Società Chimica Italiana

SCI2021

XXVII CONGRESSO NAZIONALE DELLA SOCIETÀ CHIMICA ITALIANA

LA CHIMICA GUIDA LO SVILUPPO SOSTENIBILE

14–23 SETTEMBRE 2021

INO – ORG – CSB

BOOK OF ABSTRACTS
XXVII congresso della SCI, 2021

La chimica guida lo sviluppo sostenibile
14-23 settembre 2021

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Benvenuti a SCI2021!

Il Congresso Nazionale della Società Chimica Italiana, giunto alla sua XXVII edizione, si svolgerà in modo virtuale da martedì 14 settembre a giovedì 23 settembre 2021. Come di consueto, sarà un punto di incontro e di confronto per tutto il mondo della chimica in Italia su argomenti di grande attualità.

Il congresso sarà aperto dalla ***plenary lecture*** **del Prof. Stanley Whittingham, premio Nobel per la Chimica 2019**, e prevede interventi di una serie di illustri oratori, fra cui **il premio Nobel per la Chimica 1981, Prof. Roald Hoffmann**. Il congresso si articolerà in sessioni plenarie di interesse generale e sessioni parallele, a cura delle Divisioni della Società Chimica Italiana. Nel pomeriggio di mercoledì 22 settembre sono previsti eventi satellite di interesse industriale, accessibili gratuitamente per gli iscritti al congresso.

Nelle attuali necessità di distanziamento sociale, il congresso si svolgerà tutto in modalità live telematica, con presentazioni, discussioni e tavole rotonde in diretta. Gli interventi verranno comunque registrati e resi disponibili ai partecipanti nelle due settimane successive alla chiusura del congresso, con possibilità di contatto e discussione con i presentatori.

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DELEGATI DI DIVISIONE

CHIMICA DELL'AMBIENTE E DEI BENI CULTURALI

Ezio Bolzacchini	ezio.bolzacchini@unimib.it
Lucia Toniolo	lucia.toniolo@polimi.it

CHIMICA ANALITICA

Marco Orlandi	marco.orlandi@unimib.it
Patrizia Mussini	patrizia.mussini@unimi.it

CHIMICA FARMACEUTICA

Paola Conti	paola.conti@unimi.it
Giulio Vistoli	giulio.vistoli@unimi.it

CHIMICA FISICA

Elena Selli	elena.selli@unimi.it
Moreno Meneghetti	moreno.meneghetti@unipd.it

CHIMICA INDUSTRIALE

Ilenia Rossetti	ilenia.rossetti@unimi.it
Antonella Salvini	antonella.salvini@unifi.it

CHIMICA INORGANICA

Emma Gallo	emma.gallo@unimi.it
Francesco Ruffo	francesco.ruffo@unina.it

CHIMICA ORGANICA

Alessandro Abbotto	alessandro.abbotto@unimib.it
Andrea Pace	andrea.pace@unipa.it

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DELEGATI DI DIVISIONE

CHIMICA DEI SISTEMI BIOLOGICI

Jussara Amato	jussara.amato@unina.it
Danilo Milardi	danilo.milardi@cnr.it

DIDATTICA CHIMICA

Ugo Cosentino	ugo.cosentino@unimib.it
Sergio Palazzi	studio@kemia.it

ELETTROCHIMICA

Luigi Falciola	luigi.falciola@unimi.it
Riccardo Ruffo	riccardo.ruffo@unimib.it

SPETTROMETRIA DI MASSA

Giuseppe Paglia	beppepaglia@gmail.com
Matteo Audano	matteo.audano@unimi.it

CHIMICA TEORICA E COMPUTAZIONALE

Michele Ceotto	michele.ceotto@unimi.it
Claudio Greco	claudio.greco@unimib.it

CHIMICA PER LE TECNOLOGIE

Alessandro Sacchetti	alessandro.sacchetti@polimi.it
Fabio Ganazzoli	fabio.ganazzoli@polimi.it

TECNOLOGIA FARMACEUTICA

Nunzio Denora	nunzio.denora@uniba.it
Rosario Pignatello	rosario.pignatello@unict.it

XXVII Congresso Nazionale della Società Chimica Italiana
"SCI 2021", 14-23 settembre 2021

	14 settembre	15 settembre	16 settembre	17 settembre
09:30-10:30		**Lavori Divisioni** **14 Sessioni Parallele** **1 (ABC) + 2 (FAR) + 2 (FIS) + 3 (INO) + 2 (TEC) + 3 (ELE) + 1 (TFA)**	**Lavori Divisioni** **14 Sessioni Parallele** **3 (ANA) + 3 (FIS) + 2 (IND) + 3 (ORG) + 1 (CSB) + 1 (ELE) + 1 (TEC)**	**Lavori Divisioni** **14 Sessioni Parallele** **2 (ABC) + 2 (FAR) + 2 (FIS) + 3 (INO) + 1 (TEC) + 3 (ELE) + 1 (TFA)**
10:30-11:00				
11:00-11:30				
11:30-12:00				
12:00-12:30			Break	
12:30-13:00			**ASSEMBLEE DIVISIONALI** **14 sessioni parallele** **(12:30 - 14:45)**	
13:00-14:00		Break		Break
14:00-14:30		ePoster Session		ePoster Session
14:30-15:00				
15:00-16:00	**APERTURA DEL CONGRESSO** *Saluti* **Maria Cristina MESSA** Ministro del MUR **Maria Chiara CARROZZA** Presidente CNR **Plenary Lecture del Prof. Stanley WHITTINGHAM** **PREMIO NOBEL PER LA CHIMICA 2019** Binghamton University, State University of New York, USA	**Lavori Divisioni** **14 Sessioni Parallele** **3 (ANA) + 2 (FAR) + 1 (IND) + 4 (ORG) + 1 (CSB) + 1 (DID) + 1 (MAS) + 1 (TEO)**	Sessione plenaria 2 ***La Chimica per il Benessere e la Qualità della Vita*** **Gunda I. GEORG** University of Minnesota, Department of Medicinal Chemistry, USA	**Lavori Divisioni** **14 Sessioni Parallele** **3 (ANA) + 1 (IND) + 1 (ABC) + 4 (ORG) + 1 (CSB) + 1 (DID) + 1 (MAS) + 2 (TEO)**
16:00-16:30	Sessione plenaria 1 ***Chimica, la Scienza al Centro***		**Juliane HOLLENDER** Swiss Federal Institute of Aquatic Science and Technology	
16:30-17:00	**PREMIAZIONE DELLE MEDAGLIE SCI 2020**		**Luis Liz MARZAN** CIC biomaGUNE, San Sebastián, Spain	
17:00-:17:30	Break		**Patrick COUVREUR** Université Paris-Sud France	
17:30-18:00	***Elsevier's Lecture*** **Ralf METZLER** Theoretical Physics, University of Potsdam, Germany		**Mark NOE** vice-Presidente della Pfizer	
18:00-18:30	Live Q&A Sessione 1	Discussione	Live Q&A Sessione 2	Discussione
18,30-19,30	ePoster	e-poster	e-poster	e-poster

	20 settembre	21 settembre	22 settembre	23 settembre
09:30-10:30	**Lavori Divisioni** **3 Sessioni Parallele**	**Lavori Divisioni** **14 Sessioni Parallele**	Gruppo Giovani **Yan LIANG** University of Science and Technology of China	**Lavori Divisioni** **13 Sessioni Parallele**
10:30:11:00	**3 (ORG)**	**2 (ABC) + 2 (FAR) + 2 (FIS) + 3 (INO) + 1 (TEC) + 3 (ELE) + 1 (TFA)**		**3 (ANA) + 3 (FIS) + 1 (IND) + 3 (INO) + 3 (ORG)**
11:00-11:30			**2 Sessioni Parallele**	
11:30-12:30				
12:30-13:00	**Break**			

13:00-14:00	**ASSEMBLEA GENERALE (13:00 - 14:45)**	Break	Break	Break
14:00-15:00		ePoster Session	ePoster Session	ePoster Session
15:00-16:00	Sessione plenaria 3 ***La Chimica per la Cultura*** **Prof. Roald HOFFMANN** **PREMIO NOBEL PER LA CHIMICA 1981** Department of Chemistry Cornell University Ithaca USA	**Lavori Divisioni** **12 Sessioni Parallele** **3 (ANA) + 1 (IND) + 4 (ORG) + 1 (CSB) + 1 (DID) + 1 (MAS) + 1 (TEO)**	**Eventi Satellite** **5 Sessioni Parallele** **- Principi attivi e formulazioni in ambito cosmetico** **- Ruolo della Chimica nella produzione e controllo dei farmaci biotecnologici** **- Valorizzazione di scarti di filiere produttive** **- Sostenibilità di polimeri e compositi** **- La conversione e lo stoccaggio dell'energia chimica in energia elettrica, nella vita odierna e nella società futura**	Sessione plenaria 4 ***La Chimica per l'Industria del Futuro*** **Luigi NICOLAIS** Research Policy Advisor to MUR **Avelino CORMA** Institute of Chemical Technology Polytechnical University of Valencia, Spain
16:00-16:30	**Maria Perla COLOMBINI** Dipartimento di Chimica e Chimica Industriale, Università di Pisa			**Lidia ARMELAO** Direttore del Dipartimento di Scienze Chimiche e Tecnologia dei Materiali, CNR
16:30-17:00	Break			Break
17:00-18.00	TAVOLA ROTONDA **Divulgazione scientifica e immagine della Chimica** Partecipano: **Piero Angela** **Silvano Fuso** **Massimo Polidoro** **Luigi Campanella** Coordina: **Giorgio Cevasco**			**Nausicaa ORLANDI** Presidente Federazione Nazionale Ordini Chimici e Fisici **Mario MARCHIONNA** Corporate Head Technology Innovation Saipem
18:00-18:30	Live Q&A Sessione 3	Discussione	Live Q&A	Live Q&A Sessione 4
18:30-19:30	ePoster	e-poster	e-poster	**CONCLUSIONI E CHIUSURA DEL CONGRESSO**

Programma dei LAVORI di DIVISIONE - 15 settembre mattina

Divisione CHIMICA DELL'AMBIENTE E DEI BENI CULTURALI (ABC)
ABC 01

09.30-09.35		**Antonio Marcomini**	*Opening*
09.35-10.00	**ABC IL001**	**Demetrios Anglos**	*Exploring heritage materials and objects via laser spectroscopies*
10.00-10.15	**ABC OR001**	**Gianluigi de Gennaro**	*Sars-CoV-2 airborne transmission: indoor and outdoor implications*
10.15-10.30	**ABC OR002**	**Eleonora Balliana**	*Silk and sanitizing solutions: the need to protect visitor and artworks*
10.30-10.45	**ABC OR003**	**Luca Ciacci**	*Combining the highest degradation efficiency with the lowest environmental impact in zinc oxide based photocatalytic systems*
10.45-11.00	**ABC OR004**	**Cecilia Velino**	*PROCRAFT project: conservation strategies of aircraft heritage from excavation to museum*
11.00-11.30	**break**		
11.30-11.45	**ABC OR005**	**Luca Ferrero**	*Airborne microplastics over the Baltic: influence of sea emissions*
11.45-12.00	**ABC OR006**	**Alessandra Bigogno**	*An indoor air pollution evaluation of the Quarto Stato museum*
12.00-12.15	**ABC OR007**	**Elena Badetti**	*Grafting on metal oxide nanoparticles surface reduces the toxicity of catechols*
12.15-12.30	**ABC OR008**	**Alessandro Ciccola**	*The new shades of the XX century: investigation of ACNA dyes through Raman spectroscopy and HPLC-MS*
12.30-12.45	**ABC OR009**	**Angelo Fenti**	*In Situ Electrochemical Oxidation for Destructive Treatment of PFAS*
12.45-13.00	**ABC OR010**	**Sabina Licen**	*Data fusion techniques based on Self-Organizing Map algorithm for the integration of different source/frequency instrumental data and ancillary information for environmental impact assessment*

Divisione CHIMICA FARMACEUTICA (FAR)
FAR 01

09.30 - 10.00	**FAR KN001**	**Giuseppe Campiani**	*Old but Gold: tracking the new guise of histone deacetylases as biomarkers and therapeutic targets in rare diseases. The role of isoform 6*
10.00 - 10.30	**FAR KN002**	**György M. Keserű**	*The role of the secondary binding pocket in GPCR pharmacology*
10.30 - 10.45	**FAR OR001**	**Agnese Pippione**	*Targeting prostate cancer with multiple-targeting ligands: activity on both AKR1C3 enzyme and androgen receptor*

10.45 - 11.00	**FAR OR002**	**Andrea Spinaci**	*Synthesis and characterization of new A3 adenosine receptors ligands as potential anti-cancer agents*
11.00 - 11.15	**break**		
11.15 - 11.45	**FAR KN003**	**Tracey Pirali**	*The power of multi-component reactions in drug discovery: soft drugs, PROTACs and more*
11.45 - 12.00	**FAR OR005**	**Simona Musella**	*Identification and characterization of a potent TRPM8 antagonists with in vivo analgesic properties*
12.00 -12.15	**FAR OR006**	**Letizia Crocetti**	*Synthesis of pyrazolo[1,5-a]quinazolines as ligand of α1β3γ2-GABAA receptor subtype and molecular modelling studies*
12.15 -12.30	**FAR OR007**	**Carmine Ostacolo**	*Discovery of CP86, a potent neuronal Kv7 channel activator with in vivo anticonvulsant effects*
12.30 - 13.00	**FAR KN004**	**Marco Radi**	*Navigating the antiviral drug discovery space: exploring different routes toward new broad-spectrum agents*

FAR 02

10.30 - 10.45	**FAR OR003**	**Francesca Musumeci**	*Design, synthesis, and biological evaluation of a new series of pyrazolo[3,4-d]pyrimidines active as SGK1 inhibitors. A lead optimization study*
10.45 - 11.00	**FAR OR004**	**Giuseppe La Regina**	*New pyrroles derivatives as anti-glioblastoma and anti-chronic myeloid leukemia agents*
11.00 - 11.45	**break**		
11.45 - 12.00	**FAR OR008**	**Laura Scalvini**	*N-Acylethanolamine acid amidase (NAAA): mechanism of palmitoylethanolamide hydrolysis revealed by mechanistic simulations*
12.00 -12.15	**FAR OR009**	**Leonardo Brunetti**	*Multiple causes, multiple targets: FAAH as a centerpiece for therapy of multifactorial pathologies*
12.15 -12.30	**FAR OR010**	**Rita Turnaturi**	*Influence of the N-substituent of (−)-cis-N-Normetazocine in the modulation of the functional profile at MOR, DOR and KOR: from agonist to antagonist through multitarget ligands*

Divisione CHIMICA FISICA (FIS)

FIS 01

Physical chemistry for Nanomaterials I

09:30-10:00	**FIS KN001**	**Marco Laurati**	*Blunt-end driven assembly of star-like dsDNA coated colloids*
10:00-10:15	**FIS OR001**	**Carlo Nazzareno Dibenedetto**	*Fabrication and spectroscopic investigation of Quantum Dots dimers*
10:15-10.30	**FIS OR002**	**Giovanni LiDestri**	*Forces between nanoparticels at the air/water interface: the role of the ligand chain length*
10:30-10.45	**FIS OR003**	**Davide Peddis**	*Interplay between inter- and intraparticle interactions in bi-magnetic core/shell nanoparticles*
10:45-11:00	**FIS OR004**	**Maryam Abdolrahimi**	*XAS Study of Molecular Coated Manganese Zinc Ferrite Nanoparticles*
11:00-11.15	**FIS OR005**	**Sawssen Slimani**	*Hybrid Spinel Iron Oxide Nanoarchitecture Combining Crystalline and Amorphous Parent Material*
11:15-11.30	**FIS OR006**	**Marco Fabbiani**	*Porous materials for hybrid functional nanocomposites: metal and organic nanowires confined in zeolites and mesoporous silica*
11.30-11.45	**break**		

Physical chemistry for Nanomaterials II

11:45-12:00	**FIS OR007**	**Grazia ML Messina**	*Surfactant vesicles and polysaccharides interactions with cellulose nanocrystals*
12:00_12:15	**FIS OR008**	**Simona Ricci**	*Highly efficient green inkjet printed nanostructured electrodes and SERS substrates*
12:15-12.30	**FIS OR009**	**Marcello Condorelli**	*Ag nanoflowers as single particle SERS active platform*
12:30-12:45	**FIS OR010**	**Valentina Mameli**	*57Fe Mössbauer Spectroscopy and DC magnetometry for the identification of Fe-bearing ultrasmall nanophases in inorganic ordered porous matrixes*
12:45-13:00	**FIS OR011**	**Giovanni Ferraro**	*Controlled decoration of plastic surfaces with metal nanostructures*
13:00-13:15	**FIS OR012**	**Roberta Ruffino**	*“Distorted” self-assembly of polymer thin films at nano-curved surfaces*

FIS 02

PhysicalChemistry for Biomedical Applications I

09:30-10:00	**FIS KN002**	**Paola Sassi**	*Spectroscopic markers of heart failure: a Raman and FTIR study*
10:00-10:15	**FIS OR013**	**Nunzio Tuccitto**	*Quantum Dots Enable Digital Communication Through Biological Fluids*

10:15-10.30	**FIS OR014**	**Elisabetta Fanizza**	*Plasmonic mesoporous silica coated copper sulfide nanoparticles as Near Infrared absorbing photothermal agents*
10:30-10.45	**FIS OR015**	**Rossella Labarile**	*Coating photosynthetic Rhodobacter sphaeroides with polydopamine*
10:45-11:00	**FIS OR016**	**Marco Fornasier (Vincitore del Premio Semerano)**	*A polyphosphoester analog of Pluronic F127 enhances the biocompatibility of monoolein-based cubosomes*
11:00-11.15	**FIS OR017**	**Alberta Terzi**	*X-ray Scattering Scanning Microscopies – novel diagnostic tools of pathologic tissues. A focus on aneurysms, breast cancer and diabetes*
11:15-11.30	**FIS OR018**	**Federica D'Aria**	*G-quadruplex within KRAS gene promoter: a physicochemical study*
11.30-11.45	**break**		

PhysicalChemistry for Biomedical Applications II

11:45-12:00	**FIS OR019**	**Vincenzo De Leo**	*Liposome/Polymer Assembly for Oral Delivery of Curcumin*
12:00_12:15	**FIS OR020**	**Monica Mura**	*Nanoantibiotics: design of multifunctional MSN nanosystems containing both antibiotic and copper ions to combat bone infection*
12:15-12.30	**FIS OR023**	**Elena Piacenza**	*Innovative and green synthesis of biocompatible Selenium nanoparticles in a confined environment with promising antimicrobial activity*
12:30-12:45	**FIS OR024**	**Jennifer Gubitosa**	*Green synthesis of Gold nanoparticles by using grape seeds wastewater: physico-chemical characterization and investigation of their related antioxidant features for cosmetic and biomedical applications*

Divisione CHIMICA INORGANICA (INO)

INO 01

9.30 - 10.30	**INO PZ001**	**Frank Neese**	*Deciphering Inorganic Chemistry Riddles Through a Combination of Spectroscopy and Quantum Chemistry*
10.30 - 10.45	**INO OR001**	**Roberto Gobetto**	*Innovative Mn and Re catalysts for CO2 Photo- and Electro-Reduction*
10.45 - 11.00	**INO OR002**	**Ilaria Barlocco**	*Disclosing the role of Gold on Palladium - Gold alloyed catalysts in formic acid decomposition*
11.00 - 11.15	**INO OR003**	**Cristina Pavan**	*Nearly free silanols on silica surface: a new paradigm for particle toxicology*
11.15-11.30	**break**		

11.30 - 11.45	**INO OR004**	**Massimo Christian D'Alterio**	*A combined theoretical and experimental investigation of a new class of [N,O-] imidazo[1,5-a]pyrid-3-yl)phenolate Zn(II) catalysts for the ring opening polymerization of lactide*
11.45 - 12.00	**INO OR005**	**Linda Leone**	*Highly selective indole oxidation promoted by a Mn-containing mini-enzyme*
12.00 - 12.15	**INO OR006**	**Javier Martí-Rujas**	*Synthesis and structural properties of isostructural Zn(II) M12L8 poly-[n]-catenane using the 2,4,6-tris(4-pyridyl)benzene (TPB) ligand*
12.15 - 12.30	**INO OR007**	**Francesco Fagnani**	*Three novel families of cyclometalated platinum(II) complexes with remarkable luminescence properties*
12.30 - 13.00	**INO IL001**	**Viktoria Gessner**	*Metallated Ylides: Powerful Reagents for the Stabilization of Reactive Main Group Species and Ligands in Catalysis*

INO 02

10.30 - 10.45	**INO OR008**	**Michele Benedetti**	*"NMR effective molecular radius" of coordinated ammonia*
10.45 - 11.00	**INO OR009**	**Chiara Salvitti**	*Redox reactivity of transition metal dioxide anions towards sulfur dioxide in the gas phase*
11.00 - 11.15	**INO OR010**	**Silvia Ruggieri**	*New chiral heteroleptic Eu(III)/Tb(III)/Yb(III)-based luminescent complexes designed for different applications*
11.15-11.30	**break**		
11.30 - 11.45	**INO OR011**	**Tiziano Marzo**	*Oxaliplatin binds angiogenin and exerts high antiangiogenic effects in PC-3 cancer cells at non-cytotoxic concentration*
11.45 - 12.00	**INO OR012**	**Luca Spitaleri**	*Covalently conjugated gold–porphyrin nanostructures*
12.00 - 12.15	**INO OR013**	**Nicola Panza**	*Ferrate salts as stand-alone catalysts for chemical fixation of CO2 into epoxides and aziridines*
12.15 - 12.30	**INO OR014**	**Elena Lucenti**	*Cyclic triimidazole: an appealing and versatile ligand for the preparation of emissive d9 and d10 metal derivatives*

INO 03

10.30 - 10.45	**INO OR015 premio Wiley**	**Thomas Scattolin**	*Palladium organometallic complexes as promising anticancer agents*
10.45 - 11.00	**INO OR016**	**Caterina Damiano**	*Efficient and low-cost metal-free Porphyrin/TBACl system for the CO2 valorization into N alkyl and N aryl oxazolidin-2-ones*
11.00 - 11.15	**INO OR017**	**Carlo Nervi**	*Transition metal complexes as redox catalysts for CO2 conversion*
11.15-11.30	**break**		

11.30 - 11.45	**INO OR018**	**Cristina Tubaro**	*Gold(I) and gold(III) complexes with thioether- and phosphonium- functionalized N-heterocyclic carbene ligands*
11.45 - 12.00	**INO OR019**	**Marco Baron**	*Manganese(III) complexes with tetradentate O^C^C^O ligands: synthesis, characterization and preliminary catalytic studies on the CO2 cycloaddition with epoxides*
12.00 - 12.15	**INO OR020**	**Roberto Esposito**	*MOF catalyzed ketalization of glycerol into solketal*
12.15 - 12.30	**INO OR021**	**Francesco Ferretti**	*Heterocycles from nitro compounds: CO surrogates in the Pd catalyzed synthesis of carbazoles*

Divisione CHIMICA PER LE TECNOLOGIE (TEC)
TEC 01

09.30 - 10.00	**TEC IL001**	**Alberto Rainer**	*Nanogels as smart drug delivery systems*
10.00 - 10.15	**TEC KN001**	**Claudia Espro**	*Hydrothermal Carbonization as a sustainable approach for the single-step upgrading of industrial citrus processing waste into platform chemicals and biocarbon*
10.15 - 10.30	**TEC KN002**	**Fabrizio Monica**	*Chemistry of materials for energy technologies*
10.30 - 10.40	**TEC OR001**	**Virginia Venezia**	*Biowaste as valuable resource: humic acids valorization into multifunctional materials*
10.40 - 10.50	**TEC OR002**	**Francesco Mauriello**	*Sustainable Valorization of Anchovy Leftovers into Value Added Chemicals, Products and Energy*
10.50 - 11.00	**TEC OR003**	**Carlo Punta**	*Eco-design of Cellulose NanoSponges for water decontamination*
11.00 - 11.10	**TEC OR004**	**Ermelinda Bloise**	*CNSL components as green building-blocks for bio-based nanovesicles*
11.10 - 11.30	**Discussion**		
11.30 - 11.50	**Break**		
11.50 - 12.00	**TEC OR005**	**Manfredi Caruso**	*N-Hydroxyphthalimide role in Aerobic Oxidations: Homogeneous versus Heterogeneous Catalysis*
12.00 - 12.10	**TEC OR006**	**Laura Riva**	*Co-Polymeric Nanosponges from Cellulose Biomass as Heterogeneous Catalysts for Organic Reactions*
12.10 - 12.20	**TEC OR007**	**Serena Regina**	*Use of a bio-derived polymer as crosslinking agent for stable-polyvinyl alcohol membrane development*
12.20 - 12.30	**TEC OR008**	**Simona Sabbatini**	*Thermal-Oxidative Stability of PHBV/LDH Nanocomposites*
12.30 - 12.50	**Discussion**		

12.50 - 13.00	**TEC OR009**	**Angela Marotta**	*Furan as platform molecule in the production of greener epoxy-resins*
13.00 - 13.10	**TEC OR010**	**Franca Castiglione**	*Insights on Ionic Liquids structure and dynamics: NMR methods and recent advances*
13.10 - 13.20	**TEC OR011**	**Giselle de Araujo Lima e Souza**	*Ionic conductivity and thermal characterization of DBU-based protic ionic liquids*
13.20 - 13.30	**TEC OR012**	**Maria Enrica Di Pietro**	*Deep Eutectics: what is inside the solvents for the 21st century?*
13.30 - 13.50	**Discussion**		

TEC 02

10.30 - 10.40	**TEC OR013**	**Giulio Pota**	*Mesoporous Silica Nanoparticles: a powerful platform for biocatalysis*
10.40 - 10.50	**TEC OR014**	**Antonella Satira**	*Tandem Catalytic Upgrading of Limonene and Methyl Levulinate promoted by Pd-based Catalysts*
10.50 - 11.00	**TEC OR015**	**Francesco Parrino**	*Synthesis, characterization, and photocatalytic activity of Eu doped ZnO prepared by supercritical antisolvent precipitation route*
11.00 - 11.10	**TEC OR016**	**Cristina Leonelli**	*Microwave-assisted synthesis and isopropanol extraction in the preparation of TiO2 nanoparticle suspensions*
11.10 - 11.30	**Discussion**		
11.30 - 11.50	**Break**		
11.50 - 12.00	**TEC OR017**	**Aurelio Bifulco**	*Hybrid Strategies for the Improvement of the Flame Retardancy of in-situ Silica-Epoxy Nanocomposites cured with Aliphatic Hardener*
12.00 - 12.10	**TEC OR018**	**Isabella Lancellotti**	*Chemical stabilization in a single step process: geopolymerization of tannery wastewater pollutants*
12.10 - 12.20	**TEC OR019**	**Ambra M. Fiore**	*Hematite nanoparticles as promising catalyst*
12.20 - 12.50	**Discussion**		
12.50 - 13.00	**TEC OR021**	**Vincenzina Barbera**	*Functionalization of graphene related materials with biosourced C-3 and C-6 building blocks. From synthesis to applications*
13.00 - 13.10	**TEC OR022**	**Sabina Alessi**	*Polymer/rubber nanofibrous interleaves for the enhancement of delamination resistance of CFRP laminates*
13.10 - 13.20	**TEC OR023**	**Laura Tripaldi**	*Silica Hairy Nanoparticles in Rubber Nanocomposites*
13.20 - 13.30	**TEC OR024**	**Mariachiara Miceli**	*Titanosilicalite as Nickel Support for Methanation Reaction*
13.30 - 13.50	**Discussion**		

Divisione ELETTROCHIMICA (ELE)

ELE 01

09.30 - 10.00	**ELE_KN01**	**Patrizia Mussini**	*Enantioselective Voltammetry & Chiroptical Spectroscopy: Exploring Intriguing Analogies and Connections*
10.00 - 10.15	**ELE_OR02**	**Elisabetta Petri**	*Electrochemically responsive soft actuators*
10.15 - 10.30	**ELE_OR03**	**Carmelo Lo Vecchio**	*NiFe oxide co-catalyst for an enhanced water splitting in photo-electrochemical cells*
10.30 - 10.45	**ELE_OR04**	**Marco Piccinni**	*Synthesis and water dispersion of nickel-iron layered double hydroxides for energy storage applications*
10.45 - 11.00	**ELE_OR05**	**Daniele Rocco**	*Anodic Dimerization of New Donor-Acceptor Oligothiophenes: Electrochemical and Solvatochromic Behavior*
11.00 - 11.15	**break**		
11.15 - 11.45	**ELE_KN06**	**Peter Fischer**	
11.45 - 12.00	**ELE_OR07**	**Giovanni Crivellaro**	*A complex electrochemistry triggering the operation of Vanadium Redox Flow Batteries*
12.00 - 12.15	**ELE_OR08**	**Giampaolo Lacarbonara**	*A spectroelectrochemical study of copper chloro-complexes for high performance copper redox flow batteries*
12.15 - 12.30	**ELE_OR09**	**Jorge Montero**	*Ferrocene and viologen derivatives as electrolytes for pH neutral aqueous organic redox flow batteries*

ELE 02

09.30 - 10.00	**ELE KN10**	**Giovanni Valenti**	*New Insights Into Electrogenerated Chemiluminescence Mechanism for the Enhancement of Bioanalytical Performance*
10.00 - 10.15	**ELE OR11**	**Sara Bonacchi**	*SpectroElectrochemistry of Metal Nanoclusters:new insights into the origin of the photoluminescence*
10.15 - 10.30	**ELE OR12**	**Marco Mazzucato**	*How Decisive is the Iron Precursor Ligand in Fe-N-C Single-Site Formation and Activity for Oxygen Reduction Reaction?*
10.30 - 10.45	**ELE OR13**	**Mattia Parnigotto**	*Water Loss Predictive Tests in Flooded Lead-Acid Batteries*
10.45 - 11.00	**ELE OR14**	**Mattia Reato**	*Electron Transfers in Films of Atomically Precise Metal Nanoclusters*
11.00 - 11.15	**break**		
11.15 - 11.45	**ELE KN15**	**Alessandro Minguzzi**	*In situ/operando X-ray absorption spectroscopy: a swiss-knife for studying (photo)electrodes*

11.45 - 12.00	**ELE OR16**	**Francesco De Bon**	*Para substituted pyridines ligands forms highly active catalysts for ATRP*
12.00 - 12.15	**ELE OR17**	**Danilo Dini**	*EQCM analysis of the process of electrochemical insertion in regioregular alkyl-susbtituted polyterthiophene during n-doping*
12.15 - 12.30	**ELE OR18**	**Matteo Grattieri**	*Bio-inspired intact bacteria-based biohybrid photoanodes*

ELE 03

09.30 - 10.00	**ELEKN19**	**Marc Koper**	*Advances and challenges in understanding the electrocatalytic conversion of carbon dioxide*
10.00 - 10.15	**ELEOR20**	**Maruccia Elisa**	*Nitrogen-containing ordered mesoporous carbons applied as CO2 adsorbents and anode materials in energy storage devices*
10.15 - 10.30	**ELEOR21**	**Fortunati Alessia**	*Ionic liquids for capture and electrochemical Conversion of CO2*
10.30 - 10.45	**ELEOR22**	**Moro Miriam**	*Carbon Nanostructures decorated with Cerium Oxide as selective electrocatalysts for CO2 reduction*
10.45 - 11.00	**ELEOR23**	**Guzman Hilmar**	*CuZnAl-based oxide catalysts for the electrochemical CO2 conversion*
11.00 - 11.15	**break**		
11.15 - 11.45	**ELEKN24**	**Monica Santamaria**	*Electrochemical surface treatments to improve corrosion resistance of light alloys*
11.45 - 12.00	**ELEOR25**	**Zoli Maddalena**	*Facile and scalable synthesis of Cu2O-SnO2 catalyst for the photoelectrochemical CO2 conversion*
12.00 - 12.15	**ELEOR26**	**Magni Mirko**	*Cathodic Plasma Electrolysis & Recovery of Zinc as Coating*
12.15 - 12.30	**ELEOR27**	**Poli Federico**	*Sustainable strategies to improve MFC power output by green supercapacitors and supercapacitive components*

Divisione TECNOLOGIA FARMACEUTICA (TFA)
TFA 01

09.30 - 10.00	**TFA IL001**	**Elias Fattal**	*Lipid and dendrimer-based nanomedicines for siRNA*
10.00 - 10.30	**TFA IL002**	**Stefano Colloca**	*Set up of large scale production process for GRAd-COV2 vaccine*
10.30 - 10.45	***Discussion***		
10.45 - 11.00	**break**		

15 settembre - mattina

11.00 - 11.15	**TFA OR001**	**Ilaria Arduino**	*Microfluidic preparation and characterization of iRGD-functionalized solid lipid nanoparticles for targeted delivery*
11.15 - 11.30	**TFA OR002**	**Angela Bonaccorso**	*Response Surface Methodology for the optimization of Nanogels Polyelectrolyte Complex intended for Ovalbumin nasal delivery*
11.30 - 11.45	**TFA OR003**	**Ilaria Filippin**	*Cellulase as active excipient in HPMC prolonged-release matrices: a novel approach to zero-order kinetics*
11.45 - 12.00	**TFA OR004**	**Stefania Petralito**	*Remote magneto-mechanical actuation of magnetoliposomes by alternating or pulsed magnetic fields*
12.00 - 12.15	**TFA OR005**	**Emma Piacentini**	*Controlled and tunable polymeric micro/nano particles production using membrane technology*
12.15 - 12.30	**TFA OR006**	**Giovanna Rassu**	*Crocetin as both neuroprotective agent and cross-linker for sericin for obtaining new nasal bioactive nanoparticles*
12.30 - 12.45	**TFA OR007**	**Federica Rinaldi**	*Rifampicin loaded liposomes for Mycobacterium abscessus infection treatement: intracellular uptake and antibacterial activity evaluation*
12.45 - 13.00	**TFA OR008**	**Mattia Tiboni**	*An affordable approach to scalable nanomedicine manufacturing: 3D printed microfluidics*
13.00 - 13.15	**TFA OR009**	**Siyuan Deng**	*Development and Characterization of a Novel Redox-responsive Core-shell Structure Nanohydrogel as Intracellular Delivery System*
13.15-13.30	***Discussion***		

Programma dei LAVORI di DIVISIONE - 15 settembre pomeriggio

Divisione CHIMICA ANALITICA (ANA)
ANA 01

15.00 - 15.10	**ANA PL001**	**Claudio Minero**	*INTRODUZIONE*
15.10 - 15.30	**ANA PZ001**	**Luigia Sabbatini**	*Contaminarsi fa bene alla ricerca*
15.30 - 15.50	**ANA PZ002**	**Luigi Mondello**	*Recent Developments in Mass spectrometry and Cutting Edge Scientific Innovation to Characterize Complex Samples*
15.50 - 16.10	**ANA IL001**	**Susy Piovesana**	*New trends for the enrichment and liquid chromatography-mass spectrometry analysis of peptides with protein post-translational modifications*
16.10 - 16.30	**ANA KN001**	**Flavio A. Franchina**	*The value of multidimensional chromatography coupled to mass spectrometry for the non-targeted metabolite profiling of natural products*
16.30 - 16.45	**ANA OR001**	**Alessia Arena**	*Mineral oil investigation in omega-3 rich lipid supplements by using multidimensional liquid-gas chromatography*
16.45 - 17.00	**ANA OR002**	**Carmela Maria Montone**	*Untargeted characterization and quantitative analysis of underivatized fatty acids in Chlorella vulgaris microalgae*
17.00 - 17.15	**ANA OR003**	**Lorenzo Cucinotta**	*Simultaneous Enantiomeric and Isotopic Ratio evaluation of target terpenes in Cannabis sativa essential oils through Enantio-MDGC-C-IRMS*
17.15 - 17.30	**ANA OR004**	**Gemma De Grazia**	*Evaluation of cryogenic effect for target VOCs isolation by a preparative multidimensional gas chromatographic system*
17.30 - 17.45	**ANA OR005**	**Rosangela Elliani**	*DEVELOPMENT OF A RAPID AND SIMPLE PROTOCOL FOR THE ASSAY OF PARABENS AND BISPHENOLS IN HUMAN SALIVA BY SOLID-PHASE MICROEXTRACTION-GAS CHROMATOGRAPHY-TRIPLE QUADRUPOLE MASS SPECTROMETRY*
17.45 - 18.00	**ANA OR006**	**Antonio Ferracane**	*Simultaneous determination of 88 multi-class pesticide residues in four vegetable matrices using reduced QuEChERS extraction and flow-modulated comprehensive two-dimensional gas chromatography-triple quadrupole mass spectrometry*
18.00 - 18.15	**ANA OR007**	**Micaela Galletta**	*Evaluation of use of hydrogen as carrier gas in flow-modulation comprehensive two-dimensional gas chromatography-time-of-flight mass spectrometry*

18.15 - 18.30	**ANA OR008**	**Anna Illiano**	*LC-MRM/MS assay for the quantification of some hormonal proteins in serum and follicular fluid of women undergoing in vitro fertilization*

ANA 02

15.50 - 16.10	**ANA KN002**	**Clemente Bretti**	*Removal of environmentally relevant cations: polymer inclusion membranes (PIMs)*
16.10 - 16.30	**ANA KN003**	**Francesco Pellegrino**	*A New Strategy for Overcoming the Volcano in Water Photosplitting: Controlled Periodic Illumination*
16.30 - 16.45	**ANA OR009**	**Raghav Dogra**	*Preliminary evaluation of Magnetic Nanoparticles for glyphosate contaminated water remediation*
16.45 - 17.00	**ANA OR010**	**Federico Girolametti**	*Evaluation of mercury content in red mullet (Mullus barbatus) muscle from the Adriatic Sea in relation to biological factors and sampling area: risk assessment for human consumption*
17.00 - 17.15	**ANA OR011**	**Marco Minella**	*Experimental evaluation of Fenton oxidation coupled with membrane distillation for produced water treatment: benefits, challenges and effluent toxicity*
17.15 - 17.30	**ANA OR012**	**Donatella Nardiello**	*Nanoconfined liquid phase nanoextraction: an innovative extraction technique for ex-situ and in-situ rapid and quantitative determination of benzene derivatives in seawater*
17.30 - 17.45	**ANA OR013**	**Gabriella Pinto**	*Characterization of polyphenolic compounds in food and industrial wastes*
17.45 - 18.00	**ANA OR014**	**Luca Rivoira**	*Iterative protocols for the extraction and quantitation of microplastics from marine sediments and oysters*
18.00 - 18.15	**ANA OR015**	**Saul Santini**	*Validation of a new method for the simultaneous determination of different classes of PBT chemicals in biota samples*
18.15 - 18.30	**ANA OR016**	**Davide Vivado**	*Study of iron speciation in coastal seawater samples of the Ross Sea (Antarctica) by CLE-AdSV*

ANA 03

15.50 - 16.10	**ANA IL002**	**Erika Scavetta**	*Organic Electrochemical Transistors as low cost chemical sensors*
16.10 - 16.30	**ANA IL003**	**Chiara Zanardi**	*Graphene-based electrodes for the detection of biomarkers in sweat*
16.30 - 16.45	**ANA OR017**	**Andrea Bonini**	*A Label-free impedance biosensing assay based on CRISPR/Cas12a collateral activity for bacterial DNA detection*

16.45 - 17.00	**ANA OR018**	**Tiziano Di Giulio**	*Molecularly imprinted polymers-based impedimetric sensor for metal-ion mediated recognition of a dipeptide*
17.00 - 17.15	**ANA OR019**	**Laura Fabiani**	*Magnetic beads combined with carbon black-based screen-printed electrodes for COVID-19: A reliable and miniaturized electrochemical immunosensor for SARS-CoV-2 detection in saliva*
17.15 - 17.30	**ANA OR020**	**Eleonora Macchia**	*Selective Single-Molecule Detection of clinically relevant biomarkers with an Organic Transistor*
17.30 - 17.45	**ANA OR021**	**Federica Mariani**	*Healthcare monitoring using wearable pH sensors*
17.45 - 18.00	**ANA OR022**	**Vincenzo Mazzaracchio**	*A TiO2 /KuQuinone modified screen-printed photoelectrochemical sensor for NADH detection*
18.00 - 18.15	**ANA OR023**	**Gheorghe Melinte**	*Enhancement of lysozyme detection process by using a gold clusters-based electrochemical aptasensor*
18.15 - 18.30	**ANA OR024**	**Filippo Silveri**	*Redox-active graphene film integrated into a smart device for pesticide biosensing*

Divisione CHIMICA FARMACEUTICA (FAR)
FAR 03

15.00 - 15.45	**FAR MD001**	**Kenneth A. Jacobson**	*Pratesi Medal Lecture - Design and Therapeutic Potential of Adenosine and P2Y Receptor Ligands*
15.45 - 16.00	**FAR PZ001**	**Ciro Milite**	*Modulators of Coactivator-Associated Arginine Methyltransferase 1 (CARM-1): There and Back Again*
16.00 - 16.15	**FAR PZ002**	**Mariateresa Giustiniano**	*Isocyanide Chemistry from the Ground (state) to the Star(s): what's the point for a medicinal chemist?*
16.15 - 17.00	**FAR MD002**	**Antonello Mai**	*Giacomello Medal Lecture - Lecture for the receipt of the "Giordano Giacomello" medal by the Medicinal Chemistry Division of the Italian Chemical Society*
17.00 - 17.15	**break**		
17.15 - 17.30	**FAR OR011**	**Marilia Barreca**	*Inhibition of non-Hodgkin lymphoma cell growth by pyrrolo[1,2]oxazole derivatives*
17.30 - 17.45	**FAR OR012**	**Laura Braconi**	*A new strategy to overcome multidrug resistance (MDR) in cancer cells: P-gp and hCAXII multitarget inhibitors*
17.45 - 18.00	**FAR OR013**	**Daniela Carbone**	*Synthesis and preclinical evaluation of a new generation of 1,2,4-triazine-based PDK modulators: a novel therapeutic approach to halt cancer growth.*

18.00 -18.15	**FAR OR014**	**Arianna Gelain**	*Unraveling the interaction mechanism of a benzothiadiazole-2,2-dioxide derivative with STAT3: towards novel direct inhibitors*

FAR 04

17.15 - 17.30	**FAR OR015**	**Lucia Tamborini**	*Flow-based redox biotransformations for food and pharma applications*
17.30 - 17.45	**FAR OR016**	**Federica Ianni**	*Stability of chlorogenic acid as model system after household microwave treatment*
17.45 - 18.00	**FAR OR017**	**Ilaria Frosi**	*Comparison of different extraction methods to recover bioactive compounds from corn waste (Zea mays L.)*
18.00 -18.15	**FAR OR018**	**Martina Contente**	*Valorization of food wastes and residues through glycosidases*

Divisione CHIMICA INDUSTRIALE (IND)

IND 01

Sessione congiunta con Gruppo Interdivisionale Catalisi

15.00 - 15.30	**IND KN001 Medaglia Piero Pino**	**Nicoletta Ravasio**	*Catalysis and Green Deal*
15,30 - 15,40	**IND OR001**	**Eleonora Aneggi**	*Solvent free selective oxidation of benzyl alcohol over supported Ru catalysts*
15.40 - 15.50	**IND OR002**	**Denise Cavuoto**	*The role of support wettability and acidity in the hydrogenation of γ-valerolactone over Cu/SiO2 catalyst*
15.50 - 16,00	**IND OR003**	**Tommaso Tabanelli**	*Improved Catalytic Transfer Hydrogenation of alkyl levulinates with alcohols over ZrO2 based catalysts*
16.00 - 16.10	**IND OR004**	**Eleonora Vottero**	*Reconstruction phenomena in a Pt/γ-Al2O3 catalyst under hydrogenation conditions*
16.10 - 16.20	**IND OR005**	**Maila Danielis**	*Structural Evolution and Enhanced Steam Deactivation Resistance of PtPd/CeO2 Methane Oxidation Catalysts Prepared by Dry Milling*
16.20 - 16.30	**IND OR006**	**Gabriella Garbarino**	*Effect of promoters on the performances of Ni-Al2O3 catalysts for CO2 hydrogenation*
16.30 - 16.45	**Discussion**		
16.45 - 17.00	**break**		
17.00 - 17.20	**IND KN002**	**Walter Cabri**	*The Twelve Principles of Green Chemistry Translation Guide for Palladium Catalyzed Cross Coupling Reactions for Active Pharmaceutical Ingredients Sustainable Productions"*
17.20 - 17.30	**IND OR007**	**Roberto Sole**	*The alkoxycarbonylation of protected propargyl alcohols*

17.30 - 17.40	**IND OR008**	**Aleksandr Voronov**	*Unexpected O-5-exo-dig Cyclization of Propargyl Ureas to Oxazoline-2-amines Catalyzed by Silver Salts*
17.40 - 17.50	**IND OR009**	**Francesco Taddeo**	*Kinetics of solketal synthesis promoted by Iron(III) complex*
17.50 - 18.00	**IND OR010**	**Vinayak. Botla**	*Palladium/Norbornene-Catalyzed Synthesis of 2-Iodobiaryls*
18.00 - 18.10	**IND OR011**	**Stefano Econdi**	*Heterogeneous catalysts for the liquid-phase degradation of simulants of organophosphorus chemical warfare agents*
18.10 -18.30	**Discussion**		

Divisione CHIMICA ORGANICA (ORG)

ORG 01

15.00 - 15.30	**Benvenuto e premiazione (sessioni unificate)**		
15:30 - 16:00	**ORG PZ001**	**Anna Bernardi**	***Medaglia Adolfo Quilico*** *At the crossroad between Chemistry and Biology: interfering with the sugar code using glycomimetics*
16.00 - 16.15	**ORG OR001**	**Alessandro Ajo**	*Nanocages and capsules for drug and peptides delivery*
16.15 - 16.30	**ORG OR002**	**Silvana Alfei**	*Cationic Copolymers: A Promising Option in the Treatment of Drug Resistance in Neuroblastoma Cells*
16.30 - 16.45	**ORG OR003**	**Davide Audisio**	*Direct Carbon Isotope Exchange of Pharmaceuticals via Reversible Decyanation*
16.45 - 17.00	**ORG OR004**	**Sara Battista**	*Antibacterial and physicochemical properties of quatsomes formulated with L-prolinol-derived surfactants*
17.00 - 17.30	**Break**		
17.30 - 17.45	**ORG OR005**	**Roberta Bernini**	*Hydroxytyrosol, much more than an antioxidant*
17.45 - 18.00	**ORG OR006**	**Andrea Calcaterra**	*Diels-Alder type adducts from Morus nigra as potent inhibitors of Micobacterium tuberculosis PtpB*
18.00 - 18.15	**ORG OR007**	**Fabrizio Chiodo**	*Carbohydrate-Mediated "Innate" Considerations in Designing Vaccine-Candidates*
18.15 - 18.30	**ORG OR008**	**Martina Cirillo**	*Selective Integrin Ligands Promote Cell Internalization of the antineoplastic agent Fluorouracil*

ORG 02

16.00 - 16.15	**ORG OR009**	**Mariapina D'Onofrio**	*Chemoselective disulfide-coupling for the semisynthesis of ubiquitinated forms of the Alzheimer's associated protein tau*

16.15 - 16.30	**ORG OR010**	**Maria Giulia Davighi**	*New potential carbonic anhydrase inhibitors based on mono and multivalent sugars and iminosugars*
16.30 - 16.45	**ORG OR011**	**Cristina De Castro**	*N-glycan from Paramecium bursaria Chlorella virus MA-1D: reevaluation*
16.45 - 17.00	**ORG OR012**	**Jenny Desantis**	*Design, synthesis, and evaluation of small molecules Proteolysis Targeting Chimeras (PROTACs) to induce androgen receptor degradation*
17.00 - 17.30	**Break**		
17.30 - 17.45	**ORG OR013**	**Cristina Di Carluccio**	*Investigation of the molecular recognition of sialoglycans bound to Siglec-like adhesins of Streptococcus gordonii*
17.45 - 18.00	**ORG OR014**	**Rossella Di Guida**	*Structural characterization of the lipooligosaccharide and capsular polysaccharide from the psychrotrophic bacterium Pseudoalteromonas nigrifaciens Sq02*
18.00 - 18.15	**ORG OR015**	**Maria Funicello**	*Switching the anticancer effect to HIV protease inhibition: new heteroaryl-amidic compounds with a pseudo-symmetric core*
18.15 - 18.30	**ORG OR016**	**Dario Gentili**	*Synthesis of small molecules with potential antiviral acitivity against Sars-CoV-2*

ORG 03

16.00 - 16.15	**ORG OR017**	**Vincenzo Algieri**	*Regioselective Synthesis of 1,3,4,5-Tetrasubstituted Pyrazoles by Eliminative Enaminone-Nitrilimine 1,3-Dipolar Cycloaddition*
16.15 - 16.30	**ORG OR018**	**Michael Andresini**	*Nitrogen transfer to sulfenamides: synthesis of sulfinamidines and unexplored sulfinimidate esters as valuable precursors of protected sulfilimines*
16.30 - 16.45	**ORG OR019**	**Marco Ballarotto**	*Substituted 6H-benzo[c]chromenes: synthetic approach via a Diels-Alder/aromatization sequence and computational investigation*
16.45 - 17.00	**ORG OR020**	**Bruno Mattia Bizzarri**	*Aminomaleonitrile inspired prebiotic chemistry as a novel microwave assisted multicomponent tool for the synthesis of imidazole and purine derivatives with anti-influenza activity*
17.00 - 17.30	**Break**		
17.30 - 17.45	**ORG OR021**	**Diego Caprioglio**	*The oxidation of phytocannabinoids: a systematic investigation*
17.45 - 18.00	**ORG OR022**	**Marco Colella**	*Use of flow technology for the development of a sustainable synthesis of azetines and azetidines*
18.00 - 18.15	**ORG OR023**	**Dario Corbisiero**	*Enantioselective Synthesis of Polyfunctionalized Isoxazoline Rings: Development of a Methodology for the preparation of Tumor-Oriented Small Molecules*

18.15 - 18.30	**ORG OR024**	**Massimiliano Cordaro**	*Synthetic Approaches to Molecular Diversity of BODIPY*

ORG 04

16.00 - 16.15	**ORG OR025**	**Vincenzo Mirco Abbinante**	*Highly-fluorinated aromatic diimides for organic electronics:from synthesis to thin-film preparation*
16.15 - 16.30	**ORG OR026**	**Rita Argenziano**	*Functional films from 5,6-dihydroxyindole oligomers and long chain diamines partnership*
16.30 - 16.45	**ORG OR027**	**Giacomo Biagiotti**	*Tailoring the structure of the BODIPY probe in the design of functional fluorescent materials*
16.45 - 17.00	**ORG OR028**	**Davide Blasi**	*Trityl-brominated radicals as building blocks for doublet CPL emitters*
17.00 - 17.30	**Break**		
17.30 - 17.45	**ORG OR029**	**Alberto Bossi**	*Porphycenes, a lesser known tetrapyrrolic macrocycle with intriguing properties suitable for in situ sensing*
17.45 - 18.00	**ORG OR030**	**Adriano Parodi**	*Polyhydroxybutyrate as a sustainable platform for the production of chemicals and bio-polymers*
18.00 - 18.15	**ORG OR031**	**Simone Di Noja**	*Transfer of Axial Chirality to the Nanoscale Endows Carbon Dots with Circularly Polarized Luminescence*
18.15 - 18.30	**ORG OR032**	**Claudio Ferdeghini**	*Synthesis and thermal behavior of dicationic ionic liquids*

Divisione CHIMICA DEI SISTEMI BIOLOGICI (CSB)

CSB 01

15.00 - 15.05	**Opening Remarks Presidente Michael Assfalg**		
15.05 - 15.35	**CSB KN001**	**Rommie Amaro**	*Computational Microscopy of SARS-CoV-2*
15.35 - 16.00	**CSB PZ001**	**Luca Mazzei**	*Talking about urease: How the grasp on the molecular aspects of this enzyme can help in counteracting its role in microbiological pathogenesis and environmental issues*
16.00 - 16.15	**CSB OR001**	**Marta De Zotti**	*A pH-Induced Reversible Conformational Switch able to control the Photocurrent Efficiency in a Peptide Supramolecular System*
16.15 - 16.30	**CSB OR002**	**Ottavia Bellotto**	*Supramolecular hydrogels from unprotected dipeptides: a comparative study on stereoisomers and structural isomers the Photocurrent Efficiency in a Peptide Supramolecular System*
16.30 - 17.00	**Break**		
17.00 - 17.30	**CSB PZ002**	**Claudia Bonfio**	*Uncovering the emergence of modern cells*
17.30 - 17.45	**CSB OR003**	**Gianantonio Battistuzzi**	*Molecular basis of myoglobinopathy, a newly discovered molecular disease*
17.45 - 18.00	**CSB OR004**	**Lidietta Giorno**	*Selectivity and stability of biological macromolecules heterogenized to nanostructured artificial membranes*

18.00 - 18.15	**CSB OR005**	**Claudia Riccardi**	*Design, synthesis and characterization of cyclic TBA analogues*
18.15 - 18.50	**Discussione**		

Divisione DIDATTICA CHIMICA (DID)
DID 01

15:00-16:00	**DID PL001**	**Jan Apotheker**	*Developments in chemistry education*
16:00-16:30	**DID IL001**	**Mariano Venanzi**	*Sustainable chemistry for a sustainable teaching. A proposal for a first level curriculum in Chemistry at University*
16:30-16:45	**DID OR001**	**Federica Branchini**	*Teaching the notion of chemical bonding: a didactic challenge*
16:45-17:00	**DID OR002**	**Maria Antonietta Carpentieri**	*A new didactic pathway to introduce Spectroscopy by historical-epistemiological/STEM laboratorial/distance learning blended approach*
17:00-17:15	**DID OR003**	**Maria Costa**	*Virtual Reality visualizations of complex molecular structures in chemistry education. The β-CD-ASA example*
17:15-17:30	**DID OR004**	**Sandro Jurinovich**	*A didactic sequence for teaching chromatography: observation, model and practical applications*
17:30-17:45	**DID OR005**	**Dora Stella Lombardi**	*'Light and Molecules': an experimental approach to the understanding of basic concepts of Quantum Mechanics*
17:45-18:00	**DID OR006**	**Alma Moretta**	*Additional Learning Requirements (OFA) in Math for Environmental Science degree course: a review for a better understanding of the difficulties of students entering university*
18:00-18:15	**DID OR007**	**Davide Peddis**	*From the astro to the nano scale: a learning by doing teaching pathway*
18:15-18:30	**DID OR008**	**Antonio Testoni**	*Chemistry, history and complexity*
18:30-18:45	**DID OR009**	**Sergio Palazzi**	*A colorful new morning - teaching applied chemistry in pandemic times*

Divisione SPETTROMETRIA DI MASSA (MAS)
MAS 01

15.00 - 15.15	**Welcome**		
15.15 - 15.55	**MAS PL001**	**Giuseppina Maccarone**	*The Role of Mass Spectrometry in the – omics Era*
15.55 - 16.10	**MAS OR001**	**Daniela Cecconi**	*Integrated lipidomics and proteomics reveal cardiolipin remodelling, upregulation of HADHA and long chain fatty acids in pancreatic cancer stem cells*
16.10 - 16.25	**MAS OR002**	**Silvia Pedretti**	*Metabolomic approaches to investigate the role of the mitochondrial*
16.25 - 16.35	**Break**		

16.35 - 17.15	**MAS PL002**	**John A. McLean**	*High dimensional molecular phenomics in systems, synthetic, and chemical biology*
17.15 - 17.30	**MAS OR003**	**Isabella Piga**	*Spatial proteomics to map tissue alterations during the progression of fibrosis in an IPF and Nintedanib-treated mouse model*
17.30 - 17.45	**MAS OR004**	**Federico Fanti**	*Quantitative analysis of resolvins in biological matrices by means LLE-μSPE-HPLC-MS/MS*
17.45 - 18.00	**MAS OR005**	**Elettra Barberis**	*A Combined GCxGC-MS and GC-MS Approach to Discovery and Validate New Potential Biomarkers for Prostate Cancer Diagnosis*

Divisione TEORICA E COMPUTAZIONALE (TEO)

15:00 -15:20	**TEO KN001**	**Emilia Sicilia**	*Computations for investigating anticancer activity of metal-based compounds beyond cisplatin*
15:20 - 15:40	**TEO PZ001**	**Greta Donati**	*Exploring Chemistry through Multiple Time and Size Scales*
15:40 - 15:50	**TEO OR001**	**Marco Bertani**	*Improving empirical force fields for molecular dynamics simulations of oxide glasses. The importance of three-body interactions in rigid-ion models*
15:50 - 16:00	**TEO OR002**	**Arianna Massaro**	*First-principles study of Oxygen redox activity in P2-type NaxNi0.25Mn0.68O2 high energy cathode for Na-ion batteries*
16:00 - 16:10	**TEO OR003**	**Mirko Vanzan**	*An atomistic insight on the hot-electron injection mechanism*
16:10 - 16:20	**TEO OR004**	**Sergio Tosoni**	*Computational characterization of single-atom species on metal-supported oxide thin films*
16:20 - 16:30	**TEO OR005**	**Ida Ritacco**	*Spontaneous Production of Ultrastable Reactive Oxygen Species on Titanium Oxide Surfaces Modified with Organic Ligands*
16:30 - 17:00	**break**		
17:00 - 17:20	**TEO PZ002**	**Alessandro Erba**	*The Role of Fock Exchange in Relativistic Density Functional Theory*
17:20 - 17:30	**TEO OR006**	**Luca Brugnoli**	*Development and application of a ReaxFF Reactive Force Field for Cerium Oxide/Water Interfaces*
17:30 - 17:40	**TEO PO005**	**Anna Ranaudo**	*Computational study on the structural stability of mutated Affitins*
17:40 - 17:50	**TEO OR008**	**Noelia Faginas-Lago**	*Molecular Simulations of CO2/N2/H2O Gaseous Mixture Separation in Graphtriyne Membrane*
17:50 - 18:00	**TEO OR009**	**Francesca Fasulo**	*Electrode-electrolyte interface in solid-state lithium batteries: new insights from density functional embedding theory*

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18:00 - 18:10	**TEO OR010**	**Mariagrazia Fortino**	*Multi-replica biased sampling for photoswitchable p-conjugated polymers*
18:10 - 18:30	**discussion**		

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Divisione CHIMICA ANALITICA (ANA)

ANA 04

09.30 - 09.50	**ANA IL004**	**Cosima Damiana Calvano**	*Allergenicity assessment of novel foods by identifying marker peptides using bioinformatics and LC-ESI-MS/MS*
09.50 - 10.10	**ANA OR024**	**Danilo Corradini**	*Separation and Detection of Charged and Neutral Biomolecules in Plants and Food Matrices by Capillary Zone Electrophoresis*
10.10 - 10.15	**break**		
10.15 - 10.30	**ANA OR025**	**Antonella Cavazza**	*Analytical approaches for safety assessment in the development of innovative packaging solutions*
10.30 - 10.45	**ANA OR026**	**Tatiana Chenet**	*Evaluation of the presence of plastics in two fish species of the Mediterranean Sea and potentially correlated harmful effects*
10.45 - 11.00	**ANA OR027**	**Paola Arena**	*A Holistic Approach to the Characterization of High-Value Generating Molecules from the Wastes of Tuna Fishery Industry*
11.00 - 11.15	**ANA OR028**	**Federica Dal Bello**	*Insects food for the future*
11.15 - 11.30	**ANA OR029**	**Debora fabbri**	*Integrated approach for the analysis of some pesticides in vegetables and food matrices fastidiosa*
11.30 - 11.45	**ANA OR030**	**Paola Agata E. Donato**	*Triacylglycerol Fingerprinting in Vegetable Oils by means of Subcritical Solvent Chromatography*
11.45 - 12.00	**ANA OR031**	**Marco Iammarino**	*Exploring the potentiality of capillary ion chromatography (CIC) as analytical technique for the determination of food additives*
12.00 - 12.15	**ANA OR032**	**Fabio Salafia**	*Use of ultra-high performance liquid chromatography to characterize non-volatile compounds in Italian beers*
12.15 - 12.30	**ANA OR033**	**Emanuela Trovato**	*Characterization of volatile and non volatile compounds in citrus beer to evaluate product quality for food frauds prevention.*

ANA 05

09.30 - 09.50	**ANA KN004**	**Alessandra Biancolillo**	*Variable selection with a focus on multi-way and multi-block data*
09.50 - 10.10	**ANA KN005**	**Cristina Malegori**	*Near infrared hyperspectral imaging combined with multivariate image analysis: potential and limitations for the identification of microplastics in aquatic samples*
10.10 - 10.15	**break**		
10.15 - 10.30	**ANA OR034**	**Giacomo Baccolo**	*Automate chemometric approach for peak identification and quantification in untargeted GC-MS data*

10.30 - 10.45	**ANA OR035**	**Denise Biagini**	*Oxylipin storm in COVID-19: a new perspective in classifying disease severity*
10.45 - 11.00	**ANA OR036**	**Francesca Di Donato**	*Authentication of donkey's milk by Near Infrared Spectroscopy coupled with chemometric classifiers*
11.00 - 11.15	**ANA OR037**	**Fabio Fornari**	*Connecting the dots between theory and practice: discovering new functional cocrystals through supervised pattern recognition*
11.15 - 11.30	**ANA OR038**	**Sabina Licen**	*SOMEnv: an R package for mining environmental monitoring datasets by Self-Organizing Map and k-means algorithms with a Graphical User Interface*
11.30 - 11.45	**ANA OR039**	**Lisa Rita Magnaghi**	*Optode & Chemometrics: Milk Freshness at a Glance*
11.45 - 12.00	**ANA OR040**	**Elisa Robotti**	*Optimization of the process of anaerobic digestion of FORSU by experimental design techniques*
12.00 - 12.15	**ANA OR041**	**Giorgia Sciutto**	*A chemometric strategy to exploit the complementary information from a combined XRF-Vis-NIR hyperspectral imaging system*
12.15 - 12.30	**ANA OR042**	**Federica Turrini**	*'Specialty' or 'Gourmet' oils: a multivariate statistical approach for the rapid identification of their botanical species*

ANA 06

09.30 - 09.50	**ANA KN006**	**Serena Arnaboldi**	*Unconventional Electrochemical Approaches for the Direct Readout of Chiral Information*
09.50 - 10.10	**ANA KN007**	**Isacco Gualandi**	*Electrosynthesis of Layered Double Hydroxides for analytical applications*
10.10 - 10.15	**break**		
10.15 - 10.30	**ANA OR043**	**Riccarda Antiochia**	*Wearable electrochemical microneedles-based nanoporous gold sensor for real time catecholamine detection*
10.30 - 10.45	**ANA OR044**	**Paolo Inaudi**	*Solid state electrochemical behaviour and spin multiplicity in charge transfer co-crystals of DBTTF:F4TCNQ*
10.45 - 11.00	**ANA OR045**	**Andreas Lesch**	*Large-scale production of electroanalytical sensors by combined inkjet printing and light-induced synthesis of metal nanoparticles*
11.00 - 11.15	**ANA OR046**	**Antonella Miglione**	*Combined paper-based substrates for electrochemical detection of copper ions in serum*
11.15 - 11.30	**ANA OR047**	**Patrizia R. Mussini**	*Enantiomer discrimination in voltammetry in media of high structural order at the electrochemical interphase implemented with chirality*

11.30 - 11.45	**ANA OR048**	**Laura Pigani**	*Cannabinoids fast detection in real matrices: an electrochemical sensors' approach*
11.45 - 12.00	**ANA OR049**	**Angelo Tricase**	*Electrochemical Characterization of supramolecular structure in Self-Assembled Monolayers*
12.00 - 12.15	**ANA OR050**	**Martina Vizza**	*Specific ion effect in electrochemistry: the deposition of copper in the presence of different background electrolytes*

Divisione CHIMICA FISICA (FIS)

FIS 03

Enerchem I

09:30-10:00	**FIS KN003**	**Emanuela Gatto**	*Photocurrent Generation in Supramolecular Bio-Inspired Nanoarchitectures on Gold Surface*
10:00-10:15	**FIS OR025**	**Cristina Artini**	*A novel approach for the evaluation of the defect clusters content in doped ceria through in-situ high pressure x-ray diffraction*
10:15-10.30	**FIS OR026**	**Chiara Milanese**	*Super activated biochar for solid state hydrogen storage and supercapacitors preparation*
10:30-10.45	**FIS OR027**	**Emanuela Sartori**	*Emissive Layered Perovskite Nanocrystals*
10:45-11:00	**FIS OR028**	**Giovanni Di Liberto**	*Theoretical Description Semiconductors Interfaces: insights from DFT*
11:00-11.15	**break**		

Enerchem II

11:15-11.30	**FIS OR029**	**Vanira Trifiletti**	*Synthesis of bismuth-based hybrid perovskites for thermoelectrics*
11.30-11.45	**FIS OR033**	**Mariarosaria Tuccillo**	*Operando study of a cobalt free Li-rich layered oxide materials (LRLO) in a lithium cell*
11:45-12:00	**FIS OR031**	**Simone Sansoni**	*Laser ablation in solution for a more sustainable perovskite-based optoelectronics*
12:00-12:15	**FIS OR030**	**GianLuca Chiarello**	*Photothermocatalytic steam reforming of methanol for H2 production*
12:15-12.30	**FIS OR032**	**Annalisa Polo (Vincitrice del Premio Semerano)**	*Effects of Mo6+ doping on the performance of BiVO4 photoanodes for solar water oxidation*

FIS 04

Physical Chemistry for Environment I

09:30-10:00	**FIS KN004**	**Luigi Gentile**	*Ecofriendly Isolation of Cellulose from buckwheat chaff*
10:00-10:15	**FIS OR039**	**Vito Rizzi**	*From agricultural wastes to a resource: Kiwi Peels as recyclable adsorbent to remove emerging pollutants from water*

10:15-10.30	**FIS OR035**	**Giuseppina Anna Corrente**	*Hydrochemical study of the Turbolo basin: evaluation of the spatial and seasonal variation of surface water quality*
10:30-10.45	**FIS OR036**	**Vanessa Miglio**	*Silica Monolith for the Removal of Pollutants from Gas and Aqueous Phases*
10:45-11:00	**FIS OR037**	**Gabriele Mulas**	*Investigation of mechanochemically driven CO2 conversion over Olivine powders*
11:00-11.15	**break**		

Physical Chemistry for Environment II

11:15-11.30	**FIS OR038**	**Pier Luigi Gentili**	*Establishing a link between Chemistry and Complexity Science to promote Sustainability*
11.30-11.45	**FIS OR034**	**Sebastiano Campisi**	*Tin-functionalized hydroxyapatite as an "ecofriendly bridge" joining water remediation and air protection processes*
11:45-12:00	**FIS OR040**	**Paolino Caputo**	*Use of Food Substances as chemical additives in the industrial field*
12:00_12:15	**FIS OR041**	**Alessio Zuliani**	*Environmentally friendly ZnO/Castor oil polyurethane composites for the efficient gas-phase adsorption of acetic acid*
12:15-12.30	**FIS OR042**	**Antonio Tursi**	*Synthesis and Enhanced Capture Properties of a New BioMOF@SWCNT-BP: Recovery of the Endangered Rare Earth-Elements from Aqueous Systems*

FIS 05

Spectroscopic Applications I

09:30-10:00	**FIS KN005**	**Elena Groppo**	*Revisiting the use of probe molecules in the characterization of heterogeneous olefin polymerization catalysts by IR spectroscopy*
10:00-10:15	**FIS OR043**	**Giampaolo Marcolin**	*Solvent-dependent Characterization of Fucoxanthin through 2D Electronic Spectroscopy Reveals New Details on the Intramolecular Charge Transfer State Dynamics*
10:15-10.30	**FIS OR044**	**Alessandra Forni**	*Multiple prompt and long-lived emissions from solid state purely organic materials*
10:30-10.45	**FIS OR045**	**Rosachiara Antonia Salvino**	*NMR in chiral partially ordered media: a tool for achieving conformational traits of small flexible enantiomers in solution*
10:45-11:00	**FIS OR046**	**Nicola Peruffo**	*Selective Switching of Multiple Plexcitons in Colloidal Materials: Directing the Energy Flow at the Nanoscale*

Spectroscopic Applications II

11:15-11.30	**FIS OR047**	**Elisabetta Collini**	*The effect of hydrogen bonds on the ultrafast relaxation dynamics of a BODIPY dimer*
11.30-11.45	**FIS OR048**	**Francesca Martini**	*Structure and dynamics of "cool" organic pigments by solid state NMR*

11:45-12:00	**FIS OR049**	**Margherita Bolognesi**	*Bidimensional black Phosphorus: surface functionalization, heterostructures with organic molecules, applications*
12:00_12:15	**FIS OR050**	**Annamaria Panniello**	*BODIPY-functionalized Quantum dots platform for high efficiency FRET processes*
12:30-12:45	**FIS OR093**	**Eleonora Vottero**	*C-H terminations in activated carbons and related catalysts:an Inelastic Neutron Scattering spectroscopy and DFT study*

Divisione CHIMICA INDUSTRIALE (IND)
IND 02

Sessione congiunta con Gruppo Interdivisionale Catalisi

09.30 - 9.40	**IND OR012**	**Annalisa Sacchetti**	*Bio-oils valorization by selective catalytic hydrogenation: a comparison between batch and continuous flow systems*
9.40 - 9.50	**IND OR013**	**Alessandra Toso**	*Pd/CeO2 as Passive NOx Adsorbers: key properties and NOx adsorption mechanism*
9.50 - 10.00	**IND OR014**	**Sebastiano Campisi**	*A green route to the catalytic nitrous oxide decomposition by transition metal doped hydroxyapatites*
10.00 - 10.10	**IND OR015**	**Luca Consentino**	*Ce doped WO3-TiO2 cordierite monoliths for Selective Catalytic Reduction of NOx by NH3*
10.10 - 10.20	**IND OR016**	**Roberto Fiorenza**	*The solar photothermo-catalytic approach for the VOCs degradation and the subsequent CO2 conversion*
10.20 - 10.30	**IND OR017**	**Melissa Greta Galloni**	*Cu, Fe, and CuFe exchanged hydroxyapatites as eco-friendly catalysts for NH3-SCR reaction*
10.30 - 10.45	**Discussion**		
10.45 - 11.00	**break**		
11.00 - 11.20	**IND KN003**	**Pierdomenico Biasi**	*From University to Industry: examples on how university-industry collaborations in catalysis can be effective and successful*
11.20 - 11.30	**IND OR018**	**Fabiana Vento**	*Photodegradation of Xenobiotics from Polluted Water Using a New PMMA-TiO2 Based Nanocomposite*
11.30 - 11.40	**IND OR019**	**Vincenzo Russo**	*Heterogeneous photodegradation for the removal of ibuprofen from water*
11.40 - 11.50	**IND OR020**	**Alessandro Allegri**	*Aquivion® PFSA-based spray-freeze dried composite materials for the conversion of furfuryl alcohol to levulinates*
11.50 - 12.00	**IND OR021**	**Somayeh Taghavi**	*Biomass-derived levulinic acid hydrogenation to GVL using bifunctional biochar-based catalysts*
12.00 - 12.10	**IND OR044**	**Giulia Zoppi**	*Green hydrogen production from wastewater derived from lignin-rich hydrothermal liquefaction*
12.10 - 12.30	**Discussion**		

IND 03

09.30 - 9.50	**IND KN004**	**Michele Laus**	*Polymer brush technology: the true and the false in grafting to processes*
9.50 - 10.00	**IND OR023**	**Stefano Gazzotti**	*1,3-Dioxolan-4-Ones as powerful tool for the synthesis of functionalized PLA-based materials with tailored properties*
10.00 - 10.10	**IND OR024**	**Carla Calabrese**	*Hybrid organic-inorganic materials based on polydopamine-like chemistry*
10.10 - 10.20	**IND OR025**	**Alessandro Piovano**	*ß-ketoimine Cr complexes for the production of functional polyolefins: exploring the metal-ligand bond as a key point of the catalysts*
10.20 - 10.30	**IND OR026**	**Edoardo Podda**	*Self-Healing and Shape-Memory Hydrogels by Micellar Polymerization*
10.30 - 10.40	**IND OR027**	**Riccardo Chiarcos**	*Evidence of Preferential Grafting of Short Chains in Grafting To Reactions of Hydroxy-Terminated P(S-r-MMA) Copolymers*
10.40 - 10.55	**Discussion**		
10.55 - 11.10	**break**		
11.10 - 11.20	**IND OR028**	**Antonietta Cozzolino**	*Axially oriented guest induced crystallization in syndiotactic polystyrene unstretched fiber*
11.20 - 11.30	**IND OR029**	**Manohar Golla**	*Axially Oriented Co-crystalline Phases of Poly(2,6-dimethyl-1,4-phenylene)oxide and host-guest orientations*
11.30 - 11.40	**IND OR030**	**Camilla Parmeggiani**	*Liquid crystal elastomer based artificial muscles for cardiac repair*
11.40 - 11.50	**IND OR031**	**Daniele Martella**	*Cell instructive polymers based on liquid crystals*
11.50 - 12.00	**IND OR032**	**Nicole Mariotti**	*Bio-based and waste-derived polyurethanes for energy systems*
12.00 - 12.30	**Discussion**		

Divisione CHIMICA ORGANICA (ORG)

ORG 05

10.00 - 10.30	**ORG PZ005**	**Marco Lucarini**	***Premio alla ricerca Chimica Organica nei suoi Aspetti Metodologici*** *Novel Spin-Labelled Mechanically Interlocked Molecules as Models for the Interpretation of Biradical EPR Spectra*
10.30 - 10.45	**ORG OR033**	**Fabio Buonsenso**	*Non-equilibrium dynamic chromatography: investigation of the reduction process of α-lipoic acid promoted by dithiothreitol*
10.45 - 11.00	**ORG OR034**	**Marta Da Pian**	*Combined use of forensic science in sexual assault: a case report*

11.00 - 11.15	**ORG OR035**	**Graziano Di Carmine**	*Aldol Reaction between Benzaldehyde and Hydroxyacetone Promoted by Silica SBA-15 supported proline: Unraveling the Solvent Effect on the Catalyst Behavior Using NMR Relaxation*
11.15 - 11.30	**ORG OR036**	**Elena Ermini**	*New 1-6 self-immolative spacer for the release of thiols under nitroreductase activation*

ORG 06

10.30 - 10.45	**ORG OR037**	**Germana Esposito**	*Molecular Networking: a powerful tool to dereplication of natural products*
10.45 - 11.00	**ORG OR038**	**Roberta Franzini**	*Chromatographic and spectroscopic investigation of chiral aza-dibenzocyclooctynes and their analogues obtained by azido-click reaction.*
11.00 - 11.15	**ORG OR039**	**Marco Galeotti**	*Hydrogen Atom Transfer based aliphatic C-H bond oxidation of hydrocarbons bearing cyclopropyl moieties. The role of hyperconjugation.*
11.15 - 11.30	**ORG OR040**	**Chiara Lambruschini**	*Photoisomerization of ferulic acid derivatives*

ORG 07

10.30 - 10.45	**ORG OR041**	**Francesca Ghirga**	*Development of ArnT-mediated colistin resistance diterpene-based inhibitors*
10.45 - 11.00	**ORG OR042**	**Laura Goracci**	*Exploring PROTACs metabolism: a structure-activity relationship study*
11.00 - 11.15	**ORG OR043**	**Concetta Imperatore**	*Toward marine inspired multitarget drugs for diabetes mellitus and its complications: design and synthesis of novel dual Protein Tyrosine Phosphatase 1B and Aldose Reductase ligands*
11.15 - 11.30	**ORG OR044**	**Marco Masi**	*Phytotoxins produced by fungal pathogens of legume crops*

Divisione CHIMICA DEI SISTEMI BIOLOGICI (CSB)

CSB 02

09.30 - 10.00	**CSB KN002**	**Paola Turano**	*Bioinorganic chemistry of ferritin nanocages*
10.00 - 10.15	**CSB OR006**	**Veronica Ghini**	*NMR as a tool to monitor the individual response of immunotherapy*
10.15 - 10.30	**CSB OR007**	**Luigi Russo**	*μs-ms conformational dynamics control the formation of prion protein intermediate states involved in amyloid fibrils*
10.30 - 10.45	**CSB OR008**	**Sabrina Elkhanoufi**	*New, highly sensitive off/on EPR probes to monitor enzymatic activity*
10.45 - 11.00	**CSB OR009**	**Alessia Distefano**	*A MS and SPR coupled approach to fully characterize IDE activity modulation*

11.00 - 11.15	**Break**		
11.15 - 11.30	**CSB OR010**	**Alessandro D'Urso**	*The increased thermodynamic stability of miRNAs might be the reason of stronger repressive activity*
11.30 - 11.45	**CSB OR029**	**Anna Di Porzio**	*Identification of a short peptide that preferentially binds to the G-quadruplex structure in the c-MYC oncogene promoter*
11.45 - 12.00	**CSB OR012**	**Chiara Platella**	*Targeting cancer-related DNA G-quadruplex structures by naphthalene diimide ligands*
12.00 - 12.15	**CSB OR013**	**Alessandra Romanelli**	*Self-assembly of PNA-peptide conjugates*
12.15 - 12.45	**Discussione**		

Divisione ELETTROCHIMICA (ELE)
ELE 04

09.30 - 10.00	**ELE IL28**	**Sara Rebeccani**	*PEDOT doped with Sulphonated Polyarylethersulphones as electroactive material in electroanalytical applications*
10.00 - 10.15	**ELE IL29**	**Cecilia Wetzl**	*Graphene-based functional materials for electrochemical imaging*
10.15 - 10.30	**ELE IL30**	**Lorenzo Ripani**	*Microkinetic modeling for the electrochemical CO2 reduction reaction in bicarbonate electrolyte*
10.30 - 10.45	**break**		
10.45 - 11.00	**ELE IL31**	**Riccardo Brandiele**	*Synthesis and characterization of materials for PEM-FC, based on Pt alloyed nanoparticles supported on next generation mesoporous carbon*
11.00 - 11.15	**ELE IL32**	**Annalisa Polo**	*Ternary Oxide Semiconductor Photoanodes for Solar Energy Conversion*
11.15 - 11.45	**ELE IL33**	**Laura Rotundo**	*Electroreduction of carbon dioxide by Re(I) and Mn(I) bipyridine complexes*

Divisione CHIMICA PER LE TECNOLOGIE (TEC)
TEC 03

9.30 - 9.40	**TEC OR025**	**Paola Di Matteo**	*Phenolic compounds in alcoholic and low-alcoholic beer by fast HPLC-PDA-MS/MS analysis: impact of malt composition, hops and dealcoholization process.*
9.40 - 9.50	**TEC OR026**	**Elhussein M. F. M. H. Ahmed**	*Early-Detection of Xylella fastidiosa in Olive Trees by Hyperspectral Reflectance and Non-targeted Metabolomics*
9.50 - 10.00	**TEC OR027**	**Nazeeha Ayaz**	*Hydrophobin coated superfluorinated nanoparticles for 19F-MRI cell tracking*
10.00 - 10.10	**TEC OR028**	**Elena Dilonardo**	*S-PEEK membranes optimized for Vanadium Redox Flow Battery: the effects of sulphonation degree and filler content on operative conditions and set-up configurations*

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10.10 - 10.20	**TEC OR029**	**Giuseppe Marcì**	*Selective photocatalytic partial oxidation of aromatic alcohols to aldehydes in aqueous suspensions of C3N4 obtained by polycondensation of melamine and cyanuric/barbituric acids*
10.20 - 10.40	**Discussion**		
10.40 - 10.50	**TEC OR030**	**Giancarlo Terraneo**	*Crystalline Molecular Rotors Assembled through Halogen Bonding*
10.50 - 11.00	**TEC OR031**	**Valentina Dichiarante**	*Multi-branched perfluoro-tert-butoxyl scaffolds for the functionalization of surfaces and nanomaterials*
11.00 - 11.10	**TEC OR032**	**Gabriella Munzi**	*A dinuclear Zn(II) Schiff-base complex as molecular tweezer: binding properties and sensing towards biogenic diamines*
11.10 - 11.20	**TEC OR033**	**Martina Lippi**	*Dynamic 1D Bispidine-based Coordination Polymers for Adsorption Applications*
11.20 - 11.30	**TEC OR034**	**Daniele Narzi**	*Mechanism of oxygen evolution and Mn4Ca cluster restoration in the natural water-oxidizing catalyst*
11.30 - 11.50	**Discussion**		

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Divisione CHIMICA DELL'AMBIENTE E DEI BENI CULTURALI (ABC)

ABC 02

09.30-10.00	**ABC KN001**	**Edith Joseph**	*Green methods for metals conservation*
10.00-10.15	**ABC OR023**	**Francesco Abate**	*The evolving perspective on the study of ancient bronze coins*
10.15-10.30	**ABC OR024**	**Cecilia Velino**	*Investigation of the corrosive effects of ambient particulate matter on bronze through accelerated sampling and ageing*
10.30-10.45	**ABC OR025**	**Maria Labate**	*The leading role of diagnostics for cultural heritage in historic studies and conservation: Sarezzano reliquary busts as a case study*
10.45-11.00	**ABC OR026**	**Andrea Timoncini**	*Characterization of bacteria community on bronze and marble statues*
11.00-11.15			
11.15-11.30			
11.30-11.45	**ABC OR027**	**Roberta Zanini**	*Laser Ablation ICP-MS elemental imaging to investigate corroded surfaces of ancient glass*
11.45-12.00	**ABC OR028**	**Lucrezia Gatti**	*A new analytical strategy for the characterization of diagenetic pathways in ancient bones and teeth.*
12.00-12.15	**ABC OR029**	**Raffaella Lamuraglia**	*Archaeometric investigation on Roman frescoes from the archaeological site of Aquileia*
12.15-12.30	**ABC OR030**	**Francesca Porpora**	*Diammonium hydrogen phosphate and Ca (OH)2 nanoparticles for consolidation of ancient bones: evaluation of performances*
12.30-12.45	**ABC OR052**	**Serena Spadavecchia**	*Evaluation of the effectiveness of coatings for the protection of outdoor terracotta artworks through artificial ageing*
12.45-13.00	**ABC OR032**	**Giulia C. Lodi**	*The assessment of the organic composition of historical remedies and drugs through a multidisciplinary approach*

ABC 03

09.30-09.45	**ABC OR034**	**Antonino Fiorentino**	*New photo-Fenton like process for roof harvested rainwater disinfection*
09.45-10.00	**ABC OR035**	**Elisa Gaggero**	*Removal of contaminants of emerging concern by enzymatic treatment with fungal laccases*
10-10.15.00	**ABC OR036**	**Giulia Guerra**	*Zinc and Iron Based Metal-Organic Frameworks as Ofloxacin Adsorbents in Polluted Waters*
10.15-10.30	**ABC OR037**	**Giuseppe Mascolo**	*Biodegradability enhancement of non-ionic surfactants in industrial wastewater by UV/H2O2 pre-treatment*

10.30-10.45	**ABC OR038**	**Giuseppe Mascolo**	*Remediation of groundwater contaminated with PCBs and PAHs by photocatalysis employing nano-sized TiO2 supported onto steel mesh*
10.45-11.00	**ABC OR039**	**Mirco Volanti**	*Biogas to Syngas through the Combined Steam/Dry Reforming Process: An Environmental Impact Assessment*
11.00-11.15			
11.15-11.30			
11.30-11.45	**ABC OR040**	**Sapia Murgolo**	*Assessment of a sustainable biofilter technology for reducing the environmental spread of CECs and odour emissions*
11.45-12.00	**ABC OR041**	**Federica Piras**	*Vacuum-UV as pre- and post-treatment to biofiltration: a novel integrated treatment scheme for wastewater reuse*
12.00-12.15	**ABC OR042**	**Concetta Pironti**	*A study of the biocidal effectiveness of permaleic acid (PMA): new promising application in disinfection process*
12.15-12.30	**ABC OR043**	**Annarosa Gugliuzza**	*2D Materials Engineered Membranes for a New Vision on Water Desalination*
12.30-12.45	**ABC OR044**	**Giuseppe Vitola**	*Membrane biofunctionalization for pesticide removal in surface water and vegetative water*
12.45-13.00	**ABC OR045**	**Domenico Cipriano**	*Protocol implementation of odour Proficiency Tests (PTs)*

Divisione CHIMICA FARMACEUTICA (FAR)
FAR 05

09.30 - 10.00	**FAR KN005**	**Yimon Aye**	*Leveraging precision electrophile signaling toward drug discovery*
10.00 - 10.30	**FAR KN006**	**Antimo Gioiello**	*Enabling synthesis and technologies to develop bile acid- inspired lead compounds*
10.30 - 10.45	**FAR OR019**	**Francesca Ferlenghi**	*A sulfonyl fluoride derivative selectively inhibits EGFRL858R/T790M/C797S by covalent modification of the catalytic lysine*
10.45 - 11.00	**FAR OR020**	**Angelica Artasensi**	*Novel potential DPP IV/ CA II inhibitors for the treatment of Type 2 Diabetes*
11.00 - 11.30	**FAR KN007**	**Andrea Stevenazzi**	*The selective inhibition of histone deacetylase 6 (HDAC6)*
11.30 - 11.45	**FAR OR023**	**Giannamaria Annunziato**	*Investigational studies on cyclopropane− carboxylic acid derivatives targeting O acetylserine sulfhydrylase as colistin adjuvants*
11.45 - 12.00	**FAR OR024**	**Simone Lucarini**	*Phenotype screening of a bisindole chemical library identifies URB1483 as a new antileishmanial agent with topoisomerase IB as molecular target*

12.00 - 12.15	**FAR OR025**	**Santo Previti**	*Development of peptidyl Michael acceptors for S3 pocket investigation of rhodesain, cysteine protease of Trypanosoma brucei rhodesiense*
12.15 - 12.30	**FAR OR026**	**Valentina Straniero**	*Development of benzodioxane-benzamides inhibitors of FtsZ as potent broad-spectrum antimicrobial agents*
12.30 - 13.00	**FAR KN008**	**Anna K.H. Hirsch**	*Addressing underexplored anti-infective targets*

FAR 06

10.30 - 10.45	**FAR OR021**	**Maria Dichiara**	*Design, synthesis and pharmacological evaluation of 4-carbamothioylphenyl sigma-1 receptor antagonists for pain treatment*
10.45 - 11.00	**FAR OR022**	**Giacomo Rossino**	*Identification of novel Sigma 1 receptor antagonists based on arylalkanolamine scaffold for the treatment of neuropathic pain*
11.00 - 11.30			
11.30 - 11.45	**FAR OR027**	**Marilena Muraglia**	*To042: prospective lead compound for the treatment of myotonic syndromes*
11.45 - 12.00	**FAR OR028**	**Sebastiano Intagliata**	*Development of mutual prodrugs of 5-fluorouracil and heme oxygenase 1 inhibitor as anticancer agents*
12.00 -12.15	**FAR OR029**	**Luca Pinzi**	*LigAdvisor: a web server to perform in silico explorations on crystallographic ligands and known drugs for polypharmacology and drug repurposing*
12.15 -12.30	**FAR OR030**	**Lucilla Turco**	*NMR contributions to process chemistry sustainability in the pharmaceutical research area*

Divisione CHIMICA FISICA (FIS)

FIS 06

Physical Chemistry for Biomedical Applications III

09:30-10:00	**FIS KN006**	**Debora Scuderi**	*Free electron Laser and IRMPD spectroscopy*
10:00-10:15	**FIS OR052**	**Rita Gelli**	*Insights into biologically-relevant calciprotein particles: effect of stabilizing agents on the formation and crystallization mechanisms*
10:15-10.30	**FIS OR053**	**Alessandra Del Giudice**	*Regulation of the photosynthetic AB-GAPDH via self-assembly*
10:30-10.45	**FIS OR054**	**Davide Tocco**	*Investigation of Fe-BTC and Z MOFs as carrier for Aspergillus.sp Laccase*
10:45-11:00	**FIS OR055**	**Pasquale Sacco**	*Biopolymer-based platforms for cell mechanosensing and regenerative medicine*

11:00-11.15	**FIS OR057**	**Marta Penconi**	*Advancing near-IR phosphorescence with Ir(III) complexes bearing a single emitting ligand: properties and OLED applications*
11.15-11.45	**break**		

Sessione congiunta con TEO

11:45-12:00	**FIS OR058**	**Fabio Gabas**	*Divide and Conquer Semiclassical Initial Value Representation: a valuable theoretical tool for vibrational spectroscopy of biological systems*
12:00_12:15	**TEO OR011**	**Giacomo Saielli**	*A computational view of ionic liquid crystals*
12:15-12.30	**FIS OR060**	**Tommaso Giovannini**	*Energy-Based Molecular Orbital Localization in specific Molecular Regions*
12:30-12:45	**TEO OR012**	**Alessio Petrone**	*Electronic attosecond dynamics: Ab initio treatment of photo-induced excitonic states*
12:45-13:15	**FIS KN007**	**George Froudakis**	*Designing Novel Nanoporous Materials for Applications in Energy and Environment. From Multi-Scale Modeling to Materials Informatics*

FIS 07

Sessione congiunta con CSB

09:30-10:00	**FIS KN008**	**Roland Winter**	*Temperature, Pressure, and Cosolute Effects on Liquid–Liquid Phase Separation and Condensates of Proteins: Physical Chemistry and Biological Implications*
10:00-10:15	**FIS OR067**	**Francesca Baldelli**	*Superfluorinated Exosomes for Sensitive in Vivo Tracking by 19F-MRI*
10:15-10.30	**FIS OR063**	**Cristina Carucci**	*Drug loaded polymer coated silica nanoparticles as drug delivery route against bacteria*
10:30-10.45	**FIS OR064**	**Francesca Biscaglia**	*Engineered Peptides on Gold Nanostructures for Enhanced Targeting Activity in Cancer Diagnosis*
10:45-11:00	**FIS OR065**	**Ilaria Clemente**	*Cubic and lamellar mesophases obtained from algal biomass as drug carriers with high potentiality*
11:00-11.15	**CSB OR026**	**Angelo Spinello**	*Small-molecule modulators of spliceosome-mutant cancers as a new therapeutic strategy against hematologic malignancies*
11:15-11.30	**CSB OR027**	**Nunzia laccarino**	*Effects of sequence and base composition on the CD and TDS profiles of i DNA*
11.30-11.45	**break**		

Sessione congiunta con ELE

11:45-12:15	**FIS KN009**	**Maria Vittoria Dozzi**	*CuWO4-based photoanodes for solar energy conversion: effects of Mo6+ doping and coupling with BiVO4*
12:15-12:30	**ELE OR038**	**Gennaro Sannino**	*Development of SnO2 composites as electron transport layer in un-encapsulated CH3NH3PbI3 solar cells*

12:30-12:45	**FIS OR069**	**Guillermo Escolano Casado**	*Cu-functionalized hydroxyapatites: a study of their physico-chemical properties and their potential as electrocatalysts*
12:45-13:00	**ELE OR039**	**He Xiufang**	*Investigation of the mechanism of Pt3Fe3 clusters for the hydrogen evolution reaction and for the oxygen reduction reaction*
13:00-13:15	**FIS OR071**	**Simone Di Muzio**	*Thermodynamics of the hydrolysis of lithium salts: pathways to the inorganic SEI components*

Divisione CHIMICA INORGANICA (INO)

INO 04

9.30 - 9.50	**INO PZ002 (Premio Dottorato 2020)**	**Anna Dall'Anese**	*Palladium catalyzed copolymerizations: from ligand architecture to macromolecule microstructure*
9.50 - 10.10	**INO PZ003 (Premio Dottorato 2020)**	**Giacomo Picci**	*Novel supramolecular architectures based on weak interactions*
10.10 - 10.30	**INO PZ004 (Premio Dottorato 2020)**	**Fortuna Ponte**	*Anticancer drugs: a detailed computational analysis of "non classical" compounds mechanism of action*
10.30 - 10.45	**INO OR022**	**Andrea Biffis**	*Gold catalyzed direct alkyne hydroarylations in ionic liquids: a powerful tool in organic synthesis*
10.45 - 11.00	**INO OR023**	**Luca Conti**	*Ru(II) polypyridyl complexes as promising light-responsive agents for biological application*
11.00 - 11.15	**INO OR024**	**Filippo Campagnolo**	*Development of sustainable and green methodologies for homogeneous gold(I) catalysis*
11.15-11.30	**break**		
11.30 - 11.45	**INO OR025**	**Matteo Atzori**	*Magneto-chiral dichroism in chiral molecular magnets*
11.45 - 12.00	**INO OR026**	**Stefano Scoditti**	*Anticancer and photophysical properties of a N^C^N-coordinated Pt(II) complex*
12.00 - 12.15	**INO OR027**	**Paolo Cleto Bruzzese**	*17O spin density studies of single-metal sites in Cu-CHA zeolites*
12.15 - 12.30	**INO OR028**	**Federica Santulli**	*A single catalyst for the synthesis and chemical depolymerization of polylactide*
12.30 - 13.00	**INO PZ005 (Premio Nasini 2020)**	**Enrico Ravera**	*Paramagnetic NMR in bioinorganic chemistry in the 'twenties*

INO 05

10.30 - 10.45	**INO OR029**	**Mauro Ravera**	*Pt(IV) bifunctional complexes as anticancer agents: "is this true glory?"*

10.45 - 11.00	**INO OR030**	**Alessia Giordana**	*Solid acid catalysts for glucose hydrolysis: quantification of Lewis and Brønsted acid sites using 2,6-dimethylpyridine*
11.00 - 11.15	**INO OR031**	**Giorgio Facchetti**	*New sp3 diphosphine-based rhodium catalysts for the asymmetric addition of aryl boronic acids to azaarenes*
11.15-11.30	**break**		
11.30 - 11.45	**INO OR032**	**Marco Chino**	*Design of a miniaturized FeS4 protein*
11.45 - 12.00	**INO OR033**	**Paolo Centomo**	*Selectivity enhancement of coordinating solvents on the direct synthesis of hydrogen peroxide*
12.00 - 12.15	**INO OR034**	**Tania Pecoraro**	*Luminescent self-assemblies of Pt(II) complexes in vivo*
12.15 - 12.30	**INO OR035**	**Cristiana Cesari**	*Homometallic and heterometallic ruthenium hydride carbonyl cluster*

INO 06

10.30 - 10.45	**INO OR036**	**Andrea Rossin**	*Thiazole-based Metal-Organic Frameworks for applications in CO2 storage/utilization and luminescence sensing*
10.45 - 11.00	**INO OR037**	**Patrizio Campitelli**	*Amino-decorated zinc bipyrazolate MOFs, an example of carbon dioxide capture and reuse (CCR)*
11.00 - 11.15	**INO OR038**	**Giorgio Tseberlidis**	*Sol-gel deposition of Cu2XYS4 thin-films with tunable bandgap as absorbers for photovoltaic applications*
11.15-11.30	**break**		
11.30 - 11.45	**INO OR039**	**Francesca Deganello**	*Recycling inorganic waste into sustainable materials for energy and environment*
11.45 - 12.00	**INO OR040**	**Damiano Ricciarelli**	*Energy vs charge transfer in manganese doped lead halide perovskites*
12.00 - 12.15	**INO OR041**	**Marco Bellini**	*Electrocatalysis for energy: from nanostructured to molecular approach*
12.15 - 12.30	**INO OR042**	**Chiara Domestici**	*Novel mononuclear and dinuclear Ir-Cp* complexes bearing phosphonate and carboxylate ancillary and anchoring ligands as homogeneous and heterogenized water oxidation catalysts*

Divisione ELETTROCHIMICA (ELE)

ELE 05

09.30 - 10.00	**ELE_KN34**	**Matteo Bonomo**	*NiO/ZrO2 nanocomposites as photocathodes of tandem DSCs with higher photoconversion efficiency with respect to parent single-photoelectrode p-DSCs*
10.00 - 10.15	**FIS_OR068**	**Giuseppe Arrabito**	*Inkjet Printing Quasi-Miscible Droplets for Pseudo-Planar Organic Heterojunctions*
10.15 - 10.30	**ELE_OR35**	**Alessandro Facchin**	*Oxygen Reduction Reaction monitoring at Iron Single Site Catalyst: Electrochemical Scanning Tunnelling Microscopy of Iron Octaethylporphyrin*
10.30 - 10.45	**FIS_OR070**	**Mariangela Curcio**	*Laser irradiation of Bio-waste derived carbon as anode for Li-ion batteries*

10.45 - 11.00	**ELE_OR36**	**Barbara Vercelli**	*Doping or Aggregation: the case of Conjugated Polyelectrolytes PCPDTBT-2SO3K and PCPDTBT-SO3K*
11.00 - 11.15	**FIS_OR130**	**Elena Messina**	*Electrochemical study of Smart Nanocarriers forImproved Corrosion Protection of Reinforced Concrete*
11.15 - 11.30	**ELE_OR37**	**Marco Malferrari**	*Light-Induced Electrochemical Processes at Semiconductor-Films/Water Interface Modulate Cell Redox Balance*

ELE 06

09.30 - 10.00	**ELE_KN40**	**Stefania Rapino**	*Cancer Metabolic Profile Detected by Scanning ElectroChemical Microscopy*
10.00 - 10.15	**ANA_OR137**	**Ilaria Ragazzini**	*A simple and industrially scalable method for making a PANI-modified cellulose touch sensor*
10.15 - 10.30	**ELE_OR42**	**Nikolaou Pavlos**	*Ultrasensitive Hepatitis B Virus whole genome detection by Electrochemiluminescence*
10.30 - 10.45	**ANA_OR136**	**Cosimino Malitesta**	*Electrosynthesised ion imprinted polymers in development of sensor for Cd(II) ions determination in water*
10.45 - 11.00	**ELE_OR44**	**Patrik Sfragano**	*A bicyclic peptide-based biosensor for the electrochemical detection of a cancer-related protease*
11.00 - 11.15	**ANA_OR134**	**Veronica Caratelli**	*A Paper-Based Electrochemical Device for the Detection of Pesticides Inspired by Nature: a Flower-Like Origami Biosensor*
11.15 - 11.30	**ELE_OR43**	**Silvia Comis**	*Determination of emerging contaminants with electrochemical sensors based on titania nanoporous films: effect of sol aging on their electrochemical performances*
11.30 - 11.45	**break**		
11.45 - 12.00	**ANA_OR135**	**Noemi Colozza**	*A multiparametric electrochemical device for degradation monitoring in reinforced concrete*
12.00 - 12.15	**ELE_OR41**	**Alessanra Zanut**	*DNA-based Nanoswitches: insights into electrochemiluminescence signal enhancement*

ELE 07

11.30 - 12.00	**ELE_KN045**	**Marta Feroci**	*Solvent-supporting electrolyte system in electrolysis: not only chemical environment and charge carrier*
12.00 - 12.15	**ELE_OR04 6**	**Angeloclaudio Nale**	*Interplay between porosimetric parameters, densitometric parameters and catalytic activities of "Core-Shell" ORR Electrocatalysts*
12.15 - 12.30	**ELE_OR04 7**	**Gioele Pagot**	*Ion Coordination and Dynamics in Ionic Liquid-based Electrolytes for Hybrid Al/Mg Batteries*
12.30 - 12.45	**ELE_OR04 8**	**Carpanese Maria Paola**	*Copper-based perovskite electrodes for reversible solid oxide cells*
12.45 - 13.00	**ELE_OR04 9**	**Duranti Leonardo**	*Multi-functional Fuel Electrode for Reversible Solid Oxide Cells*

Divisione CHIMICA PER LE TECNOLOGIE (TEC)

TEC 04

9.30 - 10.00	**TEC IL002**	**Lvova Larisa**	*Recent advances in potentiometric sensors for environmental purposes: from single ion-selective electrodes to multisensor analysis*
10:00 - 10:10	**TEC OR035**	**Moulaee Kaveh**	*A new electrochemical platform for fast and efficient determination of dominant non-psychoactive cannabinoids in Cannabis Sativa*
10:10 - 10:20	**TEC OR036**	**Ferlazzo Angelo**	*Crown ether functionalized graphene quantum dots as electrochemical and fluorescence based sensors for the selective detection of potassium and sodium ions*
10:20 - 10:30	**TEC OR037**	**Zribi Rayhane**	*Electrochemical and sensing properties of 2D-MoS2 nanosheets produced via liquid cascade centrifugation at different rate*
10:30 - 10:40	**TEC OR038**	**Bella Federico**	*Hybrid solar cells operating in aqueous environment*
10:40 - 10:50	**TEC OR039**	**Grisorio Roberto**	*A new synthetic approach for size-tunable and stable CsPbBr3 nanocubes with near-unity photoluminescence quantum yield*
10:50 - 11:00	**TEC OR040**	**Bortolami Martina**	*BMIm-BF4: a versatile ionic liquid for BF3 generation and reactions*
11:00 - 11:15	**Discussion**		

Divisione TECNOLOGIA FARMACEUTICA (TFA)
TFA 02

09.30 - 10.00	**TFA IL003**	**Mauro Bonini**	*Release in oral solid nutraceutical forms: case studies.*
10.00 - 10.30	**TFA IL004**	**Marco Fidaleo**	*A lesson from Vitamin B12: from the biological issues to the design of a nutraceutical formulation*
10.30 - 10.45	**Discussion**		
10.45 - 11.00	**break**		
11.00 - 11.15	**TFA OR010**	**Annalisa Bianchera**	*Crystallization of stable doped mannitol polymorphs and in vitro assessment of their safety as carriers for lung delivery*
11.15 - 11.30	**TFA OR011**	**Luca Casula**	*Multicomponent nanosuspension for the bronchial asthma inhalation therapy*
11.30 - 11.45	**TFA OR012**	**Luca Cerri**	*Spray patch based on hyaluronic acid and chitosan microparticles medicated with olive leaf extract*
11.45 - 12.00	**TFA OR013**	**Maria Chiara Cristiano**	*EtoGel: combined systems for new ethosomes application in joint diseases treatments*
12.00 - 12.15	**TFA OR014**	**Tiziana Esposito**	*Castanea sativa waste as dermo-functional ingredient into a topical delivery system: from the design and development of the formulation to in vitro stability and in vivo skin tolerability and efficacy*
12.15 - 12.30	**TFA OR015**	**Diego R. Perinelli**	*Development of topical formulations using hydrolyzed keratin as an alternative to the commonly employed emulsifying agents*

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12.30 - 12.45	**TFA OR016**	**Teresa Silvestri**	*Biodegradable microparticles for the treatment of the posterior eye segment diseases*
12.45 - 13.00	**TFA OR017**	**Elena Giuliano**	*Poloxamer– and poloxamine-based hydrogels as biocompatible systems for the delivery of active compounds*
13.00 - 13.15	**TFA OR018**	**Umberto M. Musazzi**	*Printing of cutaneous patches loaded with propranolol for the treatment of infantile hemangiomas*

Programma dei LAVORI di DIVISIONE - 17 settembre pomeriggio

Divisione CHIMICA ANALITICA (ANA)

ANA 07

15.00 - 15.20	**ANA PZ003**	**Mariosimone Zoccali**	*Is There a Real Need for Multidimensional Chromatography Strategies with the Current Availability of Powerful Mass Spectrometry Platforms?*
15.20 - 15.40	**ANA KN008**	**Giovanni Ventura**	*AllerT: a Matlab-based workflow for putative allergens identification in novel foods via LC-ESI-MS/MS analysis*
15.40 - 16.00	**ANA OR051**	**Domenica Mangraviti**	*Differentiation and profiling of Morocco species belonging to Lamiaceae Family by Ambient Mass Spectrometry methods*
16.00 - 16.15	**ANA OR052**	**Nicole Marittimo**	*Advancements in Direct-MS using SPME coupled to Liquid-EI and CI*
16.15 - 16.30	**ANA OR053**	**Katia Arena**	*Characterization of bioactive compounds from natural products using focusing-modulated comprehensive two-dimensional liquid chromatography coupled to mass spectrometry*
16.30 - 16.45	**ANA OR054**	**Eleonora Oliva**	*Analysis of phenolic compounds in plant matrices by means of HPLC-MS/MS with targeted and semi-untargeted approach*
16.45 - 17.00	**ANA OR055**	**Tania Salerno**	*The Coupling of Gas Chromatography - Mass Spectrometry with Infrared Spectroscopy for Reliable Identification of Unknowns in Complex Samples*
17.00 - 17.15	**ANA OR056**	**Danilo Sciarrone**	*Reliability of monodimensional vs multidimensional GC-C-IRMS data: a critical evaluation*
17.15 - 17.30	**ANA OR057**	**Peter Q. Tranchida**	*Options of 1D GC, flow-modulation signal-enhanced 1D GC and flow-modulation comprehensive 2D GC in a single instrument: a proof-of-concept study*
17.30 - 17.45	**ANA OR058**	**Cecile Valsecchi**	*Enhanced LC-MS/MS spectra matching through multi-task neural networks and molecular fingerprints*

ANA 08

15.20 - 15.40	**ANA IL005**	**Alessandra Bianco Prevot**	*Organic Pollutant Removal using Photo-Fenton Processes in the presence of Fe(III) complexing agents*
15.40 - 16.00	**ANA IL006**	**Paola Fermo**	*In-situ and micro-destructive investigation for the analysis of degradation products present on marble surfaces*
16.00 - 16.15	**ANA OR059**	**Francisco Ardini**	*Evaluation of potential source areas for atmospheric lead reaching Ny-Ålesund (Svalbard) from 2010 to 2019*
16.15 - 16.30	**ANA OR060**	**Stefano Bertinetti**	*Strontium isotopic analysis of microsamples by inductively coupled plasma - tandem mass spectrometry*

16.30 - 16.45	**ANA OR061**	**Luca Carena**	*Photochemistry of furfuryl alcohol in/on snow at -30°C: photoreactivity with singlet oxygen and by direct photolysis*
16.45 - 17.00	**ANA OR062**	**Silvia Illuminati**	*Year-round records of bulk aerosol composition over the Victoria Land (Antarctica)*
17.00 - 17.15	**ANA OR063**	**Elisa Calà**	*Identification of aloe and other dyes by means of SERS and HPLC-DAD-MS in the embroidery of a 15th century English folded almanac*
17.15 - 17.30	**ANA OR064**	**Emilio Catelli**	*Rediscovering the lost color. Advanced vector quantization algorithm and hyperspectral imaging for digital restoration of color films*
17.30 - 17.45	**ANA OR065**	**Giovanna Marussi**	*The Third-Century monetary crisis: chemical analysis of Denarii and Antoniniani*
17.45 - 18.00	**ANA OR066**	**Rosaria Anna Picca**	*Synthesis and spectroscopic characterization of synergistic nanomaterials for stone artwork protection*

ANA 09

15.20 - 15.40	**ANA KN009**	**Paolo Bollella**	*Enzyme based Amperometric Biosensors: From Direct Electron Transfer to Chimeric Enzymes*
15.40 - 16.00	**ANA OR067**	**Giuseppe Arrabito**	*Printing Biology: engineering analytical platforms by molecular inks*
16.00 - 16.15	**ANA OR068**	**Noemi Bellassai**	*Design of dual-functional polymer on plasmonic biosensor for detection of circulating tumor DNA point mutations*
16.15 - 16.30	**ANA OR069**	**Alessandro Bertucci**	*Artificial Biomolecular Communication Regulated by Synthetic DNA Translators*
16.30 - 16.45	**ANA OR070**	**Alessandra Maria Bossi**	*Soft molecularly imprinted nanoparticles for protein recognition in sensing and assays*
16.45 - 17.00	**ANA OR071**	**Stefano Cinti**	*A microfluidic paper-based chip patterned with Prussian Blue to determine sweat urea*
17.00 - 17.15	**ANA OR072**	**Erica Del Grosso**	*Transient control of DNA-based systems*
17.15 - 17.30	**ANA OR073**	**Marco Giannetto**	*Smart immunosensors for point-of-care serologic test to determine the level of immunity by Covid-19 infection or by SARS-CoV-2 vaccination*
17.30 - 17.45	**ANA OR074**	**Antonia Lopreside**	*Reagent-free paper biosensor based on genetically modified bioluminescent protein for cancer biomarker detection*
17.45 - 18.00	**ANA OR075**	**Lucia Sarcina**	*Selective detection of Xylella fastidiosa with a Surface Plasmon Resonance based immunoassay*

Divisione CHIMICA DELL'AMBIENTE E DEI BENI CULTURALI (ABC)

ABC 04

15.00-15.15	**ABC OR051**	**Dominique Scalarone**	*CAPuS project: research and higher education allied for the Conservation of Art in Public Spaces*

15.15-15.30	**ABC OR013**	**Ilaria Serafini**	*Advances in analytical methodologies applied to cultural heritage: first application of DLLME to characterize dyes in ancient textiles*
15.30-15.45	**ABC OR014**	**Slimani Sawssen**	*Caput Mortuum purple hematite pigment: Investigation of magnetic properties*
15.45-16.00	**break**		
16.00-16.15	**ABC OR015**	**Andrea Brunelli**	*Colloidal behavior of titanium dioxide nanoparticles in artificial and in Venice lagoon waters in the presence of standard or natural colloidal particles*
16.15-16.30	**ABC OR016**	**Felice Simeone**	*Assessment of the Cytotoxicity of Metal oxide Nanoparticles on the Basis of Immediately Available Physical-Chemical Parameters.*
16.30-16.45	**ABC OR017**	**Cristina De Ceglie**	*The effect of a karst-fractured aquifer on wastewater quality: an UHPLC-HRMS study*
16.45-17.00	**ABC OR018**	**Francesco Saliu**	*Plastic and its associated contaminants: determination of PAEs in coral reef invertebrates by in vivo SPME-LC-MS/MS*
17.00-17.15			
17.15-17.30	**ABC OR019**	**Armando Zarrelli**	*Characterization of degradation byproducts of Sartans: elucidation of their degradation pathway and ecotoxicity assessment*
17.30-17.45	**ABC OR020**	**Marco Mantovani**	*Microalgal treatment of the liquid fraction from hydrothermal carbonization process (HTC) in a circularity perspective*
17.45-18.00	**ABC OR021**	**Giulia Guidotti**	*Poly(diethylene 2,5-furanoate): a biobased promising candidate for compostable high-performant packaging*
18.00-18.15	**ABC OR022**	**Valeria D'Ambrosio**	*Lipids extraction from sewage sludge using green biosolvent for a sustainable production of biodiesel*

Divisione CHIMICA INDUSTRIALE (IND)

IND 04

Sessione congiunta con Gruppo Interdivisionale Energie Rinnovabili - Enerchem

15.00 - 15.30	**IND KN005 Chini Lecture**	**Carlo Perego**	*CO2 utilization: from waste to resource*
15.30 - 15.40	**IND OR033**	**Martina Serafini**	*Nanostructured Cu-based Electrocatalysts on a Carbonaceous Gas Diffusion Layer for the Electrochemical Reduction of CO2*
15.40 - 15.50	**IND OR034**	**Simelys Hernandez**	*How to exploit thermochemical catalysts to make efficient & sustainable CO2 electroreduction to added value products*
15.50 - 16.00	**IND OR035**	**Ivan Grigioni**	*High rate CO2 electroreduction to formate with a InP colloidal quantum dots derived catalyst*
16.00 - 16.10	**IND OR036**	**Federico Bella**	*Preliminary investigation of anodic materials for potassium batteries*
16.10 - 16.20	**IND OR037**	**Maria Grazia Musolino**	*Solvothermal synthesis of doped hematite/reduced graphene oxide nanocomposites for sodium-ion batteries*

16.20 - 16.30	**IND OR038**	**Emilia Paone**	*Reductive Upgrading of Biomass Derived Furan promoted by Spent Lithium-Cobalt Batteries as an Efficient Heterogeneous Catalyst*
16.30 - 16.40	**IND OR039**	**Matteo Bonomo**	*Thermosetting polyurethanes resins: application as cheap, sustainable and scalable encapsulants for (flexible) Perovskite Solar Cells*
16.40 - 16.55	***Discussion***		
16.55 - 17.10	**break**		
17.10 - 17.20	**IND OR040**	**Andrea Fasolini**	*Low Temperature Methane Steam Reforming in a H2-selective Pd Membrane Reactor*
17.20 - 17.30	**IND OR041**	**Tiziano Montini**	*Visible-light-driven coproduction of diesel precursors and hydrogen from lignocellulose-derived methylfurans*
17.30 - 17.40	**IND OR042**	**Nicola Sangiorgi**	*Improved water stability of CsPbBr3 thin film photoelectrodes*
17.40 - 17.50	**IND OR043**	**Cosimo Micheletti**	*Luminescent Solar concentrators based on Aggregation-Induced Emission*
17.50 - 18.00	**IND OR022**	**Giuseppe Pipitone**	*Aqueous phase reforming of biorefinery by-products towards sustainable hydrogen production*
18.00 - 18.10	**IND OR045**	**Francesco Conte**	*H2 production by photoreforming of glucose*
18.10 - 18.30	***Discussion***		

Divisione CHIMICA ORGANICA (ORG)
ORG 08

15.00 - 15.30	**ORG PZ006**	**Daniela Montesarchio**	***Premio alla ricerca Chimica Organica per le Scienze della Vita*** *G-Quadruplexes to the fore: towards DNA-targeting magic bullets*
15.30 - 16.00	**Break**		
16.00 - 16.15	**ORG PZ014**	**Anna Esposito**	***Premio Tesi di Dottorato Chimica Organica per le Scienze della Vita*** *Exploring the therapeutic potential of L-deoxyiminosugars in rare diseases*
16.15 - 16.30	**ORG OR045**	**Cristina Minnelli**	*Epigallocatechin-3-gallate-based Inhibitors Targeting EGFR to Overcome Drug Resistance in Advanced NSCLC*
16.30 - 16.45	**ORG OR046**	**Lucía Morillas Becerril**	*Specific and nondisruptive interaction of guanidium-functionalized gold nanoparticles with neutral phospholipid bilayers*
16.45 - 17.00	**ORG OR047**	**Maria Luisa Navacchia**	*Dihydroartemisinin-bile acid hybridization as an effective approach to enhance dihydroartemisinin anticancer activity*
17.00 - 17.30	**Break**		
17.30 - 17.45	**ORG OR048**	**Ferran Nieto Fabregat**	*Gram-negative bacteria LPS recognition by DC-SIGN*

17.45 - 18.00	**ORG OR049**	**Anna Notaro**	*Mimiviruses possess the biosynthetic pathways to produce bacteria-like sugars in a clade-specific manner*
18.00 - 18.15	**ORG OR050**	**Alessandro Palmioli**	*On-cell saturation transfer difference NMR for the identification of FimH ligands and inhibitors*
18.15 - 18.30	**ORG OR051**	**Daniela Perrone**	*Synthesis and preclinical evaluation of antisense oligonucleotides conjugated with ursodeoxycholic acid for the treatment of Duchenne muscular dystrophy*

ORG 09

16.00 - 16.15	**ORG PZ013**	**Mirko Maturi**	***Premio Tesi di Dottorato Chimica Organica per l'Ambiente, l'Energia e le Nanoscienze*** *Advanced Functional Organic-Inorganic Hybrid (Nano)Materials: from Theranostics to Organic Electronics and Additive Manufacturing*
16.15 - 16.30	**ORG OR052**	**Mariacecilia Pasini**	*Sustainable by Design Carbon Dots as promising material for luminescent and biomedical applications*
16.30 - 16.45	**ORG OR053**	**Vincenzo Patamia**	*A new hybrid porous multifunctional material based on Loofah-Halloysite*
16.45 - 17.00	**ORG OR054**	**Marina Massaro**	*Synthesis and characterization of different mussel inspired materials for several applications*
17.00 - 17.30	**Break**		
17.30 - 17.45	**ORG OR055**	**Giulia Neri**	*Fluorinated Polymers and Fluorescent Graphene as Innovative Nanotheranostic Materials*
17.45 - 18.00	**ORG OR056**	**Alessandra Operamolla**	*Cellulose nanocrystals for paper consolidation*
18.00 - 18.15	**ORG OR057**	**Luca Pettazzoni**	*Transamidation-based vitrimers from renewable sources*
18.15 - 18.30	**ORG OR058**	**Serena Riela**	*Improvement of properties of halloysite and some other «friends» by chemical modifications*

ORG 10

16.00 - 16.15	**ORG OR059**	**Claudio Curti**	*Merging Vinylogy with Organocatalysis: Direct, Asymmetric Entry to Chiral Fused Uracil Derivatives*
16.15 - 16.30	**ORG OR060**	**Daniele Fiorito**	*Synthetic studies towards Bastimolide B*
16.30 - 16.45	**ORG OR061**	**Paola Costanzo**	*Highly oleophilic and reusable polyurethane composites for the removal of oils from fresh water and seawater*
16.45 - 17.00	**ORG OR062**	**Andrea Mezzetta**	*Reactive Deep Eutectic Solvents (ReDESs): an underexploited option for organic chemistry*
17.00 - 17.30	**Break**		
17.30 - 17.45	**ORG OR063**	**Lorenzo Di Terlizzi**	*Visible light-driven α-arylation of enol silyl ethers via arylazo sulfones.*

17.45 - 18.00	**ORG OR064**	**Lucia Ferrazzano**	*Greening peptide synthesis: new options for a sustainable chemistry*
18.00 - 18.15	**ORG OR065**	**Valeria Nori**	*Organocatalysed Michael addition of masked acetaldehyde to nitroalkenes in water*
18.15 - 18.30	**ORG OR066**	**Rita Mocci**	*Mechanochemical Fischer Indolisation: Exploration of a Timeless Reaction in a New Guise*

ORG 11

16.00 - 16.15	**ORG OR067**	**Allegra Franchino**	*Merging organo- and Au(I) catalysis for asymmetric or silver-free reactions of alkynes*
16.15 - 16.30	**ORG OR068**	**Gianluigi Albano**	*Infrared irradiation-assisted solvent-free Palladium-catalyzed (hetero)aryl-aryl coupling via C-H bond activation*
16.30 - 16.45	**ORG OR069**	**Fabio Bellina**	*Pd/Ag-mediated dehydrogenative alkynylation of imidazoles*
16.45 - 17.00	**ORG OR070**	**Silvia Gaspa**	*Photocatalyzed amides synthesis from alcohols by visible light*
17.00 - 17.30	**Break**		
17.30 - 17.45	**ORG OR071**	**Fabrizio Medici**	*Stereoseletive [2+2] photocycloaddition: a viable strategy for the synthesis of enantiopure cyclobutane derivatives*
17.45 - 18.00	**ORG OR072**	**Francesco Messa**	*Ligand-Free Cobalt-Catalyzed Cross-Coupling Reaction Between Organoaluminum Reagents and (Hetero)Aryl and Alkyl Bromides*
18.00 - 18.15	**ORG OR073**	**Giorgia Zanchin**	*Imino-pyridine Cr complexes as precatalyst for the polymerization of olefins: synthesis and catalytic tests with NEt3 as additive*

Divisione CHIMICA DEI SISTEMI BIOLOGICI (CSB)

CSB 03

15.00 - 15.30	**CSB KN003**	**Luc Brunsveld**	*Stabilization of Protein-Protein Interactions; from the fundamentals of cooperativity to applications in drug discovery*
15.30 - 15.45	**CSB OR014**	**Alessio Romerio**	*Design, synthesis and Biological evaluation of New, glycolipid-based Toll-Like Receptor 4 (TLR4) Modulators*
15.45 - 16.00	**CSB OR015**	**Giusy Tassone**	*Evidence of amino-thiadiazoles as innovative inhibitors of human glutaminyl cyclase, validated target for neurodegenerative disorders*
16.00 - 16.15	**CSB OR016**	**Francesco Tadini-Buonisegni**	*Modulation of Ca2+-ATPase transport activity by pharmacologically relevant compounds*
16.15 - 16.30	**CSB OR017**	**Michela Pisani**	*Insulin loaded in liquid crystalline mesophases: effects on carrier structure and insulin stability*
16.30 - 17.00	**Break**		

17.00 - 17.30	**CSB KN004**	**Elena Sgaravatti**	*Research and development of active ingredients from vegetable cells or crops to be used in the Health care, Food and Personal care sectors*
17.30 - 17.45	**CSB OR018**	**Valeria Romanucci**	*New curcumin mimics based on tyrosol scaffold: investigation of neuroprotective and anticancer activity*
17.45 - 18.00	**CSB OR019**	**Roberto Tira**	*Modulation of Tau aggregation with natural coffee compounds*
18.00 - 18.10	**CSB OR020**	**Rita Pagano**	*Phosphate-linked Silybin dimers: synthesis and investigation of biological activity*
18.10 - 18.20	**CSB OR021**	**Massimiliano Gaeta**	*Hybrid Porphyrin/DOPA-melanin Film as Versatile Biomaterial for Water Remediation*
18.20 - 18.50	**Discussione**		

Divisione DIDATTICA CHIMICA (DID)
DID 02

15:00-15:30	**DID IL002**	**Carlo Fiorentini**	*The teaching of chemistry from the perspective of citizenship*
15:30-15:45	**DID OR010**	**Teresa Cecchi**	*Chemistry: a Precious Discovery in the Dantesque World*
15:45-16:00	**DID OR011**	**Maria Irene Donnoli**	*A Carbon atom journey*
16:00-16:15	**DID OR012**	**Elena Lenci**	*Peer review of scientific articles: a teaching experience*
16:15-16:30	**DID OR013**	**Silvia Prati**	*Increasing the engagement of non-chemistry major students: examples of didactic strategic*
16:30-18:30	**Panel Discussion**	**Silvia Bencivelli (coordinator) Pellegrino Conte Paola Govoni Piersandro Pallavicini Valentina Domenici**	*Chemistry: how, where, when and why*

Divisione SPETTROMETRIA DI MASSA (MAS)
MAS 02

15.00 - 15.40	**MAS PL003**	**Nikolai Kuhnert**	*Mass spectrometry in coffee science: From bean to drink to human*
15.40 - 16.10	**MAS KN001**	**Tata Alessandra**	*Non-targeted authentication of food products: the synergic combination of ambient mass spectrometry, data fusion and machine learning"*
16.10 - 16.25	**MAS OR006**	**M.A. Acquavia**	*Influence of mixed starter cultures of Hanseniaspora osmophila and Saccharomyces cerevisiae on wine flavor profile explored through HS-SPME/GC-MS*
16.25 - 16.35	**Break**		

16.35 - 17.05	**MAS KN002**	**Linda Monaci**	*Future challenges in MS based technologies applied to the safety of foods.*
17.05 - 17.20	**MAS OR007**	**Rosalia Zianni**	*Lipidomic approach to evaluate the effect of X-ray irradiation treatment on the lipid profile of Camembert cheese*
17.20 - 17.35	**MAS OR008**	**Fabiola De Marchi**	*High-resolution mass spectrometry approaches finalized to identification of new glycoside compounds in grape*
17.35 - 17.50	**MAS OR009**	**Ciro Cannavacciuolo**	*Analysis by high-resolution mass spectrometry of polyphenolic alkaloids fraction from Portulaca oleracea*
17.50 - 18.05	**MAS OR010**	**Lucia Bartella**	*Paper Spray tandem mass spectrometry: an innovative approach to assess flavonoid content in citrus drinks*

Divisione TEORICA E COMPUTAZIONALE (TEO)

TEO 02

15.00 - 15.30	**TEO KN002**	**Alfonso Pedone**	*Exploiting Machine Learning Methods in Atomistic Simulations of Oxide Glasses*
15.30 - 15.45	**FIS OR059**	**Adriana Pecoraro**	*First-principles study of Mn and Fe co-doped BaZrO3 as PC-SOFC cathode for the Oxygen Reduction Reaction*
15.45 - 16.00	**TEO OR013**	**Leonardo Guidoni**	*Quantum Chemistry using Quantum Computers*
16.00 - 16.15	**FIS OR061**	**Marco Medves**	*TDDFT methods for large systems: new computational schemes and automatic generation of density fitting basis*
16.15 - 16.30	**TEO OR014**	**Elena Tocci**	*Molecular view on crystals nucleation and growth on different PVDF polymorphs*
16:30 - 17:00	**Discussion**		

TEO 03

15:00 - 15:10	**TEO OR015**	**Matteo Capone**	*Multi-Scale Charge-Transfer Modeling in Enzyme Catalysis*
15:10 - 15:20	**TEO OR016**	**Guelber Cardoso Gomes**	*Computational study of dicationic ionic liquids based on imidazole*
15:20 - 15:30	**TEO OR017**	**Elisa Bernes**	*An experimental and theoretical investigation on the electronic structure of indole, 2,3-dihydro-7- azaindole, and 3-formylindole in the gas phase by synchrotron-based spectroscopic techniques*
15:30 - 15:40	**TEO OR018**	**Yasi Dai**	*Addressing the Frenkel and charge transfer character of exciton states with a model Hamiltonian based on dimer calculations: application to large aggregates of perylene bisimide*

17 settembre - pomeriggio

15:40 - 15:50	**TEO OR019**	**Stefano Motta**	*Study of ligand binding to HIF-2α through Path-Metadynamics*
15:50 - 16:00	**TEO OR020**	**Alessandra Gilda Ritacca**	*The multifaceted roles of copper ion in human body explored by computational tools*
16:00 - 16:10	**TEO OR021**	**Anna Rovaletti**	*Unravelling the reaction mechanism of Mo/Cu CO dehydrogenase using QM/MM calculations*
16:10 - 16:20	**TEO OR022**	**Sara Del Galdo**	*How water density responds to the presence of a crowding agent*
16:20 - 16:30	**TEO OR023**	**Francesco Ferdinando Summa**	*SYSMOIC: A Program Package for the Calculation of Origin-Independent Electron Current Density and Derived Magnetic Properties in Molecular Systems*
16:30 - 17:00	**break**		
17:00 - 17:20	**TEO KN003**	**Fabrizia Negri**	*Modelling extended-core π systems and their aggregates: charge transport and optoelectronic properties*
17:20 - 17:40	**TEO PZ003**	**Giovanni Di Liberto**	*Rational Design of Semiconductor Interfaces for Photocatalysis*
17:40 - 18:00	**TEO PZ004**	**Eduardo Schiavo**	*First Principles Approaches for Heterogeneous Functional Materials*
18:00 - 18:30	**Discussion**		

Programma dei LAVORI di DIVISIONE - 20 settembre mattina

Divisione CHIMICA ORGANICA (ORG)
ORG 12

9.30 - 10.00	**ORG PZ004**	**Pierangelo Gobbo**	***Medaglia Giacomo Ciamician*** *A synthetic chemistry approach to the fabrication of protocells and protocellular materials*
10.00 - 10.30	**ORG PZ007**	**Francesco Giacalone**	***Premio alla ricerca Chimica Organica per l'Ambiente, l'Energia e le Nanoscienze*** *Nanocarbon-based Hybrid Materials as Efficient and Sustainable Heterogeneous Catalysts*
10.30 - 10.45	**ORG OR074**	**Loredana Maiuolo**	*Polysubstituted 1,2,3-Triazoles: synthesis and biological application*
10.45 - 11.00	**ORG OR075**	**Michele Mancinelli**	*Atropisomeric Azaborines: Axial Chirality at the Boron-Carbon Bond*
11.00 - 11.15	**ORG OR076**	**Francesca Franco**	*Formal α-trifluoromethylthiolation of carboxylic acid derivatives via N-acyl pyrazoles*
11.15 - 11.30	**ORG OR077**	**Claudia Sciacca**	*Synthesis of nitrogenated analogues of honokiol as potential bioactive compounds*
11.30 - 11.45	**ORG OR078**	**Damiano Tanini**	*The unexpected role of Se(IV) vs Se(VI) species in the on water selenium-catalysed oxidation of anilines*
11.45 - 12.00	**ORG OR079**	**Claudio Zippilli**	*Double strategies for regioselective one-pot C-H oxidative functionalization of coumarins*

ORG 13

10.30 - 10.45	**ORG OR080**	**Chiara Liliana Boldrini**	*Eco-friendly deep eutectic solvent electrolyte solutions for dye-sensitized solar cells*
10.45 - 11.00	**ORG OR081**	**Gabriella Buscemi**	*Polydopamine/ethylenediamine nanoparticles embedding a bacterial photoenzyme for solar energy conversion*
11.00 - 11.15	**ORG OR082**	**Mattia Forchetta**	*Design of KuQuinone-Co3O4 nanoparticle hybrid dyads for photoelectrochemical applications*
11.15 - 11.30	**ORG OR083**	**Giulio Goti**	*Fluorescent Materials for the Enhancement of the Photosynthetic Efficiency*
11.30 - 11.45	**ORG OR084**	**Norberto Manfredi**	*Photo(electro)catalytic water splitting using Calix[4]arene-Based dyes*
11.45 - 12.00	**ORG OR085**	**Lorenzo Zani**	*Construction of tailored, donor-acceptor heterocyclic compounds for solar energy conversion*

ORG 14

10.30 - 10.45	**ORG OR086**	**Achille Antenucci**	*How do arenediazonium salts behave in Deep Eutectic Solvents? A combined experimental and computational approach*
10.45 - 11.00	**ORG OR087**	**Laura Baldini**	*Halogen-bonded architectures of multivalent calix[4]arenes*
11.00 - 11.15	**ORG OR088**	**Daniele Del Giudice**	*pH Transient Variation Triggered by Nitroacetic Acid Allowing Dissipative Control in Supramolecular Systems*
11.15 - 11.30	**ORG OR089**	**Oscar Francesconi**	*A tweezers-shaped receptor for the biomimetic recognition of the GlcNAc2 disaccharide in water*
11.30 - 11.45	**ORG OR090**	**Giorgio Olivo**	*Supramolecular Remote C(sp3)-H Oxidation*
11.45 - 12.00	**ORG OR091**	**Daniele Rosa-Gastaldo**	*Tuning the folding properties of synthetic recognition-encoded oligomers*

Programma dei LAVORI di DIVISIONE - 21 settembre mattina

Divisione CHIMICA DELL'AMBIENTE E DEI BENI CULTURALI (ABC)

ABC 05

09.30-09.45	**Presentation**		
09.45-10.00	**ABC OR046**	**P. Guzmán García Lascurain**	*Agar foam for the cleaning of art surfaces: a new approach*
10.00-10.15	**FIS OR 129**	**David Chelazzi**	*pHEMA/PAA and pHEMA/PVP semi-IPNs: physico-chemical characterization and use for bronze cleaning*
10.15-10.30	**FIS OR128**	**Francesco Armetta**	*Unusual corrosion of bronze helmets discovered in Mediterranean seabed*
10.30-10.45	**ABC OR047**	**Francesca Ramacciotti**	*Advanced systems for the cleaning of Cultural Heritage*
10.45-11.00	**FIS OR 127**	**Leonardo Severini**	*Ultrasound-stimulated PVA microbubbles as removal tool for adhesive tapes from cellulose-based materials*
11.00-11.15	**ABC OR048**	**Elisabetta Zendri**	*Evaluation of a new setup to improve the electro-kinetic desalination of porous materials in Cultural Heritage*
11.15-11.30	**break**		
11.30-11.45			
11.45-12.00	**ABC OR049**	**Marco Valente Chavez Lozano**	*Deep Eutectic Solvents (DES) based on choline chloride and betaine for cleaning gelatin residues from cellulose nitrate cinematographic films.*
12.00-12.15	**ABC OR050**	**Giuseppe Lazzara**	*Halloysite nanotubes: a versatile material for conservation of cultural heritage*
12.15-12.30	**ABC OR012**	**Francesca Nardelli**	*Insights into the oil paint polymeric network by Solid State NMR*
12.30-12.45	**ABC OR031**	**Carolina Rigon**	*Discovering the Maya ritual practices through the study of pigmented human bones remains by Archaeometry investigation*
12.45-13.00		**Antonio Marcomini**	*Conclusioni*

ABC 06

09.30-09.50	**ABC KN002**	**Fabrizio Passarini**	*The tool of LCA to analyse and improve the sustainability of chemical processes*
09.50-10.00	**IND OR046**	**Prisco Prete**	*New biodegradable catalysts for photo-Fenton like process for wastewater treatment reuse in a circular economy perspective*

10.00-10.10	**ABC OR053**	**Damiano Sgherza**	*Integrating biodegradation and ozone-catalysed oxidation for treatment of biomass gasification wastewater*
10.10-10.20	**IND OR047**	**Stefano Andrea Balsamo**	*One-pot synthesis of TiO2-rGO photocatalysts for the degradation of groundwater pollutants*
10.20-10.30	**ABC OR054**	**Luisa Barbieri**	*An integrated system for a new controlled release fertilizer based on lightweight ceramic aggregates starting from waste materials and bio-products*
10.30-10.40	**IND OR048**	**Ermelinda Falletta**	*Efficient day-and-night NO2 abatement by polyaniline/TiO2 composites*
10.40-10.50	**ABC OR055**	**Pietro Calandra**	*Reutilization of residues from municipal wastes pyrolysis to improve and regenerate asphalts*
10.50-11.00	**Discussion**		

Modellazione ambientale e caratterizzazione chimica degli aerosol atmosferici/Environmental

11.15-11.30	**ABC OR056**	**Loris Calgaro**	*Exposure modelling of emerging contaminants in the Venice lagoon - a case-study on active pharmaceutical ingredients*
11.30-11.45	**ABC OR057**	**Federtica Zennaro**	*Modelling eutrophication processes in the Venice Lagoon: a multivariate Machine Learning approach*
11.45-12.00	**ABC OR058**	**Pierluigi Barbieri**	*Bioaerosol detection, pathogen airborne transmission and abatement studies: capacity building, experimental results and perspectives from the COVID-19 pandemic*
12.00-12.15	**ABC OR059**	**Manuel Amedeo Cefali**	*Evaluation of PMx chemical composition and planning of a vegetable-green barrier in a high traffic site in Milan*
12.15-12.30	**ABC OR060**	**Niccolo Losi**	*Aerosol characterization from the tropics to the North Pole*
12.30-12.45	**ABC OR061**	**Alessandro Mancini**	*X-Ray Diffraction of Non-Exhaust Emissions generated from Braking: How to Assess the Phase Composition of the Crystalline Fraction*
12.45-13.00		**Antonio Marcomini**	*Conclusioni*

Divisione CHIMICA FARMACEUTICA (FAR)

FAR 07

09.30 - 10.00	**FAR KN009**	**Anders Bach**	*Targeting protein-protein interactions involved in oxidative stress using fragment-based drug discovery*

21 settembre - mattina

10.00 - 10.30	**FAR KN010**	**Giancarlo Aldini**	*Chemical and molecular mechanisms of cellular and extra-cellular antioxidants*
10.30 - 10.45	**FAR OR031**	**Marco Catto**	*A second life for MAO inhibitors: from CNS diseases to cancer*
10.45 - 11.00	**FAR OR032**	**Stefano Sainas**	*Apoptotic and differentiating therapy for AML using potent human dihydroorotate dehydrogenase inhibitor*
11.00 - 11.30	**FAR KN011**	**Tiziano Bandiera**	*Discovery of a picomolar potency corrector of F508del-CFTR chloride channel*
11.30 - 11.45	**FAR OR035**	**Francesca Spyrakis**	*Identification of carbapenemase broad-spectrum inhibitors through in silico methodologies*
11.45 - 12.00	**FAR OR036**	**Serena Massari**	*1,2,4-Triazolo[1,5-a]pyrimidines: efficient one-step synthesis and functionalization as antiviral agents*
12.00 -12.15	**FAR OR037**	**Alessandra Altomare**	*An integrated metabolomic and proteomic approach for the identification of covalent inhibitors of the main protease (Mpro) of SARS- COV-2 from crude natural extracts*
12.15 -12.30	**FAR OR038**	**Antonella Messore**	*Discovery of non-DKA derivatives endowed of selective activity against ribonuclease H function of the HIV-1 reverse transcriptase*
12.30 - 13.00	**FAR KN012**	**Pedro Gois**	*Exploring B-complexes as likers for targeting drug conjugates*

FAR 08

10.30 - 10.45	**FAR OR033**	**Claudia Sorbi**	*Constrained 1,4-dialkylpiperazines as dopamine transporter (DAT) inhibitors to fight psychosis and cocaine addiction*
10.45 - 11.00	**FAR OR034**	**Elisa Uliassi**	*Psychotropic-based bifunctional compounds for neurodegenerative diseases*
11.00 - 11.30			
11.30 - 11.45	**FAR OR039**	**Salvatore Di Maro**	*Peptides from bench to clinical studies: our experience with CXCR4*
11.45 - 12.00	**FAR OR040**	**Azzurra Stefanucci**	*A novel β-hairpin peptide derived from the ARC repressor selectively interacts with the major groove of B-DNA*
12.00 -12.15	**FAR OR041**	**Stefano Tomassi**	*Shading the activity of a CXCR4-interacting peptide by 1,4- and 1,5-disubstituted [1,2,3]-triazole-based cyclization*

12.15 -12.30	**FAR OR042**	**Rosa Bellavita**	*Grafting Temporin L peptides: old tactics for new antimicrobial weapons*

Divisione CHIMICA FISICA (FIS)

FIS 08

Cultural Heritage and Environment

09:30-10:00	**FIS KN010**	**Gabriella Di Carlo**	*Corrosion protection in Concrete Heritage: from material design to in situ validation*
10:00-10:15	**FIS OR072**	**Lorenzo Lisuzzo**	*Pickering Emulsions Based on Wax and Halloysite Nanotubes for the Treatment of Archeological Woods*
10:15-10.30	**FIS OR073**	**Vanessa Rosciardi**	*Biocomposite Poly(Vinyl Alcohol)/Starch cryogels: green tailorable tools for the cleaning of painted artworks*
10:30-10.45	**FIS OR074**	**Rosangela Mastrangelo**	*Cleaning Pollock's and Picasso's masterpieces: the physical chemistry behind the scenes*
10:45-11:00	**FIS OR075**	**Giovanna Poggi**	*Adaptive castor-oil based organogels: synthesis, characterization and use for the selective and controlled cleaning of works of art*
11:00-11.15	**FIS OR076**	**Michele Baglioni**	*Nanostructured Fluids For Polymeric Coatings Removal: Surfactants Affect the Polymer Glass Transition Temperature*
11:15-11.30	**FIS OR077**	**Sara Morandi**	*Pd-promoted zeolites for low-temperature NOx adsorption*
11.30-11.45	**break**		

Physical Chemistry of Sensors

11:45-12:00	**FIS OR078**	**Lucio Litti**	*Surface Enhanced Raman Scattering toward applications*
12:00_12:15	**FIS OR079**	**Stefano Toffanin**	*Organic optoelectronic components in highly integrated systems for plasmonics sensing in food security/quality*
12:15-12.30	**FIS OR080**	**Simona Bettini**	*SERS-SPR COUPLING FOR ULTRASENSITIVE DETECTION OF DOPAMINE IN ARTIFICIAL CEREBROSPINAL FLUID.*
12:30-12:45	**FIS OR081**	**Cristina Chirizzi**	*A bimodal imaging probe for combined Raman microscopy and 19F-MRI*
12:45-13:00	**FIS OR082**	**Giovanni De Filpo**	*Novel pressure sensors based on elastomeric PDLC films*
13:00-13:15	**FIS OR083**	**Francesco Tavani**	*Investigating the interfacial solvation properties of the Mg2+ ion by operando soft X-ray absorption spectroscopy at ambient pressure and simulations*

FIS 09

Physical Chemistry of Materials I

09:30-10:00	**FIS KN011**	**Luciano Galantini**	*From Molecules to Supracolloidal Atomium like Superstructures: Building from the Bottom-Up with Steroidal Amphiphiles*
10:00-10:15	**FIS OR084**	**Mario Prosa**	*Organic light-emitting transistors: advanced materials and innovative architectures towards a real-setting application*
10:15-10.30	**FIS OR085**	**Pietro Calandra**	*Mixing liquid amphiphiles to prepare organic fluids fully responsive to a magnetic field*
10:30-10.45	**FIS OR086**	**Valerio Loianno**	*A Hyphenated Approach Combining Pressure-Decay and In Situ FT-NIR Spectroscopy to Monitor Penetrant Sorption and Concurrent Swelling in Polymers*
10:45-11:00	**FIS OR087**	**Maria Rosaria Plutino**	*Design and development of multifunctional hybrid surface coatings for advanced and smart applications on textiles*
11:00-11.15	**FIS OR088**	**Federico Begni**	*Hyper Cross - Linked Polymers as additives for preventing aging of PIM1 membranes*
11:15-11.30	**FIS OR089**	**Chiara Nomellini**	*WO3-BiVO4 heterojunction: effects of WO3 nanostructuring on the photoelectrochemical performance*

Physical Chemistry of Materials II

11:45-12:00	**FIS OR090**	**Alberto Girlando**	*Charge-Transfer Soft Ferroelectrics*
12:00_12:15	**FIS OR091**	**Marco Sanna Angotzi**	*Designing Spinel Ferrite-Based Nano-Heterostructures Through Versatile Solvothermal Approaches*
12:15-12.30	**FIS OR092**	**Stefano Alberti**	*Physico-Chemical Characterization of Polydimethylsiloxane Electrospun Fibers*
12:15-12.30	**FIS OR051**	**Alessandro Piovano**	*A deep description of the electronic properties of Ti sites in Ziegler-Natta catalysts from advanced spectroscopic methods*
12:45-13:00	**FIS OR094**	**Matteo Busato**	*Structural Characterization of Deep Eutectic Solvents Mixtures with Water and Methanol*
13:00-13:15	**FIS OR095**	**Michele Porto**	*Use of REOBs and industrial by-products additives for new bitumen-like material formulation: chemical physical and mechanical characterization*

Divisione CHIMICA INORGANICA (INO)

INO 07

9.30 - 10.50	**INO PZ006 (Premio Dottorato 2021)**	**Fabio Pirro**	*De novo design of multi-domain metalloenzymes*
9.50 - 10.10	**INO PZ007 (Premio Dottorato 2021)**	**Matteo Vanni**	*Reactivity of Black Phosphorus with Pd Compounds*
10.10 - 10.30	**INO PZ008 (Premio Dottorato 2021)**	**Alessandra Barbanente**	*Targeted Delivery of Anticancer Platinum Complexes to Bone Tumors and Metastases "non classical" compounds mechanism of action*
10.30 - 10.45	**INO OR043**	**Rita Mazzoni**	*Cyclopentadienone-NHC Iron(0) electrocatalysts for water oxidation*
10.45 - 11.00	**INO OR044**	**Anna Pintus**	*Ammonium salts of oxalic acid derivatives: a new family of agents for the conservation of carbonate stone substrates of artistic value*
11.00 - 11.15	**INO OR045**	**Andrea Fermi**	*Visible-light activated metallaphotoredox catalysis enabled by TiIV complexes: new routes for C-C bond formation*
11.15-11.30	**break**		
11.30 - 11.45	**INO OR046**	**Riccardo Pedrazzani**	*Correlating solid-state analysis and catalysis: exploring secondary π-interactions effects in Au(I) catalyzed reactions*
11.45 - 12.00	**INO OR047**	**Rossana Galassi**	*When metallaphilia makes the difference: the case of stacked coinage metals Trinuclear Cyclic Compounds*
12.00 - 12.15	**INO OR048**	**Alessia Belloni**	*FTIR-HSI analysis of triple-negative breast cancer (TNBC)*
12.15 - 12.30	**INO OR049**	**Francesca Gambassi**	*A Cu(II)-MOF based on a propargyl carbamate-functionalized isophthalate ligand*
12.30 - 13.00	**INO IL002**	**Anke Weidenkaff**	*Circular Materials for the Energy Transition*

INO 08

10.30 - 10.45	**INO OR050-ad hoc**	**Marzio Rancan**	*Hierarchical chiral transfer in bright lanthanides quadruple stranded helicate-cages by host-guest interaction*
10.45 - 11.00	**INO OR051**	**Giuseppe Ferrauto**	*Hydrophobic interactions between macrocyclic Gd-complexes and polyaromatic systems as route to enhance the longitudinal water relaxivity in Magnetic Resonance Imaging*

11.00 - 11.15	**INO OR052**	**Salvatore Impemba**	*Dinuclear Thioether-amide Aluminum Complexes in the Ring Opening Polymerization of Cyclic Esters*
11.15-11-30	**break**		
11.30 - 11.45	**INO OR053**	**Paolo Pelagatti**	*Put light on inside a microporous MOF to decipher the guest arrangement and guest- release properties*
11.45 - 12.00	**INO OR054**	**Francesca Garello**	*Biodegradable polyelectrolyte/magnetite capsules for MR imaging and magnetic targeting of tumors*
12.00 - 12.15	**INO OR055**	**Letizia Liccardo**	*CeOx/TiO2 Hollow Spheres as efficient photocatalyst for the degradation of organic pollutants in wastewater*
12.15 - 12.30	**INO OR056**	**Denise Lovison**	*Highly active ruthenium complexes: synthesis and evaluation of the anticancer activity through interaction with relevant biomolecules*

INO 09

10.30 - 10.45	**INO OR057**	**Gabriele Manca**	*Reactivity of imidazolate Au(I) cyclictrinuclearcompounds, CTCs, with iodine or MeI: a computational/experimental study*
10.45 - 11.00	**INO OR058**	**Luca Andreo**	*DFT and semi-empirical GFN2-xTB methods: experimental and computational characterization of an Iron(II) carbene complex*
11.00 - 11.15	**INO OR059**	**Mario Prejanò**	*How lanthanide ions affect the catalytic activity of methanol dehydrogenase: a computational point of view*
11.15-11.30	**break**		
11.30 - 11.45	**INO OR060-ad hoc**	**Daniela Marasco**	*Transition metal complexes as neurodrugs: insights into their modulation of amyloid aggregation*
11.45 - 12.00	**INO OR061**	**Laura Del Coco**	*X. fastidiosa affecting olive trees in Salento: metal ions in soil, plants and treatment compounds*
12.00 - 12.15	**INO OR062**	**Antonino Famulari**	*Unveiling electronic and structural properties of, peroxygenase-like cytochrome P450, CYP116B5hd*
12.15 - 12.30	**INO OR063**	**Davide Corinti**	*Elusive intermediates in the reactivity of platinum(IV) prodrugs: a new perspective on their bioactivation*

Divisione CHIMICA PER LE TECNOLOGIE (TEC)

TEC 05

09.30 - 10.00	**TEC IL003**	**Alessandro Gori**	*Liquid biopsy at the crossroads of chemistry and technology: the extracellular vesicles case study*

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10.00 - 10.15	**TEC KN003**	**Serena De Santis**	*Fourier transform IR micro-spectroscopy of biological tissues: a promising tool for diagnostic and assessment of tissue functionality.*
10.15 - 10.30	**TEC KN004**	**Andrea Melchior**	*Diclofenac adsorption on carbon-based nanomaterials: a molecular dynamics study*
10.30 - 10.40	**TEC OR041**	**Francesca Baldassarre**	*Utilization of biosourced materials in chemical nanotechnologies developing controlled release systems for human and plants health*
10.40 - 10.50	**TEC OR042**	**Paola Astolfi**	*Structural characterization and in-vitro anticancer activity of nanovectors for delivery of bioactive coumpounds*
10.50 - 11.00	**TEC OR043**	**Arianna Rossetti**	*3D integration of pH-cleavable drug-hydrogel conjugates on magnetically driven smart microtransporters*
11.00 - 11.10	**TEC OR044**	**Falcone Giovanni**	*Calcium Alginate hydrogels in Semi Solid Extrusion 3D printing: physico-chemical requirements for high printing performance*
11.10 - 11.30	**Discussion**		
11.30 - 11.40	**TEC OR045**	**Anita Ceccucci**	*Mixed oxide Cerium coating for improved titanium nanotubes bioactivity*
11.40 - 11.50	**TEC OR046**	**Clelia Dispenza**	*Adipose stem cell spheroids-laden hydrogels for minimally invasive bone and cartilage regeneration interventions*
11.50 - 12.00	**TEC OR047**	**Emanuela Muscolino**	*k- Carrageenan and PVA blends as bioinks to 3D print scaffolds for cartilage reconstruction*
12.00 - 12.10	**TEC OR048**	**Edoardo Testa**	*Adducts of functionalized graphene layers with Ag nanoparticles for antimicrobial applications*
12.10 - 12.30	**Discussion**		
12.30 - 12.50	**break**		
12.50 - 13.00	**TEC OR049**	**Martina Sanadar**	*A novel luminescent Europium(III) complexes for citrate detection*
13.00 - 13.10	**TEC OR050**	**Gaspare Varvaro**	*Co/Pd-based synthetic antiferromagnetic multi-stacks for biomedical applications*
13.10 - 13.20	**TEC OR051**	**Alessandra Vitale**	*Coupling electrospinning and photo-induced crosslinking to produce shape-stable rubber nanofibrous membranes*
13.20 - 13.30	**TEC OR052**	**Antonino Rizzuti**	*Analysis of the chemical profile of sparkling wines fermented with autochthonous yeast strains using a non-targeted metabolomic approach*
13.30 - 13.50	**Discussion**		

13.50 - 14.00	**CONCLUSIONE**

Divisione ELETTROCHIMICA (ELE)

ELE 08

09.30 - 10.00	**ELE_IL50**	**Piotr Zelenay**	*Oxygen Reduction at Platinum Group Metal-Free Fuel Cell Catalysts:Piotr Recent Progress*
10.00 - 10.15	**ELE_OR51**	**Alessandro Facchin**	*From Redox-like to Heterogeneous Electrocatalysis at Metal-Octaethylporphyrins@HOPG investigated by EC-STM*
10.15 - 10.30	**ELE_OR52**	**Lucia Mazzapioda**	*Non-stoichiometric Metal Oxide Particles as Active Electrode Component in PEM Fuel Cells*
10.30 - 10.45	**ELE_OR53**	**Simone Bonizzoni**	*Aquivion®-based Alkaline Membrane for Fuel Cell and Electrolyzer Applications*
10.45 - 11.00	**ELE_OR54**	**Antunes Staffolani**	*Identification of Solid Oxide Cells Processes by Distribution of Relaxation Times: Model Creation and Validation*
11.00 - 11.15	**break**		
11.15 - 11.45	**ELE_KN55**	**Lior Elbaz**	*Design of Aerogel-based Electrocatalysts for ORR*
11.45 - 12.00	**ELE_OR56**	**Davide Cademartori**	*Anode-supporting substrates with hierarchical porosity manufactured with freeze tape casting for reversible solid oxide cells*
12.00 - 12.15	**ELE_OR57**	**Vincenzo Baglio**	*Electrospun MnCo2O4/CNF as Oxygen Electrode for Alkaline Zn-Air Batteries*
12.15 - 12.30	**ELE_OR58**	**Eleonora Pargoletti**	*Disclosing the Electrocatalytic Behavior of Doped-MnO2 for Lithium-Air Batteries*

ELE 09

09.30 - 10.00	**ELE_IN59**	**Doron Auerbach**	
10.00 - 10.15	**ELE_OR60**	**Keti Vezzù**	*Innovative Olivine Cathodes for High-Voltage Lithium Batteries*
10.15 - 10.30	**ELE_OR61**	**Akiko Tsurumaki**	*Highly Versatile Gel Polymer Electrolytes for High Voltage Lithium Batteries*
10.30 - 10.45	**ELE_OR62**	**Marisa Falco**	*Protic ionic liquid electrolytes in lithium metal cells*
10.45 - 11.00	**ELE_OR63**	**Lorenzo Mezzomo**	*Long life lithium metal batteries employing dendrite-eating nanocomposite solid-state electrolytes based on hybrid fillers.*
11.00 - 11.15	**break**		

11.15 - 11.45	**ELE_KN64**	**Michele Pavone**	*Heterogeneous functional materials for post-Li energy storage devices, new insights and design principles from quantum chemistry*
11.45 - 12.00	**ELE_OR65**	**Ernestino Lufrano**	*Study of lithiated Nafion-based nanocomposites membranes as single lithium-ion conducting electrolytes for lithium batteries*
12.00 - 12.15	**ELE_OR66**	**Anna Mangini**	*Li-ion Batteries with Innovative Silicon Anodes: Study of Electrolytes Based on Carbonates*
12.15 - 12.30	**ELE_OR67**	**Alessandro Brilloni**	*Novel methods for increasing energy and reducing environmental impact of lithium batteries.*

ELE 10

09.30 - 10.00	**ELE_KN68**	**Tealdi Cristina**	*Fast but not so fast: can we improve intercalation in cathode materials for rechargeable batteries?*
10.00 - 10.15	**ELE_OR69**	**Toigo Christina**	*Rheological properties of aqueous sodium alginate slurries*
10.15 - 10.30	**ELE_OR70**	**Leonardo Sbrascini**	*Enhanced Performance of a Sustainable Si/C Anode for High Energy Density Lithium-ion Batteries*
10.30 - 10.45	**ELE_OR71**	**Daniele Versaci**	*Carbon nitride based double layer approach for enhancing Li-S battery performances*
10.45 - 11.00	**ELE_OR72**	**Hamideh Darjazi**	*Improvement of NMC layered cathode materials by combined doping/coating and evaluation of electronic-ionic transport properties by electrochemical impedance spectroscopy*
11.00 - 11.15	**break**		
11.15 - 11.45	**ELE_KN73**	**Teofilo Rojo**	*Recent progress in electrode materials for next generation sodium ion batteries*
11.45 - 12.00	**ELE_OR74**	**Giovanna Maresca**	*Sodium-conducting, ionic liquid electrolytes for Na battery systems*
12.00 - 12.15	**ELE_OR75**	**Shahid Khalid**	*Aqueous sodium battery enabled by super-concentrated binary electrolyte.*
12.15 - 12.30	**ELE_OR76**	**Michele Tribbia**	*Improved zinc electrodeposition in mild-acidic aqueous Zn-ion batteries*

Divisione TECNOLOGIA FARMACEUTICA (TFA)

TFA 03

09.30 - 10.00	**TFA IL005**	**Manuela Estima Gomes**	*Using magnetic stimulus to bioengineer tendon tissue and tissue models: new tools to understand and stimulate regenerative pathways*

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10.00 - 10.30	**TFA IL006**	**Marco Romanelli**	*Inflammation in wound healing: the role of drug delivery*
10.30 - 10.45	**Discussion**		
10.45 - 11.00	**break**		
11.00 - 11.15	**TFA OR019**	**Giuseppina Sandri**	*Polysaccharides based scaffolds for skin tissue engineering*
11.15 - 11.30	**TFA OR020**	**Giulia Vanti**	*Development and Optimisation of a Locally- acting Microemulgel to Improve the Biopharmaceutical Properties of Cannabidiol for Dermatological Delivery*
11.30 - 11.45	**TFA OR021**	**Silvia Pisani**	*Engineered tubular scaffold for full-thickness esophageal replacement*
11.45 - 13.30	**Tavola Rotonda**	**Michele Schlich**	*Valorizzazione del dottorato in tecnologia farmaceutica al di fuori dell'accademia. Cosa si aspetta un'azienda da un dottore di ricerca rispetto ad un laureato?*

Programma dei LAVORI di DIVISIONE - 21 settembre pomeriggio

Divisione CHIMICA ANALITICA (ANA)

ANA10

15.00 - 15.20	**ANA PZ004**	**Martina Catani**	*Boosting the downstream processing of biopharmaceuticals by means of multicolumn continuous chromatography*
15.20 - 15.40	**ANA IL007**	**Maurizio Quinto**	*Rotating Magnetic Chromatography, a new technique for micro-particle and cell separation*
15.40 - 16.00	**ANA IL008**	**Roccaldo Sardella**	*Role of mobile phase composition in enantioselective liquid chromatography*
16.00 - 16.15	**ANA OR076**	**Federica Bianchi**	*Nanomaterials for improved sensitivity in sample treatment*
16.15 - 16.30	**ANA OR077**	**Irene Coralli**	*Secondary reactions in the analysis of microplastics by Py-GC-MS*
16.30 - 16.45	**ANA OR078**	**Simona Felletti**	*Investigation of the chemoselectivity of normal phase stationary phases towards the separation of cannabinoids*
16.45 - 17.00	**ANA OR079**	**Giuseppina Gullifa**	*Potential Health Impact Assessment of New Pocket Pen- Vaporizers: Vapor Characterization Using SPME-GC/MS*
17.00 - 17.15	**ANA OR080**	**Jacopo La Nasa**	*Analytical pyrolysis coupled with gas chromatography/mass spectrometry and solvent extraction for the characterization of microplastics and polymer additives*
17.15 - 17.30	**ANA OR081**	**Roberta La Tella**	*Evaluation of carbon - clad zirconia columns as stationary phases for superheated water liquid chromatography*
17.30 - 17.45	**ANA OR082**	**Marcello Locatelli**	*Fabric Phase Sorptive Extraction: an innovative tool for TDM and pharmacotoxicological studies using unconventional biological matrices*
17.45 - 18.00	**ANA OR083**	**Sara Palmieri**	*Molecular imprinted polymer coupled to LC-MS/MS for maleic hydrazide determination in food samples*
18.00 - 18.15	**ANA OR084**	**Marco Roverso**	*Determination of lactose in low-lactose milk by direct liquid injection and high-resolution mass spectrometry*

ANA11

15.20 - 15.40	**ANA KN010**	**Silvia Berto**	*Study and application of chemical models to measure the urine saturation with calcium salts*
15.40 - 16.00	**ANA OR085**	**Chiara Abate**	*Sequestering ability of carnosine towards some potentially toxic divalent metal cations in aqueous solution*

16.15 - 16.30	**ANA OR087**	**Denise Bellotti**	*Understanding the thermodynamics and coordination chemistry of metal-binding proteins: the common thread to elucidate metal acquisition processes at host/pathogen interface*
16.30 - 16.45	**ANA OR088**	**Rosita Cappai**	*Complex formation equilibria of a kojic acid derivative with different metal ions*
16.45 - 17.00	**ANA OR089**	**Salvatore Cataldo**	*CYCLODEXTRIN-BASED NANOSPONGES FOR LEAD(II) ION ADSORPTION FROM AQUEOUS SOLUTIONS*
17.00 - 17.15	**ANA OR090**	**Ottavia Giuffrè**	*O-phosphorylethanolamine and O-phosphorylcholine in aqueous solution: acid-base behavior and speciation with Mg2+*
17.15 - 17.30	**ANA OR091**	**Anna Irto**	*Thermodynamic parameters on the interaction of divalent and trivalent metal cations with 3-hydroxy-4-pyridinones*
17.30 - 17.45	**ANA OR092**	**Luana Malacaria**	*Studies on the complexation between quercetin and some first-row transition metal cations in aqueous solution*
17.45 - 18.00	**ANA OR093**	**Rossella Migliore**	*Recognition of antibiotics by calixarene-based micellar aggregates in aqueous solution: binding features and driving forces*
18.00 - 18.15	**ANA OR094**	**Davide Spanu**	*On-line ion trapping by frontal chromatography ICP-MS: a low-cost strategy for the fast speciation of inorganic pollutants*

ANA12

15.20 - 15.40	**ANA KN011**	**Flavio Della Pelle**	*2D Nanomaterials: among functional natural compounds and affordable sensor designs*
15.40 - 16.00	**ANA KN012**	**Barbara Roda**	*Celector(R): the cell chromatography for quality control of living cells*
16.00 - 16.15	**ANA OR095**	**Jessica Brandi**	*Identification of protein biomarkers responsible for meat tenderness in bovine Longissumus dorsi muscle by Kohonen self-organizing maps and multivariate analysis*
16.15 - 16.30	**ANA OR096**	**Simone Cavalera**	*Anti-Retroviral Drugs Monitoring in Urine and Saliva: A Rapid and Sensitive Lateral Flow Immunoassay for Tenofovir*
16.30 - 16.45	**ANA OR097**	**Andrea Cerrato**	*An innovative analytical platform for cannabis chemovar differentiation based on untargeted metabolomics and chemometrics*

16.45 - 17.00	**ANA OR098**	**Angela Di Capua**	*Use of online buffer exchange coupled to native-mass spectrometry to elucidate the stoichiometry of the Salmonella FraR (transcriptional repressor)-DNA complex*
17.00 - 17.15	**ANA OR099**	**Fabio Di Nardo**	*Exploiting silver nanoplates as colorimetric label in Lateral Flow Immunoassay*
17.15 - 17.30	**ANA OR100**	**Nicolò Interino**	*UPLC-Q-TOF-MS/MS analysis of bile acids and their main metabolite profile in farm animal faeces and species-specific correlation with gut microbiota*
17.30 - 17.45	**ANA OR101**	**Valentina Marassi**	*Nanosphere, polymer, self-assembled material? Clearing up the confusion on polydopamine through multidetection-FFF*
17.45 - 18.00	**ANA OR102**	**Monica Mattarozzi**	*Insights into aptamer-protein interactions for analytical applications: egg white lysozyme as case study*
18.00 - 18.15	**ANA OR103**	**Lapo Renai**	*Untargeted metabolomics reveals different postprandial serum metabolome profiles after single intake of Vaccinium myrtillus and Vaccinium corymbosum*

Divisione CHIMICA INDUSTRIALE (IND)

IND 04

Sessione congiunta con Gruppo Interdivisionale Green Chemistry - Chimica Sostenibile

15.00 - 15.20	**IND KN006**	**Rafael Luque**	*Benign by design strategies for a more sustainable future: the valorisation concept*
15.20 - 15.30	**IND OR049**	**Anna Gagliardi**	*Upgrading of Ethanol: Boosting the Guerbet Reaction with a Redox Co-Catalyst*
15.30 - 15.40	**IND OR050**	**Ilenia Rossetti**	*Sustainable process design for the valorization of bioethanol as platform chemical*
15.40 - 15.50	**IND OR051**	**Maela Manzoli**	*Enabling technologies to boost cellulose selective valorisation over bifunctional catalyst*
15.50 - 16.00	**IND OR052**	**Silvia Tabasso**	*Green deep eutectic solvents and microwave technology towards a closed loop biorefinery*
16.00 - 16.10	**IND OR053**	**Nicola Di Fidio**	*Microwave-assisted FeCl3-catalysed production of glucose from giant reed and cardoon cellulose fraction and its fermentation to new generation oil by oleaginous yeasts*
16.10 - 16.20	**IND OR054**	**Alessia Ventimiglia**	*Theoretical study of glucose oxidation to glucaric acid using gold based catalyst*
16.20 - 16.35	***Discussion***		
16.35 - 16.50	**break**		
16.50 - 17.10	**IND KN007**	**Volker Hessel**	*Sustainability as Process Design Guidance for Flow and Plasma Chemistry*
17.10 - 17.20	**IND OR055**	**Valeria Pappalardo**	*Heterogeneous catalysis in the esterification of natural antioxidants*

17.20 - 17.30	**IND OR056**	**Carmelina Rossano**	*Amberlite IR120 as catalyst for the levulinic acid esterification reaction in batch and continuous operation*
17.30 - 17.40	**IND OR057**	**Silvia Giorgi**	*Synthesis of new biopolymers by biomasses valorization*
17.40 - 17.50	**IND OR058**	**Riccardo Bacchiocchi**	*Innovative heterogeneous catalysts for the reduction of levulinic acid derivatives to γ-valerolactone and consecutive reduction products*
17.50 - 18.00	**IND OR059**	**Francesco Mauriello**	*Hydrogenolysis of aromatic ethers under lignin-first conditions*
18.00 - 18.30	**Discussion**		

Divisione CHIMICA ORGANICA (ORG)
ORG 15

15.00 - 15.30	**ORG PZ002**	**Paolo Tecilla**	***Medaglia Angelo Mangini*** *Self-organized Supramolecular Systems for Catalysis, Sensing and Transport*
15.30 - 16.00	**ORG PZ009**	**Elena Lenci**	***Premio alla ricerca Chimica Organica per le Scienze della Vita Junior*** *Combining Diversity-Oriented Synthesis and chemoinformatics to generate small molecules libraries*
15.50 - 16.00	**Break**		
16.00 - 16.15	**ORG OR092**	**Molly Pither**	*Elucidation of the Chemical Structure of Lipopolysaccharides Isolated from the Commensal Bacteria Veillonella parvula*
16.15 - 16.30	**ORG OR093**	**Debora Pratesi**	*The glycomimetic approach for selective inhibition of Carbonic Anhydrases*
16.30 - 16.45	**ORG OR094**	**Deborah Quaglio**	*Resorc[4]arene-based site directed immobilization of antibodies for immunosensors development*
16.45 - 17.00	**ORG OR095**	**Roberto Rossi**	*Problem solving in Pharmaceutical processes: isolation, characterization and synthetic preparation of unknown impurities in 4-piperidinepropanol manufacture*
17.00 - 17.30	**Break**		
17.30 - 17.45	**ORG OR096**	**Laura Russo**	*Chemoselective synthesis of triple-functionalizes nanoparticles for multimodal in vivo imaging of pancreatic β-cells*
17.45 - 18.00	**ORG OR097**	**Giovanni Sacco**	*Affinity enhancement of peptide ligands for tumor overexpressed receptors*
18.00 - 18.15	**ORG OR098**	**Cristina Manuela Santi**	*Synthesis of an analogue of Neisseria meningitidis A capsular polysaccharide for the development of a glycoconjugate vaccine*
18.15 - 18.30	**ORG OR099**	**Federica Santino**	*Rational Design of Pseudoproline-Containing K-Opioid Receptor-Selective Peptidomimetics*

ORG 16

15.30 - 16.00	**ORG PZ010**	**Manuel Orlandi**	***Premio alla ricerca Chimica Organica nei suoi Aspetti Metodologici Junior*** ***Catalyst Design via Computational Means:*** *Correlations Bridge Experiments and Calculations*
16.00 - 16.15	**ORG OR100**	**Valentina Pirota**	*Selective hydrolysis of water-soluble naphthalene diimides driven by core-substitution*
16.15 - 16.30	**ORG OR101**	**Simone Potenti**	*4-Fluorothreonine as a test case: the effects of fluorination on molecular properties*
16.30 - 16.45	**ORG OR102**	**Michele Ricci**	*Application of ASCA modelling tools on a PDO hard cheese: Analysis of the effects on physical parameters of Trentingrana*
16.45 - 17.00	**ORG OR103**	**Federica Sabuzi**	*Computational study of substituted phenols pKa*
17.00 - 17.30	**Break**		
17.30 - 17.45	**ORG OR104**	**Carla Rizzo**	*New supramolecular fluorescent NDI-gels as bioimaging materials*
17.45 - 18.00	**ORG OR105**	**Maria Sologan**	*Functionalized gold nanoparticles for MRI applications*
18.00 - 18.15	**ORG OR106**	**Benedetta Maria Squeo**	*Thiophene substituted aza-BODIPY as promising metal-free, pure NIR emitter for OLEDs*
18.15 - 18.30	**ORG OR107**	**Kristian Vasa**	*Design and synthesis of macromolecular and nanostructured carbonic anhydrases-based materials*

ORG 17

15.30 - 16.00	**ORG PZ011**	**Sara Meninno**	***Premio alla ricerca Chimica Organica per l'Ambiente, l'Energia e le Nanoscienze Junior*** *Powerful Strategies to Functionalized Molecules in One- Pot, Mild Conditions and Benign Solvents*
16.00 - 16.15	**ORG OR108**	**Giulio Bertuzzi**	*Novel Visible-Light Mediated Protocols for the Synthesis of N Heterocycles and Site-Selective Functionalizations*
16.15 - 16.30	**ORG OR109**	**Tommaso Bortolato**	*Radical α-Trifluoromethoxylation of Ketones by Means of Organic Photoredox Catalysis*
16.30 - 16.45	**ORG OR110**	**Mattia Di Maro**	*A ball-milling green synthetic procedure for the preparation of novel macromolecular stabilizers for polyolefinic-based materials*
16.45 - 17.00	**ORG OR111**	**Salvatore Marullo**	*Cholinium-based ionic liquids as catalysts for the glycolysis of post-consumer PET waste*
17.00 - 17.30	**Break**		
17.30 - 17.45	**ORG OR112**	**Angelica Mero**	*Treatment of biomass food waste by exploiting Natural Deep Eutectic Solvents and bio based-Ionic Liquids*

17.45 - 18.00	**ORG OR113**	**Elisabetta Monciatti**	*Hydroaminomethylation of terminal alkenes in water: microwave and micellar catalysis roles*
18.00 - 18.15	**ORG OR114**	**Matteo Tiecco**	*Organocatalytic activity of chiral L-Proline-based Deep Eutectic Solvents*
18.15 - 18.30	**ORG OR115**	**Federica Valentini**	*Catalytic biomass valorization towards hydrogen transfer reactions using formic acid and derivates as safe H-source*

ORG 18

15.30 - 16.00	**ORG PZ012**	**Nicolas D'Imperio**	***Premio alla ricerca Chimica Organica per lo Sviluppo di Processi e Prodotti nell' Industria Junior*** *Olefins from carbonyls. Development of new phosphorus-based cross-coupling reactions*
16.00 - 16.15	**ORG OR116**	**Valerio Fasano**	*How Big is the Pinacol Boronic Ester as a Substituent?*
16.15 - 16.30	**ORG OR117**	**Susanna Bertuletti**	*From carbonyls to chiral alcohols via asymmetric biocatalysis: exploiting the substrate promiscuity of hydroxysteroid dehydrogenases (HSDHs)*
16.30 - 16.45	**ORG OR118**	**Denisa Bisag**	*Catalyst- and substrate- dependent chemodivergent reactivity of stabilised sulfur ylides with salicylaldehydes*
16.45 - 17.00	**ORG OR119**	**Giulia Brufani**	*Imidazolium based heterogenous catalyst for the synthesis of cyanohydrintrimethylsylil ether and β-azido ketones*
17.00 - 17.30	**Break**		
17.30 - 17.45	**ORG OR120**	**Emanuela Calcio Gaudino**	*Highly Efficient Microwave-assisted synthetic protocols under Pd based β-cyclodextrin heterogeneous catalyst*
17.45 - 18.00	**ORG OR121**	**Francesco Calogero**	*Photoredox allylation and propargylation of aldehydes catalytic in titanium*
18.00 - 18.15	**ORG OR122**	**Vincenzo Campisciano**	*Al(III) Porphyrin–Imidazolium Salt Copolymer onto Carbon Nanotubes as Catalyst for the Synthesis of Cyclic Carbonates*
18.15 - 18.30	**ORG OR123**	**Francesca Foschi**	*Copper-Catalyzed/Hypervalent Iodine(III)-Mediated Dimerization/Cyclization of 2-Benzylamino-phenols: Synthesis of Fluorescent Oxazolo-phenoxazines*

Divisione CHIMICA DEI SISTEMI BIOLOGICI (CSB)

CSB 04

15.00 - 15.30	**CSB KN005**	**Angela Casini**	*Gold-templated reactions in biological systems: from medicine to catalysis*

15.30 - 15.45	**CSB OR022**	**Francesco Bellia**	*Hyaluronate–Carnosine conjugates: copper(II) complexes and antioxidant properties*
15.45 - 16.00	**CSB OR023**	**Daniele Vitone**	*The speciation of zinc complexes with chloroquine ligand*
16.00 - 16.15	**CSB OR024**	**Valentina Oliveri**	*8-Hydroxyquinoline Hybrids Differentially Interact with α-Synuclein*
16.15 - 16.30	**CSB OR025**	**Giancarlo Terraneo**	*Halogenation Dictates Architectures and Properties of Amyloid Peptides*
16.30 - 17.00	**Break**		
17.00 - 17.30	**CSB KN006**	**Amedeo Caflisch**	*Fragment-based drug design*
17.30 - 17.45	**FIS OR066**	**Federica Rizzi**	*Role of the FZD10 delivering exosomes in cellular proliferation of gastrointestinal cancer*
17.45 - 18.00	**FIS OR062**	**Ivana Miletto**	*Functionalized Upconversion Nanoparticles for Theranostic*
18.00 - 18.15	**CSB OR028**	**Gabriele Travagliante**	*Spectroscopic study on interactions of porphyrins and micro-RNA*
18.15 - 18.50	**Discussione**		

Divisione DIDATTICA CHIMICA (DID)
DID 03

15:00-15:30	**DID IL003**	**Eleonora Aquilini**	*Caring for yourself, the environment and others in primary school*
15:30-15:45	**DID OR014**	**Sergio Palazzi**	*Towards a material archive of dyestuffs from the XX century*
15:45-16:00	**DID OR015**	**Ugo Cosentino**	*The School-University joint interventions provided in the National Recovery and Resilience Plan*
16:00-18:00	**Panel Discussion**	**Riccardo Iacona (Coordinator)** **Vincenzo Balzani** **Andrea Segrè** **Vittorio Maglia** **Giovanni De Feo**	*360-degree sustainability*

Divisione SPETTROMETRIA DI MASSA (MAS)
MAS 03

15.00 - 15.40	**MAS PL004**	**Encarnación Moyano**	*Mass spectrometry for the environmental analysis of halogenated organic pollutants*
15.40 - 16.10	**MAS KN003**	**Sara Bogialli**	*Mass spectrometry for the monitoring and protection of the environment*
16.10 - 16.25	**MAS OR011**	**Carolina Barola**	*Temporal trend of per- and polyfluoroalkyl substances in air samples collected at the rural site of Monte Martano (Central Italy)*
16.25 - 16.35	**Break**		

16.35 - 17.15	**MAS PL005**	**Antony Memboeuf**	*How can energetics in CID MS/MS help the analytical chemists?*
17.15 - 17.30	**MAS OR012**	**Angela Tartaglia**	*Fabric Phase Sorptive Membrane Array: A Novel Approach for Non-Invasive In Vivo Sampling*
17.30 - 17.45	**MAS OR013**	**Raffaella Pascale**	*An interplay between FT-ICR MS and LC-LTQ MS/MS for Metabolic Profiling of Peperoni di Senise PGI Bell Peppers*
17.45 - 18.00	**MAS OR014**	**Eugenio Aprea**	*Volatile organic compounds in Gorgonzola cheese and their relationship with sensory descriptors and consumers' liking*
18.00 - 18.15	**MAS OR015**	**Flaminia Vincenti**	*New Synthetic Opioids: Development of Analytical Methods for Their Characterization and Determination by Means of HPLC-HRMS/MS*

Divisione TEORICA E COMPUTAZIONALE (TEO)
TEO 04

15:00 -15:20	**TEO KN004**	**Mauro Stener**	*Predictive optical photoabsorption of metal clusters via efficient TDDFT simulations*
15:20 - 15:40	**TEO PZ005**	**Lorenzo Cupellini**	*Multiscale investigation of chlorophyll fluorescence quenching in plant light-harvesting complexes*
15:40 - 15:50	**TEO OR024**	**Chiara Aieta**	*Quantum nuclear densities from semiclassical on-the-fly molecular dynamics*
15:50 - 16:00	**TEO OR025**	**Filippo Lipparini**	*An easy and efficient strategy to compute an accurate SCF guess for ab-initio molecular dynamics simulations*
16:00 - 16:10	**TEO OR026**	**Marco Mendolicchio**	*Accuracy and Reliability in the Simulation of Vibrational Spectra: A Comprehensive Benchmark of Generalized Vibrational Perturbation Theory to the Second Order (GVPT2)*
16:10 - 16:20	**TEO OR027**	**Fulvio Perrella**	*Improving accuracy and efficiency of ADMP Extended Lagrangian Molecular Dynamics*
16:20 - 16:30	**TEO OR028**	**Diego Sorbelli**	*Probing the electronic structure of gold dihydride with state-of-the-art relativistic approaches*
16:30 - 17:00	**break**		
17:00 - 17:20	**TEO PZ006**	**Nicola Tasinato**	*Computational Strategies for Environmental Chemistry*
17:20 - 17:30	**TEO OR029**	**Francesco Di Maiolo**	*Theoretical Approaches to Quantum Molecular Dynamics in Out of Equilibrium Environments*
17:30 - 17:40	**TEO OR030**	**Lorenzo Donà**	*Extending and assessing composite electronic structure methods to the solid state*
17:40 - 17:50	**TEO OR031**	**Federica Lodesani**	*An in-depth look into the mechanism of crystallization of lithium disilicate: a metadynamics study*

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17:50 - 18:00	**TEO OR032**	**D. K. Andrea Phan Huu**	*Molecular spectroscopy in condensed phases: an antiadiabatic approach to the medium polarizability*
18:00 - 18:10	**TEO OR033**	**Pierpaolo Pravatto**	*Tunneling splitting and the stochastic description of activated processes*
18:10 - 18:30	**discussione finale**		

Programma dei LAVORI di DIVISIONE - 23 settembre mattina

Divisione CHIMICA ANALITICA (ANA)

ANA13

09.30 - 09.50	**ANA IL009**	**Anna Laura Capriotti**	*The progress in peptidomics: new strategies for purification and untargeted identification of short peptides*
09.50 - 10.00	**break**		
10.00 - 10.15	**ANA OR104**	**Adriana Arigò**	*Analytical methods in clinical lipidomics: HPLC and SFC comparison for the analysis of lipid mediators in clinical samples*
10.15 - 10.30	**ANA OR105**	**Alfonsina D'Amato**	*nLC-MS/MS data integration of quantitative proteomics and lipidomics to study the effects of bioactive compounds*
10.30 - 10.45	**ANA OR106**	**Chiara De Luca**	*Multicolumn Countercurrent Solvent Gradient Purification (MCSGP) process for the intensification of the polishing step of a bioactive peptide mixture*
10.45 - 11.00	**ANA OR107**	**Dounia El Fadil**	*Enzyme inhibition coupled to Molecular Imprinted Polymers for acetazolamide determination in biological samples*
11.00 - 11.15	**ANA OR108**	**Alessio Lenzi**	*Determination of salivary short chain fatty acids and hydroxy acids in heart failure patients by in-situ derivatization and Hisorb-probe sorptive extraction coupled to thermal desorption and gas chromatography- tandem mass spectrometry*
11.15 - 11.30	**ANA OR109**	**Marcello Manfredi**	*Metaproteomics and metabolomics investigation of microbiome alterations in pediatric obese subjects*
11.30 - 11.45	**ANA OR110**	**Francesca Merlo**	*A simple and Fast Multiresidue Method for determination of hormones in vegetables and fruits*
11.45 - 12.00	**ANA OR111**	**Giuseppe Micalizzi**	*Microwave distillation technique for the isolation of Cannabis Sativa L. essential oils and GC-MS/FID analysis for terpenes and terpenoids characterization.*
12.00 - 12.15	**ANA OR112**	**Daniele Naviglio**	*"Cholesterol is not considered a nutrient of concern for overconsumption" (Dietary Guidelines for Americans 2015)*

ANA14

09.30 - 09.50	**ANA IL010**	**Nicola Cioffi**	*Analytical Challenges in the Fight Against Biological Threats. The case of Nanoantimicrobials Inhibiting the Persistency of SARS-CoV-2*
09.50 - 10.00	**break**	**break**	
10.00 - 10.15	**ANA OR113**	**Maria Luisa Astolfi**	*A rapid analytical method for the determination of 45 elements in extra-virgin olive oils*

10.15 - 10.30	**ANA OR114**	**Laura Barone**	*Innovative spectroscopic approach for bloodstains identification*
10.30 - 10.45	**ANA OR115**	**Deborah Biggio**	*Surface characterization of CuZn37 alloys in contact with artificial saliva: the role of organic compounds*
10.45 - 11.00	**ANA OR116**	**Beatrice Campanella**	*A multi-analytical approach for the study of immortalized hippocampal neurons after mild heat shock*
11.00 - 11.15	**ANA OR117**	**Roberta D'Agata**	*Ultrasensitive plasmonic assay and specifically-designed PNA probes for circulating microRNAs detection: towards a liquid biopsy*
11.15 - 11.30	**ANA OR118**	**Danilo Donnarumma**	*Identification and quantification of toxic compounds and essential molecules in the context of tuna fishery industry waste valorization*
11.30 - 11.45	**ANA OR119**	**Walter Giurlani**	*Film thickness determination of metal multilayers by XRF multivariate analysis using Monte Carlo simulated standards*
11.45 - 12.00	**ANA OR120**	**Giulia Gorla**	*Low-cost miniaturized NIR spectrometer as an analytical tool for monitoring kefir fermentation process*
12.00 - 12.15	**ANA OR121**	**Min Li**	*XAS study of Manganese Hexacyanoferrate cathode material in aqueous Zn-ion batteries at three K-metal edges*
12.15 - 12.30	**ANA OR122**	**Maria Chiara Sportelli**	*Analytical characterization of laser-ablated silver nanoparticles for safe and biodegradable food packaging applications*

ANA15

09.30 - 09.50	**ANA OR123**	**Raffaela Biesuz**	*SAFER Smart Labels at work on fish*
09.50 - 10.00	**break**		
10.00 - 10.15	**ANA OR124**	**Sara Gaggiotti**	*Liquid phase exfoliated Transition Metal Dichalcogenides for gas sensing*
10.15 - 10.30	**ANA OR125**	**Laura Montali**	*A clover-like paper biosensor for mercury (II) on-site monitoring with a combined bioluminescent-colorimetric detection*
10.30 - 10.45	**ANA OR126**	**Andrea Pastore**	*pH Colorimetric sensor Arrays based on acid-base indicators enhanced by surfactants*
10.45 - 11.00	**ANA OR127**	**Angela Punzo**	*Application of whole-cell analytical bioassay based on turn-on chemiluminescence dioxetane probe sensing to quantify intracellular H2O2 in nutraceutical and biomedical fields*
11.00 - 11.15	**ANA OR128**	**Simona Ranallo**	*Non-natural antibody-protein communication mediated by a synthetic DNA responsive device*

11.15 - 11.30	**ANA OR129**	**Annalisa Scroccarello**	*Colorimetric paper-based analytical device for direct evaluation of olive oil phenols*
11.30 - 11.45	**ANA OR130**	**Francesca Torrini**	*A competitive microplate bioassay to detect gonadorelin in urine samples via a polynorepinephrine-based molecular imprinted polymer*
11.45 - 12.00	**ANA OR131**	**Mohamad Ahmad**	*A spatial perspective to retrieve spatial-spectral signatures from overlapped components in spectroscopic imaging data*
12.00 - 12.15	**ANA OR132**	**Rosalba Calvini**	*Quantification of rind percentage in grated Parmigiano Reggiano cheese by NIR-hyperspectral imaging and evaluation of the effect of factors related to sample preparation and composition*
12.15 - 12.30	**ANA OR133**	**Eleonora Mustorgi**	*Multivariate online monitoring of a powder blending process using a miniaturized near infrared sensor*

Divisione CHIMICA FISICA (FIS)

FIS 10

Physical Chemistry of Biomaterials

09:30-10:00	**FIS KN012**	**Roberto De Santis**	*Design for biointerface engineering*
10:00-10:30	**FIS KN013**	**Julietta Rau**	*New trends in the development of biomedical implants with multifunctional surfaces*
10:30-10.45	**FIS OR096**	**Monica Dettin**	*Chitosan covalently functionalized with peptides mapped on Vitronectin and BMP-2 for bone tissue engineering*
10:45-11:00	**FIS OR097**	**Angela De Bonis**	*Study of the bioactivity of thin glass-ceramic films deposited on electrospun polymeric scaffolds by nanosecond PLD*
11:00-11.15	**FIS OR021**	**Lorenzo Degli Esposti**	*Crystallization of amorphous calcium phosphate to hydroxyapatite nanoparticles: new insights in the field of biomaterials and biomineralization*
11:15-11.30	**FIS OR099**	**Alessio Carmignani**	*Study of the impact of size on the properties of polydopamine nanoparticles and their interaction with glioblastoma multiforme cells*

Computational and Applied Chemistry

11.45-12.00	**FIS OR100**	**Laura Orian**	*Methylmercury toxicity: insight from a theoretical physical-chemical description*
12:00_12:15	**FIS OR101**	**Marta Corno**	*Ab-initio modelling of Fe2NiP-H2O interaction: a phosphate factory for Early Earth*
12:15-12.30	**FIS OR102**	**Mirko Leccese**	*First-principles study of the C/Si interface: the influence of graphene corrugation on the H adsorption and abstraction reactions*

12:30-12:45	**FIS OR103**	**Brunella Bardi**	*Excited-state symmetry breaking in an aza-nanographene dye*
12:45-13:00	**FIS OR104**	**Rosangela Santalucia**	*HCN adsorption and reactivity at the Mg2SiO4 surface:a laboratory model of the chemistry on interstellar dust grains*

FIS 11

Physical Chemistry for Environment and Materials I

09:30-10:00	**FIS KN014**	**Cataldo Simari**	*Reversible and low-cost CO2 capture by quaternary-ammonium-functionalized aromatic polymers*
10:00-10:15	**FIS OR105**	**Claudio Cara**	*High value-added mesostructured silica from hexafluorosilicic acid (FSA): from a hazardous waste to precious silicon source.*
10:15-10.30	**FIS OR106**	**Rodolfo Esposito**	*A sustainable approach to formulation chemistry:structure and dynamics of bio-based complex mixtures*
10:30-10.45	**FIS OR107**	**Mariafrancesca Baratta**	*Photocatalytic degradation of organic pollutants in water using an innovative TiO2/SWNT membrane*
10:45-11:00	**FIS OR108**	**Chiara Lo Porto**	*Plasma deposition of TiO2-based nanocomposite coating for photocatalytic degradation of organic pollutants in water*
11:00-11.15	**FIS OR110**	**Stefano Marchesi**	*The NMR relaxometry as a powerful tool to study the uptake of paramagnetic ions from water by synthetic saponite clays*
11:15-11.30	**FIS OR109**	**Giulia Siciliano**	*Synthesis and characterization of polydopamine coated SPIONs for Cu2+ ions removal of from water*
11.30-11.45	**break**		

Physical Chemistry for Environment and Materials II

11:45-12:00	**FIS OR111**	**Nicola Blangetti**	*Template assisted sol-gel synthesis of Fe-doped TiO2 with photocatalytic activity under visible light*
12:00_12:15	**FIS OR112**	**Chiara Nannuzzi**	*Physico-chemical characterization of high surface area TiO2*
12:15-12.30	**FIS OR113**	**Massimo Dell'Edera**	*Nano-TiO2 based material for environmental and antibacterial application*
12:30-12:45	**FIS OR114**	**Marco Montalbano**	*Combining Morphology, Surface Fluorination and Au Nanoparticles Deposition on TiO2: Effects on Rhodamine B Photodegradation*
12:45-13:00	**FIS OR115**	**Maria Francesca Colella**	*Chemical-physical methods to investigate properties of vegetable oils and fats*
13:00-13:30	***Conclusioni***		

FIS 12

Thermodynamics and Kinetics I

09:30-10:00	**FIS KN015**	**Andrea Scorciapino**	*Development of a thermodynamic and kinetic model for passivemigration of ion carriers across lipid bilayers*
10:00-10:15	**FIS OR116**	**Marco Paolantoni**	*When the Solute is Completely Slaved to the Solvent:Jump Reorientation of Formamide in Water*
10:15-10.30	**FIS OR117**	**Federico Rossi**	*Shape Transformation of Artificial Vesicles Induced by an Interplay between Osmosis and pH Change*
10:30-10.45	**FIS OR118**	**Martina Maria Calvino**	*Shelf-life prediction of paracetamol formulations by non-isothermal thermogravimetry*
10:45-11:00	**FIS OR119**	**Chiara Pelosi**	*Stability of protein-polymer conjugates in solution*
11:00-11.15	**FIS OR120**	**Stefano Salvestrini**	*Kinetics and mechanism of 4-hydroxybenzoic acid degradation by persulfate/MnO2 oxidation*
11:15-11.30	**FIS OR121**	**Valentina Migliorati**	*Unraveling the solvation properties of Lanthanide (3+) ions: from molecular solvents to Ionic Liquid based systems*

Thermodynamics and Kinetics II

11:45-12:00	**FIS OR122**	**Marcello Budroni**	*Between dissipative structure and applications: chemical oscillations*
12:00_12:15	**FIS OR123**	**Olga Russina**	*NATURE OF SOLVATION OF CYCLODEXTRINS IN (PROTIC) IONIC LIQUIDS AND DEEP EUTECTIC SOLVENTS*
12:15-12.30	**FIS OR124**	**Duccio Tatini**	*Specific ions effects in green oleate-based formulations: how salts can influence the structure and rheology of viscoelastic systems*
12:30-12:45	**FIS OR125**	**Marianne Moedlinger**	*Structures and phase equilibria in the ternary Cu-As-Sb system (a preliminary investigation)*
12:45-13:00	**FIS OR126**	**Alessandro Damin**	*Cu+ bi-pyridine based homoleptic complexes as catalysts for partial oxidation reactions: a Raman study*

Divisione CHIMICA INDUSTRIALE (IND)

IND 06

09.30 - 10.00	**IND KN008 Medaglia Mario Giacomo Levi**	**Siglinda Perathoner Gaetano Iaquaniello**	*Waste-to-chemicals: a low-carbon innovative solution for circularity*
10.00 - 10.10	**IND OR060**	**Stefania Lucantonio**	*Experimental study of interactions between biomass pellets and oxygen carriers for chemical looping gasification in fluidized beds*

10.10 - 10.20	**IND OR061**	**Lucia Fagiolari**	*Electrodes and electrolytes for aqueous dye-sensitized solar cell*
10.20 - 10.30	**IND OR062**	**Francesca Rosso**	*Carbon Dioxide Absorption Mechanism in Biocompatible Ionic Liquids Solutions*
10.30 - 10.40	**IND OR063**	**Giuliano Giambastiani**	*"To Dissipate or not to Dissipate extra-Heat? This Is the Question!" How to Reduce Energy Wastes in a Challenging Process at the Heart of P2G Chain*
10.40 - 10.50	**IND OR064**	**Matteo Borella**	*A study of Kraft lignin conversion and possible upgrading to valuable compounds*
10.50 - 11.05	***Discussion***		
11.05 - 11.20	**break**		
11.20 - 11.40	**IND KN009**	**Paolo Vacca**	*New generation of specialty zeolites for sustainable chemistry*
11.40 - 11.50	**IND OR065**	**Giorgio Ferrari**	*Multifunctional Hardening Accelerator for Low-Clinker Binders*
11.50 - 12.00	**IND OR066**	**Rosa Vitiello**	*Optimization of HASE polymers effect in formulation of cement using Design of Experiment*
12.00 - 12.10	**IND OR067**	**Matteo Guidotti**	*Are Aqueous Hydrogen Peroxide and Sodium Percarbonate Efficient in the Inactivation of SARS-CoV 2?*
12.10 - 12.20	**IND OR068**	**Carlo Pirola**	*Chemical Plants Active Learning by Virtual Immersive Laboratory: the Eye4edu Project*
12.20 - 12.30	**IND OR069 Premio Tesi di Dottorato**	**Veronica Papa**	*Manganese- and Cobalt Based Catalysts for Homogeneous Hydrogenation*
12.30 - 12.40	**IND OR070**	**Elena Ghedini**	*Biomasses, Drug Delivery and Hi-Tech formulative protocols*
12.40 - 12.50	**IND OR071**	**Maryam Hmoudah**	*Assessment of the robustness of iron-based metal organic framework (MIL-88A) in aqueous environment*
12.50 - 13.00	***Discussion***		

Divisione CHIMICA INORGANICA (INO)
INO 10

9.30 - 10.00	**INO PZ009 (Premio Malatesta)**	**Roberta Sessoli**	*The contribution of coordination chemistry to the second quantum revolution*
10.00 - 10.30	**INO PZ010 (Premio Nasini 2021)**	**Edoardo Mosconi**	*Computational Modeling of Perovskite for Photovoltaic Applications*
10.30 - 10.45	**INO OR064-ad hoc**	**Iole Venditti**	*Functionalized silver nanoparticles for water pollution monitoring: sensitivity, selectivity and the challenge of eco-safe behavior*

10.45 - 11.00	**INO OR065**	**Diego Tesauro**	*New aromatic NHC-gold complexes as anticancer agents: protein target evaluation and cytotoxic activity*
11.00 - 11.15	**INO OR066**	**Farid Hajareh Haghighi**	*Silane-functionalized TiO2 nanoparticles decorated with Ag nanoparticles for dual antimicrobial effects*
11.15-11.30	**break**		
11.30 - 11.45	**INO OR067**	**Francesca Tessore**	*Porphyrins for second order nonlinear optics*
11.45 - 12.00	**INO OR068**	**Annaluisa Mariconda**	*Sulfonated N-heterocyclic carbene silver(I) and gold(I) water soluble complexes: catalytic and cytotoxic activity*
12.00 - 12.15	**INO OR069**	**Riccardo Freccero**	*Widening the tin solid-state chemistry: unusual bonding scenario in the LaMgSn2 rare-earth stannide*
12.15 - 12.30	**INO OR070**	**Veronica Ghini**	*NMR reveals the metabolic changes induced by Auranofin in ovarian cancer cells*
12.30 - 13.00	**INO IL003**	**David P. Giedroc**	*Metals, molecules and metabolism: Molecular mechanisms of bacterial metallostasis*

INO 11

10.30 - 10.45	**INO OR071**	**Antonio Zucca**	*Advances in Pt(II) rollover chemistry*
10.45 - 11.00	**INO OR072**	**Marco Lunardon**	*Hybrid transition metal dichalcogenide/graphene microspheres for hydrogen evolution reaction*
11.00 - 11.15	**INO OR073**	**Silvia Mostoni**	*Porphyrin functionalized ZnO/SiO2 hybrid nanoparticles as scintillator agent*
11.15-11.30	**break**		
11.30 - 11.45	**INO OR074**	**Alfonso Annunziata**	*Square-planar vs. trigonal bipyramidal molecular geometry in glucoconjugate triazole Pt(II) complexes: synthesis, in-solution behaviour and anticancer properties*
11.45 - 12.00	**INO OR075**	**Giada Mannias**	*Iron(III) trimesate xerogel by ultrasonic irradiation*
12.00 - 12.15	**INO OR076**	**Christian Rossi**	*Exploiting the transformative features of metal halides for the synthesis of CsPbBr3@SiO2 core-shell nanocrystals*
12.15 - 12.30	**INO OR077**	**Luciano Marchiò**	*Supramolecular assemblies in silver bispyrazolylmethane complexes: phase transitions and the role of the halogen bond*

INO 12

10.30 - 10.45	**INO OR078**	**Adolfo Speghini**	*Fine-tuning of the size of luminescent CaF2 nanoparticles*
10.45 - 11.00	**INO OR079**	**Antonio Santoro**	*Responsive Self-Assembled Dynamic Helicates*
11.00 - 11.15	**INO OR080**	**Chiara Mazzariol**	*Synthesis in confined space of luminescent nanostructures of undoped and Eu(III)-doped calcium molybdate*
11.15-11.30	**break**		
11.30 - 11.45	**INO OR081**	**Marta Stucchi**	*The synergistic and photochromic effect of Au nanoparticles on a Silver-waste derived TiO2 photocatalyst*

11.45 - 12.00	**INO OR082**	**Diego Olivieri**	*Efficient palladium catalyzed bis-alkoxycarbonylation of olefins for the synthesis of useful succinic acid derivatives*
12.00 - 12.15	**INO OR083**	**Luca Rigamonti**	*Multivariate approach to the analysis of structural data of iron(II) spin crossover complexes and cobalt(II) single molecule magnets*
12.15 - 12.30	**INO OR084**	**Simonetta Geninatti**	*Histidine containing PLGA nanoparticles as novel theranostic agents for Boron Neutron Capture Therapy*

Divisione CHIMICA ORGANICA (ORG)
ORG 19

9.30 - 10.00	**ORG PZ003**	**Pierangelo Metrangolo**	***Medaglia Giorgio Modena*** *A Journey through the Word of Halogen Bonding*
10.00 - 10.30	**ORG PZ008**	**Jacopo Roletto**	***Premio alla ricerca Chimica Organica per lo Sviluppo di Processi e Prodotti nell'Industria*** *The art of Process Development in API manufacturing*
10.30 - 10.45	**ORG OR124**	**Andrea Sartori**	*Dual Conjugates Targeting αVβ3/αVβ6 Integrins and Tyrosine Kinase Receptors as antifibrotic agents*
10.45 - 11.00	**ORG OR125**	**Angela Scala**	*Synthesis and biological profile of novel three-arms star-shaped PLA-PEG amphiphilic copolymers*
11.00 - 11.15	**ORG OR126**	**Monica Scognamiglio**	*Isolation and structural elucidation of oleanane saponins from Bellis sylvestris Cyr. involved in plant-plant chemical interactions*
11.15 - 11.30	**ORG OR127**	**Alba Silipo**	*Herbaspirillum Root189 LPS glycan chain decorations affect LPS bioactivity, membrane properties and prevent plant immune recognition*
11.30 - 12.00	**Break**		
12.00 - 12.15	**ORG OR128**	**Laura Siracusa**	*Secondary metabolic profiles and anticancer actions from fruit extracts of immature pomegranates*
12.15 - 12.30	**ORG OR129**	**Rachele Stefania**	*Enhanced relaxivity by hydrophobic interactions of macrocyclic Gd-HPDO3A complexes linked to pyranine*
12.30 - 12.45	**ORG OR130**	**Luca Valgimigli**	*Oxygen Uptake Kinetics as a Powerful Tool to Investigate Tyrosinase Enzyme Inhibition*
12.45 - 13.00	**ORG OR131**	**Danilo Vona**	*Enzyme immobilization on polydopamine-coated living microalgae cells for bioremediation*

ORG 20

10.30 - 10.45	**ORG OR132**	**Matteo Corrieri**	*Metal-Free Synthesis of Azacarbolines Enabled by Hypervalent Iodine-Promoted Intramolecular Oxidative Cyclization*

10.45 - 11.00	**ORG OR133**	**Federico Frateloreto**	*Functionalization of C-H bond using self-assembling supramolecular iron(II) complexes*
11.00 - 11.15	**ORG OR134**	**Andrea Gualandi**	*Photoredox allylation of aldehydes mediated by bismuth and cobalt*
11.15 - 11.30	**ORG OR135**	**Marco Lombardo**	*Visible Light Photocatalytic Synthesis of Oxygenated Heterocyclic Compounds*
11.30 - 12.00	**Break**		
12.00 - 12.15	**ORG OR136**	**Michela Lupi**	*A Hydrogen Bond Donor / Lewis Base (HBD/LB) catalytic route to enantioenriched hetero[4]helicenes*
12.15 - 12.30	**ORG OR137**	**Giulia Martelli**	*Fast Heck-Cassar-Sonogashira Cross-Coupling Reactions with Palladium Catalyst Recycling and Green Solvent/Base recovery*
12.30 - 12.45	**ORG OR138**	**Silvia Gazzola**	*2- and 6-Purinylmagnesium Halides in Dichloromethane: Scope and Insights Into the Solvent Influence on the C- Mg Bond*
12.45 - 13.00	**ORG OR139**	**Angelo Nacci**	*Nanostructured catalysts for a circular economy*

ORG 21

10.30 - 10.45	**ORG PZ015**	**Gabriele Laudadio**	***Premio Tesi di Dottorato Chimica Organica nei suoi Aspetti Metodologici*** *New synthetic methods enabled by photochemistry and electrochemistry in flow*
10.45 - 11.00	**ORG OR140**	**Andrea Francesca Quivelli**	*Mild Approaches for Copper-Catalysed Coupling Reactions: Ligand-Free Ullmann-type C–N and C–O Bond Formation in Deep Eutectic Solvents*
11.00 - 11.15	**ORG OR141**	**Marco Rabuffetti**	*Stereoselective monoreduction of bulky 1,2-dicarbonyls catalyzed by a benzyl reductase from Pichia glucozyma (KRED1-Pglu)*
11.15 - 11.30	**ORG OR142**	**Daniele Ragno**	*Regiodivergent Isosorbide Acylation by Oxidative NHC-Catalysis in Batch and Continuous-Flow*
11.30 - 12.00	**Break**		
12.00 - 12.15	**ORG OR143**	**Giorgio Rizzo**	*Palladium anchored on Silk Fibroin as suitable catalyst for Suzuki-Miyaura Cross-Coupling Reactions*
12.15 - 12.30	**ORG OR144**	**Patrizio Russo**	*Novel Synthesis of Thienofuranone Derivates by Pd-Catalyzed Carbonylation Reaction*
12.30 - 12.45	**ORG OR145**	**Gabriele Lupidi**	*Vitamin B2 Promoted Tandem Nef-Henry Reactions for the synthesis of Symmetrical β-Nitro Alcohols from Nitroalkanes*

12.45 - 13.00	**ORG OR146**	**Ida Ziccarelli**	*Synthesis of Isobenzofuranones, Isochromenones and Thienopyranones by a Pd-Catalyzed Oxidative Carbonylation Approach*

Società Chimica Italiana | SCI2021

CHIMICA INORGANICA (INO)

- Orals
- Posters

Metallated Ylides: Powerful Reagents for the Stabilization of Reactive Main Group Species and Ligands in Catalysis

Viktoria H. Gessner

Chair of Inorganic Chemistry II, Ruhr-Universität Bochum, Universitätsstraße 150, 44801 Bochum, Germany; viktoria.gessner@rub.de

Reactive main group compounds such as low-valent or cationic species have received intense research interest in the past years due to their unique structures and reactivities, above all their propensity to act as transition metal mimics.[1] The isolation of such electron-deficient compounds requires a careful molecular design which usually involves the use of sterically demanding and electron-donating substituents. Especially, amino groups are privileged substituents which provide thermodynamic stability due to their propensity to function as strong π-donor ligands. Thus, they are often applied in low-valent species (such as carbenes) or cationic main group compounds. Like amino substituents phosphorus ylides can act as strong donor ligands with flexible spatial and electronic properties.[2]

Recently, our group has reported on the class of α-metallated ylides as versatile reagents for the facile introduction of ylide-substituents.[3] This presentation will give an overview over the synthesis and properties of these highly electron-rich species and their application in main group chemistry. Besides their use of main group chemistry for the stabilization of low-valent compounds with unique electronic properties (Figure 1),[4] also their application in the preparation of strongly donating phosphines (YPhos ligands) for catalytic applications will be discussed.[5]

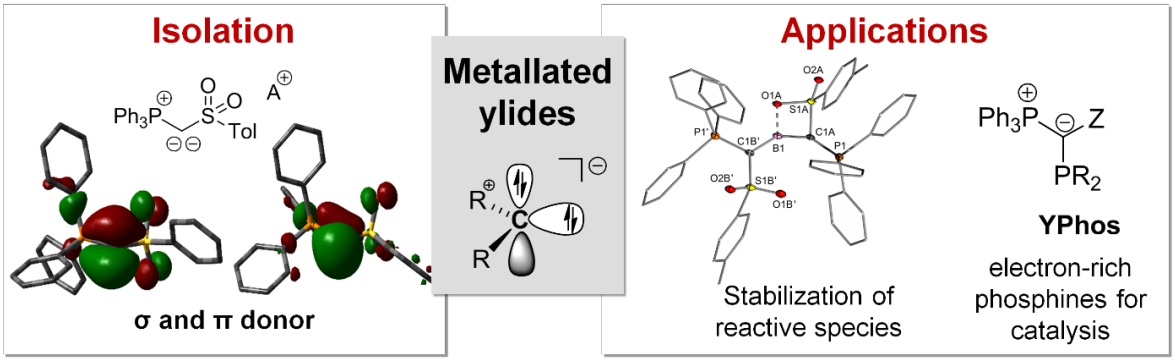

Figure 1. Metallated ylides: From their isolation to applications in main group chemistry and catalysis.

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Circular Materials for the Energy Transition

A. Weidenkaff, W. Xie, R. Yan, S. Yoon, R. Wagner-Wenz

Materials and Ressources, Technical University of Darmstadt
anke.weidenkaff@mr.tu-darmstadt.de

Sustainable energy conversion technologies require sustainable substitution materials. The implementation of green chemistry for synthesis and production processes and an efficient circularity of the energy converters with a programmable long lifetime are being introduced as a suitable approach in this talk.

The design of sustainable high performance materials is based on theoretical predictions, life cycle assessment and profound knowledge on composition-structure-property relationships, defect chemistry, ion mobility assessment, and the criticality analysis of applied elements to improve the cycle life of energy converters.

Metals, molecules and metabolism: Molecular mechanisms of bacterial metallostasis

David P Giedroc[a]

[a] *Department of Chemistry, Indiana University, Bloomington, IN 47405-7102 USA*

Transition metals are required for all forms of life, playing roles as catalytic and structural cofactors in proteins. In a process termed nutritional immunity,[1] the human host sequesters essential transition metals from the invading pathogen which we hypothesize leads to undermetallation of essential metal-dependent enzymes, thus globally impacting metabolism and inhibiting growth. The host metal-sequestering host protein calprotectin (CP), a major player of this innate immune response, attenuates growth of the major human nosocomial pathogen *Acinetobacter baumannii*, notably via Zn^{II} and Fe withholding.[2] We hypothesize that given the fact that Zn^{II}- and Fe-cofactored metalloenzymes are scattered throughout metabolism, CP stress may well re-wire or prioritize metabolism as a means to adapt to this important stressor. Recent efforts using global profiling approaches to understand this metabolic adaptation, and the function of a candidate COG0523-family zinc metallochaperone which we term ZigA (Zur-induced GTPase) in this process will be discussed.[3] I will describe cellular mechanisms of prioritization of flavin biosynthesis and the regulation of protein synthesis by CP stress, as well as new approaches to elucidate specific perturbations of the metalation status of metalloproteome in *A. baumannii* when stressed by CP. A long-term goal of these studies is to identify new (metallo)enzyme targets for the development of novel antimicrobial strategies. Supported by a grant from the US National Institutes of Health (R35 GM118157).

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Innovative Mn and Re catalysts for CO_2 Photo- and Electro-Reduction

R. Gobetto, C. Nervi, L. Rotundo, A. Tiozzo

Dept. of Chemistry, University of Turin, Italy, Via P. Giuria n° 7, 10125 Torino, Italy

The reduction of CO_2 emissions into the atmosphere has become a major environmental goal. Carbon capture and storage (CCS) has the capacity to effectively meet climate change targets, but CCS can be too expensive to be used widely. It is important to shift from a model of utilization or storage to one of utilization and storage (CCUS). It has been demonstrated that CO_2 could be used as it is captured, rather than during its storage, using an approach based on combinatorial chemistry [1]. Carbon dioxide photo- and electro-reduction has been suggested as a potential strategy to transform solar and intermittent sources of energy into valuable chemicals such as CO, HCOOH, hydrocarbons, and alcohols. [2.3] The choice of an efficient and selective catalyst for photo- and electro-chemical reduction of CO_2 is mandatory in terms of durability, stability, and improved TON efficiencies. A rational design of highly active and robust catalysts that could generate high current density and high selectivity is critical for large-scale application. We investigated innovative Mn and Re bipyridine complexes by varying the electronic and coordination properties of the metal centre in order to understand the structure-function relationships and to compare the catalytic activities with the previously published results [4,5]. Efficient homogeneous catalyst still has several benefits, including the possibility to covalently attach the molecular catalysts on the electrode surface that are able to convert CO_2 to CO and HCOOH also in aqueous media [6]. The mechanistic characterization and comparison to related complexes will be discussed.

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Disclosing the role of Gold on Palladium - Gold alloyed catalysts in formic acid decomposition

Ilaria Barlocco[a*], *Alberto Roldan*[b], *Alberto Villa*[a]

[a]*Dipartimento di Chimica, Università degli Studi di Milano, via Golgi 19, I-20133Milano, Italy;* [b]*Cardiff Catalysis Institute, School of Chemistry, Cardiff University, Main Building, Park Place, CF10 3AT, Cardiff, United Kingdom*

Sustainable energy sources are needed to mitigate the increasing dependence on fossil fuels and their high environmental impact. Hydrogen is recognised as an efficient alternative energy carrier because of its high energy density and innocuous products upon utilisation. Despite this, its direct use is hindered due to the shortage of economically and sage hydrogen storage technologies therefore, alternative methods to store and transport it is of vital importance[1]. In line with the U.S. Department of Energy, formic acid (FA) is an attractive hydrogen carrier due to its high volumetric hydrogen content (4.4 wt%), non-toxic character, and stability in liquid phase at standard temperature and pressure[2]. A controlled catalytic FA dehydrogenation is required to release hydrogen on-demand, nevertheless, its decomposition occurs in two competing pathways. The most exothermic route is the desired dehydrogenation reaction; it produces hydrogen and carbon dioxide. The second pathway is the dehydration reaction producing carbon monoxide[3]. Among all the studied heterogeneous catalysts, Pd/C have been deeply investigated because of its superior activity at room temperature. In contrast, the examined Pd/C catalysts quickly deactivate because of the high affinity with CO, which blocks the active sites[4]. To overcome the poisoning, it has been shown that the introduction of a second metal forming alloy catalysts, especially gold, overcame this problem and generates also ultrapure hydrogen at low temperature[5]. Herein, I present the synthesis of bimetallic Palladium-Gold nanoparticles with different Pd:Au ratios and the corresponding Pd and Au monometallic catalysts obtaining by sol immobilization method, in order to disclose the effect of gold on PdAu alloyed nanoparticles. The obtained materials were characterized by means of TEM, XPS and ICP - OES. The catalytic performance of the catalysts was evaluated in the liquid phase dehydrogenation of FA at room temperature, obtaining enhanced activity, stability and selectivity compared to the monometallic systems. The activity plot showed a volcano trend with a maximum for Pd_6Au_4 catalyst (3539 h^{-1}). Moreover, an increasing in conversion at 2h of reaction is observed for most of the bimetallic systems, in particular for Pd_6Au_4 and Pd_8Au_2 (73% and 68%, respectively). Moreover, an inhibition of the dehydration pathway was observed for gold-containing catalysts. For the most promising materials, an excellent stability was obtained during six consecutive runs in comparison to Pd@HHT that rapidly deactivates because of leaching, coalescence and CO-poisoning. DFT models of Pd_{15}, Au_{15} and Pd_9Au_6 clusters were then employed to better understand the beneficial effect of gold observed in the experimental results. While Au_{15} was not able to interact with FA, Pd_{15} and Pd_9Au_6 could exothermically adsorb the substrate, according to our results. Nonetheless, the adsorption energy of formic acid on Pd_{15} is 5.266 eV higher than the Pd_9Au_6 one, confirming the superior activity of the bimetallic system. Moreover, considering the pathways observed for both systems, for Pd_9Au_6 the favourite route was the formation of carbon dioxide and hydrogen, while Pd_{15} could follow both the dehydrogenation and dehydration pathways, in agreement with the analyses performed on the products.

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[3] M. Grasemann, G. Laurenczy, *Energy Environ. Sci.* **2012**, *5*, 8171–8181.
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Nearly free silanols on silica surface: a new paradigm for particle toxicology

Pavan C.,[a,b,c] Santalucia R.,[a] Leinardi R.,[a,b] Fabbiani M.,[a] Yakoub Y.,[c] Uwambayinema F.,[c] Bellomo C.,[a,b] Lagostina V., [a] Chilla G.,[a] Rebba E.,[a] Mino L.,[a] Ugliengo P.,[a] Tomatis M.,[a,b] Martra G.,[a] Lison D.,[c] Fubini B.,[a,b] Turci F.[a, b]

[a]Department of Chemistry, University of Turin, Italy, [b]"G. Scansetti" Interdepartmental Centre for Studies on Asbestos and Other Toxic Particulates, University of Turin, Italy; [c]Louvain centre for Toxicology and Applied Pharmacology, Université catholique de Louvain, Belgium.

Respirable crystalline silica (RCS) is the leading cause of occupational respiratory disease worldwide. Inhalation of RCS is associated to inflammatory lung reactions, which can lead to silicosis, cancer, and autoimmune diseases [1]. Amorphous (nano)silica has been generally considered less harmful than crystalline forms; but recent studies pointed out acute inflammatory and pro-fibrotic effects for some types of pyrogenic silicas [2]. The extreme variability of silica forms, the surface heterogeneity, depending on the source and preparation methods, and the variable toxicity effects, generated one of the most intriguing enigmas in particle toxicology, *i.e.* deciphering which physico-chemical features explain and predict the variable hazard of crystalline and amorphous silica [3]. Despite extensive research efforts in the past 50 years, a possible unifying factor remained elusive.

Using a set of *ad hoc* prepared synthetic and natural quartz particles, we have identified a unique subfamily of surface moieties as a key initiator of the toxicity of silica particles [4]. These moieties, namely "nearly-free silanols" (NFS), appear on the surface of quartz particles when crystals are fractured, and their amount can be modulated by thermal treatments. The peculiar spatial arrangement of NFS was demonstrated as the most energetically favorable for establishing interactions with cell membrane components, and to induce key events of the silica adverse outcome pathway (*Fig.1*). The toxic activity of NFS was also confirmed with pyrogenic and vitreous amorphous nanosilicas, and our recent findings suggest that NFS could impart toxic properties to other silica polymorphs and hydroxylated surfaces. Overall, we found that the variation of NFS abundance accounts for the origin and variability of the toxicity of silica, opening a new perspective for tailoring less toxic silica dusts and for improving technological applications of silica.

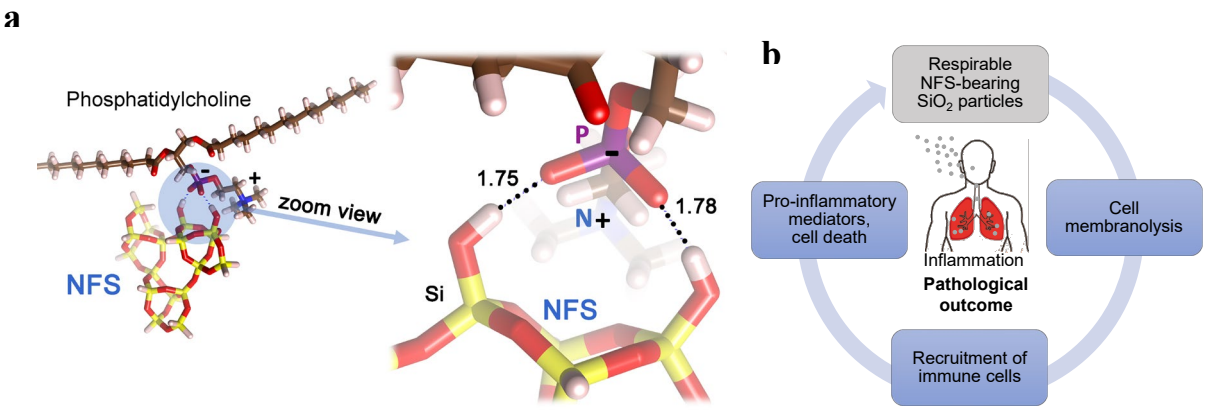

***Fig. 1**: (a) A cluster model of nearly-free silanols (NFS) interacting with phosphatidylcholine, a building block of cell membranes, as the molecular initiating event that trigger (b) cell membranolysis and a cyclic activation of inflammatory cells, which might lead to persistent lung inflammation and chronic pathological outcomes.*

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A combined theoretical and experimental investigation of a new class of [N,O$^-$] imidazo[1,5-a]pyrid-3-yl)phenolate Zn(II) catalysts for the ring opening polymerization of lactide

Massimo Christian D'Alterio,[a] *Ilaria D'Auria,*[a] *Stefano Brenna,*[b] *Claudio Pellecchia*[a]

[a]*Dipartimento di Chimica e Biologia "A. Zambelli", Università Degli Studi di Salerno, Via Giovanni Paolo II 132, 84084 Fisciano (SA). E-mail: mdalterio@unisa.it;* [b]*Dipartimento di Scienza e Alta Tecnologia, Università degli Studi dell'Insubria, Via Valleggio, 9 - 22100 Como*

The well-known problem about the plastic pollution calls for the development of environmentally benign polymers, and Poly(lactic acid) (PLA) is a perfect candidate since it is biodegradable and is obtained by biomass.[1] The industrially employed catalyst for PLA production is the Tin (II) 2-ethylhexanoate, but since its toxicity and its low control toward secondary reaction (e.g. transesterification) research is pushing toward the finding of new catalysts.[2]
Herein, we report the results of a promising new family of Zn(II) complexes bearing monoanionic [N,O$^-$] (Imidazol[1,5-a]pyrid-3-yl)phenols ligands[3] variously substituted in para position of the phenolic ring (-R) and in position 1 of imidazopyridinic ring (-R') for the L-Lactide (L-LA) Ring Opening Polymerization (ROP) both in mild (20-100°C, solvent) and in harsh conditions (190 °C, neat) (Figure 1).

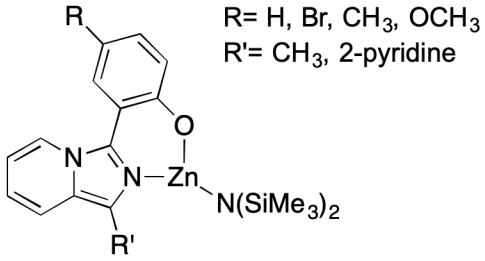

Figure 1. Zinc(II) Complexes with (imidazo[1,5-a]pyrid-3-yl)phenol ligand
R: para-substituent to the phenol, R': position 1 of imidazopyridinic ring

The catalyst bearing the 2-pyridine moiety (-R') and H (-R) resulted to be the best performer in mild reaction conditions, in line with some of the most active catalysts reported in literature.[4,5] However, the exploitation of such an active catalyst in harsh conditions is not obvious. Catalysts bearing the methyl moiety as -R' and various substituents as -R performed far better in neat at 190 °C.
To understand the behavior of our systems we performed a combined Kinetical and DFT investigations and we explained, for example, the non-trivial role of the 2-pyridine moiety in enhancing the activity in mild conditions.

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Highly selective indole oxidation promoted by a Mn-containing mini-enzyme

Linda Leone[a], *Daniele D'Alonzo*[a], *Ornella Maglio*[a,b], *Vincenzo Pavone*[a], *Flavia Nastri*[a] *and Angela Lombardi*[a]

[a] *Department of Chemical Sciences, University of Napoli "Federico II," Via Cintia 21, Napoli 80126, Italy;* [b] *Institute of Biostructures and Bioimages—National Research Council, Via Mezzocannone 16, Napoli 80134, Italy*

Indole is a widespread heterocyclic scaffold among natural compounds and its oxygenated derivatives have gathered significant interest in different areas of research. In particular, 2- and 3-oxindole derivatives represent valuable scaffolds for drug design.[1] Whereas 2-oxindole is a stable and commercially available molecule, accessing 3-oxindole is quite difficult, due to the high susceptibility of this compound to spontaneous oxidation.[2] Several approaches have been developed to access the 3-oxindole scaffold, rarely involving the direct oxygenation of indole.[3] Indeed, indole oxidation represents a real challenge from a catalytic standpoint, since it typically leads to complex mixtures of oxygenated products at different positions of the aromatic ring.
Here we present the oxidation of indole promoted by a synthetic metalloenzyme, Mn-Mimochrome VI*a (Mn-MC6*a). This mini-enzyme consists of a manganese-deuteroporphyrin active site embedded within two small peptide chains.[4] Mn-MC6*a promotes the selective oxidation of indole at its C3 position (Figure 1), achieving the highest product selectivity (86% at pH 8.5) reported among native[5,6] and artificial heme-enzymes.[7–9]

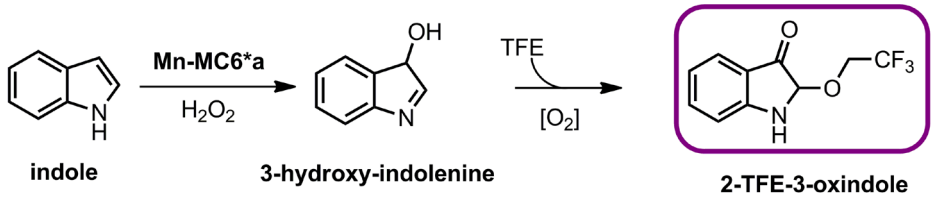

Figure 1. Indole oxidation catalyzed by Mn-MC6*a.

The peculiar conditions required to stabilize catalyst folding and, consequently, to optimize its reactivity, also allow for the isolation of a highly reactive product. Indole oxidation catalyzed by Mn-MC6*a leads to a 3-oxindole derivative in which a solvent molecule (2,2,2-trifluoroethanol, TFE) is incorporated at the most reactive C2 position of the oxidized product. We also propose a possible reaction pathway, based on the effects of pH, co-solvent, and indole substitution on the reaction outcome.

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Synthesis and structural properties of isostructural Zn(II) M12L8 poly-[*n*]-catenane using the 2,4,6-tris(4-pyridyl)benzene (TPB) ligand.

J. Martí-Rujas[a], *A. Famulari*[a], *S. Torresi*[a], *S. Elli*[a], *A. Sacchetti*[a]

[a]*Department of Chemistry, Materials and Chemical Engineering "Giulio Natta", Politecnico di Milano, Piazza L. da Vinci 32, 20133 Milan, Italy.*

The use of mechanical bonds for the synthesis of catenanes is a challenging process because of the many factors controlling the interpenetration process.[1,2] We report the kinetic control in the presence of various aromatic solvents of a poly-[*n*]-catenane (1). The polymeric structure is composed of interlocked $\mathbf{M_{12}L_8}$ icosahedral nanometric cages with internal voids of *ca*. 2500 Å^3.[3] Using the symmetric exotridentate tris-pyridyl benzene (**TPB**) ligand and ZnX_2 (where X = Cl and Br) with appropriate templating solvent molecules due to the good ligand aromatic interactions are used, the metal-organic nanocages can be synthesized very fast, homogeneously, and in large amounts as microcrystals and single crystals (Figure 1). Synchrotron single-crystal X-ray data (100 K) allowed the resolution of aromatic guest molecules at the internal walls of the $\mathbf{M_{12}L_8}$ cages, while in the centre of the nanocages the solvent is disordered and not observable by X-ray diffraction data. Using **TPB** and $ZnBr_2$, it is observed that in the absence of aromatic guest molecules the product of the fast crystallization is an amorphous phase. The amorphous material re-constructs and forms a crystalline phase in appropriated aromatic solvents. Solid-state quantum mechanics provided a rationalization of the results, in particular, solid-state approaches, showed theoretical evidence of the kinetic nature in the formation of the polycatenation of the $\mathbf{M_{12}L_8}$ nanocages by the analysis of the packing energy considering monomeric and dimeric cages.

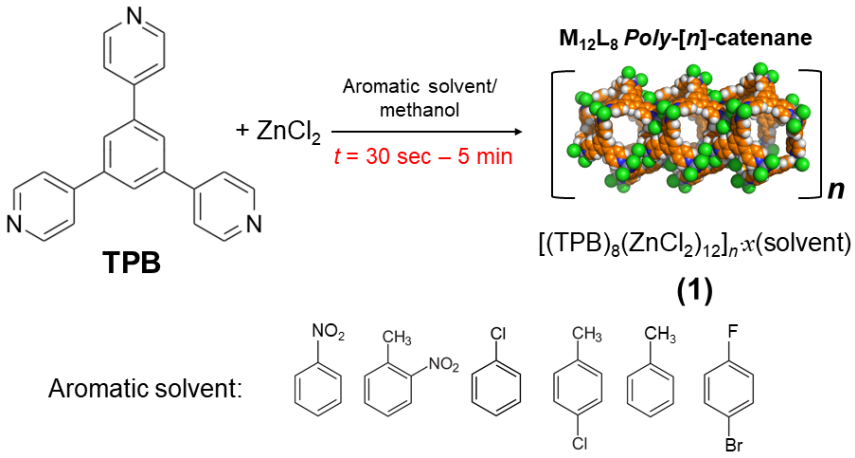


Figure 1. Synthesis of the $\mathbf{M_{12}L_8}$ interlocked nanocages forming the poly-[*n*]-catenane **1** under aromatic control.

[1] S. Torresi, A. Famulari, J. Martí-Rujas *J. Am. Chem. Soc.* **2020**, *142*, 9537-9543.

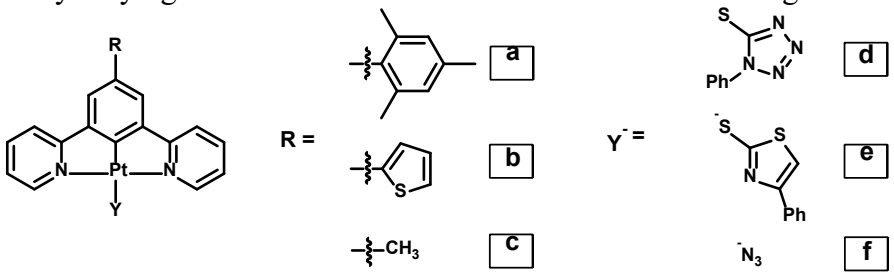
Three novel families of cyclometalated platinum(II) complexes with remarkable luminescence properties

Francesco Fagnani [a], *Alessia Colombo* [a], *Claudia Dragonetti* [a], *Dominique Roberto* [a] *and Daniele Marinotto* [b]

[a] *Dipartimento di Chimica, Università degli Studi di Milano and INSTM UdR Milano, Italy;* [b] *Istituto di Scienze e Tecnologie Chimiche SCITEC-CNR, Milano, Italy*

Among the many materials that can be employed for the production of OLEDs, transition metal complexes are certainly very promising, since the presence of the heavy metal atom allows for an efficient intersystem crossing from the excited singlet states to a triplet state, from which emission can occur. Otherwise, the population of the triplet states would be lost through non-radiative decays, reducing the overall efficiency of the system. A very appealing family of compounds is represented by the cyclometalated 1,3-di-(2-pyridyl)benzene Pt(II) complexes, bearing a chloride as ancillary ligand on the metal atom. The structural rigidity of the N^C^N ligand is at the basis of the excellent quantum yields (QY) of these molecules, which present luminescent properties widely tunable by means of the introduction of various substituents on both the benzene and the pyridine rings. A further step in the study of this class of complexes is the substitution of chloride by different ancillary ligands. Some arenethiolates have been introduced, but a strong decrease of the QY was observed [1]. However, we recently found that replacement of chloride by 1-phenyl-1*H*-tetrazole-5-thiolate preserves the great luminescence of the related Pt(II) complex bearing a cyclometalated 5-mesityl-1,3-di-(2-pyridyl)benzene [2].

In this work, we present three derivatives for each of the three known chloro Pt(II) complexes, **PtCl1**, **PtCl2** and **PtCl3**, substituted on the benzene ring with a mesityl, a 2-thienyl, and a methyl moiety, respectively (Figure). The investigated ancillary ligands are 1-phenyl-1*H*-tetrazole-5-thiolate, 4-phenylthiazole-2-thiolate, and azide. Many among these new complexes present a high absolute QY (ca 0.90) in solution of dichloromethane. Besides, their good solubility in CH_2Cl_2 is an important tool for the efficient preparation of solution-processable OLEDs, whose emission range can be modulated by varying the nature of the substituent on the tridentate ligand.



PtCl1:	R = **a**	Y^- = **Cl^-**	**PtCl2:**	R = **b**	Y^- = **Cl^-**	**PtCl3:**	R = **c**	Y^- = **Cl^-**
Pt1:	R = **a**	Y^- = **d**	**Pt4:**	R = **b**	Y^- = **d**	**Pt7:**	R = **c**	Y^- = **d**
Pt2:	R = **a**	Y^- = **e**	**Pt5:**	R = **b**	Y^- = **e**	**Pt8:**	R = **c**	Y^- = **e**
Pt3:	R = **a**	Y^- = **f**	**Pt6:**	R = **b**	Y^- = **f**	**Pt9:**	R = **c**	Y^- = **f**

Figure

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"*NMR effective molecular radius*" of coordinated ammonia

Michele Benedetti, Federica De Castro, Paride Papadia, Daniela Antonucci, Francesco P. Fanizzi

Department of Biological and Environmental Sciences and Technologies (DiSTeBA), University of Salento, Via Monteroni, 73100 Lecce, Italy.

The problem of fully understanding the phenomena influencing the δ NMR signals frequencies, related to the physical properties of a molecule, deserved a particular attention in the recent literature. [1,2] In this work, we studied a model set of square-planar $[Pt(NH_3)_aX_b]^n$ (a + b = 4; X_b = combination of b halido ligands; n = 2 – b) complexes, finding that the δ(^{195}Pt) NMR chemical shift linearly decreases on increasing the platinum bonded halido ligands' ionic radii overall sum (Figure 1A). [3] This confirms that even in the case of platinum-ammonia derivatives the NMR shielding can be attributed to the pseudo ring currents, circulating around the M–X bonding axis. Interestingly, the presented data show that even the NH_3 ligands are characterized by a constant NMR shielding ability towards the central metal. This has been rationalized in term of "*NMR effective molecular radius*" of the NH_3 ligand, affecting the observed δ(^{195}Pt), as similarly found in previous works for the simpler halido ligands. [1,2] Interestingly, a δ(^{15}N) decrease is also observed in Pt bonded NH_3 ligands when the ionic radii of *cis* halido ligands is increased, the opposite occurs if the ionic radius of a *trans* halido ligand is increased (Figure 1B). The two effects stem from both shielding electric ring currents affecting the *cis* ligands and prevailing *trans*-influence due to coordinated halido ligands.

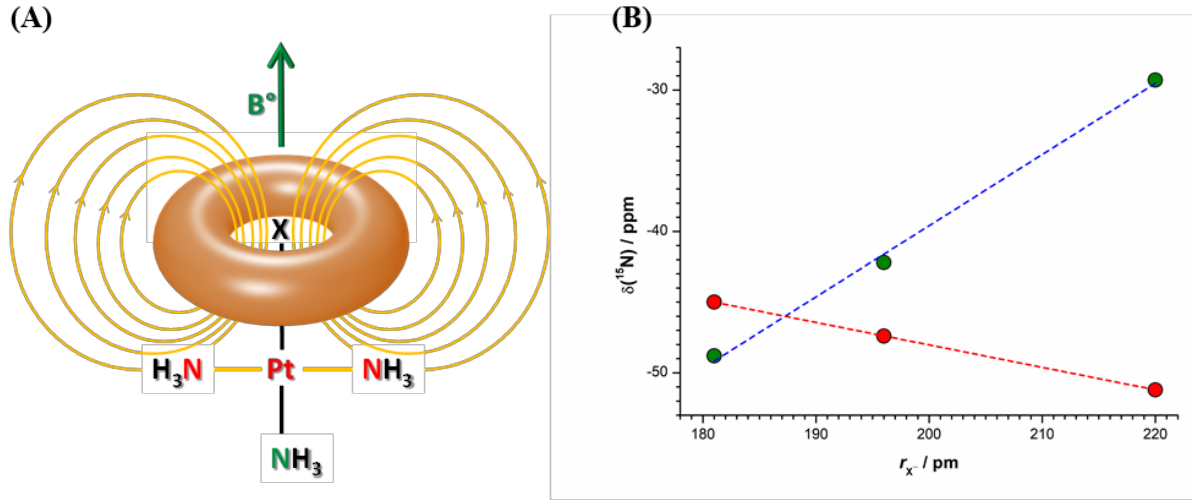

Figure 1. (A) Schematic representation of a model $[Pt(NH_3)_3X]^+$ (X = Cl, Br, I) complex. The orange torus and arrows represent the electric *pseudo*-ring currents and the induced magnetic field generated in the platinum bonded X^- ligand by an applied B° magnetic field, respectively. These produce a chemical shift reduction of both δ(^{195}Pt) and δ(^{15}N) NMR signals of the central Pt and *cis* *N*-donors (evidenced in red). Instead, *trans*-influence needs to be taken into account to explain the opposite effect observed for the ^{15}N NMR signal of the *N*-donor in *trans* to X (evidenced in green). **(B)** δ(^{15}N) NMR chemical shifts, reported as a function of the halido ligand ionic radius, r_{X^-}, for the *cis* (red data points) and *trans* (green data points) to X ammonia ligands, in the model series of square-planar Pt(II) $[PtX(NH_3)_3]^+$ (X = Cl, Br, I) complexes.

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Redox reactivity of transition metal dioxide anions towards sulfur dioxide in the gas phase

Chiara Salvitti[a], *Marzio Rosi*[b], *Federico Pepi*[a], *Anna Troiani*[a], *Giulia de Petris*[a]

[a]*Dipartimento di Chimica e Tecnologie del Farmaco, Sapienza Università di Roma, P.le Aldo Moro 5, 00185 Roma, Italy;* [b]*Dipartimento di Ingegneria Civile ed Ambientale, Università di Perugia, Via Duranti 93, 06125 Perugia, Italy*

Transition metal oxides (TMO) have long been known as effective catalysts in a variety of chemical transformations [1]. As an example, mineral oxides constituting miniaturized atmospheric aggregates provide reactive surfaces for the oxidation of tropospheric-sourced SO_2 [2-4]. This air pollutant represents the key precursor of the sulfate aerosols that are responsible for climate changes, acid rainfalls, and severe haze events, such as the "London fog" episode occurred in 1952 [5]. Interestingly, the oxidative properties of TMOs are predominantly due to the $O^{\cdot-}$ radical on the metal surface, as demonstrated by several studies carried out in the condensed phase [6-8]. Nonetheless, the catalytic features of the active sites can be masked by interfering factors observed in bulk, such as solvent and counter-ion effects, that prevent the elucidation of the reaction mechanism.

A successful approach to circumvent this problem is to perform gas-phase studies of mass-selected cluster ions generated at their electronic ground states. The reactivity of these species can be investigated by mass spectrometric techniques under single-collision conditions and the results, thus obtained, complemented by comprehensive computational studies. This strategy allows one to assess the elementary steps of a chemical reaction and investigate the effects of stoichiometry, spin distribution, and charge state on cluster reactivity at a strictly molecular level [9,10].

As a result, we report on the reactivity of the first-row transition metal dioxide anions ($CrO_2^{\cdot-}$, CoO_2^-, $NiO_2^{\cdot-}$, CuO_2^- and $ZnO_2^{\cdot-}$) towards SO_2 by combining ion-molecule reaction experiments and theoretical calculations.

An unprecedented fast and efficient oxidation of SO_2 to sulfate radical anion is promoted by dioxide anions of the late transition metals, Cu and Zn. A double oxygen transfer is indicated as the energetically-favoured reaction mechanism that switches to a single oxygen anion transfer, leading to $SO_3^{\cdot-}$, when a water molecule is ligated to $ZnO_2^{\cdot-}$. Interestingly, when the spin density is highly localized on the metal centre, as in the case of $CrO_2^{\cdot-}$, the anion acts as a reductant towards SO_2, whereas only the consecutive addition of two SO_2 molecules is observed with the earlier transition metals, Ni and Co.

In conclusion, owing to the borderline-acid nature of SO_2, the spin distribution alternatively located on the metal centre or on the terminal oxygen atoms of $MO_2^{-/\cdot-}$ anions is crucial in affecting the redox properties and the gas-phase reactivity of these species.

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New chiral heteroleptic Eu(III)/Tb(III)/Yb(III)-based luminescent complexes designed for different applications

Silvia Ruggieri,[a] Fabio Piccinelli,[a] Lorenzo Di Bari,[b] Martina Sanadar,[c] Andrea Melchior,[c] Andrea Gualandi [d] and Chiara Nardon [a]

[a]Laboratorio Materiali Luminescenti, DB, Università di Verona, Strada Le Grazie 15, 37134 Verona; [b]Dipartimento di Chimica e Chimica Industriale, via Moruzzi 13, 56124 Pisa; [c]Dipartimento Politecnico di Ingegneria e Architettura, Laboratorio di Tecnologie Chimiche, Università di Udine, via Cotonificio 108, 33100 Udine; [d]Dipartimento di Chimica ''G. Ciamician'', Università di Bologna, Via Selmi 2, 40126 Bologna.

The chemistry of luminescent complexes of trivalent lanthanide (Ln) ions is gaining remarkable attention thanks to their promising applications in several technological fields, such as the biomedicine as optical probes or biosensors and the realization of OLED[1] or solar concentrators[2]. For instance, heteroleptic complexes bearing both β-diketonates and chiral ligands[3,4] are capable to emit left and right circularly-polarized (CP) light with different intensities. Such complexes can find a possible application as phosphors in CP-OLED, emitting CP light in the visible spectral range. Thus, we recently have focused on the synthesis of a new class of chiral Ln(III)-based complexes of the type [Ln(bpcd)(tta)] and [Ln(bpcd)(cum)] (**Figure 1**) wherein *bpcd* = 2,2'-(((1R,2R or 1S,2S)-cyclohexane-1,2-diyl)bis((pyridin-2-ylmethyl)azanediyl))diacetate; *tta* = 2-thenoyltrifluoroacetyl-acetonate; *cum* = 3-acetyl-4-hydroxy-2H-chromen-2-one in order to evaluate them as luminescent species in CP-OLED devices.
It is worth highlighting that the use of Yb(III)-based complexes would propel the circularly-polarized emission in the near infrared (NIR) region, thus increasing the versatility and applicability of such a technique (*e.g.,* design of advanced security inks[5]).

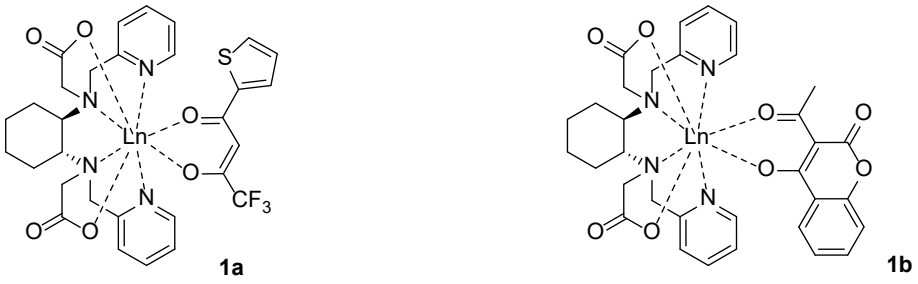

Figure 1. Chemical structure of the investigated neutral complexes. **1a**: Ln = Eu and Yb; **1b**: Ln = Eu, Tb and Yb. Here the 1R, 2R enantiomers are represented.

All the complexes have been spectroscopically characterized both in solution and in the solid state, leading to promising preliminary data. Their stability (by spectrophotometric titration experiments), structure (by DFT calculations) and CP luminescence are currently under investigation.

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Oxaliplatin binds angiogenin and exerts high antiangiogenic effects in PC-3 cancer cells at non-cytotoxic concentration

Tiziano Marzo,[a] Giarita Ferraro,[b] Lorena Maria Cucci,[c] Alessandro Pratesi,[d] Örjan Hansson,[e] Cristina Satriano,[c] Antonello Merlino [f] and Diego La Mendola [a]

[a]Department of Pharmacy, University of Pisa, Via Bonanno Pisano 6, 56126, Pisa, Italy; [b]Department of Chemistry 'Ugo Schiff', University of Florence, Via della Lastruccia 3, 50019, Sesto Fiorentino (FI), Italy; [c]Department of Chemical Sciences, University of Catania, Viale Andrea Doria 6, 95125, Catania, Italy; [d]Department of Chemistry and Industrial Chemistry, University of Pisa, Via G. Moruzzi 13, 56124, Pisa, Italy; [e]Department of Chemistry and Molecular Biology, University of Gothenburg, Medicinaregatan 9C, PO Box 462, SE-40530 Göteborg, Sweden; [f]Department of Chemical Sciences, University of Naples Federico II, Via Cintia 21, I-80126 Napoli, Italy.

Angiogenin is a potent angiogenic protein that is overexpressed in many types of cancer at concentration values correlated to the tumor aggressiveness [1-2]. Here, by means of an integrated multi-technique approach based on crystallographic, spectrometric and spectroscopic analyses [3], we demonstrate that the anti-cancer drug oxaliplatin efficiently binds angiogenin. Microscopy cellular studies, carried out on the prostate cancer cell line PC-3, show that the protein/drug adducts formed by using oxaliplatin at non-cytotoxic concentrations (sub-μM range), inhibit the angiogenin prompting effect on cell migration, which is a typical feature of angiogenesis process. Overall, our findings point to angiogenin as an actual target of oxaliplatin, thus suggesting a novel mechanism for the antineoplastic activity of the platinum drug and opening the avenue to novel approaches in the combined anti-cancer anti-angiogenic therapy.

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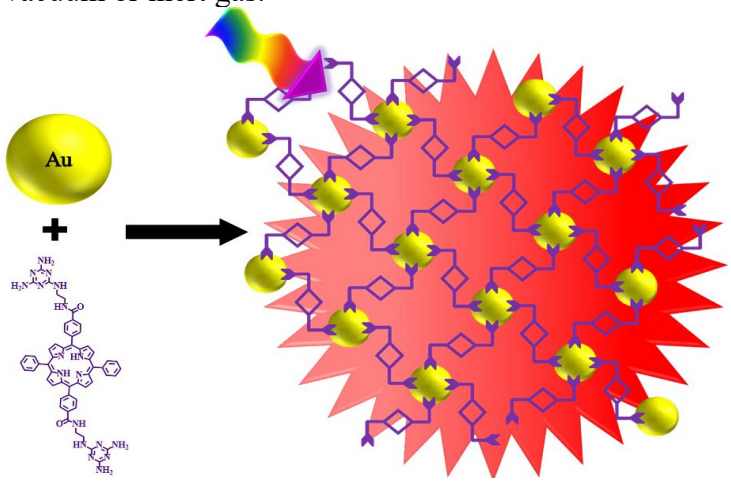
Covalently conjugated gold–porphyrin nanostructures

L. Spitaleri,[a,b] C. M. A. Gangemi,[a] R. Purrello,[a,b] G. Nicotra,[c] G. Trusso Sfrazzetto,[a,b] G. Casella,[d] M. Casarin,[e] A. Gulino[a,b]

[a]Department of Chemical Sciences, University of Catania, V.le A. Doria 6, 95125 Catania, Italy; [b]INSTM UdR of Catania, V.le A. Doria 6, 95125 Catania, Italy; [c]CNR-IMM, Strada VIII, 5, 95121 Catania, Italy; [d]Department of Earth and Sea Sciences, University of Palermo, Via Archirafi 22, 90123 Palermo, Italy; [e]Department of Chemical Sciences, University of Padova, Via Francesco Marzolo 1, 35131 Padova, Italy

Hybrid molecular–nanoparticle materials, obtained with a bottom-up approach, are suitable for the fabrication of functional nanostructures showing structural control and well-defined properties, i.e. optical, electronic or catalytic properties, in the perspective of applications in different fields of nanotechnology.[1] Gold nanoparticles (Au NPs) exhibit important chemical, electronic and optical properties, due to their size, shape and electronic structures.[2] In fact, Au NPs containing no more than 30-40 atoms are only luminescent because they can be considered as large molecules with discrete energy levels, while nano-sized Au NPs only show the surface plasmon resonance.[3] Hence, it appears that gold nanoparticles can alternatively be luminescent or plasmonic and this represents a severe constraint for their use as an optical material. The aim of this work was the fabrication of nanoscale assembly of Au NPs covalently anchored to each other by means of novel bi-functional porphyrin molecules, that work as bridges between different gold nanoparticles. This functional architecture shows a strong surface plasmon, due to the Au nanoparticles, and a strong luminescence signal coming from porphyrin molecules, thus, behaving like an artificial organized plasmonic and fluorescent network.[4] The self-assembly geometry of this porphyrin on the Au NPs was studied by investigation of the conformational properties of the porphyrin derivative at the DFT level. The morphology, electronic structure and optical properties of the conjugated Au NPs – porphyrin system were investigated by TEM, XPS, UV–vis and Luminescence. The present nanostructures can be used for plasmon-enhanced fluorescence, photocatalysis, nonlinear optics, etc. under atmospheric conditions since our system is not reactive to air nor to water and does not need to be stored in a vacuum or inert gas.



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Ferrate salts as stand-alone catalysts for chemical fixation of CO_2 into epoxides and aziridines

N. Panza,[a] F. Cargnoni,[b] R. Soave[b] M. Trioni[b] A. Caselli[a,b]

[a]Department of Chemistry, Università degli Studi di Milano, via Golgi 19, 20133 Milano, Italy. [b]CNR-SCITEC, Istituto di Scienze e Tecnologie Chimiche "G. Natta", via Golgi 19, 20133 Milano, Italy.

The exponential increase of carbon dioxide (CO_2) emission in the atmosphere, as the terminal product of all the carbon-based process for energy production (i.e. burning fossil fuels), have become an alarming problem which threaten the whole environment[1] and the utilization of CO_2 as a feedstock for chemical production is becoming remarkably attractive[2]. Thus, an enormous number of catalytic systems have been reported to be active in the transformation of CO_2 and epoxides into cyclic carbonates, which find application in both industrial and fine chemistry. Most of these catalytic systems relies on a metal Lewis acid complex and an ammonium salt as nucleophilic co-catalyst[3]. We have recently disclosed that a well-defined Zn(II) complex of a pyridine containing macrocyclic ligand (Pc-L) is a competent catalyst for the CO_2 cycloaddition to terminal epoxides without the need of any nucleophilic co-catalyst[4]. We disclosed also that a "ferrate" salt of a protonated Pc-L ligand proved to be even more active than the previous zinc complex under relative mild reaction condition (100°C, 8 bar CO_2 pressure) without any added co-catalyst (Figure 1)[5].

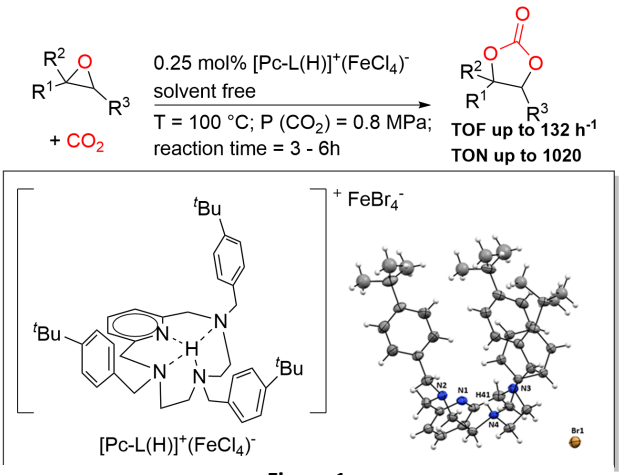

Figure 1

We report here the results obtained by using even simpler tetrabutylammonium ferrate salts (TBAFeX$_4$ with X = Cl, Br). TON values up to 1493 were obtained in the synthesis of styrene carbonate from styrene oxide and CO_2 using TBAFeBr$_4$. The catalyst can be recycled up to 3 times without any loss in activity or selectivity. TBAFeCl$_3$Br proved to be the best catalyst in terms of selectivity and a broad scope of epoxides was investigated. Early results on the reaction of aziridines with CO_2 to yield oxazolidinones using ferrate catalysts are promising. DFT studies were performed to study the reaction mechanism. A plausible equilibrium between the ferrate FeX_4^- and $FeX_3 + X^-$ in the neat epoxide could be responsible for the activity of this system, where the iron salt act as a Lewis acid activating the epoxide and X^- as a nucleophile for the ring opening reaction. The straightforwardness of the synthesis and handling of these salts compared to their iron and ammonium precursors, the possibility to modify the cationic and the anionic part of these salts, added to their impressive reactivity, open up the possible use of these catalyst in the valorisation of industrial flue gas.

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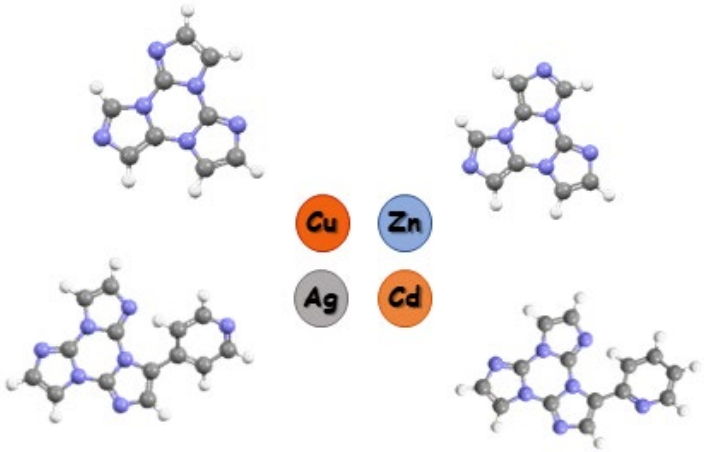
Cyclic triimidazole: an appealing and versatile ligand for the preparation of emissive d^9 and d^{10} metal derivatives

Elena Lucenti,[a] Alessandra Forni,[a] Chiara Botta,[a] Lucia Carlucci,[b] Marina S. Fonari,[c] Victor Ch. Kravtsov,[c] Daniele Malpicci,[ab] Daniele Marinotto,[a] Elena Cariati[ab]

[a]CNR-SCITEC, Istituto di Scienze e Tecnologie Chimiche "Giulio Natta", Milano, Italy; [b]Dipartimento di Chimica, Università degli Studi di Milano, Milano, Italy; [c]Institute of Applied Physics, Chisinau, Moldova.

The rich and peculiar photophysical properties of triimidazo[1,2-*a*:1',2'-*c*:1",2"-*e*][1,3,5]triazine or cyclic triimidazole (**TT**) and its pyridine-substituted derivatives, comprising dual fluorescence, molecular phosphorescence, supramolecular room temperature phosphorescence and crystallization induced emission, have been recently highlighted and associated to the formation of H aggregates due to strong π–π interactions in the crystal structure [1].
Moreover, we exploited the coordination possibilities of **TT**, displaying three available nitrogen atoms at the vertexes of a regular triangle, to prepare emissive mono-, di- and three-dimensional coordination networks of Cu(I) and Ag(I) [2-3]. In addition, the versatility of this ligand and its pyridine derivatives has been assessed through the realization of a library of Cu(II), Zn(II) and Cd(II) mononuclear and binuclear complexes displaying new architectures and various coordination modes [4-6]. The combined photophysical, theoretical and crystallographic study of these derivatives has allowed to elucidate some aspects involved in their emissive behavior such as the heavy-metal effect or the role of H aggregates, providing further knowledge on the realization of new solid-state materials with tunable emissions.



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[2] E. Lucenti, E. Cariati, A. Previtali, D. Marinotto, A. Forni, V. Bold, V. Ch. Kravtsov, M. S. Fonari, S. Galli, L. Carlucci, *Cryst. Growth Des.* **2019**, *19*, 1567.
[3] D. Malpicci, E. Lucenti, A. Forni, D. Marinotto, A. Previtali, L. Carlucci, P. Mercandelli, C. Botta, S. Righetto, E. Cariati, *Inorg. Chem. Front.* **2021**, *8*, 1312.
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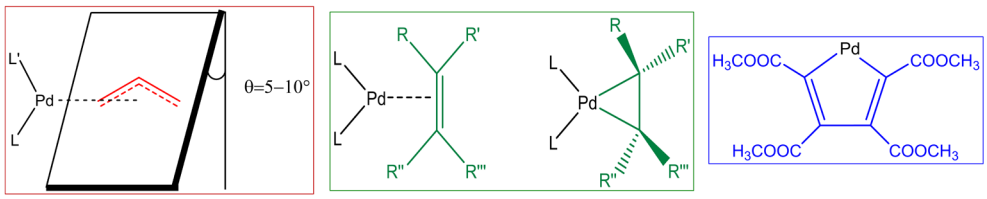
[5] E. Melnic, V. Ch. Kravtsov, E. Lucenti, E. Cariati, A. Forni, N. Siminel, M. S. Fonari, *New J. Chem.* **2021**, *45*, 9040.
[6] M. S. Fonari, V. Ch. Kravtsov, V. Bold, E. Lucenti, E. Cariati, D. Marinotto, A. Forni, *Cryst. Growth Des.* **2021**, *21*, 4184.

Palladium organometallic complexes as promising anticancer agents

Thomas Scattolin,[a,b] *Enrica Bortolamiol,*[a] *Flavio Rizzolio,*[a,b] *and Fabiano Visentin*[a]

[a]*Dipartimento di Scienze Molecolari e Nanosistemi, Università Ca' Foscari, Venezia-Mestre, Italy; Pathology Unit, Department of Molecular Biology and Translational Research, Centro di Riferimento Oncologico di Aviano (CRO) IRCCS, Aviano, Italy*

The severe limitations of chemotherapeutic protocols based on platinated agents, which are ascribable to non-negligible side effects on liver, kidneys, and brain and intrinsic or acquired resistance phenomena observed in some types of tumour [1], have prompted the development of new generations of anticancer agents based on metals other than platinum. The last two decades have seen a growing interest in coordination and organometallic palladium compounds as potential alternative anticancer drugs, inspired by its similar coordination chemistry to that of platinum. The good antiproliferative activity toward several tumor cell lines and their mode of action, which, in the few cases studied, appears sometimes quite different from that of cisplatin and its analogues, are the main reasons for the increasing popularity of palladium compounds as therapeutic agents [2]. A critical aspect that initially discouraged the study of palladium complexes as potential anticancer agents was their higher kinetic lability compared to that of their platinum congeners. The rapid hydrolysis of Pd-Ligand bonds generally results in the formation of very reactive species that are unable to reach the target biomolecules inside cancer cells. A possible strategy to reduce or even overcome this limitation, was the use of polydentate and/or bulky monodentate ligands strongly bound to the metal center [2]. Among these, palladium organometallic compounds have come to the fore for their good stability due to the presence of at least one strong Pd-C bond.
In this contribution we propose an overview of our recent results obtained with Pd(II)-allyl [3], Pd(0)-olefin [4] and palladacyclopentadienyl [5] complexes as promising anticancer candidates.
As a matter of fact, some of the tested compounds combined potent *in vitro* antiproliferative activity toward cisplatin-sensitive and cisplatin-resistant cell lines with a poor cytotoxicity toward normal cells. Interestingly, these properties were confirmed also on more complex biological systems such as tumoroids and organoids extracted from real patients.
Preliminary investigations dealing with their mechanism of action were obtained by means of immunofluorescence techniques, suggesting, in most of cases, a different mode of action compared to classical platinated anticancer agents.



η^3-allyl-Pd(II) fragment | η^2-olefin-Pd(0) fragment | Palladacyclopentadienyls

[1] R. Oun, Y. E. Moussa, N. J. Wheate, *Dalton Trans.*, **2018**, *47*, 6645.
[2] A. R. Kapdi, I. J. Fairlamb, *Chem. Soc. Rev.*, **2014**, *43*, 4751.
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[4] T. Scattolin, N. Pangerc, I. Lampronti, C. Tupini, R. Gambari, L. Marvelli, F. Rizzolio, N. Demitri, L. Canovese, F. Visentin, *J. Organomet. Chem.*, **2019**, *899*, 120857.
[5] T. Scattolin, I. Caligiuri, N. Mouawad, M. El Boustani, N. Demitri, F. Rizzolio, F. Visentin, *Eur. J. Med. Chem.*, **2019**, *179*, 325.

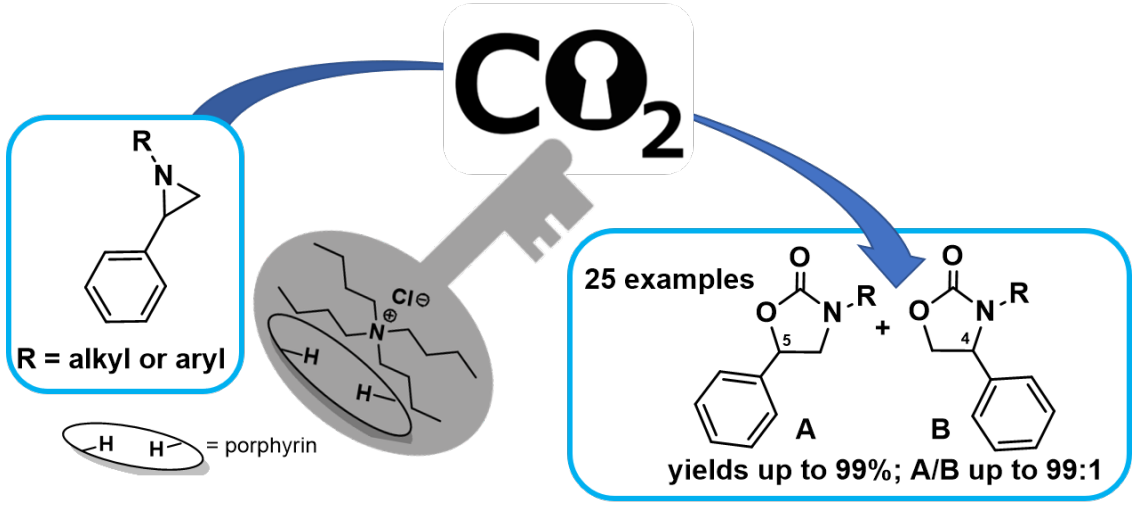
Efficient and low-cost metal-free Porphyrin/TBACl system for the CO_2 valorization into *N*-alkyl and *N*-aryl oxazolidin-2-ones

Caterina Damiano[a], *Paolo Sonzini*[a], *Matteo Cavalleri*[a], *Gabriele Manca*[b] *and Emma Gallo*[a]

[a]*Department of Chemistry, University of Milan, Via Golgi 19, I-20133 Milano, Italy;* [b]*Istituto di Chimica dei Composti OrganoMetallici, ICCOM-CNR, Via Madonna del Piano 10, I-50019 Sesto Fiorentino, Italy.*

Carbon dioxide is the primary greenhouse gas responsible for one-quarter of the atmospheric emissions. The need to reuse and valorize wastes to produce added value compounds has rendered the abundant CO_2 one of the most attractive C1 source for the synthesis of fine-chemicals and pharmaceuticals [1]. Considering the importance in developing eco-friendly synthetic processes, high attention has been devoted to the CO_2 cycloaddition to three-membered ring compounds, such as epoxides and aziridines to synthesize respectively cyclic carbonates and oxazolidin-2-ones with 100% of atom economy [2].

Unlike the commonly reported procedures, that usually involve harmful metal catalysts or promoters, we developed an eco-compatible, commercially available, and low-cost methodology able to efficiently promote the synthesis of *N*-alkyl and *N*-aryl oxazolidin-2-ones by the CO_2 cycloaddition to aziridines [3]. The combination of TBACl (tetrabutyl ammonium chloride) and 1% mol of $TPPH_2$ (tetraphenyl porphyrin) catalyzed the synthesis of a wide range of oxazolidin-2-ones in yields up to 99% and A/B regioselectivities up to 99:1, by employing a moderate CO_2 pressure and temperature (1.2 MPa and 125 °C) (Scheme 1). Collected data revealed that the catalytic performance was only slightly influenced by the porphyrin steric features and was not affected by the electronic properties of the catalyst. In addition, the combination of experimental results and DFT calculations allowed suggesting a reaction mechanism in which the $TPPH_2$/TBACl adduct played the key-role. The exoergonically formed adduct activated the aziridine ring towards the nucleophilic attack of the halogen atom by reducing the free energy barrier which is required for the uncatalyzed CO_2 coupling to *N*-alkyl and *N*-aryl aziridines.



Scheme 1. CO_2 cycloaddition to *N*-alkyl and *N*-aryl aziridines promoted by the $TPPH_2$/TBACl system.

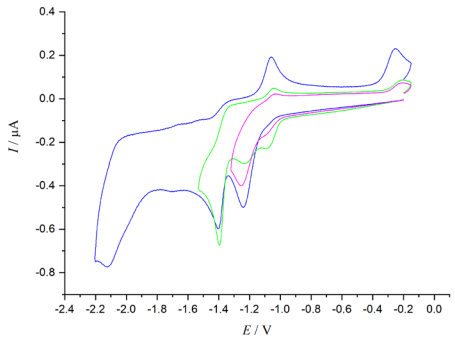
[1] a) A. W. Kleij, M. North, A. Urakawa, *ChemSusChem* **2017**, 10, 1036; b) Y. Yang, J.-W. Lee, *Chem. Sci*. **2019**, 10, 3905.
[2] D. Intrieri, C. Damiano, P. Sonzini, E. Gallo, *J. Porphyr. Phthalocyanines* **2019**, 23, 305.
[3] a) P. Sonzini, C. Damiano, D. Intrieri, G. Manca, E. Gallo, *Adv. Synth. Catal*. **2020**, 362, 2961; b) C. Damiano, P. Sonzini, G. Manca, E. Gallo, *Eur. J. Org. Chem*. **2021**, DOI: 10.1002/ejoc.202100365.

Transition metal complexes as redox catalysts for CO_2 conversion

Carlo Nervi,[a] Roberto Gobetto,[a] Laura Rotundo,[a] Arianna Tiozzo,[a] Alice Barbero,[a] Jan Fiedler[b]

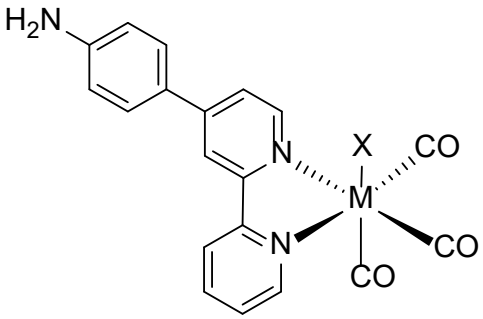
[a]Department of Chemistry, University of Turin, vi P. Giuria 7, 10125, Torino, Italy; [b]The J. Heýrovsky Institute of Physical Chemistry, Dolejsková 3, Prague, Czech Republic

Greenhouse gas anthropogenic emissions, in particular CO_2 with about 37 Gton/year, substantially contributes to the temperature increase of the Earth. In 2020, 87% of the Earth's surface was significantly warmer than the 1951-1980's average temperature. Conversion of CO_2 to renewable fuels is, in perspective, a valid strategy to pursue for mitigating the environmental effects.



In this contribution the electrochemical reduction of CO_2 catalyzed by selected transition metal complexes are presented [1]. Cyclic Voltammetry has been used to highlight catalytic activities in homogeneous solutions, exhaustive electrolysis to determine the TON values and DFT calculations as well as spectroelectrochemistry to investigate the details of the mechanism.

For example, the complexes *fac*-M(4(4-aminophenyl)-2,2′-bipyridine)$(CO)_3X$ (M=Mn, Re, X=Br, Cl) have been thoroughly studied in homogeneous solutions. The electrochemical behavior of the manganese derivative (M=Mn, X=Br) in acetonitrile solutions displays three irreversible reductions, the third being ligand-centered and located at rather negative potentials. Under CO_2 there is no apparent catalytic activity, but the presence of proton source (i.e. addition of 5% water) boosts the current of the second reduction.



To increase stability, TON and TOF values of this class of complexes, we link by a strong C-N covalent bond the intact organometallic complex to the electrode surface. This strategy has the following advantages: 1) it allows the design of organometallic catalyst, 2) it improves dramatically stability and durability as well as TON values, 3) it overcomes the problem of catalyst solubility, allowing to use any solvent (for example water, in which the complex is not soluble), 4) it minimizes slowness of the electron transfer because molecular distance between electrode and metal complex, 5) it minimize the amount of required catalyst, and finally 5) it allows the design of any electrode geometry.

This results in an impressive catalytic activity using water as solvent [2].

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Gold(I) and gold(III) complexes with thioether- and phosphonium-functionalized N-heterocyclic carbene ligands

Riccardo De Marco,[a,b] Marco Baron,[a] Laura Orian,[a] Claudia Graiff,[c] Thierry Achard,[b] Stéphane Bellemin-Laponnaz,[b] Marzio Rancan,[d] Lidia Armelao,[a,e] Cristina Tubaro[a,d]

[a] Dipartimento di Scienze Chimiche, Università degli Studi di Padova, via Marzolo 1, 35131 Padova, Italy; [b] Institut de Physique et Chimie des Matériaux de Strasbourg, CNRS-Université de Strasbourg UMR7504, 23 rue du Loess BP 43, 67034 Strasbourg, France; [c] Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università degli Studi di Parma, Parco Area delle Scienze 17/A, 43124 Parma, Italy; [d] ICMATE-CNR, Via F. Marzolo 1, 35131 Padova, Italy; [e] Dipartimento di Scienze Chimiche e Tecnologie dei Materiali, Consiglio Nazionale delle Ricerche, Piazzale A. Moro 7, 00185 Roma, Italy.

In the last few decades late transition metal complexes bearing N-heterocyclic carbene ligands (NHCs) have found several successful applications, for example as homogenous catalysts, metallodrugs or luminescent materials. The success of this class of ligands can be attributed to numerous factors like their strong donating ability, which confers to the corresponding metal complexes a very high stability, their straightforward synthetic procedure and the possibility to tune their steric and electronic properties by changing the nitrogen or backbone substituents. Additionally, it is possible to introduce a second donor group (usually P, O or N) in the pendant nitrogen substituent, thus possibly giving bidentate ligands.[1]

In this regard, complexes with N-heterocyclic carbenes bearing a thioether pendant function or a phosphonium function could find application in the field of medicinal chemistry as anticancer drugs.

Particularly, the sulfur atom on the ligand could exert a chemoprotective effect towards biological molecules, taking advantage of the potential hemilabile behavior involving a strong σ-donor function (the NHC moieties) and a weaker one (the sulfur atom). The chemoprotective action and cytotoxic properties of sulfur-containing NHC ruthenium and platinum complexes have been recently reported.[2]

Regarding the triphenylphosphonium moiety (TPP), it has been demonstrated that it acts as a delocalized lipophilic cation, efficiently penetrating mitochondrial membranes and accumulating in mitochondria. Therefore, using TPP moiety could be a great strategy to afford mitochondria-targeted organometallic compounds.[3]

In this contribution, we describe our recent results on the coordinating properties of this type of ligands towards gold(I) (Figure 1) and gold(III) metal centers.

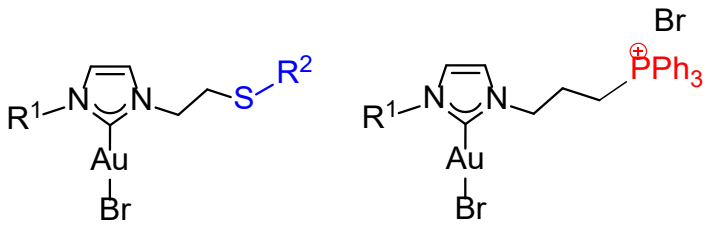


Figure 1. Gold(I) complexes with thioether and phosphonium functionalized NHC ligands

[1] H. V. Huynh, *The Organometallic chemistry of N-heterocyclic carbenes* **2017**, Hoboken, NJ: John Wiley & Sons, Inc.

[2] a) W. Chen, J. Egly, A. I. Poblador-Bahamonde, A. Maisse-Francois, S. Bellemin-Laponnaz, T. Achard, *Dalton Trans.* **2020**, *49*, 3243. b) J. Egly, M. Bouché, W. Chen, A. Maisse-François, T. Achard, S. Bellemin-Laponnaz, *Eur. J. Inorg. Chem.* **2018**, 159.

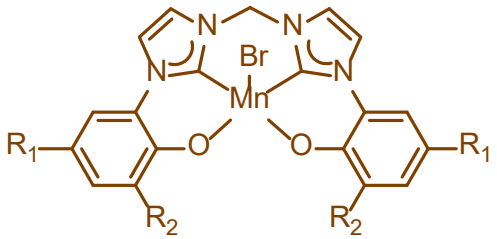
[3] J. Zielonka, J. Joseph, A. Sikora, M. Hardy, O. Ouari, J. Vasquez-Vivar, G. Cheng, M. Lopez, B. Kalyanaraman, *Chem. Rev.* **2017**, *117*, 10043.

Manganese(III) complexes with tetradentate O^C^C^O ligands: synthesis, characterization and preliminary catalytic studies on the CO_2 cycloaddition with epoxides

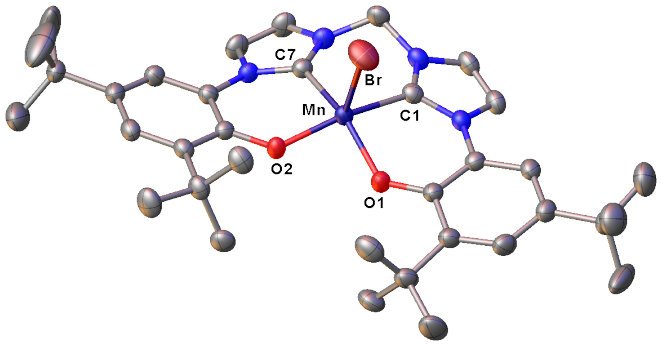
M. Baron,[a] G. Meloni,[a] L. Beghetto,[a] C. Graiff,[b] P. Centomo,[a] M. Mba-Blàzquez,[a] C. Tubaro,[a] A. Biffis[a]

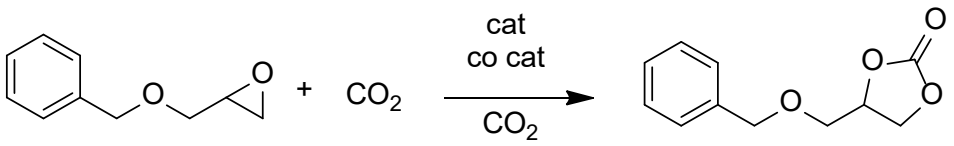
[a]Dipartimento di Scienze Chimiche, Università degli Studi di Padova, Via F. Marzolo 1, 35131 Padova, Italy; [b]Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università degli Studi di Parma, Parco Area delle Scienze 17/A, 43124 Parma, Italy.

Tetradentate bis(phenolate) ligands of general formula $[ODDO]^{2-}$ (D = neutral donor) are very popular in coordination chemistry and homogeneous catalysis. The most studied version of these ligands is the $[ONNO]^{2-}$, with Salen, Salan and Bapem metal complexes that find application in different catalytic reactions, the most famous of which is the manganese catalyzed asymmetric olefin epoxidation developed by Jacobsen.[1] The $[OSSO]^{2-}$ and $[OPPO]^{2-}$ ligand families have also been reported and used, with group (IV) metals, in olefin polymerization reactions.[2,3] Less known and developed is the $[OCCO]^{2-}$ version of this type of ligands,[4] in which the neutral donors are carbon donors. In this contribution we report on the synthesis and characterization of three tetradentate bis(N-heterocyclic carbene)-bis(phenolate) manganese(III) metal complexes. The obtained organometallic species of general formula [MnBr(OCCO)], have been used in the cycloaddition of CO_2 with epoxides to obtain the corresponding cyclic carbonates. Preliminary catalytic data will be presented.



[MnBrL^1] R = R = H
[MnBrL^2] R^1 = *t*Bu, R = H
[MnBrL^3] R^1 = R = *t*Bu
1 2





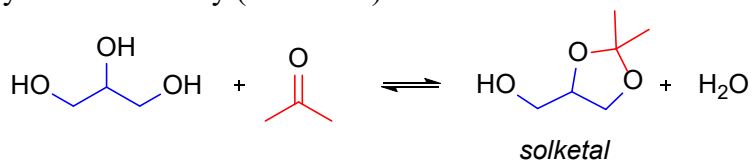
[1] Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112* (7), 2801–2803.
[2] Nakata, N.; Toda, T.; Ishii, A. *Polym. Chem.* **2011**, *2* (8), 1597–1610.
[3] Long, R. J.; Jones, D. J.; Gibson, V. C.; White, A. J. P *Organometallics* **2008**, *27* (22), 5960–5967.
[4] Kunert, R.; Philouze, C.; Jarjayes, O.; Thomas, F. *Inorg. Chem.* **2019**, *58* (12), 8030–8044.

MOF catalyzed ketalization of glycerol into *solketal*

*Massimo Melchiorre,[a] Maria Elena Cucciolito,[b,c] Vincenzo Russo,[b,c] Martino Di Serio, [b,c] Francesco Ruffo[b,c] and Roberto Esposito.[b,c]**

[a]ISUSCHEM s.r.l.; [b] Università degli Studi di Napoli Federico II; [c]Consorzio Interuniversitario di Reattività Chimica e Catalisi.

The world demand of biofuels has led to the increasing production of biodiesel and the consequent market invasion of the byproduct of its synthesis, glycerol, whose production reaches 20 ktons per year. The large availability of this variously functionalizable molecule is an opportunity to set up virtuous routes to produce different commodities starting from wastes of other industrial productions. *Solketal* is the ketal obtained by the acid catalyzed ketalization of glycerol with acetone and has many uses in industry (Scheme 1).[1]



Scheme 1. Ketalization of glycerol with acetone.

In the recent past, our research group found that different iron(III) salts and complexes are very active homogeneous catalysts for this reaction.[2]
In this work the high activity of this metal is unified with the opportunity to recover and recycle the catalyst adopting a heterogeneous iron(III) catalyst belonging to the category of *MOF*s. These interesting materials mix advantages of both heterogeneous, such as recyclability, and homogeneous catalysis, such as the fine tuning and rationalizing of the chemical environment of the metal center.
The chosen MOF is the *MIL88A* because of the simple synthesis, which is carried out in water, and its stability in polar solvents. In the optimized conditions (reflux temperature, 5% mol cat./mol glycerol, 8:1 acetone to glycerol molar ratio) the catalysts can be recycled several times, reaching very high conversions within 1.5h (Figure 1).

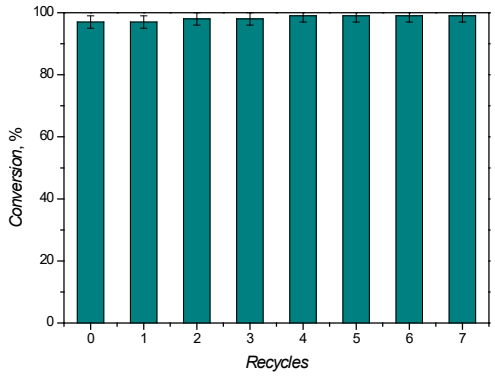


Figure 1. Recycles of the *MIL88A* in the ketalization of glycerol with acetone.

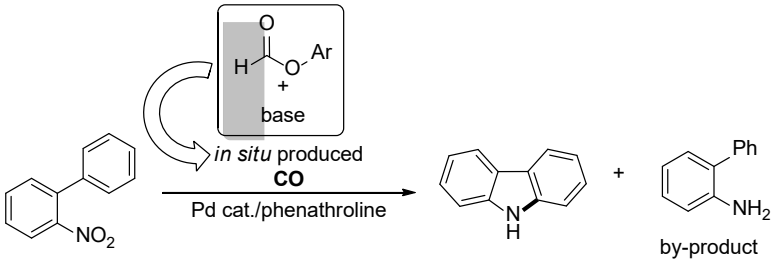
[1] C.-H. Zhou, J. N. Beltramini, Y.-X. Fan, G. Q. Lu, *Chem. Soc. Rev.* **2008**, *37*, 527-549.
[2] a) R. Esposito, M. E. Cucciolito, A. D'Amora, R. Di Guida, F. Montagnaro, F. Ruffo, *Fuel Process. Technol.* **2017**, *167*, 670-673; b) R. Esposito, U. Raucci, M. E. Cucciolito, R. Di Guida, C. Scamardella, N. Rega, F. Ruffo, *ACS Omega* **2019**, *4*, 688-698; c) F. Taddeo, R. Esposito, V. Russo, M. Di Serio, *Catalysts* **2021**, *11*, 83.

Heterocycles from nitro compounds: CO surrogates in the Pd-catalyzed synthesis of carbazoles

Francesco Ferretti, Doaa Ramadan, Fabio Ragaini

[a] *Dipartimento di Chimica, Università degli Studi di Milano, via Golgi 19, Milano, 20133, Italy.*
Email: francesco.ferretti@unimi.it

Palladium complexes with phenanthroline ligands are so far the most effective catalysts for the reductive cyclization of nitroarenes by carbon monoxide to yield a variety of N-heterocyclic compounds.[1] Despite the high efficiency of many of these reactions, they have not become of widespread use. This is mainly attributed to the need for pressurized CO (requiring specific safety measures). In the aim of turning this kind of reaction into a "general tool" for the synthetic chemist, we developed a procedure based on the use of formates as an *in situ* source of CO. The reaction can be performed in a glass pressure tube, a cheap equipment accessible to every laboratory. The method was employed for the synthesis of indoles[2] and oxazines,[3] affording the products in very good to excellent yields. However, when applied to the cyclization of *o*-nitrobiphenyls to carbazoles the method gave only poor yields. Herein we report a modified catalytic protocol for carbazole synthesis that tolerates both air and moisture and can be easily scaled up to gram scale reaction. Studies on the role of the metal in the cyclization step will be also discussed.



Scheme 1. Reductive cyclization of 2-nitrobiphenyls to carbazoles using formates as CO source.

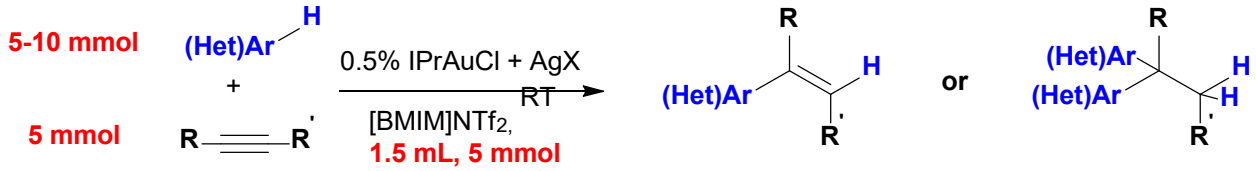
[1] a) Ferretti, D. R. Ramadan, F. Ragaini, *ChemCatChem* **2019**, *11*, 4450; b) F. Ferretti, D. Formenti, F. Ragaini, *Rend. Fis. Acc. Lincei* **2017**, *28*, 97; c) F. Ragaini, S. Cenini, E. Gallo, A. Caselli, S. Fantauzzi, *Curr. Org. Chem.* **2006**, *10*, 1479.
[2] D. Formenti, F. Ferretti, F. Ragaini, *ChemCatChem* **2018**, *10*, 148.
[3] M. A. EL-Atawy, D. Formenti, F. Ferretti, F. Ragaini, *ChemCatChem* **2018**, *10*, 4707.

Gold catalyzed direct alkyne hydroarylations in ionic liquids: a powerful tool in organic synthesis

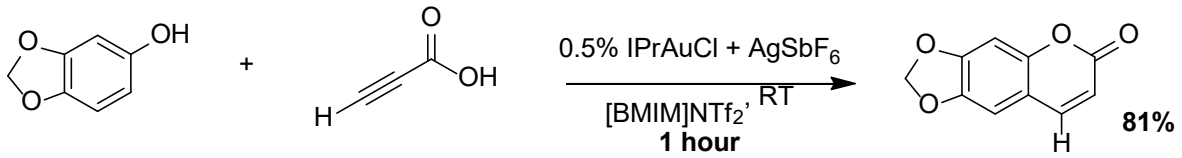
Pietro Bax, Sara Bonfante, Andrea Biffis

Dipartimento di Scienze Chimiche, Università di Padova, via Marzolo 1, 35131 Padova, Italy.

Among the numerous C-H bond functionalization reactions that have been disclosed and developed in recent years, the direct hydroarylation of alkynes shows great potential for practical applications, since it produces no waste and often exhibits a high, tunable and peculiar chemo-, regio- and stereoselectivity.[1,2]



We have recently disclosed that cationic gold(I) complexes in ionic liquids (ILs) as reaction media. display high activities under neutral conditions in direct alkyne hydroarylation reactions.[3] Furthermore, we have demonstrated that in the case of aromatic heterocycles as substrates the reaction chemoselectivity between mono- and bis-hydroarylation products can be controlled, acting in particular on the solubility of reagents and products in the IL. In this contribution, we report on optimization studies involving both the ligand L supporting the gold(I) centre and the characteristics of the employed IL, in particular the nature of the anion. Further to this, we present our latest efforts towards the practical exploitation of this reaction for the sustainable preparation of organic products of technological interest. In particular, we have targeted the one pot synthesis of coumarins from phenols and propiolic acids/esters, in which phenol hydroarylation is followed by a cyclization step. The effect of the substituents at the aromatic ring and at the alkyne are discussed. We demonstrate that the reaction can be performed with a variety of substituted substrates while maintaining a high level of catalytic efficiency.



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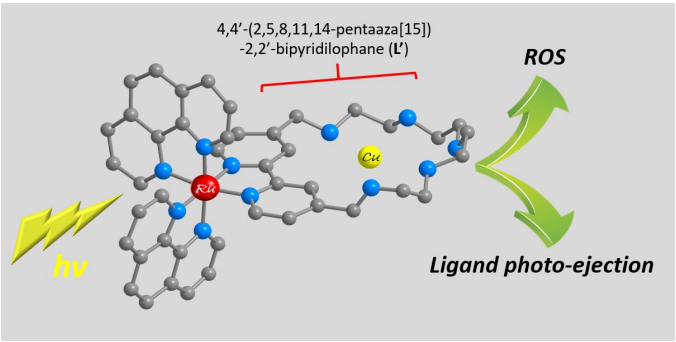
Ru(II) polypyridyl complexes as promising light-responsive agents for biological application

Luca Conti,[a] Gina Elena Giacomazzo,[a] Claudia Giorgi,[a] Annalisa Guerri,[a] Marco Pagliai,[a] Silvia Ciambellotti,[a,b] Paola Turano [a,b] Francesca Cencetti,[c] and Barbara Valtancoli[a]

[a]Department of Chemistry 'Ugo Schiff', Via della Lastruccia 3, 50019, Sesto Fiorentino, Italy; [b]Magnetic Resonance Center (CERM), University of Florence, 50019 Sesto Fiorentino, Italy; [c]Department of Experimental and Clinical Biomedical Sciences, University of Florence, Italy.

The widely known drawbacks associated to the use of commonly employed antitumoral drugs, as *cis*-platin for example, along with the increasing multidrug resistance of bacterial pathogens make it urgent to develop new and effective antitumoral as well as antimicrobial agents, which should be based on a new class of compounds, rather than on analogues of known scaffolds.
In this scenario, ruthenium(II) polypyridyl complexes represent an attractive class of compounds due to their rich chemical-physical repertoire, which includes good singlet oxygen sensitizing properties, absorption profiles that can be modified by a fine choice of the spectator ligands and good ability to interact with key biological targets, such as proteins or DNA[1].
In this work we studied a series of ruthenium(II) polypyridyl compounds featuring different ancillary ligands and containing peculiar polyamino-macrocycles, (such as **L'** in Figure). The



polyamino residues not only confer to the resulting compounds high solubility in water without altering the singlet oxygen sensitizing properties of the ruthenium centers but even strengthen their interaction with ct-DNA, thus providing optimal candidates in the PDT (photodynamic therapy) approach. Moreover, these moieties can also host additional metal ions, such as the Fenton-active Cu(II) ion, affording mixed Ru(II)/Cu(II) species able to reinforce the production of ROS (reactive oxygen species). Following a first chemical-physical characterization, the biological potential of the most promising compounds was tested against A375 human melanoma[2] and A2780 ovarian cancer cells, as well as against *B. subtilis*, chosen as a model of gram-positive bacteria[3].
In addition, the design of the ruthenium scaffolds was varied to achieve the ligand-photoejection of bioactive compounds upon exposure to low-energy visible light, thus providing alternative mechanisms of action independent by the presence of molecular oxygen, required to produce ROS species through a classical PDT approach.
The aim of this contribute is to highlight the versatility of ruthenium(II) polypyridyl complexes in the development of effective therapeutic agents with widespread biological application.

[1] F. E. Poynton, S. A. Bright, S. Blasco, D. C. Williams, J. M. Kelly, T. Gunnlaugsson, *Chem. Soc. Rev.*, **2017**, *46*, 7706-7756.
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Development of sustainable and green methodologies for homogeneous gold(I) catalysis

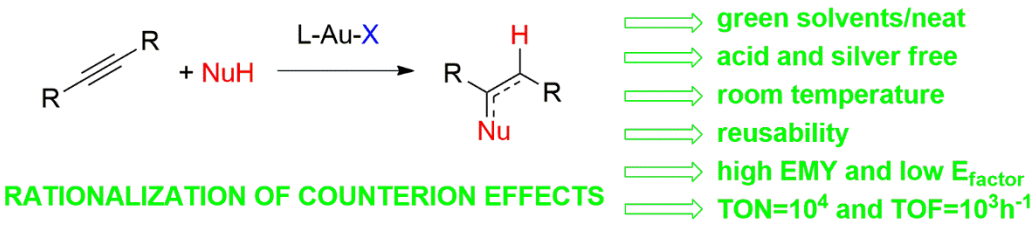
Jacopo Segato,[a] Filippo Campagnolo,[a] Diego Sorbelli,[b] Alessandro Del Zotto,[a] Leonardo Belpassi, [b]Paola Belanzoni, [bc] and Daniele Zuccaccia [a]

[a]Dipartimento di Scienze Agroalimentari, Ambientali e Animali, Sezione di Chimica, Università di Udine, Via Cotonificio 108, I-33100 Udine, Italy; [b]Istituto di Scienze e Tecnologie Chimiche "Giulio Natta" (SCITEC), Consiglio Nazionale delle Ricerche c/o, Dipartimento di Chimica, Biologia e Biotecnologie, Università degli Studi di Perugia, Via Elce di Sotto 8, 06123 Perugia, Italy; [c]Department of Chemistry, Biology and Biotechnology, University of Perugia, via Elce di Sotto 8, 06123 Perugia, Italy.

Gold(I) complexes of general formula [L-Au$^{+\cdots}$X^{-}] are successfully employed as catalysts in the activation of the triple carbon-carbon bond towards nucleophilic attack. A key role in such reactions is played by the counterion (X^{-}).[1]

There are very few examples of gold homogeneous catalysts that work in green and sustainable conditions (without using silver and acid additives, with low catalyst loading, at RT, with recovery of the catalytic system, in neat conditions[2] or in neoteric solvents). In this contribution, we report systematic experimental and theoretical data about the role of the anion in gold(I) catalysis obtained by combining multinuclear NMR spectroscopy and Density Functional Theory calculations. We have studied the cycloisomerization of N-propargylcarboxamide,[3] the Meyer–Schuster rearrangement of 1-phenyl-2-propyn-1-ol via 4-endo-dig cyclization[4] and the methoxylation of alkynes.[5]

The overall experimental evidence, supported by computational results, confirms that the anion plays a crucial role in all steps of the reaction mechanism: pre-equilibrium, nucleophilic attack, and protodeauration.[4] This complete rationalization of the counterion effect allowed us to: 1) develop a highly efficient methodology under solvent-, silver-, and acid-free conditions[5] and 2) replace traditional volatile organic solvents with more eco-friendly ones.



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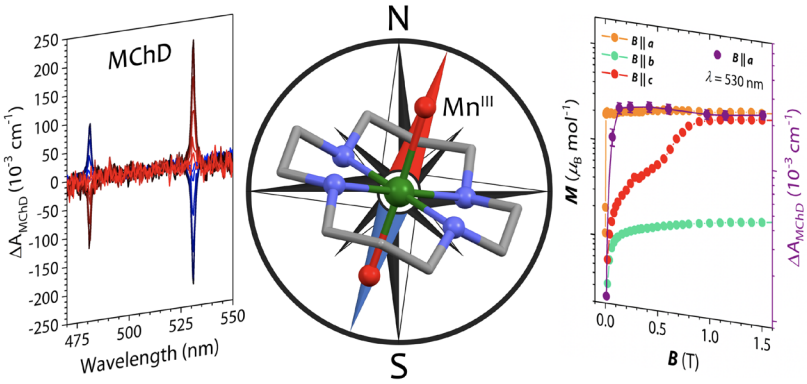
Magneto-chiral dichroism in chiral molecular magnets

Matteo Atzori,[a] Elizabeth Hillard,[b] Andrea Caneschi,[c] Roberta Sessoli,[c] Herbert Ludowieg,[d] Jochen Autschbach,[d] Fabrice Pointillart,[e] Boris Le Guennic,[e] Jeanne Crassous,[e] Geert Rikken,[a] Cyrille Train[a]

[a]Laboratoire National des Champs Magnétiques Intenses (CNRS), Grenoble, France; [b]Université de Bordeaux, Pessac, France; [c]Università degli Studi di Firenze, Firenze, Italy; [d]State University of New York, New York, USA; [e]Université de Rennes, Rennes, France.

Magneto-Chiral Dichroism (MChD) is a fascinating but scarcely investigated manifestation of light-matter interaction specific of chiral magnetized systems. It features an unbalanced absorption or emission of unpolarized light that depends on the relative orientation of the applied magnetic field and the light wavevector and the absolute configuration of the system.[1,2] Its relevance is related to potential technological applications, such as the optical read-out of magnetic data, and its possible implication as a mechanism for the emergence of life homochirality.

With this communication I will provide an overview of the most recent results we have achieved on this topic, that are aimed at understanding the microscopic parameters and the chemical ingredients that are key to observe strong MChD responses. I will present the MChD observed up to ca. 40 K in a chiral ferrimagnet with a high T_c based on Mn^{II} and Cr^{III} ions,[3] the key-role of spin-orbit coupling in driving MChD signals in a single-chain magnet based on tetragonally distorted Mn^{III} ions,[4] and the strong MChD observed for a chiral Yb^{III}-helicene complex detected by near-infrared light absorption.[5] Finally, I will present the first comparison between experimental MChD spectra and those theoretically calculated through quantum chemical calculations, showing the fundamental role of vibronic coupling in enhancing the intensity and determining the shape of the MChD signals of chiral Ni^{II} complexes.[6]



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[6] M. Atzori *et al. Sci. Adv.* **2021**, *7*:eabg2859.

Anticancer and photophysical properties of a N^C^N-coordinated Pt(II) complex

Stefano Scoditti[a], *Eslam Dabbish*[a], *Gloria Mazzone*[a] *and Emilia Sicilia*[a]

[a]*Department of Chemistry and Chemical Technologies, Università della Calabria, 87036, Arcavacata di Rende (CS), Italy*

Pt(II) complexes are very effective anticancer agents that are used in a lot of chemotherapeutic regimens administered in clinical enviroments. These complexes, with general structure $[Pt(X)_2(L)_2]$, are still among the most frequently used drugs. However, they appear to be toxic because of their chemical reactivity and instability. These issues, have represented an impetus for the development of novel Pt-based anticancer chemotherapeutic drugs that, working with different modes of action, can have maximal curative potential and less systemic toxicity and internal resistance.
Cyclometalated platinum(II) complexes containing tridentate π-conjugated organic ligands have been receiving an increase of interest as they display rich and diverse photoluminescent properties that are sensitively affected by the local environment[1,2]. These complexes can exert their cytotoxic action via classical mode of action, aquation and subsequently covalent binding to the DNA base pairs or by reversible interactions such as intercalation. In fact, the planar motif of the ligand can render the complex able to establish non-covalent π- π interactions.
The investigation of the antiproliferative properties of this kind of complexes has demonstrated that they are promising photosensitizers under visible light, capable to produce singlet oxygen[2]. The photophysical properties of the complex Pt(N^C^N)Cl, where the N^C^N ligand is 2,6-dipyrido-4-methyl-benzenechloride, are investigated in detail by means of DFT and its TD-DFT time-dependent extension together with Molecular Dynamics simulations. The suitability of the investigated complex to act as a photosensitizer has been verified calculating spectroscopic properties for both the unperturbed complex and its aquated and guanine bound forms. Using Molecular Dynamics simulation outcomes as starting point, the photophysical properties of both the DNA intercalated complex and the complex bound to DNA have been evaluated aiming at establishing how such interactions can affect the activity of the complex under examination.

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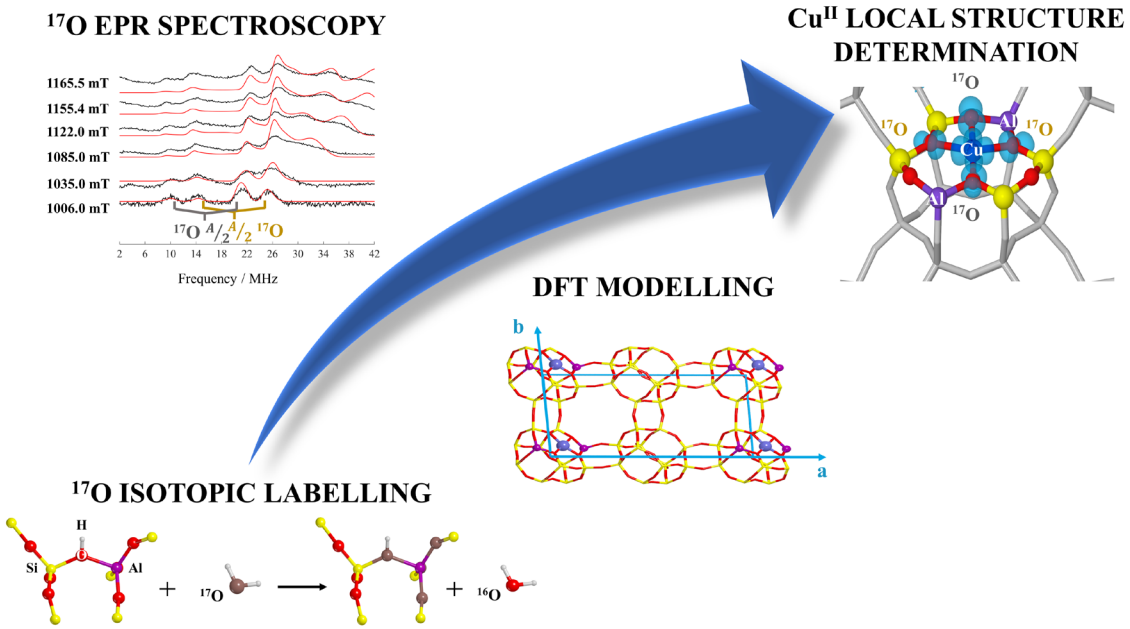
^{17}O spin density studies of single-metal sites in Cu-CHA zeolites

Paolo Cleto Bruzzese,[a,b] Enrico Salvadori,[b] Stefan Jäger,[c] Martin Hartmann,[c] Bartolomeo Civalleri,[b] Andreas Pöppl[a] and Mario Chiesa[b]

[a]Felix Bloch Institute for Solid State Physics, Universität Leipzig, Linnéstr. 5, 04103 Leipzig, Germany; [b]Dipartimento di Chimica, Università di Torino and NIS Centre, via P. Giuria 7, 10125, Torino, Italy; [c]Erlangen Center for Interface Research and Catalysis (ECRC), Egerlandstr. 3, 91058 Erlangen, Germany



Copper-exchanged Chabazite zeolites have received remarkable research interest in the last decades due to their incredible capabilities in NO_x removal and direct conversion of methane to methanol.[1,2] The catalytic properties of Cu-based catalysts are strictly related to the degree of covalency in the ligand-metal bond which is the key to activate electron transfer pathways,[3] enhance catalyst stability and stabilize intermediate species in redox reactions.[4,5] Detailed information on the Cu-O bonding interaction can be obtained through the detection of the ^{17}O hyperfine interaction, which is a direct reflection of the spin delocalization over the coordinating ligands and a direct probe of the metal-ligand covalent character. By selective ^{17}O isotopic labelling of the zeolite framework, in conjunction with advanced EPR methodologies and DFT modelling, we recover the ^{17}O hyperfine interactions associated with Cu-O bonds. This enables to determine the local structure of single site Cu^{II} species, to assess the siting of Al in the most stable Cu coordination and to follow the migration of Cu^{II} species across the zeolite channels as a function of hydrating conditions.

This work is part of a project that has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie Grant agreement no. 813209.

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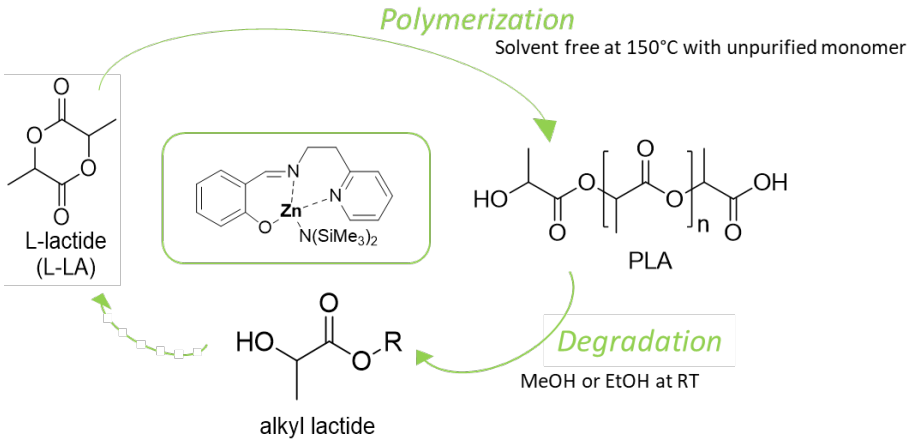
A single catalyst for the synthesis and chemical depolymerization of polylactide

Federica Santulli,[a] *Marina Lamberti*,[a] *Mina Mazzeo*[a]

[a]*Dipartimento di Chimica e Biologia "Adolfo Zambelli", Università degli Studi di Salerno, Via Giovanni Paolo II, 84084 Fisciano, SA, Italy, e-mail: fsantulli@unisa.it*

Petrochemical-based plastics have a significant impact on modern society, as underlined by their innumerable applications, and deep interweavement with human life.
Although these materials have been designed to last over time, today about 40% are used in the short-term packaging field and their end life destiny is mainly the storage in landfills or dispersion into the environment [1]. Over the years this behavior led to a strong accumulation of plastic in the oceans and on land, causing a derangement of the global ecosystems. Despite the highly negative impact that plastics have on the environment, it is almost impossible to eliminate them. Therefore, the implementation of a circular model economy of plastics is mandatory.
In this context, biodegradable polymers produced by renewable resources represent a great opportunity [2].
Among biopolymers, the best candidate as commodity is polylactide (PLA) that, thanks to its good mechanical properties, can be used in various fields such as agriculture, textiles, and packaging. However, its end life destiny is currently aligned to a linear productive model and thus, despite its potentialities, this material still contributes to plastic pollution. A desirable end- of- life path for PLA is chemical recycling through alcoholysis in which the product, alkyl lactate, can be converted into lactide, making it an entirely circular economy process, or used as a green solvent in chemical industries [3].
In this work, a new and easy-to-obtain zinc complex was synthesized, which revealed to be exceptionally efficient to promote both the synthesis and the chemical depolymerization of PLA.



In detail, the zinc complex showed a remarkable activity in the polymerization of lactide under industrial conditions, i.e., high temperature, without any solvent and by using unpurified monomers. The same system efficiently promoted the depolymerization of commercial PLA products via ethanolysis performed at room temperature and in the absence of solvent.

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Pt(IV) bifunctional complexes as anticancer agents: "*is this true glory?*"

Mauro Ravera,[a] *Maria Grazia Bottone*,[b] *Elisabetta Gabano*[a]

[a]*Dipartimento di Scienze e Innovazione Tecnologica, Università del Piemonte Orientale, Viale Michel 11, 1521 Alessandria (Italy).* [b]*Dipartimento di Biologia e Biotecnologie "L. Spallanzani", Università di Pavia, Via Ferrata 9, 27100 Pavia, (Italy).*

Since the approval of cisplatin as an anticancer agent in the distant 1978, a large number of platinum compounds have been proposed with the aim of finding improved drugs. As a result of these enormous efforts, the new Pt-based drugs that received approval can be counted on the fingers. Advancements in the understanding of cancer and of the intimate mechanism by which Pt interacts with "biological environment" were the driving force behind a current paradigm shift in metal-based drug research. In this paradigm shift the attention moved from the design of a molecule with a single target (DNA) to compounds targeting different and multiple pathways or biological networks, with greater selectivity, also by virtue of "non-classical" operating mechanisms.
Octahedral Pt^{IV} complexes are an attractive alternative to square-planar Pt^{II} compounds. The rationale behind their development was that the nontoxic Pt^{IV} prodrugs, upon entry into the reducing environment of the tumor tissue, would be activated by a $2e^-$ reduction, to form their cytotoxic Pt^{II} active metabolite with concomitant loss of the two axial ligands. Moreover, the coordination of a second anticancer agent in an axial position allows the combination of two complementary drugs into a single molecule (*bifunctional drug*) able to target multiple pathways (on paper at least) [1].
To date, a significant number of Pt^{IV} complexes with a variety of bioactive ligands have been synthesized and investigated [2,3]. However, bifunctional Pt^{IV} prodrugs are generally more active than their Pt^{II} parent by virtue of the axial ligands that impart increased lipophilicity and, hence, cell uptake. The key point is to understand if the axial ligand plays a true, active role.
In this framework, two Pt^{IV} complexes containing perillic acid (4-isopropenylcyclohexene-1-carboxylic acid) were synthesized and tested *in vitro* on several human tumor cell lines, including some highly chemoresistant malignant pleural mesothelioma cells. In particular, the complex *cis*,*cis*,*trans*-$[Pt^{IV}Cl_2(NH_3)_2(perillato)_2]$ (**2**, Figure 1) exhibited excellent antiproliferative and antimetastatic activity on A-549 lung tumor cells at nanomolar concentrations [4].

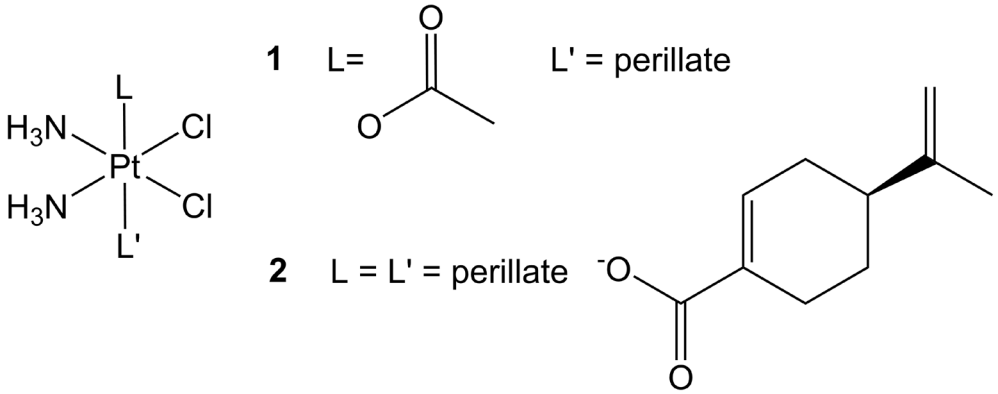

Figure 1: Sketch of the compounds under investigation

[1] D. Gibson, *J. Inorg. Biochem.* **2021**, *217*, 10.
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Solid acid catalysts for glucose hydrolysis: quantification of Lewis and Brønsted acid sites using 2,6-dimethylpyridine

Alessia Giordana[a], *Cristina Pizzolitto*[b], *Michela Signoretto*[b], *Marco Daturi*[c], *Lorenza Operti*[a], *Giuseppina Cerrato*[a]

[a]*Dipartimento di Chimica, Università degli Studi di Torino;* [b]*Dipartimento di Scienze Molecolari e Nanosistemi, Università Ca' Foscari Venezia;* [c]*Laboratoire Catalyse&Spectrochimie, ENSICAEN, Université de Caen*

Alternative feedstocks are necessary to reduce dependence on non-renewable sources, and among them biomass represents the only renewable source of organic molecules for the manufacturing of chemicals and fuels, nowadays mainly derived from petrol. Catalysts cover great importance in the development of sustainable processes.
In this research we focus our attention on the valorisation of glucose, the sugar degradation products of cellulose. The mechanism of acid catalyzed glucose hydrolysis is supposed to start via isomerization to fructose, and continue through dehydration in 5-hydroxymethylfurfural that could be possibly hydrolyzed into levulinic acid. [1] The first step is supposed to be Lewis acid catalyzed, while dehydration/hydration reactions are catalyzed by Brønsted acid sites.
In this reaction we employed two acid solid catalysts having both kinds of acid sites, sulfated zirconia and sulfonated SBA, that show different selectivity [2]. The nature of surface acid sites of these catalysts was investigated using FTIR spectroscopy and 2,6-dimethylpyridine (2,6-DMP) as probe molecule [3]. To obtained quantitative data, molar absorption coefficients of relevant modes were determined by volumetric method, and used to calculate Lewis/Brønsted ratio. Results suggest that selectivity in acid catalyzed glucose hydrolysis depends on the amount and the strength of acid sites.

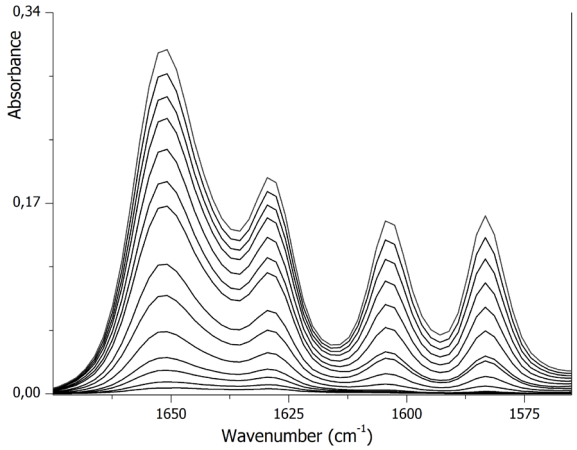

Figure 1. Differential spectra for increasing amounts of 2,6-DMP on SBA-SO_3H catalyst.

[1] (a) B. Agarwala, K. Kailasamb, R.S. Sangwana, S. Elumalai, *Renew. Sust. Energ. Rev.* **2018**, *82*, 2408; (b) S. Kanga, J. Fub, G. Zhang, *Renew. Sust. Energ. Rev.* **2018**, *94*, 340.
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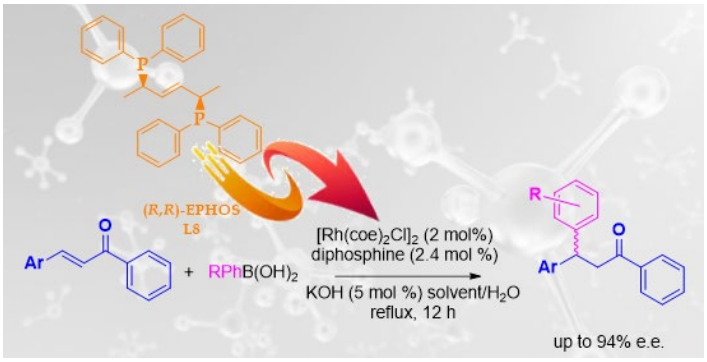
New sp^3 diphosphine-based rhodium catalysts for the asymmetric addition of aryl boronic acids to azaarenes

Giorgio Facchetti,[a] *Marco Fusè*,[b] *Tania Pecoraro*[c] *and Isabella Rimoldi*[a]

[a]*Department of Pharmaceutical Sciences, Università degli Studi di Milano, Via Venezian 21, 20133 Milano, Italy;* [b]*Scuola Normale Superiore, Piazza dei Cavalieri 7, 56126 Pisa, Italy;* [c]*Department of Molecular Biochemistry and Pharmacology, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milan, 20156, Italy*



Enantioselective catalysis using metal complexes provides one of the most general and flexible methods for the synthesis of chiral compounds [1,2]. In these regards, the proper combination of the selected metal with the correctly designed enantiopure ligand is the determining step for obtaining synthetic processes with high efficiency. Catalytic asymmetric conjugate reaction [3] stands out as one of the most useful method for the preparation of chiral compounds but although routinely employed, its application to the synthesis of chiral azaarenes has been scarcely investigated. Starting from our established expertise in the synthesis of chiral phosphine ligands [4,5] and in the field of asymmetric homogeneous catalysis, we prepared a novel chiral phosphorus ligand, hereafter called (*R*,*R*)-EPHOS, designed and synthesized starting from the optically active 1,4-(*E*)-2-butene taking inspiration from the *cis* analogue (*R*,*R*)-ZEDPHOS ligand. This new diphosphine features a stereogenic sp^3 carbon atom combined to the presence of a C_2 axial chirality, the one typically present in atropoisomeric diphosphines. Computational studies, supported by ^{31}P-NMR analyses shed light on the different coordination mode to the rhodium centre respect to (*R*,*R*)-ZEDPHOS, suggesting the ability of (*R*,*R*)-EPHOS to form complexes with phosphorus atoms disposed in *trans* configuration with respect to each other, with the C=C bond of the ligand in the metal centre coordination sphere. (*R*,*R*)-EPHOS together with other chiral diphosphines, was applied to the asymmetric rhodium catalyzed 1,4-addition of different substituted arylboronic acids to azaarenes. When applied to (*E*)-1-phenyl-3-(pyridin-2-yl)prop-2-en-1-one (**1**), (*R*,*R*)-EPHOS-based catalytic system afforded the product **1a** in a remarkable 94% e.e. [6].

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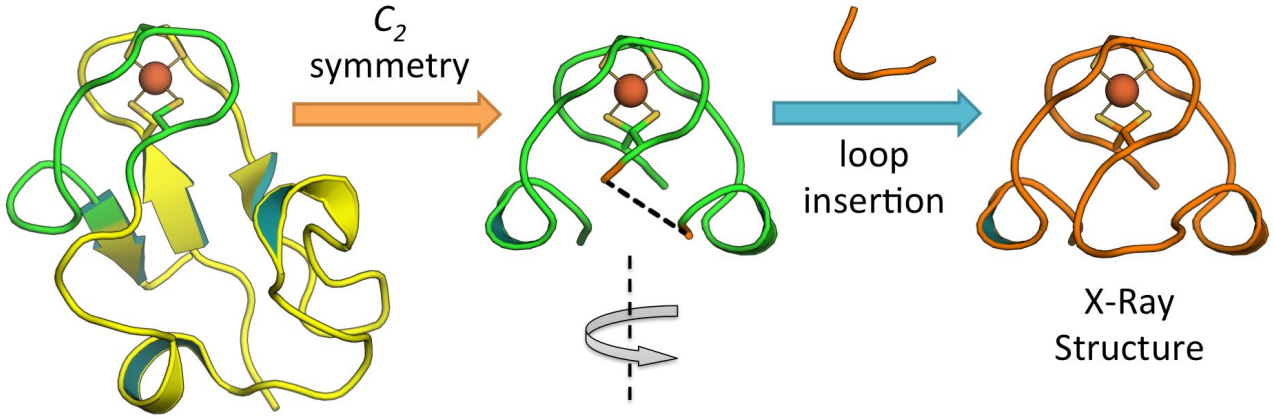
Design of a miniaturized FeS_4 protein

Marco Chino[a], *Salvatore La Gatta*[a], *Linda Leone*[a], *Luigi Di Costanzo*[a], *Angela Lombardi*[a], *Vincenzo Pavone*[a]

[a]*Department of Chemical Sciences, University of Naples "Federico II". Via Cintia 21, 80126 Napoli, Italy. marco.chino@unina.it*

Despite the great success of computational protein design in recent years,[1,2] the structure/function correlation of iron-binding proteins designed from scratch remained elusive. Explicitly, the rational arrangement of the first and second coordination interactions able to purposely select and stabilize the very labile iron chemistry is still a difficult task[3]. Besides in repurposed natural scaffolds or by exogenous ligands like porphyrins and polypyridines[4], iron-bound de novo proteins have never been structurally characterized before. We present, for the first time, the structural and functional features of a fully designed FeS_4 protein, namely METPsc. Inspired by natural rubredoxins, this miniaturized protein does not hold any sequence correlation to the known congeners, as assessed by BLASTP. Strikingly, METPsc 28-long sequence stores all the information required to fold around the metal in a tetrahedral geometry and to function as an electron-transfer protein, as confirmed by crystallography, UV-Vis and EPR spectroscopy, and cyclic voltammetry. Finally, we exploited its terminal electron acceptor properties in an artificial electron chain triggered by visible light. Its applicability in optoelectronics and light-harvesting biodevices is being explored.



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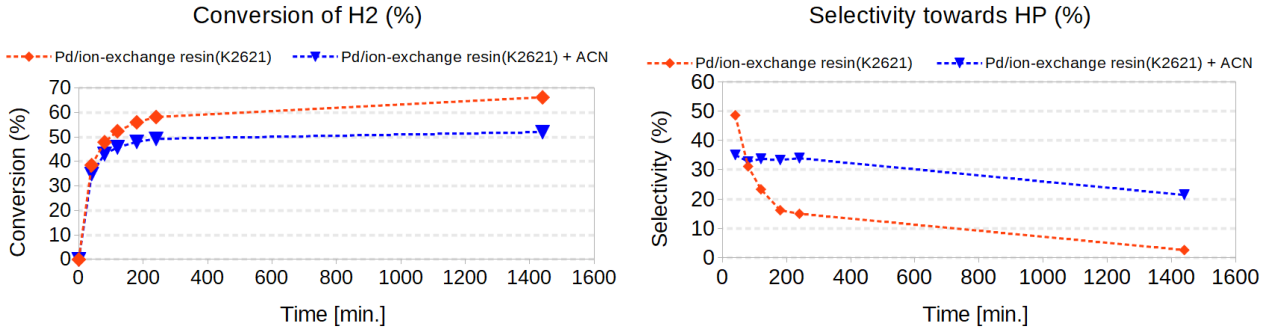
Selectivity enhancement of coordinating solvents on the direct synthesis of hydrogen peroxide

Francesco Sandri[a], *Francesco De Boni*[a], *Laura Orian*[a], *Francesco Sedona*[a], *Marco Zecca*[a], *Paolo Centomo*[a]

[a]*Dipartimento di Scienze Chimiche, Università di Padova, via Marzolo 1-I35131 Padova (Italy)*

The direct synthesis (DS) of hydrogen peroxide (HP) is a hot topic in heterogeneous catalysis, aimed at extending the scope of HP as an oxidant in chemical processes.[1,2] The DS is typically catalyzed by supported nanostructured palladium or palladium alloys. The selectivity of the catalysts is still a crucial issue. The use of inorganic acids and chloride or bromide ions as promoters is a well known and very effective way to enhance it, but due to corrosion problems this approach is unfit to industrial scale-up.[3] However. halides ions are well known ligands to palladium(II) and we occurred to us that other good coordinating, non-corrosive species could work as well. Thus, we investigated on the use of acetonitrile (ACN) as a co-solvent, in addition to methanol. The presence of ACN in general lowers the hydrogen conversion, similarly to halide ions. We found that it behaves also a selectivity enhancer if the support of the active metal bears groups apt to the ion-exchange of cations. With some differences depending on the polymer morphology, palladium catalysts supported on ion-exchange resins show remarkably improved HP selectivity and productivity in the presence of ACN, with only a moderate, if any, decrease in H_2 conversion. It was found to be particularly effective in semi-continuous tests at very long time on-stream, with selectivity several hundred percent higher than over the unpromoted catalysts, a very interesting finding from the technological point of view.



The characterization with XPS and HR-TEM showed that modifications of the Pd nanoparticles occur in the presence of ACN: In particular we observed the oxidation of the metal and its reconstruction to smaller nanoparticles. Palladium(II) complexes stabilized by ACN coordinated to the metal centers, which can be retained by the ion-exchange groups of the supports, could be the key of all the effects observed. Accordingly, other coordinating co-solvents, such as dimethylsulfox ide and dimethylformamide, were found to behave similarly, although to different extents depending on their nature. Different levels of palladium leaching with different co-solvents were detected too. Finally DFT calculations were carried out to correlate the stability of the palladium(II) complexes with the different co-solvents as ligands with their effects on the DS reaction. In conclusion, we report a novel catalytic system for the DS of HP at high conversion and selectivity, formed by palladium nanoparticles supported on ion-exchange resins, in which for the first time coordinating co-solvents are found to act as selectivity enhancers.

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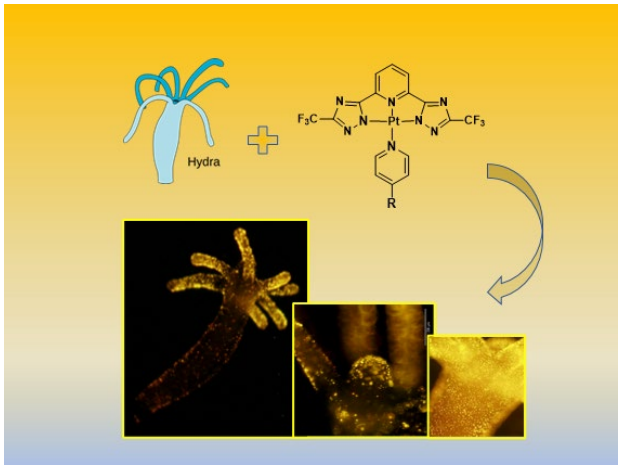
Luminescent self-assemblies of Pt(II) complexes *in vivo*

Tania Pecoraro[a], *Giorgio Facchetti*[b], *Isabella Rimoldi*[b], *Claudia Tortiglione*[c], *Alessandro Aliprandi*[d], *Luisa De Cola*[b]

[a]*Department of Molecular Biochemistry and Pharmacology, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, 2056 Milano;* [b]*Università degli Studi di Milano, 20133 Milano;* [c]*Consiglio Nazionale delle Ricerche Napoli, Campania,* [d]*Université de Strasbourg, ISIS, & CNRS UMR 7006, Strasbourg, France*

Recently, significant research efforts have been focused on the development of new Pt(II) complexes for their application as luminescent probe for cellular imaging. This application is limited by the quenching exerted by dioxygen in water and biological fluids because of the long lived luminescent excited states. This severe drawback could however be overcome by exploiting the high tendency of such square planar compounds, containing conjugated ligands, to self-assembly in supramolecular structures. This phenomenon can significantly enhance the emissive properties of Pt(II) compounds, because of the formation of new excited states (metal-metal ligand charge transfer, MMLCT) and an increasing rigidity due to the packing of the units, and as a consequence, also a slower or negligible diffusion of dioxygen. The assemblies therefore can become better probes for imaging application due to their enhanced emission and reduced reactivity.[1] In this regard, our research group has already demonstrated the aggregation induced emission for Pt(II) complexes[2,3] in different media. In this contribution we describe the synthesis and characterization of a series of luminescent amphiphilic platinum compounds, soluble in water, based on a N^N^N pyridil-triazolate functionalized with different ancillary ligands (see figure) and their behaviour *in vivo*. An invertebrate freshwater polyp, Hydra vulgaris, was treated with the bright orange phosphorescent complexes at only 20 μM concentration. The compounds self-assembly in vivo and in particular accumulate in the tentacles of the animal. Interestingly preliminary results suggest not only the imaging behaviour of the systems, but an increase in the cell proliferation and a wound healing ability.



Studies are in progress to rationalize such important results.

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Homometallic and heterometallic ruthenium hydride carbonyl cluster

Cristiana Cesari,[a] *Stefano Zacchini*.[a]

[a]*Dipartimento di Chimica Industriale "Toso Montanari", Università di Bologna, Viale Risorgimento 4, 40136 Bologna, Italy.*

Metal hydrides are widely investigated for applications in catalysis and hydrogen storage. Ruthenium forms several hydride compounds, including mononuclear coordination and organometallic complexes, molecular clusters and nanoclusters as well as Ru-H nanoparticles. Ru hydride compounds are involved in several catalytic processes, moreover, molecular Ru-H complexes and clusters have been employed as models for the location of hydride ligands in Ru nanoparticles used in hydrogenation processes.[1]
Herein, we report a straightforward one-pot synthesis of $[H_3Ru_4(CO)_{12}]^-$ operating at mild condition, rather than using the multistep synthesis previously reported in the literature.[2] Furthermore, reduction reactions performed on the already known ruthenium hydride clusters led to isolate new di- and tri- anionic ruthenium carbonyl cluster such as $[Ru_3(CO)_9(CO_3)]^{2-}$ and $[HRu_4(CO)_{12}]^{3-}$ (Figure 1). Ruthenium hydrides are very important for fundamental and applicative purposes, additionally, they can be used for the preparation of heterometallic polyhydride carbonyl clusters. The synthesis and characterization of new heterometallic ruthenium clusters and the investigation of their catalytic activity in hydrogenation reactions will be also presented.

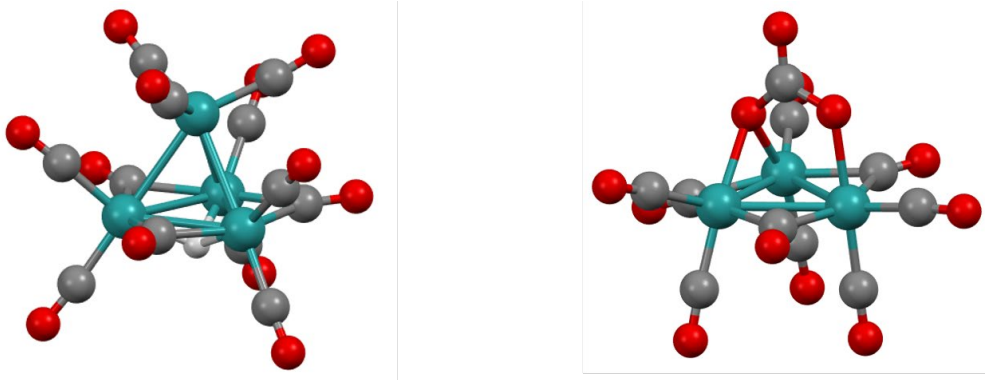

Figure 1. Molecular structures of $[HRu_4(CO)_{12}]^{3-}$ (left) and $[Ru_3(CO)_9(CO_3)]^{2-}$ (right).

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Thiazole-based Metal-Organic Frameworks for applications in CO_2 storage/utilization and luminescence sensing

Andrea Rossin,[a] *Giuliano Giambastiani*,[a] *Giulia Tuci* [a]

[a]*Consiglio Nazionale delle Ricerche - Istituto di Chimica dei Composti Organometallici (ICCOM-CNR), Via Madonna del Piano 10, 50019 Sesto Fiorentino (Firenze).* a.rossin@iccom.cnr.it

The design, synthesis and characterization of Metal-Organic Frameworks (MOFs) for assorted applications is nowadays one of the most fruitful research fields in inorganic chemistry and materials science. The high versatility in MOFs design, obtained through a judicious combination of metallic nodes and organic linkers along with their high crystallinity degree are key features that can be exploited in a plethora of applicative fields.[1] While MOFs featuring fully carbocyclic spacers are ubiquitous, much fewer examples are found with (N,S)-containing heterocycles like thiazole. Thiazoles are electron-deficient systems bearing a basic N atom suitable for interaction with acidic molecules; they are intrinsically fluorescent[2] and they can be found in several naturally occurring biomolecules like luciferin (the active component generating luminescence in fireflies). In this lecture, some representative examples of MOFs built with tailored thiazole-containing linkers will be presented, along with their exploitation in the fields of CO_2 storage and conversion (CCS/CCU technology)[3] and luminescence sensing of polluting ions in wastewaters (Figure 1).[4]

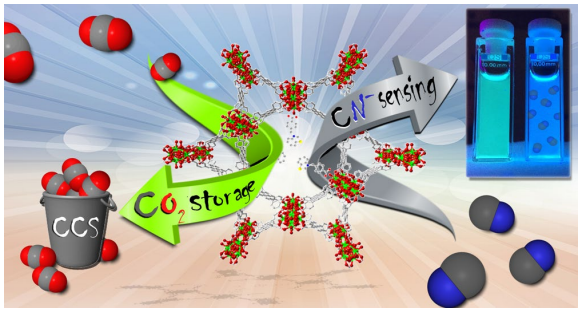

Figure 1. A benzothiazolium-functionalized NU-1000 MOF for CO_2 storage and CN^- luminescence sensing. From reference [4].

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Acknowledgments
The PRIN 2017 Project Multi-e (20179337R7) "Multielectron transfer for the conversion of small molecules: an enabling technology for the chemical use of renewable energy" is acknowledged for support to this work.

Amino-decorated zinc bipyrazolate MOFs, an example of carbon dioxide capture and reuse (CCR)

Patrizio Campitelli[a], *Giorgio Mercuri*[b], *Kostiantyn V. Domasevitch*[c], *Corrado Di Nicola*[a], *Claudio Pettinari*[b], *Simona Galli*[d], *Andrea Rossin*[e]

[a]*School of Science and Technology and* [b]*School of Pharmacy, University of Camerino, Via S. Agostino 1, 62032 Camerino;* [c]*Taras Shevchenko National University of Kyiv, Volodymyrska, Str.64/13, 01601 Kyiv;* [d]*Department of Science and High Technology, University of Insubria, Via Valleggio 11, 22100 Como;* [e]*Institute of Chemistry of Organometallic Compounds, Via Madonna del Piano 10, 50019 Sesto Fiorentino*

Carbon dioxide emissions in atmosphere have been increasing more and more since the Industrial Revolution due to anthropogenic activities. It is well known that this gas is responsible for global warming and, indirectly, of depletion of stratospheric ozone; moreover, the increase of CO_2 concentration in waters is causing the acidification of oceans with negative consequences on sea life.[1] Metal-Organic Frameworks (MOFs) seem to be a valid solution to counteract this fast growth, due to the surprising ability of some MOFs in selective adsorption of CO_2, in its storage and also conversion into other products (Carbon Dioxide Capture and Reuse, CCR). In this communication, two isomeric forms of diamino-decorated zinc bipyrazolate MOFs Zn(3,3'-L) and Zn(3,5-L) (L = diamino-4,4'-bipyrazolate) (Figure 1a) have been synthesized by solvothermal route[2] in DMF and characterized by IR, TGA/DTA, EA. XRPD analysis shows in both cases 3D (4,4)-connected network structures with 1D squared channels, isostructural with respect to Zinc MOFs based on 3-amino-4,4'-bipyrazole and 4,4'-bipyrazole linkers previously reported.[3,4] The textural properties (BET surface area, pore size distribution) and the ability as CO_2 adsorbents were investigated through N_2 and CO_2 adsorption, together with their potential as heterogeneous catalysts in the solvent-free conversion of epichlorohydrin or epibromohydrin and carbon dioxide into the corresponding cyclic carbonates at 393K and p_{CO2} = 5 bar (Figure 1b).

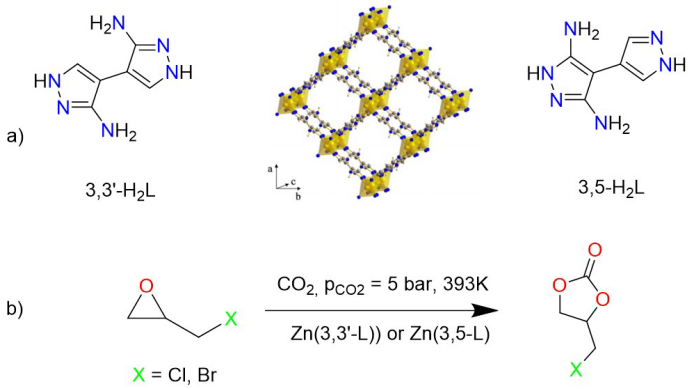

Figure 1 a) Schematic representation of 3,3'-H_2L and 3,5-H_2L linkers structure and of the topology of their corresponding Zinc MOFs. b) Reaction scheme of epichlorohydrin/epibromohydrin and carbon dioxide to yield cyclic carbonate.

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Sol-gel deposition of Cu_2XYS_4 thin-films with tunable bandgap as absorbers for photovoltaic applications

Giorgio Tseberlidis[a], *V. Trifiletti*[a], *Luigi Frioni*[a], *S. Riva*[a], *A. H. Husien*[a], *Maurizio Acciarri*[a] *and Simona Binetti*[a]

[a]*University of Milano-Bicocca, Department of Materials Science and Solar Energy Research Center (MIB-SOLAR), Via Cozzi 55, Milan (Italy)*

In current days, the PV research is focused on finding low cost and easily processable materials. Here we propose a simple chemical procedure for the synthesis and characterization of earth-abundant chalcogenide thin-films with tunable bandgap, leading to well-defined phases of Cu_2XYS_4 (with X = Zn, Fe, Mn; Y = Sn, Ge). The deposition process is straightforward and very cheap, based on the sol-gel technique, where the thin films are produced thanks to a direct drop-casting of the precursor solution, followed by a gelation process and heat treatment in Ar atmosphere for short time to generate the desired crystalline phase of the quaternary alloy. Metal acetate precursors were proved to have a primary role in creating a network in the sol-gel transition by coordinating and so pre-organizing the metals in solution, together with thiourea (as the only source of sulfur) and DMSO or DMF as solvents.[1] Moreover, the addition of dopant amounts of KCl into the precursor solution was experimentally demonstrated to be beneficial for the grain growth and material quality, both crucial for the final solar device performance.
The so-synthesized layers have been characterized by UV-Vis, μ-Raman, XRD, EDX spectroscopy measurements and their morphology was studied by SEM imaging proving the very good quality of the material. The band gap, obtained from transmittance measurements, ranges from 1.4 to 2.1 eV depending on the combination of the chosen metal precursors, suggesting this class of materials as suitable candidate as top absorber in a tandem device architecture, and promising single-junction prototypes of working solar-devices have been produced.[2,3,4]

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Recycling inorganic waste into sustainable materials for energy and environment

Francesca Deganello[a], *Valeria La Parola*[a], *Maria Luisa Testa*[a], *Leonarda Francesca Liotta*[a], *Giuseppe Pantaleo*[a], *Elisa Isabel García-López*[b], *Giuseppe Marcì*[c]

[a]*Istituto per lo Studio dei Materiali Nanostrutturati (ISMN), Consiglio Nazionale delle Ricerche (CNR), Via Ugo La Malfa 153, 90146 Palermo, Italy;* [b]*Dipartimento di Scienze e Tecnologie Biologiche Chimiche e Farmaceutiche (STEBICEF), Università degli Studi Di Palermo, Viale delle Scienze Ed. 16, 90128 Palermo, Italy;* [c]*Dipartimento di Ingegneria (DI), Università degli Studi Di Palermo, Viale delle Scienze Ed. 6, 90128 Palermo, Italy.*

In the transition toward sustainability, waste recycling is highly desired, especially by industries, which tend to produce huge amount of waste in their production cycle. In this presentation, inorganic waste is used as a source of elements as well as a microstructural template in the solution combustion synthesis [1] of mixed oxides for environmental and energy applications. Three types of inorganic waste are examined: aluminum, rust, and active carbon waste. Overall, the use of inorganic waste in the synthesis in replacement of commercial reagents brings inherent peculiarities to the final material, due to the waste's microstructure, morphology, and matrix composition. Major issues in this synthesis procedure are the presence of inorganic impurities in the waste, the scarce reactivity of the waste in its original form, the lack of information on the exact waste composition as well as the waste reproducibility [2]. Different solutions are here proposed to overcome the main obstacles encountered. Finally, it is evidenced how systematic experiments and careful characterization play a primary role in obtaining efficient materials.

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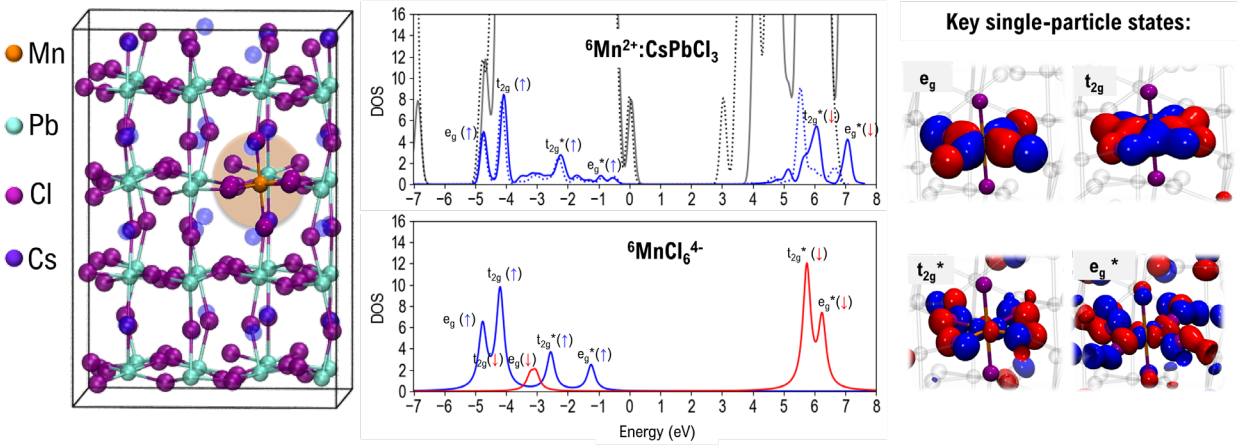
Energy vs charge transfer in manganese doped lead halide perovskites

*Damiano Ricciarelli,[a,b] Daniele Meggiolaro,[b] Paola Belanzoni,[a,b] Edoardo Mosconi,[b] * Filippo De Angelis[a,b,c*]*

[a] Department of Chemistry, Biology and Biotechnology, University of Perugia, Via Elce di Sotto 8, 06123 Perugia, Italy; [b]Computational Laboratory for Hybrid/Organic Photovoltaics (CLHYO), Istituto CNR di Scienze e Tecnologie Chimiche "Giulio Natta" (CNR-SCITEC), Via Elce di Sotto 8, 06123 Perugia, Italy; [c]CompuNet, Istituto Italiano di Tecnologia, Via Morego 30, 16163 Genova, Italy.

Metal halide perovskites (MHPs) are a game-changer class of materials in photovoltaics and optoelectronics. [1] Besides their success in solar cells, perovskite nanocrystals (NCs) have shown outstanding optical properties in light-emitting diodes, with near unity emission quantum yield and wide color tuning.[2] To further diversify the emission color gamut of MHP NCs, Mn^{2+} doping has been successfully implemented [3]. Similar to what is observed in binary semiconductors, in MHPs a dual-color emission from the perovskite host exciton is observed, along with a broad Mn^{2+} ($^4T_1 \rightarrow {}^6A_1$) ligand field transition at ~ 2.0 eV. The contention between energy transfer, host-to-dopant direct photon exchange, and charge transfer, host-to-dopant photon exchange mediated by an intermediate specie (for example an oxidized Mn), in sensitizing dopant luminescence in Mn-doped perovskites is investigated by state-of-the-art DFT calculations on $APbX_3$ (X = Cl, Br, and I; A=Cs, Methylammonium). The accurate simulation of doped NCs electronic structure considering various charge and spin states is provided together with a further in-depth structural/mechanistic analysis of Mn sensitization as a function of the perovskite composition. Our analysis, peer-reviewed and published on ACS Energy Letters [4], supports both the energy and charge transfer mechanisms, we hence highlight points in favor of the former and of the latter. Furthermore, the available experimental data [5] show overlapping features with the thermodynamics/kinetics of Mn oxidation investigated by us. This work represents a robust foundation for an atomic-scale understanding of Mn sensitization in inorganic semiconductors and can possibly help the scientific community for a successful engineering of these compounds.



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Electrocatalysis for energy: from nanostructured to molecular approach

Marco Bellini [a], *Maria V. Pagliaro* [a], *Francesco Bartoli* [a], *Hamish A. Miller* [a], *Andrea Marchionni*[a], *Jonathan Filippi* [a], *Alessandro Lavacchi* [a], *Werner Oberhauser* [a] *and Francesco Vizza* [a].

[a]*Istituto di Chimica dei Composti OrganoMetallici (ICCOM) – Consiglio Nazionale delle Ricerche (CNR), Via Madonna del Piano 10, 50019 Sesto Fiorentino (Fi), Italia.*

Hydrogen has the largest energy density of all fuels and is considered the more suitable energy source (properly H_2 is an energy vector) for matching a clean and carbon neutral future energetic scenario. This rather old technology was theorized almost 50 years ago but still doesn't have a widespread application due to severe limitations. The high cost and the poor sustainability for large scale application of electrochemical devices for hydrogen production and conversion to electricity are the main limitations. In fact, proton exchange membrane electrolyzers (PEMs) and fuel cells (PEMFCs) employ catalysts based on high amounts of rare noble metals, such as Pt, Ir, Ru and Pd. In addition, proton exchange membranes, such as the DuPont Nafion®, are very expensive materials.

The reduction of precious metal loadings to negligible amounts keeping constant catalyst activity is a possible route for making fuel cells and electrolyzers sustainable devices. Traditional electrocatalysts are based on metal nanoparticles dispersed on conductive supports where only the particles surface atoms are involved in electrocatalysis. Replacing nanoparticles with metal complexes is a way for making accessible each metal center of the catalyst. A molecular catalyst offers other advantages with respect to nanosized materials, such as control of the selectivity of the oxidation reaction occurring in direct fuel cells fed with liquid and renewable fuels such as alcohols and formic acid. So direct fuel cells can convert a biomass-derived fuel not only into electricity but also into high purity chemicals. [1]

A second route to make fuel cells and electrolyzers sustainable devices is the replacement of proton exchange membranes with anion exchange membranes (AEMs) because in alkaline environment several nanostructured catalysts based on cheap metals can be used (in acidic environment most of the transition metals would be subject to corrosion phenomena). Thanks to the development over the last few years of high efficiency and stable alkaline membranes, we have developed anodic and cathodic nanostructured catalysts based on cheap metals like iron and nickel which are assembled together in alkaline fuel cells and eletrolyzers able to reach an activity close to the state of the art PEM based devices. [2][3] As example an iron phthalocyanine cathode based H_2/O_2 fed fuel cell set up in our laboratory delivered a remarkable power density of 1 W cm^{-2} (figure 1). [3]

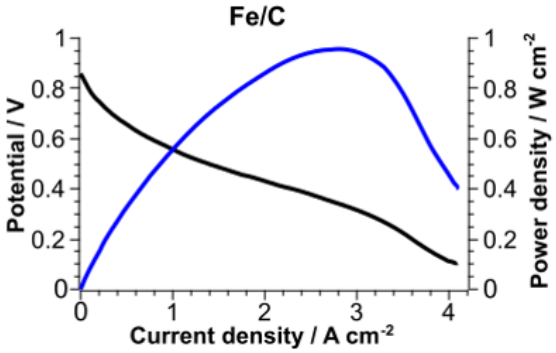

Figure 1. AEMFC performance with a 0.03 mg_{Fe} cm^{-2} cathode.

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Novel mononuclear and dinuclear Ir-Cp* complexes bearing phosphonate and carboxylate ancillary and anchoring ligands as homogeneous and heterogenized water oxidation catalysts

Chiara Domestici,[a] *Leonardo Tensi,*[a] *Elisa Boccalon,*[b] *Francesco Zaccaria,*[a] *Ferdinando Costantino,*[a] *Cristiano Zuccaccia,*[a] *and Alceo Macchioni*[a]

[a]*Department of Chemistry, Biology and Biotechnology University of Perugia and CIRCC, Via Elce di Sotto, 8 - 06123 Perugia, Italy;* [b]*Department of Industrial Engineering, University of Salerno, Via Giovanni Paolo II, 132 - 84084 Fisciano (SA), Italy*

Water oxidation (WO) to molecular oxygen is considered the ideal reaction for producing electrons and protons for the photo- and electro-synthesis of renewable fuels. [1] However, the development of efficient water oxidation catalysts (WOCs) for practical applications remains an open challenge. Among others, supported systems appear particularly promising since they combine the distinctive advantages of homogeneous and heterogeneous catalysts. Recently, our group has explored some design strategies for preparing heterogenized Ir-WOCs, by combining Cp* ancillary ligand, which usually imparts high activity, with carboxylated and phosphonated anchoring ligands. First, we explored dinuclear Cp*Ir catalysts bearing EDTA and EDTMP ligands (Figure **1a**), which exhibit good performances both in homogeneous and heterogeneous phase.[2] These studies suggested that the phosphonate arm could easily dissociate from the coordinately saturated Ir center and act as anchoring moiety, whereas the amino acidate fragment remains more tightly bound at the metal. Based on these observations, we then explored hybrid carboxylate and phosphonate ligands like glyphosate and glyphosine.[3] The performances of this novel heterogenized Ir-WOCs will be discussed.

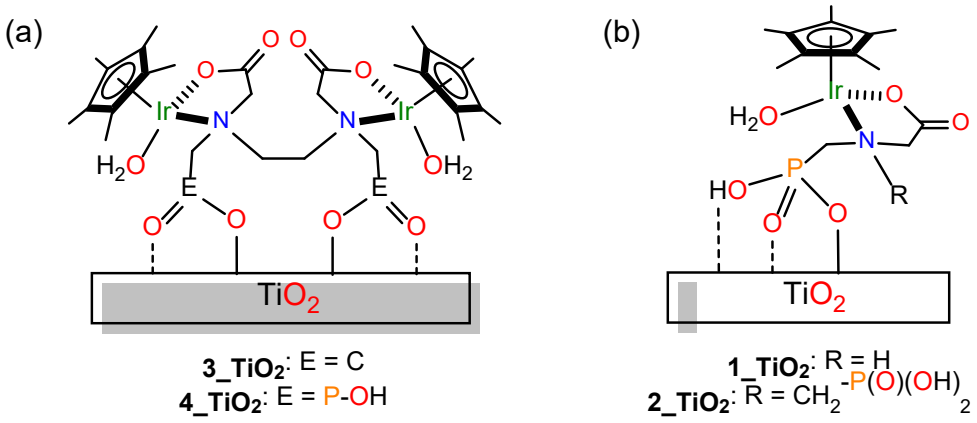

Figure 1. Sketches of the Cp*Ir heterogenized WOCs bearing phosphonate and carboxylate ligands.

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Cyclopentadienone-NHC Iron(0) electrocatalysts for water oxidation

Andrea Cingolani,[a] Isacco Gualandi,[a] Erika Scavetta,[a] Cristiana Cesari,[a] Valerio Zanotti,[a] Stefano Zacchini,[a] Paola Franchi,[b] Marco Lucarini,[b] Emilia Sicilia,[c] Gloria Mazzone,[c] and Rita Mazzoni[a]

[a]Department of Industrial Chemistry "Toso Montanari", viale Risorgimento, 4 40136 Bologna (IT);[b]Department of Chemistry "Giacomo Ciamician", via Selmi, 2 40126 Bologna (IT);[c]Department of Chemistry and Chemical Technologies, Via Bucci, 12C, Arcavacata di Rende (Cs-IT). rita.mazzoni@unibo.it

Despite the considerable effort in the development of homogeneous water oxidation catalysts (WOC), the most are based on expensive metals such as ruthenium and iridium.[1] Finding sufficiently efficient and robust catalysts based on abundant and affordable first-row transition metals, such as iron, is still crucial for the design of economically viable water splitting process, as competitive green alternative for energetic applications (eg. solar fuel). The majority of Fe-WOC catalysts available employ sacrificial oxidants (e.g. CAN or periodate) which recently demonstrated to be often involved in the reaction mechanism aside from being simply innocent one-electron acceptors.[2] A cleaner way to move electrons is represented by electrochemistry. The few examples of molecular iron electrocatalysts that are reported in literature still suffer from quite low efficiencies and high overpotential.[2,3]

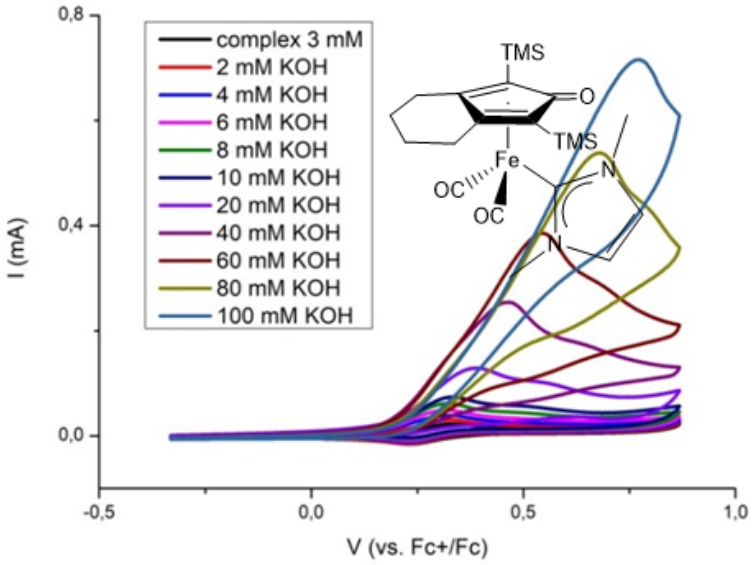

Figure 1. CVs in 3mM solution (THF/H_2O, 4:1 containing 0.1 M $LiClO_4$) of iron catalyst with increasing [OH^-].

Here we report on low valent iron complexes bearing cyclopentadienone and N-heterocyclic carbene ligands active in water oxidation under basic conditions (Figure 1).[4] The catalysts show competitive efficiency in term of TOF and overpotential. Redox reactivity of the complexes and DFT calculations will be also discussed.

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Ammonium salts of oxalic acid derivatives: a new family of agents for the conservation of carbonate stone substrates of artistic value

Anna Pintus,[a] Massimiliano Arca,[a] Laura Giacopetti,[a] Paola Meloni,[b] Gianfranco Carcangiu,[c] Domingo Gimeno,[d] Antonia Navarro Ezquerra,[e] Jordi Rius,[f] Oriol Vallcorba,[g] Enrico Podda[a]

[a]Università degli Studi di Cagliari, Dipartimento di Scienze Chimiche e Geologiche, S. S. 554 Bivio per Sestu, 09042 Monserrato (CA), Italy; [b]Laboratorio di didattica e ricerca Colle di Bonaria, Via Ravenna snc, 09125 Cagliari, Italy; [c]Consiglio Nazionale Delle Ricerche (CNR), Istituto di Scienze dell'Atmosfera e Del Clima (ISAC), S.S. 554 bivio per Sestu, 09042 Monserrato (CA), Italy; [d]Facultat de Ciències de la Terra, Universitat de Barcelona, c/Martí i Franquès s/n, 08028 Barcelona, Spain; [e]Departamento de Tecnología de la Arquitectura, EPSEB-UPC, Avda. Doctor Marañón, 44-50, 08028 Barcelona, Spain; [f]Institut de Ciència de Materials de Barcelona (CSIC), Campus de la UAB, 08193 Bellaterra, Spain; [g]ALBA Synchrotron Light Source – CELLS, 08290 Cerdanyola del Vallès, Barcelona.

Since antiquity, carbonate stones, such as limestone and marble, have been widely used as materials of buildings and sculptures. Unfortunately, these lithotypes are vulnerable to various forms of physical, chemical, and biological weathering when exposed outdoors. Among the variety of conservation products employed to reduce degradation effects, organic consolidants (e.g. acrylic and epoxy resins), lack chromatic and physical compatibility with the substrate and tend to undergo photo-oxidative decay, while the penetration depth of inorganic compounds such as diammonium hydrogen phosphate and ammonium oxalate (AmOx) is not completely satisfactory due to solubility issues. Over the past years, the efforts of researchers have mostly focused on improving the application procedures of the aforementioned products in order to overcome their shortcomings; here we report instead an innovative approach based on newly synthesized, more soluble derivatives of AmOx. In particular, a new library of monoester compounds of general formula NH_4(ROC(O)COO), and monoamides NH_4(RNHC(O)COO) was prepared, and the salts were characterized by both experimental and theoretical means. The most promising products in terms of solubility were applied to artificially weathered marble samples and biomicritic limestone specimens, and their properties before and after the treatments were compared thorough mercury intrusion porosimetry, electronic microscopy, colorimetric and diffractometric measurements, determination of water transport properties, and pull-off tests, showing promising results in terms of homogeneity and thickness of the newly formed passivating layer, consolidating abilities, and hygric properties. The interaction of the new materials with calcite was also modeled and investigated through DFT calculations.

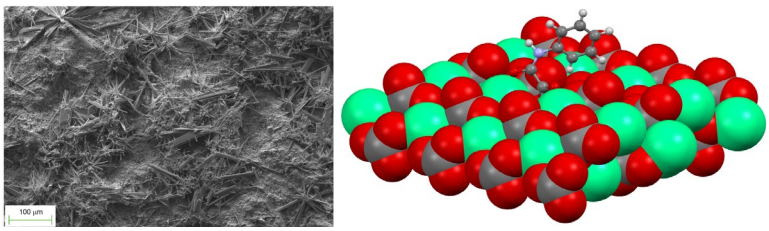

Figure 1. SEM image of the crystalline phase obtained from ammonium N-phenyloxamate on biomicritic limestone (left) and DFT-optimized N-phenyloxamate anion interacting with a portion of calcite lattice (right).

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Visible-light activated metallaphotoredox catalysis enabled by Ti^{IV} complexes: new routes for C-C bond formation

Andrea Fermi,[a] *Andrea Gualandi*,[a] *Francesco Calogero*,[a] *Simone Potenti*,[a] *Marco Di Matteo*,[a] *Martino Mazzarini*,[a] *Simone Guazzi*,[a] *Giacomo Bergamini*,[a] *Pier Giorgio Cozzi*[a]

[a]*Dipartimento di Chimica "G. Ciamician", Università di Bologna, via Selmi 2, 40126 Bologna, Italy*

The use of visible light in photoredox catalysis recently emerged as powerful and sustainable tool in organic synthesis, enabling the production of radical species by means of electron- or energy transfer.[1] Specifically, the merger of photoredox-enabled radical chemistry with metal-assisted catalytic cycles rapidly soared as an effective approach to open the way to new reaction pathways, especially those able to generate highly reactive nucleophilic species.[2]
Recently,[3,4] our attention has been focused on Ti^{IV} complexes such as Cp_2TiCl_2, whose uncommon redox behaviour facilitates the access to radical intermediates with peculiar regio- and chemoselectivity otherwise not feasible by using other metal complexes. The combination between the reactivity of Cp_2TiCl_2 and the photoredox properties of isophthalonitrile derivatives, a cheap and easily prepared class of organic dyes, allowed its use in metallaphotoredox catalysed reactions. The analysis of photo-induced electon transfer events in the presence of such Ti^{IV} complexes helped us in the design of C-C bond formation reactions: allylation and propargylation of aldehydes have been successfully achieved, allowing access to a wide range of unsaturated alcohols in high yields in sacrificial conditions.

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Correlating solid-state analysis and catalysis: exploring secondary π-interactions effects in Au(I) catalyzed reactions

Riccardo Pedrazzani,[a] *Marco Bandini* [a] *Magda Monari*[a]

[a]*Dipartimento di Chimica "Giacomo Ciamician", Alma Mater Studiorum – Università di Bologna, via Selmi 2, 40126, Italy*

Homogeneous gold(I) catalysis has faced an exponential growth during the last 20 years, when new transformations have been achieved by the low reactive-thought noble metal, especially through C-C unsaturated bonds.[1,2] This trend was paralleled by a growing interest in organometallic synthesis and application of phosphines[3] and *N*-heterocyclic carbenes (NHC)[4] ligand-based complexes. Herein, most attention has been devoted to the structure/activity relationship with a focus on steric as well as electronic parameters. On this topic, Toste elegantly rationalized an interesting correlation between solid state data and catalytic outcome, to predict regio-divergent Au(I)-catalyzed reaction.[5]

In this work we present our recent findings in the development of fine-tunable NHC-Au(I) complexes (NHC = ImPy: imidazo[1-5,a]pyridinium core, Figure 1)[6,7] enabling the overall control of the electronic as well as catalytic activity of the metal center *via* secondary Aryl…Au π-interactions.

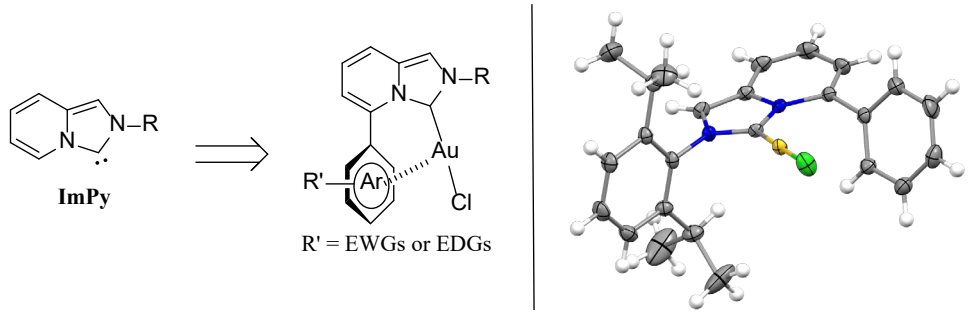

Figure 1. ImPy core (left), schematic representation of NHC-Au(I) complexes presented (centre), molecular drowing of one ImPy-Au(I) synthetized (right).

The synthetized complexes are tested in the catalytic dearomatization of 1,3-dimethyl napht-2-ol with *N*-phenyl tosylallenamide.[8] Catalytic performances correlated to the solid-state information will be discussed in the communication.

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When metallaphilia makes the difference: the case of stacked coinage metals Trinuclear Cyclic Compounds

Lorenzo Luciani,[a] Vladimir Nesterov,[b] Mohammad Omary,[b] Alceo Macchioni,[c] Cristiano Zuccaccia,[c] Rossana Galassi[a]

[a]School of Science and Technology, Chemistry Division, University of Camerino, Via Sant'Agostino 1,Camerino, I-62032, Italy; [b]Department of Chemistry, University of North Texas, Denton, Texas 76203, United States of America; [c]Department of Chemistry, Biology and Biotechnology, University of Perugia and CIRCC, via Elce di Sotto 8, Perugia, I-06123, Italy

Since the early appearance in '70s [1], cyclic trinuclear coinage metals compounds (CTCs), consisting of finite triangular metal(I) frames supported by bridging N,N or C,N ligands, have steadily gained a lot of interest, lastly becoming promising materials for optoelectronics [2]. By means of closed shell d^{10}-d^{10} and electrostatic interactions, CTCs spontaneously self-assembly affording to extended columnar or oligomeric supramolecular entities in the solid state and, depending on the solvent, also in solution. Moreover, according to their π-acid or π-basic properties, they recognize metal cations, organic or organometallic moieties; upon recognition, the modulation of sophisticated luminescence properties is observed, making these compounds interesting in the field of sensing [3], [4], [5]. A key point of the study of these materials emerges when CH_2Cl_2 or THF solutions of CTCs of different nature (π-basic or π-acid, with different bridging ligands or diverse metals) are mixed, two possible stackings can be observed: i) made of different homonuclear CTCs (see figure 1) or ii) of heteronuclear CTCs where an exchange of metals or metals and ligands occurs [5]; both structures are built up by heteronuclear closed shell interactions with these latter stronger than the homonuclear ones. Some theoretical studies and experimental work by X-ray diffraction methods, NMR and UV-visible spectroscopies have been carried out to disclose aspects of the intricate stereo-electronic effects governing this chemistry. The results will be the subject of this contribution.

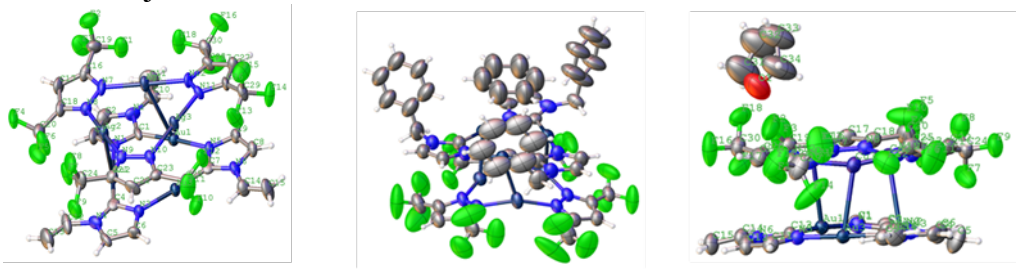

Figure 1. ORTEP plots for 1:1 stacked Ag_3/Au_3 and Cu_3/Au_3 CTCs.

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FTIR-HSI analysis of triple-negative breast cancer (TNBC)

Alessia Belloni[a], Valentina Notarstefano[a], Chiara Pro[a], Giorgia Gioacchini[a], Alfredo Santinelli[b,c], Elisabetta Prete[c], Paola Lorenzini[c], Simona Cerioni[c], Vincenzo Catalano[d], Donatella Sarti[d], Anna Maria Baldelli[e], Francesco Graziano[e], Elisabetta Giorgini[a]

[a]Dipartimento di Scienze della Vita e dell'Ambiente, Università Politecnica delle Marche, Ancona (Italy); [b]Sezione di Anatomia Patologica, Dipartimento di Scienze Biomediche e Sanità Pubblica, Università Politecnica delle Marche, Ancona (Italy); [c]U.O.C. Anatomia Patologica, A.O. Ospedale Riuniti Marche Nord, Pesaro (Italy); [d] U.O.C. Oncologia, A.S.U.R AV1 - Ospedale di Urbino, Urbino (Italy); [e]U.O.C. Oncologia, A.O Ospedali Riuniti Marche Nord, Pesaro (Italy).

Breast cancer is widely diffused in the world and Triple Negative Breast Cancer (TNBC) is considered as most malignant subtypes, accounting for 12%-17% all invasive breast cancers in Western population [1]. It's about a complex disease characterized by the lack of expression of estrogen receptor (ER), progesterone receptor (PR) and Human Epidermal Receptor 2 (HER2) [2]. Nowadays, routinely chemotherapy drugs represent the unique treatment for patients both in early and advanced stage; since an approved target therapy still remains absent, recurrence and resistance to chemotherapy agents represent frequent events [3]. At the time, several routinely analytical techniques, such as histology, immunohistochemistry and other 'omics' technologies, have highlighted the high heterogeneity of TNBC; this finding suggest the occurrence of several typologies and sub-variants of the tumour itself, well explaining the variability of response to treatments [4]. Compared to these assays, Fourier Transform Infrared Spectroscopy - HyperSpectral Imaging (FTIR-HSI) analysis represents a valid and well-assessed tool to investigate cancer biopsies, able to distinguish biochemical differences among heterogenous tissues without using any labels or staining [5]. This technique allows to detect possible changes in biochemical fingerprint of samples, differentiating between healthy and pathological tissues [6].

In this light, we have analysed TNBC paraffin-embedded biopsy samples by FTIR-HSI with the aim (1) to evaluate the mechanisms of interaction of the tumour mass with the surrounding stromal tissue, and (2) to define new spectral biomarkers able to improve the classification of TNBCs in relation with similar histological features and tumour grading. In particular, the analysis was focused on three different regions for each TNBC biopsy: the healthy gland epithelium, the tumoral mass, and the surrounding stroma. In Fig. 1A, the IR maps of representative sections of healthy gland, tumour mass, and surrounding stroma are reported, together with the corresponding average spectra (Fig. 1B).

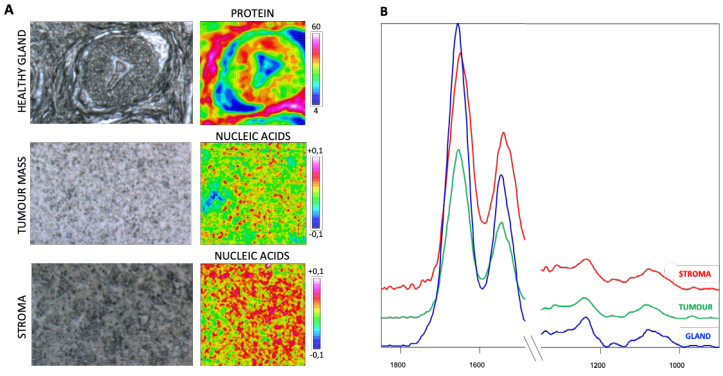

Fig.1. (A) FTIR Hyperspectral imaging analysis of a healthy gland, tumour mass, and surrounding stroma; (B) Average FTIR spectra of healthy gland (blue); tumour mass (green) and surrounding stroma (red).

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A Cu(II)-MOF based on a propargyl carbamate-functionalized isophthalate ligand

F. Gambassi, M.C. Cassani, D. Nanni, I. Ragazzini, B. Ballarin

Dept. of Industrial Chemistry "Toso Montanari", Bologna University, Viale Risorgimento 4, I-40136, Bologna, Italy

A copper-based metal-organic frameworks (Cu(II)-MOF) functionalized with a new linker, a 5-substituted isophthalic acid bearing a propargyl carbamate group was prepared, intended to provide a support for gold species for potential catalytic applications.[1] The novel material was fully characterized using several complementary techniques. Synchrotron X-ray diffraction data analysis, in particular, revealed that this MOF, labelled Cu(II)-MOF contains a complex network of 5-substituted isophthalate anions bound to Cu(II) centers, arranged in pairs within paddlewheel fragments, with a short Cu···Cu distance (Fig. 1).

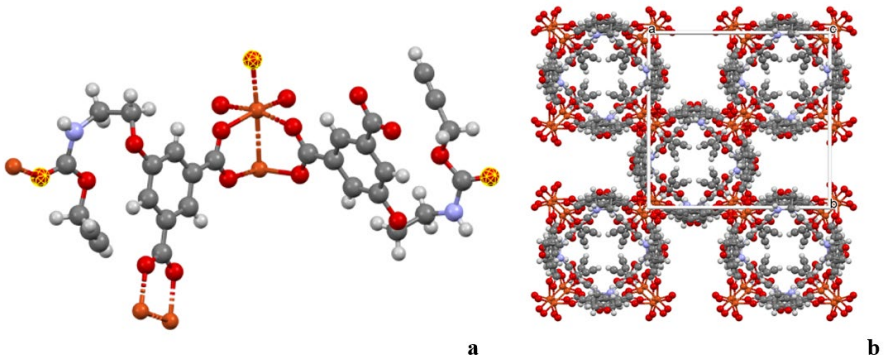

Figure 1. The paddlewheel moiety of Cu(II)-MOF (a). The MOF complex netwotk (b)

Quite unexpectedly, the apical atom in the paddlewheel structure belongs to the carbamate carbonyl oxygen atom. Such extra coordination by the propargyl carbamate groups influences the MOF porosity, a feature that was also confirmed by BET measurements.[1]

[1] Manuscript submitted for publication.

Hierarchical chiral transfer in bright lanthanides quadruple stranded helicate-cages by host-guest interaction

Marzio Rancan,[a] Jacopo Tessarolo,[b] Alice Carlotto,[c] Silvia Carlotto,[c] Maria Rando,[c] Lucrezia Barchi,[c] Elisa Bolognesi,[c] Roberta Seraglia,[d] Gregorio Bottaro,[a] Maurizio Casarin,[c] Guido Clever,[b] Lidia Armelao [c,d]

[a]ICMATE-CNR, Via Marzolo 1, 35131 Padova, Italy; [b]Department of Chemistry and Chemical Biology, TU Dortmund University, 44227 Dortmund, Germany; [c]Dipartimento di Scienze Chimiche, Università di Padova, via F. Marzolo 1, 35131 Padova, Italy; [d]ICMATE-CNR, Corso Stati Uniti 4, 35127 Padova; DSCTM-CNR, Piazzale A. Moro 7, 00185 Roma.

Two lanthanide (Ln = La, Eu and Gd) quadruple stranded helicate-cages $[Ln_2L^B{}_4]^{2-}$ and $[Ln_2L^M{}_4]^{2-}$ are here reported. Both the photophysics and then the host-guest properties with achiral and chiral guest were investigated. As proved by XRD and DFT calculations, these cages are present in solution as an equilibrating racemic mixture of left- and right-handed helicates and eventually the mesocate form. The equilibrium between the two opposite helical configurations can be orchestrated by encapsulation of a chiral guest, *i.e.* through a hierarchical chiral information transfer from a chirality at a primary level (the chiral guest) to the helicate composed of achiral components manifesting supramolecular chirality at a secondary level. Asymmetric induction by the chiral guest was studied by CD and CPL and a helicity inversion mechanism based on a Bailar twist was proposed and studied by DFT. The different chiral response of the two cages depends on both the host-guest affinities and the helical rearrangement activation energies that is strongly correlated to the cage's ligand scaffold rigidity.

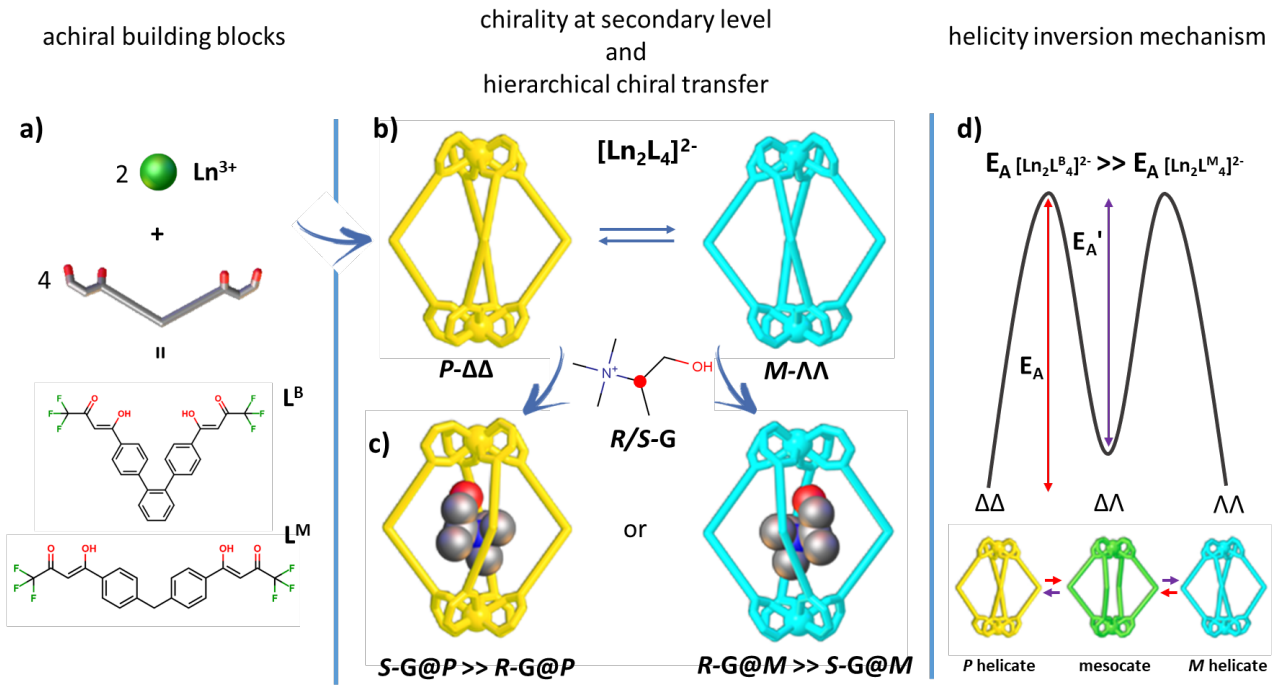

Figure 1. a) Achiral building blocks: Ln^{3+} ions and ligands L^B and L^M. b) Self-assembly of a racemic mixture of quadruple stranded helicate-cages. c) Hierarchical chiral transfer from the chiral guest to the host. d) Bailar twist-based helicity inversion with activation energies related to the ligand nature.

Hydrophobic interactions between macrocyclic Gd-complexes and polyaromatic systems as route to enhance the longitudinal water relaxivity in Magnetic Resonance Imaging

Enza Di Gregorio[a], Luciano Lattuada[2], Alessandro Maiocchi[2], Silvio Aime[a], Giuseppe Ferrauto[a], Eliana Gianolio[a]

[a]Molecular Imaging Center, Department of molecular biotechnologies and health sciences, Via Nizza 52, 10126 Torino (It); [b]Bracco Imaging Spa, Bracco Research Centre, Via Ribes 5, Colleretto Giacosa, Torino (It)

Magnetic Resonance Imaging (MRI) is the election imaging technique for the diagnosis and monitoring of numerous diseases. About 40–45% of MRI scans (*ca*. 38 million per year) are performed with the use of Gadolinium based contrast agents (GBCAs).
The recent findings related to Nephrogenic Systemic Fibrosis (NSF) and Gd-retention strongly required caution in the use of GBCAs [1]. Hence, chemistry becomes central in looking for i) more stable and ii) more efficient GBCAs (*i.e.* enhanced relaxivity). Different routes to enhance relaxivity were exploited so far, as i) the set-up of non-covalent binding interactions with macromolecules present in solution (*e.g.* albumin), ii) the increase of the number of coordinated or second sphere water molecules, iii) the increasing of prototropic exchange rates [2,3].
Herein, we describe the increase of relaxivity attainable through reversible binding interactions between the hydrophobic region of macrocyclic GBCAs and pyrene derivatives.
Macrocyclic (ProHance, Gadovist, Dotarem) and linear (Magnevist, Omniscan, MultiHance) GBCAs were tested. The increase of relaxivity upon the addition of pyrene derivatives was assessed by ^{1}H-relaxometry and ^{1}H-/^{17}O-NMR. The binding parameters K_a (association constant) and R_b (relaxivity of the adduct) between GBCAs and the pyrene derivatives were calculated by using the Proton Relaxation Enhanced technique. ^{1}H-NMRD profiles were measured *w.* or *w/o* pyrene derivatives at variable B_0 (0.24mT-1.5 T). Further insights into the formation of the adduct were obtained i) by high resolution ^{1}H-NMR of YbHPDO3A complex *w.* or *w/o* pyrene derivatives, ii) by Chemical Exchange Saturation Transfer (CEST)-MRI and iii) by x-ray crystallography.
The *in vivo* proof of concept of the enhancement of contrast was obtained by MRI of tumor-bearing mice *pre* and *post* injection of clinical doses of Gd-HPDO3A or Gd-HPDO3A/HPTS adduct.
A high binding affinity of macrocyclic GBCAs toward pyrene derivatives was observed. The supramolecular adducts display a significant increase of relaxivity. No enhancement was observed for linear GBCAs. This is due to the increase of the molecular reorientation time (τ_R) and second sphere water molecules (for the presence of $SO3^-$ and OH).
NMR spectra of the Yb-HPDO3A/ pyrene mixture and x-ray crystallography of Gd-HPDO3A/pyrene mixture fully support the formation of the supramolecular adduct.
When HPTS/Gd-HPDO3A ratio is 3:1 (*m/m*), >90% of Gd-HPDO3A is in the associated adduct and there is a 40% relaxation enhancement in respect to the value observed for Gd-HPDO3A alone (*i.e.* 6.5 $mM^{-1}s^{-1}$ *vs*. 9.2 $mM^{-1}s^{-1}$ in blood serum).
In T_{1w}-MRI of tumor-bearing mice there is the increase of signal enhancement from 53% (upon *i.v.* of only Gd-HPDO3A) to 125% (upon *i.v.* of Gd-HPDO3A/HPTS adduct).
By concluding, a novel tool to enhance the relaxivity of macrocyclic GBCAs is shown, occurring through reversible hydrophobic interaction, already avaiable at clinical doses.

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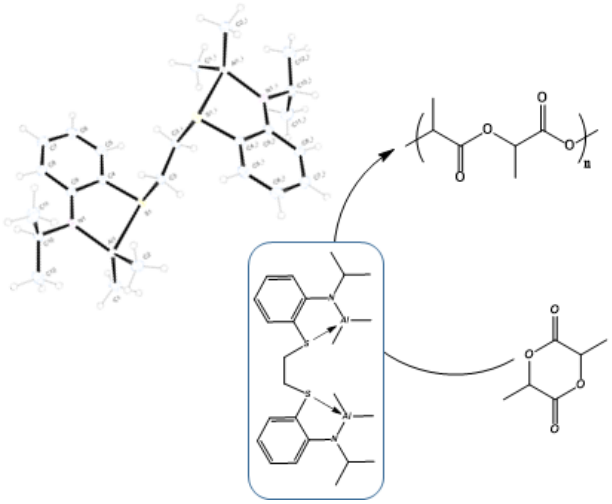
Dinuclear Thioether-amide Aluminum Complexes in the Ring Opening Polymerization of Cyclic Esters

Salvatore Impemba[a], *Giuseppina Roviello*[b], *Stefano Milione*[a], *Carmine Capacchione*[a]

[a]*Department of Chemistry and Biology, University of Salerno, via Giovanni Paolo II, 132 Fisciano I-84084, Salerno, Italy;* [b]*Department of Engineering University of Naples Parthenope Centro Direzionale Napoli, Isola C4, 80143, Napoli, Italy.*

The aliphatic polyesters can be considered a sustainable alternative to conventional polymers of petrochemical origin. The ring opening polymerization (ROP) catalyzed by metal complexes of cyclic esters allows obtaining aliphatic polyesters with controlled molecular masses using mild reaction conditions and avoids the formation of small molecules byproducts.[1] Aluminum complexes are particularly attractive in the *ROP* of cyclic esters due to high Lewis acidity and good abilities in controlling the molecular weight and molecular weight distribution.[2] Currently, there is interest in the preparation of aluminum dinuclear systems as they have proved to be more active than monuclear systems thanks to the collaboration between the two metal centers.[3] In this work, a new class of aluminum dinuclear complexes coordinate by linear dianionic tetradentate *NSSN* ligand is reported. The ligands feature two amide functions coupled with two thioether groups linked by different central bridges to increase or decrease the distance between the two metal centers. Moreover, the ligands differ for the substituent on the aniline nitrogen atoms, i.e. isopropyl or cyclohexyl substituents. The corresponding *Al* complexes were obtained through the reaction between the neutral ligands and trimethyl aluminum and they were characterized by NMR spectroscopy and, in some cases, by X-ray diffraction analysis. The catalytic performances of complexes in the *ROP* of cyclic esters, such as L-lactide, were investigated. The aluminum complex featuring a two-carbon bridge resulted more active than those complexes with longer bridge. This result clearly suggests a cooperative effect between the two metal center that leads to a favorable increase in the catalytic activity.



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Put light on inside a microporous MOF to decipher the guest arrangement and guest-release properties

Alessia Bacchi, Davide Balestri, Paolo Pio Mazzeo, Federica Bianchi, Maria Careri, Fabio Fornari, Paolo Pelagatti

[a] *Department of Chemical Sciences, Life Science and Environmental Sustainability, University of Parma, Parco Area delle Scienze 17/A, 43124 Parma, Italy, paolo.pelagatti@unipr.it*

Mixed-ligand MOFs are a class of crystalline materials deriving from the self-assembly of two different linkers with a metal nucleus [1]. The judicious choice of the components allows to reach microporous 3D frameworks whose porosity can be controlled by a careful selection of the two linkers. The functionalization of the linkers with hydrogen-bond active groups can impart to the materials high host-guest propensity towards several organic molecules, such as phenol derivatives. Natural phenol-derivatives represent an important class of substances naturally found in essential oils extracted from several plants and featured by antibacterial and antioxidant properties. The inclusion of essential oil components in microporous mixed-ligand MOFs can then lead to materials capable of a controlled release of active substances that can found application in several fields, such as food preservation and plant-disease control. To understand the release properties of a material, the knowledge of the molecular organization adopted by the guest molecules inside the host framework is highly desirable.

In this communication we present the crystal engineering approach optimized in our laboratory to make functional mixed-ligand MOFs having different framework dimensionality, porosity and types of entanglement [2]. The structural elucidation of the guest arrangement inside selected MOFs will be described and correlated with their release properties [3-4].

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Biodegradable polyelectrolyte/magnetite capsules for MR imaging and magnetic targeting of tumors

Francesca Garello[a], Yulia Svenskaya[b], Ekaterina Lengert[b], Anastasiia Kozlova[c], Roman Verkhovskii[c], Valeria Bitonto[a], Maria Rosaria Ruggiero[a], Sergey German[d,e], Dmitry Gorin[e], Enzo Terreno[a]

[a]University of Torino, Molecular and Preclinical Imaging Centres, Department of Molecular Biotechnology and Health Sciences, Torino, Italy; [b]Saratov State University, Remote Controlled Systems for Theranostics laboratory, Research and Educational Institute of Nanostructures and Biosystems, Saratov, Russian Federation; [c]Saratov State University, Biomedical Photoacoustics Laboratory, Saratov, Russian Federation; [d]Institute of Spectroscopy of the RAS, Laboratory of Optics and Spectroscopy of Nanoobjects, Troitsk, Russian Federation; [e]Skolkovo Institute of Science and Technology, Center of Photonics and Quantum Materials, Moscow, Russian Federation

The tireless research for effective drug delivery approaches is prompted by poor target tissue penetration and limited selectivity against diseased cells [1]. To overcome these issues, various nano- and micro-carriers have been developed so far, but some of them are characterized by slow degradation time, thus hampering repeated drug administrations. The aim of this study was to pursue a selective delivery of magnetic biodegradable polyelectrolyte capsules in a mouse breast cancer model, using an external magnetic field.

To achieve this goal, four different kinds of magnetic polyelectrolyte capsules were fabricated via layer-by-layer assembly [2] of biodegradable polymers on calcium carbonate templates. Magnetite nanoparticles were embedded either into the capsules' shell (sample S) or both into the shell and the inner volume of the capsules (samples CnS, where n is the number of nanoparticle loading cycles). Samples were first characterized in terms of their relaxometric and photosedimentometric properties. *In vitro* magnetic resonance imaging (MRI) experiments, carried out on RAW 264.7 cells, allowed the selection of two lead samples that proceeded for the *in vivo* testing on a mouse breast cancer model. In the set of *in vivo* experiments, an external magnet was applied for 1 hour following the intravenous injection of the capsules to improve their delivery to the tumor, and MRI scans were acquired at different time points post administration.

All samples were considered non-cytotoxic as they provided more than 76% viability of RAW 264.7 cells upon 2 h incubation. Sample S appeared to be the most efficient in terms of T_2-MRI contrast, but less sensitive to external magnet navigation, since no difference in MRI tumor signal with and without the magnet was observed (-15 ± 5 % and -18 ± 4 %, respectively). On the other side, sample C_6S was efficiently delivered to the tumor tissue, with a three-fold T_2-MRI contrast enhancement upon the external magnet application (-12 ± 2 % vs -4 ± 2 %). The effective magnetic targeting of C_6S capsules was also confirmed by the reduction in T_2-MRI contrast in the spleen if compared with the mice untreated with magnet values (-43 ± 7 vs -65 ± 5 %, respectively) and the presence of dense and clustered iron aggregates in tumor histology sections even 48 h after the magnetic targeting.

In conclusion, the reported strategy of magnetic biodegradable polyelectrolyte capsules' design allows for the development of a drug delivery system effective in terms of both external magnetic field-guided targeting of tumors and MRI monitoring. Summation of these properties with the polyelectrolyte capsule biocompatibility and the ability of co-loading with an anticancer drug holds the prospect for an effective theranostic platform development aiming at improved anticancer therapy.

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CeO_x/TiO_2 Hollow Spheres as efficient photocatalyst for the degradation of organic pollutants in wastewater

Letizia Liccardo[a], *Alberto Vomiero*[a,b], *Elisa Moretti*[a]

[a]*Department of Molecular Sciences and Nanosystems, Ca' Foscari University of Venice, Via Torino 155, 30172 Venezia Mestre, Italy;* [b]*Division of Materials Science, Department of Engineering Sciences and Mathematics, Luleå University of Technology, 97187 Luleå, Sweden*

Environmental pollution is one of the main problems for future survival, and pesticides, synthetic dyes and pharmaceutical compounds largely contribute to water, soil, and air contamination[1,2]. To date, water contamination associated with dyes and drugs is a great environmental emergency and their removal could be investigated using conventional and advanced biological, chemical, and physical treatment processes[2].

Solar light-based processes are the most challenging and promising possibility, since they are able to promote photochemical degradation, being at the same time low cost and eco-friendly. TiO_2-based materials are one of the most employed class of photoactive materials. However, there are many relevant drawbacks, among which the titania large band gap (3.0-3.2 eV) that limits its use in the UV region, thus it cannot be used as efficient solar light harvester[3]. Many ways have been exploited to overcome these limits[4], but a growing interest has emerged on the metal ions doping strategy. On this point, cerium oxides display suitable optical and catalytic properties associated with the $Ce^{3+/}Ce^{4+}$ redox couple, to boost the photocatalytic activity of bare titania, shifting the absorption band towards visible light[5,6]. This can lead to the development of innovative and efficient nanostructured photocatalysts able to exploit solar light in order to promote pollutants photodegradation for water remediation.

In detail, the preparation, and the photocatalytic activity behavior of novel nanostructured Ce-Ti mixed oxides hollow spheres for the photodegradation of some of the most employed dyes and drugs (i.e., methylene blue and metronidazole) will be further discussed. Cerium doped-TiO_2 samples were characterized by many techniques: surface and bulk chemistry was evaluated using X-ray diffraction (XRD) and X-ray photoelectron Spectroscopy (XPS); morphological and textural characterization was carried out by scanning and high-resolution transmission electron microscopy (SEM, HRTEM); porosity was measured by N_2 physisorption; the optical properties by diffuse reflectance UV-Vis spectroscopy. A comparison between the photoactivity under UV and solar light irradiation was made, correlating the catalytic performances with the optical, morphological, and compositional properties of the investigated samples.

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Highly active ruthenium complexes: synthesis and evaluation of the anticancer activity through interaction with relevant biomolecules

Denise Lovison,[a] *Lorenzo Allegri*,[b] *Chiara Nardon*,[c] *Dario Alessi*,[a] *Giuseppe Damante*,*[b] *and Walter Baratta**[a]

[a]*Dipartimento di Scienze Agroalimentari, Ambientali e Animali, Università di Udine, Via Cotonificio 108, I-33100 Udine, Italy;* [b]*Dipartimento di Area Medica – Istituto di Genetica Medica, Università di Udine, Via Chiusaforte, F3, I-33100 Udine, Italy;* [c]*Dipartimento di Biotecnologie, Università di Verona, Strada Le Grazie 15, 37134 Verona, Italy.*

Nowadays metal compounds are widely used in medicine as therapeutic and diagnostic agents. Due to their versatile biochemical properties, ruthenium-based compounds have shown to be promising anti-cancer agents as alternatives to cisplatin and its derivatives.[1] The aim of our work is to investigate the effects of the new ruthenium(II) complexes [RuX(CO)(dppb)(phen)]X [X = acetate, pivalate, thioacetate; dppb = 1,4-bis(diphenylphosphino)butane; phen = 1,10-phenanthroline] [2] on anaplastic thyroid cancer and colon carcinoma cells. Interestingly, these compounds display IC_{50} values as low as 40 nM after 72h of incubation.

Based on these considerations, we also demonstrate that the introduction of a chiral diphosphine, namely (*R*,*R*)-Skewphos, leads to the formation of a single stereoisomer, which shows a remarkably difference in *in vitro* biological activity with respect to the corresponding enantiomer with the (*S*,*S*)-Skewphos. In addition, the most promising complexes demonstrated water solubility with formation of labile aquo species which easily react with relevant biomolecules such as *L*-cysteine (*L*-Cys), glutathione (GSH) and NADH. The resulting Ru-Cys, Ru-SG and RuH derivatives, respectively, may play a crucial role in the redox imbalance of cancer cells, resulting in cell death via apoptosis.

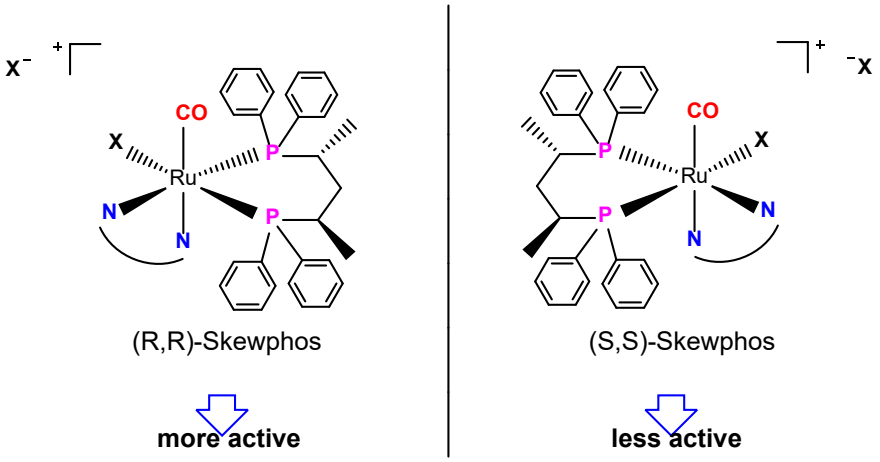

Figure 1. Ruthenium enantiomers and their differences in cytotoxicity.

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Reactivity of imidazolate Au(I) cyclictrinuclearcompounds, CTCs, with iodine or MeI: a computational/experimental study

Gabriele Manca,[a] *Lorenzo Luciani*,[b] *Rossana Galassi*[b]

[a]*Istituto di Chimica dei Composti Organo-Metallici, CNR-ICCOM, Sesto Fiorentino, 50019, Italy;* [b]*School of Science and Technology, Chemistry Division, University of Camerino, Camerino, I-62032, Italy*

Cyclic trinuclear complexes (CTCs) of d^{10} metal frames, obtained through the reaction between angular ditopic anionic bridging ligands and 11th group elements M(I) complexes, have aroused considerable attention due to their potential application in optoelectronics and molecular recognition [1]. Experimental evidences show that the reaction of gold(I) CTCs, featuring imidazolate bridging ligands, with different substrates (CH_3I and I_2) result to the formation of carbene, bis-carbene or square planar complexes depending on the nature of both the reactants depending on and of the substituent at the imidazolyl ring. Herein, we report the results of a detailed computational investigation of the reactivity by considering two different substituents at the ring ligand: methyl or benzyl groups. All the electronic and steric factors ruling the reactivity have been pointed out and, in particular, the not innocent behaviour of the imidazolyl rings in the activation of C-I bonding. Experimentally, the X-ray crystal structure demonstrates that the reaction between the gold(I) CTC - having 1-methyl-imidazolate as bridging ligand- with MeI provides the formation of a square planar gold complex with the formation of new Au-I and Au-CH_3 linkages. In Figure 1 is reported the optimized structure obtained by computational calculations within Gaussian 16 package. Such a reactivity, beyond to the classic addition of iodine traditionally classified as "oxidative addition", has been explained accordingly to the newly introduced Inverted Ligand Field concept [2]. A reasonable explanation has been also provided for the role of the different substituents at the imidazolyl ring in the reactivity.

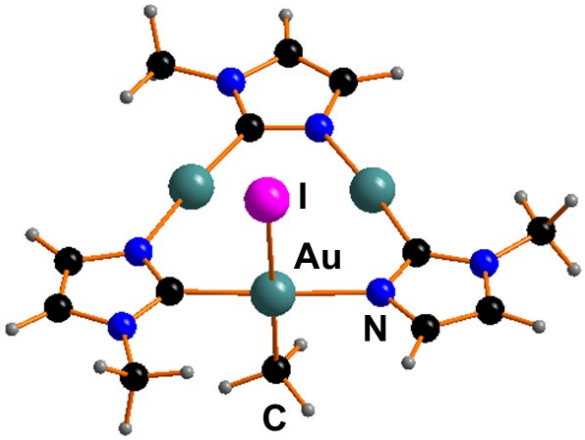

Figure 1. Optimized structure for the product of the first CH_3I molecule activation by the gold(I) CTC.

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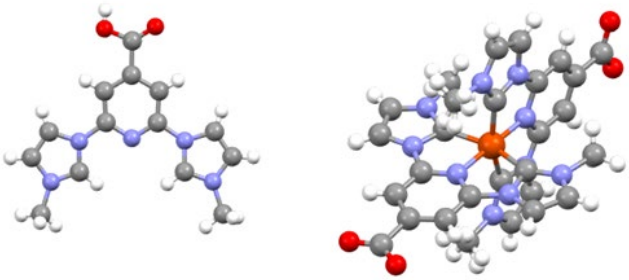
DFT and semi-empirical GFN2-xTB methods: experimental and computational characterization of an Iron(II) carbene complex

Luca Andreo, Alessia Giordana, Emanuele Priola, Roberto Rabezzana, Eliano Diana

Università degli Studi di Torino, Dipartimento di Chimica, via P.Giuria 7, 10125 Torino

First-row transition metal complexes with strong σ-donor ligands are receiving increasing attention for their photophysical and photochemical properties and for their relatively low cost with respect to second and third-row metal complexes. Chemists rely on computational chemistry for predicting and studying the properties of these complexes, such as geometries, vibrational frequencies and electronic spectra, by employing well-established DFT and TD-DFT methods for accurate descriptions of such systems; however, the computational cost of properties calculation increases rapidly with large systems, especially for the investigation of excited states.
In this contribution, we present and compare results of calculations on a newly synthesized Iron(II) carbene complex [1]. We provide results obtained by the widely used B3LYP hybrid density functional method [2] and by GFN2-xTB [3], a semi-empirical DFTB method, in combination with sTDA [4], a method for calculating electronic spectra, implemented in the xtb program [5]. The results obtained thus far through the tight-binding method with a low computational cost are comparable with the ones obtained through the traditional DFT-B3LYP method, which is more computationally demanding. The astonishing accuracy with respect to experimental data and the very fast calculation speed make the semi-empirical method an alluring tool for inorganic chemists to predict and study electronic properties of medium-large metal-organic systems.



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How lanthanide ions affect the catalytic activity of methanol dehydrogenase: a computational point of view

Mario Prejanò,[a,b] *Tiziana Marino*,[a] *Nino Russo*[a]

[a]*Department of Chemistry and Chemical Technologies, University of Calabria, 87036 Arcavacata di Rende, Cosenza, Italy;* [b]*Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, SE-10691 Stockholm, Sweden.*

In the last fifteen years, the inorganic biochemistry has been enriched by the novelty of biological relevance of rare earth elements. In particular, the discovered methanol dehydrogenase (MDH), from *Methylacidiphilum fumariolicum* SolV (MfSoLV) bacterium, requires lanthanides (Lns) as evidenced by the presence of Ce in active site of the enzyme, to carry out the catalytic dehydrogenation of methanol in formaldehyde.[1,2] This process is essential for methanol- and methane- utilizing bacteria. Despite the need of lanthanides for such microorganisms is a proven fact, [3] the exact role played in the course of catalysis by the metals is still subject of debate. In detail, recent cell's growth experiments carried out on MfSoLV evidenced 200 times slower growth of bacteria culture in presence of Eu, with respect to early lanthanides (La, Ce and Pr). Interestingly, the growth was not detected in presence of Yb, the second to last atom of the series.
Among the possible hypothesis for explaining such behavior, the *lanthanide contraction effect* (*LCE*), a well-known periodic property of the series, has been considered as the principal explanation. [3,4] According to this, such *LCE* should affect the formation of enzyme-substrate (ES) complex and consequently the reaction of MDH. A recent work on Ce-MDH demonstrated that the reactivity of the system cannot be solely ascribable to the formation of ES complex and for this reason further investigations are required, [5] for in-depth understanding of the effect of lanthanides in MDH's active site. The results of systematic DFT-based investigation on catalysis of Ln-dependent MDHs are presented. Firstly, attention is focused on electronic description of Ln (La-Lu)-ES complexes. Next, results on catalytic mechanism of Ce-, Eu- and Yb-dependent MDH are presented. The characterization of intermediates and transition state along the reaction mechanism provides information on the effect of *LCE* affecting all steps of the catalytic mechanism. In addition, the analysis of energy profiles provides explanation for the decreasing efficiency of MDH, observed proceeding in the series.
This indications can prove useful insights for developing of new catalytic machineries and of enzymes that adopt new-to-nature transformations.

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Transition metal complexes as neurodrugs: insights into their modulation of amyloid aggregation

Sara La Manna, Daniele Florio and Daniela Marasco

Department of Pharmacy, University of Naples Federico II, 80131, Naples, Italy

Transition metal complexes present unique features: the oxidation, spin states and coordination geometries of metal ions can be tuned through a systematic variation of their ligands [1]. The abilities of these compounds to interact with proteins through coordinative, oxidative and hydrolytic mechanisms provide many application fields as metallo-drugs [2]. Neurodegenerative diseases are caused, at molecular level, by uncontrolled amyloid aggregation and, hence, many drug discovery processes are oriented to evaluate new compounds able to modulate self-recognition mechanisms. Among others, metal complexes demonstrated able to interfere with amyloid aggregation involving mainly progressive substitutions of ligands. Our recent studies outlined the abilities of Pt(II-IV), Pd (II), Au(III) and Ru(II) compounds [3] [4] [5] [6] to affect self-recognition: structural and functional investigations allowed to unveil their inhibitory effects on the cytotoxicity of several amyloid system models and pointed out their potential therapeutic application. Thioflavin T, CD UV-vis and MS analyses indicated: i)the inhibition of aggregation, ii)the stabilization of soluble β-structures, iii)IC50 values in the micromolar range. Furthermore, several complexes demonstrated able to reduce amyloid cytotoxicity in human SH-SY5Y neuroblastoma cells.

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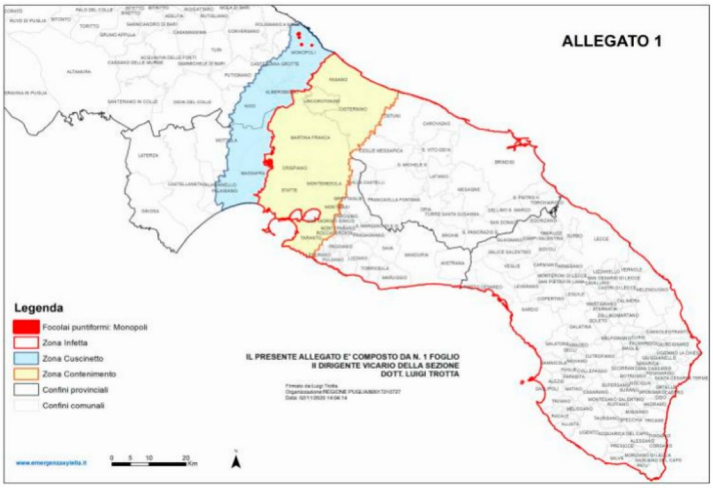
X. fastidiosa affecting olive trees in Salento: metal ions in soil, plants and treatment compounds

Laura Del Coco[a], *Chiara Roberta Girelli*[a], *Federica Angilè*[a], *Danilo Migoni*[a], *Marco Scortichini*[b], *Francesco Paolo Fanizzi*[a]

[a]*Department of Biological and Environmental Sciences and Technologies (Di.S.Te.B.A.), Salento University, Prov.le Lecce-Monteroni, 73100 Lecce, Italy;* [b]*Research Centre for Olive, Fruit Trees and Citrus Crops, Council for Agricultural Research and Economics (CREA), 00134 Roma, Italy*



Xylella fastidiosa subsp. *pauca* is associated with the "olive quick decline syndrome" in Salento (Apulia, Italy) [1]. Since 2015, multidisciplinary studies were carried out, in order to provide a sustainable control strategy for this pathogen that damages the multi-millennial olive agroecosystem of Salento [2]. Among the very few suggested treatments the use of a biocomplex constituted by citric acid chelates of Zn and Cu ions (Dentamet®) was extensively tested [2]. The NMR metabolomic approach revealed, upon the treatments, a consistent variation of the xylematic profiles for both susceptible (Ogliarola salentina and Cellina di Nardò) and somehow resistant cultivars (Leccino) [3]. A specific study on the ionomic profiles focused on micronutrients of soil and leaves that might be associated with this outbreak. For this purpose, infected plants, (NTR, not treated with Dentamet®,) in comparison with treated (TR) and not infected plants (NI), located in different geographical districts of Apulian and Lucanian regions were studied. Both soil and olive leaf samples of Cellina, Ogliarola salentina, Leccino and Coratina cultivars (for a total of ~125 samples) were analyzed for macro and micronutrients content by using ICP-AES spectroscopy analysis. This investigation [4] and previous experimental data [5] corroborate the observed decrease of Mo in soil and a low bioavailability of Cu and Mo in the leaves of *X. fastidiosa* infected plants. Moreover, a high relative content of Ca and Mg and a low relative content of Na were found in NI olive leaf samples. A high relative zinc content in leaves characterized treated with respect to untreated trees. On the other hand, among the not-infected trees, *Xylella*-resistant Leccino showed higher manganese content when compared with the higher pathogen sensitive Ogliarola salentina and Cellina di Nardò. According to these results, soil and olive leaf ionome could provide basic information for the epidemiologic study and possible control of *X. f.* subsp. *pauca* in Apulia.

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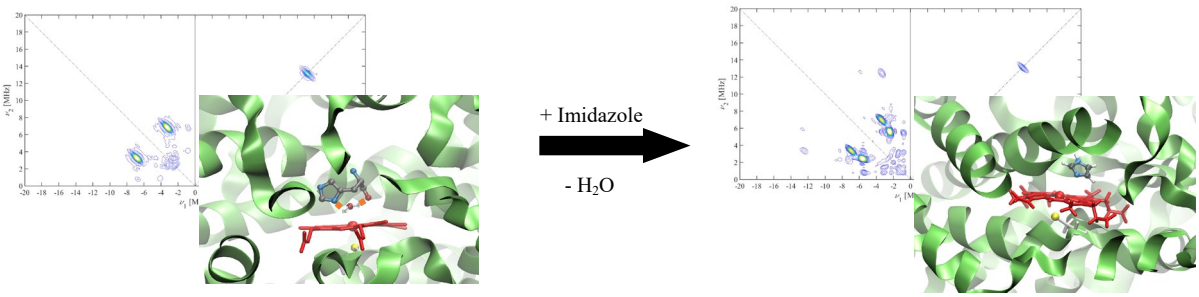
Unveiling electronic and structural properties of, peroxygenase-like cytochrome P450, CYP116B5hd

Antonino Famulari,[a,b] Danilo Correddu,[c] Giovanna Di Nardo,[c] Gianfranco Gilardi,[c] Mario Chiesa,[b] Inés García-Rubio[d,a]

[a]Department of Condensed Matter Physics, Faculty of Sciences, University of Zaragoza, Calle Pedro Cerbuna 12, 50009, Zaragoza, Spain; [b]Department of Chemistry, University of Turin, Via Giuria 9, 10125, Torino, Italy; [c]Department of Life Sciences and Systems Biology, University of Turin, Via Accademia Albertina 13, 10123, Turin, Italy; [d]Centro Universitario de la Defensa, Carretera de Huesca s/n, 50090, Zaragoza, Spain;



CYP116B5 is a class VII self-sufficient P450 peroxygenase involved in different oxidative reaction of aromatic compounds.[1],[2] Interestingly, the isolated heme domain of this enzyme (CYP116B5hd) is able to perform catalysis using the so-called peroxide shunt, a shortcut of cytochrome P450 catalytic cycle where hydrogen peroxide is directly used to generate compound 0, which precedes the reactive compound I. Indeed, CYP116B5hd showed a higher stability to hydrogen peroxide-induced oxidative heme damage when compared to classical P450 cytochromes.[3]

In this contributions, the heme domain of CYP116B5hd is assessed by means of EPR techniques with the aim of, for the first time, correlating its electronic structure and coordination environment with its ability to use H_2O_2 for function. The similarity of the *g*-tensor with that of CYP450 monooxygenases iron reflect an electronic ground state very similar to classical P450-monooxygenases and different from P450-peroxygenases, which is not a critical hindrance for peroxygenase activity.[4],[5] On the other hand, for the imidazole-inhibited protein, we report g-values that are very close to the ones reported for CYP152 peroxigenases. The detection of hyperfine interactions, through HYSCORE experiments, was crucial to identify imidazole axial coordination and tell it apart from other effects like polarity, presence and distribution of charges or conformational changes in the heme site that also affect the ground state orbital for Fe^{III}.

This work is part of a project that has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 813209.

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Elusive intermediates in the reactivity of platinum(IV) prodrugs: a new perspective on their bioactivation

Davide Corinti,[a] Maria Elisa Crestoni,[a] Simonetta Fornarini,[a] Gilles Frison,[b] Eslam Dabbish,[c] Emilia Sicilia,[c] Elisabetta Gabano,[d] Elena Perin,[d] and Domenico Osella[d]

[a]Università di Roma "La Sapienza", P.le A. Moro 5, I-00185 Roma, Italy, [b]LCM, CNRS, Ecole Polytechnique, Institut Polytechnique de Paris, 91128 Palaiseau, France, [c]Università della Calabria, Ponte P. Bucci Cubo 14c, 87035 Arcavacata di Rende (CS), Italy. [d]Università del Piemonte Orientale, Viale T. Michel 11, 15121 Alessandria (AL), Italy.

Platinum(IV) complexes are promising candidates for the development of safer and orally available platinum-based antineoplastic drugs due, in particular, to their slower ligand substitution kinetics compared to currently usedPt(II) drugs. In fact, a preliminary reduction step (from octahedral Pt(IV) to square-planar Pt(II) complexes) is considered mandatory for their cytotoxic activity.[1]
Pt(IV) complexes have been examined as gaseous deprotonated species and their fragmentation was proven to be effective in producing reduced platinum complexes.[2] In particular, ions with the exotic Pt oxidation state of +3 were also observed, attracting our attention on the possibility of isolate and characterize these elusive species. In this contribution it will be shown how IR ion spectroscopy (IRIS) can be conveniently used to obtain structural information, helping to define the nature of the complex. Experimental data are interpreted by calculations at DFT, MP2 and CCSD levels showing the localization of the radical to be shared between the d_{xz} orbital of platinum and the nitrogen p_z of the amino group, which is acting as a non-innocent ligand.[3]
Pt(IV) reduction in the cell, however, is usually mediated by biological reductants. In this context, a an inquiry into the reduction reactivity involving ascorbic acid, is also presented in this contribution. The reduction trend of cisplatin-based prodrugs presenting different axial ligands [2,4] is interpreted through a combination of techniques including kinetic studies in solution, ESI-mass spectrometry, IRIS and calculations at the DFT level. In particular, ESI-MS was able to reveal the encounter complex of the platinum(IV) prodrugs with ascorbic acid. This complex was subsequently assayed using IRIS, allowing to obtain significant structural information.[3] Moreover, the fragmentation pattern showed the presence of Pt(II) containing fragments, thus proving the reduction process to occurwhen the encounter complex is activated (Figure 1). Finally, DFT calculations on the free-energy surface of the reduction reaction have assessed the importance of characteristic interactions between the axial ligands and ascorbic acid for the bioactivation of the sampled Pt(IV)-complexes.

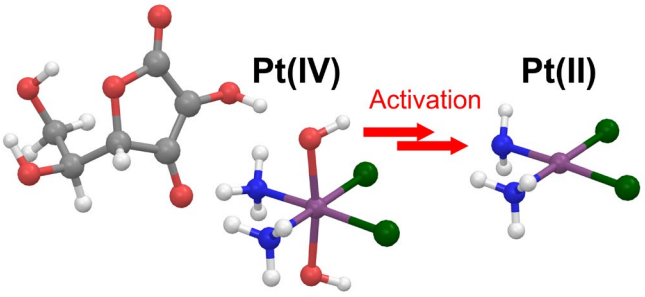

Figure 1. (Photo)-activation of non-covalent complexes of Pt(IV) prodrugs and ascorbic acid produces cytotoxic cisplatin.

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Functionalized silver nanoparticles for water pollution monitoring: sensitivity, selectivity and the challenge of eco-safe behavior

Iole Venditti[a], Paolo Prosposito[b], Luca Burratti[b], Ilaria Corsi[c], Arianna Bellingeri[c], Carlo Punta[d], Laura Riva[d], Martina Marsotto[a], Federica Bertelà[a], Giovanna Iucci[a], Chiara Battocchio[a]

[a]Department of Sciences, University of Roma Tre, via della Vasca Navale 79, 00146 Rome (IT); [b]Department of Industrial Engineering, University of Rome Tor Vergata, Via del Politecnico 1, 00133 Rome, (IT); [c]Department of Physical, Earth and Environmental Sciences and INSTM Local Unit, University of Siena, Siena, 53100 (IT); [d]Department of Chemistry, Materials, and Chemical Engineering G. Natta and INSTM Local Unit, Politecnico di Milano, Piazza Leonardo da Vinci 32, Milano, I-20133 (IT)

Silver nanoparticles (AgNPs) are widely used in many advanced technologies, especially in sensors, due both to their versatile, easy and cheap preparations and ~~both to~~ their peculiar physico-chemical properties [1-3]. Furthermore, eco-design strategy has recently been proposed with the aim to combine all their best performances and, in the same time, to evaluate and minimize the risk for natural ecosystems and living beings [4].
In this framework innovative AgNPs are presented. They are properly functionalized with citrate (Cit) and L-cysteine (L-cys) and this choice of capping agents allows both the detecting Hg (II) in water and assure low toxicity in the short and long term [5,6]. The local surface plasmon resonance (LSPR) at λ max = 400 nm, the Dynamic Light Scattering (DLS) measurements ($<2R_H> = 8 \pm 1$ nm) and Transmission Electron Microscopy (TEM) studies ($Ø = 5 \pm 2$ nm) confirm the system nanodimension and the stability in water. Moreover, the molecular and electronic structures of AgNPs were investigated by FTIR, SR-XPS, and NEXAFS techniques, in view of sensing applications. In fact, these AgNPs were tested as plasmonic sensor in water with 16 different metal ions, finding sensitivity to Hg (II) in the range 1-10 ppm. For these AgNPs, environmental safety assessment (ecosafety) was performed by using a standardized ecotoxicity bioassay as algal growth inhibition test (OECD 201, ISO 10253:2006), coupled with determination of Ag (I) release in fresh and marine water exposure media, by means of ICP-MS. These latest studies confirmed low toxicity and low Ag(I) release in water. Furthermore, being extremely efficient in detection, their eco-safe application will be improved by combining in a hybrid system the AgNPs with polymer-based matrices, in particular with cellulose, following an eco-design approach. In fact, preliminary studies allowed to obtain innovative AgNPs-cellulose system, prepared with the aim to reach many advantages: easily production, low costs, possible reuse, and eco-safe behavior.

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New aromatic NHC-gold complexes as anticancer agents: protein target evaluation and cytotoxic activity

Diego Tesauro[a], *Filippo Prencipe*[b], *Luisa Ronga*[c], *Enrique Alcoceba Alvarez*[c], *Ryszard Lobinski*[c], *Melchiorre Cervello*[d], *Giuseppe Felice Mangiatordi*[b], *Michele Saviano*[b],

[a]*Department of Pharmacy and Interuniversity Research Centre on Bioactive Peptides (CIRPeB), University of Naples "Federico II", via Mezzocannone 16, 80134 Naples, Italy;* [b]*Istituto di Cristallografia (IC), CNR Via Amendola 122/O 70126 Bari Italy;* [c]*Université de Pau et des Pays de l'Adour, E2S UPPA, CNRS, IPREM, Pau, France;* [d]*Istituto per la Ricerca e l'Innovazione Biomedica (IRIB), CNR, Via Ugo la Malfa 153, 90146 Palermo, Italy.*

Among the non-platinum antitumor agents, gold complexes have increased attention owing to their strong antiproliferative effects, which generally occur through non-cisplatin-like mechanisms of action [1]. The choice of auxiliary ligands can tune the stability of the complexes *in vivo*. N-heterocyclic carbene (NHC) ligands can stabilize the gold(I) and furthermore they can guarantee the necessary lipophilicity to favorite the penetration through the mitochondrial membrane. Therefore, several neutral and cationic gold carbene species have been synthesized and characterized in the last years [2]. Several studies have revealed that many cytotoxic gold compounds, either NHC-gold(I) complexes are potent Thioredoxin Reductase (TrxR) inhibitors [3]. Within this frame we have designed selected gold(I) complexes based on aromatic ligands reported in Figure. These ligands were synthesized adapting literature procedure. Monocarbene and biscarbene gold complexes were prepared after the transmetalation of corresponding silver compounds. All products were characterized by ^{1}H, ^{13}C NMR and Mass Spectrometry (MS). In turn to achieve more insight about the interaction of NHC-gold compounds, we studied by MS the interaction of our NHC-gold(I) compounds with the synthetic pentapeptide: H-Cys-Trp-Gy-Pro-Cys-NH_2, derived by the active site of thioredoxin enzyme comprising the thioredoxin system. The formation of 1:1 gold-peptide adducts was observed for our gold complexes and reasonably related to the interaction of gold with peptide thiol. In a selected case, the enzyme inhibition will be explored about a possible alternative target in the thioredoxin system of NHC-gold complexes. Overall, antiproliferative effects will be also evaluated *in vitro* for the new complexes by cancer cells biological assays.

Peptide: H-CysTrpGlyProCys-NH_2

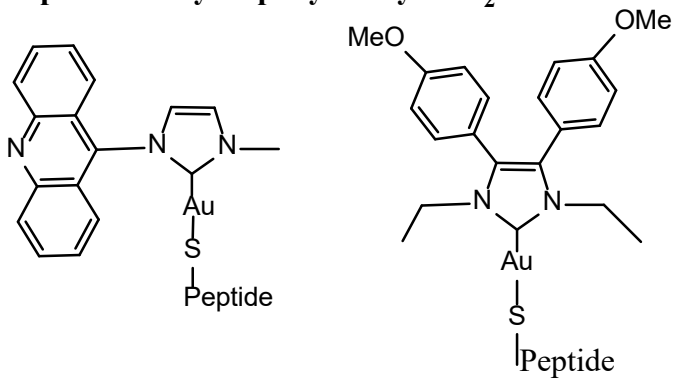

Figure: Example of observed MS adducts

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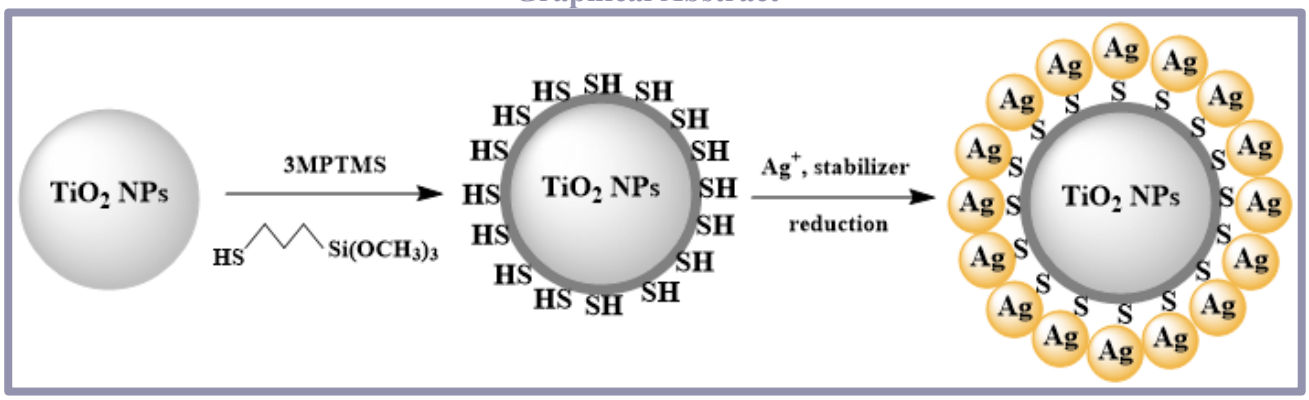
Silane-functionalized TiO_2 nanoparticles decorated with Ag nanoparticles for dual antimicrobial effects

Farid Hajareh Haghighi, Martina Mercurio, Sara Cerra, Tommaso A. Salamone, Ilaria Fratoddi

Department of Chemistry, Sapienza University of Rome, Piazzale Aldo Moro 5, 00185, Rome, Italy

TiO_2 and Ag nanoparticles (NPs) have attracted considerable attention in recent years due to the interesting antibacterial application of a single nanoplatform of these two components [1,2]. The direct TiO_2-Ag conjugation is still challenging and opens applicative perspectives as a multifunctional nanotool for dual antimicrobial activity.
In the present work, (3-mercaptopropyl)trimethoxysilane (3MPTMS) was selected as a bifunctional linker bearing –SH and –O moieties to mediate the chemical attachment of soft AgNPs to hard TiO_2NPs.
Moreover, the 3MPTMS linker can improve the stability and biocompatibility of TiO_2-Ag nanoconjugate. Regarding the synthesis, commercially available TiO_2NPs with a mean size of 50 nm were firstly functionalized with 3MPTS (hydrolyzed form of 3MPTMS) through the formation of
Ti–O–Si bonds and then Ag ions were coordinated to the –SH groups of the TiO_2NPs-3MPTS followed by reduction to the AgNPs forming the final TiO_2-3MPTS-Ag nanohybrid. Different reducing agents were tested for both reduction of the coordinated-Ag^+ and stabilization of the resultant AgNPs on the surface of TiO_2NPs-3MPTS. The stability, size, morphology, and chemical composition of the nanoparticles were evaluated by extensive characterizations including FTIR-ATR, FESEM-EDS, and DLS. Thanks to multidisciplinary collaborations, the *in vitro* antibacterial property of this TiO_2-Ag nanohybrid is in progress.

Graphical Abstract



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Porphyrins for second order nonlinear optics

Francesca Tessore,[a] Gabriele Di Carlo,[a] Alessio Orbelli Biroli,[b] Alessandra Forni,[c] Stefania Righetto.[d]

[a]Dipartimento di Chimica, Università degli Studi di Milano, UdR INSTM, via C. Golgi 19, 20133 Milano; [b]Dipartimento di Chimica, Università di Pavia, via Taramelli 12, 27100 Pavia; [c]CNR-SCITEC Istituto di Scienze e Tecnologie Chimiche "Giulio Natta" c/o Università degli Studi di Milano, via C. Golgi 19, 20133 Milano; [d]Dipartimento di Scienze della Terra e dell'Ambiente, Università di Pavia, via A. Ferrata 1, 27100 Pavia.

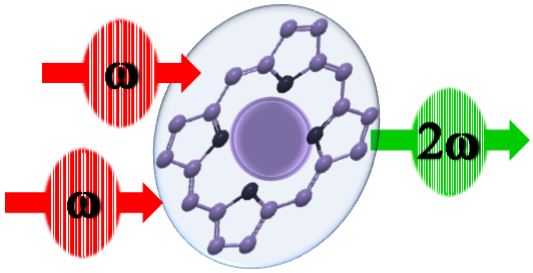

Figure 1: *schematic representation of a porphyrin-based NLO-phore*

In the last twenty-five years, many organic and organometallic molecular chromophores have attracted attention in the scientific community for the significant second order NLO properties, mainly arising from a donor - π-delocalized spacer - acceptor push-pull structure. Among them, porphyrins and metal porphyrins are very appealing, thanks to the thermal and chemical stability and the quite good solubility. The electron-rich extended 18-electron π-conjugated core of porphyrins can act as a spacer between the donor and the acceptor group in the push-pull system, or it can be itself the donor or the acceptor part of the push-pull architecture.

The four *meso*, the eight β-pyrrolic and the two axial positions allow a wide variety of chemical functionalizations, so that many different substituents can be linked to the core and to the metal centre. Moreover, by changing the metal center, its oxidation state, the type of the axial ligands, or the nature of the substituents at the periphery of the macrocycle, a fine-tuning of the electronic properties and a large second order NLO response can be achieved.[1]

Through experimental EFISH measurements and TD-DFT computational studies, the effect of the metal,[2] of the nature and of the position of the substituents,[3] and of the presence of aggregation phenomena in solution[4,5] have been investigated in depth.

This contribution aims to provide an account of the main results achieved so far by our research group for porphyrin-based NLO-phores, with a particular focus on the not-negligible role of third order contributions to the quadratic hyperpolarizability of A_4 β-substituted Zn^{II} porphyrins.

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Sulfonated N-heterocyclic carbene silver(I) and gold(I) water soluble complexes: catalytic and cytotoxic activity

Mariconda A.[a], *Sirignano M.*[b], *Longo P.*[b]

[a]*Department of Science, University of Basilicata, Viale dell'Ateneo Lucano 10, 85100 Potenza, PZ, Italy;* [b]*Department of Chemistry and Biology, University of Salerno, via Giovanni Paolo II,1321-84084, Fisciano, SA*

Late transition metal complexes have been mainly used in catalysis. In the twenty-first century, new catalytic systems have been developed aimed at developing processes with a lower environmental impact, reducing or eliminating the use and generation of hazardous substances. For this purpose water is the ideal reaction solvent[1] and consequently the research is oriented towards the development of water-soluble catalysts, possibly recyclable. In addition, the frequently water-insolubility of reaction products (organic compounds) makes their separation and recovery process easier.
The design and application of new water-soluble transition metal catalysts is often realized by attacking a group with the desired properties [2,3], *i.e.:* sulfonated groups.
After the discovery and characterization in 1991, by Arduengo, of the first N-heterocyclic carbene (NHC),many transition metals coordinated with NHC ligands have been used in organometallic catalysis, but only a few of them have been investigated in aqueous phase.[4] Our research fits into this context with the synthesis, characterization and use in catalysis of novel sulfonated N-heterocyclic carbene of silver(I) and gold(I) complexes (Figure 1).

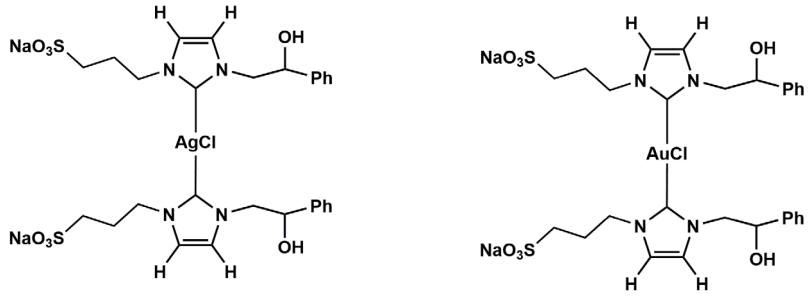

Figure 1. Novel sulfonated N-heterocyclic carbene of silver(I) and gold(I) complexes

We studied the catalytic performance of new complexes in various chemical reactions of alkynes: three-component coupling reactions (alkynes, aldehydes, amines), hydration and hydroamination.
Moreover, since recently, the metal complexes of N-heterocyclic carbenes have attracted much attention as potential anticancer agents[5], the synthesized complexes were screened for their cytotoxic activity against hepatocellular carcinoma (HepG2) and human hepatocyte (IHH), using MTT assay.

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Widening the tin solid-state chemistry: unusual bonding scenario in the $LaMgSn_2$ rare-earth stannide

Riccardo Freccero [a,b], *Pavlo Solokha* [a], *Serena De Negri* [a]

[a]*Dipartimento di Chimica e Chimica Industriale, Università degli Studi di Genova, via Dodecaneso 31, 16146 Genova (Italy);* [b]*Max-Planck-Institut für Chemische Physik fester Stoffe, Nöthnitzer Strasse 40, 01187 Dresden (Germany)*

Intermetallics are a large family of inorganic compounds investigated both for their structural peculiarities, including approximants and quasicrystals, and for their physical properties, such as superconductivity, heavy-fermion behaviour and multiferroicity. Their study has traditionally been somewhat neglected by chemists, due to the impossibility to apply the classical concepts of chemical bonding to these compounds, characterized by a low number of valence electrons. Nevertheless, some electron counting rules have been successfully conceived and applied. For example, in classical Zintl phases, formed by an electropositive metal and an electronegative *p*-block element, the number of covalent bonds realized by the latter is described on the basis of the 8–*N* rule. Chemical bonding analysis for *p*-elements containing compounds that violate the Zintl-Klemm rule is of great interest as unexpected and unprecedented bonding scenarios are often revealed. This is the case of the LuGe phase, where the "excess" electrons are the main responsible for the formation of Lu_4 four-atomic bonds [1].

In this work, the chemical bonding of the ternary $LaMgSn_2$ rare-earth stannide [2] was studied applying cutting-edge quantum-chemical techniques in position space. The two Sn atoms show different distributions of ELI-D attractors: one has an attractor along the shortest Sn–Sn contact (2.93 Å) plus three "lone-pairs" pointing to Mg and La; the other Sn shows four maxima in the "lone-pairs" region (see Figure). This topology seems to rule out the presence of additional Sn–Sn covalent bonds (d = 3.19 Å) supporting the formal electron-deficient scenario: $(La^{3+})(Mg^{2+})[(1b)Sn^{3-}][(0b)Sn^{4-}] \times 2p^{+}$. Nevertheless, a careful analysis of the ELI-D relative Laplacian suggests that the longer Sn–Sn interactions should be also interpreted as bonding. A similar scenario was reported for some antimonides (*e.g.* Li_2Sb) where the longest contacts were interpreted as one-electron bonds [3]. This leads, for the title compound, to a new ionic formulation: $(La^{3+})(Mg^{2+})[(2b)Sn^{2-}][(1b)Sn^{3-}]$ where each Sn gains one net single bond. Further analyses have evidenced that the Sn "lone-pairs" would be better described as multi-atomic polar-covalent interactions between Sn and the surrounding Mg and La metals. Particularly interesting is the presence of a 2-center covalent Sn–Mg interaction.

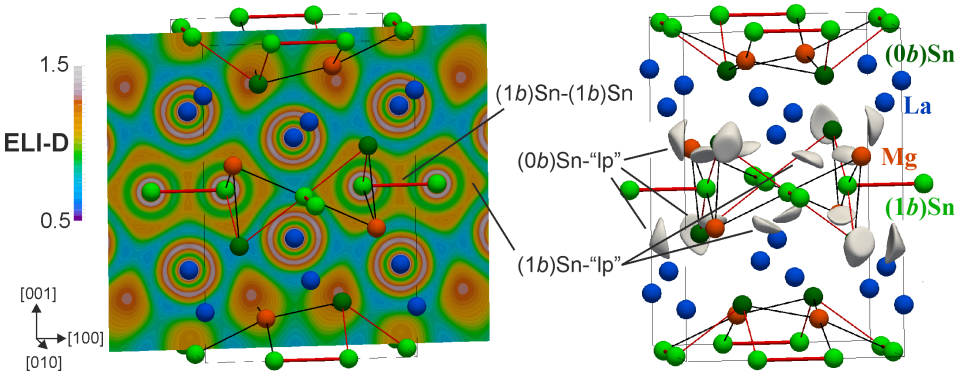

Figure. ELI-D distribution in the (020) plane (left) and isosurfaces (right) for $LaMgSn_2$.

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NMR reveals the metabolic changes induced by Auranofin in ovarian cancer cells

Veronica Ghini[a,b], *Lara Massai*[b], *Tania Gamberi*[c], *Luigi Messori*[b], *Paola Turano*[a,b]

[a]*Center of Magnetic Resonance, University of Florence, Italy;* [b]*Department of Chemistry, University of Florence, Italy;* [c]*Department of Experimental and Clinical Biomedical Sciences, University of Florence, Italy.*

Gold-based compounds constitute a variegate family of very promising metallodrugs for cancer treatment. Despite several mechanistic studies demonstrated that the gold compounds possess mechanisms of action that are distinct from those of the well-known anticancer platinum-drugs, their precise mechanisms of action remain to be elucidated to a large extent. Auranofin (AF hereafter) is a metal-based drug consisting of a gold(I) center linearly coordinated to triethylphosphine and to a thiosugar ligand [1]. Typically, AF behaves as a prodrug undergoing activation through release of the thiosugar ligand. AF interacts very weakly with DNA while manifesting a remarkable affinity and selectivity for proteins bearing free cysteines and selenocysteines [2]. Thioredoxin reductase, a selenoenzyme governing the intracellular redox balance, is believed to be its primary target [3].
Here, ^{1}H NMR-spectroscopy was used as an efficient and highly reproducible platform for the analysis of A2780 ovarian cancer cells after AF treatment. The chemical identity and concentration of metabolites detected in cell lysates and their respective growing media can be viewed as a global fingerprint that unambiguously describes the response to drug treatment [4-5].
An early and large increase in intracellular glutathione is highlighted as the main effect of the treatment accompanied by small but significant changes in the levels of a few additional metabolites. The observed biochemical alteration can be interpreted in terms of the cross-talk between the thioredoxin and glutathione redox systems [5].

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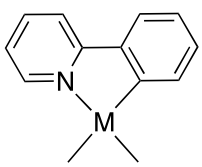
Advances in Pt(II) rollover chemistry

Antonio Zucca, Luca Maidich, Davide Vitale, Maria I. Pilo and Sergio Stoccoro

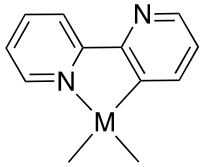
University of Sassari, Department of Chemistry and Pharmacy, 07100 Sassari, Italy; zucca@uniss.it

The chemistry of cyclometalated complexes has become one of the most important fields of organometallic chemistry. During the years cyclometalation studies have evolved from the search of new C-H bond activation methods and coordination modes to its present standpoint into applications.

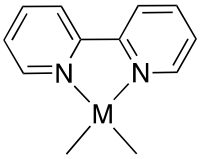
In addition to classical cyclometalated complexes, new families of less conventional derivatives have appeared in the literature, such as that of rollover compounds. In rollover cyclometalation a bidentate heterocyclic ligand, after chelation, displaces one of the donor atoms from the metal and, after an internal rotation, activates a remote C-H bond to give a rollover complex.[1] The resulting derivatives display properties which differ from those of the classical cyclometalated species, mainly due to the presence of an uncoordinated donor atom, which can serve as a site for coordination, protonation, cyclometalation and other chemical reactions, being also able to assist catalytic processes. Due to their flexibility, these complexes can act, *inter alia*, as catalysts, antitumor drugs, chemosensors and photoluminescent agents.



classical cyclometalated complex
(2-phenylpyridine)

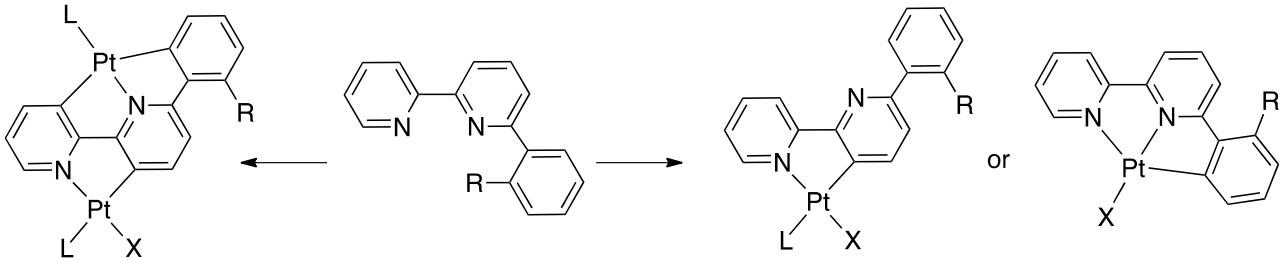


rollover cyclometalated complex
(2,2'-bipyridine)



classical chelated complex
(2,2'-bipyridine)

Following our long-standing interest in this field[2] we report here our latest results on the Pt(II) rollover chemistry of 2,2'-bipyridines. In particular we will report a preliminary study on the relationship between classical and rollover cyclometalated Pt(II) complexes, by comparing isostructural and isoelectronic complexes of cycloplatinated 2-phenylpyridine and 2,2'-bipyridine and our latest investigations on Pt(II) rollover chemistry. As an example, addition of aryl substituents on the bipyridine scaffold can result in multiple C-H bond activations affording mono and dinuclear species according to reaction conditions.



Other aspects of rollover behaviour include reactions with acids, which may result in retro-rollover reactions, methane evolution, or nitrogen protonation, affording abnormal-remote pyridylenes.

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Hybrid transition metal dichalcogenide/graphene microspheres for hydrogen evolution reaction

Marco Lunardon, Jiajia Ran, Stefano Agnoli and Gaetano Granozzi

Department of Chemical Sciences, University of Padova, Via F. Marzolo 1, 35131 Padova, Italy.

Here, we report the successful fabrication of transition metal dichalcogenides (TMDCs)/graphene hybrid systems with well-controlled 3D morphologies following a highly scalable procedure that combine electrospraying and freeze-drying techniques. This novel approach produces a unique center-diverging microchannel spherical structure, named graphene oxide aerogel microspheres (GOAM)[1] used as a scaffold to incorporate TMDCs. The aim was to prove that it is possible to integrate into a 3D graphene network the functional properties of TMDC-based electrocatalysts without altering the microchannel central divergence morphology and to create intimate contacts between the two materials, which increase the final hydrogen evolution reaction (HER) activity while maintaining accessible the TMDC catalytic sites.

For the synthesis of the TMDC component two different approaches were explored. Through the first method (top-down), we used exfoliated TMDC nanosheets that were later introduced in a graphene oxide (GO) suspension, and assembled into the mechanically stable, center diverging nanohybrids by consecutive steps of electrosprayig, freeze-drying and mild thermal annealing (450°C).[2] Once demonstrated the interesting HER activity of these hybrid systems, to optimize the active sites, we investigated a bottom-up approach by introducing in the initial GO suspension a suitable precursor (ammonium tetrathiomolybdate) that, after the electrospraying, freeze-drying steps, and thermal annealing, eventually nucleates small TMDC nanoparticles inside the GOAMs (see Figure 1). We demonstrated that the second approach improves the uniformity and dispersion of the catalytic sites in the 3D graphene network and offers better HER performance. Moreover, such bottom-up approach allows a facile preparation of Ni-doped MoS_2/prGOAMs hybrid catalysts [3] that exhibited an excellent HER activity with an outstanding overpotential of 0.160 V to achieve 10 mA/cm^2 in alkaline conditions.

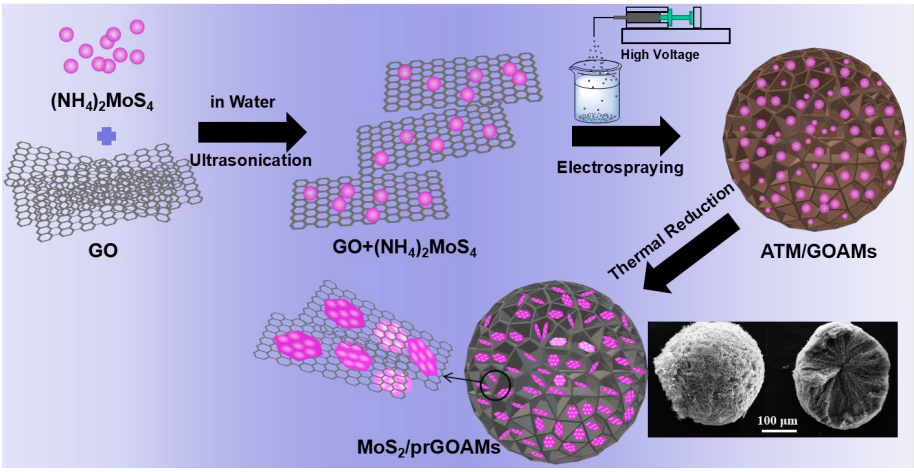

Figure 1. Schematic illustration of the bottom-up synthesis of the MoS_2/prGOAMs.

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Porphyrin functionalized ZnO/SiO_2 hybrid nanoparticles as scintillator agent

Silvia Mostoni[a,b], Roberta Crapanzano[a], Irene Villa[c], Massimiliano D'Arienzo[a,b], Barbara Di Credico[a,b], Mauro Fasoli[a], Anna Vedda[a], Roberto Scotti[a,b]

[a]Department of Materials Science, University of Milano Bicocca, Via Roberto Cozzi 55, 20125 Milano; [b]INSTM, University of Milano Bicocca, Via Roberto Cozzi 55, 20125 Milano; [c]Institute of Physics of the Czech Academy of Science (FZU), Cukrovarnicka 10/112, 16200 Prague, Czech Republic.

ZnO coupled with organic photosensitizers (PS) is a potential candidate material as scintillator agent for cancer treatment under X-ray. In these conditions, ZnO nanoparticles (NPs) convert the X-ray into UV-Vis emission, promoting the PS excitation and leading to the production of reactive oxygen species (ROS). Its photostability and biocompatibility make ZnO suitable for in vivo applications. However, the efficient coupling of ZnO with different PS (typically porphyrin) is still a controversial issue, as it requires both a high ZnO luminescence yield and a good overlapping of ZnO emission-PS absorption spectra, along with a suitable energy transfer between ZnO and PS.
In this perspective, the aim of this work is to design ZnO-porphyrin structures with high energy transfer efficiency for application in anti-cancer therapies and imaging that exploit ionizing radiations. Thus, the work focused on the development of porphyrin functionalized ZnO hybrid NPs anchored on SiO_2 NPs as carrier and on the investigation of their optical properties and ZnO-PS interaction, aiming at the understanding of the role of ZnO-PS proximity on their optical behavior.
The material synthesis followed a three-steps procedure: i) ZnO NPs were anchored onto silica NPs (both porous and non-porous), used as support and carrier; ii) then, the surface of ZnO/SiO_2 NPs was functionalized with 3-aminopropyl)triethoxysilane (APTES) as silane-grafting agent, by hydrolysis and condensation reactions; iii) the functionalized ZnO/SiO_2 NPs were reacted with increasing amounts of PS (tetrakis(4-carboxyphenyl)porphyrin(TCPP), by using amino:TCPP molar ratios equal to 1:0,1, 1:0,25, 1:0,5 and 1:1), in order to promote the formation of a covalent bond between amino groups of APTES linked onto ZnO/SiO_2 and COOH groups of TCPP. The structural and surface characterization confirmed the presence of amorphous ZnO NPs of 5-6 nm on SiO_2 surface. The ZnO/SiO_2 functionalization with APTES and TCPP was assessed by Infrared Spectroscopy, Thermogravimetric Analysis and Elemental Analysis. APTES was confirmed to be linked to the ZnO/SiO_2 surface and increasing TCPP amounts were detected depending on the TCPP loading, up to 3,0 wt% of TCPP over SiO_2, as confirmed by the absorption spectra of TCPP-functionalized ZnO/SiO_2. The optical properties of TCPP-functionalized ZnO/SiO_2 were preliminary tested in dimethylformamide, used as solvent reaction for TCPP anchoring on SiO_2. The Photoluminescence Analysis (PL) revealed a high luminescence of ZnO NPs, with no detrimental effects given by the addition of APTES. Besides, it showed the absence of non-radiative energy transfer between ZnO and TCPP in all the materials, while a radiative one occurred, in which ZnO emitted photons are re-absorbed by TCPP. This energy transfer is not visible in a mechanical mixing of ZnO and TCCP. Hence, an optical interaction between ZnO and TCPP in the materials was partially achieved upon functionalization. Differently, TCPP emission was hugely enhanced under X-ray irradiation in the Radioluminescence Analysis (RL), whereas no enhancement was detectable in the mechanical mixing. The RL spectra indicated that this enhancement could be generated by both re-absorption of ZnO emitted photons and by ionizing radiation energy deposition in the porphyrin surroundings, whose efficiency depend on the TCPP arrangement and spatial distribution.
In conclusion, this work paves the way to the deeper understanding of the correlation between the synthesis and the optical interactions of ZnO scintillator coupled with organic moieties to improve their luminescence performances.

Square-planar *vs.* trigonal bipyramidal molecular geometry in glucoconjugate triazole Pt(II) complexes: synthesis, in-solution behaviour and anticancer properties[1]

Alfonso Annunziata,[a,b] Emiliano Bedini,[a] Maria Elena Cucciolito,[a,b] Davide Liberti,[a] Domenico Loreto,[a] Daria Maria Monti,[a] Antonello Merlino,[a] Francesco Ruffo[a,b]*

[a] *Dipartimento di Scienze Chimiche, Università di Napoli Federico II, Via Cintia 21, I-80126, Napoli (NA), Italy.;* [b] *Consorzio Interuniversitario di Reattività Chimica e Catalisi, via Celso Ulpiani 27, I-70126 Bari, Italy*

Platinum compounds have assumed a prominent role in anticancer chemotherapies, despite the occurrence of severe side effects and drug resistance which limit their effects. In last years, we focused our research on the design of organometallic Pt-complexes bearing sugar-based ligands, as valid alternative to the more common platinum coordination compounds.[2,3] The presence of a sugar fragment in the coordination sphere of the complex improves the biocompatibility of the agent, allows to tune its physical-chemical properties (e.g. lipophilicity and water solubility) and it can improve its the selectivity toward cancer cells.[4] Among the proposed molecules, five-coordinate Pt(II) complexes in which glucose fragments are linked to the metal through triazole-based ligands (**1Pt** in **Figure 1**) showed to be more active than cisplatin although no selectivity was observed.[5]

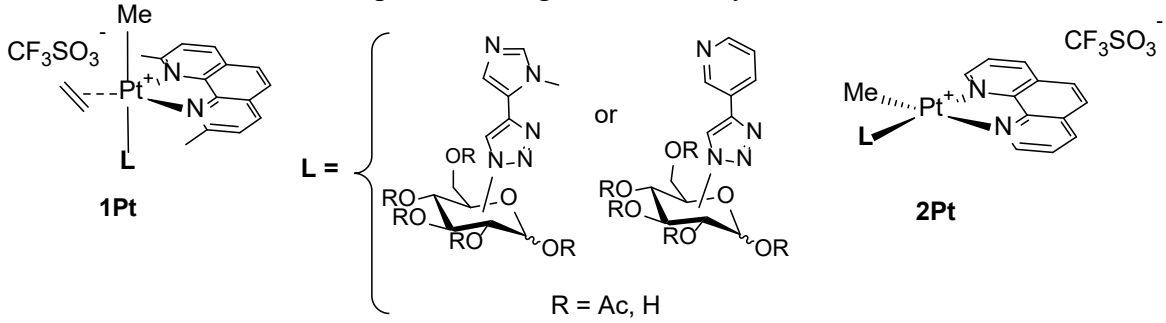

Figure 1

On this basis, the related family of compounds **2Pt** (in **Figure 1**) in the more common square-planar geometry has been synthetized and characterized. In-solution studies disclosed that **2Pt** complexes are more inert than **1Pt** toward ligand substitution, both in organic and mixed water-organic solvents, retaining the glucose-based ligand which was quickly substituted by the solvent in five-coordinate analogues **1Pt**. This observation agrees with the lack of selectivity observed for the class. Such preliminary investigations encouraged us to perform a comparative study between two families, by evaluating their cytotoxicity and their reactivity with model biological molecules. The results allowed us to shed light on the molecular geometry-activity relationship between two classes of Pt-based anticancer agents sharing the oxidation state and the nature of the ligands in two different geometries.

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Iron (III) trimesate xerogel by ultrasonic irradiation

Giada Mannias [a], *Martina Pilloni* [a,b], *Aharon Gedanken* [b], *Vijay Bhooshan Kumar* [b], *Alessandra Scano* [a] *and Guido Ennas* [a].

[a]*Department of Chemical and Geological Sciences, University of Cagliari and INSTM unit, S.S. 554 bivio Sestu, 09042 Monserrato (CA), Italy;* [b]*Department of Chemistry, Bar-Ilan University, Ramat-Gan 5290002, Israel.*

Metal-Organic Frameworks (MOFs) are crystalline porous coordination polymers composed of organic-inorganic building units [1]. Structures built on iron (III) and 1, 3, 5-benzenetricarboxylate (BTC or trimesate), also known as Fe-BTC materials, have attracted enormous attention because of their high biocompatibility, low cost, redox behavior and stability in air, water and organic solvents [2]. All these features have made Fe-BTC MOF a suitable candidate for the application in several fields, including catalysis, gas storage and separation, drug-delivery and protein immobilization [3]. The first type of iron (III) trimesate MOF synthesized was MIL-100(Fe) [4]. The traditional synthesis of this system consists in the solvothermal method, which is time-consuming, expensive and implies the use of large amounts of solvents (e.g. HF) [4]. Hence, several alternative green approaches, including mechanochemical and sonochemical methods, have been proposed in order to obtain this material in a shorter time under mild and low-cost conditions [5]. We present here a green method for the synthesis of a microporous Fe-BTC MOF at room temperature in water, using ultrasonic (US) irradiation. We conducted two groups of experiments using different ultrasonic apparatus to investigate, respectively, the time effect of US irradiation and the influence of pH in terms of microstructure, thermal stability and textural properties of the material. A gel was obtained in all synthesis as the effect of cavitation due to US irradiation. After a drying process, accompanied by a shirking effect, a transparent, glassy xerogel was obtained (Fig. 1). The gel and monolithic states hold great promise for novel application of MOFs, owing to providing a minimal mass transfer resistance and an increased gas adsorption capability, compared to powders [6]. All the samples obtained were characterized by X-ray powder diffraction (XRPD), Fourier transform infrared spectroscopy (FTIR), thermal analysis and nitrogen physisorption. We observed significant differences in surface areas and micropore volume, although the samples showed similar microstructure by FTIR and PXRD.

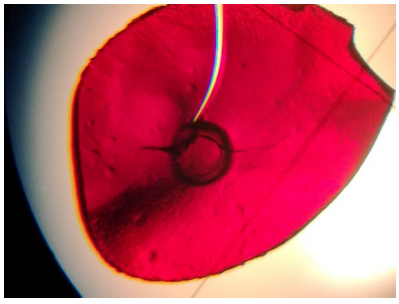

Fig. 1. Fe-BTC xerogel from the shrinking process during slow drying of gel at room temperature observed with an optical microscope.

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Exploiting the transformative features of metal halides for the synthesis of $CsPbBr_3$@SiO_2 core-shell nanocrystals

Christian Rossi,[a,b] *Riccardo Scarfiello,*[c] *Dmitry Baranov,*[b*] *Rosaria Brescia,*[d] *Luca Goldoni,*[e] *Gianvito Caputo,*[b] *Luigi Carbone,*[c] *Luca De Trizio,*[b] *Liberato Manna,*[b] *Diego Colombara.*[a,b*]

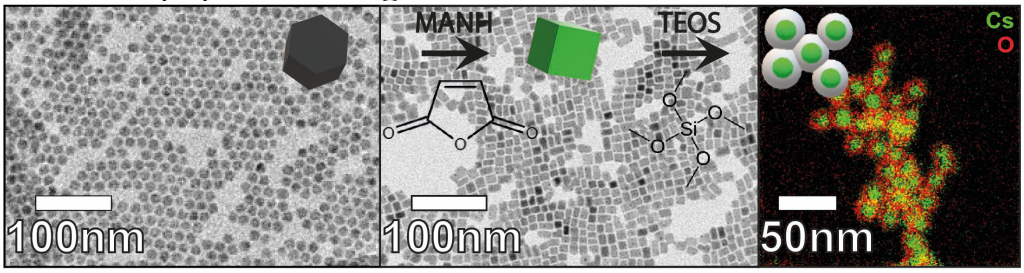
[a]*Department of Chemistry and Industrial Chemistry, University of Genova, via Dodecaneso 31, 16146 Genova, Italy;* [b]*Nanochemistry Department, Italian Institute of Technology, via Morego 30, 16163 Genova, Italy.;* [c]*CNR NANOTEC, Institute of Nanotechnology, c/o Campus Ecotecne, via Monteroni, 73100 Lecce, Italy;* [d]*Electron Microscopy Facility, Istituto Italiano di Tecnologia, via Morego 30, 16163 Genova, Italy.* [e]*Analytical Chemistry Lab, Istituto Italiano di Tecnologia, via Morego 30, 16163 Genova, Italy.*

Lead halide perovskite (LHP) nanocrystals (NCs) are an emerging semiconductive material with a great potential for applications in optoelectronic devices such as photodetectors, solar cells, light-emitting diodes, etc.[1] Such an interest in LHP NCs is motivated by their easy synthesis combined with tunable and bright photoluminescence (PL) and strong absorption.[2] Despite their impressive optoelectronic properties, LHP NCs experience fast degradation when exposed to UV irradiation, high temperature, moisture, acidic or alkaline environments and polar solvents.

Silica has emerged as the most promising material for LHP NCs stabilization.[3] However, such enhanced stability is achieved with bulk silica which cannot be employed in technologies that require colloidal stability (e.g. inkjet printing). As a consequence, the community is moving to colloidally stable LHP NCs@SiO_2 core@shell systems.

The complexity of growing silica shells onto preformed LHP NCs arises from NCs degradation under the conditions needed to grow silica, i.e. the acidic or alkaline environments that catalyze growth. Interestingly, *Baranov et al.* stabilized $CsPbBr_3$ NCs in an acidic environment through the reaction of the non-luminescent Cs_4PbBr_6 NCs with poly(maleic anhydride-alt-1-octadecene) (PMAO). In particular, the oleylamine capping ligands react with the polymer promoting the formation of the luminescent $CsPbBr_3$ NCs and acidifying the reaction environment due to maleamic acid formation.[4]

In our study, we exploited the acidic environment produced by the reaction of maleic anhydride (MANH, the reactive monomer of PMAO) with the oleylamine ligand of Cs_4PbBr_6 to prepare $CsPbBr_3$@SiO_2 in presence of tetraethyl orthosilicate (TEOS). XRD showed the partial conversion of the Cs_4PbBr_6 into the $CsPbBr_3$ NCs which was confirmed by their green emission. The $CsPbBr_3$@SiO_2 were further coated with SiO_2 enhancing the stability towards polar solvents and removing the residual Cs_4PbBr_6 NCs. These results provide interesting insights onto the mechanism of silica shell formation. Namely, Both the acidic environment and the Cs_4PbBr_6 NCs as starting material are needed to prepare $CsPbBr_3$@SiO_2.



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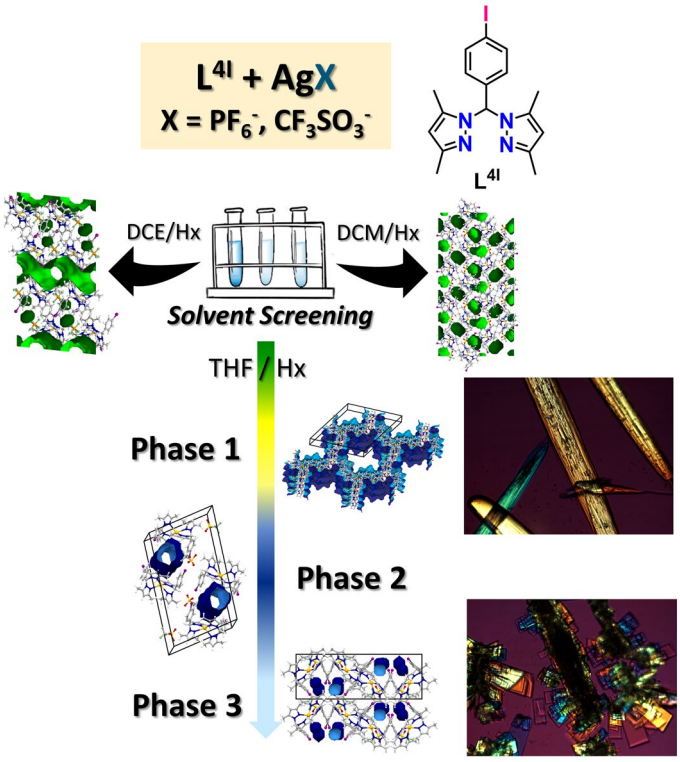
Supramolecular assemblies in silver bispyrazolylmethane complexes: phase transitions and the role of the halogen bond

Giulia Bonfant, Davide Balestri, Luciano Marchiò

Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale (Chemistry Unit), Università di Parma, 43124, Parma, Italy, luciano.marchio@unipr.it

Here we report a systematic investigation of how the halogen bond [1] can modulate the supramolecular arrangement of silver complexes [2]. The compounds are synthetized by complexing two different Ag(I) salts ($AgPF_6$, $AgCF_3SO_3$) with X-phenyl(bispyrazolyl)methane (X = Br, I). The halogen functions are located in *meta* or *para* (L^{3I}, L^{4I}) positions on the phenyl ring in order to provide different directionalities of the X function with respect to the N,N coordination system. In all compounds, the presence of halogen bonds in the crystalline structure was confirmed by X-ray diffraction on single crystal. The solvent of crystallization influences the crystal packing, and $[Ag(L^{4I})_2]PF_6$ gives rises to three different solvates when crystallized in dichloroethane/hexane, dichloromethane/hexane and THF/hexane, respectively [3]. Both complexes $[Ag(L^{4I})_2]PF_6$ and $[Ag(L^{4I})_2]CF_3SO_3$ crystallized from THF/hexane are characterized by the presence of three different phases. The single-crystal evolution from Phase 1 (a honeycomb structure with large 1D channels comprising 56% of the unit cell volume) to Phase 3 (solventless) occurs by the stepwise decrease in the crystallization solvent content.



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Fine-tuning of the size of luminescent CaF_2 nanoparticles

Giacomo Lucchini[a], Chiara Cressoni[a], Emil Milan[a], Nicola Da Roit[a], Francesca Parolini[b], Nicola Pinna[c], Mariapina D'Onofrio[b], Adolfo Speghini[a]

[a]Nanomaterials Research Group, Department of Biotechnology, University of Verona and INSTM, RU of Verona, Strada le Grazie 15, 37134 Verona, Italy; [b]Chemistry of Biomacromolecules, Department of Biotechnology, University of Verona, Strada le Grazie 15, 37134 Verona, Italy; [c]Institut für Chemie and IRIS Adlershof, Humboldt-Universität zu Berlin Brook-Taylor-Str. 2, 12489 Berlin, Germany.

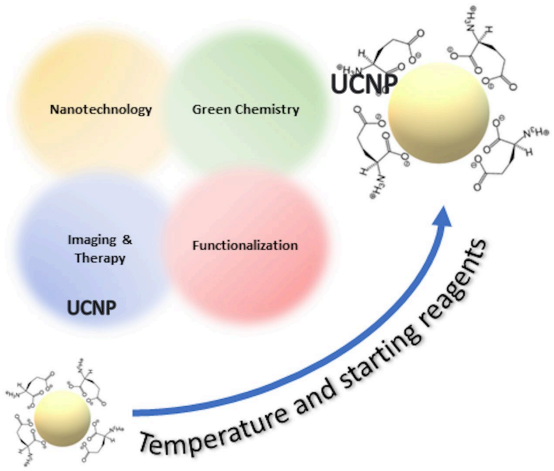
Luminescent Lanthanide ions doped fluoride nanoparticles are valuable in several modern technological and biomedical applications as diagnostic probes and as therapeutic agents in nanomedicine.[1-3]

In this communication, we describe an investigation on CaF_2 nanoparticles (NPs), properly activated with luminescent Ln^{3+} ions (e.g., Yb^{3+}, Nd^{3+}, Tm^{3+}, Er^{3+}), which exhibit strong upconversion (UC) emissions in the optical range upon near infrared (NIR) laser excitation.

These UCNPs have been prepared using a "green chemistry", microwave assisted hydrothermal technique, using hydrophilic and biocompatible molecules as capping agents, as citrate or glutamate moieties. The coordination of these capping molecules on the surface of the UCNPs confers excellent colloidal stability and open the way to further functionalization on the nanoparticle surface.

A facile microwave assisted hydrothermal synthesis allows to prepare UCNPs directly dispersed in aqueous solutions, with the possibility of fine-tuning the nanoparticle size. We have investigated how the variation of the experimental conditions, as the reaction temperature and the starting reagents concentrations, impacts on the particle size. Preliminary results indicate that the particle size of the UCNPs can be easily varied in a range of tenths of nanometers, with a good monodispersion, also influencing the UC emission.

To test the biocompatibility of the prepared UCNPs, the cytotoxicity has been also evaluated by cell viability assays.



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Responsive Self-Assembled Dynamic Helicates

Antonio Santoro[a,b], *Jan Holub*[a,c], *Marta A. Fik-Jaskółka*[a,d,e], *Ghislaine Vantomme*[a,f], *Jean-Marie Lehn*[a]

[a]*Laboratoire de Chimie Supramoléculaire, ISIS, Université de Strasbourg, 8 Allée Gaspard Monge, 67000 Strasbourg, France;* [b]*Present address: Department of Chemical, Biological, Pharmaceutical and Environmental Sciences, University of Messina, Viale F. Stagno d'Alcontres 31, 98166 Messina, Italy;* [c]*Present address: Institute of Chemical Research of Catalonia (ICIQ) Avinguda Països Catalans 16, 43007 Tarragona, Spain;* [d]*Present address: Faculty of Chemistry, Adam Mickiewicz University, Uniwersytetu Poznańskiego 8, 61-614 Poznań, Poland;* [e]*Present address: Centre for Advanced Technology, Adam Mickiewicz University, Uniwersytetu Poznańskiego 10, 61-614 Poznań;* [f]*Present address: Institute for Complex Molecular Systems, Laboratory of Macromolecular and Organic Chemistry, Eindhoven University of Technology, P.O. Box 513, 5600 MB Eindhoven, The Netherlands;*

The understanding and the application of reversible covalent reactions and coordination chemistry together with the proper design of the molecular frameworks, allow one to achieve not only well-defined output architectures but also different grades of complex behaviour.
The systems investigated offer an additional level of complexity by combining self-sorting on two levels: 1) the build-up of the ligand strand constituents from their components through dynamic covalent chemistry; 2) the assembly of the helicates from the ligands and the metal cations through dynamic metallosupramolecular chemistry. The information encoded in the ligands constituent molecule was read differently (and accurately at the same time) by metal cations that varied in the coordination algorithms. It enabled the selective formation of a specific type of helicates from a wide library of helicates formed by the possible combination of subcomponents.

Synthesis in confined space of luminescent nanostructures of undoped and Eu(III)-doped calcium molybdate

Chiara Mazzariol[a], *Francesca Tajoli*[a], *Alexander Evgenyevitsch Sedykh*[b], *Paolo Dolcet*[c], *Klaus Müller-Buschbaum*[b,d], *Silvia Gross*[a,c]

[a]*Department of Chemical Sciences, University of Padova, 35131, Italy;* [b]*Institut für Anorganische und Analytische Chemie, Justus-Liebig-Universität Gießen, 35392, Germany;* [c]*Institut für Technische Chemie und Polymerchemie (ITCP), Karlsruher Institut für Technologie (KIT), 76131, Germany;* [d]*Center for Materials Research (LAMA), Justus-Liebig-Universität Gießen, 35392, Germany*

In recent years, many efforts have been devoted to obtain inorganic nanomaterials with controlled size, shape and crystalline phase, features which all play a relevant role in determining the final functional properties [1]. In this regard, the synthesis of inorganic nanostructures in confined space, which is defined as an enclosed nanoscale volume with limited accessibility, is a challenging and promising route to achieve these goals, since it allows to explore non-conventional crystallization pathways and finely control on reaction outcomes [2].

In this work, the restricted enviroment of water droplets in inverse minimeulsion has been employed as a synthetic pathway to inorganic nanostructures with controlled size and shape. The reaction is supposed to take place in an independent way inside the 'nanoreactors', that are identified as the nanodroplets of inverse water-in-oil miniemulsions, in the size range of 50-300 nm [3]. Within this framework, calcium molybdate $CaMoO_4$ has been chosen as a model system to investigate how the confined space affects the final features of the synthesized nanoparticles. Calcium molybdate is a promising photoluminescent material, due to its intrinsic photoluminescence properties, its chemical and thermal stability. It finds applications in many fields as phosphor, laser material and in light emitting diode, especially when doped with rare earth ions (e.g., Eu^{3+}, Tb^{3+}, Yb^{3+}, Dy^{3+}) [4,5].

The synthesis of the target inorganic system has been performed via inverse miniemulsion and, as a reference, in batch (without spatial confinement). Calcium molybdate has been synthesized both undoped and Eu(III)-doped at different doping percentages (Eu:Mo = 1, 3, 5, 7 at%.). The results thereby obtained through the two different synthetic routes have been related to the effect of the spatial confinement of the reaction environments on the final features. In particular, significant effects ascribable to the confined space have been found in the i) size and shape of the nanoparticles (XRD, TEM and SEM); ii) effectiveness of the doping with Eu(III) ions (XRD, ICP-MS, XAS); and iii) photoluminescence properties (photoluminescence excitation and emission spectra, emission lifetime, quantum yield, and emission intensity).

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The synergistic and photochromic effect of Au nanoparticles on a Silver-waste derived TiO_2 photocatalyst

M. Stucchi[a], D. Meroni[a], C. L. Bianchi[a] and L. Prati[a]

[a]*Dipartimento di Chimica, Università degli studi di Milano*

Noble metals nanoparticles (NPs) absorb light in the visible range because of the surface plasmon resonance (SPR) phenomenon [1]. Silver NPs coupled with TiO_2 show many advantages regarding materials energy and sustainability, including plasmon-enhanced photocatalytic activity [2][3]. However, the use of noble metals is limited by their high cost and search for alternatives is one of the greatest interest topics of nowadays. Alternatives can be found in the use of inexpensive and earth-abundant elements or, even, in the use of waste. In particular, wastewater from metal refineries have high concentration of residues of precious metals.
Here, valorisation of silver processing industries wastewater was carried out for the first time recovering Ag for preparing Ag-modified TiO_2 (3%wt). This material resulted active in ethanol photocatalytic oxidation (Fig. 1a). The addition of a small amount of Au nanoparticles (as low as 0.5% wt.) synthesized by sol-immobilization [4] produced a strong synergistic effect not only improving the activity of the photo-catalyst but also modifying the final product distribution (Fig. 1b). Indeed, full conversion of EtOH was reached in about 1 hr (compared to more than 3 hrs in the case of Ag/TiO_2) and CO_2 as main product was obtained (compared to acetaldehyde in the case of Ag/TiO_2). TEM characterization revealed the presence of big Ag NPs (about20 nm) on which, in some cases, small gold nanoparticles have been deposited (about 2-3 nm). Besides the SPR-induced extension of light absorption of TiO_2, Au addition to $Ag\text{-}TiO_2$ also leads to synergistic photochromic effects under UV irradiation that, to the authors' best knowledge, have never been previously reported.

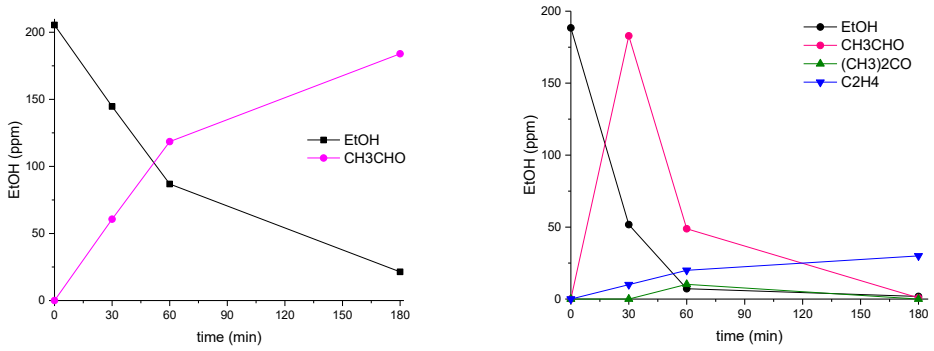

Fig. 1 EtOH UV photo-oxidation by $Ag\text{-}TiO_2$ (a) and by $0.5\%Au/Ag\text{-}TiO_2$

Therefore, the interaction between Au and Ag nanoparticles produces a synergistic effect that changes the photocatalytic activity, as well as the behaviour of the sample under irradiation and forms a novel promising photocatalyst material from waste products.

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Efficient palladium catalyzed bis-alkoxycarbonylation of olefins for the synthesis of useful succinic acid derivatives

Diego Olivieri,[a] Riccardo Tarroni,[a] Gabriele Manca,[b] Carlo Mealli,[b] Carla Carfagna[a]

[a]Department of Industrial Chemistry "T. Montanari", University of Bologna, Viale Risorgimento 4, 40136 Bologna (BO), Italy. E-mail: diego.olivieri2@unibo.it; [b]Istituto di Chimica dei Composti OrganoMetallici, CNR-ICCOM, Via Madonna del Piano 10, I-50019 Sesto Fiorentino, Florence (FI), Italy.

Succinic acid is an important intermediate for the production of commodity chemicals and the world market potential of its derivatives is estimated to be around 270.000 t/year.[1] Above all, succinates find applications in various industrial fields, such as cosmetics, agricultural chemistry, food industry and material science.[2] In this context, based on our knowledge on the carbonylation reactions of unsaturated substrates, we have recently developed an efficient, low-cost and one-pot methodology for the synthesis of succinic acid derivatives. In particular, we were able to carry out the bis-alkoxycarbonylation of olefins using palladium/aryl α-diimine complexes as catalysts, obtaining succinates in high yields and selectivities, under mild reaction conditions. The reaction proceeds utilizing *p*-benzoquinone as oxidant and *p*-TSA as additive, in the presence of an alcohol, which acts both as a solvent and as nucleophile, under 4 bar of carbon monoxide at 20°C. The most active catalysts are easily formed *in situ* by mixing $Pd(TFA)_2$ and the nitrogen ligands **1a** or **1b**, in THF (Figure 1, left). This process has also been successfully applied to particularly low-reactive olefins, such as 1,2-disubstituted olefins,[3] including unsaturated fatty acid methyl esters, or acrylic esters and acrylic amides.[4] Interestingly, when internal olefins are utilized, the process turned out to be diastereospecific and no Pd-catalyzed isomerization of the double bond has been observed.[5] Our studies, in addition to providing a complete library of succinates, allowed us to highlight some relevant aspects of the catalytic cycle of the bis-alkoxycarbonylation reaction, through mechanistic investigations carried out with ab-initio calculations (Figure 1, right).[6]
Here, our latest results on the bis-alkoxycarbonylation process will be presented.

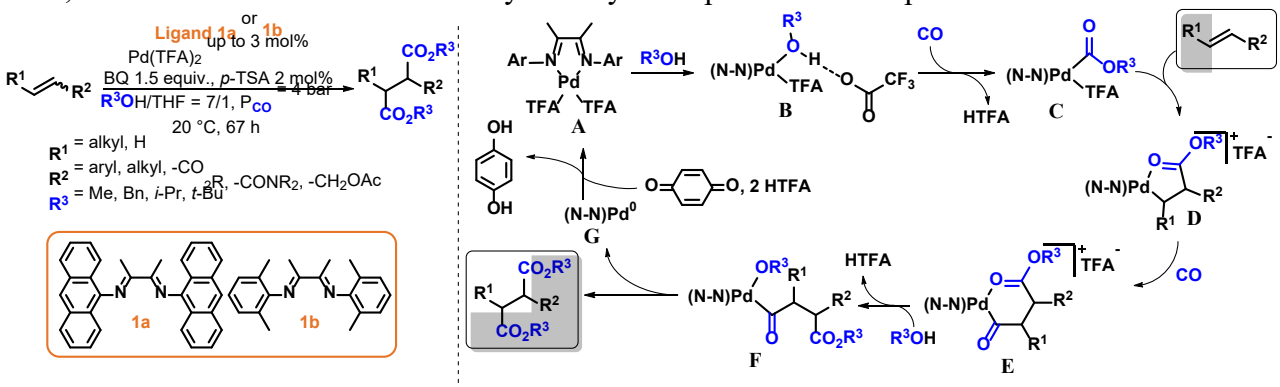

Figure 1 – Bis-alkoxycarbonylation reaction of olefins.

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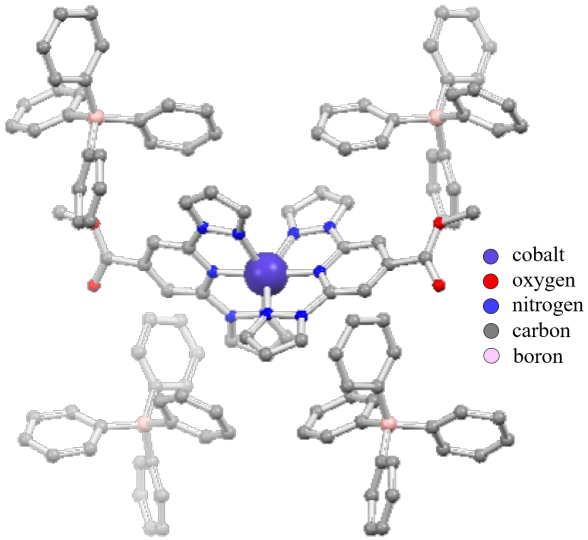
Multivariate approach to the analysis of structural data of iron(II) spin crossover complexes and cobalt(II) single molecule magnets

Lorenzo Marchi,[a] Simone Fantuzzi,[a] Marina Cocchi,[a] Rita Mazzoni,[b] Stefano Zacchini,[b] Dawid Pinkowicz,[c] Luca Rigamonti[a]

[a]Dipartimento di Scienze Chimiche e Geologiche, Università degli Studi di Modena e Reggio Emilia, via G. Campi 103, 41125 Modena, Italy; [b]Dipartimento di Chimica Industriale 'Toso Montanari', Università degli Studi di Bologna, viale Risorgimento 4, 40136 Bologna, Italy; [c]Faculty of Chemistry, Jagellonian University, Gronostajowa 2, 30-387 Krakow, Poland. Contact: luca.rigamonti@unimore.it

Iron(II) and cobalt(II) *bis*-pyrazolilpyridyl (bpp-R) complexes, with general formula $[M(bpp\text{-}R)_2](X)_2 \cdot solv$, where M = Fe and Co, R = substituent on the bpp ligand (mainly on the central pyridyl ring), X^- = anion, and solv = co-crystallized solvent molecules, possess magnetic properties of interest. In particular, iron(II) derivatives can undergo spin transition from high spin (S = 2, HS) to low spin (S = 0, LS),[1] showing the spin crossover (SCO) phenomenon,[2] while cobalt(II) compounds can behave as single molecule magnets (SMMs) with consequent slow relaxation of the magnetization at low temperature.[3] Both magnetic features are mainly influenced by the distortion of the octahedral coordination environment around the metal centre. This is in turn governed by the crystal packing, which depends on the substituent R of the bpp ligands, the anion X^- and the possible co-crystallized solvent. An innovative chemometrics[4] aided approach (from design of experiment to QSPR) to study all these co-acting factors will be presented. Synthetic efforts toward new compounds with modulated substituent R (NH_2, Me, COOMe, NO_2) and anion X^- (NO_3^-, ClO_4^-, BF_4^-, TfO^-, PF_6^-, SbF_6^-, CF_3COO^-, BPh_4^-) will be also reported. The structural characterization through X-ray diffraction experiments of the complexes isolated as single crystals, together with the magnetic properties of selected derivatives, will be part of this contribution.



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Histidine containing PLGA nanoparticles as novel theranostic agents for Boron Neutron Capture Therapy

Jacopo Sforzi[a], Diego Alberti[a], Rachele Stefania[a], Alberto Lanfranco[b], Annamaria Deagostino[b], Silvio Aime[a], Simonetta Geninatti Crich[a]

[a]Department of Molecular Biotechnology and Health Sciences; University of Turin, via Nizza 52, 10126, Turin, Italy; [b]Department of Chemistry, University of Turin, via P. Giuria 7, 10125, Turin, Italy.

Boron Neutron Capture Therapy (BNCT) is a promising option for tumoral treatment, relying on the selective delivery of boron atoms to cancer cells, followed by the irradiation with a neutron beam of the diseased organ The innovation of this study lies on the development and test of a nanosized theranostic agent, able to maximize the selective uptake of boron atoms in tumor cells and, at the same time, to quantify (by MRI) the in vivo boron biodistribution. This is crucial to determine the optimal neutron irradiation time and to calculate the delivered radiation dose. In this study we used the theranostic compound AT101 (10 B enriched ligand-C-[N-(DOTAMA-C6)carbamoylmethyl]C′-palmitamidomethyl-o-carborane), a compound containing a Gadolinium atom for imaging purposes, and 10 boron atoms in the carborane structure for BNCT purposes.
AT101 has been internalised into PLGA (Poly, (lactic-co-glycolic acid)) nanoparticles: these nanoparticles have been coated with DSPE-PEG-2000 and prepared with and without a 50% of a PLGA conjugated with a polyhistidine chain (n=15). They were incubated with AB-22 and MET-5α a mesothelioma and healthy mesothelium cell lines, respectively. Interestingly, in mesothelioma cell line (AB22), the nanoparticle containing polyhistidine has a double rate of internalisation in the tumoral cells compared to the control one without the Poly-His feature. This therapy can potentially affect only tumor cells with a lethal dose of radiations, even in case of spreading and infiltrative cases. These promising insights on the possibility to selectively direct a theranostic dual agent directly into tumoral cell, with the possibility to analyse the drug uptake in a certain organ using MRI, may be an important, versatile and new starting point for the future of BNCT technology and cancer theranostics.

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Deciphering Inorganic Chemistry Riddles Through a Combination of Spectroscopy and Quantum Chemistry

Frank Neese

[a] *Max Planck Institut für Kohlenforschung, Kaiser Wilhelm Platz 1, D-45470 Mülheim an der Ruhr, Germany; neese@kofo.mpg.de*

From the point of view of theoretical chemistry, coordination chemistry deal with the most complicated part of the periodic table: open shell transition metals. In fact, transition metal ions, play a fundamental and decisive role in many areas of chemistry, including biochemistry, catalysis and materials science. Coordination chemistry has a rich history and a highly developed culture to investigate transition metal ions with a large array of advanced spectroscopic methods ranging from X-ray spectroscopy, through absorption spectroscopy to magnetic resonance spectroscopy and magnetism. As a consequence, there is a wealth of experimental data that needs to be interpreted in order to gain deep insights into the geometric and electronic structure of these systems and their reactivity. Traditionally, the language that has been used is that of ligand field theory, a semi-empirical theory tailored to transition metal complexes. However, in recent years, very powerful quantum chemical methods became widely available that allow for highly accurate numerical predictions. However, this does not make ligand field theory obsolete. In the lecture I will argue quite to the contrary and show how quantum chemistry, ligand field theory and experimental spectroscopy can be used to great advantage in studying the reaction mechanisms of even the most challenging catalytic systems including metalloenzymes.[1,2]

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Palladium catalyzed copolymerizations: from ligand architecture to macromolecule microstructure

Anna Dall'Anese,[a] Barbara Milani[a]

[a] *Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Trieste,Via Licio Giorgieri, 1, , 34127 Trieste, Italy.*

Polyolefins account for more than 55% of the plastic market demand worldwide.[1] These materials, however, suffer of scarce surface properties that can be improved thanks to the introduction of polar groups into the polyolefin skeleton leading to functionalized polyolefins. Moreover, the presence of functional groups could trigger controlled polymer degradation.[2] The synthesis of these macromolecules is a highly challenging reaction and the direct, controlled, homogeneously catalyzed copolymerization of olefins with polar vinyl monomers represents the most environmentally friendly technology to achieve it. In the past two decades, many catalytic systems, preferentially based on Pd(II) complexes with a great variety of ligands, have been reported.[3] However, their catalytic performances do not fulfill the requirements for a potential industrial application, thus better performing catalysts are needed.

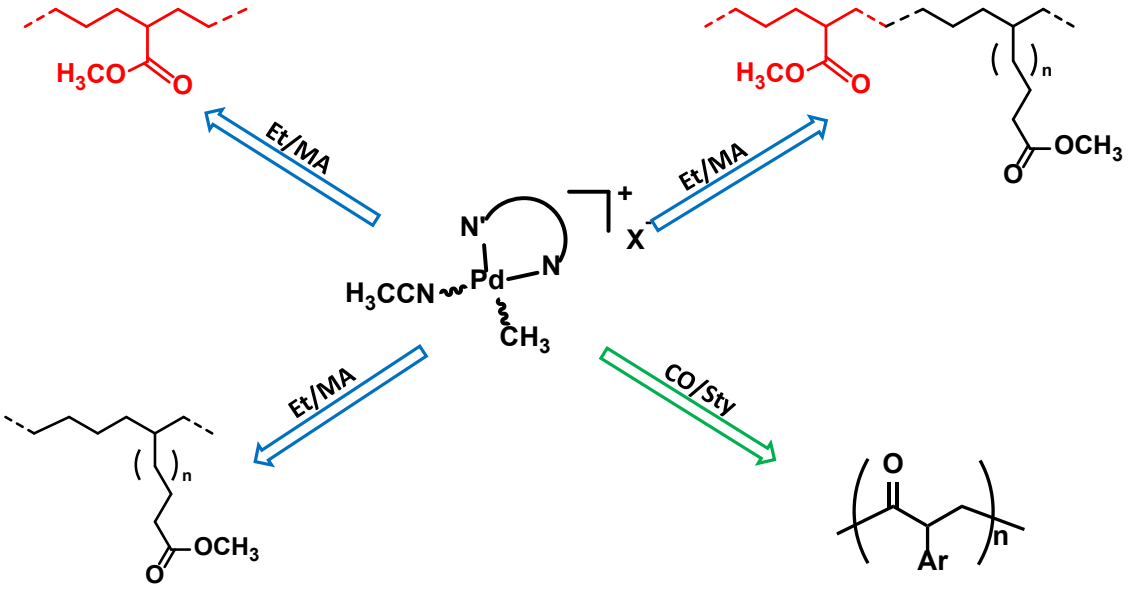

Figure. Types of copolymers that can be obtained according to ligand design in Pd(II) complexes.

The research work carried out in the frame of this PhD thesis deals with the development of new homogeneous catalysts, based on palladium(II) complexes with bidentate nitrogen-donor ligands (N-N'), for the target reaction (Figure). The research strategy consisted in applying to ligand designs three key features - desymmetrisation, bulkiness, and variation on ligand backbone - with the ultimate goal of studying how they affect not only the catalyst activity but also the macromolecules architecture. For instance we will highlight how the ligand backbone affects the enchainment of the polar monomer or how the desymmetrisation determines the macromolecule stereochemistry[5].

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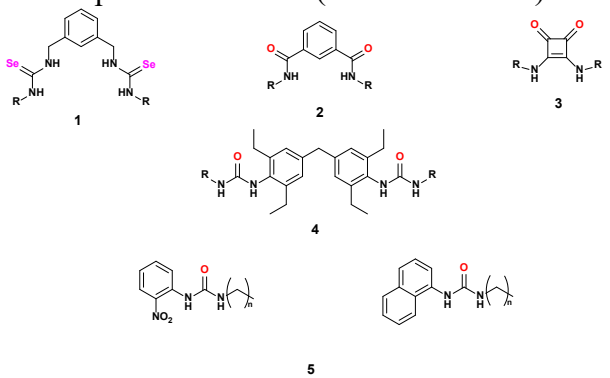
Novel supramolecular architectures based on weak interactions

Giacomo Picci *[a], *Claudia Caltagirone* [a]

[a] *Dipartimento di Scienze Chimiche e Geologiche, Università degli Studi di Cagliari, SS 554 Bivio per Sestu, 09042 Monserrato (CA), IT Email: gpicci@unica.it*

The importance of weak, noncovalent interactions in biological systems was first appreciated at the beginning of the 20th century with an improved understanding of hydrogen bonding and substrate–receptor interactions. Weak interactions are crucial for the formation of "host–guest" complexes forming well-defined architectures and acknowledged with the 1987 Nobel Prize in Chemistry. Since then, a variety of supramolecular systems that respond to signals, molecular machines and switches, well-defined networks, and self-assembling macrostructures have been developed. [1] A wide number of receptors based essentially on the hydrogen bond interaction for anion species are designed and synthesized in the last decades, because of the fundamental interest towards anions. Among them, the urea and amide moieties are the most largely employed due to their easy synthesis and due to the presence of NH acid protons able to interact with anions *via* hydrogen bond. On the other hand, the possibility to act as both H-bond donor and acceptor makes them ideal candidates for the development of self-assembled materials, and in particular as potential low molecular weight gelators. The work described herein will be focused on the design, the synthesis and the study of a new series of molecules containing different anion binding scaffolds that are able to act as receptors for anions in competitive media, to transport anions through phospholipids membranes or, as building blocks for the development of new materials (Scheme 1).

First, a novel family of bis-selenoureas receptors (**1** in Scheme 1) were synthesised and their affinity towards different anion species were tested by means ^{1}H-NMR titrations in DMSO-d_6. [2] A novel family of amide-based receptor were reported (**2** in Scheme 1). Specifically, the role of the halogen substituents on the anion binding properties and on the activity as anion transporters of a series of isophthalamides and dipicolineamides both in solution and in the solid state was investigated. [3] With the same aim, a new family of symmetric squaramide- based receptors functionalised with different fluorophores for anion recognition, transport and cell imaging were studied (**3** in Scheme 1). [4] The synthesis, gelation tests and characterization of eight LMWGs based on the urea moiety scaffold were explored in the last part of this work (**4-5** in Scheme 1).



Scheme 1. Model structures of the supramolecular architectures discussed in this work

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Anticancer drugs: a detailed computational analysis of "non classical" compounds mechanism of action

Fortuna Ponte [a], Emilia Sicilia [a]

[a] Dipartimento di Chimica e Tecnologie Chimiche, Università della Calabria, 87036 Arcavacata di Rende (CS), Italy

In the past, metal-based compounds have been widely used in the treatment of disease conditions, but the lack of a clear distinction between the therapeutic and toxic doses has been a major challenge. The discovery of the cytotoxic effects of cisplatin by Barnett Rosenberg in 1960 is a milestone in the history of metal-based compounds used in the treatment of cancers, which forms the foundation for the modern era of metal-based anticancer drugs. Platinum drugs, such as cisplatin, carboplatin and oxaliplatin, are the mainstay of the metal-based compounds in the treatment of cancer. Nevertheless, despite the pervasiveness of platinum drugs in cancer treatment regimens, a number of attendant disadvantages exist. For instance, no single-agent is equally effective against all cancer types and some types appear to be inherently resistant to treatment with any of the currently approved platinum agents. In addition to such resistance, populations of cancer cells can acquire resistance over time through a process of somatic evolution. Moreover, a number of side-effects, ranging from minor to dose-limiting in toxicity, accompanies treatment with platinum agents. Therefore, decades of research efforts have been devoted to the search and the synthesis of safer and more effective and selective agents, either containing platinum or alternative metals, acting with similar or different mechanisms. In order to accomplish this aim is of decisive importance the elucidation of the mechanism of action of the drugs.

Another strategy that has been used by chemists involves the use of drug delivery systems, and many different approaches have been examined to encapsulate platinum drugs within macromolecules, including macrocyclic species, which are responsible for creating supramolecular host-guest structures. The encapsulation slows down and prevents the drug degradation by proteins and peptides. One of the most widely studied class of synthetic supramolecular macrocycles are Calix[n]arenes (CX), whose properties, as molecular hosts and delivery systems, are of increasing interest.

Recently, beside conventional therapies, alternative treatment strategies have been proposed such as Photodynamic Therapy (PDT).

PDT is a non-toxic therapeutic technique, clinically approved and minimally invasive, used for the treatment of several types of cancers based on the generation of reactive oxygen species (ROS), that act as cytotoxic agents. Three components are required in PDT applications: a photosensitizer (PS), a light of a specific wavelength and tissue oxygen.

The aim of this research project was to study, through the strategies of the theoretical and computational chemistry, such as density functional theory (DFT), time dependent DFT (TD-DFT) and metadynamics, the mechanism of action of "non classical" platinum and transition metal non-platinum compounds, for some of them in collaboration with experimentalists, and the rationalization of their behaviors.

Paramagnetic NMR in bioinorganic chemistry in the 'twenties

Enrico Ravera

[a] *Centro di Risonanze Magnetiche, Università degli Studi di Firenze;* [b] *Dipartimento di Chimica "Ugo Schiff", Università degli Studi di Firenze;* [c] *Consorzio Interuniversitario Risonanze Magnetiche di Metalloproteine*

The interest in the elucidation of the properties of paramagnetic compounds is steadily increasing, because of the applications in healthcare (MRI contrast agents), quantum information processing (single ion magnets, qubits) and biomedicine (metalloproteins). Together with this growing interest, the applications of paramagnetic NMR are increasing as well (Figure 1), because of the unique ability of NMR to detect structural and dynamical features at the atomic level [1].

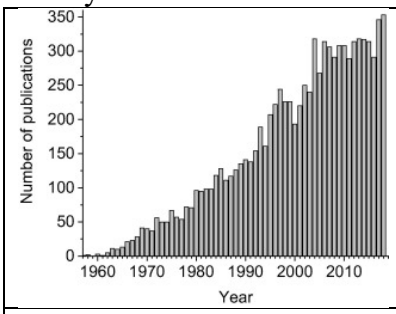

Figure 1. Number of published papers dealing with paramagnetic NMR (as determined from a search with scopus)

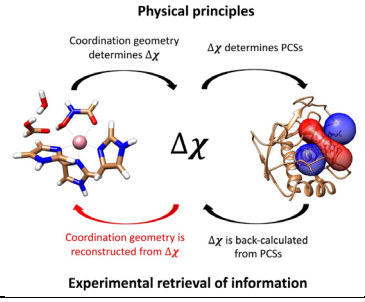

Figure 2. Pseudocontact shifts have been introduced by our lab [2] since 1996 to provide structural restraints in metalloproteins far from the metal center (top). Depending on the magnetic susceptibility, PCSs can also be used to reconstruct the metal coordination geometry through QC calculations (bottom).

The possibilities offered by NMR have been dramatically boosted by the accessibility and quality of Quantum Chemical methods for the calculation of paramagnetic NMR observables. We have tested the performance of QC methods in the prediction of proton hyperfine shifts of two archetypical high-spin pentacoordinate nickel(II) complexes (NiSAL-MeDPT and NiSAL-HDPT [3]), which, for a variety of reasons, turned out to be perfectly suited to challenge the QC predictions to the finest level of detail [4]. Furthermore, we have shown that it is possible to determine the coordination environment of the paramagnetic metal in the protein at a resolution inaccessible to other techniques (figure 2) [5].

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De novo design of multi-domain metalloenzymes

Fabio Pirro[a,b], Marco Chino[a], William F. DeGrado[c], Angela Lombardi[a]

[a] Department of Chemical Sciences, University of Napoli Federico II, 80126 Napoli, Italy; [b] Present address: School of Chemistry, University of Bristol, Cantock's Close, Bristol, UK; [c] Department of Pharmaceutical Chemistry and the Cardiovascular Research Institute, University of California, San Francisco, CA 94158-9001

The course of evolution required the recombination of protein domains to perform ever-growing complex functions. The presence of an additional domain in a multi-domain protein expands, alters, or modulates the functionality with respect to the isolated one-domain protein.[1] Taking inspiration from Nature, artificial proteins have been engineered combining different domains to develop bioinspired molecular machines, able to respond to external stimuli.[2]
Here, we report a new computational strategy to design de novo multi-domain proteins. The new methodology led to the first example of an artificial metalloenzyme, in which allostery was designed completely from scratch.[3,4]
In particular, DF (Due Ferri), a diiron phenol oxidase domain, and PS (Porphyrin-binding Sequence), a zinc porphyrin binding domain, were selected as individual proteins to be combined and give DFP (Due Ferri Porphyrin).[5] The multiple junctions were identified to colocalize the two domains, and obtain a more extensive structural coupling between them.
Noteworthy, DFP not only preserves the structural and functional properties of the parental proteins, but also shows a modulation in cooperation between the two domains. The catalytic characterization of 4-aminophenol oxidation demonstrated Michaelis-Menten kinetic in the phenoloxidase activity, and high-lightened a 4-fold tighter K_m and a 7-fold decrease in k_{cat} upon binding of the designed zinc porphyrin ZnP (Zn-meso-(trifluoromethyl)porphin). Molecular Dynamics simulations suggested that the presence of ZnP restrains the conformational freedom of a second-shell Tyr, that have been previously shown to largely affect the reactivity of the diiron center.
Subsequently, the binding fitness of the zinc porphyrin was changed to investigate the bidirectionality of the allosteric regulation. In the presence of the different zinc porphyrin ZnDP (Zn-Deuteroporphyrin IX), the ferroxidase and phenol oxidase activities were still. DFP3 showed an excellent affinity for ZnDP, only one order lower in magnitude compared to the designed ZnP. Most importantly, the ZnDP affinity was modulated by the presence of zinc bound to DFP3, showing a 3-fold decrease in KD, and demonstrating the presence of a back-regulation.
The photosensitizing properties of zinc porphyrin-DFP3 complexes were tested in the oxidation of the biological redox cofactor NADH. The photocatalytic characterization highlighted the paramount role of the protein scaffold not only in increasing the reaction rate, but also in protecting the zinc porphyrins from highly reactive species. The lower binding fitness of DFP3 towards ZnDP hindered this protection, enabling a major permeability of these species and leading to the zinc porphyrin photobleaching.
The high reactivity and versatility of such systems are a promising starting point for the de novo design of artificial photosystems for the storage of light energy in chemical fuels. [6]

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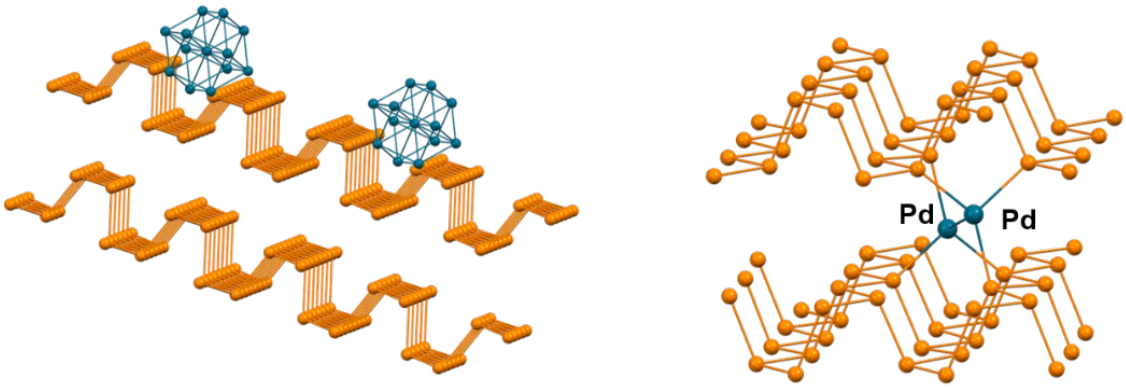
Reactivity of Black Phosphorus with Pd Compounds

Matteo Vanni[1], Marco Bellini[1], Silvia Borsacchi[2,3], Lucia Calucci[2,3], Maria Caporali[1], Stefano Caporali[4], Francesco D'Acapito[5], Marco Geppi[2,6], Andrea Giaccherini[7], Andrea Ienco[1], Gabriele Manca[1], Antonio Massimiliano Mio[8], Giuseppe Nicotra[8], Werner Oberhauser[1], Manuel Serrano-Ruiz[1], Martina Banchelli[9], Francesco Vizza[1], Maurizio Peruzzini[1]

[1]CNR-ICCOM, Sesto Fiorentino, Italy [2]Center for Instrument Sharing of the University of Pisa (CISUP), Pisa, Italy [3]CNR-ICCOM, SS Pisa, Italy [4]Department of Industrial Engineering, University of Florence, Italy [5]CNR-IOM-OGG, c/o ESRF, Grenoble, France [6]Department of Chemistry and Industrial Chemistry (DCCI), University of Pisa, Italy [7]Department of Earth Sciences, University of Florence, Italy [8]CNR-IMM, Catania, Italy [9]CNR-IFAC, Sesto Fiorentino, Italy

Since its first reported exfoliation in 2014, the interest in 2D black phosphorus (2D BP) and its chemical functionalization has grown dramatically [1], though a satisfactory structural description of the modified materials is seldom achieved. Herein, the functionalization of 2D BP starting from molecular Pd precursors is presented, leading either to supported Pd NPs (Pd/BP) or to interlayer Pd−Pd discrete units (Pd_2/BP). An in-depth solid-state characterization of the new materials was carried out by means of XPS, HAADF-STEM, XRD, NMR MAS and XAS. Remarkably, XAS analysis, backed up by DFT modelling, was crucial in revealing the existence of Pd_2 moieties stacked amidst BP layers in Pd_2/BP. The potential application of these heterogeneous systems as catalysts was demonstrated in distinct processes, namely the selective hydrogenation of chloronitrobenzene to chloroaniline and the hydrogen evolution reaction (HER) from acidic medium.



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Thanks are expressed to the European Council for funding the project PHOSFUN (AdG to M.P.).

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Targeted Delivery of Anticancer Platinum Complexes to Bone Tumors and Metastases

Alessandra Barbanente[a], Barbara Palazzo[b], Michele Iafisco[c], Giovanni Natile[a], Sander Leeuwenburgh[d], and Nicola Margiotta[a].

[a] *Chemistry Department, University of Bari "Aldo Moro", Via E. Orabona 4, 70125 Bari, Italy.*
[b] *Ghimas S.p.A., c/o Distretto Tecnologico High Tech Scarl, Campus Ecotekne, Via per Monteroni, 73100 Lecce, Italy.*
[c] *Institute of Science and Technology for Ceramics (ISTEC), National Research Council (CNR), Via Granarolo 64, 48018 Faenza, Italy.*
[d] *Department of Dentistry – Regenerative Biomaterials, Radboud Institute for Molecular Life Sciences, Radboud University Medical Center, Philips van Leydenlaan 25, 6525 EX Nijmegen, The Netherlands.*

Bone is a likely site of metastases deriving from non-osseous tumors. Thus, bone metastases originate when cancer cells from the primary tumor relocate to bones. Platinum-based chemotherapeutics, such as cisplatin, are commonly used for treatment of bone cancers where these drugs induce cancer cell death by binding to DNA and forming unrepaired Pt–DNA adducts. Unfortunately, Pt-based anticancer chemotherapy is associated with severe side effects because of poor specificity, therefore a current field of research in medicinal inorganic chemistry is to develop therapeutic strategies leading to the selective treatment of bone tumors and metastases.
In this context, the drug targeting and delivery (DTD) strategy represents a powerful tool for delivering the drug selectively to the biological target so minimizing systemic toxicity and drug resistance. Thus, in this lecture different bone-specific delivery strategies will be presented spanning from the synthesis of Pt-based drugs carrying specific targeting moieties (active targeting) to the loading of the platinum drug onto hydroxyapatite nanoparticles (HA) as specific delivery system. Doping of HA with other elements, such as selenium, has also been exploited [1] since it is known that selenite, a typical supplementation form of selenium, can inhibit the proliferation of various kinds of cancer cells via its apoptosis-inducing effect. An additional strategy is represented by the local implantation, after resection of a tumor from the bone, of multiple chemotherapeutic agents to synergistically improve the curative effect and to ensure prolonged delivery over the time. The anticancer ability of selenite-doped HA nanoparticles loaded with a HA-binding anti-tumor platinum drug has been tested *in vitro* on co-cultured cancer cells and bone marrow stem cells [2], while i*n vivo* experiments have been performed using an embryonic zebrafish xenograft model to determine the antitumor activity and selectivity of HA loaded with Pt drugs and their suitability for clinical application [3]. Finally, an active-DTD approach has been developed in which a Pt-drug has been linked to a pyrophosphate carrier ligand that can drive the drug to the calcium-rich tumor tissues [4],[5].
Although the development of drugs that induce selective toxicity to cancer cells without harming healthy cells represents a non-easy task, our results are encouraging and represent an initial promising step in the right direction.

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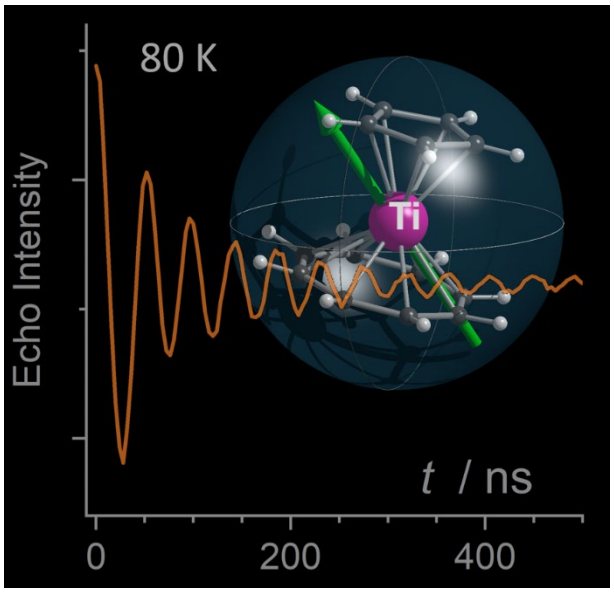
The contribution of coordination chemistry to the second quantum revolution

Roberta Sessoli Dipartimento di Chimica "U. Schiff", Università degli Studi di Firenze, Sesto Fiorentino, Italy.

E-mail: Roberta.sessoli@unifi.it

In the field of quantum technology several physical realizations of the basic unit, or qubit, are currently investigated. Actually, the most advanced platform is constituted by superconducting circuits, but spin systems continue to attract interest as intrinsic highly coherent two-level systems, which can be easily manipulated by electromagnetic radiations and act as ultrasensitive quantum sensors as in the case of nitrogen-vacancy defects in diamond.

Though molecules exhibit shorter spin coherence times than spin impurities in extended lattices, they have the advantage that they can be replicated in large quantities and their magnetic properties tuned through molecular synthetic strategies.[1] They can be designed to host several qubits with a precise control of their interaction allowing for the realization of quantum gates and quantum simulator. The wide library of electron and nuclear spin combinations is particularly attracting for quantum error correction. In addition, they can retain most of their magnetic features once they are put in contact with conducting substrates, a necessary step for integration in devices.



Our research has been focused on the rationalization of the main parameters governing spin dynamics in magnetic molecules, with a special attention for vibrational properties, indeed the Achille's heal of magnetic molecules.[2] Our efforts have been directed also to molecules that can be deposited on a surface and addressed using scanning probe techniques, such as metal phthalocyanines[3] and organometallic sandwich compounds.[4] More recently we have extended our interest to an innovative protocol of spin initialization based on spin selectivity in the electron transfer through chiral linkers.[5]

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Computational Modeling of Perovskite for Photovoltaic Applications

Edoardo Mosconi [a]

[a] *Computational Laboratory for Hybrid/Organic Photovoltaics (CLHYO), Istituto CNR di Scienze e Tecnologie Chimiche "Giulio Natta" (CNR-SCITEC), Perugia, 06123 Italy*

Hybrid AMX_3 perovskites (A=Cs, CH_3NH_3; M=Sn, Pb; X=halide) have in the last years revolutionized the scenario of emerging photovoltaic technologies.
Despite the extremely fast progress, the materials electronic properties which are key to the photovoltaic performance are relatively little understood.
Density Functional Theory electronic structure methods have so far delivered an unbalanced description of Pb- and Sn-based perovskites. We developed an effective GW method incorporating spin-orbit coupling[1] which allows us to accurately model the electronic, optical and transport properties of halide perovskites, opening the way to new materials design. In particular, the different $CH_3NH_3SnI_3$ and $CH_3NH_3PbI_3$ electronic properties are discussed in light of their exploitation for solar cells and found to be dominantly due to relativistic effects.
By applying our computational approach, we moved to investigate the effect of the chlorine doping for the mixed halide perovskites ($MAPbI_{3-x}Cl_x$)[2] and the role of the different A cation.[3] In parallel, a series of computational simulation carried out using Car-Parrinello molecular dynamics have been performed investigating the nature of the perovskites/TiO_2 interface,[4] the role of moisture in the perovskite degradation[5] process and the effect of the defect on the device working mechanism.[6]
The overall picture of our theoretical investigations underlines a crucial role of computational investigation, casting the possibility of performing predictive modeling simulations, in which the properties of a given system are simulated even before the materials laboratory synthesis and characterization. At the same time, computer simulations are shown to offer the required atomistic insight into hitherto inaccessible experimental observables.

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Framework coordination of single-ion Cu^{2+} sites in hydrated ^{17}O-ZSM-5 zeolite

Arianna Actis[a], Enrico Salvadori[a] and Mario Chiesa[a]

[a] *Department of Chemistry and NIS Centre, University of Torino, Via Giuria 7, 10125 Torino (Italy)*

Cu exchanged zeolites have been in the spotlight since 1970 for their activity in relevant catalytic processes, such as selective catalytic reduction of nitrogen oxides[1] or CH_4/CH_3OH and CH_3OH /propylene conversion[2]. Despite the extent of the studies devoted to these materials, the interfacial coordination chemistry of the metal, i.e. the formation of the inner-sphere coordination complex with framework atoms and/or coordinating molecules, is still a relevant topic both in basic research and in applied heterogeneous catalysis. The aim of this project is to gain an atomistic structural description of the coordination chemistry of single-ion Cu^{2+} sites in ZSM-5, assessing the nature of the Cu-O bond with coordinating oxygen donor atoms of the framework and water molecules. Isolated Cu^{2+} species are prepared in ZSM-5 through oxidation of the corresponding Cu^{+} species, introduced via gas phase reaction with CuCl, and then hydrated. Selective ^{17}O isotopic labelling of the oxide ions, either as framework oxygen[3] or belonging to solvating water, together with pulsed ENDOR spectroscopies applied to ^{17}O and ^{1}H nuclei, reveals an equatorial coordination of both zeolite framework oxide ions and solvating water molecules toward Cu^{2+} ions. These results, together with the absence of any ^{17}O signal attributable to weak axially coordinated water molecules confirmed by HYSCORE experiment, allow to conclude that in this system single-ion Cu^{2+} sites adopt a square planar coordination geometry and maintain a strong interaction with the zeolite framework even in presence of solvating water molecules. Furthermore, the analysis of the Fermi contact term and of the dipolar contribution to the hyperfine coupling allows to derive the spin density on oxygen orbitals and to prove that the Cu-O bond in ZSM-5 has a non-negligible covalent character. This result outlines the structural definition and atomic resolution afforded by EPR hyperfine techniques in the description of structure-function relationships.

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Perfluorinated Zn^{II} porphyrins for water photooxidation

Cecilia Albanese,[a] Gabriele Di Carlo,[a] Francesca Tessore,[a] Alessio Orbelli Biroli,[b] Stefano Caramori[c]

[a] Dipartimento di Chimica, Università degli Studi di Milano, UdR INSTM, via C. Golgi 19, 20133 Milano; [b] Dipartimento di Chimica, Università di Pavia, via Taramelli 12, 27100 Pavia; [c] Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Ferrara, via L. Borsari 46, 44121 Ferrara.

The intense UV-Vis absorptions, the high electrochemical and photochemical stabilities, the electronic properties which can be tuned quite easily through appropriate structural modifications make Zn^{II} porphyrins very attractive *n*-type sensitizers in photoelectrosynthetic cells for hydrobromic acid and water splitting.[1,2]

To allow the thermodynamically demanding process of water oxidation, the porphyrin must have a sufficiently high ground-state oxidation potential. This key feature can be achieved by endowing the core with electron-withdrawing groups, able to induce a significant electron deficiency.

Following this approach, we have prepared some novel β-substituted A_4-type and *meso*-substituted A_3B-type Zn^{II} porphyrins, carrying pentafluorophenyl moieties and different π-spacers and anchoring groups (Figure 1), and we have used them to sensitize the wide band-gap semiconductor SnO_2.[3,4]

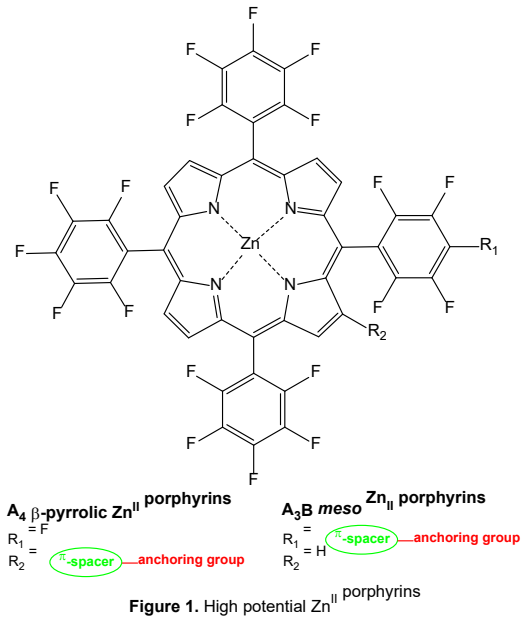

Figure 1. High potential Zn^{II} porphyrins

The present contribution aims to show the results of the photoelectrochemical investigation of the photoanodes and the evaluation of their performances with hydrobromic and ascorbic acid as sacrificial agents, carried out in order to explore the electronic transfer ability of the dyes in the absence of kinetic barriers possibly limiting dye regeneration. The best performing photoanode with respect to charge separation and collection has been coupled to the efficient Ir^{IV} water oxidation catalyst reported by Brudvig,[5] confirming the ability of the molecular substrate to carry out water oxidation, and leading to a faradaic yield over 95% for photoinduced oxygen evolution.

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Pd(II) catalysts for the synthesis of functionalized polyolefins: the control of polar monomer enchainment

Chiara Alberoni, [a] *Gabriele Balducci,* [a] *Claudio Pellecchia,* [b] *Barbara Milani* [a]

[a] *Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Trieste, Via Licio Giorgieri 1, 34127 Trieste, Italy*
[b] *Dipartimento di Chimica e Biologia "A. Zambelli", Università di Salerno, via Giovanni Paolo II 132, I-84084 Fisciano (SA), Italy.*

Functionalized polyolefins have a large use in different sectors of industry. However, they are currently produced by radical polymerization or post-polymerization functionalization, requiring harsh reaction conditions and resulting in a poor control of the macromolecule microstructure. [1] The most powerful and environmentally friendly approach to synthesize them would be the direct, controlled, homogeneously catalyzed copolymerization of ethylene with polar vinyl monomers.
In literature, several examples of Pd(II) complexes with different ancillary ligands belonging either to the family of α-diimines or anionic phosphine sulfonate derivatives are reported. Nevertheless, the discovery of highly efficient catalysts is still lacking. [2]
As an alternative strategy to ligand design, we have now investigated the introduction of an hemilabile, potentially bidentate ligand, on the fourth coordination site of palladium, and, as such, we chose thiophenimines, N-S. A new class of Pd(II) complexes, of general formula [Pd(Me)(N-S)(N-N)][PF_6], has been synthesized and characterized, both in solution by NMR spectroscopy and in solid state by X-Ray analysis (Figure).

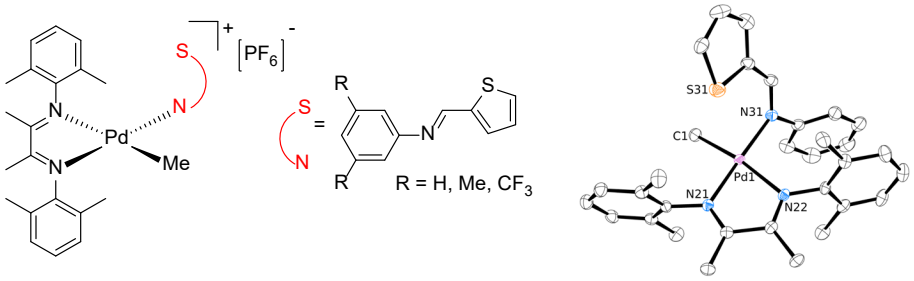

Figure. The studied Pd(II) complexes and ORTEP representation of one of them.

A detailed investigation of the catalytic behavior of these complexes in the copolymerization of ethylene with methyl acrylate (MA) was carried out by studying the effect of reaction medium, ethylene pressure and temperature. The most significant results are related to the effect of these parameters on the way of incorporation of MA in the synthesized copolymers.

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Phosphine and anionic ligand influences in glioblastoma 4° cancer treatment using ruthenium diphosphine carbonyl complexes.

Dario Alessi,[a] Pierfrancesco del Mestre,[b] Denise Lovison,[a] Maurizio Ballico,[a], Irene G. Rolle,[b] Daniela Cesselli,[b] Antonio P. Beltrami[b] and Walter Baratta*[a]*

[a] *Dipartimento di Scienze Agroalimentari, Ambientali e Animali, Università di Udine, Via Cotonificio 108, I-33100 Udine, Italy*
[b] *Dipartimento di Area Medica, Università di Udine, Via Colugna 50, I-33100 Udine, Italy*

Ruthenium diphosphine carbonyl complexes of general formula [Ru(dppb)(CO)(X)(phen)]X (X = OAc^-, SAc^-, $OPiv^-$, Cl^-, NCS^-; phen = 1,10-phenantroline) had already proven their efficacy against anaplastic thyroid cancer cells.[1] Since this class of compounds demonstrated high cytotoxicity in vitro, related complexes were synthetized using different phosphine ligands, namely dppe and the chiral BINAP. These complexes were tested against glioblastoma 4° cancer cells (U87), obtaining encouraging results and affording IC_{50} values ranging between 0.08-1.48 µM. The IC_{50} value seems to be largely dependent on the nature of the phosphine ligand, whereas the type of ligand X provides a less notable effect in dppe compounds and a marginal effect in BINAP compounds. In order to investigate the mechanism of the cytotoxic activity, the complex behavior in aqueous media and the formation of aquo specie, via X exchange, was studied by NMR analysis.

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Functionalization of Ti surface with antimicrobial layered double hydroxides

[a]Morena Nocchetti, [a]Marzia Bini, [a]Anna Donnadio, [a]Valeria Ambrogi, [a]Riccardo Vivani, [b]Davide Campoccia, [b]Valentina Mariani, [b]Stefano Ravaioli, [b,c]Lucio Montanaro, [b,c]Carla Renata Arciola

[a] Department of Pharmaceutical Sciences, University of Perugia, Via del Liceo 1, 06123 Perugia, Italy
[b]Laboratorio di Patologia delle Infezioni Associate all'Impianto, IRCCS Istituto Ortopedico Rizzoli, via di Barbiano 1/10, 40136 Bologna, Italy.
[c]Department of Experimental, Diagnostic and Specialty Medicine, University of Bologna, via San Giacomo 14, 40126 Bologna, Italy

Pure titanium has been employed since early 1950s in biomedical fields, especially in orthopedics, due to its good biocompatibility and suitable elastic modulus matching the human cortical bone. However, the aseptic loosening of the pure titanium implant and the bacterial infections are the two leading causes of implant failure. The most convenient way to combat implant related infections [1] is the development of an anti-infective Ti surface, able to inhibit or prevent bacterial adhesion and to limit bacterial proliferation. In this context, surfaces able to release antibiotics or metal nanoparticles or covered with antimicrobial polymers, enzymes and peptides were studied [2]. Among different materials that can be used as coating of Ti surface, layered double hydroxides (LDHs) could represent a multifunctional material able to confer both osteoconductive and antimicrobial properties [3]. LDHs are layered solids described by the general formula $[M(II)_{1-x}M(III)_x(OH)_2](A^{n-})_{x/n}\cdot nH_2O$ were M(II) is a divalent cation (i.e. Zn, Mg, Cu, Co), M(III) a trivalent cation (i.e. Al, Ga, Fe) and A^{n-} the anions that balance the positive charges of the lamellae. They are characterized by a very high compositional versatility due to the possibility to use different bivalent and trivalent cations and exchange A^{n-} with a huge variety of anions. This work deals with the development of synthetic strategies to prepare stable and biologically active LDH titanium coatings. The alkali and acid titanium etching are used to promote the nucleation and growth of LDH on the titanium surface ensuring a good anchorage of the crystals. A combination of metal cations such as Mg^{2+}, showing good osteoinductive properties and Zn^{2+} and Ga^{3+}, having antibacterial action, were used to prepare LDH coating [4]. Synthetic strategies as urea and sol-gel method were investigated to functionalize activated Ti surface with ZnAl, MgAl, ZnAlGa, MgAlGa and MgGa. The Ti@LDH composites were characterized by FE-SEM, EDS, XRPD analysis and ATR-FTIR. Different morphologies of the LDH grown on Ti were obtained and as an example, FE-SEM images of titanium surface functionalized with MgAlGa and ZnAlGa LDH crystals are reported in Figure 1.
A set of these coatings, in particular ZnAlGa and MgAlGa LDH, are under investigation for their antibacterial/antibiofilm activity.

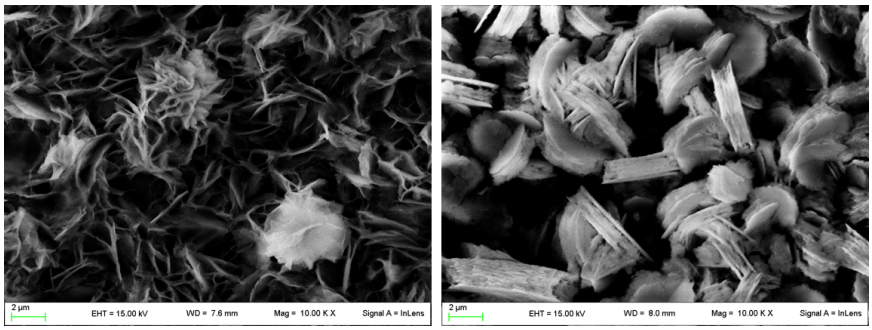

Figure 1. FE-SEM images of MgAlGa (left) and ZnAlGa (rigth) grown on Ti.

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New anticancer copper complexes containing ligands conjugated with biologically active molecules

L. Bagnarelli,[a] M. Pellei,[a] C. Santini,[a] F. Del Bello,[b] W. Quaglia,[b] G. Giorgioni,[b] M. De Franco,[c] C. Marzano,[c] C. Battocchio,[d] G. Iucci,[d] I. Schiesaro,[d] I. Venditti,[d] V. Gandin[c]

[a] School of Science and Technology, Chemistry Division, University of Camerino, Italy; [b] School of Pharmacy, Medicinal Chemistry Unit, University of Camerino, Italy; [c] Department of Pharmaceutical and Pharmacological Sciences, University of Padova, Italy; [d] Department of Science, Roma Tre University, Italy

Copper complexes might represent suitable alternatives to the platinum-based drugs for the treatment of tumors.[1] Our efforts have been recently focused on design and synthesis of novel Cu(I) and Cu(II) complexes with heteroscorpionate ligands based on bis(azol-1-yl)acetic acids conjugated with biologically active species such as the N-methyl-D-aspartate receptor antagonist (6,6-diphenyl-1,4-dioxan-2-yl)methanamine (NMDA-ANT) [2, 3] and Lonidamine [4] (LND). In particular, LND, an antineoplastic drug able to sensitize tumors to radio-, chemo- and photodynamic-therapy, has been converted into 2-hydroxyethylester and 2-aminoethylamide derivatives to be conjugated with chelating ligands (Figure 1).

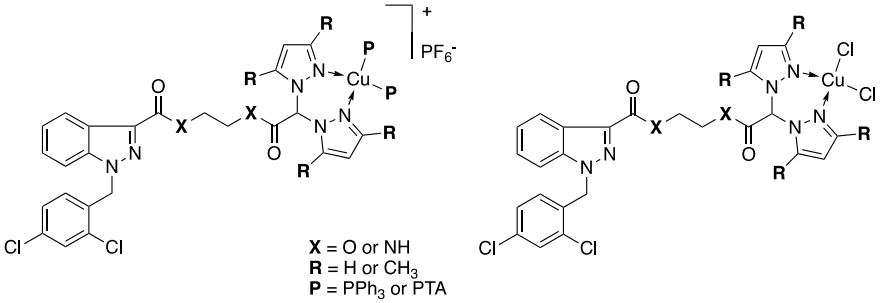

Figure 1. Cu(I) and Cu(II) complexes of heteroscorpionate ligands conjugated with Lonidamine.

Both the above-mentioned groups (NMDA-ANT and LND) have been chosen with the aim to synthesize complexes acting through a synergistic mechanism of action due to the presence of both copper and moieties able to interact with the cancer cells in the same chemical entity. In particular Cu(II) complexes have been obtained using $CuCl_2$ as an acceptor while Cu(I) complexes have been synthesized employing as starting materials $[(CH_3CN)_4Cu(I)]$ and phosphanes such as triphenylphosphine (PPh_3) and 1,3,5-triaza-7-phosphaadamantane (PTA) in order to modulate the lipophilic and hydrophilic properties of the resulting compounds. The molecular and electronic structure of such complexes were probed by Synchrotron Radiation-induced X-ray Photoelectron Spectroscopy and Near Edge X-ray Absorption Fine Structure spectroscopy to obtain further information about the influence of the metal coordination on the electronic structure of the ligands, and in the near edge (XANES) and extended (EXAFS) regions to understand the local coordination chemistry and electronic structure around Cu. All the novel complexes have shown a significant *in vitro* antitumor activity against several human cancer cell lines of different histology and cisplatin resistant or with multi-drug resistant phenotype, being significantly more active than the reference drugs and the related free ligands, even against 3D spheroids of lung, pancreatic and ovarian cancer cells, which more closely mimic the heterogeneity and complexity of *in vivo* tumors.

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Study of nickel-molybdenum alloy based catalysts for hydrogen evolution reaction and oxygen evolution reaction in a anion exchange membrane electrolyzer

Francesco Bartoli [a,b], Hamish A. Miller [a], Maria V. Pagliaro [a], Marco Bellini [a], Andrea Marchionni [a], Jonathan Filippi [a], Francesco Vizza [a].

[a]ICCOM-CNR; [b] University of Siena

The hydrogen economy is becoming more feasible in recent years due to technological progresses in materials development. Such improvements have allowed a reduction in manufactory cost from year to year, making hydrogen competitive with the solutions currently available on the market. To this regard, the best way to produce H_2 is by water electrolysis, that is one of the most abundant and renewable sources of hydrogen present in nature. Unfortunately, some problems remain due to the use of critical raw materials employed for the fabrication of the catalysts, like Platinum Group Metal (PGM) and the membrane stability and permeability. In order to make these technologies available to a large market, many efforts have been made to limit or eliminate precious metals from the catalysts. Here we report PGM free catalysts for anion exchange membrane electrolyzer based on Nickel-Molybdenum alloys and iron oxide-hydroxide: $MoNi_4:MoO_{x-3}/Ni_{foam}$ for the cathode and $Fe\text{-}MoNi_4:MoO_{x-3}/Ni_{foam}$ for the anode (Figure 1).

These materials have some interesting advantages; firstly a facile hydrothermal synthesis, this procedure requires only the metal salts and water, representing also a "green" alternative with respect other pathways, once the mixed oxide are grown on the Ni_{foam} surface , thermal annealing under reducing atmosphere leads to the formation of $MoNi_4:MoO_{x-3}/Ni_{foam}$. An iron oxide-hydroxide anode can be prepared by simply dipping the lamina of $MoNi_4:MoO_{x-3}/Ni_{foam}$ in a solution of $FeCl_3$. Tests carried out in a complete AEM electrolyzer demonstrate improved performances, showing very good stability with a current loading of 500 mA/cm^2 for 1 day at 60 °C, keeping the potential around 1.8 V. Further improvements are aimed to bring the current density to 1 A/cm^2 maintaining the same cell potential.

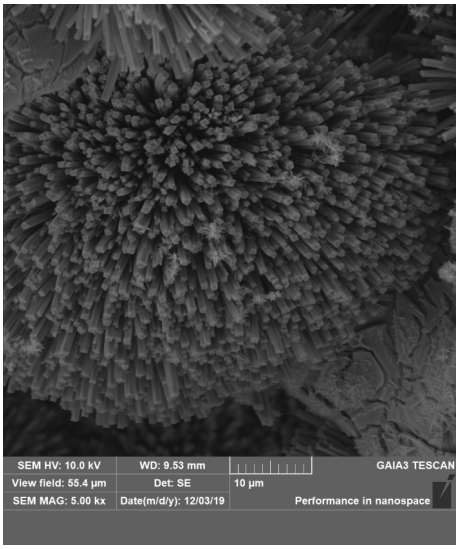

Figure 1: SEM image of $MoNi_4:MoO_{X-3}/Ni_{foam}$

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Gold nanorods functionalized with copper containing coordination compounds showing promising antiviral activity: structural and morphological characterization

Chiara Battocchio[a], Iole Venditti[a], Giovanna Iucci[a], Luca Tortora[b], Eleonora Marconi[a,b], Martina Marsotto[a], Marisa Colone[c], Annarica Calcabrini[c], Annarita Stringaro[c], Maura Pellei[d], Carlo Santini[d]

[a] *Roma Tre University, Dept. of Sciences, Via della Vasca Navale 79, 00146, Rome - Italy*
[b] *LASR3 Surface Analysis Laboratory, INFN Roma Tre, via della Vasca Navale 84, Rome, Italy*
[c] *National Center for Drug Research and Evaluation, Italian National Institute of Health, Viale Regina Elena, 299, 00161, Rome, Italy*
[d] *School of Science and Technology, Chemistry Division, University of Camerino, via S. Agostino 1, 62032 Camerino, Macerata, Italy.*

The global imperative for infectious disease research is to develop new antibacterial and antiviral drugs since several fatal infectious diseases caused by pathogenic viruses and bacteria are responsible for the gravest health concerns over the world [1]. In particular, the outbreak of the SARS-CoV-2 since early 2020 poses dramatic problems to the health systems as no truly effective drugs are yet available therefore, the identification of innovative strategies selectively interfering with the pandemic disease is a thrilling challenge for chemical and biochemical research. For this purpose, extensive screenings are conducted on thousands of molecules using combinatorial libraries or in silico docking experiments to discover new effective antiviral agents [2]. Among other, metal-based agents are an attractive class of drugs for their versatile applications in medicinal inorganic chemistry [3]. The great structural versatility, compared to purely organic molecules, depends on the combination of different metal ion(s) with distinct ligand(s) in the same molecular entity. Metals can coordinate ligands in a precise three-dimensional configuration thus allowing the tailoring of the molecule to recognize and interact with a defined molecular target.
Copper-based agents are an attractive class of drugs for their versatile applications in medicinal inorganic chemistry [4] and several Cu species have been reported to exhibit significant antiviral activity [5]. Copper is a fundamental micronutrient for the functioning of human immune cells and it can kill some infectious DNA or RNA viruses, including bronchitis virus, poliovirus, human immunodeficiency virus type 1 (HIV-1); moreover, it blocks PLpro-2, which is crucial for SARS-CoV-1 replication [6]. Altogether, these observations strongly encourage to explore the potential of Cu-based drugs against COVID-19 disease.
Recently, new chelating ligands showing potential activity against SARS-CoV-2 have been prepared by our research group, and the coordination chemistry of related Cu(I/II) complexes has been detailly investigated. In addition, to enhance their solubility in water, these copper-based coordination compounds have been conjugated to the surface of nanocarriers: gold nanoparticles of spherical or rod-like shape. Here, we will present the structural and morphological investigation carried out on the Cu(I/II) coordination compounds both pristine and charged on the nanoparticles surface, as well as some interesting results from the photoluminescence studies.

Acknowledgements: The Grant of Excellence Departments, MIUR (ARTICOLO 1, COMMI 314 – 337 LEGGE 232/2016), is gratefully acknowledged by authors of Roma Tre University.

[1] D.M. Morens, et al., *Nature* **2004**, *430*, 242.
[2] K. Świderek, V. Moliner, *Chem. Sci.* **2020**, *11*, 10626.
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[4] C. Santini, et al., *Chem. Rev.* **2014**, *114*, 815.
[5] M.C. Linder, M. Hazegh-Azam, *Am. J. Clin. Nutr* **1996**, *63*, 797S.
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Fracturing and surface reconstruction kinetics of crystalline silica in a toxicological perspective

Bellomo C.[a], Pavan C.[a], Lagostina V.[a], Paganini M. C.[a], Chilla G.[a], Mino L.[a], Turci F.[a].

[a]*Dipartimento di Chimica, Università degli Studi di Torino, via Giuria 7, 10125, Torino, Italy.*

Crystalline silica is a very well-known toxic material. It is the cause of silicosis, one the most common occupational diseases, and of other severe pathologies, including lung cancer.[1] In the last decades, a huge research effort has been carried out to find correlations between the toxic potential of crystalline silica and its surface chemistry. Several studies evidenced that freshly ground crystalline silica exhibits a greater toxicity than aged dusts.[1,2] Among several hypotheses to explain this variability in toxicity effects, we recently found out that a specific population of silanols, named "nearly free silanols" (NFS), occurs at quartz surface after fracturing. NFS were variably present also on amorphous silica and they were shown to have a crucial role in initiating silica toxic effects.[3] Such findings pose relevant new questions on the formation and the evolution over time of silanol species, during and after fracturing. To answer those questions, a set of crystalline silicas of synthetic origin[4] were milled down to a respirable size (Fig 1a) and their structural properties, solid-state defects, NFS content, and membranolytic activity towards model membranes, were analyzed. The milling procedure was performed in an orbital and mixer ball miller under different atmospheres: a) argon, b) air and c) argon saturated with $H_2O_{(vap)}$. Surface reconstruction processes under the same three different atmospheres were followed by EPR spectroscopy at several time points and in parallel NFS and membranolytic activity toward red blood cells (RBC) were measured. The milled quartzes showed a remarkable variability of solid-state radicals, and a striking larger amount of them was generated in totally inert atmosphere in respect to the other two atmospheres (Fig 1c). Also, the silanol content and the hemolytic activity were modulated by both milling and storing atmospheres (Fig 1b) and, quite surprisingly, by the type of milling performed (orbital vs mixer milling). In conclusion, we are now able to describe how the quartz surface evolves over time, depending on the milling and storing atmosphere. This finding reveals the dynamic structure of the silica surface which might be related to its variable toxicity potential and suggests procedures aimed at detoxification/safer design of silica-based materials.

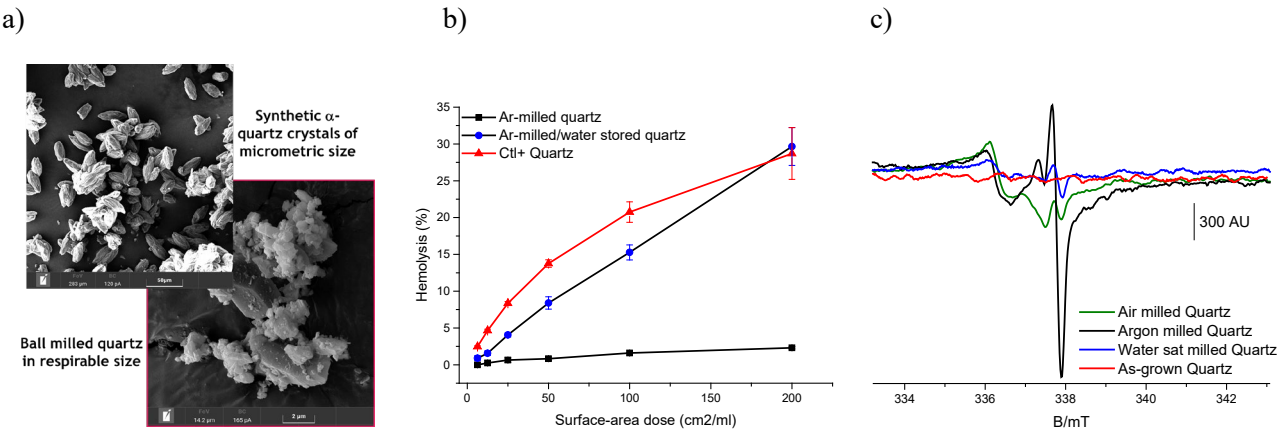

***Figure 1**: a) FESEM images of quartz before and after milling; b) Hemolytic activity of the quartz milled in Ar and stored in Ar or contacted with water vapor; c) different CW-EPR of quartzes milled in different atmospheres.*

[1] IARC, *Monograph Vol. 100C,* **2012;** IARC *Monograph Vol. 68,* **1997**
[2] Vallyatan et al, *Am. Rev. Respir. Dis.,* **1988**, *138*, 1213.
[3] Pavan et al, *Proc. Natl. Amer. Soc. USA,* **2020**, *117 (45*), 27836.
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Preparation and characterization of crystalline nanosilica for toxicological applications

Bellomo C.[a], Pavan C.[a], Turci F.[a]

[a] *Dipartimento di Chimica, Università degli Studi di Torino, via Giuria 7, 10125, Torino, Italy.*

Exposure to respirable crystalline silica is one of the main causes of occupational respiratory diseases, which includes silicosis and lung cancer.[1ab] Although the variability of silica toxicity, in both crystalline and amorphous forms, hampers a clear paradigm which correlates chemical features and toxicity, it is reported that fractured crystalline silica has a toxic potential greater than intact quartz.[1c] Several questions remain unanswered on fractured quartz, including the potential toxicity of the nanometric fraction of crystalline silica (nano-CS) that has been shown to adhere on the respirable micrometric particles after milling (Fig. 1a). Health protection organizations, including the International Agency of the Research on Cancer (IARC)[1ab], and the Agency of Food, Environmental and Occupational Health and Safety (ANSES), [2a] posed the issue on the relevance of nano-CS for the toxic activity of fractured quartz, because of its variable amount and the unknown structural nature. To study toxicological properties of nano-CS, a highly pure quartz of synthetic origin (in micrometric size and of SSA < 0.1 m^2/g) was ball milled to obtain ultrafine particles that could be classified by EU CLP regulation as "nanomaterial".[2b] To achieve the nanometric size, ball milling was optimized coupling dry and wet milling steps, using water as a dispersing agent. This procedure generated particles with a SSA ranging from 37 (for less energetic millings) to 55 m^2/g (for prolonged millings), in good agreement with the SSA of nanometric silica (e.g., Aerosil50 with 50 m^2/g). The particle morphology was assessed by FESEM (Fig. 1b), the structural modifications induced by milling were evidenced by HR-TEM and XRPD (Fig 1c), using the Rietveld method, and the size of the primary particles were evaluated by dynamic light scattering (DLS). The nano-CS obtained exhibited: i) a partial amorphization (amorphous content ranged from negligible to more than 20 wt.%), and the presence of two distinct domains of scattering having nanometric (less than 50 nm) and submicrometric (800nm-1µm) size; ii) a strong tendency to form agglomerates and/or aggregates in water, which could be partially separated with ultrasounds and surfactants. In conclusion, the proposed procedure represents a good strategy to prepare ultrafine particles for the toxicological investigation of the nanometric fraction of quartz.

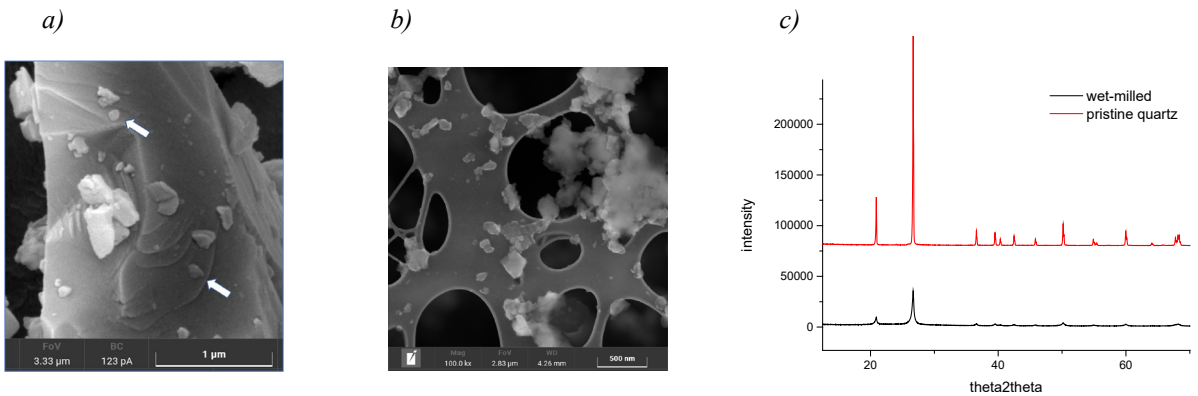

Figure 1*: a) FESEM image of nano-CS on quartz micrometric particles; b) FESEM image of the nano-CS obtained by milling; c) XRPD comparison between pristine micrometric quartz crystals and wet ultrafine milled quartz.*

[1] a)IARC, *Monograph Vol. 100C,* **2012;** b)IARC *Monograph Vol. 68,* **1997** c) Pavan et al, *Proc. Natl. Acad. Sci USA,* **2020**, *117 (45*), 27836 ; d) Turci et al, *Part Fibre Toxicol,* **2016**, *13*, 32.

[2] a) ANSES Opinion - Request No **2015-SA-0236** –*Crystalline silica*. b) SCoEaNIHR, E. S., **2010**, 'Scientific Basis for the Definition of the Term "nanomaterial"', *European Commission.*

[Pt(DMSO)(η¹-C_2H_4OMe)(phen)]$^+$ inhibits migration and invasion in neuroblastoma SH-SY5Y cells

[a] *Erika Stefàno,* [b] *Antonella Muscella,* [c] *Michele Benedetti,* [c] *Federica De Castro,* [c] *Danilo Migoni,* [a] *Giorgia N. Iaconisi,* [c] *Francesco P. Fanizzi,* [a] *Santo Marsigliante.*

[a] *Cellular Physiology Laboratory of DiSTeBA;* [b] *Cellular Pathology Laboratory of DiSTeBA;* [c] *General and Inorganic Chemistry Laboratory of DiSTeBA, University of Salento, Via Monteroni, 73100 Lecce, Italy.*

Among the new Pt-complexes with antitumor properties, phenanthroline derivatives aroused high interest due to their entirely different mode of action [1].
We examined cytotoxic effects of two new Pt(II)-complexes containing 1,10-phenantroline (phen), [Pt(phen)(DMSO)(η¹-CH_2CH_2OMe)]$^+$ and [Pt(phen)(NH_3)(η¹-CH_2CH_2OMe)]$^+$, in eight human cancer cell line. Among them, the DMSO-containing complex exhibited a great antiproliferative potential, especially in neuroblastoma cell line (SH-SY5Y). Moreover, the reduction of cell viability occurred starting from the first hours of treatment, compared to cisplatin [2]. Therefore, not only the inhibition of tumor proliferation by [Pt(phen)(DMSO)(η¹-CH_2CH_2OMe)]$^+$, but also migration and invasion processes were evaluated more deeply.
The antimetastatic effect was studied through wound healing (Figure 1) and tumor spheroids-based assay. SH-SY5Y were treated with sublethal concentration (0.1-1 μM) of the new Pt-complex and cisplatin to assess their ability to inhibit cell migration. Both Pt-complexes inhibited wound closure, but the new compound was found to be more effective than cisplatin (Figure 1). Likewise, [Pt(phen)(DMSO)(η¹-CH_2CH_2OMe)]$^+$ inhibited migration areas of tumor spheroids while cisplatin had no significant effects. These results suggest that the new Pt(II)-complex acts not only by inhibiting cancer cells proliferation, but also preventing cell motility and invasion; this could lead to the reduction of metastatic potential.

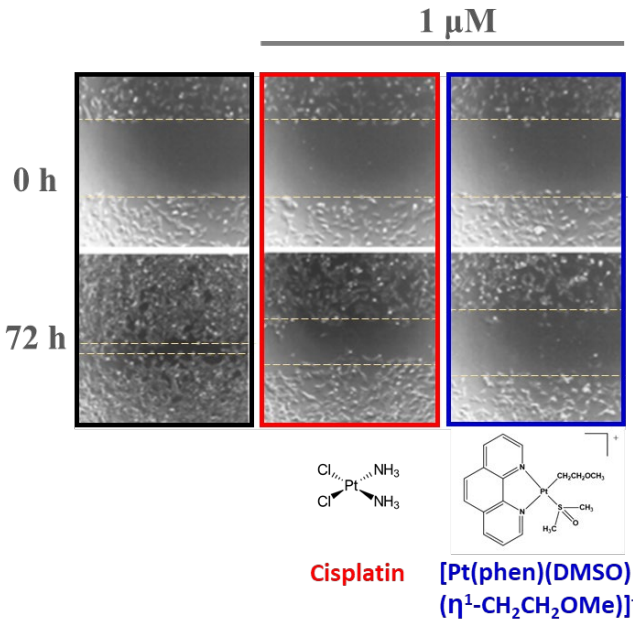

Figure 1. [Pt(phen)(DMSO)(η¹-CH_2CH_2OMe)]$^+$ and cisplatin treatment inhibits cell migration and wound closure.

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Rational synthetic approaches towards NHC stabilized molecular gold nanoclusters

Matteo Bevilacqua, Marco Roverso, Sara Bogialli, Andrea Biffis

Dipartimento di Scienze Chimiche, Università di Padova, Via Marzolo 1, 35151 Padova (PD).

Gold nanoparticles (AuNPs) and polynuclear gold(I) complexes are among the most studied chemical entities for their peculiar bioactivity, luminescence behavior and catalytic properties. Between these two worlds, there is another which has not been sufficiently characterized: the world of molecular gold nanoclusters (AuNCs). At variance with more common AuNPs, these species present molecular features, as a precise stoichiometric formula and orbital structure. The most important problem linked with these compounds is their synthesis and stabilization, until now mostly achieved using thiolate ligands; these species are useful to stabilize the clusters but tend to saturate the metal surface, which impairs an eventual catalytic activity. Thus, other kind of ligands are currently studied as alternative stabilizers, like phosphines (PR_3) and N-heterocyclic carbene (NHC) ligands. In particular, the latter impart a stability which is comparable with that attained with thiolate ligand.

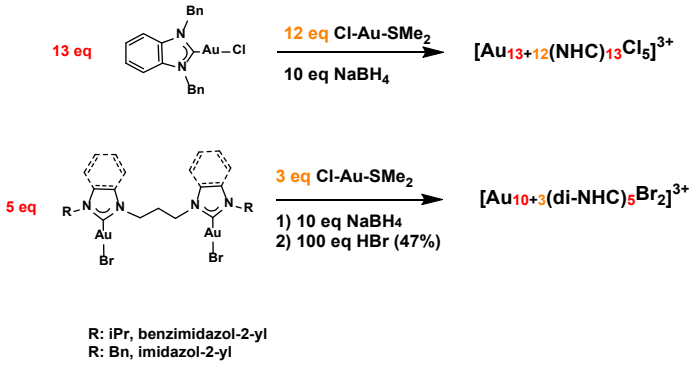

Figure 1: stoichiometric AuNCs synthesis

AuNCs synthesis has been performed in two general ways: gold complex reduction using sodium borohydride as reducing agent[1] and ligand exchange starting from a preformed nanocluster[2]. Our work is focused on synthesis of new AuNCs stabilized with poly- and mono-NHC using two novel synthetic ways: a "stoichiometric" approach and a "stepwise-addition" approach. With the first method, reported in Figure 1, using mono- or di-NHC gold(I) complex and another Au(I) complex as "gold source" during reduction we can obtain clusters with the reduction approach that are otherwise difficult to synthesize or are obtained in low yield. The stepwise-addition approach (Figure 2) is an innovative method to obtain mixed PR_3-NHC AuNCs. Starting from an Au_{11} PR_3-stabilized cluster and a di-NHC gold(I) complex we can obtain a new Au_{13} cluster, with total consumption of reagents. To analyze these species, we use in first way high resolution ESI-MS, the most powerful tool to understand the stoichiometry of AuNCs: we have confirmed cluster formation in solution and have determined the effect of some reagents during synthesis (acid addition for example). We have also rationalized the effect of the steric and electronic features of the employed NHC ligand on AuNCs. Work currently in progress involves purification of these AuNCs, to obtain pure clusters as much as possible to have a better characterization on them, characterization concerning UV-Vis adsorption and emission bands and structure information derived from single crystal X-Ray diffractometry.

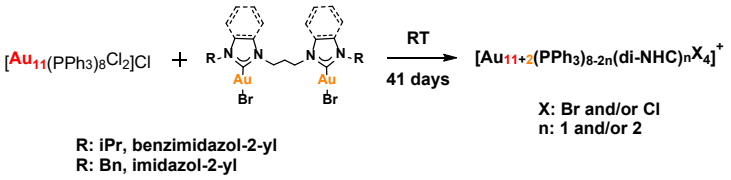

Figure 2: stepwise-addition AuNCs synthesis

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Cationic η^3-indenyl palladium complexes bearing phosphine and N-heterocyclic carbene ligands

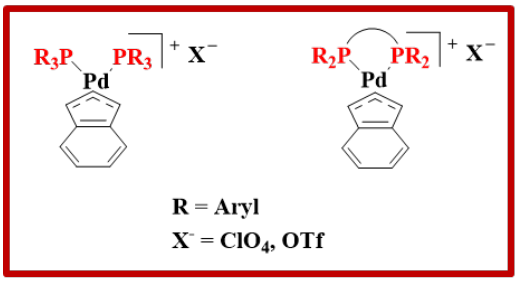
Enrica Bortolamiol,[a] Thomas Scattolin,[a] Francesco Fama, [a] Giacomo Isetta, [a] Flavio Rizzolio,[a,b] and Fabiano Visentin[a]

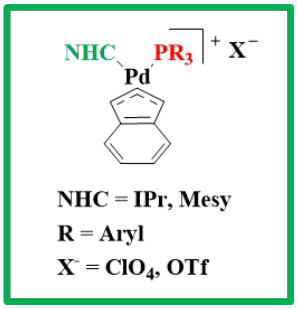
[a] *Dipartimento di Scienze Molecolari e Nanosistemi, Università Ca' Foscari, Venezia-Mestre, Italy;*
[b] *Pathology Unit, Department of Molecular Biology and Translational Research, Centro di Riferimento Oncologico di Aviano (CRO) IRCCS, Aviano, Italy*

The metal transition complexes bearing Indenyl ligand (Ind) are more performant in several catalytic applications and stoichiometric reactions than Cyclopentadienyl (Cp) analogues.
In their seminal works , Zargarian and co-workers, observed how this flexible and responsive nature of M-Ind bonding strictly depends on the electronic configuration of the metal centre. Moreover, they synthetized the first Indenyl palladium complexes bearing phosphine and isocyanide ligands [1]. More recently, Hazari's and Nolan's [2] groups described the synthesis and catalitical activity of many neutral Indenyl-palladium complexes based on N-heterocyclic carbene ligands (NHCs) but, to date, no studies on the biological properties of this category of compounds has been reported.
Since the discovery of cisplatin, organometallic compounds with metal centre other than platinum are investigated as antiproliferative agents to reduce side effects and resistance during the therapeutic treatment. Within this context, in the last years, palladium-based complexes have received an increasing interest in medicinal chemistry. Palladium derivatives are generally more soluble in water than their platinum congeners and show often different reactivity in the biological environment; these features promote in some cases different mechanisms of action. On the other hand, to limit the faster ligand dissociation pattern of palladium complexes a good option is represented by the choice of phosphines and NHCs as ancillary ligands.

Recently, our group have studied the antiproliferative activity of different palladium organometallic derivatives such as Pd(II)-allyl, Pd(0)-olefin [3] and palladacyclopentadienyl. Pd(II)-η^3-allyl organometallic fragment has given us the most promising results as anticancer agents and on this basis we have planned to extend to related Pd(II)(η^3-indenyl) derivatives our studies.

In this contribution, we propose a new synthetic route to obtain cationic Indenyl palladium complexes with monodentate and chelated phosphine and NHC ligands in order to test their capability as antiporliferative agents toward different cancer cells.





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Synthesis and characterization of new Rh-Au carbonyl clusters

Guido Bussoli, [a] *Cristina Femoni,* [a] *Maria Carmela Iapalucci,* [a] *Silvia Ruggieri.* [b]

[a] *Dipartimento di Chimica Industriale "Toso Montanari", Università di Bologna, Viale Risorgimento 4, 40136 Bologna, Italy.*
[b] *Dipartimento di Biotecnologie, Università di Verona, Strada Le Grazie 15, 37134, Verona, Italy.*

In-depth studies of the chemistry of gold took off relatively recently and started with the first organometallic compounds, followed by molecular clusters, [1] colloids and nanoparticles (AuNPs) [2] and, most recently, atomically-precise gold nanoclusters. [3] The lack of heterometallic Rh-Au clusters encouraged us to investigate this system in order to try to obtain new Rh species with gold encapsulated in the metal cage. Both Au(I) and Au(III) complexes can be used to prepare clusters with gold embedded in their metal frameworks. [4] Herein we report the results of the redox condensation between the precursor cluster $[Rh_7(CO)_{16}]^{3-}$ and $[AuCl_4]^-$ or $Au(SEt_2)Cl$.

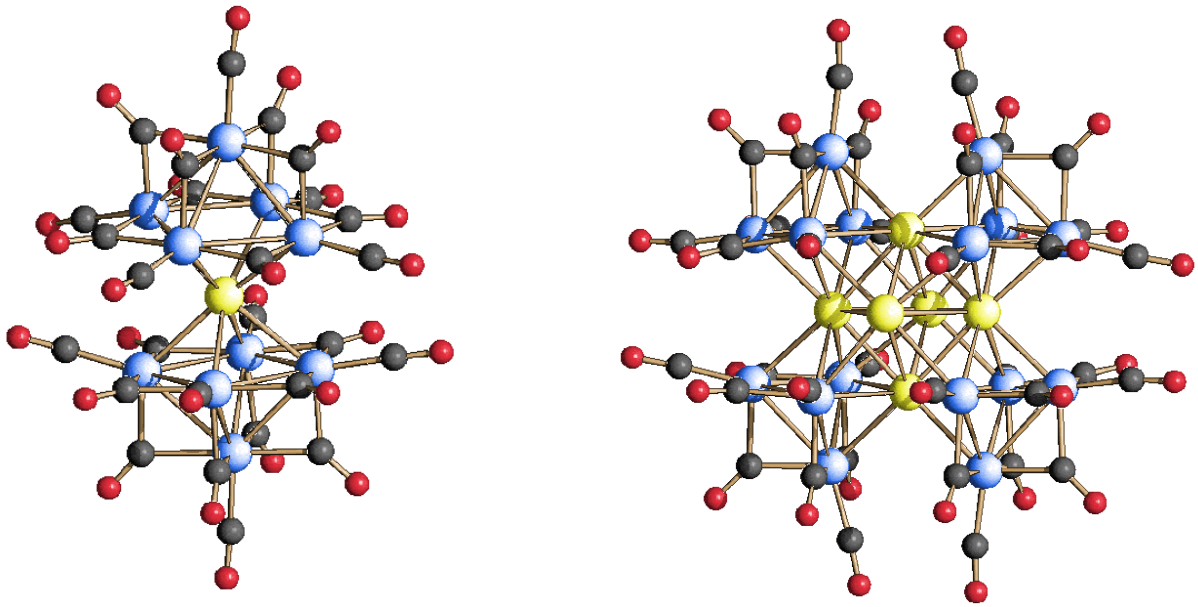

Figure 1. Molecular structures of $[Rh_{10}Au(CO)_{26}]^{3-}$ (left) and $[Rh_{16}Au_6(CO)_{36}]^{6-}$ (right).

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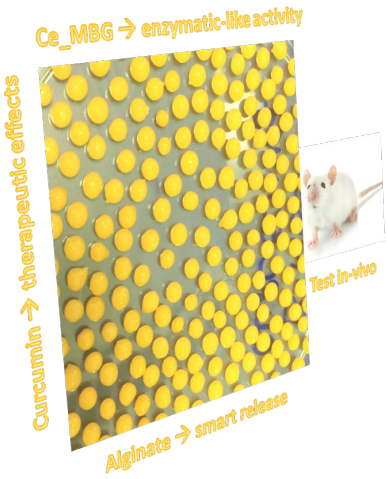
Cerium-containing mesoporous silica systems with enzymatic-like activity for Curcumin delivery

Debora Carrozza,[a] Matteo Mari,[a] Erika Ferrari,[a] Gigliola Lusvardi,[a] Gianluca Malavasi [a]

[a] Department of Chemical and Geological Sciences, University of Modena and Reggio Emilia, via G. Campi 103, 41125, Modena, Italy

213134@studenti.unimore.it, debora.carrozza@hotmail.it

Cancer genesis and progression is caused by homeostatic errors occurring within the tumor microenvironment [1], related or not with genetic mutations, dealing with all components of the cancer tissue, and implying many alterations, including increased oxidative status [2].
Many natural occurring antioxidants have been investigated so far, among them Curcumin, a promising bioactive phytochemical extracted from turmeric (*Curcuma longa* L.), demonstrated to have interesting antioxidant and anticancer properties, particularly against colorectal cancer, one of the mostly spread ones. However, it is difficult to move from in vitro studies to clinic applications due to availability issues: low aqueous solubility, rapid phase II metabolism, chemical and metabolic instability resulting in poor oral bioavailability [3].
Recently, we demonstrated that the introduction of small amounts of CeO_2 (nanoceria) into mesoporous bioactive glasses (MBG) confers antioxidant properties such as the catalase mimetic activity [4]. Thus, the redox properties of nanoceria determine its ability to protect tissues against oxidative stress, representing and interesting stable inorganic option to organic radical scavengers.
The aim of this work is to investigate the possibility to develop an improved antioxidant material that benefit of both the therapeutic features of curcumin and the antioxidant properties of cerium-based MBG. In order to overcome curcumin issues and increase bioavailability, encapsulation strategy in delivery systems is explored, particularly the use of polysaccharide hydrogel beads that are suitable for utilization in the food industry [5].
The encapsulated hybrid material was obtained by the injection-gelation approach: a biopolymer solution containing the bioactive components (curcumin/Cerium containing MBG) is injected into the ‘‘hardening’’ calcium solution under conditions that promote the gelation of the injected biopolymer. The Ce-MBG/alginate curcumin-containing beads were fully characterized, curcumin release was tested in simulated biological fluids (gastrointestinal, intestinal). Antioxidant activity was investigated by catalase mimetic activity and DPPH assays. Bioavailability was finally tested in a preliminary pilot *in vivo* study using Wistar rat model.



Concluding, the hybrid material sums up the features of is components, in fact it is able to ***i)*** resist in the gastrointestinal tract with a subsequent drug release in intestinal environment ***ii)*** promote enzymatic-like activities (catalase) able to reduce H_2O_2 a potent ROS ***iii)*** benefit of antioxidant and potentially anticancer activity of curcumin ***iv)*** increase curcumin bioavailability.

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Bimetallic Au-Ag systems for electrocatalytic applications

Stefano Cattaneo[a], Anna Testolin[a], Valentina Pifferi[a], Antonella Balerna[b], Luigi Falciola[a] and Alberto Villa[a].

[a] Dipartimento di Chimica, Università degli Studi di Milano, Via Golgi 19, 20133 Milano, Italy; [b] INFN, Laboratori Nazionali di Frascati, 00044 Frascati (RM), Italy:

Bimetallic gold-silver nanoparticles have recently attracted extended scientific attention due to their superior and unique chemical and physical properties compared to their monometallic counterparts.[1] The alloying of these two metals, in fact, can enhance both optoelectronic and catalytic properties and for this reason, AuAg systems find application in several fields, such as catalysis, optoelectronics, surface-enhanced Raman spectroscopy and as biosensors. These new properties can be ascribed to a synergistic effect of the two metals, and in particular to ligand and ensemble effects.[2] The presence and extent of these effects are intimately related to the chemical-physical properties of the nanoparticles, such as particle size and chemical composition.[3]
In this work, bimetallic Au-Ag nanoparticles were synthesised using a sol-immobilisation method in order to obtain different bimetallic structures, such as random alloys and core-shell structures (Fig. 1 - left). The colloids were then deposited onto carbon nanofibers. The as prepared catalysts were thoroughly characterised with different complementary techniques such as high resolution transmission microscopy coupled with energy-dispersive X-ray spectroscopy (HRTEM-EDX), cyclic voltammetry (CV) and X-ray absorption fine structure spectroscopy (XAFS). All these techniques gave a comprehensive view on the chemical-physical properties of the different materials. The catalysts were then finally tested in the electrocatalytic reduction of organic halides, where the two metals showed a synergistic effect reducing both acetobromo-α-D-glucose (Fig. 1 – right) and benzyl bromide at higher potentials compared to the respective monometallic counterparts.

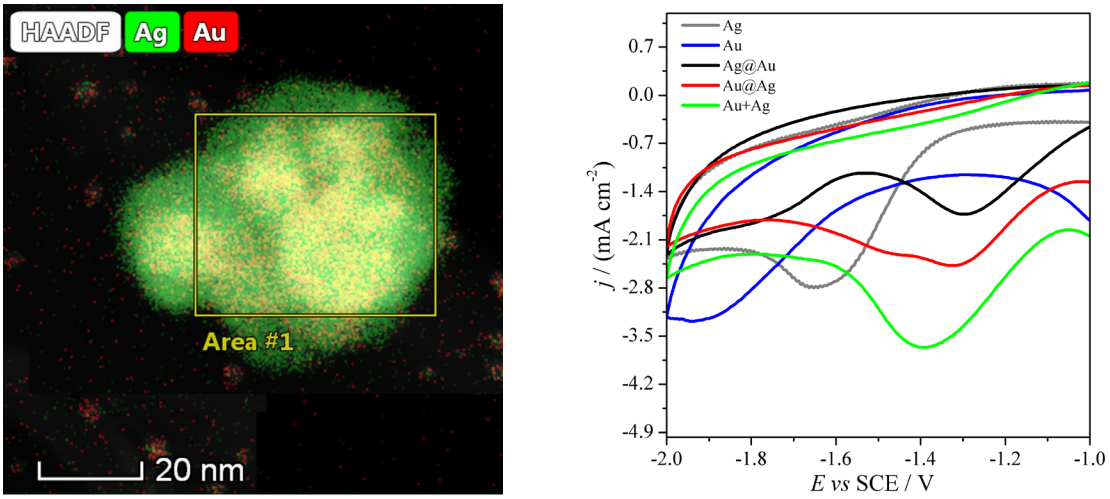

Figure 1: (left) EDX-HAADF image of an agglomerate of Au-core Ag-shell (Ag@Au) nanoparticles supported onto carbon nanofibers. (right) CV of bimetallic and monometallic catalysts registered in ACN with 0.1 M TBAP solution as supporting electrolyte, at 100 mV s^{-1}, in the presence of 2 mM of Acetobromo-α-D-glucose.

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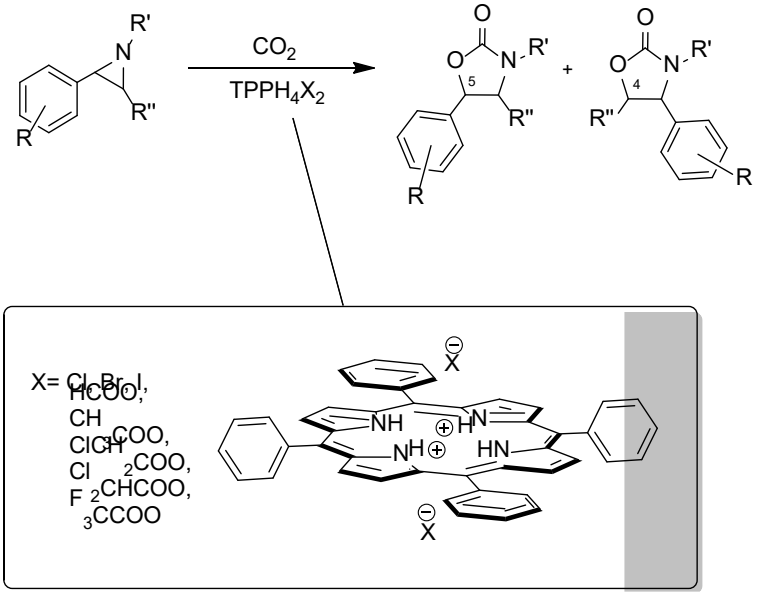
Catalytic activity of protonated porphyrins in the CO_2 cycloaddition to aziridines

Matteo Cavalleri, Caterina Damiano, Paolo Sonzini, and Emma Gallo

Department of Chemistry, Università degli Studi di Milano, via Golgi 19, 20133 Milano, Italy

Oxazolidinones are largely used as intermediates as well as chiral auxiliaries[1] in organic synthesis and constitute a class of active antibacterial and antibiotic compounds[2].
One of the most interesting methodologies for the synthesis of oxazolidinones is the CO_2 cycloaddition to aziridines, which employs this greenhouse gas as a renewable C1 synthon instead of other carbon sources derived from oil-based feedstock.
Recently, we reported the metal-free synthesis of oxazolidin-2-ones by the carbon dioxide cycloaddition to aziridines, which was promoted by $TPPH_2$/TBACl ($TPPH_2$=tetraphenyl porphyrin; TBACl=tetrabutyl ammonium chloride) catalytic system[3]. In this reaction, the porphyrin core plays a fundamental role to improve the TBACl nucleophilic reactivity with the consequent improving of both the catalytic performance and the reaction regioselectivity[3].
Triggered by these good results, we investigated the possibility to perform the CO_2 cycloaddition to aziridine in the absence of the TBACl co-catalyst by using di-protonated porphyrins, which show the nucleophilic agent as the counteranion.
Di-protonated porphyrins, obtained by reaction of free porphyrins with different acids, show the two counteranions on the two faces of the porphyrin plane[4]. The reaction performed well in the presence of protonated porphyrin molecules to suggest a good nucleophilic activity of the two counteranions, which can attack the aziridine and be responsible for the ring-opening reaction and the consequent CO_2 cycloaddition.
The catalysts screening, optimization of reaction conditions and the reaction scope are here reported.



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Methylmethacrylate-based polymeric nanoparticles as platform for multimodal imaging

S. Cerra[a,*], *V. Dini*[b], *T.A. Salamone*[a], *F. Hajareh Haghighi*[a], *F.A. Scaramuzzo*[c], *R. Matassa*[d], *M. Marsotto*[e], *C. Battocchio*[e], *A. Cartoni*[a], *I. Fratoddi*[a]

**Email: sara.cerra@uniroma1.it*

[a] *Department of Chemistry, Sapienza University of Rome, Piazzale Aldo Moro 5, 00185, Rome, Italy;* [b] *National Center for Innovative Technologies in Public Health, Istituto Superiore di Sanità – National Institute of Health, Viale Regina Elena 299, 00161 Rome, Italy;* [c] *Department of Basic and Applied Sciences for Engineering (SBAI), Sapienza University of Rome, Via Antonio Scarpa 14, 00161 Rome, Italy;* [d] *Department of Anatomical, Histological, Forensic and Orthopaedic Sciences, Section of Human Anatomy, Sapienza University of Rome, Via A. Borelli 50, 00161, Rome, Italy;* [e] *Department of Sciences and CISDiC, Roma Tre University, Via della Vasca Navale 79, 00146 Rome, Italy.*

Cancer therapy using nanomaterials has progressed significantly over the years. Radiation therapy, chemotherapy, or combination of these is used to deal with the serious threats of malignancy. However, surgical resection is the most effective therapy since it reduces the probability of tumor recurrence. While some tumors can be resected easily, others may be in hard-to-reach locations. Radioguided surgery (RGS) is a technique that may enable the surgeon to evaluate in real time the completeness of the tumor lesion resection [1]. With high development in nanoscience, nanostructured polymers have attracted high interest especially in cancer diagnosis and therapy due to their unique properties, such as porous structure, and high surface than their bulk counterparts [2,3]. This work concerns the preparation and characterization of methylmethacrylate-based copolymeric nanoparticles *via* surfactant-free emulsion polymerization using radical initiator at 80°C. Acrylic acid and N,N-dimethylacrylamide were used as comonomer to obtain P(MMA-co-AA) and P(MMA-co-DMAA) polymeric NPs. The effects of monomers ratio and initiator were studied to optimize average particle hydrodynamic diameter and polydispersity index of the final particles. Then, the obtained polymeric nanoparticles were loaded with ^{89}Y, as a model of β^- radioisotope ^{90}Y, by addition of an aqueous solution of YCl_3. NPs as imaging probe were obtained by physical encapsulation of xanthene dye fluorescein isothiocyanate isomer I (FITC) into the inner core of the copolymeric NPs. The obtained NPs were used for *in vitro* biocompatibility evaluation in human glioblastoma cell line. The copolymers were characterized by FTIR, and the composition was determined by ^{1}H-NMR and XPS spectroscopies. The morphology and particle size distribution were determined through dynamic light scattering (DLS), atomic force microscopy (AFM) and electron microscopies (SEM/TEM). As a proof of concept, bright fluorescence of FITC encapsulated NPs was studied via fluorescence microscopy.

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Metal-oriented tertiary structural motifs: a minimal set of bricks for metal coordination in proteins

Marco Chino[a], Fabio Pirro[a], and Thomas Lemmin[b]

[a]*Department of Chemical Sciences, University of Naples "Federico II". Via Cintia 21, 80126 Napoli, Italy.*
[b]*DS3Lab, System Group, Department of Computer Sciences, ETH Zurich, 8092 Zürich, Switzerland*

Metal cofactors are often essential for the proper folding of polypeptide chains or function of folded proteins[1]. However, the full potential of protein ligands to bind any given metal cofactors and tune their chemistry has not been exhaustively explored by evolution[2–4]. It has been shown that the protein structural space is highly degenerate and can be recapitulated with a finite set of structural units, such as elements of tertiary structure called TERMs (TERtiary Motifs).[5] Here, we build on this concept and report the development of a dataset of highly specialized metal-binding elements: MetalTERMs. Over 100'000 MetalTERMs were identified from sites in which the metal was bound only by protein residues and water molecules. Subsequently, MetalTERMs were clustered according to their root-mean-square-deviation, the total number of residues and the number of non-contiguous segments. We find that the number of clusters rapidly drops with the increase in complexity of the tertiary arrangement, and that MetalTERMs composed of at most three segments can recapitulate about 90% of the whole dataset. This would indicate that medium to long-range mutations have most likely only a marginal effect on the metal coordination sphere, and would therefore corroborate the well-established adoption of the miniaturization approach for designing metalloproteins from scratch. Our analyses have also enabled us to identify new-to-nature combinations of most recurring MetalTERMs, which could eventually lead to the design of unprecedented catalysts.

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Magnetic iron oxide nanoparticles for the heterogenization of catalytic organometallic complexes

R. Colaiezzi, A. Lazzarini, A. Di Giuseppe, M. Crucianelli

Department of Physical and Chemical Sciences, University of L'Aquila, Via Vetoio (COPPITO 1-2), 67100, L'Aquila, Italy

The importance of the recyclability of a heterogeneous catalyst is an aspect that is arousing much interest in the scientific community [1]. Silica-coated magnetic iron oxide nanoparticles (MNP) were synthesized to be used as a starting core for easily recoverable heterogeneous catalyst supports. Both the properties of the magnetic core and the cover shell have been finely tuned, with particular attention in optimizing the thickness of the silica layer. A complete set of characterization techniques, partially shown in Figure 1 (ATR-IR, XPS, XRD, SEM, TEM, ICP-MS, BET, AGFM), was employed to reveal the characteristics of the catalyst.

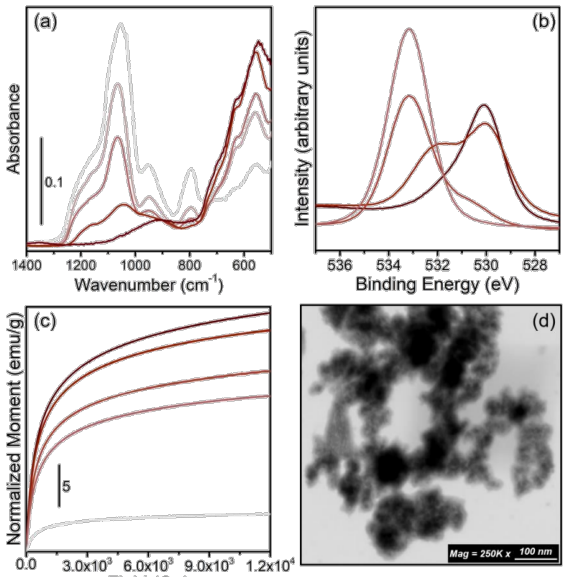

Figure 1. Overview of techniques employed for the characterization of the coated nanoparticles: (a)ATR-IR spectroscopy, (b) XPS, (c) AGFM, (d) STEM.

We are currently developing a procedure for the heterogenization of organometallic complexes based on V and Mo containing Schiff Bases in the organic ligand. For this reason, the efficiency of the coating is essential to provide a tailored anchor point for the active phase of the catalyst. The oxidation of cis-cyclooctene with tert-butyl hydroperoxide in the presence of MNP was used as a reaction probe to verify the reactivity, if any, of the coated NPs, as it is, and the effectiveness of the silica shield [2]. The results of these tests showed its chemical inertness confirming the absence of side reactions catalyzed by iron oxide or modifications of the magnetic core. This reaction was also used as a model reaction for preliminary catalytic tests, which showed high yields and selectivity, as well as good recyclability.

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Supporting planetary exploration with high fidelity lunar dust simulants for toxicological studies.

Ingrid Corazzari[a,b,c], Serena Esposito[d], Antonello Marocco[e], Michele Pansini[e], Maela Manzoli[a], Chiara Bellomo[a,b,c], Cristina Pavana[b,c], Francesco Turcia[b,c]

[a] Dipartimento di Chimica, Università di Torino; [b] "G. Scansetti" Interdepartmental Center for Studies on Asbestos and Other Toxic Particulate, Università di Torino; [c]Topical Team on Celestial Dust Toxicity (T3CD); [d]DISAT, Politecnico di Torino; [c]Department of Civil and Mechanical Engineering and INSTM Research Unit, Università degli Studi di Cassino e del Lazio Meridionale.

With the Artemis program NASA plans to bring humans to the Moon by 2024 with the aim of establishing a permanent human. Artemis program envisages long duration missions and planetary operations (including extra vehicular activities and in situ resource utilization), which entail numerous risks. One of the major concerns is represented by the exposure to the fraction of lunar soil with size < 20 μm, known as lunar dust (LD). Several Apollo crew members reported that after exposure to LD (fig. 1A) they suffered detrimental effects, including respiratory and eye irritation. This suggests that LD has the potential to induce toxic outcomes. There is high concern especially for the effects due to a long-duration exposure, which is expected during Artemis program (fig.1B), has been expressed. The potential toxicity of LD resides in its unique physico-chemical features that could impart exceptional reactivity to the particle surface. In particular, LD possesses some unique characteristics as a consequence of the peculiar environmental conditions in which it is formed and exists. The continuous bombardment by micro-meteorites creates freshly-fractured surfaces, whose reactivity is preserved by the absence of an oxidative atmosphere. Moreover, nanophase zero-valent iron (np-Fe0), which is a peculiarity of LD never observed in terrestrial mineral dusts, was claimed to be responsible for the LD remarkable oxidative reactivity [1]. Since the amount of LD samples returned from Apollo is too limited to be widely distributed to the scientific community, the majority of the studies on the toxicity of LF are and will be based on simulants. Several terrestrial mineral dusts have been proposed as LD analogues in virtue of their elemental and mineralogical features, but all of them lack some peculiar yet toxicologically relevant features of LD [2]. For this reason NASA strongly recommended the creation of a high fidelity standardized simulant for toxicological studies that could be widely distributed and widely employed by research laboratories. We propose here a preparative approach based on a strictly controlled procedure. Synthetic quartz and np-Fe°-rich simulant (prepared following the synthetic procedure described in [3] and [4]) were subjected to a highly controlled and efficient milling under inert atmosphere to mimic some of the Moon environmental conditions with the dual purpose of reducing the particle size to the respirable range and activating the reactivity through the creation of freshly formed reactive moieties. The milled dusts were studied in terms of particle size distribution, morphology, presence of surface radicals and reactive centers (EPR), oxidative properties (terephthalate assay/fluorimetry) [5], and the capability to induce in vitro cell membrane damage.

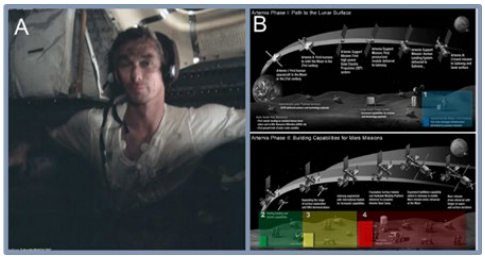

Figure 1 A. Apollo 17 astronaut is G. Cernan covered in LD after an EVA;B.T3CD's qualitative estimation of the exposure to LD during the several steps of Artemis program

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Biocompatible lanthanide-doped KY_3F_{10} colloidal nanocrystals for multimodal imaging

Chiara Cressoni[a], Giacomo Lucchini[a], Marco Gerosa[b], Federica Vurro[b], Federico Boschi[b], Antonello Spinelli[c], Pasquina Marzola[b], Adolfo Speghini[a]

[a] *NRG, Department of Biotechnology, University of Verona and INSTM, RU Verona, Strada Le Grazie 15, I-37134 Verona, Italy*
[b] *Department of Computer Science, University of Verona and INSTM, RU Verona, Strada Le Grazie 15, I-37134 Verona, Italy*
[c] *Preclinical Imaging Facility, IRCCS Ospedale San Raffaele, Via Olgettina 60, 20132 Milano, Italy*

Lanthanide ions (Ln^{3+}) doped KY_3F_{10} hosts has recently been investigated for their interesting luminescence properties [1], that could pave the way for many applications in nanomedicine, especially for bioimaging, sensing, drug delivery and photodynamic therapy. From a synthetic point of view, environmental-friendly syntheses to obtain colloidal nanoparticles are nowadays highly desirable. Hydrothermal treatments are particularly useful, as they are usually associated to low energy costs and short reaction times [2].
In this communication we investigated luminescent KY_3F_{10} nanoparticles, activated with Er^{3+}, Yb^{3+} and Nd^{3+}, as dispersible colloids prepared by a facile microwave-assisted synthesis, that allows to decrease the reaction times to finely control the size and structure of the nanomaterials. Biocompatible capping agents have been also considered to improve colloidal stability as well as biological cell internalization processes.
We prepared a core@shell multifunctional architecture [3] to develop optical and Magnetic Resonance Imaging (MRI) contrast agents. The nanomaterials under investigation are also useful as nanothermometers, as some emissions in the optical range (e.g. in the first and second biological windows), change their relative intensity on varying the temperature. These features offer the possibility to exploit the lanthanide doped nanomaterials for optical imaging and, at the same extent, temperature sensing. Furthermore, Gd^{3+} ions have been considered as dopants to provide strong paramagnetic properties for MRI. The X-ray absorptions of the doping lanthanide ions are also considered for CT imaging. Preliminary biocompatibility investigations of the prepared nanomaterials have revealed very low cytotoxicity in different human cell lines. Biodistribution within mice models has also been investigated to investigate *in-vivo* applications.

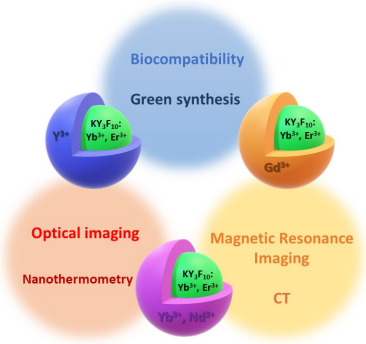

Figure 1. *KY_3F_{10}: Yb,Er nanoparticles with multifunctional core@shell architectures*

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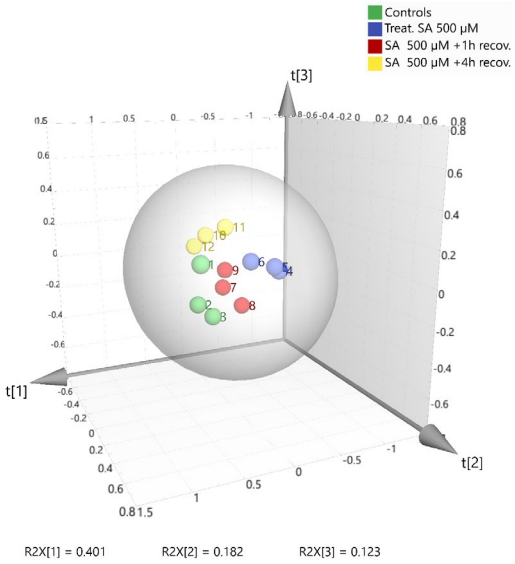
SH-SY5Y neuronal cultures stressed with sodium arsenite as model cells for the study of amyotrophic lateral sclerosis: a ^{1}H-NMR metabolomic investigation

Federica De Castro,[a] Viviana Vergaro,[a,b] Michele Benedetti,[a] Alessandro Romano,[c] Annamaria Nigro,[c] Francesca Pezzuto,[c] Giuseppe Ciccarella, [a,b] Francesco Paolo Fanizzi.[a]

[a] Dipartimento di Scienze e Tecnologie Biologiche ed Ambientali, Università del Salento & UdR INSTM di Lecce, Via Monteroni, I-73100 Lecce, Italy ;[b] CNR NANOTEC - Istituto di Nanotecnologia c/o Campus Ecotekne, Università del Salento, Via Monteroni, 73100 Lecce, Italy; [c] Division of Neuroscience, Institute of Experimental Neurology, IRCCS San Raffaele Scientific Institute, I-20132 Milan, Italy

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease that results in the degeneration of both upper and lower motor neurons and the presence of intra-neuronal aggregates in the affected tissue. These lead to muscle weakness and often to paralysis [1].
Previous studies indicated that neurodegenerative diseases are caused by mitochondrial DNA mutation, oxidative stress damage, excitatory toxin and immune related inflammation. Among these factors, oxidative stress plays an important role [2]. Nevertheless, the exact mechanisms underlying ALS remain unclear. The neuroblastoma SH-SY5Y cells possess many characteristics of neurons, thus representing one of the most used models for studying mechanism involved in neurotoxicity. Recently, it has been reported that the exposure to sodium arsenite (SA) induces cell oxidative stress followed by formation of cytoplasmic stress granules, typical of the ALS disease [3]. For these reasons, the SA stressed neuron-like SH-SY5Y cells are actually used as model for ALS studies. However, the specific mechanisms responsible for the stress granules formation are still unknown. For this reason, in the present work, a ^{1}H NMR metabolomics approach was used to study the metabolic alteration induced by SA in SH-SY5Y cells. NMR based metabolomics was also performed to evaluate the reliability of the used cellular model for the study of ALS, see Figure.



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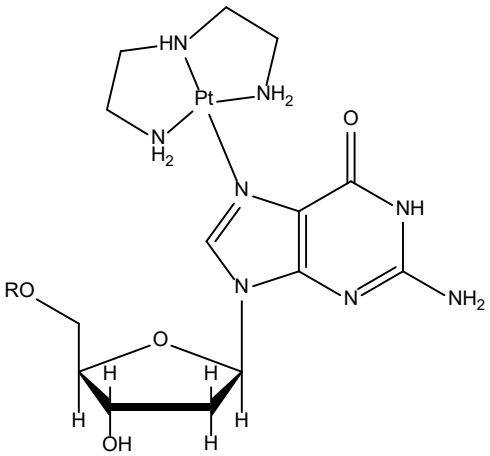
Study of the uptake of platinated nucleotides through plasmatic cell membrane

Erik De Luca [a], Federica De Castro [a], Amilcare Barca [a], Chiara R. Girelli [a], Alessandro Romano [a], Francesco P. Fanizzi [a], Tiziano Verri [a] and Michele Benedetti [a]

[a] *Dipartimento di Scienze e Tecnologie Biologiche ed Ambientali, Università del Salento, Via Monteroni, I-73100 Lecce, Italy.*

Notwithstanding the general progresses made in antitumor therapy, cancer remains one of the main causes of death. Platinum-based anticancer drugs are between the most effective anticancer drugs for the treatment of malignant tumors. However, due to severe side effects and resistance phenomena induced by treatments with platinum drugs, the search for alternative platinum compounds with enhanced efficacy and lower toxicity is highly desired. [1] In this context, we previously synthesized and characterized a series of platinated antimetabolites, of the type [Pt(dien)(*N7*-G)] (dien = diethylenetriamine; G = guanosine derivative), showing *in vitro* the possibility to specifically target DNA, without affecting the RNA. [2-3] As known, the first major barrier for drug delivery is the crossing of the plasma cell membrane. This is a pre-requisite for cell uptake of drugs and other biologically active molecules. For this reason, we have assayed the capability of our compounds to be internalized by tumor cells membrane. In human (h) cells and tissues are known two families of nucleoside transporters (i.e. *equilibrative* nucleoside transporters, hENTs, and *concentrative* nucleoside transporters, hCNTs). Such classes of transporters are known to generally mediate the transport of both physiological nucleosides and molecular analogues, the last sometimes effective as chemotherapeutic agents. [4] In this work, we evaluated, in a model HeLa cancer cell line, the possible uptake of platinated nucleotides, $[Pt(dien)(dGuo)]^{2+}$ and [Pt(dien)(dGTP)] (Scheme 1), in order to identify and quantify their possible cell membrane transport. Preliminary results evidenced a marked sodium-dependent transport of the platinated nucleotides, condition associated to the hCNT mediated transport.



Scheme 1. Chemical structure of platinated nucleosides. R= H; $H_4P_3O_9$.

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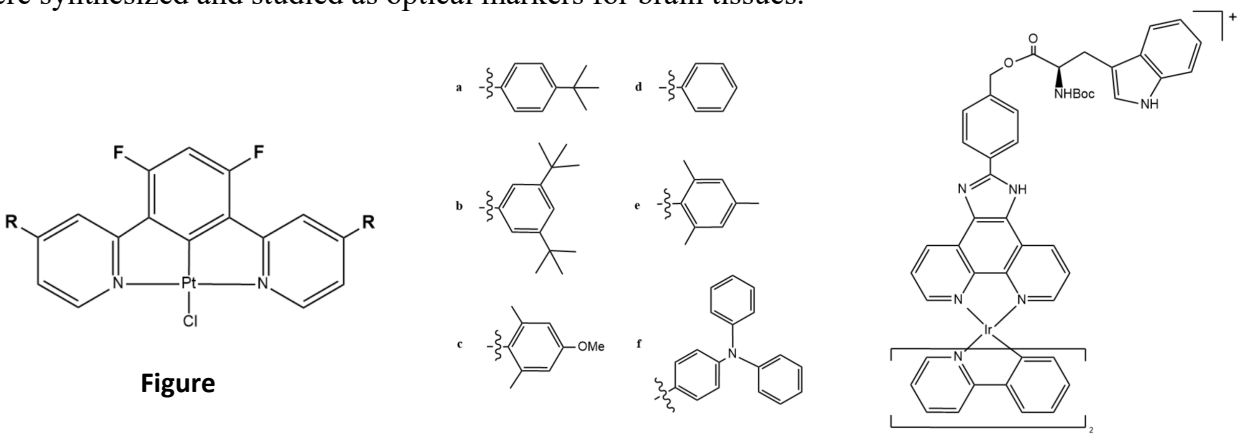
Innovative highly hindered cyclometalated Pt(II) and bioconjugated Ir(III) complexes: broadening the bioimaging and photodynamic therapy frontiers.

Giulia De Soricellis [a], Alessia Colombo [a], Claudia Dragonetti [a], Dominique Roberto [a], Daniele Marinotto [b], Massimiliano Massi [c], Bertrand Carboni [d] and Veronique Guerchais [d]

[a] *Dip. di Chimica, Università degli Studi di Milano and INSTM UdR Milano, Italy*
[b] *CNR-SCITEC, Milan, Italy*
[c] *Curtin Institute of Functional Molecules and Interfaces, Curtin University, Perth, Australia*
[d] *University of Rennes 1, Institut des Sciences Chimiques de Rennes ISCR, Rennes, France*

The role of transition metal complexes in life science has gained increasing interest, due to their outstanding photophysical properties. In particular, the ability of heavy metals to undergo spin-orbit coupling and the long life-time of their excited states, have led to extensive studies focused on phosphorescent organometallic complexes.[1,2] Remarkably, through minor modifications of the coordination sphere, it is possible to finely tune the photophysical properties. Furthermore, the introduction of biologically relevant substituents allows to target specific organelles, circumscribing their action locally.[3] These features make organometallic complexes very attractive for a broad range of applications in the biological environment, e.g. for bioimaging or for photodynamic therapy. Indeed, the excited states of these complexes can be exploited for the emission of photons thus obtaining bright images of cells and of their components, [4] or to selectively cause the death of cancer cells through formation of cytotoxic species.[5]
In this context, a series of innovative cyclometalated fluorinated Pt(II) complexes functionalized with bulky aryl substituents on the para position of the pyridine rings were synthesized. The enhanced steric hindrance provides an effective strategy to prevent aggregation, a phenomenon that leads to energy loss. Furthermore, a tryptophan conjugated ligand and the deriving cationic Ir(III) complex were synthesized and studied as optical markers for brain tissues.



Figure

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Mo doped $ZnIn_2S_4$ for photocatalytic nitrogen fixation

Tarekegn Heliso Dolla, [a] *Tiziano Montini* [a]

[a] *Department of Chemical and Pharmaceutical Sciences, INSTM Trieste Research Unit and ICOOM-CNR Trieste Research Unit, University of Trieste, Italy*

Photocatalytic nitrogen fixation is considered as a promising technology to solve the high-energy demand in industrial ammonia synthesis. However, because of the requirements of reaction conditions, its development is still limited by the poor reaction efficiency and low yield of ammonia [1]. In this study, to explore the activity of a visible light active $ZnIn_2S_4$ materials for photocatalytic nitrogen reduction reaction (PCNRR), Mo doped $ZnIn_2S_4$ nanostructures were developed through a facile hydrothermal route [2,3]. It is observed that the Mo doping enhanced the photocatalytic performance of the $ZnIn_2S_4$. With an optimum 1 mol % Mo doping, the NH_3 production of about 40 $\mu mol\ g^{-1}\ h^{-1}$ is achieved under visible light irradiation and in the presence of a hole scavenger. The Mo can act as activation center by enhancing the N_2 adsorption and activation and reducing the charge recombination.

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Wild animal hair as biological indicator of trace metals

S. Squadrone[a], S. Falsetti[a], A. Griglione[a], S. Robetto[b], R. Orusa[b], M.C. Abete[a]

Istituto Zooprofilattico del Piemonte, Liguria e valle d'Aosta, via Bologna 148, Turin, Italy
[a] CReAA; National Reference Center for the surveillance and monitoring of animal feed
[b] CERMAS National Reference Center for Wild Animal Disease

Trace elements are essential for all living organisms. Their presence in excess or in defect often results in pathological states in animals and humans. Lead (Pb) and cadmium (Cd) and mercury (Hg) are toxic elements, while copper (Cu), zinc (Zn) manganese (Mn), nickel (Ni), and iron (Fe) are necessary for life. Animal hair is a useful biomonitoring tool for assessing the presence of metals in the ecosystem [1] since it reflects the animal's diet. Hair in fact accumulates and concentrates metals at higher levels than organs and indicates an exposure of months or years before. CERMAS and CReAA have always collaborated in the monitoring of metals in wild animals. Hair samples (n=50) were collected in North-western Italy in 2019. Samples were weighed then added with 1.5 mL of 30% hydrogen peroxide, and 7 mL of 70% nitric acid and mineralized an ETHOS 1 microwave oven (Milestone S.r.l.). The detection of metals was performed by the Inductively Coupled Plasma-Mass Spectrometer (ICP-MS) Xseries II, (Thermo Scientific, Bremen, Germany) as already described [2]. The analysis of 16 trace elements (Table 1) performed on the hair of badger (*Meles meles*), wild boar (*Sus scrofa*), marmot (*Marmota marmota*), wolf (*Canis lupus*) and fox (*Vulpes vulpes*) has clearly shown that animals with omnivorous and mainly vegetarian diet such as badger, marmot and wild boar have a hair metal content (Al, As, Cr, Cu, Fe, Ni, V) higher than carnivores (wolf and fox).Element concentrations found in the investigated species were below levels related to toxicosis in mammals [3].

This research was funded by the Italian Ministry of Health (Project n. IZS PLV 19/11RC)

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Table 1 Trace elements in wild animal hair (mg/kg)

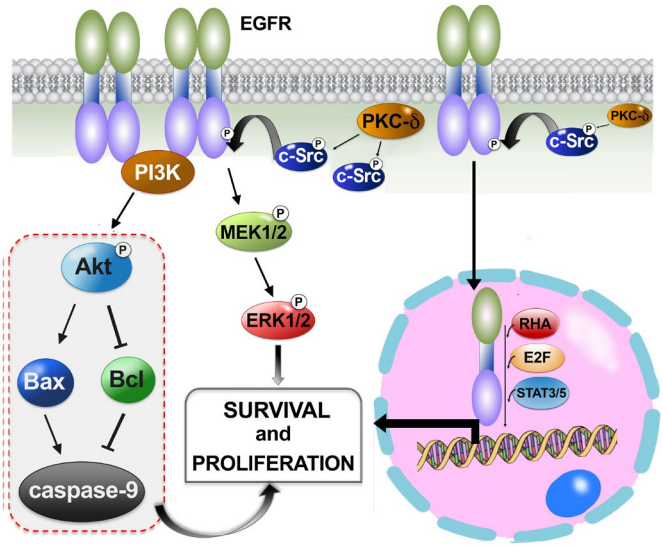
	badger	***wild boar***	***marmot***	***wolf***	***fox***
Al	849	708	428	124	162
As	1,1	0,27	1,0	0,43	0,41
Cd	0,023	0,059	0,087	0,011	0,024
Cr	2,5	1,5	2,1	0,85	1,1
Cu	52	28	45	21	22
Fe	852	441	504	199	127
Hg	0,52	0,066	< 0,010	0,044	0,28
Mn	27	24	33	64	68
Ni	1,7	1,6	2,1	0,61	1,8
Pb	0,83	2,3	1,1	0,19	0,33
Pd	< 0,010	0,011	0,017	< 0,010	< 0,010
Pt	0,011	< 0,010	< 0,010	< 0,010	< 0,010
Rb	1,0	1,4	1,8	0,31	0,35
Sn	0,051	0,043	0,088	0,025	0,041
V	1,6	1,2	0,73	0,61	0,41
Zn	131	121	185	124	148

Intracellular mechanisms underlying resistance to Pt drugs in MCF-7 human breast cancer cell line

Muscella Antonella, Stefàno Erica, Calabriso Nadia, De Pascali Sandra Angelica, My Giulia, Iaconisi Giulia Natalia, Fanizzi Francesco Paolo, Marsigliante Santo.

Department of Biological and Environmental Science and Technologies (DiSTeBA), University of Salento, Via Prov. le Lecce-Monteroni, 73100 Lecce, Italy.

Platinum complexes are currently used for breast cancer therapy, but, as with other drug classes, a series of intrinsic and acquired resistance mechanisms hinder their efficacy. A typical example of cisplatin resistant tumour cells is MCF-7 strain commonly used as reference in comparative activity studies. Previous works demonstrated the antitumor activity of the Pt Complex [Pt(O,O'-acac)(γ-acac)(DMS)] [1] (1) against MCF7 with a distinct mechanisms of action from cisplatin, especially with regard to cellular targets. To gain more insights into the mechanisms underlying platinum complexes resistance in breast cancer, we generated a [Pt(O,O'-acac)(γ-acac)(DMS)]-resistant MCF-7 cells denoted as 1R. These latter are characterized by increased proliferation rates and aggressiveness with higher PKC-δ, BCL-2, MMP-9 and EGFR protein expressions and also by increased expression of various genes covering cell cycle regulation, invasion, survival, and hormone receptors. The 1R cells also displayed high levels of activated signaling kinases Src, AKT and ERK/2. Subject to (1) effect, 1R cells showed a relevant EGFR activation due to PKC-δ and Src phosphorylation that provoked proliferation and survival through MERK1/2/ERK1/2 and PI3K/Akt pathways. In addition, EGFR shuttled from the plasma membrane to the nucleus maybe acting as co-transcriptional factor.



The data suggest that growth and survival of 1R strain rely upon a remarkable increase in EGFR level which, in collaboration with an enhanced role of PKC-δ and Src kinases supports the resistant cells. It could therefore be assumed that combination treatments targeting both EGFR and PKC-δ/Src kinases may result in better therapeutic outcomes for patients with breast cancer.

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In vivo visualization of a Gd-containing contrast agent through its effect on the properties of a fluorescent pyrene-based dye. Insights for improving imaging-guided surgery?

Enza Di Gregorio[a], Chiara Furlan[a], Eliana Gianolio[a] , Zsolt Baranyai[b], Giuseppe Ferrauto[a,], Silvio Aime[a]*

[a] *Molecular Imaging Center, Department of molecular biotechnologies and health sciences, Via Nizza 52, 10126 Torino (It)*
[b] *Bracco Imaging Spa, Bracco Research Centre, Trieste (It)*

To resect tumors, surgeons are guided from their tactility and from the information gained in pre-acquired diagnostic images (CT, MRI, etc.). Gd-contrasted MR images are often of great relevance as the superb resolution of this technique allows to get a very accurate delineation of the tumor lesion[1]. It is straightforward to say that the access to Gd distribution in the surgery theatre would represent a highly valuable support for a complete tumor resection [2].
We wonder whether it would be possible to detect the distribution of Gd-bearing contrast agents by seeking specific effects on the fluorescence response of selected molecules. We report on the exploitation of hydrophobic interactions occurring between macrocyclic Gd complexes (*e.g.* Gadoteridol) and polycyclic fluorescent dyes normally used in biological assays (*e.g.* HPTS).
For this purpose, the HPTS fluorescence was titred in presence of Gadoteridol (by spectrofluorometer and IVIS optical imaging). Insights into the interaction between the two molecules were obtained by x-ray crystallography.
In vivo experiments have been carried out on murine cancer models. Murine breast cancer cells (TS/A) were subcutaneously administrated to Balb/c mice ($5x10^5$cells) and tumors imaged 10 days after the cells' implantation (volume of *ca*. 150 mm^3). Then, mice were divided into two groups. The first group has been *i.v*. injected with 0.6 μmol/kg HPTS; the second group received the *i.v*. co-administration of the HPTS/GdHPDO3A adduct (0.6 μmol/kg HPTS+ 0.6 mmol/kg GdHPDO3A).
UV-Vis and fluorescence emission spectra for 100 nM of HPTS solutions in the presence of Gadoteridol show that by creasing the concentration of the macrocycle, there is a significant enhancement in the absorption and emission spectra of HPTS. Results were corroborated by optical fluorescence imaging in phantom and in mice. This indicates that HPTS and GdHPDO3A interact together by forming supramolecular adduct. The presence of a 2:1 GdHPDO3A:HPTS adduct is reported by x-ray crystallography. The interaction occurs only with TSAP isomer of GdHPDO3A.
When Gadoteridol is applied to mice at a dose consistent with the clinical one (*e.g.*, 0.6 mmol / Kg corresponding to 0.05 mmol/kg in humans), the HPTS administered at the dose of 0.6 μmol / Kg is sufficient to yield a detectable enhancement in the fluorescence images.
The enhancement of the fluorescent signal quickly reaches a maximum for both systems being higher when Gd-HPDO3A is present than for HPTS alone (70% *vs*. 42%). Interesting differences were also observed as far as concerns the wash-out in the fluorescent response.
In conclusion, in this work we reported a method for the visualization of Gd-complexes in tumors by using fluorescence imaging. The effect is detectable at clinical doses of GBCA and at a not toxic dose of HPTS. The possibility of visualizing the tumor margins during the surgery, by using a fluorescence signal reporting on the distribution of the GBCA, appears to be an innovative tool to bridge the information available in the surgery theatre with the pre-surgery Gd- contrast enhanced MR images.

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Photoreactivity studies of Cr(I) complexes by EPR spectroscopy

David Fioco[a,b], Andrea Folli[a], Emma Richards[a], Richard Wingad[a], Mario Chiesa[b], Damien Murphy[a]

[a]*School of Chemistry, Cardiff University, Main Building, Park Place, Cardiff, CF10 3AT.* [b]*Dipartimento di Chimica, Via Pietro Giuria 7, 10125 Torino, Italy*

Linear α-olefins (LAO) are a versatile class of organic compounds employed in a wide variety of industrial processes, ranging from the more common C4-C8 which are used in the production of polyethylene, linear aldehydes and short chain fatty acids to C20-C30 that are employed in the production of heavy linear alkyl benzenes as well as low molecular weight polymers to tune the rheological properties of waxes. Linear α-olefins are typically produced employing chromium complexes as catalysts [1]. For LAOs of C4 and C8 the reaction proceeds through a ring growth process in which ethylene inserts in free coordination sites around the metal centre to form 5 term ring (1-butene) to 9 (1-octene). Forming these free coordination sites requires a preliminary activation step, normally performed by chemical activation with Et_2Al_6 (TEA) or other Aluminium based alkylating agents. Chromium can access a variety of oxidation states from 0 to VI. Among the paramagnetic electronic configurations, oxidation states I, III, and V are often studied by Electron Paramagnetic Resonance (EPR) spectroscopy.

The complex $[Cr(CO)_4(Ph_2P(CH_2)_3PPh_2)]^+$ was investigated for photoreactivity experiments using UV-A (365nm, 50nm bandwidth [2]. All evidence collected so far has demonstrated that UV radiation can break the Cr-C and Cr-P bonds, as expected from previous studies on Cr(0) complexes [3]. While the end product of this reaction $[Cr(CO)_2(Ph_2P(CH_2)_3PPh_2)_2]^+$ is unlikely to have any catalytic activity, two of the other species that are formed, *mer*-$[Cr(CO)_3(\kappa^1\text{-dppp})(\kappa^2\text{-dppp})]^+$ and $[Cr(CO)_2dppp)(\eta^6\text{-arene})]^+$, initially reported by Rieger and Rieger [3], are here being investigated for their potential catalytic activity towards ethylene oligomerisation.

An analogous coordination compound, $[Cr(CO)_3((Ph_2P(C_2H_4))NH)]^+$, is also under investigation. As a novel complex, a full EPR characterization is under way. Preliminary studies display photoreactivity under UV-A (365nm, 50nm bandwidth) irradiation similar to the one exhibited by $[Cr(CO)_4(Ph_2P(CH_2)_3PPh_2)]^+$. Additional studies with TEA are also underway to determine if activation (chemical or photochemical) can be achieved and if the activated complex possesses catalytic activity towards ethylene oligomerization reaction.

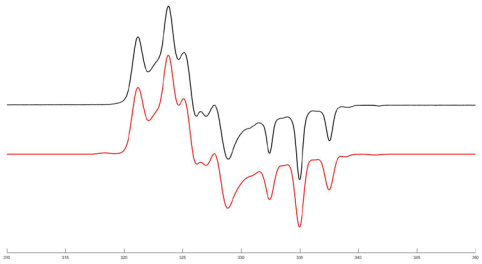

***Figure 1**: cw-X band spectrum (black) and simulation (Red) of $[Cr(CO)_3((Ph_2(C_2H_4))NH)]^+$ recorded at 120K.*

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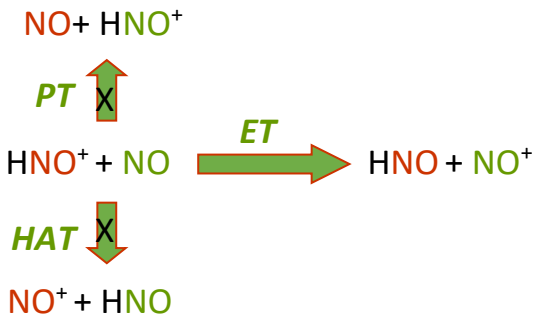
Charge transfer prevails over proton and hydrogen atom transfer in the reaction of protonated and neutral nitric oxide

Dandamudi Usharani,[a] *Maria Elisa Crestoni*,[b] *Simonetta Fornarini*[b]

[a] *Department of Food Safety and Analytical Quality Control Laboratory, CSIR-Central Food Technological Research Institute, Mysuru, Karnataka, India;* [b] *Dipartimento di Chimica e tecnologie del farmaco, Sapienza Università di Roma*

Simple triatomics such as neutral and charged HNO/$[HNO]^{+\cdot}$ play relevant roles in a variety of contexts. Nitroxyl, HNO is a reactive intermediate in the oxidation of atmospheric nitrogen, in the combustion of nitrogen containing fuels, and in the reaction of NH_2 radical with O_3 and O_2 in the troposphere. Another area where nitroxyl is recognized to exert a major function is in various biological processes.[1] It behaves as elusive intermediate, though, which limits its maximum concentration and lifetime. In this contribution we report on an assay of elementary reaction paths that may engage the $[HNO]^+$/NO couple.[2] To this end the ion is allowed to react with neutral NO in the cell of an FT-ICR mass spectrometer. In spite of the very simple reacting partners, different reactive processes may compete.

The thermal gas-phase reaction of $[HNO]^+$ with nitric oxide (NO) has been studied using FT-ICR mass spectrometry complemented by high level quantum chemical calculations. Both NO and $[HNO]^+$ are odd electron species and in consideration of this open shell configuration one could expect hydrogen atom transfer reactivity. We succeeded in discriminating among different competitive paths that could be envisioned, by using D- and ^{15}N-labelling in the reagent species. Different combinations of reacting partners have allowed to unequivocally observe an exclusive electron transfer (ET) reactivity. This outcome is well accounted for by the energy profile for the possible pathways calculated at CCSD(T)/aug-ccpVTZ//B3LYP/def2-TZVP level of theory. The seemingly barrierless ET process (as predicted by classical Marcus theory) is exoergonic by 20.8 kcal/mol. The two reaction partners may alternatively yield an adduct, endowed with partially covalent character, where a noticeable extent of charge transfer has taken place. This $[HNO\cdots NO]^+$ adduct may proceed by undergoing transfer of hydrogen, entailing largely hydride character. However, in agreement with a calculated barrier of ca. 12 kcal/mol, no experimental evidence is obtained for the occurrence of this alternative route.



This work was performed as Trans national access project in the frame of the European Network of Fourier-Transform Ion-Cyclotron-Resonance Mass Spectrometry Centers (Horizon 2020 Programme EU_FT-ICR_MS, grant number 731077)

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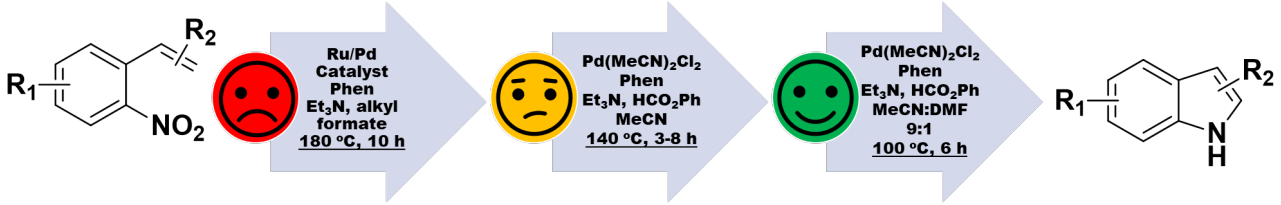
From *o*-nitrostyrenes to indoles: metal catalyzed reductive cyclization of *o*-nitrostyrenes using formate esters as CO surrogates

Manar Ahmed Fouad,[a] *Francesco Ferretti,*[a] *Fabio Ragaini* [a,*]

[a] *Dipartimento di Chimica, Università degli Studi di Milano, via Golgi 19, Milano, 20133, Italy*

Over thirty years ago, Cenini and co-workers reported the first reductive cyclization reaction of *o*-nitrostyrenes to indoles utilizing carbon monoxide as the reductant, employing different transition metals as catalysts under forcing conditions (220 °C, 80 bar CO).[1] Despite the high efficiency and the high atom-economical character of these reactions, they have not become of widespread use. This is mainly due to the need to use pressurized CO, requiring safety measures that are not accessible in most synthetic organic laboratories. Our group introduced alkyl and aryl formats as efficient, powerful, low-toxic, and cheap *in-situ* CO-releasers, that avoid to employ pressurized CO and autoclaves, in the metal-catalyzed reductive cyclization reactions of *o*-nitrostyrenes to indoles. A cheap glass pressure tube can be used as the reaction vessel which transforms this kind of reaction into a "General Tool" to the synthetic chemist. Owing to the minimal cost of alkyl formates, the initial investigation was directed to their use as CO releaser. A bimetallic Ru/Pd-catalytic system was required to achieve both the formate decomposition and the *o*-nitrostyrene reductive cyclization with satisfactory yields. However fulfilling results were accomplished uniquely under harsh conditions (180 °C, up to 10 h). On the other hand, when phenyl formate was employed, complete conversions and good selectivities were accomplished at lower temperature (140 °C) and using a Pd/phenanthroline complex as the catalyst.[2] Nevertheless, the temperature was still moderately high and resulted in a low selectivity in the cyclization of some substrates. Here we report the results of a further optimization that permitted us to improve both selectivity and yield. The milder reaction temperature and a mixed CH_3CN/DMF solvent system allowed to get improved yield for several substrates including some for which previous conditions failed to afford the indole.



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Deep chemical characterisation of Al_2O_3 as catalytic support for gas exhaust abatement processes

Marina Franca[a,b], Andrea De Toni[c], Franz Dornhaus[c] and Silvia Gross[a,b]

[a] Department of Chemical Sciences, University of Padova, 35131, Italy; [b] INSTM Consortium, Firenze, 50121, Italy; [c] Umicore AG & Co KG, Hanau, 63457, Germany

In the field of automotive catalysts and supports for gas exhaust abatement, alumina, Al_2O_3, finds wide applicability as support for catalytically active nanoparticles. Al_2O_3 can be found in numerous crystallographic polymorphs, depending on structure and hydration degree.[1,2]
The most common ones among these are α-Al_2O_3 and γ-Al_2O_3, which can be employed as catalyst supports due to their features: enhanced catalytic activity thanks to the structure and high specific surface area (SSA) regarding γ-Al_2O_3, and thermodynamic stability concerning α-Al_2O_3.[2,3]
This work is developed within the framework of catalysis processes for the gas exhaust abatement, by adopting Al_2O_3 as catalyst support for precious group metal particles, to achieve the oxidation of several exhaust gases, such as NO, CO and hydrocarbons.[4]
Seven benchmark aluminas provided by different external suppliers were characterised with the aim of studying the main characteristics and differences that can be paramount for the catalytic process as catalyst supports. The powders were analysed through different analytical tools: XRD to determine the crystal structure, FT-IR and Raman Spectroscopies to define Al and O local environment, TEM in order to investigate the morphology, BET to determine the SSA, XPS for the evaluation of the surface composition and chemistry.
Eventually, with the aim of observing whether and to which extent Pt nanoparticles can affect alumina characteristics, Pt-Al_2O_3 samples were also studied adopting many of the above-mentioned techniques.

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Truffle farming and nanomaterials: a new technology for the optimization of the mycorrhization process and release of "helper" microorganisms

I. Fratoddi[a] , E. Bodo, [a] S. Cerra[a], T.A. Salamone[a], F. Hajareh. Haghighi,[a] M. Bovi[b], M. Bonaconza[b], E. Kuzminsky[c], C. Morales-Rodriguez[c], S. Pagliarani[c], A. Vannini[c]

[a]Department of Chemistry, Sapienza University of Rome, Piazzale Aldo Moro 5, 00185, Rome, Italy; [b]Nanomnia srl via di Mezzo 46, 37059 Zevio, Verona; [c]Department for Innovation in Biological, Agrifood and Forest Systems (DIBAF), Università Della Tuscia. Via S. Camillo de Lellis, Viterbo, 01100, Italy.

Truffle farming is synonymous with specialized plantations where the quality of the starting material, that is the plant with the mycorrhiza, determines its productivity and economic sustainability. The mycorrhizal phase still represents a crucial point in the process and the study of the rhizospheric microbiome in the process of mycorrhizal symbiosis through the action of 'helper' microorganisms is of crucial importance. The TANA project is part of this complex context, in which research groups from the University of Tuscia, Sapienza, in collaboration with the start-up Nanomnia, thanks to funding from LazioInnova regional funding agency for innovation of Regione Lazio, have proposed a new synergistic approach for the enhancement and optimization of truffle farming processes thanks to the combined use of nanotechnologies.

Indeed, numerous inorganic compounds, bacteria and viruses contribute to the complexity of the soil biota; among these, bacteria are the most abundant and many of them are classified as MHB (mycorrhiza helper bacteria) because they are able to stimulate the formation of mycorrhizal symbiosis and its vitality. In this context, nanomaterials can act as carriers for bioactive species and at the same time can be effective in stabilizing and protecting encapsulated molecules / microorganisms (fungi and bacteria), favoring their gradual release into the environment.

The study of inorganic nanoparticles and polymer / nanoparticle composites, to be used as carriers of microorganisms in the soil, has the main purpose of improving the development of the rhizosphere by providing a consistent source of fungi and bacteria capable of interacting with the root system and the microbiome of the soil. Polysaccharides are among the most stable and most efficient biomaterials to meet the needs that the encapsulation of microorganisms requires. Among these, alginate, a natural polymer extracted from brown algae, is the most used because it is non-toxic to humans and the environment, inexpensive and suitable for encapsulating living cells. It is therefore possible to prepare alginate beads with a controlled diameter and, with a simple methodology, also create formulations by encapsulating mycorrhizogenic fungi and MHB bacteria at the same time. Furthermore, it is possible to encapsulate inorganic nanoparticles (AgNPs) which at low doses show beneficial effects on the growth and development of the rhizosphere thanks to a slow controlled release.

The specific objective of TANA is therefore to develop a new biotechnological manufacturing product based on the use of nanotechnologies, functional to the truffle supply chain for *Tuber melanosporum* (precious black truffle) in the process phase that concerns the production of high quality mycorrhized plants, for productive plantations.

Bifunctional Pt(IV) prodrugs based on the histone deacetylase inhibitor 2-(2-propynyl)octanoate

Elisabetta Gabano,[a] Maria Grazia Bottone,[b] Angelica Facoetti,[c] Mauro Ravera[a]

[a] Dipartimento di Scienze e Innovazione Tecnologica, Università del Piemonte Orientale, Viale T. Michel 11, 15121 Alessandria, Italy; [b] Laboratorio di Biologia Cellulare e Neurobiologia, Dipartimento di Biologia e Biotecnologie "L. Spallanzani", Università di Pavia, Via Ferrata 9, 27100 Pavia, Italy; [c] Centro Nazionale di Adroterapia Oncologica (Fondazione CNAO), Str. Campeggi 53, 27100 Pavia, Italy

Bifunctional Pt(IV) prodrugs contain one biologically active ligand that is released, after reduction of the complexes, together with the corresponding cytotoxic Pt(II) species. The higher lipophilicity of this kind of Pt(IV) *combo* improves the accumulation and the potency of the conjugate with respect to its components used alone.

In this framework 2-(2-propynyl)octanoic acid, an inhibitor of histone deacetylase able to cause a decreased histone-DNA interaction allowing for chromatin relaxation and decondensation, was combined in racemic or in enantiomeric form with cisplatin [1-3] and [$PtCl_2$(cyclohexanediamine)] [4,5]. The resulting complexes were tested on various cancer cell lines proving to be much more active than their Pt(II) precursors, without significant differences among isomers. The good activity of the complexes is due to both their high cell uptake and the synergism between the released metabolites.

The cisplatin-based bifunctional complex **1** (Figure 1) was tested also in combination with carbon ion hadrontherapy on human glioblastoma, the most common cancer of the central nervous system. Complex **1** was able to induce cell death, through different pathways, at concentrations lower than cisplatin and with effects persistent in long-term treatments. This effect was further amplified when the treatment was followed by exposure to carbon ion radiation [6].

Finally, complex **1** caused a remarkable reduction of the tumor mass (94%) in a model of solid tumor (murine Lewis lung carcinoma), compared to the control, whereas cisplatin induced a tumor regression of 75%. A good accumulation of **1** was observed in the tumor mass without significant body weight loss [1].

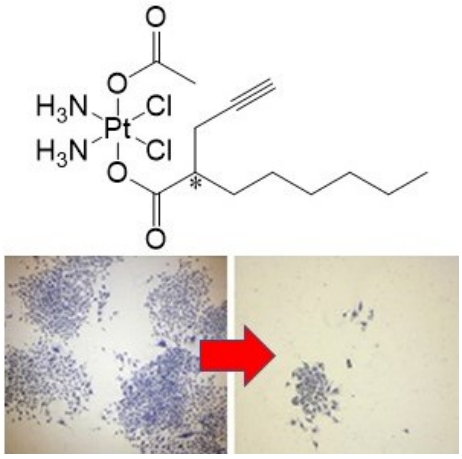

Figure 1. (*OC*-6-44)-acetatodiamminedichlorido (2-(2-propynyl)octanoato)platinum(IV), **1**, and treated glioblastoma cells.

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Deep chemical characterisation of Al_2O_3 as catalytic support for exhaust gas abatement processes

Marina Franca[a,b], Andrea De Toni[c], Franz Dornhaus[c] and Silvia Gross[a,b]

[a] *Department of Chemical Sciences, University of Padova, 35131, Italy;* [b] *INSTM Consortium, Firenze, 50121, Italy;* [c] *Umicore AG & Co KG, Hanau, 63457, Germany*

In the field of automotive catalysts and supports for exhaust gas abatement, alumina, Al_2O_3, finds wide applicability as support for catalytically active nanoparticles. Al_2O_3 can be found in numerous crystallographic polymorphs, depending on structure and hydration degree.[1,2]
The most common ones among these are α-Al_2O_3 and γ-Al_2O_3, which can be employed as catalyst supports due to their features: enhanced catalytic activity thanks to the structure and high specific surface area (SSA) regarding γ-Al_2O_3, and thermodynamic stability concerning α-Al_2O_3.[2,3]

This work is developed within the framework of catalysis processes for the exhaust gas abatement, by adopting Al_2O_3 as catalyst support for precious group metal particles, to achieve the oxidation of several exhaust gases, such as NO, CO and hydrocarbons.[4]
Seven benchmark aluminas provided by different external suppliers were characterised with the aim of studying the main characteristics and differences that can be paramount for the catalytic process as catalyst supports. The powders were analysed through different analytical tools: XRD to determine the crystal structure, FT-IR and Raman Spectroscopies to define Al and O local environment, TEM in order to investigate the morphology, BET to determine the SSA, XPS for the evaluation of the surface composition and chemistry.
Eventually, with the aim of observing whether and to which extent Pt nanoparticles can affect alumina characteristics, Pt-Al_2O_3 samples were also studied adopting many of the above-mentioned techniques.

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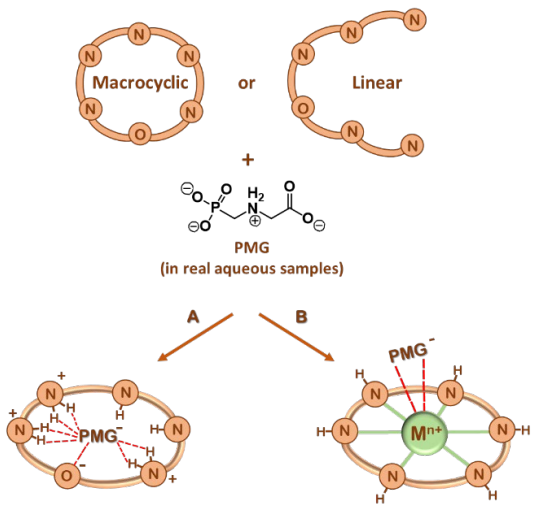
New molecular systems for the monitoring of environmental pollutants

Gina Elena Giacomazzo,[1] Luca Conti,[1] Claudia Giorgi,[1] Marco Pagliai,[1] Luca Giorgi,[2] Vieri Fusi,[2] Mauro Formica,[2] Luca Mancini,[2] Barbara Valtancoli [1]

[1] *Department of Chemistry 'Ugo Schiff,' Via della Lastruccia 3, 50019, Sesto Fiorentino, Italy.*

[2] *Department of Pure and Applied Sciences, University of Urbino "Carlo Bo", via della Stazione 4, 61029 Urbino, Italy*

Among the most important environmental pollutants, N-(phosphonomethyl)glycine (glyphosate or PMG) plays a central role due to his widespread use as broad spectrum herbicide worldwide.[1] However, despite the need for a massive monitoring program, sensors for the fast and cheap PMG determination direct in field are still rare. With this regard, various methods have been developed, based on liquid/gas chromatography (LC/GC), capillary electrophoresis (CE) and mass spectrometry (MS) analysis. However, because of the high polarity of such analyte, most of these methods requires derivatization procedures and thus the optimization of a high number of parameters.[2] Our approach is based on the use of a novel series of molecular receptors optimally designed for the specific recognition of PMG, as well as of its primary metabolite AMPA (Aminomethylphosphonic acid) in aqueous samples. Its non-symmetrical structure, together with the zwitterionic nature in a wide range of pH values, make difficult the design of appropriate receptors able to bind this substrate. Based on these considerations, we focused on macrocyclic and linear polyamines with a negatively charged fragment (phenol or bi-phenol). The polyamine frameworks in fact, improve not only the water solubility of these compounds, but also confers the capability to bind anions in aqueous solution via mainly electrostatic and hydrogen bond interactions. In addition, the presence of a deprotonated phenol spacer can strengthen the interaction of the potential receptors towards PMG and AMPA, providing additional charge-charge interactions with the guest ammonium function. The formation of supramolecular anion assemblies between the receptors and the targeted guests in aqueous medium was investigated through potentiometric measurements affording to obtain the logK values for the formation of the resulting adducts (route A, scheme 1). Analogues measurements were performed on metal-complexes of the correspondent ligands, exploiting the capacity of the coordinated metal center to strengthen the binding affinity towards the anionic guests (route B, scheme 1). Besides the potentiometric measurements, the fluorescent properties of the metal complexes were explored while DFT calculations aimed at achieving a better understanding of the interaction between receptors and the targeted species.



Scheme 1. *Formation of supramolecular anion assemblies*

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Solvent-based approaches for the fractionation of technical lignosulfonates

Matteo Gigli,[a,b] Paolo Guzzonato,[a] Claudia Crestini,[a,b]

[a]Department of Molecular Sciences and Nanosystems Ca'Foscari University of Venice, Via Torino 155, 30172 Mestre (VE)
[b]Italian Research Center for Colloids and Surface Science (CSGI), University of Florence, Via della Lastruccia 3, 50019 Sesto Fiorentino (FI)

Lignin is the most abundant aromatic biopolymer on Earth. Although it represents a highly valuable resource towards the synthesis of low molecular weight compounds and (nano)materials of interests for a wide range of applications, its intrinsic heterogeneity and variability, further enhanced by the harsh conditions employed during its extraction by pulp and paper and biorefinery industries, hamper its full valorization. With the aim of obtaining lignin structures with more homogeneous physicochemical characteristics, in the last years various fractionation strategies have been studied.[1] While Kraft and Organosolv lignins have been deeply investigated, and both solvent- and membrane-based methodologies have been optimized for these materials, the fractionation of lignosulfonates (LS) has been carried out almost exclusively by means of ultrafiltration membranes, because of the high water solubility of LS, which makes solvent-based approaches not very straightforward. However, the following drawbacks can be highlighted: I) high cost of the membranes, II) the separation into different cuts occurs on molecular weight basis rather than based on the different chemical functionalities of the lignin molecules.
In this framework, the present contribution is focused on the development of solvent-based protocols for the fractionation of LS. Specifically, both sequential solvent fractionation and fractional precipitation have been tested towards the extraction of homogeneous cuts from softwood and hardwood lignosulfonates. Operational conditions (e.g. nature and sequence of the solvents, lignin concentration, etc.) have been screened to maximize the yield and to guarantee the extraction of fractions with well-defined properties. The obtained fractions have been characterized in terms of molecular weight and polydispersity by gel permeation chromatography and chemical structure by NMR (^{31}P and HSQC) and elemental analysis. A clear relationship between the used solvent and the physicochemical characteristics of the cut, independently of the starting LS, has been evidenced. Thus, the results here presented open up new possibilities for the achievement of specific LS cuts to be successively transformed into high added-value specialties.

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New ruthenium(II)-tris(pyrazolyl)methane complexes

A. Gobbo[a], L. Biancalana[a], M. Guelfi[a], F. Marchetti[a], G. Pampaloni[a], S. Zacchini[b]

[a] Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via Moruzzi 13, 56124 Pisa (Italy)
[a] Dipartimento di Chimica Industriale "Toso Montanari", Università di Bologna, Viale Risorgimento 4, 40136 Bologna (Italy)

Ruthenium(II) complexes containing an arene ligand have aroused a huge interest for their applications in catalysis and in medicinal chemistry.[1] The replacement of the arene with the tridentate ligand tris(pyrazolyl)methane (tpm) is expected to increase the stability of the coordination compound; however, the chemistry of Ru(II)-tpm complexes has been sparingly explored heretofore, and the apparent complexity of the synthetic steps has limited the number of known compounds belonging to such family. [2]
Here, we present a facile synthetic route to access a series of new ruthenium(II)-tpm complexes from the easy available [RuCl(tpm)(PPh_3)$_2$]Cl. [3] The synthesis of this key precursor was first improved and optimized for gram-scale preparations. Selective mono-substitution of the labile PPh_3 ligand allowed the coordination of a variety of neutral ligands such as pyridines, phosphines/phosphites, nitriles and isocyanides within the Ru(II)-tpm scaffold in high yields. In addition, we focused our attention to the incorporation of small bioactive molecules in metal complex, in view of a potential biological applications. Facile esterification of 4-pyridinemethanol ligand allowed the introduction of organic moieties with known biological functions such as ethacrynic acid (a glutathione S-transferase inhibitor), chlorambucil (chemotherapy medication) and NSAIDs (cyclooxygenase inhibitors).
The new complexes were fully characterized by spectroscopic experiments and a number of structures were elucidated by single crystal X-ray diffraction. Most of them display an appreciable water solubility, of the order of 10^{-3} M. The stability of the new complexes in water, water/DMSO, and cell culture solutions was evaluated by NMR spectroscopy, revealing a substantial robustness except for reversible chloride/water substitution. The octanol/H_2O partition coefficients were assessed by UV-Vis spectroscopy. The evaluation of the catalytic and biological applications of the new complexes are in progress.

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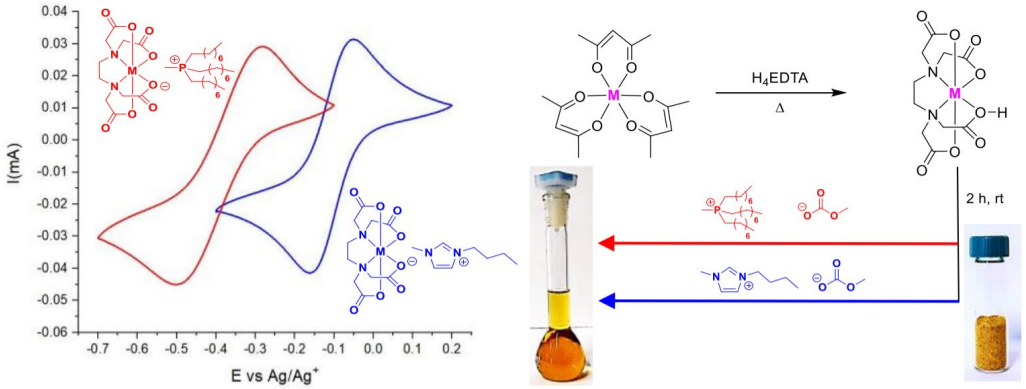
Novel ionic liquids based on trivalent metal–EDTA complexes

L. Guglielmero[a,b], A. Mero[b], A. Mezzetta[b], F. D'Andrea[b], C. S. Pomelli[b], L. Guazzelli[b]

[a] DESTEC, University of Pisa, Largo Lazzarino, 56122, Pisa, Italy; [b] Dept. of Pharmacy, University of Pisa, Via Bonanno 33, 56125, Pisa, Italy.

Ethylenediaminetetraacetic acid (EDTA) is a well-known, formidable chelating agent able to form water soluble metal complexes with di- and trivalent cations, making its use attractive in several large-scale applications. The chelation of redox active metal centers, reducing the electron transfer activation energy, appears a viable method to improve their electrochemical kinetic performances[1,2] and offers interesting perspectives from an electrochemical point of view and as innovative electrolytes for redox flow batteries.[3-5] In this context, a new simple and highly performing synthetic approach has been proposed and successfully tested for the preparation of two series of ionic liquids (ILs) consisting in metal-EDTA complex ([MEDTA]) anions and 1-butyl-3-methylimidazolium ([BMIM]) or trioctylmethylphosphonium ([TOMP]) cations. Due to the complementary solubility characteristics imparted by the [BMIM] and the [TOMP] cations, the electrochemical properties of the prepared ILs have been investigated in both aqueous and non-aqueous solvents, shedding light on the influence of solvent environments on metal-EDTA complexes redox behavior.



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XPS spectroscopy investigation of the surface of Ti-Cu and Ti-Cu-Ag thin films produced by PVD magnetron sputtering, showing biocompatibility and antibacterial properties

Giovanna Iucci[a], Saqib Rashid[b], Gian Marco Vita[a], Luca Persichetti[a], Rostislav Daniel[c], Daniela Visaggio[a], Martina Marsotto[a], Edoardo Bemporad[b], Paolo Ascenzi[a], Giovanni Capellini[a], Marco Sebastiani[b], Alessandra di Masi[a], Chiara Battocchio[a]

[a] *Università degli Studi Roma Tre, Engineering Department, via della Vasca Navale 79, 00146 Rome, Italy ;*
[b] *Università degli Studi Roma Tre, Department of Science, Viale Guglielmo Marconi, 446, 00146 Rome, Ital;y*
[c] *Department of Materials Science, Montanuniversität Leoben, Franz-Josef-Straße 18, Leoben, 8700, Austria*

One of the main goals of tissue engineering is the preparation of biomaterials showing good biocompatibility and antibacterial activity at the same time.
Multi-element thin films are a new class of nano-engineered materials showing an excellent combination between high strength and biocompatibility. In particular, Ti-based thin films can be produced by Physical Vapor Deposition (PVD), to obtain biocompatible films with improved surface hardness for applications in human implants. Additions of Au, Cu, Zn or Ag to Ti-based films can induce potential antibacterial behavior [1]; copper addition, for instance, is considered a promising solution for the preparation of biomedical materials, due to its antibacterial activity, related to the liberation of Cu^{+1} and Cu^{+2} ions [2, 3].
In this framework, Ti-Cu and Ti-Cu-Ag thin films were produced by physical vapor deposition magnetron sputtering (MS-PVD), with the aim of obtaining concurrent biocompatibility and antibacterial properties. The prepared films were characterized by X-ray diffraction (XRD), nanoindentation, atomic force microscopy (AFM) and X-ray photoelectron spectroscopy, to investigate their structural, mechanical and surface properties. By using surface chemical and morphological characterization, combined with cell growth studies and antibacterial testing, significant antibacterial properties combined with biocompatibility have been observed.
TiCu thin films shows complete amorphous structure, but addition of silver changes the film structure to partially crystalline at 20% Ag and completely crystalline at 30% Ag. XPS spectroscopy yielded information the chemical composition of the sample surface and the oxidation state of the elements. Titanium is completely oxidized to Ti (IV), copper partially oxidized to Cu (II) and partially in metallic state and for silver the unoxidized metallic component is predominant and oxidation takes place to a very limited extent. Finally, biocompatibility and antibacterial activity were investigated by biological assays.
In summary, the formation of mixed copper and titanium oxide on the surface of Ti-Cu and Ti-Cu-Ag thin films induces high biocompatibility and remarkable antibacterial properties.

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Kinetic and mechanistic studies of a de novo designed dicopper protein

Salvatore La Gatta[a], Marco Chino[a], Ornella Maglio[a,b], Flavia Nastri[a], Angela Lombardi[a]

[a]Departm. of Chemical Sciences, Univ. of Napoli Federico II, Via Cintia 21, Napoli 80126, Italy; [b]Inst. of Biostructures and Bioimages-National Res. Council, Via Mezzocannone 16, Napoli 80134, Italy

The type III copper center (T3Cu) plays a major role in biology, since it is able to bind and, eventually, activate molecular oxygen[1]. Over the years, bioinorganic chemists have tried to replicate the peculiar reactivity and spectroscopic features of T3Cu centers. Small mimetic complexes are able to host the Cu_2O_2 core, nevertheless they do not present catalytic activity in aqueous solution under mild condition[2]. In this exciting research environment, the Artificial Metallo-Enzymes Group (AMEG) has been developing the DR (Due Rame) class of artificial metalloproteins by a de novo design approach. ApoDR1 is a dimer that binds two copper ions and, as T3Cu proteins, adopts a four-helix bundle structure, bearing three histidine residues per monomer (Figure 1). Previous studies have demonstrated that DR1 catalyzes the oxidation of 3,5-di-*tert*-butylcatechol (DTBC) to the corresponding o-quinone, 3,5-di-*tert*-butyl-o-benzoquinone (DTBQ), cycling between copper(I) and copper(II) under mild conditions[3].

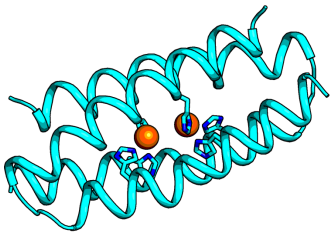

Figure 1. Cu(II)-DR1 designed model

Here we present a complete kinetic study of the DR1 catalyzed catechol oxidation, which allowed to determine the kinetic parameters (K_m and k_{cat}). Interestingly, the kinetic progress curves are characterized by two phases: (i) a fast burst phase, in which DTBC rapidly binds and reduce the DR1 di-cupric site; (ii) a slower conversion step, in which DTBQ is formed with very low efficiency. To get insights into the catalytic pathways for catechol oxidation by DR1, the progress curves were analyzed through different kinetic models. All models gave estimated rate constants, which suggested that the decrease in the conversion rate, after an initial burst phase (Figure 2, black arrow), was due to the rate-limiting re-oxidation step of the *deoxy*-DR1 di-cupreous center by molecular oxygen (Figure 2, red arrow), as proposed for other model compounds of Catechol Oxidases[4]. Similar analysis performed on the kinetic data for a less hydrophobic substrate, namely 4-*tert*-butylcatechol (4TBC), strongly supported the hypothesis that DR1 is also performing catalase activity (Figure 2, green arrow), consuming hydrogen peroxide. Such uncoupled reactivity may be responsible for the slow reoxidation of the *deoxy*-form.

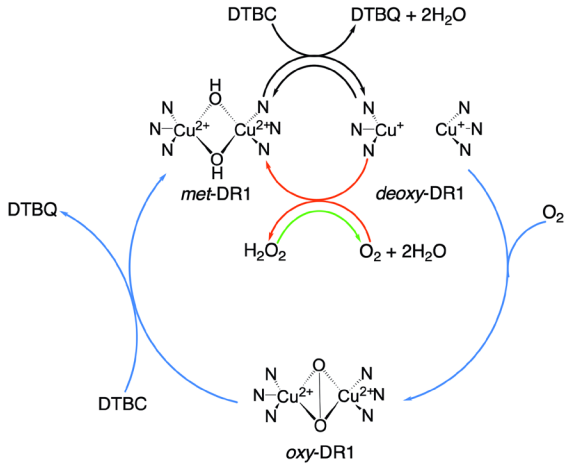

Figure 2. Hypothesized reaction mechanisms for catechol oxidation by DR1

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Solid state CW X-band EPR studies of silica radicals generate by milling of synthetic quartz

V. Lagostina [a], C. Bellomo [a], C. Pavan [a,b], M. C Paganini [a], and F. Turci [a,b]

[a] *Department of Chemistry, University of Turin, via P. Giuria 7, 10125, Torino*
[b] *"G. Scansetti" Interdepartmental Center, University of Turin, via P. Giuria 9, 10125, Torino*

Silica, in its crystalline or in amorphous form, is a popular material in many industrial productions and processes. Inhalation of crystalline silica particles, however, can induce inflammatory lung reactions that lead to silicosis and/or lung cancer. This brings the crystalline silica, in quartz or cristobalite form, to be classified in group 1 by the International Agency for Research on Cancer (IARC) as human lung carcinogen.[1] Quartz is industrially used always in the form of milled dusts (quartz flour) and IARC evaluation pointed out that freshly milled quartz dusts are more toxic than aged ones, suggesting peculiar reactivity and chemical evolution at the particle surface.
During milling, the fracturing of the crystals may generate the homolytic cleavage of ≡Si-O-Si≡ bonds with the formation of ≡SiO• and ≡Si• radicals, especially in inert atmosphere. These types of species, they reactivity and their chemical can be studied by using the EPR spectroscopy.[2]
This work aims to evaluate the formation and the evolution of bulk and surface radical species formed on quartz crystals subjected to different milling experiments and different aging environments.
Synthetic quartz crystals of micrometric size were milled for 1 h (three steps of 20 minutes) at 250 rpm in a ball mill with zirconia jar and 5 mm balls. To evaluates the effects of atmosphere during milling, the jar is closing into two different conditions: in argon (inside a glove box) or in air. Then, the fresh milling materials are transferred in an EPR cell and afterwards measured with an ADANI EPR spectrometer at room temperature. The milling argon-quartz sample is then studied in different conditions. Firstly, we considered the effect of thermal treatments, from 100 to 400 °C, in dynamic vacuum or with 100 mbar of oxygen to obtain information about the nature and chemical environment of the radicals. To discriminate among bulk and surface species and gain insight on their reactivity, we measured the EPR spectra in the presence of small molecules in gas phase, including H_2O and O_2. The EPR spectra were analyzed with EasySpin[3] (Matlab toolbox) to describe the *g*-tensors of the observed species according to experimental and theoretical data.

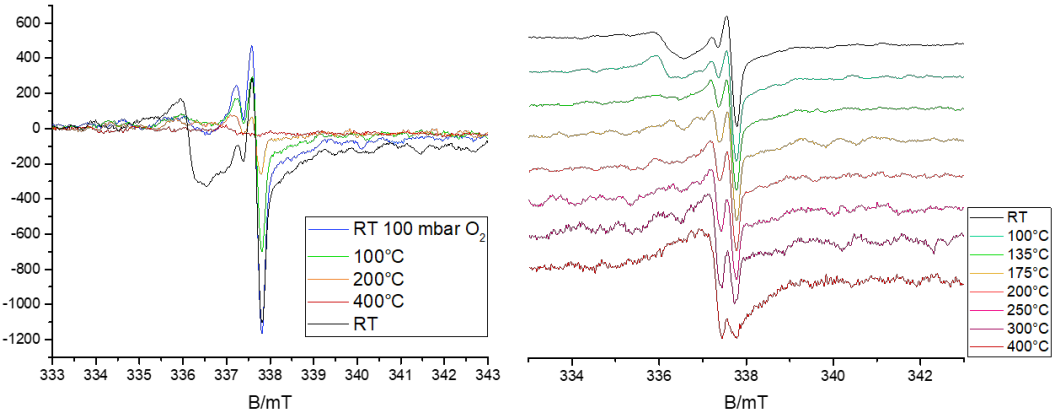

Figure 1: CW X-band EPR spectra of synthetic quartz milled in Ar during O_2 (left) and vacuum treatments (right)

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Synthesis and characterization of heterobimetallic Au(I)/M(IV) bridging hydrides (M=Mo,W)

Martina Landrini,[a] Rohan Patel,[b] David L. Hughes,[b] Leonardo Tensi,[a] Alceo Macchioni,[a] Luca Rocchigiani.[a,b]

[a] Department of Chemistry, Biology and Biotechnology, University of Perugia, Perugia, IT; [b] School of Chemistry, University of East Anglia, Norwich, UK.

Gold hydrides are postulated as important intermediates in many heterogeneous and homogeneous catalytic reactions, even though they have been considered as too unstable to be isolated for a long time.[1] The recent discoveries of the first stable Au(I) and Au(III) terminal hydrides paved the way for a better understanding of the properties of the Au–H bond and their reactivity is starting to be rationalized.[2] However, their synthesis remains challenging and very few ligand systems are compatible with this chemistry. Taking inspiration from seminal work by Stone and Venanzi,[3] some of us recently showed that bridging LAu(μ-H)$_2$WCp$_2$ complexes offer an interesting platform to study the interactions between a cationic gold centre and a hydride ligand, with enhanced thermal stability, ligand tolerance and potential for photochemical hydride transfer.[4]

In this contribution, we will show how different ligands and metal hydrides fragments, featuring variable donor/acceptor ability and steric demand, modulate the properties of the Au(μ-H)$_2$M core. In particular, we focused on the effect of steric bulk of N-heterocyclic carbene and phosphine ligands in determining the structure, stability and spectroscopic features of bimetallic gold-tungsten adducts [(L)Au(μ-H)$_2$WCp$_2$][SbF$_6$] (Figure 1a). We also explored the suitability of Cp$_2$MoH$_2$ as a hydride donor for gold(I) cations (Figure 1a), probing the role of electronegativity of the second metal in driving the hydride transfer to gold. NMR spectroscopy and X-ray diffraction (Figure 1b) are used to compare the heterobimetallic complexes and to provide a rationale that will help future developments in hydrogen transfer reactivity and, hopefully, catalytic application.

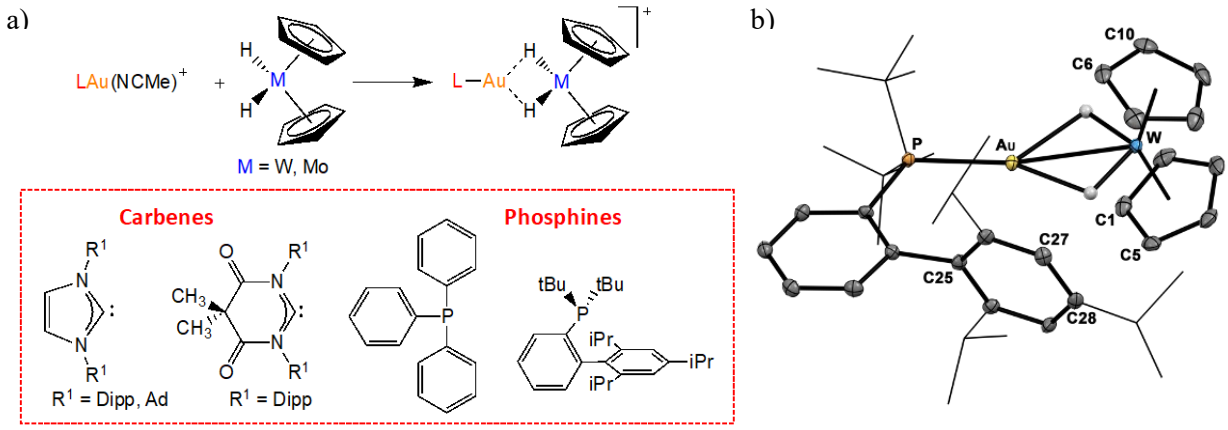

Figure 1. a) Bimetallic adducts synthesised,
b) X-Ray structure of [(^{t}BuXPhos)Au(μ-H)$_2$WCp$_2$]$^+$.

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Anticancer activity of a tris-phosphane gold compound

Lorenzo Luciani,[a] Rossana Galassi,[a] Alessia Cogo,[b] Maria Luisa Di Paolo,[c] Lisa Dalla Via[b]
[a]Scuola di Scienze e Tecnologie, Università degli studi di Camerino, Sezione Chimica, via Sant'Agostino, 1, 62032 Camerino, MC, Italia

[b] Dipartimento di Scienze del Farmaco, Università degli Studi di Padova, via F. Marzolo 5, 35131 Padova
[c] Dipartimento di Medicina Molecolare, Università degli Studi di Padova, viale G. Colombo 3, 35131 Padova

In the continuous effort to find new metal-based compounds alternative to platinum related anticancer drugs, 11th group metals phosphane compounds have been thoroughly taken in consideration. Copper is a bio essential metal [1] while gold and silver are not endogen metals and their anticancer activity is featured by a potent and wide antiproliferative action along with variable systemic toxicity and generally lower selectivity between healthy and cancer cells [2], [3]. Interestingly, some of us have found that some heteroleptic triphenylphosphine/azolate compounds with gold(I) as metal, are very active also *in vivo* in the treatment of Basal Like Breast Cancer, whose diagnosis is rather severe and still without an efficacious therapy [4]. From this study, it was highlighted that the presence of hydrophilic groups, such as COOH or OH, in the triarylphosphane ligands hampers the anticancer activity. With the aim to increase the polarity of the triarylphosphane ligand without affecting the activity, we considered the preparation of ester ligands starting from the 4-diphenylphosphane-benzoic acid; the resulting phosphanes are less sigma donators than the PPh_3, carrying to the synthesis of poly-phosphane M(I) compounds. Hence, homolog series of L_3MX type compounds (where M = Au and X = Cl, M= Cu and X = BF_4 and M = Ag and X = PF_6) were obtained with the 4-methoxy or 4-ethoxy-diphenylphosphane benzoate, L^{MeO} or L^{EtO}. The corresponding L_3MX compounds have been characterized by analytical and spectroscopic methods and their formation was associated to large $\Delta\delta$ recorded in the ^{31}P NMR spectra of the complex with respect the free ligand (30-35 ppm in $CDCl_3$). They exhibit rather good bench stability and some dynamic behavior in $CDCl_3$ solution, even though stability studies in cell culture media highlighted an acceptable trend upon time. The three complexes have been tested by an *in vitro* assay on human tumor cell lines, showing a significant antiproliferative effect. Interestingly, the ligand appeared ineffective in the same experimental conditions. In this contribution, the investigation on the intracellular targets and the possible mechanism of action of the L_3AuCl complex will be presented. A comparison with L_3AgPF_6 is attempted, to identify mechanistic similarities/differences in biological effects between the complexes.

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NMR investigation of octahedral post-metallocene Salan complexes

Anna Dall'Anese,[a,b] Dmitry Uborsky,[c,b] Christian Ehm,[d,b] Roberta Cipullo,[d,b] Cristiano Zuccaccia,[a,b] Alexander Z. Voskoboynikov,[c,b] Vincenzo Busico [d,b] Alceo Macchioni[a,b]

[a]Dipartimento di Chimica, Biologia e Biotecnologie, Via Elce di Sotto, 8, 06123 Perugia (PG), Italy [b]DPI, P.O. Box 902, 5600 AX Eindhoven, the Netherlands [c] Department of Chemistry, Lomonosov Moscow State University, 1/3 Leninskie Gory, 119991 Moscow, Russia [d]Dipartimento di Scienze Chimiche, Università di Napoli Federico II, Via Cintia, 80126 Napoli, Italy

Post-metallocene and, particularly, octahedral post-metallocene catalysts are rapidly gaining importance in olefin polymerization. Compared with metallocenes, they are easier to synthesize and exhibit superior performance at high temperature.[1] Differently from *ansa*-metallocenes, for which the stereorigidity imposed by the ligand framework allows for a close structural relationship with the parent precatalytic complexes,[2] post-metallocene precatalysts, upon activation, might form several isomers, some of which can also be dormant or even inactive; the ones that are active, can establish relatively fast equilibria, or undergo *in situ* ligand modification. All those phenomena make detailed NMR studies on the activation of octahedral post-metallocenes particularly challenging.[3]

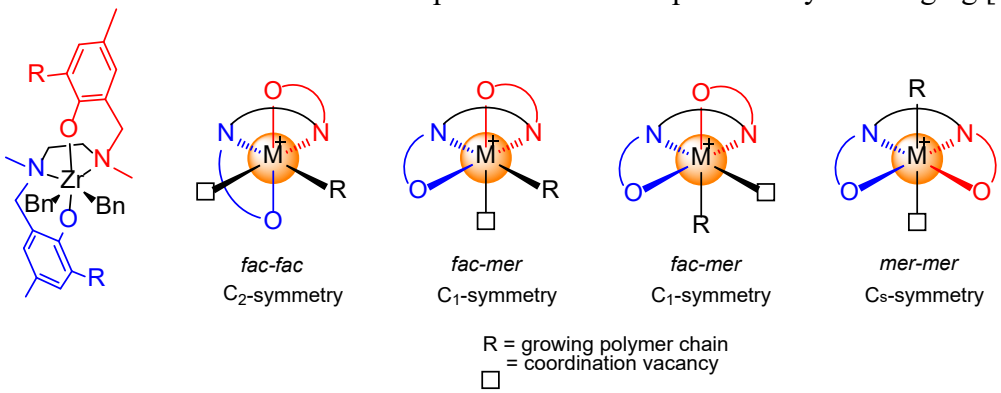

Figure 1. General [ONNO] Salan-type complex (left) and different isomers derived upon activation of octahedral post-metallocenes complexes bearing [ONNO] Salan-type ligands).

We hereby report a thorough NMR study on the activation, speciation and dynamics of octahedral post-metallocenes belonging to the class of the [ONNO]- or Salan complexes (Figure 1). The configuration adopted in solution by the active species was analysed by combining dynamic NMR data with other 1D and 2D NMR techniques and contrasted with that determined in the solid state by X-ray single-crystal diffraction experiments. Variable-temperatures ^{1}H,^{1}H EXSY and line shape NMR analysis, in particular, allowed the activation parameters of the ion pair symmetrisation process to be estimated. They evidenced the crucial role played by the nature of the substituent on the *ortho*-position of the phenoxy amine ring in determining the overall behaviour in solution of Salan complexes. Finally, some correlations were derived between the fluxionality of the complexes in solution and their activity in propene polymerization. All these findings, and more, will be discussed in the present contribution.

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Luminescent organometallic iridium complexes: synthesis of neutral and cationic derivatives and their application in electrochemiluminescence

*Mattia Manzotti[a], Marta Penconi[a], Clara Baldoli[a], Daniele Marinotto[a], Alessio Orbelli Biroli[a,b], Francesco Paolucci[c], Giovanni Valenti,[c] Antonino Licciardello[d], Alberto Bossi[a]**

[a] Istituto di Scienze e Tecnologie Chimiche "G. Natta", CNR-SCITEC, v. Fantoli 16/15, I-20138 Milano (Italy), and SmartMatLab Center, v. Golgi 19, II-20133 Milano (IT); [b] Dipartimento di Chimica, Università di Pavia, via Taramelli 12, 27100 Pavia, (IT); [c] Dipartimento di Chimica "Giacomo Ciamician", Università degli Studi di Bologna, Via Selmi 2, Bologna (IT); [d] Dipartimento di Scienze Chimiche, Università di Catania, V.le Andrea Doria, 6 - 95125 Catania, (IT)

The current developments of optoelectronics and bionanoscience take great advantage from the ability of organic, organometallic and hybrid compounds to fulfill specific needs and requirements. Phosphorescent transition-metal complexes, in particular octahedral iridium(III) ones, have been the target of intense researches given their high stability and excellent photophysical properties, such as high luminescence quantum efficiency and short radiative lifetime; in addition, they can be easily engineered in order to judiciously tune their optical absorption and emission colour, electronic energy levels, steric hindrance and solid-state packing.[1] Iridium complexes quickly became the emitters of choice in organic light-emitting diodes (OLEDs, the reference technology employed in energy-saving display), and they are now becoming successful emitters in many other technological fields. In particular, electrochemiluminescence (ECL) applications are looking at the use of these complexes as alternatives to the widely studied ruthenium(II)polypyridine complexes.[2,3]
In this contribution, we will present the synthesis of a family of cyclometalated heteroleptic Ir(III) complexes with emission centered in the blue, green and nearIR spectral regions (Figure 1). Their optical properties will be discussed in correlation to their neutral or cationic nature and preliminary ECL studies shown. In particular, the development of an efficient system for nearIR electrochemiluminescence can have a significant impact in the design of novel tools for bioimaging and clinical diagnostics.

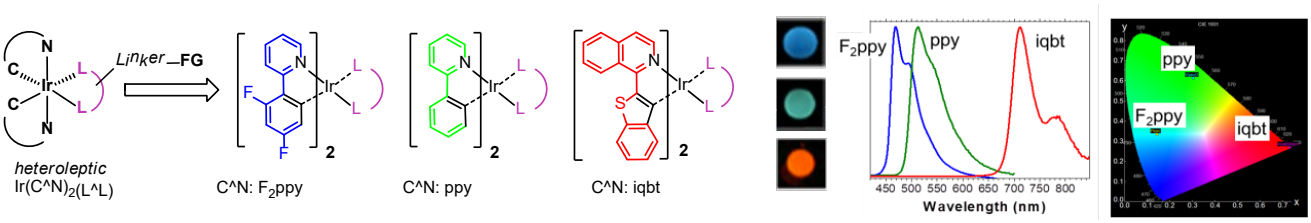

Figure 1. General structure of the studied heteroleptic Ir(III) complexes and their corresponding phosphorescence emission.

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Amino-pyrimidine curcumin derivative: metal ligand for theranostic applications

Matteo Mari,[a] Debora Carrozza,[a] Michele Iori,[b] Pier Cesare Capponi,[b] Sara Rubagotti,[b] Mattia Asti,[b] Erika Ferrari [a]

[a] Department of Chemical and Geological Sciences, University of Modena and Reggio Emilia, via G. Campi 103, 41125, Modena, Italy; [b] Radiopharmaceutical Chemistry Section, Nuclear Medicine Unit, Azienda USL-IRCCS Reggio Emilia, via Amendola 2, 42122, Reggio Emilia, Italy.

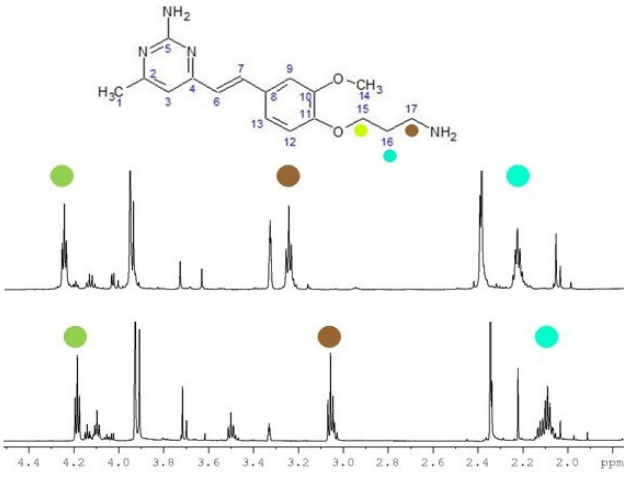

Figure 1. *^{1}H NMR spectra of: MPYC3NH2 in MeOD-d_4 (bottom) and K_2PtCl_4:MPYC3NH2 1:1 after 1 week in MeOD-d_4/D_2O (top) at 298 K @ 600 MHz.*

Curcumin is well known for its countless therapeutic properties, including antitumor, anti-inflammatory, and antimetastatic activities, as well as inhibitory of angiogenesis [1]. These features, together with its high affinity for colon-rectal cancer cells, makes it a feasible targeting vector for theranostic purposes [2]. On the other hand, curcumin issues are: low solubility in water, low rate of intestinal absorption and rapid degradation in physiological media. The latter could be attributed to the presence of the β-diketo moiety that make it a challenging compound to deal with.

Platinum complexes, cisplatin and oxaliplatin above all, are nowadays widespread and well-known therapeutics for the treatment of several cancers, mainly prostate, ovarian and colorectal [3]. On the other hand, copper isotopes, are used for both diagnosis and therapy in nuclear medicine applications [4].

Developing ligands for copper(II) and platinum(II) based on a curcumin structure with improved water solubility and stability may lead to theranostic compounds that benefit of either the metal properties and the antiproliferative activity of curcumin as well. To accomplish this purpose, the new compound MPYC3NH2 (**Figure 1**) was synthesized. In this new derivative, the β-diketo moiety was replaced with an amino-pyrimidine ring and the phenolic group was functionalized with an amino-alkyl chain. This terminal amine is meant to act both as coordinating agent and as reactive group for further structural modifications. The molecular weight below the cut-off value of 500 Da in combination with the presence of polar groups may account for sufficient water solubility and cellular uptake. A complete $^1H/^{13}C$ NMR characterization with both 1D and 2D techniques was carried out, as well as the acid-base behaviour by spectrophotometric techniques. UV-vis data allowed to evaluated protonation stability constants. UV-vis complexation studies were performed with Cu^{2+} while the complexation with Pt^{2+} was investigated by ^1H and ^{195}Pt NMR. As shown in **Figure 1**, proton spectra point out downfield shifts of signals belonging to the amino-alkyl chain. This outcome indicates the formation with slow kinetics of a metal-complex species. In particular, the ^1H-NMR most affected signal is the one belonging to the -CH_2 directly bound to the amine group, while the shift affecting the -CH_2 protons in β and γ positions is less evident.

Concluding, these preliminary results are encouraging and suggest that these studies may lead to a new class of compounds although further biological studies need to be carried out.

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Optimization of a green synthesis of zinc oxide nanoparticles exploiting an algae-mediated biogenic approach

Chiara Mazzariol[a], Susanna Tinello[a,b], Carlo Pilotto[a,b], Francesca Gambaro[b], Tomas Morosinotto[b] and Silvia Gross[a]

[a] Department of Chemical Sciences, University of Padova, 35131, Italy; [b] Department of Biology, University of Padova, 35131, Italy

Nowadays the optimization of synthetic pathways compliant with the principles of Green Chemistry for obtaining inorganic nanomaterials with relevant functional properties is a very important challenge. Indeed, common objectives in the development of such synthetic strategies are the exploitation of sustainable procedures, based upon low amount of toxic or hazardous chemicals, environmentally friendly solvents (water), low temperature and pressure of processes, low energy consumption. For the synthesis of inorganic nanomaterials, biology provides exciting opportunities and solutions. A synthetic approach supported by the exploitation of the possibilities offered by nature is more cost-effective and environmentally friendly when compared to classical chemical and physical synthetic routes. Actually, enzymes, microorganisms and plants extracts can be used as green scaffolds, in particular as reductants and stabilizers [1], to promote the formation of various inorganic metallic and binary nanoparticles [2,3].

Within this framework, the current work focuses on a one-pot approach for the green production of zinc oxide ZnO nanoparticles using microalgae and microalgae's extract. Microalgae are microorganisms of choice in biotechnology thanks to their wide range of potential bio-applications responding to an economic, circular and eco-sustainable perspective [4]. On the other hand, zinc oxide ZnO nanoparticles have attracted significant attention in recent years due to their wide range of applications, such as in electronics, optics and biomedical systems [3]. Nanoparticles synthesized from microalgae in aqueous solution are characterized through different analytical tools: XRD to determine the crystalline phase; TEM and SEM to define the size, size distribution and morphology. Particular attention has been paid on the evaluation of the microalgae extract's role in the synthesis of ZnO, starting from different zinc salts precursors and different species of microalgae. First results show that the temperature and the concentration of microalgae employed in the synthetic procedures are key factors for determining the size of the zinc oxide nanoparticles.

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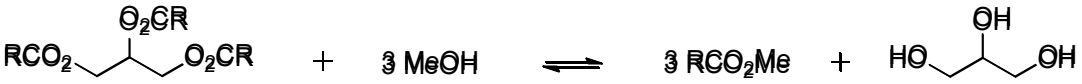
Homogeneous salen Fe(III) catalysts for biodiesel synthesis

Massimo Melchiorre [a], Angela Amoresano [b], Roberto Esposito [b, c], Gabriella Pinto [b], Maria E. Cucciolito [b, c] and Francesco Ruffo [b, c]*

[a] *ISusChem S.r.l., Piazza Carità, 32, 80134, Napoli, Italy;* [b] *Dipartimento di Scienze Chimiche, Università degli Studi di Napoli Federico II, Complesso Universitario di Monte S. Angelo, via Cintia 21, 80126 Napoli, Italy;* [c] *Consorzio Interuniversitario di Reattività Chimica e Catalisi (CIRCC), via Celso Ulpiani 27, 70126 Bari, Italy.*

Global warming and depletion of fossil resources have highlighted the weakness of the linear economy, favoring the development of the circular economy. [1] In this framework, biofuels production is a key point with a high industrial potential: EU biodiesel manufacture (Scheme 1) was estimated 21 million tons in 2017. [2]



Scheme 1 *– Biodiesel synthesis*

Waste oils are feedstock of choice, but these substrates often have high free acidity, water and many other pollutants that can deactivate the catalytic species used in the process. Therefore, one of the most challenging issues is the design of robust catalysts able to resist to the large variety of ingredients present in the oily matrix of waste vegetable oils. [3]
Recently, our research group came across monomeric and μ-oxo dimeric salen Fe(III) complexes as catalysts for the esterification and transesterification of levulinic acid and methyl levulinate. [4] Here we report the study of a panel of this class of Fe(III) catalysts (Figure 1) to promote biodiesel production, along with the optimization of the reaction conditions (temperature, molar ratio MR, time, catalyst, catalyst loading).

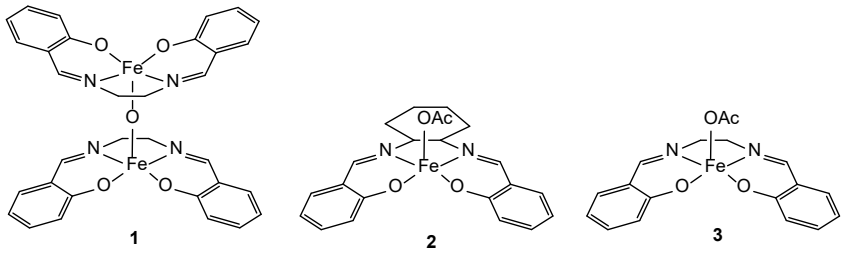


Figure 1 *– catalysts panel*

Proven the efficacy with fresh vegetable oil feedstock, the catalytic system has also been successfully validated with acid vegetable oils (up to AV 2.8 mg_{KOH}/g_{oil}) achieving 95% yield in optimized condition (2h at 180°C, cat. **3** 0.1% mol, methanol/oil 20/1), which paves the way to the use of these catalysts with real waste oil feedstock.
Further details will be given in the poster.

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Selenophene-based mixed-linker metal-organic frameworks: synthesis, characterization and luminescent properties

Giorgio Mercuri [a,c], Patrizio Campitelli [b], Corrado Di Nicola [b], Giuliano Giambastiani [c], Andrea Rossin [c], Andrea Fermi [d], Giacomo Bergamini [d], Marco Moroni [e], Simona Galli [e]

[a] *School of Pharmacy and* [b]*School of Science and Technology, University of Camerino, Via S. Agostino 1, 62032 Camerino;*
[c] *Consiglio Nazionale delle Ricerche - Istituto di Chimica dei Composti Organometallici (CNR-ICCOM), via Madonna del Piano 10, 50019, Sesto Fiorentino (Firenze);*
[d] *Dipartimento di Chimica "G. Ciamician", Università di Bologna, 40126 Bologna, Italy;*
[e] *Dipartimento di Scienza e Alta Tecnologia, Università dell'Insubria, 22100 Como, Italy.*

Metal-Organic Frameworks (MOFs) are a class of nanoporous materials that in recent years have gained great attention for their widespread application in several fields of materials science (catalysis, luminescence, gas storage and separation). MOFs have an extraordinary versatility in their design achieved through a tailored combination of organic linkers and inorganic nodes. This characteristic gives to MOFs unique advantages, including control of their pore size, high specific surface areas [1] and the possibility to include suitable functional groups on their linkers' skeleton [2]. In this work, we describe the synthesis and full characterization of the bicyclic ditopic linker 2,2'-biselenophene-5,5'-dicarboxylic acid (H_2SpSp) specifically designed for MOFs construction. Afterwards, the corresponding zirconium MOF $[Zr_6O_4(OH)_4(SpSp)_{3.8}Cl_{4.4}]$ (**1**) has been prepared and the crystallographic analysis has revealed that it is isostructural with its bitiophene and bithiazole analogues. Therefore, three new mixed-linker MOFs containing biselenophene (H_2SpSp), bithiophene (H_2ThTh) and bithiazole (H_2TzTz) linkers have been synthesized, in detail the two double-mixed $[Zr_6O_4(OH)_4(SpSp)_{2.6}(ThTh)_{1.3}Cl_{4.2}]$ (**2**) and $[Zr_6O_4(OH)_4(SpSp)_2(TzTz)_{1.8}Cl_{4.4}]$ (**3**), as well as the triple-mixed $[Zr_6O_4(OH)_4(SpSp)_{1.6}(ThTh)_{1.2}(TzTz)_{1.4}Cl_{3.6}]$ (**4**). Compounds **1**-**4** have been tested for luminescent applications, emitting at wavelengths falling in the blue-green visible region under UV irradiation [3].

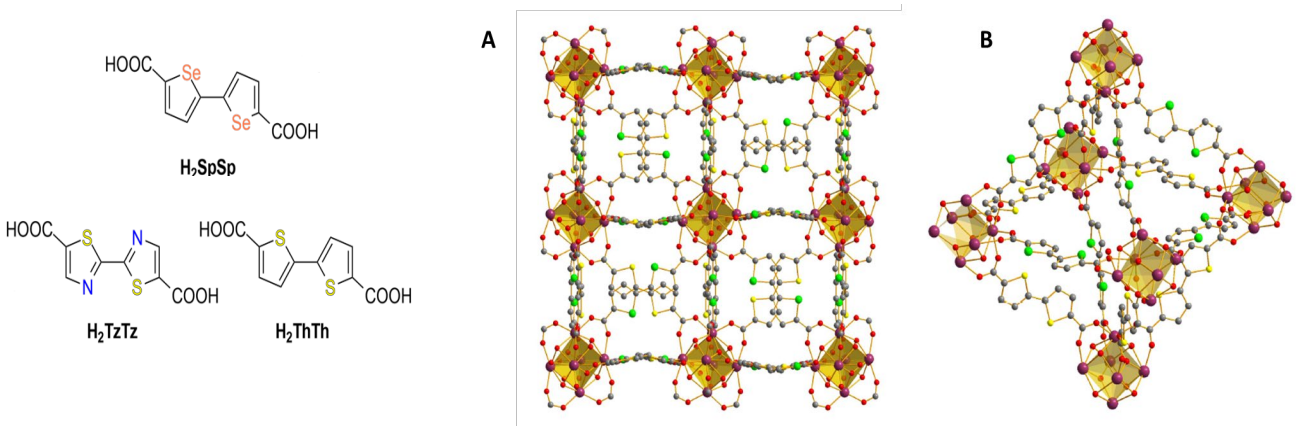

Figure 1*: the structure of the three ligands (left). Representation of the crystal structure of* ***4S*** *(right): (A) portion of the crystal structure viewed along the [001] crystallographic direction; (B) the octahedral cage.*

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The strong role of imidazolium salt on the catalytic performance of a ruthenium based anionic pre-catalyst for the Guerbet reaction

Alessandro Messori,[a] Nicola Monti,[a] Anna Gagliardi,[a] Cristiana Cesari,[a] and Rita Mazzoni[a]

[a] *Department of Industrial Chemistry "Toso Montanari", viale Risorgimento, 4, 40136, Bologna IT*

Biofuels represent a promising route to reduce our dependence on fossil fuels. Bio-ethanol is a bio-derived platform chemical that can be transformed into butanol and higher alcohols: species with higher energy density and better capability of being mixed with conventional fuel. Among the others, Guerbet reaction represents an appealing pathway for bio-ethanol refinery [1] especially when it is derived from waste or second generation (non-food) biomass.
Our group recently demonstrate **3a** (Figure 1) as an efficient pre-catalyst for the Guerbet reaction.[2] Here we report on the synthesis of a small library of similar complexes **3b-d** bearing imidazolium or ammonium cations (Figure 1) in order to rationalize the role of the countercation in Guerbet catalysts of type **3**.

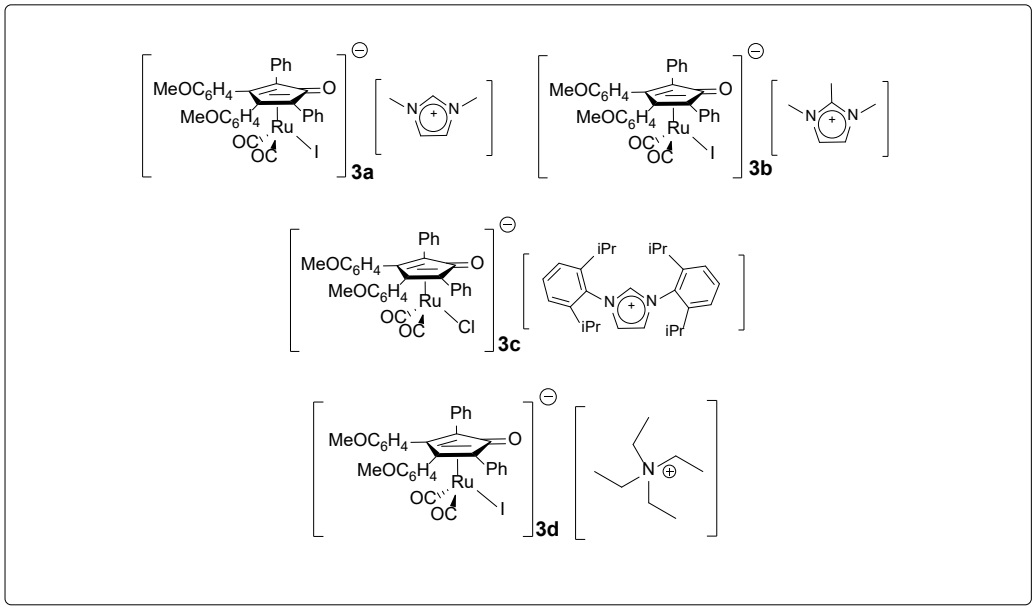

Figure 1 *Pre-catalysts* ***3a-d*** *employed in this work*

The catalytic screening revealed that conversion, alcohols selectivity and carbon loss are highly dependent on the counterion, demonstrating a detrimental effect of NCN substituents for imidazolium salts in complexes **3b** and **3c**, negative effect is also pronounced while employing tetraethylammonium **3d** or Na^+ as the counterions. Results from the screening and designed reactivity will be discussed in correlation with steric encumbrance, acidity and hydrogen bonding which may affect the complex behavior in the mixture employed for the reaction: EtOH, EtO^-, high temperature (150 °C) and products from side reactions.

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Zinc single sites anchored on silica as curing activators for rubber

Paola Milana[a], Silvia Mostoni[a], Antonio Susanna[b], Massimiliano D'Arienzo[a], Barbara Di Credico[a], Roberto Scotti[a]

[a]Department of Materials Science, INSTM, University of Milano-Bicocca, Via R. Cozzi, 55, 20125 Milano, Italy
[b]Pirelli Tyre SpA, Viale Sarca 222, 20126 Milano, Italy

Rubber materials are nowadays used for many applications, ranging from shoes, adhesives, and gloves. Since most rubber is used to produce tires, both sulfur vulcanization and reinforcing fillers such as silica nanoparticles (SiO_2 NPs) are used to obtain highly performant tires. To enhance the rate of the curing process, activators (ZnO), accelerators (sulfenamides) and co-activators (fatty acids) are usually used. [1] Although the mechanism is not completely understood, it has been recognized that ZnO plays a key role, because it promotes the formation of Zn (II)- sulfurating complexes during the first steps of the reaction, determining both the kinetic and the nature of the cross-linked products. However, the low affinity of ZnO towards the rubber entails its high consumption to achieve a good distribution in the matrix, leading to a non-negligible environmental impact [2].

By considering the main role of zinc in the vulcanization mechanism, the aim of this work is to substitute ZnO with a novel curing activator based on Zn (II) single sites, directly anchored on filler surface with the goal to increase the zinc availability and reactivity towards the polymer chains, thus reducing its amount in rubber materials. Zn (II) ions were anchored on the surface of SiO_2 NPs, through the coordination with different functional groups, to obtain double function fillers acting both as curing activator and reinforcing agents. Therefore, (3-aminopropyl) triethoxysilane, (3-Mercaptopropyl) trimethoxysilane, (N-[3-(Trimethoxysilyl) propyl] ethylenediamine) and a carboxyl-based silane, obtained by a ring opening reaction between succinic anhydride and (3-aminopropyl) triethoxysilane, were chosen as functionalizing reactants to link, respectively, amino, thiol, etilendiamine and carboxyl ligands on the silica surface. The synthetic procedure includes the functionalization of silica particles by hydrolysis and condensation of the silane-grafting agents, followed by the reaction with a Zn (II) precursor. The functionalization of silica NPs was confirmed by many characterization techniques, among which Infrared Spectroscopy (FTIR) and Thermogravimetric Analysis (TGA), showing the formation of isolated zinc centers. The curing activators were used to vulcanize (170°C, 5 minutes) silica/isoprene nanocomposites (IR NCs), without using micro-crystalline ZnO. Comparing the results, amino ligand has the highest efficiency, providing the best curing efficiency and kinetic. Regarding both etilendiamine and carboxyl groups, a good vulcanization efficiency was observed, combined with a slower kinetic with a delay in the first step of reaction, probably due to their chelating nature. Finally, the thiol group showed the worst activity because it strongly bonds Zn (II) ions. In fact, the different curing activity and mechanical behavior of the final composites are correlated to the different stability of the Zn (II)-ligand complex, with a decrease of the kinetic efficiency as the complex stability increases. When Zn (II) ions are more strongly bonded to the ligand, their reactivity towards curative reactants and sulfur is hindered. Zn (II) single sites anchored on silica are very efficient activators of the vulcanization process, with the ability to modulate their reactivity by tuning the chemical nature of the zinc complex, strictly dependent on the type of ligand. These results are promising for an industrial application in rubber vulcanization, as possible alternative to the conventional use of ZnO.

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Ethylene/methyl acrylate copolymerization: effect of palladium catalyst on methyl acrylate enchainment

Barbara Milani,[a] Chiara Alberoni,[a] Gabriele Balducci,[a] Maurizio Polentarutti[b]

[a] Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Trieste, Via Licio Giorgieri 1, 34127 Trieste, Italy; [b]Elettra Sincrotrone, Trieste

The synthesis of functionalized polyolefins through the direct, controlled, homogeneously catalyzed copolymerization of ethylene with polar vinyl monomers is a highly challenging reaction, recognized as the "polar monomer problem".[1] The ideal catalyst, in addition to show a high productivity, has to be able to control the key parameters of the produced macromolecules, like molecular weight and molecular weight distribution, amount of polar monomer incorporated and way of incorporation. With respect to the latter parameter, in the ethylene/methyl acrylate (MA) copolymerization catalyzed by Pd(II) complexes two ways of MA incorporation have been found depending on the ancillary ligand: either at the end of the branches of the macromolecules, when α-diimines are used,[2] or into the main chain, when phosphino-sulfonate derivatives are present.[3]
We have now investigated two series of Pd(II) complexes, [Pd(Me)(MeDAB)(L)][PF_6] and [Pd(Me)(iPrDAB)(L)][PF_6], featuring as α-diimine the bis(aryl)-1,4-diazabutadienediimine with aryl rings 2,6-disubstituted with methyl (MeDAB) or iso-propyl (iPrDAB) groups and having a monodentate ligand L belonging to the family of pyridines (Figure left).

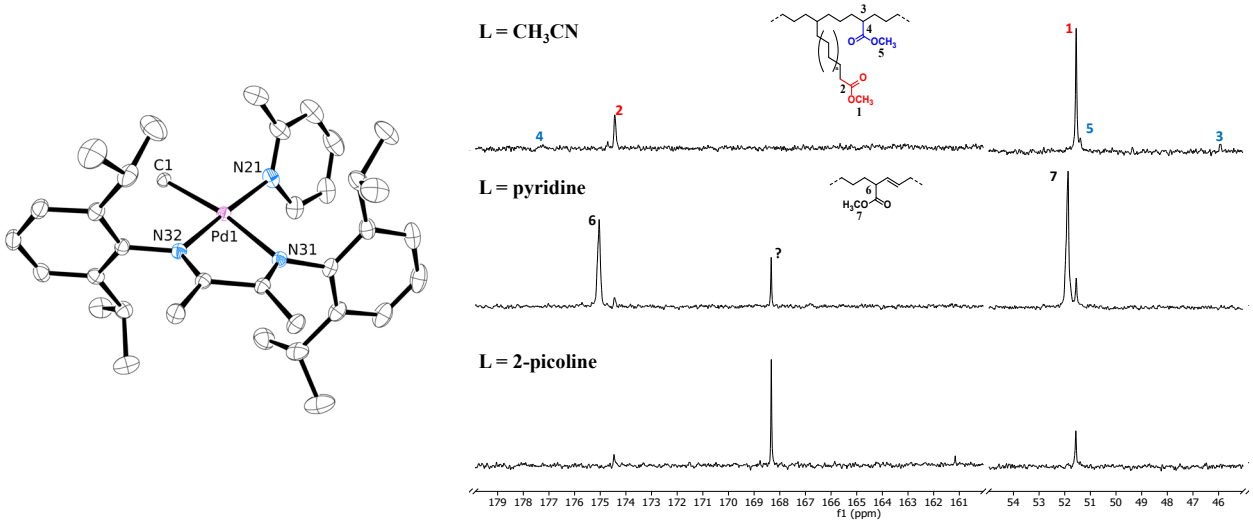

Figure. left: ORTEP drawing of [Pd(Me)(iPrDAB)(2pic)]$^+$; right: ^{13}C-NMR spectra of ethylene/MA copolymers synthesized with [Pd(Me)(iPrDAB)(L)][PF_6], region of carbonyl and methinic signals.

These complexes were tested as catalysts in the ethylene/MA copolymerization and, despite the expected inhibiting effect of the L ligand on productivity with respect to that of the parent compound where L is the labile CH_3CN, we found, for the first time, a remarkable effect of L on the way of enchainment of the polar monomer (Figure right). This effect suggests that, during the catalytic process, L remains close to the palladium center affecting the propagation step of the copolymerization reaction.

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Complexes of lanthanide ions (Yb^{3+} and Nd^{3+}) embedded in poly(lactic-co-glycolic acid) (PLGA) nanoparticles as bioprobes emitting in the Near Infrared Spectral Range

S. Mizzoni,[a] C. Nardon,[a] S.C. Gaglio, M. Perduca, [a] E. Cavalli[b] and F. Piccinelli[a]
[a]Laboratorio dei materiali luminescenti, Univ. Verona, Verona, Strada Le Grazie 15, 37134 Verona, Italy
[b]Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Univ. Parma, Parco Area delle Scienze, 11/a - 43124 Parma, Italy
e-mail: silvia.mizzoni@univr.it

Whereas photosensitization of visible emission from Eu^{3+} and Tb^{3+} in complexes containing chromophoric ligands is a wellestablished phenomenon with a large number of current applications,[1] analogous emission from Yb^{3+} and Nd^{3+} in the near-infrared remains relatively unexplored. More recently, considerable interest in near-IR luminescence from ytterbium(III), neodymium(III), erbium(III), and praeseodymium(III) has emerged, as the detection of photons in this spectral region has become increasingly efficient.[2]
Although the luminescence lifetimes from neodymium(III), ytterbium(III), etc. are shorter than their europium(III) and terbium(III) analogues, this should still permit time-gating techniques to be applied, while also providing greater tissue penetration and image resolution in the fluorescence microscopy of biological systems[3].
In the present contribution, we synthesized and investigated the spectroscopic properties of the complexes [(Ln(**L**$_1$)(tta)]; Ln= Yb^{3+}, Nd^{3+} **L**$_1$=2,2'-N,N'-((1R,2R/1S,2S)-(cyclohexane-1,2-diylbis(azaneylylidene))bis(methaneylylidene))bis(quinolin-8-ol); tta =2-thenoyltrifluoroacetyl-acetonate] and [(Ln(**L**$_2$)(tta)2] complexes where **L**$_2$=(N,N′-bis(2-pyridylmethylidene)-1,2-(R,R + S,S)-cyclohexanediamine) (**Figure 1**).
Subsequently, these complexes were embedded in Poly(lactic-co-glycolic acid) (PLGA) matrix by using a composition Poly(lactic(75%)-co-glycolic acid(25%), briefly PLGA 75:25, giving nanoparticles characterized by a monodispersed distribution of the size (diameter around 40-50 nm). The results of this study and some preliminary evidence reveal that these new complexes are promising candidates for bio-imaging applications.

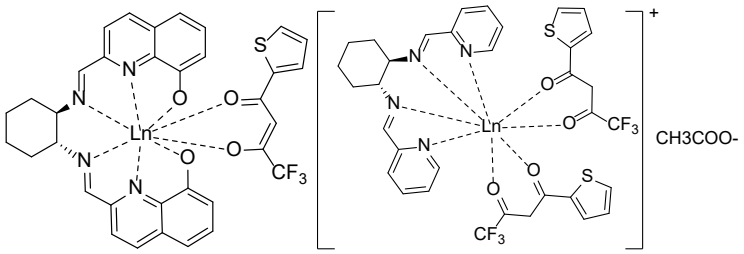

Figure 1: Ln(**L1**)(tta), Ln = Yb and Nd (left) and [Ln(**L2**)(tta)$_2$]CH_3COO (right) complexes depicted in the (R,R) stereochemistry of the chiral ligands. The (S,S) enantiomer has been also investigated.

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Au-decorated Ce-Ti mixed oxides for efficient photo-assisted CO preferential oxidation

Elisa Moretti [a], Mojtaba Gilzad Kohan [b], Alberto Vomiero [a,b], Antonia Infantes Molina [c]*

[a] *Department of Molecular Sciences and Nanosystems, Ca'Foscari University of Venice, Via Torino 155/B, 30172 Mestre Venice, Italy.*
[b] *Division of Materials Science, Department of Engineering Sciences and Mathematics, Luleå University of Technology, 97187 Luleå, Sweden.*
[c] *Department of Inorganic Chemistry, Crystallography and Mineralogy, University of Málaga, Campus de Teatinos, E 29071 Málaga, Spain.*

The investigation of CeO_2-based materials is a research hotspot for environmental and energy-related applications[1-3]. Tuning the morphological features of a catalyst has emerged as an important strategy to improve catalytic activity and there has been extensive research to develop highly active ceria-based systems rationally designed with a controlled morphology at the nano/microscale.
The present work aims to investigate the photocatalytic behavior of Au nanoparticles supported on CeO_2-TiO_2 nanostructured matrices in the CO preferential oxidation in H_2-rich stream (photo CO-PROX), assessing not only the role of each component in the system and on the catalytic response, but also how a peculiar morphology can affect the photocatalysis. CeO_2 samples containing different TiO2 loadings (0-20 wt%) were synthesized by a surfactant-free and environmentally friendly slow co-precipitation method. Au NPs (< 1.0 wt% loading) were deposited on the surface of the CeO_2-TiO_2 mixed oxides by deposition-precipitation. Crystalline structure, morphological, textural, and optical properties were investigated by several techniques. As shown by SEM and HR-TEM measurements, the samples appeared organized in a hierarchical needle-like structure, with homogenously distributed Au NPs decorating the Ce-Ti mixed oxides. The Au/CeO_2-TiO_2 systems showed a morphology dependent behavior in the photo CO-PROX under simulated solar light irradiation at r.t. and P_{atm}, resulting much more active than a benchmark sample with a non-organized structure. A clear morphology-functionality correlation was found, with CO conversion maximized for a TiO_2 content equal to 15 wt%. These results may represent a significant advancement toward the development of an effective strategy for exploitation of hydrogen as a viable clean fuel in stationary, automotive and portable power generators.

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Synthesis of sulfur-containing polymers: copolymerization of carbon disulfide with epoxides by [OSSO]-type catalysts

Fatemeh Niknam, Carmine Capacchione

Department of Chemistry and Biology "Adolfo Zambelli", University of Salerno, Via Giovanni Paolo II, 84084 Fisciano, SA, Italy

Polymers containing sulfur atoms have attracted great attention because of their interesting features, such as optical, electrical properties, and resistance to heat, chemicals, and radiation.[1] Carbon disulfide (CS_2), a sulfur analogue of CO_2, is a sustainable and low-cost monomer that has long been used as a sulfur source in organic chemistry. The carbon of CS_2 is more electrophilic than that of CO_2 because of the weaker π donor-ability of the sulfide atom.[2] However, up to now, the polymerization of CS_2 with other monomers such as epoxides is rarely reported.[3, 4] Oxygen/sulfur scrambling for both the polymeric products and the cyclic by-products, is a notable feature of the copolymerization reaction of CS_2 with epoxides, producing different valuable products.[5] In this contribution, effective catalytic systems based on bis-thioether-diphenolate [OSSO]-type Cr and Fe complexes are described in the coupling reaction of CS_2 with Propylene oxide (PO), Cyclohexene oxide (CHO), and 1-Hexene oxide (HO). According to O/S scrambling, different polymeric and cyclic products were observed and fully characterized by ^{1}H NMR and ^{13}C NMR spectroscopy. The schematic of [OSSO]-type complexes and some of the products with the reaction conditions are shown in Figure 1.

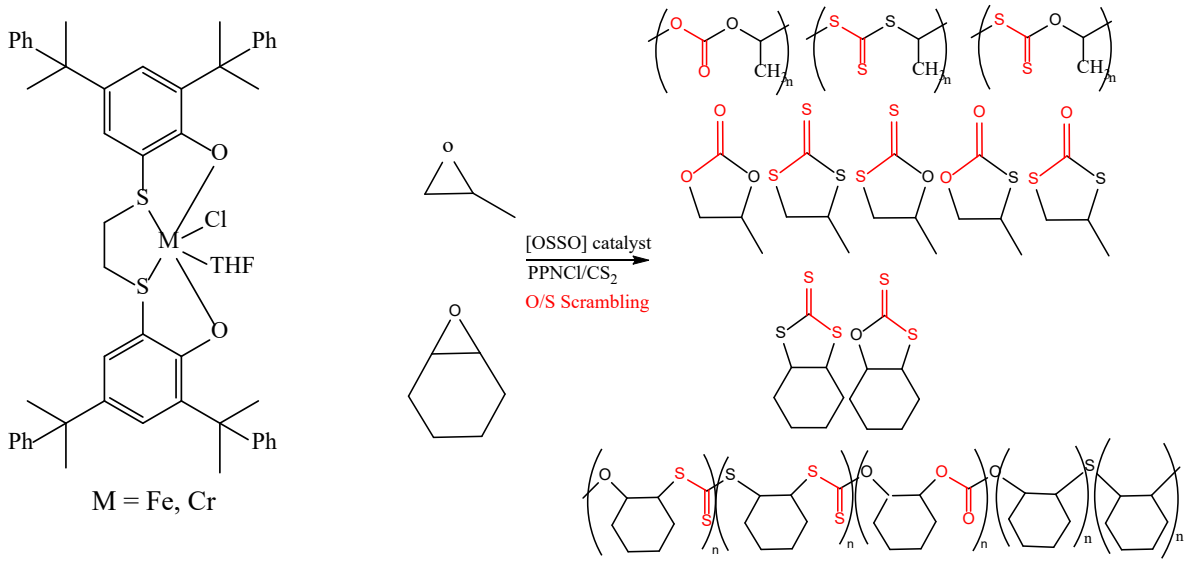

Figure 1: Left: The [OSSO]-type complexes. Right: The Reaction conditions for CS_2/Epoxide couplings: time = 24 h, catalyst = 0.1 mol%, CS_2/Epoxide ratio = 2, Co-cat/cat ratio = 0.5, 1, and 2 mol%, and Co-cat = PPNCl (bis(triphenylphosphine)iminium chloride)

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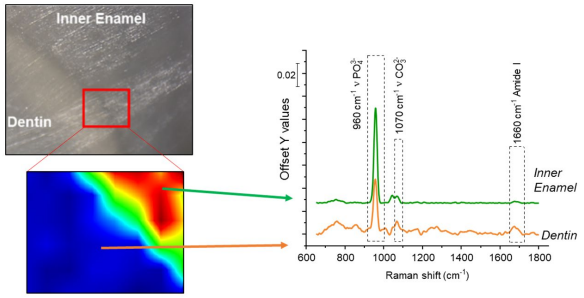
New insights from Raman MicroSpectroscopy and Scanning Electron Microscopy on the microstructure and chemical composition of vestibular and lingual surfaces in permanent and deciduous human teeth

Valentina Notarstefano[a], Giulia Orilisi[b], Riccardo Monterubbianesi[b], Vincenzo Tosco[b], Flavia Vitiello[b], Giampaolo Giuliani[c], Angelo Putignano[b], Giovanna Orsini[b]

[a] Department of Life and Environmental Sciences, Università Politecnica delle Marche, Ancona; [b] Department of Clinical Sciences and Stomatology, Università Politecnica delle Marche, Ancona; [c] Department of Materials, Environmental Sciences and Urban Planning, Università Politecnica delle Marche, Ancona

Teeth are characterized by a specific chemical composition and microstructure, which are also related to their nature, permanent and deciduous, and to the sides, lingual and vestibular. Enamel and dentin are the major components of the human dental crown, exhibiting different function, composition and structure [1]. Enamel is composed of up to 96-97% by weight of inorganic matter, 2-3% of water, and 1% of non-collagenous organic material; its microstructure mainly consists of carbonated and fluorinated hydroxyapatite (HA) crystals, arranged in prisms [2]. Dentin, less mineralized, prevents enamel from fracturing and protects the pulp chamber; it is a typical composite material consisting of inorganic HA crystals (~70% by weight) and organic collagen matrix proteins (~20%) [3]. A deeper knowledge on the differences in the chemical composition and microstructure of lingual and vestibular sides of permanent and deciduous teeth could be useful in clinical practice to develop new strategies in restorative dentistry and in the choice of materials with the best performances. In this study, Raman MicroSpectroscopy (RMS), Scanning Electron Microscopy (SEM), Energy Dispersive X-ray Spectrometry (EDS), and Vickers MicroHardness (VMH) were exploited to characterize the microstructure and chemical/elemental composition of enamel and dentin in permanent and deciduous human teeth, by considering both lingual and vestibular sides [4]. All the employed techniques evidenced differences between permanent and deciduous teeth: SEM microphotographs evidenced areas with an irregular appearance in the vestibular and lingual sides, which presented also different VMH values. Furthermore, RMS and EDS displayed a different chemical and elemental composition in outer and inner enamel and dentin, in terms of Mineral/Matrix, Crystallinity, Carbonates/Phosphates, and of concentrations by weight (%) of calcium, phosphorous, carbon, magnesium, and sodium. Interestingly, a good linear correlation was found between RMS spectral profiles and EDS and VMH measurements, suggesting that RMS can be considered a useful and non-destructive diagnostic tool for obtaining multiple information on calcified tissues.



Representative Raman map acquired at the interface between dentin and inner enamel of a permanent tooth. Corresponding spectra are also reported.

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Expanding the biological potentials of curcumin-like ligands to half-sandwich ruthenium(II) and osmium(II) metal complexes

Noemi Pagliaricci [a], Lorenzo Pietracci [b], Riccardo Pettinari [a], Alessia Tombesi [b], Fabio Marchetti [b], Corrado Di Nicola [b], Stefania Scuri[a], Loredana Cappellacci[a].

[a] School of Pharmacy and [b] School of Science and Technology, Chemistry Division, University of Camerino, via S. Agostino 1, 62032 Camerino MC, Italy.

Curcumin is the major bioactive ingredient extracted from the rhizome of the plant *Curcuma longa* (turmeric) that has several medicinal properties, such as anti-inflammatory, antioxidant, anticancer effects, and it is widely studied as a chemo-preventive agent in clinical oncology. However, curcumin shows low absorption, poor bioavailability, low water solubility and all these factors reduce its use and efficiency[1]. On this respect, curcumin bioconjugates could overcome this problem by showing enhanced cellular uptake; furthermore, curcumin-metal complexes can improve the bioavailability and gain even more diverse potential health benefit[2]. Half-Sandwich Ru(II) and Os(II) complexes represent good candidates for this purpose since their well-known antitumoral activities[3]. Recently, (η^6-arene)metal(II) complexes containing curcuminoid ligands were reported as potent anticancer agents[4]. In this work we report the synthesis of novel Ru(II) and Os(II) *p*-cymene derivatives containing curcuminoid bioconjugates with palmitoyl residue (1*E*,3*Z*,6*E*)-3-hydroxy-5-oxohepta-1,3,6-triene-1,7-diyl)bis(2-methoxy-4,1-phenylene)dipalmitate (p-curcH) and (1E,3Z,6E)-3-hydroxy-5-oxohepta-1,3,6-triene-1,7-diyl) bis(4,1-phenylene) dipalmitate (p-bdcurcH) (Figure 1). The chloride ligand has been then replaced by the 1,3,5-triaza-7-phosphaadamantane ligand (PTA) and ionic derivatives [M(η^6-cym)(p-curc)(PTA)][SO_3CF_3] and [M(η^6-cym)(p-bdcurc)(PTA)][SO_3CF_3] (M = Ru^{II} or Os^{II}) have been obtained and fully characterized (Figure 1). The cytotoxicity of the complexes has been evaluated in vitro against human ovarian carcinoma cells (A2780 and A2780cisR), as well as against non-tumorous Human Embryonic Kidney cells (HEK293).

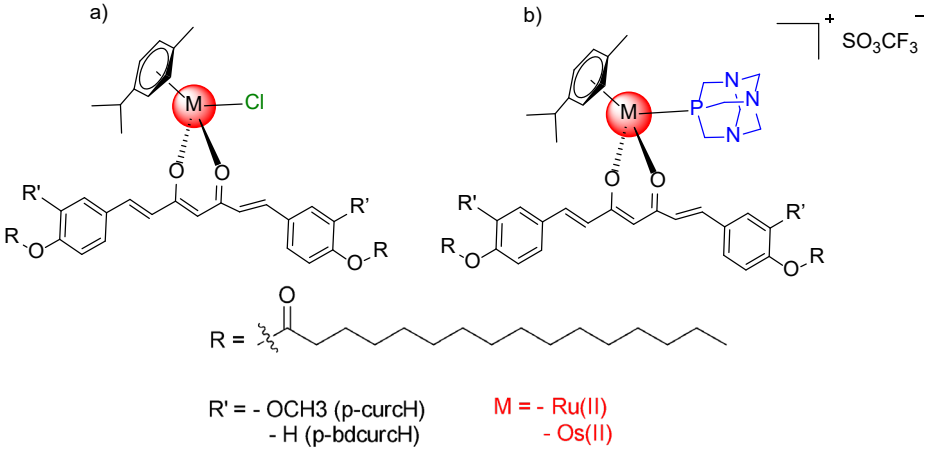

Figure 1 Ru(II) and Os(II) complexes of bioconjugate curcumins.

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Laccase-mediate oxidative upgrade of technical lignins and their fractions

Nicolò Pajer [a], Matteo Gigli [a], Valentina Beghetto [a] and Claudia Crestini [a]

[a] Department of Molecular Sciences and Nanosystems, Università Ca' Foscari Venezia, Via Torino, 155 Mestre - 30172 Mestre (VE)

Lignin, the most abundant aromatic biopolymer on Earth, is mainly obtained as by-product of pulp and paper and biorefinery industrial processes. Therefore, it represents a potential low-cost source of many compounds that can be used for a wide variety of applications ranging from food (e.g. vanillin) to building blocks for the synthesis of renewable plastics. Biotechnological approaches involving the use of lignolytic enzymes such as laccases, lignin peroxidases or manganese peroxidases have been studied with the aim of oxidatively depolymerising lignin into high added-value molecules.
However, the structural heterogeneity, which depends both on the botanical origin and on the industrial approach used for lignin isolation, significantly limits yields and selectivity of these approaches. To overcome this issue, fractionation revealed a winning strategy to extract lignin cuts with more homogeneous characteristics.
In this contribution, we coupled the two above-described strategies with the purpose of enhancing the concentration of valuable products derived from laccase-mediated oxidation of lignin. Specifically, softwood kraft lignin (SKL) and wheat straw organosolv lignin (WSL) have been firstly fractionated into an acetone soluble (AS) and an acetone insoluble (AI) cut. After an in-depth characterization to determine both the molecular weight and the hydroxyl group content of the starting lignins and the obtained fractions, laccase-mediated treatments have been carried out. Both process conditions and laccase concentration have been varied to maximize the yield of extracted compounds, whose nature and content have been determined by GC-MS analysis.
The used laccase, without the addition of any mediator molecules, demonstrated good catalytic action on all the tested substrates. However, the results evidenced a much higher activity of the enzyme on AS fractions with respect to AI and pristine lignin samples, resulting in an increased concentration of extracts and a significant reduction of the hydroxyl group content of the residual lignin with respect to untreated and control samples. Furthermore, GPC measurements on the residual lignin highlighted that laccases also induced a certain degree of repolymerisation, as an increase of the molecular weight has been detected.

MoO_3/Al_2O_3 and MoO_3/SiO_2 based catalysts for ethanol oxidative dehydrogenation to acetaldehyde

*G. Pampararo [a] *, G. Garbarino [b], G. Busca [b], P. Riani [a]*

[a] DCCI, University of Genova, Via Dodecaneso 31, 16146 Italy, [b] DICCA, University of Genova, Via all'Opera Pia 15, 16145, Italy

In recent years, mainly to attain sustainability, the interest in using biomass as carbon source to produce chemicals has emerged. Among these, ethanol produced by fermentation of lignocellulosics is expected to become a primary intermediate. It can be used as a feedstock to produce several platform molecules [1]. One of the most important secondary intermediates is acetaldehyde, that allows to produce several industrial chemicals [2]. The production of acetaldehyde from ethanol was applied in early times with the dehydrogenation route. However, selectivity is very high mostly at moderate conversion and catalyst deactivation occurs relatively fast. This led us to explore, as an alternative, also the oxidative dehydrogenation route. For this reaction vanadia and noble metals systems are mostly investigated [3-5]. Supported molybdena-based catalysts have also been reported to be active for this reaction in earlier literature [6]. The aim of this work is to investigate how adding silica, may affects the nature of the molybdena/alumina interaction, thus achieving better catalytic performances.

Pure MoO_3 and supported molybdena samples with different MoO_3 loading (1÷12 % $wt_{MoO3}/wt_{support}$) over γ-Al_2O_3, SiO_2-(1 and 5 wt.%) doped γ-Al_2O_3 and SiO_2 were prepared by incipient wetness impregnation technique. Catalysts were extensively characterized by BET, XRD, FE-SEM microscopy, UV-vis and IR spectroscopies. The introduction of silica modifies the distribution of dispersed molybdate species deposed on alumina, reducing the amount of polymeric species. Instead, over pure SiO_2 molybdenum is found both as molybdate species and as bulk MoO_3. All samples, including pure MoO_3, were tested in ethanol oxidative dehydrogenation in Temperature Programmed Surface Reaction (TPSR) conditions. Best performing catalysts were also tested in steady state and time on stream experiments. The best catalyst for the production of acetaldehyde is 12 wt.% MoO_3 over 1 wt.% SiO_2 on alumina, giving rise to acetaldehyde yield of 60% at 573 K in steady state conditions.

The effect of molybdenum content and of different supports will be discussed as a function of catalyst performance and stability.

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Theoretical study of arsenoplatin-1 complex activation and multitarget platination mechanisms

Angela Parise,[a,b] Nino Russo,[a] Tiziana Marino[a]

[a] Dipartimento di Chimica e Tecnologie Chimiche, Università della Calabria, Via Pietro Bucci, 87036 Arcavacata di Rende, CS, Italy; [b] Université Paris-Saclay, CNRS, Institut de Chimie Physique UMR8000, Orsay, France

Platinum(II)-based molecules are the most commonly used anticancer drugs in the chemotherapeutic treatment of tumours but possess serious side effects and some cancer types exhibited resistance with respect to these compounds (e.g. cisplatin). For these reasons, the research of new compounds that can bypass this limitation is in continuous development. Recently, mixed Pt(II)-As(III) systems have been synthesized and tested as potential anticancer agents. The first representative of this novel class of anti-cancer agents, the arsenoplatin-1 complex, **AP1** [Pt(μ-NHC(CH_3)O)$_2$ClAs(OH)$_2$], displays an higher activity profile relative to the parent drugs As_2O_3 and cisplatin in many cancer cell lines *in vitro* tested.

Based on clinical used platinum(II) drugs, we have explored the pro-drug activation process of the arsenoplatin-1, using density functional theory (DFT). Then we focused our attention on the platination mechanism of DNA, the main cellular target for Pt anticancer complex, by **AP1**. For this new compound it appears that guanine base is the preferred site with respect to adenine as with other platinum-containing compounds. A comparison with cisplatin is performed in order to highlight the contribution of arsenic in the anticancer activity of this new proposed anticancer agent.[1]

Recent structural studies [2] have shown that **AP1** bound to the bovine pancreatic ribonuclease (RNAse A) with platinum(II) that binds to the N-atoms of the solvent exposed His105 and the catalytic His119 side chains of the protein, preserving the Pt–As bond. (Figure 1)

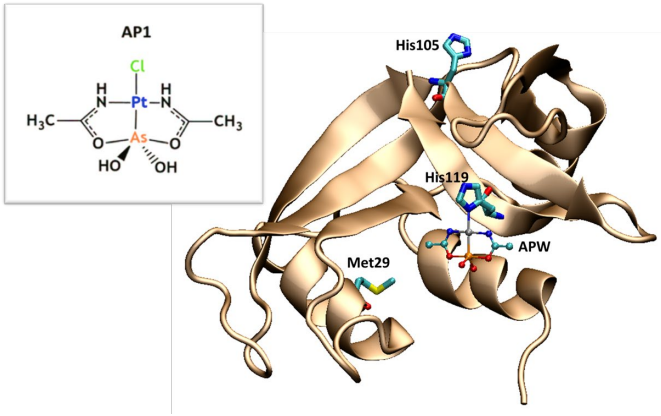

*Figure 1 Representation of **AP1** and binding sites of the **AP1** moieties of RNase A (PDB code 5NJ7 [2]).*

Since His119 residues are implicated in the catalytic activity of the RNase A enzyme, the binding of **AP1** on this site generates the inhibition of the enzyme function, as indicated by a catalytic activity assay.[2]

In this contribution we present a detailed metalation process of RNase A by **AP1** through quantum chemical investigation that uses a large QM-cluster model of the active site employing both the B3LYP and M062X functionals.[3] The role of water molecules in the active site is also analysed.

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Dusts from kitchen benchtops: physicochemical features modulating their toxicity

Pavan C.,[a,b,c] Tomatis M.,[a,b] Leinardi R.,[a,b] Corazzari I.,[a,b] Bellomo C., [a,b] Santalucia R.,[a] Chilla G.,[a] Mino L.,[a] Fubini B.,[a,b] Maharjan P.,[d] Pisaniello D.,[d] Turci F.[a,b]

[a] Department of Chemistry, University of Turin, Italy; [b] "G. Scansetti" Interdepartmental Centre for Studies on Asbestos and Other Toxic Particulates, University of Turin, Italy; [c]Louvain centre for Toxicology and Applied Pharmacology, Université Catholique de Louvain, Belgium; [d]Adelaide Exposure Science and Health School of Public Health, University of Adelaide, Australia

New outbursts of silicosis and lung-associated pathologies were reported in the last decade among workers manufacturing an engineered material known as "artificial stone" (AS) [1]. AS is a novel class of composite materials for the fabrication of kitchen and bathroom benchtops and is composed by high percentages of quartz (up to 98%), pigments, and polymeric resins.
Dusts released by abrasion during AS polishing were collected at workplaces in conventional and simulated operations. AS dusts were characterized for particle size distribution, morphology, and elemental composition, and studied for their ability to catalyse free radical generation in acellular tests. Dust ability to induce lysis of model cellular membranes and *in vitro* toxicity were assessed. AS dusts exhibited morphological features close to quartz but contained larger amounts of transition metal ions (mainly, Fe, Cu, and Ti), potentially responsible for the high reactivity in eliciting reactive oxygen species (ROS) *in chemico*. Unlike a reference quartz of known toxic activity, AS dusts were neither membranolytic nor induced cellular toxicity *in vitro*. The presence on the particle surface of residues of the resin accounts for this attenuated behaviour, as membranolysis and cytotoxicity increased after thermal degradation of the resin, likely when the bare quartz surface was made available for particle-cell interaction [2]. Spectroscopic investigations of the AS surface, before and after heating, revealed that the resin-deprived particles show peculiar hydroxyl moieties, namely the "nearly free silanols - NFS", that we recently discovered as the major initiator of quartz toxic activity [3]. Moreover, we observed that membranolytic activity was restored on AS dusts incubated in simulated artificial lysosomal fluid (ALF) (representative of the more acidic environment within the lung) for 2 months. This finding suggests that the prolonged contact of AS dust with components of the cellular fluid could degrade the resin and reveal surface NFS, which explain the toxicity of these dusts (*Fig. 1*). Our results may contribute to clarify the mechanisms underlying the severity of the disease that is being observed on workers exposed to AS dusts, encouraging safer occupational practices and safer-by design approaches on the materials.

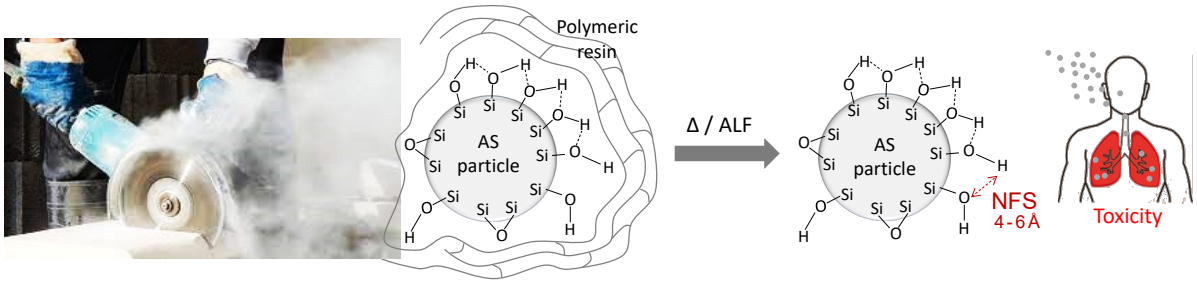

Fig.1 *Dusts released by artificial stone (AS) cutting are coated by a polymeric resin which is removed by thermal treatments and permanence in artificial lung fluid (ALF). Restoring of bare quartz surfaces and nearly free silanols (NFS) could initiate toxicity responses within the lungs, when AS particles are inhaled.*

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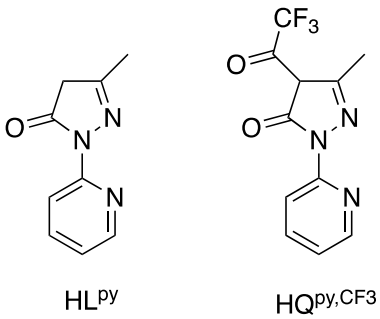
New arene-Ru(II) compounds as potential anticancer agents

Lorenzo Pietracci[a], Noemi Pagliaricci[b], Fabio Marchetti[a], Riccardo Pettinari[b], Stefania Scuri[b], Loredana Cappellacci[a], Corrado Di Nicola[a], Alessia Tombesi[a].

[a] School of Science and Technology and [b]School of Pharmacy, University of Camerino, Via S. Agostino 1, 62032 Camerino.

As platinum-based anticancer drugs suffer from a number of side effects, the battle against tumours is directing toward more selective and efficient non-platinum-based anticancer and antimetastatic agents [1]. In recent years half-sandwich Ru(II) complexes have emerged as potential alternatives to platinum-based drugs due to several attractive properties such as redox-accessible oxidation states, biocompatible ligand exchange rates, covalent binding with DNA and/or proteins, combined with a low toxicity [2]. Our research group has contributed to expand this field by investigating the coordination chemistry and the antitumor prospective of the (arene)Ru(II) complexes with a family of exotic β-diketones, namely the acylpyrazolones, based on a pyrazole fused to the chelating ring [3]. In this work we investigated as ligands 5-methyl-2-(pyridin-2-yl)-2,4-dihydro-3H-pyrazol-3-one (HL^{py}) and the corresponding acylpyrazolone with the 2,2,2-trifluoroacetyl fragment, i.e. 5-methyl-2-(pyridin-2-yl)-4-(2,2,2-trifluoroacetyl)-2,4-dihydro-3H-pyrazol-3-one ($HQ^{py,CF3}$), both containing a pyridine ring (Figure 1). They are both able to react with (arene)Ru(II) acceptors affording neutral complexes with good solubility in alcoholic solvents and those of L^{py} also in water. They have been fully characterized in solution and solid state, also by X-ray diffractometry (Figure 2). The cytotoxicity of the free ligands and Ru(II) complexes has been evaluated against human ovarian carcinoma cells (A2780 and A2780cisR, cisplatin sensitive and cisplatin resistant, respectively), and non-tumorous human embryonic kidney SV40 transformed (HEK293T) cells.



HL^{py} $HQ^{py,CF3}$

Figure 1

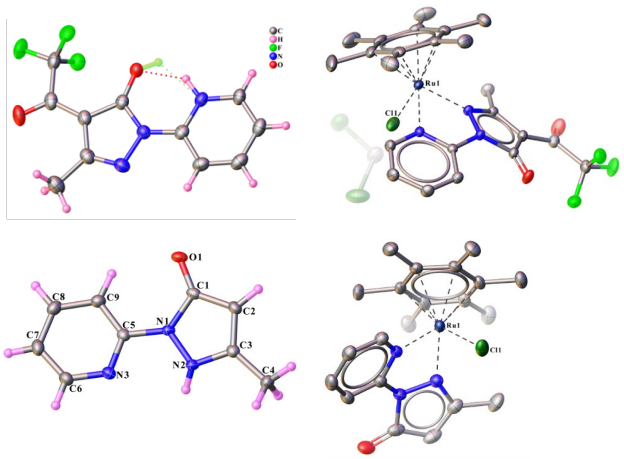


Figure 2

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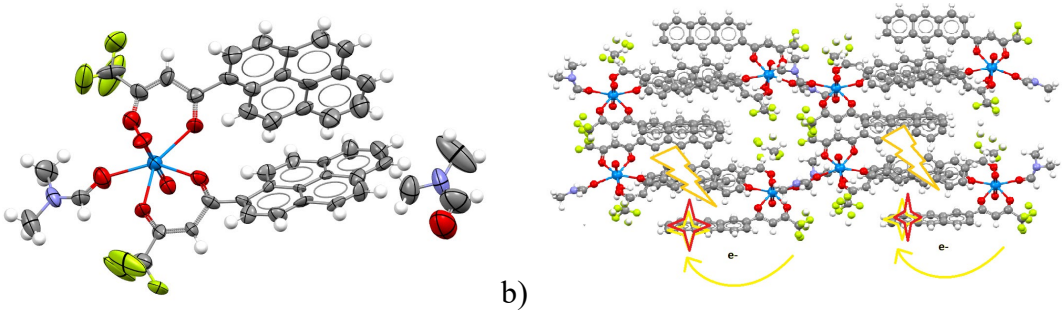
Uranyl β-diketonates with polycyclic aromatic substituents as autoluminescent complexes: a structural and electronic characterization

Emanuele Priola,[a] Jacopo Andreo,[b] Eugeny V. Alexandrov,[c] Paola Benzi,[a] Davide M. Proserpio,[d] Vladislav Blatov,[c] Lorenza Operti [a] and Eliano Diana[a]

[a]Department of Chemistry, University of Turin, Via Pietro Giuria 7, 10125 Turin, Italy, [b]Dipartimento di Chimica Generale ed Inorganica, Chimica Analitica, Chimica Fisica, Università di Parma, Viale G. P. Usberti 17A, 43100 Parma (Italy), [c]Samara Center for Theoretical Materials Science (SCTMS), Samara State Technical University, Molodogvardeyskaya St. 244, Samara 443100, Russia, [d]Dipartimento di Chimica, Università degli Studi di Milano, Via Golgi 19, 20133 Milano, Italy

Radioluminescence is one of the most fascinating properties related to radioactivity. All radioactive materials spontaneously emit photons through several physical phenomena. However, an extremely high radioactivity and sample quantity are required to make it perceivable, as most of these phenomena present low emission efficiency. The most interesting exception to this general rule is scintillation, a luminescence whose energy source is a direct ionizing particle or a high-energy photon. These interact with the scintillator (a phosphor with scintillating property) triggering multiple excitations and leading to a burst of light, whose intensity depends only on the particle nature and energy and the scintillator efficiency.[1] The scintillator can usually be an inorganic salt (es. $ThBr_4$) or an organic fragment like naphthalene or anthracene.[2] In a previous publication, we manage to obtain a MOF with a scintillating organic fragment crystallized with Thorium radioactive centers to create the first autoluminescent material.[3] In this prosecution, we synthetized and characterized a series of 5 new uranyl(VI) β-dichetonates with anthracene, pyrene, naphthalene and fluorene substituents and we checked them as the first autoluminescent molecules. The effect of the change of metal center from thorium to uranium will be commented, especially regarding the structural and electronic behavior. There findings will be interesting in the field of actinide detection and in technologies for new generation nuclear energy.



a) b)

Figure 1. a) molecular structure of $[UO_2(DMF)(acac\text{-}R)]$ (R= pyrene) and (b) solid state mechanism of autoluminescence;

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A FTIRI focus on the macromolecular features of swordfish (*Xiphias gladius*) Zona Radiata

Chiara Pro[a], Luca Marisaldi[a], Valentina Notarstefano[a], Alessia Belloni[a], Edoardo Acri[a], Giorgia Gioacchini[a], Oliana Carnevali[a], Elisabetta Giorgini[a]

[a] Dipartimento di Scienze della Vita e dell'Ambiente, Università Politecnica delle Marche, via Brecce Bianche, 60131 Ancona (Italy)

Swordfish is a large pelagic fish, with high commercial and ecological value. Despite this, the reproductive biology is up to date and not well known. The term oogenesis includes all the developmental and maturation processes that lead to the formation of mature egg ready to be fertilized. A crucial role in fertilization processes is played by the zona radiata (ZR), a glycoprotein layer surrounding the plasma membrane of mature eggs. ZR is mainly composed by three glycoproteins (ZPA, ZPB, and ZPC), and it changes in composition, thickness and structure during oogenesis, becoming highly ordered and architecturally complex in the mature stage.

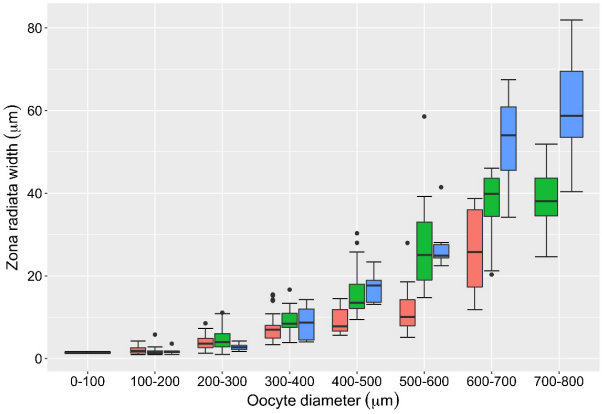

Fig. 1. Correlation between oocyte diameter and ZR thickness in Balearic Islands (blue), Sicily (green), and Sardinia (red).

The aim of this study is to evaluate a possible correlation between ZR thickness and composition and the geographical fishing area. At this purpose, swordfish oocytes collected in three different regions of the Mediterranean Sea were analyzed: Balearic Islands, Sicily, and Sardinia. Histological analysis showed a different thickness of the ZR, depending not only by the developmental stage (oocyte diameter) but also by the fishing zone (Fig. 1). FTIRI imaging analysis confirmed this finding. False colour images reported in Fig. 2, show the topographical distribution of the most relevant biomolecules in IR maps collected on ZR of vitellogenic and mature oocytes from Balearic Islands, Sicily, and Sardinia. In particular, the following macromolecules were checked: lipids (LIP), fatty acids (FA), proteins (PRT), glycosylated compounds (GLY) and phosphates (PH). Specific band area ratios were also analyzed (LIP/CELL, FA/LIP, PHOSPHO/CELL, PRT/CELL, CARBO/CELL), showing differences in composition between vitellogenic and mature oocytes both within the same fishing area (mainly in LIP and FA composition), and among the three different areas (vitellogenic oocytes in LIP, FA, PRT and GLY composition, while mature ones in PRT and GLY composition).

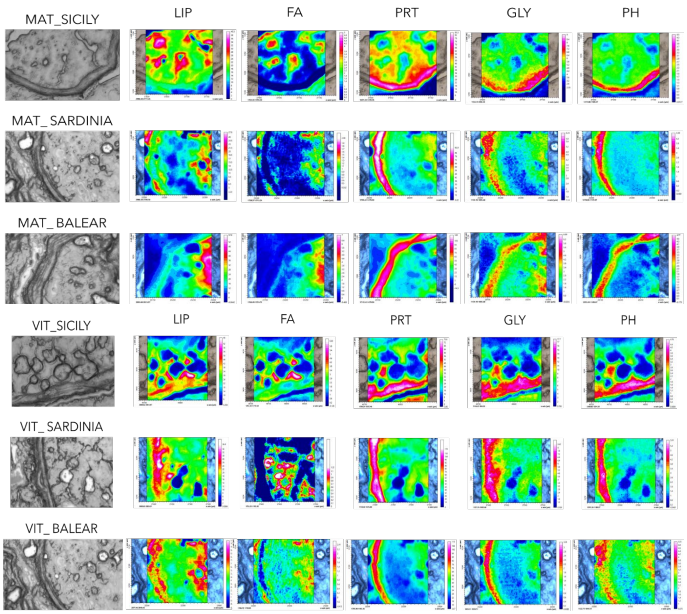

Fig. 2. FTIRI imaging analysis of ZR of vitellogenic and mature swordfish oocytes from Balearic Islands, Sicily, and Sardinia; topographical distribution of lipids (LIP), fatty acids (FA), proteins (PRT), glycosylated compounds (GLY) and phosphates (PH).

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Homo and heterometallic lanthanide cages as luminescent ratiometric thermometers

Maria Rando,[a] Luigi Bosi,[a] Alice Carlotto,[a] Roberta Seraglia,[b] Silvia Carlotto,[a] Gregorio Bottaro,[c] Lidia Armelao,[a,d] Marzio Rancan[c]

[a] Dipartimento di Scienze Chimiche, Università di Padova, Via Marzolo 1, 35131 Padova, Italy; [b] ICMATE-CNR, Corso Stati Uniti 4, 35127 Padova; [c] ICMATE-CNR, Via Marzolo 1, 35131 Padova, Italy; [d] DSCTM-CNR, Piazzale A. Moro 7, 00185 Roma.

Metallo-supramolecular architectures generated from metal ions and well-designed polytopic ligands are an excellent bench test for supramolecular and self-organization concepts and a wide source of new functional materials.
In this contribution, the self-assembly of homo and heterometallic lanthanide-based cages of general formula $[Ln_2L_4]^{2-}$ will be discussed. In particular, the formation of heterometallic cages have been followed, studied, and quantified through electrospray ionization mass spectrometry as a function of the lanthanide ionic radius.
The europium cages are highly luminescent at room temperature, with high brightness values, and with a low temperature dependent luminescence. On the other hand, the terbium cages luminescence is strongly dependent on the temperature. This paves the way for the design of ratiometric luminescent thermometers by mixing the Eu and Tb systems. The ratiometric thermometers show a wide temperature range of applicability (ca. 200 K where the relative sensitivity is > 1 $\%K^{-1}$) ranging from cryogenic to physiological temperatures. The ability to follow and quantify the formation of the heterometallic cage allowed us to evaluate its effect on the thermometric properties.

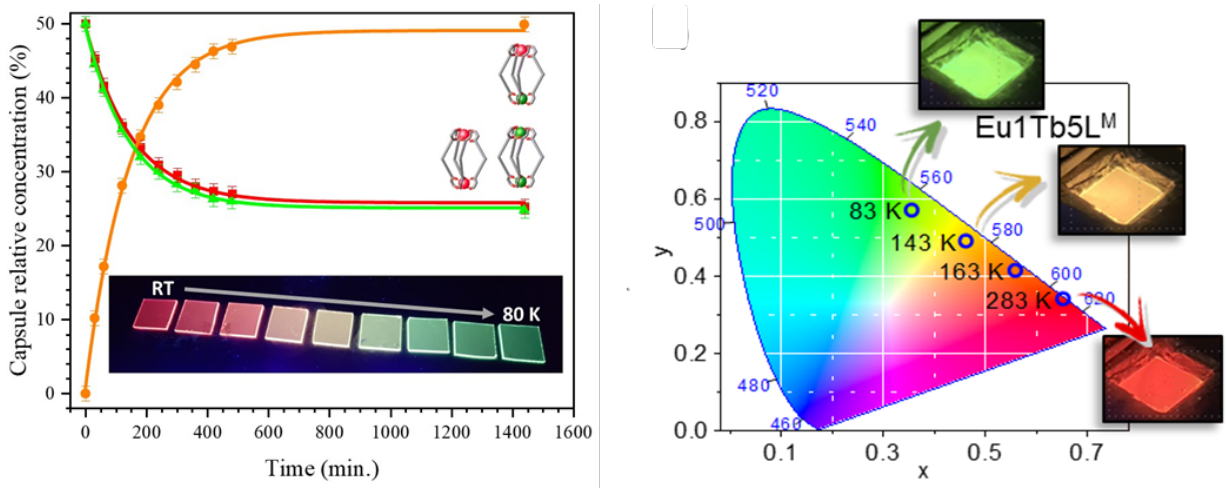

Figure 1. Kinetic of the heterometallic cage $[EuTbL_4]^{2-}$ formation and ratiometric lanthanide cages luminescent thermometers

Artificial mini-enzymes on nanogold surfaces

Emilia Renzi,[a] Rocco di Girolamo,[a] Marco Chino,[a] Angela Lombardi[a] and Flavia Nastri[a]

[a]Department of Chemical Sciences, University of Naples "Federico II", via Cintia, 21, 80126, Naples, (Italy)

Nanomaterials (NMs) have drawn great interest over the last decades in a variety of research areas, including biosensing, catalysis and diagnostics. In the field of enzyme immobilization, gold-containing nanomaterials (AuNMs) play a central role as excellent platforms due to a high surface area-to-volume ratio as well as with a versatile surface chemistry. Especially gold nanorods have been identified as promising candidates for the construction of highly effective biosensors.[1] In this context, the conjugation of AuNMs with artificial heme-enzymes, known as Mimochromes (MCs),[2] enables the construction of versatile hybrid bio-systems. Indeed, preliminary results on Fe(III)-Mimochromes demonstrated their successful immobilization onto gold electrode surfaces and conjugation to AuNPs while retaining redox and catalytic properties.[3,4] Driven by these interesting results, the work here presented focused on the construction of bionanoconjugates, selecting the artificial heme-peroxidase Fe(III)-MimochromeVI*a (FeMC6*a) as the biomolecular building block and gold nanorods (AuNRs) as the target support. The immobilization was achieved by carrying out two different approaches: on one hand, FeMC6*a was derivatized with lipoic acid, in order to be directly grafted on the surface of AuNRs (**Figure 1**). On the other hand, the SPAAC (strain-promoted azide-alkyne cycloaddition) chemistry guaranteed the fast-covalent immobilization of the mini-enzyme modified with a pegylated spacer to carry an aza-dibenzocyclooctyne (DBCO) moiety. In this case, AuNRs were properly modified to expose azide moieties (**Figure 1**).

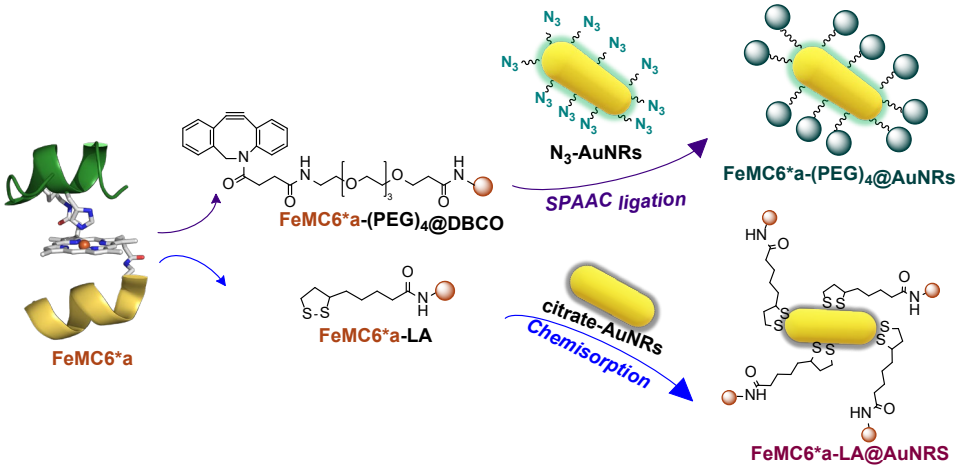

Figure 1: Schematic representation of the two methodologies employed to prepare FeMC6*a-based bionanoconjugates.

The two methodologies proved to be easy and efficient, allowing the attachment of several copies of FeMC6*a to gold nanorods. The catalytic properties of the resulting hybrid bio-nanomaterials were evaluated using model oxidation reactions. Both approaches afforded functional bio-nanoconstructs, which retained peroxidase activity, although decreased catalytic performances were observed, if compared to that of the freely diffusing FeMC6*a. However, the developed methods represent a proof of concept that the artificial metalloprotein FeMC6*a can be firmly anchored on nanomaterials and support the development of stable and functional FeMC6*a-AuNMs conjugates.

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Novel gallium(III) complexes of tridentate Schiff base hydrazones as potential anticancer agents

Daphne Romani [a], Federico Verdicchio [b], Corrado Di Nicola [a], Riccardo Pettinari [b], Alessia Tombesi [a].

[a]School of Science and Technology and [b]School of Pharmacy, Chemistry Division, University of Camerino, Italy

Gallium-based anticancer complexes have attracted considerable attention due to the proven ability of gallium cations to inhibit tumour growth, enhanced bioavailability and moderate toxicity compared to gallium salts[1,2]. The complexation of Ga(III) with hydrazones can increase the biological activity of the metal and is considered to be an important strategy for the development of cytotoxic drugs. Recently, pyrazolone-based hydrazones were obtained from the reaction of 4-acyl-5-pyrazolones and 2-hydrazinopyridine and used to coordinate Ru(II) affording complexes with anticancer activity[3]. More in general, these ligands possess interesting features, such as antioxidant, antifungal and anti-microbial properties[4]. In this study we present recent achievements on the synthesis and characterization of novel cationic Ga(III) complexes of 4-hydrazone-5-pyrazolones and a systematic investigation of their solution and solid state chemistry, together with the anticancer activity toward some representative tumour cell lines. Moreover, their antibacterial potential has been tested against *S. aureus* and *E. coli*.

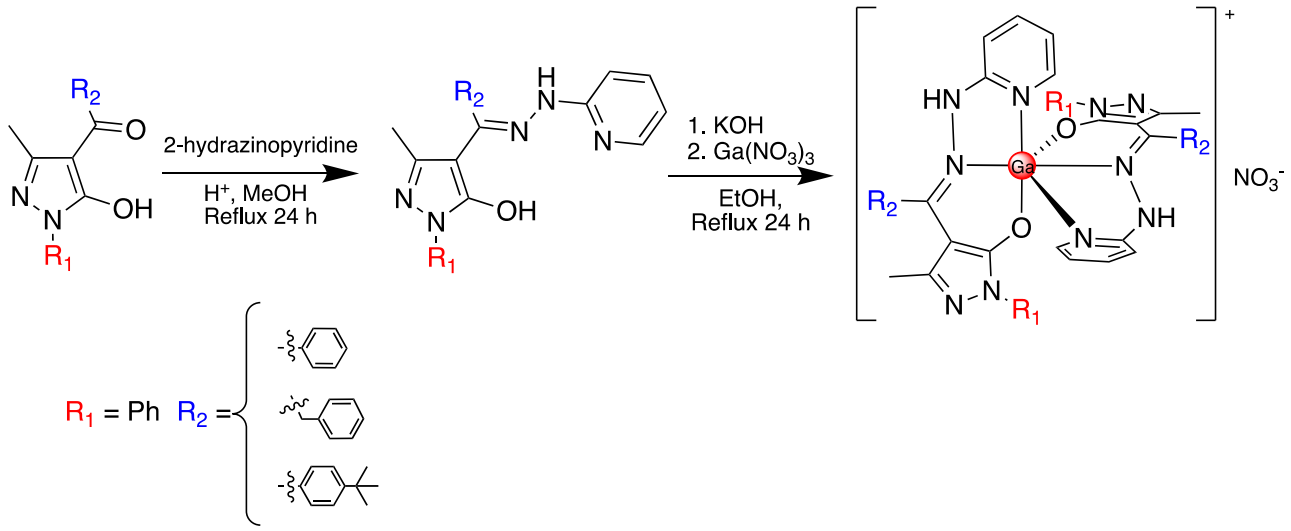

Figure 1: Synthesis of hydrazone ligands and their Ga(III) complexes.

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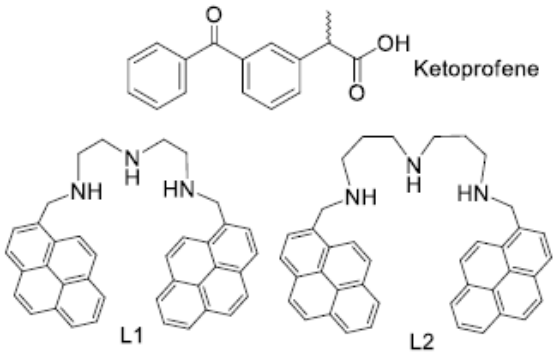
Recognition of non-steroidal anti-inflammatory drugs with fluorescent polyamine receptors and their Zn(II) complexes

Giammarco Maria Romano [a], Andrea Bencini [a]

[a] *Dipartimento di Chimica "Ugo Schiff", Università di Firenze, Via della Lastruccia 3, 50019 Sesto Fiorentino, Florence, Italy*

In the last few years, the interest in the development of new sensing systems for certain consumer drugs, such as antibiotics and non-steroidal anti-inflammatories drugs (NSAIDs), has progressively increased. Indeed, their wide use and presence in the environment, in particular in water, can lead to a continuous consumption from living beings, with possible long term toxic effects. They are part of the "emerging pollutants", whose use, in most cases, is not yet subjected to exact normative.



The purpose of the present work is the development of new fluorescent molecular sensors for NSAIDs. Here we use two fluorescent triamine receptors, L1 e L2, and their Zn(II) complexes as optical probes for one of the most used NSAIDs, ketoprofen. In fact, ketoprofen, and NSAIDs in general, present in their structure a carboxylic group, normally deprotonated at neutral pH, and aromatic units. The two synthesized receptors are constituted by a polyamine chain, which can protonate in aqueous solution a neutral pH and two pyrene units, as signalling units, with a marked hydrophobic character. From this point of view, the two receptors possess optimal structural characteristics for NSAIDs recognition; the triamine chain, when protonated, can interact via charge-charge and hydrogen bonding interactions with the anionic carboxylate group of ketoprofen, while the pyrene units can give hydrophobic and/or π-stacking interactions with the aromatic portions of the NSAID.

A notable feature of the fluorescence spectra of both receptors, at neutral pH, is the presence of a red-shifted emission band at around 460 nm due to an intramolecular excimer formed via an association of two end pyrene fragments within the molecule. The emission intensity of this band undergoes a significant increase as a result of interaction with ketoprofen at pH 7. The interaction between carboxylate group and ammonium groups of the receptor may lead to a localization of acid protons on adjacent amino groups to fluorescent units. In fact, when deprotonated, amino groups can quench the pyrene fluorescence emission by electronic photoinduced transfer (PET effect), which is inhibited by protonation as result of the interaction with ketoprofen.

Furthermore, polyamine chains can form stable complexes with metal cations, in particular transition metals, which can be used as anchoring points for substrate, including ketoprofen, which can bind to metal cations via its carboxylate group. The Zn(II) complexes of L1 and L2 , are also characterized by the presence of the red-shifted excimer emission band, which increases as result of coordination of ketoprofen

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Materials having *self-healing* ability by intermolecular interactions

Simona Russo [a], Elisa Calabrese [b], Marialuigia Raimondo [b], Annaluisa Mariconda [c], Liberata Guadagno [b], Pasquale Longo [a]

[a] *Department of Chemistry and Biology, University of Salerno, via Giovanni Paolo II,132I-84084, Fisciano, SA, Italy*
[b] *Department of Industrial Engineering, University of Salerno, via Giovanni Paolo II,132I-84084, Fisciano, SA, Italy*
[c] *Department of Science, University of Basilicata, Viale dell'Ateneo Lucano 10, 85100 Potenza, PT, Italy*

A huge challenge, nowadays, is the design of materials with self-healing capabilities. The aviation industry is particularly interested in making materials with this type of property for the construction of structural elements, such as fuselages, because they are subject to wear and maintenance costs are high. However, the self-healing ability is of interest for the realization of any type of artifact. [1-2]

With this contribution, we want to show the possibility to have composite materials with self-healing ability through non-covalent interactions. The copolymer Poly(PEGMA-co-UPy) [3], with various percentages of PEGMA and HEMA-Upy, is blended with epoxy resins , for applications in the aeronautical field, or in polymer matrices, such as polylactic acid (PLA), for other applications. This copolymer Poly(PEGMA-co-UPy) confers self-healing properties to the resulting composite materials, thanks to the reversibility of hydrogen bond interactions through the polymer chains (Figure 1).

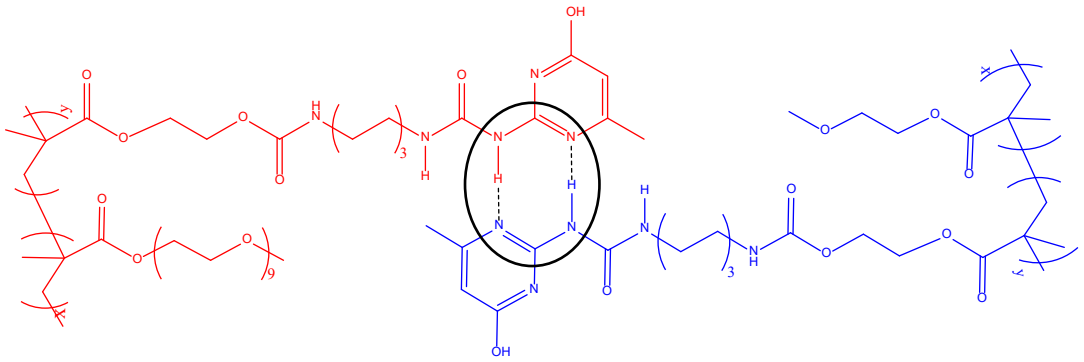

Figure 1. Hydrogen bonds between two copolymer chains

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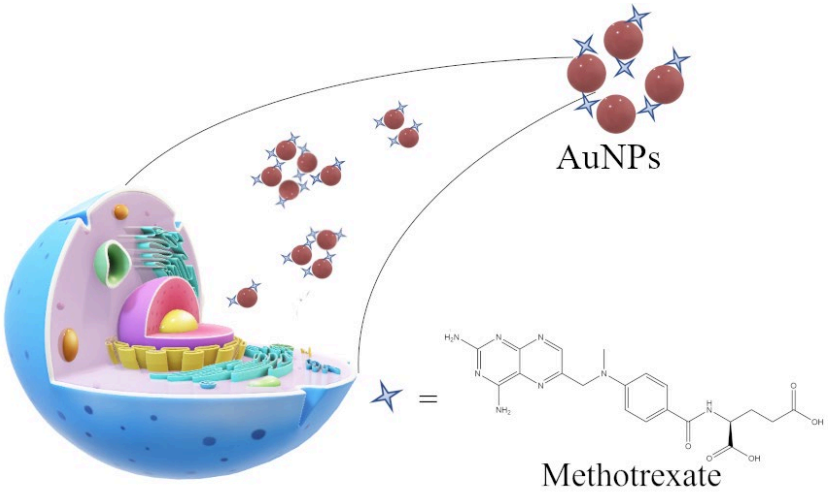
Functionalised gold nanoparticles loaded with methotrexate for the treatment of neuroblastoma: synthesis, characterisation, and *in vitro* study

Tommaso A. Salamone[a], Lavinia Rutigliano[b], Sara Cerra[a], Farid Hajareh Haghighi[a], Marzia Mongillo[a], Ilaria Fratoddi[a], Enzo Agostinelli[c]

[a] Department of Chemistry, Sapienza University of Rome, 00185 Rome, Italy; [b] Department of Molecular Medicine, 00161, Rome, Italy.; [c] Department of Sense Organs, Policlinico Umberto I, 00161 Rome, Italy.

Nanomaterials as drug delivery probes have shown great potential over time [1,2]. Herein, gold nanoparticles are used as a platform for the delivery of methotrexate (MTX), a drug which is used in a wide range of treatments, including cancer [3] and psoriasis [4]. In this work, gold nanoparticles (AuNPs) functionalised with two different thiols, 3-mercaptopropane-1-sulfonate (3MPS) and 2-(diethylamino)ethanethiol (DEA) are synthesised following a single phase wet chemical reduction, using sodium borohydride as the reducing agent and the thiols as stabilisers. MTX was loaded on the synthesised nanoparticles following a previous report[5], the loading percentage was found to be >90% and the release over time negligible. Both the as-synthesised AuNPs and the drug loaded AuNPs have been extensively characterised by means of UV-visible spectroscopy, FT-IR spectroscopy, NMR, Dynamic Light Scattering, ζ-potential measurements, together with morphological characterisations such as TEM and SEM. A preliminary *in vitro* study was carried out to evaluate the biological activity of the drug loaded gold nanoparticles towards two different neuroblastoma cell lines, SJNKP and IMR5 with overexpressed c-Myc and two adenocarcinoma cell lines, LoVo and LoVo DX.



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Aluminium configuration and conformation in porous cement architectures

Mohammed Salha,[a], Enrico Bodo,[a], Gregory A. Chass[b]

[a] University of Rome, 00185, Roma, Italy; [b] School of Biological and Chemical Sciences, Queen Mary University of London, London E1 4NS, United Kingdom

Modern cements are high in strength, and endeavor to the long-term toughness of ancient Roman structures. However, the atomistic structure and nanoscopic role of each element in cement remains poorly understood; the Calcium-(Alumino-)Silicate-Hydrogel (C-(A-)S-H) phase in particular, as well as Aluminium's role in toughening. [1-4] Molecular cluster C-(A-)S-H nanoparticles (~1—3 nm^3) were therefore investigated by high-level Density Functional Theory (DFT) complemented by *Ab initio* molecular dynamics simulations (AIMD) to resolve their nano structures and dynamical flexibilities. The configurational ordering of Al at terminal (Q1) vs. bridging (Q2) positions was also investigated. It was found that Al assisted in retention of higher chain-length and that the increased flexibility of Al-O-X bond angles (X = Si, H, Al) was sustained by Al, serving as hinge-points in the networks. Structurally, alumino-silicate units with differing Al-coordinations (4-, 5- and 6-coordinate) were characterised, with 5-coordinate facilitating distortion and interconversion, equating to increased flexibility and potential for dispersion of mechanical stresses. The Al-doped structures were amorphous with irregular pores with an overall increased free volume (Vf), relative to Al-poor ones, evidencing Al's role in the stabilisation of dry and hydrated pore architectures. The findings suggest atomistic contributions of Al-atoms to toughening in cements and may promote Al-tailored structuring and applications towards reproducing the damage tolerances observed in heritage cements.

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Multivariate-assisted approach to neuromelanin's synthesis first steps

Fabio Schifano[a,b], Lisa Rita Magnaghi[b], Stefania Nicolis[b], Simone dell'Acqua[b], Michela Sturini[b], Luigi Casella[b], Enrico Monzani[b]

[a]University School for Advanced Studies, Piazza della Vittoria 15, 27100 Pavia, Italy; [b]Department of chemistry, University of Pavia, Viale Taramelli 12, 27100 Pavia, Italy

Neuromelanins (NMs) are the melanins mainly found in human's pigmented neurons of Substantia Nigra (SN) and Locus Coeruleus (LC), where exert a protecting role sequestering, respectively, un-stored dopamine (DA), norepinephrine (NE) and toxic metal ions, such as iron and copper.[1,2] Under the pathological conditions found in brains of Parkinson's Disease (PD) patients, NMs can exacerbate oxidative stress damage: dying neurons can release NM, causing the microglia activation,[3] which, in turn, can disrupt NM causing the release of toxic metals and compounds bound to NM, leading to a vicious cycle of chronic inflammation.[1]
Aim of our work is to understand how metal-catalyzed oxidation of catecholamines is affected by chemical-physical parameters such as type of metal ion (iron, copper or both), pH, ionic strength and the presence of neuronal peptides. The reactivity studies have been performed following both the DA oxidation by UV-Vis spectroscopy and the metal's concentration by ICP-OES. A multivariate approach, based on different chemometric tools (DOE, PCA and 3W-PCA), was exploited to extract information. These methods are powerful data reduction tools that allow to handle and interpret large data-sets, such as full spectra, without any data manipulation or extrapolation; but allow also to extract valuable information from spectra with several overlapped bands or baseline related problems.
The results clearly indicate that copper is more reactive than iron in melanin formation. Furthermore, when both metal ions are present, the oxidation rate and the type of product are in between of the situation with the two metals taken alone and no cooperation is observed. Of particular importance is that, following the absorbance changes with time, it is possible to asses weather the reaction is driven by iron, copper or the two metal ions together in the medium. As for the effect of ionic strength of the medium, the rate of DA oxidation decreases with the increase of the ionic strength. Future perspectives are directed toward the study of the effects of neuronal related peptides on DA oxidation and melanin synthesis.

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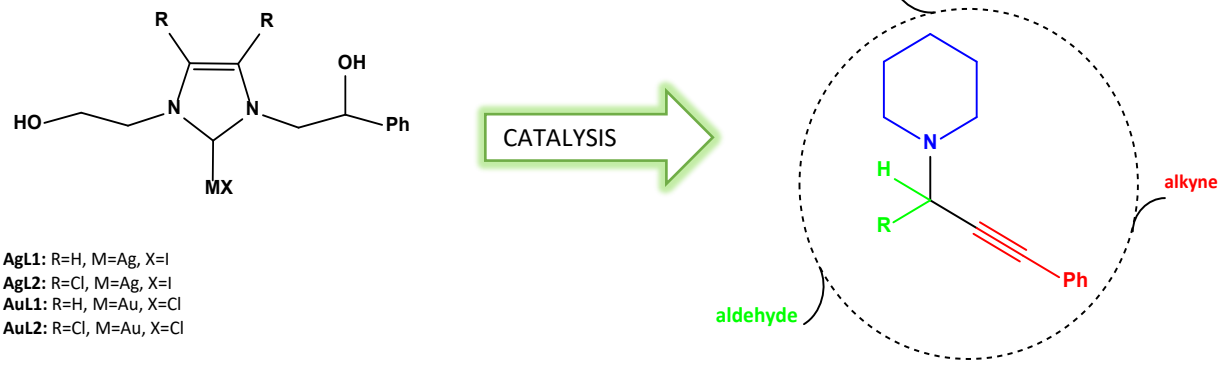
A^3 coupling reaction catalyzed by NHC silver and gold complexes

Marco Sirignano [a], Annaluisa Mariconda [b], Pasquale Longo[a]

[a] *Department of Chemistry and Biology (DCB), University of Salerno, via Giovanni Paolo II, 132I-84084, Fisciano, SA, Italy*
[b] *Department of Science, University of Basilicata, Viale dell'Ateneo Lucano 10, 85100 Potenza, PT, Italy*

In recent years, homogenous catalysis promoted by silver (I) and gold (I/III) compounds has attracted remarkable interest [1]. The use of silver (I) compounds (i.e., AgCl, AgBr, Ag_2SO_4) and gold (I/III) salts (AuCl, $AuCl_3$, $NaAuCl_4$) in many organic transformations has been studied and reported in literature [2]. The synthesis of important organic molecules with these catalytic systems can occur through the π coordination of alkenes, allenes and alkynes or through the σ coordination of scaffolds of heteroatoms (ethers, epoxides, immines, carbonyls and aziridines) [3] at the metal center [2]. The main limitation in the use of these inorganic salts is the formation of colloidal compounds, thus reducing the catalytic activity and turnover number.
Stabilization of the metal center by means of an ancillary ligand is essential for improving the catalytic activity. N-heterocyclic carbene ligands (NHC) allowed the synthesis of highly stable and active catalysts, used in various organic transformations [5].
The NHC complexes of silver and gold have been shown to be able to catalyze the trimerization reaction of aldehyde, alkyne, and amine (A^3-coupling reaction) to lead propargylamines [3],[6].
Herein we reported the synthesis, the characterization, and the catalytic activity in A^3-coupling reaction of two silver and two gold complexes bearing N-heterocyclic carbene ligands unsymmetrically N-substituted having hydrogen or chlorine on backbone. The gold complexes have showed a better catalytic activity than the silver analogues for all aldehyde used (p-formaldehyde, cyclohexylaldehyde and benzaldehyde).



AgL1: R=H, M=Ag, X=I
AgL2: R=Cl, M=Ag, X=I
AuL1: R=H, M=Au, X=Cl
AuL2: R=Cl, M=Au, X=Cl

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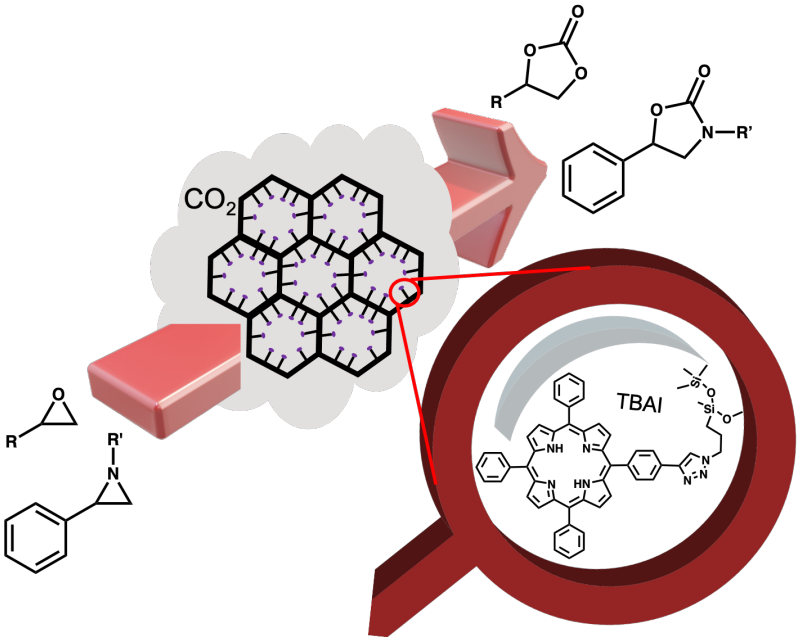
A new heterogeneous catalyst for the cycloaddition reaction of carbon dioxide to three membered heterocycles

Paolo Sonzini, Matteo Cavalleri, Caterina Damiano and Emma Gallo

[a] *Department of Chemistry, Università degli Studi di Milano, via Golgi 19, 20133 Milano, Italy*

Oxazolidinones constitute a versatile class of organic compounds, which, besides being useful intermediates and chiral auxiliaries in organic synthesis,[1] present interesting antibacterial and antibiotic properties.[2] The best pharmaceutical performances have been usually observed for *N*-aryl oxazolidin-2-ones (NAOs), such as Linezolid, Tedizolid and Toloxatone, which are FDA-approved drugs.[3] On the other hand, cyclic carbonates are used either as solvents in chemical processes and in batteries or as precursors of a great variety of organic molecules.[4] One of the most interesting methodologies for the synthesis of NAOs and cyclic carbonates is the use of greenhouse CO_2 as a renewable C1 synthetic building block in cycloaddition reactions to aziridines and epoxides, respectively.

Considering our recent report on the catalytic efficiency of the $TPPH_2$/TBACl system ($TPPH_2$ = *meso*-tetraphenyl porphyrin) in the metal-free synthesis of NAOs and *N*-alkyl oxazolidinones,[5] we have investigated the heterogenization of porphyrins onto SBA-15 silica in order to improve the sustainability and industrial attractiveness of the system. The so-obtained heterogeneous catalyst was used to promote the cycloaddition reaction of carbon dioxide to three-membered heterocycles. Here we report the synthesis and characterization of the SBA-15@porphyrin material and its utilization, in combination with ammonium salts, in the reaction of carbon dioxide with both aziridines and epoxides.



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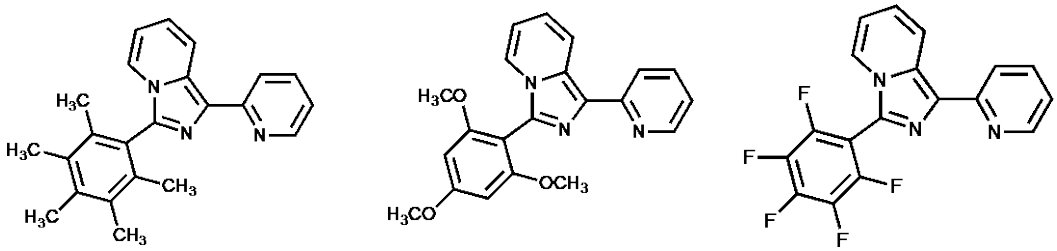
Synthesis and characterization of gold(III) derivatives with 3-substituted 1-(2-pyridyl)imidazo-[1,5-*a*]pyridine ligands

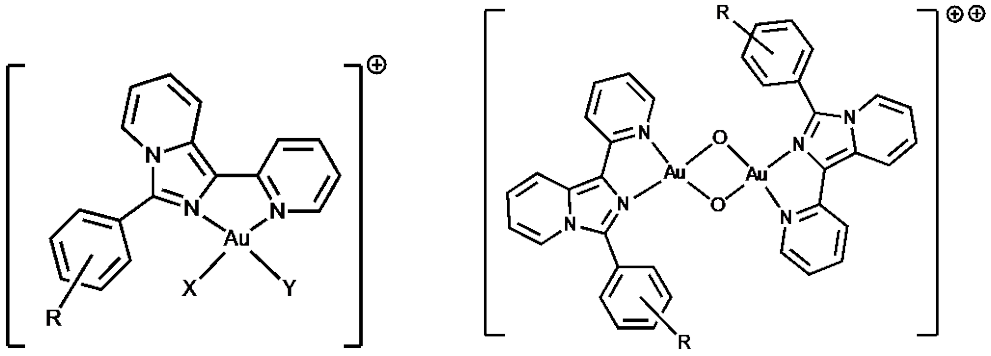
Sergio Stoccoro, Sara Pischedda, Kholoud Zribi, Giacomo Senzacqua, Alessandro Ledda and Antonio Zucca*

Dipartimento di Chimica e Farmacia – Università degli Studi di Sassari, Via Vienna 2, 07100 Sassari

Coordination chemistry of gold is still attracting considerable attention due to applications of many derivatives in various fields including catalysis and medicinal chemistry.[1] A number gold(III) complexes with nitrogen ligands are known, most of which are bipyridine and phenanthroline derivatives.[2] Following our interest in the coordination chemistry of 3-substituted 1-(2-pyridyl)-imidazo[1,5-*a*]pyridines ligands[3] here we report the synthesis of new gold(III) complexes with a series of these ligands (L^n):



Until now, only cationic adducts $[Au(L^n)XY][PF_6]$(X=Y= Cl, OH; X≠Y=Cl, OH) have been obtained, where the ligands act as classical chelating bidentate N^N ligand. Due to their interesting chemistry, different experimental conditions are under investigation aimed to obtain the corresponding bis μ-(O^{2-}) complexes [4] and cyclometalated derivatives.[3]



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Investigations of the antibacterial activity of a series of bis(pyrazolato)-based metal-organic frameworks

Alessia Tombesi [a], Sonila Xhafa [a], Fabio Marchetti [a], Claudio Pettinari [b], Corrado Di Nicola [a], Riccardo Pettinari [b], Stefania Scuri [b].

[a] School of Science and Technology and [b]School of Pharmacy, University of Camerino, Via S. Agostino 1, 62032 Camerino.

It is widely known that pathogens are becoming resistant towards large use antibiotics, making treatment of infections critical in recent years. The development of novel anti-microbial agents that operate through different mechanisms to those of the known classes of antibiotics assumes great importance.[1] Over the past decade, metal-organic frameworks (MOFs) have shown to be successfully employed as antimicrobial materials for food, medical, and environmental fields. These hybrid porous materials consist of metal ions linked by organic binding ligands, possessing uniform structures with high specific surface area and tuneable physical and chemical properties. MOFs can act as antimicrobial agents releasing metal ions, such as Ag(I), Cu(II), Co(II), and Zn(II), to prevent bacterial development and infections or oxidizing the protein and fatty acids on the bacterial membranes without the release of metal ions.[2] In addition, MOFs nanoparticles with suitable size can cross the bacterial cell membranes resulting in their destruction. Starting from this assumption, we have decided to investigate the antibacterial activity of zinc and copper MOFs based on different bis(pyrazolyl)-tagged ligands such as $[M(BPZ)]_n$ (M = Zn(II), Cu(II), H_2BPZ = 4,4′-bipyrazole),[3] $[M(BPZ\text{-}NH_2)]_n$ (M = Zn(II), Cu(II); H_2BPZNH_2 = 3-amino-4,4'-bipyrazole)[4] and [Zn(Me_4BPZPh)], [Cu_2(Me_4BPZPh)] (H_2Me_4BPZPh = bis-4′-(3′,5′-dimethyl)-pyrazolylbenzene)[5] (Figure 1). Their antimicrobial activity has been be tested against Gram-negative (*P.s aeruginosa*, *E. coli*), Gram-positive (*S. aureus*) bacteria and also against fungi (*C. albicans*), as representative agents of infections.

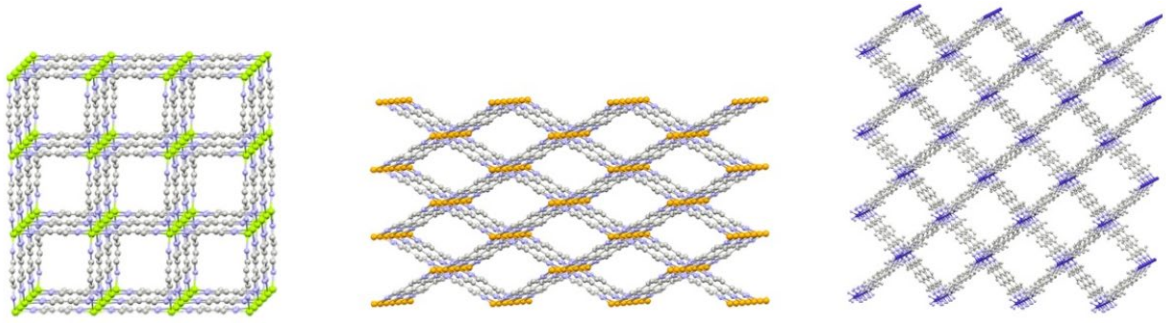

Figure 1 Representation of the crystal structure of (a) $[Zn(BPZ)]_n$ (b) [Cu(BPZ)]n and (c) [Zn(Me_4BPZPh)].

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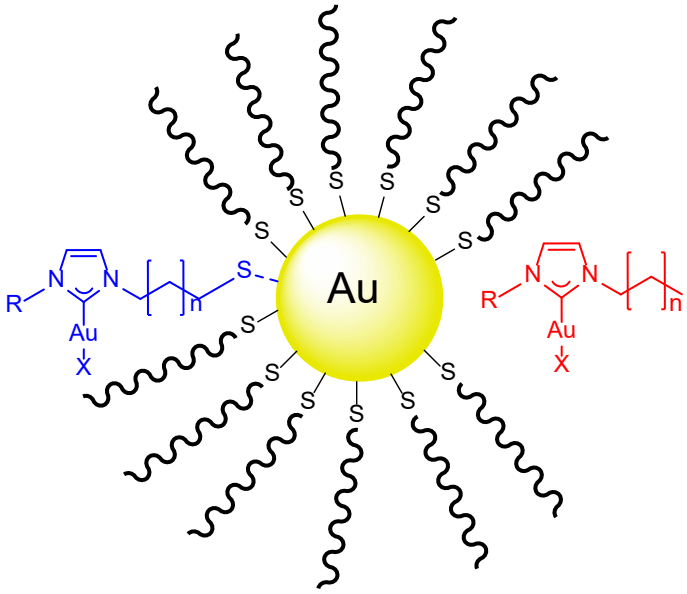
NHC – gold(I) complexes as catalysts encapsulated within monolayer-protected gold nanoparticles

Federica Tresin,[a] Cristina Tubaro,[a] Andrea Biffis,[a] Fabrizio Mancin,[a] Giordano Zanoni,[a] Riccardo Cendron [a]

[a] *Dipartimento di Scienze Chimiche, Università di Padova, via Marzolo 1, 35131 Padova.*

Gold complexes have become extremely important within the field of homogeneous catalysis and, in particular, gold(I) complexes bearing N-heterocyclic carbene (NHC) ligands have been studied as catalysts in a wide range of technologically relevant organic reactions[1]. The encapsulation of these complexes within a supramolecular system, in this case monolayer-protected gold nanoparticles, may influence their activity and selectivity[2]. Consequently, the gold(I) complexes have been designed so that their encapsulation within the nanoparticles can be facilitated by lipophilic interactions using long alkyl chains as N-substituents on the carbene ring, or by covalent interactions with a thiol present at the end of the chain. Preliminary results regarding these two synthetic approaches will be presented herein.



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Characterization of NiTi shape memory alloys

Rubina Troiano[a], Gaetano D'Amora[a], Pietro Magarò[b], Carmine Maletta[b], Pasquale Longo[a] Gaetano Guerra[a]

[a] *Dipartimento di Chimica e Biologia "A. Zambelli", Università degli Studi di Salerno, Fisciano (SA), Italy*
[b] *Dipartimento di Ingegneria Meccanica, Università degli Studi della Calabria, Rende (CS), Italy*

In recent years, the interest in shape memory alloys (SMA) is increased due to their use in many industrial fields, such as automotive, biomedical[1] and aerospace[2]. The present work is focused on the Nichel-Titanium alloys, known as nitinol. Nitinol alloys are generally composed by near-equiatomic composition of nichel and titanium (50/50) and exhibits two main proprieties: shape memory effect and super-elasticity[3]. Both properties are associated to the occurrence of a solid-solid phase transformation involving their austenite (A) and martensite (M) phases[4].
In this contribution, wires of NiTi alloys are characterized by different techniques. In particular, X-ray diffraction[5] and differential scanning calorimetry[6] measurements are used to investigate Martensite- Austenite transition temperature[7] (Figure 1), and mainly their dependence on mechanical strain and on the crystalline phase perfection.

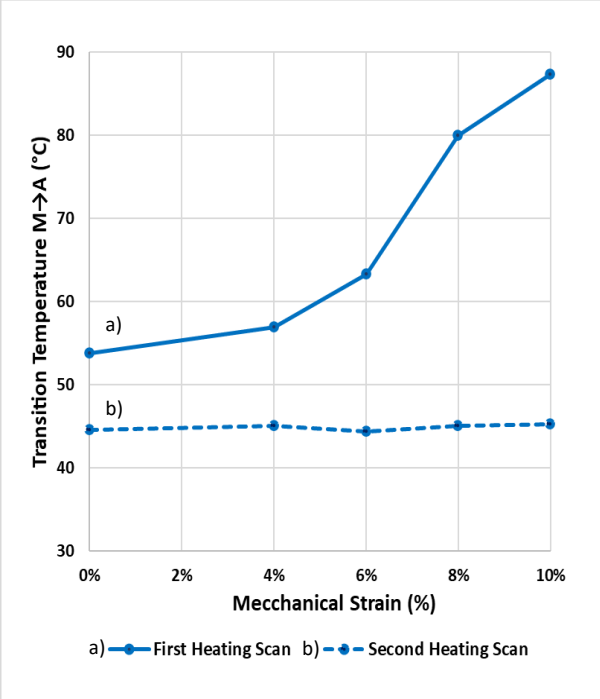

Figure 1. *Influence of mechanical strain on transition temperature M→A of CH samples in a) first Heating scan b) second Heating scan.*

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Synthesis and characterization of novel Zn(II) pyrazolone based hydrazone complexes

Federico Verdicchio [a], Daphne Romani [b], Riccardo Pettinari [a], Claudio Pettinari [a], Alessia Tombesi [b]

[a] School of Pharmacy and [b]School of Science and Technology, Chemistry Division, University of Camerino, via S. Agostino 1, 62032 Camerino MC, Italy.

4-Acyl-5-pyrazolones are O_2-donor ligands whose structure can be easily varied upon functionalization of the acyl fragment to induce different properties to the corresponding metal complexes[1]. This versatile class of ligands can be further modified by reaction with hydrazines affording hydrazone ligands (HN^{R_1,R_2})[2] that can be employed to coordinate Zn^{2+} acceptors, resulting in a set of new monomeric Zinc(II) complexes whose structure is a function of the hydrazone moiety (Figure 1). In detail, with a pyridine ring the ligand acts as tridentate N,N,O-donor, whereas all other groups bring to bidentate N,O-donor ligands with an octahedral Zn environment containing two additional water molecules in *trans* position to each other (Figure 2). However, with a 4-methylbenzenesulfonohydrazide group the steric hindrance prevents the coordination of water and a tetrahedral environment has been observed in the solid state by X-ray crystal studies (Figure 2). The antimicrobial activity of ligands and complexes has been investigated against representative *gram+*, *gram-* and fungal strains.

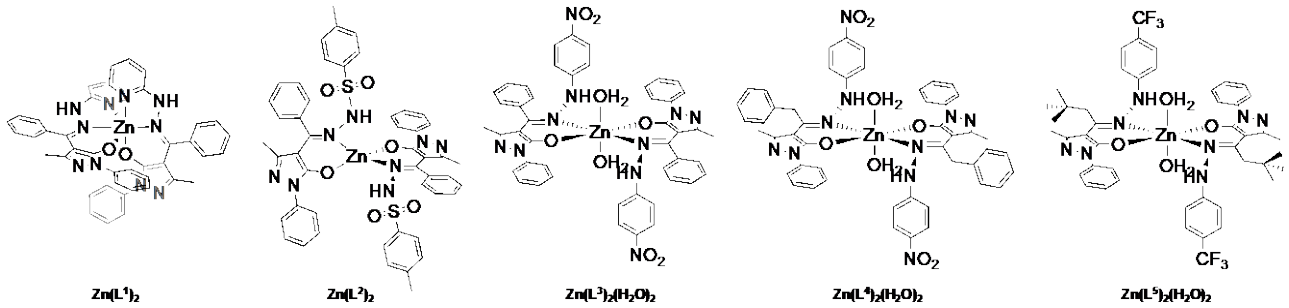

Figure 1

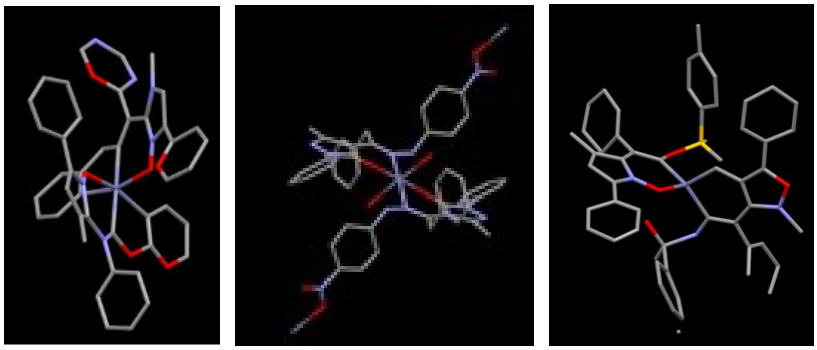

Figure 2

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CO_2 hydrogenation to methanol over PdCu/ZnO catalysts

Alessandro Vomeri,[a] Jonathan Ruiz Esquius,[b] Hasliza Bahruji,[c] Nikolaos Dimitratos,[a] Laura Prati,[a] Alberto Villa[a]*

[a] *Università degli Studi di Milano;* [b] *Cardiff University,* [c] *Brunei University*

The increasing CO_2 concentration in the atmosphere is a global concern, which is going to lead to irreversible climate changes in the near future. Catalytic hydrogenation is being investigated as a very promising route to assess the ever-increasing need for CO_2 transformation into value-added chemicals. Here, the synergistic properties of Pd and Cu metal active sites have been studied towards CO_2 hydrogenation to methanol. Indeed, Cu(0) and Cu(I) have been extensively recognised in the literature as active phases for the reaction[1–5], and it has also been reported that Pd enhances the catalytic activity by H_2 spillover and boosts the performance of Cu-based catalysts[6,7]. Moreover, the use of ZnO as support results in a structural and electronic promoter for Cu-based catalysts[8]. Three catalysts based on Cu (30%wt.), doped with Pd (0.05:1 and 0.01:1 molar to Cu) and supported on ZnO have been prepared by hydrothermal synthesis coupled with Chemical Vapor Impregnation (CVI). Characterization by XRD and XPS analyses allowed us to determine the presence of different metal phases and the metal oxidation state after reduction treatments.
As a main result, we found that catalysts reduction at high temperature prior to the reaction resulted in a high amount of metallic Cu and small amounts of bimetallic alloys of the three metals depending on the relative amount of Cu and Pd. This allowed to obtain very active and selective catalysts compared to a widely employed commercial catalyst ($CuO/ZnO/Al_2O_3$, Alfa Aesar 45776) (Fig. 1).

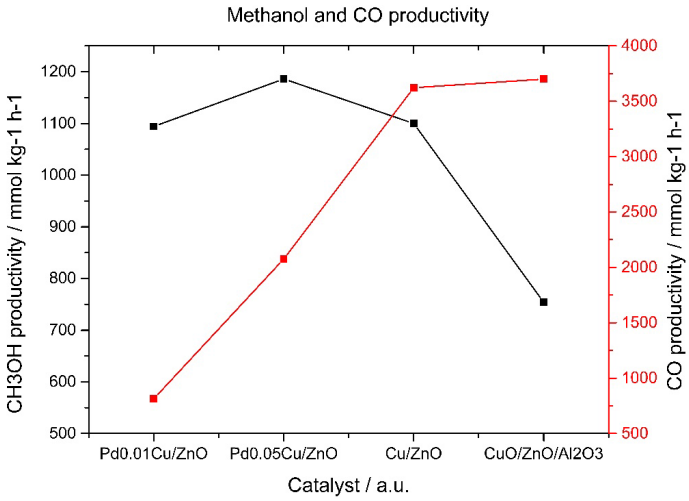

Fig. 1. Methanol and CO productivity for the series compared to the commercial catalyst Alfa Aesar 45776.

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Synthesis and characterization of novel zinc complexes of Schiff bases with photochemical and biological properties

Sonila Xhafa [a], Alessia Tombesi [a], Fabio Marchetti [a], Claudio Pettinari [b], Corrado Di Nicola [a], Stefania Scuri [b]

[a] School of Science and Technology and [b]School of Pharmacy, University of Camerino, Via S. Agostino 1, 62032 Camerino.

Schiff base ligands are an important family of compounds, capable to perform crucial biological activities (e.g. antimicrobial, antioxidant, anti-inflammatory, anticancer, antifungal etc.), that can be enhanced after complexation with transition metal ions[1]. In this context, metal-derivatives antioxidants have received great attention in order to identify their capacity in scavenging free radicals that are related to various disorders and diseases[2]. Schiff-bases show fluorescence, but systematic studies of photo-luminescence of Schiff-base complexes of Zn(II), especially their potential applications in optical and optoelectronic devices (such as organic light emitting diodes and lasers), bio-imaging and chemo-sensors are not well explored[3]. In this study, a series of new zinc(II) complexes with Schiff bases of pyrazolones[4] have been synthesized and fully characterized (Figure 1). The antibacterial activity of ligands and complexes has been tested measuring the Minimum Inhibitory Concentration (MIC) against Gram-positive *S. aureus* and Gram-negative *E. coli* bacteria. Moreover, they have been investigated in the role of antioxidants as effective scavengers of Reactive Oxygen Species (ROS). Furthermore, the optical properties of all of the complexes were investigated by UV/Vis absorption and luminescence spectroscopy both in solution and in the solid state.

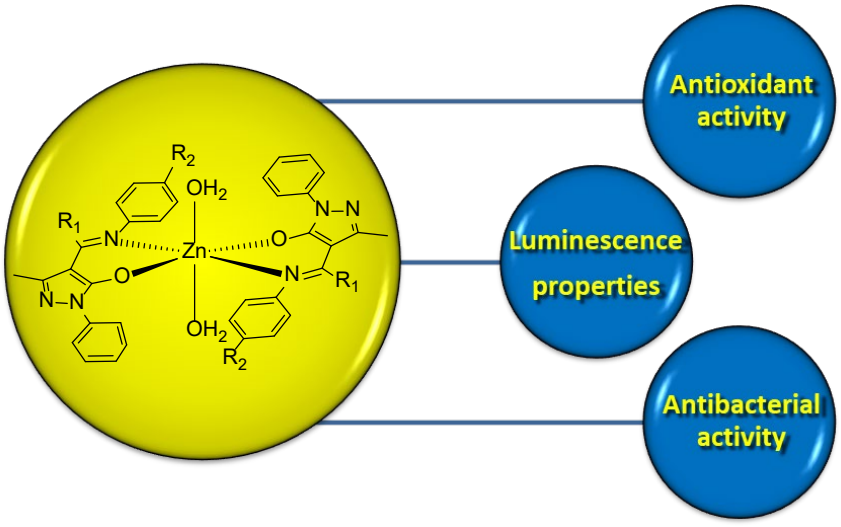

Figure 1

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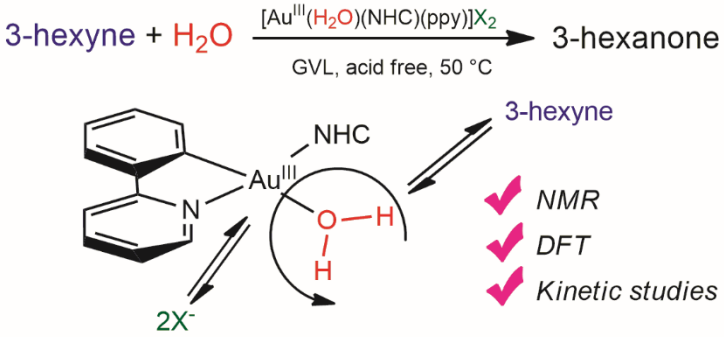
Acid-free hydration of alkynes catalyzed by the gold(III) complex [(ppy)Au(L)Cl]Cl

Jacopo Segato,[a] Flavio Sabatelli,[c] Alessandro Del Zotto,[a] Leonardo Belpassi,[b] Paola Belanzoni, [bc] and Daniele Zuccaccia [a]

[a] Dipartimento di Scienze Agroalimentari, Ambientali e Animali, Sezione di Chimica, Università di Udine, Via Cotonificio 108, I-33100 Udine, Italy.
[b] Istituto di Scienze e Tecnologie Chimiche "Giulio Natta" (SCITEC), Consiglio Nazionale delle Ricerche c/o, Dipartimento di Chimica, Biologia e Biotecnologie, Università degli Studi di Perugia, Via Elce di Sotto 8, 06123 Perugia, Italy
[c] Department of Chemistry, Biology and Biotechnology, University of Perugia, via Elce di Sotto 8, 06123 Perugia, Italy.

Gold(I) catalysis is an area of research of vital importance with many reported examples. Conversely, gold(III)-catalyzed reactions are still in their infancy and the development of knowledge on Au(III) catalysis and stoichiometric reactions, as done for Au(I), is mandatory. Over the last few years, our group has been engaged in the rationalization of important features of gold(I) catalysis,[1] such as the identification of the rate determining step, as well as of the nature of catalytic species and intermediates, and the highlighting of the importance of both ligand (L) and counterion (X) in L-Au-X species. Our most relevant results were obtained in the hydration of alkynes promoted by L-Au-X in both neat conditions and green solvents.[2]
In order to improve the knowledge about the mechanism of Au(III)-mediated hydration of alkynes (Figure), in this contribution [4] we investigated the structure, reactivity and catalytic properties of [(ppy)Au(NHC)Cl]Cl and [(ppy)Au(PPh_3)Cl]OTf complexes [ppy = 2-phenylpyridine, NHC = 1,3-bis(2,6-di-isopropylphenyl)-imidazol-2-ylidene] in γ-valerolactone, under acid-free conditions, by means of solution NMR spectroscopic and computational (DFT) techniques. Importantly, we have found that no reduction of gold takes place during catalysis and both ppy and NHC ligands do not decoordinate from the metal ion. Furthermore, we observed that the preequilibrium[5] is the rate determing step of the reaction.



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Layered Double Hydroxides based on metals with anti-infective properties

[a]*Paola Ricci,* [a]*Anna Donnadio,* [b]*Tamara Posati,* [b]*Marta Giannelli,* [a]*Morena Nocchetti*

[a]*Department of Pharmaceutical Sciences, University of Perugia, via del Liceo 1, 06123 Perugia Italy;* [b]*National Research Council of Italy, Institute of Organic Synthesis and Photoreactivity (CNR-ISOF) Via Piero Gobetti 101, 40129 Bologna, Italy*

Bacterial adhesion and surface colonization can lead to numerous undesirable consequences and are an emerging problem of global concern. So potential remedies are of the utmost necessity and urgency. Transmission via contaminated surfaces has been recognized as an important route for the spreading of pathogens and today, the COVID-19 pandemic has intensified the world's attention toward the spread of contamination facilitated by "high touch" surfaces. In this scenario, the antimicrobial properties of metal-based compounds are potential sustainability solutions for the treatment of infections and also towards communicable diseases. Recently, great efforts have been made to develop nanostructured composite materials in the form of thin coatings, where bioactive species are immobilized on inorganic nanostructured matrices to avoid the development of multidrug-resistant bacterial strains. In this context, layered inorganic materials such as layered double hydroxides (LDHs) [1] are good candidates for this application, as they are characterized by a high structural and chemical variety and therefore offer the possibility of preparing materials with characteristics suitable for the purpose [2]. The properties of these layered inorganic materials allow their use as polymeric fillers for the preparation of composites and the design of anti-infective coatings. In this work, LDHs based on Mg, Cu, Zn, Ga with anti-infective properties were prepared via hydrothermal treatment and by double-microemulsion water-in-oil technique [3] and tested for the anti-infective activity. The obtained LDH particles were characterized by XRD, TGA, ICP, SEM and TEM. The morphological analysis showed that the particles have different size ranging from some hundreds to few tens of nanometers (figure 1).

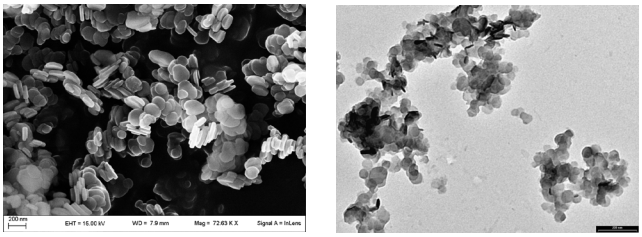

Figure 1. SEM and TEM images of LDHs prepared by hydrothermal treatment on the left and by double-microemulsion water-in-oil technique on the right.

The LDHs were used as filler for PLGA in order to obtain composite films. In vitro preclinical tests will be performed on the specimens to assay under static conditions the performance of the treated material surfaces in comparison with neat polymers or no-treated surfaces.

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PVC grafted zinc oxide nanoparticles as inhospitable surface to microbes

[a,d]Anna Donnadio,[b]Luca Roscini, [c]Alessandro Di Michele, [a]Valentina Corazzini, [b,d]Gianluigi Cardinali, [a]Valeria Ambrogi

[a]Department of Pharmaceutical Sciences, University of Perugia, via del Liceo 1, 06123 Perugia Italy; [b]Department of Pharmaceutical Sciences, University of Perugia, Borgo XX giugno, 06121 Perugia, Italy; [c]Department of Physics and Geology, University of Perugia, Via A. Pascoli, 06123 Perugia, Italy; [d]Centro di Eccellenza CEMIN - Materiali Innovativi Nanostrutturali per applicazioni Chimica Fisiche e Biomediche, University of Perugia, via Elce di Sotto 8, 06123 Perugia, Italy.

Polyvinyl chloride (PVC) is a low-cost and durable polymer used in pipes, food packaging, biomedical devices. However, PVC suffers from microbial colonization by microorganisms present in the living environment and this results in a rise in nosocomial infections leading to severe economic and medical consequences. For this reason, the modification of the PVC surface to obtain an antibacterial material could diminish the risk of infections. In this study, antimicrobial PVC was obtained by a coating of ZnO nanoparticles achieved by grafting mercaptopropyltrimethoxysilane onto PVC [1] followed by the growth of zinc oxide nanoparticles covalently bonded on the polymer surface. The relationship, between the physicochemical features of modified-surface PVC and antimicrobial activity on *Candida albicans* (CMC 2020) and *Staphylococcus aureus* (PI 6870) isolated in Pisa hospital from patient blood culture and diabetic foot, respectively, was investigated. Zinc oxide with controllable morphologies (rods, rod flowers, and petal flowers) was grown up on the polymer surface by a hydrothermal process, tuning the base type and concentration. SEM and EDX analysis showed that the coatings were homogeneous.

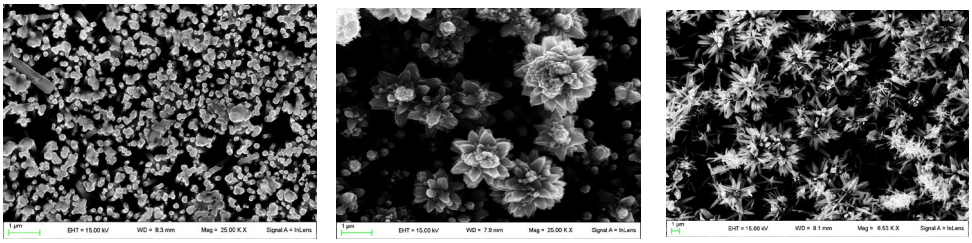

Figure 1. SEM images of the different morphologies of ZnO onto PVC surface.

ZnO coated PVC showed a better antibacterial performance than the controls. The antimicrobial activity was more pronounced for rod flower morphology, because of their differences in microscopic parameters such as specific Zn-polar planes. This work provides an important hint for the safe use of PVC for biomedical devices by the structure surface tuning without injuring polymer bulk properties and a reduced risk of the covalently bonded nanoparticle dispersion in the host and the environment.

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CHIMICA ORGANICA (ORG)

- Orals
- Posters

Nanocages and capsules for drugs and peptides delivery

Alessandro Ajó [a], Maria Sancho-Albero [b] and Luisa De Cola [a,b]

[a] *Università degli Studi di Milano, 20133 Milano*

[b] *Department of Molecular Biochemistry and Pharmacology, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, 20156 Milano*

The problem related to the delivery of biomolecules rely on their fragility and low solubility that prevent a systemic administration and requires a protection during their circulation.

Amongst the many nanocarriers proposed in the literature, liposomes and polymeric[1] systems have been quite successful but the number of biomolecules entrapped and the size of the nanocarriers remain a problem. However more recently silica has emerged as delivery system.[2]

In this study we report two different multifunctional carriers based on organosilica nanoparticles, NPs, able to entrap not only small molecules but also large biomolecules. Such NPs can also be an active component of a more complex soft structures, hybrid hydrogels.

Breakable capsules have been synthesized with a backbone of silica and disulfide bonds allowing the breakability within a reducing environment such as glutathione present in every cell and in very large amount in cancer tissues.[3] To reduce the size 10 and 20 nm silica nanocages were also synthesized according to modify literature procedures[4] and we have shown that small molecules can be entrapped and release on demand. Furthermore, they can be functionalized with a broad range of chemical groups including cell and barrier penetrating peptides.

Preliminary experiments are ongoing to demonstrate the Blood Brain Barrier, BBB, penetration of such systems.

The systems have a very high monodispersity and the cage structure confer very special properties such as their escape from macrophages[5]

These materials present different advantages such as high biocompatibility, degradability, large surface area for drug loading, stability and low costs.[6]

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Cationic Copolymers: A Promising Option in the Treatment of Drug Resistance in Neuroblastoma Cells

Silvana Alfei [a,], Barbara Marengo [b], Giulia Elda Valenti [b] and Cinzia Domenicotti [b]*

[a] Department of Pharmacy, University of Genoa, Viale Cembrano, 16148 Genoa, Italy; [b] Department of Experimental Medicine (DIMES), University of Genova, Via Alberti L.B., 16132 Genoa, Italy

Drug resistance is a multifactorial phenomenon that limits the action of antibiotics and chemotherapeutics, thus making urgent the development of new therapeutic strategies capable of inducing cytotoxic effects circumventing chemoresistance. Natural and synthetic cationic peptides and polymers has given satisfactory results both in microbiology, as antibacterial agents, and in the oncological field, resulting effective against several tumors, including human neuroblastoma (NB) [1,2]. To this end, we synthetized, characterized, and tested on etoposide-sensitive (HTLA-230) and -resistant (HTLA-ER) human NB cells [3], two ammonium chloride polystyrene-based copolymers P5 (Figure 1a) and P7 (Figure 1c).

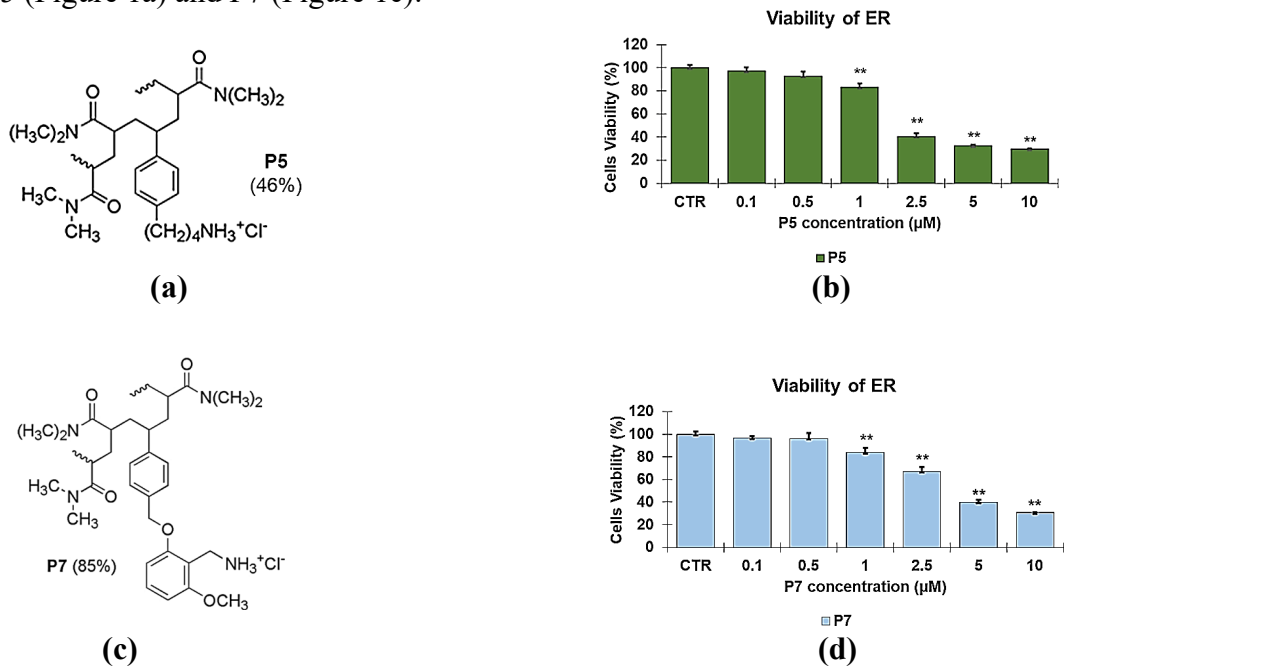

Figure 1. Structure of copolymer P5 (a) and P7 (c). ER NB cells viability when exposed to increasing concentrations of P5 (b) and P7 (d).

Both copolymers were water-soluble, showed a positive surface charge, due to nitrogen atoms which resulted protonated in the whole physiological pH range, and showed values of Z-potential favorable to stability in solution [4]. P5 and P7 exhibited excellent buffer capacity, useful to escape lysosome deactivation once inside cells, nanosized particles and were able to reduce NB cell viability in a concentration-dependent way (Figure 1b and 1d) [4]. Interestingly, a significant increase in reactive oxygen species (ROS) production was observed in both NB cell populations treated with P5 or P7 establishing, for both copolymers, an unequivocal correlation between cytotoxicity and ROS generation [4]. Unexpectedly, the ROS-related cytotoxic effects of both copolymers were even higher on HTLA-ER cells, thus proving that P5 and P7 could be promising template macromolecules for the development of new chemotherapeutic agents able to fight NB chemoresistance [4].

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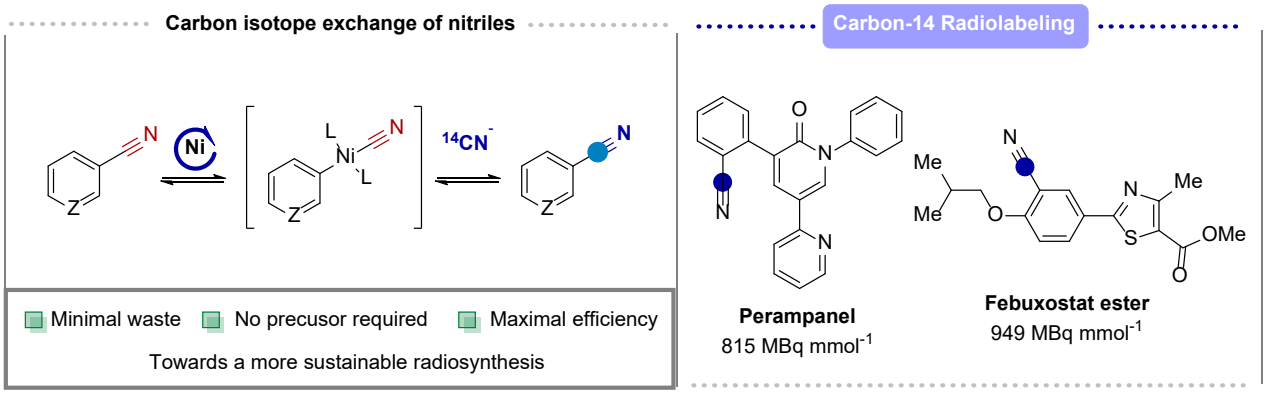
Direct Carbon Isotope Exchange of Pharmaceuticals via Reversible Decyanation

Minghao Feng, [a] *Joao De Oliveira,* [a,b] *Antoine Sallustrau,* [a] *Gianluca Destro,* [a] *Sebastien Roy,* [c] *Thibault Cantat,* [a] *Charles S. Elmore,* [b] *Jorg Blankenstein,* [c] *Frédéric Taran,* [a] *Davide Audisio* [a]*

[a] *Université Paris Saclay, CEA, DMTS, Service de Chimie Bio-organique et Marquage, Gif-sur-Yvette, France* [b] *Isotope Chemistry, Pharmaceutical Science, R&D, AstraZeneca, Gothenburg, Sweden.* [c] *Isotope Chemistry, Integrated Drug Discovery Sanofi R&D, Vitry-sur-Seine, France.*

Carbon-14 radiolabeling is a unique tool that, in association with β-counting and β-imaging technologies, provides vital knowledge on the fate of synthetic organic molecules such as pharmaceuticals and agrochemicals [1]. Traditional multistep synthesis and the associated costs have limited its utilization. While hydrogen isotope exchange reactions are routinely utilized for deuterium and tritium labeling, in the field of carbon isotope, this concept has long remained unexplored and it was thus far limited to the utilization of $^{14}CO_2$ [2].
Recently, we report on a nickel-catalyzed dynamic carbon isotope exchange with $Zn(^{14}CN)_2$, a readily available source of radiocarbon [3]. This new process expands the concept of late-stage carbon radiolabeling with substrates bearing Csp^2 nitriles and provides a direct access to end-use labeled pharmaceuticals.



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Antibacterial and physicochemical properties of quatsomes formulated with L-prolinol-derived surfactants

Sara Battista,[a] *Mariana Köber*,[b,c] *Pierangelo Bellio*,[d] *Giuseppe Celenza*,[d] *Guillem Vargas-Nadal*, [b] *Jaume Veciana*,[b,c] *Nora Ventosa*, [b,c] *Luisa Giansanti*[a]

[a] *Dipartimento di Scienze Fisiche e Chimiche, Università degli Studi dell'Aquila, Via Vetoio, 67010 Coppito (AQ) (Italy);* [b] *Institut de Ciència de Materials de Barcelona (ICMAB-CSIC), Esfera UAB; Campus UAB s/n; E-08193 Cerdanyola del Vallès, Spain;* [c] *Networking Research Center on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Campus Universitari de Bellaterra, E-08193 Cerdanyola, Spain;* [d] *Dipartimento di Scienze Cliniche Applicate e Biotecnologie, Università degli Studi dell'Aquila, Via Vetoio, 67010 Coppito (AQ) (Italy).*

Quatsomes are homogeneous and very stable vesicles composed of cholesterol (chol) and micelle-forming quaternary ammonium surfactants. In this investigation quatsomes containing chol and one of the six synthetic *L*-prolinol derivatives (Figure 1) were prepared according to *Depressurization of an Expanded Liquid Organic Solution-Suspension* methodology.[1] These structurally related surfactants, that differ for the chain length (12, 14 or 16 carbon atoms) and for the headgroup charge (cationic or zwitterionic), have previously been shown to increase the efficacy of several active principles when included in liposomal delivery systems.[2] They can't be components of conventional liposomes at high percentages due to their high detergent action. Consequently, their inclusion in quatsomes grants two main advantages: *i*) to obtain homogeneous nanovesicles that are stable over months *ii*) to include in the formulations 50 molar percentage of surfactant, thus enhancing their pharmacological potential. Quatsomes were widely characterized from the physicochemical point of view to find out the relation between their composition and the aggregates properties. Moreover, (+)-usnic acid (UA), a natural substance that shows several pharmacological activities, [3] was also included in quatsomes to investigate their potentiality as drug delivery systems. The dependence of the antibacterial/antioxidant activity of each formulation was correlated to the molecular structure of the components and, in the presence of UA, also to the inclusion procedure.

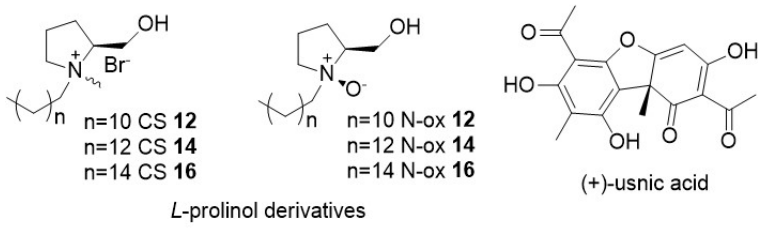

Figure 1. Quatsomes synthetic components and (+)-usnic acid

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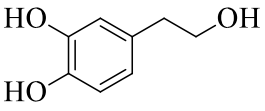
Hydroxytyrosol, much more than an antioxidant

Roberta Bernini, Elisa Pannucci, Mariangela Clemente, Luca Santi

Dipartimento di Scienze Agrarie e Forestali, Università degli Studi della Tuscia, Viterbo

Hydroxytyrosol (HTyr) is a low-molecular weight phenol available on a large scale and in high purity in our laboratories thanks to a patented synthesis starting from tyrosol [1].



Hydroxytyrosol (HTyr)

HTyr is a bioactive constituent of olive fruits (16.6 mg/Kg) [2]. During the production of extra virgin olive oil, a high quantity of wastes consisting of free-oil olive pulp (solid) and olive mill wastewaters (liquid) is obtained. Based on the hydrophilic properties, this process tends to deplete HTyr from olive oil enriching the wastes. They represent a serious environmental problem for olive oil producers due also to remarkable content in organic matter such as polyphenols, which are responsible for high toxicity. However, according to the circular economy approach [3], these wastes represent a source of precious compounds to valorize. In this context, standardized HTyr-enriched extracts are obtained from olive oil by-products through sustainable processes based on membrane technologies [4]. HTyr is of high interest for the food and pharmaceutical industry mainly for the strong antioxidant activity [5]. In this communication, several studies performed on pure HTyr and HTyr-enriched extracts obtained by olive oil by-products as well as the synthesis of novel HTyr-derived compounds of pharmacological interest in collaboration with other research groups will be described [6].

This work was supported by the Ministero dell'Università e della Ricerca with the PRIN 2017 (20175XBSX4) entitled "Targeting Hedgehog pathway: virtual screening identification and sustainable synthesis of novel Smo and Gli inhibitors and their pharmacological drug delivery strategies for improved therapeutic effects in tumors".

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Diels-Alder type adducts from *Morus nigra* as potent inhibitors of *Micobacterium tuberculosis* PtpB

Andrea Calcaterra,[a] Alessandra Mascarello,[b] Mattia Mori,[c] Bruno Botta,[a] Hernán Terenzi[b]

[a] Dipartimento di Chimica e Tecnologie del Farmaco, Sapienza Università di Roma, P.le Aldo Moro 5, 00185, Roma, Italy; [b] Centro de Biologia Molecular Estrutural, CEBIMEUFSC, Universidade Federal de Santa Catarina, Campus Trindade, 88040-900, Florianopolis, SC, Brazil; [c] Dipartimento di Biotecnologie, Chimica e Farmacia, Università degli Studi di Siena, Via Aldo Moro 2, 53100, Siena, Italy.

Mycobacterium tuberculosis (Mtb) protein tyrosine phosphatases B (PtpB) is an essential key extracellular protein, that have been recognized as potential molecular targets for the development of new therapeutic strategies against tuberculosis (TB). [1-3] Recently, the naturally occurring Diels-Alder-type adduct kuwanol E (Fig.1) have been reported by our group to be a potent inhibitor of PtpB (K_i = 1.6 ± 0.1 mM). [4] Herein, we isolated additional Diels-Alder type adducts from *Morus nigra* roots bark that are capable to inhibit PtpB at sub-micromolar concentrations. [5] The two most potent compounds, namely kuwanon G and kuwanon H (Fig. 1), showed lower K_i with respect to kuwanol E in competitive inhibition assays, moreover the kinetics and mass spectrometry studies suggested their interaction with the active site of the enzyme. These interactions have been further characterized by molecular docking, intrinsic fluorescence analysis, and isothermal titration calorimetry. Finally, kuwanon G showed inhibition of Mtb growth by 61.3% in a Mtb survival assay inside macrophages. All these findings highlight that the common Diels-Alder-type adduct scaffold is relevant for the development of PtpB inhibitors as drug candidates for the treatment of TB.

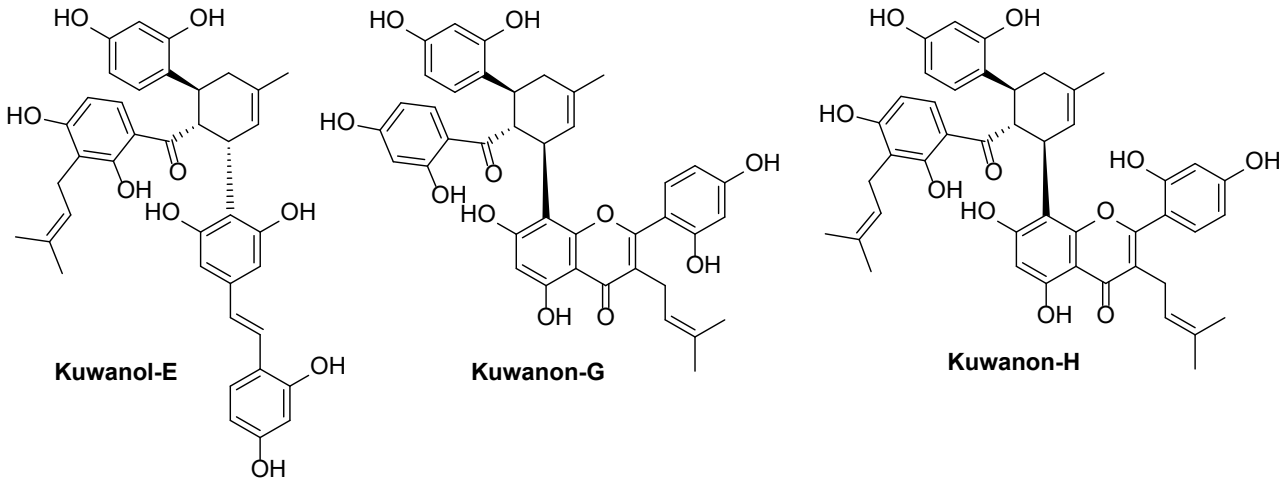

Figure 1. Chemical structure of Diels-Alder type adducts from M. nigra root bark.

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Carbohydrate-Mediated "Innate" Considerations in Designing Vaccine-Candidates

Fabrizio Chiodo [a,b]

[a] *Institute of Biomolecular Chemistry, National Research Council (CNR), Pozzuoli, Napoli, Italy*
[b] *Finlay Vaccine Institute, 200 and 21 Street, Havana 11600, Cuba*

Carbohydrates play key immunological roles at the host-pathogens interface, and these interactions are extremely important while designing vaccine-candidates against infectious diseases. The traditional mechanism of action of conjugate-vaccines considers the peptides generated from the immunogenic carrier proteins (toxoids etc) to be responsible of T-cells activation, B-cells maturation and antibodies production. However, in conjugate-vaccines, the carbohydrates could play a two-faced role: they are the antigens able to elicit specific anti-carbohydrate immune responses, and at the same time they could work as an immune-potentiator to enhance the immune responses to themselves. We demonstrated the active involvement of some *S. pneumoniae* polysaccharides in determining a series of *in vitro* innate immune responses in human. Peripheral blood mononuclear cells were stimulated with approved and in clinical use *S. pneumoniae* Cuban carbohydrate-based vaccine coupled to the carrier tetanus toxoid and different read-out have been measured. In addition, we also recently applied a rational "glyco-approach" to design different subunit SARS-CoV-2 vaccine-candidates now in clinical trial in Cuba. In conclusion, our results aim at considering carbohydrate-mediated "innate" interactions while designing vaccine-candidates against infectious diseases.

Selective Integrin Ligands Promote Cell Internalization of the antineoplastic agent Fluorouracil

*Martina Cirillo[a], Monica, Baiula[b], Giulia Martelli[a], Valentina Giraldi[a], Elisa Gasparini[a], Santi Mario Spampinato[b], Daria Giacomini[a]**

[a] *Department of Chemistry "G. Ciamician", University of Bologna, Via Selmi 2, 40126 Bologna, Italy;*
[b] *Department of Pharmacy and Biotechnology, University of Bologna, Via Irnerio 48, 40126 Bologna, Italy*

Drug conjugates for cancer therapy consist of an antineoplastic drug and a targeting receptor ligand and they have the aim to overcome the heavy side effects of unselective anticancer agents. Our project is based on the study of agonist and antagonist integrin ligands as targeting head of molecular cargoes for the selective delivery of 5-fluorouracil (5-FU) to cancer or non-cancer cells.
Integrins are adhesion receptors that mediate dynamic adhesive cell-cell and cell-matrix interactions; because of the important roles of integrins and their ligands in biological development, immune responses, leukocyte traffic, haemostasis, and cancer, their potential as therapeutic tools is now widely recognized. [1]
Our research group recently developed a library of novel agonist integrin ligands characterized by a beta-lactam scaffold [2,3] and demonstrated that these compounds could promote integrin trafficking and endocytosis.
At first two fluorescent β-lactam-based integrin ligands were synthesized and tested for an effective and selective internalization mediated by $\alpha_4\beta_1$ or $\alpha_5\beta_1$ integrins in Jurkat and K562 cells, respectively. Afterwards, three conjugates composed by the β-lactam ligand, suitable linkers, and 5-FU were realized (Figure 1).

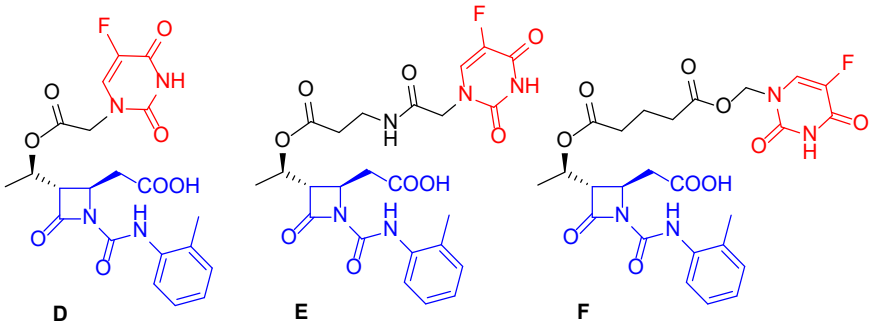

Figure 1. New 5-FU-conjugates designed to evaluate the selectivity of the anticancer effect.

Finally, the three 5FU-conjugates **D**, **E**, and **F** were evaluated by apoptosis assays in Jurkat, K562, and HEK 293 cells.

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Chemoselective disulfide-coupling for the semisynthesis of ubiquitinated forms of the Alzheimer's associated protein tau

Mariapina D'Onofrio,[a] Francesca Munari,[a] Carlo G. Barracchia,[a] Francesca Parolini,[a] Daniele Trivellato,[a] Roberto Tira,[a] and Michael Assfalg[a]

[a] *University of Verona, Department of Biotechnology, Strada le Grazie, Verona, Italy*

The microtubule-associated protein tau is an intrinsically disordered protein, abundant in neuronal axons, where it promotes microtubule assembly and stabilization. Abnormal accumulation of tau is associated with Alzheimer's disease, frontotemporal dementia, and other neurodegenerative disorders collectively referred to as tauopathies [1]. Post-translational modifications are key regulators of tau function and dysfunction. Ubiquitinated tau has been shown to accumulate in both early and intermediate stages of disease, and is a component of neurofibrillary tangles [2]. Mounting evidence suggests that, beyond acting as a signal for degradation, ubiquitination plays a role in modulating tau aggregation [3].

To facilitate our understanding of how ubiquitin influences the structural transitions and interactions that precede the irreversible accumulation of tau, we have optimized a semisynthetic strategy that allows for the site-specific introduction of single or multiple ubiquitin molecules on the protein substrate. We used disulfide-directed ubiquitination as an efficient method to produce modified proteoforms in high yield for subsequent biophysical investigation. The method is based on a disulfide forming reaction between a cysteine residue on tau and a ubiquitin molecule bearing a C-terminal thiol. We successfully produced tau modified with a single mono-ubiquitin, or di-ubiquitin, in different positions, and characterized their functional interactions and aggregation propensity [4,5].

To further characterize the transition of tau toward toxic species we are exploring cysteine-selective bioconjugation to produce multiple mono-ubiquitined tau protein. To increase the yield of the bioconjugate, we operate in denaturing conditions to overcome problems related to steric hindrance. Our results allowed us to establish relationships between the sites and type of ubiquitin modification and the molecular behavior of tau proteoforms.

Acknowledgements: This work was supported by a grant from the Alzheimer's Association (AARG-17-529221).

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New potential carbonic anhydrase inhibitors based on mono and multivalent sugars and iminosugars

Maria Giulia Davighi [a] Camilla Matassini,[a] Francesca Cardona,[a] Andrea Goti [a], Andrea Angeli,[b] Fabrizio Carta, [b] Claudiu T. Supuran [b]

[a] Dipartimento di Chimica 'Ugo Schiff', University of Firenze, via della Lastruccia 3-13, 50019 Sesto Fiorentino (FI), Italy. E-mail: mariagiulia.davighi@unifi.it. [b] Dipartimento Neurofarba, Sezione di Scienze Farmaceutiche e Nutraceutiche, Università degli Studi diFirenze, 50019 Florence, Italy;

Human carbonic anhydrases are ubiquitous zinc enzymes that catalyse the reversible hydration of carbon dioxide to bicarbonate and proton, a fundamental reaction connected to many important physiological processes based on gas exchange, ion transport and pH balance. There are 15 known isoforms in humans (hCAs) belonging to the α-family which differ for tissue distribution and cellular localization and which have become targets for the design of inhibitors (CAIs) with biomedical applications (e.g. diuretic, antiglaucoma, anticonvulsant, antiobesity drugs).[1] Most of these inhibitors contain a primary sulfonamide moiety, which binds to the CA active-site zinc ion essential for the catalytic activity. Nevertheless, the large number of hCA isoforms requires new increasingly selective inhibitors to avoid side effects due to the indiscriminate inhibition of isoforms not involved in a certain pathology.[1] Following the 'sugar approach', the introduction of a sugar moiety permitted the development of more selective inhibitors with polar or charged tails, thus impairing their ability to diffuse through lipid membranes.[2] Carbohydrates are widespread in biologically activity compounds, influencing their pharmacokinetics, drug targeting, and mechanism of action. Another strategy recently developed to address the selectivity of CAIs relies on the use of multivalent CA-directed pharmacologic agents; especially, carbohydrate–protein interactions are notably weak at the monomer level but are enhanced if the ligand is displayed in a multivalent way.[3] In this communication we report the synthesis and biological evaluation of monovalent and multivalent compounds containing both the sulfonamide group and a sugar or azasugar moiety (Figure 1), in order to highlight the presence of a multivalent effect and the behaviour of azasugar vs. sugar moieties.

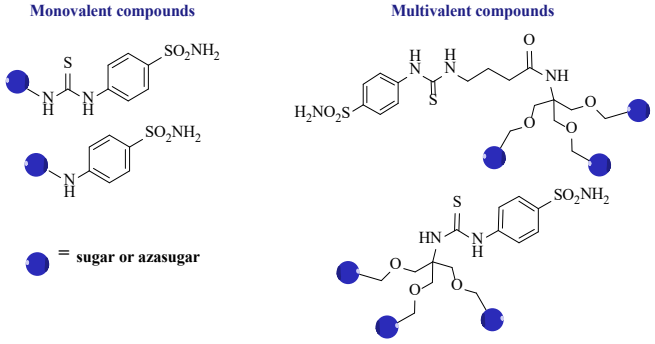

Figure 1: potential mono and multivalent carbonic anhydrase inhibitors.

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N-glycan from Paramecium bursaria Chlorella virus MA-1D: re-evaluation of the oligosaccharide common core structure

Immacolata Speciale,[a] Eric Noel,[b] Irina Agarkova,[b] Antonio Molinaro,[c] James Van Etten,[b] Cristina De Castro[a]

[a] University of Napoli, Department of Agricultural Sciences; [b] Nebraska Center for Virology, University of Nebraska, Lincoln, NE 68583-0900, [c]University of Napoli, Department of Chemical Sciences

Paramecium bursaria Chlorella virus MA-1D is a chlorovirus able to infect *Chlorella variabilis* strain NC64A, a symbiont of the protozoan *Paramecium bursaria*. This virus has a 339-kb genome encoding ca. 366 proteins and 11 tRNAs. Similarly to other chloroviruses [1-4], its major capsid protein (MCP) is decorated with *N*-glycans, whose structure has been here established by using nuclear magnetic (NMR) spectroscopy. This analysis discloses the presence of two *N*-linked oligosaccharides that differ in the not stoichiometric presence of three monosaccharides, with the largest made of eight monosaccharides organized in a highly branched fashion. Importantly, the N-glycan structures share several traits with those of the other chloroviruses, as that of the prototype strain, PBCV-1, except the one that regards the oligosaccharide of the conserved core region, that in this virus misses the distal xylose unit (Figure 1). This finding makes us to reconsider the essential features of the common core region of chloroviruses.

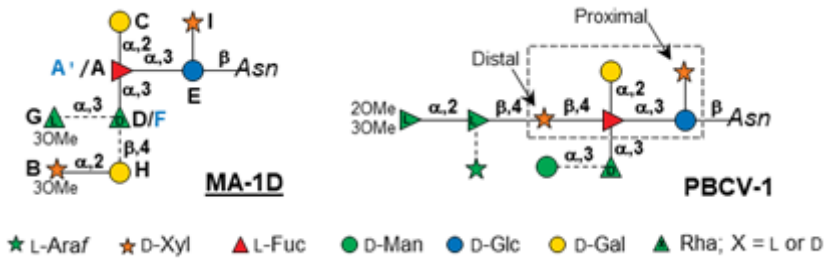

Figure 1. N-glycan structure of *Paramecium bursaria* MA-1D virus. *N*-glycans of the prototype chlorovirus PBCV-1 [1], is given for comparison. Monosaccharides connected by dashed lines are non-stoichiometric substituents. Grey box encloses the conserved pentasaccharide core structure common to all chloroviruses analyzed to date. All sugars are in the pyranose form except where specified. Letter labels on MA-1D glycan structure are those used during NMR assignment: black letters identify the largest glycoform; in blue those referring to the short one.

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Design, synthesis, and evaluation of small molecules Proteolysis Targeting Chimeras (PROTACs) to induce androgen receptor degradation

Desantis Jenny,[a,#] *Michela Eleuteri,*[a] *Aurora Valeri,*[b] *Isaac Yi Kim,*[c] *and Gabriele Cruciani*[a]

[a] *Department of Chemistry, Biology and Biotechnology, University of Perugia, 06123 Perugia, Italy;* [b]*Molecular Horizon, srl, Bettona 06084, Italy;* [c] *Rutgers Cancer Institute of New Jersey and Division of Urology, the State University of New Jersey, New Brunswick, New Jersey, USA;* [#] *present address: Department of Molecular Medicine, University of Padua, 35121 Padova, Italy.*

In recent years, the proteolysis targeting chimeras (PROTACs) technology has gained tremendous attention thanks to its promise for the discovery and development of completely new therapeutic interventions focused on the degradation of disease-related proteins.[1] PROTACs are hetero-bifunctional small molecules in which a protein of interest (POI) ligand and an E3 ubiquitin ligase ligand are linked together through an appropriate linker.[2] The forced close proximity between POI and E3 ligase triggers POI polyubiquitylation and its subsequent proteasomal-dependent degradation.[2] To date, a number of literature studies have proven insights into the feasibility of PROTAC strategy in inducing the degradation of several proteins involved in a variety of cancer types and other diseases.[1,2] Additionally, several PROTACs have entered clinical trials and some of them have shown encouraging results, such as the first oral PROTACs ARV-110 and ARV-471, thus resulting in a greater enthusiasm for PROTAC research.[3]

Recently, we decided to exploit the targeted proteasomal-dependent degradation of the androgen receptor splice variant 7 (AR-V7) in order to identify an innovative treatment for lethal prostate cancer.[4] Indeed, although second-line antiandrogen therapy (SAT) is the standard of care in men with castration-resistant prostate cancer (CRPC), resistance inevitably occurs.[5] One of the major mechanism of resistance to SAT involves the emergence of androgen-receptor (AR) splice variants, such as AR-V7, which are constantly activated and lack the AR domains that are targeted by existing AR-directed therapeutics.[6]

In the present study, the design, synthesis, and *in vitro* biological characterization along with preliminary pharmacokinetic studies of a series of AR-V7 degraders will be presented.

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Investigation of the molecular recognition of sialoglycans bound to Siglec-like adhesins of *Streptococcus gordonii*

Cristina Di Carluccio[a], Barbara A. Bensing[b], Antonio Molinaro[a,c], Roberta Marchetti[a], Alba Silipo[a]

[a] Departement of Chemical Sciences, University of Naples Federico II, Naples, Italy; [b] San Francisco Veterans Affairs Medical Center and University of California, San Francisco, USA; [c] Graduate School of Science Osaka University 1-1 Machikaneyama, Toyonaka, Osaka, Japan.

Streptococcus gordonii and *Streptococcus sanguinis*, commensal species among the normal oral microbiota, become opportunistic pathogens that can cause infective endocarditis (IE) when they enter the bloodstream [1]. The presence on the microbial surface of "Siglec-like" serine-rich repeat adhesins may increase the propensity of streptococci to cause IE. These adhesins contain Siglec-like binding regions (SLBRs) that recognize α2-3 sialylated glycan structures, including O-linked glycans displayed on salivary MUC7, platelet GPIb and several mucin-like plasma proteins [2].
GspB and Hsa are Siglec-like serine-rich repeat adhesins of *S. gordonii* strains M99 and Challis, respectively, that can mediate *Streptococcus* adhesion to platelet membrane glycoproteins. Although their high-resolution crystal structures have been published [3,4], the determinants of ligand specificity have not been fully explained. Thus, unveiling the molecular mechanism of host glycans recognition by Siglec-like adhesins represents a prerequisite to deep understand the different selectivity and flexibility of the streptococcal adhesins towards sialoglycans. We indeed explored the recognition and binding process of SLBRs of GspB, highly selective, and Hsa, which instead shows broader sialoglycans specificity (figure 1). Our outcomes were achieved by a combination of NMR ligand-based methods, such as Saturation Transfer Difference NMR, WaterLOGSY and transferred NOESY, as well as computational approaches, including CORCEMA-ST analysis, docking and Molecular Dynamics [5,6].

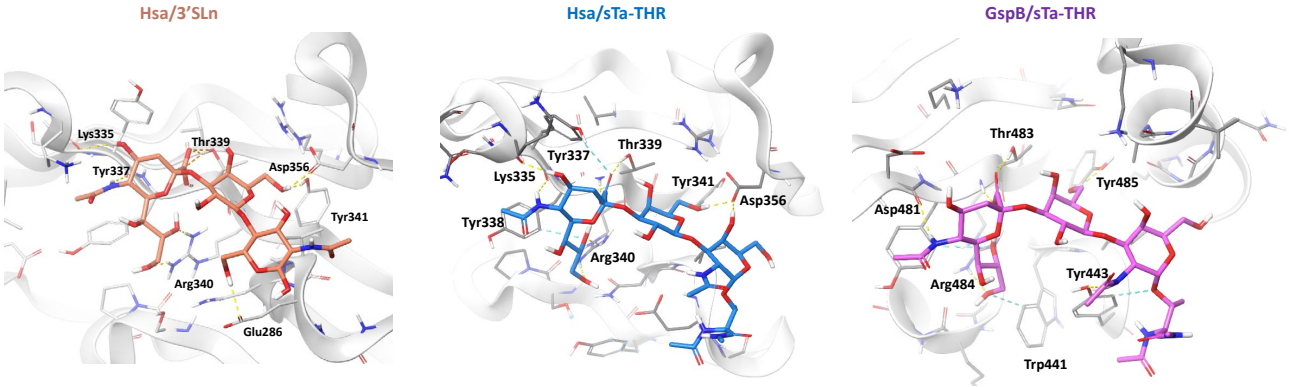

Figure 1. 3D view of Hsa and GspB with different sialoglycans. 3'SLn: 3'-Sialylactosamine; sTa-Thr: sialyl-T-antigen linked to a threnonine.

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Structural characterization of the lipooligosaccharide and capsular polysaccharide from the psychrotrophic bacterium *Pseudoalteromonas nigrifaciens* Sq02

Rossella Di Guida[1], Angela Casillo[1], Maria Michela Corsaro[1]

[1]Department of Chemical Sciences, University of Naples Federico II, Complesso Universitario Monte S. Angelo, Via Cintia 4, 80126, Naples, Italy

The dominant part of the biosphere is cold, the polar regions and the oceans representing 14 and 71% of the earth's surface, respectively. These regions are the natural habitat for cold adapted bacteria. These species are able to thrive at low temperatures since have developed a wide range of physiological and structural adaptations,[1] many of which are only beginning to be understood. The discovery and understanding of the adaptation mechanisms are the keys to a more global view of the ecological roles of microbial communities in cold ecosystems. Moreover, these species and their biomolecules have promising biotechnological applications as cell factories for the production of heat-sensitive compounds and in a wide range of industry from pharmaceutical to cosmetic and food, and environmental biotechnology.[2]

The aim of this project is the structural characterization of lipopolysaccharides (LPSs) and exopolysaccharides (EPSs) isolated from cold adapted Gram-negative bacteria, to understand the relationship between the structure of these macromolecules and their involvement in cold adaptation. Among the bacteria examined there is *Pseudoalteromonas nigrifaciens* Sq02, grown at 18 °C, a psychrotrophic bacterium isolated from the intestine of a Seriola quinqueradiata, a fish species native to the northwest Pacific Ocean. It has been demonstrated that the LOS of this bacterium and that isolated from *Pseudoalteromonas haloplanktis* TAC 125,[3] a psychrophilic bacterium belonging to the same genus, show an identical structure. Moreover, *Pseudoalteromonas nigrifaciens* Sq02 produces a capsular polysaccharide (CPS), the structure of which was established by chemical and spectroscopic experiments. This polysaccharide contains the rare monosaccharide 2-acetamido-2-deoxy-D-mannuronic acid.

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Switching the anticancer effect to HIV protease inhibition: new heteroaryl-amidic compounds with a pseudo-symmetric *core*

Maria Funicello, [a] *Rosarita D'Orsi*, [a] *Lucia Chiummiento*, [a] *Paolo Lupattelli*, [a] *Maria Francesca Armentano* [a] *and Federico Berti.* [b]

[a] *Dipartimento di Scienze, Università della Basilicata, Via Ateneo Lucano 10, 85100 Potenza*
[b] *Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Trieste, Via Giorgieri 1, 34127 Trieste*

During the past two decades, great efforts have been devoted to the discovery of new drugs for the treatment of human immunodeficiency virus (HIV) infection. Among the different biochemical targets for antiviral therapy development, HIV-1 protease remains the most addressed, and its inhibitors continue to play an important role in the treatment of the infection. (1) During our investigation on new peptidomimetics and non peptidic inhibitors we found beneficial effect of heteroaryl rings. (2,3)

In this communication we will report the synthesis of compounds prepared starting from a common hydroxyetylaminic core with the presence of either H or benzyl as R_1 group (Figure 1) who was involved in the linkage with different heteroarylcarboxy acids (X = O, NH, S) and solfonyl chlorides (R_3 = 4-OMe, 3,4-di-OMe, 4-NO_2). Potential change and improvement of the biological activity by modifying the structure in P2 and/or in P2' moieties will be discussed. In particular, a new series of compounds containing both heterocycles moiety and pseudo-symmetric hydroxyethylaminic *core* were obtained in few steps and high yields by using a simple synthetic path. Furthermore, diversity-oriented synthesis was studied to change different functionalities according to needs. Some synthetic intermediates showed important anti-cancer effects (4) which were lost in some cases when the heteroaryl group was present in the final HIV-1 protease inhibitors.

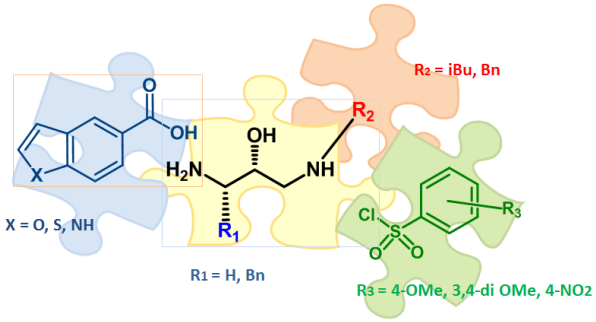

Figure 1

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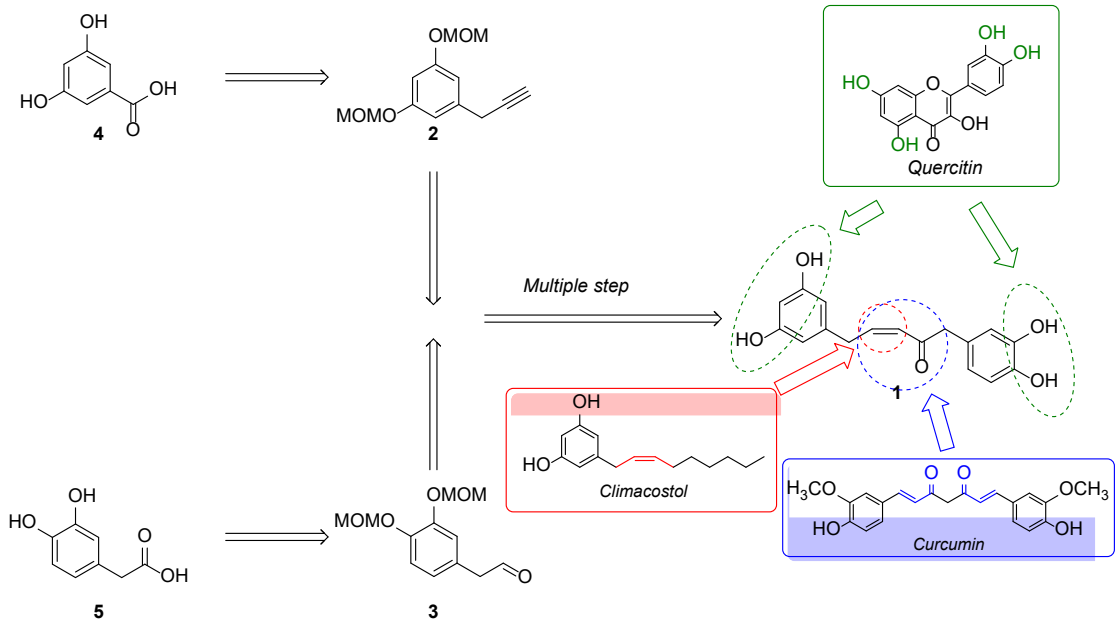
Synthesis of small molecules with potential antiviral acitivity against Sars-CoV-2.

Gentili, D.; Aravindashkan, V.P.; Pastore, G.; Giacomantonio, R.; Lippolis, M.; Gabrielli, S.; Cimarelli,C.; Marcantoni, E.

University of Camerino, School of Science and Techonology, Chemistry Division

Virus infection is one of the most important diseases that afflict human living all over the worlds. Especially, with the outbreaks of pandemic situation of COVID-19 (Sars-CoV-2), the scientists had focused their energy and efforts to fight this situation.[1] Vaccines are one of the most powerful instrument to fight viruses, but these will work only if most of population is vaccinated, moreover virus could persist in wildfire host.[2] Recently Abian *et al.*[3] showed by computational molecular study that Quercitin is a potentional inhibitor of SARS-CoV-2 protease 3CLPro and it could became a very important tool for treatment for the people already affected by this dreadful virus. Therefore the use of small molecules, in symbiosis with vaccines, could be a powerful tool to face against this siutaion. Inspired by all these works, we had evaluated the affinity of Climacostol, already synthesized in our laboratory,[4] to SARS-CoV-2 3CLPro, and an analogue of it, such as compound **1**, is very close to the behavior of Quercitin. A synthetic strategy was designed starting from two easy commercial available molecules such as the 3,5-dihydroxybenzoic acid **4** and 3,4-dihydroxyphenyl acetic acid **5**.



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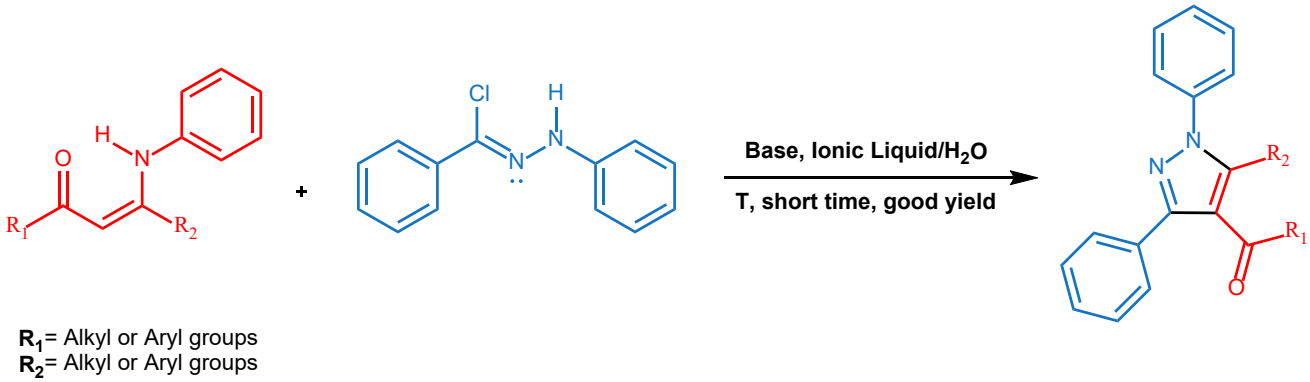
Regioselective Synthesis of 1,3,4,5-Tetrasubstituted Pyrazoles by Eliminative Enaminone-Nitrilimine 1,3-Dipolar Cycloaddition

Vincenzo Algieri,[a] Fabrizio Olivito,[a] Matteo Antonio Tallarida,[a] Antonio Jiritano,[a] Loredana Maiuolo,[a] Paola Costanzo,[a] Cristina Algieri,[b] Salvatore Nesci,[b] Antonio De Nino.[a]

[a] Department of Chemistry and Chemical Technologies - CTC, University of Calabria, Via P. Bucci, Cubo 12C, 87036 – Rende (CS), IT; [b] Department of Veterinary Medical Science - DIMEVET, University of Bologna, Ozzano dell'Emilia (BO), IT. vincenzo.algieri@unical.it

Pyrazoles are five-membered heterocycles composed of two adjacent nitrogen atoms and three carbons. Pyrazole core is rare in natural compounds, so the only way to be produced is organic synthesis. They are applicated in many fields: agrochemical, industrial, clinical and pharmaceutical [1]. At least thirty-three years, pyrazole-containing drugs have been marketed to treat many diseases as bacterial infections, cancers and neurologic disorders, confirming their high versatility and pharmacological efficiency. Many general and practical approaches including the involvement of transition-metal catalysts, photoredox reactions, one-pot multi-component process, new reactants, and novel reaction type have led to fruitful advances in the field of the synthesis and functionalization of pyrazole derivatives [2]. Generally, the pyrazole synthesis leads to the formation of mixtures of regioisomers [3] whereby highly regioselective methods are necessary to improve the accessibility of these heterocycles. In this context, our research group has developed a regioselective approach for synthesis of 1,3,4,5-tetrasubstituted pyrazoles through an eliminative 1,3-dipolar cycloaddition reaction between *in situ*-generated nitrilimine from hydrazonyl chloride and enaminone as described in **Scheme 1**.



Scheme 1. *1,3-Dipolar Cycloaddition between in situ-generated nitrilimine from hydrazonyl chloride and variously substituted enaminones.*

The reaction is conducted in an eco-friendly system composed of ionic liquid and water that can be reused for different cycles never losing its efficiency. Moreover, all synthesized heterocycles are produced with high yields and elevated regioselectivity because only a single regioisomer is observed. In addition, the obtained pyrazoles will be subjected to preliminary studies to evaluate their biological activity on mitochondrial oxidative phosphorylation.

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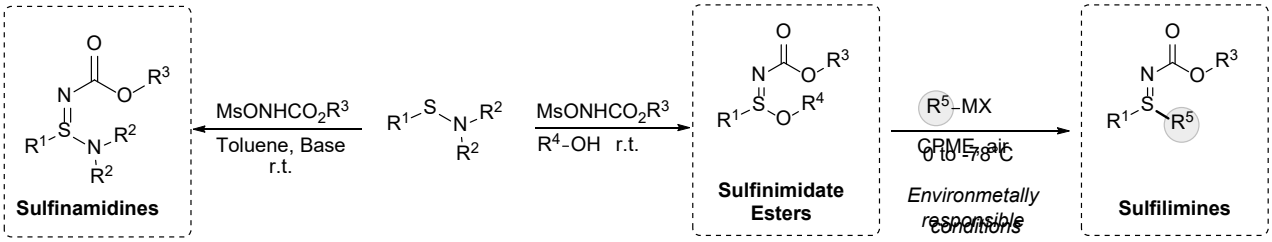
Nitrogen transfer to sulfenamides: synthesis of sulfinamidines and unexplored sulfinimidate esters as valuable precursors of protected sulfilimines

Michael Andresini,[a] Mauro Spennacchio,[a] Fulvio Ciriaco,[b] Leonardo Degennaro,[a] Renzo Luisi[a]*

[a]Flow Chemistry and Microreactor Technology FLAME-Lab, Department of Pharmacy-Drug Sciences, University of Bari "A. Moro", Via E. Orabona 4, Bari 70125, Italy; [b] Department of Chemistry, University of Bari "A. Moro", Via E. Orabona 4, Bari 70125, Italy

Despite the growing interest for bioisosteres within modern drug discovery programs, the synthesis of trivalent imidated sulfur-bearing compounds, exception made for sulfilimines, remains a severely underdeveloped topic in organic chemistry.[1,2] In this communication, we report the first general tactic for the imidation of sulfenamides with *N*-mesyloxycarbamates that enables the preparation of hardly accessible sulfinamidines and sulfinimidate esters, and the first evidence of their synthetic potential.[3] A range of substituted *S*-aryl, heteroaryl, and alkyl sulfenamides were found to react with the nitrogen source, leading to the corresponding *N*-protected sulfinamidines in the presence of a base and upon mild conditions. With our delight, the reaction of sulfenamides with *N*-mesyloxycarbamates in primary or secondary alcohols resulted in the selective conversion into the corresponding sulfinimidate esters with the formal replacement of the aminic portion by solvent. Computational studies and NMR experiments helped to suggest a reasonable reaction mechanism, while detailed structural information have been obtained from single crystal X-ray analysis of selected compounds. Moreover, the electrophilic character of sulfinimidate esters has been disclosed, and diverse *N*-protected sulfilimines were easily prepared from organomagnesium and organolithium compounds through a formal nucleophilic substitution reaction upon environmetally bening conditions.



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Substituted 6H-benzo[c]chromenes: synthetic approach via a Diels-Alder/aromatization sequence and computational investigation

Marco Ballarotto[a], *Andrea Temperini*[a]

[a] *Department of Pharmaceutical Sciences, University of Perugia, Via del Liceo, 1, Perugia, Italy*

The 6*H*-benzo[c]chromene core is a commonly observed scaffold in natural products and synthetic biologically active molecules and for this reason it occupies a prominent role in medicinal chemistry.[1,2] A few notable examples are cannabinol, ligand of CB1 and CB2 receptors, Ganocochlearin C, a natural product isolated from *Ganoderma Cochlear*, and AL-438, a synthetic glucocorticoid receptor modulator. Due to its pharmacological importance, the development of a protocol for an efficient synthesis of this scaffold is an ambitious target for both medicinal and organic chemists.

The published synthetic strategies are based on transition metal catalysis to form the biaryl bond and although this approach allows for the rapid synthesis of variably substituted compounds for screening purposes, the low functional group tolerance and the required purification from the catalyst hinder the possibility for production on a larger scale.[3]

Here we report our results towards a transition metal-free synthetic protocol for highly substituted 6*H*-benzo[c]chromenes. The *de novo* construction of the fused benzene ring has been achieved through a Diels-Alder cycloaddition followed by aromatization of the intermediate cycloadduct to obtain the desired compounds. Starting from commercially available salicylaldehydes, α,β-unsaturated carbonyl compounds and alkynes substituted with an electron withdrawing group, the chromene core is quickly assembled in a 3-step sequence in good yields.

DFT calculations were then performed to try to understand the observed regioselectivity and differences in reactivity. The obtained results highlight the presence of a concerted but slightly asynchronous transition state, and the energetic analysis is in accordance with the experimental results.

In conclusion, the developed protocol allows for the rapid synthesis of differently substituted compounds based on this scaffold, thanks to the modularity of the approach and the short reaction sequence.

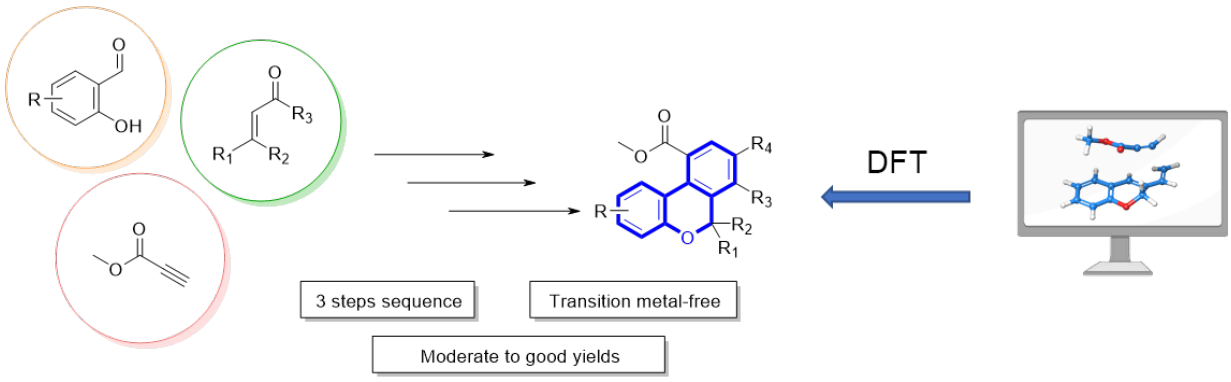

Figure 1: General scheme for the synthesis of benzo[c]chromenes.

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Aminomaleonitrile inspired prebiotic chemistry as a novel microwave assisted multicomponent tool for the synthesis of imidazole and purine derivatives with anti-influenza activity.

Bruno Mattia Bizzarri

University of Tuscia, Viterbo 01100, Italy, Biological and Ecological Sciences Department (DEB)

It is well recognized that Multi-Component Chemistry (MCC) played a key role in molecular evolution thanks to the capability of generating high chemical diversity starting from two or more reagents.[1] Recently, prebiotic MCC involving formamide (NH_2CHO), a product of barrier less hydrolysis of HCN,[2] afforded a robust chemical framework for the contemporary synthesis of sugars, carboxylic acids, amino acids and several types of heterocyclic compounds, including purine and pyrimidine nucleobases and nucleosides.[3-9] What if we may use the prebiotic based MCC as a tool for the synthesis of libraries of complex heterocyclic derivatives viable not only to LUCA's (in its modern version) but for viruses too? In this context, amino imidazole carbonitrile derivatives decorated with α-amino acids have been synthesized by a three component microwave assisted reaction inspired by the prebiotic chemistry of aminomaleonitrile. These compounds have been successively used as annulation synthons for the preparation of 8,9-disubstituted-6,9-dihydro-1H-purin-6-ones by reaction with formic acid, as a simple C-1 donor reagent. Some of the novel heterocycles showed a significant activity against influenza virus.

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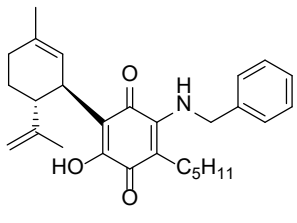
The oxidation of phytocannabinoids: a systematic investigation

Diego Caprioglio,[a] *Daiana Mattoteia*,[a] *Giovanni Appendino*[a]

[a] *Dipartimento di Scienze del Farmaco, Università del Piemonte Orientale, Novara*

Quinones are a remarkable class of bioactive compounds whose broad occurrence in terrestrial and marine organisms mirrors their role in mitochondrial and plastidial electron transport. Due to their polarized bonds, quinones have a remarkable potential of engagement in both covalent and non-covalent intermolecular interactions.[1] Cannabinoquinoids, the non-narcotic oxidized form of phytocannabinoids, have attracted considerable attention for their potent bioactivity, culminating in the discovery of VCE-004.8 (**1**), a compound under phase 2 clinical development with orphan drug status by EMA and FDA for the management of scleroderma.[2]

Spurred by the growing interest for this class of compounds, we have systematically investigated the oxidation of phytocannabinoids to cannabinoquinones under a variety of experimental conditions (base-catalyzed aerobic oxidation, oxidation with metals, oxidation with hypervalent iodine reagents),[3] discovering that the regiochemistry of oxidation, a critical maneuver for bioactivity, depending not only on the nature of the oxidant, but also on post-oxidative prototropic- and valence tautomeric equilibria that isomerize *ortho*-quinones to *para*-quinones.[4] Attempts to telescope the synthesis of aminoquinones by transition-metal promoted one-step oxidation, aza-Michael addition, and dehydrogenation will be presented.



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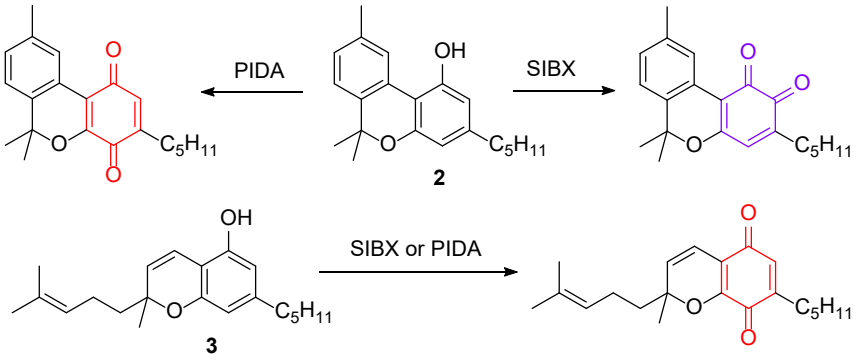

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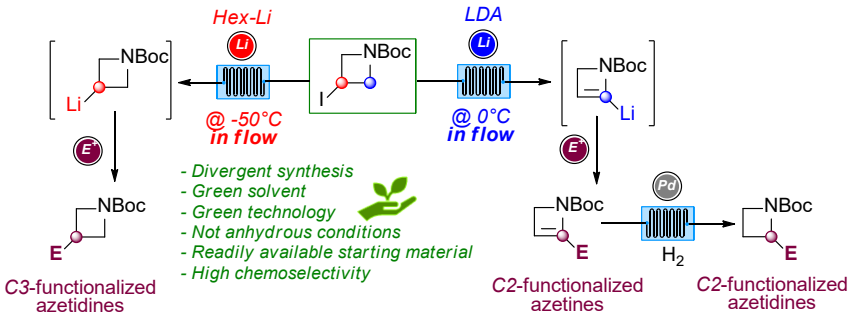
Use of flow technology for the development of a sustainable synthesis of azetines and azetidines

Marco Colella,[*a] *Pantaleo Musci,*[a] *Debora Cannillo,*[a] *Leonardo Degennaro,*[a] *Renzo Luisi*[a]

[a] *Department of Pharmacy – Drug Sciences, University of Bari "A. Moro" Via E. Orabona 4, 70125 – Italy FLAME-Lab –Flow Chemistry and Microreactor Technology Laboratory.*

In 2014, has been estimated that 59% of U.S. FDA approved small-molecule drugs holds a nitrogen heterocycle.[1] Although historically less studied than its higher homologues belonging to the class of *N*-containing heterocycles, the azetidine nucleus is present in various biologically active compounds of both natural and synthetic derivation.[2] Sufficient robustness and strong molecular rigidity are the main features that encourage the introduction of this motif in compounds for applications in medicinal chemistry. Moreover, beneficial effects on the pharmacokinetic profile of pharmaceutically relevant structures connected with the introduction of this small and strained ring have been reported.[3] In recent years, our group has developed new strategies for azetidine ring decoration by using organolithium chemistry.[4] Moreover, in the last decade, we gave our contribution to demonstrate how the well-documented benefits of flow microreactor technology perfectly fit with organometallic chemistry, allowing not only to refine old transformations (process intensification) but also to expand the synthetic "toolbox" with new reactivity patterns, previously considered inaccessible.[5] In this contribution, we attempted to merge these two long-lasting interests by reporting the generation of two different lithiated four-membered azaheterocycles under continuous flow conditions. *N*-1-Boc-3-iodoazetidine acts as a platform to prepare both C3-lithiated azetidine and C2-lithiated azetine by simply selecting the lithiating agent. In this work, we highlighted how the flow approach enables to manage the lithiated intermediates at higher temperatures with respect to batch. This, in combination with the use of the ecofriendly cyclopentyl methyl ether (CPME) as the solvent, allows the development of sustainable processes. Moreover, further manipulation of 2-substituted azetines will be described.



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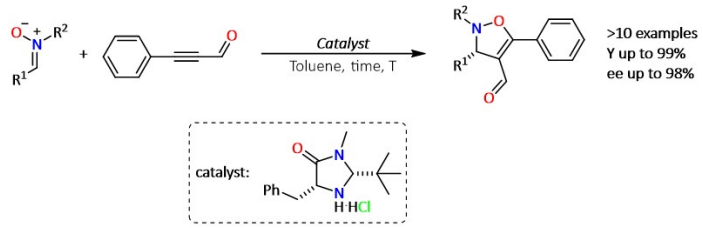
Enantioselective Synthesis of Polyfunctionalized Isoxazoline Rings: Development of a Methodology for the preparation of Tumor-Oriented Small Molecules

Dario Corbisiero,[a] Alessandra Tolomelli,[a]

[a] *Department of Chemistry, University of Bologna, Via Francesco Selmi, 2, 40126 Bologna, Italy.*

Cancer represents one of the most relevant and widespread diseases in the modern age. One critical point of cancer-associated pathologies is the difficult identification of a single etiology for their onset. Among them, inflammation is a determining step, involving several cellular receptors. In this context, integrins play a fundamental role in the regulation/upregulation of cellular phenomena. In fact, these transmembrane receptors are responsible for the communication between cells and with extracellular matrix ligands. Therefore, among the different possible integrins we focused our attention on $\alpha_V\beta_3$ and $\alpha_5\beta_1$ receptors, overexpressed on the surface of cancer cells and involved in the outbreak of inflammations. Historically, our group was involved in the racemic synthesis of isoxazoline ligands towards these specific integrin subtypes.[1] Nevertheless, since in medicinal chemistry is relevant to understand the activity of each enantiomer of a bioactive molecule, we investigated the enantioselective synthesis of isoxazoline rings. Unfortunately, there are only few examples about the enantioselective synthesis of Δ^4-isoxazoline scaffold and many of them have some limitations about functional groups and/or synthetic results (conversions, yields and enatiomeric ratio). Combining our necessity to synthesize peptidomimetic isoxazoline-based molecules with the idea to bridge a gap in their synthetic methodology, we developed the synthesis of the aforementioned scaffolds through an organocatalyzed 1,3-dipolar cycloaddition reaction (Huisgen reaction) between commercial, easy to prepare and bench stable starting materials (Scheme 1). This approach allows to achieve high results in terms of yields and enantiomeric ratios, opening new possibilities for the exploitation of these small molecules as suitable bioactive platforms. Moreover, we expanded the library of the already reported isoxazoline rings introducing several functional groups and allowing a diversified polyfunctionalization of the scaffold.



Scheme 1 - Enantioselective synthesis of isoxazoline rings

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Synthetic Approaches to Molecular Diversity of BODIPY

Massimiliano Cordaro[a]

[a] *Dipartimento di Scienze Chimiche, Biologiche, Farmaceutiche e Ambientali - Università di Messina*

Among the dyes, the BODIPYs have something more, especially from the point of view of the synthetic organic chemist. The chemical-physical characteristics of this class of compounds of primary interest to the scientific community are known. [1] There is an additional feature that makes them unique, that is, the possibility to design a variety of BODIPY derivatives through procedures by pre- and post-functionalization, whose only limit is the imagination. In the last years, in the framework of several collaborative projects, we have focused our research interest on the synthesis and applications of various BODIPY derivatives (Figure 1) [2,3,4,5,6,7].

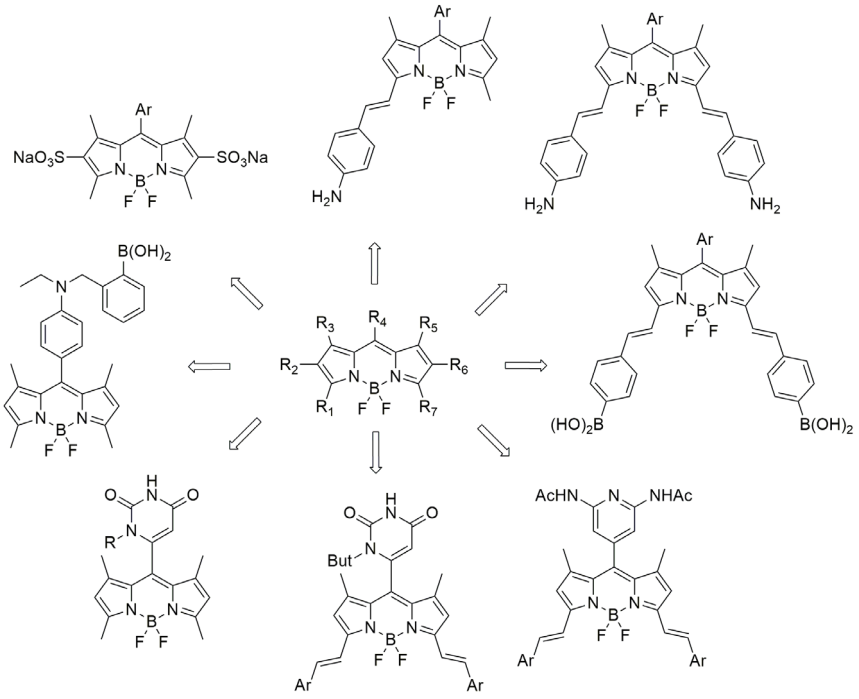

Figure 1

The presentation will highlight the potential of BODIPY-type dyes through an comprehensive analysis of the results on the studied derivatives. Practical inspirations and possible ways of developing new BODIPY will be proposed, focusing on potential applications.

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Highly-fluorinated aromatic diimides for organic electronics: from synthesis to thin-film preparation

Vincenzo Mirco Abbinante,[a] Gonzalo García-Espejo,[a] Candida Pipitone,[b] Gabriele Calabrese,[c] Silvia Milita,[c] Francesco Giannici,[b] Antonietta Guagliardi,[d] Norberto Masciocchi[a]

[a] Dipartimento di Scienza e Alta Tecnologia & To.Sca.Lab, Università dell'Insubria, via Valleggio 11, I-22100 Como; [b] Dipartimento di Fisica e Chimica, Università di Palermo, Edificio 17, I-90128 Palermo; [c] Istituto di MM, CNR, via Gobetti 105, I-40129 Bologna; [d] Istituto di Cristallografia & To.Sca.Lab, CNR, via Valleggio 11, I-22100 Como.

Organic electronics require the availability of molecular or polymeric materials simultaneously possessing semiconducting properties, chemical and thermal stability, easy processability and filmability. [1] Among the most promising materials, those based on aromatic diimides bearing (fluo-)aliphatic chains have recently raised the interest of the entire organic semiconductor community. [2] Having studied the effect of constitutional isomers on the molecular properties of amino-aromatic pendant residues in a recent paper, [3] we present here the synthesis, characterization, and thin film formation properties of a number of highly fluorinated naphthalene diimides (NDIs), that possess extreme stability, a variety of π-π interactions in the solids, higher solubility in most organic solvents and easy deposition as thin films, by solution-based processes or even by sublimation. Such fluorinated derivatives, containing up to 14 F atoms per molecule, are highly hydrophobic, possess significantly low LUMO energies and, being based on electron-withdrawing groups, are prone to *n*-doping, an electronic feature which is of utmost relevance for enhancing electron mobility and, for thermoelectric properties. [4] X-ray powder diffraction and grazing incidence characterization provided structural and morphological information, while diffuse reflectance and photoluminescence spectroscopies, DFT modeling and a variety of thermal analyses shed light on the electronic and chemical stability of these species. The synthesis and the structural and spectroscopic features of these materials, shown in **Figure 1**, will be presented. Funding by MIUR, through project PRIN 2017L8WW48, is heartily acknowledged.

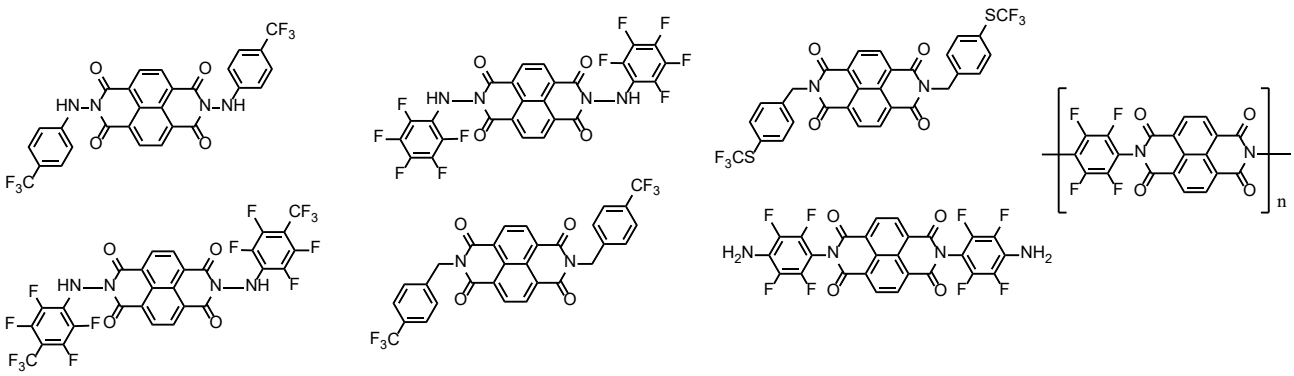

Figure 1: Schematic picture of the investigated fluorinated-diimide compounds.

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Functional films from 5,6-dihydroxyindole oligomers and long chain diamines partnership

R. Argenziano, M.L. Alfieri, L. Panzella, A. Napolitano, M. d'Ischia

[a]*Department of Chemical Sciences, University of Naples Federico II, via Cintia 4, I-80126 Naples, Italy rita.argenziano@unina.it*

The development of innovative and versatile dip-coating technologies for surface functionalization has been a very active issue over the past decade following the discovery of the extraordinary wet adhesion properties of polydopamine, a black insoluble eumelanin-like material inspired to the robust adhesion properties of catechol- and amine-rich mussel byssus proteins.[1] New opportunities have derived from the discovery that hexamethylenediamine (HMDA) markedly enhances film deposition from the polymerization of dopamine and a variety of catechol substrates, including the key eumelanin precursor 5,6-dihydroxyindole (DHI), leading to films with attractive properties in terms of morphology and functionalities.[2] Recent studies have provided evidence for the remarkable antioxidant properties of synthetic eumelanins from the other primary melanin precursor 5,6-dihydroxyindole-2-carboxylic acid (DHICA) and its methyl ester (MeDHICA).[3]

In the present work the oxidative polymerization of MeDHICA was run in aqueous buffers at pH 9.0 in the presence of HMDA at different molar ratios. The most promising results were obtained using MeDHICA and HMDA at 1 mM at 1:1.5 molar ratio. Under these conditions, yellowish coatings (< 40 nm thick by AFM analysis) with regular and homogeneous morphology (SEM analysis) were obtained with moderately hydrophobic properties (WCA= 67°) turning to hydrophilic upon exposure to gaseous HCl. The coatings turned darker in color by exposure to gaseous ammonia in the solid state, by dipping into oxidant solutions or following UV exposure, and could be removed by washings with DMSO. Film deposition was pH-dependent, markedly decreasing at pH 7 or 12, and was specifically induced by HMDA, as monoamines or shorter diamines were less effective in inducing coating formation. LC-MS, MALDI-MS and NMR analysis of the films indicated the presence of HMDA and monomeric MeDHICA accompanied by dimers and small oligomers (up to the tetramer level) and no detectable MeDHICA-HMDA covalent conjugation products. Overall, available experimental results coupled with theoretical data concurred to support a mechanism for film deposition involving the spontaneous assembly of self-organized networks of MeDHICA in the deprotonated anion form (computed pKa = ca. 7.5) and HMDA as the dication in an approximate ratio of 1:0.5, held together mainly by electrostatic interactions. The films displayed potent antioxidant properties in three different assays and exerted significant protective effects from oxidative stress on HaCat cells stimulated with UV radiation.

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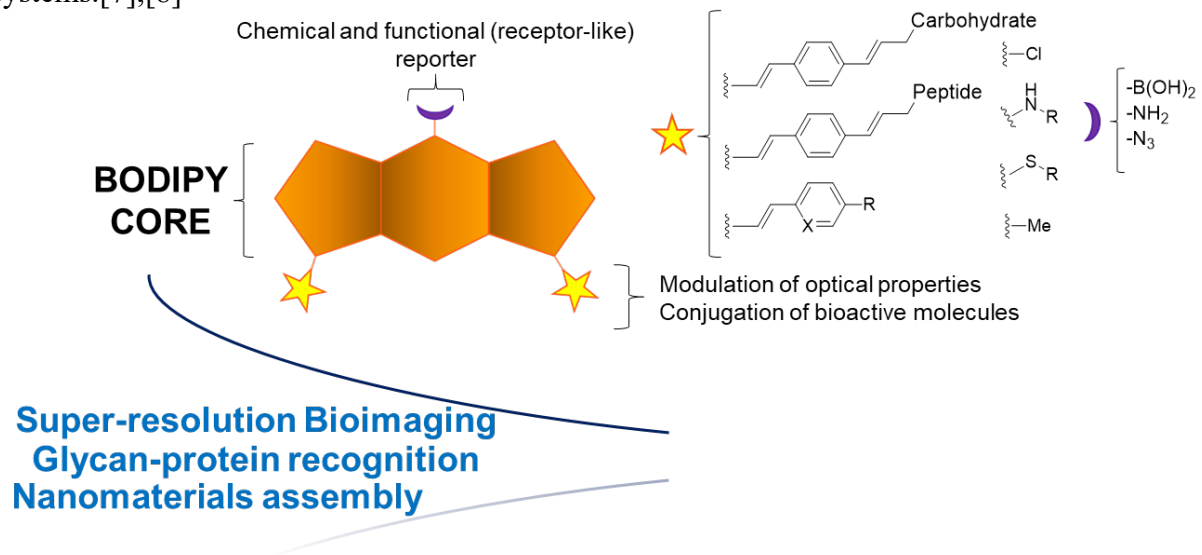
Tailoring the structure of the BODIPY probe in the design of functional fluorescent materials

G. Biagiotti,[a] *S. Cicchi*,[a] *B. Richichi*[a]

[a] *Department of Chemistry "Ugo Schiff", University of Firenze, Via della Lastruccia 13, 50019 Sesto Fiorentino FI, Italy*

Recent advances in fluorescence microscopy techniques have allowed increasingly detailed assessment of complex dynamic events in biological systems at a resolution down to the molecular scale.[1],[2] Accordingly, today, the design and the synthesis of high performance and reliable tools for bio-imaging is a highly sought-after goal. In this field, 4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene (named BODIPY) derivatives, [3] thanks to their unique and fascinating optical properties and biocompatibility, have been prompted as one of the most intriguing dyes in different research areas across (nano)materials to life science. [4]
In this communication, we describe our findings on the development of high performance functional and modular BODIPY-based probes with tunable and enhanced optical properties. Notably, the *meso* and the 3-5 positions of the BODIPY core have been orthogonally modified allowing the conjugation of either nanomaterials, biopolymers, biomolecules and small bioactive molecules (Fig.).[5],[6] The versatility and feasibility of our approach, that allowed us to access to two main classes of BODIPY probes, will be outlined by referring on the applications of our BODIPY conjugates (Fig.) which include super-resolution bio-imaging, nanomaterials assembly and labelling, trackable drug delivery systems.[7],[8]



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Trityl-brominated radicals as building blocks for doublet CPL emitters

Davide Blasi,[a,b] *Imma Ratera,*[b] *Jaume Veciana.*[b]

[a] *Dipartimento di Chimica, Università degli Studi di Bari "Aldo Moro", 70125, Bari, Italy;*
[b] *Institut de Ciència de Materials de Barcelona (ICMAB-CSIC), Campus Universitat Autònoma de Barcelona, 08193, Bellaterra (BCN), Spain.*

Less than five years ago, luminescent triaryl methyl radicals were just considered a family of "exotic" emitters. Currently, they represent one of the most interesting alternatives to phosphorescent materials in organic optoelectronic devices.[1] In fact, their doublet spin multiplicity, due to the presence of an odd electron mainly located in the central sp_2 methyl carbon, makes it possible to overcome the problems associated to the spin statistics which affect conventional fluorescent species in electroluminescent devices.[2] Using luminescent organic radicals as emitting layer in OLEDs, it is possible to achieve values of internal quantum efficiency of 100% in a spectral range between 700-800 nm, with an emission life-time of few ns.[3] Some of triaryl methyl radicals are also capable to form excimers when trapped into-rigid hosts.[4] These supramolecular radical-pairs are stable, with a luminescence in the deep-red/NIR region, and they represent the only known completely organic system showing a magnetic-sensitive emission.[5] Furthermore, due to their propeller-shape, polychlorotriphenyl methyl radicals exist in a racemic mixture of Minus (M) and Plus (P) enantiomers depending on the left or right-handed torsion of the three aromatic rings protecting the odd electron. Tris(2,4,6-trichlorophenyl)methyl (**1**) and perchlorotriphenylmethyl (**2**) radicals exhibit an intrinsic circularly polarized luminescence (CPL) with an opposite sign associated to each pair of conformers.[6] **1** and **2** show a luminescence dissymmetry factor $|g_{lum}| = 0.5 - 0.8 \cdot 10^{-3}$ respectively with a $|g_{abs}| / |g_{lum}| \approx 1$. Unfortunately, both species tend to racemize at room temperature, making not possible any application in optoelectronics. Based on the structure of **1**, the first polybromotriphenyl methyl radical was synthesized.[7] Tris(2,4,6-tribromophenyl)methyl radical (**3**) adopts the same crystallographic configuration of its polychlorinated analogous **1**. The two enantiomers M and P own an intrinsic CPL at 595 nm with a $|g_{lum}| = 0.7 \cdot 10^{-3}$, but thanks to the bulky dimensions of the six bromine atoms in *ortho* positions, no evidence of racemization can be observed up to 60°C. This aspect, together with the higher chemical versatility offer by the presence of bromine atoms in the three *para* positions, make the radical **3** the best candidate for the synthesis of new open-shell CPL emitters for optoelectronic applications.

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Porphycenes, a lesser known tetrapyrrolic macrocycle with intriguing properties suitable for *in situ* sensing

*Marta Penconi[a], Jacek Waluk[b], Rossella Yivlialin[c], Marcello Campione[d], Gianlorenzo Bussetti[c], Alberto Bossi[a]**

[a] *Istituto di Scienze e Tecnologie Chimiche "G. Natta", CNR-SCITEC, v. Fantoli 16/15, I-20138 Milano (Italy), and SmartMatLab Center, v. Golgi 19, II-20133 Milano (IT);* [b] *Institute of Physical Chemistry, Polish Academy of Science, 01-224 Warsaw, Kasprzaka 44/52 (PL); Faculty of Mathematics and Science, Cardinal Stefan Wyszyński University, Dewajtis 5,01-815 Warsaw (PL);* [c] *Department of Physics, Politecnico di Milano, p.za Leonardo da Vinci 32, I-20133 Milano (IT);* [d] *Department of Earth and Environmental Science, Università degli Studi di Milano – Bicocca, p.za della Scienza 4, I-20126 Milano (IT);*

Email: alberto.bossi@cnr.it

The research in sensor miniaturization for application in medicine, environmental analysis, explosive tracing, etc., is rapidly increasing. Optical sensors, i.e., transducers based on the resultant optical signal modulation following detection of analytes, play a fundamental role among the various chemical detection systems thanks to their easy working operation and wide range of applications (e.g. vapor sensors for acids or volatile compounds). An "hot topic" in the sensing field is the search of stable materials processable by different techniques thus enabling for the realization of a broad range of sensing setups.

Porphycene (H_2Po), a tetrapyrrolic 18π electrons chromophore whose structure is reported in Fig.1a, is a constitutional isomer of the widely known porphyrin family and differs from them in the pattern of connection of the four pyrrole rings, such that two of them are bound directly to each other at the α position.[1] The different size of the inner core of the molecule and the reduced symmetry of the skeleton with respect to porphyrins endow porphycenes with unique stability and optical features suitable for the exploitation as ultrafast responsive material for sensing.

Herein we report the study on vacuum deposited H_2Po thin film by means of UV-Vis-NIR optical spectroscopies (absorption, emission, and surface differential reflectivity-SDR) and surface microscopies (i.e. AFM). We demonstrate a spectacular chromatic change (transmission and reflection mode Fig.1b-d) when the film is exposed to acid and verified the fast reversibility of the process.

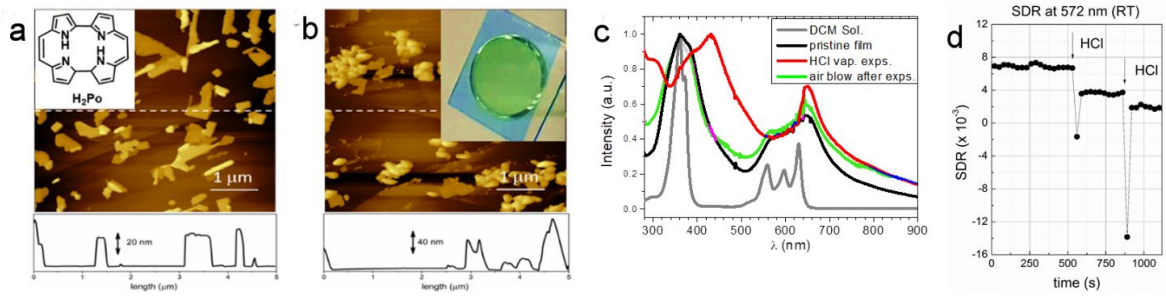

Figure 1: Topography and spectroscopy of the H2Po thin film. a) pristine sample (inset, molecular structure); b) sample after the exposure to HCl vapors and recovery of the SDR optical spectrum (inset, visual observation of the film color *exposed* to acid vapors-green area- and *unexposed*-blue one); c) comparative UV-Vis absorption of the film on quartz slide before and after exposure to HCl vapors; d) SDR signals of the film on HOPG substrate before and after exposure to HCl vapors.

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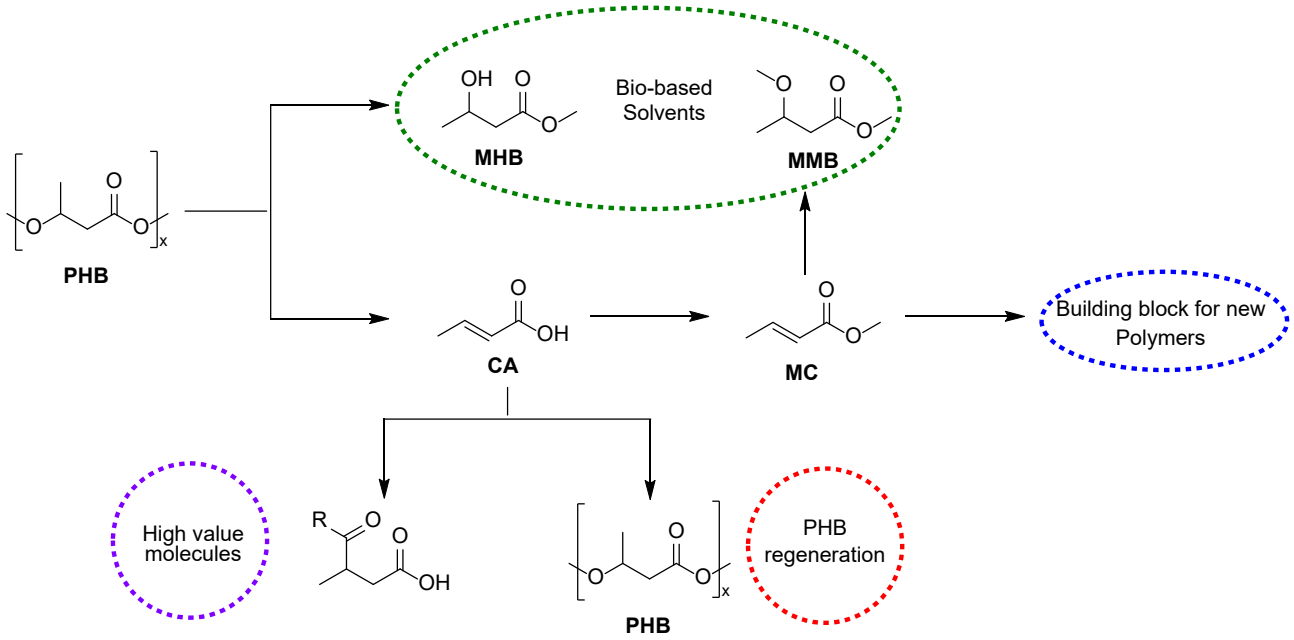
Polyhydroxybutyrate as a sustainable platform for the production of chemicals and bio-polymers

Adriano Parodi, [a] *Chiara Samorì,* [a] *Paola Galletti* [a]

[a]*Dipartimento di Chimica "Giacomo Ciamician", University of Bologna, via Sant'Alberto 163, Ravenna, Italy*

Polyhydroxyalkanoates (PHAs) are biobased and biodegradable polyesters of hydroxy acid monomers bio-synthesized by different kinds of bacteria through the aerobic conversion of various feedstock, and potentially capable to replace fossil-based plastics thanks to similar mechanical and physical proprieties. The development of technologies that allow the production of this biopolymer from wastes through the use of mixed microbial cultures, can open the possibility to produce PHA in a more economically sustainable way. In the context of PHA production and valorization, our research group is developing new strategies for: i) recycling the homopolymers polyhydroxybutyrate (PHB) into newly PHB; ii) using PHB as a sustainable platform for the synthesis of chemicals that can be used in the same PHB production cycle (e.g. highly efficient solvents for PHB recovery) or iii) for totally different applications, such as the synthesis of high value molecules[1] or the manufacturing of new polymers.



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Transfer of Axial Chirality to the Nanoscale Endows Carbon Dots with Circularly Polarized Luminescence

Simone Di Noja [a], *Francesco Amato* [a], *Francesco Zinna* [b], *Giulio Ragazzon* [a], *Lorenzo Di Bari* [b], *Maurizio Prato* [a,c,d]

[a] *Department of Chemical and Pharmaceutical Sciences, CENMAT, Center of Excellence for Nanostructured Materials, INSTM UdR, Trieste, University of Trieste, via Licio Giorgieri 1, 34127, Trieste, Italy*

[b] *Department of Chemistry and Industrial Chemistry, University of Pisa, via Moruzzi 13, 56124, Pisa, Italy*

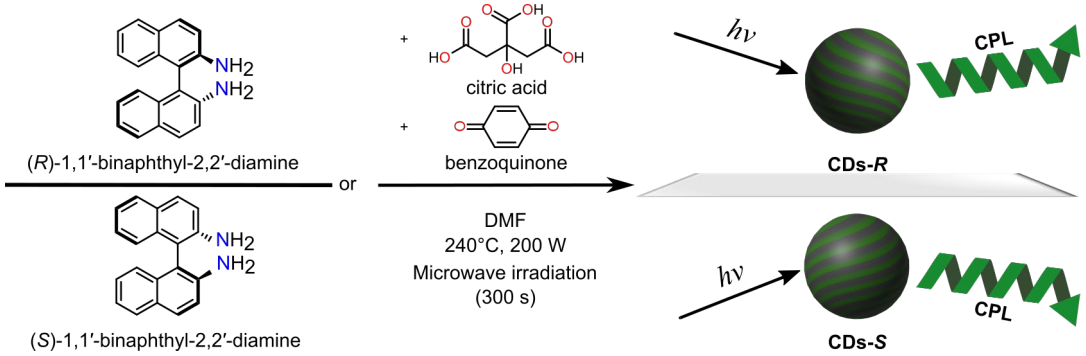
[c] *Center for Cooperative Research in Biomaterials (CIC biomaGUNE), Basque Research and Technology Alliance (BRTA), Paseo de Miramón 182, 20014, Donostia San Sebastián, Spain*

[d] *Basque Fdn Sci, Ikerbasque, Bilbao 48013, Spain*

Carbon Dots (CDs) are carbon-based nanoparticles that have recently gained great interest as novel luminescent materials.[1][2] The properties of CDs largely depend on the type of precursors employed during the synthetic process. Our group has developed a general strategy to expand CDs properties, by using *ad hoc* molecular precursors which can transfer their features to the nanomaterial.[3]

Leveraging on our expertise in the preparation of chiral CDs,[4] we have now engineered atropisomeric CDs. Our approach consists in one-pot microwave-assisted solvothermal synthesis, using citric acid, benzoquinone, and either (*S*)-1,1'-binaphtyl-2,2'-diamine or its (*R*)-atropisomer. The novel CDs – as assessed by AFM and ^{1}H-NMR analyses – show similar structural and morphological properties, regardless of the atropisomer employed. These nanoparticles, having a medium size of 3.47 nm, exhibit fluorescence emission in the green region, with a maximum at 480 nm. Chirality of the obtained nanoparticle is confirmed by nicely specular circular dichroism spectra. Remarkably, these atropisomeric nanoparticles show opposite CPL bands which retrace the luminescence profile.

This study affords atropisomeric nanoparticles having better optical properties compared to the starting materials (e.g. emission in the green *vs* blue region). Transferring axial chirality to the nanoscale affords CDs which exhibit CPL intrinsically, without the use of an external chiral agent.



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Synthesis and thermal behavior of dicationic ionic liquids

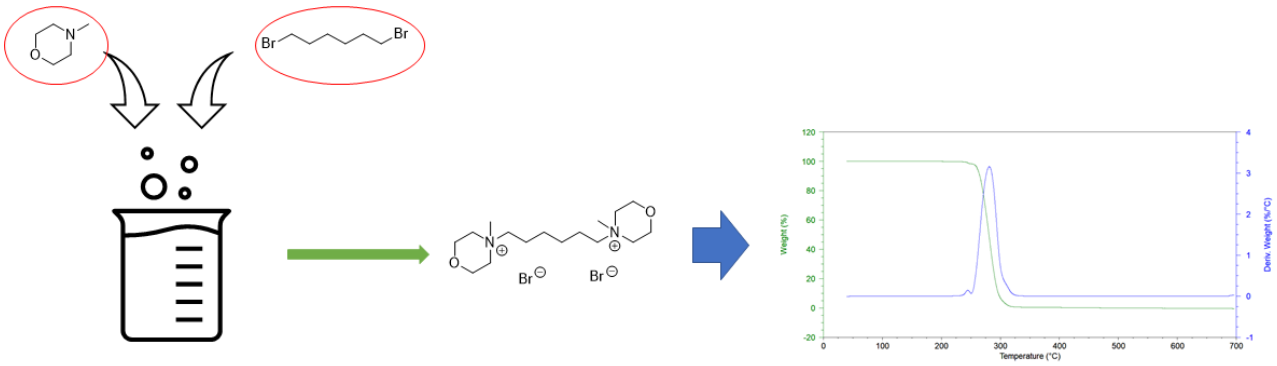
Claudio Ferdeghini,[a] Andrea Mezzetta,[a] Christian Silvio Pomelli [a] Lorenzo Guazzelli,[a]

[a] *Dipartimento di Farmacia, Università degli studi di Pisa*

As the problematic to find new ways to sustainable development becomes more and more urgent, ionic liquids (ILs) appear to be a very promising option due to their properties. Indeed, through a careful selection of the constituting ions, ILs can respect many principles of green chemistry.[1] Among these organic salts, the subclass of dicationic ionic liquids (DILs) showed peculiar physico-chemical properties and an even potentially greater range of applications.[2] However, DILs have been far less studied than their monocationic parents, and only little is known about their possibilities and most structures still need to be characterized in details.

The most common way to synthetize ILs (and DILs) is the reaction between a heterocyclic compound and a halogenated (or di-halogenated) alkyl chain. This simple reaction allows for preparing very large number of compounds. The possible structural variations are not restricted to the cationic moiety, but may involve the type of linker between the positively charged headgroups as well as the nature of anion. Hence, the structural space and the related properties can be fine-tuned to tackle very disparate challenges.

In the present work, the synthesis of various families of DILs with different length of the linker and different cationic moieties is presented. To better understand the potential field of application, the thermal stability and thermal behavior of these compounds have been investigated. Interestingly, differences in their degradation pathways as a function of the length of the spacer have been observed.



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Non-equilibrium dynamic chromatography: investigation of the reduction process of α-lipoic acid promoted by dithiothreitol.

Fabio Buonsenso [a]; *Marco Pierini* [a]

[a] *Dipartimento di Chimica e Tecnologie del Farmaco, Università degli Studi di Roma "La Sapienza", Piazzale Aldo Moro 5, 00185 Roma (Italy)*

By definition, effective chromatographic separations of complex mixtures are characterized by a series of baseline well-resolved peaks. However, if during the discrimination process the analysed species were involved into a secondary dynamic equilibrium concomitant with their chromatographic repartition equilibria, the related peaks will be linked by a plateau zone, giving rise to a so-called "*dynamic chromatogram*" (**DyCh**), whose shape and height reflects the particular retentive behaviour of the molecules reacted during the run and contains kinetic information concerning the secondary process suffered by these molecules. In this way, a suitable analysis of such **DyCh***s* constitutes a valid tool for estimating the activation parameters associated to the process secondary to the chromatographic one. In particular, iterative simulation of experimental **DyCh***s* performed by means of a dedicated software can provide an accurate measurement of the kinetic constants governing the secondary process, and so also the thermodynamic activation barriers connected to it. [1, 2] In this study we present the first example of dynamic chromatography measurements carried out in non-equilibrium conditions and performed to study a REDOX reaction taking place during the chromatographic separation process of the involved species. The reaction under consideration is represented by the reduction of lipoic acid promoted by dithiothreitol (DTT, Figure 1), added in mobile phase as the reducing agent. The resulting **DyCh***s*, registered under different conditions of pH, temperature and DTT concentrations, were analysed by means of the home-made computer program Auto-DHPLC-y2k [2], so allowing the determination of the second order kinetic constants relevant to the REDOX reaction as a function of pH and temperature.

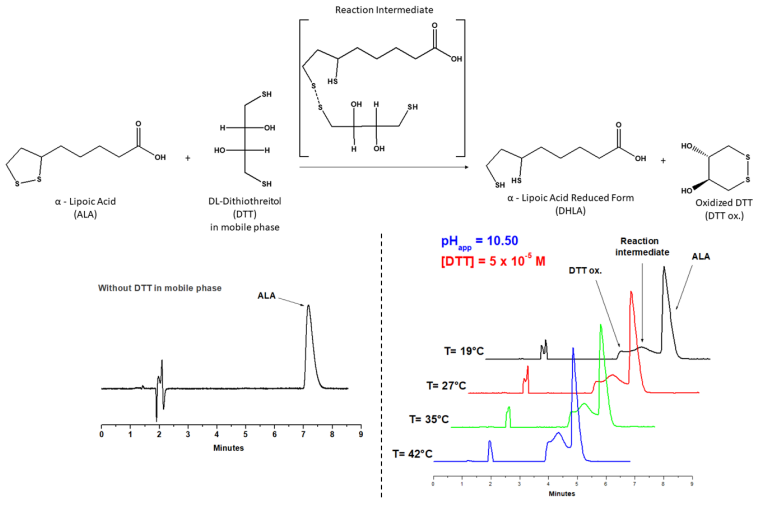

Figure 1: Picture above: lipoic acid reduction reaction scheme using DTT as a reducing agent. Picture below: left side, chromatogram of ALA without DTT in mobile phase; right side, dynamic chromatograms, carried out at different temperatures, of the reduction process.

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Combined use of forensic science in sexual assault: a case report

Marta Da Pian [a], *Valerio Causin* [a], *Micaela Maria Bonetto* [a], *Katiuscia Barison* [a], *Luciana Caenazzo* [b], *Pamela Tozzo* [b]

[a] *Universitá degli Studi di Padova - DISC, via Marzolo 1, 35131, Padova, Italy;* [b] *Universitá degli Studi di Padova – DMM, via Gabrielli 63, 35121, Padova, Italy; marta.dapian@unipd.it*

DNA analysis has been widely used in the forensic field in order to contribute to identifying the perpetrator of a crime. Forensic investigation in sexual assaults usually focuses on locating and identifying biological fluids, followed by DNA analysis [1]. The identification of certain compounds present in condoms can be useful to reconstruct the occurred event, especially in cases of sexual assaults where the DNA analysis did not show the presence of a male profile and where RNA analysis did not show the presence of sperm markers [2].

Herein we describe the case of a woman reporting to be victim of sexual assault, who was not able to provide accurate information concerning the dynamics of the event, except for the use of a condom during the assault.

We started from a Short Tandem Repeat (STR) analysis on vaginal and rectal swabs which showed only the presence of vaginal and skin markers. In this situation, the identification of condom compounds residues on vaginal swabs became important as it contributes to the weight of evidence related to the available circumstantial data and to other collected evidence [3]. We therefore developed a protocol based on IR an NMR spectroscopy to successfully analyze and correlate the organic residue of the condoms' lubricant to the condom's brand.

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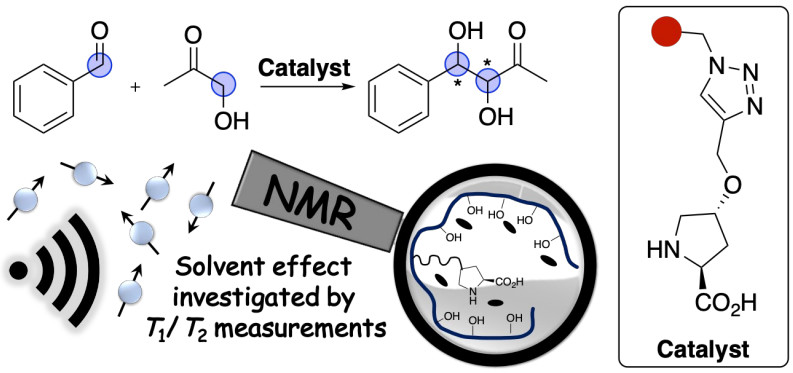
Aldol Reaction between Benzaldehyde and Hydroxyacetone Promoted by Silica SBA-15 supported proline: Unraveling the Solvent Effect on the Catalyst Behavior Using NMR Relaxation

Graziano Di Carmine[a,b], Lorenzo Poletti[a], Daniele Ragno[a], Christopher Parlett[b,c,d], Armando Carlone[e], Alessandro Massi[a], Carmine D'Agostino[b] and Olga Bortolini[a]

[a] *Department of Chemical, Pharmaceutical and Agricultural Sciences (DOCPAS); University of Ferrara, Via Luigi Borsari 46, I-44121, Ferrara, Italy.*
[b] *Department of Chemical Engineering and Analytical Science (CEAS); The University of Manchester, M13 9PL, Manchester, U.K.*
[c] *Diamond Light Source; Harwell Science and Innovation Campus, OX11 0DE, Didcot, Oxfordshire, U. K.*
[d] *Catalysis Hub, Research Complex at Harwell; Rutherford Appleton Laboratory, OX11 0FA, Harwell, Oxfordshire, U. K.*
[e] *Dipartimento di Scienze Fisiche e Chimiche; University of L'Aquila, Via Vetoio 42, I-67100, L'Aquila, Italy.*

The beginning of new millennium is recognized as the dawn of modern organocatalysis for organic chemists. Since 2000 the number of publications on this topic has been grown dramatically, imposing the organocatalysis as the new frontier among the conventional catalysis. Even though organocatalyzed reactions which compose the toolbox of organic chemists has been increased in number during these two decades, some issues remain challenges. The most important drawback of organocatalysis lies on the low turnover number (TON) if compared with metal- and bio-catalysis[2]. Heterogenization of organocatalysts has been established as the main way to overcome this problem, preferably by implementation with flow reactors. Several methods to immobilize organocatalysts have been disclosed in the years but some questions about the differences in terms of reactivity and selectivity observed moving from homogeneous to heterogenous conditions remain puzzling. In our previous work we reported as NMR relaxation measurements can be employed to explain how the solvent nature plays a different role switching from homogeneous to heterogenous conditions for polystyrene supported triazolium organocatalyst[2]. Herein, we report a deep insight into the solvent effect in the proline-SBA-15 supported catalyst employed in Aldol reaction between benzaldehyde and hydroxy acetone.



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New 1-6 self-immolative spacer for the release of thiols under nitroreductase activation

E. Ermini,[a] *P. Tolu*, [a] *M. Taddei*,[a]

[a] *Dipartimento di Biotecnologie, Chimica e Farmacia, Università di Siena, Via A. Moro 2, 53100 Siena (Italy)*

Thiols are a particular class of molecules having essential roles in biological systems. They can work as potent metallo-enzyme inhibitors, complex metals present in proteins and they are excellent electron donors. Thanks to this wide range of activities, thiols are potentially useful compounds in therapy, although the diversity of targets makes them often non-selective.

The weakness of drugs containing thiols is often the lack of selectivity and the use of pro-drugs or bioconjugation are potential solutions to the issue. However, the weak acidity of thiols makes them not suitable for self-immolative spacer groups. The use of thiocarbonate or thiocarbamate as pro-drug is also limited by the instability of these groups in water/organic based media.[1]

In this communication we describe a new 1-6 self-immolative spacer suitable for enzyme mediated release of thiols. As the aromaticity of the system is supposed to influence the disassembly kinetics of these spacers, we thought that poorly aromatic five membered heterocycles could be useful as scaffolds for the release of low acidity compounds such as thiols.

We applied this linker to ST7612, a powerful HDAC inhibitors containing thiol with in vitro activity in the nanomolar range (IC_{50} = 50 nM on NCI-H460 cells) associated with a remarkable in vivo antitumor activity.[2] The release kinetic was done through rreduction of the nitro moiety with nitroreductase, an enzyme over-expressed in hypoxic conditions including solid tumour cells and bacterial infected tissues.[3]

Computational studies were also carried out to understand the behaviour of this new promising system potentially useful also for other functional groups.

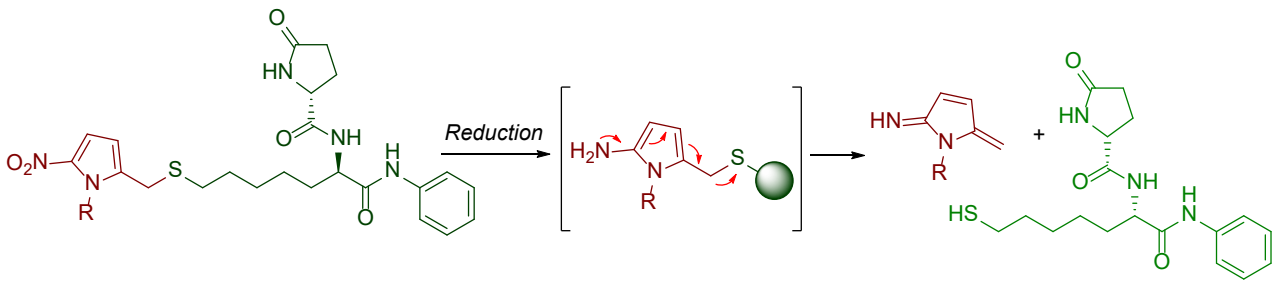

Figure 1

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Molecular Networking: a powerful tool to dereplication of natural products

G. Esposito,[a] *R. Teta*,[a] *G.Della Sala*,[b] *A. Mangoni*,[a] *L. Milella*,[c] *M. Lega*[d] *and V. Costantino*[a]

[a] *Dipartimento di Farmacia, Università degli Studi di Napoli "Federico II", Napoli, Italy;* [b] *Dipartimento di Biotecnologie Marine, Stazione Zoologica Anton Dohrn, Villa Comunale, 80121 Napoli, Italy;* [c] *Dipartimento di Scienza, Università della Basilicata, Italy;* [d] *Dipartimento di Ingegneria, Università di Napoli Parthenope, Centro Direzionale di Napoli, Isola C 4, 80143 Napoli, Italy*

The nature providing a large number of unusual skeletons from plants, marine organisms, and microorganisms is the main inspiration for novel lead compounds in drug discovery programs.

The challenge in natural product research is the fast identification of novel natural products from complex extracts, containing hundreds or thousands of different compounds, including primary metabolites, contaminants and known natural substances. This process, referred to as dereplication, is best achieved by high resolution liquid chromatography coupled with tandem mass spectrometry (LC-HRMS^2).[1] However, LC-HRMS^2 provides huge amounts of data that are hard to be examined manually. Molecular networking (MN) has been proven to be a powerful tool for the analysis of the results of LC-MS^2 experiments, allowing an automated identification of structural similarity between metabolites, which is inferred from the relatedness of their MS^2 spectra.[2] The Feature Based Molecular Networking approach, consisting of the preprocessing of LC-MS^2 raw data using software like MZmine,[3,4] has been shown to generate remarkably better networks when used with LC-MS^2 data obtained from crude extracts.

In our research group, the value of molecular networking was demonstrated in different applications.

In the discovery of natural products MN led to the isolation of four new antiproliferative polyketides, smenolactones A-D,[5] and two new hybrid peptide/polyketides, smenamide F and G, from the organic extract of *S. aurea*.

In the environmental field MN has speeded up the analysis of extracts of cyanoHAB sample from Avernus lake that let us to detect the presence of toxic cyanopeptides, i.e., microcystins, micropeptins, anabaenopeptins, and aeruginopeptins.

In the food field molecular networking was exploited for metabolomics analysis of pomace extracts. In particular, the feature-based network has allowed us to reveal how the chemical composition of these samples changes considering pomace from different origin areas or obtained with different extraction methods.

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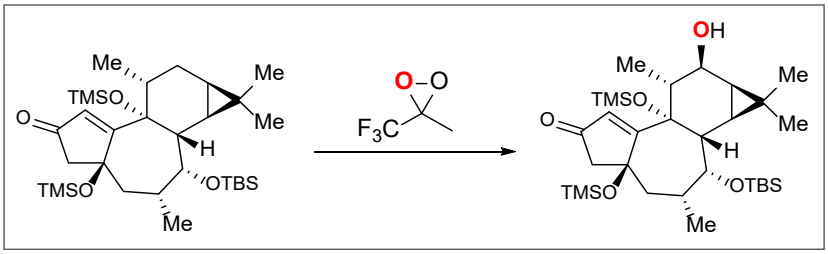
Hydrogen Atom Transfer based aliphatic C–H bond oxidation of hydrocarbons bearing cyclopropyl moieties. The role of hyperconjugation.

Marco Galeotti, Sergio Sisti, Michela Salamone and Massimo Bietti

Dipartimento di Scienze e Tecnologie Chimiche, Università "Tor Vergata", Via della Ricerca Scientifica, 1, I-00133 Rome, Italy

The selective functionalization of nonactivated aliphatic C−H bonds represents one of the most challenging reactions in modern organic synthesis.[1] Among the available methodologies, those based on hydrogen atom transfer (HAT) to radical[2] and radical-like species[3] have proven to be successful in pursuing this challenging goal. The factors that govern reactivity and selectivity in HAT from aliphatic C−H bonds have been discussed in detail.[1],[3c],[4] Within this framework, cyclopropyl groups have been shown to activate toward functionalization adjacent aliphatic C–H bonds by hyperconjugation. An outstanding example of this activation has been recently reported by Baran in a key step of the synthesis of (+)-phorbol, employing trifluoromethyldioxirane (TFDO) as the HAT reagent.[5] Oxidation occurs site- and stereoselctively at the C–H bond α- to the cyclopropyl group (**Scheme 1**), pointing toward the importance of these effects and their possible role in the elaboration of strategies for the synthesis of complex molecules.



Scheme 1. Site- and stereoselective C–H bond hydroxylation promoted by TFDO in a key synthetic step of the synthesis of (+)-phorbol.

In order to plan complex molecule total syntheses that involve one or more C–H functionalization steps, a deep knowledge of all the factors that govern C–H bond reactivity and selectivity is needed. Along this line, in order to obtain information on the role of hyperconjugation in HAT-based aliphatic C–H bond functionalization, we have investigated in detail the oxidation of bicyclo[n.1.0]alkanes (n = 3-6), spiro[2.5]octane and of some of their derivatives promoted by dioxiranes, with particular attention being devoted to the role of the cyclopropyl group on the site- and stereoselectivity of these processes. The results thus obtained will be presented.

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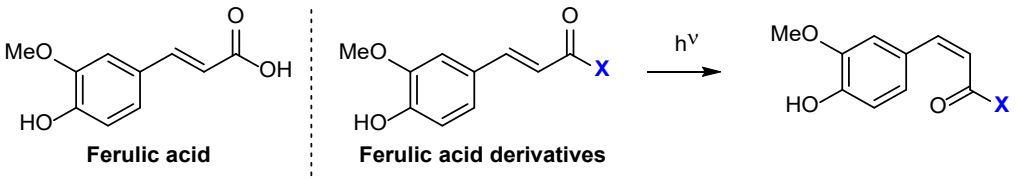
Photoisomerization of ferulic acid derivatives

Chiara Lambruschini, Luca Banfi, Andrea Basso, Lisa Moni, Alessia Mori, Federica Risso, Renata Riva

[a] *Department of Chemistry and Industrial Chemistry, University of Genova, Via Dodecaneso, 31, 16146 Genova, Italy*

Ferulic acid (FA) is a ubiquitous natural phenol and one of the most important phenolic acid. FA is found in many plants and can be extracted from lignin,[1] a non-edible fraction of biomass. Therefore, ferulic acid is a bio-based building block obtained from a renewable feedstock and an its valorization is an important goal.
Ferulic acid and its derivatives are well-known anti-oxidants, can be used as solar screens and have been studied as potential drugs. We have reported the biological properties of some feruoyl amides as inhibitors of beta-amyloid aggregation[2] and as anti-oxidant and lipid-lowering compounds.[3]
In this context, we discovered that one of our feruloyl amide was almost completely converted to the (Z) isomer under solar light. Although the photoisomerization of cinnamic acids is a well-known process, in all previous reports regarding ferulic acid derivatives the isomerization was only partial, at the photostationary state.
Herein, we report a thorough study on the photoisomerization of feruloyl derivatives aiming to shed a light on the structural requirements for a complete isomerization. These finding can open to the design of photo-responsive feruloyl conjugates, that can find application in both material and pharmaceutical sciences.



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Development of ArnT-mediated colistin resistance diterpene-based inhibitors

Francesca Ghirga,[a] Maria Luisa Mangoni,[b] Fiorentina Ascenzioni,[c] Francesco Imperi,[d] Mattia Mori, Bruno Botta [a]

[a] Department of Chemistry and Technology of Drugs, "Department of Excellence 2018−2022", Sapienza University of Rome, P.le Aldo Moro 5, 00185 Rome, Italy; [b]Department of Biochemical Sciences, Sapienza University of Rome, Laboratory Affiliated to Pasteur Italia-Fondazione Cenci Bolognetti, P.le Aldo Moro 5, 00185 Rome, Italy; [c] Department of Biology and Biotechnology Charles Darwin, Sapienza University of Rome, Laboratory Affiliated to Pasteur Italia-Fondazione Cenci Bolognetti, Via dei Sardi 70, 00185 Rome, Italy; [d] Department of Science, Roma Tre University,00146 Rome, Italy; [e] Department of Biotechnology, Chemistry and Pharmacy, "Department of Excellence 2018−2022", University of Siena, via Aldo Moro 2, 53100 Siena, Italy

Colistin is a last-line antibiotic for the treatment of multidrug resistant Gram-negative bacterial infections.1 Recently, a natural ent-beyerene diterpene was identified as a promising inhibitor of the enzyme responsible for colistin resistance mediated by lipid A aminoarabinosylation in Gram-negative bacteria, namely, ArnT (undecaprenyl phosphate-alpha-4-amino-4-deoxy-l-arabinose arabinosyl transferase).[1,2] To explore structure–activity relationship (SAR) and validate the versatility of the diterpene scaffold as a key platform for further development of ArnT-mediated colistin resistance inhibitors with improved activity, a library of semisynthetic analogues of hit were designed, synthesized and tested against colistin-resistant Pseudomonas aeruginosa strains, including clinical isolates.[3,4] Microbiological assays coupled with molecular modeling demonstrated that an ent-beyerane scaffold bearing an oxalate like group at C-18/C-19, or a sugar residue at C-19 to resemble L-Ara4N is an essential requirement for a more efficient inhibition of bacterial growth likely resulting from a more efficient inhibition of ArnT activity. Importantly, the easy accessibility of ent-beyerane scaffold from Stevia rebaudiana secondary metabolites will provide a cost-effective key platform for the development of promising colistin resistance inhibitors.

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Exploring PROTACs metabolism: a structure-activity relationship study

Laura Goracci,[a] Jenny Desantis,[a,#] Aurora Valeri,[b] Beatrice Castellani,[a] Michela Eleuteri,[a] Gabriele Cruciani[a]

[a] Department of Chemistry, Biology and Biotechnology, University of Perugia, 06123 Perugia, Italy; [b] Molecular Horizon, srl, Bettona 06084, Italy; #present address: Department of Molecular Medicine, University of Padua, 35121 Padova, Italy.

In the last two decades, many efforts have been made to decode the metabolic fate of drugs. Indeed, predicting or measuring pharmacokinetic properties of new chemical entities is today integral to the drug discovery process. Despite signs of progress in the field, all available ADME tools have been calibrated mainly using traditional small molecules, which mainly accomplish the Lipinski rules. In the comfortable space of small molecules, the accuracy and sensitivity of the models are usually very good.[1] More recently, the chemical space of drug-like compounds has expanded, including the emerging class of hetero-bifunctional PROteolysis TArgeting Chimeras (PROTACs). PROTACs are hetero-bifunctional molecules composed of a ligand for the protein of interest (POI), another ligand to recruit an E3 ubiquitin ligase, and a linker to concatenate the two ligands. The formation of the ternary complex composed of the POI, the PROTAC, and the E3 ligase allows the E2 ubiquitin-conjugating enzyme to transfer ubiquitin to the surface of the POI, inducing its proteasomal-dependent degradation. One of the main advantages of PROTACs is that they can degrade proteins regardless of their function, thus turning into druggable also the "undruggable", due to their innovative mechanism of action. Therefore, PROTACs represent an innovative class of compounds that overcome traditional limitations, opening a new therapeutic strategies and, at the same time, breaking the rules used so far with the potential to revolutionize drug discovery.[2] Despite the increasing number of publications about the synthesis, biological evaluation, and mechanism of action of PROTACs, the characterization of the pharmacokinetic properties of this class of compounds is still minimal. Therefore, we recently reported on the metabolism of a series of 40 PROTACs in cryopreserved human hepatocytes at multiple time points. In addition, a subset of compounds was also tested for metabolism by human cytochrome P450 3A4 (CYP3A4) and human aldehyde oxidase (hAOX) for more in-depth data interpretation, and both enzymes resulted active in PROTACs metabolism.[3] The accurate design of the dataset allowed us to highlight a first structure-property relationship for PROTACs metabolism and, more recently, the effect of other enzymes is under investigation.

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Toward marine inspired multitarget drugs for diabetes mellitus and its complications: design and synthesis of novel dual Protein Tyrosine Phosphatase 1B and Aldose Reductase ligands

Concetta Imperatore,[a] Marcello Casertano,[a] Paolo Paoli,[b] Antonella Del Corso,[c] Marialuisa Menna [a]

[a] Department of Pharmacy, University of Naples "Federico II", via D. Montesano 49, 80131 Naples, Italy; [b] Department of Experimental and Clinical Biomedical Sciences, University of Florence, Viale Morgagni 50, 50134 Firenze, Italy; [c] Department of Biology, University of Pisa, Via S. Zeno 51, 56123, Pisa, Italy.

Protein tyrosine phosphatase 1B (PTP1B) and aldose reductase (AR) enzymes are two emerging targets differently involved in the onset of type 2 diabetes mellitus (T2DM).[1] Diabetes mellitus is a complex disease and is one of the leading causes of death worldwide. Its development implies numerous metabolic dysfunctions and the onset of hyperglycaemia-induced chronic complications. The opportunity to design inhibitors capable to bind orthosteric and allosteric regions of both PTP1B and AR is a promising tool for the discovery of new designed multiple ligands for T2DM treatment. Marine environment offers an enormous pool of chemical structures with uncommon and different structural motifs with a wide range of pharmaceutical applications.[2] Phosphoeleganin (**1**, Figure 1), a marine-derived phosphorylated polyketide,[3,4] has been identified as novel dual inhibitor of PTP1B/AR. Therefore, in order to gain further insights into structural requirements for dual PTP1B/AR inhibition and to develop the identified natural hit to a promising lead candidate, a fragment-based approach inspired by phosphoeleganin has been performed.

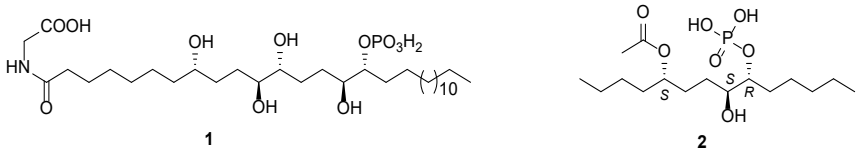

Figure 1. Structures of phosphoeleganin (**1**) and its simplified bioactive analogue (**2**).

The development of a versatile and efficient synthetic protocol was carried out due to effectively generate a small library of triol derivatives inspired to the functionalized polyol portion of phosphoeleganin. All the prepared synthetic simplified analogues have been tested for the inhibition of both enzymes and preliminary SAR studies have been performed. The obtained results evidenced that fragmentation of the molecule caused the loss of the activity on AR enzyme; moreover, a new phosphorylated triol (**2**, Figure 1) with a potent and selective inhibitory activity against PTP1B, has been identified, encouraging the further investigation of other structural motifs of **1** in search of new and more potent multitarget inhibitors.

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Phytotoxins produced by fungal pathogens of legume crops

Marco Masi,[a] Francisco Sautua,[b] Stefany Castaldi,[c] Rachele Isticato,[c] Marcelo Anibal Carmona,[b] Antonio Evidente[a]

[a] *Dipartimento di Scienze Chimiche, Università di Napoli Federico II, Complesso Universitario Monte S. Angelo, Via Cintia 4, 80126 Napoli, Italy*
[b] *Facultad de Agronomía, Cátedra de Fitopatología, Universidad de Buenos Aires, C1053 CABA, Buenos Aires, Argentina*
[c] *Dipartimento di Biologia, Università di Napoli Federico II, Complesso Universitario Monte S. Angelo, 80126 Napoli, Italy*

Despite their importance for the agriculture and the environment, the production of food legumes is decreasing in most of the farming systems. One of the major causes is the low and irregular yield of production due to biotic and abiotic stresses. Among the biotic constraints pathogenic fungi are the causal agents of the highest losses. They can produce phytotoxic metabolites involved in disease development and in symptom appearance. The isolation and chemical and biological characterization of these compounds is the first step to understand their role in the development of disease symptoms and select plant genotypes resistant to the pathogens [1]. Recently, a strain of the pathogenic *Ascochyta lentis* was isolated from lentil (*Lens culinaris*) and studied to ascertain its capability to produce bioactive metabolites. From its cultures three new anthraquinone derivatives and five known analogues were isolated. Four of them showed phytotoxicity on host and non-host plants [2]. During the last years different fungi were identified as the causal agents of several diseases on soybean (*Glycine max* L.), one of the most important crop in the world. In fact, soybean grains are utilized globally as a critical substrate for foods, feeds, fuels, and biobased materials. Thus, studies are needed to investigate the production of phytotoxic metabolites by these fungi belonging to different genera. In particular, strains of *Macrophomina phaeolina*, *Colletotrichum* spp. and *Cercospora* spp. were isolated from infected soybean plants in Argentina and Spain, grown in vitro and their cultures extracted and purified. Two new penta- and tetrasubstituted cyclopentenones, named phaseocyclopentenones A and B (**1** and **2**), together with guignardone A (**3**) (Fig. 1), were isolated from *M. phaseolina* cultures [3]. This communication will give an overview on the work carried out on the isolation and chemical and biological characterization of phytotoxins produced by fungal pathogens of legume crops and will illustrate the results obtained.

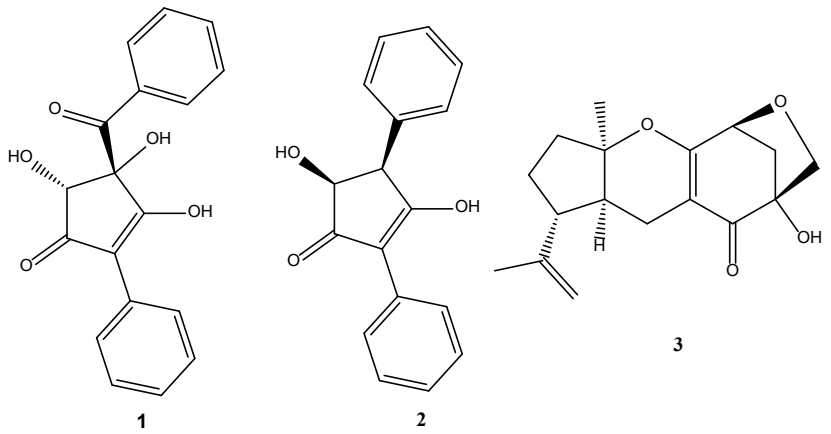

Figure 1. The structures of phaseocyclopentenones A and B (**1** and **2**), and guignardone A (**3**)

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Epigallocatechin-3-gallate-based Inhibitors Targeting EGFR to Overcome Drug Resistance in Advanced NSCLC

Minnelli Cristina[a], Laudadio Emiliano, Galeazzi Roberta[a], Mobbili Giovanna[a]

[a] Dipartimento di Scienze della Vita e dell'Ambiente, Università Politecnica delle Marche, via Brecce Bianche, 60131 Ancona, Italy; [b] Dipartimento di Scienze e Ingegneria della Materia, dell'Ambiente e Urbanistica, Università Politecnica delle Marche, via Brecce Bianche, 60131 Ancona, Italy

Epithelial Growth Factor Receptor (EGFR) is a kinase protein frequently overexpressed and aberrantly activated in non-small cell lung cancer (NSCLC). The occurrence of missense mutations induces local conformational changes and possible miss-folding of these proteins, causing the arise of resistance even to modern anticancer drugs. The use of Osimertinib (OS), a tyrosine kinase inhibitor (TKIs), has led to improved outcomes for advanced NSCLC patients. However, its efficacy is compromised by a tertiary mutation of the covalent anchor point Cys-797 to a less reactive serine occurring in 27% of all OS pre-treated patients [1] (Figure 1).

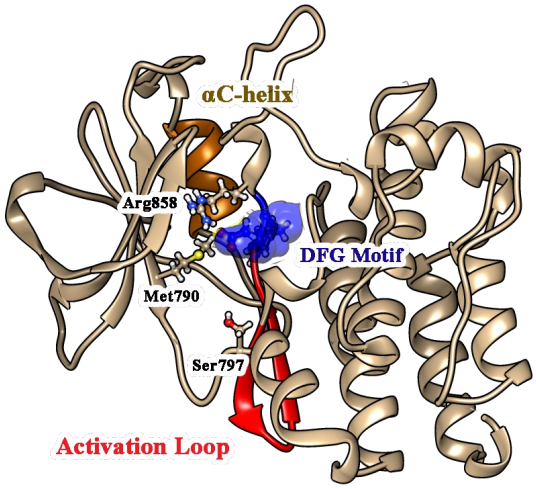

Figure 1. Structure of Epidermal Growth Factor (EGFR) Tyrosine Kinase Domain and the main mutated amminoacids involved in resistance mechanism.

Among the known anticancer agents that have recently been found to inhibit wild-type EGFR phosphorylation, there is Epigallocatechin-3-gallate (EGCG), a major biologically active constituent of green tea. This powerful polyphenol molecule has been used as a scaffold for the design of novel ATP-competitive inhibitors to overcome the EGFR drug resistance. Computational studies have been employed to shed insights on the molecular mechanisms of the EGCG kinase inhibition in the wild-type and mutated EGFR forms [2]. Cell-based experiments were also performed to ascertain the sensitivity of NSCLC mutant cells to EGCG. From the overall results obtained, the amminoacids mutations directly influence the binding affinity of EGCG, resulting in a different efficacy of EGCG inhibition. The collected data have been therefore used for drug design of novel EGCG-based inhibitors targeting the TK domain of the EGFR mutated forms. This aim was achieved through the identification of the key residues involved in the coordination of Mg^{2+} at the EGFR hydrophobic ATP binding pocket and considering the mutated amminoacids. Novel EGCG-based inhibitors were synthetized, characterized, and tested for their inhibitor EGFR activity in NSCLC cell lines. Results showed that the introduction of specific groups on EGCG structure that can interact with Arg858 displays an improvement of the binding affinity independently of the occurrence of the additional mutation C797S.

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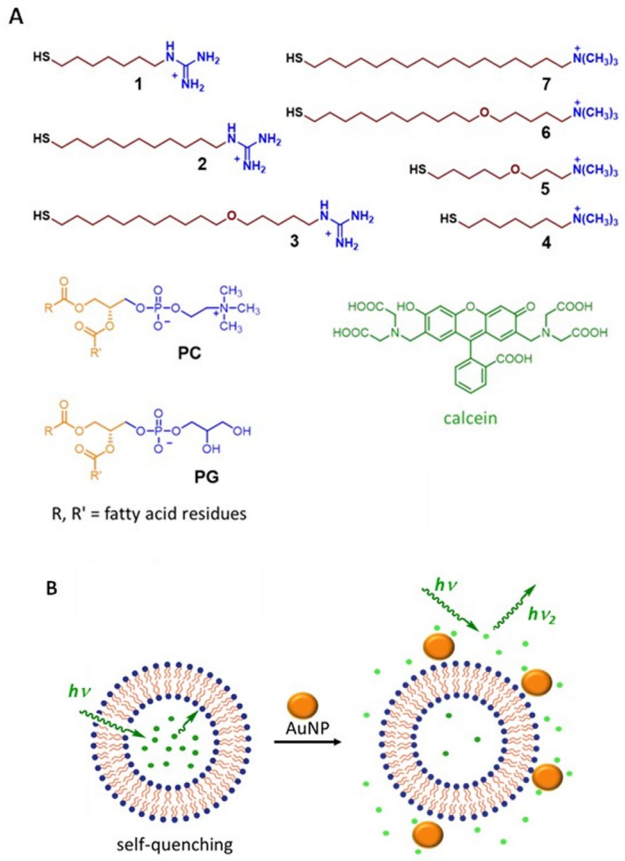
Specific and nondisruptive interaction of guanidium-functionalized gold nanoparticles with neutral phospholipid bilayers

Lucía Morillas-Becerril,[a] Sebastián Franco-Ulloa,[b] Ilaria Fortunati,[a] Roberto Marotta,[b] Xiaohuan Sun,[c] Giordano Zanoni,[a] Marco De Vivo,[b] and Fabrizio Mancin[a]

[a] Dipartimento di Scienze Chimiche, Università di Padova, via Marzolo 1, 35131 Padova, Italy; [b] Laboratory of Molecular Modeling and Drug Discovery, Istituto Italiano di Tecnologia, Via Morego 30, 16163 Genoa, Italy; [c] School of Chemistry and Chemical Engineering, Yangzhou University, Yangzhou, Jiangsu, 225002, P. R. China



Understanding and controlling the interaction between nanoparticles and biological entities is fundamental to the development of nanomedicine applications.[1] In particular, the possibility to develop nanoparticles capable to directly target neutral lipid membranes would be advantageous to numerous applications aiming at delivering nanoparticles and their cargos into cells and biological vesicles.[2-5] In this study,[6] we analyzed experimentally and computationally the interaction between liposomes and gold nanoparticles (AuNPs) featuring a cationic headgroups (1-7) in their protecting monolayer.

We found that only guanidinium-coated AuNPs can bind to neutral phosphatidylcholine liposomes, inducing nondisruptive membrane permeabilization. Atomistic molecular simulations revealed that this ability is due to the multivalent H-bonding interaction between the phosphate residues of the liposome's phospholipids and the guanidinium groups. Our results demonstrate that the peculiar properties of arginine magic, an effect responsible for the membranotropic properties of some naturally occurring peptides,[7] are also displayed by guanidinium-bearing functionalized AuNPs.

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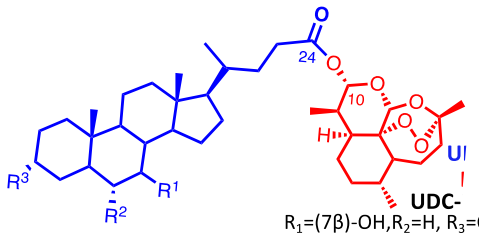
Dihydroartemisinin-bile acid hybridization as an effective approach to enhance dihydroartemisinin anticancer activity

Elena Marchesi,[a] Lorenzo Preti,[a] Massimo L. Capobianco,[b] Paolo Marchetti,[a] Lih-Ching Hsu,[c] Daniela Perrone[a] and Maria Luisa Navacchia[b]

[a] Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, 44121 Ferrara, Italy; [b]Institute of Organic Synthesis and Photoreactivity National Research Council Via P. Gobetti, 101, 40129, Bologna, Italy; [c] School of Pharmacy, National Taiwan University, No. 33, Linsen S. Road, Taipei 10050, Taiwan.

Combination therapy approaches can help to overcome drug resistance and to reduce toxicity. While there is considerable literature on the use of pharmacophores in combination with chemotherapeutics or phytochemicals, pharmacophore hybridization, involving the conjugation of at least one bioactive molecule through a covalent bond, is a more recent approach. Herein we report a new series of hybrids integrating two natural molecules such as dihydroartemisinin (DHA) and selected endogenous bile acids (BAs) through different linkage positions and linker nature (ester moiety, triazole, succinic chain). DHA, the main active metabolite of Artemisinin, a sesquiterpene lactone obtained from the plant *Artemisia annua*, is a well-known drug for the treatment of malaria. Previous studies have demonstrated that DHA exhibits also antitumor effects toward a variety of human cancers and has a potential for repurposing as an anticancer drug. Nevertheless, its short half-life may limit the application in cancer therapy. In this light, the conjugation approach can represent an interesting tool for the development of novel anticancer DHA based drugs. The biological study on BA-DHA hybrids was targeted toward a selection of human cancers such as hepatocellular carcinoma,[1,2] leukemia[1] and Diffuse Large B Cell Lymphoma[3] in order to evaluate BA-DHA hybrids anticancer activity and investigate the mechanisms of action. The hybridization efficiency was clearly highlighted by the enhanced cytotoxicity and cytoselectivity of the hybrids respect to the parent molecules.



UDC- R_1=(7β)-OH,R_2=H, R_3=OH	1.8	11.7	2.16	18.5	0.19	10.5

Figure. Sketch: molecular structure of hybrid UDC-DHA conjugated at C-24 position of ursodeoxycholic bile acid by condensation with OH-10 of DHA. Table: hybrid UDC-DHA antiproliferative effect against selected cancer cell lines.

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Gram-negative bacteria LPS recognition by DC-SIGN

Ferran Fabregat Nieto[a], *Antonio Molinaro*[a], *Franck Fieschi*[b], *Roberta Marchetti*[a], *Alba Silipo*[a]

[a] *Dipartimento di Scienze Chimiche, Università degli Studi di Napoli Federico II, Via Cinthia, 4, 80126 Napoli, Italy*

[b] *CNRS, CEA, Institut de Biologie Structurale Universitè Grenoble Alpes 71 avenue des Martyrs, 38000 Grenoble (France)*

Lectins play an important role in the innate immune system, being involved in the recognition of carbohydrates epitopes exposed on cell surfaces.[1] Due to their ability to recognise carbohydrate structures, lectins emerged as potential receptors for bacterial lipopolysaccharides (LPS). LPSs are heat stable amphiphilic molecules known for being the major component of the external leaflet of the Gram-negative bacteria outer membrane. They are one of the main virulence factors of bacteria and they are involved in host-microbe interaction processes.[2] LPSs are constituted by three portions: the lipid A, the core and the so called O-antigen when constituting the smooth form. However, if the O-antigen moiety is missing, they are characterized by a rough form and are known as lipooligosaccharides (LOS).[3]

Despite growing interest in investigating the association between host receptor lectins and exogenous glycan ligands, the molecular mechanisms underlying bacterial recognition by human lectins are still not fully understood.[4] Therefore, here is tackled the important question of envelope microbial glycans recognition by lectins, focusing our attention on dendritic cell-specific intracellular adhesion molecules (ICAM)-3 grabbing non-integrin (DC-SIGN).

In detail, a novel molecular interaction between the DC-SIGN and LPS isolated from different Gram-negative bacteria such as *Escherichia coli* and *Bacteroides vulgatus* has been unveiled. NMR ligand base techniques, like trNOESY, STD and DOSY NMR, combined with computational studies, were pivotal to prove the ability of DC-SIGN to recognise glycan moieties exposed on Gram-negative bacterial surfaces.

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Mimiviruses possess the biosynthetic pathways to produce bacteria-like sugars in a clade-specific manner

Anna Notaro[a,b], Olivier Poirot[b], Sebastien Nin[b], Michela Tonetti[c], Cristina De Castro[a], Chantal Abergel[b]

[a] Department of Agricultural Sciences, University of Naples. Naples. Italy.; [b]Aix–Marseille University, Centre National de la Recherche Scientifique, Information Génomique & Structurale, Unité Mixte de Recherche 7256 (Institut de Microbiologie de la Méditerranée, FR3479, IM2B), 13288 Marseille Cedex 9, France; [c]Department of Experimental Medicine and Center of Excellence for Biomedical Research, University of Genova. Genova. Italy

The discovery of giant viruses has broken many long-lasting beliefs on viruses [1]. For instance, it was evidenced that the members of the *Megamimivirinae* family possess many genes related to the production and manipulation of sugars [2]. It was soon proposed that these genes were involved in the glycosylation of the layer of fibrils surrounding their icosahedral capsid, a hallmark of the whole family. The best characterized prototype is *Mimivirus* (clade A) [1] for which we have recently shown that the fibrils were decorated by two polysaccharides [3], thus breaking the dogma that viruses decorate the capsid proteins with small oligosaccharides [4]. In the present study, we extended the study to the entire family, investigating the type of sugars present and the corresponding biosynthetic processes for each clade, using a combination of chemical methods and bioinformatics approaches. As a result, we have demonstrated that there is clade-specific glycosylation trend in the *Megamimivirinae* family, with at least one exception we will discuss. Indeed, each clade has characteristic and unusual sugars, such as viosamine for clade A, fucosamine for clade B and quinovosamine for clade C. Interestingly, all these sugars have been found in the bacterial world, often linked to pathogenesis. Furthermore, we have identified all the biosynthetic pathways that lead to the formation of these sugars as activated nucleotides. Similarly, to what happens in bacteria, we have shown that the genes involved in the production and assembly of sugars in the *Megamimivirinae* are organized in complex gene clusters. To conclude, the glycosylation of the giant viruses seems to be very complex and shows how far we are form a complete understanding of the viral glycosylation, opening new avenues in this field. Finally, we can consider giant viruses as a new source of active carbohydrates enzymes that could be used for biotechnological purposes.

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On-cell saturation transfer difference NMR for the identification of FimH ligands and inhibitors

Alessandro Palmioli [a], Paola Sperandeo [b], Sara Bertuzzi [a,c], Alessandra Polissi [b], Cristina Airoldi [a]

[a] BioOrg NMR Lab, Department of Biotechnology and Biosciences, University of Milano-Bicocca, P.zza della Scienza, 2, 20126 Milan, Italy; [b] Department of Pharmacological and Biomolecular Sciences, University of Milano, Via Balzaretti, 9/11/13, 20133 Milano, Italy; [c] Chemical Glycobiology Lab, Center for Cooperative Research in Biosciences (CIC-bioGUNE), 48160 Derio, Spain.

FimH is a mannose-binding bacterial adhesin expressed at the apical end of type 1 pili of uropathogenic bacterial strains and responsible for their D-mannose sensitive adhesion to host mammalian epithelial cells. [1] Because of these properties, FimH is a key virulence factor and an attractive therapeutic target for urinary tract infection. [2]
Here, we describe the development of an on-cell NMR method for the rapid screening of FimH ligands and the structural identification of ligand binding epitopes. [3] For this purpose, we prepared synthetic D-mannose decorated dendrimers, we tested their ability to prevent the FimH-mediated yeast agglutination, and thus we used the compounds showing the best inhibitory activity as models of FimH multivalent ligands to set up our NMR methodology.
Our experimental protocol, based on on-cell STD NMR techniques, is a suitable tool for the screening and the epitope mapping of FimH ligands aimed at the development of new antiadhesive and diagnostic tools against urinary tract infection pathogens. Notably, the study is carried out in a physiological environment, i.e. at the surface of living pathogen cells expressing FimH.

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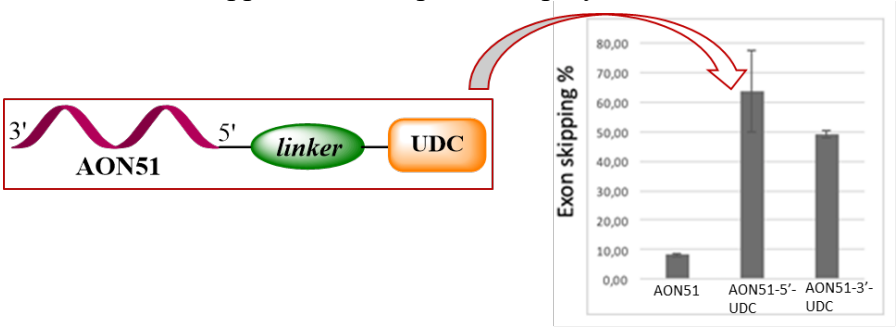
Synthesis and preclinical evaluation of antisense oligonucleotides conjugated with ursodeoxycholic acid for the treatment of Duchenne muscular dystrophy

D. Perrone[a], E. Marchesi[a], L. Preti[a], B. Palmieri[b], P. Braghetta[c], M. L. Capobianco[d], A. Medici[a], P. Rimessi[e], M. Sibilla[c] and M. Bovolenta[f]

[a]Department of Chemistry, Pharmaceutical and Agricultural Sciences, University of Ferrara; [b]Department of General Surgery and Surgical Specialties, University of Modena and Reggio; [c]Department of Molecular Medicine, University of Padova; [d]Institute of Organic Synthesis and Photoreactivity National Research Council; [e]Unit of Medical Genetics, Department of Medical Sciences, University of Ferrara, [f]Department of Translational Medicine, University of Ferrara.

Duchenne muscular dystrophy (DMD) is an X-linked recessive disease due to mutations in the dystrophin gene usually resulting in the complete absence of the protein. Currently, there are many therapeutic approaches aimed at restoring a functional dystrophin gene and/or muscular regeneration processes. One of the most promising is exon skipping based on the use of antisense oligonucleotides (AONs), to recognize specific pre-mRNA sequence target and modulate the splicing with restoration of the reading frame encoding for the dystrophin protein. AONs, used for exon-skipping approaches are short single stranded molecules of chemically modified RNA, resulting in improved efficacy and nuclease resistance. The main AON chemistries used for clinical treatment of DMD include the phosphorodiamidato morpholino (PMO), the 2'*O*-Me-phosphorothioato (2'OMePS) and 2'-*O*, 4'-*C*-ethylene-bridged (ENA) oligonucleotides [1]. Nevertheless, certain issues such as, poor delivery of AONs to all tissues affected by the disease, including skeletal and cardiac muscles and toxicity, remain to be solved for a long-life therapeutic use of modified AONs [2]. For this purpose, the conjugation of AONs with other molecular entities can represent an attractive strategy. Recently, we have conjugated several hydrophobic compounds at the 5'- and/or 3'-ends of the 2'OMePS antisense oligonucleotide targeting human *DMD* exon 51 (AON51), to improve AON bioavailability [3]. Particularly, AON51 conjugated at 5'-or 3'-end with ursodeoxycholic acid (UDCA), a secondary bile acid with anti-apoptotic and anti-inflammatory properties, showed a skipping efficiency greater than 40% compared to naked AON51, when tested on myotubes obtained by differentiation of a cell line of immortalized human myoblasts derived from a DMD patient. Furthermore, the immunofluorescence analysis showed restored expression of the dystrophin and correct localization at the sarcolemma only in the myotubes treated with AON51-UDC conjugates. Our recent proof-of-concept animal study confirmed effectiveness of UDCA-based-AON conjugates and encourage further studies to evaluate their applicable therapeutic employment in DMD treatment.



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Sustainable by Design Carbon Dots as promising material for luminescent and biomedical applications

Paola Lagonegro[a], Umberto Giovanella[a], Christian Bellacanzone[b], Camilla Marzuoli[b,c], Mariarosa Antognazza[b] and Mariacecilia Pasini[a]

[a] *Istituto di Scienze e Tecnologie Chimiche "Giulio Natta" (SCITEC)-CNR, via corti 12, Milano, Italy.*
[b] *Center for Nano Science and Technology @PoliMi, Istituto Italiano di Tecnologia, via Pascoli 70/3, 20133 Milano, Italy.*
[c] *Politecnico di Milano, Dipartimento di Fisica, P.zza L. Da Vinci 32, 20133 Milano, Italy.*

In the last 10 years the interest on carbon dots (CDs) has been progressively increased in different fields. Their remarkable advantages in terms of low toxicity, chemical inertness, tunable fluorescence, good water solubility, and physicochemical properties make them suitable not only for sustainable luminescent applications but also for bio-based applications and in particular in the biomedical field [1], [2]. Another peculiarity of CDs is that their synthesis fully responds to the principles of the circular chemistry.
In the present work, we show the synthesis, characterization and preliminary applications of nitrogen-doped CDs (N-CDs). N-CDs synthesized by one-step hydrothermal methods starting from waste/renewable materials as citric acid and urea (Figure 1). TEM, XRD and FT-IR analysis confirmed the nature of the N-CDs. UV-Vis absorption and photoluminescence spectra showed that optical properties of N-CDs can be tuned over the visible spectrum simply by changing the ratio between reagents and reaction conditions.
Particularly, N-CDs with absorption above 470 nm were selected to evaluate their cytotoxicity and internalization at 24 and 72h. On the basis of the obtained results their photocatalytic activity will be test with the aim to modulate the generation of reactive oxygen species (ROS)[3].

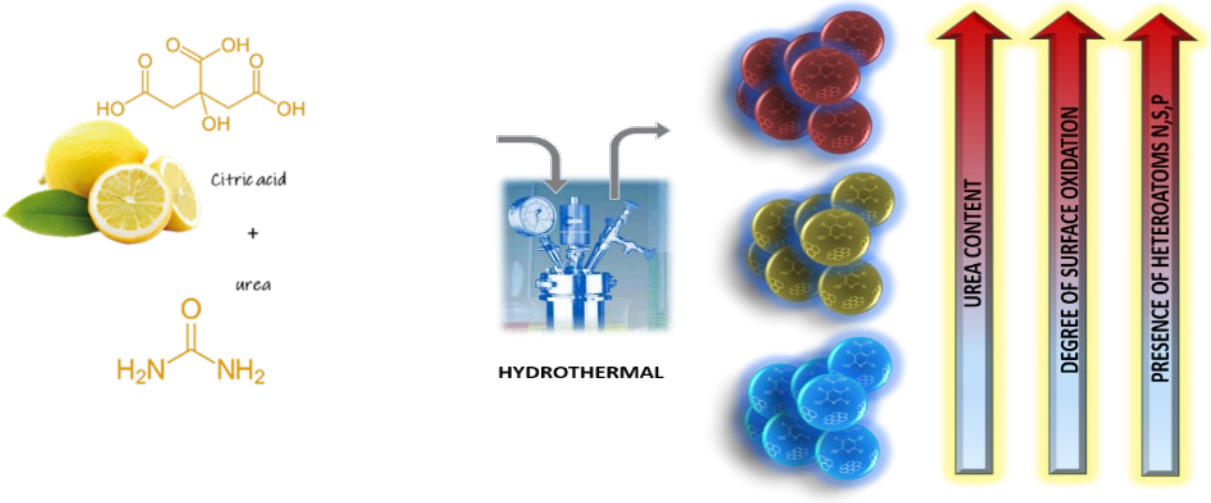

Figure 1. Schematic representation of CDs preparation and tailoring strategy.

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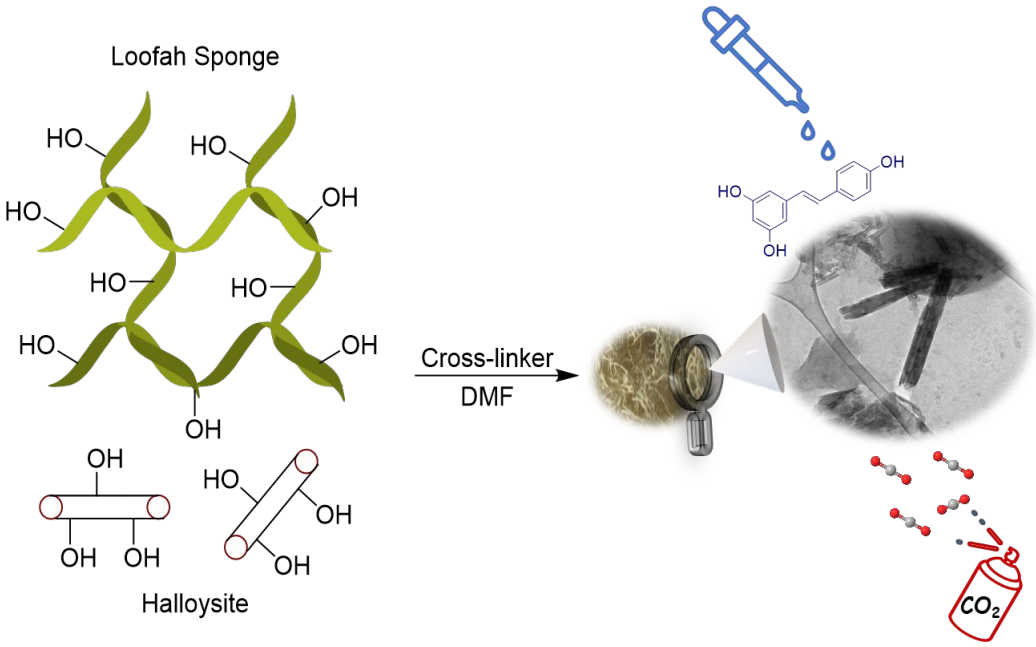
A new hybrid porous multifunctional material based on Loofah-Halloysite

Vincenzo Patamia,[a] Roberto Fiorenza,[b] Massimo Zambito Marsala,[c] Stefano A. Balsamo,[b] Vincenzina Barbera,[c] Salvatore Scirè,[b] Antonio Rescifina[a]

[a]Department of Drug and Health Sciences, University of Catania, V.le A. Doria, 95125 Catania, Italy
[b]Department of Chemical Sciences, University of Catania, V.le A. Doria, 95125 Catania, Italy
[c]Department of Chemistry, Materials and Chemical Engineering "G. Natta", Politecnico di Milano, Via Mancinelli 7, Milano, 20131, Italy

The advancement of materials science and technology has led researchers to look at nature to find new materials with high performance and low cost. Among these, the Loofah sponge (LS) has been widely used as a natural material in industrial applications, thanks to its polyporous structure and light consistency.[1] This work aims to functionalize the LS fibers with Halloysite, a clay mineral of the kaolin group,[2] to improve its adsorption performance. Two different crosslinkers were used for functionalization, and the new composites were characterized by Fourier-transform infrared spectroscopy (FT-IR in ATR mode), Thermogravimetric analysis (TGA), Scanning Electron Microscopy (SEM) and High-Resolution Transmission Electron Microscopy (HR-TEM). The composites were applied for the carbon dioxide capture studies, showing superior adsorption capacities compared to the single components, LS and Halloysite, and to materials currently used in industry, such as BEA and MOR zeolites. Furthermore, this new composite has proved to be an excellent candidate for the delivery of Resveratrol. The preliminary results underline the synergistic effect of functionalization in increasing the adsorption properties compared to the starting materials and the possibility of using this new low-cost porous system in various fields such as gas adsorption and drug delivery.



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Synthesis and characterization of different mussel inspired materials for several applications

Marina Massaro,[a] Maria Laura Alfieri,[b] Marco d'Ischia,[b] Michelangelo Gruttadauria,[a] Giuseppe Lazzara,[c] Leonarda F. Liotta,[d] Serena Riela[a]

[a] *Dipartimento STEBICEF, Sez. Chimica, Università degli Studi di Palermo, Viale delle Scienze, Ed. 17, 90128 Palermo, Italy.*
[b] *Dipartimento di Scienze Chimiche, Università di Napoli Federico II, Via Cinthia 4, I-80126 Napoli, Italy.*
[c] *Dipartimento di Fisica e Chimica, Università degli Studi di Palermo, Viale delle Scienze, Ed. 17, 90128 Palermo, Italy.*
[d] *Istituto per lo Studio dei Materiali Nanostrutturati (ISMN)-CNR, Via Ugo La Malfa 153, 90146 Palermo, Italy.*

Polydopamine (PDA) is widely used as hydrophilic coating for several applications. Up to now, most of the methods studied to improve or manipulate PDA properties are multistep and time-consuming, and there is a need for versatile strategies aimed at controlling and modifying the properties of PDA. Furthermore, the polymerization process requires alkaline conditions or the use of oxidants, causing uncontrolled precipitation of polymer in the reaction medium [1]. Thus, development of selective methodologies for the site-controlled functionalization of surfaces appears to be an important goal for various technological and biomedical applications.
Halloysite nanotubes (HNTs) are an aluminosilicate clay, belonging to the kaolin group, which possess predominant hollow tubular morphology and tunable surface chemistry. Due to their high mechanical strength and good biocompatibility, HNTs provide a versatile core structure for the design of functional nanosystems of potential technological and biomedical interest [2].
Herein we report the synthesis and characterization of mussel-inspired nanomaterials, based on the combination of organic and inorganic components, which have found applications both in the biological field and environmental remediation [3,4].
Acknowledgements: PRIN2017-2017YJMPZN

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Fluorinated Polymers and Fluorescent Graphene as Innovative Nanotheranostic Materials

Giulia Neri [a], Anna Piperno [a], Francesco Cellesi [b], Francesca Baldelli Bombelli [b], Pierangelo Metrangolo [b]

[a] Department of Chemical, Biological, Pharmaceutical and Environmental Sciences, University of Messina, V.le F. Stagno d'Alcontres 31, 98166 Messina, Italy; [b] Department of Chemistry, Materials, and Chemical Engineering "Giulio Natta", Politecnico di Milano V. Luigi Mancinelli, 20131 Milan (Italy)

Nowadays the development of nanoscale devices with multifunctional properties (such as specific cell targeting, therapeutic agent's delivering, and medical imaging), represents a significant step forward in nanomedicine. [1]
These systems showed unique properties compared to the corresponding bulk ones. In particular, the design of all-in-one nanosystems can lead to an enhancement of the biocompatibility and colloidal stability, resulting in well-tuned therapeutic and diagnostic actions.
In this context we developed and characterized a new generation of ^{19}F MRI nanotheranostic devices based on poly(lactic-co-glycolic acid) (PLGA) and hyperbranched polyether copolymers [2,3]. Such systems showed promising results as ^{19}F MRI contrast agents, while preserving good cytocompatibility and drug nanocarrier ability.
In the field of nanomedicine we additionally designed and studied the behavior of a new fluorescently labeled cationic cyclodextrin− graphene nanoplatform (GCD@Ada-Rhod), by investigating its intracellular trafficking and ability to deliver plasmid DNA and microRNA [4]. Moreover, the changes in the expression of genes involved in angiogenesis processes, extracellular matrix (ECM) modification and tumor metastasis were examined [5].

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Cellulose nanocrystals for paper consolidation

Alessandra Operamolla,[a] Claudia Mazzuca,[b,c] Laura Capodieci,[d] Francesca Di Benedetto,[d] Leonardo Severini,[c] Mattia Titubante,[c] Andrea Martinelli,[e] Valter Castelvetro[a] and Laura Micheli[b,c]

alessandra.operamolla@unipi.it

[a] Dipartimento di Chimica e Chimica Industriale, Università di Pisa, via Giuseppe Moruzzi, 13, 56124 Pisa; [b] Dipartimento di Scienze e Tecnologie Chimiche, Università degli Studi di Roma Tor Vergata e [c] Unità CSGI (Consorzio Interuniversitario per lo Sviluppo dei Sistemi a grande Interfase) di Roma, Via della Ricerca Scientifica, I-00173 Rome, Italy; [d] Laboratory for Functional Materials and Technologies for Sustainable Applications (SSPT-PROMAS-MATAS), ENEA – Italian National Agency for New Technologies, Energy and Sustainable Economic Development, S.S. 7 Appia km 706, I-72100 Brindisi (Br), Italy; [e] Dipartimento di Chimica, Università degli Studi di Roma " Sapienza" - Piazzale Aldo Moro 5, 00185 Roma

Cellulose nanocrystals (CNCs) [1] are renewable and nontoxic [2] elementary fibrils with a high aspect ratio (width 5-50 nm and length 100-500 nm), low density (1.6 g/cm³) and high tensile strength (Young's modulus 100–140 GPa). [3] Thanks to the presence of pending hydroxyl groups, a wide variety of functionalities can be anchored on their surface, offering the opportunity to modify their self-assembling behavior or to tune their intriguing properties. CNCs are ideal building blocks for smart architectures where environmentally friendly and multifunctional substrates are desired and have a straightforward connection to paper technology and paper-based devices. [4]
Only recently, nanocelluloses have been suggested as consolidation treatment for the conservation of ancient paper artefacts.[5] They do not necessitate any adhesive for their application on paper, because they are composed of the same biopolymer: cellulose.
Herein, we present an innovative but fundamental contribution to the field of Cultural Heritage and of paper restoration [6]: first, we describe in detail the positive effect on the paper properties of the application of a cellulose nanocrystals water suspension. We offer useful insights onto the influence of the nanocellulose functional group (sulfate vs hydroxyl) on the characteristics of the restored paper. Finally, we propose a successful approach, based on the application of a gel combined with an electrochemical monitoring facility, for removing the treatment from the paper surface, demonstrating the potential reversibility of the restoration treatment, and its safe removal once it has reached its end-of-life and needs to be replaced by a new conservation treatment.

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Transamidation-based vitrimers from renewable sources

Luca Pettazzoni[a], Francesca Leonelli[a], Andrea Martinelli[a], Valerio Di Lisio[a], Sara Alfano[a], Daniele Di Luca[a], Lorenzo Celio[a]

[a] *Department of Chemistry, "Sapienza" University of Rome, Italy*

Vitrimers are polymeric materials that behave as thermosets at room temperature but, when heated, they exhibit a plastic flow similar to thermoplastics, enabling their reprocessability[1]. This behavior is due to the presence of dynamic cross-linking functions, that at high temperature can generate an exchange process between the latter.

A series of new bio-based polyamide-polyamine vitrimers has been synthetized starting from tris(2-aminoethyl)amine and epoxidized methyl oleate, a material that can be easily prepared from renewable resources obtainable both from natural products and waste. The incorporation of free amine groups in the network enables the transamidation exchange reaction with the crosslinking amide functions (Fig 1). This reaction, that is strongly underused in vitrimers chemistry, if it is appropriately catalyzed donates a full reprocessability to the material. During our work we tested different catalyst, but our choice fell on boric acid, that is known to be a green, economic and low toxicity catalyst for transamidation reactions[2]. Different catalyst loading, ranging from 0% to 10%, have been tested, and the obtained materials have been subjected to thermal and mechanical characterization.

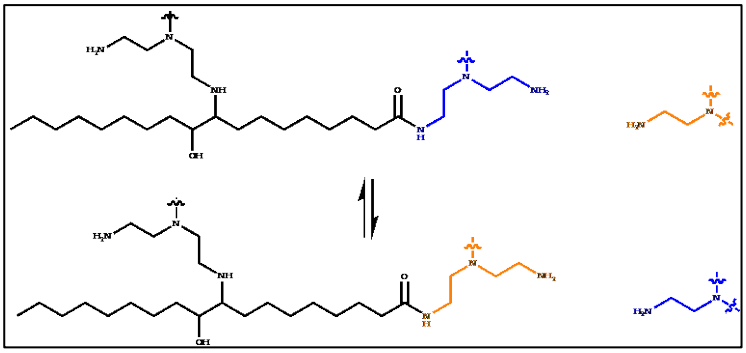

Figure 1: Transamidation exchange reaction in the network

The materials are almost insoluble in the most common organic solvents, indicating that these are densely cross-linked; at the same time, they can be easily reprocessed at 140°C for 2 hours. They demonstrate an excellent thermal stability up to 350°C and a T_g value ranging between 9 and 24°C, depending on the amount of boric acid present in the material (Table 1).

	0% $B(OH)_3$	2% $B(OH)_3$	5% $B(OH)_3$	10% $B(OH)_3$
T_g (°C)	9	10	12	24
E_a (Kj/mol)	-	150	89	65

Table 1: T_g and activation energies (E_a) for each material prepared

Using the stress-relaxation experiments performed at different temperatures, Arrhenius plots were obtained and the activation energies for the transamidation reactions in each material were calculated; as expected a lowering in the activation energy is observed as the catalyst loading increase (Table 1). Lastly, stress-strain experiments were performed on all the pristine samples and on the reprocessed ones, showing an excellent recovery of the initial elastic modulus.

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Improvement of properties of halloysite and some other «friends» by chemical modifications

Serena Riela

Dipartimento STEBICEF, Sez. Chimica, Università degli Studi di Palermo, Viale delle Scienze, Ed. 17, 90128 Palermo, Italy.

Clay minerals have been used for medical purposes from ancient times. Among them, the halloysite nanotube, an aluminosilicate of the kaolin group, is an emerging nanomaterial which possesses peculiar chemical characteristics. By means of suitable modifications, such as supramolecular functionalization or covalent modifications, it is possible to obtain novel nanomaterials with tunable properties for several applications [1,2].
Herein it is reported the covalent grafting of suitable organic moieties on the external surface of halloysite to improve the loading and release of several biologically active molecules. The resulting hybrid nanomaterials could be applied as drug carrier and delivery systems, as fillers for hydrogels, in tissue regeneration and in the gene delivery field.
In addition, combination of halloysite with other clay minerals led to the production of interesting nanomaterials with enhanced properties [3].

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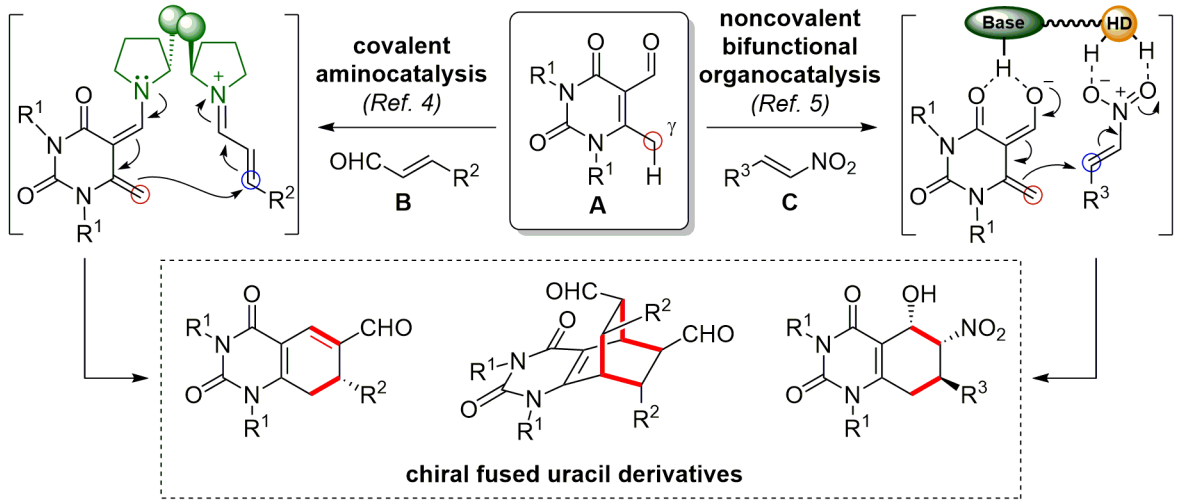
Merging Vinylogy with Organocatalysis: Direct, Asymmetric Entry to Chiral Fused Uracil Derivatives

Claudio Curti, Enrico Marcantonio, Franca Zanardi

Department of Food and Drug, University of Parma, Parco Area delle Scienze 27/A, I-43124 Parma, Italy

claudio.curti@unipr.it



In the continuous search of new potentially active molecules, differently functionalized purine and pyrimidine scaffolds represent important lead structures of chemical and pharmaceutical interest.[1] Among these variegated classes of molecules, fused-uracil derivatives (molecules featuring an uracil core "fused" with one or more functionalized rings) are particularly attractive compounds, as demonstrated by their wide bioactivity profile as anticancer, antiviral, antifungal, antibacterial, anti-inflammatory, and analgesic agents.[2] In this context, despite chiral, enantiopure uracil derivatives represent an important set of bioactive molecules, the search of efficient and stereoselective methodologies for the construction of such motives by asymmetric catalysis is largely unexplored.

As part of our ongoing studies on the development of new, catalytic, enantioselective vinylogous transformations applied to π-extended enolate-type donor systems,[3] we recently focused on remotely enolizable 6-methyluracil-5-carbaldehydes of type **A**, an underestimated class of vinylogous pronucleophiles to be engaged in direct, asymmetric [4+2] cyclizations with suitable acceptors. Indeed, under the strategic exploitation of covalent and noncovalent organocatalysis, dearomative, vinylogous enolization strategies were implemented, in which *ortho*-quinodimethane-type dienolate intermediates were efficiently trapped by either enals **B**[4] or nitroolefins **C**[5] to give differently functionalized, chiral and enantioenriched fused uracil derivatives in good yields and high stereoselectivities.

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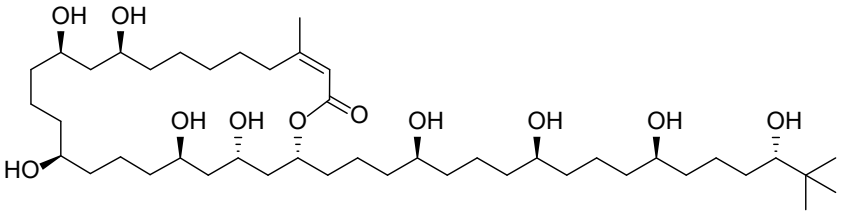
Synthetic studies towards Bastimolide B

Daniele Fiorito,[a] Selbi Keskin,[a] Varinder K. Aggarwal[a]

[a] *School of Chemistry, University of Bristol, Cantock's Close, Bristol, UK*

Bastimolide B is a polyhydroxy macrolide isolated from marine cyanobacteria displaying antimalarial activity.[1] It features a dense array of hydroxylated stereogenic centers, mainly in 1,5-relative configuration. These 1,5-polyols represent a particularly challenging structural motif for synthesis, as methods for their stereoselective construction are scarce and at best limited in scope.[2] Herein, we present a strategy for 1,5-polyol stereocontrolled synthesis based on iterative boronic ester homologation with enantiopure magnesium carbenoids.[3] By merging boronic ester homologation and transition metal-catalyzed alkene hydroboration and diboration, the backbone of Bastimolide was rapidly assembled from readily available building blocks with full stereochemical control.[4] This approach capitalizes on the assembly-line strategy devised for methyl-bearing deoxypolypropionates and it opens new directions in the stereocontrolled synthesis of hydroxylated polyketides.[5]



bastimolide B

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Highly oleophilic and reusable polyurethane composites for the removal of oils from fresh water and seawater

P. Costanzo[a], *F. Olivito*[a], *A. Jiritano*[a], *V. Algieri*[a], *M. Tallarida*[a], *L. Maiuolo*[a], *A. De Nino*[a]

[a] *Università della Calabria, Ponte Bucci, cubo 12C, 87036 Arcavacata di Rende (CS)*

Tons of crude and refined oils are transported across our lands and seas every day and the spillages represent a serious problem for environmental contamination [1]. The low biodegradability together with marked toxicity represent a threat to the entire ecosystem. The strategy for oil recovery can be chemical or physical. There are two types of chemical adsorbents: synthetics and naturals. These categories possess both advantages and disadvantages [2]. Synthetic adsorbents are usually difficult to dispose of, while the natural ones can be strongly affected by the environmental conditions, for example, the pH of the medium and the weather conditions. Composites are a type of material with enhanced properties with respect to the starting materials [3]. In our recent works, we proposed a green catalytic route, based on a single initial addition of a very cheap catalyst, for the production of polyurethane foams [4]. We decided to investigate one of these foams produced with PEG 400, Isophorone di-isocyanate and 1,2 ethylene glycol as a chain extender, to produce two composites by a micro-particle surface coating using silica and activated carbon. The polyurethane and the relative composites, completely aromatic compound free, were tested for the removal of diesel, gasoline, and oil engine from fresh water and seawater samples [Figure 1]. The best performance was given by the composite with activated carbon with enhanced adsorption up to 50% with respect to the polyurethane alone. The materials tested can be regenerated by a simple centrifugation up to 50 times without a significant loss in adsorption capacity.

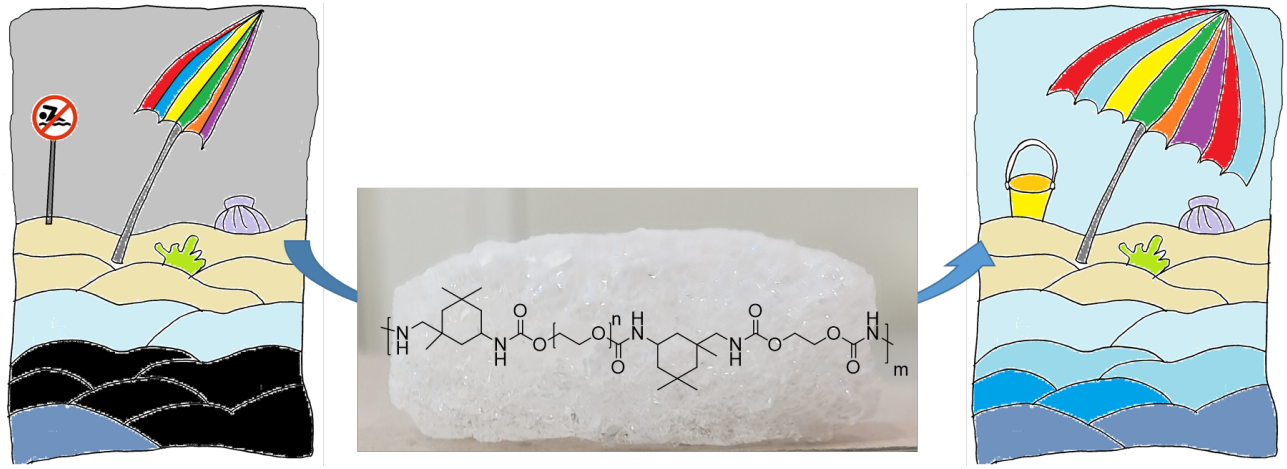

Figure 1. Structure and use of polyuretnane studied.

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Email: paola.costanzo@unical.it

Reactive Deep Eutectic Solvents (ReDESs): an underexploited option for organic chemistry

Andrea Mezzetta,[*a] *Christian Silvio Pomelli,*[a] *Lorenzo Guazzelli*[a]

[a] *Università di Pisa, Dipartimento di Farmacia, via Bonanno 33, 56126 Pisa, Italy*

Transition toward sustainable chemistry is boosting the search for solvents endowed with safe, renewable and environmentally friendly profiles which can be suitable alternative to traditional volatile organic solvents. In this context, Deep eutectic solvents (DESs) emerged as one of the most encouraging media for several research areas. DESs are binary mixtures of two distinct species which display freezing temperatures at the eutectic point well below the ideal expected ones. Usually, this deviation from ideality is rationalized considering the strong hydrogen bonding interactions between a hydrogen bond donor (HBD) and a hydrogen bond acceptor (HBA) that cause in some cases impressive freezing temperature decrement.[1] A very attractive feature of the DESs is the possibility to fine-tune their physico-chemical properties by choosing the appropriate partners, molar ratio and amount of water. This peculiar aspect holds true for a subset of DESs, the so-called Natural DESs (NaDESs), which are mixtures composed solely by natural partners (such as organic acids, plant metabolites, sugars or aminoacids). NaDESs are regarded as the most promising solvent option for the development of sustainable chemistry on account of the ease of preparation and low cost, the modulability of their physicochemical properties, their benign (eco)toxicological profiles.[2]

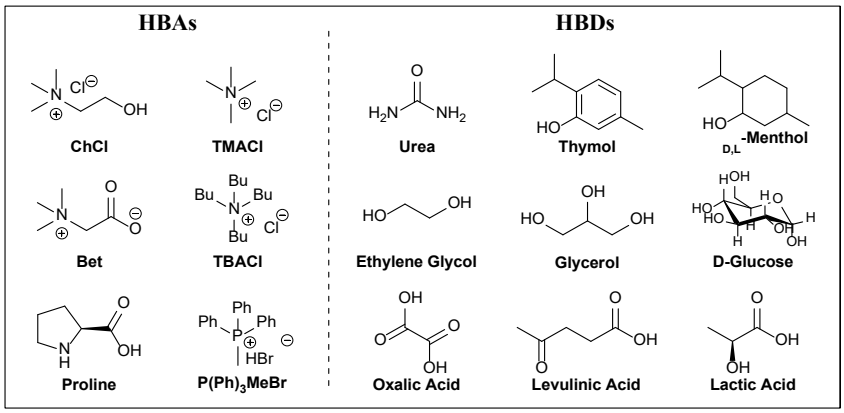

Figure 1. Common hydrogen bond acceptors (HBAs) and hydrogen bond donors (HBDs) DES partners.

In the last years, the use of DESs as *green* innocent solvents in organic synthesis has been reported for a wide range of reactions. Particular emphasis has been direct towards the possible dual solvent-catalyst role played by DESs. However, their use as reactive media has been almost completely overlooked. In the present work, the potential of reactive DESs (ReDESs) as innovative media for the synthesis of bio-derived compounds has been investigated. Sustainability aspects have been evaluated by using green metric parameters, while the effect of these innovative systems on the reaction mechanism has been assessed by means of DFT calculations.

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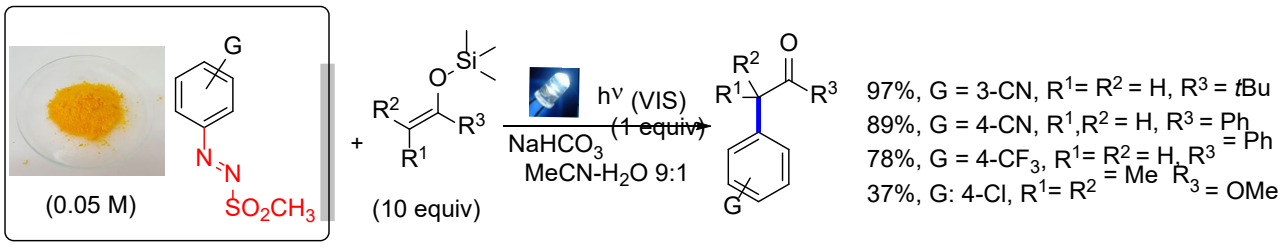
Visible light-driven α-arylation of enol silyl ethers via arylazo sulfones.

Lorenzo Di Terlizzi, Ivana Cola, Carlotta Raviola, Maurizio Fagnoni and Stefano Protti

PhotoGreen Lab, Department of Chemistry, University of Pavia, Viale Taramelli 12, Pavia 27100.
E-mail: Lorenzo.diterlizzi@universitadipavia.it

The structural motif of α-aryl ketones or esters is commonly present in both natural and artificial bioactive products.[1,2] As for the preparation of these ketones and esters, in recent years, the photoredox catalyzed α-arylation of enol acetates and silyl ethers by aryl diazonium salts has been proposed as a mild and promising alternative to traditional transition metal catalysed cross coupling reactions.[3]

Our group investigated in details the photochemistry of arylazo sulfones ($ArN_2SO_2CH_3$), yellow to orange bench-stable compounds bearing a dyedauxiliary group (DG = $-N_2SO_2CH_3$) able to impart both color and photoreactivity to the molecule.[4,5] Indeed, the photoremoval of the DG group upon visible light irradiation has been exploited for the generation of aryl radicals and their use in Ar-C and Ar-heteroatom bond formation.[4] We present herein a protocol for the synthesis of α-aryl ketones and esters under photocatalyst- and metal-free conditions by using arylazo sulfones as source of aryl radicals and enol silyl ethers as the coupling partners. The reaction is performed upon visible light (456 nm) irradiation in mixed organic/aqueous solvent and in the presence of a buffering agent ($NaHCO_3$, 1 equiv).



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Greening peptide synthesis: new options for a sustainable chemistry

Lucia Ferrazzano[a], Alessandra Tolomelli*[a], Walter Cabri*[a]

[a] *Department of Chemistry "Giacomo Ciamician", Via Selmi 2, 40128 Bologna (Italy);* [b] *Affiliation (Times New Roman, 11 pt, Italics, justified)*

Due to the increasing demand from the chemical and pharmaceutical markets for chemically synthesized peptide therapeutics, great attention has been paid to the use of greener solvents for their synthesis. In fact, several market studies estimated a consistent global grow and success of the peptide segment from 29 billion $ in 2019 to 48 billion $ in 2025, with an annual 10% increase.[1] Renaissance of peptide therapeutics has occurred in the last few years, with nowadays about 70 therapeutic peptides launched on the market and more than 100 currently running the clinical trial stages.[2] From a synthetic point of view, in pharmaceutical industry the solvents represent the main waste of a chemical process playing a key role in the toxicity of the overall process as consequence of their use only as medium in which the reactions occur.[3]
The production of peptides is mainly performed by solid-phase synthesis (SPPS), which gives access to long sequences with pharmaceutical purity grades and good yields. On the other hand, SPPS is characterized by large volumes of solvents, mainly DMF or NMP, with dramatic impact on both atom economy and production green metrics.[4] In this context, we recently contributed to the identification of alternative solvents aimed at improving the environmental health and safety profile of these protocols.[5,6] Anyway, since the role of the solvent in SPPS is to efficiently assist the swelling of the resins,[7] the couplings, the deprotections and the washings, it is difficult to find good-performing new single green solvents able to simultaneously do well in all these different steps. In order to include green solvents that have been excluded from the previous studies, we tested mixtures of solvents showing efficient properties as swelling agents and solubilization media. We reported a study on the replacement of DMF in solid-phase peptide synthesis with binary mixtures of green solvents (GM-SPPS), obtained by mixing Cyrene™ (Cyr), Sulfolane (Sul), Anisole (An), N-octylpyrrolidne (NOP) with Dimethyl or Diethyl carbonate (DMC/DEC), evaluating their efficiency in terms of swelling of the resins, coupling, deprotection and washings processes and applying the best performing protocols to the synthesis of model peptides (Aib-enkephalin and Aib-ACP) and of a pharmaceutical grade peptide (Octreotide). In particular for the mixture NOP/DMC, it is worth nothing that the solvents and the piperidine used in the deprotection step could be easily recovered by direct distillation from the process waste mixture. The process mass intiensity (PMI), being reduced by 63-66%, achieved an outstanding value representing a clear step forward in SPPS greening.

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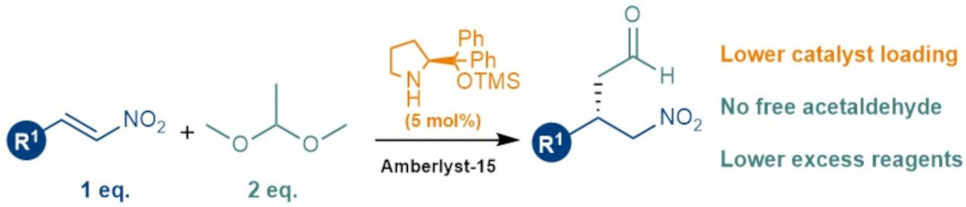
Organocatalysed Michael addition of masked acetaldehyde to nitroalkenes in water

Valeria Nori[a], Giuliana Giorgianni[a], Arianna Sinibaldi[a], Francesca Di Donato[a], Alessandra Biancolillo[a], Angelo Antonio D'Archivio[a], Aitor Landa[b], Fabio Pesciaioli[a], Armando Carlone[a]

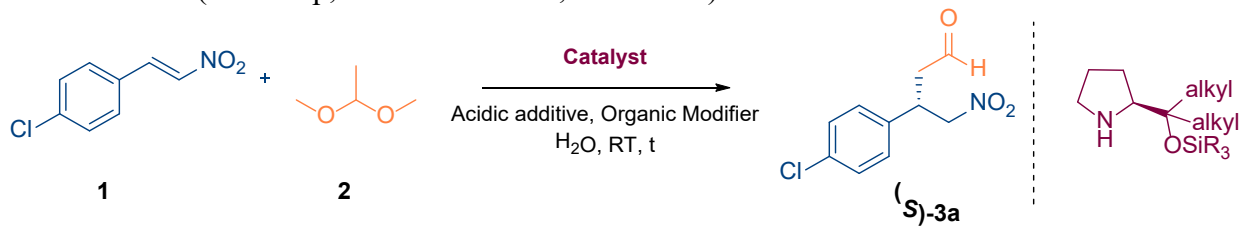
[a] *Department of Physical and Chemical Sciences, Università degli Studi dell'Aquila, via Vetoio, 67100 L'Aquila, Italy;* [b] *Departamento de Química Orgánica I, Universidad del País Vasco, Manuel Lardizabal 3. 20018-San Sebastián, Spain.*

valeria.nori@graduate.univaq.it

In our recently published work, a novel and safe reaction for the enantioselective enamine-catalysed addition of acetaldehyde to nitroalkenes is presented: this protocol makes use of a safe acetaldehyde precursor to access important intermediates to APIs and allows the use of fewer equivalents of acetaldehyde and lower catalyst loadings[1]. Therefore, we have developed an industrially useful protocol for the Michael addition of acetaldehyde to nitroalkenes, affording the corresponding products in high yields and ee. The presented reaction makes use of a masked acetaldehyde to avoid the use of a highly toxic, flammable and reactive intermediate. Furthermore, the use of an acidic resin and low amounts of an affordable organocatalyst make the overall protocol appealing for more in-depth studies to assess its application in manufacture.



Anyway, a current limitation of the presented reaction is the use of chloroform which is a class 2 solvent; in order to overcome this issue, we started a collaborative effort with Landa's research group to perform this reaction in water using their catalysts which are specifically designed for this reaction medium[2]. We optimised the reaction conditions in collaboration with D'Archivio research group performing DoE analysis and investigating several parameters and how they are correlated[3]. This would improve the industrial applicability of the process, exploiting the unique characteristics of water as solvent (*i.e.* cheap, available in bulk, hazardless).



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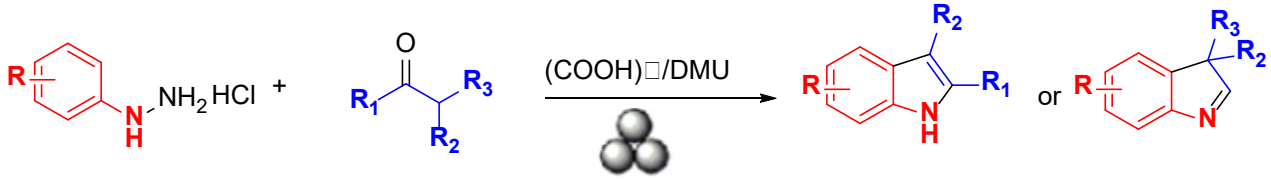
Mechanochemical Fischer Indolisation: Exploration of a Timeless Reaction in a New Guise.

Margherita Brindisi,[a] *Maria Valeria D'Auria,*[a] *Andrea Porcheddu,*[b] *Rita Mocci*,b*

[a] *Department of Pharmacy, University of Naples Federico II, Via D. Montesano, 80131 Naples (Italy); Department of Chemical and Geological Sciences, University of Cagliari, Cittadella Universitaria, S.S. 554 bivio per Sestu, 09042, Monserrato (CA)*

rita.mocci@unica.it

Due to the urgency dictated by actual environmental issues, the demand from society for clean and safe alternatives to classic chemical synthesis keeps growing. Several efforts have been dedicated to this goal, and significant steps ahead have been made. For this purpose, the mechanochemical approach has gained remarkable attention. Indeed, this technique often enables the implementation of existing methodologies more efficiently and sustainably. This peculiarity is a reason for appeal and interest from companies that can apply this kind of strategy even on a large scale by adopting suitable existing scale-up techniques. During the last decades' enormous progress has been made in this field, and several name-reaction have been reported.[1,2,3] Despite these improvements, conducting a synthesis in the absence of solvent is anything but trivial and more efforts are required to achieve a broader range of applicability. Fisher and interrupted Fischer reactions still represent the preeminent method for synthesizing the indole and spiroindole cores, two highly recurrent scaffolds in many chemical compounds with pharmaceutical and agrochemical applications, among others.[4,5,6] Fischer indole synthesis typically requires the use of strong acids in organic solvents at elevated temperatures. In the present communication, we report the results of our extensive experimentation toward the development of a mechanochemical Fischer-type protocol for the synthesis of indole derivatives. The developed methodology represents an effective mechanochemical procedure for the preparation of indole- and indolenine-based templates in short times and with high yield using a mixture of solid oxalic acid and dimethylurea. The number of examples and the variability of the nature of aldehydes, ketones and phenylhydrazines successfully converted, witness the broad scope and utility of the proposed methodology. Moreover, the newly developed protocol displays the potential to turn it into an effective coupling point for additional modification leading to compounds of pharmaceutical interest.



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Merging organo- and Au(I) catalysis for asymmetric or silver-free reactions of alkynes

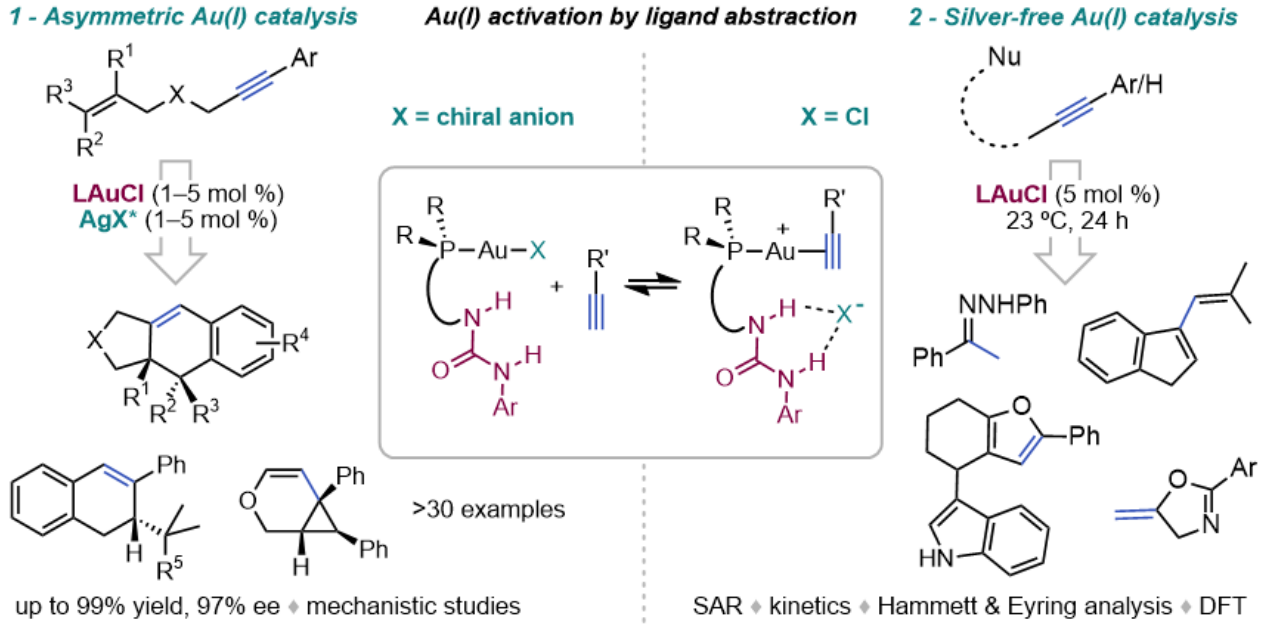
Allegra Franchino,[a] *Àlex Martí,*[a] *Stefano Nejrotti,*[a] *Antonio M. Echavarren*[a]

[a] *Institute of Chemical Research of Catalonia (ICIQ), Av. Països Catalans 16, 43007 Tarragona (Spain) and Departament de Química Analítica i Química Orgànica, Universitat Rovira i Virgili, C/ Marcel·lí Domingo s/n, 43007 Tarragona (Spain)*

Gold(I) complexes with phosphine ligands incorporating dual H-bond donor groups, such as ureas, thioureas and squaramides, were designed for carbo- and heterocyclization reactions of alkynes. Thanks to their H-bonding ability, these complexes contribute to the solution of two long-standing issues in Au(I) catalysis [1]:

1- The realization of challenging Au(I)-catalyzed enantioselective transformations of alkynes by placing the chiral information not on the ligand, but on the counterion instead [2]. The successful implementation of this strategy is demonstrated for various asymmetric 1,6-enyne cyclizations, exploiting a conceptually new H-bonded chiral anion approach [3] (Figure, left).

2- The necessity of a silver co-catalyst, which has the drawback of mandating the use of an additional metal, while sometimes negatively impacting selectivity ("silver effect") [4]. The novel phosphinosquaramide and phosphinourea Au(I) chloride complexes display good activity at room temperature in both intra- and intermolecular reactions of alkynes, in the absence of any additives [5] (Figure, right). Structure-activity relationships, comprehensive kinetic studies and DFT calculations focused on the Au–Cl bond activation highlight the key role of the H-bond donor in aiding chloride abstraction and thus enabling catalysis at the metal center.



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Infrared irradiation-assisted solvent-free Palladium-catalyzed (hetero)aryl-aryl coupling via C-H bond activation

Gianluigi Albano,[a] *Gianfranco Decandia*,[a,b] *Maria Annunziata M. Capozzi*,[a] *Angela Punzi*,[a] *Gianluca Maria Farinola*[a]

[a] *Dipartimento di Chimica, Università degli Studi di Bari "Aldo Moro", Via E. Orabona 4, 70126 Bari, Italy;*
[b] *Istituto per i Processi Chimico-Fisici CNR-IPCF, Via E. Orabona 4, 70126 Bari, Italy.*
e-mail: gianluigi.albano@uniba.it

Organic π-conjugated small molecules and polymers based on (hetero)aryl structural units have been extensively investigated in recent years. The development of efficient methods for the generation of aryl-aryl bonds is the key step to produce these compounds. Palladium-catalyzed direct C-H bond arylation of (hetero)arenes fits well with most of the 12 principles of Green Chemistry: the direct C-H bond activation eliminates the need of the preliminary preparation of air- and moisture-sensitive, expensive, and toxic organometallic reagents. [1] Although significant efforts have been made towards more sustainable conditions, including the use of recoverable catalysts and green solvents,[2] some issues still remain, in particular the need of high temperatures and long reaction times.
Non-conventional energy sources (microwaves irradiation, ultrasound sonication, mechanical milling) have recently earned attention with respect to the traditional thermal heating, although the successful use of these methodologies is limited by the access to specific and expensive instruments. The infrared (IR) irradiation could represent an appealing alternative: it is an efficient form of heating emitted by an inexpensive lamp, with high heat transfer rate, good heating homogeneity, low energy consumption and short heating time.[3] Its application to organic reactions could provide significant advantages: reduced energy requirements, shortened reaction times and even access to new mechanistic pathways, in addition to its potential compatibility with solvent-free methodologies. However, the true potential of IR-assisted reactions is still almost unexplored, especially for Pd-catalyzed chemistry.
Here we successfully applied IR irradiation to the Palladium-catalyzed direct C-H bond arylation of (hetero)arenes, performed under solvent-free conditions (Figure 1): the reaction of benzo[*b*]thiophene, thieno[3,4-*c*]pyrrole-4,6-dione, 1*H*-1,2,3-triazole and pentafluorobenzene with functionalized aryl iodides gave the corresponding coupling products in good yields after very short times. The benefits of IR irradiation have been then proved in preliminary tests of direct C-H arylation polymerization and oxidative coupling of pentafluorobenzene with thiophenes via 2-fold C-H functionalization.

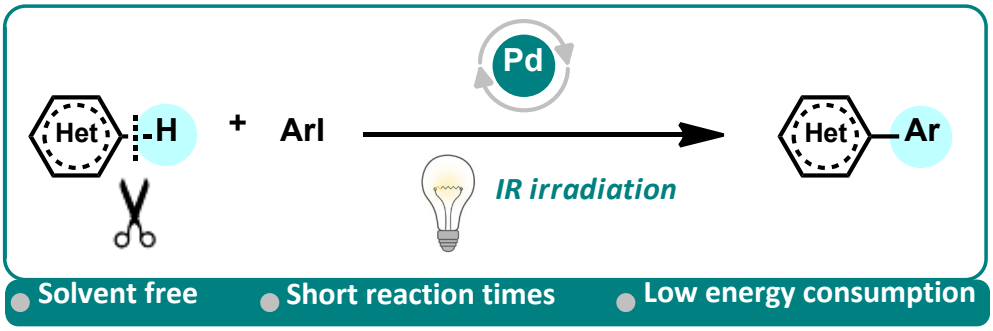

Figure 1. IR irradiation-assisted Pd-catalyzed direct C-H bond arylation of (hetero)arenes.

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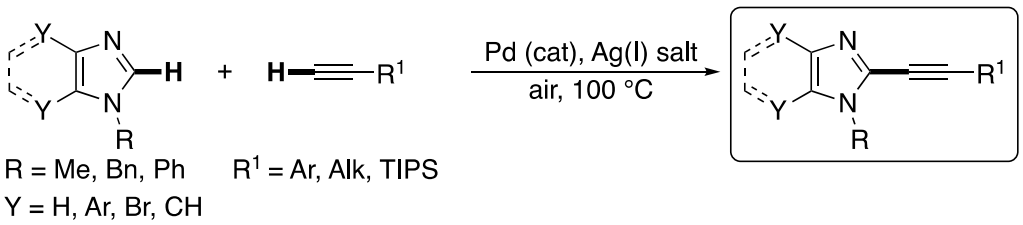
Pd/Ag-mediated dehydrogenative alkynylation of imidazoles

Fabio Bellina,[a] Matteo Biagetti,[b] Mattia Fausti,[a] Giovanni Granucci,[a] Sara Guariento,[b] Marco Lessi,[a] Cosimo Micheletti,[a] Andrea Pucci,[a] Paolo Ronchi,[b] Elisabetta Rosadoni[a]

[a] Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via Moruzzi 13, 56124 Pisa, Italy; [b] Chiesi Farmaceutici, Largo Belloli 10/A, 43122 Parma, Italy

Imidazole scaffolds are frequently found in bioactive compounds[1] and organic functional materials such as liquid crystals and fluorescent dyes.[2] Due to their widespread applications, the development of simple functional group-tolerant synthetic methods that allow the selective heterocycle elaboration under mild conditions aroused considerable attention.[3]
Recently, the transition metal-catalyzed dehydrogenative cross-coupling reactions involving aromatic Csp2-H bonds of azoles emerged as an attractive strategy for the direct functionalization of their heteroaromatic cores, due to the fact that a pre-activation of both the coupling partners, which is in contrast required by the traditional metal- catalyzed cross-coupling protocols, is not required.[4]
Over the last years we have been interested in studies aimed to broaden the substrate scope of the direct functionalization of azoles and, in particular, to develop efficient synthetic protocols for the carbon-carbon bond forming reaction by regioselective palladium-catalyzed C-H bond activation of imidazole derivatives. Our efforts to the development of an efficient procedure for the regioselective dehydrogenative alkynylation of *N*-substituted imidazoles with terminal alkynes will be the main topic of this communication.[5]



When appropriate, the chemical behavior of azoles other than imidazole will be compared and discussed, along with the results obtained when the dehydrogenative alkynylation was applied to the preparation of new synthetic push-pull heteroaromatic dyes.

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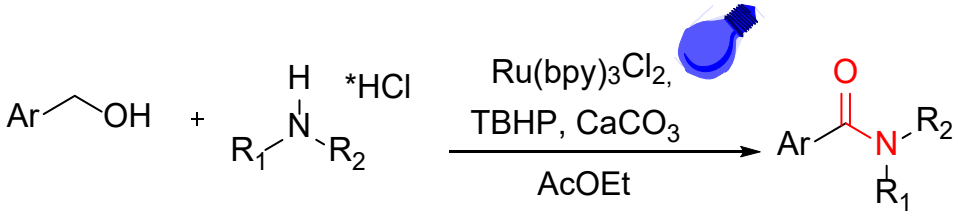
Photocatalyzed amides synthesis from alcohols by visible light

Silvia Gaspa,[a] *Andrea Farina*,[a] *Mariella Tilocca*,[a] *Andrea Porcheddu*,[b] *Luisa Pisano*,[a] *Massimo Carraro*,[a] *Ugo Azzena*,[a] *Lidia De Luca*[a]

[a] *Dipartimento di Chimica e Farmacia, Università degli Studi di Sassari, 07100 Sassari, Italy;* [b] *Dipartimento di Scienze Chimiche e Geologiche, Università degli Studi di Cagliari, Cittadella Universitaria, 09042 Monserrato, Italy.*

The amide bonds are the most studied in organic chemistry due to their common occurrence.[1] Classically, amide bonds are synthesized by acylation of amines with carboxylic acid derivatives, but this approach presents many disadvantages related to increasing production of byproducts, reduction in the yield of final products and use of highly hazardous reagents.[2] One of the most challenging research themes in modern organic synthesis is the development of new methodologies induced by visible light.[3]
In this contest, the first example of photocatalyzed amides synthesis from alcohols and amines mediated by visible light was studied.[4]



The method appears to be very general and selective, has an optimal stoichiometric molar ratio of reactants, mild reaction conditions, makes use of green reagents and eco-sustainable, bio-based solvent such as ethyl acetate. Furthermore, the use of visible light as a source of energy is very appealing from an ecological point of view.

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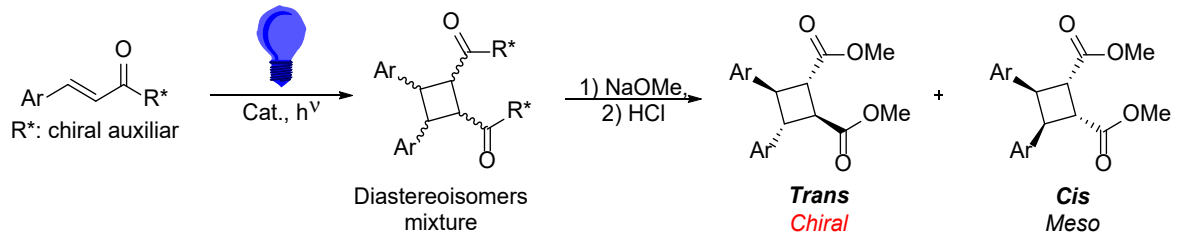
Stereoseletive [2+2] photocycloaddition: a viable strategy for the synthesis of enantiopure cyclobutane derivatives.

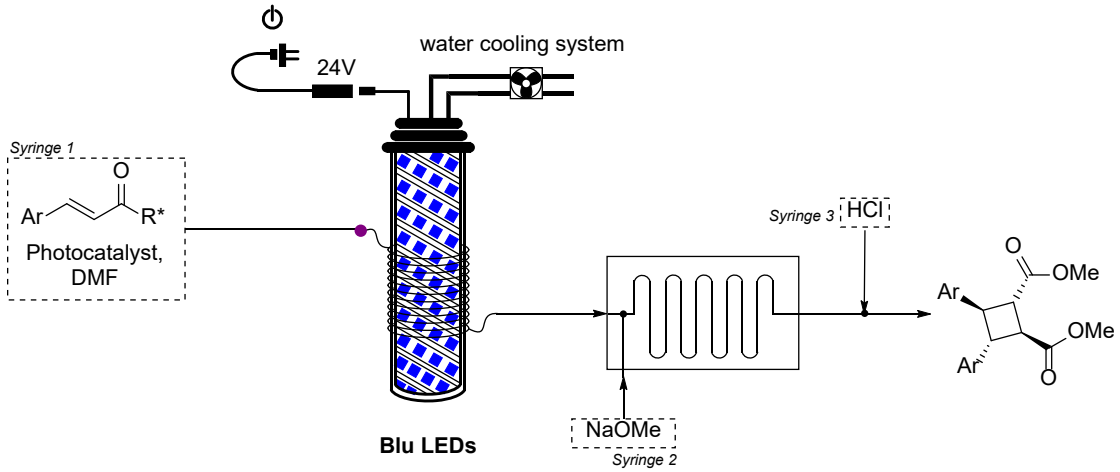
Fabrizio Medici,[a] *Sergio Rossi* [a] *Maurizio Benaglia* [a]

[a] *Dipartimento di Chimica, Università degli Studi di Milano, Via Golgi 19, 20133 Milano, Italy*

The synthesis of cyclobutanes has always attracted the attention of chemists, due to their presence in natural products and importance as biologically active compounds.[1] In the last decade, the development of photochemistry opened new routes for the 4-member carbon ring assembly. Among others, recently, Raiser and co-worker showed that starting from a cinnamic ester is possible to obtain the corresponding cyclized products in high yields.[2] Based on this seminal work, we have decided to develop a stereoselective strategy to synthesize enantiomerically enriched cyclobutane rings. To achieve this result, we introduced in the scaffold of the cinnamic derivatives a chiral auxiliary, a powerful tool widely used in asymmetric synthesis.[3]



The reaction, promoted by an iridium catalyst, under blue LEDs irradiation, of a wide range of cinnamic esters, with differently substituted aromatic rings was investigated, affording the products in 65-95% yield and, after chiral auxiliary removal, 70-98% e.e..[4] Moreover, the reaction was also performed under continuous flow conditions.[5]



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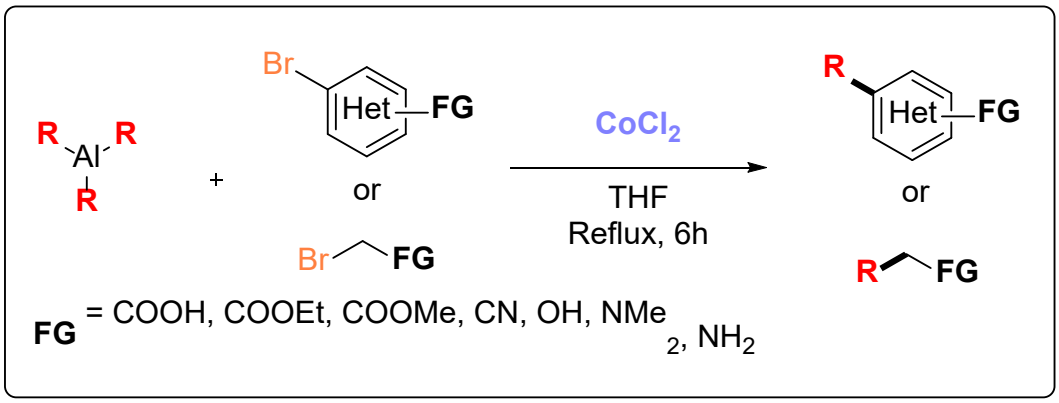
Ligand-Free Cobalt-Catalyzed Cross-Coupling Reaction Between Organoaluminum Reagents and (Hetero)Aryl and Alkyl Bromides

F. Messa,[a] G. Dilauro[a], S. Perrone[a], A. Salomone[b]

[a] *Dipartimento di Scienze e Tecnologie Biologiche e Ambientali, Università del Salento, Prov.le Lecce-Monteroni, Lecce, I-73100, Italy*
[b] *Dipartimento di Chimica, Università degli Studi di Bari, Consorzio C.I.N.M.P.I.S., Via E. Orabona 4, I-70125 Bari, Italy.*

Transition-metal catalyzed cross-coupling reactions are some of the most important C−C bond-forming protocols and have been widely applied both in academic research and in industry. Since the discovery of cross-coupling reactions in the early 1970's, a great number of catalytic systems using organoboron, organotin, organosilicon, organozinc or organozirconium, and organomagnesium as coupling reagents have been developed. In contrast, coupling reactions employing organoaluminum reagents are very rare. These reagents exhibited high chemoselectivity and good compatibility of functional groups in C−C bond formation reactions. Moreover, aluminum exhibits low toxicity and is one of the most inexpensive and earth-abundant metals. [1, 2] As part of our current research interest in developing new catalytic synthetic methodologies, [3, 4] in this communication we report a very general, cobalt catalyzed cross coupling reaction between alkyl- and aryl-aluminum compounds with alkyl- and (hetero)aryl bromides, affording the $C(sp^2)–C(sp^2)$ and $C(sp^3)–C(sp^2)$ cross-coupled products in good to excellent yields.
Catalyzed by the cheap and commercially available $CoCl_2$, without external ligands or bases, the reactions proceed smoothly with a wide range of substituted bromides, decorated by electro-donating and electro-withdrawing group, providing a versatile methodology for cobalt-mediated cross-coupling processes.



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Imino-pyridine Cr complexes as precatalyst for the polymerization of olefins: synthesis and catalytic tests with NEt_3 as additive

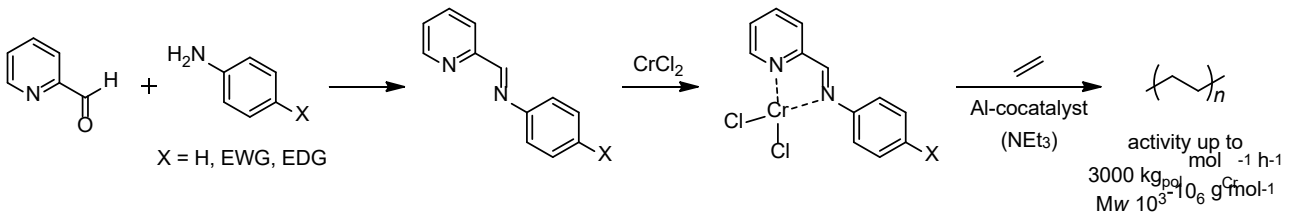
Giorgia Zanchin[a], Alessandro Piovano[b], Benedetta Palucci[a], Alessia Amodio[b], Fabio De Stefano[c], Rocco Di Girolamo[c], Elena Groppo[b], Giuseppe Leone[a]

[a] *CNR, Istituto di Scienze e Tecnologie Chimiche "Giulio Natta" (SCITEC), I-20133 Milano, Italy*
[b] *Dipartimento di Chimica, NIS Interdepartmental Research Center and INSTM Reference Center, Università degli Studi di Torino, I-10135 Torino, Italy*
[c] *Dipartimento di Scienze Chimiche, Università di Napoli "Federico II", Complesso Monte S. Angelo, I-80126 Napoli, Italy*

Iminopyridines belong to the family of redox-active ligands, among which bisimines are perhaps the most famous analogues.[1] Redox-active ligands are those that participate in redox chemistry with a metal, rather than existing as spectators. From being of marginal concern they have become the forefront of inorganic and organometallic chemistry. These ligands serve as electron reservoirs working in concert with metal ions and providing an unexpected utility in a wide range of catalytic conversions. In addition to these features, they have recently received particular consideration as ancillary ligands in coordination chemistry by virtue of their low cost, easy preparation, and fine-tunability of their steric and electronic properties.

In this context, a series of iminopyridine ligands, differing in the substitution at the *para*-position of the aryl ring, were synthesized by condensing 2-pyridinecarboxaldehyde with the appropriate primary amine; the ligands were then complexed with $CrCl_2$ to give the corresponding chromium complexes.[2,3] Spectroscopic investigations proved that in some cases an electron transfer from Cr to the ligand occurs, giving rise to complexes with a *formal* divalent oxidation state but a *physical* trivalent state, and a ligand in the monoanionic radical form $(L^{\bullet})^{-}$.

These complexes were investigated as precatalysts for the polymerization of ethylene using different aluminum cocatalysts, and eventually also the Lewis base NEt_3 as additive. In most of the cases, the polymerization brought to the synthesis of solid polyethylene, with variable molecular weight (from 10^3 to 10^6 g mol^{-1}) depending on the reaction conditions. The factors that mainly affect the polymerization are (*i*) the nature of the aluminum activator that influences the ion pair generated, (*ii*) the presence of the additive that boosts the synthesis of UHMWPE, and (*iii*) the polymerization temperature that affects the polymerization catalysis and the polymer molecular weight.



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Polysubstituted 1,2,3-Triazoles: synthesis and biological application

Loredana Maiuolo[a] *Vincenzo Algieri,*[a] *Fabrizio Olivito,*[a] *Antonio Jiritano,*[a] *Matteo Antonio Tallarida,*[a] *Paola Costanzo,*[a] *Cristina Algieri*[b], *Fabiana Trombetti*[b], *Salvatore Nesci*[b], *Antonio De Nino.*[a]

[a] *Department of Chemistry and Chemical Technologies – CTC, University of Calabria, Via P. Bucci, Cubo 12C, 87036 – Rende (CS), IT;*
[b] *Department of Veterinary Medical Science (DIMEVET), University of Bologna, Ozzano dell'Emilia (BO), IT.*

1,2,3-Triazole are five-member *N*-heterocyclic compounds bearing three nitrogen atoms in the ring that exhibit a number of important biological properties, such as antibacterial, antifungal, anticancer, antiviral, antitubercular, analgesic, anti-inflammatory, anticonvulsant, antidepressant and anti-arrhythmic activities [1].
Typically, 1,2,3-triazoles are synthesized through a 1,3 dipolar cycloaddition reaction between an azide and a terminal alkyne, the so-called AAC (azide-alkyne cycloaaddition) reaction [2]. As alternative approach, electron-deficient olefins were proposed to replace alkynes in the eliminative azide-olefin cycloaddition reaction (EAOC) [3].
In this work, we present the regioselective synthesis of a variety of polysubstituted-1,2,3-triazoles by 1,3-dipolar cycloaddition, starting from azides as dipole and substituted triple or double bonds as dipolarophile (Figure 1).

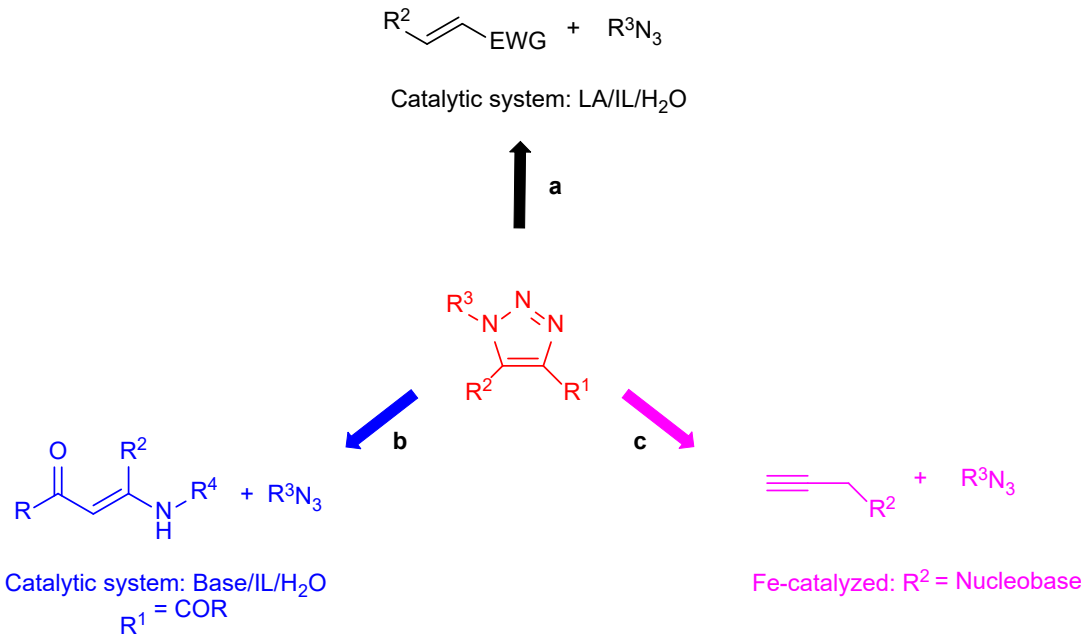

Figure 1. Synthesis of di- and trisubstituted 1,2,3-triazoles by 1,3-dipolar cycloaddition reaction.

In all cases, a highly efficient catalytic system was developed, sometimes in presence of ionic liquid as recoverable solvent for a green synthetic process. Finally, the biological activity of some synthetized triazole derivatives will be present, highlighting their promising activity for some mPTP-related human pathologies.

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Atropisomeric Azaborines: Axial Chirality at the Boron-Carbon Bond

A. Mazzanti,[a] M. Mancinelli[a]

[a]*Department of Industrial chemistry "Toso Montanari", University of Bologna, Viale del Risorgimento 4, Bologna 40136, Italy*
michele.mancinelli@unibo.it

Azaborines are organic molecules that have been receiving a lot of attention from chemists in recent years. The azaborines have in their strucrtures a B-N bond and are isosteric and isolectronic architectures of related organic compounds that have a C=C bond. The inclusion of heteroatoms and π-conjugated fragments is a strategy that allows to find new materials with different chemical and physical properties. Our studies focus on the study of azaborines containing chirality axes on B-Caryl bond. In particular 2-aryl-1,2-dihydrobenzo[e][1,2]azaborines [1] and 6-Aryl-5,6-dihydrodibenzo[c,e][1,2]azaborines [2] display restricted rotation at the boron-carbon aryl bond, yielding conformational isomers or atropisomers.

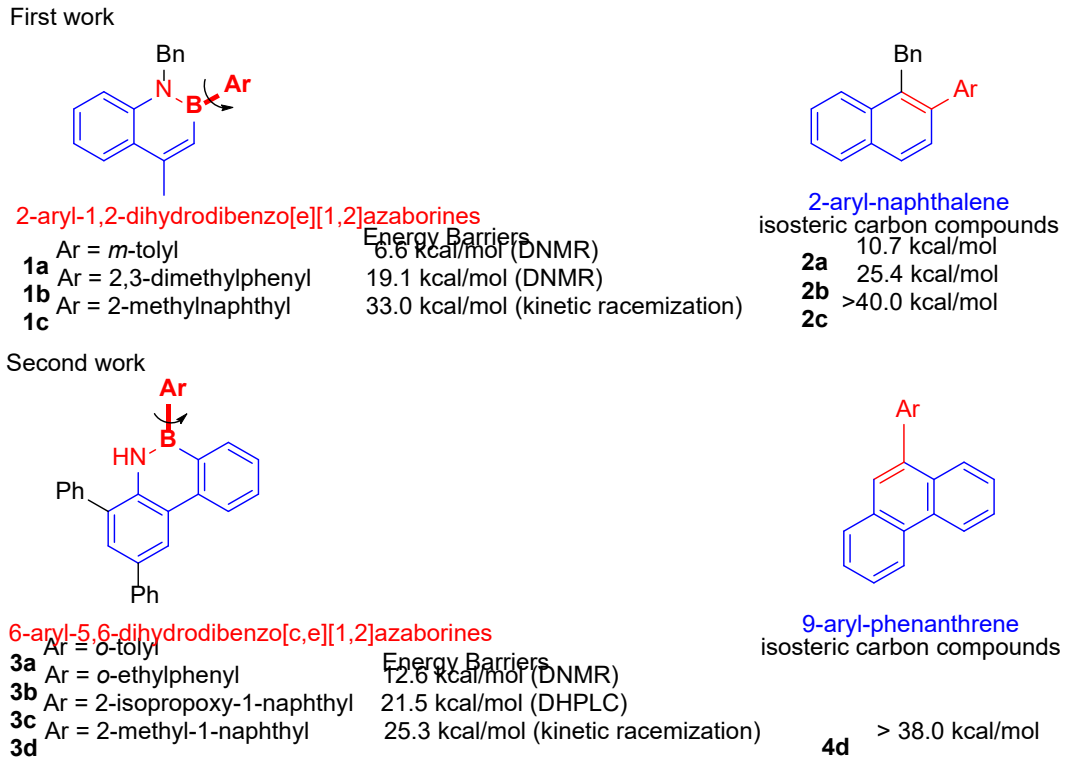

Figure 1: First and Second work on atropisomeric azaborines studies.

The stereodynamics processes were monitored by Dynamic NMR, Dynamic enantioselective HPLC or kinetic racemization measurements. The stable atropisomers 1c and 3d were separate using semi-preparative enantioselctive HPLC and their absolute configuration were determined by TD-DFT simulation of the electronic circular dichroism (ECD) spectra. The energy barrier of azaborines are smaller than their isosteric compounds, because the B-Caryl bond is longer than a normal C-Caryl bond making it easier to rotate the aryl moiety. The second work has been published as ACS Editors' Choice in The Journal of Organic Chemistry [2].

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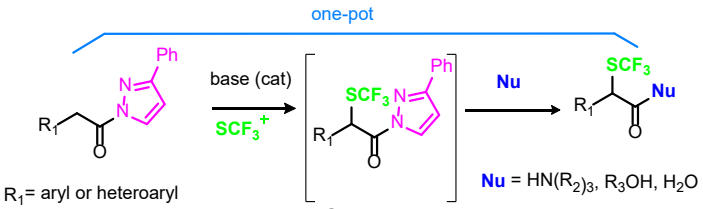
Formal α-trifluoromethylthiolation of carboxylic acid derivatives via *N*-acyl pyrazoles

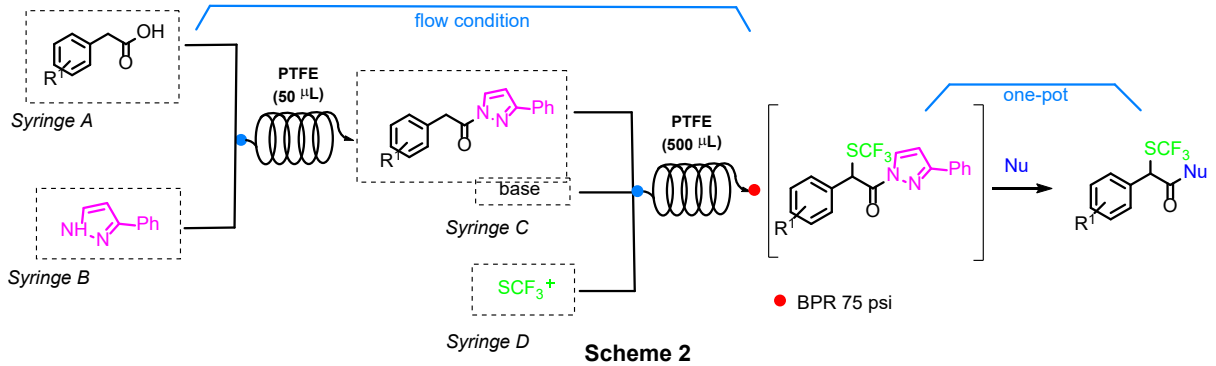
F.Franco,[a] S.Meninno,[a] M. Benaglia,[b] A. Lattanzi[a]
[a] *Dipartimento di Chimica e Biologia, Università di Salerno, Via Giovanni Paolo II, Fisciano, Italy*
[b] *Dipartimento di Chimica, Università degli Studi di Milano, Via Golgi, Milano, Italy*

The interest in the chemistry of fluorinated compounds is constantly increasing both in academic and in industrial research.[1] More specifically, continuous efforts have been devoted to the development of new protocols and technologies to produce molecules bearing the trifluoromethylthio (SCF_3) group, to take advantage of its high electron-withdrawing and lipophilic character.[2] Different methods for the introduction of trifluomethylthio group at α-position of carbonyl compounds have been intensively investigated, achieving important results for ketones, aldehydes and 1,3-dicarbonyl compounds both under batch and flow conditions.[3] However, few methods have been reported for the α-trifluoromethylthiolation of carboxylic acid derivatives. To this end, we developed a convenient metal-free and catalytic one-pot route for the introduction of SCF_3 group at α-position of carboxylic acid derivatives starting from N-acyl pyrazoles.[4] In particular, by using ester surrogates it is possible to achieve the challenging target by working under very mild reaction conditions and the corresponding products can be easily transformed back, in a one-pot fashion, into amides, esters, or carboxylic acids (Scheme 1). Moreover, the intermediates can be reduced in a one-pot fashion, using common reducing agents, to access β-SCF_3 alcohols.



Scheme 1

Based on these results, we further developed the telescopic synthesis of α-SCF_3 carboxylic acid derivatives starting directly from commercial sources by exploiting flow chemistry technology. With this strategy the environmental footprint and the reaction time of the one-pot process are considerably reduced. Waste production is minimized avoiding purification or separation of the chemical intermediates of each step (Scheme 2).



Scheme 2

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Synthesis of nitrogenated analogues of honokiol as potential bioactive compounds

C. Sciacca,[a] N.Cardullo,[a] V. Muccilli,[a] C. Tringali.[a]

Department of Chemical Sciences, University of Catania, V.le A. Doria 6, 95125,
e-mail: claudia.sciacca@phd.unict.it

The extracts from medicinal plants have been employed for centuries to treat several diseases. Extracts from *Magnolia*'s tree have been used as traditional herbal medicines in Japan, China and other countries as treatments for gastrointestinal disorders, anxiety, allergies, inflammation and other diseases thanks to their multiple therapeutic properties. Magnolol and honokiol, two neolignans with bisphenolic structure, have been identified as the main bioactive constituents from the bark and roots of *Magnolia*'s tree and have shown an array of biological properties, including antitumor, antidiabetic, anti-inflammatory, antimicrobial, antiviral, antioxidant and neuroprotective activity.[1] The above cited biological properties prompted us to plan the synthesis of magnolol and honokiol analogues as potential bioactive molecules, as a continuation of previous studies pointing out that synthetic bisphenolic neolignans show antitumor[2] and hypoglycemic[3] activity higher than the natural *leads*.

The main goal of this work was the synthesis of nitrogenated analogues inspired by honokiol and the evaluation of their biological properties to obtain new potential therapeutic agents. The synthetic strategy involves i) borylation of phenols, ii) Suzuki-Miyaura cross-coupling reaction between phenols or aniline bromides and suitable arylboronate iii) reactions of allylation and iiii) subsequent Claisen rearrangement to insert the allyl chains on the two aromatic rings (Fig.1). As first biological screening, the new compounds were evaluated for their *in vitro* inhibitory activity against metabolic enzymes such as yeast α-glucosidase (EC 3.2.1.20), porcine pancreatic α-amylase (EC 3.2.1.1, Type VI-B) and porcine pancreatic lipase (EC 3.1.1.3, Type II), with promising results.

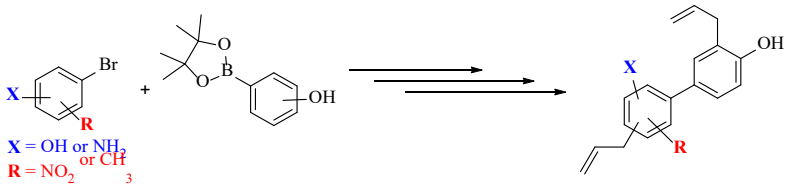

Fig.1

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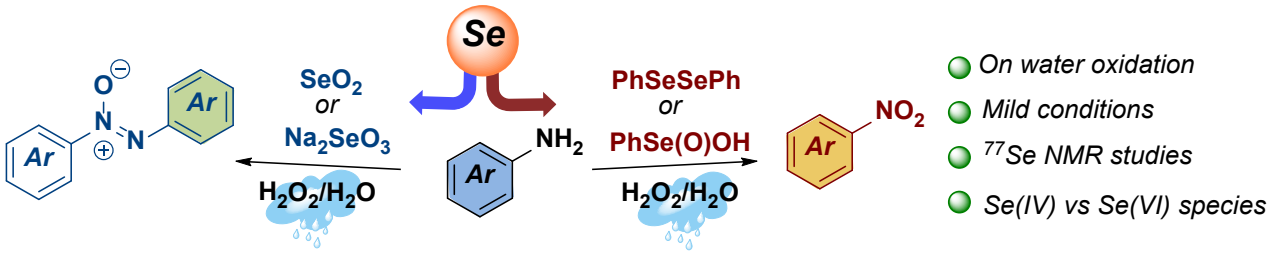
The unexpected role of Se(IV) *vs* Se(VI) species in the *on water* selenium-catalysed oxidation of anilines

Damiano Tanini, Camilla Dalia, Antonella Capperucci

[a]*Department of Chemistry 'Ugo Schiff", University of Florence, Via Della Lastruccia 3-13, Sesto Fiorentino, Firenze, Italy*

Selenium-catalysed oxidations are highly sought after in organic synthesis and in biology. Such transformations occupy a central position in organic synthesis, enabling a wide variety of valuable functional group conversions.[1] Selenium(IV) oxide, diselenides, and seleninic acids are commonly employed as catalysts in oxidation reactions often requiring hydrogen peroxide or *tert*-butyl hydroperoxide (TBHP) as oxidants.[2] In this regard, while selenium catalysed epoxidation and dihydroxylation of alkenes are well established,[1,2] oxidation of amines are far less explored and only few methodologies dealing with the synthesis of nitroso derivatives[3] or azoxyarenes[4] have been described.

Herein, we report our studies on the *on water* selenium mediated oxidation of anilines. In the presence of diphenyl diselenide or benzeneseleninic acid, anilines react with hydrogen peroxide providing direct and selective access to nitroarenes. Instead, the use of selenium dioxide or sodium selenite led to azoxyarenes. Careful mechanistic analysis and ^{77}Se NMR studies revealed that only Se(IV) species, such as benzeneperoxyseleninic acid, are the active oxidants involved in the catalytic cycle operating in water and leading to nitroarenes. While other selenium-catalysed oxidations occurring in organic solvents have been recently demonstrated to proceed through Se(VI) key intermediates,[5] the on water oxidation of anilines to nitroarenes, unexpectedly, do not. These findings shed new light on the multifaceted nature of organoselenium-catalysed transformations and open new directions to exploit selenium-based-catalysis.



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Double strategies for regioselective one-pot C-H oxidative functionalization of coumarins

Claudio Zippilli [a], Lorenzo Botta [a], Bruno Mattia Bizzari [a], and Raffaele Saladino [a]

[a]Department of Biological and Ecological Sciences, University of Tuscia, Via S.C. De Lellis s.n.c., 01100, Viterbo Italy.

Coumarins are widespread natural products exhibiting strong antiviral, anticancer, anticoagulant, and antimicrobial activity [1, 2]. The synthesis of new bioactive coumarins, through direct C-H oxidative functionalization, lacks in yield and regioselectivity so, until now, multistep reactions and the use of protecting groups are required [3]. We rationalized two divergent strategies for the one-pot and protecting group-free regioselective C-H oxidative functionalization of coumarins. The first strategy concerned the use of 2-iodoxybenzoic acid (IBX) for the regioselective *ortho*-hydroxylation of hydroxycoumarins to catechol and pyrogallol counterparts, leading to novel derivatives with high antioxidant and anti-influenza A virus activity (Figure 1, panel **a**) [4]. The selectivity of the process is driven by the carbocationic behavior of the λ5-iodanyl cyclic intermediate formed in the initial step of the reaction. The second strategy involved the H_2O_2-free and 2-methyltetrahydrofuran (2-Me-THF) mediated blue-LED-driven *in situ* activation of horseradish peroxidase in a two-liquid-phase system (2LPs) for the regioselective homodimerization of hydroxycoumarins to corresponding bicoumarins (Figure 1, panel **b**) [5]. In this latter case, the scavenging of singlet oxygen by 2-Me-THF controlled the stabilization of the peroxidase-catalyzed incipient oxygen-centered radicals, the oxidative coupling being deeply influenced by the position of the hydroxyl groups on the aromatic ring. This system led to the unprecedented synthesis of two natural bicoumarins, recently isolated from pharmacologically active extracts of *Erycibe obtusifolia* Benth (Convolvulaceae).

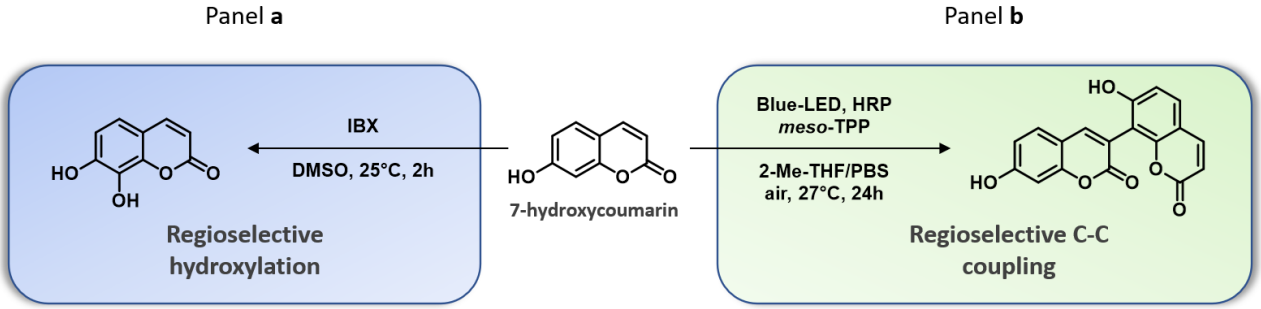

Figure 1. Panel **a**: regioselective IBX-catalyzed one-pot *ortho*-hydroxylation of 7-hydroxycoumarin to catechol counterpart; panel **b**: regioselective one-pot homocoupling of 7-hydroxycoumarin to bicoumarin, by blue-LED driven and 2-Me-THF mediated *in situ* activation of HRP.

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Eco-friendly deep eutectic solvent electrolyte solutions for dye-sensitized solar cells

C. L. Boldrini[a], *N. Manfredi*[a], *F. M. Perna*[b], *V. Capriati*[*b], *A. Abbotto*[*a]

[a] *Dipartimento di Scienza dei Materiali, Università degli Studi di Milano-Bicocca, and INSTM Milano-Bicocca Research Unit, Via R. Cozzi 55, 20125-Milano, Italy;* [b] *Dipartimento di Farmacia–Scienze del Farmaco, Università degli Studi di Bari "Aldo Moro", Consorzio C.I.N.M.P.I.S., Via E. Orabona 4, 70125-Bari, Italy*

Among photovoltaics technologies, dye-sensitized solar cells (DSSCs) offer high conversion efficiencies (15% record efficiency) and low-cost manufacturing. Unfortunately, one of the major drawbacks in these record cells is the presence of toxic volatile organic solvents (VOCs) in the electrolyte.

To overcome this problem, we have successfully tested eco-friendly reaction media such as Deep Eutectic Solvents (DESs), made of two or three safe and cheap components which are able to express hydrogen-bond interactions with each other to form an eutectic mixture with a melting point much lower than either of the individual components. DESs are simple and low-cost to synthesize, do not need purification, and they are usually biodegradable. One of the most common DES components, choline chloride (ChCl), is largely used as an additive for chicken feed. We tested both hydrophilic and hydrophobic DESs in DSSCs with promising results [1,2]. As a prototypical hydrophilic DES, we used ChCl/glycerol (1:2 mol mol^{-1}) with 40% water jointly with an hydrophilic dye, and performed an extensive optimization of the device, including different co-adsorbents and TiO_2 film thicknesses. Conversely, when using a hydrophobic DES made of menthol and acetic acid we chose a phenothiazine-based dye already studied in our group. DSSCs filled with DESs displayed a lower recombination resistance and a higher V_{oc} when compared to cells filled with an electrolyte based on standard VOCs.

We then focused on DSSCs containing innovative sugar-based natural DES electrolytes, that is ChCl with different monosaccharides, sensitized with multi-branched phenothiazine dyes developed in our group, and characterized by the presence of an alkyl or a sugar substituent [3,4]. In particular, we systematically varied the dye (alkyl functionality vs. sugar moiety), the co-adsorbent (chenodeoxycholic acid vs. glucuronic acid), and the monosaccharide present in the DES. Overall, results are consistent with a cooperative interaction among all the components containing a sugar functionality leading to a performance boost.

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Polydopamine/ethylenediamine nanoparticles embedding a bacterial photoenzyme for solar energy conversion

Gabriella Buscemi[a,b], *Danilo Vona*[a], *Roberta Ragni*[a], *Roberto Comparelli*[b], *Massimo Trotta*[b], *Francesco Milano*[c], *and Gianluca Maria Farinola*[a]

[a] *Chemistry Department, University of Bari "Aldo Moro", via Orabona 4, I-70126 Bari, Italy*
[b] *CNR-IPCF, Istituto per i Processi Chimico Fisici / Consiglio Nazionale delle Ricerche via Orabona 4, I-70126 Bari, Italy.*
[c] *CNR-ISPA, Institute of Sciences of Food Production, S. P. Lecce-Monteroni, I-73100 Lecce)*

Polydopamine (PDA) is a biocompatible material suitable for confinement and protection of biomacromolecules [1]. PDA can be easily produced *via* oxidative polymerization of dopamine by a straightforward one pot process, directly occurring around biological templates. Due to PDA dark opaque color, related to its intense light absorption, applications with biological components whose activity is light dependent require further polymer modifications to increase both affinity and efficiency [2]. Among these photo-active species, the Reaction Center (RC) from *Rhodobacter sphaeroides* is often used as a model system. RC is a transmembrane photoenzyme that behaves as a highly efficient photoconverter, able to perform light transduction into charge separated states through an electron cascade process. Therefore, RC can be exploited as photoactive element to produce photocurrents and, by engineering bioelectronic devices, to achieve eco-friendly and sustainable technology using sunlight as primary green energy source [3].
Here we demonstrate that embedding the RC in PDA aggregates and treating them with ethylenediamine (EDA) [4], the photosynthetic protein still retains both structural and functional integrity. In fact, EDA can convert some diketo- forms of the dihydroxy-indole units of PDA into Schiff bases, and it can react via Michael-like addition disrupting PDA nanostructure by interfering with π-π stacking between the aggregate polymeric chains. In this way a degradation of PDA promotes particles size reduction and significant changes of their absorption and emission properties. The obtained PDA:EDA@RC nanoparticles are promising materials for solar energy conversion, exhibiting higher water dispersity, decrease of particle size and an increased transparency of the polymer itself. Consequently, higher photocurrents were obtained in the engineered nanoparticles as compared to pure and dark PDA. The optimized confined photoenzyme produces charge separated states with a yield comparable to the pristine enzyme in solution. This allowed to overcome the main limitation of photoactive system encapsulated in bare PDA, which is the polymer low light transmission ability, yet retaining the adhesive properties of the starting material [5]. This engineered bio-hybrid system represents an example of functional nanostructures for sunlight photoconversion, addressed in a tuneable bio-compatible polymer composite, also showing the potentialities of fine chemical tailoring of polydopamine bio-interfaces.

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Design of KuQuinone-Co_3O_4 nanoparticle hybrid dyads for photoelectrochemical applications

Mattia Forchetta[a], *Federica Sabuzi*[a], *Francesca Valentini*[a], *Xavier Sala*[b], *Valeria Conte*[a], *Pierluca Galloni*[a]

[a] *Università degli Studi di Roma Tor Vergata, Dipartimento di Scienze e Tecnologie Chimiche, Via della ricerca scientifica, 00133, Roma, Italy*

[b] *Universitat Autònoma de Barcelona, Departament de Química, 08193, Bellaterra, Catalonia, Spain*

KuQuinones (KuQs) are pentacyclic, fully conjugated quinoid compounds, which exhibit a low reduction potential and a broad absorption band in the visible region.[1] These peculiar spectroscopic and electrochemical features make them excellent candidates as photosensitizers for the light-driven water oxidation. [2,3] The design of hybrid dyads, characterized by organic dyes covalently bound to abundant first row transition metal oxide nanoparticles, constitutes an appealing method to catalyze the photoinduced water oxidation reaction.[4]

In this work we studied the grafting of KuQ photosensitizers on Co_3O_4 nanoparticles, obtaining advanced hybrid photocatalysts. Diverse KuQuinone derivatives, presenting a carboxylic or a phosphonate anchoring group in side-chain, have been synthetized in order to allow their chemisorption on Co_3O_4 nanoparticles.

The hybrid dyads have been deposited on indium tin oxide (ITO) and evaluated as catalysts for the photoinduced water oxidation reaction, showing better performances with respect to the non-decorated nanoparticles.

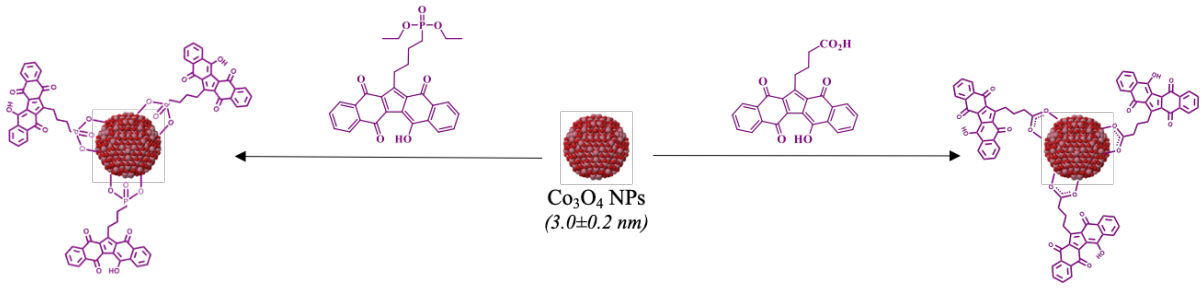

Figure 1. Graphic representation of the grafting of KuQ photosensitizers on Co_3O_4 nanoparticles.

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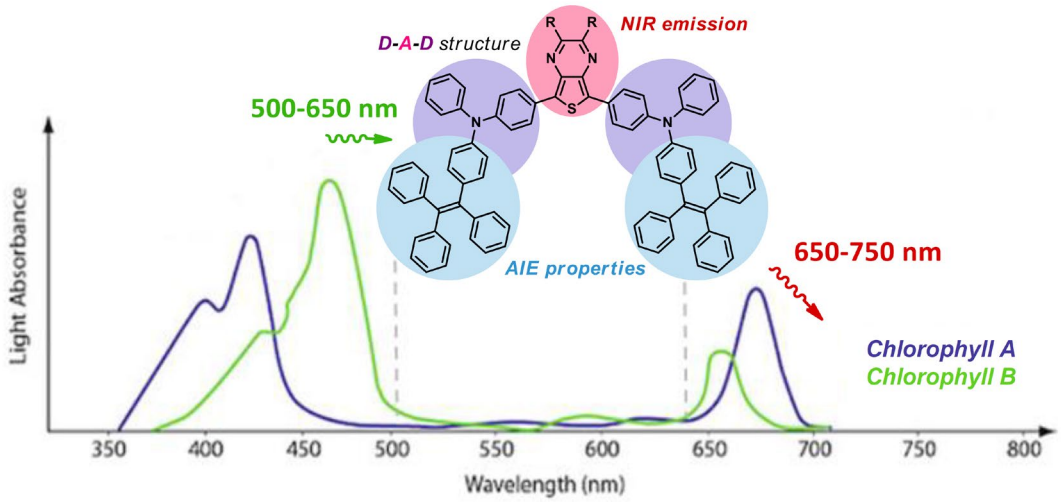
Fluorescent Materials for the Enhancement of the Photosynthetic Efficiency

Giulio Goti,[a,b] Massimo Calamante,[a,b] Carmen Coppola,[c,d] Alessio Dessì,[a] Daniele Franchi,[a] Alessandro Mordini,[a,b] Adalgisa Sinicropi,[a,c,d] Lorenzo Zani,[a] Gianna Reginato[a]

[a] Institute of Chemistry of Organometallic Compounds (ICCOM), National Research Council (CNR), Via Madonna del Piano 10, 50019 Sesto Fiorentino, Italy; [b] Department of Chemistry "Ugo Schiff", University of Florence, Via della Lastruccia 13, 50019 Sesto Fiorentino, Italy; [c] Department of Biotechnology, Chemistry and Pharmacy, University of Siena, Via A. Moro 2, 53100, Siena, Italy; [d] Consorzio per lo Sviluppo dei Sistemi a Grande Interfase (CSGI), Via della Lastruccia 3, Sesto Fiorentino, 50019, Italy

Food security and sustainable agriculture is a significant and current challenge to society in the face of growing global consumption.[1] In this regard boosting crop yields by enhancing the efficiency of the photosynthetic process to meet the rising demand of the market has been highlighted as a preferred and greener solution.[2] Sunlight is undoubtedly an unlimited, free, and sustainable energy source; however, plants can only absorb light within specific regions of the solar spectrum, within 430-480 nm and 630-680 nm. Only the absorbed light is essential for photosynthesis, which means that a considerable portion of sunlight cannot be assimilated and transformed into chemical energy. Here we present the preparation of innovative luminophores as light conversion agents,[3] able to enhance plants light uptake by absorption of unproductive wavelengths and re-emission within the absorption region of chlorophyll-based photosynthetic systems. The dyes feature a donor–acceptor–donor (D-A-D) structure, and are characterized by a modular and efficient synthesis that allows for easy tuning of their absorption and emission profiles. The intense light-harvesting ability and emissions in the deep-red and NIR region, as well as the aggregation induced emission (AIE) properties, that enhance their emissive ability in the aggregate state, make them attractive materials for the development of luminescent devices with potential application in plant growing.



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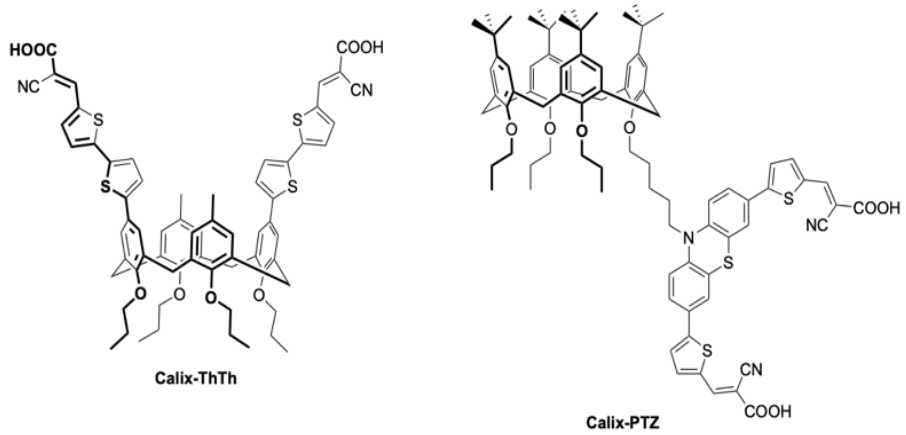
Photo(electro)catalytic water splitting using Calix[4]arene-Based dyes

Norberto Manfredi,[1,] Cristina Decavoli,[1] Chiara Liliana Boldrini,[1] Tarekegn Heliso Dolla,[2] Federica Faroldi,[3] Francesco Sansone,[3] Tiziano Montini,[2,*] Laura Baldini,[3,*] Paolo Fornasiero,[2] Alessandro Abbotto.[1,*]*

[1]Department of Materials Science and Solar Energy Research Center MIB-SOLAR, University of Milano-Bicocca, and INSTM Milano-Bicocca Research Unit, Via Cozzi 55, I-20125, Milano, Italy. [2]Department of Chemical and Pharmaceutical Sciences, INSTM Trieste Research Unit and ICCOM-CNR Trieste Research Unit, University of Trieste, Via L. Giorgieri 1, I-34127, Trieste, Italy. [3]Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco Area delle Scienze 17/A, 43124, Parma, Italy.

e-mail: norberto.manfredi@unimib.it

Direct water splitting from solar energy using photocatalytic and photoelectrochemical methods hold great potential especially when metal-free molecular components are exploited.[1,2] The use of templating functionalities to express specific interaction has been attempted in few cases with the result of an improvement of the photo(electro)catalytic properties.[3,4] In this work, we have developed two classes of calix[4]arene-based molecular photosensitizers to be used as antenna systems in photocatalytic production of hydrogen and photoelectrochemical water oxidation. The structure of the first class of dyes shows the typical donor-π-acceptor molecular architecture where a calix[4]arene scaffold is used as an embedded donor. The properties conferred by the calix[4]arene donor afforded twice larger performances compared to the corresponding linear system though showing similar quantitative optical properties.[5] The second class of sensitizers uses the calix[4]arene structure as peripheral functionalization with the effect of coordinating the water oxidation catalyst in the solution. As a matter of fact, the device sensitized with the calix[4]arene functionalized dye showed an increased photocurrent in photoelectrochemical experiments. The new molecular design paves the way to a new strategy for photo(electro)catalytic water splitting where the calix[4]arene scaffold can afford more efficient systems offering the potential for host-guest supramolecular effects.



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Construction of tailored, donor-acceptor heterocyclic compounds for solar energy conversion

Lorenzo Zani,[a] *Massimo Calamante*,[a,b] *Alessio Dessì*,[a] *Daniele Franchi*,[a] *Alessandro Mordini*,[a,b] *Gianna Reginato*[a]

[a] *Istituto di Chimica dei Composti Organometallici (CNR-ICCOM), Via Madonna del Piano 10, 50019 Sesto Fiorentino (FI), Italy. Email: lorenzo.zani@iccom.cnr.it.* [b] *Dipartimento di Chimica "U. Schiff", Università degli Studi di Firenze, Via della Lastruccia 13, 50019 Sesto Fiorentino (FI), Italy.*

Heterocyclic compounds have found extensive application as active components in optoelectronic and photovoltaic devices, either as light-harvesting or charge carrier-transporting materials.[1] In recent years, our research group focused on the design and synthesis of donor-acceptor, conjugated organic compounds endowed with a wide array of heterocyclic moieties, and investigated their use in various solar energy conversion technologies, such as dye-sensitized and perovskite solar cells,[2] photocatalytic systems for hydrogen production[3] and luminescent solar concentrators (Figure 1).[4]

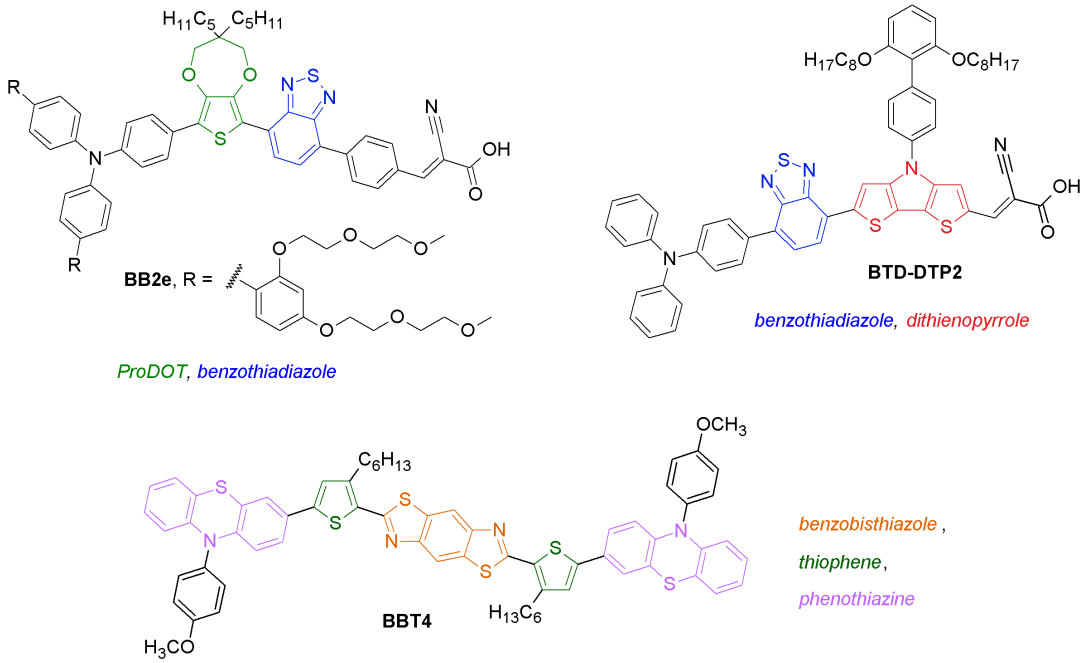

Figure 1. *Structures of organic compounds recently applied in solar energy conversion devices,[2-4] whose different heterocyclic moieties have been highlighted.*

In this communication, we will present some selected examples of our activity, illustrating the logic behind the rational design of the compounds and describing the synthetic strategies followed for their preparation, mostly based on the assembly of molecular "jigsaw pieces" by cross-coupling reactions and direct arylation procedures.[5] Finally, we will discuss the relationship between the compounds spectroscopic and electrochemical properties and the performances of the corresponding solar-powered devices.

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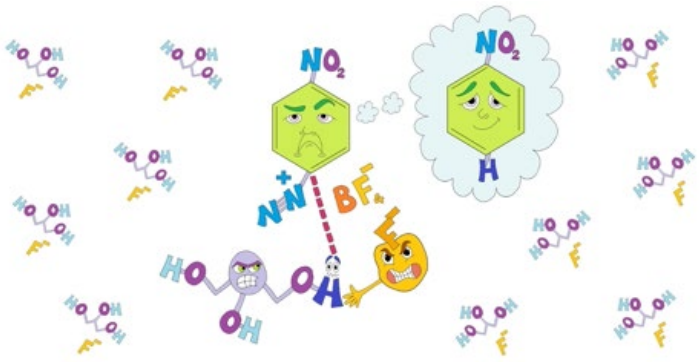
How do arenediazonium salts behave in Deep Eutectic Solvents? A combined experimental and computational approach

Achille Antenucci,[a,b] *Matteo Bonomo,*[a,b,c] *Giovanni Ghigo,*[a] *Lorenzo Gontrani,*[c] *Claudia Barolo,*[a,b] *Stefano Dughera* [a]

[a] *Dipartimento di Chimica, Università di Torino, Via P. Giuria 7, 10125 Turin, Italy;* [b] *NIS Interdepartmental Centre, Reference Centre for INSTM, University of Turin, Via Gioacchino Quarello 15/A, 10135 Turin, Italy;* [c] *Dipartimento di Chimica, Università di Roma "Sapienza", P.le A. Moro 5, 00185 Rome, Italy*

Despite the growing use of deep eutectic solvents as green reaction media in a number of organic synthetic protocols,[1] no significant reactions of diazonium salts in these solvents are known in the literature.[2] Thus, the behavior of arenediazonium tetrafluoroborates in new polyol-based DESs, whose nature is investigated by means of a combined computational and experimental approach, is reported.[3] A relatively fast (strictly depending on the electronic effects of the substituents bound to the aromatic ring) reduction reaction occurs, initiated by the formation of a glycerolate-like species, as demonstrated by an accurate computational, study aiming at elucidating the involved mechanism. Furthermore, the present study represents both an exploitation of an innovative DES-design approach[4],[5] and a description of the background behaviour of arenediazonium compounds in DESs. Both aspects may result crucial in expanding the application range of DESs as reaction media, in compliance to the 5th principle of green chemistry.



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Halogen-bonded architectures of multivalent calix[4]arenes

Laura Baldini, Alessandro Casnati, Maria Chiara Gullo, Luciano Marchiò

Dipartimento di Scienze Chimica, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco Area delle Scienze 17/A, 43124 Parma

Crystalline supramolecular networks of calixarenes are attractive structures in the field of functional materials. Thanks to the combination of an aromatic cavity available for the complexation of small guests with the ease of functionalization of the phenol moieties, the calixarene macrocycle provides a versatile synthon to produce solid-state supramolecular architectures possibly characterized by porosity.

While a wide range of solid state calixarene networks have been obtained through hydrogen bonds[1] or metal−ligand interactions,[2] it is surprising that halogen bonds (XBs) have not yet been extensively exploited. This non-covalent interaction, in fact, shows important properties like high directionality, modularity and great water stability, that make it a promising tool for the synthesis of solid state structures by design.[3]

In order to obtain self-assembled architectures via XBs of calix[4]arene macrocycles, we synthesized two tetra(iodopropargyl)calix[4]arenes (Fig. 1, left), one in the *cone* (**1**) and the other in the *1,3-alternate* conformation (**2**). The iodoalkynyl group is a ditopic synthon, able to act as both a XB donor through the iodine atom and as a XB acceptor on the C≡C triple bond. The presence of four XBing groups on the scaffold may allow the formation of robust 2D and 3D networks of calixarenes in presence of suitable multidentate XB acceptors.

In this presentation we report the solid state self-assembly properties of **1**[4] and **2** crystallized in presence and in absence of different XB acceptors. X-ray diffraction analysis of the crystals and co-crystals obtained revealed that XBs are the main driving force that organizes the synthons (Fig.1, right).

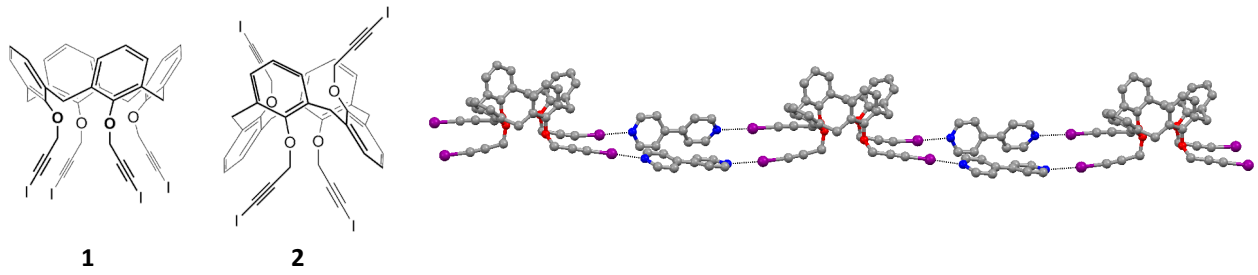

Fig.1. Left: structures of tetra(iodopropargyl)calix[4]arenes **1** an **2**. Right: co-crystal structure of **1** with 4,4'-bipyridine.

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pH Transient Variation Triggered by Nitroacetic Acid Allowing Dissipative Control in Supramolecular Systems

D. Del Giudice [a,c], *D. Mariottini* [b], *E. Spatola* [a,c], *C. Bombelli* [c], *G. Ercolani* [b], *F. Ricci* [b], *S. Di Stefano* [a,c]

[a] *Dipartimento di Chimica, Università degli Studi di Roma "La Sapienza", P. le A. Moro 5, I-00185 Rome, Italy.*
[c] *Dipartimento di Scienze e Tecnologie Chimiche, Università di Roma Tor Vergata, Via della Ricerca Scientifica, 00133 Roma, Italy*
[c] *ISB-CNR Sede Secondaria di Roma - Meccanismi di Reazione c/o Dipartimento di Chimica, Università degli Studi di Roma "La Sapienza", P.le A. Moro 5, I-00185 Rome*

Chemists have always taken a cue from Nature, being inspired by how it accomplishes complex biological processes. Most of these operate under dissipative conditions, that is the functional state persists until a fuel is supplied to the system.[1] For example, a lot of biochemical networks employ dissipative pH variation triggered by enzymes to modulate the outcomes of several biological processes.[2] Such dissipative control is also desirable in bioinspired supramolecular systems: this can be achieved both with fully biological tools (enzymes)[3] or purely abiotic chemical species.[4] Here I report on the possibility to control dissipative pH variation over time employing nitroacetic acid in NaOH aqueous solution.[5] pH cycles of the kind pH_{high}-pH_{low}-pH_{high} are obtained. It is also possible to modulate the time needed to complete the pH cycles by varying the amount of added reactants. Initially, this method was applied to modulate over time the host-guest interaction between *α*-cyclodextrin and *p*-aminobenzoic acid. Later, time-programmable pH dependent release/reuptake of a small DNA strand from DNA-based nanoreceptor was achieved.

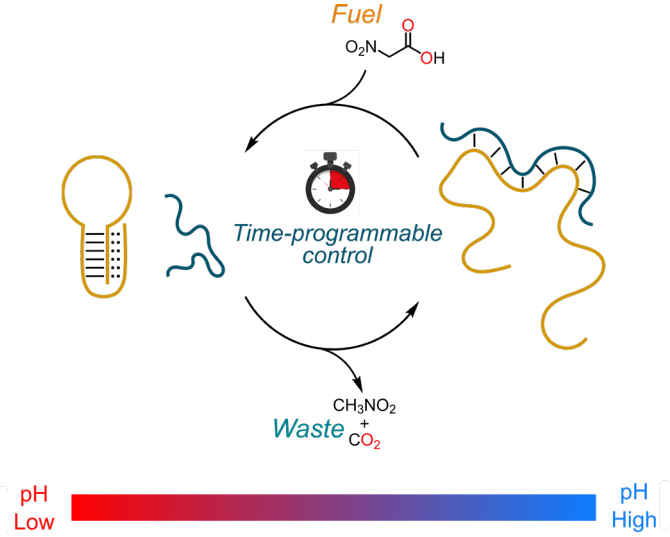

Fig. 1: Dissipative variation of the pH due to nitroacetic acid can be employed to obtain a time-programmable control over supramolecular systems. For example, this method was employed to control the release/reuptake of DNA-target from a pH-dependent DNA-based nanoreceptor.

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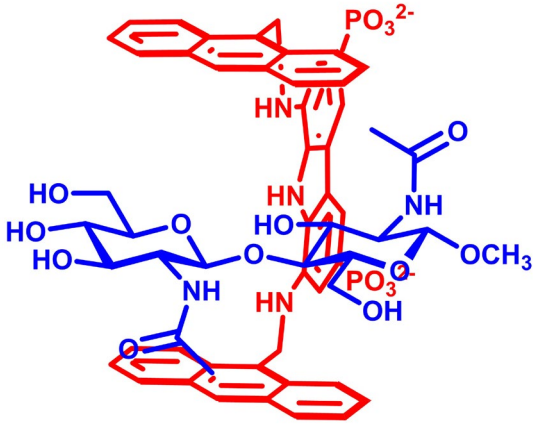
A tweezers-shaped receptor for the biomimetic recognition of the $GlcNAc_2$ disaccharide in water.

Oscar Francesconi,[a] Francesco Milanesi,[a,b] Cristina Nativi,[a] and Stefano Roelens[a]

[a] Department of Chemistry "Ugo Schiff" and INSTM, University of Florence, Polo Scientifico e Tecnologico 50019 Sesto Fiorentino, Firenze (Italy); [b] Magnetic Resonance Center CERM Via L. Sacconi 6, 50019 Sesto Fiorentino, Firenze (Italy)

Biomimetic receptors may be a convenient alternative to the use of lectins to interfere with biological processes that rely on carbohydrate recognition as a key step, such as docking of viruses to host cells.[1] The *N*,*N*'-diacetylchitobiose ($GlcNAc_2$) disaccharide plays a pivotal role in this context, because is part of the highly conserved $GlcNAc_2Man_3$ core fragment of N-glycans present on the surface of enveloped viruses, including, among others, coronaviruses. Unsurprisingly, lectins targeting $GlcNAc_2$ at the stem of N-glycosilation sites possess a broad-spectrum activity against several families of enveloped viruses.[2] Thus, effective recognition of $GlcNAc_2$ in water by a biomimetic receptor may inhibit virus-cell interaction, thereby preventing viral entry and infection.



Recently, in our research group we have developed a new family of hydrosoluble receptors for carbohydrates, featuring diaminocarbazole as a hydrogen binding unit, which turned out to be effective in water in the recognition of monosaccharides of biological relevance.[3] In this communication, we describe the design, synthesis and binding properties of a simple tweezers-shaped receptor, based on a diaminocarbazole unit, recognising the methyl-β-glycoside of $GlcNAc_2$ disaccharide with unprecedented affinity, exceeding that of more structurally complex receptors reported in the literature. Moreover, the tweezer-shaped acyclic structure exhibits marked selectivity *vs*. structurally related disaccharides, and complete discrimination between mono- and disaccharides. Molecular modeling calculations, supported by NOE data, provided a three-dimensional description of the binding mode, shedding light on the origin of the affinities and selectivities exhibited by the receptor.[4]

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Supramolecular Remote C(sp^3)-H Oxidation [Elsevier Award]

Giorgio Olivo[a], Giulio Farinelli,[a] Giorgio Capocasa,[b] Laia Vicens,[b] Federico Frateloreto,[a] Osvaldo Lanzalunga,[a] Stefano Di Stefano*[a], Miquel Costas*[b]*

[a] *Dipartimento di Chimica, Sapienza Università di Roma, Piazzale Aldo Moro 5, Rome, Italy;* [b] *QBIS-Cat, IQCC, Universitat de Girona, C/Pic de Peguera 15, 17003, Girona, Spain*

Direct C-H functionalization represents a holy grail in organic synthesis, and promises to substantially streamline drug discovery.[1] However, its potential is tapped by the difficulty of predictably controlling the reaction selectivity, i.e. discriminating a specific C-H bond from many similar others with the highly reactive species required for C-H cleavage. Current control of selectivity relies on the higher reactivity of certain sites or on a coordinating group that directs the reaction on a nearby site. This implies that remote, unactivated C-H bonds are essentially indistinguishable and cannot be targeted.

We developed a supramolecular strategy for the predictable oxidation of these remote C(sp^3)-H sites in primary amines.[2–4] Key to such elusive selectivity is the recognition and pre-organization of the substrate with benzocrown ether receptors to place remote C8 and C9 C-H bonds close to a Mn catalytic center, enabling their selective oxidation (Figure 1). We applied this strategy to the remote C8 and C9 oxidation of linear protonated alkyl amines[2] and to their substrate-selective oxidation in mixtures.[3] Moreover, this concept enabled site-selective oxidation of aminosteroids at the unactivated D-ring, with a selectivity that is orthogonal to that of undirected reactions and easily predictable via NMR analysis or simple docking of the substrate-catalyst adduct (Figure 1). We are currently aiming to rationalize and quantify this selectivity via kinetic and model studies and further exploring the potential of this supramolecular approach.

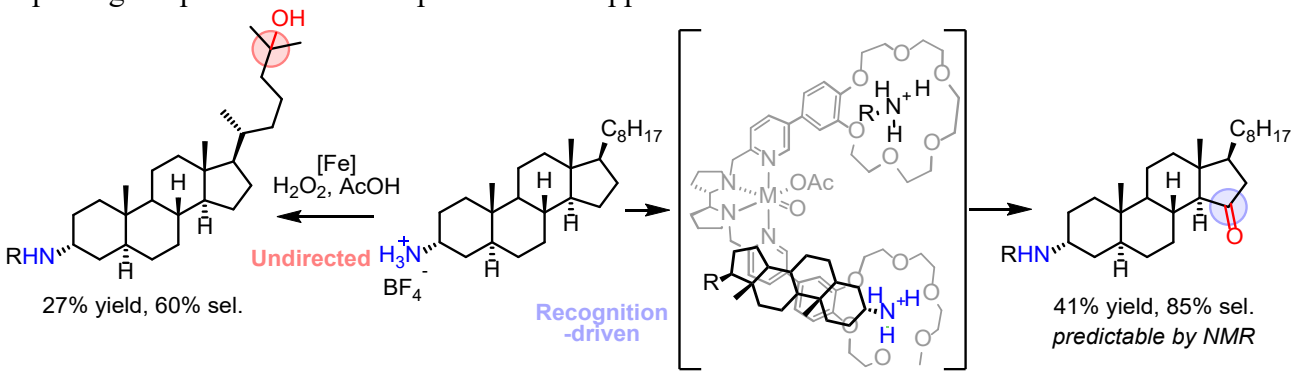

Figure 1: Recognition-driven remote C(sp^3)-H Oxidation of amines. Example on the switch in aminosteroid oxidation site-selectivity towards unactivated, remote positions via a supramolecular approach.

Acknowledgement – This research activity is supported by the "Reaxys SCI Small Research Grant" [S-ReCHOx; PI: Giorgio Olivo].

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Tuning the folding properties of synthetic recognition-encoded oligomers

Daniele Rosa-Gastaldo[a], *Luca Gabrielli*[a]

[a] *Università degli Studi di Padova, Dipartimento di Scienze Chimiche, via Marzolo 1-35121, Padova*

Inspired by DNA, researchers designed and explored synthetic supramolecular systems that form duplex structures via non-covalent interactions, exploiting a modular approach for the design of synthetic molecules that form duplexes via multiple cooperative H-bonding interactions, between recognition units that are appended to the backbone.[1,2] In mixed-sequence oligomers the possibility of introducing intramolecular H-bonds, can lead to folding equilibria that compete with duplex formation (Figure 1a). If two adjacent recognition units on an oligomer interact strongly, the folding pathway will be favored over the duplex assembly channel. Thus, the presence of 1,2-folding is a determining factor for the ability of mixed sequence oligomers to form stable duplexes.
In this work,[3] taking advantage of the flexible modular approach used, we modified the sterically hindrance of the acceptor phosphine oxide and the backbone geometry, to tune the folding properties of the oligomers (Figure 1b).

Figure 1. a) Competing self-assembly channels for AD•AD duplexes; b) structural strategies used to tune the folding properties.

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Elucidation of the Chemical Structure of Lipopolysaccharides Isolated from the Commensal Bacteria *Veillonella parvula*

M. D. Pither[a], *A.N. Jacobson*[b], *M.A. Fischbach*[b], *P. Salvatore*[c], *A.Silipo*[a], *A. Molinaro*[a], *F. Di Lorenzo*[a]

[a]*Department of Chemistry, University of Naples Federico II, Italy*
[b]*Department of Bioengineering and Therapeutic Sciences and California Institute for Quantitative Biosciences, University of California, San Francisco, California, USA*
[c]*Dipartimento di Medicina molecolare e Biotecnologie Mediche, Napoli, Italy*

The human gut microbiota harbours a complex community of microorganisms which influences human physiology, metabolism, nutrition, and immune function [1]. To remain immunologically tolerant to these commensal bacteria and preserve a symbiotic relationship elaborate biochemical mechanisms are involved. A key mechanism involves the bacterial lipopolysaccharides (LPSs), key components of the Gram-negative bacteria cell wall. LPS is a potent ligand for the host receptor Toll-like receptor 4/myeloid differentiation factor 2 (TLR4/MD2) complex [2]. These interactions are vital for the initiation of immune response to pathogens, but how LPS from commensal bacteria interact with TLR4/MD2 complex is still unclear. *Veillonella* species are known as an opportunistic pathogen, through being a component of the normal human microbiome and yet having been found to play a vital role in poly-microbial infections, specifically in respiratory and oral infections [3,4]. Additionally, research has shown that the LPS isolated from *Veillonella* possesses inhibitory activity towards pathogenic LPS and can influence the susceptibility of children to allergies and autoimmunity [5]. Since LPS are involved in the interaction between bacteria and the host, an in-depth investigation of the full structure of the LPS from *Veillonella* is a first but essential step to understand the basis of virulence and symbiotic behaviour of these bacterial species. Accordingly, our previous work shows *Bacteroides vulgatus,* another key commensal member of the human microbiota*,* produces LPS which does not elicit a potent proinflammatory response and is structurally different to pathogen-derived LPS [6].
To this aim, LPSs have been extracted from *Veillonella parvula* cells*,* grown in our laboratories, and then undergone a full structural elucidation using both mass spectrometry and nuclear magnetic resonance.

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The glycomimetic approach for selective inhibition of Carbonic Anhydrases

Debora Pratesi[a], Camilla Matassini[a], Andrea Angeli[b], Marta Ferraroni[a], Francesca Cardona[a], Claudiu T. Supuran[b], Rolando Spanevello[c], Andrea Goti[a]

[a]Dipartimento di Chimica 'Ugo Schiff', Università degli Studi di Firenze, via della Lastruccia n. 3-13, Sesto Fiorentino (FI), Italy; [b]Dipartimento Neurofarba, Sezione di Scienze Farmaceutiche e Nutraceutiche, Università degli Studi di Firenze, Via U. Schiff 6, 50019, Sesto Fiorentino, Florence, Italy; [c] Instituto de Química Rosario, Facultad de Ciencias Bioquímica y Farmacéuticas, Universidad Nacional de Rosario, CONICET, Suipacha 531, S2002LRK Rosario, Argentina.

Carbonic Anhydrases (CAs; EC 4.2.1.1) are zinc metalloenzymes which play a fundamental role both in physiological and pathological processes in humans (h). Therefore, modulation of the activity of hCAs represents an important target for drug development, which results highly challenging due to the large number of isozymes expressed and requires the discovery of selective inhibitors. By following the "sugar approach"[1] and considering our recent disclosure of two selective hCAs inhibitors based on glycomimetic-sulfonamide conjugates[2], new glycomimetic-sulfonamides have been synthesized[3] by conjugating several benzenesulfonamides to a triazole-armed azasugar with different linkers such as thioureido, ureido, amido and amine groups. These compounds were found to be potent selective inhibitors; in particular some of them showed interesting data towards the therapeutically relevant hCAs II and VII isoforms. We also synthesized new benzenesulfonamide derivates based on levoglucosenone (**1**) that is a small highly functionalized compound produced by pyrolysis of cellulose-containing urban and industrial residual materials such as waste paper[4]. In this way we have exploited renewable source for the synthesis of glycomimetic inhibitors.

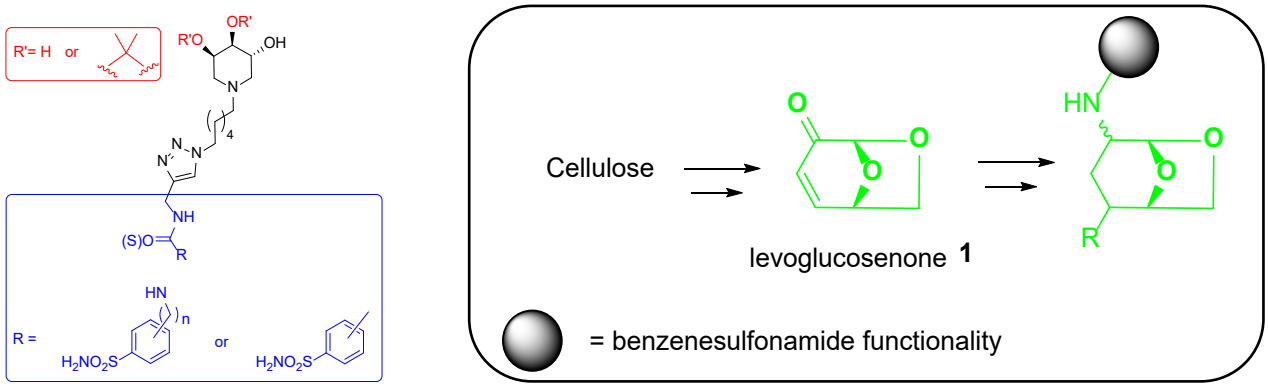

Figure 1- New glycomimetic-sulfonamide conjugates inhibitors.

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Resorc[4]arene-based site directed immobilization of antibodies for immunosensors development

Deborah Quaglio, Gabriele Favero, Marco Pierini, Bruno Botta, Franco Mazzei

Department of Chemistry and Technology of Drugs, "Department of Excellence 2018−2022", Sapienza University of Rome, P.le Aldo Moro 5, 00185 Rome, Italy

One of the main problems in the development of immunosensors is to overcome the complexity of binding antibody to the surface of the sensor. In fact, antibodies need to be immobilized with a high density and good orientation to allow the easy detection of antigens. The influence of nonspecific bindings should be minimized to improve the detection performance. Most of immobilizing methods lead to randomly oriented antibodies on the surface, which results in a low density of binding sites and alleviation of immunoaffinity of the antibodies. Therefore, oriented immobilization is required for the improvement of the performance enhancement.

Calix[4]arene derivatives have been proposed as an alternative tool for the oriented immobilization of antibodies thanks to their unique three-dimensional surface, which can be functionalized at both the upper and lower rims with several functional groups.[1] Within the calixarene family, resorcinol-derived cycloligomers, namely resorcarenes, behave as abiotic artificial receptors having enforced cavities of molecular dimension.[2]

To ensure the orientation control of antibodies on the sensor surface, we synthesized several resorc[4]arene derivatives able to self-assemble onto gold surface thanks to the thioether groups present on their structure.[3] After the spectroscopic characterization of resorc[4]arene self-assembled monolayers (SAMs) onto gold films, the surface coverage and the orientation of insulin antibody (Ab-Ins) were assessed by a surface plasmon resonance (SPR) technique and compared with a random immobilization method. Experimental results combined with theoretical studies confirmed the dipole–dipole interaction as an important factor in antibody orientation and demonstrated the importance of the upper rim functionalization of resorcarenes. Based on these findings, the resorcarene-based immunosensor is a powerful system with improved sensitivity providing new insight into sensor development.

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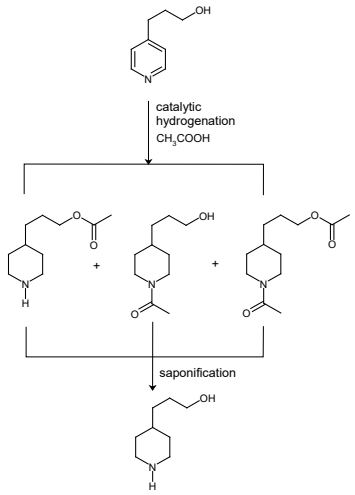
Problem solving in Pharmaceutical processes: isolation, characterization and synthetic preparation of unknown impurities in 4-piperidinepropanol manufacture.

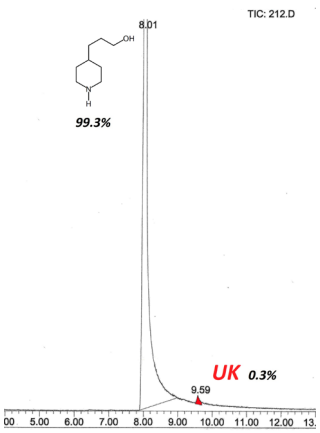
Roberto Rossi[a], *Manuela Saba*[b]

[a] *Dipharma Francis S.r.l.;* [b]*Dipharma Francis S.r.l.(current address Steroid S.p.A);*

Impurity management is a common practice in the pharmaceutical manufacture. Every time a new synthetic route is being developed, unknown impurities can pose in serious jeopardy the whole process. The identification of impurities present, and even more the understanding of their formation pathways, may enable the implementation of changes to the process to avoid problems in subsequent steps, not limited to the control of the residual impurities on the finished product. An emblematic case is here presented to show a fast response approach to a complex issue.
4-piperidinepropanol is a well-known building block, for example in the preparation of polysulfonamides [1], polyurethane polymers [2], as a synthetic reagent for the preparation of thrombin inhibitor [3], effective as a therapeutic or prophylactic agent for conditions such as depression, anxiety, Alzheimer's disease [4], or for the preparation of cardiotonic agents [5]. Our interest in such a small and simple molecule pushed us to search for our own synthetic preparation (Scheme 1) [6]. However, in the manufacturing campaign of this intermediate, a new unknown impurity was detected and found to be critical (Figure 1). Since it was higher than our specification limit (0,1% for every single UK impurity), its identification (Figure 2) and other corrective actions were required . The strategy for impurity management applied and here described allowed changes to be implemented in subsequent batches, solving the problem at its root.



Scheme 1



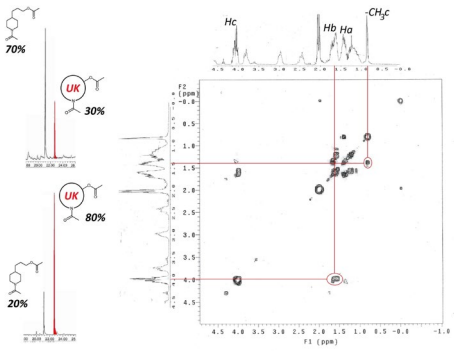


Figure1

Figure 2

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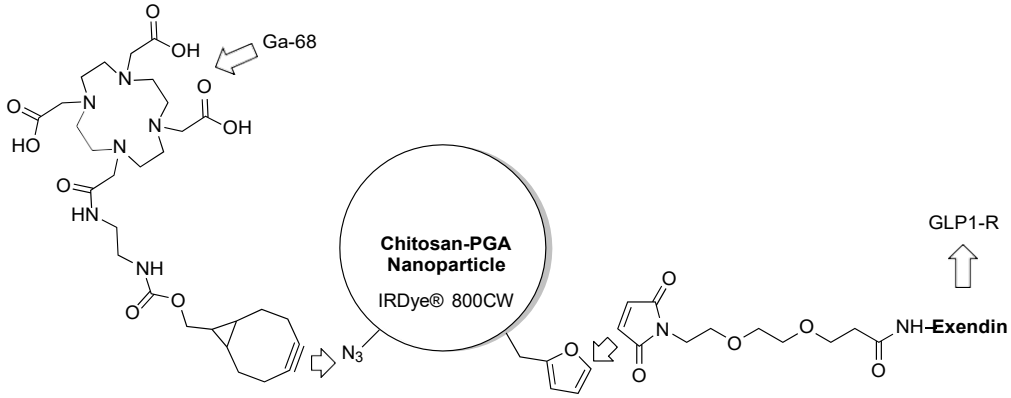
Chemoselective synthesis of triple-functionalizes nanoparticles for multimodal in vivo imaging of pancreatic β-cells

Russo L.[1], *Rossi L.*[1], *Pignatelli C.*[1], *Kerekes K.*[2], *Körhegyi Z.*[2], *Bodnar M.*[2], *Kocsi J.*[2], *Lindheimer F.*[3], *Lindner M.*[3], *Lindner S.*[3], *Bartenstein P.*[3], *Ziegler S.*[3], *Nicotra F.*[1]

E-mail: laura.russo@unimib.it

[1] *University of Milano-Bicocca, Department of Biotechnology and Biosciences, Italy,* [2] *BBS Nanotechnology, Hungary;* [3]*Department of Nuclear Medicine, Faculty of Medicine, University Hospital LMU, Germany*

Selective targeting of pancreatic β-cells has tremendous interest in regenerative strategies for diabetes and in early detection of pancreatic cancer and disfunctions. In the H2020-NMBP project iNanoBIT, aimed to develop an implantable medical device containing β-cells producing insulin, we developed multifuctional nanoparticles to test β-cells viability and functionality[1,2]. To this purpose chitosan and γ-PGA, properly combined to generate 120-170 nm nanoparticles, were functionalized with azide, thiol and furan for subsequent chemoselective linkage of a β-cells targeting agent, a chelator of radioisotopes for PET/SPECT analysis and a Near IR dye for a new optoacustic imaging approach (MSOT). As targeting agent we selected the peptide exendin-4, a ligand of GLP1-receptors of β-cells, to which a linker with a meleimido terminal group was attached at Lys27, to allow chemoselective Diels Alder reaction with the furan groups of the nanoparticles. The near IRDye® 800CW was conjugated as NHS-derivative to few amino groups of chitosan, whereas the DOTA chelator, functionalized with a cyclooctine linker, was conjugated exploiting their azido groups at the nanoparticles surface.



The chemical and morphological properties of the nanoparticles were standardized, the targeting ability and imaging performance were determined both in vitro and in vivo. PET in vivo studies in mice with Ga-68 labeled nanoparticles were performed to confirm the biocompatibility, the biodistribution and the imaging properties, whereas the pancreatic uptake was confirmed by in vitro autoradiography.

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Affinity enhancement of peptide ligands for tumor overexpressed receptors

G. Sacco,[a] A. Dal Corso,[a] D. Arosio,[b] L. Belvisi,[a] L. Pignataro,[a] C. Gennari[a]

[a] *Università degli Studi di Milano, Dipartimento di Chimica, Via C. Golgi 19, 20133 Milano;*
[b] *CNR, Istituto di Scienze e Tecnologie Chimiche "Giulio Natta" (SCITEC), Via C. Golgi 19, 20133 Milano.*

The impact of monoclonal antibodies (mAbs) in current pharmaceutical research is due to their unique ability to bind biological targets with very high affinity. On the other hand, there is a considerable interest in the development of small molecule ligands with antibody-like affinities, which may overcome some limitations of mAbs.
In the last years, we have developed general strategies to increase the binding affinity of peptide ligands bearing the Arg-Gly-Asp (RGD, Figure 1A) motif, i.e. the well-known recognition sequence of specific tumor-associated integrin receptors.
In our first approach, we designed a bicyclic peptide bearing two RGD motifs (compound **1**, Figure 1B). Compound **1** displayed enhanced inhibition of ECM protein binding to integrin receptors $\alpha_v\beta_3$ and $\alpha_5\beta_1$ as compared to monomeric RGD analogues, which led to marked biological effects in U-373 MG glioblastoma cells.[1]
Later on, we focused on the 2-hydroxybenzaldehyde tag (2HB), which can engage the ϵ-amino group of Lys residues by forming stable imines.[2] After investigating the 2HB installation into different types of reactive handles,[3] we conjugated the 2HB tag to a cyclic RGD peptide, and the resulting conjugates (compounds **2** and **3**, Figure 1B) are being investigated as novel integrin ligands, ideally showing high binding affinity through the reversible-covalent Lys engagement.

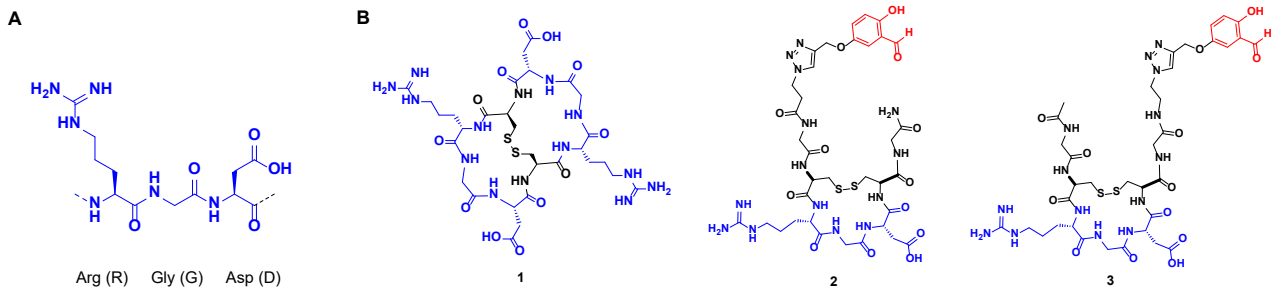

Figure 1. A) The Arg-Gly-Asp (RGD) tripeptide structure; B) Structures of the dimeric bicyclic RGD peptide **1** and the 2HB-bearing RGD peptides **2** and **3.**

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Synthesis of an analogue of *Neisseria meningitidis* A capsular polysaccharide for the development of a glycoconjugate vaccine

C.M. Santi, L. Lay

Dipartimento di Chimica - Università degli Studi di Milano - Via Golgi 19 - 20133 Milano

Neisseria meningitidis A (MenA) had been for a long time the main cause of epidemics of meningococcal meningitis in the sub-Saharan Africa. Thanks to the introduction of MenAfriVac vaccine, serogroup A related infections have almost vanished in 2017; however, the World Health Organization pointed out the importance to persist with a strict vaccination program.
Up to date, all the licensed vaccines targeting MenA are obtained from the extraction and size fragmentation of the capsular polysaccharide (CPS) from the bacterium. MenA CPS consists of (1→6)-linked-2-acetamido-2-deoxy-α-D-mannopyranosyl phosphate residues partially acetylated at C-3 and C-4. This structure, once isolated, is not stable in water due to the hydrolysis of the phosphodiester bond. Due to the instability issues, most of the licensed vaccines targeting MenA are distributed in a lyophilized form and the cold chain must be maintained during the entire process of distribution and storage.
To achieve a more stable vaccine, which could be distributed in the more convenient liquid formulation, without the need of a strict temperature control, some, more stable, structural analogues have been developed. In particular, our group synthesized MenA CPS non-acetylated phosphonoester-linked oligomers up to the trimer [1]: these analogues showed good stability, however, they resulted to be poorly immunogenic [2], even after protein conjugation [3].
Since the acetylation was proven to have an important role in the immunogenicity of natural MenA CPS [4], our goal is the synthesis of the 3-O acetylated phosphonate analogue up to the trimer.
In this communication, the synthesis of the 3-O acetylated phosphonate analogue up to the trimer will be described.

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Rational Design of Pseudoproline-Containing K-Opioid Receptor-Selective Peptidomimetics

F. Santino [a], *A. Bedini* [b], *S. Spampinato*[b], *L. Gentilucci* [a]

[a] *Department of Chemistry "G. Ciamician", University of Bologna, via Selmi 2, 40126, Bologna*
[b] *Department of Pharmacy and Biotechnology, University of Bologna, via Belmeloro 6, 40126, Bologna*

Prescription opioids are powerful painkiller medications but the scope of their misuse and abuse is constantly increasing. The most common drugs include selective agonists of the μ-opioid receptor (MOPr) such as methadone, oxycodone, hydrocodone and fentanyl. However, these molecules also produce many unwanted side effects. On the other hand, for their low abuse potential κ-opioid receptor (KOPr) agonists represent valuable alternative analgesics.

In 2018, we proposed a modified analogue of the endogenous MOPr ligand endomorfin-1 (EM1), H-Tyr-Pro-Trp-PheNH$_2$, by replacing Pro^2 with stereoisomeric β^2-homo-Freidinger lactam-like scaffolds ([Amo^2]EM1, Figure C). [1] Unexpectedly, the compound H-Tyr-Amo-Trp-PheNH$_2$ showed high affinity and selectivity for KOPr, acting as a partial agonist *in vitro*, and demonstrated analgesic activity *in vivo* in the tail-immersion test. These results were explained by the discussed possibility that peptides must adopt a cis conformation about the Tyr-Pro peptide bond to properly fit the MOPr binding site (Figure A) [2], while [Amo^2]EM1 adopts an all-trans conformation (Figure B).

Based on this assumption, we decided to introduce diverse all trans-inducing five-membered heterocycles at the position 2 of the sequence, to produce a complete loss of affinity for MOPr, while gaining affinity and selectivity for KOPr. The conformationally constrained heterocycles have been synthetized by click reaction of alkyne/azide precursors (**1**), or by in-peptide cyclization of functionalized amino acids (**2**).

The resulting EM1 mimetics have been analyzed by displacement and functional assays to determine receptor affinity and agonism/antagonism, and the receptor binding modes have been investigated by molecular docking.

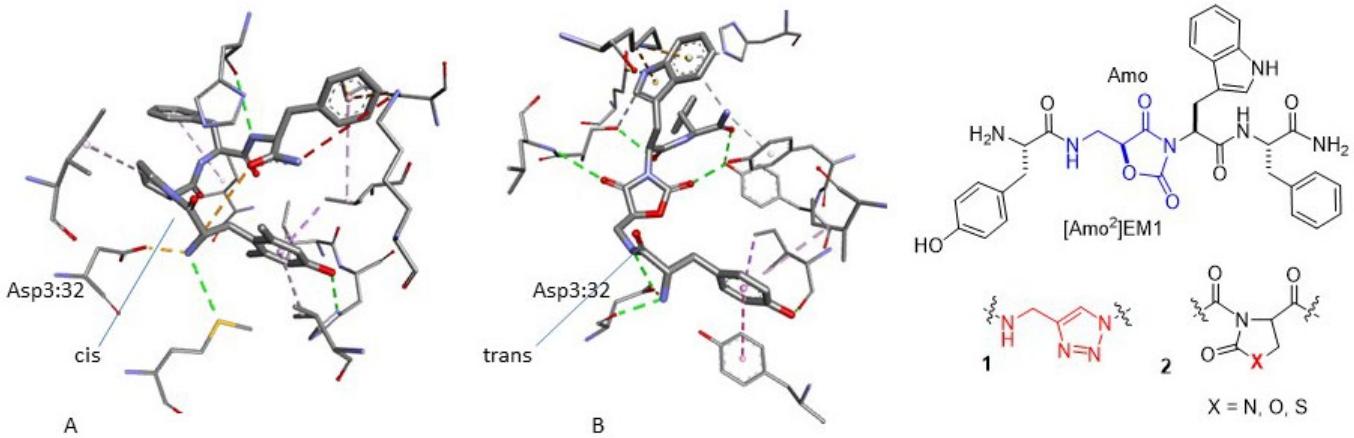

Figure. Side views of the bioactive conformations of (A) [Dmt^1]EM2 as docked in h-MOR, and (B) of [Amo^2]EM1 in MOR. (C) Structure of Amo^2]EM1 and of the all trans-inducing heterocycles **1** and **2**.

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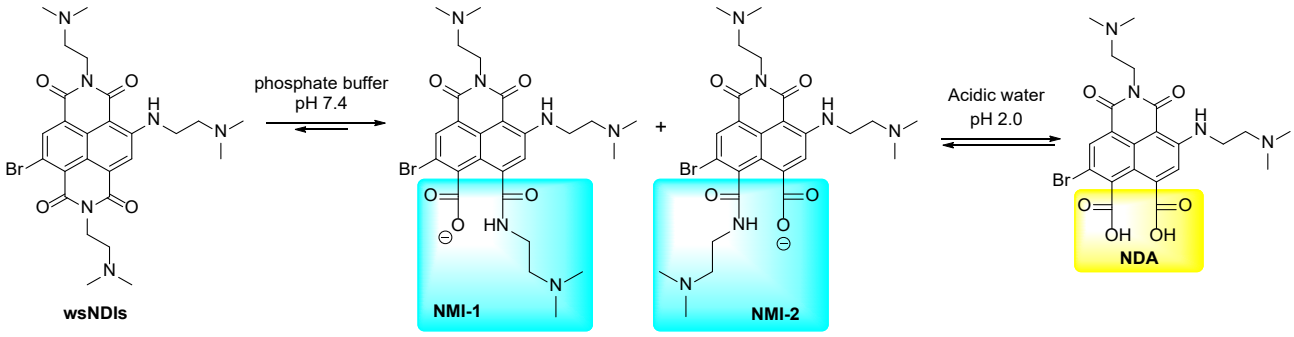
Selective hydrolysis of water-soluble naphthalene diimides driven by core-substitution

*Pirota V., Freccero M., Doria F.**

Department of Chemistry, University of Pavia, via Taramelli 10, I-27100 Pavia, Italy

Extended planar aromatic surface and useful optoelecronic properties of naphthalene diimides (NDIs) make them a versatile platform for the design of molecules ranges from material sciences to supramolecular chemistry, to biological and medical functions.[1] Distinctly, the significance of the water-soluble NDIs (wsNDIs) mostly arises from their use in medicinal chemistry for their exceptional ability to interact with nucleic acids and in particular, with their secondary non-canonical structures, such as G-quadruplexes.[2-4] Although wsNDIs are very stable in organic solvents or in acid aqueous solutions, they are quite sensitive to basic hydrolysis. Reversible hydroxide-catalyzed hydrolysis on unsubstituted wsNDIs was reported to promptly occur stepwise affording the mono-imide (NMI), which slowly hydrolyses further giving the diacid-diamide structures.[5] Despite the imide pendants can tune the hydrolytic stability, their contribution in modeling the optoelectronic properties of wsNDIs is negligible.

In this context, we studied how wsNDIs' optoelectronic and redox properties can be steered by affecting the π-system, by functionalization of the naphthalene core (i.e. nature and number of substituents). To rationalize the effect of the naphthalene core-substitution on the first step of the hydrolysis, di-, tri-, and tetra-substituted wsNDIs were synthesized, molding the substituents from two bromine to amines, the principal pendants of well-known wsNDIs. The presence of bromine, as core-substituent, promotes hydrolysis under mild conditions with unexpected high regioselectivity (**NMI**; Scheme 1). Subsequent acidification of the solution promotes the formation of diacid-imine structure (**NDA**; Scheme 1), which is the key intermediate to drive the formation of a controlled asymmetric diimide. This strategy was exploited to synthesize a small family of tetra asymmetric wsNDIs,. This innovative synthetic approach offers an effective method for the synthesis of asymmetric diimide as useful G4-ligands.



Scheme 1 – Schematic representation of reversible hydroxide-catalyzed hydrolysis on core-substituted wsNDIs.

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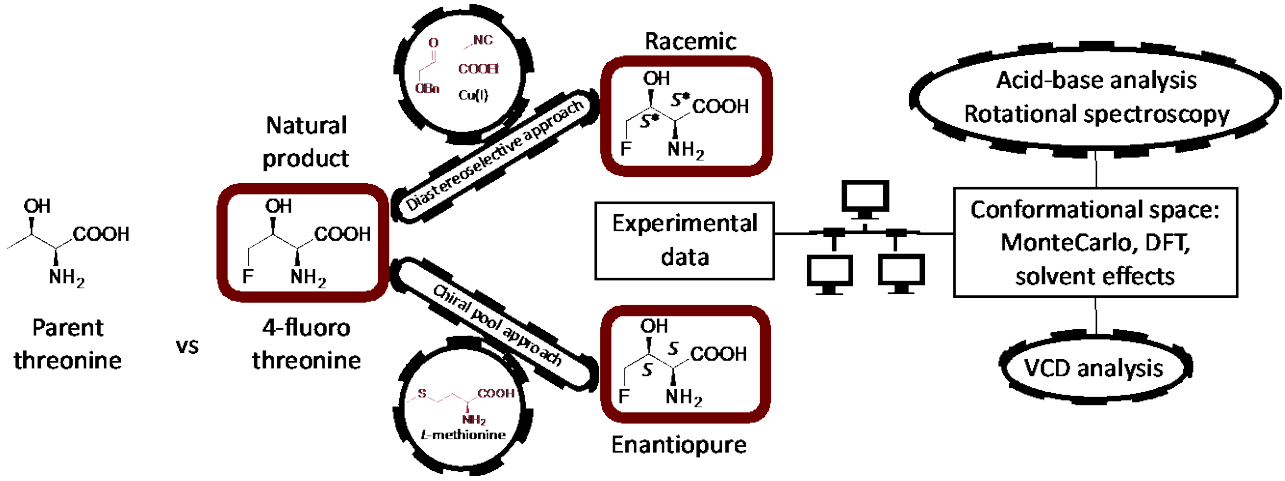
4-Fluorothreonine as a test case: the effects of fluorination on molecular properties

S. Potenti,[a,b] L. Spada,[a,b] M. Fusè,[a] G. Mancini,[a,c] A. Gualandi,[b] C. Leonardi,[d] P. G. Cozzi,[b] C. Puzzarini,[b] V. Barone[a]

[a] Laboratorio SMART, Scuola Normale Superiore, 56126 Pisa, Italy; [b] Dipartimento "G. Ciamician", Alma Mater Studiorum – Università di Bologna, 40126 Bologna, Italy; [c] Istituto Nazionale di Fisica Nucleare (INFN), 56127 Pisa, Italy; [d] Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Ferrara, 44121 Ferrara, Italy
e-mail: simone.potenti@sns.it

Starting from the beginning of the 20th century, it became clear that most molecular properties arise from the conformational behavior,[1] so we analyzed the conformational space of 4-fluorothreonine, the only fluoro amino acid of natural origin discovered so far,[2] as a test case to study the effects of fluorination. Such conformational analysis was performed by means of state-of-the-art computational methods. Indeed, we have demonstrated that our computational approach provides results and trends in remarkable agreement with experiments.[3]



Besides, 4-fluorothreonine is an interesting target even for synthetic investigation. Both racemic and enantioselective synthetic routes have been analyzed to produce synthetic material for experimental characterization. Once the experimental data are available, they can be compared with the computed ones. Indeed, comparison studies between parent threonine and 4-fluorothreonine can lead to a better description of the effect of fluorine on molecular properties.

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Application of ASCA modelling tools on a PDO hard cheese: Analysis of the effects on physical parameters of Trentingrana

Michele Ricci [a,b], Flavia Gasperi [a,b], Elena Santoro [b], Leonardo Menghi [a,b,c], Isabella Endrizzi [b], Danny Cliceri [a], Pietro Franceschi [d], Eugenio Aprea [a,b]

a University of Trento - Center Agriculture Food Environment; Via E. Mach, 1 – San Michele All'Adige (TN) – 38010 – Italy;

b Department of Food Quality and Nutrition, Research and Innovation Centre, Fondazione Edmund Mach; Via E. Mach, 1 – San Michele All'Adige (TN) – 38010 – Italy;

c University of Southern Denmark – Department of Technology and Innovation; Campusvej 55 – Odense – 5230 – Denmark;

d Unit of Computational Biology, Research and Innovation Centre, Fondazione Edmund Mach; Via E. Mach, 1 – San Michele All'Adige (TN) – 38010 – Italy;

Trentingrana is a hard long ripened cheese characterized by specific physical properties obtained by curing, a ripening period of at least 18 months, and the use of raw milk only from farms of a specific area of northern Italy. The color and the texture of the grain are two crucial factors for consumer acceptance. These properties depend on the composition of raw milk during coagulation and on both microbial activity and water dispersion during ripening. At a supply chain level, these processes are influenced by the different dairy factory where the process is handled and to the part of the year when the raw milk is produced and conferred to the dairy factory. The aim of this study is to analyze the effect of different conditions of production on the physical properties of hard long ripened cheese.

To estimate the effect of the dairy factory, the part of the year and their interactions on the physical properties of hard cheese, colorimetric and textural measurements have been systematically acquired from 317 cheese wheels sampled every 2 months for 2 years from 15 dairy factories of the Trentingrana consortium. From each wheel, 24 blocks with a length of 3 cm, a width of 1.5 cm, and a height of 1.5 cm, have been sampled and grouped in 6 levels according to their distance from the center of the wheel. Globally, 7602 measurements have been acquired. Color properties have been measured in the CIElab color space using a CR-400 colorimeter equipped with a D65 illuminant source, and texture properties have been measured using a TA-XT texture analyzer through a uniaxial penetration test to estimate the maximum force applied, the area below the force/strain curve and Young's modulus.

We developed separate linear mixed models, which also included the cheese blocks' position inside the wheel as an additional source of variability, to integrate into the model the variability within a cheese slice. The cheese wheel was considered a random factor. Each model has been validated using a permutation test and the results have been processed using ANOVA Simultaneous Component Analysis (ASCA) to compare differences and similarities between the levels of each factor at a multivariate level.

Results showed a significant effect for all the factors analyzed, except the interaction between the dairy factory and the part of the year. ASCA decomposition highlighted three different clusters of dairy factories due to textural properties, three clusters of part of the year due to textural and colorimetric properties, with a strong difference of a single couple of months comparing to other levels, and an overall increase of both colorimetric and textural properties in sampling position in relation to the distance from the center. Those results are a useful insight to understand the complex relations between process conditions and the properties of the cheese product in a real case scenario of a real-scale semi-artisanal supply chain.

This study is supported by TRENTINGRANA project (PSR 2017/2019), which provides the Consortium of technical assistance for quality control.

Computational study of substituted phenols *pKa*

Federica Sabuzi, Samuele Tarallo, Alessandro Iannini, Valeria Conte, Pierluca Galloni

[a] *Department of Chemical Science and Technologies, University of Rome Tor Vergata, Via della Ricerca Scientifica, snc – 00133 Roma*

Natural phenols, mainly of vegetable origin, are receiving more and more attention, thanks to their peculiar biological activity as anti-oxidant, anti-parasitic and anti-microbial agents. Over the last few years, we have been involved in the study of thymol, a natural terpenoid phenol, extracted from thyme essential oils. Biological studies showed that the brominated thymol derivatives[1] (namely 2-bromothymol and 2,4-dibromothymol) are significantly more effective than thymol in exerting their anti-bacterial, anti-fungal and anti-parasitic action[2]. Such results prompted us to synthesize a series of differently functionalized thymol derivatives[3], to be screened as biologically active ingredients for different purposes. Also, a suitable and sustainable delivery system, based on lignin microcapsules, has been developed for application in the cosmesis field[3].
Among the others, acidity and lipophilicity are key factors that affect phenols biological activity; in fact, they are determinant parameters for modulating the cellular membrane crossing by an active ingredient, which is needed to induce bacterial cell death.
Due to the low water solubility of thymol derivatives, the aim of this work is to find an accurate computational method for determining the acid dissociation constant of differently functionalized thymol derivatives, using DFT calculations. Different functionals and solvation models will be evaluated, to obtain an accurate protocol that will be exploited also for other organic acids. In particular, the *pKa* of thymol and its bromo- and nitro- derivatives will be calculated and compared with those of reference compounds.

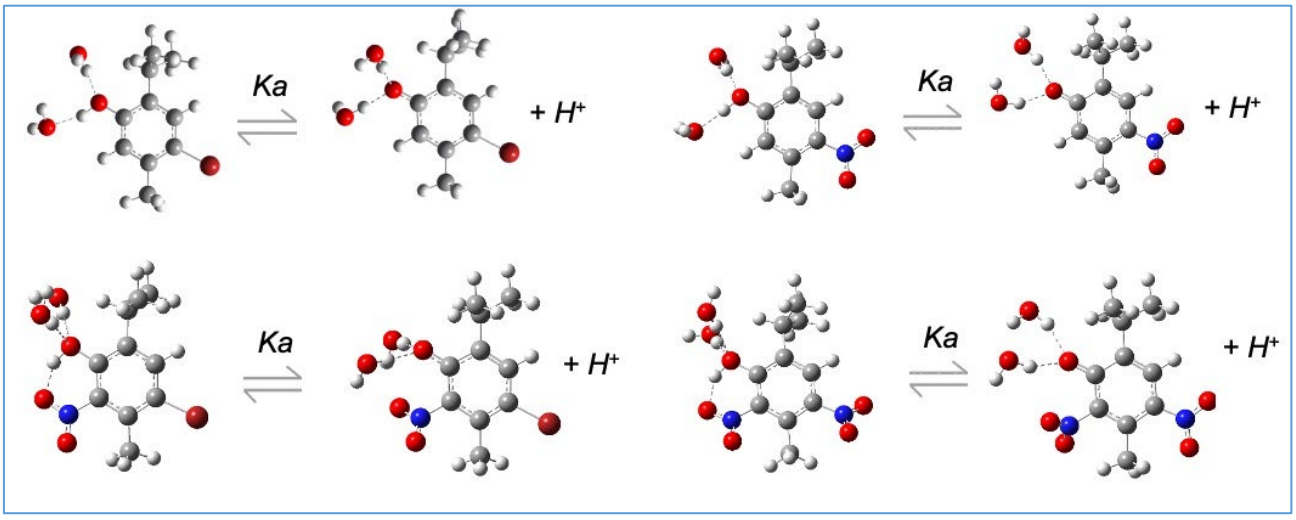

Fig. 1. Optimized geometry of bromo- and nitro- thymol derivatives and their conjugated bases, solvated with two water molecules (C atoms are represented in grey, H atoms in white, N in blue, O in red, Br in dark red).

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Supramolecular Catalytic Gels [Elsevier Award]

Carla Rizzo, Salvatore Marullo, Floriana Billeci, Francesca D'Anna

Dipartimento STEBICEF-sezione di Chimica, Università degli Studi di Palermo

Developing new catalytic systems that conjugate reaction efficiency and sustainability is still challenging. In this framework, performing organic reactions in supramolecular gels based on green solvents such as Ionic Liquids and Deep Eutectic Solvents, ILGs or eutecto-gels, allow having catalyst and solvent in one system, recovering products and reusing the system for several catalytic cycles.
These supramolecular and confined reaction media could offer, indeed, the possibility to work in mild conditions without leaching issues.[1] Some hydro- and organogels have been reported as efficient catalytic gels, but only few examples of ILGs or eutectogel have been applied as catalytic media until now.[2] Recently, some ILGs have been proved efficient media, in terms of yield and enantiomeric excess, for the enantioselective desymmetrization of cyclic meso-anhydrides.[3]

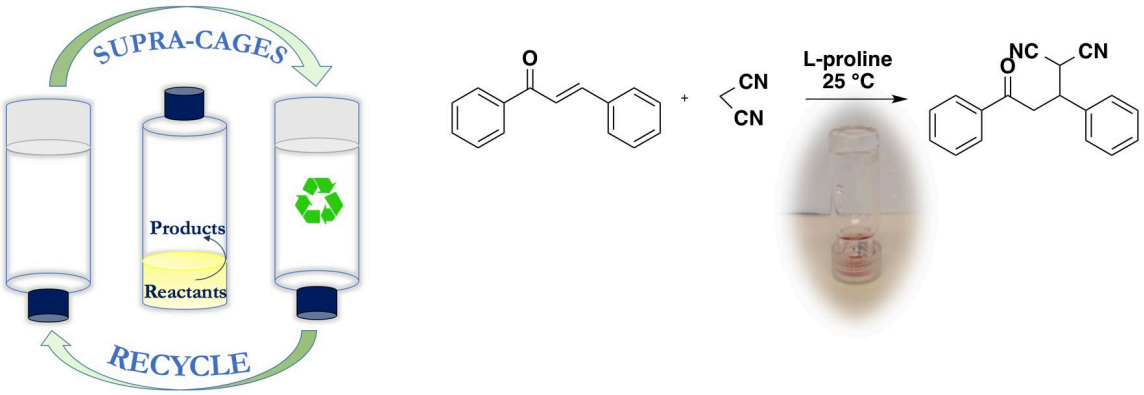

Figure 1. Schematic representation of catalytic system involving gels as reaction media and model reaction performed in a transparent eutectogel.

To further study catalysis on gel phases, after a full characterization of gel's physicochemical properties, some eutectogels were tested as catalytic reaction media for the enantioselective aldol reaction and Michael addition.
In both cases, all gels improved the reaction outcome in terms of conversion and yield. As for the stereochemical control of the reaction, good enantiomeric excess was only achieved in the case of the aldol reaction. Eutectogels proved to have a great potential as sustainable reaction media, allowing to perform processes under mild conditions. In some cases, they can be reused up to five cycles keeping the stereochemical control of the reaction. These results encourage to perform further reactions in sustainable gels.

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Functionalized gold nanoparticles for MRI applications

Maria Şologan[a,*], Francesco Padelli [b,*], Isabella Giachetti [b], Domenico Aquino [b], Mariangela Boccalon [a], Gianpiero Adami [a,c], Paolo Pengo [a] and Lucia Pasquato [a,c*]

[a] *Department of Chemical and Pharmaceutical Sciences, University of Trieste, Via L. Giorgieri 1, 34127 Trieste, Italy;*
[b] *Neuroradiology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, 20100 Milano, Italy;*
[c] *INSTM Trieste Research Unit, Via L. Giorgieri 1, 34127 Trieste, Italy.*

MRI is a very useful technique for noninvasive imaging which offers anatomical and functional information about tissues, by altering the longitudinal and transversal relaxation times (T1 and T2 respectively) of selected nuclei. The conventional MRI techniques exploit the NMR signals arising from the hydrogen of water molecules present within the tissues or from fluorine nuclei of artificial compounds introduced into the organisms[1].

Gold nanoparticles (AuNPs) protected by fluorinated ligands are, by themselves, contrast agents displaying good sensitivity for ^{19}F magnetic resonance imaging, due to the possibility to achieve a high density of fluorine nuclei by grafting suitable ligands on the gold core surface[2]. The low water solubility of these type of nanomaterials is a drawback for biological applications.
In order to overcome this, our group has previously designed and synthesized gold nanoparticles protected by ligands composed of three parts: an alkyl chain which gives stability to gold nanoparticles, a fluorinated moiety to achieve an MRI signal and a polyethylene glycol chain which imparts water solubility[3,4].

Herein, we present the synthesis, characterization and preliminary MRI studies for gold nanoparticles protected by thiols having a fluorinated part[4] or/and an alkyl chain functionalized with a DOTA derivative which complexes Gd^{3+} ions (Figure 1a), for ^{1}H and/or ^{19}F MRI (Figure 1b).[5] Moreover, gold nanoparticles protected by different ratios between ligands have been investigated in order to optimize the effect of Gd^{3+} in shortening of T1 and T2. As expected, the introduction of gadolinium chelates on fluorinated AuNPs determines a decrease of both T1 and T2 relaxation times for ^{19}F.

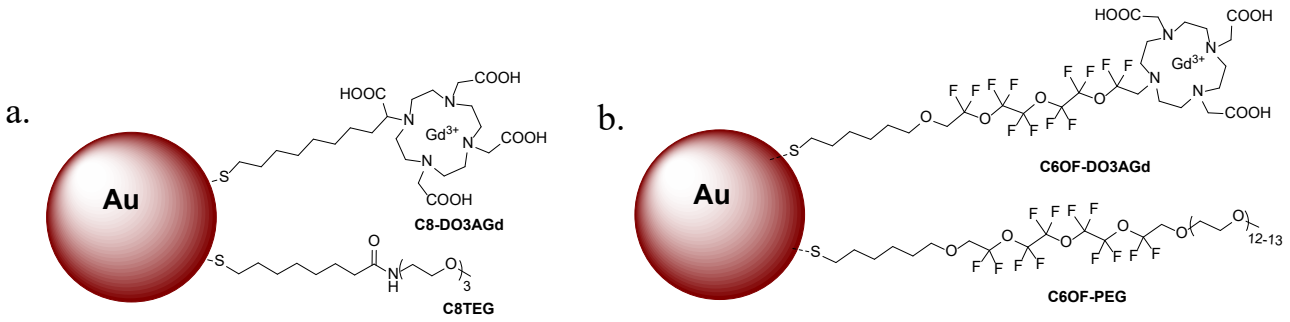

Figure 1: AuNPs for MRI applications

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Thiophene substituted aza-BODIPY as promising metal-free, pure NIR emitter for OLEDs

Benedetta Maria Squeo, Wojciech Mróz, Chiara Botta, Mariacecilia Pasini

Istituto di Scienze e Tecnologie Chimiche, "Giulio Natta" SCITEC-CNR, Via Corti, 12 – 20133 Milano (Italy);

Organic semiconductors absorbing or emitting in the near-infrared (NIR) range of the electromagnetic spectrum have emerged in the last twenty years as a novel class of materials with useful optoelectronic properties. Clearly the most appealing features are the solution processing, low-cost fabrication and the possibility of application on flexible, conformable or even stretchable substrates for organic electronics, such as organic and polymer light emitting diodes (OLED and PLED). NIR OLEDs and PLEDs [1] are particularly interesting for night vision-readable displays which are unreadable to the naked eye but could be read with night-vision goggles, or as light source for sensors that operate with NIR light. Furthermore, the semitransparency of biological tissue between 700 and 1000 nm makes these applications appealing for a broad class of biomedical applications, in particular imaging and sensing. However, obtaining organic materials with emission in pure NIR is still a goal to be pursued and in general complexes based on lanthanides are used which however have the problem of scarce abundance and are non-renewable resources.
4,4-Difluoro-4-borata-3a-azonia-4a-aza-s-indacene dyes, more commonly known as BODIPY dyes, since long time have been recognized for their excellent optical properties such as large absorption coefficients, high fluorescence quantum yields, and remarkable photostability [2,3,4] and are particularly promising as IR-emitting dyes. Replacing the C-8 in meso position in the conventional BODIPY core with an aza-N atom lowers the energy of both absorption and emission transitions and the resultant aza-BODIPY dyes absorb and emit in the spectral window 600-750 nm in solution [4].
Here we present a tetra-thiophene substituted aza-BODIPY as pure IR emitter with photoluminescence emission peaked @ 890 nm when dispersed in polystyrene film and electroluminescence tested in PLED devices peaked @ ~ 900 nm.

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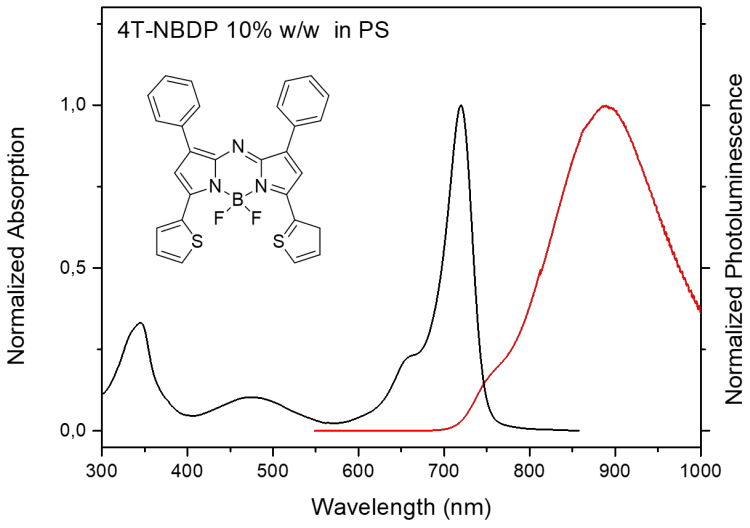

Design and synthesis of macromolecular and nanostructured carbonic anhydrases-based materials

Kristian Vasa,[a] *Viviana De Luca,*[b] *Cristina Salvatici,*[c] *Clemente Capasso,*[b] *Stefano Menichetti,*[a] *Anna Maria Papini,*[d] *Claudiu Supuran,*[e] *Fabrizio Carta,*[e] *Caterina Viglianisi,*[a] *Claudia Bello*[d]

[a] *Department of Chemistry 'Ugo Schiff', University of Florence, Via Della Lastruccia 3-13, 50019, Sesto Fiorentino, Firenze, Italy*
[b] *Istituto di Bioscienze e Biorisorse, CNR, Via Pietro Castellino 111, 80131 Napoli, Italy.*
[c] *Institute of Chemistry of Organometallic Compounds (ICCOM)-Electron Microscopy Centre (Ce.M.E.), National Research Council (CNR), via Madonna del Piano n. 10, 50019 Sesto Fiorentino, Firenze, Italy*
[d] *Interdepartmental Research Unit of Peptide and Protein Chemistry and Biology, Department of Chemistry "Ugo Schiff", University of Florence, Firenze, Italy*
[e] *Università degli Studi di Firenze, NEUROFARBA Dept., Sezione di Scienze Farmaceutiche e Nutraceutiche, Via Ugo Schiff 6, 50019, Sesto Fiorentino (Florence), Italy.*

We report the synthesis of new macromolecular and nanostructured Carbonic Anhydrases (CA)-based functional materials which combine the exceptionally kinetic performances of such enzymes with the feature of mesoporous spherical silica nanoparticles, or polyolefins. The goal of this study is transforming these materials in valid devices for CO_2 capture thus inducing or controlling pH variations. We performed and compared several methods for the encapsulation of bovine b-CA within mesoporous silica nanoparticles generated by controlled biomimetic silica precipitation induced with silaffin peptides (Cys_R5). [1] Furthermore, the b-CA was covalently conjugated to polypropylene-graft-maleic anhydride (PP-*g*-MA) *via* a ball-milling green synthetic procedure effecting chemical reactions by mechanical energy.[2] The enzymatic activity, structural, physical and chemical characteristics of the obtained materials are currently investigated with the purpose to further evolve our findings to diverse CA isoforms.

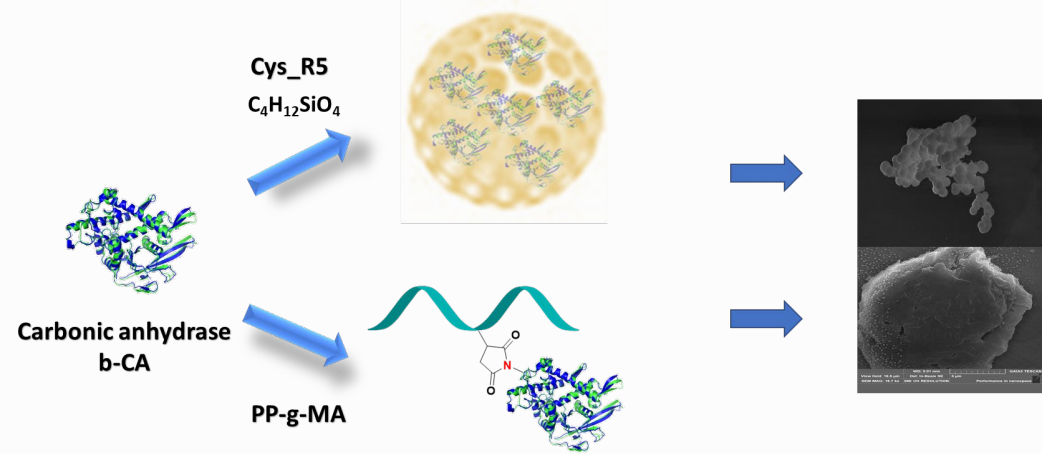

Figure. General representation of Carbonic Anhydrase immobilization

[1] C. Lechner, C. F. W. Becker, *Mar. Drugs.* **2015**, *13,8*, 5297.

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Novel Visible-Light Mediated Protocols for the Synthesis of N-Heterocycles and Site-Selective Functionalizations.

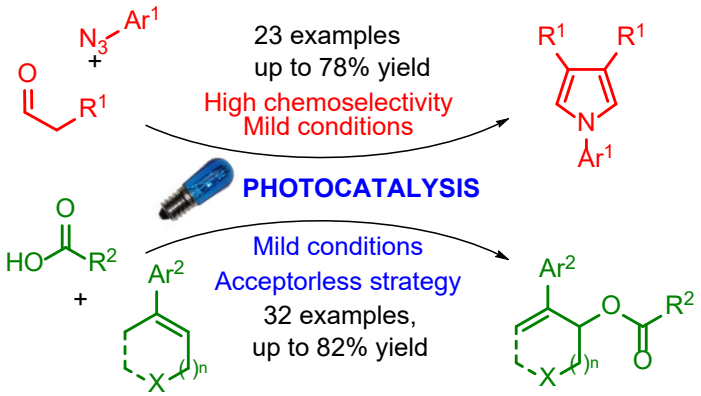
Giulio Bertuzzi, Marco Bandini

[a] *Dipartimento di Chimica "Giacomo Ciamician", Alma Mater Studiorum - Università si Bologna, via Selmi 2, 40126 Bologna, Italy.*

The advent of visible-light photoredox catalysis paved the ways for the generation of high-energy chemical species, such as radicals as well as charged intermediates, under mild reaction conditions.[1] This strategy can be efficiently exploited for synthetically challenging transformations such as site-selective functionalizations and cascade constructions of hetero-aromatic compounds. These transformations are generally carried out in the presence of stoichiometric amount of oxidants or require pre-functionalizations of starting materials. The gain of photocatalysis is to circumvent these issues, by enabling, for example, direct C-H activation of unfunctionalized substrates. Alternatively, by employing tailor-made reactants, oxidative protocols can be carried out in a catalytic oxidant-free fashion.

The synthesis of 1,3,4-trisubstituted pyrroles via visible-light mediated photoredox catalyzed condensation of arylazides and aldehydes under mild conditions is an example of the abovementioned strategies. This protocol avoids stoichiometric oxidants, affording the desired N-heterocycles in good yields. Mechanistic investigations pointed to the realization of α-carbonyl radicals with the concomitant photoinduced reduction of azides.[2]

As far C-H functionalizations are concerned, a visible-light photoredox/[Co(III)] co-catalyzed dehydrogenative functionalization of cyclic and acyclic styryl derivatives with carboxylic acids is presented. The methodology allows a chemo- and regioselective allylic functionalization of unactivated olefins, leading to allylic carboxylates in high yields. Moreover, such process can be implemented in an intramolecular variant for the preparation to intriguing tricyclic lactones.[3]



Scheme 1. New photocatalytic protocols for the synthesis of substituted pyrroles and allyl carboxylates.

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Radical α-Trifluoromethoxylation of Ketones by Means of Organic Photoredox Catalysis

Tommaso Bortolato,[a] Thibaut Duhail,[b] Javier Mateos,[a] Antonio Togni,[c] Emmanuel Magnier,[b] Guillaume Dagousset[b] and Luca Dell'Amico[a]*

[a] NanoMolCat Laboratories, Department of Chemical Sciences, University of Padova, Via Marzolo 1, 35131, Padova (Italy); [b] Université Paris-Saclay, UVSQ, CNRS, UMR 8180, Institut Lavoisier de Versailles, 78035 Versailles Cedex (France); [c]Swiss Federal Institute of Technology, ETH Zurich, Vladimir-Prelog-Weg 2, 8093 Zurich (Switzerland)

The incorporation of fluorine atoms in organic molecules is known to change dramatically their physicochemical properties. Among the emerging perfluorinated groups, the OCF_3 functionality occupies a special place due to its remarkable electronic and steric properties, associated to a good metabolic stability and special conformation.[1] Despite the growing interest in the OCF_3 moiety, synthetic methods able to deliver this functionality are scarce and often require harsh reaction conditions, unstable reagents or high excess of substrate.[2]

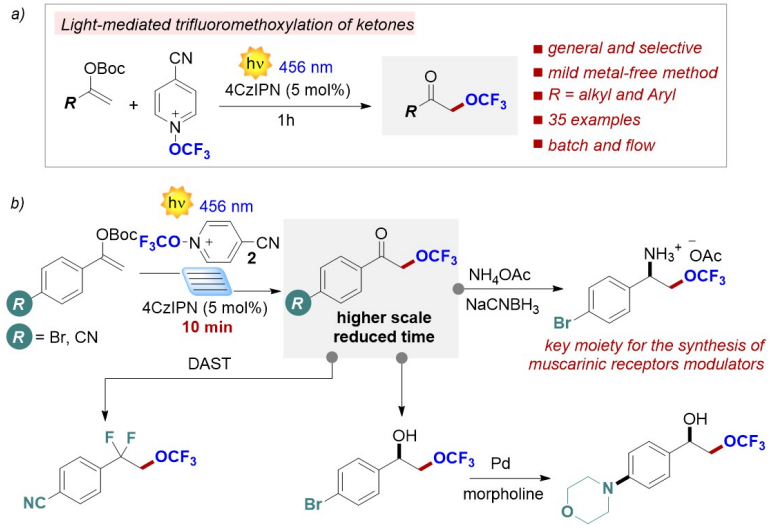

Figure 1 a) The developed light-mediated protocol for the alpa-trifluoromethoxylation of ketones. b) Scale-up of the protocol through continuous flow reactor and subsequent manipulations of the products

We have developed a practical and mild protocol for the trifluoromethoxylation of ketones by means of organic photoredox catalysis (Figure 1a).[3] To the best of our knowledge, our work discloses the first radical-based α-trifluoromethoxylation of enol derivatives, furnishing valuable trifluoromethoxylated ketones. The developed protocol is fully chemoselective, avoiding the competitive installation of the OCF_3 moiety on the aromatic ring.[4] Moreover, scale-up of the reaction with the aid of a continuous flow reactor was possible, delivering a tenfold increase of the reaction scale in reduced reaction time (10 min) with identical yield. To showcase the synthetic utility of the method, post-modifications of the scaled-up products were performed, demonstrating the versatility of the obtained molecules towards the access to biorelevant targets (Figure 1b).

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A ball-milling green synthetic procedure for the preparation of novel macromolecular stabilizers for polyolefinic-based materials

M. Di Maro,[a] *P. Stagnaro,*[b] *S. Losio,*[c] *C. Viglianisi,*[a] *S. Menichetti*[a]

[a]*Department of Chemistry 'U. Schiff', University of Florence, Via Della Lastruccia 3-13, 50019 Sesto Fiorentino, Italy*
[b]*Institute of Chemical Sciences and Technologies (SCITEC) 'Giulio Natta', Italian National Research Council, Via De Marini 6, 16149 Genova, Italy*
[c]*Institute of Chemical Sciences and Technologies (SCITEC) 'Giulio Natta', Italian National Research Council C, Via Alfonso Corti 12, 20133 Milano, Italy*

Polyolefins are widely used as packaging materials for different types of commodities in particular as *Food Contact Materials* **[1]**. Although they are relatively inert, polyolefins can undergo degradation processes caused by the presence of atmospheric oxygen and promoted by sunlight through an auto-oxidative free radical chain reaction. For this reason, various stabilizer additives, such as antioxidants or UV absorbers, are added to extend the shelf life of the material by preventing the auto-oxidation. Commonly used stabilizer additives are hindered phenols (like BHT or BHA) and hindered amine light stabilizers (HALS), able to quench the peroxyl radicals and the other related species formed during auto-oxidation. These stabilizers are, typically, low molecular weight polar compounds, showing a low miscibility in the apolar polyolefinic matrix. This promotes the physical loss of additives in the external environment, by volatilization, migration or extraction, and, in the case of *food contact material*, causes a food contamination and a potential health risk for the final consumer **[1]**. To overcome these drawbacks, in recent years we proposed different families of novel polymeric additives obtained using ethylene- and propylene-based copolymers containing tuned amounts of suitable olefinic comonomers bearing a stabilizing functionality. The macromolecular nature of such additives and the covalently linked stabilizing moieties to the polymer backbone, while guarantee a very good protection to auto-oxidation, certify an intrinsically non-releasing character, with clear advantages for packaging of foodstuff and pharmaceuticals. **[2]** In this communication, we describe the preparation of a new family of macromolecular additives, based on the grafting of maleinized polypropylene with BHT and HALS derivatives (Figure 1). The role of the polymer portion of the additives is to improve the compatibility and, likewise, the miscibility of the additives in the polymer matrix. The grafting process has been conducted in a micro ball-mill apparatus, exploiting the advantages of mechanochemistry. **[3]** Applications and scope of this innovative procedure for grafted polymers functionalization will be presented and discussed.

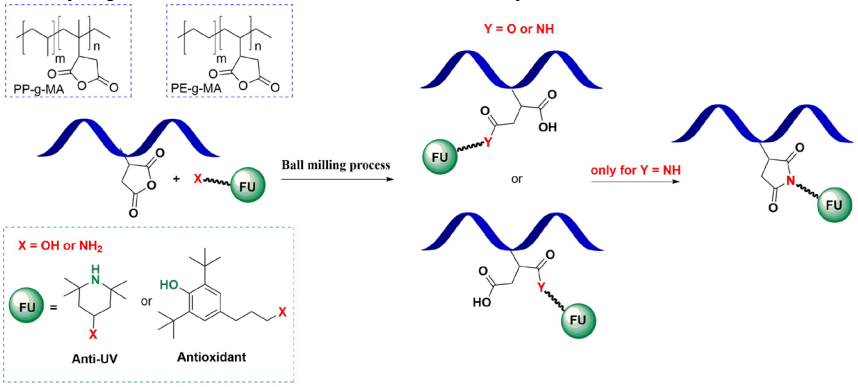

Figure 1: Scheme of the strategic approach adopted for this work.

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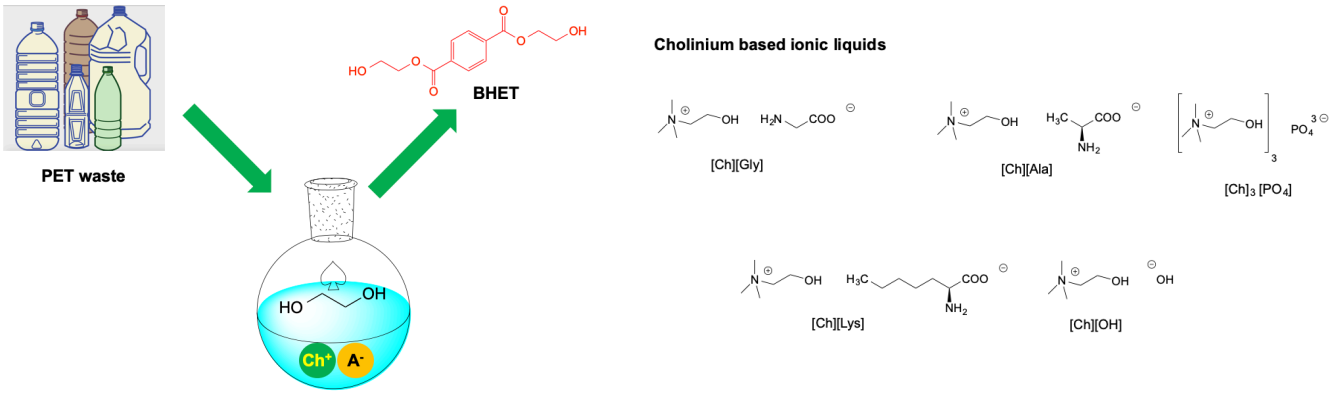
Cholinium-based ionic liquids as catalysts for the glycolysis of post-consumer PET waste

Salvatore Marullo, Carla Rizzo, Floriana Billeci, Francesca D'Anna

Dipartimento STEBICEF-sezione di Chimica, Università degli Studi di Palermo

The widespread use of plastic polymers is one of the hallmarks of the technological advancement of modern society. Due to their lightness, inertness, versatility and resistance, plastic is practically ubiquitous in every human endeavor. Unfortunately, the same properties that make these materials so successful are at the root, together with poor disposal management and slow recycling rate, of the pressing issue of plastic pollution. In this context, one polyester polymer that fits this description is polyethylene terephthalate (PET). One of the possible routes to recycle PET waste, is its depolymerization in the presence of ethylene glycol, or glycolysis, to obtain the monomer bis-(2-hydroxyethyl) terephthalate (BHET). This latter can then be polymerized back to PET or unsaturated polyester resins.[1]
Since sustainability must involve also the process used for the chemical recycling of PET, we investigated the glycolysis of different PET sources, promoted by ionic liquids composed by low- or non-toxic ions such as cholinium cations and anions comprising also amino acid-based ones.



We first searched for the optimal reaction conditions, with pristine PET pellets as substrate, finding that [Ch][gly] was the most active catalyst, affording good yields in BHET at the relatively low temperature of 150 °C.
Subsequently, we applied this protocol to different sources of PET deriving from post-consumer waste, including drinking bottles, clear or opaque, and food packages. The results obtained evidenced good yields in BHET even if in some cases an effect of the presence of additives in the starting material was observed.

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Treatment of biomass food waste by exploiting Natural Deep Eutectic Solvents and bio based-Ionic Liquids

Angelica Mero[a], Josè Gonzalez Rivera[a], Elena Husanu[a], Marinella De Leo[a], Andrea Mezzetta[a], Felicia D'Andrea[a], Christian Silvio Pomelli[a], Alessandra Braca[a], Lorenzo Guazzelli[a]

[a] *Università di Pisa, Dipartimento di Farmacia, via Bonanno Pisano 6, 56126 Pisa, Italy*

The agri-food sector annually generates huge amount of waste and by-products, whose disposal provokes serious environmental and economic issues. In this scenario, alongside with the transition towards sustainability, the full exploitation of biomass food waste and its recycle into a new chain of value *via* the development of sustainable and green process in terms of a circular economy, are of primary importance[1],[2]. In this study, natural deep eutectic solvents (NADESs) and bio based-ionic liquids (bio-ILs), as alternative to the classical volatile and toxic organic solvents have been synthesized and successfully employed for the valorization of different biomass food waste (i.e. chestnut shell, cherry pomaces and apple fibers waste). More in details, choline chloride, betaine or proline-based DESs with various classes of hydrogen bond donors have been investigated for the extraction of polyphenolic compounds, high added value compounds characterized by antioxidant, anti-carcinogenic, anti-inflammatory and anti-bacterial activity. The composition of extracts was ascertained by high performance liquid chromatography analyses (HPLC) and the polyphenols content was assessed by colorimetric assays. Then, cholinium based-ionic liquids with different aminoacidic anion have been successfully employed for the treatment of the lignocellulosic wastes. Cellulose enriched material (CRM) and lignin enriched material (LRM) were obtained, and the nature of the extracted fractions was confirmed by infrared spectroscopy (FTIR) and thermogravimetric analysis (TGA). Also, the recovery of the NADES and the bio-ILs have also been proven, which make the whole process viable and amenable for large-scale applications.

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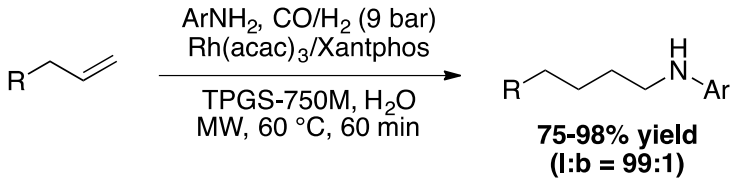
Hydroaminomethylation of terminal alkenes in water: microwave and micellar catalysis roles

Elisabetta Monciatti, Francesca Migliorini, Elena Petricci

Dipartimento di Biotecnologie, Chimica e Farmacia, Università degli studi di Siena, Via Aldo Moro, 53100 Siena, Italy

Hydroaminomethylation is a one pot tandem process representing an elegant, atom economic, and environmentally benign approach to the synthesis of amines [1]. During the years, we demonstrated that hydroformylation, hydroaminomethylation, and other similar tandem transformations can take advantages from microwave irradiation, that consents to work in milder reaction conditions [2-4]. We recently reported the possibility to improve the sustainability of hydroformylation reaction by coupling micellar and microwave catalysis [5]. Here are reported our last findings in the application of micellar catalysis on the microwave assisted hydroaminomethylation of terminal alkenes.



This sustainable process allows to obtain the linear aniline derivatives as the major regioisomers in good yields, in mild reaction conditions in term of temperature (60 °C), syngas pressure (9 bar), and time (60 min), using commercially available surfactant, catalyst, and ligand.

The protocol is of general applicability to different alkenes and anilines and the catalyst/ligand system can be recycled at least 5 times without impacting in both regioselectivity and yields.

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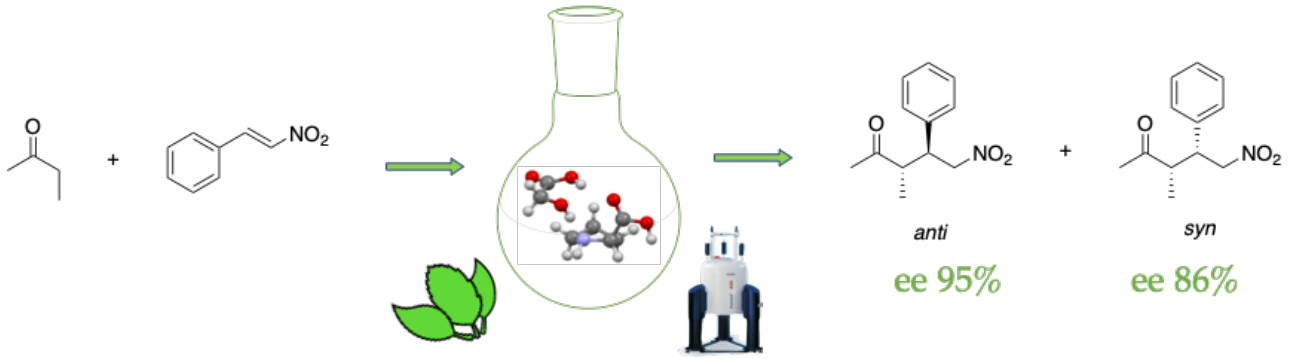
Organocatalytic activity of chiral L-Proline-based Deep Eutectic Solvents

Matteo Tiecco[a], Diego A. Alonso[b], Gianluca Ciancaleoni[c], Sarah-Jane Burlingham[b], Gabriela Guillena[b], Diego J. Ramón[b], Raimondo Germani[a].

[a]Department of Chemistry, Biology and Biotechnology, Università degli Studi di Perugia, via Elce di Sotto 8, 06124 Perugia, Italy; [b]Department of Organic Chemistry, Institute of Organic Synthesis (ISO), University of Alicante, P.O.Box 99, 03080 Alicante, Spain; [c]Department of Chemistry and Industrial Chemistry, University of Pisa, via Giuseppe Moruzzi 13, 56124 Pisa, Italy.

The impact on the environment of polluting and volatile organic solvents represents nowadays a severe matter to be faced in order to reduce the incidence on the environment of chemical applications. Deep Eutectic Solvents (DESs) represent a step ahead in this field thanks to their green properties[1]. These novel liquids are formed by weak interactions between two species and they are not toxic, biocompatible, they can be easily recycled, they have low or absent vapor pressure, they are biodegradable, they are realized without the use of any solvent with a 100% yield. Over these green properties, DESs can have a catalytic role because the properties of these liquids are derived from the properties of the molecules forming them; therefore, their characteristics are truly tunable because of the very large number of molecules available to form a DESs[2].
Following our recent results on the realization and on the use of chiral DESs in asymmetric transformations[3-5], in this presentation the results of the use of L-Proline-based Chiral Deep Eutectic Solvents (CDESs) in a probe asymmetric Michael addition will be shown. In this reaction the L-Proline acts as solvent component as well as chiral organocatalyst. Because of the complexity of the features of these innovative solvents, the results were analyzed with a structural approach with NMR measures taking in account the availability of the L-Proline, considering the strength of the association of it with the counterpart of the liquids. DFT studies were also performed and the geometry and energy of the adducts were determined and a qualitative rationale to the reaction stereoisomers distribution was given.



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Catalytic biomass valorization towards hydrogen transfer reactions using formic acid and derivates as safe H-source

Federica Valentini,[a] Benedetta Di Erasmo,[a] Maurizio Taddei,[b] Luigi Vaccaro[a]

[a] *Laboratory of Green S.O.C., Dipartimento di Chimica, Biologia e Biotecnologie, Università degli Studi di Perugia, Via Elce di Sotto 8, 06123-Perugia, Italy*
[b]*Dipartimento di Biotecnologie, Chimica e Farmacia, Università degli Studi di Siena Via A. Moro 2, 53100, Siena, Italy*

One of the most urgent challenge of the modern chemistry is the abatement of environmental impact associated to the chemical production. In this context the replacement of petrol-based chemicals and fuels with lignocellulosic biomass, a carbon-neutral renewable feedstock, is of great importance.
The majority of biomass manipulation processes consists in hydrogenation reactions allowing a wide range of value-added products, including biofuels and biofuels additives.[1] For this reason, the development of reductive chemical protocols avoiding the direct usage of molecular hydrogen, which may pose safety concerns and high costs, is essential, in view of their implementation on an industrial scale.
Among the alternative liquid organic hydrogen carriers (LOHCs), formic acid can be derived from plant biomass processing being a viable reversible and renewable hydrogen-source. Since the decomposition of formic acid can undergo towards two distinct processes (dehydrogenation and dehydration), several efforts have been dedicated to the development of efficient catalytic systems for the selective dehydrogenation of formic acid.
Our attention is dedicated to the upgrading of lignin-derived phenolic compounds.[2] Phenols are among the most naturally prevalent structural units on the planet, generally present in their polymeric form in lignin.[3] Among the hydrogen-dependent processes for phenols valorization, selective hydrogenation and the subsequent transformations affords in useful commodity chemicals such as cyclohexanone, key-intermediate in nylon 6 and nylon 66 synthesis, and aromatic or aliphatic amines. In this context our efforts are voted to the design and synthesis of novel, efficient catalytic systems able to catalyze hydrogen-transfer processes for phenolic biomass upgrading using formic acid or formate salts as safe H-source (figure 1).

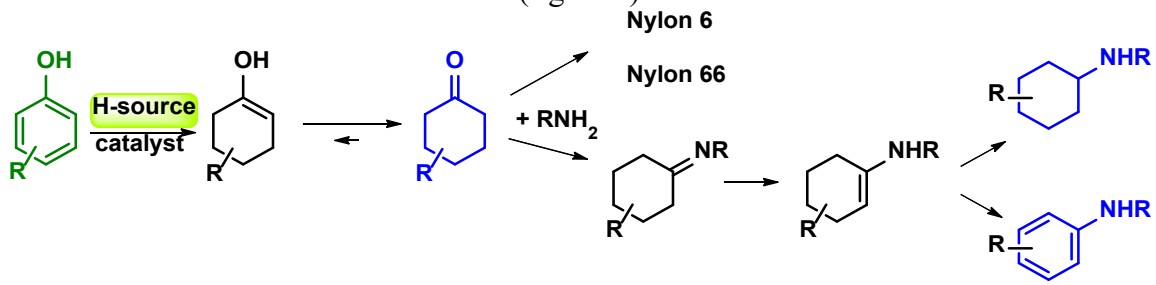

Figure 1. Catalytic conversion of lignin-derived phenolic compounds to value-added products.

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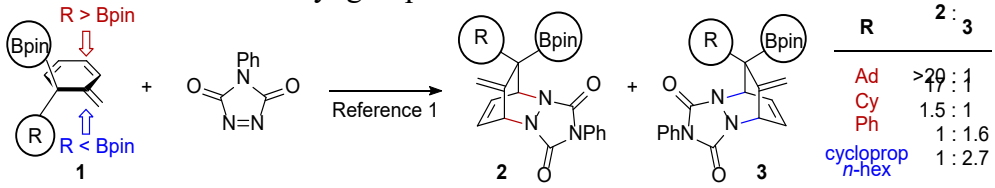
How Big is the Pinacol Boronic Ester as a Substituent?

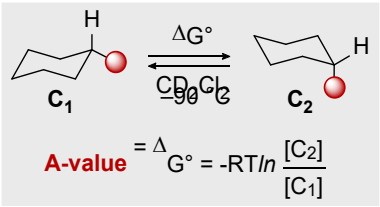
V. Fasano,[a] A. McFord,[a] C. P. Butts,[a] B. S. L. Collins, [a] N. Fey,[a] R. W. Alder, [a] V. K. Aggarwal[a]

[a]*University of Bristol, Cantock's Close, Bristol, BS8 1TS, UK*

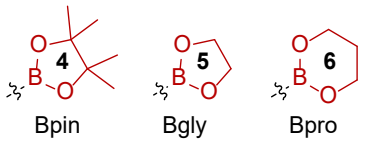
The synthetically versatile pinacol boronic ester group (Bpin) is generally thought of as a bulky moiety because of the two adjacent quaternary sp^3-hydrized carbon atoms in its diol backbone. However, recent diastereoselective reactions have cast doubt on this perception, placing Bpin's size somewhere between a 1° and 2° alkyl group.[1]



In this study[2] we have reported a detailed experimental and computational analysis of Bpin and structurally related boronic esters which allows determination of three different steric parameters for the Bpin group: the A-value,[3] ligand cone angle,[4] and percent buried volume.[5]

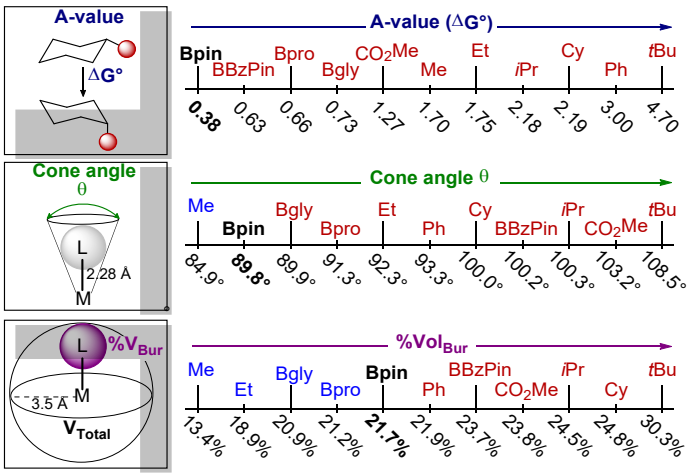


	[C1] : [C2] Observed	A-value (kcal/mol)
4	74 : 26	0.38
5	88 : 12	0.73
6	86 : 14	0.66



A-value measurements were performed recording $^{13}C\{^1H\}$ NMR spectra of CD_2Cl_2 solutions of cyclohexyl boronic esters at –90 °C. For cyclohexyl Bpin **4**, two species were identified in a 74:26 ratio (A-value of 0.38 kcal/mol). Similarly small A-values were also observed for other related boronic esters. These A-values were significantly smaller than that reported for a methyl group (1.70) or a hydroxy group (0.87), thus placing Bpin among the smallest reported A-values. However, while A-value does capture the comparatively small size of the Bpin group, it fails to fully account for the stereochemical influence of the group on the Diels-Alder reaction.[1] To better picture the size of the Bpin group, other steric descriptors were thus calculated: ligand cone angle[4] and percent buried volume.[5]

The calculated ligand cone angles were similarly small as they are also primarily determined by the planar O–B–O motif, whereas percent buried volume provided the best correlation between steric size and diastereoselectivity in a Diels–Alder reaction. In conclusion, all three parameters suggest that the Bpin moiety is remarkably small, with the planarity of the oxygen-boron-oxygen motif playing an important role in minimising steric interactions.



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From carbonyls to chiral alcohols via asymmetric biocatalysis: exploiting the substrate promiscuity of hydroxysteroid dehydrogenases (HSDHs)

S. Bertuletti,[a,b] E. Miraglia,[a,b] E. E. Ferrandi,[a] I. Bassanini,[a] D. Monti,[a] S. Riva[a]

[a] *SCITEC-CNR (Istituto di Scienze e Tecnologie Chimiche "Giulio Natta"), Via M. Bianco 9, Milan, Italy*
[b] *University of Milan, Via Mangiagalli 25, Milan, Italy*

Bacterial hydroxysteroid dehydrogenases (HSDHs) are NAD(P)H-dependent enzymes that belong to the superfamily of short-chain dehydrogenases/reductases (SDRs). These enzymes catalyze the reversible and regioselective oxidoreduction of the hydroxyl/oxo moieties of steroidal compounds recognizing the different positions of the steroidal skeleton (e.g., at C-3, C-7, and C-12). Additionally, HSDHs usually display high stereoselectivity, discriminating the hydroxyl group above the plane of the steroid molecule (β configuration) from the one below (α configuration).[1] These features make these enzymes attractive for industrial applications.
Although HSDHs have been thoroughly investigated in the last years, little is currently reported on their substrate promiscuity, i.e. the biotransformation of alcohols or ketones that differ from their natural steroidal substrates.[2]

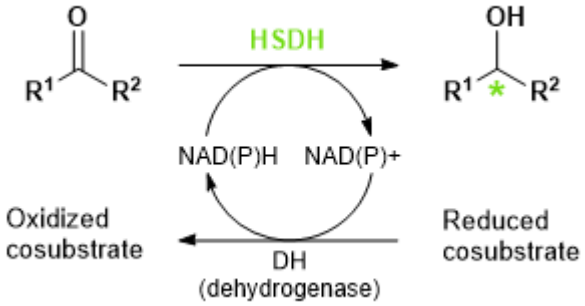

Figure 1. stereoselective reduction of ketonic moieties catalyzed by HSDHs.

To fill this gap, a library of thirteen 7α-, 7β-, or 12α-HSDHs (either already described or recently identified from metagenomic collections) was tested for the stereoselective reduction of a panel of carbonyl substrates. The screened compounds are of pharmaceutical relevance and they include α-ketoesters, α-diketones, and selected ketones that partially resemble the structural features of steroids (e.g., bicyclic ketones).[3,4]
Nearly all of the tested HSDHs showed excellent activity and stereoselectivity towards these compounds, as it has been recently partially reported by us.[3,4]

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Catalyst- and substrate- dependent chemodivergent reactivity of stabilised sulfur ylides with salicylaldehydes

G. D. Bisag,[a] S. Ruggieri,[b] M. Fochi ,[a] L. Bernardi[a]

[a] Department of Industrial Chemistry "Toso Montanari" Alma Mater Studiorum – University of Bologna. Viale del Risorgimento 4, 40136 Bologna, Italy; [b] Department of Biotechnology – University of Verona. Strada Le Grazie 15, 37134, Verona, Italy.

Sulfur ylides are formal internal salts characterised by a carbanion flanked by a positively charged sulfur atom. These ylides are able to react via typical (2 + 1) pathways (Corey-Chaykovsky epoxidation and related reactions) or can display less conventional reactivity such as insertion reactions[1] into X-H, C-H, C-X and X-Y bonds, generally characteristic of the arguably problematic diazo compounds.

This communication presents a tandem chemodivergent cyclization reaction between sulfoxonium ylides and salicylaldehydes. The literature reports the reaction of unstabilized sulfoxonium ylide with these aldehydes, giving benzofurans as products.[2] In our case,[3] reacting stabilized sulfoxonium ylides with salicylaldehydes, two different compounds are obtained, 2*H*-cromene and dihydrobenzofuran scaffolds, depending on the substituents around the aromatic ring and the presence of the catalyst (Figure 1). In particular, using electron poor salicylaldehydes, in the absence of catalyst, three different dihydrobenzofuran derivatives were achieved in excellent yields, while, using electron neutral or electron rich salicylaldehydes in the presence of 5 mol% of diphenyl phosphate, 16 examples of differently substituted 2*H*-cromenes were obtained in good yields. Mechanistic insight and comparison with the reactivity of sulfonium ylides are also given.

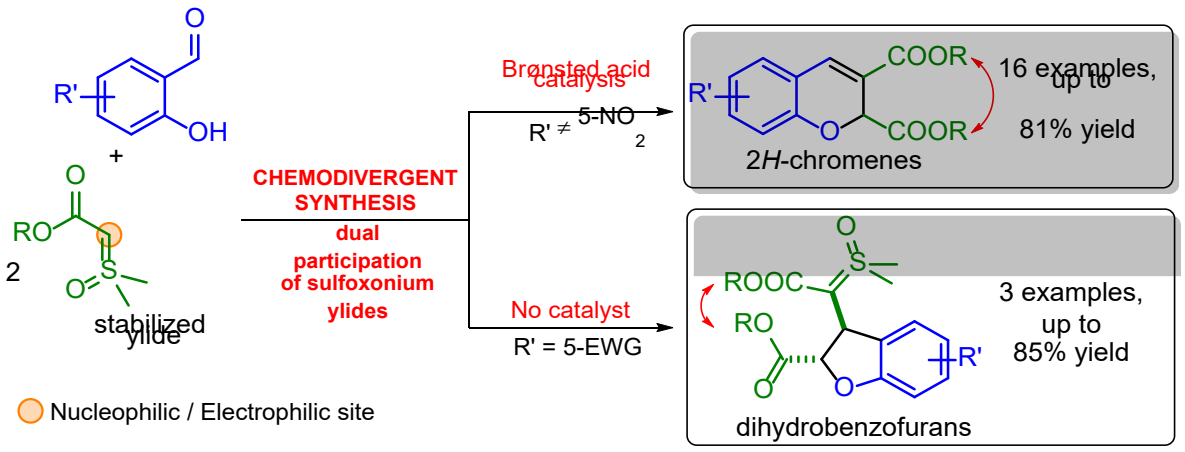

Figure 1. *Tandem chemodivergent cyclization between sulfoxonium ylides and salicylaldehydes.*

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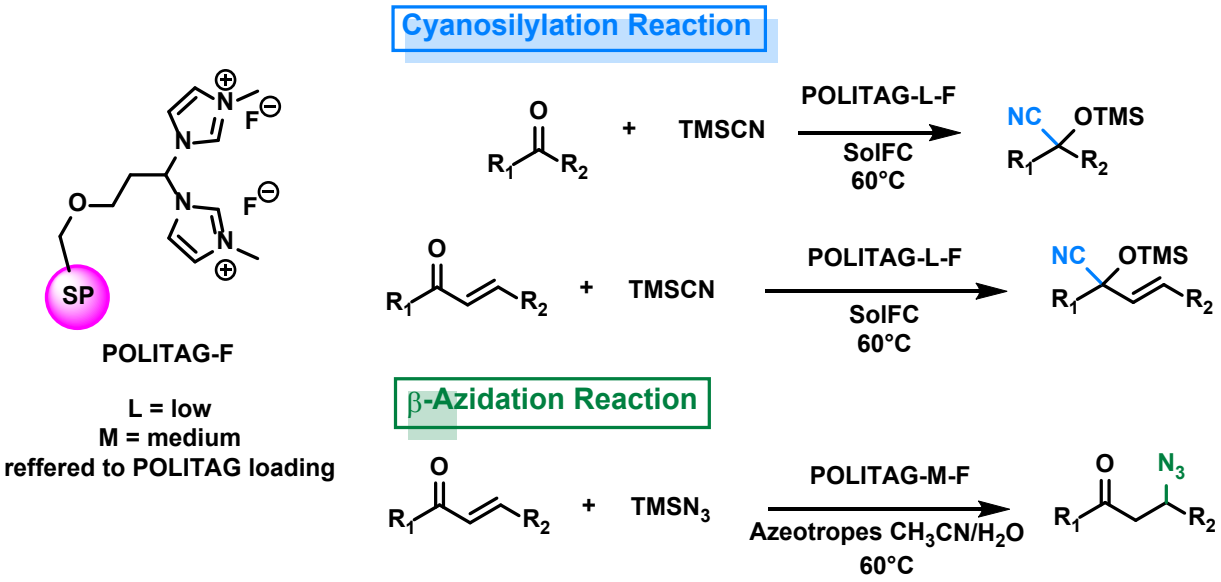
Imidazolium based heterogenous catalyst for the synthesis of cyanohydrintrimethylsylil ether and β-azido ketones

Giulia Brufani[a], Federica Valentini[a], Francesco Ferlin[b], Daniela Lanari[b], Luigi Vaccaro[a]

[a]Laboratory of Green Synthetic Organic Chemistry (Green S.O.C), Department of Chemistry, Biology and Biotechnologies, University of Study of Perugia, via Elce di Sotto 8, 06123-Perugia, Italy; [b]Department of Pharmaceutical Science, University of Study of Perugia, 06123-Perugia, Italy.

In the field of organocatalysis, imidazolium salts play a crucial role exploiting the synergistic effect in the reaction mechanism of the cationic moieties and the carefully chosen counterions.[1] However, to avoid the principal drawbacks of imidazolium salt, it is of great interest their immobilization into a solid support, favoring the recycle and limiting the needed amount.[2] Herein we report a novel class of heterogeneous fluoride-based organocatalytic system named **POLITAG-F** (POLymeric Ionic-TAG), that features a bis-imidazolium ionic-tag moiety, with fluoride as counterion. The catalyst is covalently anchored into a tailor-made polystyrene-based gel-type resin cross-linked with SPACeR.[3] **POLITAG-F** was efficiently applied in two different synthetic protocols for the synthesis of cyanohydrintrimethylsilyl ether[4] and β-azido carbonyl compounds in a waste minimized protocols under batch and continuous flow condition.



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Highly Efficient Microwave-assisted synthetic protocols under Pd based β-cyclodextrin heterogeneous catalyst

Emanuela Calcio Gaudino,[1] Silvia Tabasso,[2] Maela Manzoli,[1] Giancarlo Cravotto[1]

[1]Dipartimento di Scienza e Tecnologia del Farmaco, University of Turin, Via P. Giuria 9, 10125 Turin (Italy). [2]Dipartimento di Chimica, University of Turin, Via P. Giuria 7, 10125 Turin, (Italy).

With the growing concerns of environmental pollution and the depletion of natural resources, synthetic organic chemists are facing the challenge of designing "greener" methodologies. Effective heating is one of the key means with which to access desired chemical reactivity while ensuring suitable energy consumption. In this context, microwave (MW) dielectric heating is still today one of the most powerful tools for promoting synthetic transformations [1]. A broad array of new heterogeneous catalytic applications has been reported since Varma first introduced solid catalysts to MW-assisted organic synthesis (MAOS) [2]. In addition to their recyclability, there are several other advantages to using solid catalysts in MAOS: heterogeneous catalysts are generally excellent MW absorbers, meaning that they provide a cooperative effect in MW-assisted reactions as the catalytic material is also the source of rapid internal heating [3]. The role of cyclodextrins (CDs) in catalytic systems is manifold in organometallic reactions and the use of *ad hoc* tailored mono (or even multi-metallic b-CD-cross linked catalysts could strongly promote several sustainable synthetic protocols under MW dielectric heating. In this context, we recently described the synthesis and application of a series of recyclable palladium based β-CD catalysts (Pd/CβCAT) well suited for MW-assisted reactions. [4-5]. Due to the growing interest on more sustainable synthetic approach, we report herein a MW-assisted green protocol for the C-H direct arylation of thiophenes with substituted aryl halides. Our synthetic approach includes the use of alternative green solvents combined with the use of Pd/CβCAT. This sustainable protocol carried out in γ-valerolactone (GVL) is catalyzed by Pd nanoparticles embedded in cross-linked β-CD. In view of the excellent results achieved with activated substrates, the one-pot synthesis of a 4(3H)-quinazolinone derivative has been accomplished [6]. A pressure-resistant MW reactor, equipped with multiple gas inlets, was used for sequential (i) C-H arylation, (ii) reduction and (iii) carbonylation in the presence of the same catalyst, but under different gas atmospheres. The robust heterogeneous Pd catalyst showed limited metal leaching in GVL, making this an efficient MW-assisted process with high atom economy. The synthetic procedure can easily be scaled up to gram scale and carried out in flow mode using a modern MW flow reactor that enables heterogeneous catalysis under gas pressure, thus paving the way for safer, energy saving and more environmentally benign synthetic protocols.

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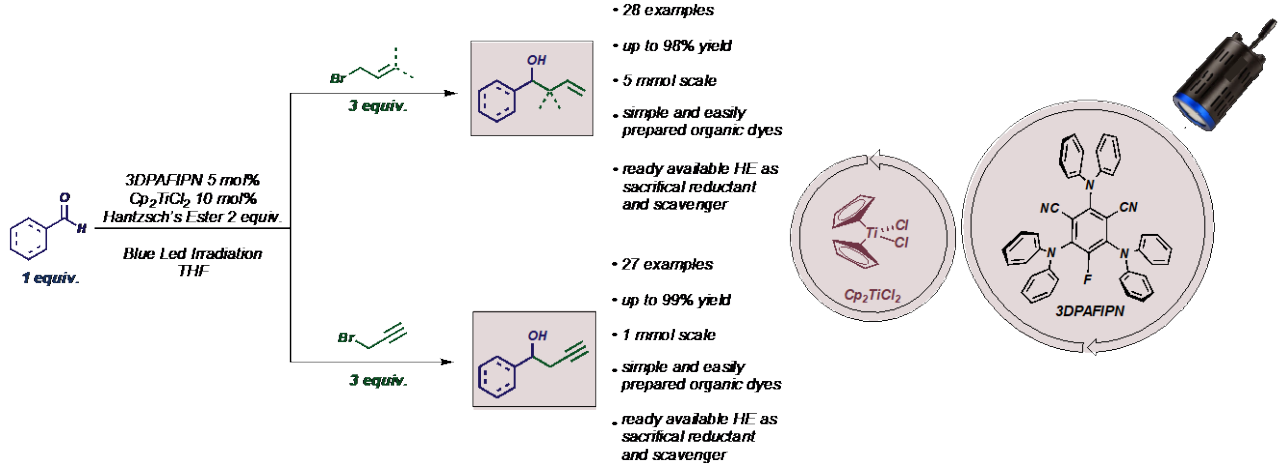
Photoredox allylation and propargylation of aldehydes catalytic in titanium

F. Calogero,[a] A. Gualandi,[a] S. Potenti[a] A. Fermi,[a] G. Bergamini,[a] P. G. Cozzi[a]

[a] *Alma Mater Studiorum, Università di Bologna, Dipartimento "G. Ciamician", 40126 Bologna, Italy.*

Functionalization of carbonyls under Barbier conditions, giving access to transient organometallic reactive nucleophilic species, is a key strategy for the preparation of functionalized building blocks in the total synthesis of natural products.[1] In the last decade, photoredox catalysis have reached an extraordinary level of advancement, introducing new and exciting methodologies in organic chemistry.[2] Now, dual metallaphotoredox catalysis, that is the combination of metal promoted processes with photoredox cycles, is in continuous development.[3]



In this context, two practical and straightforward radical-polar crossover photoredox functionalization of aldehydes mediated by titanocene complexes, giving access to a wide range of homoallylic and homopropargylic alcohols in good to excellent yields will be discussed. The two presented methodologies require the utilization of 1,3-dicyano-5-fluoro-2,4,6-tris(diphenylamino)-benzene (3DPAFIPN) as the photocatalyst, in the presence of the readily available Hantzsch's ester as sacrificial reductant and scavenger for the titanium complex.[4]

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Al(III) Porphyrin–Imidazolium Salt Copolymer onto Carbon Nanotubes as Catalyst for the Synthesis of Cyclic Carbonates

Vincenzo Campisciano,[a] Andrea Santiago-Portillo,[b] Nicolò Saladino,[a] Luca Fusaro,[b] Carmela Aprile,[b] Michelangelo Gruttadauria,[a] Francesco Giacalone[a]

[a] Department of Biological, Chemical and Pharmaceutical Sciences and Technologies University of Palermo Viale delle Scienze, Ed. 17 90128 Palermo (Italy); [b] Laboratory of Applied Materials Chemistry (CMA) University of Namur 61 rue de Bruxelles, Namur 5000 (Belgium)

The drastic climate changes we are witnessing nowadays have led to an increased awareness about the need to reduce the carbon dioxide emissions. However, despite the well-known problems related to the high concentration of CO_2 in the atmosphere, carbon dioxide constitutes also a low-priced, abundant, and sustainable C1 resource for the chemical industry.[1] It is therefore not surprising that CO_2 transformation into valuable products represents a topic of current interest both from the environmental and industrial viewpoint. Among the wide range of CO_2-derived high-value added chemicals, cyclic carbonates, obtained by means of the cycloaddition of carbon dioxide with epoxides, have aroused great research interest since they find numerous applications as chemical intermediates, polar aprotic solvents, or battery electrolytes.[2] In this context, heterogeneous metal-based catalysts represent a class of materials extensively exploited in the chemical transformation of CO_2 into cyclic carbonates. However, most of the metal-based catalytic systems require the presence of additional external nucleophilic co-catalytic species, which sometimes are used in large excess with respect to the metal center.[3] The preparation of a heterogeneous bi-functional catalyst containing both the metal center and the nucleophilic species represents the obvious solution to avoid the presence of external co-catalytic components. Therefore, we have designed and prepared a highly efficient and bifunctional heterogeneous catalyst for CO_2 fixation into epoxides based on multi-walled carbon nanotubes (MWCNTs) covered by a porous copolymeric network formed by a tetrastyrylporphyrin aluminum chloride (TSP-AlCl) monomer and a bis-vinylimidazolium (bis-imi) salt bearing bromide anion as counter ion (**Figure 1**). In such a way, a fixed local concentration of active sites corresponding to an Al/Br^- ratio of 1/8 and a fine control onto their relative position to maximize cooperation between the electrophilic and nucleophilic sites has been reached. The prepared MWCNT-TSP-AlCl-imi material has been fully characterized and revealed to be an active catalyst for the synthesis of cyclic carbonates starting from CO_2 and epoxides, even when challenging substrates have been used, showing no loss of catalytic activity during the recycling.

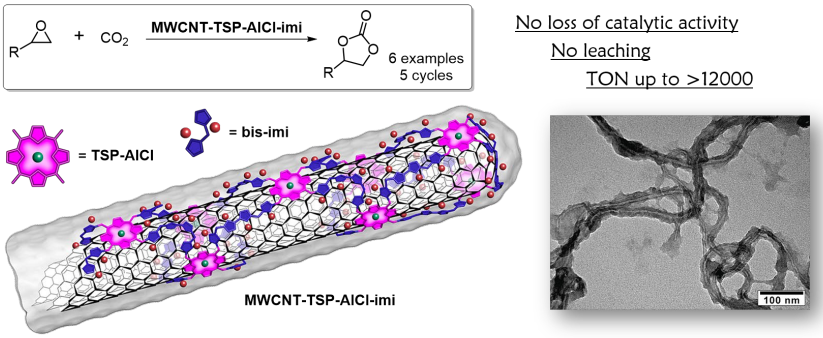

Figure 1. MWCNT-TSP-AlCl-imi catalyst used for the synthesis of cyclic carbonates.

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Copper-Catalyzed/Hypervalent Iodine(III)-Mediated Dimerization/Cyclization of 2-Benzylamino-phenols: Synthesis of Fluorescent Oxazolo-phenoxazines

Francesca Foschi, Marta Papis

Dipartimento di Scienza e Alta Tecnologia, Università degli Studi dell'Insubria, Via Valleggio 9, 22100, Como, Italy;

One-pot strategy for preparation of heterocycles is a topic of considerable interest in the organic field because allows sustainable construction of high functionalized molecules which find application in many different areas. Furthermore, transition metal-catalyzed C-H functionalization processes under oxidative conditions have had a notable development due to the possibility to use non-activated compounds as substrates.[1] In this field, copper-catalyzed reactions have been proved to be a valuable alternative to palladium-catalyzed reactions.[2,3]

In this communication we report an oxidative/copper catalyzed procedure for direct coupling of 2-benzylamino-phenols **1** to oxazolo[4,5-*b*]phenoxazines **2**. The conversion of substrates into tetracylic products involves only C-H functionalization steps with formation of two C-O and one C-N bonds. A catalytic amount of CuCl combined with a stoichiometric hypervalent iodine source allowed a regioselective access to the tetracyclic products **2** through the formation of the phenoxazine structure **II**, which is a precursor of the oxazole ring having in turn a benzylamino-phenol portion. This protocol is general and could be extended to the dimerization/cyclization of *N-N'*-dibenzyl-1,2-benzendiamines and 2-benzylamino-thiophenols.

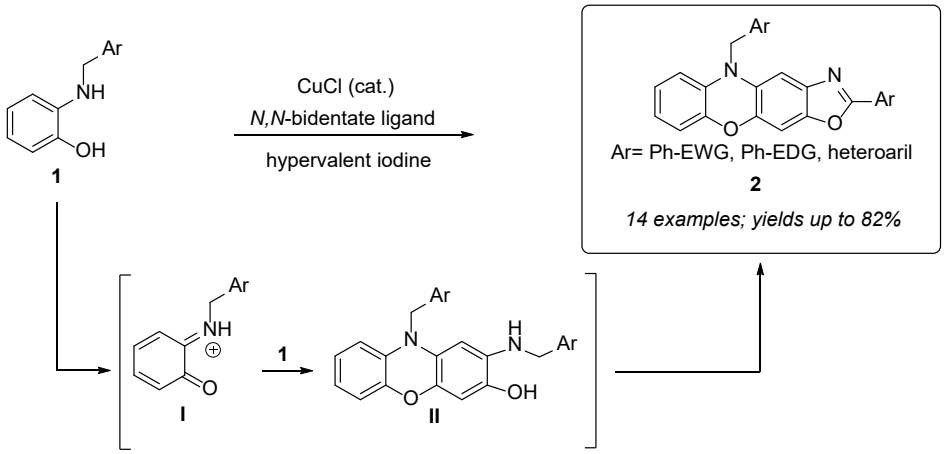

Figure 1. Dimerization/cyclization reaction of 2-benzylamino-phenols

In agreement with the light emitting properties of phenoxazine analogous, the obtained 5*H*-oxazolo[4,5-*b*]phenoxazines **2** showed fluorescent skills.

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Dual Conjugates Targeting $\alpha_v\beta_3/\alpha_v\beta_6$ Integrins and Tyrosine Kinase Receptors as antifibrotic agents

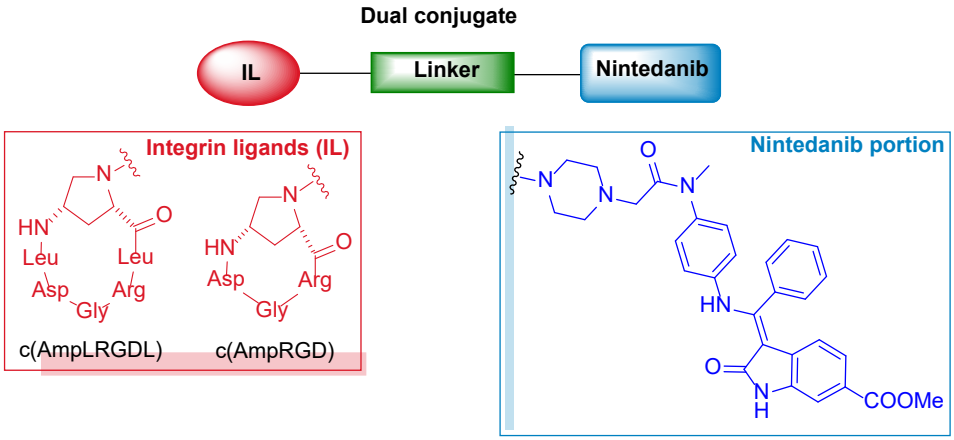
Kelly Bugatti[a], Elena Andreucci[b], Lucia Battistini[a], Silvia Peppicelli[b], Jessica Ruzzolini[b], Franca Zanardi[a], Francesca Bianchini[b], Andrea Sartori[a]

[a] Dipartimento di Scienze degli Alimenti e del Farmaco, Università di Parma, P.co Area delle Scienze 27A, 43124 Parma, Italy; [b] Dipartimento di Scienze Biomediche Sperimentali e Cliniche "Mario Serio", Università di Firenze, V.le Morgagni 50, 50134, Florence, Italy

Fibrosis is defined as excessive deposition of collagen and other ECM components in a tissue. This pathologic process can affect several organs and it is the cause of diverse chronic diseases such as, for example, liver cirrhosis, and idiopathic pulmonary fibrosis (IPF). The major pro-fibrotic mediator is transforming growth factor β (TGF-β), which is released by macrophages and stimulates the migration and proliferation of fibroblasts and myofibroblasts and the deposition of collagen and other extracellular matrix proteins.

The α_v-integrins, in particular $\alpha_v\beta_6$, are major activators of TGFβ [1], which is always expressed in a latent form. For this reason, $\alpha_v\beta_6$- and/or $\alpha_v\beta_3$-antagonists could be of interest in fibrosis disease treatment. Moreover, other cytokines stimulate the uncontrolled proliferation of fibroblasts. In fact, one of the two drugs approved for the treatment of IPF is nintedanib, a tyrosine kinase inhibitor able to block the signaling of several Growth Factors Receptors (GFRs). [2]

Six different covalent conjugates were synthesized as potential antifibrotic agents. These conjugates are constituted by an analogue of the kinase inhibitor nintedanib, which is linked to an RGD-based cyclopeptidomimetic [3] as the targeting unit by means of a robust linker moiety. The panel of these conjugates was realized by conjugating the nintedanib unit either to c(AmpRGD) cyclopeptide targeting $\alpha_v\beta_3$ or to c(AmpLRGDL) cyclopeptide targeting $\alpha_v\beta_6$, varying the linker, which was selected among three different structures differing in length, polarity and valency. Preliminary results on their antagonistic effect on the activation of L929 fibroblast cells will be reported.



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Synthesis and biological profile of novel three-arms star-shaped PLA-PEG amphiphilic copolymers

Serena Maria Torcasio,[a,b] Monica Montesi,[c] Silvia Panseri,[c] Arianna Rossi, [c] Giada Bassi,[c] Antonino Mazzaglia,[d] Anna Piperno,[b] Olivier Coulembier,[a] and Angela Scala[b]

[a] Center of Innovation and Research in Materials and Polymers (CIRMAP), Laboratory of Polymeric and Composite Materials, University of Mons, Place du Parc 23, 7000 Mons, Belgium; [b] Department of Chemical, Biological, Pharmaceutical and Environmental Sciences, University of Messina, V.le F. Stagno d'Alcontres 31, 98166 Messina, Italy (ascala@unime.it); [c] CNR-ISTEC, Institute of Science and Technology for Ceramics, National Research Council of Italy, Via Granarolo 64, 48018 Faenza, RA, Italy; [d] CNR-ISMN, Istituto per lo Studio dei Materiali Nanostrutturati, V.le F. Stagno d'Alcontres 31, 98166, Messina, Italy.

Star polymers based on amphiphilic polylactide-poly(ethylene glycol) (PLA-PEG) are biomaterials of growing interest in the biomedical field as injectable drug delivery systems. Their exclusive structure, consisting of multiple variable-length linear chains (*arms*) radiating from a central *core,* is responsible for remarkable properties unattainable by linear polymers. [1,2]
In the framework of our studies dealing with the synthesis and functionalization of biopolymers for drug delivery purposes, [3-6] we have recently designed and synthesized a three-arms star-shaped PLA-PEG copolymer decorated with the integrin-targeting RGD peptide (*star*PLA-PEG-RGD), a cell recognition motif highly expressed in tumor cells and strongly involved in the regulation of tumor angiogenesis. Taking advantages from the recent advances in polymerization strategies and coupling chemistry, the synthesis of this complex macromolecular architecture was developed in a *core-first* approach, combining the Ring Opening Polymerization (ROP) with the *click* chemistry. The multi-step synthetic route allowed precisely controlled molecular weights and proper functionalities. The star polymers were fully characterized by ^{1}HNMR spectroscopy, gel permeation chromatography (GPC) and MALDI-ToF analysis. Two model anticancer drugs, Doxorubicin (DOX) and Docetaxel (DTX), were efficiently encapsulated into the *star*PLA-PEG nanoparticles (NPs) by nanoformulation approaches (*e.g.* dialysis and nanoprecipitation); the particle size and size distribution, zeta potential, drug loading and encapsulation efficiency were investigated. Moreover, the biological profile of drug-loaded *star*PLA-PEG NPs was explored with the aim to evaluate the cytotoxicity and antiproliferative activity against different tumoral cell lines (*e.g.* osteosarcoma, glioblastoma and breast cancer cells).

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Isolation and structural elucidation of oleanane saponins from *Bellis sylvestris* Cyr. involved in plant-plant chemical interactions

Monica Scognamiglio, Joyce Rodriguez, Giovanna Valentino, Brigida D'Abrosca, Rosita Russo, Assunta Esposito, Antonio Fiorentino*

Dipartimento di Scienze e Tecnologie Ambientali, Biologiche e Farmaceutiche, Università degli Studi della Campania "Luigi Vanvitelli", Via Vivaldi 43, 81100 Caserta.

** Email: monica.scognamiglio@unicampania.it*

Saponins are triterpenoid or steroid glycosides produced by several plants and few other organisms. The interest towards these compounds is due to their potential applications in many fields, based on the wide range of biological activities they possess [1]. Furthermore, they very likely play a role in plant defence and in general in plant chemical ecology [1]. A few saponins have, for example, been reported for their phytotoxic activity [2,3]. The production of phytotoxic compounds by plants is linked to the phenomenon of allelopathy, according to which one plant species interferes (often negatively) with the growth and performance of neighbouring species, through the production and release of chemicals [4].

In a preliminary study aimed at studying chemical-mediated interactions among plants of Mediterranean area, the species *Bellis sylvestris* Cyr., belonging to the Asteraceae family, showed phytotoxic potential against the target specie *Triticum ovatum* (syn. *Aegilops geniculata*) [4].

A phytochemical study aimed at identifying the phytotoxic compounds from *B. sylvestris* was therefore carried out. Extracts were obtained from the leaf, flower head, and root components and fractionated through a combination of several chromatographic steps. The structure of the saponins was determined by the extensive use of 2D-NMR experiments, including COSY, TOCSY, NOESY, HSQC, HMBC, CIGAR-HMBC, H2BC, and HSQC-TOCSY, along with Q-TOF HRMS^2 analysis. The phytochemical analysis led to the isolation of new oleanane saponins, along with already known compounds.

The phytotoxic activity of the isolated saponins was then assessed against *T. ovatum*. The metabolites were tested at three different concentrations (i.e., 1 mM, 1 μM and 1 nM) and their effects evaluated on the root and shoot elongation. Besides the inhibition of plant growth, an upwards root growth of *T. ovatum* was observed. It was therefore hypothesized that these compounds could interfere with the gravitropic response of the target plant. This was in good agreement with a previous study reporting that saponins isolated from *Pisum sativum* L. specifically interact with AUX1 protein in regulating the gravitropic response of *Arabidopsis thaliana* roots [5].

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Herbaspirillum Root189 LPS glycan chain decorations affect LPS bioactivity, membrane properties and prevent plant immune recognition

Alba Silipo

Department of Chemical Sciences, University of Naples Federico II

Plant microbiota (1,2) is a complex co-association of microorganisms that promotes plant health and growth, primes plant immune response, assures protection from pathogens. Lipopolysaccharides (LPS) (3), outer membrane components of Gram-negative bacteria, are involved in host-microbe interaction events, such as colonization, symbiosis, virulence. How plants immunity discriminates between beneficial and pathogenic microbes and perceives LPS from plant microbiota is still an open question (4). In this frame, we evaluated structure, conformation, membrane properties and immune recognition of the LPS isolated from the plant microbiota member *Herbaspirillum* sp. Root189 by a combination of complementary techniques, including NMR, computational, biophysical, microarray, immunological approaches (5-6). We showed how *Herbaspirillum* Root189 LPS structural features tune host recognition and therefore why the LPS is well tolerated by the plant immune system. We also evaluated how the glycan chain decorations affect LPS physicochemical features and membrane properties.

Herbaspirillum LPS consists of an *O*-methylated and variously acetylated D-Rhamnose containing polysaccharide chain, whose conformational behavior and flexibility was assessed using MD simulation and NMR spectroscopy, length and solvent affinity by MS and DLS, while structure and properties of the bacterial membrane, included flexibility, density and water permeability, using Neutron Reflectometry NR analysis on asymmetric bilayer. We then investigated *Herbaspirillum* Root189 LPS bioactivity, demonstrating how the O-polysaccharide chain shielded the LPS to the plant immune system. We therefore highlighted the functional role of glycan chain decorations in the elusion of host recognition and how *Herbaspirillum* Root189 LPS can favor plant colonization.

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Secondary metabolic profiles and anticancer actions from fruit extracts of immature pomegranates

Laura Siracusa [a], Carmelo Drago [a], Claudia Giovanna Leotta [b], Luana Pulvirenti [a], Giuseppe Ruberto [a], Venera Russo [b], Giovanni Mario Pitari [b]

[a] *Istituto di Chimica Biomolecolare del CNR (ICB-CNR), Via Paolo Gaifami ,18 - 95126 Catania, Italy*

[b] *Vera Salus Ricerca s.r.l., Via A. Broggi, 10 - 96100 Siracusa, Italy*

Immature fruits from *Punica granatum* L. thinning (Fig.1) are a neglected side product of the pomegranate production with serious disposal associated costs for farmers. In this work, we assessed the compositional features and antitumorigenic activity of extracts from immature pomegranate fruits cv. "Wonderful" at two different stages of maturation, in order to allow their potential valorization. Cancer cell proliferation was quantified in human lung H1299 and colon HCT116 adenocarcinomas by crystal violet staining and spectrophotometry. The results coming from both HPLC/DAD and HPLC/ESI-MS analyses indicate that immature fruits are very rich sources of gallotannins and ellagitannins with immature fruit peels far away richer than mesocarp, arils and ripe pomegranate extracts.

Biological investigations reveal a robust anticancer activity by immature *P. granatum* fruit extracts. These observations suggest *P. granatum* byproducts from the thinning process may provide unexplored values for virtuous circular economy.

Figure 1. Immature pomegranates "baby red" (A) and "baby green" (B) object of this study.

Enhanced relaxivity by hydrophobic interactions of macrocyclic Gd-HPDO3A complexes linked to pyranine

R.Stefania [a], Valentina Dinatale [a], Lorenzo Palagi [a], S. Aime [a], E. Gianolio[a]

[a] *Department of Molecular Biotechnology and Health Sciences, University of Torino, Torino, Italy*

The increase of relaxivity of Gadolinium Based Contrast Agents (GBCAs) continues to be a task of great interest as, in principle, it would allow to use lower doses. Relaxivity enhancements have been pursued via the increase of inner- or second-sphere water molecules. Other routes rely on the formation of supramolecular adducts. We have recently described the possibility of enhancing the relaxivity of the clinically approved Gadoteridol (Gd-HPDO3A) through the reversible binding interactions between the macrocyclic Gd-HPDO3A and pyranine (HPTS) [1]. 50% enhancement in relaxivity (r_1 = 6.7 mM^{-1} s^{-1}) was attained when the Gd(III) complex and the pyranine molecule were in 1:3 molar ratio. This result prompted us to design new systems in which Gd-HPDO3A and HPTS are linked covalently in order to pursue the formation of intra-molecular self-assembling system. Here, we describe the synthesis of two CM-pyranine (trisodium 8-(carboxymethoxy) pyrene-1,3,6-trisulfonate) conjugates of the Gd-HPDO3A, with different lengths of the spacer between the two moieties. Namely, no spacer for Gd-Pyr1 and an aliphatic short spacer for Gd-Pyr2 (Figure1). The synthesis of Gd-Pyr1 started from the ring opening of N-Z-2,3-epoxypropylamine with the secondary amine of DO3A(*t*BuO)$_3$, followed by deprotection of the *N*-benzyl protecting group to afford HPADO3A(*t*BuO)$_3$. Commercially available pyranine was alkylated with methyl bromoacetate, then methyl ester was hydrolyzed to afford pure CM-pyranine. HPADO3A(*t*BuO)$_3$ and CM-pyranine were linked to form and amide bond. For the Gd-L2, HPADO3A(*t*BuO)$_3$ was reacted before with Z-6-aminohexanoic acid followed by hydrogenolytic deprotection and then coupled with CM-pyranine. The final ligands were obtained by deprotection of the *t*butyl esters using TFA and the GdIII complexes by the reaction of the ligands with $GdCl_3$ at pH = 7.0 in aqueous solution. The effect of self-assembly on the relaxivity has been investigated by following the relaxation rates increase, at 21 MHz and 298 K, as a function of the concentration of the Gd-complexes. For both the systems, the measured r_1 values increased as a function of their concentration to reach values of 9.0 mM^{-1} s^{-1} and 8.6 mM^{-1} s^{-1} for Gd-Pyr1 and Gd-Pyr2, respectively. These values are significantly enhanced if compared to the relaxivity of the parent Gd(HPDO3A) measured in the same conditions (r_1 = 4.6 mM^{-1} s^{-1}). The length of the spacer between the macrocyclic cage and the pyranine moiety doesn't seem to have a great influence on the capability of the intra-molecular interaction to occur.

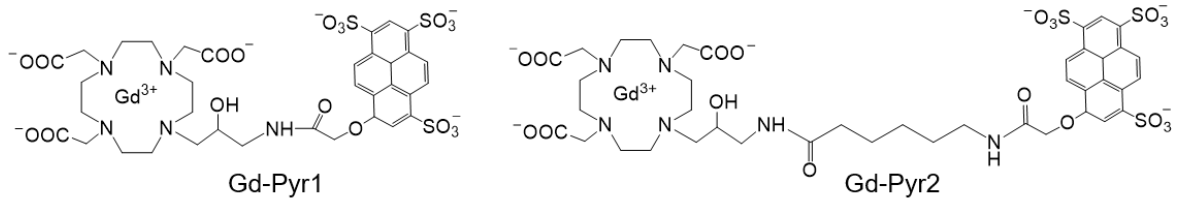

Figure_1: Structure of Gd-Pyr1 and Gd-Pyr2

In summary, we have reported that Gd(III) complexes can be coupled directly to pyranine through amide conjugates of the HPDO3A chelator to give new macrocyclic GBCAs endowed with improved relaxivities thanks to a self-assembling process based on the hydrophobic interaction between the macrocyclic tetra-aza ring and the piranine moiety.

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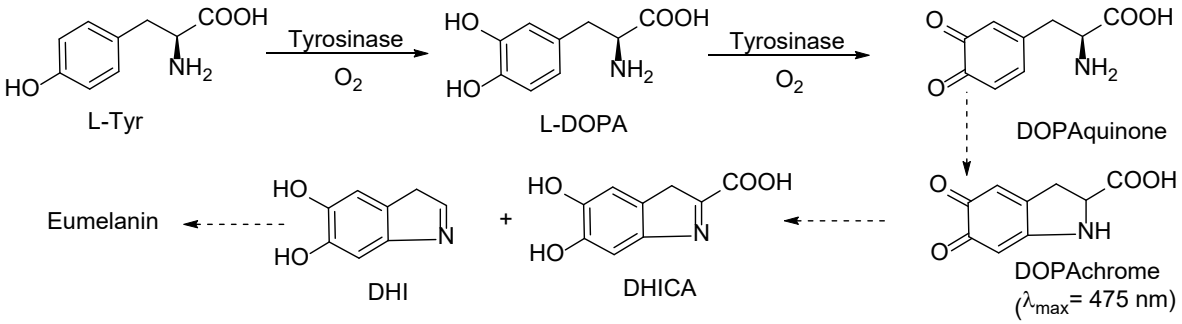
Oxygen Uptake Kinetics as a Powerful Tool to Investigate Tyrosinase Enzyme Inhibition

Yafang Guo,[a] Alice Cariola,[a] and Luca Valgimigli [a]

[a] Department of Chemistry "G. Ciamician", University of Bologna; Via S. Giacomo 11, 40126 Bologna, Italy.

Tyrosinase is a family of phenol oxidase enzymes found in a broad range of biological species, from fungi to humans, which catalyzes the oxidation of amino acid L-tyrosine to L-DOPA (monophenolase activity) and subsequently to DOPAquinone (diphenolase activity), as illustrated in the scheme. Being the key effector and controller of the biosynthesis of melanin biopolymers, tyrosinase plays a fundamental role in important processes ranging from food browning on storage to animal (and human) skin pigmentation and related disorders [1]. Not surprisingly its control by tyrosinase inhibitors has major scientific and practical relevance [2].



Conventionally, tyrosinase activity and inhibition are studied by spectrophotometric monitoring of the formation of DOPAchrome, a late product formed upon spontaneous cyclization of DOPAquinone prior to its conversion in DHICA and DHI in the synthetic path to eumelanin [3]. Since oxygen is the oxidant used in the reactions' sequence, accurate time-dependent monitoring of its consumption offers a complementary approach to monitor enzyme kinetics and inhibition. A new protocol was set up for continuous monitoring of oxygen uptake using a miniaturized IR fluorescence quenching probe, which enabled kinetic analysis of both monophenolase and diphenolase activity using, respectively, L-Tyr or L-DOPA substrates. The method was validated against the conventional spectrophotometric method then integrated with it to achieve multi-metabolite monitoring which proved advantageous to accurately investigate Tyrosinase inhibition kinetic and mechanism. Indeed, the combined method allows to clearly distinguish real inhibition from "false substrate" reaction, often encountered with phenolic and polyphenolic inhibitors. Application of the method on reference inhibitors kojic acid and glabridin (from *G. glabra*) allowed to revise previous controversial knowledge on the mechanism and kinetics of inhibition by glabridin itself, revealing a competitive Michaelis-Menten inhibition constant K_I of 13.95 nM and 61.22 nM respectively for monophenolase and diphenolase activity, *i.e.* about two orders of magnitude more effective than previous reports, which already spanned two orders of magnitude [4]. The method has lately been applied to investigate other inhibitors, a selection of which will be discussed.

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Enzyme immobilization on polydopamine-coated living microalgae cells for bioremediation

Danilo Vona[1], *Cesar Vicente Garcìa*[1], *Stefania Roberta Cicco*[2], *Roberta Ragni*[1], *Gabriella Leone*[1], *Gianluca Maria Farinola**[1]

1 Department of Chemistry, University of Bari, Via Orabona 4, 70125, Bari, Italy; 2 CNR-ICCOM Institute of organometallic chemistry-, Bari 70126, Italy

Diatoms are photosynthetic microalgae which naturally convert inorganic silicate into complex and nanostructured biosilica shells (called frustules) with peculiar properties, such as high surface area, transparency and mechanical resistance. Their *in vivo* and *in vitro* chemical modifications make them suitable for producing new generation mesoporous biosilica-based materials for photonics, sensing, optoelectronics and biomedicine [1]. Recently, we demonstrated an *in vivo* approach of functionalization of silica shells with luminescent organic small molecules, [2] organometallic emitters [3] and photoactive enhancers of photosynthesis [4]. Here, we *in vivo* functionalized living diatom single cells with polydopamine (PDA) polymer, proposed as an organic artificial shell with both intrinsic detoxification property [5] and used as an adhesive coating for entrapping enzymes such as laccase, lipase, tyrosinase and peroxidase. These enzymes are cheap and green catalysts outcompeting chemical catalysts for various applications. In details, laccase, tyrosinase and peroxidase catalyze oxidation reactions of a broad spectrum of compounds, such phenols, alkyl or arylamine and drug macrocycles, while lipase catalyzes hydrolysis and transesterification reactions with bioremediation applications. The enzyme-decorated diatoms act as easy, quick, biotic and eco-friendly living platforms for detoxifying aqueous solutions from recalcitrant xenobiotic compounds (poly-aromatic hydrocarbons (PAHs), polychlorinated biphenyl compounds (PCBs), hydrocarbons, dyes, pesticides, esters, heavy metals) from the natural environment.
We demonstrated that PDA coating and enzyme entrapment do not affect diatom cell viability: they reproduce and colonize the microenvironments while catalyzing oxidative degradation of organic pollutants. Moreover, we pave the possibility to magnetize living algae bearing enzyme moieties by incorporating also magnetic iron nanoparticles directly on diatom cells surfaces.

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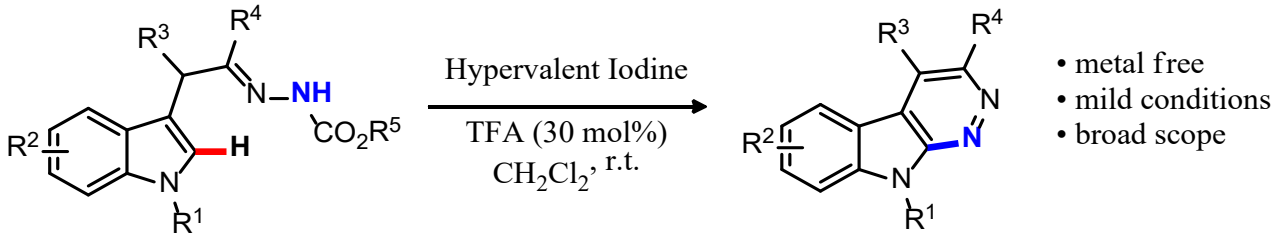
Metal-Free Synthesis of Azacarbolines Enabled by Hypervalent Iodine-Promoted Intramolecular Oxidative Cyclization

M. Corrieri, L. De Crescentini, G. Favi, F. Mantellini, G. Mari, S. Santeusanio

Department of Biomolecular Sciences, Section of Chemistry and Pharmaceutical Technologies, University of Urbino "Carlo Bo", Via I Maggetti 24, 61029 Urbino, Italy

Given the prevalence of azaheterocycles in nature and their broad application in chemistry, biology, and material sciences, the development of effective methods for the formation of C–N bonds is an intensively investigated area. Transition metal (TM)-catalyzed amination reactions[1] have been recognized as powerful methods for the direct C–N formation of (hetero)aromatic C–H bonds. However, either the high cost or toxicity of the transition metals or the harsh reaction conditions largely restricted their applications in practical synthesis. Recently, the interest in the use of hypervalent iodine reagents (HIRs)[2] as alternative metal-free promoters for C(sp^2)−N oxidative coupling reactions has significantly increased. Advantages of HIRs are mainly represented by their low toxicity, low prices and bench stability. Intrigued by HIRs chemistry and following our interest in the synthesis of fused *N*-heterocycles, we herein disclose an unprecedented synthesis of functionalized azacarbolines from readily prepared α-indolylhydrazones.[3] This method involves oxidative conditions using a combination of HIRs (including both tri and pentavalent) and catalytic amounts of trifluoroacetic acid (TFA) (Scheme 1). The procedure allows for an intramolecular coupling between the indole C2-H and the N-H donor of the hydrazone moiety. This contribution will cover the details of this procedure, the scope, the limitations, further applications of the method as well as mechanistic insights.



Scheme 1

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Functionalization of C-H bond using self-assembling supramolecular iron(II) complexes

Federico Frateloreto, Marika Di Berto Mancini, Giorgio Capocasa, Carla Sappino, Karim Abdel Hady, Giorgio Olivo, Osvaldo Lanzalunga, Stefano Di Stefano*

Dipartimento di Chimica and Istituto CNR per i Sistemi Biologici (ISB-CNR); Sezione Meccanismi di Reazione, Università di Roma "La Sapienza", P.le A. Moro, 5, 00185 Rome, Italy.

Oxidation of unactivated C-H bonds of aliphatic and aromatic substrates is a challenging reaction. In order to perform this reaction many catalysts based on transition metal complexes have been synthesized in the last years. These catalysts have to act with particular specificity in order to distinguish the various C-H bonds on a general substrate. In recent years a self-assembled iron(II) complex based on bis-iminic ligand has been synthesized. This complex is able to act as a catalyst in C-H bond oxidation of both aliphatic and aromatic substrates, using H_2O_2 as oxidant.[1]
Herein we report the preparation and characterization of new non-heme iron imine-based complexes (1, 2, 3): all of them self-assembles in CH_3CN solution from three building blocks, that are either commercially available or can easily be obtained from commercial products. These complexes display all the features for a supramolecular catalyst for H_2O_2 oxidation of aromatic and aliphatic compounds. Complex **1** is endowed with crown ethers that can act as supramolecular receptors for substrates carrying a positive charge such as an ammonium group [2].
Complexes **2** and **3** are functionalized with bulky groups (triisopropylsilyl) in order to explore the influence of steric hindrance on the selectivity of oxidation. [3]

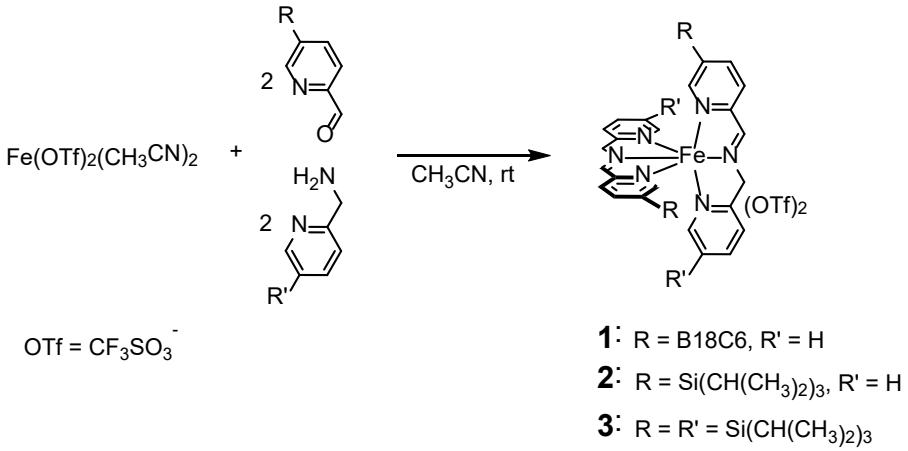

Figure 1: *In situ* generation of supramolecular imine iron complex **1**, **2** and **3**.

[1] (a)G. Olivo, G. Arancio, L, Mandolini, O. Lanzalunga, S. Di Stefano, *Catal Sci. Technol*. **2014**, *7*, 2900. (b) G. Olivo, M. Nardi, D. Vidal, A. Barbieri, A. Lapi, L. Gómez, O. Lanzalunga, M. Costas, S. Di Stefano, *Inorg. Chem*. **2015**, *54*, 10141. (c) G. Capocasa, G. Olivo, A. Barbieri, O. Lanzalunga and S. Di Stefano, *Catal. Sci. Technol*. **2017**,*7*, 5677.
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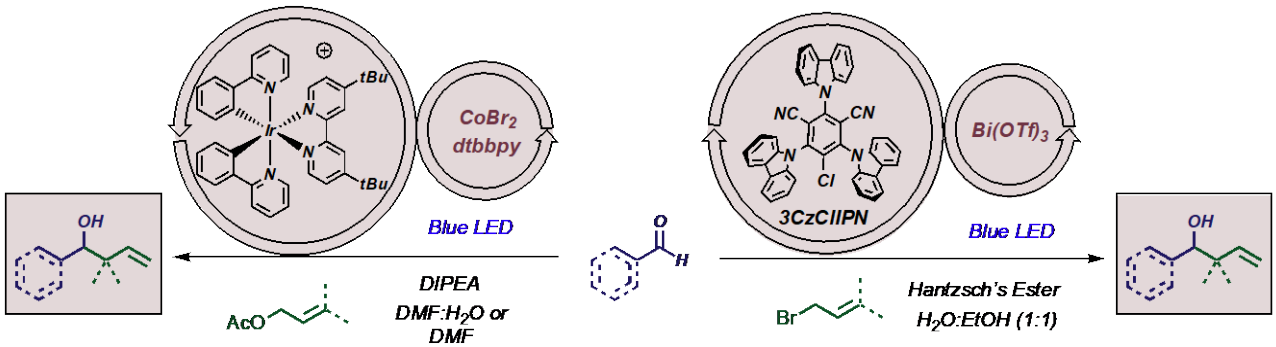
Photoredox allylation of aldehydes mediated by bismuth and cobalt

Andrea Gualandi,[a] *Francesco Calogero*,[a] *Simone Potenti*,[a] *Giacomo Rodeghiero*,[b] *Marco Di Matteo*,[a] *Martino Mazzarini*,[a] *Alessio Puggioli*,[a] *Cristina Moreno-Cabrerizo*,[c] *Charles Foucher*,[d] *Marianna Marchini*,[a] *Andrea Fermi*,[a] *Giacomo Bergamini*,[a] *Paola Ceroni*,[a] *Pier Giorgio Cozzi*[a]

[a] *Dipartimento di Chimica "G. Ciamician", Alma Mater Studiorum – Università di Bologna, Via Selmi 2, 40126, Bologna, Italy;* [b] *Cyanagen Srl, Via Stradelli Guelfi 40/C, 40138, Bologna, Italy;* [c] *Departamento de Química Orgánica and Centro de Innovación en Química Avanzada (ORFEO-CINQA), Universidad de Alicante 03080, Alicante, Spain;* [d] *École nationale supérieure de chimie de Paris 11, rue Pierre et Marie Curie, 75231, Paris, Cedex 05, France*

Allylation reactions in Barbier conditions are a useful methodology for the construction of C–C bonds. Different variations were reported in literature employing catalytic amount of metals (e.g. Ni, Co, Ti, Cr) in the presence of a stoichiometric co-reductant (often Mn or Zn) to obtain the metal catalyst in the active reduced form.
Metallaphotoredox catalysis, i.e. metal catalysis merged with photoredox catalysis, represents a formidable tool to generate nucleophilic organometallic reagents under Barbier conditions.[1] As a part of our research interest in the metallaphotoredox catalysis,[2] we combined Co[3] or Bi[4] catalysis with photoredox catalysis for efficient allylation of aldehydes. Mild reaction conditions, the use in catalytic amount of poor toxic metals and aqueous solvent, make these photoredox methodologies attractive for green and sustainable C–C bond formation processes. Substrates scope, limitations, and photophysical investigations of this new processes we will be discussed in the present communication.



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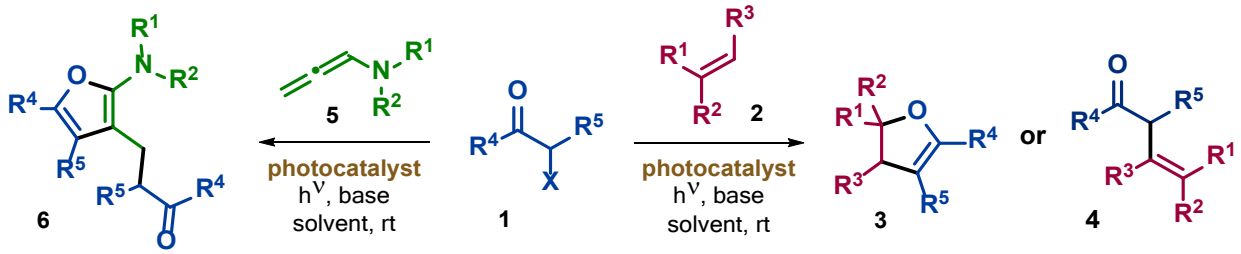
Visible Light Photocatalytic Synthesis of Oxygenated Heterocyclic Compounds

R. Veronesi, M. Lombardo and A. Quintavalla

Department of Chemistry "G. Ciamician", University of Bologna, Via Selmi 2, I-40126 Bologna, Italy

The last decade has witnessed an ever-increasing interest in the field of visible light photocatalysis, resulting in a tremendous grow of the available methodologies for the photogeneration of organic radicals and transforming photocatalysis in a reliable technique for organic synthesis.[1] In particular, visible light photoredox catalysis enables the development of efficient and sustainable radical synthetic approaches to differently functionalized heterocyclic scaffolds. As a part of our ongoing interest in the synthesis of bioactive heterocyclic compounds,[2] we report here our most recent results on the visible light photocatalytic synthesis of variably substituted dihydrofurans (3), β,γ-alkenyl ketones (4) and 2-aminofurans (6).[3] The mild reaction conditions employed and the redox-neutral nature of these transformations make them particularly attractive, being not only highly selective but also sustainable, avoiding the use of both sacrificial reactants and stoichiometric strong oxidants, that are expensive, often harmful to the environment and in many cases the cause of undesired side-reactions.



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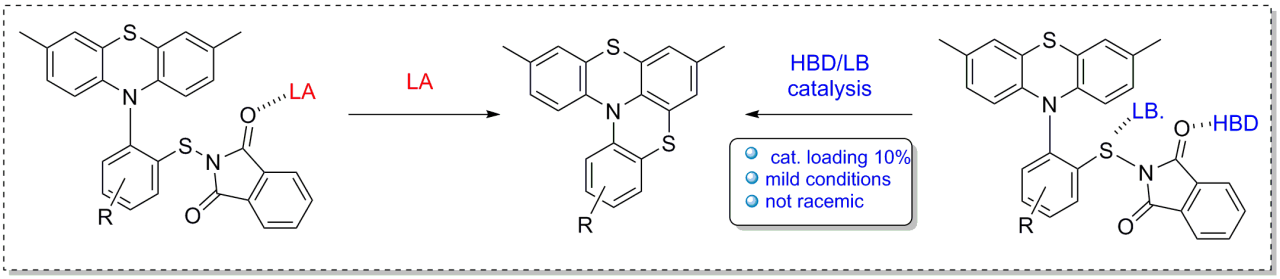
A Hydrogen Bond Donor / Lewis Base (HBD/LB) catalytic route to enantioenriched hetero[4]helicenes

Michela Lupi,[a] *Omar Salmi,*[a] *Stefano Menichetti,*[a] *Caterina Viglianisi*[a]

[a] *Department of Chemistry "Ugo Schiff", University of Florence, Via della Lastruccia 3-13, 50019 Sesto Fiorentino, Italy.*

Thia Bridged Triarylamine Hetero[4]Helicenes (TBTH[4]H) are a peculiar class of geometrically stable [4]helicenes with racemization energy barriers higher than those measured for all carbon [5]helicenes, allowing their HPLC resolution.[1] The similarity to triarylamines and phenothiazines confer interesting red-ox properties to these systems which can be oxidized to the corresponding stable radical cations.[2,3] Recently we reported the deposition of enantiopure helicenes radical cations on a pre-functionalized Au (111) surface preserving both the paramagnetism and the handnesess of these appealing molecules.[4] Thus, a synthetic approach to non-racemic TBTH[4]H is an important challenge. TBTH[4]H have been prepared via sulfenylation of triarylamines or *N*-phenylphenothiazines with the phthalimidesulfenyl chloride, followed by a Lewis Acid (LA) promoted intramolecular electrophilic cyclization.[5] However, the cyclization reaction requires excess amount of Lewis acid under quite harsh conditions. In this communication, we report a detailed survey concerning the use of a Hydrogen Bond Donor / Lewis Base catalytic system (HBD/LB) for the synthesis of these appealing curved chiral heterocycles including the possibility of controlling their absolute stereochemistry (Scheme 1).



Scheme 1

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Fast Heck-Cassar-Sonogashira Cross-Coupling Reactions with Palladium Catalyst Recycling and Green Solvent/Base recovery

G. Martelli[*,a] *T. Fantoni*[a] *S. Bernardoni*[a] *A. Mattellone*[a] *L. Ferrazzano*[a] *P. Cantelmi*[a] *D. Corbisiero*[a] *A. Tolomelli*[a] *W. Cabri*[a] *F. Vacondio*[b] *F. Ferlenghi*[b] *M. Mor*[b] *and A. Ricci*[c]

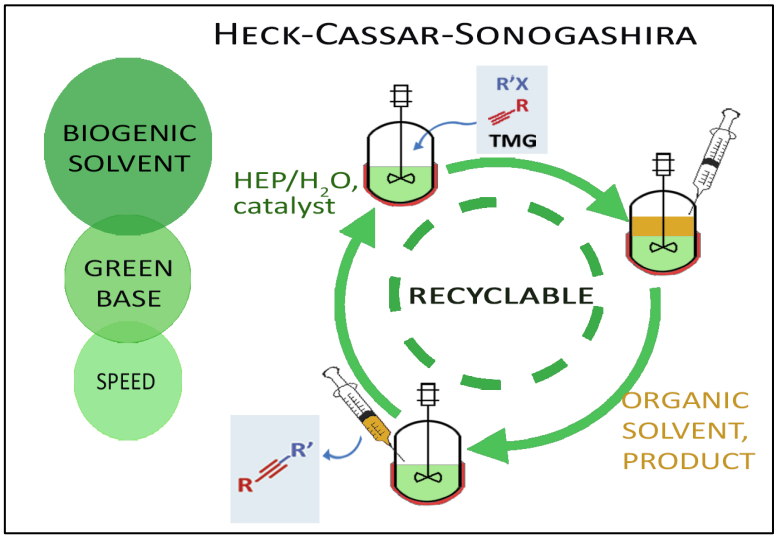
[a]*Department of Chemistry G. Ciamician, Alma Mater Studiorum, Via Selmi 2, Bologna*
[b]*Department of Food and Drug Sciences, University of Parma, Parco Area delle Scienze 27/a, Parma*
[c]*Fresenius Kabi iPsum, Innovation and Development, Via San Leonardo 23, Villadose (RO)*

Catalysis has been listed by the fathers of green chemistry as a fundamental tool to shift the paradigm of chemical processes from classical to sustainable methodologies. Switching to catalysis for carbon-carbon bond formation often involves the use of transition metals, with Pd-catalyzed reactions showing a prominent role.[1]

We recently contributed in this field with the development of a sustainable, efficient and flexible protocol for the Heck-Cassar-Sonogashira (HCS) cross-coupling: *N*-hydroxyethylpyrrolidone (HEP) and *N,N,N',N'*-tetramethyl guanidine (TMG) as green solvent/base proved to be applicable on aryl iodides and bromides affording high yields and fast conversions under mild conditions.[2]

The methodology was then further optimized, in order to satisfy the key goal of decreasing costs while increasing reaction greenness and industrial potential. The need of removing the metal from the products and of decreasing the process mass intensity (PMI) was accomplished by a HEP/water/TMG mixture with sulfonated phosphine ligands, conditions that allowed to drastically reduce the amount of catalyst and to recover solvent, base and Pd several cycles with no loss in activity, obtaining the products free from metal contamination.

With this new HCS protocol we achieved high yields, high TON/TOF values and competitive PMI (close to 3), recalculated considering solvent, base, and palladium recovery.[3] The methodology was then successfully applied to the telescoped synthesis of the anticancer drug Erlotinib (TON: 1380; TOF: 46 h^{-1}), revealing its applicability in drug discovery and industrial pharmaceutical segment.



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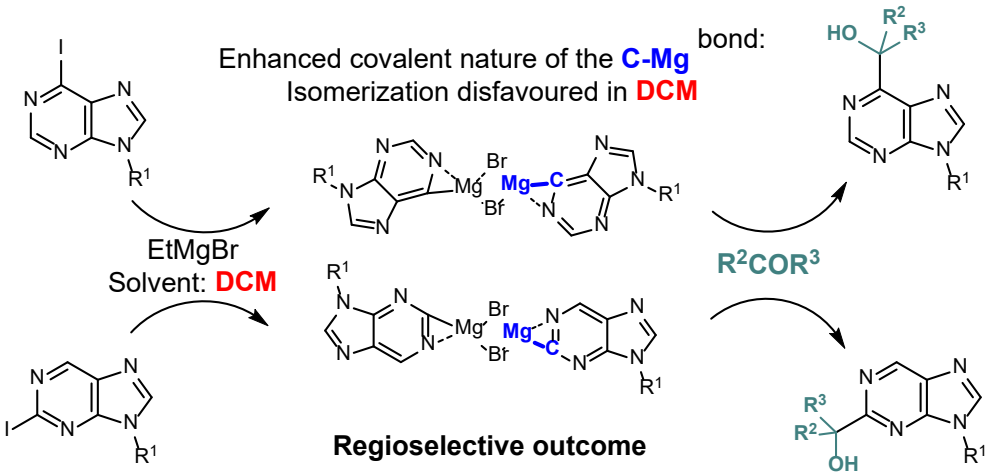
2- and 6-Purinylmagnesium Halides in Dichloromethane: Scope and Insights Into the Solvent Influence on the C-Mg Bond

Giovanni Fusi[a], Zelong Lim[b], Stephen D. Lindell[b], Enrique Gomez-Bengoa[c], Malcolm R. Gordon[b] and Silvia Gazzola[a]

[a] *Science and High Technology Department, University of Insubria, 22100, Como, Italy.*
[b] *Bayer CropScience, BCS AG-R&D-SMR-WC-WCC, Frankfurt am Main, G836, 200.*
[c] *Department of Organic Chemistry I, University of the Basque Country UPV/EHU, 20018 Donostia-San Sebastián, Spain.*

The synthesis and the functionalization of purine rings have been deeply investigated to generate potential bioactive compounds for pharmaceutical and agrochemical purposes [1]. Generally, the introduction of a carbon substituent at the C-2, C-6 and C-8 positions occurs through transition metal catalyzed cross coupling reactions of purine halides [2]. By contrast, the coupling of metalated purines with appropriate C-electrophiles has been less developed due to the low stability of the resultant purine anion in THF, which leads to a mixture of regioisomers as final product [3]. By conducting the reaction in dichloromethane, herein we demonstrated that the anion isomerization can be stopped and these stable purin-2- and 6-yl Grignards react directly with a broad scope of electrophiles. Remarkably, density functional theory calculations suggested that the choice of solvent plays a key role in this chemistry due to the more covalent nature of the C-Mg bond in DCM compared with a more ionic and basic nature in THF [4].



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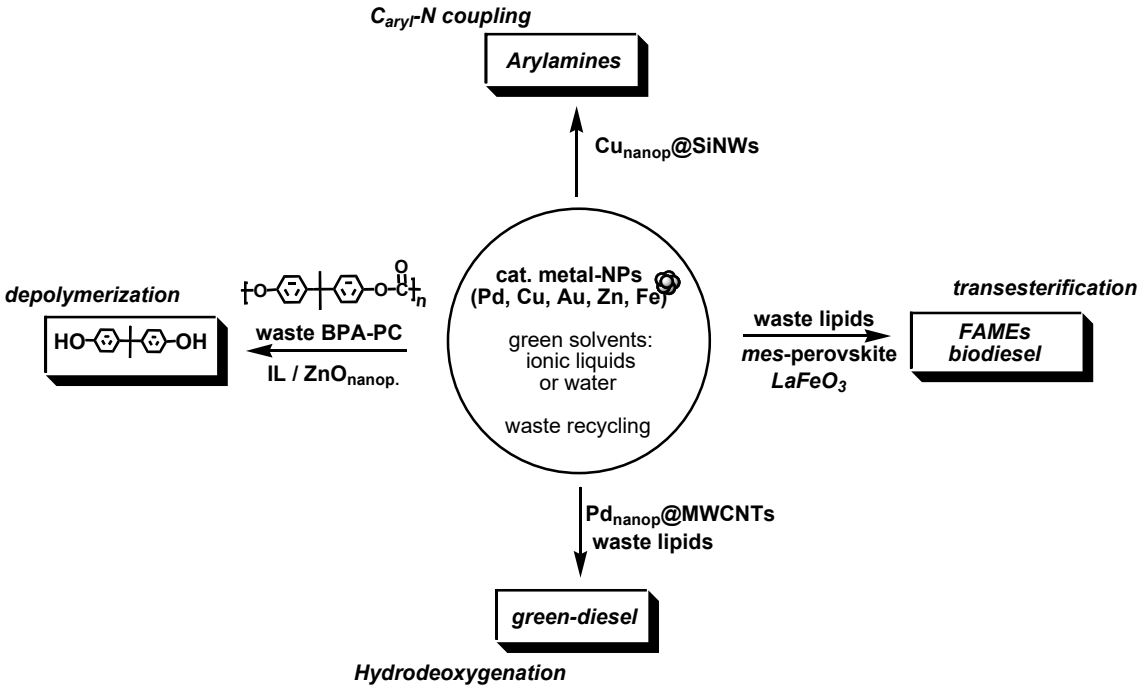
Nanostructured catalysts for a circular economy

Angelo Nacci,[a,b] Michele Casiello,[a] Onofrio Losito,[a] Andrea Aloia,[a] Francesca Russo,[a] Francesca De Robertis,[a] Nicola Nocera,[a] Caterina Fusco,[b] Antonio Monopoli,[a] Lucia D'Accolti [a,b]

[a] Chemistry Department, University of Bari Aldo Moro, Via Orabona 4, 70125 Bari, Italy; [b] CNR—Istituto di Chimica dei Composti Organometallici (ICCOM), Bari Section, Via Orabona 4, 70125 Bari, Italy.

Growing energy demand and climate change are the two sides of the same coin representing one of the main challenges that mankind has been facing since the beginning of the 21st century. Diversifying the supply of energy fonts and materials, moving from a linear to a circular development model, is the winning strategy that avoids simultaneously the depletion of resources and the accumulation of waste.
Valorization of biomass and scraps is the main route for applying these circular economy principles and to this end nanoscale materials have assumed a key role as catalysts in a wide number of applications ranging from fuel conversion, pollution abatement to fine chemicals production [1].
During the last two decades, our group has developed several catalytic protocols based on a variety of nanostructured metals and sustainable eco-friendly conditions (low temperature, green reagents, alternative reaction media like water or ionic liquids). Based on our experience in this field [2], we recently devoted attention to circular economy processes valorizing biomass and wastes. This communication deals with our recent advances in catalytic conversion of waste lipids into 1st and 2nd generation biofuels, in plastic recycling by depolymerization reactions and in C_{aryl}-N couplings catalyzed by copper nanoparticles supported on silicon nanowires (SiNWs).



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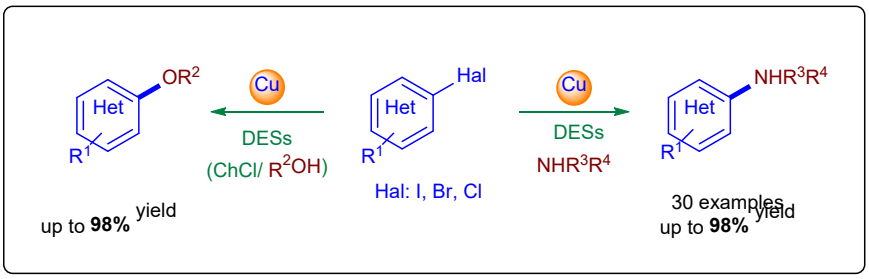
Mild Approaches for Copper-Catalysed Coupling Reactions: Ligand-Free Ullmann-type C–N and C–O Bond Formation in Deep Eutectic Solvents

Andrea F. Quivelli,[a] Paola Vitale,[a] Filippo M. Perna,[a] Vito Capriati [a]

[a]Dipartimento di Farmacia-Scienze del Farmaco, Università degli Studi di Bari "Aldo Moro", Consorzio C.I.N.M.P.I.S, Via E. Orabona 4, 1-70125 Bari, Italy;
e-mail:andreaquivelli@uniba.it

Growing efforts are continuously being made to replace harmful, carcinogenic, petroleum-based volatile organic compounds (VOCs) with inexpensive, green and bio-renewable reaction media [e.g. water, bio-based solvents] [1,2]. In this contest, the so-called Deep Eutectic Solvents (DESs) have come to the fore in the last decade. They are binary or ternary eutectic mixtures that are particularly attractive from both an ecological point of view and an economic perspective as they are biodegradable, poorly toxic and inexpensive [3,4].
Nowadays, there has been a boost in metal-catalysed and metal-mediated organic reactions run in the aforementioned unconventional solvents [5,6]. Copper-catalysed Ullmann-type cross-coupling reactions allow the synthesis of C–N and C–O bonds in VOCs (e.g., THF, toluene), however, often making use of high temperature and of expensive ligands [8–10]. In this communication, we report on two mild approaches for promoting Cu-catalysed cross-coupling reactions in choline chloride (ChCl)-based eutectic mixtures as non-innocent reaction media aimed at synthesizing secondary and tertiary aryl amines, and aryl-alkyl ethers [11]. Overall, reactions proceed smoothly in the absence of ligands, under air and moderate heating, affording the desired adducts in high yields (up to 98%).



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Stereoselective monoreduction of bulky 1,2-dicarbonyls catalyzed by a benzil reductase from *Pichia glucozyma* (KRED1-Pglu)

Marco Rabuffetti[a], Pietro Cannazza[b], Martina L. Contente[b], Andrea Pinto[b], Diego Romano[b], Pilar Hoyos[c], Andrés R. Alcántara[c], Ivano Eberini[d], Tommaso Laurenzi[d], Louise Gourlay[e], Flavio Di Pisa[e], Francesco Molinari[b]

[a] *Department of Chemistry, University of Milan, via Golgi 19, 20133 Milan, Italy;* [b] *Department of Food, Environmental and Nutritional Sciences (DeFENS), University of Milan, Via Mangiagalli 25, 20133 Milan, Italy;* [c] *Department of Chemistry in Pharmaceutical Sciences (QUICIFARM), Pharmacy Faculty, Complutense University, Plaza de Ramon y Cajal, s/n, 28040 Madrid, Spain;* [d] *Department of Pharmacological and Biomolecular Sciences (DiSFeB), University of Milan, Via Balzaretti 9, 20133 Milan, Italy;* [e] *Department of Biosciences, University of Milan, Via Celoria 26, 20133 Milan, Italy*

Enantiomerically enriched hydroxyketones are well-established intermediates for the synthesis of several bioactive compounds [1] and can be chemically obtained by stereoselective reduction of one of the carbonyl moieties of the corresponding diketones. However, enzymatic strategies are characterized by higher catalytic efficiency, milder reaction conditions, higher stereo- and regioselectivity, and fewer numbers of synthetic steps. Therefore, they can be chosen as convenient and environmentally friendly alternatives.[2]

A NADPH-dependent benzil reductase from the non-conventional yeast *Pichia glucozyma* (KRED1-Pglu) was over-expressed in *E. coli*, purified and exploited to catalyze the asymmetric monoreduction of bulky aromatic 1,2-dicarbonyl compounds (**Figure 1**). The cofactor was recycled by an enzyme-coupled system (glucose-glucose dehydrogenase (GDH) from *Bacillus megaterium*). The recombinant KRED1-Pglu showed a wide range of activity (24-97% conversion) and excellent stereoselectivity (*ee* ≥ 96% in all but one case). On the contrary, it proved either inactive or very poorly active towards most 1,3- and 1,4-dicarbonyls tested as potential substrates. In order to understand this peculiar behavior, the enzyme was crystallized (1.77 Å resolution) and its active site was investigated to identify the recognition residues involved in the desymmetrization reaction. QM and classical calculations also allowed for a proposal of the catalytic mechanism, along with an *in silico* reactivity prediction.[3]

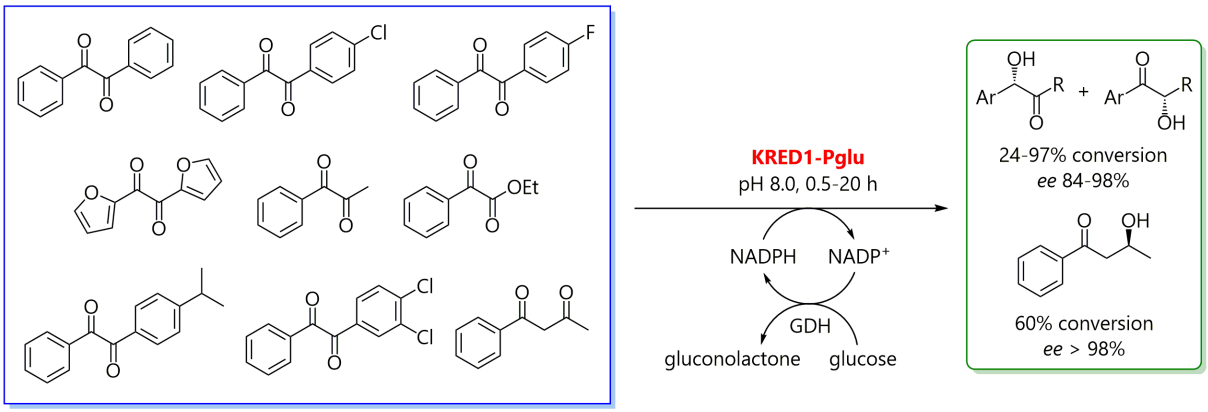

Figure 1. Stereoselective monoreductions of dicarbonyls catalyzed by KRED1-Pglu.

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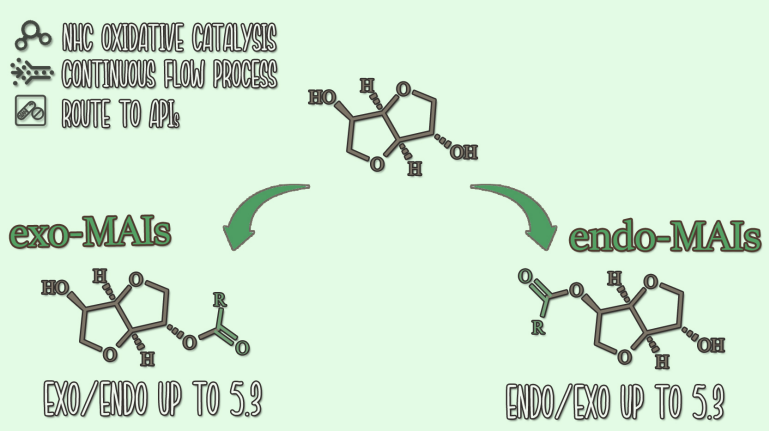
Regiodivergent Isosorbide Acylation by Oxidative NHC-Catalysis in Batch and Continuous-Flow

Daniele Ragno, Costanza Leonardi, Graziano Di Carmine, Olga Bortolini, Arianna Brandolese, Carmela De Risi, Marco Bottin and Alessandro Massi

Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Via L. Borsari, 46, 44121 Ferrara (Italy)

e-mail: daniele.ragno@unife.it

A new N-heterocyclic carbene (NHC)-catalyzed strategy for the regioselective monoesterification of isosorbide (IS) [1] at either *endo* (5-OH) or *exo* (2-OH) position is described. Site-selective acylation proceeds under oxidative conditions in the presence of a quinone oxidant using aldehydes as mild acylating agents [2,3]. Experimental evidences suggest a role of the stereoelectronic features of the acyl azolium salt intermediate in determining the selectivity of the acylation process. The solvent effect was also investigated considering conventional and sustainable solvents. Aromatic aldehydes, including bio-based furfural (FF) and 5-hydroxymethyl furfural (HMF), together with α,β-unsaturated aldehydes proved to be effective reaction partners affording monoacyl-isosorbides (MAIs) with satisfactory levels of regioselectivity (*exo/endo*: 5.3-3.5; *endo/exo*: 5.3-3.3). Additionally, the *exo*-selective triazolium salt promoter was successfully transferred into heterogeneous phase and applied to continuous-flow (CF) catalysis. In particular, the polystyrene-supported version of the selected NHC showed a catalytic activity comparable to that of the homogeneous counterpart in terms of both conversion efficiency (TON = 108) and regioselectivity (*exo/endo* up to 5.3). Also, the corresponding packed-bed mesoreactor was operated with long-term stability (ca. 110 hours on stream) to produce the 2-benzoyl-IS (1.32 mmol h^{-1} $mmol_{cat}^{-1}$), which is the key intermediate in the synthesis of a commercial active pharmaceutical ingredient (API), namely the vasodilator isosorbide-5-mononitrate (IS-5MN).



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Palladium anchored on Silk Fibroin as suitable catalyst for Suzuki-Miyaura Cross-Coupling Reactions

G. Rizzo[a], G. Albano[a], G. M. Farinola[a]*

[a] Dipartimento di Chimica, Università degli Studi di Bari "Aldo Moro", Via Edoardo Orabona 4, 70126 Bari, Italy. e-mail: giorgio.rizzo@uniba.it;

Silk Fibroin (SF) was the first ever reported organic support for catalysis, leading to the fascinating field of organocatalysis. It is known that SF is an efficient support for Palladium[1], Platinum[2] and Rhodium[3] in the hydrogenation reactions. A SF-Palladium catalyst for Suzuki-Miyaura cross-coupling reactions was prepared and optimized[4], often giving the desired pure biaryl as the only product in mild conditions, thus avoiding tedious purification steps and chromatography techniques. Pd/SF was also suitable for gram-scale reactions and for the synthesis of a key pharmaceutical intermediate. In the literature are known different biopolymers as supports in catalysis, such as cellulose, starch, lignin, alginic acids and keratine[5] but SF represents a valid alternative to these supports since the metal loading is very low, any additional ligand or toxic organic solvent are required, reactions can be completed in very short times at low temperatures, and they require only water and ethanol as solvents. It is worth emphasizing that Pd/SF showed an exceptionally high recyclability (up to 19 cycles): typically both biopolymer-based and synthetic supports do not exceed five or more recycling processes. Moreover, it has been demonstrated that Pd/SF exhibits a purely heterogeneous catalytic mechanism without any metal leaching during the reactions.

Figure 1. *Preparation of Palladium supported on Silk Fibroin catalyst for Suzuki-Miyaura cross-coupling reactions.*

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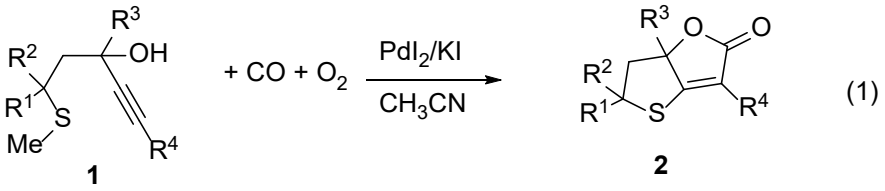
Novel Synthesis of Thienofuranone Derivates by Pd-Catalyzed Carbonylation Reaction

Raffaella Mancuso, Patrizio Russo, Alex De Salvo, Domenico Santandrea, Bartolo Gabriele

Laboratory of Industrial and Synthetic Organic Chemistry (LISOC) Department of Chemistry and Chemical Technologies, University of Calabria, Via P. Bucci, 12/C, 87036 Arcavacata di Rende (CS), Italy
patrizio.russo@unical.it

After recent studies on the inhibitory activity of molecules with a furofuranone core, which showed an important antiproliferative activity on various human breast cancer cell lines[1], the possibility of synthesizing thienofuranone molecules has been investigated, also considering that no examples are currently known of synthetic approached for this type of heterobicyclic compounds.

In the present work, we report a general synthesis of thienofuranone derivatives **2** based on a PdI_2/KI-catalyzed oxidative S-cyclization-cyclocarbonylation process (Eq. 1)



R^1, R^2, R^3= H, Me
R^4= Aryl, Alkyl

(55%-81%)

Eq. 1

The protection of the thiol group with a methyl group in the substrates is of fundamental importance, as it avoids the possible formation of disulfide bonds under oxidative conditions. The methyl group on sulfur is, in fact, easily removed under the reaction conditions by the iodide anion to give methyl iodide, which in its turn convert into MeOH by reaction with water.

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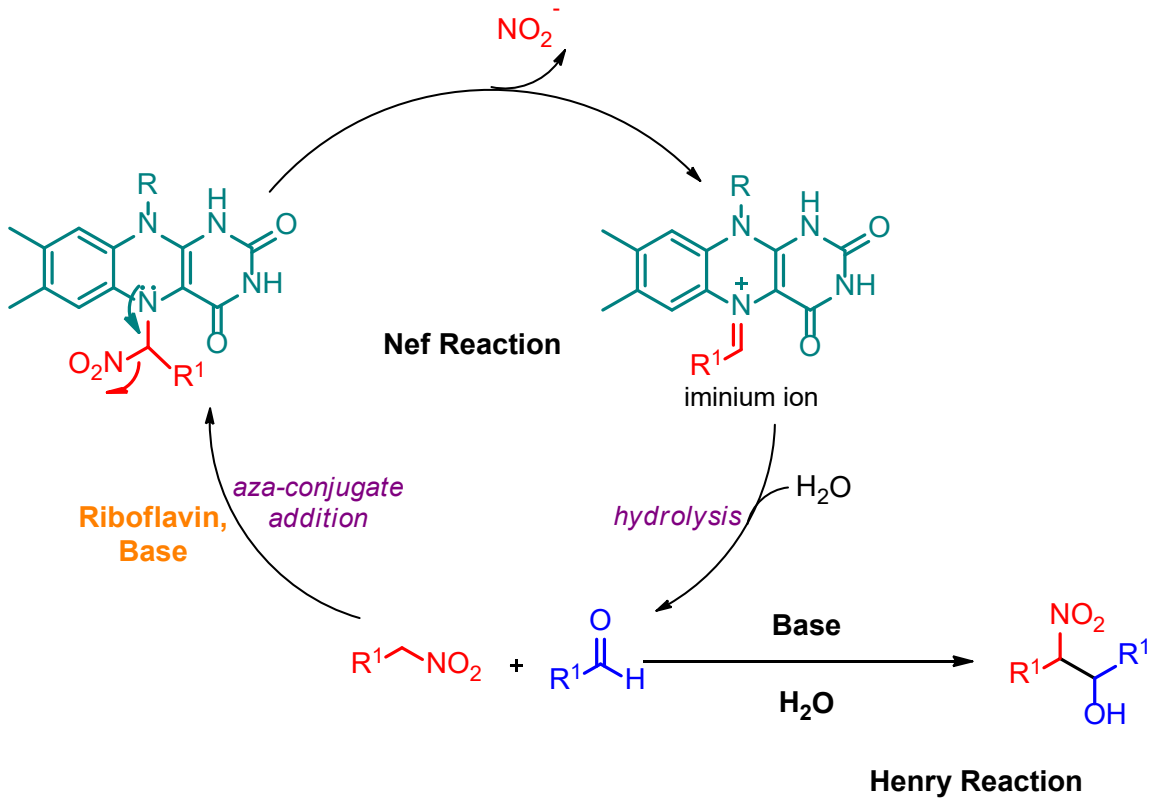
Vitamin B2 Promoted Tandem Nef-Henry Reactions for the synthesis of Symmetrical β-Nitro Alcohols from Nitroalkanes

G. Lupidi,[a] *A. Palmieri*,[a] *M. Petrini*[a]

[a] *School of Science and Technology, Chemistry Division, University of Camerino, Via S. Agostino 1, 62032 Camerino*

Over the past several decades, the chemistry of nitroalkanes has been recognized as one of the most flourishing area in synthetic chemistry.[1] Nitroalkanes serve as pivotal intermediates in the synthesis of natural products,[2] biologically active pharmaceutical ingredients (APIs),[3] and other useful compounds. Recently, Thapa *et al.* reported flavinium salts-based catalysts for generating nitrite anions from nitromethane.[4] Inspired by this work, we decided exploit natural small molecules as promoter for classical reactions. We have disclosed a new methodology for the synthesis of functionalized symmetrical β-nitro alcohols under mild reaction conditions by Riboflavin-promoted Nef reaction on primary nitroalkanes coupled with a tandem Henry reaction.



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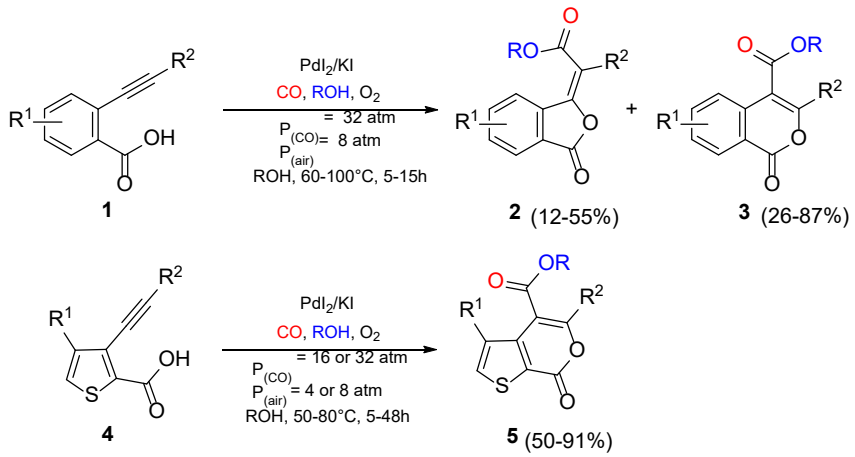
Synthesis of Isobenzofuranones, Isochromenones and Thienopyranones by a Pd-Catalyzed Oxidative Carbonylation Approach

Ida Ziccarelli, Raffaella Mancuso, Romina Strangis, Bartolo Gabriele

Laboratory of Industrial and Synthetic Organic Chemistry (LISOC) Department of Chemistry and Chemical Technologies, University of Calabria Via Pietro Bucci 12/C, 87036 Arcavacata di Rende (CS), Italy
ida.ziccarelli@unical.it

PdI_2-catalyzed oxidative carbonylation of acetylenic substrates bearing a suitably placed nucleophilic group is a powerful methodology for the direct synthesis of carbonylated heterocycles [1].

We report here a novel method for the synthesis of isobenzofuranones **2**, isochromenones **3** and thienopyranones **5** based on PdI_2/KI-catalyzed oxidative oxidative heterocyclization-alkoxycarbonylation of 2-alkynylbenzoic acids **1** and 3-alkynylthiophene-2-carboxylic acids **4** (Scheme 1).



Scheme 1

In the presence of catalytic amounts of PdI_2 (2 mol%) in conjunction with KI (20 mol%) and under relatively mild reaction conditions (50-100 °C under 20 or 40 atm of a 4:1 mixture of CO-air), different 2-alkynylbenzoic acid **1** and 3-alkynylthiophene-2-carboxylic acids **4** were converted into the corresponding carbonylated heterocycles **2**, **3** and **5** through and ordered sequence of steps, involving a 5-*exo-dig* or a 6-*endo-dig* cyclization, carbon monoxide insertion, and nucleophilic displacement by an external alcohol (also used as solvent).

Reactions led to the desired products in moderate to high yields and the structure of some representative products has been confirmed by XRD analysis.

The heterocyclic derivatives synthesized in this work may be of interest owing to their potential bioactivity and, in particular, for the possible identification of novel anticancer agents [2].

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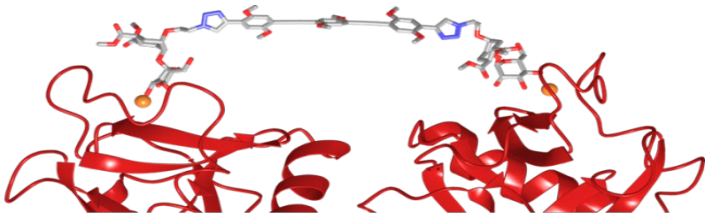
At the crossroad between Chemistry and Biology: interfering with the sugar code using glycomimetics

Anna Bernardi

Università degli Studi di Milano, Dipartimento di Chimica, via Golgi 19, Milano

The recognition of carbohydrates by specific sugar-binding proteins called *lectins* mediates a number of physiological and pathological events, that are increasingly being elucidated and appreciated as central to the flow of information in cell-cell and cell-environment communication. Understanding and controlling sugar-encoded information can advance fundamental knowledge of biological events and generate new approaches to the treatment of many diseases, ranging from cancer to microbial infections.

Over the past two decades, we have been working on the rational design and the synthesis of structural and functional mimics of oligosaccharides, with the aim of disrupting sugar/protein interactions that control biologically relevant events. Our design strategy takes advantage of the 3D structures of known oligosaccharides and of available structural information on the protein/ligand complexes. The small-molecule, monovalent ligands obtained are often endowed with limited protein affinity, owing to specific characteristic of lectins binding sites, but display improved drug-like properties compared to natural sugars. High-affinity antagonists are then obtained by multivalent presentation on multimeric scaffolds, such as dendrimers, polymers or nanoparticles. [1]



The presentation will deal with selected examples of our work in this area. [2-8]

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Self-organized Supramolecular Systems for Catalysis, Sensing and Transport

Paolo Tecilla

Department of Chemical and Pharmaceutical Sciences, University of Trieste, Via Giorgieri, 1, I-34127 Trieste, Italy; ptecilla@units.it

The emergence of Supramolecular Chemistry in the eighties brought new perspectives to chemistry and a new way of viewing classical chemical interactions and processes. In particular, the concept of molecular recognition and, even more important, the concept of self-organization and their associated functions allowed to explore new phenomena and new properties that arise from the organized interaction of multiple chemical entities. In this context, the classical tools of Physical Organic Chemistry have been fundamental to rigorously describe the observed phenomena and to dissect the various effects involved.

Following this unifying approach, over the years, we have investigated several supramolecular systems starting with colloidal aggregates and in particular micelles and liposomes. Micelles can be considered as self-assembled microreactors in which, by using properly functionalized surfactants or lipophilic molecules, it is possible to concentrate in the confined space of the colloidal aggregate different reactive functions that can cooperate in the catalysis of chemical reactions. In particular, metallocatalyzed hydrolysis reactions of esters (carboxylic, phosphoric and also DNA) have been studied obtaining important results in terms of acceleration of the reactions and enantioselectivity in the hydrolysis of amino acid esters [1].

The same concept of self-assembly have been applied in micelles and in silica nanoparticles to the development of sensors for metallic species. The novelty here is that the self-organization of the metal ion receptor and the fluorescent dye in the supramolecular aggregate allows communication between the two components ensuring transduction between the recognition event and the generation of the optical signal [2].

More recently the attention has shifted to the control of self-association phenomena in phospholipid membranes to mimic the transport functions of natural ion channels. In this field some digression towards unimolecular receptors allowed to improve the selectivity in the trans-membrane transport of anions which is relevant in the perspective treatment of genetic diseases such as Cystic Fibrosis.

At the end of this long journey in the supramolecular chemistry of self-organized system, the take-home message is that, as in life, also in chemistry the cooperation of different entities in a self-organized system can lead to unpredicted results that go far beyond the simple sum of the individual properties.

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A Journey through the World of Halogen Bonding

Pierangelo Metrangolo

[a] *SupraBioNanoLab-DCMIC "Giulio Natta", Politecnico di Milano, Italy, E-mail: pierangelo.metrangolo@polimi.it; Web-site: www.suprabionano.eu;* [b] *Center for Nano Science and Technology, Italian Institute of Technology;* [c] *Centre of Excellence in Hybrid Biosynthetic Materials, Aalto University, Finland;* [d] *Nanotechnology Institute (Nanotec), National Research Council, Italy;* [e] *VTT-Technical Research Centre of Finland.*

In recent years, halogen bonding has grown from a scientific curiosity to one of the most interesting noncovalent interactions for constructing supramolecular assemblies (Figure 1) [1]. According to the recently proposed IUPAC provisional recommendation [2], "A halogen bond occurs when there is evidence of a net attractive interaction between an electrophilic region associated with a halogen atom in a molecular entity and a nucleophilic region in another, or the same, molecular entity". This definition acknowledges the qualitative analogy between halogen bonding and the ubiquitous hydrogen bonding. In this lecture, I will survey my 20 years of research, starting from small molecule crystal engineering and arriving to the relevant implications of *in-vivo* halogenation mechanisms [3].

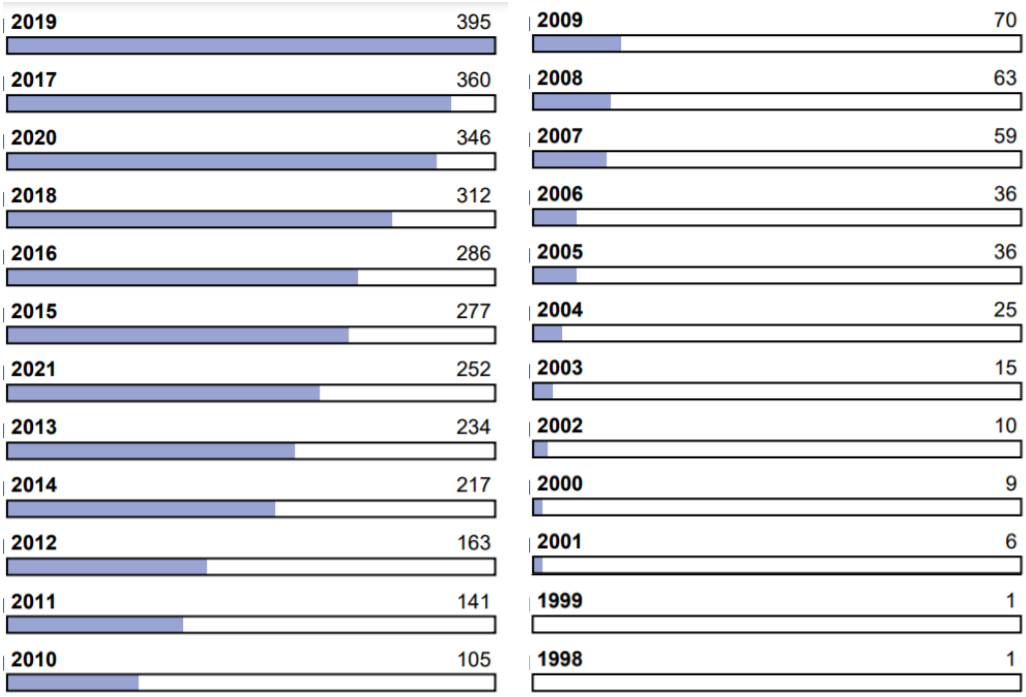

Figure 1. Numbers of papers published in the last 20 years reporting the wording *Halogen Bonding* (source SciFinder 29/07/2021).

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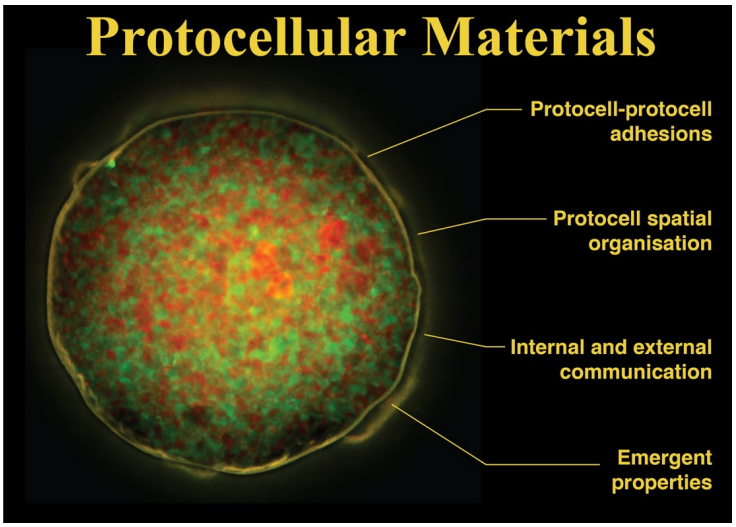
A synthetic chemistry approach to the fabrication of protocells and protocellular materials

Pierangelo Gobbo[a]

[a] *School of Chemistry, University of Bristol (UK)*



Recreating the structure and functions of living tissues is one of the grand challenges of our time. One way to overcome this challenge is by relying on synthetic cells (or "protocells") as foundational units to build free-standing structures with complex three-dimensional architectures that we call "protocellular materials" (PCMs) (see figure). In this seminar I will give a brief introduction of this young and emerging research field and report our most recent scientific breakthroughs. These were achieved by combining in an original and synergistic manner key aspects of organic chemistry and materials science with fundamental concepts of bottom-up synthetic biology.[1] I will describe our techniques to generate protocell-protocell adhesions and control the assembly of protocell building blocks into PCMs with complex three-dimensional architectures. Finally, I will explain how we can chemically program the PCMs to display emergent bio-inspired behaviours such as collective contractility, non-equilibrium sensing and photoinduced O_2 production.[2-4]

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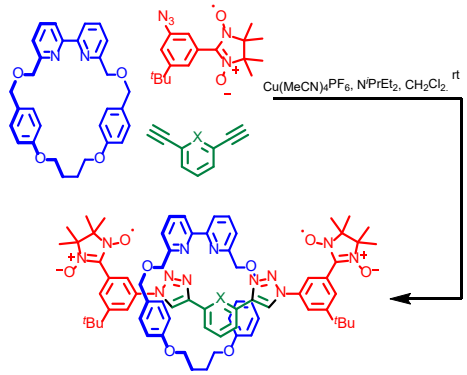
Novel Spin-Labelled Mechanically Interlocked Molecules as Models for the Interpretation of Biradical EPR Spectra

Lorenzo Gualandi,[a] Paola Franchi,[a] Elisabetta Mezzina,[a] Stephen M. Goldup[b] , Marco Lucarini[a]

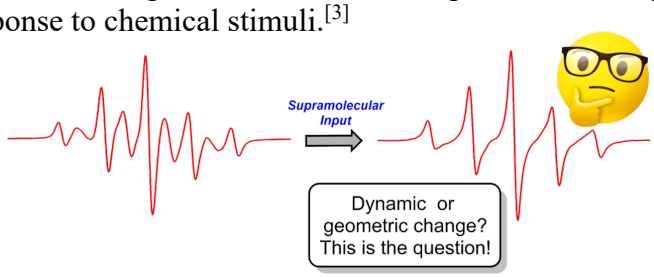
[a]Department of Chemistry "Giacomo Ciamician", Alma Mater Studiorum - University of Bologna, Italy
[b]Department of Chemistry, University of Southampton, UK

Nitroxide biradicals are commonly employed to probe interactions between molecules in chemistry and biology.[1] Biradicals are particularly useful for this because the spin-spin exchange magnetic interaction between the two radical centers depends strongly on the distance between them.[2] However, the observed EPR spectral shape, from which the exchange interaction is determined, can result from different combinations of average radical-radical coupling constant, *J*, and the rate of exchange between populated states with different values of *J*. Thus, careful attention is necessary when interpreting the spectra of biradicals when they are employed as spin probes. These details are often overlooked, at least in part because it is often challenging to separate their relative importance.



To unambiguously demonstrate this principle, and so highlight the importance of more nuanced analysis, we synthetized and investigated a family of mechanically interlocked rotaxane biradicals bearing nitronyl nitroxide units at the at both axle termini as shown in the scheme.[3] Our hypothesis was that comparison of the EPR spectrum of each rotaxane with that of the corresponding non-interlocked axle would allow us to separate the effects of through bond coupling, conformational preference and rate of exchange between the available conformations. Pleasingly, our hypothesis proved to be correct; by comparing the EPR spectra of the non-interlocked axles and their rotaxane counterparts we demonstrated that, as predicted using the theoretical model suggested more than 50 years ago by Luckhurst[4], apparently similar spectra can arise in biradical systems with different average values of *J* and conformational dynamics.

In principle, threading a linear axle component bearing radical units on its termini through a macrocycle to form a rotaxane should change its conformational properties (influencing through space interactions), without significantly altering the electronic properties of the system (through bond exchange). Here we demonstrate that this hypothesis is indeed correct; by studying biradical rotaxanes in comparison to their non-interlocked axles we show in solution that the qualitative form of the EPR spectra may be the same for different combinations of *J* and rate of conformations interconversion. Not only do our results validate the theoretical model of Luckhurst, they strongly reinforce the requirement that great attention must be paid when interpreting changes in the spectra of biradicals in response to chemical stimuli.[3]



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G-Quadruplexes to the fore: towards DNA-targeting magic bullets

Daniela Montesarchio

Department of Chemical Sciences, University of Naples Federico II, Via Cintia, 21, I-80126 Naples (Italy)

In the context of precision medicine, DNA is considered as the main privileged target. However, the search for potential drugs selectively binding specific genomic regions is still one of the most challenging tasks, considering the high structural homogeneity of duplex DNA.
In contrast, DNA G-quadruplexes (G4s) exhibit a remarkable polymorphism, with a large variety of different architectures and peculiar foldings, very promising for the design of high affinity ligands, discriminating duplex DNA.[1] Then, in addition to the different unimolecular conformations which guanine-rich oligonucleotides (ODNs) can adopt, consecutive G4 monomers can also form different multimers, *i.e.* higher-order aggregates consisting of adjacent G4 monomers interacting *via* the loops or π-π stacking, *e.g.* those of the telomeric DNA 3'-overhang consisting of tens of TTAGGG repeats.[2]
From a biological point of view, the location of guanine-rich sequences in genomes is non-random, with putative G4-forming tracts found in functional and highly conserved human, as well as viral, genomic regions, *e.g.* those of gene promoters, telomeres and transcription factor binding sites. Changes in G4 formation/stability can deeply affect protein expression, telomerase activity and genome stability.[3] These findings confirmed that the G4s – mainly at the level of telomeres and regulatory regions of oncogenes - may be selective targets for therapeutic intervention, particularly in cancer. In detail, two main approaches have been developed as therapeutic strategies:

G4s occurring in telomeres or oncogenes as prospective targets for cancer treatment[4];
synthetic G4-forming ODNs acting as aptamers to recognize cancer-related proteins[5].

In this field, we studied: *i*) cancer-related G4-forming aptamers, natural or modified, targeting VEGF-A[6] and nucleolin[7,8]; *ii*) several small molecule libraries as selective ligands of G4s in anticancer therapy[9-12]. The G4-CPG assay[13], an affinity-chromatography-based method, allowed identifying, for each investigated family, the best candidates, then analyzed in solution in their interaction with G4- and duplex-forming ODNs and in their antiproliferative activity on cancer and non-cancer cells.

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Nanocarbon-based Hybrid Materials as Efficient and Sustainable Heterogeneous Catalysts

Francesco Giacalone[a]

[a] *Department of Biological, Chemical and Pharmaceutical Sciences and Technologies, University of Palermo, Viale delle Scienze, Ed. 17 90128 Palermo (Italy)*

Nowadays, nanocarbons such as fullerene, nanotubes, graphene, nanohorns etc. are emerging as useful platforms in the preparation of last generation nanocatalysts,[1] due to a series of characteristics which include high chemical inertness, thermal stability and mechanical resistance, high surface area along with a lightness that other conventional materials cannot match. Carbon nanoforms are nanoobjects with well-defined structure and dimensions often displaying sharp size distribution, which allow for a homogeneous dispersion of the functionalities and active sites all over their surface, allowing obtaining reproducible hybrids with reproducible properties.

In the last recent years, our research group has investigated the use of different nanocarbons as support for anchoring catalytic moieties directly or for covalently linking dendrimers and polymers for the stabilization of metal nanoparticles (Figure 1). One of our main goal is the functionalization of carbon nanoforms by means of radical polymerization, that represents a very efficient strategy both in terms of atom economy and for the limited production of waste due to the excellent yields and high functionalization degree of the so-obtained hybrids.

In such a way, the resulting hybrids have been successfully employed as recyclable nanocatalysts in organocatalysis[2] (oxidation of alcohols, Knoevenagel reaction, fixation of CO_2), as well as in organometallic catalysis[3] (Suzuki and Heck reaction) showing in some case synergistic effect or enhanced performances compared to other supported catalysts.

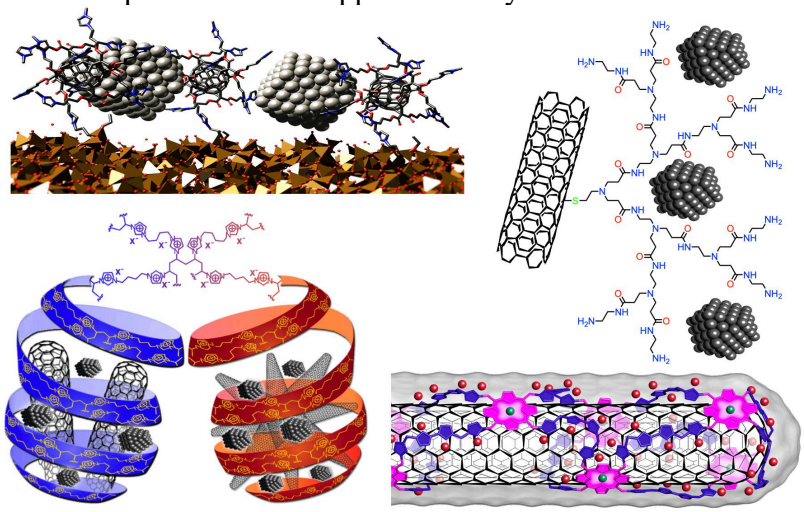

Figure 1. Cartoon of nanocarbon-based hybrid catalysts

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The art of Process Development in API manufacturing

Jacopo Roletto[a], Paolo Paissoni[a], Alessandro Barozza[a]

[a] *Procos S.p.A. (Cameri - NO)*

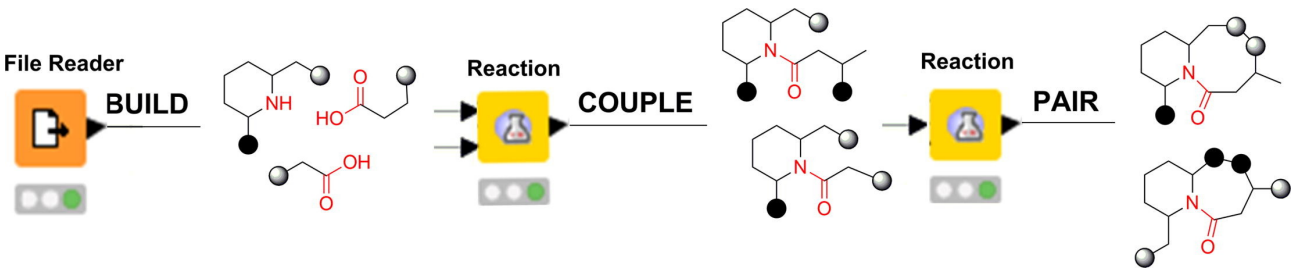
A different perspective of the Process Development activities where main focus is not the ability to synthesize the Active Pharmaceutical Ingredient but to avoid the formation of many other molecules called "impurities" is discussed. Like an artist who precisely chisels away from the marble block all superfluous material to get his sculpture, the process chemist precisely sets up a manufacturing process to assure high quality of the API controlling all impurities at extremely low level. Besides trivial impurities simply coming from starting materials, for some "side reaction" impurities a wide comprehension of the chemical mechanism combined with a multidisciplinary approach including analytical development and chemical engineering competences is fundamental to reach the proper control. Cases studies of process development involving innovative thinking will be reported

Combining Diversity-Oriented Synthesis and chemoinformatics to generate small molecules libraries

Elena Lenci, Andrea Trabocchi

Dipartimento di Chimica "Ugo Schiff", Università degli Studi di Firenze, Via della Lastruccia 13, 50019, Sesto Fiorentino (FI), Italia

Small molecule libraries are a well-established tool for the identification of new hit compounds. In both virtual and experimental libraries, the structural complexity and diversity of library members is a crucial factor in increasing the chance of a successful outcome in the screening campaign. In this context, Diversity-Oriented Synthesis has proven to be very effective, as the compounds generated are structurally complex and differ not only for the appendages, but also for the molecular scaffold. Libraries developed around privileged scaffolds are particularly relevant, as they can bring drug-like properties in the final compounds. In this context, lactams stand out as a class of privileged compounds, as they show a broad variety of potential therapeutic applications, including cancer, diabetes and infectious diseases. In our research group, we have been focusing the attention in the preparation of sp^3-rich lactam scaffolds by applying diversity-oriented couple/pair process, particularly those that can be used as peptidomimetic compounds [1]. For examples, the synthesis of morpholin-3-one derivatives using the Castagnoli-Cushman reaction has allowed for the discovery of novel BACE1 inhibitors. Also, we reported the chemoinformatic analysis of beta-, gamma-, delta- and epsilon-lactams present in databases of approved drugs, natural products, and bioactive compounds from the large public database ChEMBL, identifying the main biological targets in which the lactams have been evaluated [2]. Finally, we automated the design of a virtual library of lactams by applying a Diversity-Oriented Synthesis strategy called Build/Couple/Pair, in order to generate lactams that are not represented in the known lactam chemical space [3]. The assessment of the drug-like and lead-like properties of the enumerated lactams provide the valence of this novel *in silico* designed library for medicinal chemistry applications.



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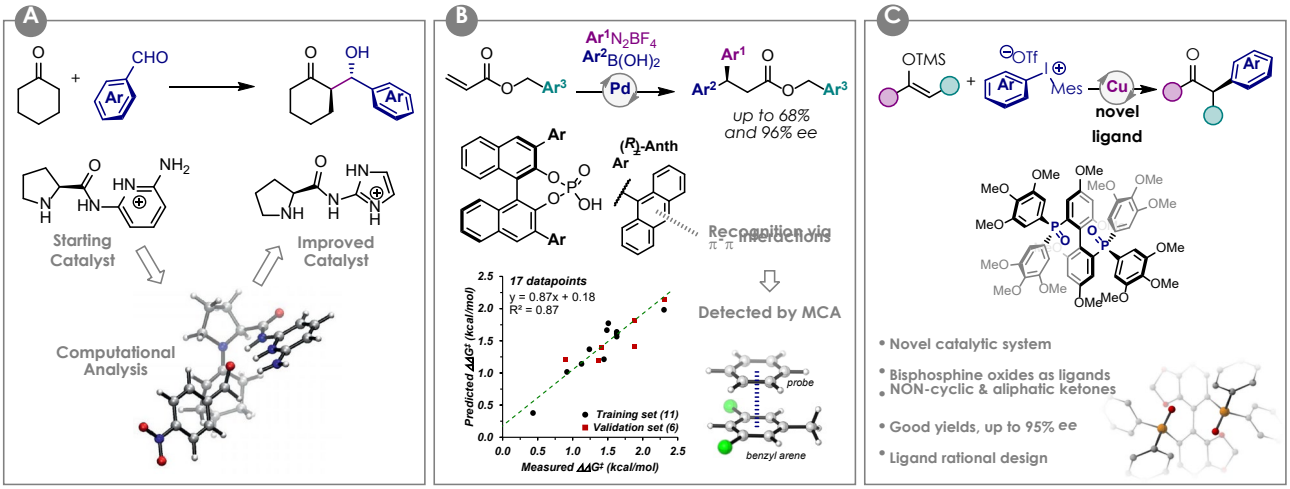
Catalyst Design via Computational Means: Correlations Bridge Experiments and Calculations

Manuel Orlandi[a]

[a]*Department of Chemical Sciences, University of Padova, via Marzolo 1, 35131 Padova.*

The development and optimization of new enantioselective catalytic transformations can be a challenging task. This is generally achieved via extensive reaction screening based on empiricism (trial-and-error) or with occasional systematic approaches such as Design of Experiments or High Throughput Screening. Contextually, mechanistic analyses are typically performed at the end of the optimization process, with computational studies being a supplement for further refinement of chemical understanding. However, more recently, new strategies have been devised that simultaneously interrogate the reaction mechanism and identify key features for the rational design of improved catalysts. Among these, Multidimensional Correlation Analysis (MCA) rely on the establishment of mathematical relationships of the experimental reaction outcome (e.g. enantio-, regio-, and chemo-selectivity) as a function of calculated physical organic molecular descriptors.[1] By this approach, experiments and calculations are linked and provide both mechanistic understanding and performance prediction.

In this communication, the use of classical computational approaches for the optimization of an organocatalytic reaction with a known mechanism will be discussed first (Figure A).[2,3] Then, a complex enantioselective Pd-catalyzed reaction will be presented.[4] In this case, conclusions concerning the reaction stereochemical model were drawn thanks to the unprecedented combination of classical TS analysis and MCA (Figure B). Finally, it will be shown how MCA has been successfully used for the rational optimization of an enantioselective Cu-catalyzed reaction for which the mechanism was not known and classical TS analysis could not be performed (Figure C).[5]



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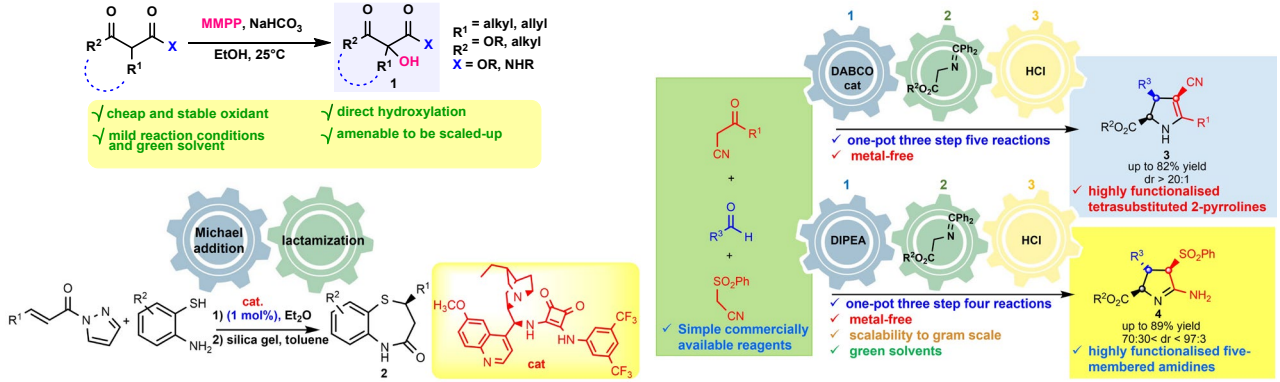
POWERFUL STRATEGIES TO FUNCTIONALIZED MOLECULES IN ONE-POT, MILD CONDITIONS AND BENIGN SOLVENTS

Sara Meninno

University of Salerno Via Giovanni Paolo II 132 – 84084 Fisciano (Italy)

One of the current challenges faced by the scientific community is to reconcile the pressing need to develop efficient and sophisticated chemical processes, to access functionalized and complex molecules, with the limited ability of our planet to absorb pollution. A solution consists in the design of new processes to avoid the use of scarce precious metals, using cheap organic promoters and reagents of low toxicity, high stability to air and moisture, and working in green solvents under mild and less hazardous reaction conditions.[1] In this direction, recently our group reported a mild and convenient protocol for the first direct α-hydroxylation of α-substituted malonates, β-ketoesters, and β-ketoamides via the Rubottom oxidation by cheap and stable oxidant MMPP, which proceeds at room temperature in EtOH as green solvent (Scheme 1).[2]

One-pot and tandem methodologies are highly attractive considering their advantages in minimizing waste production while avoiding purification or separation of intermediates. Over the years, our group has been focusing on the development of organocatalytic one-pot methodologies for the stereoselective synthesis of differently functionalized heterocyclic scaffolds.[3] In particular, considering the prominent role played by nitrogen-containing heterocycles in the fields of natural products, market drugs, agrochemicals and dyes, we recently paid attention to the design of one-pot and cascade processes to easily access novel *N*-unprotected-tetrasubstituted *trans*-2-pyrrolines **3** and amidines **4** starting from commercially available reagents and exploiting fundamental consecutive organic reactions (5 or 4 steps) in benign solvents (Scheme 1).[4] In a similar way, the first enantioselective synthesis of popular drugs benzothiazepines **2** has been realized, minimizing the number of operations despite the number of transformations involved, paving the way for the concise preparation of the antidepressant drug (*R*)-(-)-thiazesim in an extremely easy and more sustainable way.[5]



Scheme 1

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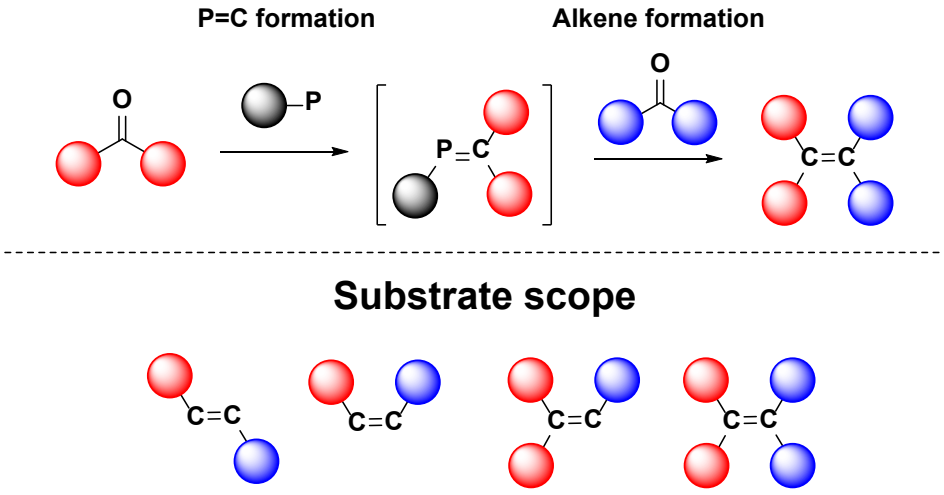
Olefins from carbonyls –

Development of new phosphorus-based cross-coupling reactions

Nicolas D´Imperio,[a] *Anna Arkhypchuk,*[a] *Sascha Ott*[a]

[a]*Department of chemistry Ångström, Uppsala University, Uppsala, Sweden*
nicolas.dimperio1991@gmail.com

Phosphaalkenes have been known for several decades. Since their discovery,[1] phosphaalkenes have been mainly used in coordination and polymer chemistry.[2] Only recently we have been able to convert differently substituted phosphaalkenes into olefins, with the net result of creating new carbonyl cross-coupling olefinations. In this presentation, we show our procedures in which two aldehydes have been selectively coupled to *E* and *Z* 1,2-disubstited alkenes,[3] trisubstituted olefins have been obtained by the coupling of a ketone and an aldehyde,[4] and ultimately tetrasubstituted olefins have been formed from two ketones.[5]



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Advanced Functional Organic-Inorganic Hybrid (Nano)Materials: from Theranostics to Organic Electronics and Additive Manufacturing

Mirko Maturi[a]

[a] *Department of Industrial Chemistry "Toso Montanari", University of Bologna*

During my PhD studies, I worked the synthesis and surface modification of gold nanorods (GNRs) for applications as theranostic agents able to combine the diagnostic properties of photoacoustic imaging applied to near-infrared absorbing plasmonic nanostructures with the therapeutic effects of chemotherapy and photothermal therapy.[1] Besides, an application of chemometrics based on multivariate analysis is showed on photoacoustic imaging data obtained with PEGylated gold nanorods as contrast agents.[2]
In a second part, I will present the implementation of ceramic ($BaTiO_3$) nanoparticles coated with a hydrophilic organic ligand and formulated in piezoionic gels to produce a pressure sensor.[3] In a further work, a synthetic lipophilic ligand is attached to $BaTiO_3$ nanoparticles, allowing for its homogeneous dispersion in PDMS matrices to study the piezoelectric behaviour of the nanocomposites. Finally, I describe the possibility to employ surface stabilized ultrathin gold nanowires (AuNWs) dispersed in low concentration in thin PDMS film as capacitive strain sensors.
In the last chapter, I describe the synthesis and formulation of a novel and biobased photocurable resin for stereolithography which is functionalized with phosphorescent iridium complexes able to provide efficient light emission even at very low concentrations.[4]

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Exploring the therapeutic potential of L-deoxyiminosugars in rare diseases

Anna Esposito,[a] Maria De Fenza,[a] Eliana De Gregorio,[b] Daniele D'Alonzo,[a] Annalisa Guaragna[c]

[a] Dept. of Chemical Sciences, University of Naples Federico II, Via Cintia, 80126 Naples, Italy; [b] Dept. of Molecular Medicine and Medical Biotechnologies, University of Naples Federico II, Via S. Pansini, 80131 Naples, Italy; [c] Dept. of Chemical, Materials and Production Engineering, University of Naples Federico II, P. V. Tecchio 80, 80125 Naples, Italy

Within the class of glycomimetics, the unnatural L-iminosugars, non-superimposable mirror images of the natural D-iminosugars, represent promising therapeutic agents as alternative to their D-counterparts [1]. Indeed, even though D-iminosugars have been identified as therapeutic candidates for several medical purposes including malignancies, viral infections and rare diseases, the progression of these molecules to marketed drugs has been often hampered by their poor *in vivo* selectivity [2]. Conversely, the less explored L-iminosugars have shown higher selectivity often acting as inhibitors or enhancers of some glycosidases and glycosyltransferases surpassing in some cases the pharmacological potential of their D-enantiomers [1]. Based on these findings, herein we report a synthetic route aimed to the preparation of novel *N*-alkyl-L-deoxyiminosugars and cholesterol–iminosugar conjugates (**Figure 1**) to explore the role of both the chirality and lipophilicity on the therapeutic potential of iminosugars in the treatment of Cystic Fibrosis (CF), a rare disorder characterized by chronic inflammation and polymicrobial infections [3].

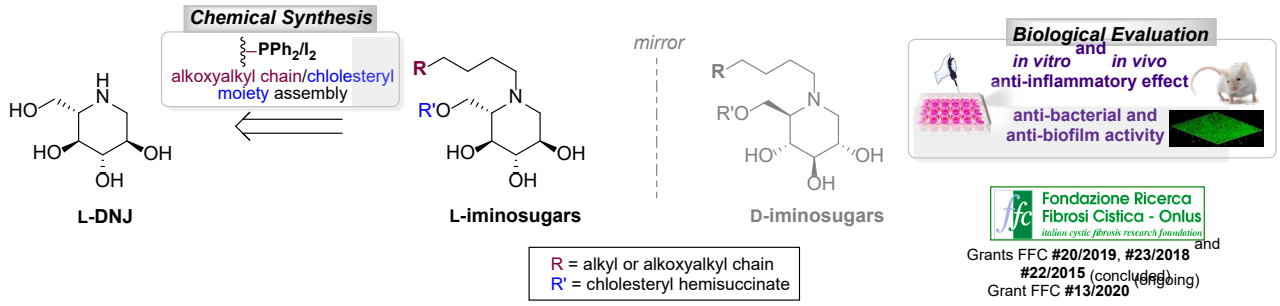

Figure 1. L-deoxyiminosugars as dual acting drugs in CF treatment.

The established PS-TPP/I_2 activating system was herein exploited for the assembly of the alkyl chains on the unnatural L-DNJ [4], as well as, for the conjugation of the iminosugars with the cholesteryl moiety enabling to obtain the target compounds in a one-pot procedure [5]. Biological assays revealed a promising *in vitro* and *in vivo* anti-inflammatory activity of the syntesized compounds [4]. On the other hand, *N*-alkyl L-deoxyiminosugars also exhibited an interesting *in vitro* antibacterial and antibiofilm activity [6] pointing out the potential of these glycomimetics to act as dual acting drugs in CF treatment as both anti-inflammatory and antibacterial agents.

This work was funded by Italian Cystic Fibrosis Research Foundation grants number FFC #20/2015, #23/2018, #20/2019 and by the currently ongoing grant #13/2020 (adopted by Gruppo di Sostegno FFC di Milano Magenta, Delegazione FFC di Treviso Montebelluna, Delegazione FFC di Imola Romagna, Gruppo di Sostegno FFC di Crotone "Vita in te ci credo", Delegazione FFC di Monterotondo Roma).

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New synthetic methods enabled by photochemistry and electrochemistry in flow.

Gabriele Laudadio[a], Timothy Noël[b]

[a]Department of Chemistry, Scripps Research, 10550 North Torrey Pines Road, La Jolla, California 92037, United States; [b]Flow Chemistry Group, Van't Hoff Institute for Molecular Sciences(HIMS), University of Amsterdam, Science Park 904, 1098 XH, Amsterdam, The Netherlands.

The employment of traceless reagents like photons or electrons in synthetic organic chemistry has recently witnessed a renaissance, since these techniques allow more selective, sustainable, and effective transformations. [1,2] However, the scale-up of photochemical or electrochemical reactions may be difficult because of mass transfer or light penetration issues. These limitations can be overcome by combining these approaches with continuous-flow technology, which creates a safe and reliable platform for scalable, fast, and efficient processes. [3,4]

Regarding photochemistry, decatungstate-catalyzed hydrogen atom transfer (HAT) reactions in continuous-flow were developed, namely i) a C(sp3)–H oxidation employing oxygen as sole oxidant, [5] ii) a room temperature, photochemical alkylation of Michael acceptors with volatile gases. [6]

Regarding electrochemistry, the continuous-flow technology was adopted for the synthesis of valuable functional groups from inexpensive commodity chemicals, leading to reliable electrochemical protocols to obtain sulfonamides, [7] sulfonyl fluorides [8] and substituted aziridines. [9]

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Supramolecular hydrogels from a heterochiral tripeptide and a carbon nanostructure

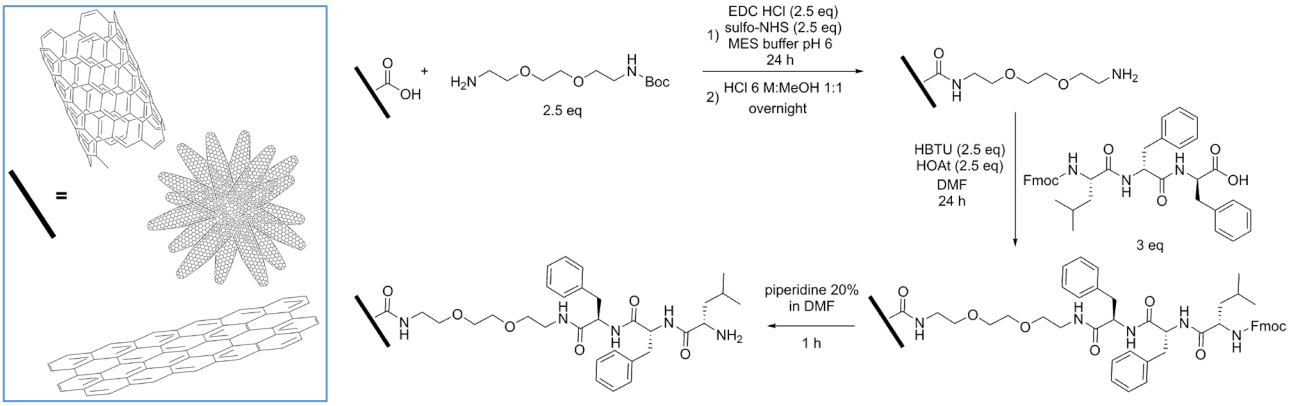
Simone Adorinni[a], *Petr Rozhin*[a], *Alessandro Beltram*[a], *and Silvia Marchesan*[a]

[a] *Dip. di Scienze Chimiche e Farmaceutiche, Università di Trieste, Via L. Giorgieri 1, 34127 Trieste, Italy*

Peptides are attractive building blocks for supramolecular hydrogels.[1] In particular, simple tripeptides are advantageous thanks to the simplicity and low cost of their preparation, inherent biocompatibility, and biodegradability. Thanks to these properties they can be used in a wide range of fields such as drug-delivery, tissue-engineering, bio-sensing, and bio-imaging. Moreover, the capability of these materials could be significantly expanded by adding carbon nanostructures to enhance their mechanical features, and to introduce a large variety of additional properties to attain *smart* materials, which change in response to physico-chemical stimuli.[2]

Supramolecular hydrogels have been prepared through the self-assembly of the uncapped heterochiral tripeptide Leu-^{D}Phe-^{D}Phe in the presence of one of three different oxidized carbon nanomaterials (*i.e.*, multi-walled carbon nanotubes or CNTs, single-walled carbon nanohorns or CNHs, and graphene oxide or GO), as 1D (CNTs), 2D (GO), or 3D (CNHs) model structures.[3] GO and CNTs showed a good level of interaction with peptide fibrils, leading to homogenous hydrogel networks. Conversely, CNHs tended to self-aggregate, yielding a heterogeneous material. Interestingly, hydrogels based on CNTs acquired self-healing ability, which was rationalized with the favourable interactions between peptides and CNTs, as the former coated the latter, and both peptide fibrils and CNTs displayed analogous anisotropic morphology leading to a highly interconnected network.

To gain deeper insights into the self-healing behaviour and the importance of carbon nanomorphology relative to chemical interaction with the peptide, in this work the tripeptide Leu-^{D}Phe-^{D}Phe was covalently linked on the surface of the three oxidized nanomaterials (Scheme 1) prior to assembly in the presence of free peptide. The systems are being characterized with several techniques, such as thermogravimetric analysis (TGA), Raman and infrared spectroscopy, rheology, transmission electron microscopy (TEM), and circular dichroism, to reveal fine details that will ultimately allow an optimized design of *smart* hydrogels with enhanced properties.



Scheme 1: Reactions for covalent functionalization of oxidized carbon nanomaterials.

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Targeting GRP receptor: from the characterization of bombesin/GRP-R interaction to the design, synthesis and preliminary biological characterization of new non-peptide bombesin antagonists

*Alessandro Palmioli,[a,b] Gabriella Nicolini,[b,c] Farida Tripodi,[a] Alexandre Orsato,[a,d] Cecilia Ceresa,[b,c] Elisabetta Donzelli,[b,c] Martina Arici,[a] Marcella Rocchetti,[a] Barbara La Ferla,[c] and Cristina Airoldi [a,b]**

[a]*Department of Biotechnology and Biosciences, University of Milano - Bicocca, P.zza della Scienza 2, 20126, Milan, Italy;* [b]*Milan Center for Neuroscience, University of Milano-Bicocca, P.zza dell'Ateneo Nuovo 1, 20126, Milano, Italy;* [c]*School of Medicine and Surgery, Experimental Neurology Unit, University of Milano - Bicocca, Via Cadore 48, 20900 Monza, MB, Italy;* [d]*Departamento de Química, CCE, Universidade Estadual de Londrina, CEP 86057-970 Londrina, Paraná, Brazil.*

We report the rational design, synthesis, and *in vitro* preliminary evaluation of a new small library of non-peptide ligands of Gastrin Releasing Peptide Receptor (GRP-R), able to antagonize its natural ligand bombesin (BN) in the nanomolar range of concentration.
GRP-R is a transmembrane G-protein coupled receptor promoting the stimulation of cancer cell proliferation. Being overexpressed on the surface of different human cancer cell lines, GRP-R is ideal for the selective delivery to tumor cells of both anticancer drug and diagnostic devices. What makes very challenging the design of non-peptide BN analogues is that the 3D structure of the GRP-R is not available, which is the case for many membrane-bound receptors. Thus, the design of GRP-R ligands has to be based on the structure of its natural ligands, BN and GRP.
We recently mapped the BN binding epitope by on-cell STD-NMR [1] and then we exploited the same spectroscopy, combined with MD, to define BN conformation in proximity of biological membranes, where the interaction with GRP-R takes place [2]. The gained structural information was used to identify a rigid *C*-galactosidic scaffold able to support pharmacophore groups mimicking the BN key residues' side chains in a suitable manner for binding to GRP-R [2].
Our BN antagonists represent hit compounds for the rational design and synthesis of new ligands and modulators of GRP-R. The further optimization of the pharmacophore groups will allow to increase the biological activity. Due to their favorable chemical properties and stability, they could be employed for the active receptor-mediated targeting of GRP-R positive tumors.

Acknowledgement
The authors acknowledge AIRC for funding My First AIRC project 17030 - Targeting of Gastrin-Releasing Peptide receptor expressing tumors: NMR characterization of Bombesin/GRP-R interaction.

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Chiral diketopyrrolo[3,4-*c*]pyrrole dyes with remarkable chiroptical properties in thin films

Gianluigi Albano,[a] *Andrea Taddeucci,*[b,c] *Francesco Zinna,*[b] *Maria Annunziata M. Capozzi,*[a] *Gennaro Pescitelli,*[b] *Angela Punzi,*[a] *Gianluca Maria Farinola,*[a] *Lorenzo Di Bari*[b]

[a] *Dipartimento di Chimica, Università degli Studi di Bari "Aldo Moro", Via E. Orabona 4, 70126 Bari, Italy;*
[b] *Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via G. Moruzzi 13, 56124 Pisa, Italy;*
[c] *Diamond Light Source, Ltd., Chilton, Didcot OX11 0DE, United Kingdom.*
e-mail: gianluigi.albano@uniba.it

Chiral organic π-conjugated systems have recently known a significant development as semiconducting active layers for optoelectronic and nanotechnology applications. In fact, chirality is an appealing tool for controlling the structural organization of π-conjugated molecules constituting the active layers of the devices;[1] moreover, it opened the way to highly specialized applications exploiting the interaction with circularly polarized (CP) light.[2] Therefore, a current research goal is to obtain thin films of chiral organic materials with high discrimination of CP-light in absorption (electronic circular dichroism, ECD) or in emission (circularly polarized luminescence, CPL).
The experimental ECD signal of thin films is the sum of two main contributions: i) the intrinsic isotropic component of circular dichroism, termed CD_{iso}, which is invariant upon sample orientation; ii) the LDLB, arising from the combined effect of linear dichroism (LD) and linear birefringence (LB), which is invariant upon sample rotation around the optical axis of spectropolarimeter, but it inverts the sign by sample flipping.[3] Interestingly, thin films displaying a substantial LDLB contribution have been only rarely reported in the literature to date.[4-6]
Here we synthesized two new 1,4-diketo-3,6-dithienylpyrrolo[3,4-*c*]pyrrole dyes, functionalized with inexpensive chiral groups from natural sources (*i.e.*, citronellyl moieties) through 1,2,3-1*H*-triazole scaffolds conjugated as terminal rings to the central core (**Figure 1**), studying their chiroptical features in thin films. Although they only differ in the achiral side chains (*n*-octyl *vs.* TEG), we surprisingly found very different properties: a substantial CD_{iso} in one case, a very large LDLB in the other. The effect of deposition technique and post-deposition operations will be also evaluated.

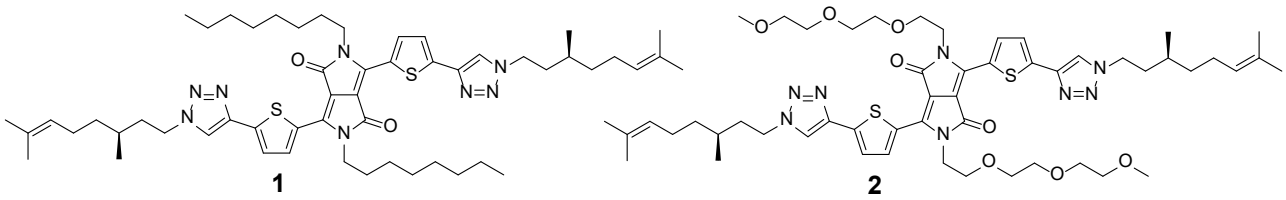

Figure 1. Chemical structure of chiral diketopyrrolo[3,4-*c*]pyrrole dyes studied in this work.

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Coupling interrupted Fischer and multicomponent Ugi-Joullie' to chase chemical diversity: from batch to sustainable flow synthesis of peptidomimetics.

A.I. Alfano[a], H. Lange [b] and M. Brindisi [a]*

[a] *Department of Pharmacy, Via Domenico Montesano, 84, Naples;* [b] *Department of Earth and Environmental Sciences, Piazza della Scienza 1 e 4, I-20126, Milan*

Organic synthesis is an enabling science with immense impact in many areas of research, including modern medicine and biology. The need for sustainable and green research to reduce the global carbon footprint leads to the emerging importance of "green chemistry".[1] In this frame, fFlow chemistry processes are particularly useful, since they can potentially conjugate the need for increased space-time yields with sustainability requirements. [2] In our quest towards the implementation of flow chemistry methodologies for the synthesis of privileged scaffolds,[3] we reported the application of this technology-based greener synthesis approach to the formation of privileged (spiro)indolenine and (spiro)indoline frameworks [4]. Our flow chemistry protocol for the synthesis of 3,3-disubstituted indolenines is chemically based on interrupted Fischer indolisation reactions. The telescoped approach allowed generation of a library of indolenines and indolines with limited solvent consumption and work-up procedures, and required minimum operator input. This newly developed protocol also displays the potential to turn into an effective coupling point for additional flow reactions for multistep syntheses.

Accordingly, we sought to interrogate the outcome of spiroindolenines as substrates for the generation of peptidomimetic frameworks through Ugi-type multicomponent reactions (MCR) reactions. Isocyanide-based MCR, are widely established as useful tools for creating novel peptidomimetic structures, owing to the fact that diamide "peptoid" motifs are inherently created in the course of these reactions.[5] Upon a preliminary batch investigation, batch-to-flow transition was implemented. The developed protocol is of general utility for the synthesis of peptidomimetic frameworks in a safe, environmentally friendly, and cost-effective mode that additionally could be amenable to larger scale manufacturing.

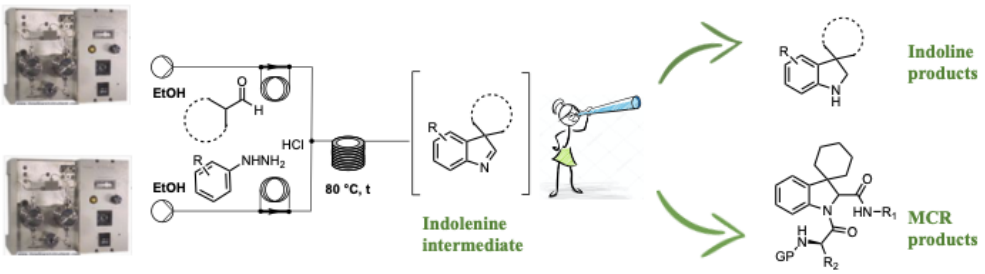

Figure 1. Telescoping approach.

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Physicochemical Characterization of two Cationic Copolymers Effective on Etoposide-Sensitive and Resistant Neuroblastoma Cells

Silvana Alfei [a,], Barbara Marengo [b], Giulia Elda Valenti [b] and Cinzia Domenicotti [b]*

[a] *Department of Pharmacy, University of Genoa, Viale Cembrano, 16148 Genoa, Italy;* [b] *Department of Experimental Medicine (DIMES), University of Genova, Via Alberti L.B., 16132 Genoa, Italy*

New therapeutic agents as antibiotics and chemotherapeutics capable of inducing cytotoxic effects and employed in the treatment of lethal human diseases as cancer and infections need also to circumvent the increasing chemoresistance, which limits their action. Natural and synthetic cationic peptides and polymers have given appealing results both in microbiology, and in the oncological field, where they resulted effective against several tumors, including human neuroblastoma (NB) [1,2]. To this end, we recently synthetized two polystyrene-based cationic copolymers (P5 and P7, Figure 1a and 1b), which proved a potent ROS-related cytotoxicity against both etoposide-sensitive (HTLA-230) and -resistant (HTLA-ER) NB cells [3]. Interestingly, the cytotoxic effects of P5 and P7 were even higher on HTLA-ER cells, thus proving that they could be promising template macromolecules for the development of new chemotherapeutic agents able to fight NB chemoresistance.

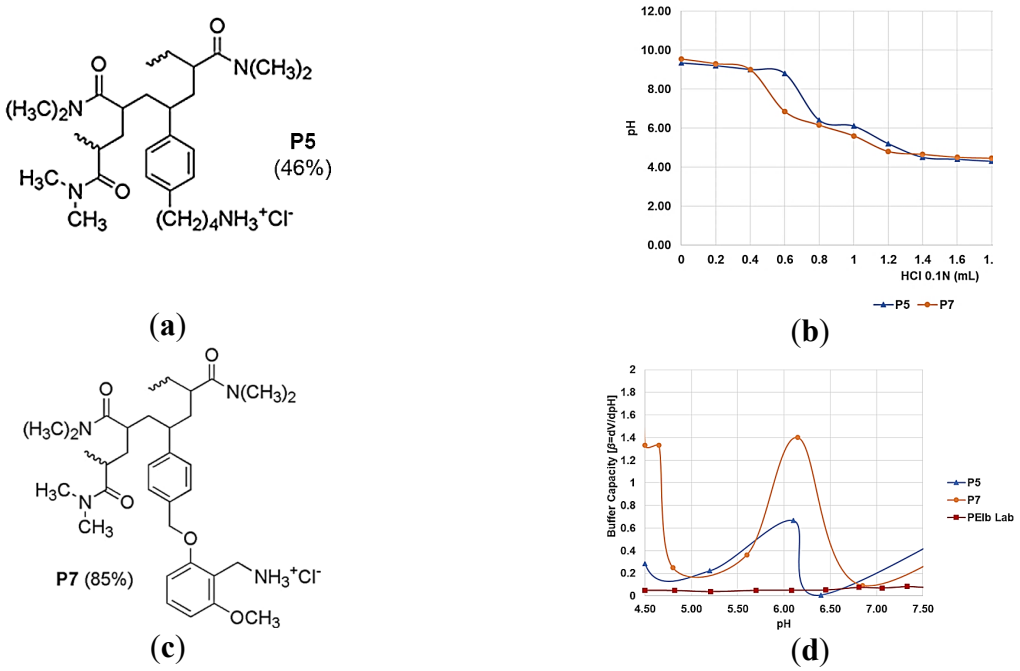

Figure 1. Structure of copolymer P5 (a) and P7 (c). Potentiometric titration curves (b) and buffer capacity curves (d) of P5 and P7.

Water-solubility, surface charge, protonation profile in the physiological pH range, Z-potential, polydispersity index, buffer capacity, and particles size are pivotal features for the feasibility of biomedical application of new bioactive macromolecules. In our poster, in addition to show the spectroscopic characterization of P5 and P7, we have reported their complete physicochemical characterization. As an example, Figure 1 shows the potentiometric titration curves (b) of P5 and P7, which were used to determine their protonation profile (not shown) and buffer capacity curves shown in Figure 1d, and compared to that of branched PEI b, a standard reference cationic polymer.

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INVESTIGATION OF THE CHEMICAL STRUCTURE OF POLYSACCHARIDES PRODUCED BY *LACTOBACILLUS REUTERI*

Samantha Armiento,[1] Antonio Molinaro,[1] Ravi Verma,[2] Sin-Hyeog Im,[3,4] Cristina De Castro[4]

[1]Università degli studi di Napoli, Dipartimento di Scienze Chimiche, 80126 Napoli (NA)
[2]ImmunoBiome Inc. Pohang, Korea
[3]Pohang University of Science and Technology (POSTECH), Korea
[4]Università degli studi di Napoli, Dipartimento di Agraria, Portici (NA)

Lactobacillus reuteri is a pro-biotic Gram-(+), facultative anaerobic bacterium, that colonizes mostly the gastro-intestinal human tract. The abundance of *L. reuteri* varies among different individuals. Notably, the decrease of *L. reuteri* in humans in the past decades is correlated with an increase in the incidences of inflammatory diseases over these periods. It is a bacterium of considerable interest as it is able to benefit the host organism thanks to several effects [1]. Probably, many biological activities of bacteria are mediated by a complex mixture of different carbohydrate polymers that coat their surfaces or are released into the extracellular media [2]. In general, Lactobacillus strains can synthesize capsular polysaccharides (CPS), which are important substances that exhibit many important technological as well as health-promoting properties [3]. In this work, the capsular material from *Lactobacillus reuteri* has been purified and analyzed and our results demonstrate that the coat of this bacterium consists of a heterogeneous mixture of three types of glycans, a glucogalactan, a galactan, and teichoic acids. The identification of the three glycans was possible after extensive purification steps which included both size exclusion and ion exchange chromatography, and that led to the isolation of the teichoic acid in pure forma and to a mixture of the two neutral polysaccharides.

Each sample was then extensively characterized by 2D NMR and the structural data collected were counterchecked by chemical analysis [4].

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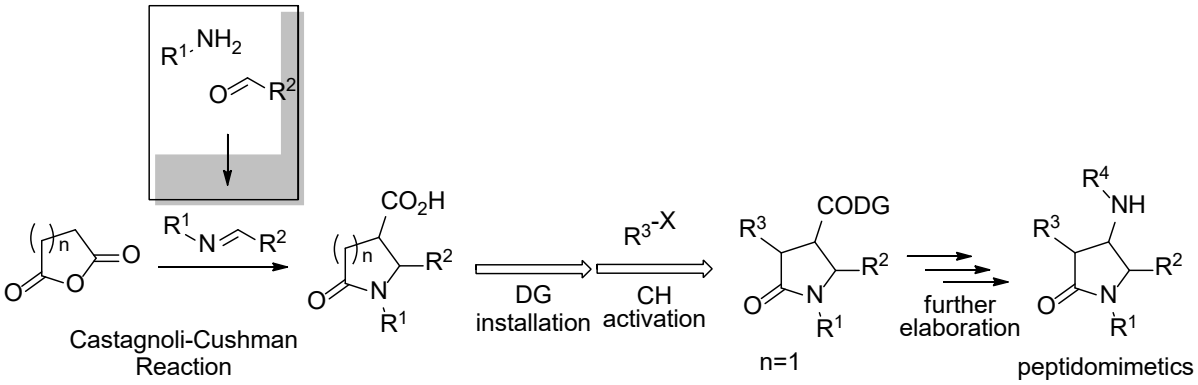
Synthesis of cyclic amino acids via C-H functionalization for the development of peptidomimetics

Lorenzo Baldini, Andrea Trabocchi

Dipartimento di Chimica "Ugo Schiff", Università degli Studi di Firenze, via della Lastruccia 13, 50019 Sesto Fiorentino, Firenze

The possibility to make a precise nonacidic C-H bond reacting allows to generate a site of functionalization otherwise unexploitable, and this is obviously of great interest for organic chemists. Unsurprisingly, selective transition metal-assisted C(sp^2/sp^3)-H activation reactions have been set up on a wide range of substrates [1-2], including amino acids and derivatives [3-5]. To achieve selectivity, a Directing Group (DG) is often used, due to its ability to chelate metal ions, which can be exploited for bringing the catalytic metal centre closer to the C(sp^2/sp^3)-H bond of interest and making the distance as the distinctive parameter [6]. In this view, we aimed at functionalizing heterocyclic amino acid precursors coming from multicomponent processes (MCRs), such as the Castagnoli-Cushman reaction, taking advantage of the COOH handle coming out from the reaction to install suitable DG for the functionalization of the heterocycle. We developed a range of compounds containing aryl substituents that may be further processed to achieve novel constrained amino acids for application in peptidomimetic chemistry.



General strategy for the functionalization of an example of Castagnoli-Cushman reaction products

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New organic fluorophores for Luminescent Solar Concentrators

M. Bartolini[a,b], M. Calamante[a,b], A. Mordini[a,b], G. Reginato[a], L. Zani[a]

[a] Institute of Chemistry of Organometallic Compounds (CNR-ICCOM), Via Madonna del Piano 10, 50019 Sesto Fiorentino, Italy; [b] Department of Chemistry "U. Schiff", University of Florence, Via della Lastruccia 13, 50019 Sesto Fiorentino, Italy. E-mail: mbartolini@iccom.cnr.it

Luminescent Solar Concentrator (LSC) is an old-but-gold technology, which nowadays is rising as a promising alternative optical device for the sunlight harvest and production of energy.[1] Due to the low-priced materials and their innovative aesthetic properties, LSCs find an easy integration in architectural systems, such as roofs, windows, canopies, and greenhouse, matching the current push toward more sustainable and energy efficient structures (e.g., BIPVs, NZEBs).

The working mechanism of LSC devices focuses on trapping incident solar radiation, converting the spectrum to the wavelength band of interest, and concentrating the light by total internal reflection to the edge of the panel where a photovoltaic (PV) solar cell is attached. As consequence, the choice of the proper fluorophore is fundamental to achieve good performances. It needs to meet several criteria: broad absorption range, large Stokes shift, high fluorescence quantum yield, precise matching between dye emission wavelength and PV absorption band, good optical efficiency, and good dispersion in the host materials.[2]

Organic molecules are one of the most interesting classes of luminophores, which could largely satisfy LSC requirements. In the last years, we have been interested in the synthesis of new D-π-A organic dyes showing an intense light absorption and high versatility, due to their close relationship between molecular design and optoelectronic tunability.[3] Starting from this class of molecules, we decided to synthesize a new series of fluorophores specifically designed for LSC application, perform a complete spectroscopic characterization, and eventually build and test the actual devices.

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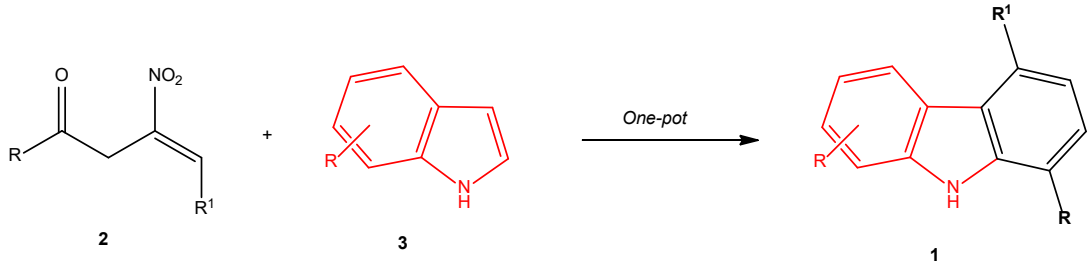
Novel one-pot synthesis of poly-substituted carbazole systems starting from functionalized nitroolefins and indoles

Benedetta Bassetti,[a], *Gabriele Lupidi*,[a] *Roberto Ballini*,[a] *Marino Petrini*,[a] *and Alessandro Palmieri*[a]

[a] *Green Chemistry Group, School of Science and Technology, Chemistry Division, University of Camerino, Via S. Agostino n. 1, 62032 Camerino (MC), Italy*

Carbazoles (**1**) constitute one of the most important class of nitrogen-containing heterocycles, largely present in a wide range of natural products and pharmaceuticals, because of their antimicrobial, anti-inflammatory, anticancer and antiviral activity.[1] Moreover, carbazoles find application in material sciences as photoconductors, light-emitting diodes (LEDs), and as components in photovoltaic devices and solar cells.[2]
For all these reasons, the interest in their chemistry has grown extensively in the last decades and considerable efforts have been devoted to streamlining their synthesis.[3]
In this context and taking into account our experience using functionalized nitroolefins,[4] we developed a new one-pot synthesis of poly-substituted carbazoles starting from β-nitro-β,γ-unsaturated-ketones (**2**) and indoles (**3**). This process is based on two consecutive steps involving an initially fluorinated solvent-promoted Friedel-Craft reaction of indoles to nitroolefins followed by an acidic and microwave assisted intramolecular cyclization, that affords the title targets (**1**).



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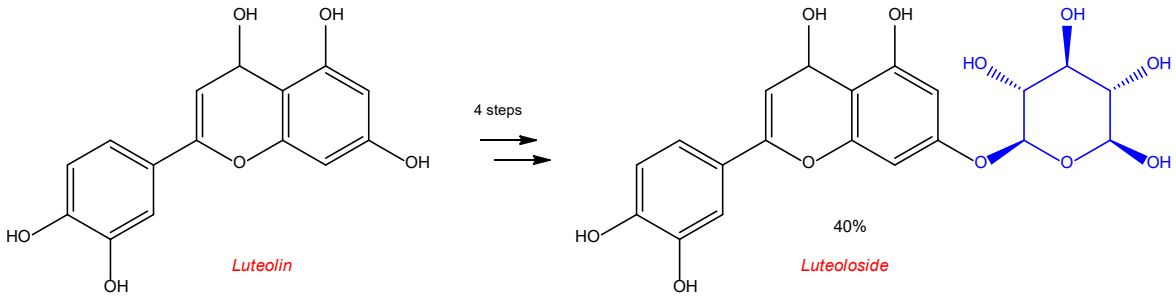
A new useful approach for the conversion of Luteolin into the glycosylated Luteoloside

Benedetta Bassetti,[a] *Roberto Ballini*,[a] *Daniele Ciceri*,[b] *Pietro Allegrini*,[b] *and Alessandro Palmieri* [a]

[a] *Green Chemistry Group, School of Science and Technology, Chemistry Division, University of Camerino, Via S. Agostino n. 1, 62032 Camerino (MC), Italy;* [b] *Indena S.p.A., Viale Ortles n.12, 20139, Milan, Italy*

Flavonoids are a pivotal class of natural products, that are ubiquitous in fruits and vegetables, constituting a fundamental component in the human diet.[1] Their importance is due to the wide number of biological effects exhibited, such as anti-oxidative, anti-inflammatory, anti-degenerative, antimicrobial and anti-carcinogenic.[2]
In this context, luteoloside seems to be one of the most promising flavonoids, however, it is mainly isolated and obtained by extraction from various plant sources and its concentration is generally lower than the other flavonoids and the presence of analogues complicates further the purification. A valuable alternative to overcome these issues can be the synthetic approach, however only few protocols are reported in literature.[3]
In order to overcome these limitations, we present a new effective conversion of luteolin into luteoloside capable to sustain in vivo bioactivity studies in terms of scale-up, and to grant also analytical standards for the quantification in food and medicinal plants. Our synthetic approach is based on four steps and provides the desired product in ~40% overall yield.



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Synthesis of fused furans derivatives starting from the ring-opening of nitrothiophenes

A. Benzi, L. Bianchi, G. Petrillo, C. Tavani*

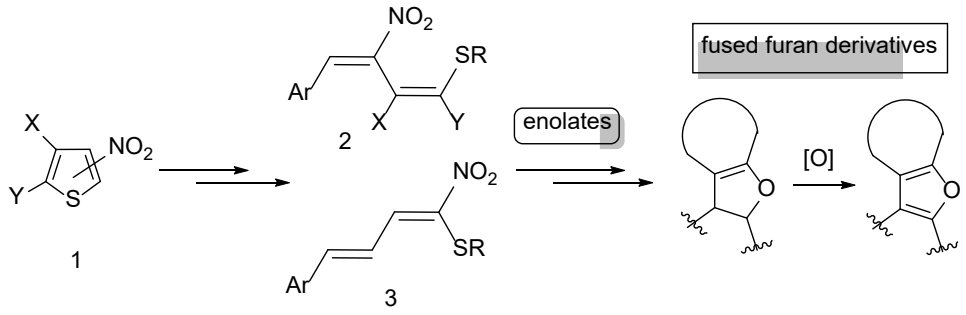
Department of Chemistry and Industrial Chemistry, University of Genova, Via Dodecaneso 31, I-16146 Genova, Italy

e-mail: alice.benzi@edu.unige.it

Exploiting the reactivity with nucleophiles of nitrobutadienes **2**,**3**, obtained from the initial ring-opening of suitably substituted nitrothiophenes **1**,[1] a wide range of heterocyclic derivatives, containing nitrogen, oxygen and sulphur, can be prepared, through ring-closing processes.[2]

The reaction between such versatile building-blocks as **2** and **3** and enolates generated *in situ* leads to highly-functionalized fused furan derivatives (Scheme), whereby the dienes behave twice al electrophiles while the enolates behave as C- and O-nucleophiles, in sequence.

Latest results will be presented.



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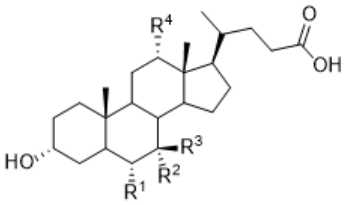
Regioselective biocatalyzed α/β inversion of Hyocholic Acid's 7-OH

S. Bertuletti,[a,b] I. Bassanini,[a] E. E. Ferrandi,[a] D. Monti,[a] S. Riva.[a]

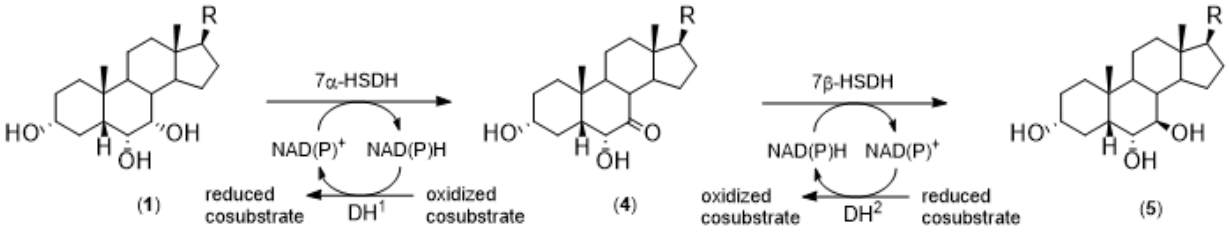
[a] *SCITEC-CNR (Istituto di Scienze e Tecnologie Chimiche "Giulio Natta"), Via Mario Bianco 9, Milano, Italy*
[b] *Università Statale di Milano, Via Mangiagalli 25, Milano, Italy*

Hyocholic acid (3α,7α,12α-trihydroxy--5β-cholan-24-oic acid, **1**) is a bile acid which can be extracted from pig gall. It might be considered as a suitable alternative to cholic acid (**2**) for the preparation of ursodeoxycholic acid (UDCA, **3**), a drug widely used for the treatment of cholestatic diseases.[1]



1: R^1=R^2=OH; R^3=R^4=H
2: R^2=R^4=OH; R^1=R^3=H
3: R^3=OH; R^1=R^2=R^4=H

In order to achieve this goal, one of the required structural changes would be the stereoinversion of the C-7 hydroxyl group. To this respect, a valuable solution might be offered by the use of hydroxysteroid dehydrogenases (HSDHs), a group of NAD(P)-dependent dehydrogenases that are able to selectively act on the hydroxylated group of the steroidal skeleton.[2] On this respect, years ago we reported on the C-7 α/β stereoinversion of differently substituted hydroxysteroids.[3] As shown in the Scheme, it was a two-steps procedure involving the regioselective oxidation with a 7α-HSDH followed by stereoselective reduction with a 7β-HSDH. With the HSDHs at disposal at that time it was possible to oxidize hyocholic acid to its 7-oxo derivative (**4**), but the subsequent reductive step failed.



Recently a search of HSDH homologues in in-house or public available (meta)genomes has allowed us to identify, clone and produce novel 7α-, 7β-, or 12α-HSDHs, which were tested as biocatalysts for the stereoselective reduction of a panel of substrates.[4] As an extension, the NAD or NADP-dependent 7β-HSDHs were tested on the 7-oxo derivative (**4**) and more than one of them were able to catalyze the desired stereoselective reduction to the 7β-derivative of hyocholic acid (**5**).

The enzymatic stereoinversion of **1** to **5** has been optimized in terms of the *in situ* enzymatic regeneration of the suitable NAD(P)(H) cofactors.

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New supramolecular fluorescent NDI-gels as bioimaging materials

Floriana Billeci,[a] Carla Rizzo,[a] Patrizia Cancemi,[b] Miriam Buttacavoli,[b] Salvatore Marullo,[a] Francesca D'Anna.[a]

[a] *Università degli Studi di Palermo, Dipartimento STEBICEF, Viale delle Scienze, Ed. 17, 90128 Palermo, Italy;*
[b] *Università degli Studi di Palermo, Dipartimento STEBICEF, Viale delle Scienze, Ed. 16, 90128 Palermo, Italy*

Supramolecular gels are widely applied in biological fields. The noncovalent nature of the interactions responsible of 3D network formation leads to useful reversible gel-sol transitions. These can be tuned by external stimuli such as p*H*, temperature, enzymes, and pressure without compromising the mechanical properties and making the systems suitable as intelligent carriers and versatile bio-agents. The proper combination of gelator and solvent is the key to tailor the system to a specific application.[1]

In this work we have designed fluorescent gelators combining emissive properties of the 1,8-naphthalimide (NDI) with the ones of alkyl ammonium salts.[2] This allowed obtaining new fluorescent materials potentially suitable for in vivo and in vitro imaging.[3] In details, the structure has been modulated varying the length of the linker (n = 2 or 3) between cation and NDI, the length of the alkyl chain on the cation (C_{12} or C_{14}) and the anion (Br or gluconate) (Figure 1).

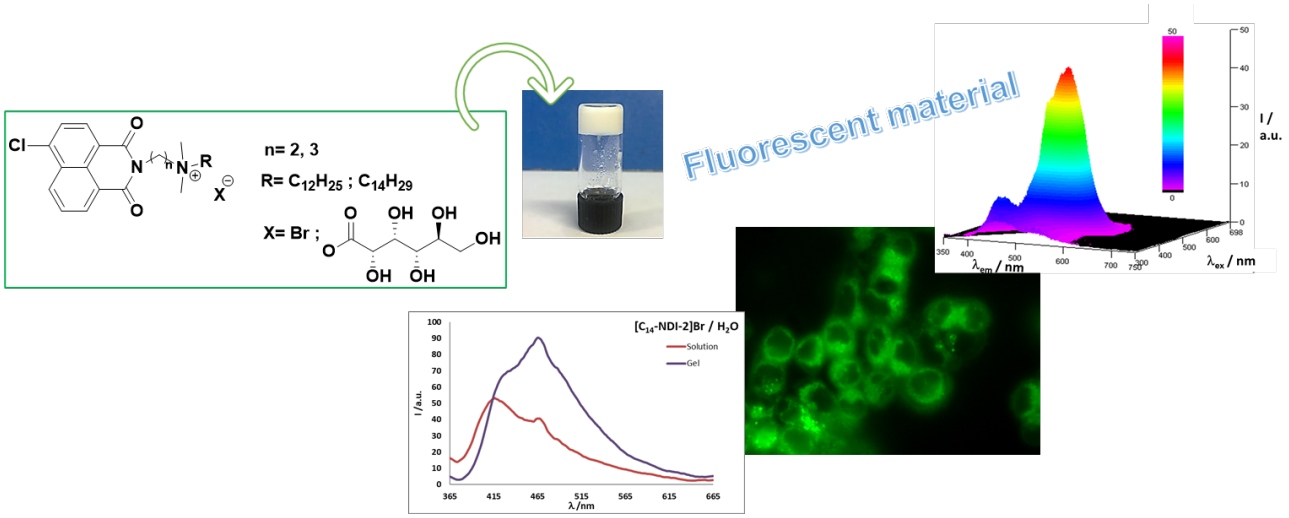

Figure 1 - Structures of salts and examples of fluorescent spectra and fluorescence in cells.

The salts were used as gelators to obtain fluorescent gelatinous matrices. These soft materials have been characterized by mechanical investigations such as thixotropy and rheology, showing interesting reversible response to external stimuli. Moreover, UV-vis and fluorescence measurements have been carried out. Both solution and gel phases showed interesting fluorescent properties, with gels presenting more intense emission than the solution of the corresponding gelator and solvent. The biological investigations led also to interesting properties. Solutions and gels have been tested for bioimaging, showing blue and green fluorescence and confirming the possible application in this field. Moreover, MTT tests reveal the effect of salt structures on cytotoxicity. In particular, for the cell lines tested (HELA, MDA, HCT, RPE), the anion gave the main contribution on cellular toxicity, with gluconate salts showing the higher toxicity.

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Design and synthesis of peptide and peptidomimetic ligands for the Extra-Domain B of Oncofetal Fibronectin

L. Bisbal Lopez, A. Dal Corso, C. Gennari

Università degli Studi di Milano, Dipartimento di Chimica, Via C. Golgi, 19, 20133, Milano, Italy

The high expression of alternatively spliced isoforms of extracellular matrix (ECM) proteins is a well-known hallmark of solid tumors. In particular, fibronectin is one of the most abundant ECM components and its tumor-specific (oncofetal) isoforms play a key role in tumor development. Within the structure of oncofetal fibronectin, the extra-domain B (EDB) is a promising biomarker for cancer detection and diagnosis, as it is expressed in tumors but not in healthy tissues.

While EDB has been investigated as a clinical target for antibody therapeutics, the development of small and synthetically accessible EDB ligands may open to a wide range of applications. The most promising EDB ligand reported in the literature is known as "Aptide" **1**, a 26-mer peptide based on a central scaffold (red in Figure 1) connecting two peptide arms (blue in Figure 1).[1] Besides the specific peptide sequence, the scaffold's β-hairpin structure was showed to be important for EDB binding.[2]

Aiming at the development of peptidomimetic analogues of **1**, we designed and synthesized a library of compounds (general structure described by **2**). More specifically, the Asparagine-Glycine residues should induce the β-hairpin conformation, which is further stabilized either by the formation of a disulfide bridge between the two Cysteine residues or by the introduction of different Cys-crosslinkers. Binding studies against the isolated EDB receptor are being performed in collaboration with the Marie Skłodowska-Curie Network partner Philochem AG (Otelfingen, CH), providing preliminary data for further synthetic activities.

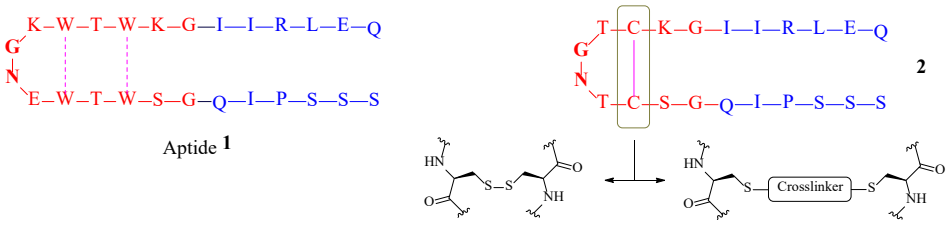

Figure 1. Schematic representation of the EDB-binding Aptide **1** and of the library of its derivatives **2**, bearing the Asp-Gly β-turn inducer and different modalities (e.g. disulfide bond or Cys crosslinkers) to lock the scaffold conformation.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 861316.

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Monitoring the forced degradation of lansoprazole over the time: how cheminformatic tools can support data interpretation

Stefano Bonciarelli [a], *Jenny Desantis* [b], *Laura Goracci* [a], *Lydia Siragusa* [c], *Ismael Zamora* [d] *and Elisabeth Ortega-Carrasco* [d]

[a] *Department of Chemistry, Biology and Biotechnology, University of Perugia, Via Elce di Sotto 8, 06123 Perugia;* [b] *Department of Molecular Medicine, University of Padua, Via A. Gabelli 63, 35121 Padua, Italy;* [c] *Molecular Horizon SRL, Via Montelino 30, 06084 Bettona, Italy;* [d] *Lead Molecular Design, SL, Rambla del Celler 113 local, 08173 Sant Cugat del Vallès, Spain*

Nowadays, stress testing are routinely performed in pharmaceutical companies in the early stage of drug development process in order to decrease the risk of failure due to stability problems and to the uncover of potentially toxic degradation products.[1] Forced degradation studies are usually performed to evaluate the effect of pH, moisture, heat, or other adverse conditions related to transport or packaging issues, on the potency, purity, and hence on the safety profile of a drug.[2] Regulatory agencies and in particular the International Conference of Harmonization (ICH) clearly defines strict guidelines to be applied to perform forced degradation studies.[3] Among the methods used for the identification and characterization of forced degradation products, high-performance liquid chromatography coupled with high resolution mass spectrometry (HPLC-HRMS) represents the analytical technique commonly used to estimate the degradation impurities allowing both elucidation of the structure of the degradation products and monitoring of the whole degradation pathway of a drug. However, these studies are usually performed by evaluating the degradation products at a single time point, making sometimes data interpretation a challenging task. For example, low abundant products could be of uncertain attribution, being close to the noise level and one product could be a result of a second or a third generation of chemical transformations. Monitoring the degradation process at several time points could be a promising approach to overcome both above mentioned issues, but data analysis become time consuming. Here we evaluated the use of MassChemSite and WebChembase, two specific developed tools for automatic reaction monitoring, for the study of the forced degradation of lansoprazole, an inhibitor of gastric H+/K+-ATPase, under acidic, oxidative, basic and neutral stress conditions.[4] The degradation products, as well as the kinetic behaviors and the computational performances are discussed.

[1] K. M. Alsante, A. Ando, R. Brown, J. Ensing, T. D. Hatajik, W. Kong, Y. Tsuda, *Adv. Drug Deliv. Rev.* **2007**, 59, 29–37.
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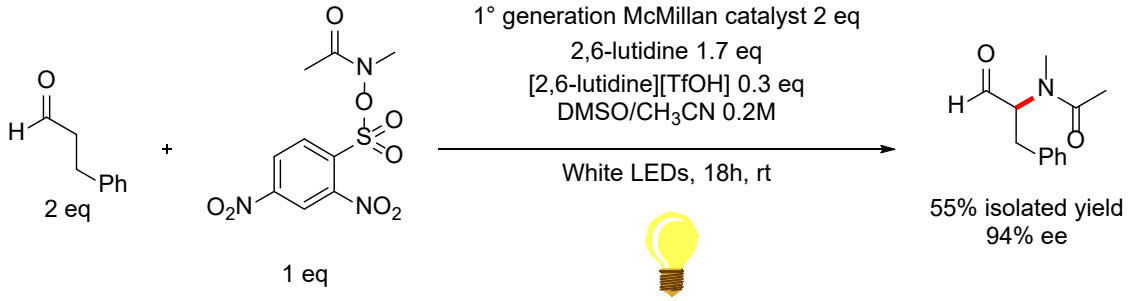
Amidyl radicals in light-promoted stereoselective reactions

Monica Fiorenza Boselli[a], *Maurizio Benaglia*[a], *Alessandra Puglisi*[a]

[a] *Università degli Studi di Milano, Via Golgi 19, Milano*

Organic compounds bearing nitrogen substituents are always present into pharmaceutical and agrochemical products, so to develop new green and cheap methodologies to build up CN bonds is a key step for chemists. In 2013, McMillan and co-workers[1] have developed a new strategy to introduce enantioselectively NBoc moieties in alpha position to aldehydes exploiting the organocatalysis and nitrogen electrophilic radicals generated by light. More recently, Leonori and co-workers[2] have studied the amidyl radicals, which have an electrophilic behavior and usually react with π systems like aromatic rings or in intramolecular cyclizations or in 1,5-HAT (*hydrogen atom transfer*).

Our research group has recently started to study introduction of amides/lactams in alpha position to aldehyde by exploiting amidyl radical chemistry. Preliminary tests on a model reaction gave the product in 55% of yield and 94 % e.e.[3]



The results are promising and studies are currently underway to develop an efficient, catalytic, enantioselective alpha amidation.

Moreover, flow chemistry could be an interesting tool to increase the performance of a reaction catalyzed by light because in microchannels with an internal volume < 1mm the light transmittance does not decrease exponentially like in batch conditions.[4] Indeed, it is possible to have higher and more homogeneous photon flux, resulting in shorter reaction times and consequently less side-product formation due to over-irradiation, often observed in batch.

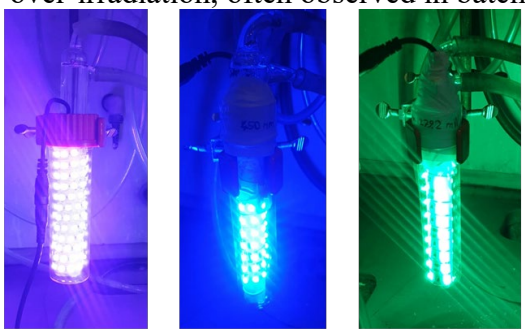


Figure 1 Handmade Flow Photoreactor

After improving the standard conditions, our aim will be to study a flow version of this alpha amidation in meso tubes exploiting a photoreactor built in our laboratory (Figure 1).

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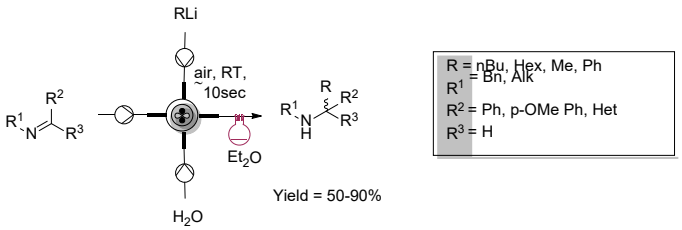
[4] *C. Sambiagio and T. Noël, Trends in Chemistry, 2020, 2, 2*

Continuous flow, Fast “on water” organolithium addition to imines

J. Brucoli [a], A. Puglisi [a], M. Benaglia [a]

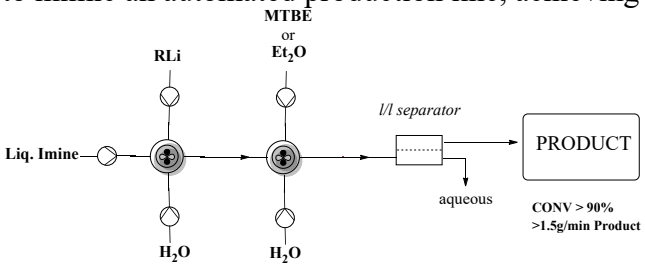
[a] *Dipartimento di Chimica - Università degli Studi di Milano, via Golgi 19, Milano*

The chemistry of polar organometallic compounds in unconventional reaction media has opened up new opportunities in synthesis.[1-3] Based on recent findings on the addition of highly polar organometallic to imines “on-water”,[4] we decided to extend the applicability of the method using continuous technologies with the aim to restrict the gap between laboratory and industry.
These routes provide fast access to secondary amines, which are often useful “building blocks” for natural products and active pharmaceutical ingredients (APIs).[5] Continuous technologies ensure high productivity and efficiency, and represent a valuable alternative to traditional batch systems when exothermic and hazardous reactions are involved or when mixing is a crucial parameter.[6]



Scheme 1: *Fast "on-water" organolithium addition to imines using a CSTR for the synthesis of secondary amines*

A variety of secondary amines (Yield 50-90%) are produced “on-water” in continuous flow using a CSTR (fReactor)[7] starting from different imines and commercial organolithium solutions (nBuLi 2.5M in Hexane, HexLi 2.3M in Hexane, MeLi 1.6M in Et_2O, PhLi 1.9M in Bu_2O).
A full in-flow process using 2 CSTRs (fReactor) and a membrane separator is then reported in order to mimic an automated production line, achieving an extraordinary level of productivity.



Scheme 2: *Full automated continuous process for the production and separation of secondary amines*

[1] C. Vidal, J. García-Álvarez, A. Hernàn-Gòmez, A. R. Kennedy, E. Hevia, *Angew. Chem.* Int. Ed. **2014**, *53*, 5969.
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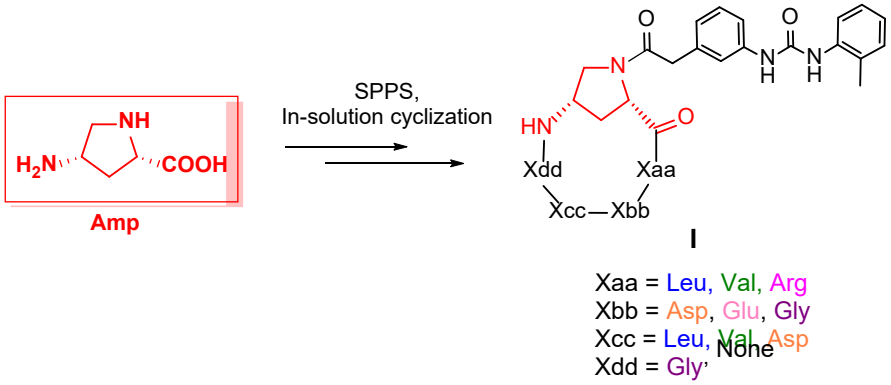
New small-molecule cyclic peptidomimetics as potential modulators of the $\alpha_4\beta_1$ integrin receptor

Bugatti K.,[a] Sartori A.,[a] Portioli E.,[a] Bruno A.,[a] Baiula M.,[b] Bianchini F.,[c] Zanardi F.,[a] and Battistini L.[a]

[a]Department of Food and Drug, University of Parma, Parco Area delle Scienze 27A, 43124 Parma, Italy; [b]Department of Pharmacy and Biotechnology, University of Bologna, Via Irnerio 48, 40126 Bologna, Italy; [c]Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, Viale Morgagni 50, 50134, Florence, Italy. Email: kelly.bugatti@unipr.it

Integrins are heterodimeric cell surface receptors used by cells to communicate with the extracellular matrix; they play key roles in different physiological processes and, for this reason, their altered activity is related to different pathologies including cancer development, metastasis spread, autoimmune diseases and fibrosis, rendering these receptors attractive targets in biomedical research.[1] The $\alpha_4\beta_1$ integrin, belonging to the leucocyte specific receptors, has emerged as an interesting biological target, given its primary role in mediating chronic inflammation, autoimmune diseases, and cancer-related inflammation.[2] In particular, the sole approved $\alpha_4\beta_1$-related drug – namely, the dual $\alpha_4\beta_1/\alpha_4\beta_7$ inhibitor antibody Natalizumab – is used for the treatment of multiple sclerosis and Chron's disease, though its possible serious side effects have partially compromised wide applicability of this drug in the clinics. Thus, the search for new small-molecule $\alpha_4\beta_1$ inhibitors is still highly pursued.



Based on the matured experience in the synthesis and application of integrin-targeted cyclopeptides containing the 4-aminoproline (Amp) scaffold as turn-inducer,[3] we report the design and synthesis of a panel of new small-molecule cyclic peptidomimetics of type **I**. The synthesized molecules contain the Amp scaffold properly functionalized with the 4-[(*N*-2-methylphenyl)ureido]-phenylacetyl group (MPUPA) and grafted into a $\alpha_4\beta_1$-recognizing peptide sequence (LDV and analogues). The collection of the cyclopeptidomimetics has been created by solid-phase synthesis, followed by in-solution cyclization reactions. These compounds have been evaluated for their possible biological activity toward $\alpha_4\beta_1$ integrin by cell adhesion inhibition assays. The results of this endeavour and preliminary SAR studies are herein highlighted, opening the way to the development of $\alpha_4\beta_1$ ligands with optimized receptor affinity and selectivity.

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Thin-Film Luminescent Solar Concentrators with outstanding optical efficiency by using D-A-D Quinoxaline Fluorophores

Costanza Papucci,[a,b,c] Alessio Dessì,[a] Carmen Coppola,[b,d] Adalgisa Sinicropi[a,b,d] Cosimo Micheletti,[e] Rima Charaf,[e] Mariangela di Donato,[a,f] Maria Taddei,[a,f] Paolo Foggi,[f,g,h] Lorenzo Zani,[a] Gianna Reginato,[a] Andrea Pucci,[e] Massimo Calamante,[a,c] Alessandro Mordini.[a,c]

[a] *a Institute of Chemistry of Organometallic Compounds (CNR-ICCOM), Via Madonna del Piano 10, 50019 Sesto Fiorentino, Italy;*
[b] *Department of Biotechnology, Chemistry and Pharmacy, University of Siena, Via A. Moro 2, 53100, Siena, Italy;*
[c] *Department of Chemistry "U. Schiff", University of Florence, Via della Lastruccia 13, 50019 Sesto Fiorentino, Italy;*
[d] *CSGI, Consorzio per lo Sviluppo dei Sistemi a Grande Interfase, Sesto Fiorentino 50019, Italy;*
[e] *Department of Chemistry and Industrial Chemistry, University of Pisa, Via Giuseppe Moruzzi 13, 56124 Pisa, Italy;*
[f] *LENS, European Laboratory for Non-Linear Spectroscopy, via N. Carrara 1, Sesto Fiorentino 50019, Italy.*
[g] *Department of Chemistry, Biology and Biotechnology, University of Perugia, via Elce di Sotto 8, 06123 Perugia, Italy*
[h] *INRIM (Istituto Nazionale di Scienza Metrologica), Strada delle Cacce 91, 10135 Torino, Italy*

Luminescent solar concentrators (LSCs) is a technology developed since the 1970s[1] with the aim of obtaining large-area, semi-transparent and cheap photovoltaic devices capable of concentrating solar radiation on small solar cells at their margins. Specifically, they consist of a panel of a standard plastic material (e. g., poly(methyl methacrylate), PMMA) in which a fluorescent compound, able of absorbing direct and indirect sunlight radiation and emitting it at a different, usually longer wavelength, is dispersed. Commonly used fluorescent compounds can be quantum dots, perovskites, rare-earth complexes and organic molecules[2]. Thanks to the different refractive indexes of air and the plastic material, the emitted radiation is mainly concentrated via total internal reflection at the edge of the panel, where the solar cells are usually placed, making the device less dependent on light orientation. This, together with the aesthetic characteristics (colour and shape tunability), allows their use in building-integrated photovoltaics (BIPVs)[3].
In order to obtain high-performance LSC devices, a careful study of the materials used for their assembly must be performed, both concerning the selection of the fluorophore and the plastic material in which it is dispersed[2].
We recently synthetized and investigated the properties of a series of organic fluorophores with donor-acceptor-donor (D-A-D) structure, characterized by a benzo[1,2-d:4,5-d']bisthiazole[4] and quinoxaline as acceptor core. The optical properties of the molecules were investigated in solution as well as after dispersion in PMMA and its copolymer with more apolar cyclohexyl methacrylate repeating units. The variation of the absorption and emission maxima, the fluorescence quantum yields andthe optical efficiency of the corresponding LSC devices were eventually determined. Due to the very good fluorophores compatibility with the polymeric matrices, LSCs with optical features superior to the state-of-the-art were obtained [4].

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[4] a) C. Papucci, *et.al., EurJOC* **2018**, *20*, 2657; b) Papucci, *et.al., Dye. Pigment*. **2021**, 188.

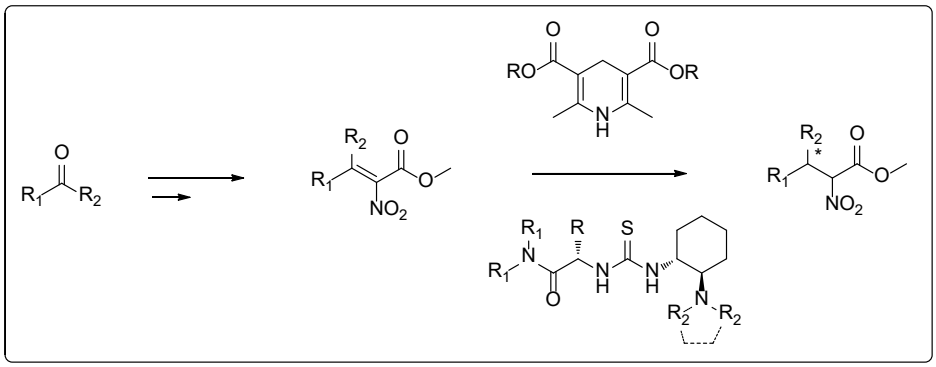
SYNTHESIS AND ENANTIOSELECTIVE REDUCTION OF TETRASUBSTITUED NITROALKENES

Patricia Camarero González [a], Maurizio Benaglia [a], Sergio Rossi [a], Alessandra Puglisi [a], Miguel. A.Sanz [b]

[a] *Department of Chemistry University of Milan, Via Camilo Golgi 19, Milano Italy*
[b] *Taros Chemicals,Emil Figge Straße 76A, Dortmund Germany*

Nitro compounds and nitroalkenes are versatile compounds in synthetic organic chemistry. They can be used as dienophiles in a Diels-Alder reaction or as electrophiles in addition reactions with many different nucleophiles. These compounds can be easily prepared by Henry condensation of an aldehyde or ketone followed by the dehydration of the correspond β-nitroalcohol[1]. Trisubstituted nitroalkanes, have been extensively studied in literature; however, the synthesis of tetrasubstituted nitroalkenes remains a challenge. Here we are reporting a novel method of synthesis for tetrasubstituted nitroalkenes (Scheme 1) by conversion of commercially available ketones into their α,β-unsaturated esters followed by a nitration with an appropriate nitrate agent[2], which allowed to obtain the product in a reproducible manner.

Furthermore, the enantioselective reduction[3] of these molecules has also been studied using different bifunctional thiourea catalysts and Hantzsch ester as a reductive agent to form the corresponding nitroalkane. Mechanistic studies have also been performed to predict the predominant configuration of the final molecule.



Scheme 1: Synthesis and enantioselective reduction of tetrasubstituted nitroalkenes

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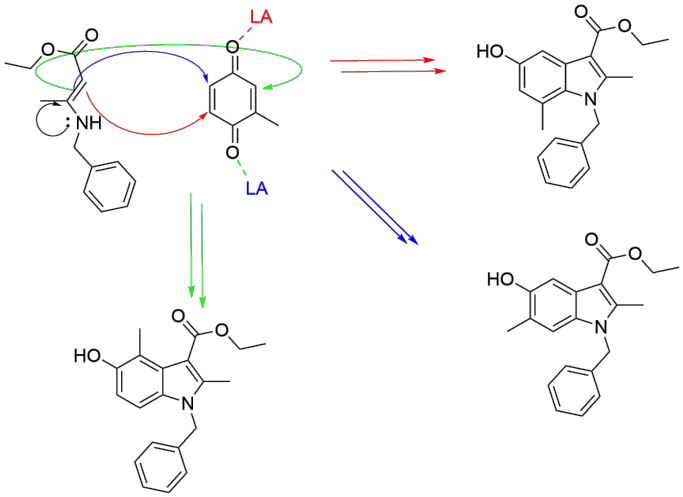
Iron catalyzed Nenitzescu indole synthesis from substituted benzoquinones

Giuseppe Satta [a,b], Andrea Beccu [a,b], Silvia Gaspa [a], Lidia De Luca [a], Ugo Gavino Azzena [a,b], Luisa Pisano [a,b], Massimo Carraro [a,b]

[a] Department of Chemistry and Pharmacy, University of Sassari, via Vienna 2, 07100 - Sassari. e-mail: mcarraro@uniss.it; [b] Consorzio Interuniversitario Reattività Chimica e Catalisi (CIRCC), Bari, Italy

Nenitzescu indole synthesis is a well-established reaction to obtain substituted 5-hydroxyindoles from quinones and enamines.[1] The reaction can be performed without a catalyst at high temperatures or with the activation from mild Lewis acids. [2] During our investigations to substitute zinc halogenide and dichloromethane we found that CPME is a suitable solvent, and that iron chloride can give acceptable yields of product. Interestingly, when a substituted quinone is utilized, $FeCl_3$ gives (somehow unexpected and) unique results in term of yields and selectivity.



The selectivity was assessed and explained with the help of ^{1}H-NMR (predicted and experimental), DFT calculated local electronic densities of frontier orbitals and IR spectroscopy.

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Cigarette butts as feedstock for Levulinic Acid production

Michele Casiello,[a] Onofrio Losito,[a] Caterina Fusco,[b] Amelita G. Laurenza,[c] Vincenzo Pantone,[c] Antonio Monopoli,[a] Angelo Nacci,[a,b] and Lucia D'Accolti[a,b]

[a] Chemistry Department, University of Bari Aldo Moro, via Orabona 4, 70125 Bari, Italy; [b] CNR—Istituto di Chimica dei Composti Organometallici (ICCOM), Bari Section, via Orabona 4, 70125 Bari, Italy; [c] Ambra SRL Via Mitilini 11 Pomarico, Matera, 75016, Italy.

Valorization of wastes for production of fine chemicals and energy is the main route for a circular development model and is the winning strategy that avoids simultaneously the depletion of resources and the scraps accumulation. Levulinic acid (LA) is considered one of the twelve most promising industrial bio-intermediates and amongst the most innovative building blocks of chemical industry, due to its conversion in several high-value bio-based chemicals and materials (Fig. 1) [1]. The main end users of LA are agricultural, pharmaceutical, and cosmetic sectors. According to the most recent studies, it is estimated that the world market demand for LA will grow 150-200 times over the next 7-8 years.

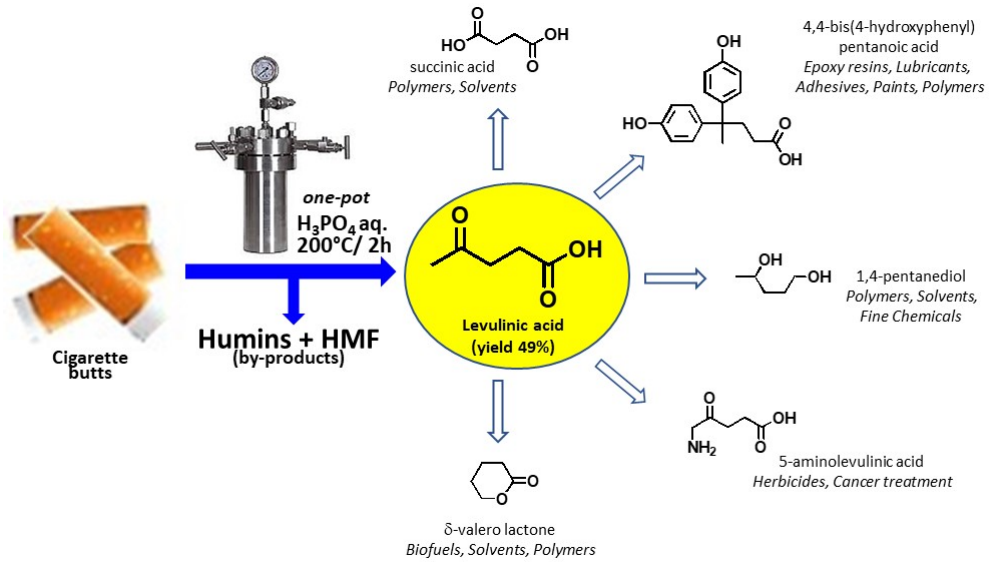

Figure 1. Levulinic acid as a key industrial intermediate

The well-known approach to convert lignocellulosic materials (wood, paper, food crops wastes) into LA is the thermal treatment with strong Brønsted acids (e.g. H_2SO_4). Despite the high yields, this strategy is difficult to apply at an industrial level, due to the plants corrosion [2]. Concerning cellulosic starting materials agricultural scraps are commonly used, but recently municipal paper wastes are gaining attention. Among these latters, cigarette butts represent a neglected and no cost reservoir of cellulose acetate, that is virtually boundless if considering that about 5.5 trillion cigarettes are produced each year.

This communication deals with the use of cigarette filters as feedstock for production of Levulinic acid by thermal hydrolysis catalysed by phosphoric acidic. The protocol avoids the use of more aggressive H_2SO_4 and HCl, thus minimizing corrosion phenomena of plants. Notably, by simply modifying acid catalyst (e.g. using CH_3COOH), another top value-added fine chemical such as 5-hydroxymethylfuraldehyde (HMF) is obtained, thus widening the scope of the method.

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Synthesis and Molecular Modeling Studies of Strobilurin-SDHI Based Hybrid fungicides

Giorgia Catinella [a], Cecilia Pinna[a], Andrea Kunova [a], Luca Palazzolo [b], Fabio Forlani [a], Loana Musso [a], Paolo Cortesi [a], Ivano Eberini [b, c], Andrea Pinto [a] and Sabrina Dallavalle [a]

[a] Department of Food, Environmental and Nutritional Science (DeFENS), University of Milan, 20133 Milan, Italy; [b] Department of Pharmacological and Biomolecular Sciences (DiSFeB), University of Milan, 20133 Milan, Italy; [c] Data Science Research Center (DSRC), University of Milan, 20133 Milan, Italy

Pyricularia oryzae causes one of the most aggressive fungal diseases of cultivated rice worldwide [1]. The election classes of fungicides for the control of the infection are Qo Inhibitors (QoIs, e.g. azoxystrobin), melanin biosynthesis inhibitors (e.g. tricyclazole), demethylase 2 inhibitors (DMI, e.g. prochloraz) and succinate dehydrogenase inhibitors (SDHIs, e.g. boscalid), ideally combined or alternated to ensure that the fully efficacy is preserved [2]. In Italy, only strobilurins and demethylation inhibitors (DMI) are currently approved [3].
However, the increasing development of resistance causes the failure of disease control with severe consequences on crop production. In particular, the resistance to strobilurins is most often determined by a single amino acid substitution from glycine to alanine (G143A).
To expand the collection of fungicides against *P. oryzae* and, more importantly, to overcome the pathogen resistance developed against rice crops, a new chemical strategy can be the construction of multitarget compounds. With this aim, we carried out a structural investigation of new fungicides obtained by combining the pharmacophores of two classes of marketed antifungal compounds: strobilurins and SDH inhibitors.
This study focused on the structural modifications of a previously obtained hit candidate, containing the strobilurin pharmacophore connected by a proper linker to the carboxamide pharmacophore of a commercial SDH inhibitor [4, 5]. A collection of compounds was synthetized changing the spatial orientation of the two pharmacophores, modifying the length and the nature of the linker and the substitution patterns of the SDHI pharmacophore to investigate the key structural determinants of their activity.
All the new molecules were tested against wild-type and strobilurin-resistant strains of *P. oryzae*; the introduction of substituents with different steric and stereoelectronic properties on the SDHI benzamide ring had a major effect on the activity of dual compounds. In fact, one of these compounds showed a very promising biological activity on both strains (>80% inhibition). Moreover, to investigate the binding mode of the compound with cytochrome *bc1* we developed a three-dimensional model of *P. oryzae* cytochrome *bc1* in complex with azoxystrobin. The *in silico* analysis suggests that the new compounds have the same molecular recognition mechanism of azoxystrobin for the *P. oryzae* cytochrome bc1 Qo binding site.

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Enantioselective CO_2 Fixation Via Nickel Catalyzed di-Functionalyzation of Alkenes

Alessandro Cerveri,[a] *Marco Bandini*.[a,b]

[a]*Dipartimento di Chimica "Giacomo Ciamician", Alma Mater Studiorum – Università di Bologna, via Selmi 2, 40126, Bologna, Italy.*
[b]*Consorzio CINMPIS, via Selmi 2, 40126, Bologna, Italy*
e-mail: alessandro.cerveri2@unibo.it

In organic chemistry, carboxylic acids are an important synthetic goal for their high relevance in bio-medicinal chemistry. Over the past decade, steps towards the chemoselective catalytic electrophilic as well as nucleophilic activation of CO_2, have been taken, and the 3d-TM catalyzed carboxylation reactions have been developed toward highly efficient synthesis of complex carboxylic acids.[1] However, the adoption of carboxylation reactions in enantioselective catalytic procedures is still underdeveloped,[2] and to overcome this challenge we proposed Ni-catalyzed intramolecular reductive Heck-coupling followed by CO_2-based carboxylation for the synthesis of 3,4-dihydrobenzofuran-3-ylacetic derivatives, featuring a defined quaternary stereogenic center (**Figure 1**).

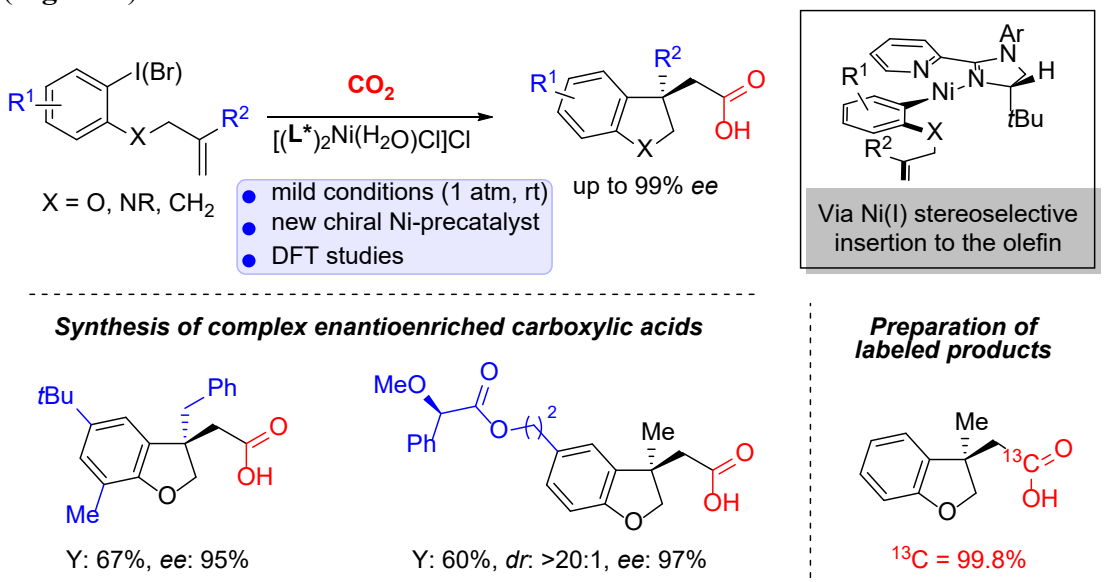

Figure 1

The reaction mechanism has been addressed through a combination of experimental and computational studies, enabling what is proposed to be a Ni(I)-assisted truncated Heck-coupling event, along with a stereodiscrimination model based of non-covalent interactions.

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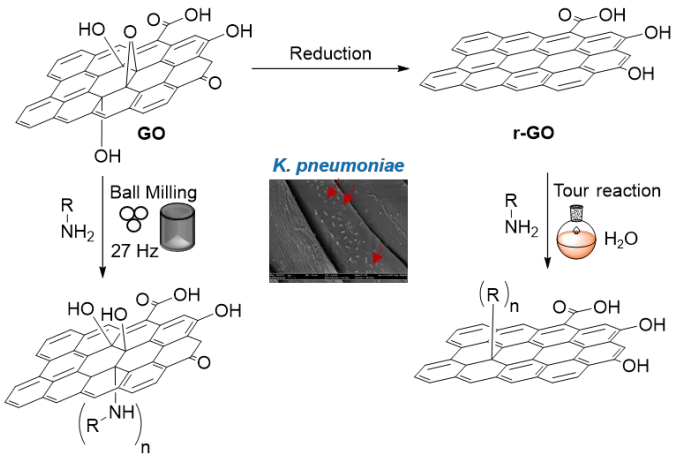
Surface Engineering of Graphene-based materials: tailored synthetic processes on gram scale (from the bench to industrial-driven applications)

Giacomo Biagiotti,[a,b] *Stefano Cicchi,*[a,b] *Barbara Richichi* [a,b]

[a] *Department of Chemistry "Ugo Schiff", Università di Firenze, Via della Lastruccia 3-13, 50019, Sesto Fiorentino, Italy.*
[b] *INSTM (Consorzio Interuniversitario Nazionale per la Scienza e Tecnologia dei Materiali) Via G. Giusti, 9, 50121 Firenze (ITALY).*

Reduced graphene oxide (**r-GO**) and graphene oxide (**GO**) thanks to their high surface area and their intrinsic physical and biological properties are unique carbon-based materials, which have generated great expectations.[1] Despite many impressive achievements in their surface engineering, the scale up of the functionalization processes, aimed at obtaining graphene-based materials with tailor-made properties, is a drawback in handling these materials thus, limiting industrial-driven applications, in particular, when significant batches are required and the use of organic solvents is avoided.[2-3]
In this communication. we report on the efficient and custom engineering (on gram scale) of **GO** and **r-GO** surface with bioactive molecules (up to 20% of loading) by exploiting different surface chemistry (*i.e.,* the conventional (in batch) solution-based Tour reaction in water and a dry mechanochemical approach). [4]
Then, taking advantage on the interdisciplinary collaborations with experts in their field, we proved that our approach gives access to engineered nanomaterials with improved physical and biological properties, which have been employed as antimicrobial additives on cotton fabrics providing stable physical interactions with the cotton matrix.[4]



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We thank POR FESR 2014−2020, Regione Toscana, Project: GlycoGLAB 4.0: nanoadditivo multiproprietà ad attività assorbente e preservante.

Chemoselective Addition of Lithium Phosphides to Aldehydes and Epoxides in *Deep Eutectic Solvents*

Luciana Cicco,[a] *Alba Fombona-Pascual,*[b] *Alba Sánchez-Condado,*[b] *Paola Vitale,*[a] *Filippo Maria Perna,*[a] *Vito Capriati,*[a] *Alejandro Presa Soto,*[b] *Joaquín García-Álvarez* [b]

[a] *Dipartimento di Farmacia-Scienze del Farmaco, Università di Bari "Aldo Moro" Consorzio C.I.N.M.P.I.S, Via E. Orabona 4, 1-70125 Bari, Italy;* [b] *Departamento de Química Orgánica e Inorgánica, IUQOEM (Unidad asociada al CSIC), Universidad de Oviedo, E-33071, Oviedo, Spain).*

Within the arsenal of organic synthesis, the chemistry of compounds of *s*-block elements (typically organolithium and Grignard reagents) has become one of the most useful tools to forge new C–C.[1] Although a variety of synthetic methods has been developed so far to create C–N,[2] C–O[3] and C–S[4] bonds, the number of protocols for the construction of new C–P connections is much more limited. Pioneering, independent studies from Hevia, García-Alvarez, and our own group have shown that the rate of alkylation/arylation of unsaturated functional groups (e.g., carbonyl compounds, imines, double bonds) by highly polar organometallic compounds successfully competes with protonation, when using environmentally responsible protic solvents like water and the so-called *Deep Eutectic Solvents* (*DESs*).[5,6] In this communication, we wish to report that *DESs* can be used as environmentally friendly reaction media to promote a fast (within 3 s reaction time) and chemoselective addition of in-situ generated highly polarized lithium phosphides ($LiPR_2$) to both aldehydes and epoxides, working at room temperature (RT) and under aerobic conditions, thereby granting access to *α*- and *β*-hydroxy-phosphine oxides, respectively, in very good yields (up to 94%, **Figure 1**).[7]

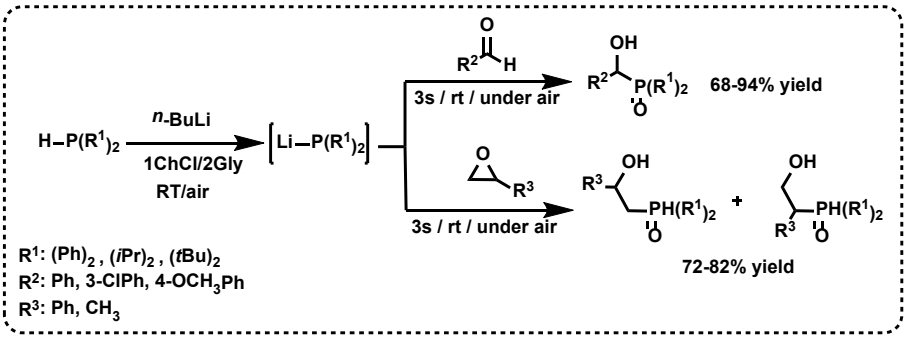

Figure 1. In-situ generation of lithium phosphides and their one-pot chemoselective addition to aldehydes and epoxides, working under air, at RT, in 1ChCl/2Gly mixture. ChCl = choline chloride, Gly = glycerol

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An efficient and eco-friendly synthesis of alkyl gallates over the ion-exchange resin Amberlyst-15

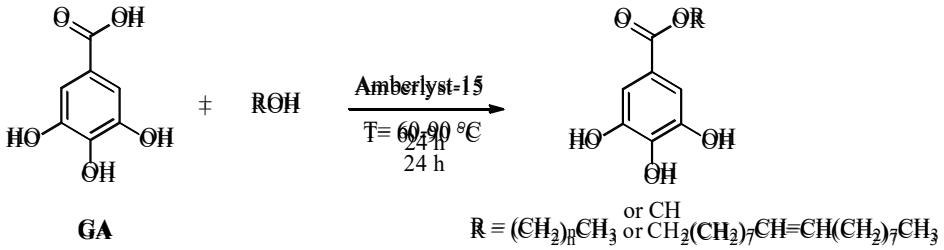
Mariangela Clemente,[a] Annalisa Romani,[b] Luca Santi,[a] Giancarlo Fabrizi,[c] Roberta Bernini[a]

[a] Dipartimento di Scienze Agrarie e Forestali, Università degli Studi della Tuscia, Viterbo; [b] Dipartimento di Statistica, Informatica, Applicazioni "G. Parenti", Laboratorio PHYTOLAB, Università degli Studi di Firenze; [c] Dipartimento di Chimica e Tecnologie del Farmaco, Sapienza Università di Roma, Roma

Gallic acid (GA) is a low-molecular weight phenolic compound exhibiting antioxidant, antimicrobial and anticancer activity [1]. Despite these remarkable properties, its applications such as dietary supplement and stabilizer of foods and cosmetics in non-aqueous media are limited for the high hydrophilic character. With the aim to overcome these drawbacks, lipophilic alkyl gallates were prepared via a direct esterification reaction with alkyl alcohols using strong acids such as sulfuric acid [2].

In this communication we describe a mild and eco-friendly procedure for the synthesis of C1-C18 alkyl gallates starting from GA and the appropriate alcohol. The reactions were performed at 60-90°C in heterogenous phase in the presence of Amberlyst-15, a macroreticular ion-exchange resin having strongly acidic sulfonic groups [3]. After 24 h, the corresponding alkyl gallates were isolated in satisfactory yields (84-98%); by-products were not observed (Scheme).

Scheme



At the end of the reaction, the resin was recovered and reused for at least five times without loss of efficiency. For the simplicity, efficiency and eco-friendliness, this procedure represents a green way for the synthesis of alkyl gallates, lipophilic compounds characterized by relevant biological activities including anti-cancer properties [4].

This work was supported by PIN SCRL - Servizi Didattici e Scientifici, University of Florence and the Ministero dell'Università e della Ricerca with the PRIN 2017 (20175XBSX4) entitled "Targeting Hedgehog pathway: virtual screening identification and sustainable synthesis of novel Smo and Gli inhibitors and their pharmacological drug delivery strategies for improved therapeutic effects in tumors".

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Sol-gel synthesis of Ce(III) doped – TiO_2 NPs and their application in PMMA matrix

Tommaso Compagnucci[a], Serena Gabrielli[a], Francesco Lanero[b], Enrico Marcantoni[a], Genny Pastore[a], Maria Savina Pianesi[b]

[a] *School of Science and Technologies, Università degli Studi di Camerino, 62032 Camerino, Italy*
[b] *Delta srl, Via Tambroni Armaroli 2, 62010 Montelupone, Italy*

Nowadays, the use of semiconductors in photocatalysis is mostly due to their ability to photo-degrade organic pollutants and bacteria[1]. For non-food plastic products, TiO_2 nanoparticles (NPs) have received great consideration because of its intriguing photocatalytic activity, low cost, no secondary pollution and nanometric size. Although the great activity, some relevant drawbacks are still open: i) the need of a UV light source to activate the photocatalyst; ii) limited photonic efficiency; iii) the quite challenging use of nano-sized particles.[2] So, the main focuses are both the shift of the photocatalytic activity toward the visible light and, furthermore, to avoid the most common employment as photoactive coatings (e.g. through spraying techniques), due to the tendency of coatings to spoil, causing the release of not-bounded NPs and efficiency loss over time. Aiming to overcome these problems, two different investigations are in progress. One is the study that relies on the Ce(III) ion doping of TiO_2 NPs, that is an interesting approach to achieve both the raising of photonic efficiency and the activity shift to the visible region.[3] For this purpose, the sol-gel synthesis method is the one largely employed because of its simplicity and the possibility to apply it to an industrial scale (Figure 1a). The second investigation is related to their direct application inside the PMMA matrix (polymethylmethacrylate) aided by the use of a coupling agent, able to create a covalent bond between inorganic and organic phases, thus avoiding the free release of NPs from the material surface. Therefore, the so-called silanization of TiO_2 NPs with the organosilane coupling agent γ-methacryloxypropyltrimethoxysilane (MPS) and the co-polymerization with PMMA has been performed (Figure 1b)[4]. The photocatalytic activity of these materials will be tested through the degradation of a representative dye (methylene blue) in aqueous media.

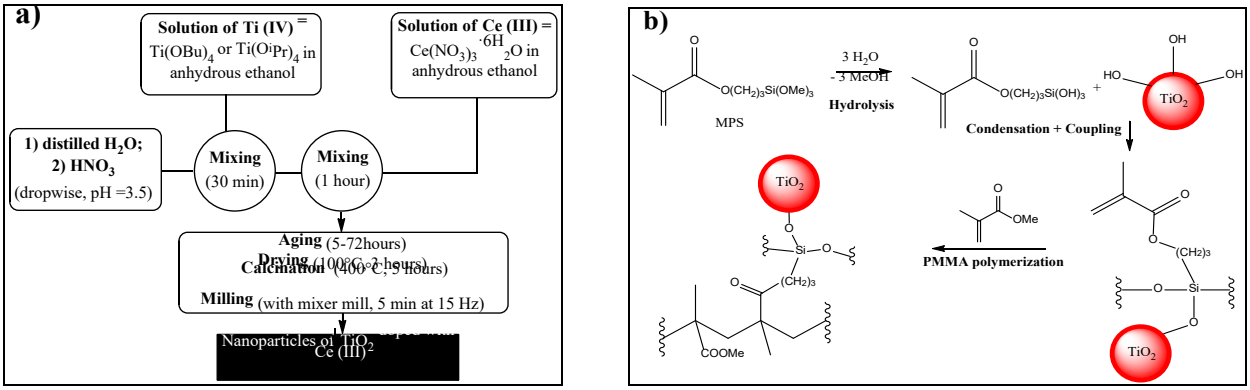

Figure 1. *a)* Ce(III) doped TiO_2 NPs synthesis; *b)* Silanization and PMMA co-polymerization with NPs.

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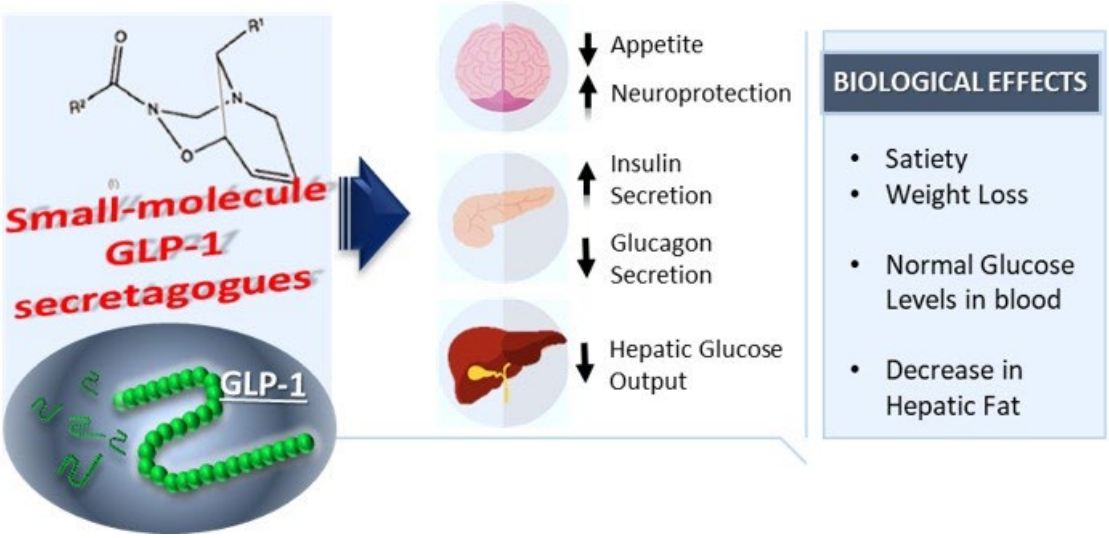
Development of novel small molecules as anti-diabesity agents relying on GLP-1 secretion pathway

*Lucrezia M. Comparini, Lisa Giannessi, Federico Dani, Sebastiano Di Pietro, Mauro Pineschi**

Dipartimento di Farmacia, Via Bonanno 33, 56126 Pisa, Italy. E-mail: lucrezia.comparini@phd.unipi.it

Diabesity is a neologism coined by WHO to indicate the strict association between type 2 diabetes and obesity. Diabesity represents an important health problem with a socio-economic impact expected to grow in the future. GLP-1 is an incretin hormone that plays a pivotal role in our body. The activation of GLP-1 is an established mechanism to treat diabetes and obesity and several peptide agonists, very close in structure to native GLP-1, are now in the market [1]. Such peptides have very high costs, an administration route which is normally by injection and several adverse side effects such nausea and vomiting. Therefore, there is a huge interest in the pharma industry for novel treatments of diabesity and related pathologies by oral administration increasing the patient compliance and also reducing costs as small molecules are generally much cheaper to produce than peptides. Recently, our research group synthesized compounds having an innovative 1,3-diaza-4-oxa-[3.3.1]-bicyclic nonene scaffold and showing a good GLP-1 secretagogue activity and pharmacokinetic profile [2-4]. We now report the chemical diversification of the library of compounds with an emphasis on late stage manipulations.



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DFT and TDDFT investigation of novel organic catechol-based sensitizers for type II Dye Sensitized Solar Cells (DSSCs)

Carmen Coppola[a,b], Alessio D'Ettorre[a], Maria Laura Parisi[a,b,c,e], Lorenzo Zani[c], Gianna Reginato[c], Massimo Calamante[c,d], Alessandro Mordini[c,d], Maurizio Taddei[c,e], Riccardo Basosi[a,b,c], Adalgisa Sinicropi[a,b,c,e]

[a]*Università di Siena, R²ES Lab, Dipartimento di Biotecnologie, Chimica e Farmacia, Via Aldo Moro 2, 53100 Siena, Italy*
[b]*CSGI, Consorzio per lo Sviluppo dei Sistemi a Grande Interfase, Via della Lastruccia 3, 50019 Sesto Fiorentino, Italy*
[c]*CNR – Istituto di Chimica dei Composti Organometallici (CNR-ICCOM), Via Madonna del Piano 10, 50019 Sesto Fiorentino, Italy*
[d]*University of Florence, Department of Chemistry "U. Schiff", Via della Lastruccia 13, 50019 Sesto Fiorentino, Italy*
[e]*Università di Siena, Dipartimento di Biotecnologie, Chimica e Farmacia, Via Aldo Moro 2, 53100 Siena, Italy*

In the last two decades, Catechol-based (Cat-) molecules have attracted much attention as light harvesting materials for type II Dye Sensitized Solar Cells (DSSCs), which are characterized by a *one-step* electron injection mechanism that implicates the direct transfer of electron from the dye to the conduction band of TiO_2, the semiconductor [1-3]. Indeed, upon binding to TiO_2, Cat-dyes are involved in the DTCT, dye-to-TiO_2 charge transfer, process which consists in exhibiting broad absorptions all over the spectral range of light [1-4]. Nevertheless, they have hardly been employed as sensitizers for DSSCs, as their efficiency had never exceeded 2.5% [1]. Hence, in order to develop more efficient Cat-based type II dyes, it is fundamental to increase our knowledge about the *one-step* mechanism and the DTCT features, strongly affected by the substituents to the catechol moiety [3-7]. With this aim, in this work, a series of Cat-based molecules, **Cat-I** to **Cat-XV**, is presented [8]. They have been endowed with strong or moderated electron-donating or electron-withdrawing substituents, directly linked to the Cat unit or through an ethylene π spacer. In order to test their suitability as sensitizers for type II DSSCs, Density Functional Theory (DFT) and Time Dependent DFT (TDDFT) methods have been applied to investigate the electronic structures and the excited state properties of free and $(TiO_2)_9$-bound **Cat-I-XV**. In particular, the influence of different substituents and the effect of the π spacer have been investigated relatively to the DTCT properties and to the electron injection mechanism. The results of calculations suggest that fully conjugated molecules, regardless of the kind of substituent, could perform better as type II dyes. Indeed, they show red-shifted DTCT bands, formed by the interaction of d orbitals of Ti and p orbitals of catechol oxygens, leading to a strong electron coupling which fosters type II mechanism.

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Quantification of Health Claim-relevant Tyrosol and Hydroxytyrosol in Extra Virgin Olive Oil by RP-HPLC After Direct Hydrolysis

Martin Fischnaller[a], Oliver M. D. Lutz[a], Danilo Corradini[b], Alexios-Leandros Skaltsounis[c], Panagiotis Stathopoulos[c], Thomas A.E. Jakschitz[a], Guenther K. Bonn[a,d,]

[a]Austrian Drug Screening Institute, Innsbruck, Austria [b]Consiglio Nazionale delle Ricerche, Institute for Biological Systems, Montelibretti, Rome, Italy [c]Department of Pharmacognosy and Natural Products Chemistry, University of Athens, Greece [d] Institute for Analytical Chemistry and Radiochemistry, University of Innsbruck, Austria.

According to EU regulations, a food health claim is any message or label which states, suggests, or implies that a food has characteristics or/and contains substances that are beneficial for the human health. To ensure that the claims made are truthful, it is necessary that the substances that are the subject of the claim are present in the final product in quantities that are sufficient to produce the claimed physiological effect. Such health claims are authorized for use in EU after scientific assessments performed by the European Food Safety Authority (EFSA). In the EU there is an authorized health claim that 'olive oil polyphenols contribute to the protection of blood lipids from oxidative stress', which is based on the numerous scientific investigations showing significantly reduced levels of oxidised low density lipoprotein (LDL) in plasma after extra virgin olive oil consumption. EFSA has concluded that the claim may be used only for olive oil that contains at least 5 mg of hydroxytyrosol and its derivatives per 20 g of olive oil.
This communication describes and discusses a rapid and thoroughly optimized extraction and RP-HPLC quantification method for the determination of hydroxytyrosol and tyrosol occurring in extra virgin olive oil (EVOO) in free and bound forms, after their direct hydrolysis in the oil and not in the extracted phenolic samples. Since direct hydrolysis of the olive oil is the central element of the proposed method, the reaction temperature, time, reagent concentration and reagent type have been optimized. Furthermore, the influence of co-solvents has been investigated, possibly aiding the intermittent miscibility of the two phases during hydrolysis. The method has been validated and applied to fourteen commercially available EVOO samples that have also analyzed by a conventional RP-HPLC method based on the extraction of the polar phenols with a methanol/water mixture before hydrolysis. The communication also discusses certain shortcomings of the EU health claim (regulation 432/2012) and the commonly used quantification method presented by the International Olive Council.

This project has received funding by the Research Executive Agency of the European Union in the framework of MSCA-RISE Action of the H2020 Programme, Project 734899 Olive-Net.

DNA vs PNA as thrombin aptamers: the role of electrostatic interactions

Federica Curti [a], *W. Knoll*[b], *M. Careri and R. Corradini*[a]

[a] *Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parma, Italy;*
[b] *Austrian Institute of Technology GmbH, Vienna, Austria*

During the last years, thrombin binding aptamer (TBA) was one of the most extensively studied oligonucleotide G-quadruplex aptamers and the search for modifications that are able to improve its chemical and clinical properties is still ongoing [1]. In a research program dealing with the development of innovative systems [2], we designed of a similar binding system by replacing the phosphate backbone of the DNA-TBA with a DNA-mimic probe based on Peptide Nucleic Acids (PNAs) [3]. PNAs are well known ligands that offer enhanced base pairing binding properties compared to DNA/RNA system, can be easily synthetized in the laboratory, and are very resistant to both chemical and enzymatic degradation.
The PNA probes have been synthesized by keeping the same nucleobases sequence of the well-known 15-mer DNA-HD1 anti-thrombin aptamer and it was possible to compare a completely neutral PNA-HD1 sequence and a PNA-HD1 baring glutamic acid residues. Both PNAs and DNA aptamer performances with human thrombin were followed via fluorescence anisotropy to preliminary investigate the importance of the electrostatic interactions and the role of the lone nucleobases when interacting with the protein binding sites. Regarding the DNA aptamer-thrombin complex, it was possible to observe a significant change in its behavior when exposed to different ionic strength solutions, leading to a destabilization of the complex by increasing the ionic strength. Unfortunately, an extremely week signal was observed when the PNA aptamer was used, that is reflective of the predominant electrostatic nature of this aptamer-protein system. Moreover, the intramolecular G-quartet structure of both PNA and DNA systems was monitored with UV-melting profiles, which can reveal the presence of quadruplex structures [4]. Details will be presented in the poster.

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A molecular network based approach to fight viral infections: Focus on *Paulownia tomentosa* (Thunb.) steud. and SARS-COV-2

Matteo Micucci[a], Alberto Chiarini[a], Laura Beatrice Mattioli[a], Roberta Budriesi[a], Marisabel Mecca[b], Luigi Todaro[c], Domenico Nuzzo[d], Pasquale Marrazzo[d], Valentina di Liberto[e], Fabio Magurano[f], Maurizio D'Auria[b]

[a] University of Bologna, Department of Pharmacy & Biotechnology, Italy; [b] Dipartimento di Scienze, Università della Basilicata, Italy; [c] School of Agricultural Forestry, Food, and Environmental Science, Università della Basilicata, Italy; [d] Istituto per la Ricerca e l'Innovazione Biomedica, CNR, Palermo, Italy; [e] Dipartimento di Biomedicina, Neuroscienze e Diagnostica Avanzata, Università di Palermo, Italy; [f] Italian National Reference Laboratory for measles and rubella, Departement of Infectious Diseases, Istituto Superiore di Sanità, Rome, Italy.

Coronaviruses (CoVs) are positive single-stranded RNA enveloped viruses infecting animals. These viruses have determined pneumonia and colds until the emergence of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002 and Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012 from zoonotic sources. A novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing severe acute respiratory disease emerged recently in Wuhan, China, in December 2019 and produced the actual pandemy. [1] In addition to the actual preventive and therapeutical strategies, other tools to decrease viral infection diffusion and its severity are required. Several plants are used, in Folk Medicine, for the treatment of many diseases including those related to respiratory infections. Many phytocomplexes and isolated compounds affect a plethora of molecular networks influencing each other. In the field fo COVID-19, our research is aimed at finding phytocomplexes acting on host and guest.

Paulownia tomentosa (Thunb.) steud. has been used, in Folk Medicine, for the treatment of respiratory diseases. Some flavonoids isolated from this plant were shown to inhibit SARS-CoV papain-like protease in vitro [2]. In this work, we evaluated the antiviral effects of a Paulownia tomentosa (Thunb.) steud. wood extract against sars-cov-2 in vitro, its activity towards lung epitelial H292 cell viability and oxidative stress, its ability to affect trachea and lungs smooth muscle contraction through in vitro biological assays. The chemical investigation of the wood extract was exerted using a GC-MS system. The extract showed a significant antiviral activity and demonstrated a cytoprotective effect towards butyl hydroperoxide-induced damage, at least in part decreasing oxidative stress. Furthermore, the extract did not affect significantly tranchea neither lung smooth muscle contraction, showing an in vitro good toxicological profile. The cytoprotective effects occurred at concentrations ranged between 0,01 and 0,1 mg/mL, at which it did not affects mooth muscle contraction parameters.

These experiments suggest the potential application of this phytocomplex acting through a guest and host targeting approach in COVID-19.

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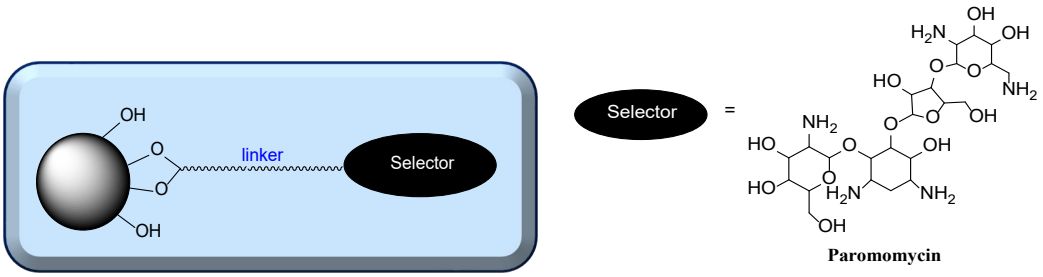
A novel stationary phase for hydrophilic interaction chromatography

Martina De Angelis,[a] Francesco Gasparrini,[a] Alessia Ciogli[a]

[a] Dipartimento di Chimica e Tecnologie del Farmaco, Sapienza Università di Roma, P.le Aldo Moro 5, 00185 Roma, Italy

Hydrophilic interaction liquid chromatography (HILIC) provides an alternative approach complementary to reversed phase (RP), being suited for separation of small polar and ionized compounds. Typically, HILIC system involves polar stationary phases and aqueous-polar organic mobile phase (mainly acetonitrile). [1] Beside the most commonly used stationary phases (diol, amino, amido), several other selectors for HILIC applications, with large structure variability, have been emerged in literature. [2,3] In this contest, a new stationary phase for HILIC applications has been prepared and packed into HPLC column. The selector immobilized on 2.7 µm totally porous silica particles, is the aminosugar paromomycin, an aminoglycoside active against many bacteria. [4]



The prepared stationary phase, rich in hydroxyl and amine functions, has been tested in both HILIC and RP conditions and results were compared with commercially available HILIC columns. In addition, due to the chiral nature of selector, the potential on the enantioselective chromatography has been investigated.

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Green Synthesis of Plant Protection Peptides

Laura Gabbatore,[a] Angela Bolzonello,[b] Luca Sella,[b] Laura Morbiato,[a] Silvio Tundo,[b] Francesco Favaron,[b] Marta De Zotti[a]

[a] Department of Chemistry, University of Padova, 35131 Padova (Italy); [b] Department of Land, Environment, Agriculture and Forestry, University of Padova, 35020 Legnaro, PD (Italy). marta.dezotti@unipd.it

European Union actively seeks eco-friendly and effective alternatives to synthetic pesticides. Fungal species belonging to the *Trichoderma* genus are commonly used as biocontrol agents against several crop pathogens, but their efficacy is often unreliable. Among their secondary metabolites, peptaibols are a peculiar family of helical peptides with antimicrobial activity. Their plant-protection properties and structural stability, even under critical pH and temperature conditions, make them promising active agents, but they come as a complex mixture of congeners with a composition - and efficacy - heavily dependent on the environmental conditions. Besides, their poor water-solubility hampers an efficient delivery for practical use in crop protection.
In this presentation, we describe a versatile solid-phase peptide synthesis strategy, designed to reduce the impact on the environment, applied to produce water-soluble analogs of the natural short-length peptaibol trichogin GA IV. We tested our analogs *in vitro* against the important fungal plant pathogen *Botrytis cinerea* and other ascomycete phytopathogens (*Bipolaris sorokiniana*, *Fusarium graminearum*, *Penicillium expansum*). Compared to trichogin, which was completely inactive against those fungi, three analogs wholly inhibited fungal growth at low micromolar concentrations [1]. The most effective peptides significantly reduced disease symptoms by *B. cinerea in vivo* on both common bean and grapevine leaves and ripe grape berries without visible phytotoxic effects. An in-depth conformational analysis allowed us to build a 3D-structure-activity relationship finding that the relative position of the basic residues is crucial to increase peptide fungicidal activity.

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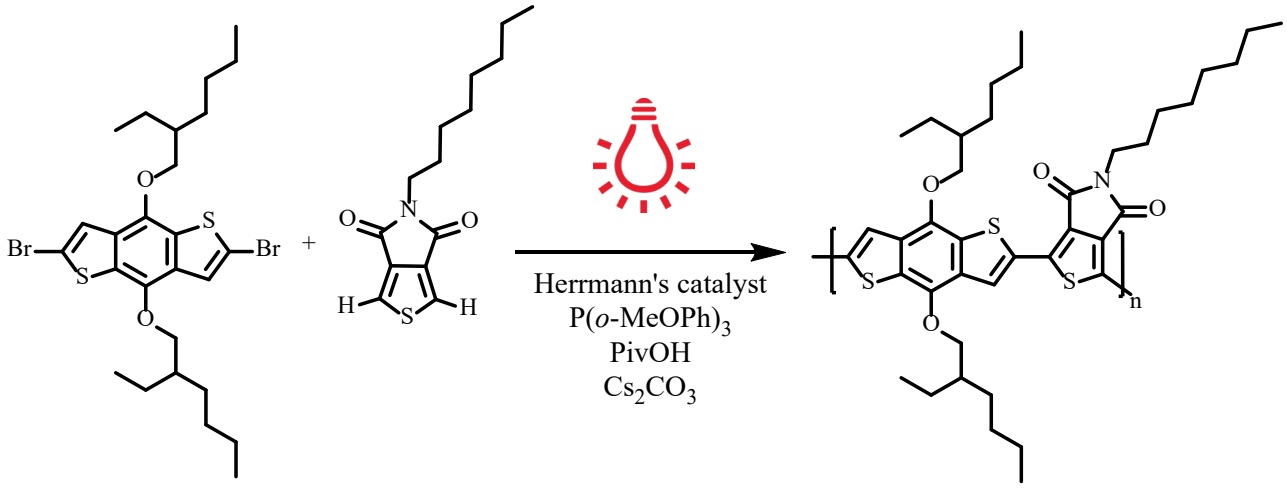
Infrared irradiation-assisted Pd-catalyzed direct (hetero)arylation polymerization

Gianfranco Decandia[a,b], *Gianluigi Albano*[a], *Angela Punzi*[a], *Gianluca M. Farinola*[a]*

[a] *Dipartimento di Chimica, Università degli Studi di Bari "Aldo Moro", Via E. Orabona 4, 70126 Bari, Italy*
[b] *Istituto per i Processi Chimico-Fisici CNR-IPCF, Dipartimento di Chimica, Via E. Orabona 4, 70126 Bari, Italy*

Conjugated polymers are functional materials with a wide range of applications: from field-effect transistor to organic photovoltaics, from sensors to bioimaging materials.
Generally, the polymerization process is catalyzed by a transition metal, typically Palladium, and it involves several organometallic reagents and aryl halides to form new carbon-carbon bonds. One of the major drawbacks is the preliminary preparation of the organometallic reagents, often air- and moisture-sensitive, expensive or even toxic[1].
Recently, direct arylation polymerization has attracted much attention as an environmentally friendly alternative to classic cross-couplings since it does not need organometallic compounds and does not form metallic salts as by-products. The main disadvantage is represented by the use of harmful solvents (*e.g.*, DMF, DMA, toluene, etc.)[2], which, lately, have been replaced by more sustainable ones, such as 2-methyltetrahydrofuran and cyclopentyl methyl ether (CPME)[3].



In this work, the synthesis of a donor-acceptor polymer, composed of 4,8-bis((2-ethylhexyl)oxy)benzo[1,2-b:4,5-*b'*]dithiophene (BDT) as the electron-donating unit and 5-octyl-thieno[3,4-*c*]pyrrole-4,6-dione (TPD) as the electron-accepting unit has been performed. Polymerizations have been carried out using CPME as the solvent and an infrared (IR) lamp as the energy source: IR irradiation heating, actually, has proven to be a good alternative to conventional energy sources[4] and provides good yields and high molecular weights in just one hour reaction.

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Organic dye-based photosystems for the evolution of solar fuels

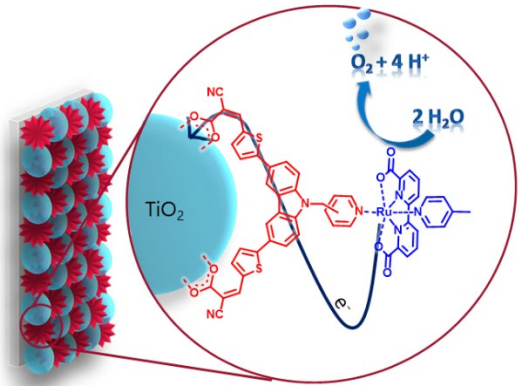
C. Decavoli, C. L. Boldrini, N. Manfredi, A. Abbotto

Dipartimento di Scienza dei Materiali, Università degli Studi di Milano-Bicocca, e Unità di Ricerca INSTM di Milano-Bicocca, via Roberto Cozzi 55, 20125 Milano, Italy, e-mail: c.decavoli@campus.unimib.it

The continuous increase in global energy demand can no longer be satisfied exclusively by fossil fuels since it is no longer sustainable for our planet. Currently, the scientific community is looking for new materials to efficiently convert renewable energy sources. Great interest has been given to the mimesis of natural photosynthesis, a process that allows obtaining oxygen and organic compounds using only water, carbon dioxide, and solar radiation. Although we are still far from making a real artificial leaf, there a couple of devices that mimic the first step of natural photosynthesis that is the production of oxygen and hydrogen, using only water and sunlight. Among these, one is the dye-sensitized photoelectrochemical cell (DS-PEC). The central element of this device is a semiconductor (SC), on whose surface a dye and a water oxidation catalyst (WOC) are typically anchored. The irradiated dye has the strategic task of generating the hole/electrons couple, of being stable over a long time irradiation, of absorbing a large portion of the visible spectrum, and of guaranteeing a fast charge transfer to the SC while avoiding charge recombination paths.[1] However the binding of the WOC onto the SC surface competes with the absorption of the dye and thus reduces the light harvesting of the system. A possible development of these systems is the synthesis of a single molecule, a dyad, composed by the union of the two essential elements for a DS-PEC, dye and WOC. In this way, it is possible to obtain the highest light harvesting and a faster charge transfer, reducing the detrimental charge recombination reactions between SC and WOC since the latter is kept away from the electrode surface. In literature only few examples of this kind of systems are present, but until now the dyads based on metal-free organic dyes are a rarity.

Here, I will present a new way of producing organic dye-based dyads exploiting a covalent bond between the dye and a ligand of the ruthenium WOC.[2] I investigated different designs of the dye, which modified the structure of the dyads depending on the nature of the donor moiety, on the distance between the ligand and the donor moiety and on the linkage position on the axial ligand.

These dyads have been investigated in water-splitting DS-PEC, showing excellent faradaic efficiencies, thus triggering new perspectives for the design of efficient molecular dyads based on metal-free dyes for DS-PEC water splitting.



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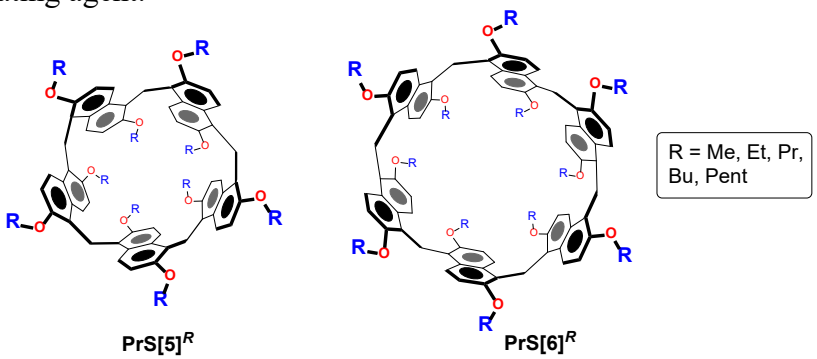
Prism[*n*]arene Macrocycles:

A New Tool in Supramolecular Chemistry

Rocco Del Regno,[a] Paolo Della Sala,[a] Carmen Talotta, [a] Placido Neri,[a] Silvano Geremia,[b] Neal Hickey,[b] Amedeo Capobianco,[a] Luca Di Marino, [a] Carmela Calabrese,[a] Carmine Palo,[a] Aldo Spinella,[a] Carmine Gaeta[a]

[a] *Dipartimento di Chimica e Biologia, "A. Zambelli" Università di Salerno Via Giovanni Paolo II, I-84084, Fisciano, Italy.*
[b]*Centro di Eccellenza in Biocristallografia, Dipartimento di Scienze Chimiche e Farmaceutiche Università di Trieste Via L. Giorgieri 1, I-34127, Trieste, Italy*

The synthesis of new macrocycles is one of the most explored field in supramolecular chemistry. At this regard, the design of macrocyclic hosts with an extended aromatic cavity plays a central role, thanks to their potential applications in molecular recognition.[1] Very recently, we have introduced the prism[n]arenes,[2] novel macrocycles based on methylene-bridged 1,5-naphthalene units. These derivatives have been synthesized by a thermodynamic templated synthesis.[3] In details, **PrS[5]^{Me}** or **PrS[6]^{Me}** was selectively removed from the equilibrium mixture by using the complementary ammonium-templating agent.[2]



The length of the alkyl chains on the rims of prismarenes plays a "special role",[4] driving the cyclization of prismarenes. In fact, **PrS[6]^{Et}** and **PrS[6]^{nPr}** are achieved in high yields and in short reaction times independent of the nature of the solvent, while the yield of prism[6]arene decreases (from 75 % to 8 %) as the chain length increases from ethoxy to pentoxy. **PrS[6]^{Et}** and **PrS[6]^{nPr}** adopt, both in solution and in the solid state, a folded cuboid-shaped conformation, in which four inward oriented alkyl chains fill the cavity of the macrocycle. On these bases, we proposed that the cyclization of **PrS[6]^{Et}** and **PrS[6]^{nPr}** occurs through an intramolecular thermodynamic self-templating effect.[4] In other words: the self-filling of the internal cavity of **PrS[6]^{Et}** and **PrS[6]^{nPr}** stabilizes their cuboid structure, driving the equilibrium toward their formation.
The **PrS[n]^{R}** here described show a deep π-electron rich aromatic cavity thanks to which exhibits a great affinity for the quaternary ammonium guests, originating from favorable cation··· π and $^{+}$NC−H··· π interactions.

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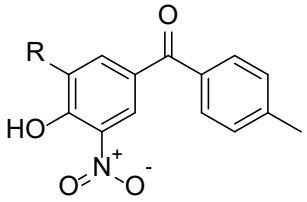
Tolcapone analogues as stabilizers of the amyloidogenic protein transthyretin

Valentina Loconte[a], Michele Cianci[b], Ilaria Menozzi[c], Davide Sbravati[c], Davide Dell'Accantera[c], Francesco Sansone[c], Alessandro Casnati[c], Rodolfo Berni[c]

[a] iHuman Institute, ShanghaiTech University, 201210 Pudong, Shanghai, China; [b] Department of Agricultural, Food and Environmental Sciences, Polytechnic University of Marche, 60131 Ancona, Italy; [c] Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, 43124 Parma, Italy

Transthyretin (TTR) is an amyloidogenic homotetramer involved in the transport of thyroxine[1] and retinol in blood and cerebrospinal fluid.[2] Tolcapone (Fig.1) is an FDA approved drug for Parkinson's disease able to interact with the thyroxine-binding sites both of the wild type and pathogenic mutant forms of TTR.[3] In this way, tolcapone works as stabilizer of the TTR tetramer and, as consequence, inhibits the amyloidogenic activity of this protein that is related to its disassembly, cause of amyloid fibrils formation.[4] In tackling the TTR related amyloidosis, tolcapone has two limiting features: a short life-time in the plasma due to rapid glucuronidation of OH group in 3 position that produces a rapidly eliminated metabolite[5] and a too low lipophilicity that jeopardizes an efficient crossing of the brain-blood barrier (BBB). In our work,[6] we are preparing and studying more lipophilic analogs of tolcapone, such as 3-O-methyltolcapone and 3-deoxytolcapone (Fig.1).



R=OH, tolcapone
R=OCH_3, 3-O-methyltolcapone
R=H, 3-deoxytolcapone

Fig.1: Structures of tolcapone, 3-deoxytolcapone and 3-O-methyltolcapone

Their features should improve BBB penetration and pharmacokinetics, thus resulting advantageous for the pharmacological treatment of TTR amyloidoses affecting the central nervous system. We will report on the synthesis of the tolcapone analogs and their properties as ligands and stabilizers of the TTR tetramer.

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C-H Bonds Oxidation Promoted by Nonheme Iron(IV)-oxo Complexes Mediated by *N*-hydroxyphthalimide: Change of Selectivity by Effect of HAT Mediators

Marika Di Berto Mancini[a], Federico Frateloreto[a], Andrea Del Gelsomino[a], Stefano Di Stefano[a], Osvaldo Lanzalunga[a], Andrea Lapi[a], Giorgio Olivo[a] and Stefano Sajeva[a]*

[a]*Dipartimento di Chimica and Istituto CNR per i Sistemi Biologici (ISB-CNR), Sezione Meccanismi di Reazione, Università di Roma "La Sapienza", P.le A. Moro, 5, 00185 Rome, Italy)*

Oxidation processes mediated by *N*-hydroxyphthalimide (NHPI) have attracted a special attention in recent years. For example, NHPI is an efficient mediator in the aerobic oxidation of organic compounds promoted by laccase.[1] NHPI plays also an important role as redox mediator under electrochemical conditions.[2] We have recently discovered that NHPI is an efficient mediator in the oxidations of organic compounds promoted by nonheme iron(IV)-oxo complexes, biomimetic models of the active species formed in nonheme iron oxygenases.[3] Kinetic studies with the nonheme iron(IV)-oxo complex, $[(N4Py)Fe^{IV}(O)]^{2+}$, showed a faster decay of the oxidant in the presence of NHPI. The increase of reactivity is associated to the oxidation of the mediator to the corresponding aminoxyl radical PINO (Figure 1, step a) which efficiently abstracts hydrogen atoms from the substrates regenerating the mediator NHPI (Figure 1, step b). The mediation effect of NHPI in this system is in accordance with the results of product analysis showing that higher product yields are observed in the presence of the mediator.

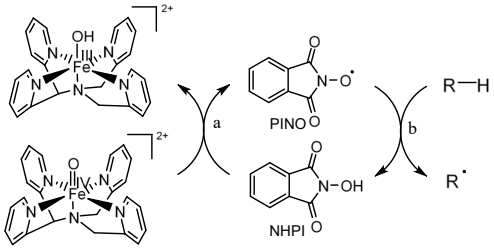

Figure 1: NHPI mediated oxidation of organic compounds promoted by $[(N4Py)Fe^{IV}(O)]^{2+}$.

A change of selectivity in the C-H functionalization of alkylaromatic componds and alcohols is observed in the presence of the NHPI mediator as a result of the different polar effects operating in the HAT processes promoted by $[(N4Py)Fe^{IV}(O)]^{2+}$ and the phthalimide-N-oxyl radical (PINO) (Figure 2).

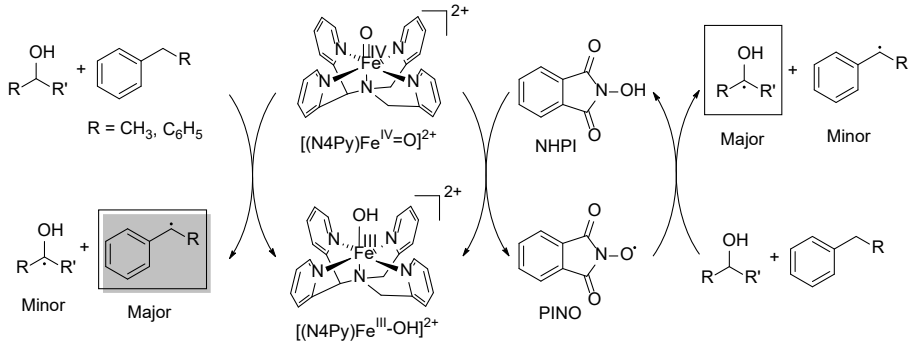

Figure 2: Change of selectivity in the oxidation promoted by $[(N4Py)Fe^{IV}(O)]^{2+}$ with NHPI.

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Bioactive metabolites produced by two *Diplodia* spp., pathogens of Mediterranean forest plants

Roberta Di Lecce,[a] Marco Masi,[a] Giulia Marsico,[b] Benedetto Teodoro Lunaldeddu,[c] Lucia Maddau,[d] Stefano Superchi,[b] Gennaro Pescitelli[e] and Antonio Evidente[a]

[a]*Dipartimento di Scienze Chimiche, Università di Napoli Federico II, Complesso Universitario Monte Sant'Angelo, Via Cintia 4, 80126, Napoli, Italy*
[b]*Dipartimento di Scienze, Università della Basilicata, Viale dell'Ateneo Lucano 10, 85100 Potenza, Italy*
[c]*Dipartimento Territorio e Sistemi Agro-Forestali, Università di Padova, Viale dell'Università 16, Legnaro 35020, Italy*
[d]*Dipartimento di Agraria, Sezione di Patologia Vegetale ed Entomologia, Università degli Studi di Sassari, Viale Italia 39, 07100, Sassari, Italy*
[e]*Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via Moruzzi 13, 56124 Pisa, Italy*

Pathogenic fungi are involved in some canker forms of forest plants and fungal-plant interactions represent biochemically complex processes that are being studied. These fungi are able to produce phytotoxins, i.e. secondary metabolites, which are virulence factors and are involved at different stages of pathogenesis. These metabolites belong to several classes of natural compounds and could show interesting biological activities in agriculture and in medicine.[1]
Forest plant diseases in the Mediterranean area are a public interest issue, considering the resulting huge losses to the wood industry and landscape.
Species of *Diplodia* are cosmopolitan in temperate regions and exhibit diverse life-styles spanning from endophytes to aggressive pathogens.[1] The improvement of new diseases caused by these pathogens during the last decades is highlighting the importance to investigate the involved metabolites.
Diplodia olivarum has arised as an aggressive pathogen on various plant hosts in Italy, as carob tree, wild olive and lentisk.[2,3,4] It induce sunken cankers with characteristic wedge-shaped wood necrosis on branches and stems. The fungus was grown on two media and from the corresponding organic extracts a new cleistanthane *nor*-diterpenoid together with other diterpenoids and an isocoumarin were isolated.
Diplodia sapinea is the most known and economically important pathogen of conifers worldwide. This fungus had attacked severely pine plantations in the southern hemisphere causing large-scale dieback and tree mortality.[5] Recently, an ongoing expansion of *D. sapinea* in Tunisia has been inducing branch canker and dieback of maritime pine.[6] Two new phytotoxins have been isolated from the organic extract of its culture filtrate.
This communication will be focused on the structure elucidation and biological characterization of the secondary bioactive metabolites produced by the two *Diplodia* spp..

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Chemistry and Immunology of Lipopolysaccharides from commensal bacteria: is it time for a paradigm shift?

Flaviana Di Lorenzo

[a] *Department of Chemical Sciences, University of Naples Federico II, Naples 80126, Italy*

Lipopolysaccharides (LPS) from gut commensal and mutualistic bacteria trigger immunomodulatory responses on the basis of their chemical structures. However, only a few gut commensal/mutualistic LPS have been structurally elucidated so far. Therefore, the molecular motifs crucial for LPS−host interactions at the gut level remain obscure. In this communication, I will focus on the LPS of two mutualists of the human intestine: *Bacteroides vulgatus* and *Alcaligenes faecalis*. I will show that *B. vulgatus* LPS does not induce pro-inflammatory cytokines release and that its administration is enough to reestablish intestinal immune homeostasis in a mouse model for experimental colitis.[1] I will also present that the LPS structural characterization revealed an unprecedented structure based on a hypo-acylated and *mono*-phosphorylated lipid A, a galactofuranose-containing core oligosaccharide (OS), and an O-antigen built up of mannose and rhamnose. This particular structure is reflected in an intriguing ability, in human *in vitro* cellular models, to produce anti-inflammatory cytokines and to induce the synergistic activation of TLR4- and TLR2-mediated signaling pathways.[2] As for *A. faecalis*, this is the sole Gram-negative inhabiting gut lymphoid tissues, Peyer's patches (PPs), which are the largest sites for the initiation and regulation of intestinal IgA responses. *Alcaligenes* spp. LPS is necessary to maintain a homeostatic environment in PPs, without triggering any harmful response. Here I will highlight that also *A. faecalis* LPS has an unreported structure with a *mono*-phosphorylated core OS, which contains a huge number of *N*-acetyl hexosamines.[3] The lipid A is a mixture of tetra- to hexa-acylated species. Finally, I will show that these differently acylated lipid A have been synthesized and their immunological properties tested, revealing that only the hexa-acylated one is able to induce NF-κB activation in TLR4-expressing cells, which was however massively weaker than upon stimulation by the highly immunostimulant *E coli* LPS.[3]

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Catalytic deoxygenation of sunflower oil using reduced metal catalysts supported on Fly Ash Cenosphere

Giuseppe Di Vito Nolfi[a], Leucio Rossi[a], Katia Gallucci[b]

[a]Dipartimento di Scienze Fisiche e Chimiche. Università degli Studi dell'Aquila. Via Vetoio snc – Coppito; 67100. L'Aquila ; [b] Universita `degli studi dell' Aquila DIIIE, 67100 L' Aquila, Italy

Catalytic deoxygenation (DO) of vegetable oils effectively converts oils into Green Diesel (nC$_{15}$-C$_{18}$ hydrocarbons), a biofuel fully compatible with mineral diesel[1]. In the DO process, the vegetable oil was converted in hydrocarbons following three different pathways: HDO (hydrodeoxygenation), DCO (decarbonylation) and DCO$_2$ (decarboxylation)[2]. In this work, the DO of sunflower oil was investigated using reduced state transition metal catalysts supported on fly ash cenospheres (FAC). FAC are by-products of coal combustion and using them as a support means recycling a waste material. Several catalysts (named XY(n/m)/FAC where X and Y are the metals, and n and m the %$_{wt}$ of the metal oxides) are synthesized via wet impregnation method followed by calcination and reduction. They were tested in a batch reactor at T: 320°C, P$_{H2}$: 40bar, t: 6h, 20g Hexane, oil 2g, catalyst 0.2g After 6 hours, the mixture underwent transesterification before being analyzed with gas chromatograph. The data obtained are shown in figure 1.

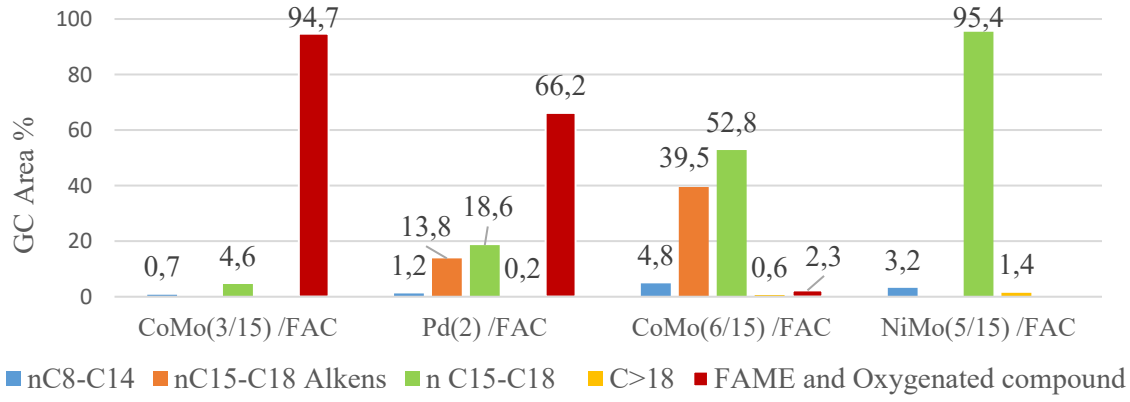

Figure 1 Distribution of products in reaction mixture after DO

Among the catalysts tested, the most active are NiMo(5/15)/FAC and CoMo(6/15)/FAC leading to 100% and 98% conversion respectively. NiMo(5/15)/FAC produce 95.4%$_{wt}$ of n-C$_{15}$-C$_{18}$ saturated hydrocarbons (68.2% of C$_{18}$ and 19.1% of C$_{17}$ and thus high HDO selectivity); CoMo(6/15)/FAC yields 92.3%$_{wt}$ of n-C$_{15}$-C$_{18}$ (39.2% of C$_{18}$ and 7.5% of C$_{17}$), with a high degree of n-C$_{15}$-C$_{18}$ unsaturated hydrocarbon (39.5%). It is interesting to note that increasing Co load in the CoMo catalyst (CoMo(3/15) to CoMo(6/15)) leads to a significant increase in conversion (13% to 98%). In summary, we have shown that cenospheres can act as a cost-effective recycled material, and an efficient support metal catalyst in the synthesis of Green Diesel from vegetables oils with high activity and selectivity towards diesel range hydrocarbons.

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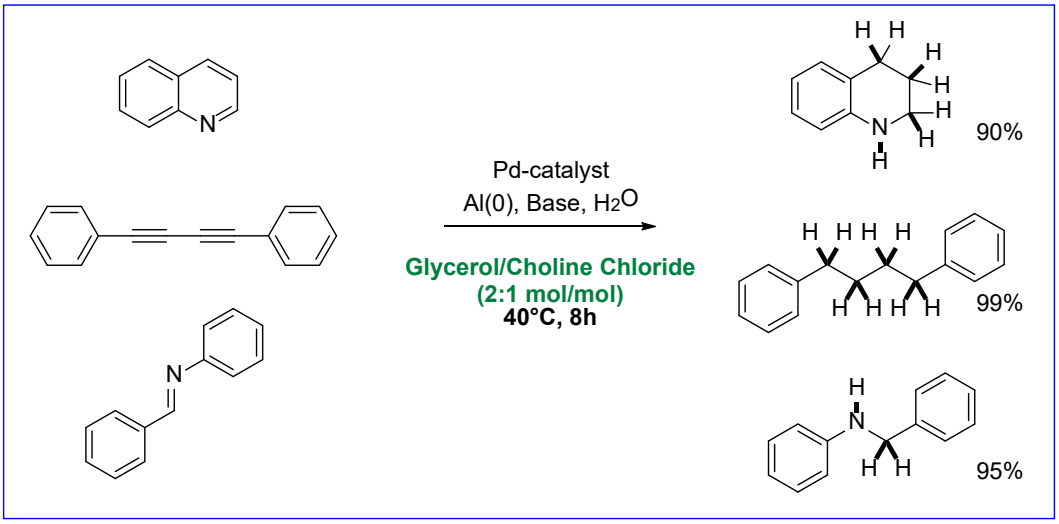
Pd-catalyzed Reductions in Deep Eutectic Solvents by Using Aluminum and Water as Hydrogen Source

Giuseppe Dilauro[a], Serena Perrone[a], Francesco Messa[a], Andrea N. Paparella[a], Antonio Salomone[b]

[a] Dipartimento di Scienze e Tecnologie Biologiche ed Ambientali, Università del Salento, Prov.le Lecce-Monteroni, I-73100 Lecce, Italy; [b] Dipartimento di Chimica, Consorzio C.I.N.M.P.I.S., Università degli Studi di Bari "Aldo Moro", Via E. Orabona 4, I-70125 Bari, Italy

The reduction of organic functional groups, using metal-catalyzed hydrogenations, is one of the most employed strategy in organic chemistry for the synthesis of both fine and bulk chemicals.[1] Hydrogen is an explosive gas and its production needs extensive energy and generates a considerable amount of carbon dioxide. Therefore, the development of cost-effective reduction methods that use safe reagents, environmentally-friendly solvents and prevent or minimize waste formation represents a challenge of great interest in sustainable chemistry. As part of our ongoing efforts in the discovery of sustainable synthetic methodologies,[2] an alternative and safe palladium-catalyzed hydrogenation reaction in Deep Eutectic Solvents (DESs) is here described.[3] The use of aluminum powder in combination with water and a base in DESs, results in an environmentally-responsible system for the controlled *in-situ* generation of hydrogen. Our optimized protocol is effective for the reduction of a wide range of functional groups, containing C–C, C–N, C–O, N–O multiple bonds as well as for the dearomatization of (hetero)aromatic compounds, and leads to the desired products in yield up-to 99%. The simplicity, cost, tunability, scalability and the environmentally benign character of both catalytic system and DESs, offer numerous advantages over the currently available methods that employ external and dangerous H_2 source and harsh, volatile organic solvents.



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Divergent, stereospecific mono/difluoromethylation of boronic esters

V. Fasano,[a] N. Winter,[a] A. Noble,[a] V. K. Aggarwal[a]

[a]*University of Bristol, Cantock's Close, Bristol, BS8 1TS, UK*

There is considerable interest in incorporating fluorine into agrochemicals and pharmaceuticals.[1] Whilst a number of methods have been reported for installing CH_2F and CHF_2 groups, they are mainly limited to radical reactions, which are invariably racemic.[2] We have studied the divergent, stereospecific reaction of fluoroiodomethyllithium with boronic esters to give α-fluoro-boronic esters.[3] The use of the highly unstable fluoroiodomethyllithium was key to allowing rapid 1,2-migration over competing decomposition of the carbanion. Indeed, DFT calculations suggested that the more fluorine atoms attached to carbon, the higher the barrier to 1,2-migration and the lower the barrier to dissociation, which in turn lead to carbanion decomposition.

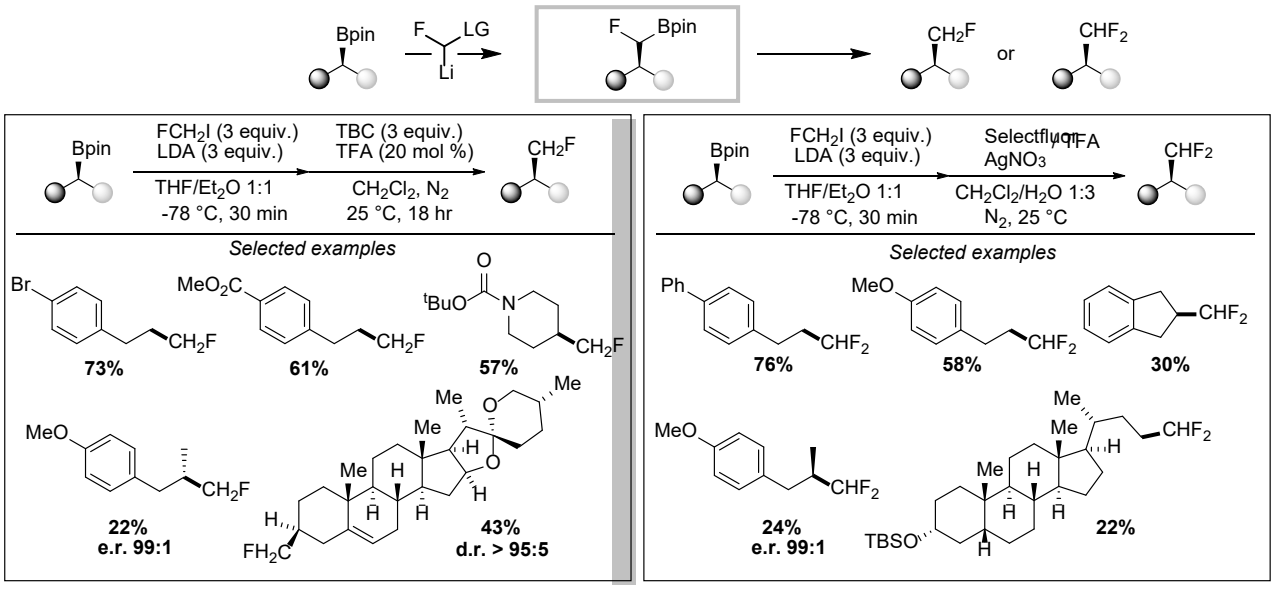

Figure 1. Divergent, stereospecific fluoromethylation of boronic esters.

The unique α-fluoro-boronic esters intermediates can be readily transformed into the corresponding mono- or difluoromethylated compounds through proto- or fluorodeboronation, respectively. Furthermore, the reactions were fully stereospecific, as shown by transforming an enantioenriched secondary boronic ester into the corresponding fluoromethylated products in high e.e.

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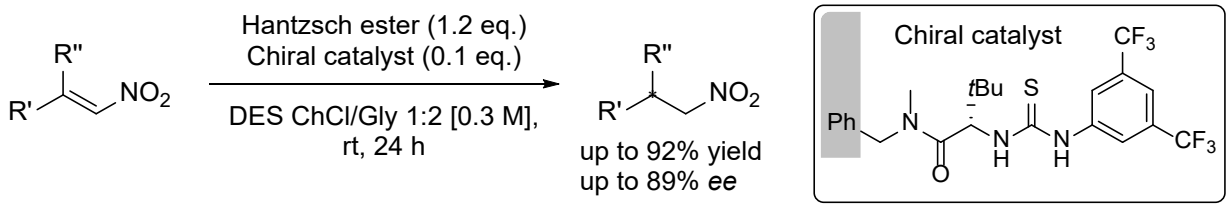
Catalytic enantioselective reduction of nitroalkenes in DESs

C. Faverio,[a] *M. Benaglia*[a]

[a] *Università degli Studi di Milano, Via Golgi 19, Milano*

The shift toward sustainable chemical processes that fulfill the principles of green chemistry, is recognized as a priority by the scientific community. In this context, one of the major culprits of waste production in chemical industries is the use of solvents, therefore the study of alternative and environmentally benign solvents is a topic that is gaining a steadily increasing attention.
Deep Eutectic Solvents (DESs)[1] are mixture of two or three components, typically derived from natural sources, which are capable of forming hydrogen bond interactions with each other, thus leading an eutectic mixture with a melting point lower than either of the individual components. DESs were firstly studied by Abbott[2] and co-workers in 2003 and, since then, a considerable number of applications, spanning from metal processing to biodiesel purification, were published. The attention dedicated worldwide to DESs is linked to their unique features, to be easily prepared without the need of further purification, to be non-volatile, non-flammable and biodegradable.
In 2016, our research group[3] disclosed the possibility to run stereoselective reactions catalyzed by a chiral primary amine in bio-based eutectic mixtures. In particular, three different activation mode based on covalent interaction between the catalysts and the substrate were studied.
Herein, we report our efforts for the development of the first organocatalytic reduction involving hydrogen bonding interactions among the substrate, the reagent and the catalyst in deep eutectic solvents which are made in turn of hydrogen bonds. We optimized the reduction of *β,β*-disubstituted nitroalkenes with Hantzsch ester (di-*tert*-butyl-1,4-dihydro-2,6-dimethyl-3,5-pyridinedicarboxylate) in the presence of thiourea-based chiral bifunctional catalysts to promote the formation of enantioenriched *β*-branched nitroalkanes, that was published by List[4] and co-workers, employing DESs as reaction medium instead of traditional organic solvents.



Several DESs were tested, obtaining the best results with a mixture of choline chloride and glycerol. The reduction protocol involves milder reaction conditions and shorter reaction time with the respect to the original publication and opens the way to the possibility of recycling the DES.

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Probing molecular recognition of sialoglycans by Nuclear Magnetic Resonance and Molecular Modelling

Rosa Ester Forgione[a], *Antonio Molinaro*[a], *Roberta Marchetti*[a], *Alba Silipo* [a]

[a]*Dipartimento di Scienze Chimiche, Università degli Studi di Napoli Federico II, Strada Comunale Cinthia, Italy;* [b]*Department of Chemistry, Graduate School of Science, Osaka University, Osaka, Japan*

The interplay between sialoglycans and their receptors lays the foundation for numerous molecular recognition processes like cell–cell interactions, information transfer and pathogenesis.[1] Of particular interest is their role as selective mediators in disease, defense, and symbiosis,[2] making sialoglycans ideal candidates to design effective diagnostic tools or therapeutic drugs. To date, several sialic acid-based drugs have already been designed and currently employed as therapeutics, diagnostics and vaccines and many others are expected to come in the next years.[3]
To this purpose, the atomic level characterization of sialoglycans binding upon their receptors sets the basis for the design and development for novel therapeutics. In this context, we applied nuclear magnetic resonance (NMR), computational and biophysical techniques to provide a deeper comprehension of the biological processes underlying sialoglycans recognition by therapeutically relevant sialic acid binding proteins, such as Siglecs[4][5] (Sialic acid binding immunoglobulin-type lectins) as well as neuraminidases.[6] Our studies allowed for the rigorous definition of the bioactive conformation and the binding epitope of natural occurring sialoglycans and their analogues and afforded the atomistic description of the 3D complexes structures. The obtained outcomes represented a first step toward the development of more effective drugs to prevent life threatening diseases, including cancer and autoimmune disorders.[7]

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Ferrocene/C$^{\alpha,\beta}$-didehydroalanine conjugates to investigate the role of dipolar moments in peptides

Saverio Santi,[a] Annalisa Bisello,[a] Roberta Cardena,[a] Silvia Tomelleri,[a] Renato Schiesari,[a] Barbara Biondi,[b] Marco Crisma,[b] Fernando Formaggio[a,b]

[a] Department of Chemistry, University of Padova, 35131 Padova, Italy; [b]Institute of Biomolecular Chemistry, Padova Unit, CNR, 35131 Padova, Italy

Electron/charge transfer processes are relevant phenomena in proteins. In this connection, the dipole moment generated by α-helices plays an important role. Our work aims at reinforcing this finding through synthesis and electrochemical studies of peptide systems having no dipole moments.
We exploited the natural, but non coded, C$^{\alpha,\beta}$-didehydroalanine (ΔAla) α-amino acid. It prefers the fully-extended conformation, also known as 2.0$_5$-helix, where the amide carbonyls have antiparallel orientations (Figure 1).[1] Therefore, the C=O dipoles cancel each other out and do not create a significant dipole moment. We chose ferrocene (Fc) as electrochemical probe because it is endowed with an excellent stability in different environments without losing its electrochemical features.[2]
We synthesized three -(ΔAla)$_n$- (n = 1-4) segments having one or two Fc moieties covalently bound (Figure 1, left). A thorough conformational investigation revealed that our conjugates adopt the fully-extended conformation, both in solution (2D-NMR and IR absorption) and in the crystal state (X-ray diffraction). The cyclic voltammetry analysis agreed with such conclusion as no influence of dipole moments was observed.[3] Thus, at variance from the charge/electron conductive properties of α-helices, fully-extended α-peptide stretches act as insulators.

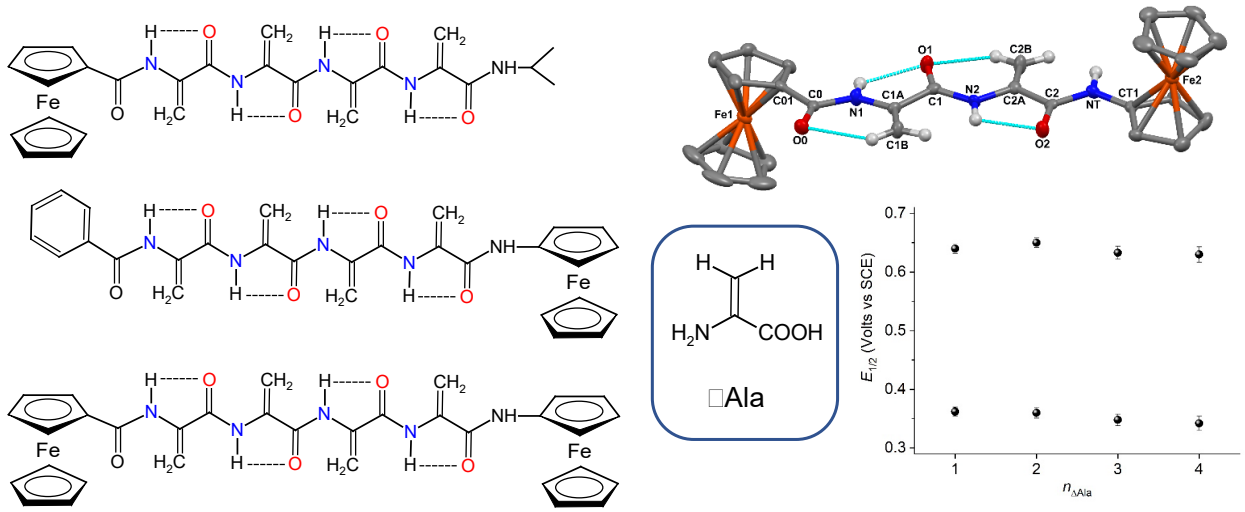

Figure 1. *Left:* the 3 longest Fc/peptides investigated. *Top right:* X-Ray diffraction structure of the dipeptide with two Fc moieties. *Bottom right:* Plot of the Fc oxidation potentials for the series with two Fc. The negligible variations upon peptide lengthening support the absence of influence from dipole moments.

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An iron catalyzed, regiodivergent methodology for the reductive opening of epoxides

L. Tadiello,[a] T. Gandini,[b] B. M. Stadler,[a] S. Tin,[a] H. Jiao,[a] J. G. de Vries,[a] L. Pignataro,[b] C. Gennari[b]

[a]*Leibniz-Institute für Katalyse e.V., Albert-Einstein-Straße 29a, Rostock (Germany)*

[b]*Università degli Studi di Milano, Dipartimento di Chimica, Via Camillo Golgi 19, Milano (Italy)*

The reductive opening of epoxides represents an appealing access route to alcohols and is alternative to other well-established strategies such as C=O reduction or alkene hydration. Traditionally, this transformation has been carried out using stoichiometric amounts of metal hydrides such as $LiAlH_4$, whereas catalytic versions are attractive but rarely precedented. In particular, catalytic hydrogenation (CH) represents the most environmentally friendly way to perform epoxide opening, since H_2 is a cheap and clean reductant and no stoichiometric waste is produced. The known CH methodologies for epoxide opening, including the recent breakthroughs made by the research groups of Norton[1] and Beller,[2] still suffer from some limitations, such as use of noble metals/expensive ligands or high catalytic loading. In this work, a new approach for the homogeneous CH of epoxides is presented, using the cheap and easily synthesized (cyclopentadienone)iron complex **1** as pre-catalyst.[3] The CH of aromatic epoxides was successfully performed with a high degree of regioselectivity in favor of the primary alcohol product. Applying the same pre-catalyst to the more challenging aliphatic epoxides, we discovered that it is possible to switch the regioselectivity from linear to branched alcohol products by simply varying the Lewis acid additive.

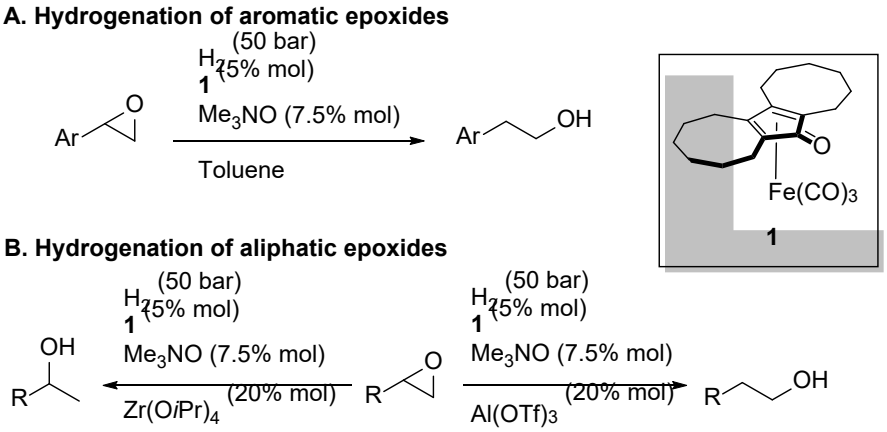

Figure 1. Catalytic hydrogenation of epoxides carried out in this work

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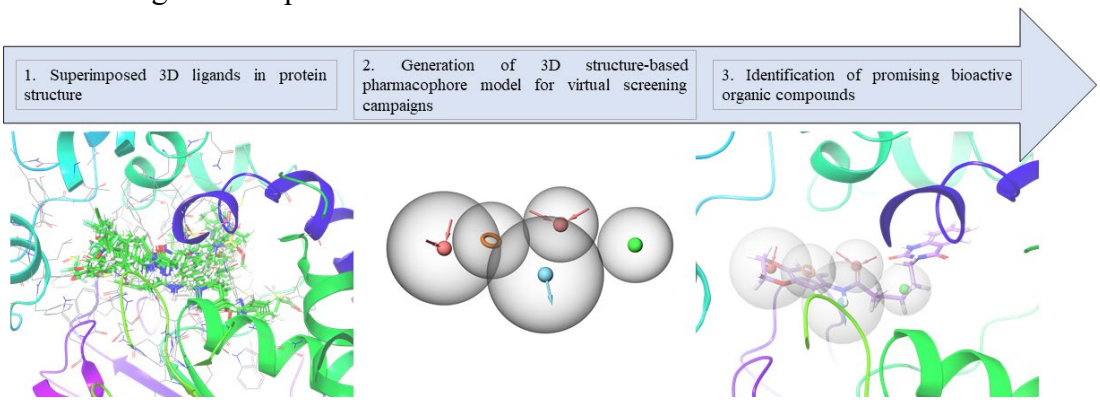
3D structure-based pharmacophore models for the identification of bioactive compounds and for accelerating the drug repositioning

Erica Gazzillo[a], Gianluigi Lauro[a], Maria Giovanna Chini[b], Ines Bruno[a], Stefania Terracciano[a], Assunta Giordano[a, c], Giuseppe Bifulco[a].

[a]Department of Pharmacy, University of Salerno, Via Giovanni Paolo II 132, 84084, Fisciano, Salerno, Italy.
[b]Department of Biosciences and Territory, University of Molise, C.da Fonte Lappone, Pesche 86090, Italy
[c]Institute of Biomolecular Chemistry (ICB), Consiglio Nazionale delle Ricerche (CNR), Via Campi Flegrei 34, I-80078, Pozzuoli, Napoli, Italy.
egazzillo@unisa.it

Computational techniques are useful for facilitating the identification of potentially active compounds, their optimization in terms of pharmacokinetic properties, potency, and selectivity. In this scenario, *in silico* techniques have been shown to be particularly useful in the field of the drug repurposing strategy[1]. With the aim of accelerating the drug repositioning process, we have developed and applied a new computational protocol that takes advantage of "structure-based 3D pharmacophore" models, built with software Phase software of Schrödinger Suite[2-4]. To validate the computational protocol, we have focused on bromodomain-containing protein 9 (BRD9) [5,6] and soluble epoxide hydrolase (sEH) [7], two targets of our interest involved in inflammatory and cancer pathologies, following our research project supported by the Italian Association for Cancer Research (AIRC). 3D-structure-based pharmacophore models have been then built for these targets and used as selection filters in virtual screening campaigns for the repositioning of commercially available organic compounds and in-house libraries. In this way, we have implemented a rapid computational workflow leading to the identification of a small set of small molecules featuring a promising activity on the two targets. These preliminary data have prompted us to optimize and implement the proposed workflow for identifying "structure-based 3D pharmacophore" models in an automated fashion, useful to speed up drug repositioning campaigns and to guide the drug design of new bioactive organic compounds.



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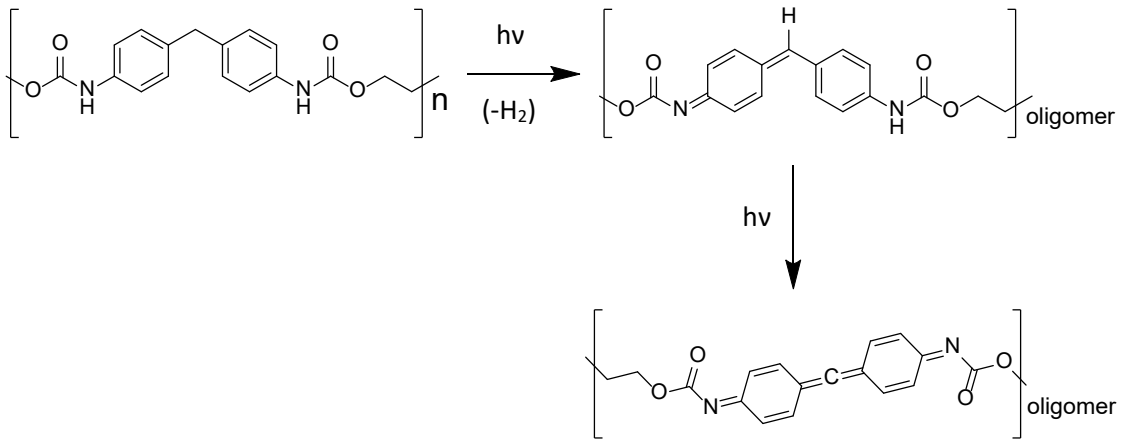
Spot-like yellowing issues of illumination products due to migration effects

Roberto Giacomantonio,[a] Serena Gabrielli,[a] Massimo Gattari,[b] Genny Pastore,[a] Leonardo Piattoni,[b] Francesca Stella,[a] Enrico Marcantoni,[a]

[a] *School of Science and Technologies, Università degli Studi di Camerino, 62032, Camerino, Italy.*
[b] *iGuzzini-Illuminazione S.p.A., Via Mariano Guzzini 37, 62019, Recanati, Italy*

Yellowing phenomena in polymer materials have been extensively studied because of their practical importance.[1,2] The problem deserves a lot of attention when it occurs in a finished product for ease of migration. Yellowing is mainly due to a variety of irreversible degradation reactions (Thermal, photo oxidation, radiation, oxidation), and given that these reactions cannot be switched back, additives are designed to mitigate the unwanted yellowing phenomenon.[3,4]



Scheme 1. UV degradation of aromatic polyurethane.

The structures responsible for the yellowing have very high molar extinction coefficients and, as a consequence, very low concentrations of the products are sufficient to give a visible yellowing. Because concentrations are low, it is rather difficult to determine the molecular structures of yellowing compounds using various in situ spectrophotometric techniques. Searches are needed to find out the origin and the cause of the unwanted phenomenon.
We focused our attention on the identification of particular spot-like yellow zone appearing under natural weathering onto the surface of a commercially available extruded polysiloxane profile. According to Scheme 1, the migration of the degradation product into polyurethane jacked cable in polysiloxane transparent material is the cause of the unwanted yellowing. Accelerated UV tests were also performed to reproduce the real service life of the product, and to provide a solid method to reproduce the migration yellowing phenomenon.

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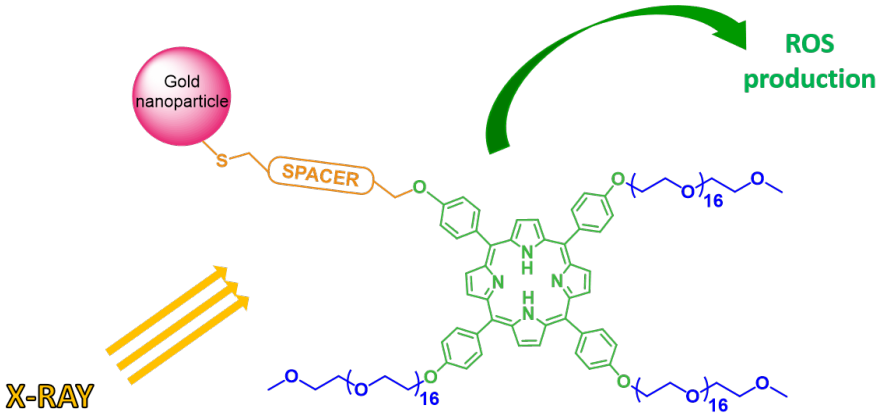
Synthesis of hybrid systems for biomedical applications through the functionalization of nanostructures

G. Gullo, E. Vaioli and F. Bigi

Department of Chemistry, Life Sciences an Environmental Sustainability, University of Parma, Parco, Area delle Scienze 17/A, 43124 – Parma, Italy

Photodynamic therapy (PDT) is a clinical approach for cancer treatment based on the activation of a photosensitizer using visible or near-infrared light to generate reactive oxygen species, in particular singlet oxygen, that induce the death of cancerous cells. Examples of effective photosensitisers (PS) for PDT treatment of cancer include organic molecules such as porphyrins, phthalocyanines and related tetrapyrroles. Recently, a great interest has been devoted to the preparation and the study of AuNPs conjugated with photosensitizer to obtain enanched fluorescence emission and PDT effect. It is known that AuNP complexes generally quench the fluorescence emission of nearby chromophores. However, many papers reported that it is possible to obtain a synergistic effect with an enanched PDT effect under laser irradiation[1]. The main drawback of classical PDT is due to the impossibility to treat deep seated tumors, being visible light employed. Thus, many efforts have been spent to overcome this limit using X-ray irradiation. In addition to the approach of *self-lighting photodynamic therapy*, based on X-ray scintillating nanoparticles conjugated with photosensitizers[2], the combination of PS and AuNP has been proposed, taking into account that under X-ray irradiation, havy elements increase the dose delivery to surrounding tissues and that also PS can increase the ROS production[3,4]. A further strategy recently published is the incorporation of PS and AuNPs into liposomes[5], to improve the *in vivo* stability, circulation lifetime, and cellular uptake. Aiming at including PS@AuNP in liposomes, here we present the synthesis of water soluble PS suitable for conjugation to AuNP. In particular, the (4-hydroxyphenyl)porphyrin functionalized with three polyethylenglycole chains was synthetized and the covalent binding with a thiol-ending linker was studied (*figure*).



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Continuous Flow Optimization of the Asymmetric α-Benzylation of Aldehydes

F. Herbrik,[a] Prof. A. Puglisi,[a] Prof. M. Benaglia,[a] Dr. M. Sanz[b]
[a]*University of Milan, Via Golgi 19, Milan,* [b]*Taros Chemicals GmBH, Emil-Figge Strasse 76°, Dortmund*

In 1912 Giacomo Ciamician shared a vision of the future with the rest of the world, in which he describes the advent and later widespread utilization of solar energy for chemical synthesis.[1] Almost 100 years later David MacMillan shared his works on the asymmetric α-alkylation of aldehydes by merging photoredox and organocatalysis in an unprecedented way and for an otherwise elusive chemical transformation.[2] The negative exponential attenuation of light through the reaction solution (fully described by the Lambert-Beer-Law) presents a harsh physical reality for upscaling purposes in the chemical industry, as the bulk of a batch reactor will not get efficiently irradiated.

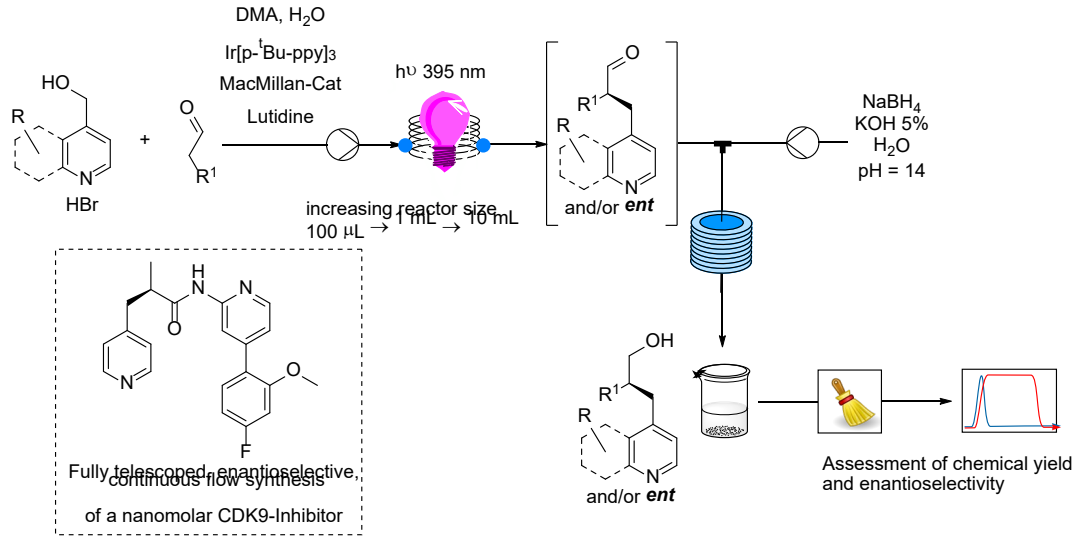

Figure 1. Illustration of the 2-step telescoped process for the synthesis and characterization of the previously described α-benzylation of aldehydes.[3]

The present work showcases the scalability that arises from employing continuous flow methodologies, exploiting the larger surface-to-volume ratio of tubular micro- and meso-reactors. An upscaling by a factor of 100 was undertaken and the productivity was compared to traditional batch methods. Due to the far increased reaction rate a slight improvement of enantioselectivity was also observed. Using the far improved methodology, a fully telescoped synthesis of a powerful API for the treatment of several forms of cancer was undertaken *in continuo*.

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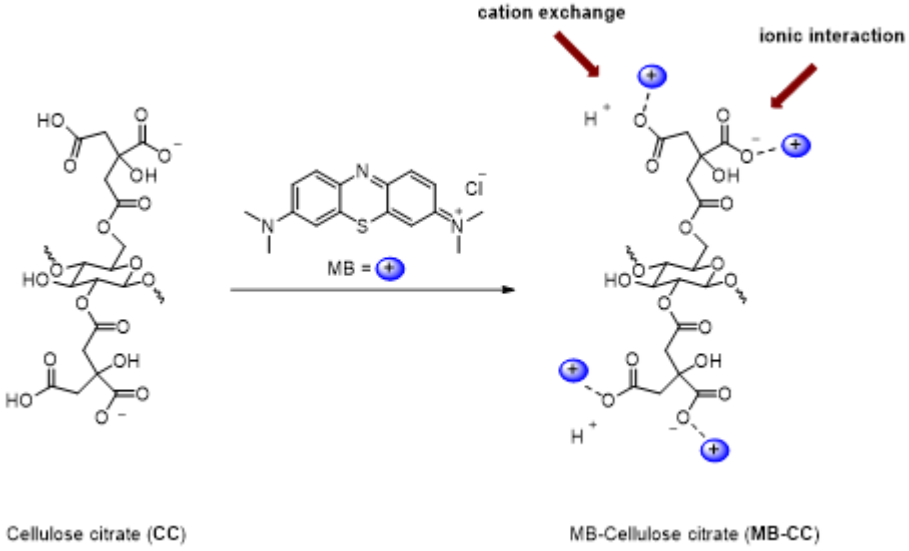
Synthesis of cellulose citrate and its application for the removal of cationic dyes from contaminated water

Antonio Jiritano,[a] Fabrizio Olivito,[a] Vincenzo Algieri,[a] Matteo Antonio Tallarida,[a] Paola Costanzo,[a] Loredana Maiuolo,[a] Antonio De Nino[a]

[a] Dipartimento di Chimica e Tecnologie Chimiche, Università della Calabria, Ponte P. Bucci, 87036 Arcavacata di Rende (CS), Italy. E-mail: antonio.jiritano@unical.it

In the recent years there was an increasing concern regarding the environmental pollution [1]. Water is the most abundant element present on our planet, and for this reason one of the most common targets for contamination. Organic dyes together to pharmaceuticals and pesticides represent one of the most dangerous threats. Every year tons of these chemicals are produced from industries in the field of textile, cosmetics, food processing, paper, agriculture and many others. Producing bio-adsorbents from biomass is a convenient process due to the wide availability of this primary source and to the biodegradability and low impact of the produced materials on the environment [2, 3]. In this context, we carried out a green and sustainable esterification reaction, starting from micro-crystalline cellulose and citric acid in a solvent-free reaction [4]. Cellulose citrate was obtained in high yield in a pure form using only acetone as the washing solvent. This product was tested as a cation exchange resin, for the adsorption of the cationic dye methylene blue from water. The mechanism of adsorption at different pH was depicted in the following Scheme 1.



Scheme 1. Mechanism of methylene blue adsorption on cellulose citrate.

The activity of cellulose citrate was evaluated at different times, temperature, pH and concentration, with the best performance under 100 mg/L. The mechanism followed the Langmuir isotherm relative to a monolayer adsorption.

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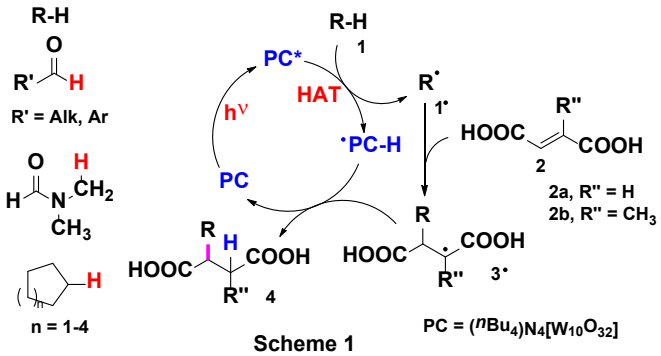
Photocatalyzed functionalization of α,β-unsaturated carboxylic acids

[1]Alexandra Jorea, [2]Maurizio Fagnoni, [2]Davide Ravelli, [3]Rodrigo M. Romarowski, [3]Stefania Marconi [3]Ferdinando Auricchio

[1]Department of Surgery, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy
[2]PhotoGreen Lab, Department of Chemistry, University of Pavia, viale Taramelli 12, 27100 Pavia, Italy.
[3]Computational Mechanics and Advanced Materials Group, University of Pavia, via Ferrata 3, Pavia, Italy
e-mail: alexandra.jorea01@universitadipavia.it

The selective functionalization of α,β-unsaturated carboxylic acids with nucleophilic reaction partners is not an easy task because of the presence of acidic hydrogens, possibly leading to mixtures of products. In this project, we explored the functionalization of these acids under radical-mediated photocatalyzed processes, complementing our recent work on the derivatization of crotonic acid. [1] Our group is deeply involved in the development of photocatalytic methods for the photogeneration of C-centered radicals and the ensuing addition onto electron-poor olefins. [2] This strategy is based on the use of tetrabutylammonium decatungstate (TBADT, $(n\text{Bu}_4\text{N})_4[\text{W}_{10}\text{O}_{32}]$) as the photocatalyst. [3] Upon absorption of a photon, this compound is able to cleave homolytically (often with high chemo- and regioselectivity) C–H bonds in a variety of organic derivatives through a Hydrogen Atom Transfer (HAT) step. [4] Accordingly, we achieved the smooth C(sp^3)–H functionalization of aldehydes, amides and alkanes (see R-H **1** in Scheme 1 below). [3,4]
In this work we applied this approach to two α,β-unsaturated dicarboxylic acids with different steric hindrance on the double bond, namely fumaric (**2a**) and citraconic (**2b**) acids (Scheme 1). Thus, the photogenerated radical **1**• was trapped by **2** to give radical adduct **3**•, in turn involved in the regeneration of the photocatalyst (via a back-HAT step) and leading to the desired product **4**. In the case of **2b** functionalization, the selectivity in the addition step onto the two non-equivalent positions of the double bond has been likewise evaluated, showing a dependency on the nature of the photogenerated radical.
Notably, these reactions could be easily adapted to flow conditions, by adopting a home-made reactor or a 3D printed microreactor made of PP (polypropylene).



Scheme 1

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Enantioselective Phase-Transfer Catalysis under Continuous Flow Conditions

Milena Krstic[a], Maurizio Benaglia[a], Miguel Sanz[b], Alessandra Puglisi[a]*

[a] *Dipartimento di Chimica, Università degli Studi di Milano, Via Golgi 19, 20133 Milano, Italy*
[b] *Taros Chemicals, GmbH & Co. KG, Emil-Figge-Str 76a, 44227 Dortmund, Germany*

Chiral phase-transfer catalysis in batch, as the most reliable method for the enantioselective synthesis of optically active α-amino acid derivatives using achiral Schiff base esters has been well-developed in the last 40 years. [1] Phase-transfer catalysts derived from the Cinchona alkaloids (such as Corey or Lygo catalyst) as well as Maruoka catalyst were mainly used for this type of asymmetric transformation. [2,3] Recently continuous flow technology has become of great interest in the academy and industry, since it offers safer process operating conditions and higher efficiency than can be obtained with traditional batch processing. [4]
Taking into account all the benefits of the continuous flow process, our main goal was to develop sustainable asymmetric phase transfer in flow synthesis of quaternary aminoacids. Non-proteinogenic α,α-dialkyl-α-amino acids or their derivatives represent an important building blocks for the synthesis of various biologically active compounds. [5]
Yiming Mo et al. examined the phase-transfer benzylation of N-(diphenylmethylene) glycine *t*-butyl ester catalyzed by cinchonidine-derived compound under various residence times and agitation intensities in continuous stirred-tank reactor (CSTR). [6] So far, continuous flow asymmetric phase transfer reactions for the preparation of amino acid derivatives containing a quaternary stereocenter has not yet been published.

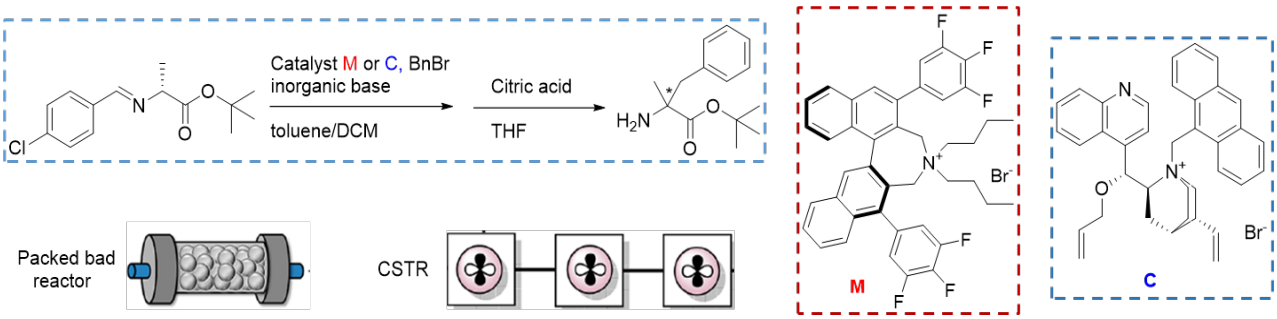

Figure 1. Asymmetric phase transfer benzylation under continuous flow conditions

Herein, we wish to report on the first example of phase transfer benzylation of alanine Schiff base ester, under continuous flow conditions. Different flow setup was used to perform the first step (packed bad reactor filled with the glass beads as well as the continuous stirred-tank reactor).
Better results were achieved using CSTR units (provides intensive agitation and better mass transfer). The second step, mild hydrolysis of the imine, has also been implemented successfully, to afford the deprotected amino ester in very high enantioselectivity.

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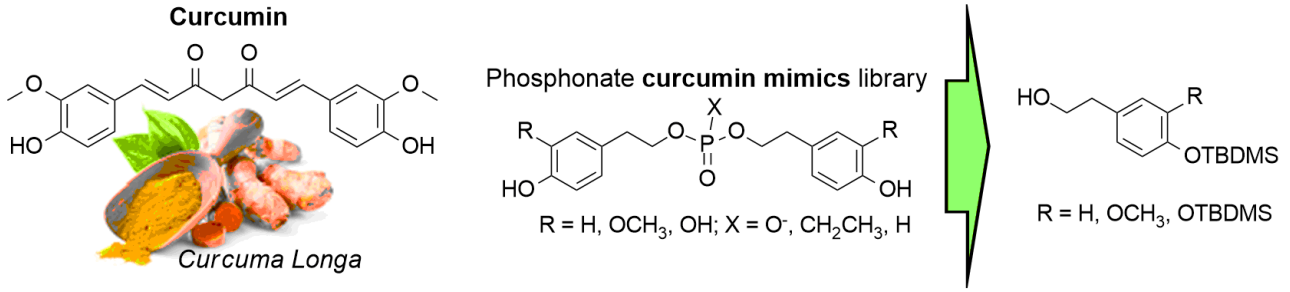
Synthesis and characterization of new curcumin mimics based on tyrosol phosphonates[1]

Antonio Lembo, Valeria Romanucci, Rita Pagano, Armando Zarrelli and Giovanni Di Fabio

Department of Chemical Sciences, University of Naples Federico II, Via Cintia 4, Naples, 80126 Italy

Curcumin, the main component of *Curcuma Longa*, is a bioactive natural compound with a wide range of pharmacological properties, including neuroprotective and antitumor activities.[2,3] However, its clinical application has been limited because of its low solubility, stability, and bioavailability. The presence of the active methylene group and β-diketone moiety contributes to the instability of curcumin under physiological conditions, poor absorption, and fast metabolism.[4] Many efforts have been made to replace the central diketone structure with a moiety that increases water solubility and improves bioavailability while keeping the methoxy–tyrosol portion unaltered. Several strategies that combine two polyphenolic "fragments" to obtain libraries based on polyphenol dimers have been proposed.[5] The dimerization or linking of moieties may enhance and/or alter their biological activity, and each scaffold with lipophilic or hydrophilic moieties can substantially modify their behaviour in lipidic or aqueous cell compartments, providing new hybrid compounds with enhanced efficacies. We recently studied the fibrillogenic activity of phosphodiester tyrosol-based dimers (X = O^-) and explored the synthesis of structures containing building blocks known for their pharmacological activities as tyrosol (TYR), hydroxytyrosol (HDT), and homovanillyl alcohol (HVA).[6]



The serum and Alkaline phosphatase (ALP) assays of these compounds showed remarkable stability even after several days. Similar behavior was observed in simulated intestinal fluid (SIF) and simulated gastric fluid (SGF). The good stability observed for these molecules prompted us to consider them mimics of curcumin and to test the neuroprotective and anticancer activities.
To expand the structural variety of mimics as inhibitors of Aβ protein aggregation and anticancer drugs, we propose here, the synthesis of a mini library of derivatives based on tyrosol scaffolds in which the two phenolic moieties are linked by a phosphonate bridge (X = CH_2CH_3 or H in Figure). The synthetic route was realised by starting from suitable protected building blocks based on tyrosol, obtained in few straightforward steps. All building blocks were coupled by a phosphoramidite chemistry and the final derivatives were purified by flash chromatography and then by RP-HPLC leading to desired mimics in good yields (50-75%). The identities of mimics were ascertained by 1D and 2D-NMR experiments and ESI-MS analysis. Preliminary studies on the radical scavenger activity as well as their stability in simulated fluid (sIF and sGF) are discussed.

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Expanding the Toolbox of Heterogeneous Asymmetric Organocatalysts: Bifunctional Cyclopropenimine Superbases for Enantioselective Catalysis in Batch and Continuous-Flow

Costanza Leonardi [a], Arianna Brandolese [a], Lorenzo Preti [a], Lorenzo Poletti [a], Olga Bortolini [a], Eleonora Polo [b], Paolo Dambruoso [b], Daniele Ragno [a], Graziano Di Carmine [a], and Alessandro Massi[a]

[a]*Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Via L. Borsari, 46, 44121 Ferrara (Italy)*

[b]*Istituto per la Sintesi Organica e la Fotoreattività, Consiglio Nazionale delle Ricerche, Via P. Gobetti, 101-40129 Bologna, Italy.*

In recent years, chiral cyclopropenimines have been coming to light as effective Brønsted base orgacatalysts in enantioselective direct deprotonation reactions by activating pronucleophiles with a wide range of pK_a values [1]. In particular, the strong basicity of cyclopropenimines (pK_{BH^+} ~26 in MeCN) resides in the presence of a latent, aromatic 2π-electron cyclopropenium ion which is generated upon protonation of the cyclopropenimmine scaffold.

However, due to their inherent strong reactivity, cyclopropenimines are difficult to access in terms of preparation and purification. In this direction, organocatalyst heterogenization offers unique opportunities by facilitating the catalyst handling, recycling, and an easy product/catalyst separation.

In this context, we describe an unprecedent immobilization strategy onto solid supports of chiral 2,3-bisaminocyclopropenimine (Lambert catalyst), which is a privileged bifunctional organocatalyst for highly enantioselective Michael reactions [2].

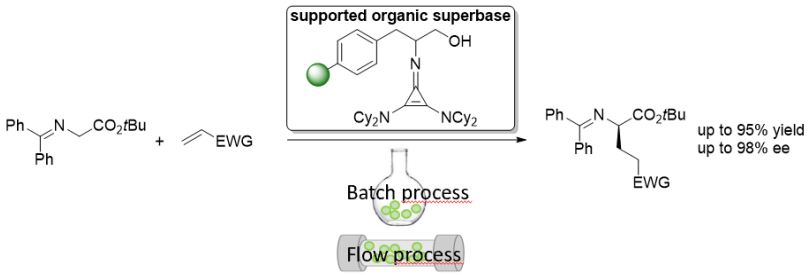

Figure 1: Supported cyclopropenimine catalyst in model Michael reaction in heterogeneous phase

The activity and recyclability of the supported cyclopropenimine were tested under batch conditions in a model Michael reaction. Our immobilization strategy preserved in heterogeneous phase the activity and stereoinduction ability which the Lambert catalyst displayed in homogeneous phase. In addition, the immobilized cyclopropenimine exhibited a great stability, which we exploited to demonstrate for the first time the compatibility of asymmetric organo-superbase catalysis with a continuous-flow set-up through the fabrication and long-term operation of the corresponding packed-bed mesoreactor.

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Chemical characterization of recycled and bio-based polymers for predictive applications

Martina Lippolis,[a] Genny Pastore,[a] Serena Gabrielli,[a] Giorgio Caporaletti,[b] Maurizio Mezzelani,[b] Manuela Cortese,[a] Enrico Marcantoni[a]

[a] *School of science and technologies, Organic Chemistry Division, University of Camerino, Italy.*
[b] *Fratelli Guzzini s.p.a. u.s., c.da Mattonata 60, 62019 Recanati Mc – Italy.*

A circular economy approach using sustainable, recyclable and bio-based materials can be used to minimize negative environmental impact of petroleum-based polymers[1, 2], although the use of recycled and bio-based materials is limited by difficulties that companies find in optimizing all processability parameters (**Figure 1**). Such as, recycled and bio-based materials can result in different chemical-physical-mechanical characteristics compared to the virgin one. Further, in order to make processable and performing these kinds of polymers it is necessary to add some specific additives, make blends or composite materials[3, 4]. In fact, one of the main issues is related to the chemical variability composition associated to the different type of companies that produce the materials resulting in a very challenging optimization of production parameters and prediction of final product functionalities.

This study is based on the implementation of an industrial software, such as Moldex, which can simulate injection molding processes. In fact, chemical characterization, and other parameters are necessary to offer reliable results, and these data are not available for recycled and bio-based materials due to their variability in composition.

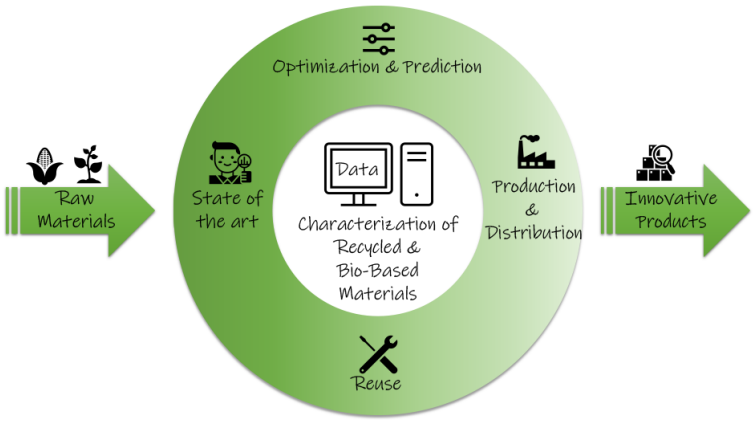

Figure 1. Importance of chemical characterization in bio-circular economy.

In this work, different type of recycled polyolefins and bio-based materials has been characterized leading to the insertion of the correct parameters in the software.

All recycled and bio-based composites have been characterized by several techniques, such as FTIR, TGA, NMR and SEM analysis with the scope of improving the production and to make a comparative study concerning the different behavior of virgin, recycled and natural based plastics.

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New NiNP@rGO Nanocomposites as Heterogenous Catalysts for Thiocarboxylation Cross-Coupling Reactions

Lorenzo Lombardi[*,a] *Raffaello Mazzaro,*[b] *Andrea Brunetti,*[a] *Massimo Gazzano,*[a] *Alessandro Kovtun,*[c] *Vittorio Morandi,*[b] *Giulio Bertuzzi*[a] *and Marco Bandini*[a,d]

[a] *Dipartimento di Chimica "Giacomo Ciamician", Alma Mater Studiorum – Università di Bologna, via Selmi 2, Bologna.*
[b] *Institute for Microelectronics and Microsystems (IMM) – CNR, via Gobetti 101, 40129, Bologna.*
[c] *Istituto per la Sintesi Organica e Fotoreattività (ISOF) – CNR, via Gobetti 101, 40129 Bologna.*
[d] *Consorzio CINMPIS, Università di Bologna, via Selmi 2, Bologna, Italy.*
e-mail: lorenzo.lombardi10@unibo.it

Despite the extensive exploitation of Ni mediated cross-coupling strategies, some protocols still suffer limitations due to the employment of highly reactive and sensitive [Ni(0)] species as pre-catalysts.[1] In this direction, the support of metallic Ni nanoparticles (NPs) onto inert matrix is considered as a valuable strategy to access easy-to-handle active Ni entities.[2]
A new type of ligand-free Ni nanoparticles supported on rGO was prepared and fully characterized via crystallographic (XRD-powder), spectrometric (ICP-MS) as well as spectroscopic tools (SEM/STEM/EDS, BET XPS, FT-IR).
The metal composite was effectively employed in the unprecedented nickel catalyzed cross-coupling reaction of aryl/vinyl iodides and potassium thioacetate. A pool of sulphur-containing aryl as well as vinyl derivatives was obtained in high yields (up to 82%), operationally simple reaction conditions (reagent grade xylenes, 150°C) with wide functional group tolerance.

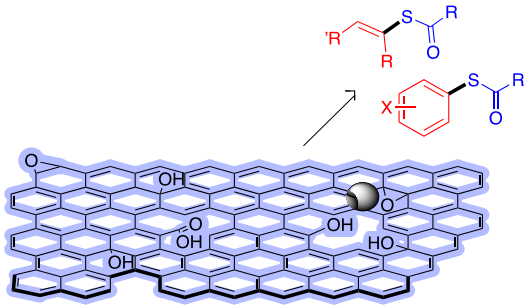

Figure 1. Graphical sketch of the present C-S bond forming cross-coupling mediated by Ni@NP-rGO.

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Extraction approach for minor macrocyclic condensed tannins from grape berry skins: optimization of the extraction variables, purification and LCMS characterization

Edoardo Longo,[a,b] Vakare Merkyte,[a,b] Daniela Eisenstecken,[c] Peter Robatscher,[c] Emanuele Boselli[a,b]

[a]Faculty of Science and Technology, Free University of Bozen-Bolzano, Piazza Università 5, 39100 Bolzano (Italy); [b]Oenolab, NOI Techpark, via A. Volta 13, 39100 Bolzano (Italy); [c]Laboratory for Flavours and Metabolites, Laimburg Research Centre, Laimburg 6, Vadena, 39040 Ora (Italy)

Correlating the profiles of condensed tannins and phenolic compounds in grape and wine with the viticultural (e.g., grape variety, clone, *terroir*, vintage, climate) and enological (e.g., winemaking practices, fermentations, ageing) variables is a current task of the research in enological chemistry [1,2]. The complexity associated to the profile of these oligo-/poly-meric flavanols arises from the intrinsic variability of their constituents (type of monomers) and binding modes, along with a dependence on their stability and their tendency to evolve overtime (e.g., by further polymerization or depolymerization). Nonetheless, cyclic proanthocyanidins (c-PAC), minor condensed tannins with an interesting macrocyclic structure, have demonstrated better stability towards harsh conditions that would cause instead degradation of their conventional (non-macrocyclic) analogues [3,4]. These compounds could represent an example of stabler makers of varietal authenticity [5] if their stability proved to hold for the entire c-PAC profile and also in wine overtime. Consequently, the study of these compounds is being pursued in order to define their relationships with enological and viticultural variables, the only limitation being the lack of suitable chemical standards and limited concentrations in grape and wine samples in general. In this report, a direct isolation approach for this phenolic fraction, which favors them *vs* their conventional analogues, is presented. An exploratory Plackett-Burman design was applied to evaluate the significant variables affecting the extraction performance and selectivity (such as extraction time, temperature, etc.), while several procedures proposed by the literature have been tested for purification, involving ion-exchange resin purification and gel filtration, followed by mass spectrometric characterization. The optimized methods could be suitable for implementing a food-grade process and scaling-up, with potential application to recovery of secondary products of winemaking, such as grape pomace left over from large-scale white wine vinifications. The conditions for the extraction and purification are reported along with the related mass spectrometric characterizations.

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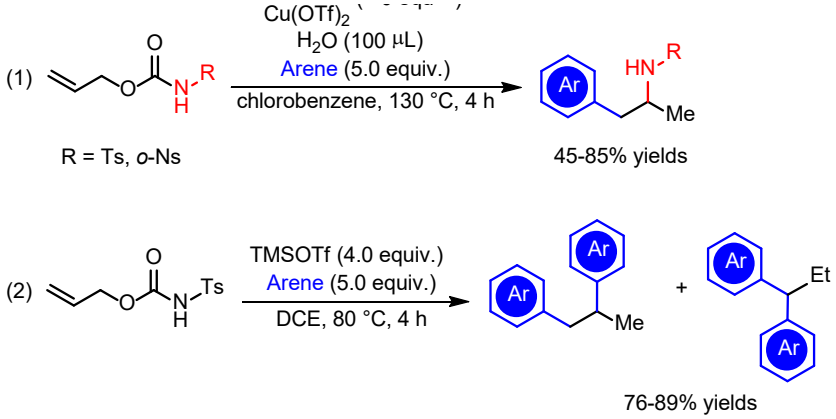
O-Allyl Carbamates: Acid-Mediated Decarboxylative Arylation/Hydroamination *vs* Diarylation

Camilla Loro,[a] Julie Oble,[b] Francesca Foschi,[a] Giovanni Poli,[b] and Gianluigi Broggini[a]

[a] Dipartimento di Scienza e Alta Tecnologia, Università degli Studi dell'Insubria, 22100, Como, Italy;
[b] Sorbonne Université, Faculté des Sciences et Ingénierie, CNRS, Institut Parisien de Chimie Moléculaire, IPCM, 4 place Jussieu, 75005 Paris, France

O-Allyl carbamates represent a highly attractive class of substrates due to their multifaceted chemical behavior. For example, the Shi group has recently reported a remarkable divergent intramolecular *exo*- vs *endo-trig* amination / functionalization sequence, depending on the applied reaction conditions.[1] Moreover, these substrates allow synthetically interesting decarboxylative *O*→*N* allylic rearrangements.[2] However, decarboxylative transformations of *O*-allyl carbamates involving double functionalization of the allyl moiety are still lacking. Following our interest in alkene difunctionalization,[3] we have now developed two new acid-mediated decarboxylative di- or tri-functionalization of *O*-allyl carbamates. More specifically, in the presence of $Cu(OTf)_2$ as additive, hydrocarbon or electron-rich arenes undergo a selective decarboxylative arylation/hydroamination process (Equation 1). On the other hand, TMSOTf as additive leads to 1,2- and/or 1,1-diaryl-propane derivatives, as a function of the steric hindrance of the arene (Equation 2).



Equation 1: arylation/hydroamination sequence; equation 2: diarylation sequence.

Furthermore, *p*-xylene gave an indane structure, besides the expected corresponding 1,1- and 1,2-diaryl-substituted propanes. This new reactivity involves the generation of four carbon-carbon bonds in a single synthetic operation. The detailed mechanism of these transformations will be discussed in detail.

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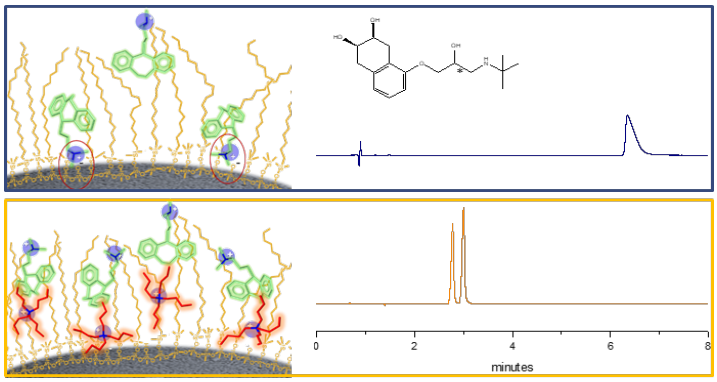
Dynamic electrostatic repulsion reversed phase: an useful elution mode for control of basic compounds and for enhancing diastereoselectivity in chromatography

S. Manetto,[a]

[a]*Dipartimento di Chimica e Tecnologie del Farmaco, Sapienza Universita` di Roma, p.le A. Moro 5, 00185 Roma, Italy.*
e-mail: simone.manetto@uniroma1.it

Many compounds of pharmaceutical interest are bases, and reversed phase chromatography (RPC) is the first choice for determining their purity. However, due to the complexity of the surface of the silica particles, the analysis of basic molecules poses some problems [1]. In particular, free silanols in dissociated form, work as cation exchange sites with the protonated basic analytes creating a second mechanism that overlaps with the hydrophobic interactions (e.g. van der Waals) of the solutes on the stationary phase. The ionic interaction shows slower kinetics than the hydrophobic interaction between the analyte and C18 chains, leading to peak asymmetry and loss of efficiency. Various approaches have been developed to decrease the activity of silanols, such as the use of acidic pH, the use of ion-pair additives or the use of new generation columns.
One of these is the use of surface-charged hybrid organic/inorganic (CSH) packaging materials, which involves using positively charged fragments chemically bonded to the silica surface. In 2014, Gritti and Guiochon coined the term RPLC electrostatic repulsion interactions (ER-RPLC) to describe this new mixed-mode [2]. A comparison was then made between different strategies: 4 commercial C18 columns were selected.
We have observed that the addition of a positively charged hydrophobic ion pair agent can dynamically charge the surface of the particles. In analogy to the term coined by Gritti, we have decided to call this dynamic mode ERRP [3]. The positively charged hydrophobic ion pair agent studied is tetrabutylammonium, which interacts both with C18 through hydrophobic interactions and with silanols, furthermore operating at acid pH creates a second interaction of an electrostatic repulsive type with positively charged analytes. In addition, beyond improving efficiency and symmetry, diastereoselectivity increased unexpectedly. It was possible to resolve the nadolol diastereoisomers, which were not resolved with the same column in RP and not even with the CSH column with the technology we had taken as a model [4].



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Metal Catalysis for Sustainable Transformations in Aqueous Micellar Conditions

[a]S. Maramai, [a]E. Ermini and [a]M. Taddei

[a]Dipartimento di Biotecnologie, Chimica e Farmacia, Dipartimento di Eccellenza 2018-2022 - Università degli Studi di Siena, Via Aldo Moro 2 – 53100 (SI) Italy

Micellar catalysis has been proposed as an efficient and green alternative to perform organic transformations in aqueous medium[1]. The use of surfactants generating supramolecular aggregates allows to solubilize organic lipophilic molecules in water, with the formation of nanoreactors, containing all reactants and catalyst in very high concentrations, thus speeding up the reaction rates of many different metal-catalysed reactions, such as Suzuki-Miyaura,[2] and Heck cross-coupling,[3] hydrogen borrowing processes,[4] and others. Recently, we evaluated the use of transition metal nanoparticles (NPs) in the selective hydrogenation reaction of aromatic nitro groups under aqueous micellar conditions. Using NPs with a source of hydrogen at room temperature represents a sustainable and green process for obtaining aromatic and heteroaromatic amines, a versatile class of intermediates for the synthesis of fine chemicals and pharmaceuticals. In addition, this methodology also introduces a biocompatible approach for the release of biologically active compounds from nitro-containing aromatic carriers. In fact, the selective reduction of this group to the corresponding aniline can induce a rearrangement process of the system leading to the release of a loaded drug, either by intramolecular cyclization or system elimination (Figure 1).

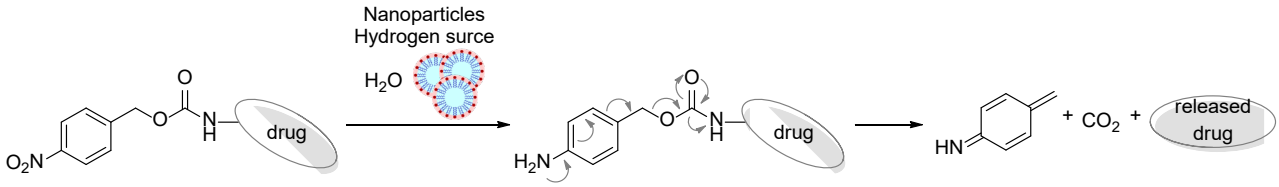

Figure 1. Example of an aromatic nitro group reduction with NPs under micellar conditions with possible 1,6-elimination of the system and drug release.

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Design and solid-phase synthesis of 5'-modified gRNA with lipophilic moiety to improve CRISPR/Cas9 genome-editing

Elena Marchesi[a], *Lorenzo Preti*[a], *Matteo Bovolenta*[b] *and Daniela Perrone*[a]

[a] *Department of Chemistry, Pharmaceutical and Agricultural Sciences, University of Ferrara, Luigi Borsari 46, 44121 Ferrara, Italy;* [b]*Department of Translational Medicine, University of Ferrara, Fossato di Mortara 64/B, 44121 Ferrara, Italy*

CRISPR/Cas genome editing is a groundbreaking technique able to efficiently introduce specific alterations in a genome. The CRISPR/Cas9 system is a ribonucleoprotein (RNP) complex containing the Cas9 protein and a single guide RNA (sgRNA), a ~100 nt sequence that could be chemically synthesized or generated enzymatically by *in vitro* transcription (IVT). As expected, the use of unmodified guide RNAs in biological systems highlights similar problems observed for RNAs: rapid degradation in serum and in intracellular environment and activation of undesired innate immune response. Since it is difficult to control the chemical modification patterns when generating sgRNAs by IVT, early reports employ chemically synthesized sgRNAs for introducing specific chemical modifications (e.g., backbone, furanose sugar, or nucleobase) attempting to increase genome editing efficiency through RNA stabilization [1-3]. Moreover, sgRNAs are highly charged macromolecules that cannot passively diffuse across the cell membrane, requiring the aid of a delivery agent. The use of targeting ligands conjugated to oligonucleotides (ONs) has been extensively studied to overcome the delivery challenges [4]; in particular, hydrophobic lipid-based conjugates are an attractive strategy for ONs delivery due to their association with serum lipoproteins, which increases bioavailability, as well as their ability to facilitate receptor-mediated membrane permeability [5]. Therefore, to overcome the sgRNAs delivery limitation, we designed a chemical modified guide conjugated with suitable ligands. Taking advantage of our consolidated experience in the synthesis of modified oligonucleotides conjugated to lipophilic molecules [6], we report a full solid-phase total synthesis of a 97-mer sgRNA 5'-modified with a lipophilic moiety and chemically modified with 2'OMe 3'PS on the flanking ends (Figure 1). Our design would improve gRNA stability, cellular uptake, bioavailability and hopefully increase potency of genome editing.

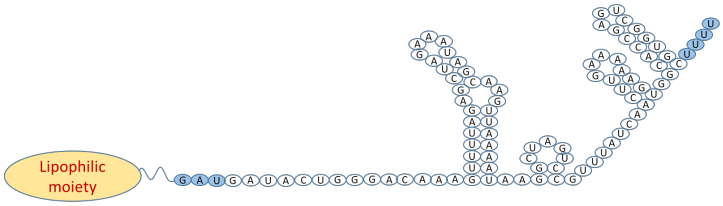

Figure 1: schematic representation of the RNA guide.

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Siglecs as Novel Immunotherapy Targets

Roberta Marchetti [a]

[a] *Department of Chemical Sciences, University of Naples Federico II, Via Cinthia, 4, 80126 Napoli, Italy*

Siglecs (Sialic acid-binding immunoglobulin type lectins) are a family of cell surface transmembrane receptors belonging to I-type lectins, predominantly expressed by immune cells. Individual family members exhibit preferences for sialosides of various linkages to underlying glycan motifs, but the physiological ligands they interact with are largely unknown.[1]

Many Siglecs, such as Siglec-2,[2,3] Siglec-7 and Siglec-10,[4] are inhibitory receptors involved in the down-regulation of cell signalling upon the interaction with sialylated glycans that act as determinants of self. Interestingly, clinically relevant pathogens have the ability to decorate their surface with glycans that mimic self-associated molecular patterns, bind to inhibitory Siglecs, and escape immune surveillances.

Thus, Siglecs are nowadays considered glyco-immune checkpoints and exhibit a great therapeutic potential for the treatment of autoimmune, neurodegenerative and cancer diseases.
In this context, we investigated the molecular mechanisms underlying sialoglycans recognition by Siglecs using a combination of biophysical, spectroscopic and computational approaches, with the aim to carry out a dynamic characterization of their interactions in solution. NMR spectroscopy, and in particular ligand-based NMR techniques including STD- NMR and tr-NOESY, were used to evaluate the interacting epitope and the bioactive conformation of sialoglycans in solution. Homology modeling, docking and MD studies, together with CORCEMA-ST protocol, were implemented to obtain and validate 3-D ligands/receptor complexes, highlighting the crucial interactions between the binding partners. Comprehensively, our outcomes have improved our knowledge of the molecular interaction occurring between Siglecs and sialyloglycans, providing a structural point of view for the design and development of high-affinity ligands able to control the receptor functionality.

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Self-Assembly Behaviour Control of an Amyloidogenic-Derived Peptide by Iodination of a Custom Amino Acid

A. Marchetti[a], *C. Pigliacelli*[a], *A. Pizzi*[a], *U. Rost*[b], *U. Diederichsen*[b], *G. Terraneo*[a] *and P. Metrangolo*[a]

[a] *SupraBioNanoLab-DCMIC "Giulio Natta", Politecnico di Milano, Milan, Italy*
[b] *Institute of Organic and Biomolecular Chemistry, Georg-August-Universität, Göttingen, Germany*

The use of halogenated compounds as markers for crystallographic phasing of big biomolecules and biostructures such as proteins, oligomers, and lipid bilayers, is a consolidated practice enabled by the combination of their anomalous scattering and minimal impact of halogenation on the probed system [1]. Although this is true in many applications, when iodination is performed on systems ruled by weak interactions, the set of noncovalent interactions enabled by iodine atoms (*e.g.*, halogen bond) dramatically impacts the overall system's behaviour. In the last few years, the engineering of amyloidogenic peptides, a class of fibril-forming amino acid sequences, has greatly benefitted from halogenation of aromatic residues [2]. In this work, we explored the impact of iodination of an aliphatic residue on amyloidogenic peptides self-assembly by synthesizing a custom iodine-labelled amino acid and inserting it into an amyloidogenic-derived peptide sequence. The analysis of its fibril forming proclivity, both in the solid state and in solution, confirmed the amplification of the fibrillogenic behaviour of the iodinated peptide with respect to its non-iodinated counterpart. Despite being a minimal modification, the introduction of iodine atoms greatly improved the formation of ordered and crystalline structures, as confirmed by the peptide single crystal X-ray structure. Moreover, if the self-assembly is carried out in the presence a gold(III) salt, gold nanoparticles embedded in a peptide matrix are spontaneously obtained, demonstrating that iodination triggers new functions to amyloidogenic sequences [3].

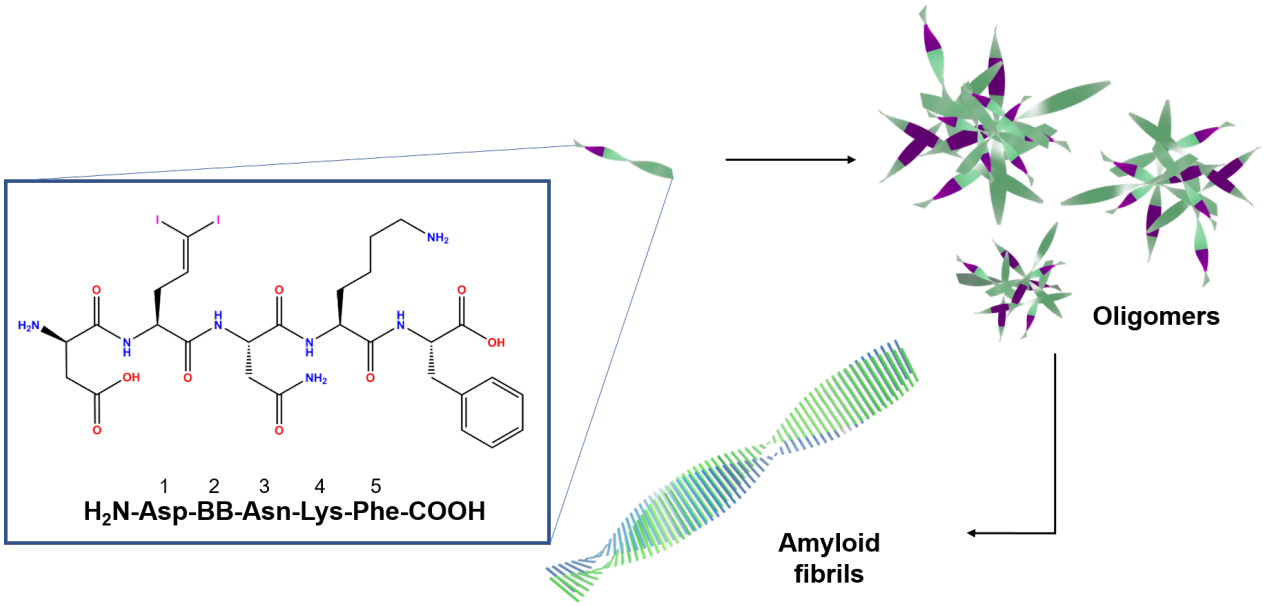

Figure 1: Chemical structure of the iodinated peptide (left) and a cartoon schematically reporting its self-assembly behaviour (right).

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Recognition mechanisms of bacterial glycans by host immune receptors

Angela Marseglia[a], Antonio Molinaro[a], Alba Silipo[a], Roberta Marchetti[a]

[a] *Department of Chemical Sciences, University of Naples "Federico II", Via Cinthia 4, 80126, Napoli, Italy.*

All cells of living organisms are covered by a layer of glycans that acts as an interface between the outer environment and the cell membrane. Glycans exhibit broad structural diversity and are involved in fundamental molecular and biological mechanisms, including protein folding, cell adhesion, signal transduction, receptor activity modulation and immunological and pathological processes. Particularly, glycans are involved in the interaction mechanisms of bacteria with eukaryotic host. Glycans serve as counter receptors for different proteins, including lectins [1]. These are exposed on the surface of innate immune cells and represent an important class of Pathogen Recognition Receptors (PRRs) characterized by their ability to recognize glycans.

These PRRs may contribute to initial recognition of bacterial glycans, thus providing an early defense mechanism against bacterial infections, but some of them may also be exploited by bacteria to escape immune responses.

Several human pathogens have indeed developed the capability to cover their surface with glycans mimicking eukaryotic SAMPs (Self Associated Molecular Patterns) structures, able to interact with inhibitory host receptors, thus eluding host immune responses and promoting infections.

Among them, the ESKAPE (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter species*) pathogens exhibit multidrug resistance and virulence and represent a global threat to human health. [2].

Thus, given their therapeutic relevance, we aim to elucidate, at a molecular level, the recognition of glycoconjugates isolated from Gram-negative bacteria, such as capsular polysaccharides from *A. baumannii,* by inhibitory host receptors, as Siglec-10.

In order to dissect the fine details of the recognition of feared pathogens from immune response, we use a multidisciplinary approach based on different and advanced biophysical techniques, mainly NMR spectroscopy, combined with computational studies.

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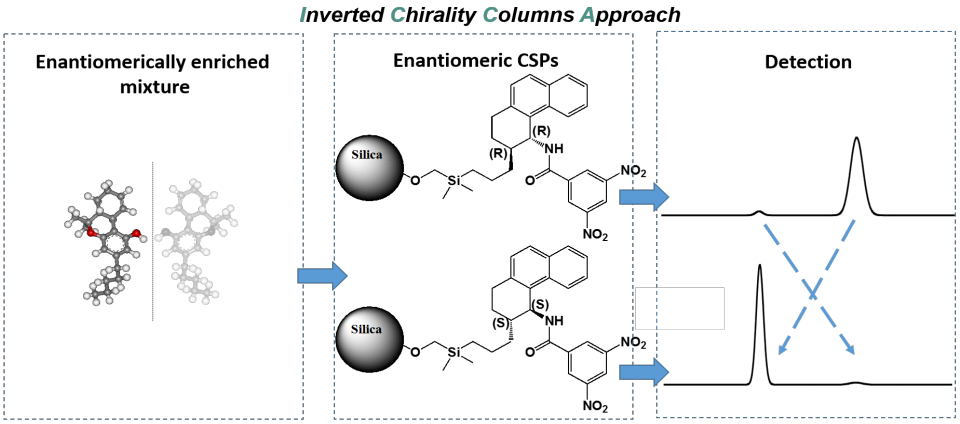
Inverted chirality column approach for tackling stereochemical puzzles in organic chemistry, natural products, and pharmaceutical chemistry

G. Mazzoccanti,[a]
[a]*Dipartimento di Chimica e Tecnologie del Farmaco, Sapienza Universita` di Roma, p.le A. Moro 5, 00185 Roma, Italy.*
e-mail: giulia.mazzoccanti@uniroma1.it

Chirality describes a spatial arrangement of a molecule in which simple symmetry operations, such as reflection at a molecular level, do not lead to self-imaging. The study of chiral molecules often foresees the separation of enantiomers as an obligatory step. Several techniques have been used, and, liquid chromatography using chiral stationary phases (CSPs) is a crucial instrument with a wide range of applications. Therefore, unlike the typical puzzle, the solutions to the problems of enantioseparation can be boundless, as they have to combine the knowledge of organic chemistry (e.g., synthesis of the chiral selector and its anchoring on the silica surface), of materials science (e.g., the study of the different supports that can be used), of physical chemistry (the study of the different processes that can occur within the chromatographic system), and analytical chemistry (e.g., sample preparation). This characteristic effort traces the evolution of the discipline. Nevertheless, one of the principal problems encountered in the stereoselective analysis of complex molecules with one or more stereogenic elements is that the minor enantiomer, or the racemate, are often not available as reference samples and frequently are very difficult to synthesize. This is especially the case of natural products, usually produced as single enantiomer; or, frequently, as enantiomerically enriched mixtures with extreme enantiomeric excess (*ee*). Hence, it becomes evident the importance of determining the enantiomeric purity, in naturally occurring samples, in both single and in more complex mixtures, as well as the importance of the evaluation of stereochemical efficiency of enantioselective synthetic pathways, even in non or partially purified crude reaction mixtures. To overcome this limitation, our group has previously developed a method for identifying enantiomeric couples and accurate quantification of the minor enantiomer in trace analysis, named the "inverted chirality columns approach" (ICCA). [1-3] The approach is founded on the swapping between two columns packed with CSPs having the same bound selector but with an opposite configuration. In the same experimental conditions, it is possible to observe the inversion of the elution order of a given enantiomeric pair according to supramolecular recognition by the *reciprocal principle of selectand-selector systems.* [4] An efficient protocol of general applicability is proposed to the scientific community for the control of stereochemistry in highly enriched chiral products in the field of enantioselective synthesis, natural products, and pharmaceutical chemistry by using cutting-edge techniques such as the enantioselective ultra high-performance chromatography (*e*UHPC), based on sub-2-μm CSPs developed in our laboratories.



Identification of enantiomeric couples and *ee* evaluation *in complex mixtures, in the absence of the reference enantiomers and without chiroptical detection*

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Chemical Modification of Carbon Nanotubes with Sulfonylamides

[a]*Alessandro Mercadante,* [a]*Vincenzo Campisciano,* [b]*Valeria La Parola,* [a]*Michelangelo Gruttadauria,* [a]*Francesco Giacalone*

[a] *Department of Biological, Chemical and Pharmaceutical Sciences and Technologies University of Palermo Viale delle Scienze, Ed. 17 90128 Palermo (Italy);* [b] *Istituto per lo Studio dei Materiali Nanostruttuarati (ISMN-CNR), Via Ugo La Malfa 153, 90146, Palermo (Italy).*

In recent decades, carbon nanotubes (CNTs) have attracted enormous interest in the scientific community for their potential use in a wide range of applications, from nanotechnology to countless applications in everyday life, from electronics to energy to biomedicine. However, the full and large-scale exploration of the extraordinary capabilities of nanotubes remains linked to their poor solubility and dispersibility in solvents, which, to a certain extent, prevents their wider application and limits their potential, as they create tangled three-dimensional CNT networks built by van der Waals forces. One possible way to overcome these drawbacks lies in their chemical modification. Chemical modification is based on the covalent bonding of functional groups on the CNTs and it can be carried out on the tips of the nanotubes or on their side walls[1]. This process can be carried out by reaction with certain molecules with high chemical reactivity. Manipulation strategies usually include oxidation reactions under adverse reaction conditions, which very often alter the electronic properties and induce damage in an uncontrolled manner, presenting numerous limitations, especially in terms of reproducibility. To this end, new strategies for functionalizing CNTs, which allow surface modification, are always welcome. In the present work, we show a new strategy for the aziridination of carbon nanotubes. This reaction involves the use of sulfonylamides, which are widely exploited and are an important building block in organic synthesis, that are surface-bonded to form the corresponding aziridines (Figure 1). The sulfonamides ($R\text{-}SO_2NH_2$) can already bind the group of interest in the R- portion, or they can be easily post-modified with task-specific moieties that may allow better dispersion, or may exert catalytic activity[2].

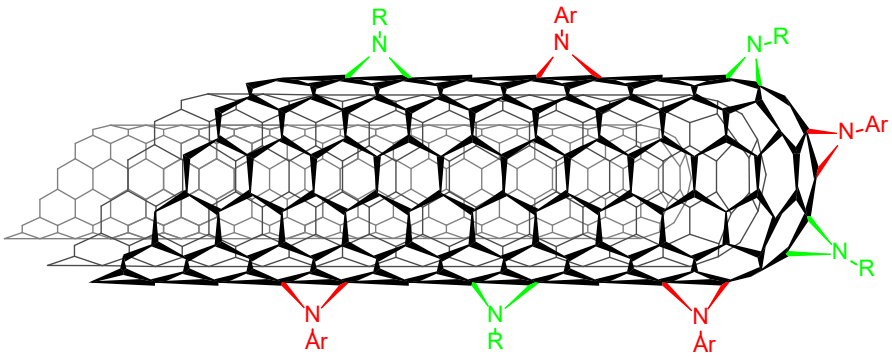

Figure 1

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Tuning the Siglec-Sialylated Glycans Axis: Design and Synthesis of Novel Analogs and Mimetic

Monica Civera,[a] Oscar Francesconi,[b] Martina Fruscella,[b] Roberta Marchetti,[c] Francesco Milanesi,[b] Marco Montefiori,[a] Cristina Nativi,[b] Francesco Papi,[b] Sara Sattin,[a] Alba Silipo [c]

[a] Department of Chemistry,University of Milan, Via Golgi 19, I-20131, Milano (Italy); [b] Department of Chemistry ''Ugo Schiff'' and CERM,University of Florence, Polo Scientifico e Tecnologico, I-50019, Sesto Fiorentino, Firenze (Italy); [c] Department of Chemical Sciences,University of Naples ''Federico II'', Strada Comunale Cinthia 26, I-80126, Napoli (Italy)

Siglecs are inhibitory receptors expressed on immune cells which recognize sialylated epitopes. Of note, some pathogens like *C. jejuni*, and *N. meningitides* are coated with silylated-glycans that, mimicking self-like ligands, can bind to Siglecs triggering tolerance to the pathogen.[1] Effective tools to interfere in this process are analogs or mimetics of sialic acid. Several compounds with nanomolar affinities for different Siglecs isoforms have been reported,[2] most of which are not selective. Some of the most relevant Siglecs (2,7 and 10) are known to bind different oligosaccharidic epitopes (**Figure 1**) in which sialic acid is the terminal unit.[1] In this study we aim to design novel analogs or mimetics of binding epitopes of Siglec-2, 7 or 10. The design is supported by preliminary molecular modeling studies. The interactions between the target Siglec and new compounds will be characterized by NMR.

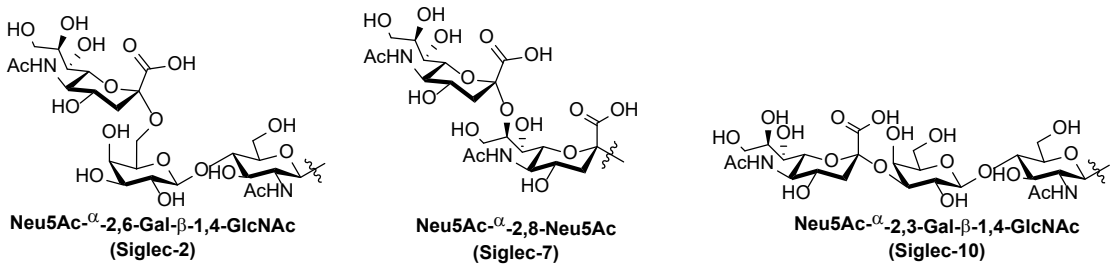

Figure 1: Examples of epitopes recognized by Siglec 2, 7 and 10.

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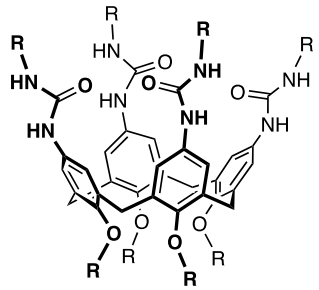
The self-assembly and disassembly of octatolylurea calix[4]tube

Anna Notti,[a] Giuseppe Gattuso,[a] Marco Milone,[a] Melchiorre F. Parisi,[a] Ilenia Pisagatti,[a] Silvano Geremia,[b]

[a] Dipartimento di Scienze Chimiche, Biologiche, Farmaceutiche ed Ambientali, Università di Messina, viale F. Stagno d'Alcontres 31, 98166 Messina; [b] Centro di Eccellenza di Biocristallografia, Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Trieste, via L. Giorgieri 1, 34127 Trieste

Urea-substituted calix[4]arenes **1** have attracted much attention for their ability to spontaneously self-assemble, both in solution and in the solid state, into homo- and heterodimeric capsules held together by a cyclic array of hydrogen bonds between their ureido groups [1]. Inspired by this self-assembly motif [2] and in connection with our current interest in the design of linear supramolecular polymers [3], we have recently looked at the congener family of calix[4]tubes **2** [4]. These tubular molecules bear a criptand-like binding site and have, as a result, been used as selective ionophores but, because of the inertness of their alkyl wide-rim substituents, have so far been employed as building blocks of supramolecular arrays only in one instance after suitable derivatization [5].
In the present contribution, we describe the synthesis and structural features of octatolylurea calix[4]tube **3** along with a preliminary study on the fine-tuning of its self-assembly behaviour in solution.



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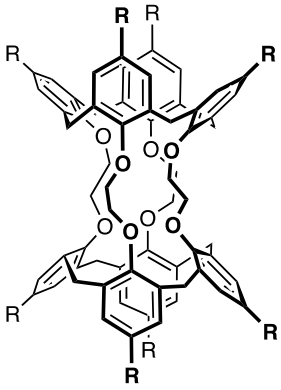

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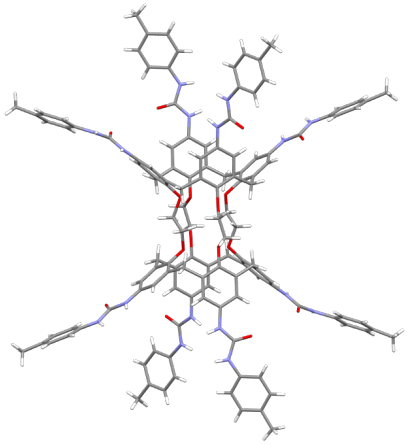

3

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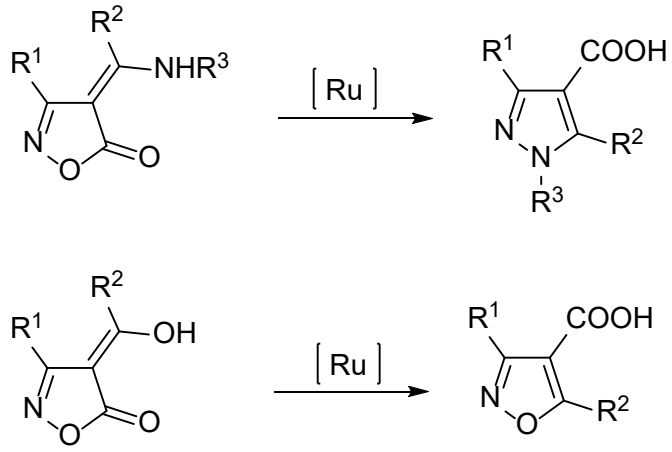
An efficient rearrangement of Isoxazolones to Pyrazole- and Isoxazole-4-carboxylic acids through Ruthenium-catalysis

[a]Letizia Molteni, [a]Egle M. Beccalli, [b]Camilla Loro

[a] *DISFARM, Sezione di Chimica Generale e Organica "A. Marchesini" Università degli Studi di Milano, via Venezian 2, 20133 Milano, Italy*
[b] *Dipartimento di Scienza ed Alta Tecnologia, Università degli Studi dell'Insubria, Via Valleggio 11, Como 22100, Italy*

Patents dealing with isoxazol-5-one derivatives are numerous, as a consequence of the importance of this ring in compounds of interest in the pharmacological fields and as agricultural chemicals.[1] Isoxazolinones are also interesting synthetic building blocks, due to the presence of different functionalizations, an imine-like C=N bond and the reactive N-O bond able to react in the presence of transition metal catalyst, showing different ring transformations.[2] We reported here the study on the 4-aminomethylene- and 4-hydroxymethylene-isoxazol-5-one derivatives under ruthenium catalysis, exploiting the relative ease of ring opening through the insertion of the metal and the formation of a metal nitrenoid intermediate.[3] The resulting rearrangement afforded different heterocycles, pyrazoles and isoxazoles bearing the carboxylic group as substituent in position 4.



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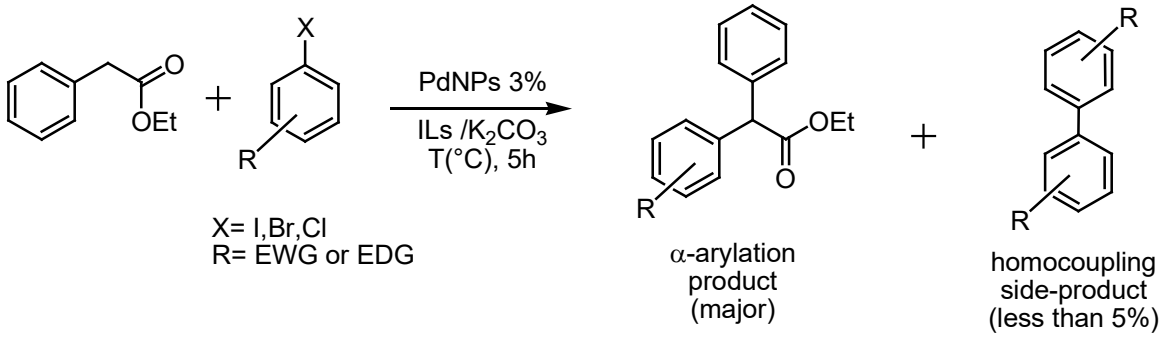
Ligand-free palladium nanoparticles catalysed α-arylation of esters and ketones with aryl halides in ionic liquids

Antonio Monopoli,[a] *Michele Casiello*,[a] *Daniele Nuzzo*,[a] *Caterina Fusco*,[b] *Angelo Nacci*,[a,b] *Lucia D'Accolti* [a,b]

[a] *Chemistry Department, University of Bari Aldo Moro, Via Orabona 4, 70125 Bari, Italy;* [b] *CNR—Istituto di Chimica dei Composti Organometallici (ICCOM), Bari Section, Via Orabona 4, 70125 Bari, Italy.*

During the last two decades, α-arylation of carbonyl compounds has gained great attention due to the significance of many obtained products in the pharmaceutical industry [1]. As an example, important 2-aryl alkanoic derivatives such as Ibuprofen® or Naproxen® can be synthesized by this way. However, the strong basic conditions often required for this reaction and the high reactivity of some substrates which can enable side-reactions, have limited the number of investigations on this topic, until now [2].
Nanostructured metal catalysts in combination with ionic liquids can be an alternative strategy that enables the coupling of haloarenes with different carbonyl compounds with high efficiency and selectivity. In line with our findings on the use of ionic liquids as reaction media capable of enhancing nanocatalysts performances, we present here an easy and efficient protocol for the *α*-arylation of ketones and esters catalysed by palladium nanoparticles dispersed and stabilized by ionic liquid solvents. The ratio between the substrate and the aryl halide, the nature of the base and the temperature were carefully optimized to avoid undesired homocoupling products (see scheme below). To the best of our knowledge, this represents the first example of α-arylation of ketones and esters carried out in ionic liquids under ligand-free conditions.



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Optimization and production in *E. coli* of crucial proteins involved in host-pathogen interactions.

Miguel Moreira[a], Roberta Marchetti[a], Alba Silipo[a]. Antonio Molinaro[a]

[a] Dipartimento di Scienze Chimica, Università degli studi di Napoli Federico II, Via Cintia 4, I-80126, Napoli, Italy

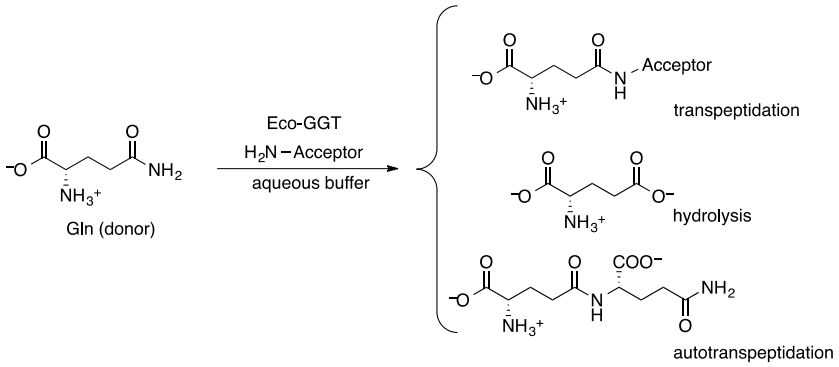
Host-pathogen interactions are often mediated and rely on the intricate and dynamic interactions between proteins and carbohydrates. These molecular interactions are the mantlepiece of several pathogenic mechanisms and immune responses. The unveiling of the atomic details of such interactions is crucial not only to the fundamental understanding of the interactions but also for the development of therapeutic approaches towards these pathogens. However, to study such interactions, large amounts of the target proteins are usually necessary. Furthermore, the dynamic study of such interactions is usually done through spectroscopic NMR techniques that may require the production of such proteins in isotopically labelled forms. This production, although theoretically possible in eukaryotic systems, is often cumbersome and impractical from a monetary standpoint. Switching to prokaryotic systems creates other problems. Although protein expression can be achieved, the prokaryotic cells lack most of the protein folding machinery present in eukaryotic cells and thus challenging proteins can fold abnormally, aggregate and precipitate in inclusion bodies or even not be fully produced. In this work we developed and optimized protocols to inexpensively and recombinantly express in E. coli several proteins crucial for host-pathogen interactions in human bacterial infections.

An overall framework for the *E. coli* γ-glutamyltransferase-catalyzed transpeptidation reactions

Valeria Somma,[a] Cinzia Calvio,[b] Marco Rabuffetti,[a] Erlinda Rama,[b] Giovanna Speranza,[a] Carlo F. Morelli[a]

[a] Dipartimento di Chimica, Università degli Studi di Milano, via Golgi, 19 – 20133 Milano; [b] Dipartimento di Biologia e Biotecnologie, Università degli Studi di Pavia, via Ferrata, – 27100 Pavia

Despite the interest raised by γ-glutamyl derivatives of proteinogenic or modified amino acids as flavor enhancers or biologically active compounds, their supply at a large scale and at reasonable costs remains a challenge [1]. Enzymatic synthesis has been recognized since time as a possible affordable alternative with respect to both the low-yielding isolation procedures from natural sources, and chemical synthesis made non-economical by the need of protection/deprotection steps. The γ-glutamyltransferase from *E. coli* (Eco-GGT) has already been proposed for the enzymatic synthesis of various γ-glutamyl derivatives [2]. However, hydrolysis and auto-transpeptidation of the donor substrate have been identified as the enzyme-catalyzed side reactions lowering the final yield of the desired product (Scheme). In addition, experimental conditions needed to be adjusted from time to time specifically for the different acceptor substrates. Thus, an overall picture of the activities exerted by the enzyme seems to have escaped rationalization. In this work, some representative acceptor amino acids have been tested in reactions catalyzed by Eco-GGT towards glutamine as the donor of the γ-glutamyl moiety. Reactions were monitored following formation and distribution of products in time. This approach allowed to rationalize the effect of donor/acceptor molar ratio on the outcome of the transpeptidation reaction and on the distribution of the different byproducts, figuring out a general scheme for Eco-GGT-catalyzed reactions.



Our results can aid in shedding light on the still elusive acceptor binding site of the enzyme and they can help in the employment of the enzyme as a biocatalyst for preparative purposes. As a demonstration, a γ-glutamyl dipeptide with flavor-enhancing properties was obtained through an *E. coli* GGT-catalyzed reaction in an isolated yield that for the first time reached 60%.

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The present work was carried out within the TailGluTran Project, funded by Fondazione Cariplo, grant no. 2016-0741.

Supported Polyimidazolium Network on Carbon Nanoforms for the Conversion of CO_2 into Cyclic Carbonates

[a,b] A. Morena; [a]V. Campisciano; [b]A. Comés; [a]F. Giacalone; [a]M. Gruttadauria; [b]C. Aprile

[a] Dipartimento di Scienze e Tecnologie Biologiche, Chimiche e Farmaceutiche, Università di Palermo, Viale delle Scienze s/n, Ed. 17, 90128, Palermo (Italy)
[b] Département de Chimie, Université de Namur, Rue de Bruxelles, 5000, Namur (Belgium)

The high environmental impact of CO_2 today has motivated the scientific community to find effective alternatives to reuse this molecule. One of the reactions that aims to exploit CO_2 is the reaction with epoxides, high internal energy molecules that can make the process thermodynamically favorable.[1] The high energy input required for the transformation of carbon dioxide can be further reduced through the coordination of the epoxide oxygen with a metal center acting as Lewis acid or through the formation of hydrogen bonds.[2] Recently, heterogeneous catalytic systems based on supported ionic liquid phases with halide counterions represent a promising class of materials.
Three different carbon nanoforms (CNFs), single-walled and multi-walled carbon nanotubes (SWCNTs, MWCNTs) and carbon nanohorns (CNHs), have been used as support for the direct polymerization of a bis-vinylimidazolium salt endowed with a hydroxyl group and the resulting hybrid materials have been characterized. Transmission electron microscopy confirmed that all the CNFs act as template on the growth of the polymeric network, which perfectly covers the nanocarbons forming a cylindrical (SWCNTs, MWCNTs) or spherical (CNHs) coating.[3] Interestingly, despite the loss of part of the polymeric coating, the activity increases upon recycling of the materials, and this behavior was probably ascribed to their change of morphology that led to materials with higher surface areas and with more accessible catalytic sites.

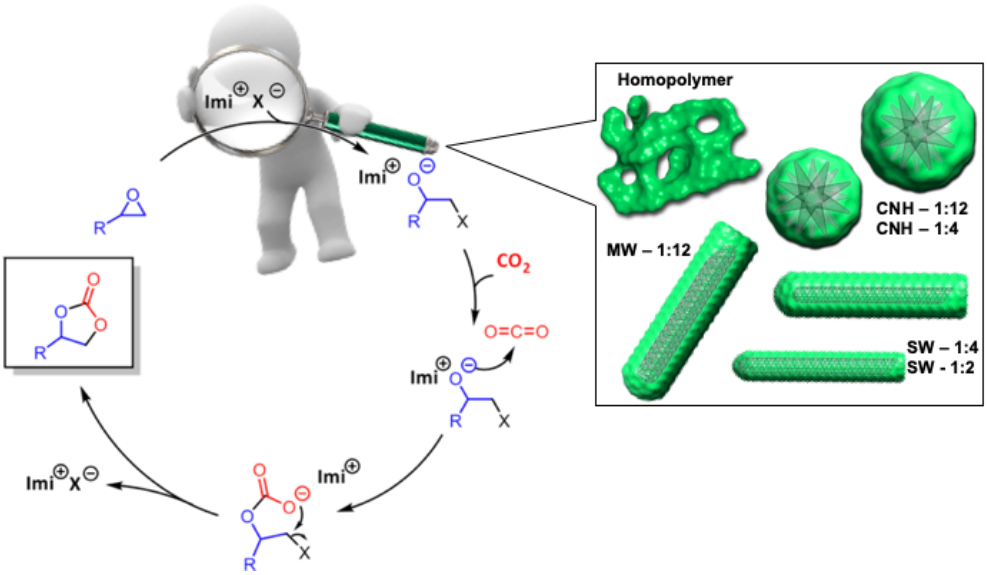

Figure 1: Mechanism for the fixation of CO_2 into epoxides and representation of the hybrid materials.

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Natural polyphenols and synthetic analogues as potential hypoglycemic and antiobesity agents

V. Muccilli, C. Sciacca, N. Cardullo, C. Tringali.

Department of Chemical Sciences, University of Catania, V.le A. Doria 6, 95125, e-mail: v.muccilli@unict.it

Obesity is a metabolic disorder resulting from an excessive accumulation of body fat. It is associated with a huge spectrum of comorbidities, such as the onset of cardiovascular diseases, diverse types of cancer, osteoarthritis, and hypertension. Moreover, the incidence of obesity is frequently associated with the incidence of Type 2 diabetes (T2D, Diabetes mellitus), a metabolic disorder characterized by insulin hormone dysfunction, and as a result, by high blood glucose levels. Type 2 diabetes represents 90% of all diabetes cases and among other diet-related diseases is the primary cause of deaths. It is also noteworthy that hyperglycemia associated with Diabetes mellitus is characterized by an increase in the production of reactive oxygen species, causing oxidative tissue damage.

Various strategies have been developed for the inhibition of the enzymes involved in these dietary diseases. Pancreatic lipase is a key enzyme in dietary fat absorption, responsible for the hydrolysis of 50–70% of dietary triglycerides into monoacylglycerides and free fatty acids, which can then be absorbed by enterocytes. Inhibition of this enzyme is used to reduce dietary fat absorption. Both α-amylase and α-glucosidase are carbohydrate hydrolyzing enzymes, and their inhibition is one of the strategies to manage the T2D-related hyperglycemia. Several drugs are currently employed as inhibitors of α-amylase, α-glucosidase and pancreatic lipase although with undesired side effects.

In recent years, some natural polyphenols have been reported as inhibitors of the above digestive enzymes, involved in metabolic diseases. The present work reports some of our recent efforts aimed at discovering the inhibition properties of natural polyphenols or synthetic analogues. Some examples will be provided, namely: 1) dimeric neolignans and their synthetic analogues;[1] 2) isoflavonoids;[2] 3) C-glucosidic ellagitannins and galloylated glucoses;[3] 4) phenolic acids and their derivatives.[4]

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Exploring the potential of metallated strained heterocycles: flow generation, lithiation and functionalization of 1-azabicyclo[1.1.0]butanes

Pantaleo Musci,[a] Timo von Keutz,[b] Leonardo Degennaro,[a] David Cantillo,[b] Christian Oliver Kappe,[a] Renzo Luisi.[a]*

[a] *Flow Chemistry and Microreactor Technology FLAME-Lab Department of Pharmacy – Drug Sciences University of Bari "A. Moro" Via E. Orabona 4, Bari, 70125 (Italy);* [b]*Institute of Chemistry, University of Graz, Heinrichstrasse 28, 8010, Graz (Austria)*

Modern medicinal chemistry is increasingly turning to unconventional structural motifs to optimize drug candidates. In this scenario, 1-azabicyclo[1.1.0]butanes (ABBs) are becoming appealing structural motifs that can be employed as click reagents or precursors of azetidines.[1,2] A straightforward continuous flow process for one-pot generation, C3 lithiation and functionalization of ABB is reported in this communication.[3] The microfluidic technology allows for exquisite control of the reaction parameters and the process operates at higher temperatures and safer conditions if compared to batch mode. A plethora of 3-substituted-1-azabicyclo[1.1.0]butanes have been prepared in flow operations.

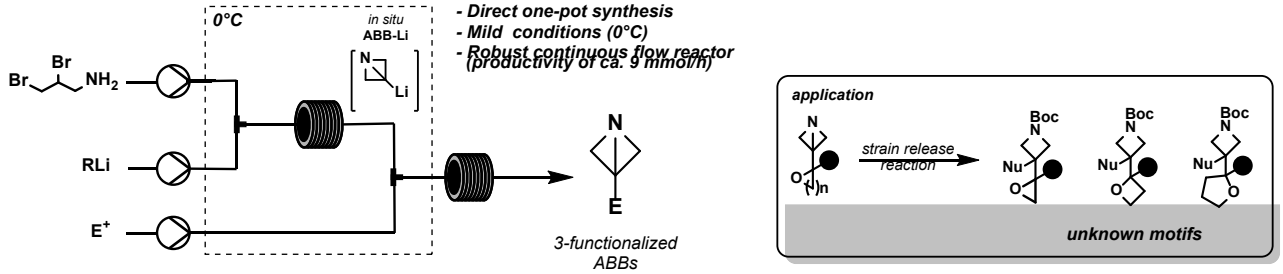

Figure 1. Microfluidic setup for the genesis, lithiation and trapping of 1-azabicyclo[1.1.0]butane and strain release process.

Moreover, the possibility to install two different strained heterocycles on the same scaffold was explored, with spotlight on a new chemical space. Oxyranyl, oxetanyl and tetrahydrofuranyl ABBs were obtained in good yields and the strain release process led to intriguing 3,3-difunctionalized azetidines bearing an oxygenated heterocycle.

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A VEGF-targeting aptamer labelled with a fluorescence light-up probe for diagnostics and theranostics

Ettore Napolitano,[a] Claudia Riccardi,[a] Domenica Musumeci,[a],[b] Filippo Doria,[c] Rosa Gaglione,[a] Angela Arciello,[a] Daniela Montesarchio,[a]

[a] *Department of Chemical Sciences, University of Naples Federico II, Naples, Italy;*
[b] *Institute of Biostructures and Bioimages, Naples, Italy*
[c] *Department of Chemistry, University of Pavia, Pavia, Italy.*

In order to develop effective theranostic systems targeting VEGF-A,[1] we here focused on the interaction between the G-quadruplex (G4)-forming V7t1[2,3,4] aptamer and a novel fluorescent cyanine.[5,6,7] V7t1 is a G-rich oligonucleotide aptamer that specifically recognizes VEGF-A, a cytokine overexpressed in cancer cells. The aim of this study is obtaining stable non-covalent complexes between the aptamer and the fluorescent probe that can be selectively internalized in cancer cells and thus recognize the target, giving a marked fluorescence light-up upon binding. Strong binding between the aptamer and the probe, ensured by cyanine stacking on terminal guanine tetrads of V7t1, could be a superior strategy for aptamer labelling over classical conjugation, based on covalent bonds between the aptamer and the probe. In fact, this system is intrinsically very simple, obtained by mixing in 1:1 ratio unmodified V7t1 and the cyanine, and does not require linkers which in principle could alter the aptamer properties and particularly its folding. The interaction between the G4-forming aptamer and the fluorescent probe was studied using different biophysical techniques, i.e. circular dichroism, fluorescence spectroscopy and native gel electrophoresis. The cyanine-aptamer complex was tested on MCF-7 and HeLa cancer cells to evaluate their cell uptake, monitored by confocal microscopy, and in vitro anticancer efficacy. Our strategy shows promise for a useful combination of the therapeutic activity of V7t1 with a sensitive fluorescence-based detection of VEGF-A, identified as useful biomarker for early cancer diagnosis.

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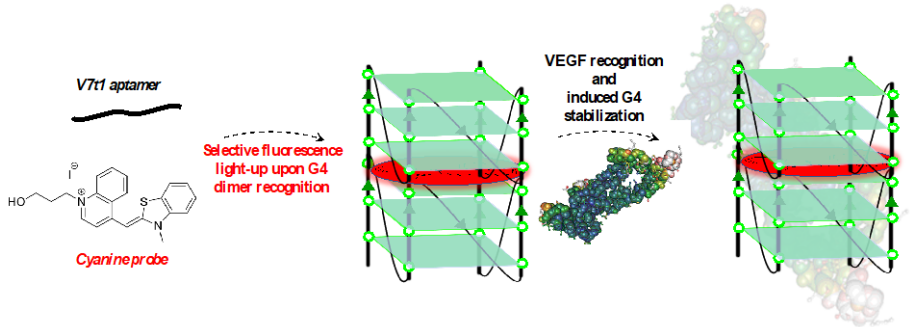

Figure 1. Selective fluorescence enhancement of the G4 dimer-cyanine complex upon VEGF interaction

New approaches for polyurethanes production: from catalysis to renewable synthesis

Fabrizio Olivito,[a] *Vincenzo Algieri,*[a] *Matteo Antonio Tallarida,*[a] *Antonio Jiritano,*[a] *Antonio Tursi,*[a] *Paola Costanzo,*[a] *Emilia Sicilia,*[a] *Loredana Maiuolo,*[a] *Antonio De Nino*[a]

[a] *Dipartimento di Chimica e Tecnologie Chimiche, Università della Calabria, Ponte P. Bucci, 87036 Arcavacata di Rende (CS), Italy. Email: fabrizio.olivito@unical.it*

Polyurethanes are a wide class of versatile polymers with a huge number of applications that cover medical, engineering, environmental and many other purposes [1]. Catalysis plays a central role for this kind of polymerization and the most common species employed are organic bases, organic acids and heavy metals compounds like tin and bismuth, that are still used today [2,3]. In this work, we initially present our methodology to prepare rigid polyurethanes foams, proving the role of non-toxics inorganic salts (i.e. sodium chloride) as optimal catalytic species. We investigated the complexation of these salts with PEG 400 in a crown ether-type manner. We used three different diisocyanates to produce three different prepolymers, and the chain extension on these intermediates were evaluated using 1,2-ethylene glycol and 1,4-butandiol. Moreover, considering that in our previous work we discovered a green reaction to convert microcrystalline cellulose into bio-oil and cellulose citrate using citric acid in a solvent-free reaction [4], in this context, we will illustrate the results obtained by converting the produced bio-oil into a polyol. We tested this polyol as a chain extender for the synthesis of a series of renewable polyurethane foams. In addition, we proved that cellulose citrate can be used as an optimal additive to improve the mechanical properties. The procedure furnished different types of materials like rigid and flexible foams that open new routes towards engineering and environmental applications. Here we report the structure of one of these products in Figure 1.

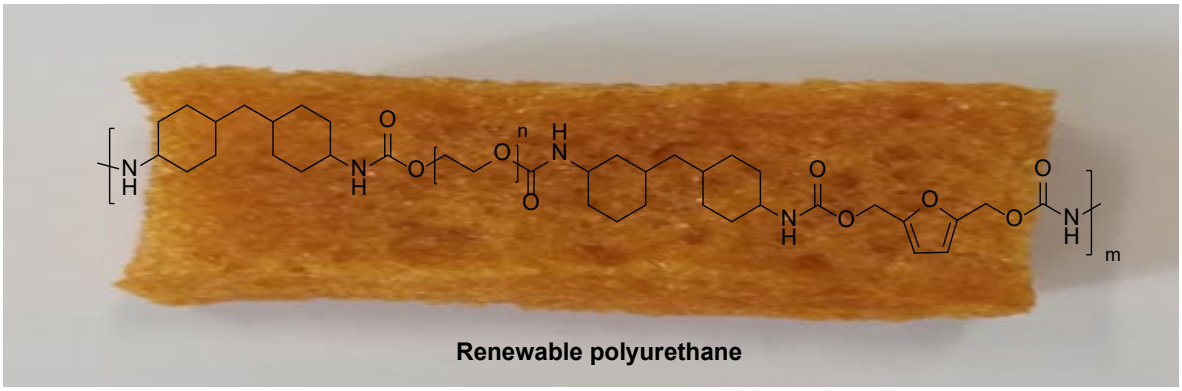

Figure 1. One of the final polyurethanes with the insertion of renewable polyol.

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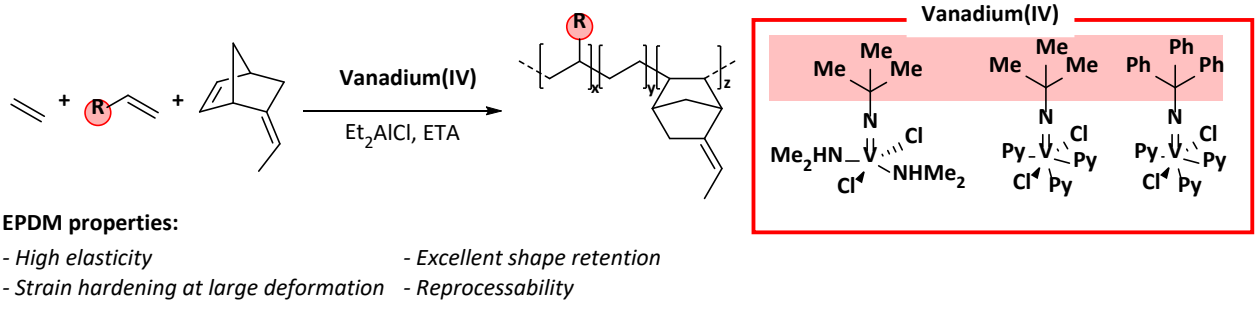
Vanadium−catalyzed olefin terpoymerization: EPDMs with tunable proprieties

Benedetta Palucci [a], Giorgia Zanchin [a], Adriano Vignali [a], Fabio Bertini [a], Giovanni Ricci [a], Giuseppe Leone [a]

[a] CNR, Istituto di Scienze e Tecnologie Chimiche "Giulio Natta" (SCITEC), via A. Corti 12, I-20133 Milano, Italy.

The research on polyolefins focuses on insertion−coordination polymerization catalyzed by molecular transition metal-based catalysts. The major advantage of insertion polymerization is that its mechanism is largely governed by the catalyst structure, which in turn strongly affects the polymer physical and mechanical properties. Amongst the transition metal series, chromium, Group IV and late metal catalysts have been highly reported. [1] Conversely, vanadium complexes have been less investigated as catalyst precursors for olefin polymerization, despite being the catalyst of choice in the production of ethylene–propylene rubber and ethylene–propylene–diene elastomer (EPDM). Herein, we report the synthesis and characterization of a series of imido vanadium(IV) complexes, differing in the ligand substitution, as well as their application in combination with Et_2AlCl and Cl_3CCO_2Et (ETA), in the terpolymerization of ethylene and 5-ethylidene-2-norbornene (ENB) with α-olefins (e.g. propylene, 1-hexene and 1-octene) (Scheme 1). [2] The resulting polymers have been characterized to study their microstructure, mode of insertion, and thermal properties. Furthermore, the mechanical properties of the obtained EPDMs have been also investigated to evaluate the resistance to strain, the material stiffness and the polymer elasticity. The resulting EPDMs behave as thermoplastic elastomers or soft elastomers, depending on the polymerization conditions and vanadium catalyst employed. Generally, the obtained EPDM thermoplastic elastomers exhibit high elongation at break, strain hardening at large deformation, excellent shape retention properties and remelting processability with no fall in properties for recycle use without the need of polymers blending and reinforcement through the addition of active fillers. Preliminary data about the terpolymerization of ethylene with ENB and α,ω-non conjugated dienes (e.g.1,5-hexadiene and 1,7-octadiene) and subsequent functionalization of the resulting polymers through a radical grafting, will be discussed.



Scheme 1. Terpolymerization of ethylene with α−olefins (e.g. propylene, 1-hexene, 1-octene) and ENB catalyzed by vanadium based catalysts.

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Luminescent Solar Concentrator: benzothiadiazole-based fluorophores for a green application

Costanza Papucci[a,b], *Massimo Calamante*[b], *Lorenzo Zani*[b], *Andrea Pucci*[c], *Gianna Reginato*[b] *and Alessandro Mordini*[b]

[a] *Department of Chemistry Via della Lastruccia 3, 50019, (FI), Italy*
[b] *ICCOM-CNR Via Madonna del Piano 10, 50019, (FI) Italy*
[c] *Department of Chemistry and Industrial Chemistry Univesrity of Pisa, Via A.G. Moruzzi 13, 56124, (PI) Italy*
e-mail: costanza.papucci@gmail.com

Luminescent Solar Concentrators (LSCs) are optical devices based on a polymeric panel (usually PMMA), doped with a fluorophore, which is capable to improve the photovoltaic efficiency of a typical PV cell, at the edge of the panel, reducing the costs of installation and materials. This, together with the aesthetic characteristics of LSCs (color and shape tunability), allows their use as building integrated photovoltaics (BIPVs). Organic compounds will be promising dyes for LSC application for their versatile spectroscopic characteristics, in particular absorption and emission range, depending on a specific structural design[1].
Microalgae are eukaryotic unicellular organisms, with dimensions 1 μm-10 μm of diameter, belonging to the class of aquatic plants; they have been used for many environmental applications, especially for CO_2 mitigation, wastewater treatments and biofuels production[2].
This work is focused on the synthesis and the spectroscopic characterization of new fluorescent organic compounds with a typical extended conjugated D-A-D structure, characterized by an absorption range not competitive with chlorophyll one (440 nm, 660 nm).
The new compounds were obtained with good overall yields, through two direct C-H arylation steps, avoiding organometallic intermediates, under mild conditions and with easy purifications.
New dyes showed good spectroscopic characteristics. In particular, their absorption maxima are compatible with chlorophyll one; furthermore, their interesting optical properties allow to employ these compounds in LSC applications and possible integration in greenhouse or in microalgae culture.

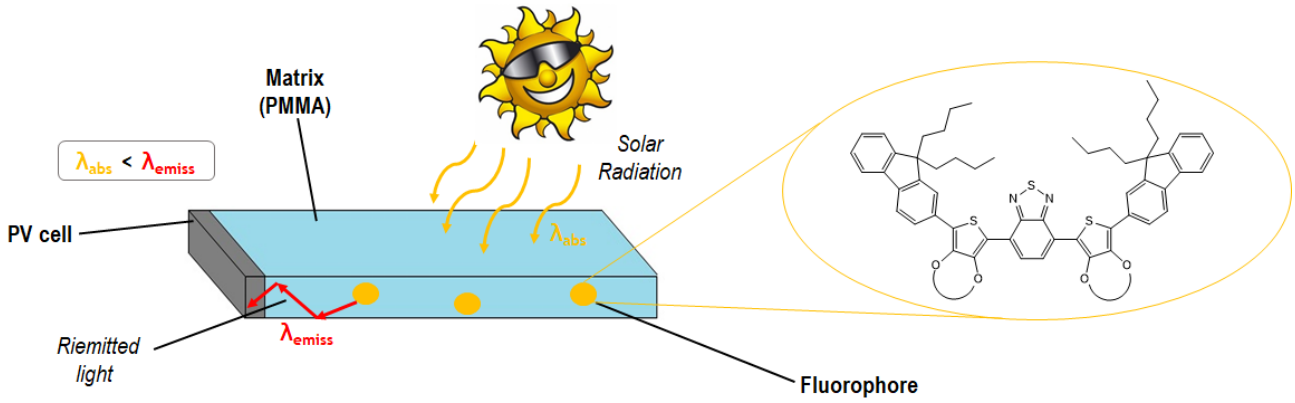

Fig.1: *General mechanism of a LSC device and a specific D-A-D organic compound employed for LSC applications.*

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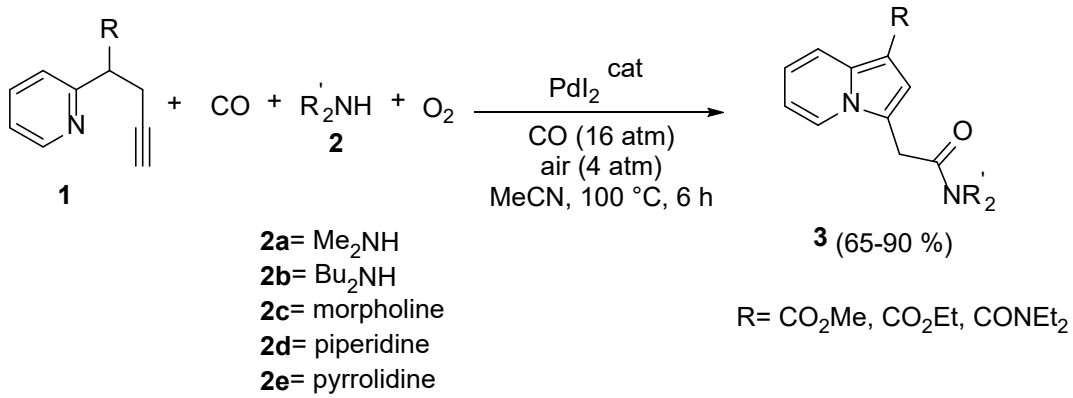
Multicomponent PdI_2/KI-catalyzed synthesis of indolizine derivatives

Marzia Petrilli, Lucia Veltri, Roberta Amuso, Bartolo Gabriele

[a] *Laboratory of Industrial and Synthetic Organic Chemistry (LISOC), Department of Chemistry and Chemical Technologies, University of Calabria, Via P. Bucci 12 C, 87036 Arcavacata di Rende (CS), Italy*

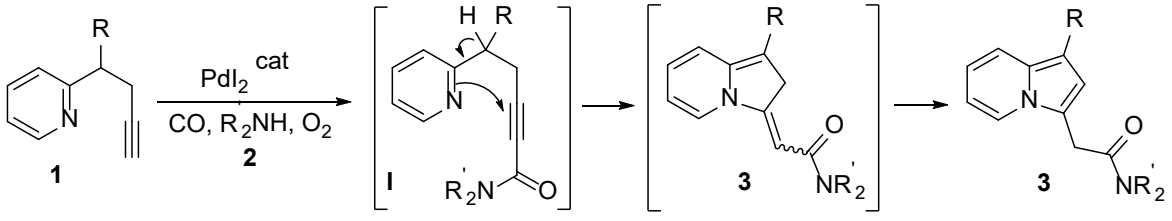
Indolizines are an important class of polyheterocyclic derivatives. The indolizine core is present in many molecules which display a wide range of pharmacological properties, such as CNS depressant, analgesic and anti-inflammatory, anticancer, antibacterial, antioxidant, larvicidal and anti-HIV activities.[1]

In this communication, we report a novel, multicomponent approach to indolizine derivatives **3** in good to high isolated yields (65–85%), based on PdI_2/KI-catalyzed oxidative aminocarbonylation [2] of 2-(but-3-yn-1-yl)pyridines **1** (Scheme 1). Reactions are carried out in the presence of a secondary amine **2** (3 equiv), using oxygen (from air) as oxidant, in the presence of 1 mol% of PdI_2 and 0.5 equiv of KI, in MeCN as the solvent, at 100 °C and under 20 atm of a 4:1 CO-air mixture.



Scheme 1: Multicomponent PdI_2/KI-catalyzed synthesis of indolizine derivatives **3** starting from 2-(but-3-yn-1-yl)pyridines **1,** amines **2**, CO and O_2.

A mechanistic hypothesis for this process is based on the sequential combination between the PdI_2/KI-catalyzed oxidative aminocarbonylation of 2-(but-3-yn-1-yl)pyridines **1** with CO, O_2 and amines **2**, followed by the intramolecular aza-Michael reaction of the initially formed 2-ynamide intermediates **I** and isomerization (Scheme 2).



Scheme 2: Mechanistic hypothesis leading to target indolizine derivatives **3** from 2-(but-3-yn-1-yl)pyridines **1**, CO, O_2, and secondary amines **2**: aminocarbonylation–aza-Michael–isomerization.

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Exploring the epigenetic reader BRD9: computational studies and synthesis of new potential binders

M. Pierri,[a] E. Gazzillo,[a] M. G. Chini,[b] G. Bifulco,[a] I. Bruno,[a] G. Lauro,[a] S. Terracciano[a]

[a] *Department of Pharmacy, University of Salerno, Via Giovanni Paolo II 132, 84084 Fisciano, Italy*
[b] *Department of Biosciences and Territory, University of Molise C.da Fonte Lappone – 86090, Pesche (IS), Italy*

Bromodomain-containing proteins (BRDs) have recently been receiving growing interest from the scientific community due to their involvement in gene expression as epigenetic readers of acetyl-lysine (KAc) modifications on histone tails, a widespread post-translational modification (PTM) implicated in the regulation of chromatin structure.[1,2] In this context, Bromodomain-containing protein 9 (BRD9) is overexpressed in many human cancers, such as acute myeloid leukemia and human squamous cell lung cancer. Therefore, the discovery of potent and selective BRD9 ligands could be useful for interrogating and elucidating the biological and pharmacological role of this reader module and for corroborating its therapeutic potential.[3] On the other hand, the discovery of small molecules, endowed with high affinity and selectivity within the BRDs families, represents a significant challenge since bromodomains show a highly conserved overall fold.[4,5] Continuing our previous studies focused on the identification of new chemical entities as BRD9 binders,[6] we recently fine-tuned structure-based 3D BRD9 pharmacophore models which provided us the possibility to overcome the above-mentioned challenge. Indeed, thanks to the application of this computational protocol, we screened large libraries of drug-like molecules identifying new heterocyclic scaffolds. Herein we report the synthetic approach of the most promising candidates.

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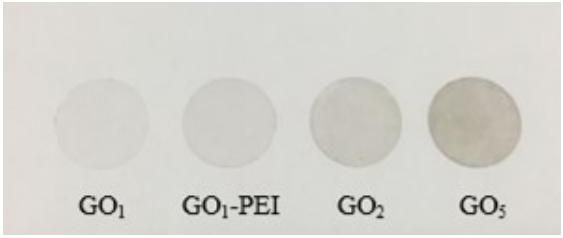
Preparation of 3D Graphene Oxide-Polyethylenimine Porous Scaffold for Cardiac Tissue Engineering

Serena Pilato,[a] Samanta Moffa,[a] Daniele Capista,[b] Maurizio Passacantando,[b] Francesca Diomede,[c] Jacopo Pizzicannella,[d] Antonella Fontana[a]

[a] Department of Pharmacy, University "G. d'Annunzio" of Chieti-Pescara, Via dei Vestini, 66100 Chieti, Italy; [b] Department of Physical and Chemical Sciences, University of L'Aquila, Via Vetoio, 67100, L'Aquila, Italy; [c] Department of Innovative Technologies in Medicine & Dentistry, University "G. d'Annunzio" of Chieti-Pescara, Via dei Vestini, 31, 66100 Chieti, Italy; [d] ASL02 Lanciano-Vasto-Chieti, "Ss. Annunziata" Hospital, Chieti, Italy

Miocardial infarction is associated with significant cell death and consequently leads to loss of heart functions. Biomaterials currently used in cardiac tissue engineering must have peculiar characteristics, such as electrical conductivity and appropriate mechanical properties, which are two parameters playing a key role in regulating cardiac cells behavior. Carbon-based nanomaterials have been considered promising candidates to mimic certain structure and function of native extracellular matrix materials for tissue engineering. In this study, a 3D porous structure composed by graphene oxide (GO) and linear polyethylenimine (PEI) was developed for cardiac repair applications. The reactions were carried out using round glass coverslips as support, previously activated under an UV-ozone lamp and incubated with (3-aminopropyl)triethoxysilane to form the silanised derivatives. The activated substrates were alternatively dipped in aqueous solutions of GO and PEI, leading to the formation of different networks with a number of graphene layers ranging from one to five separated from each other by the PEI spacers.



AFM and SEM analysis have been used to have morphological information on the graphene-based 3D networks, revealing that the functionalization of the coverslips was mostly homogeneous and that the thickness of the different samples increased proportionally with the number of incubations. The Young modulus of the networks, measured by Peak Force QNM mode of AFM, decreased with the increase of the number of layers of GO-PEI and the degree of functionalization of GO, in agreement with previous studies.[1] The XPS analysis performed on the different samples confirmed that the alternating incubations of the substrates with the solutions of GO and PEI actually led to the functionalization of GO with the formation of covalent bonds between the carboxylic and epoxy groups of GO and amino groups of PEI. Furthermore, GO-PEI scaffolds were used for in vitro studies, wherein cardiac muscle HL-1 cells exhibited good cell viability and the absence of morphological changes. Cells seeded on coverslips treated with GO_5 and GO_1-PEI showed a high number of focal adhesions and the formation of an intercellular network. Moreover, immunofluorescence staining and western blotting highlighted for GO_5 and GO_1-PEI networks an upregulation of the proteins expression Connexin-43 and Nkx 2.5, involved in muscle conduction of electric signals. Overall, it is possible to conclude that GO-PEI scaffolds promote the properties of cardiac tissue constructs and they can potentially provide a tissue model for drug studies or an attractive platform for cardiac tissue engineering.

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Highly efficient epoxidation of vegetable oils catalyzed by Aquivion perfluorosulfonic acid resin

Riccardo Polese, Elisa Pintus, Luca Nuvoli, Monica Tiana, Salvatore Pintus, Silvia Gaspa, Massimo Carraro, Lidia De Luca, Ugo Azzena, Luisa Pisano[a]

[a] *Dipartimento di Chimica e Farmacia, Università degli Studi di Sassari, Via Vienna 2, 07100, Sassari, Italy luisa@uniss.it*

The acid-promoted epoxidation of vegetable oils [1] was studied using a variety Acidic Ion Exchange Resins (AIERs) as heterogeneous acid catalyst. Quantitative and selective epoxidation was obtained upon identification of the more efficient catalyst and experimental conditions. Furthermore, optimized reaction conditions were successfully applied to the epoxidation of a waste cooking oil, thus extending our procedure to the valorization of a biowaste, an area of increasing importance within a more sustainable society [2].
The use of quantitative ^{1}H-NMR beside making accurate control of the epoxidation stoichiometry and selectivity, allowed facile and rapid quantification of mono- di- and tri-epoxides thus providing an indirect indication on the fatty acid composition of the vegetable oils, even in the presence of very low quantities of linolenic acid [3,4].

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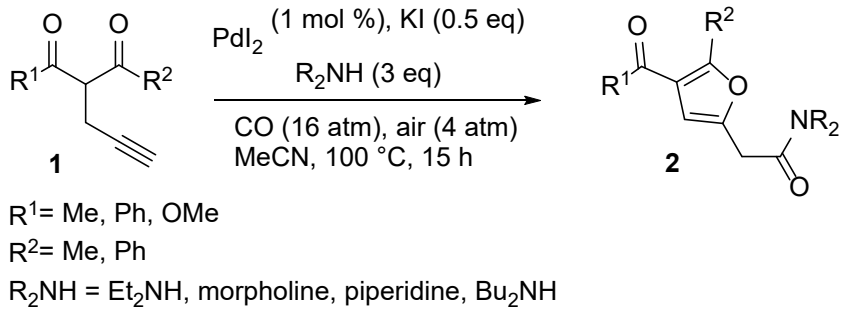
Novel synthesis of functionalized 2-(furan-2-yl)acetamides by a Pd-catalyzed oxidative aminocarbonylation approach

Lucia Veltri, Tommaso Prestia and Bartolo Gabriele

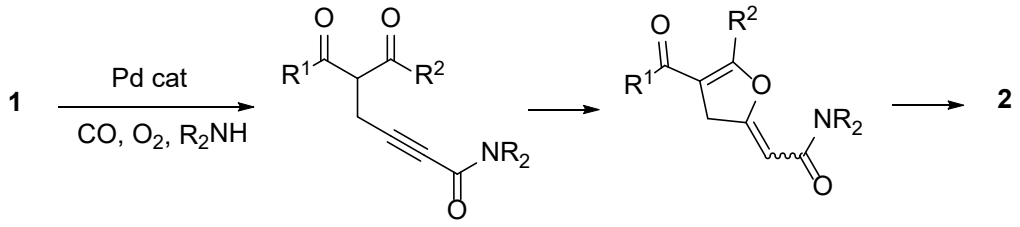
Laboratory of Industrial and Synthetic Organic Chemistry (LISOC), Department of Chemistry and Chemical Technologies, University of Calabria, Via Pietro Bucci 12/C, 87036 Arcavacata di Rende (CS), Italy

Functionalized furans are a very important class of heterocyclic compounds because the furan core is present in many biologically active compounds.[1] Moreover, they find use in many applicative fields.[2] In this contribution, we report a new multicomponent aminocarbonylative[3] approach which affords functionalized 2-(furan-2-yl)acetamides **2** in high yields (65-75%) starting from propargylated diketones or ketoesters **1** (Scheme 1).



Scheme 1

The process involves the oxidative monoaminocarbonylation of the terminal triple bond, followed by intramolecular conjugate addition and isomerization (Scheme 2).



Scheme 2

Reactions are carried out in presence of catalytic amount of PdI_2 in conjunction with KI and with a secondary amine as nucleophile (in CH_3CN as the solvent at 100° C° for 15 h, under 20 atm of a 4:1 mixture of carbon monoxide and air).

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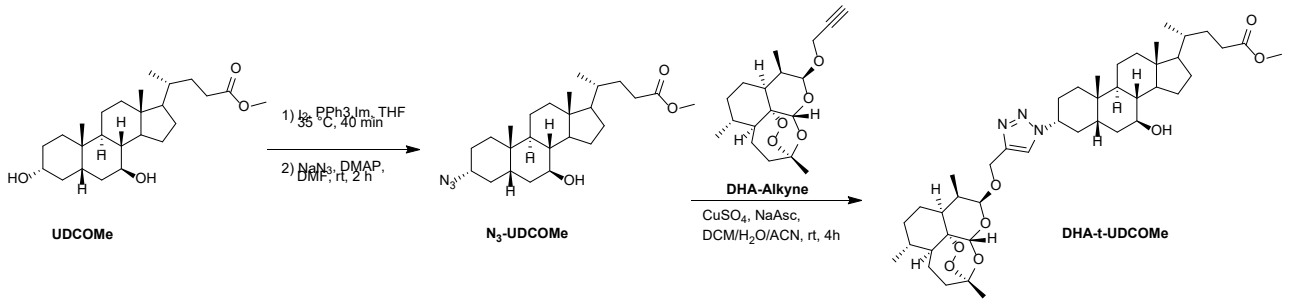
Repurposing of dihydroartemisinin-bile acids conjugates as new potential anti SARS-CoV-2 agents

Lorenzo Preti,[a] *Elena Marchesi,*[a] *Valentina Gentili,*[a] *Sabrina Rizzo,*[a] *Paolo Marchetti,*[a] *Maria Luisa Navacchia,*[b] *Daniela Perrone*[a]

[a]*Dipartimento di Scienze Chimiche, Farmaceutiche ed Agrarie, Università degli studi di Ferrara, Via Luigi Borsari, n. 46 - 44121 Ferrara;* [b]*Istituto per la Sintesi Organica e la Fotoreattività, Via P. Gobetti 101 - 40129 Bologna*

The COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to plague many countries and has caused more than 3 million deaths worldwide.[1] The use of repurposed drugs as antiviral agents is a promising strategy to meet the urgent demand for treatment of the disease. Recently, Zhong *et al*. demonstrated that artemisinin derivatives can inhibit SARS-CoV-2 replication *in vitro*.[2] Among others, Dihydroartemisinin (DHA), is widely used as a malaria treatment. Furthermore, DHA can be easily conjugated to lipophilic moieties such as bile acids, that have been found to bind to the spike protein of the SARS-CoV-2 by Fiorucci *et al*.[3] Several conjugates of DHA and bile acids, with antitumoral activity, were previously synthetized by our research group.[4] The conjugates improved the stability of DHA and were more potent against cancer cell lines than DHA itself. In our work, we focused on synthesis optimization to obtain a procedure suitable for the production of triazole linked conjugates of DHA and bile acids. The synthetic procedure for conjugation of ursodeoxycholic acid's methyl ester (UDCOMe) to DHA via triazole moiety is reported here as an example. This involves the substitution of the 3-hydroxyl with iodine, followed by substitution with sodium azide to afford the clickable N_3-UDCOMe. The azide modified bile acid was reacted through CuAAC (copper catalyzed azido-alkyne reaction) with the alkyne modified DHA to afford the triazole containing hybrid in good yield. In order to assay the antiviral property of the conjugate, it was used to treat SARS-CoV-2-infected VeroE6 cells. First, the conjugate was tested on healthy cells for the evaluation of cytotoxicity by MTT and found to be not toxic up to 100 µM. Then, 10 µM of DHA-t-UDCOMe was selected to treat VeroE6 cells during the infection with SARS-CoV-2 (100 genome equivalent per cell). The results showed that the conjugate was able to decrease the viral load of 2.735 logs after 48 hours post infection, with respect to the untreated infected cells. These preliminary results, encourage us to test different dihydroartemisinin-bile acid conjugates against the SARS-CoV-2 infection.



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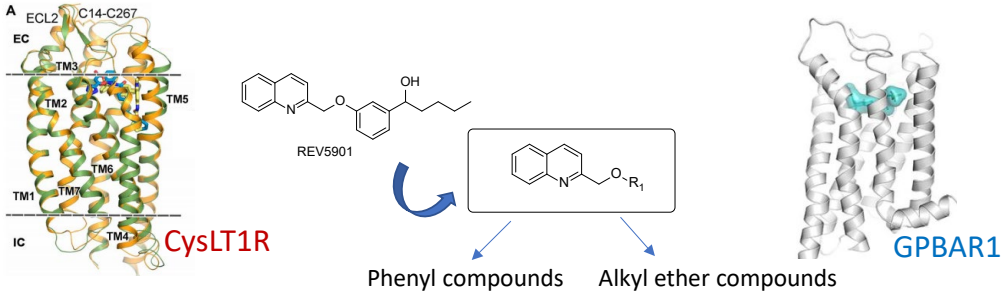
Design and synthesis of multitarget compounds acting on Cysteinyl Leukotriene Receptor 1 and G-Protein coupled Bile Acid Receptor 1

Pasquale Rapacciuolo,[a] Bianca Fiorillo,[a] Valentina Sepe,[a] Paolo Conflitti,[b] Rosalinda Roselli,[c] Giuliana Baronissi,[a] Chiara Cassiano,[a] Bruno Catalanotti,[a] Angela Zampella,[a] Vittorio Limongelli,[a,b] Stefano Fiorucci.[c]

[a]*Department of Pharmacy, University of Naples "Federico II", Via D. Montesano, 49, I-80131 Naples, Italy*
[b]*Università della Svizzera italiana (USI), Faculty of Biomedical Sciences, Euler Institute, via G. Buffi 13, CH-6900 Lugano, Switzerland*
[c]*Department of Clinical and Experimental Medicine, Nuova Facoltà di Medicina, Piazza L. Severi 1-06132 Perugia, Italy*

Leukotriene receptors are a pharmacologically subfamily of class A G protein-coupled receptors (GPCRs) composed of five members: cysteinyl leukotriene receptor 1 ($CysLT_1R$) and 2 ($CysLT_2R$), leukotriene B4 receptor 1 (LTB4-R1) and 2 (LTB4-R2), and oxoeicosanoid receptor 1 (OXER1). These receptors are activated by leukotrienes, which are eicosanoids derived from the oxidation of arachidonic acid acting as important mediators in inflammatory processes. In particular, the cysteinyl leukotrienes C4 (LTC_4), D4 (LTD_4) and E4 (LTE_4) are endogenous ligands of $CysLT_1R$ and $CysLT_2R$ with different potency and affinity. Activation of CysLTRs by one of these molecules regulates cytokine secretion, vascular permeability, fibrosis, bronchoconstriction and recruitment of effector cells and mucus.[1,2] In particular, $CysLT_1R$ is known to mediate allergic and hypersensitivity reactions and when its signaling is exacerbated it leads to pathological conditions as asthma and allergic rhinitis. The discovery of the first $CysLT_1R$ antagonists, namely montelukast, zafirlukast and pranlukast has greatly impacted the treatment of asthma and respiratory morbidities and many more $CysLT_1R$ antagonists have been developed and tested in preclinical and clinical trials. Among these, we have recently reported alpha-pentyl-3-[2-quinolinylmethoxy] benzyl alcohol (REV5901) as the first compound endowed with dual activity as $CysLT_1R$ antagonist and agonist of the G protein-coupled bile acid receptor 1 (GPBAR1),[3] another class A GPCR activated by secondary bile acids and highly expressed in liver, intestine, brown adipose tissue, muscles, and immune cells.[4,5] We reported that REV5901 has positive effects in a mouse model of colitis with reduced levels of CysLTs, $CysLT_1R$, and cyclooxygenase 1 and 2 in a GPBAR1-dependant manner.
Here, we present a series of compounds with dual activity towards $CysLT_1R$ and GPBAR1. They are derivatives of REV5901 - the first reported dual compound - with therapeutic potential in the treatment of colitis and other inflammatory processes.



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Mannich reaction for the synthesis of zwitterionic calix[4]arene-based ligands: supramolecular properties, self-assembly and interactions with proteins

Francesco Rispoli[a], *Alessandro Casnati*[a], *Francesco Sansone*[a], *Laura Baldini*[a]

[a]*Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco Area delle Scienze 17/a, 43124 Parma*

For over 20 years calixarenes have been used to build up ligands able to interfere with aggregation and functions of proteins to different extents. The positively charged cone-calix[4]arene **1,** has been tested as inhibitor of the activity of voltage-dependent potassium channels thanks to the interaction between the guanidinium groups of the calixarene and the carboxylated groups present at the channel entry[1]. Negatively charged cone-calix[4]arenes, can provide a single-point recognition of protein surface by the synergistic action of their lipophilic cavity and proper functional groups at its upper rim. An example is the tetrasulfonato calix[4]arene **2**, whose recognition ability to bind cyt c was demonstrated by Crowley et al. [2].

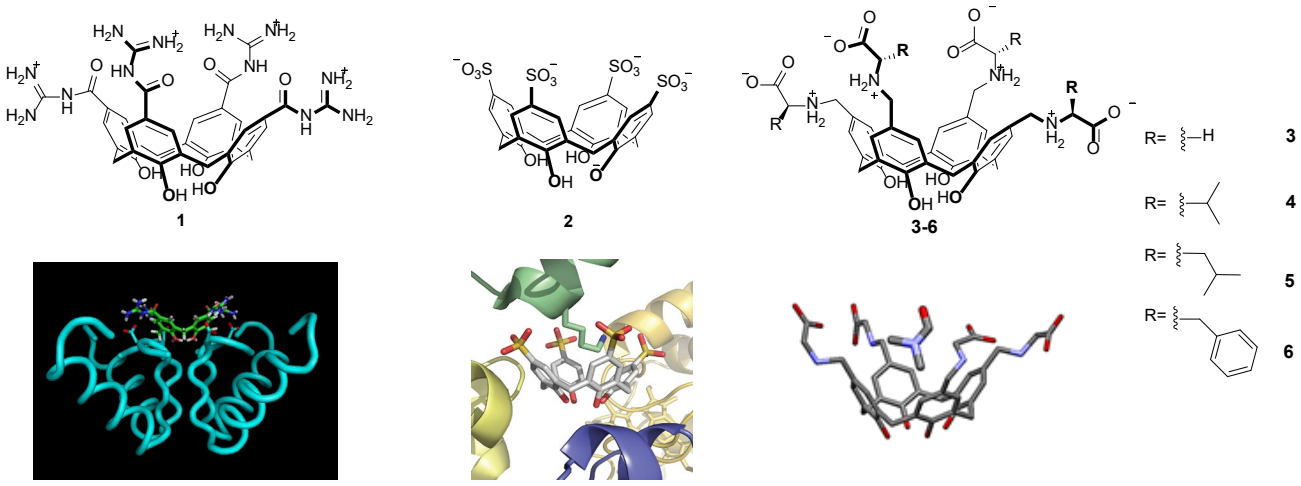

Fig 1: Positively (**1**), negatively (**2**) and zwitterionic (**3-6**) calix[4]arenes

Throughout the last years, zwitterionic moieties have raised attention as constituents of biocompatible materials [3]. The aim of this research is to functionalize the upper rim of calix[4]arene with zwitterionic moieties in order to study the possible interactions with proteins or other zwitterionic molecules. We herein exploited the use of the Mannich reaction for a fast and efficient introduction of α-amino acids on the calix[4]arene.[4] Using this method we were able to functionalize the upper rim with Glycine, Valine, Leucine and Phenylalanine. The scope and limitations of this synthesis and the supramolecular properties of the obtained receptors will be discussed.

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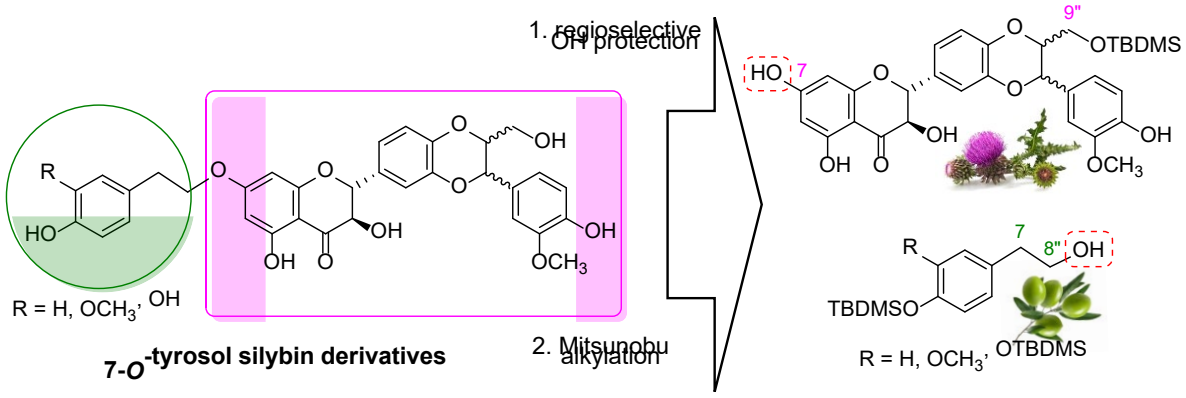
Regioselective synthesis of new 7-*O*-tyrosol silybin derivatives as promising multitarget ligands (MTL)[1]

Valeria Romanucci, Rita Pagano, Marilena Giordano, Antonio Lembo, Armando Zarrelli and Giovanni Di Fabio

Department of Chemical Sciences, University of Naples Federico II, Via Cintia 4, Naples, 80126 Italy

Multifactorial diseases, such as cancer and neurological disorders, are driven by dysregulation of different but interconnected biochemical pathways. The complexity of these pathologies makes them hardly addressable by single-target molecules. To combat these diseases, multitarget-directed ligands (MTDLs), which interfere pathogenesis with multiple targets, may achieve better therapeutic efficacy with complementary mechanisms of action. [2] In the last years a plethora of natural products was identified as lead for multitarget drug discovery that, in the light of their structural diversity, allows the discovery of new or similar pharmacophores. Here, we reported the design and synthesis of new bioactive compounds, combining two "fragments" with a simple synthetic strategy in order to obtain libraries based on lead polyphenols. To this purpose, a pharmacophore-combination strategy was used with silybins and tyrosols as the lead compounds. Silibinin is a diastereoisomeric mixture of flavonolignans extracted by the seeds of milk thistle *Silybum marianum* [L. Gaertn. (Asteraceae)] which exerts multiple activities ranging from anticancer to neurodegenerative ones.[3,4]



It has been reported that the pure diastereomers of silibinin, silybin A and silybin B, show distinct metabolic profiles and biological effects; therefore, potentially differing effects of pure silybin A and silybin B tyrosols derivatives have been also investigated. Tyrosols identified as tyrosol (TYR), homo-vanillyl alcohol (HVA) and hydroxytyrosol (HDT), are three polyphenols that deserve special consideration for their pharmacological activities such (antioxidant, anticancer, anti-inflammatory, and neuroprotective) [5,6] New compounds were synthesized by a regioselective alkylation of 7-OH group of silybins starting from appropriately protected building blocks. The library of 7-*O*-tyrosol silybin derivatives has been extended to 7-*O*-tyrosol 2,3-dehydro-silybin (DHS) derivatives by the oxidation procedure previously reported by us. DHS represents another pharmacophore that further increases the diversity of potential effects. All compounds were fully characterized by 1D, 2D-NMR and MS analyses. Preliminary antioxidant activity of all compounds highlights their strong antioxidant activity in comparison with parent metabolites.

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A new family of branched superfluorinated dendritic amphiphiles

M. Rosati,[a] G. Neri,[a] Andrea Pizzi,[a]
Nicola Demitri,[b] F. Baldelli Bombelli,[a] G. Cavallo,[a] and P. Metrangolo [a]

[a] SupraBioNanoLab-DCMIC "Giulio Natta", Politecnico di Milano, Via L. Mancinelli 7, 20131 Milan, Italy; [b] Elettra – Sincrotrone Trieste, S.S. 14 Km 163.5 in Area Science Park, 34149 Basovizza – Trieste, Italy.

E-mail: marta.rosati@polimi.it

Due to the higher electronegativity and larger dimension of fluorine than hydrogen, perfluoroalkyl chains are bulkier than their hydrogenated counterparts, characterized by greater rigidity, and generally assume a helical conformation to minimize steric hindrance. All these properties induce in perfluorocarbons peculiar self-assembling properties, thus generating functional materials with improved mechanical properties [1]. Unfortunately, linear-chain perfluorocarbons (PFCs) with more than six -CF_2 units show long-lasting persistence in the environment, high tendency to accumulate in humans and animals, and suspected toxicity [2]. The use of short branched perfluorinated chains, as those present in perfluoro-*tert*-butoxyl-functionalized pentaerythritol derivatives [3-4], guarantee the insertion of a high number of equivalent fluorine atoms with an enhanced lability and biodegradability [2]. As shown in figure 1, these molecules bear a high number of equivalent ^{19}F atoms making them exceptional probes for ^{19}F-Magnetic Resonance Imaging (MRI) applications [5]. However, superfluorinated molecules are not directly dispersible in aqueous solutions, thus chemical functionalization with hydrophilic moieties or tailored formulations are needed for obtaining their dispersibility in this medium. The development of polyglycerol dendrons functionalized at their core with linear perfluorinated chains guaranteed the formation of new self-assembling properties in solution [6]. In this work we present the synthesis and self-assembly of a new family of superfluorinated dendritic amphiphiles showing low generation bis-MPA based polyester dendrons [7] functionalized at their focal point with a new F_{27} derivative.

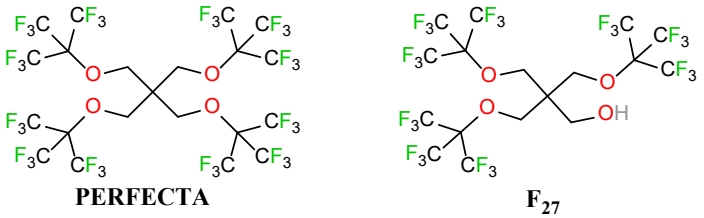

Figure 1. Chemical structure of PERFECTA, which shows 36 magnetically equivalent fluorine atoms, and of tri-perfluoro-tert-butoxyl-functionalized pentaerythritol (F_{27}). This molecule shows 27 equivalent fluorine atoms and a free hydroxyl group suitable for further functionalization.

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Extraction of astaxanthin from *Haematococcus pluvialis* with hydrophobic deep eutectic solvents

Chiara Samorì,[a,b] Laura Pezzolesi,[c] Virgina Gori,[b] Walter Pitacco,[a] Martina Vagnoni,[a] Paola Galletti [a,b]

[a]*Dipartimento di Chimica "Giacomo Ciamician", University of Bologna, via Sant'Alberto 163, Ravenna, Italy*

[b]*CIRI-FRAME, University of Bologna, via Sant'Alberto 163, 48123, Ravenna, Italy*

[c]*Dipartimento di Scienze Biologiche, Geologiche ed Ambientali, University of Bologna, via Sant'Alberto 163, 48123, Ravenna, Italy*

Astaxanthin (3,3'-dihydroxy-β,β-carotene-4,4'-dione) is a secondary carotenoid belonging to the class of xanthophylls and biosynthesized (e.g. by the microalga *Haematococcus pluvialis* or the yeast *Phaffia rhodozyma*) or accumulated (e.g. by marine invertebrates or birds) by a variety of living organisms. The chemical structure of astaxanthin is directly correlated to the organism in which it is produced or found: astaxanthin bounded with fatty acids like oleic, linoleic and palmitic acids (monoesters of astaxanthin) is the typical structure biosynthesized by *H. pluvialis* whereas astaxanthin in the free form is usually found in larger extent in shrimps, crabs, flamingos or fishes, organisms that cannot synthesize astaxanthin de novo but are capable of accumulating such pigment only when it is assumed with food [1]. The extraction of natural astaxanthin has been accomplished with a variety of hydrophobic solvents, from traditional organic compounds to unconventional alternatives like supercritical CO_2, vegetable oils, ionic liquids or deep eutectic solvents, more and more investigated for developing sustainable protocols for the recovery of bio-based pigments and bioactive compounds [2]. Deep eutectic solvents (DES) have become quite popular in this scenario, especially if composed of non-toxic and biocompatible hydrogen bond donors and acceptors (HBD and HBA, respectively) [3]. The aim of the present work is to extend the use of hydrophobic DES in the extraction of astaxanthin from *H. pluvialis*. In particular, the water immiscibility of these peculiar solvents has been exploited to develop a liquid-liquid extraction of astaxanthin, by-passing the need of harvesting and drying the microalgal culture, known to have a large impact on the overall energy consumption and economics of the extraction process. To this purpose, four hydrophobic DES based on oleic acid as HBD and various HBA (menthol, thymol, geraniol, and α-bisabolol) were prepared and applied to both freeze-dried biomass and *H. pluvialis* cultures, comparing their extraction ability and their "algae-compatibility".

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Synthesis of aryl aldehydes by Rieche formylation reactions of electron-rich phenyl boronic acids

Alessandro Santarsiere[a], *Maria Funicello*[a], *Paolo Lupattelli*[a], *Lucia Chiummiento*[a]

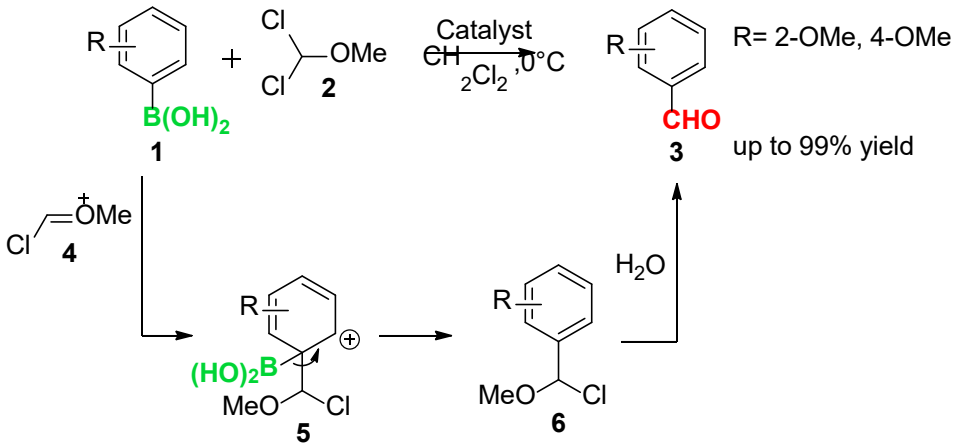
[a] *Department of Science, University of Basilicata, Via dell'Ateneo Lucano n. 10, 85100, Potenza, Italy*

Given the large availability of commercial boronic acids and their relative ease of preparation, recently several examples of transformation of boronic acids by cross-coupling, aminations, oxidations and alkylations have been reported, making these substrates highly versatile, we propose to enrich the few reported examples about their formylation [1].

For this purpose Rieche formylation has been chosen, which consists on the use of a Lewis acid as the catalyst (silver triflate, aluminiun (III) chloride, titanium (IV) chloride and iron (III) chloride) and dichloromethyl methylether (Cl_2CHOCH_3) as the formylating agent [2].

The synthesis of electron-rich aldehydes has been performed by regioselective Rieche formylation of the corresponding arylboronic acids under mild reaction conditions giving excellent yield, while electron-poor arylboronic acids are unreactive.

The proposed mechanism for this reaction has been reported in the Scheme 1. The oxonium ion **4** deriving from the ether **2** is involved in the electrophilic aromatic substitution of boronic acids **1** through the Wheland intermediate **5** and as a result, after hydrolysis of **6**, the corresponding aldehydes **3** have been obtained.



Scheme 1. Proposed Mechanism

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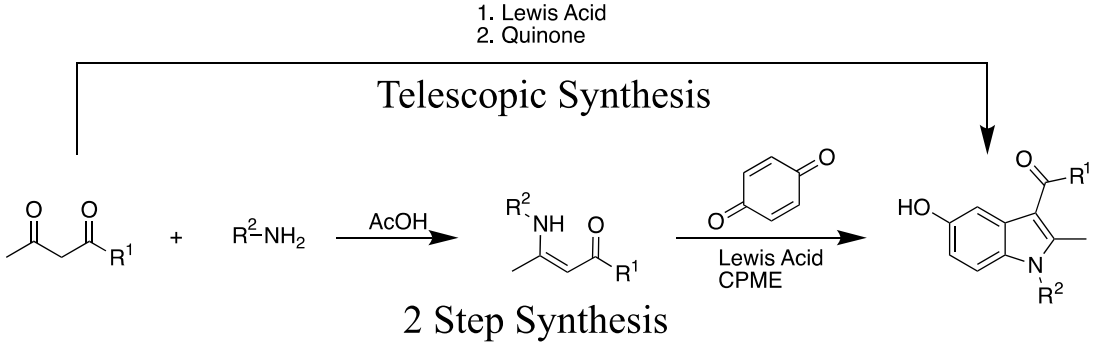
Nenitzescu Synthesis of Hydroxyindoles with Zinc, Iron and Magnesium Salts in Cyclopentyl Methyl Ether

Giuseppe Satta,[a,b] Andrea Beccu,[a] Silvia Gaspa,[a] Lidia De Luca,[a] Luisa Pisano,[a,b] Ugo Azzena,[a] and Massimo Carraro[a,b]*

[a] Department of Chemistry and Pharmacy Università degli Studi di Sassari via Vienna 2, 07100 Sassari, Italy
E-mail: g.satta@studenti.uniss.it
[b] Consorzio Interuniversitario Reattività Chimica e Catalisi (CIRCC), Bari, Italy

Indole ring is present in a great variety of biologically relevant compounds, like, e.g. the amino acid tryptophan, the hormone melatonin and the neurotransmitter serotonin as well as complex plant secondary metabolites[1]. Their application for the treatment of various pathologies, such as childhood leukemia, psychosis, different types of tumors[2], or in antiretroviral treatments(from the most common herpes to hepatitis B) increase their usefulness and stimulate development of new synthesis techniques. In 1929 Constin Nenitzescu[3] developed a specific process to synthetize 5-Hydroxyindoles starting from quinones and enamines; early processes needed use of nitromethane[4] and no catalyst, obtaining product by direct precipitation from reaction mixture with good yields and purity. Major advancements in this reaction have been done by the group of Velezheva[5,6], that developed the application of mild Lewis acids, such as zinc chloride, to perform the reaction in dichloromethane. We tried to further reduce the environmental impact of the entire process by substituting Dichloromethane with Cyclopentyl Methyl Ether (CPME) a more sustainable solvent[7]. The reduction of the environmental impact has been expressed through some Green Metrics: E Factor[8],RME, PMI. Comparing metrics calculated from this work with the ones obtained from literature, a reduction going from 2 times to one order of magnitude were achieved. In addition, the use of low temperatures in the presence of zinc, iron and magnesium salts as Lewis acids, lead to acceptable-good yields with a simple workup and an excellent recycle of the solvent.



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Cryo-dynamic HPLC and off-column HPLC in the determination of unusual atropoisomers and their extreme interconversion energy barriers.

A. Sorato [a], A. Fochetti [a], G. Fabrizi [a], A. Mazzanti [b], A. Ciogli [a]

[a] *Department of Chemistry and Technology of Drugs, University "La Sapienza", P. Le A. Moro 5 - 00185 Roma, Italy*
e-mail: andrea.sorato@uniroma1.it;
[b] *Department of Industrial Chemistry "Toso Montanari", University of Bologna, Viale del Risorgimento 4, 40136 Bologna, Italy*

Atropoisomers represent an important class of stereoisomers where restricted rotation around a single bond generates axial chirality. While most known atropoisomers belong to the biaryl class, research recently paid great attention to non-biaryl type atropoisomerism [1,2]. In this contest, we have investigated a small family of bis-2H,8H-pyrano[3,2-g]chromene derivatives (compounds 1-5) [3]. These compounds have two stereogenic axes that generate in principle 4 stereoisomers for the 4,10 derivatives and 3 stereoisomers (due to the presence of *syn* stereoisomer) in case of 4,6 derivates. By means of the enantioselective chromatographic approach, to resolve all stereoisomers for each compound, two extreme scenarios were found. The axial rotations of compounds 1-4 are very fast and it was not possible to isolate the atropoisomers. On the contrary, atropoisomers of compound 5 were very stable at room temperature. In both cases, the enantioselective chromatography has proved to be a valid tool for evaluating of the activation energies involved in the interconversion of atropoisomers. Cryo-DHLC approach was employed for compounds 1-4 down to -63°C, while off-column HPLC experiments were required for compound 5. The values of the interconversion energy barriers were 16.8 Kcal/mol (at -48°C) for the faster interconverting atropoisomers and 31 Kcal/mol (at 130°C) in the syn/anti interconversion of compound 5. Experimental data were supported by theoretical DFT calculations at the B3LYP/6-31G(d) level.

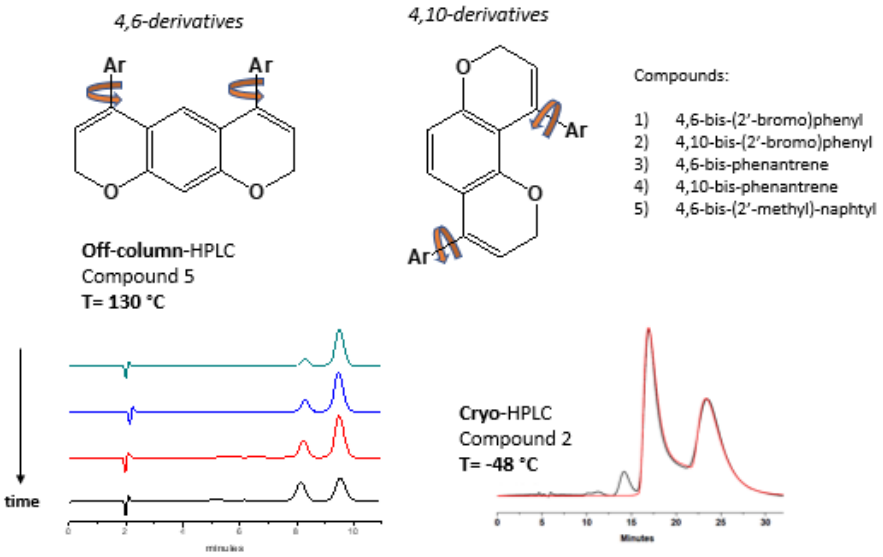

Figure 1: Investigated Compounds and chromatographic traces of diastereoisomers.

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Time Programmable Locking/Unlocking of the Calix[4]arene Scaffold by Means of Chemical Fuels

Emanuele Spatola,[a] Francesco Rispoli,[b] Daniele Del Giudice,[a] Roberta Cacciapaglia,[a] Alessandro Casnati,[b] Laura Baldini,[b], Gianfranco Ercolani,*[c] and Stefano Di Stefano*[a]*

[a] *Dipartimento di Chimica*
Università di Roma La Sapienza and ISB-CNR Sede Secondaria di Roma - Meccanismi di Reazione, P.le A. Moro 5, I-00185 Roma, Italy.
[b] *Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale Università degli Studi di Parma Parco Area delle Scienze 17/A, 43124 Parma, Italy.*
[c] *Dipartimento di Scienze e Tecnologie Chimiche Università di Roma Tor Vergata Via della Ricerca Scientifica, 00133 Roma, Italy.*

We report that the geometry of the calix[4]arene scaffold in its cone conformation can be controlled by means of chemical fuels such as 2-cyano-2-phenylpropanoic acid and its *p*-Cl, *p*-CH_3 and *p*-OCH_3 derivatives.[1] It is shown that, under the action of the fuel, the cone calix[4]arene platform assumes a "locked" shape such that two opposite aromatic rings strongly converge and the other two strongly diverge ("pinched cone" conformation). The calix[4]arene scaffold retains its "pinched cone" conformation as long as the fuel is present. Then, it can return to its original cone shape. Remarkably, the duration of the "locked" state can be controlled at will by varying the fuel structure or the amount added. Given the widespread use of the cone calix[4]arene unit as a structural platform in supramolecular architectures with different properties and functions, the fine control of the "pinched cone" / "cone" conformation equilibrium by means of chemical fuel may open the way to a large number of interesting applications.

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A new biopolymer architecture produced by *Rhizobium radiobacter* bacterium

Immacolata Speciale,[a] Flaviana Di Lorenzo,[b] Valentina Gargiulo,[b,c] Gitte Erbs,[d] Mari-Anne Newman,[e] Antonio Molinaro,[b] Cristina De Castro[a]

[a] Department of Agricultural Sciences, University of Napoli Federico II (Italy); [b] Department of Chemical Sciences, University of Napoli Federico II (Italy), [c] Institute for Research on Combustion (IRC), CNR (Italy), [d] Department of Health Technology, Technical University of Denmark (Denmark), [e] Department of Plant and Environmental Sciences, Faculty of Science, University of Copenhagen (Denmark)

The lipopolysaccharide (LPS) O-antigen structure produced by the plant pathogen *Rhizobium radiobacter* strain TT9 (previously recognized as *Agrobacterium tumefaciens* [1]) was investigated to evaluate its role a plant-microbe interaction. This analysis disclosed the presence of two LPSs with different O-antigens, named *Poly1* and *Poly2* [2].

Poly2 has a disaccharide repeating unit built up as follows [4)-α-L-rhamnose-(1→3)-α-D-fucose-(1→]$_n$. Interestingly, the less common fucose stereoisomer is present.

As for *Poly1*, the interpretation of the structure was quite complex and required the combined use of different approaches (chemical, spectroscopic and computational techniques) which revealed a new type of biopolymer composed of an alternation of a monosaccharide and an amino acid derivative. Its repeating unit, indeed, consists of the monosaccharide 4-amino-4-deoxy-3-O-methyl-D-fucose, and by the (2′*R*,3′*R*,4′*S*)-*N*-methyl-3′,4′-dihydroxy-3′-methyl-5′-oxoproline. Therefore, the polymer presents an alternation of glycosidic and amidic bonds, recognizing it as a new type of biopolymer that cannot be classified as either a polysaccharide or a protein.

Furthermore, the two O-antigens do not trigger the immune response in *Arabidopsis thaliana* facilitating the infectious process, contrary to what is expected from most plant pathogens [3], probably due to their atypical structures.

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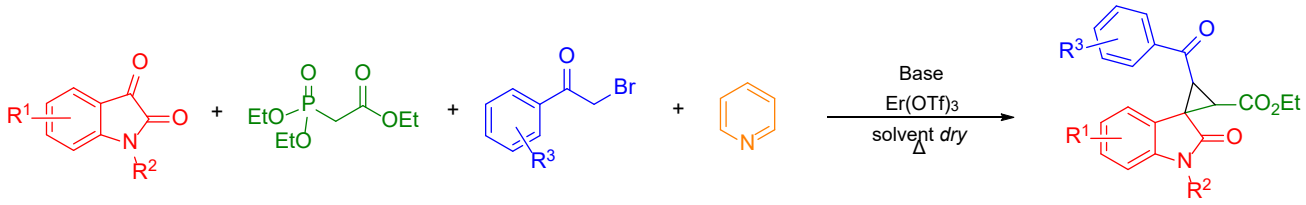
$Er(OTf)_3$-Catalyzed Multicomponent Synthesis of Spirocyclopropil Oxindoles as Potential MDM2 Protein Inhibitors

Matteo Antonio Tallarida,[a] *Vincenzo Algieri*,[a] *Fabrizio Olivito*,[a] *Antonio Jiritano*,[a] *Paola Costanzo*,[a] *Loredana Maiuolo*,[a] *Antonio De Nino*.[a]

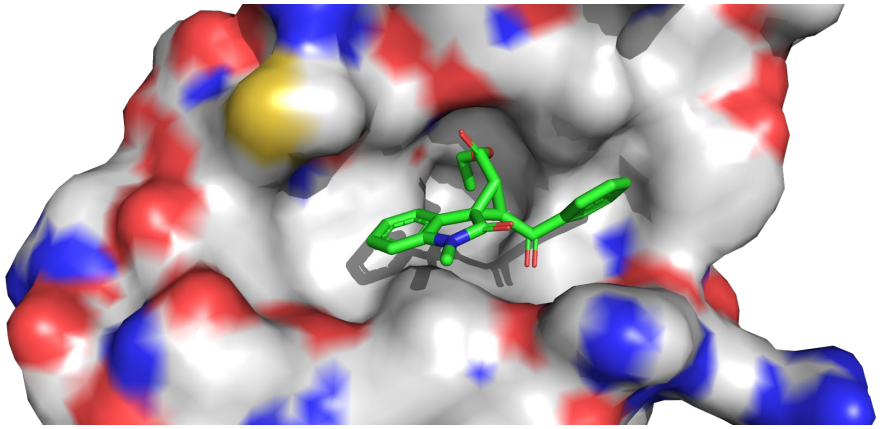
[a] *Dipartimento di Chimica e Tecnologie Chimiche-CTC, Università della Calabria, Ponte Bucci Cubo 12/C, 87036, Arcavacata di Rende (CS), IT, matteoa.tallarida@unical.it*

Spirooxindoles constitute a wide variety of compounds at the center of a vivid research interest worldwide. Such an interest is certainly related to their notable biological activities, [1] in particular as scaffolds useful in anticancer agents' development. [2] More thoroughly, spirocyclopropil oxindoles represent an emerging framework showing remarkable properties useful in medicinal chemistry too. [3] Even though numerous approaches for the multicomponental synthesis of spirooxindoles from isatin derivatives have been proposed, [4] strategies for a simple preparation of spirocyclopropil oxindoles are still lacking.

In this work, we will present the four-component synthesis of these substrates using $Er(OTf)_3$ as catalyst, starting from simple and easily accessible reagents.



Relying on the well-established potential of oxindole-containing spiro-derivatives as MDM2 protein inhibitors, [5,6] we will also illustrate a preliminary molecular docking screening performed on the hydrophobic cleft contained in the *N*-terminal domain of MDM2 protein. Inhibiting such a region would determine the disruption of the interaction of MDM2 with another protein residue, namely p53, allowing the development of new antitumoral drugs. [7]



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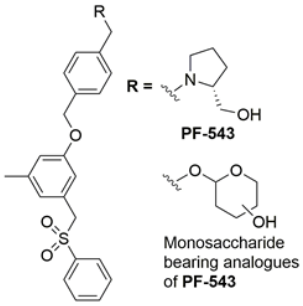
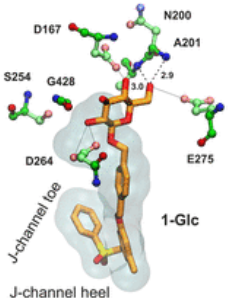
Exploiting monosaccharides in drug design: development of a new series of sphingosine kinase inhibitors

Tricomi J.,[1] Papakyriakou A.,[2] Cencetti F.,[3] Puliti E.,[3] Morelli L.,[4] Bruni P.,[3] Compostella F.,[4] Richichi B.[1]

[1]Department of Chemistry, University of Florence, Via della Lastruccia 13, 50019 Sesto Fiorentino (FI)
[2]Institute of Biosciences & Applications, NCSR "Demokritos" Athens, Greece
[3]Department of Experimental and Clinical Biomedical Sciences, University of Florence, V.le Morgagni 50, 50134 Firenze
[4]Department of Medical Biotechnology and Translational Medicine, University of Milan, Via Saldini 50, 20133 Milano

Sphingosine kinase 1 (SK1) is an enzyme localized in the cytosol, which catalyzes the production of sphingosine-1-phosphate (S1P) in an ATP-dependent manner. Solid experimental evidences implicate the S1P axis in different pathological conditions (*i.e.* cancer, inflammatory diseases, fibrosis) and aberrant S1P levels and/or SKs expression have been associated with diseases progression.[1] In this regards, different compounds have been studied aimed at the modulation of the S1P axis, either through inhibition of SK activity or by inhibition of S1P receptors signaling.[2] A wide number of SK1 inhibitors have been developed so far; however, the main issues are related to their low potency and/or specificity among SK subtypes.
In this framework, this communication describes our original approach for the rational design of SK1 inhibitors. It relies on the integration of the information coming from the SK1-co-crystal structure of known validated inhibitors into pharmacophoric models.[3] In doing so, we exploited monosaccharide residues to enhance the anchoring of the known SK1 inhibitor PF-543 at the polar head of the J-shaped substrate-binding channel [4] of SK1 (Fig. 1). Therefore, we describe the rational design and the synthesis of a series of monosaccharide-bearing PF-543 analogues. Biological data, obtained in an *in vitro* model of skeletal muscle fibrosis, supported our rationale. Indeed, our findings, obtained in TGFβ-induced fibrosis of murine myoblasts, indicate that the glucose bearing analogue inhibits SK1 enzymatic activity leading to a reduced expression of a fibrosis marker.





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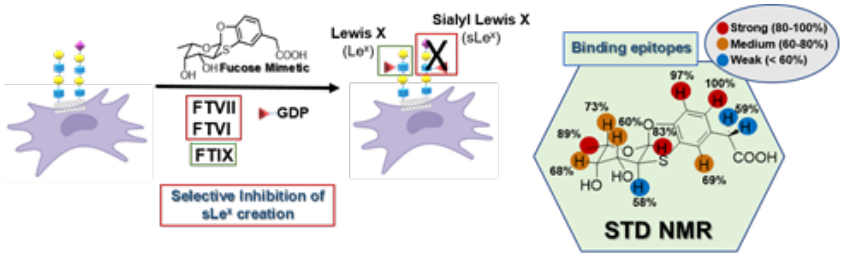
We thank COST Action CA18103 INNOGLY: INNOvation with GLYcans: new frontiers from synthesis to new biological targets.

Custom-site Modification of Cell Surface Fucosylation *via* Next Generation Fucosyltransferase Inhibitors.

Tricomi J.,[1] *Martin K. C.*,[2,3,4] *Corzana F.*,[5] *García-García A.*,[6] *Ceballos-Laita L.*,[7] *Hicks, T.*[7] *Monaco S.*,[7] *Angulo J.*,[7,8,9] *Hurtado-Guerrero R.*,[6,10,11] *Sackstein R.*,[2,3,4] *Richichi B.*[1]

[1]*Dep. of Chemistry 'Ugo Schiff', University of Florence, Sesto Fiorentino (FI), Italy.*
[2]*Dep. of Translational Medicine, and Translational Glycobiology Institute, Herbert Wertheim College of Medicine, Florida International University, Miami, FL 33199.*
[3]*Dep.of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115.*
[4] *Program of Excellence in Glycosciences, Harvard Medical School, Boston, MA 02115.*
[5] *Dep. de Química, Universidad de La Rioja, Centro de Investigación en Síntesis Química, 26006 Logroño, Spain.*
[6] *Institute of Biocomputation and Physics of Complex Systems (BIFI), University of Zaragoza, Zaragoza, Spain; Fundación ARAID, Zaragoza, Spain.*
[7] *School of Pharmacy, University of East Anglia, Norwich Research Park, NR47TJ, Norwich, UK.*
[8] *Dep. de Química Orgánica, Universidad de Sevilla, C/ Prof. García González, 1, 41012 Sevilla, Spain.*
[9] *Instituto de Investigaciones Químicas (CSIC-US), Avda. Américo Vespucio, 49, 41092 Sevilla, Spain.*
[10] *Copenhagen Center for Glycomics, Department of Cellular and Molecular Medicine, School of Dentistry, University of Copenhagen, Copenhagen, Denmark.*
[11] *Laboratorio de Microscopías Avanzada (LMA), University of Zaragoza, Zaragoza, Spain.*

Today, glycomimetics are emerging within the drug development market. These molecules possess vast therapeutic potential, and by proper modulation of their structure, researchers can overcome the inherent limits of native carbohydrates allowing to produce molecules with enhanced selectivity, potency, improved pharmacokinetic properties and locked conformations.[1] With this in mind, the possibility to custom modify cell surface glycosylation using non-toxic glycomimetics that prevent the action of glycosyltransferases holds great promise for treatment in a great variety of diseases, such as autoimmune disorders, inflammation, and cancer. Critically, such inhibitors should be selective and target only the desired glycosyltransferase, while leaving other glycosyltransferases untouched, thereby yielding the construction of only requisite glycan products.[2]



To this end, we specifically repurposed a fucose glycomimetic[2] that was previously used to block lectin binding in bacteria.[3] In so doing, we identified the next generation of selective fucosyltransferase (FT) inhibitors. This mimetic of fucose selectively and markedly interferes with the creation, of sialyl Lewis X (sLe^x) by FTVI and FTVII, but had no effect on the catalytic activity of FTIX, the α-1,3-FT that principally mediates Le^X synthesis.[4] Surprisingly, our findings indicate that our fucose mimetic and the natural donor substrate (GDP-fucose) does not compete for the same enzymatic binding site,[2] highlighting the need for further investigations and a deeper understanding of the catalytic activity of these enzymes and the inhibition mediated by the mimetic.

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We thank COST Action CA18103 INNOGLY: INNOvation with GLYcans: new frontiers from synthesis to new biological targets.
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An investigation on the KuQuinone redox species: an electrochemical and computational cross study

Francesca Valentini,[a,b] *Federica Sabuzi*,[a] *Valeria Conte*,[a] *Victor N. Nemykin*,[b,c] *Pierluca Galloni*.[a]

[a] *Department of Chemical Science and Technologies, University of Rome Tor Vergata, Rome 00133, Italy*
[b] *Department of Chemistry, University of Manitoba, Winnipeg, Manitoba R3T 2N2, Canada*
[c] *Department of Chemistry, University of Tennessee, Knoxville, Tennessee 37996, United States*

The study of the electrochemical properties of quinones is a fascinating topic in chemistry. In fact, redox reactions occurring with quinoid scaffolds are essential for most of their applications in biological systems,[1] in CO_2 reduction devices,[2] and in many other fields.[3] In this contribution, a detailed investigation of KuQuinones' (KuQ) (Figure 1 left) redox behavior will be presented.[4] The distinctiveness of such molecules is the presence in the structure of two condensed naphthoquinone units, which implies the possibility to undergo multiple one-electron reduction processes. Solvent, supporting electrolyte, and hydrogen bond donor species effects on the KuQ's electrochemical profile will be elucidated. In particular, additions of 2,2,2-trifluoroethanol as a hydrogen bond donor in solution lead to important shifts of the redox potentials toward more favorable values. DFT calculations will be also presented to clarify the nature of such hydrogen-bonded complexes. UV−vis−NIR spectroelectrochemical experiments were performed to investigate KuQ's reduced species in solution. Additionally, the effect of Lewis acid coordination on the KuQuinone electrochemical and spectroelectrochemical behavior will be also presented.

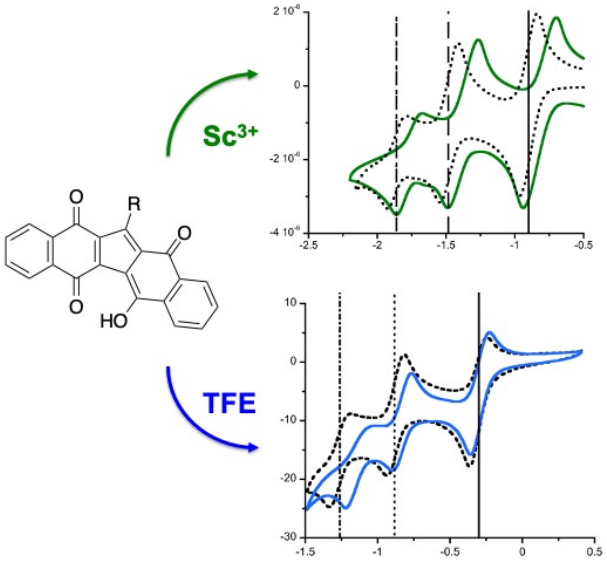

Figure 1. KuQuinone general structure (left). KuQuinone electrochemical profile in the presence of 2,2,2-trifluoroethanol (TFE) and Lewis Acid (Sc^{3+}) (right).

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Characterization of glycans isolated from *Methylobacterium extorquens PA1*

Adele Vanacore[a], Alba Silipo[a]*

*[a]Dipartimento di Scienze Chimiche, Complesso Universitario Monte Sant'Angelo, Università di Napoli Federico II, Via Cintia 4, I-80126 Napoli, Italy. *E-mail: adele.vanacore@unina.it; Tel.: +393408434005.*

The genus *Methylobacterium* is composed of pink-pigmented facultative methylotrophic (PPFM) bacteria, which are able to synthesize carotenoids and grow on reduced organic compounds containing one carbon (C1), such as methanol and methylamine [1]. *Methylobacterium* strains are commonly found in soil, dust, freshwater, sediments, and in the air [2]. Moreover, they are consistently found in association with plants, in particular as epiphytic and endophytic leaf colonizers, but also in association with plant roots [3].
Most plants, due to the demethylation of pectin, emit methanol through the stomata, especially during the early stages of leaf expansion. *Methylobacterium extorquens* can take advantage of its ability to use methanol as a source of carbon and energy, and at the same time, methylotrophy gives it a selective advantage over the colonization of the phyllosphere [4].
In recent years, a number of research projects have been launched with the aim of deepening knowledge on the mechanisms for regulating either methylotrophic pathways and genes involved. Despite the above, most, if not all, the studies on *Methylobacterium* membrane are focused on the lipid components, while there is little information on structure and function of glycoconjugates constituting *Methylobacterium* cell envelope . Therefore, we chose to characterize the structure of lipoplysaccharide (LPS) and capsular polysaccharides (CPS) isolated from *Methylobacterium extorquens* strain PA1. A combination of compositional analysis, spectrometric and spectroscopic (MS and NMR) and biophysical (DLS)investigations allowed to determine the complete structure of Methylobacterium LPS and CPS, and also to evaluate their role in the bacterial membrane. Furthermore, the structure and function of the capsular polysaccharides produced by *Methylobacterium extorquens* when grown in presence of methanol was also determine.
The characterization of these envelope glycans is certainly the first step in understanding their function, particularly with regard to the mechanism of interaction with the external environment.

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Effect of fluorination on the thermal stability of azide-tagged aminoacids

Eleonora Veronese[a], *Giancarlo Terraneo*[a], *Andrea Pizzi*[a], *Maria Isabel Martinez Espinoza*[a], *Pierangelo Metrangolo*[a]

[a] *Laboratory of Supramolecular and Bio-Nanomaterials (SupraBioNanoLab), Department of Chemistry, Materials, and Chemical Engineering "Giulio Natta", Politecnico di Milano, Via Luigi Mancinelli 7, 20131 Milan (Italy).*

The azide moiety is a widely used and versatile chemical probe with unique properties. In the field of protein and peptide chemistry, for instance, this highly reactive functional group gives the possibility to introduce structural modifications, *i.e.*, a triazole ring *via* Huisgen 1,3-dipolar cycloaddition, obtaining modified and constrained peptides and proteins, which in recent years are gaining increasing attention for biomedical purposes. In addition, azido-compounds look particularly interesting for their ability in photoaffinity labelling. Moreover, due to the polarizability of the N_3 group, they opened up new applications as probes for FT-IR and Raman spectroscopy. An intense and clear vibrational signal in these analyses unlocks a plethora of applications wherein the N_3 group acts as a biotag for different types of molecules.

For all the reasons mentioned above, it is of primary importance to obtain azido-modified amino acids, in order to include them in biocompatible systems and exploit all the previously cited properties. On the other hand, azides are known for their explosive behavior, which make them difficult to handle. [1]

Here, we present an effective strategy to overcome this limit and to obtain a safer azido-scaffold. Starting from a tetrafluoro-phenylalanine, we introduced the azide group at the *para* position of the aromatic ring, obtaining *N*-Boc-(4-azido-2,3,5,6-tetrafluoro)-L-phenylalanine tert-butyl ester (*Figure 1, left*). From thermal stability studies and single crystal X-ray structure, we were able to demonstrate that the presence of fluorine atoms is useful for the stabilization of the azide moiety *via* a pnictogen bond (*Figure 1, right*). Furthermore, fluorination enhances the potentiality of this new molecule, making it responsive also to ^{19}F-NMR. Finally, these organic azides could be useful also as reactive intermediates for the introduction of different chemical functionalities, enabling us to synthesize a series of *para*-substituted tetrafluorophenylalanines.[2]

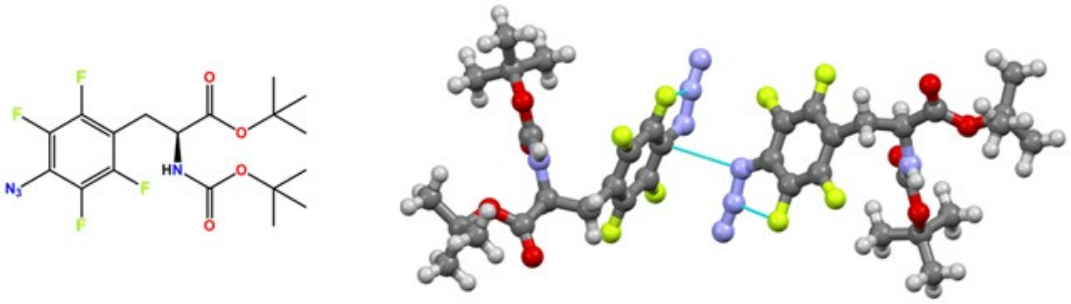

Figure 1: Chemical structure (left) and single crystal X-ray structure (right) of N-Boc-(4-azido-2,3,5,6-tetrafluoro)-L-phenylalanine tert-butyl ester. Colour code: C, grey; O, red; N, violet; F, yellow; H, white.

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A Structure-Activity Investigation on Modified Analogues of an Argininocalixarene Based Non-viral Gene Vector

Carlo Alberto Vezzoni,[a] Michela Lomazzi,[a] Valentina Franceschi,[b] Valentina Bagnacani,[a] Gaetano Donofrio,[b] Alessandro Casnati,[a] and Francesco Sansone[a]

[a] Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parco Area delle Scienze 17/A, Parma; [b] Department of Veterinary Science, University of Parma, Via del Taglio 6, Parma

The possibility of treating diseases thanks to the use of Gene Therapy[1] represents an exceptional perspective that could bring to the systematic defeat of both severe hereditary and acquired pathologies related to alterations and disorders at level of the cell genetic inheritance. The delivery of Nucleic Acids into the cells is a key point of this technique. We have already shown the extraordinary abilities of tetra-L-arginino-tetrahexyloxycalix[4]arene (Figure 1, left) to compact and internalize different type of Nucleid Acid cargos (DNA,[2] microRNA,[3] PNA[4]) into cells even known to be transfected with great difficulties by commercial non-viral gene delivery systems. This activity, accompanied by negligible toxicity, makes this calixarene a rather promising prototype of vector for Gene Therapy.

We have studied, recently, how small structural changes like: i) the nature of the lower rim substituents, ii) the type of the terminal cationic headgroups (guanidinium or primary ammonium), iii) the length of the linker between the macrocycle and the terminal cationic headgroup, iv) the presence/absence of the basic α-amino group of Arg, and v) the stereochemistry (L or D) of Arg, can affect the ability of the calixarene vectors to compact DNA and to deliver its cargo into the cells.

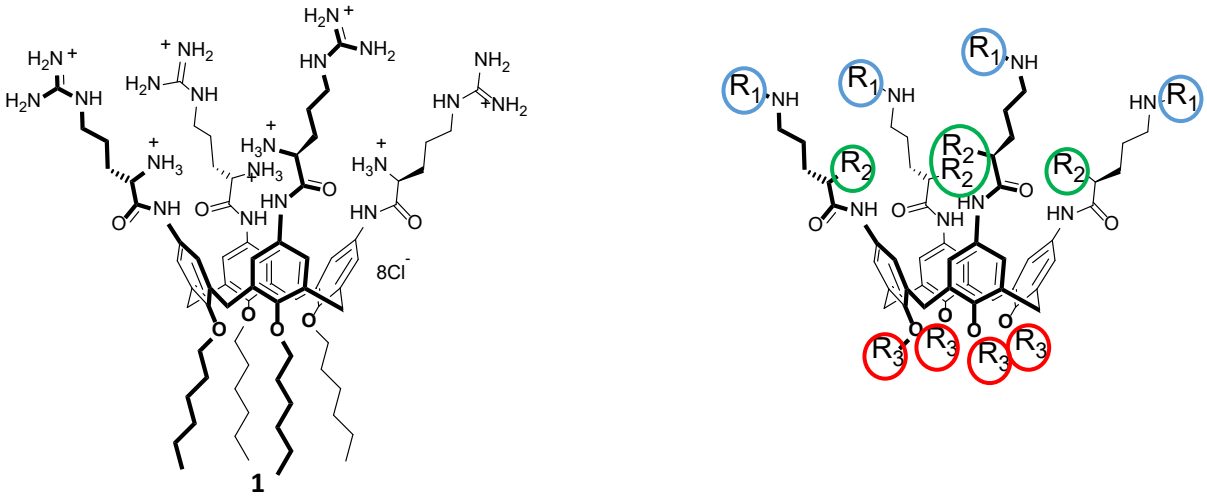

Figure 1: On the left, the tetra-L-arginino-tetrahexyloxycalix[4]arene; On the right side, a generalized calix[4]arene **1** structure, the circled R_1, R_2, R_3 groups show in which region of the molecule we decided to introduce the modifications mentioned above.

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"Sticky Diatoms": A Multi-Purpose Platform for in vivo diatom functionalization

Cesar Vicente-Garcia[a]; *Danilo Vona*[a]; *Stefania R. Cicco*[b]; *Roberta Ragni*[a]; *Gianluca Maria Farinola**[a].

[a] *Dipartimento di Chimica, Università degli Studi di Bari Aldo Moro;* [b] *CNR-ICCOM-Bari.*

Diatom microalgae are known for generating highly nanostructured biosilica shells (frustules) by *in vivo* mineralization of orthosilicic acid, rendering extraordinarily intricate pore patterns. These shells exhibit not only high surface area, but also a photonic structure, suitable for applications in photonics and optoelectronics [1]. Covalent and non-covalent approaches for the anchorage of functional elements (drugs, dyes, antibodies, metals) have already been described [2,3], with the purpose of fabricating hybrid nanostructures for applications that range from biosensing [4] to solar energy conversion [5]. The purpose of this project is to develop a versatile method for obtaining chemically "sticky" diatoms, that are susceptible to bind a plethora of useful chemical compounds, nanoparticles, macromolecules, or surfaces. This can be seen as a useful alternative to the covalent and non-covalent methodology for engineering more complex biosilica-based structures with multi-purpose functionalization. The strategy involves an *in vivo* chemical modification of diatoms with an organic silane bearing an acrylic moiety (MAPTMS), which can be easily polymerized (either while the algae are growing or after protoplasm removal), leading to a transparent and stable coating of the biosilica shells. The grafting of a specific functional compound (dye, enzyme, nanoparticle, etc.) onto the diatom's shell proceeds either by supramolecular encapsulation in the "sticky" polymer network or by covalent binding using the chemical reactivity of the acrylic functionality. In addition, thin films of the obtained biohybrid materials will be assembled onto activated surfaces for nanotechnological applications. FTIR-ATR, Raman spectroscopy and electronic microscopy characterization, together with the covalent binding of Fluorescein-O-methacrylate specifically to treated samples, supports the successful embedding of the MAPTMS into the biosilica shell and subsequent polymerization. This approach opens the way to complex and multifunctional biohybrid materials starting from our expertise to functionalize living diatom cells and exploiting the "sticky" nature of an organic polymer. Moreover, this system could also allow simultaneous poly-functionalization with different compounds, surpassing the previously reported, narrower functionalization strategies.

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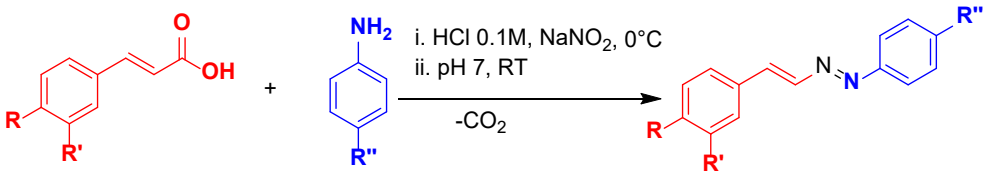
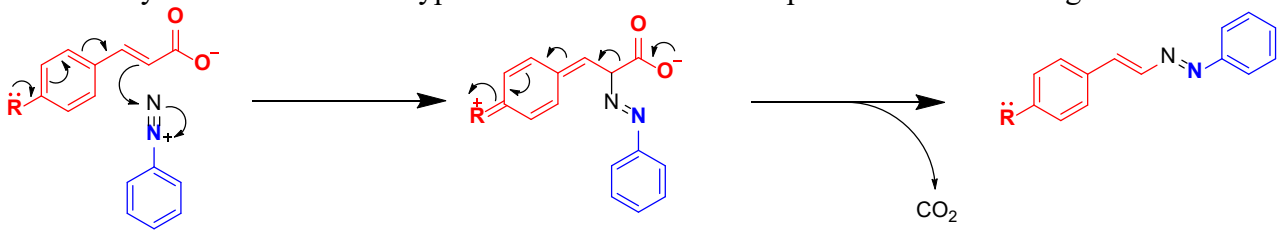
Synthesis of 1,2-diaza-1,3-dienes from cinnamic acids mediated by diazonium salts

Vida, V.[a]; Forzato, C.[a]; Berti, F.[a]

[a] *Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Trieste*



The aim of the present work is the study of the formation of 1,2-diaza-1,3-dienes from substituted cinnamic acids and anilines. Besides being known for their biological activity, cinnamic acids have aroused interest from the synthetic point of view due to the different reactions in which they can be involved, thanks to the presence of the carboxylic group and the polarized alkenyl moiety. [1] The reactivity of cinnamic acids with diazonium salts from anilines has been previously reported in Meerwein arylation reactions, leading to the formation of the corresponding stilbenes by loss of nitrogen and carbon dioxide molecules. [2][3] However, studying the reactivity of phenolic compounds in diazo-coupling reactions, the unexpected formation of diazadiene compounds by loss of CO_2 only was observed: the hypothesized mechanism is reported in the following scheme.



This communication reports the results from a screening on different cinnamic acids and anilines, to understand in which cases this unexpected reactivity takes place. It was possible to observe that the presence of different electron-donating groups -for example hydroxyl or dimethylamino groups- in *para* position with respect to the conjugated double bond of the cinnamic acid, leads to the formation of diazadienes, instead of the more conventional diazo-coupling products. The reaction happens in aqueous solution, rapidly and in very mild conditions, without any catalyst, and the products can be usually isolated easily in high yields. Formation of the desired diazadiene compounds has been confirmed by ^{1}H- and ^{13}C-NMR spectroscopy and mass spectrometry.

Thanks to the extended conjugation, these compounds have very intense colors, ranging from deep purple and red, to bright orange, and this property is currently being studied for sensory applications. The reactivity of the 1,2-diaza-1,3-diene products, which is already extensively reported in literature, [4] is being tested to analyze further possible synthetic applications.

Preliminary results for the evaluation of the biological activity of such compounds is currently under investigation, in order to determine their toxicity, antimicrobic and antitumor activity.

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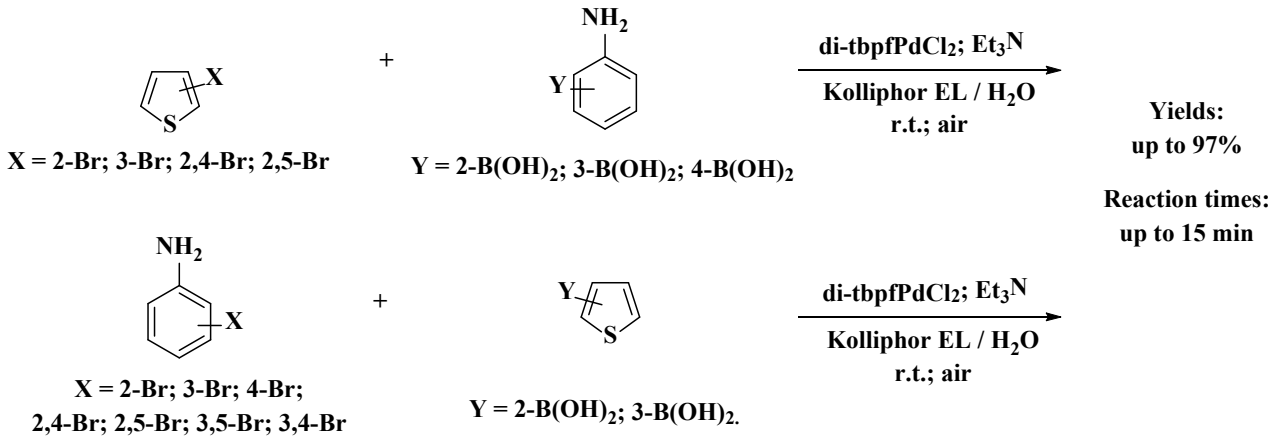
Micellar Suzuki cross-coupling between thiophene and aniline in water and under air

Dawod Salim Yousif, Silvia Tombolato, Elmehdi Ould Maina, Riccardo Po, Antonio Papagni and Luca Vaghi*

[a] *Department of Materials Science, University of Milano-Bicocca, Via Cozzi 55, 20125 Milano, Italy;* [b] *Eni Renewable Energy, Magnetic Fusion and Material Science Research Center, Eni SpA, Via Fauser 4, 28100 Novara, Italy*

The Suzuki Miyaura cross-coupling reaction plays a fundamental role in modern synthetic organic chemistry, both in academia and industry. For this reason, the search for new more effective, cheap, and environmentally compliant procedures has never stopped. Recently, micellar synthetic chemistry demonstrated to be an excellent strategy to obtain chemical transformations more efficiently, thanks to the creation of nanoreactors in aqueous environments using selected surfactants.[1,2] In particular, the cheap and commercially available surfactant Kolliphor EL has been used with success to achieve metal-catalyzed transformation in high yields and short reaction time, with the plus of using air-sensitive catalysts without the need of inert atmosphere.[3,4]



Scheme 1

In this context, Kolliphor EL methodology was applied to the Suzuki cross-coupling between thiophene and aniline, using the highly effective catalyst di-tbpfPdCl$_2$.[5] Both the reactions of 2- and 3-bromothiophene with *o*-, *m*- and *p*-aniline boronic acids, and *o*-, *m*- and *p*-bromoaniline with 2- and 3- thiophene boronic acids were tested as well as 2,4-, 2,5- and 3,5-dibromoaniline (Scheme 1). The cross-coupling products were obtained in high yields and reaction times up to 15 minutes, working at room temperature and without the need for an inert atmosphere.

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Efficient solid phase polypeptide synthesis in acetonitrile with a mesoporous polydivinylbenzene support.

Barbara Biondi[a], Daniele Trovò[b], Riccardo Leder[b], Paolo Centomo[b], Marco Zecca[b], Karel Jeřábek[c]

[a] ICB, Sede Secondaria di Padova, CNR - Dipartimento di Scienze Chimiche, Università di Padova, via Marzolo 1-I35131 Padova (Italy); [b] Dipartimento di Scienze Chimiche, Università di Padova, via Marzolo 1-I35131 Padova (Italy); [c] Institute of Chemical Process FundamentalsCZ-165 02 Prague, Czech Republic

Mesoporous polydivinylbenzenes (MPDVB) can be readily obtained by inducing microsyneretic pore formation during the homopolymerization of divinylbenzene[1]. In the expanded, pseudo-swollen state, they exhibit quite unusual textural properties, virtually independent on nature of the surrounding solvent. They offer very large surface area in mesopores which are as wide as tens of nanometers in absence of micropores (Table 1). All these features are compatible with a "mesofoam" texture, which is particularly promising for solid phase chemical applications, such as the peptide synthesis.

Table 1

Polymer	Pore volume ($cm^3.g^{-1}$)	Mean pore diameter (nm)	Surface area ($m^2.g^{-1}$)
MDVB	5.2	30	1060
MDVB-W	2.2	27	770

The chloromethylation and the subsequent transformation of MPDVB into a Wang-support for SPPS (MPDVB-W) are straightforward. MPDVB-W has somewhat smaller pore volume and lower specific surface area than parent MPDVB, but still it was possible to replace N,N-dimethylformamide with acetonitrile and to produce, under non optimized conditions, Fmoc-Leu-Leu-Val-Phe-OH and ACP-(65-74) with practically the same yield in high to very high purity (Table 2)[2]. More importantly, MPDVB-W clearly outperformed in the synthesis of ACP-(65-74) the Wang forms of gel-type polystyrene and ChemMatrix resins both in DMF and ACN.

Table 2

Support	Peptide	DMF		ACN	
		Yield (%)	Purity (%)	Yield (%)	Purity (%)
MPDVB-W	Fmoc-Leu-Leu-Val-Phe-OH	30	93	24	98
	ACP-(65-74)	43	88	22	80
PS-W	Fmoc-Leu-Leu-Val-Phe-OH	88	95	0	nd
	ACP-(65-74)	nd	very low	-	-
ChemMatrix-W	ACP-(65-74)	8	78	-	-

In conclusion, MPDVB is apparently a promising starting material for the preparation of supports which could allow at relativaly low costs the replacement of N,N-dimethylformamide with greener solvents for SPPS.

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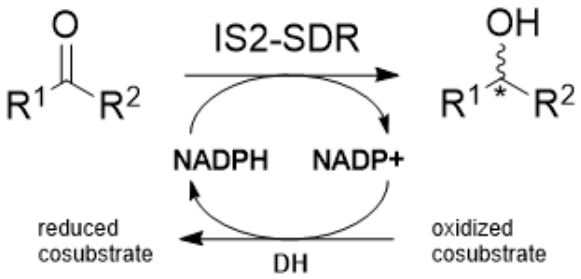
Biocatalytic asymmetric synthesis of highly diverse chiral alcohols via a promiscuous ketoreductase

S. Bertuletti,[a,b] E. Miraglia,[a,b] E. E. Ferrandi,[a] I. Bassanini,[a] D. Monti,[a] S. Riva.[a]

[a] *SCITEC-CNR (Istituto di Scienze e Tecnologie Chimiche "Giulio Natta"), Via M. Bianco 9, Milan, Italy*
[b] *University of Milan, Via Mangiagalli 25, Milan, Italy*

Short-chain dehydrogenases (SDRs) are a large superfamily of enzymes that belong to the class of oxidoreductases, mostly known to be NAD(H)- or NADP(H)-dependent. SDRs show a low sequence similarity (few residues are conserved), but a high three-dimensional structural similarity. A relevant example of SDRs is given by hydroxysteroid dehydrogenases (HSDHs), enzymes able to regio- and stereoselectively transform steroidal compounds.[1]

The search of novel thermostable HSDHs via (meta)genome mining has brought us to the discovery and isolation of a novel enzyme (named Is2-SDR) from an Icelandic metagenome, which shared a high sequence similarity with HSDHs, but it turned out to be inactive on steroidic substrates.
Despite that, Is2-SDR manifested to be a very versatile ketoreductase, being able to regio- and stereoselectively reduce a diversified panel of carbonylic substrates, that encompasses bulky and cyclic ketones, α- and β-ketoesters, and α-diketones of pharmaceutical relevance.[2,3]



Furthermore, kinetic studies and circular dichroism analyses of this enzyme have proven that it is extremely thermostable (it does not unfold up to 90°C) and highly compatible with a panel of organic solvents, either miscible or immiscible with water. These characteristics make it a promising asymmetric biocatalyst for synthetic applications.

Considering the promising nature of Is2-SDR, and due to the high synthetic interest of obtaining chiral alcohols in a highly enantiomerically enriched form, studies on the performances of free and immobilized Is2-SDR on Eupergit C are in progress, to lead its use from batch synthesis to in-flow asymmetric reduction of carbonylic substrates.

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Graphene-mediated electrical stimulation for the Selective triggering of Astrocyte Calcium signaling

R. Fabbri[a], A. Scidà[a], A. Kovtun[a], E. Saracino[a], A. Candini[a], D. Spennato[a], R. Zamboni[a],

M. Melucci[a], E. Treossi[a], V. Palermo[a], V. Benfenati[a]

[a] *Istituto per la Sintesi Organica e la Fotoreattività, Consiglio Nazionale delle Ricerche, via Gobetti 101, 40129 Bologna, Italy*

Among two dimensional (2D) nanomaterials, Graphene has been widely explored as bio-organic material interface in recent years. Due to their advantageous combination of biocompatibility, electrical conductivity, mechanical and optical properties, Graphene nanosheets are being successfully exploited to optimize the interface between implant devices and neurons. Newly, in vitro studies have shown the positive impact of Graphene nanoflakes and chemically functionalized Graphene-Oxide (GO) substrates on the viability and functional properties of brain glial cells, called astrocytes. Emerging evidence indicates the crucial role of astrocytes in the physiology and pathophysiology of the central nervous system. Besides providing structural support to neurons, astrocytes are critically involved in the control of brain homeostasis and modulation of synaptic transmission, as well as in the inflammatory reaction to device or electrode implantation. The investigation of biophysical mechanisms underlying the interaction between astrocytes and biomaterials, such as variation in intracellular calcium concentrations ($[Ca^{2+}]_i$), is essential to define new tools and technologies enabling the selective manipulation of diverse brain signaling pathways. In the present work, we exploited different properties of Graphene-based devices to study the effect of extracellular electrical stimulation on the astrocyte $[Ca^{2+}]_i$ signaling. We performed Fluo-4 calcium imaging experiments on primary rat cortical astrocytes grown on indium tin oxide coated with GO (ITO-GO) devices. Astrocytes were also plated on bare ITO and ITO coated with reduced Graphene Oxide (ITO-rGO) substrates. Unprecedentedly, our results suggest that electrical stimulation applied by different Graphene-based devices triggers diverse astrocyte $[Ca^{2+}]_i$ responses depending on the device used to deliver the stimulation. Astrocytes cultured on insulating GO display slow $[Ca^{2+}]_i$ transients, typically mediated by extracellular Ca^{2+} influx, while astrocytes on conductive ITO and rGO exhibit rapid oscillatory $[Ca^{2+}]_i$ dynamics, possibly mediated by Ca^{2+} release from the cytoplasmic stores. The potential of using GO and rGO devices to generate novel organic glial interfaces aiming at the selective modulation of astrocyte molecular pathways can be useful for uncovering the role of glial cells in neuronal circuits, in the study and treatment of neurological disorders, such as epilepsy, brain tumours, Alzheimer and Parkinson diseases.

Supported by AFOSR-3D Neuroglia, ASTROMAT; EU-GRAPHENE FLAGHIP

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Società Chimica Italiana | SCI2021

CHIMICA DEI SISTEMI BIOLOGICI (CSB)

- Orals
- Posters

Computational Microscopy of SARS-CoV-2

Rommie Amaro

Department of Chemistry and Biochemistry, University of California San Diego, La Jolla, CA 92093, USA; e-mail: ramaro@ucsd.edu

I will discuss our lab's efforts, together with collaborators, to use computational microscopy to understand the SARS-CoV-2 virus in atomic detail, with the goals to better understand molecular recognition of the virus and host cell receptors, antibody binding and design, and the search for novel therapeutics. I will focus on our studies of the spike protein, its glycan shield, its interactions with the human ACE2 receptor, our ACM Gordon Bell Special Prize winning efforts to model the SARS-CoV-2 virion, and escape variants.

Bioinorganic chemistry of ferritin nanocages

Paola Turano

CERM and Department of Chemistry, University of Florence

In Nature, 24-mer ferritins are important players in iron homeostasis. They concentrate iron inside their 8 nm inner cavity through pathways determined by electric gradient guidance and assist caged iron mineral formation via catalytic oxidation at ferroxidase centers (H-type subunits in mammalian ferritins) and biomineral growth at inner surface nucleation sites (L-type subunits in mammalian ferritins).
The ferritin nanocage is exploited for targeted drug-delivery. Tumor targeting of H human ferritin is mediated by the transferrin receptor-1; the stability of ferritin allows us to genetically or chemically modify the external surface to impart new functionalities, including targeting of alternative cell surface receptors. In terms of cargo molecules, two different strategies can be adopted. Classical metal-based drugs can freely diffuse through ferritin ion channels and efficiently bind at several protein sites. Larger chemical entities can be encapsulated via *in vitro* disassembly/reassembly procedures.
The data here presented are the results of several collaborations, as it emerges from some key references reported below.

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Stabilization of Protein-Protein Interactions: from the fundamentals of cooperativity to applications in drug discovery

Luc Brunsveld

Laboratory of Chemical Biology, Department of Biomedical Engineering and Institute for Complex Molecular Systems (ICMS), Eindhoven University of Technology, P.O. Box 513, 5600 MB Eindhoven, The Netherlands; e-mail: l.brunsveld@tue.nl

Our group combines organic synthesis, protein chemistry, structural biology, and supramolecular chemistry to perform chemical biology studies on protein-protein interactions (PPIs) with the aim to enable innovative medicinal chemistry for 'molecular glues' for PPIs. In this presentation I aim to show that a chemical biology approach to protein-protein interactions (PPIs) helps to unravel the underlying, more complex, interaction mechanisms. This conceptual approach to PPIs allows to recognize and apply concepts such as multivalency and cooperativity within the context of drug discovery. Using nuclear receptors and 14-3-3 proteins as examples, this presentation aims to provide insights into questions such as 1) How can chemical biology studies steer medicinal chemistry for PPIs? 2) What are the key biophysical characteristics of molecules that stabilize PPIs? 3) How can we find chemical starting point for PPI stabilization?

Research and development of sustainable botanicals in health care, food and personal care sectors

Elena Sgaravatti

Founder&Ceo of PlantaRei Biotech S.r.l., via AOSTA, 1, 35142, Padova, Italy; e-mail: elenasgaravatti@plantareibiotech.it

The world population is expected to reach 8.5 billion by 2030, 9.7 billion by 2050, and more than 11 billion by 2100 [1]. In order to meet the food needs of the world's growing population, crop production systems should be improved. Over the past ten years, the availability of agricultural land has been declining. Therefore, as the global population continues to increase and land supply is restricted, the task of ensuring food and nutrition security and food safety has become really challenging.
Intensive use of ecosystems to increase productivity will affect agricultural ecosystems through soil erosion, water pollution, water depletion, and loss of biodiversity, which will have an impact on plant health and plant biosafety.
According to the Food and Agriculture Organization of the United Nations, pests destroy up to 40% of the world's food crops, causing US$220 billion in trade losses each year.
Furthermore, the awareness of the usefulness of a diet rich in polyphenols and therefore the use of botanicals is constantly increasing. It is therefore urgent and critical on the one hand the adoption of innovative cultivation techniques - as plant cell culture, vertical farming etc., that allow the production of safe botanicals with the maximum saving of resources such as water, soil and solvents and on the other hand the reuse and skillful enhancement of food byproduct within a production chain as circular as possible.

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Gold-templated reactions in biological systems: from medicine to catalysis

Angela Casini

Chair of Medicinal and Bioinorganic Chemistry, Department of Chemistry, Technical University of Munich, Lichtenbergstr. 4, 85747 Garching, Germany; e-mail: angela.casini@tum.de

One of the challenges of modern inorganic chemistry is translating the potential of metal catalysts to living systems to achieve controlled non-natural transformations. To this aim, transition metal catalysts offer an opportunity of modulating bio-processes through reactions that are complementary to enzymes. In this context, gold complexes, both coordination and organometallics, have emerged as promising tools for bio-orthogonal transformations, endowed with excellent reactivity and selectivity, compatibility within aqueous reaction medium, fast kinetics of ligand exchange reactions and mild reaction conditions [1].

This lecture will summarize recent findings from our group on Au(III)-catalyzed reductive elimination in aqueous media, providing the proof-of-concept for the use of organogold compounds – cyclometalated Au(III) C^N complexes - for the efficient modification of proteins through C-atom transfer, enabling chemoproteomic studies (e.g. profiling of cysteine residues). Furthermore, the obtained mechanistic insights have allowed to extend the cross-coupling concept to other substrates, to enable C–P (Figure 1) and C–C bond formation under mild conditions [2-3].

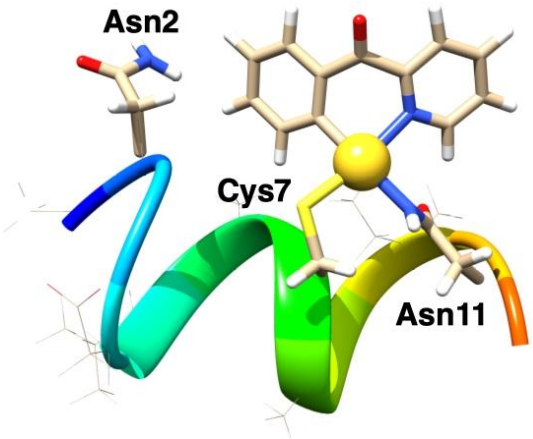

Figure 1. Cyclometalated Au(III) C^N complex adduct with model peptides templating Caryl–S cross-coupling.

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Fragment-based drug design

Amedeo Caflisch

Department of Biochemistry, University of Zurich

We have developed a program for the docking of libraries of fragments (molecules with a molecular weight smaller than 300 g/mol) that makes use of a force field energy-evaluation with an implicit model of the solvent [1]. By means of high-throughput docking we have identified small-molecule inhibitors of six human bromodomains, protein modules that bind acetylated histone tails. In the case of the CREBBP bromodomain, optimization of the initial hits by chemical synthesis of derivatives has resulted in several low-nanomolar binders with favorable ligand efficiency and high selectivity against other bromodomains [2]. Thus, the screening of fragment libraries by docking is very efficient (24,000 molecules in a day on a commodity desktop) and the hit rate, i.e., number of active molecules among the purchased compounds, is very high (typically 10% to 30%). We have validated the predicted binding modes by solving the crystal structure of about 150 bromodomain/ligand complexes. Two lead compounds for the CREBBP bromodomain and the Ephrin tyrosine kinases, respectively, have shown antiproliferative activity in mouse xenograft models [3,4].

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A pH-Induced Reversible Conformational Switch able to control the Photocurrent Efficiency in a Peptide Supramolecular System

Marta De Zotti[a], *Sascha Kubitzky*[b], *Mariano Venanzi*[c], *Barbara Biondi*[a], *Raffaella Lettieri*[c], *Emanuela Gatto*[c]

[a]*Institute of Biomolecular Chemistry, Padova Unit, CNR, Department of Chemistry, University of Padua, 35131 Padua, Italy;* [b]*Faculty of Engineering and Natural Sciences, Technische Hochschule Wildau, Wildau, 15745 Germany;* [c]*Department of Chemical Science and Technologies, University of Rome Tor Vergata, 00133 Rome, Italy; e-mail: marta.dezotti@unipd.it*

External stimuli are potent tools that Nature uses to control protein function and activity. For instance, during viral entry and exit, pH variations are known to trigger large protein conformational changes. In Nature, the electron transfer (ET) properties of ET proteins are also influenced by pH-induced conformational changes. Helical peptides are known to effectively mediate ET, acting as biomolecular wires. In this presentation, the effect on ET-through-a-peptide of a pH-controlled, reversible 3_{10}-helix to α-helix conversion is described [1]. The peptide is part of a supramolecular system, built on a gold electrode, able to convert light into current [2]. The effect of pH on the ability of the peptide SAM to generate a photocurrent was investigated, with particular focus on the effect of the pH-induced conformational change on photocurrent efficiency. The films were characterized by electrochemical and spectroscopic techniques, and were found to be very stable over time, also in contact with a solution. They were able to generate current under illumination, with an efficiency that is the highest recorded so far with biomolecular systems.

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Supramolecular hydrogels from unprotected dipeptides: a comparative study on stereoisomers and structural isomers

Ottavia Bellotto[a], *Slavko Kralj*[b], *Rita De Zorzi*[a], *Silvano Geremia*[a], *and Silvia Marchesan*[a]

[a]*Dip. Scienze Chimiche e Farmaceutiche, Università di Trieste, 34127 Trieste, Italy;* [b]*Materials Synthesis Department, Jožef Stefan Institute, 1000 Ljubljana, Slovenia*

The interest in biodegradable nanomaterials has grown exponentially especially for short peptide-based systems. Supramolecular hydrogels from unprotected short peptides (di- or tri-peptides) have been used in a wide range of biomedical applications. These systems offer several advantages over other classes of molecules (*i.e.* versatility, easy scale-up, biocompatibility), especially if they feature D-amino acids that confer higher resistance against enzymatic hydrolysis [1]. For a minimalistic strategy, the shorter is the sequence, the lower will be the cost of preparation. Recently, a single amino acid (Phe) with an aromatic N-cap was reported to yield hydrogels with mild antimicrobial activity [2]. The substitution of these groups with another hydrophobic amino acid (*i.e.* Phe [3], Leu [4], Ile or Nle) could be a preferable strategy that yields dipeptides able to gel, especially when combined with heterochirality. Heterochirality and hydrophobicity are well-known to play a key role in the self-assembly of unprotected peptides into hydrogels in aqueous systems at physiological conditions. In the case of Phe-Phe, it is worth mentioning the role of heterochirality in promoting intramolecular interactions which impeded hierarchical assembly into microtubes, stabilizing instead a homogenous population of 4-nm wide nanotubes with high cell viability [3]. All the dipeptide stereoisomers that are not enantiomers were studied for assembly into gels in phosphate buffer to unveil the relationship between chemical structure (*e.g.,* branching of the aliphatic amino-acid side chain for the three regioisomers Leu, Ile, Nle, Figure 1a) and supramolecular behaviour. Interestingly, both stable and metastable hydrogels were obtained (Figure 1b), and the heterochirality overall increased hydrophobicity and promoted self-assembly, even if not in all dipeptide systems. XRD data shed light on the key interactions and packing modes that were related to the different stability of the hydrogels. Comparative studies between different regioisomers and stereoisomers are set to identify design rules for supramolecular biomaterials derived from the self-organization of simple and low-cost building blocks that do not persist in the environment.

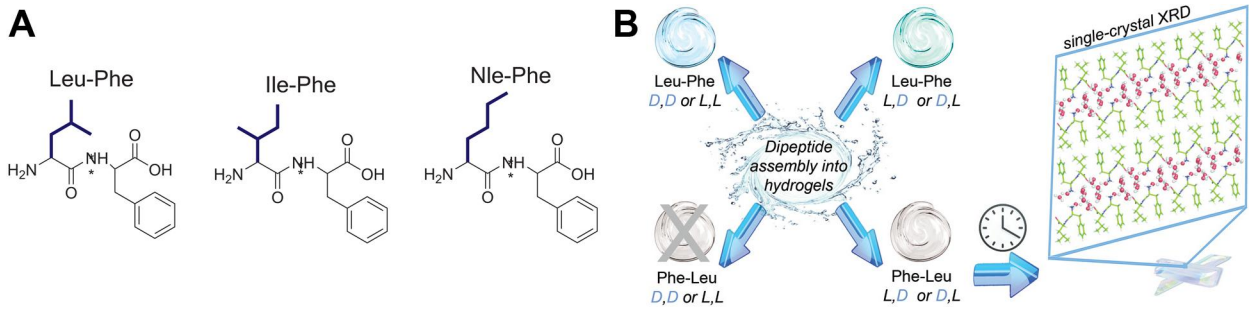

Figure 1. a) Dipeptide regioisomers studied (side-chain variations in blue). * indicates stereocenters, whose configuration was varied systematically to study the self-assembly of the corresponding stereoisomers. **b)** Example of dipeptide stereoisomers' assembly study into stable or metastable gels [4].

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Molecular basis of myoglobinopathy, a newly discovered molecular disease

Marcello Pignataro[a], Marco Borsari[a], Carlo Augusto Bortolotti[b], Giulia Di Rocco[b], Stefan Hofbauer[c], Paul G. Furtmüller[c], Christian Obinger[c], Marco Sola[b] and Gianantonio Battistuzzi[a]

[a] Department of Chemistry and Geology, University of Modena and Reggio Emilia, via Campi 103, 41125 Modena, Italy; [b] Department of Life Sciences, University of Modena and Reggio Emilia, via Campi 103, 41125 Modena, Italy; [c] Institute of Biochemistry, Department of Chemistry, Vienna Institute of BioTechnology, BOKU-University of Natural Resources and Life Sciences, Muthgasse 18, A-1190, Vienna, Austria

Myoglobin (Mb) is a small globular protein, found in high concentrations in the muscular and cardiac tissues, where it reversibly binds O_2 using a ferrous 5-coordinate eme b [1,2]. Replacement of the native His98 by a tyrosine (H98Y mutation) induces an autosomal dominant myopathy (Myoglobinopathy), resulting in muscle weakness, respiratory failure and finally in cardiac involvement [1]. To understand the molecular basis of the disease, we studied the structural and functional effects of the H98Y mutation on the reactivity and catalytic properties of the heme center and on the aggregation propensity of human Mb using a combination of physico-chemical techniques (Uv-vis, MCD and EPR spectroscopies, molecular dynamics, electrochemistry, Uv-vis spectroelectrochemistry, stopped-flow kinetics).

In a previous work [1] we demonstrate that the mutant features an impaired oxygen binding and faster heme bleaching compared to the wt protein. Here, we show that the H98Y mutant, although featuring an active site architecture only marginally different from the wt protein, has an altered reactivity also with H_2O_2. Larger binding rates and increased pseudoperoxidase activity (detoxifying action) on one hand and a larger H_2O_2-induced tendency to form high- molecular weight aggregates and to undergo heme bleaching (harmful effects) on the other were observed. These effects are the result of bond formation/cleavage events occurring at the distal and proximal heme iron binding sites, respectively. Therefore, conceivably the determinants of the disease are localized there. These findings set the bases for clarifying how these effects concur to the development of the cascade of chemical events responsible for the pathological symptoms of myoglobinopathy.

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Selectivity and stability of biological macromolecules heterogenized to nanostructured artificial membranes

Lidietta Giorno, Giuseppe Vitola, Emma Piacentini, Rosalinda Mazzei

National Research Council of Italy, Institute on Membrane Technology (CNR-ITM), Via P. Bucci 17C at Campus UNICAL, 87036, Rende (CS), Italy; email: l.giorno@itm.cnr.it; lidietta.giorno@cnr.it

The development of nanostructured artificial membranes bearing biofunctional properties can promote highly selective and efficient systems, which are needed in many fields, including chemical conversion, analytical detection, environmental monitoring. Biological macromolecules, such as enzymes, antibodies, molecular receptors, have unpaired performance in terms of catalytic activity and selectivity compared to synthetic molecules. On the other hand, biological components are labile and compromise technology robustness. The heterogenization of biocomponents with nanostructured synthetic membranes is a strategy to increase the stability of biological macromolecules. The challenge is to do not alter their native high selectivity. The lecture will discuss the influence of the membrane microenvironment and highlight the properties that influence biomacromolecules stability, selectivity, and catalytic activity. Besides physical-chemical properties, morphology and topography of nanostructures present in the porous membrane matrix play an important role. Overall, the observed kinetic properties of heterogenized enzymes and productivity of biocatalytic membranes are influenced by macromolecule's flexible conformation as well as by mass transfer through biohybrid fluidized system. Case studies of model enzymes (such as lipase, beta-glucosidase, and phosphotriesterase) loaded to polymeric membranes by entrapment, adsorption or covalent bond will be illustrated highlighting conditions where the common observed inverse relationship between increase of stability at the expenses of selectivity and catalytic activity was overcome.

Design, synthesis and characterization of cyclic TBA analogues

C. Riccardi[a], *A. Meyer*[b], *J.-J. Vasseur*[b], *F. Morvan*[b], *I. Russo Krauss*[a], *L. Paduano*[a], *D. Montesarchio*[a]

[a]*Department of Chemical Sciences, University of Naples Federico II, Via Cintia 21, I-80126, Napoli, Italy*
[b]*Institut des Biomolécules Max Mousseron, UMR 5247, Univ. Montpellier, CNRS, ENSCM, University of Montpellier, place E. Bataillon, 34095 Montpellier Cedex 5, France*

The Thrombin Binding Aptamer or TBA, a 15-mer G-rich oligonucleotide with the sequence 5′-GGTTGGTGTGGTTGG-3′, is able to selectively recognize the fibrinogen-binding exosite I of thrombin, thus inhibiting the conversion from soluble fibrinogen into insoluble strands of fibrin [1,2]. Aiming at obtaining TBA analogues better performing *in vitro* and *in vivo*, a large number of chemically modified TBA variants have been proposed in the literature [3].
In this frame, exploiting different cyclization approaches, we prepared a series of cyclic TBA analogues by covalently linking its 5′ and 3′-ends with a variety of flexible linkers (Figure) [4,5]. The first derivative – named cycTBA – was realized as a proof of concept introducing a 20-atom long linker. Compared to native TBA, it exhibited a G4 structure with exceptionally improved stability (ΔT_m of ca. +18 °C) and nuclease resistance (ca. 180-fold higher half-life). However, these very favourable structural properties were associated to a reduced biological activity, correlated to a lower thrombin binding affinity with respect to unmodified TBA, suggesting that a higher flexibility in the linker structure was necessary [4]. Therefore, a mini-library of second generation cyclic TBAs (cycTBA I-IV) was prepared, carrying circularizing linkers overall spanning from 22 to 48 atoms. A fine-tuning of the length and chemical nature of the connecting linker allowed identifying a cyclic analogue, named cycTBA II, with improved anticoagulant activity, associated with a dramatically stabilized G4 structure and enhanced enzymatic resistance in serum compared to the native linear aptamer [5]. Further studies are in progress to investigate pseudocyclic TBA analogues, where the cyclic structure is obtained not through covalent bonds but via π-π stacking interactions of different aromatic appendages inserted at the termini.

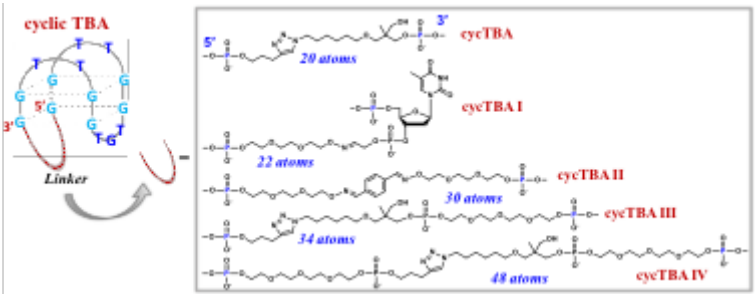

Figure. Schematic representation of a generic cyclic TBA structure with a linker connecting the 3′- and 5′-ends of the oligonucleotide sequence (left); chemical structures and length of the linkers (right) used in the cyclic TBA derivatives cycTBA and cycTBA I-IV.

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NMR as a tool to monitor the individual response of immunotherapy

Veronica Ghini[a,b], *Claudio Luchinat*[a,b], *Paola Turano*[a,b]

[a]*Center of Magnetic Resonance, University of Florence, Italy;* [b]*Department of Chemistry, University of Florence, Italy*

Metabolomics represents a powerful tool to approach precision medicine, with the final aim of monitoring the individual response to pharmacological treatments, thus improving patient stratification and management [1].
The type and abundance of metabolites detected in a biological sample can be viewed as a global fingerprint that unambiguously describe the overall status of an individual [1].
Here, NMR-based metabolomic analysis of biofluids has been used to establish a "signature", both before and after a given drug therapy, that provides information on individual treatment outcomes. This methodological approach was used in a retrospective study to predict the outcome of immunotherapy in advances non-small-cell lung cancer patients. In particular, serum metabolomic fingerprinting was used as a predictive biomarker of the effectiveness of immunotherapy treatment with monoclonal antibodies, being able to discriminate responder *vs.* non-responder subjects with high accuracy and specificity [3].
With the same methodology, the effect of tocilizumab administration was evaluated in COVID-19 patients. The presence of common plasma metabolomic signatures of COVID-19 patients, despite the heterogeneity of the clinical symptoms, was established and characterized; tocilizumab treatment resulted in at least partial reversion of the metabolic alterations due to SARS-CoV-2 infection. [4]
The presented results highlighted the pivotal role of NMR-metabolomics in personalized medicine, in which treatment decisions are taken based on the subject's individual subtype with the final aim of avoid inefficient therapy and improve patient care.

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µs-ms conformational dynamics control the formation of prion protein intermediate states involved in amyloid fibrils.

Luigi Russo[a], Giulia Salzano[b], Luigi Celauro[b], Edoardo Bistaffa[c], Fabio Moda[c], Manoj Madheswaran[a], Gianluca D'Abrosca[a], Gaetano Malgieri[a], Danilo Milardi[d], Gabiele Giachin[e], Carla Isernia[a], Giuseppe Legname[b] and Roberto Fattorusso[a]

[a]Department of Environmental, Biological and Pharmaceutical Science and Technology, University of Campania - Luigi Vanvitelli, via Vivaldi 43, 81100 Caserta, Italy; [b]Department of Neuroscience, Laboratory of Prion Biology, Scuola Internazionale Superiore di Studi Avanzati (SISSA), Trieste, Italy; [c]Fondazione IRCCS Istituto Neurologico Carlo Besta, Division of Neurology 5 and Neuropathology, Milano, Italy; [d]Institute of Crystallography, National Research Council, Catania, Italy; [e]Department of Cellular, Computational and Integrative Biology (CIBIO), University of Trento, Povo (Trento), Italy.

The conformational conversion of the prion protein (PrP) from its normal cellular form, PrPC, to the unsoluble scrapie form, PrPSc, is at the basis of the pathogenesis of the transmissible spongiform encephalopathies (TSE) [1,2,3]. The misfolding of PrPC into PrPSc may occur due to genetic mutations of the PrP gene enhancing the aggregation propensity of the protein or through infection by diseased PrPSc forms, which then act as a template for PrPC-PrPSc autocatalytic conversion [4]. Nonetheless, most reported prionpathies are the results of spontaneous conversion of PrPC into PrPSc whose mechanism has been not yet elucidated, despite the fact that several in vitro and computational studies suggest PrP high conformational flexibility as a crucial factor in aggregation mechanism [5,6]. As a matter of fact, the capability of PrPC to populate partially unfolded state (usually termed as PUFs) in equilibrium with the native state appears to be an essential step prior to convert to the β-structured toxic oligomers and successively to the fibrillar unsoluble forms. In spite of this wealth of knowledge, a high resolution description of the initial stages of the conformational transition from PrPC to PrPSc is not yet available, as well as a detailed molecular picture of PrPC folding mechanism. Here, in order to understand the structural and dynamics determinants controlling the formation of intermediate states involved in fibril assembly, we report an exhaustive NMR-Based investigation of conformational equilibria and folding mechanisms for full length and 90-231 prion proteins.

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New, highly sensitive off/on EPR probes to monitor enzymatic activity

Sabrina Elkhanoufi, Rachele Stefania, Diego Alberti, Simona Baroni, Silvio Aime, Simonetta Geninatti Cric

University of Torino, Molecular Biotechnology and Health Sciences, Torino, Italy

Many pathologic conditions are often associated with unregulated level of enzyme activity. Therefore, the detection and quantification of the enzymatic activity is extremely important for a diagnostic purpose [1]. In this contest, a particularly interesting class of enzymes is represented by carboxylesterases (CEs). These enzymes belong to the serine hydrolase superfamily and are involved in the hydrolysis of endogenous ester-containing substrates as well as ester-containing drugs, thus playing a crucial role in a variety of metabolic processes [2]. CEs are upregulated in many tumors and the assessment of their activity may be of diagnostic interest as well it may provide relevant information regarding chemotherapeutic effects of antitumor ester-containing drugs and pro-drugs. Currently CE activity is assessed by means of fluorescence and UV-based methods [3]. In this study, we propose the use of electron paramagnetic resonance (EPR) as an easy method to probe CE enzymatic activity *in vitro*. EPR has the advantage to be highly sensitive and with limited interferences from the matrix, also in the presence of turbid samples. For this application, TEMPO derivative nitroxide radicals were conjugated to a fatty acid (Dodecanoic acid) *via* the formation of an ester bond to yield **Tempo-C$_{12}$** (TC$_{12}$) and **Tempo-2-C$_{12}$** (T2C$_{12}$). In the Figure the structures of the two EPR probes and the products generated upon the CE activity are reported; in the lower part the off/on EPR signal after the hydrolysis are reported. Both compounds exhibit a low solubility in water and aggregate to form stable micelles with the lipophilic tail in the core and the nitroxide radical exposed to water. The radicals in the micellar aggregates are practically EPR silent showing a low and broad EPR signal. The hydrolysis of the ester bond catalyzed by CE generates a narrow and intense EPR signal as a consequence of the release of the nitroxide radical from the micelle, that is proportional to the enzymatic activity [4]. CEs1, CEs2 and esterase from porcine liver (PLE) were tested. The result obtained show that the micelles of TC$_{12}$ and T2C$_{12}$ have a much higher selectivity toward the CEs2, and a Limit of Detection of the same order of those ones obtained with optical methods. In conclusion, this is a new promising tool to quantitatively detect the CEs2 activity. The method can be applied for monitoring the enzymatic activity *in vivo,* eventually also through the detection of the Overhauser MRI response.

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A MS and SPR coupled approach to fully characterize IDE activity modulation.

Alessia Distefano[a], *Damiano Calcagno*[b], *Josè Giuffrida*[a], *Giuseppe Grasso*[a].

[a]*Università degli Studi di Catania, Dipartimento di Scienze Chimiche, Viale Andrea Doria, 6, 95125-Catania, Italy;* [b]*Dipartimento di Scienze Biomediche e Biotecnologiche (BIOMETEC), sez. Biochimica medica, Università di Catania, Via Santa Sofia 97, 95124 Catania, Italy; e-mail: distefano-alessia@libero.it*

Insulin-degrading enzyme (IDE) is a metalloprotease with a zinc metal core belonging to the inverzincin family, responsible for the degradation of insulin and many other peptides. IDE plays a crucial role *i)* in the onset of diabetes and *ii)* in neurodegenerative pathologies such as Alzheimer's Disease, since Aβ peptides are also recognized as substrates by IDE [1].
IDE exists in different conformational states, the closed state (IDE_c) and the open state (IDE_o), as well as in different oligomeric forms which are in equilibrium in solution. Allosteric modulators of the enzyme that induce the IDE_o are enzyme activators, as confirmed by X-ray structures [2]. In the case of large substrates, more than 30 Å, *i.e.* Insulin, a bivalent interaction occurs both through the catalytic site and the so-called exosite, thus allowing the conformational switch [3]. However, small molecules, which can be degraded by IDE themselves, can also bind the exosite to regulate IDE activity towards other substrates. For example, somatostatin, an IDE substrate, appears to enhance the degradation of insulin and $A\beta_{1-40}$ at sub-micromolar concentrations [4].
In this perspective, the search of small molecules that can modulate IDE activity and therefore can have potential therapeutic applications in the diseases mentioned above is of paramount importance. Herein, some small molecules have been investigated since they can act either as activators or inhibitors of IDE. Mass spectrometry was used to investigate the enzyme activity, whereas Surface Plasmon Resonance (SPR) technique was applied to fully characterize the biomolecular interactions involved. Besides the information obtained in this specific case, we have developed a robust experimental approach to be applied in the field of enzyme modulation activity.

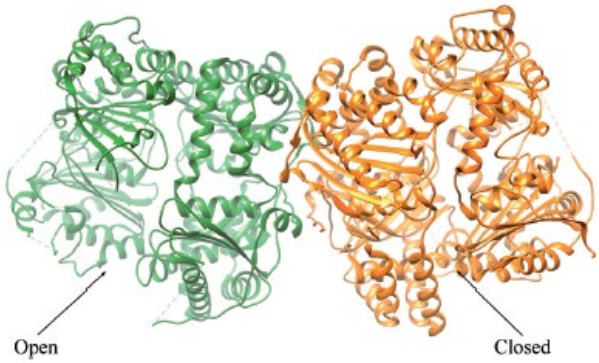

Figure 1 Representation of the three-dimensional structure of the IDE dimer.[3]

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The increased thermodynamic stability of miRNAs might be the reason of stronger repressive activity

A. D'Urso[a], *Paolo Devanna*[b], *G. Travaglianti*[a], *S. Alaimo*[c], *A. Ferro*[c], *R. Purrello*[a]

[a]*Dipartimento di Scienze Chimiche, Università degli Studi di Catania, Italia;* [b]*Neurogenetics of Vocal Communication Group, Max Planck Institute for Psycholinguistics, Nijmegen, The Netherlands;* [c]*Department of Clinical and Experimental Medicine University of Catania Italy c/o Dipartimento di Matematica e Informatica*

MicroRNAs (miRNAs) are short sequences formed by 18–24 nucleotides, that play a crucial role in gene expression by binding to the messenger RNA (mRNA) [1]. The normal expression of miRNAs is important in physiological processes, while the aberrant expression of miRNAs is often associated to the initiation and development of human diseases like cancer, genetic disorders and altered immune system function [2]. As known so far, every miRNA has a small portion of nucleotides called seed region, which is essential for the binding of the miRNA to the mRNA. However recently, has been discovered that in addition to sequence even the structure adopted by miRNAs might play an important role to reach the target [3]. Indeed in our previous paper we have reported that two endogenous miRNA sequences (miR-15a and miR-15b), having different biological activity (pathogenesis of chronic lymphocytic leukemia and progression of metastasis respectively) [4], can arrange in distinct secondary structures suggesting potential relationship between secondary structure and biological functionality.
Intrigued by the apparent correlation between the different biological behavior and the structural properties of miR-15a and miR-15b, we have investigated by Electronic Circular Dichroism (ECD) measures and ECD melting experiments, both human and bat miR-337-3p sequences in order to characterize the possible secondary structures adopted. Since the two sequences, differing only for two basis located in the external portion of the seed region, have involved in tumor progression and cognitive processes we think that them can fold in different arrangements, which might justify the distinct biological targets.

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Photoresponsive Ligands for Targeting PARP1 G-Quadruplex

A. Benassi, G. Preda, R. Perotti, V. Pirota, F. Doria, M. Freccero

Department of Chemistry, University of Pavia, Viale Taramelli 10, 27100-Pavia, Italy

Nucleic acids sequences rich in guanines can fold into supramolecular structures known as G-Quadruplexes (G4s), characterized by two or more guanine tetrads stacked one on another. Their formation has been widely detected both *in vitro* and *in vivo*, especially in telomeres, gene promoter regions and in 5'-UTR of RNAs [1]. Therefore, stabilization of these secondary structures with small molecules represents a valid strategy to interfere with important biological processes and develop innovative therapies against different types of pathologies [2]. Recently, a new G4 has been identified in the promoter region of PARP1[3], a gene encoding for an enzyme involved in repair of DNA single strand breaks. Inhibition of PARP1 is a promising approach against different types of tumors, including ovarian and breast [4]. Here we propose the synthesis of two different libraries: NDI-tetrazole and NDI-pyrazoline conjugates, to be evaluated as PARP1-G4 ligands, taking advantage of the photoreactivity of the tetrazole moiety.

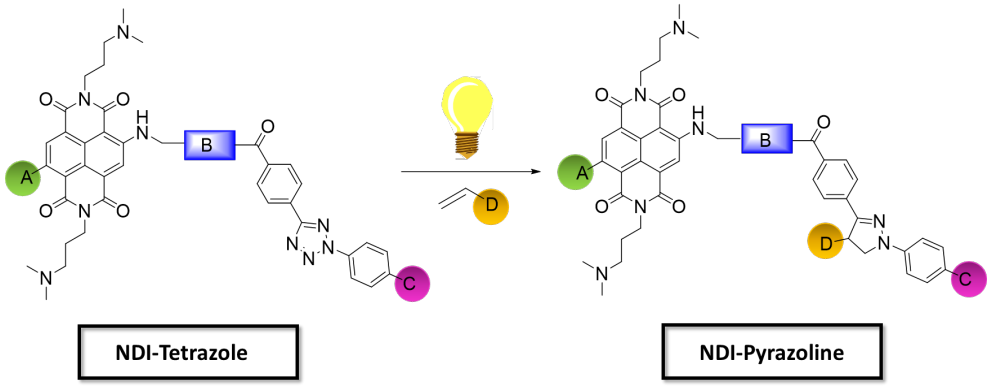

Figure 1. Light-mediated generation of fluorescent NDI-Pyrazolines from NDI-Tetrazole.

In fact, NDI conjugated to 2,5-diaryl tetrazoles can be photoactivated generating the reactive intermediate nitrilimine (NI). The resulting NI reacts with different reagents, including alkenes and nucleofiles, expanding the structural variability of the second library. Therefore, we have synthesized a small library of novel NDI-tetrazole conjugates, embedding three variable structural elements (A, B, C and D in Figure 1), to investigate their spectroscopic properties and their photoreactivity, generating NDI-pyrazoline conjugates. In the end, we have analyzed the binding properties of NDI-Tetrazoles and the corresponding NDIs-Pyrazolines towards PARP1-G4, by biophysical assays, including Circular Dichroism analysis and FRET-Melting assay, to verify their potential as novel, light-responsive, PARP1 inhibitors.

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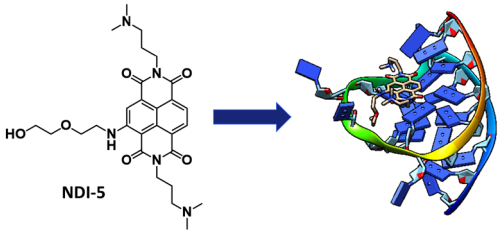
Targeting cancer-related DNA G-quadruplex structures by naphthalene diimide ligands

Chiara Platella[a], *Marko Trajkovski*[b], *Filippo Doria*[c], *Domenica Musumeci*,[a], *Valentina Pirota*[c], *Jussara Amato*[d], *Bruno Pagano*[d], *Mauro Freccero*[c], *Janez Plavec*[b], *Daniela Montesarchio*[a]

[a]*Department of Chemical Sciences, University of Naples Federico II, via Cintia 21, I-80126 Naples, Italy;* [b]*Slovenian NMR Centre, National Institute of Chemistry, Hajdrihova 19, SI-1000 Ljubljana, Slovenia;* [c]*Department of Chemistry, University of Pavia, Viale Taramelli 10, I-27100 Pavia, Italy;* [d]*Department of Pharmacy, University of Naples Federico II, via D. Montesano 49, I-80131 Naples, Italy*

G-quadruplexes are secondary structures of DNA and/or RNA formed by stacking of cyclic planar arrangements of four guanines called G-quartets, and stabilized by metal cations. These peculiar nucleic acid architectures play key roles in the regulation of tumour-specific genes as well as in molecular pathways involved in uncontrolled proliferation mechanisms common to all tumour types. Thus, selectively targeting G-quadruplex structures *in vivo* represents a very general and promising anticancer strategy [1]. The appealing possibility to treat common features of different cancers without impairing normal cells stimulated the synthesis of large libraries of putative G-quadruplex ligands. To rapidly and effectively select 'true hits', we have recently developed an affinity chromatography-based method, *i.e.* the G4-CPG (G-quadruplex on Controlled Pore Glass) assay to identify ligands able to specifically recognize biologically relevant G-quadruplex structures [2]. More specifically, we recently focused on a library of new multifunctionalized naphthalene diimides (NDIs) [3,4]. By exploiting the G4-CPG assay, **NDI-5** was found to be the most attractive compound within the investigated series. Most notably, *in vitro* cell viability tests indicated **NDI-5** as a very promising candidate drug for its strong bioactivity against human cancer cells, showing an IC_{50} value in the low nanomolar range and high selectivity in killing tumour cells, not sensibly affecting normal cells [3]. Encouraged by these results, we deemed it essential to undertake an in-depth study on the interaction of **NDI-5** with G-quadruplexes to clarify the structural details of this strong and specific binding. Therefore, we performed NMR experiments with two model G-rich oligonucleotides able to fold into stable and well-characterized oncogenic and telomeric G-quadruplex structures. NMR investigation on the **NDI-5** interactions with G-quadruplexes of different structural topologies was complemented with dynamic light scattering, circular dichroism and fluorescence spectroscopy analyses [5]. Altogether the obtained insights are now directing the design of optimized **NDI-5** analogues as effective anticancer candidate drugs to be advanced to *in vivo* targeted therapies.



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Self-assembly of PNA-peptide conjugates

Concetta Avitabile[a], Carlo Diaferia[b], Marilisa Leone[c], Enrico Gallo[d], Michele Saviano[a], Marika Riva[e], Antonella Accardo[b] and Alessandra Romanelli[e]

[a]Institute of Crystallography (CNR), via Amendola 122, 70126 Bari, Italy; [b]Department of Pharmacy, Research Centre on Bioactive Peptides (CIRPeB), University of Naples "Federico II", Via Mezzocannone 16, 80134 Naples, Italy; [c]Institute of Biostructures and Bioimaging (CNR), via Mezzocannone 16, Naples Italy; [d]IRCCS SDN, Via E. Gianturco 113, 80143 Naples, Italy; [e]Department of Pharmaceutical Sciences, University of Milan, via Venezian 21, 20133 Milan, Italy

Self-assembly of PNA based molecules is the object of many recent investigations, due to the potential applications of these compounds in nanotechnology [1,2]. PNA assemblies exhibit photoluminescence properties and morphologies that can be tuned by changing the base composition and covalently linking hydrophobic or aromatic moieties to the PNA chain to promote formation of supramolecular structures [3,4]. Forces that stabilize the assembled structures typically are hydrogen bonds or aromatic interactions; in case of nucleic acids, Watson-Crick pairing drives self-assembly while, in case of peptides, backbone hydrogen bonds and interactions between aromatic side chains trigger the formation of structures, such as nanotubes or ribbons. Molecules containing both aromatic peptides and nucleic acids could in principle exploit different forces to self-assemble. In this work we investigated the self-assembly of systems containing both peptide and nucleic acids, in the form of Peptide Nucleic acids, with the aim to understand which forces play a major role and determine formation/structure of aggregates. We therefore synthesized conjugates of the peptide FF to the Peptide Nucleic Acid dimer "gc" and characterized their aggregates by different spectroscopic techniques, including NMR, CD and fluorescence. Interesting results in term of forces that drive the self-aggregation can be derived.

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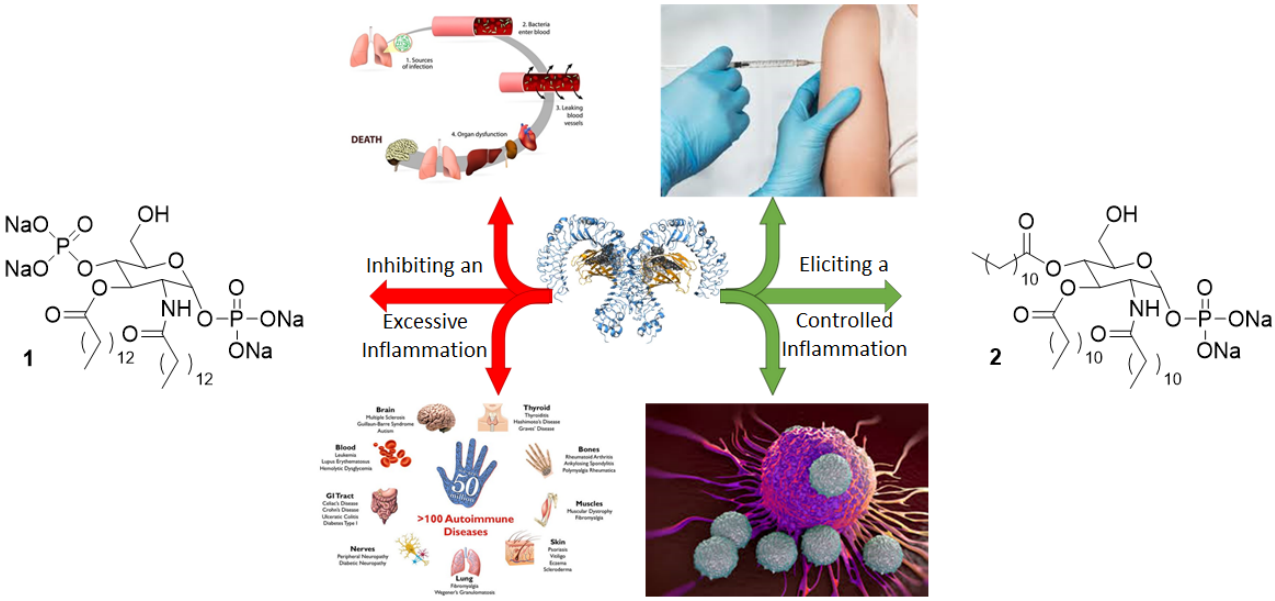
Design, synthesis and Biological evaluation of New, glycolipid-based Toll-Like Receptor 4 (TLR4) Modulators

Alessio Romerio, Andrea Luraghi, Ana R. Franco, Mohammed M. Shaik, Nicolé Gotri, Valentina Artusa, Simona D'amato, Francesco Peri

Università di Milano-Bicocca, Department of Biotechnology and Biosciences, Milano

Innate Immunity is the first defense line in multicellular organisms against internal of external threats. It acts through inflammation, triggered by the recognition of specific Pathogen or Damage Associated Molecular Patterns (PAMPs or DAMPs) by specific pattern-recognition receptors (PRRs). Toll-Like Receptor 4 (TLR4) is one of the most important PRRs, and it responds to gram-negative bacteria lipopolysaccharide (LPS) [1].
TLR4 modulation is emerging as an important therapeutic approach in several clinical settings: TLR4 inhibition has a potent anti-inflammatory effect; on the other hand, TLR4 mild activation can be used to stimulate immunity in vaccine adjuvants or to develop cancer immunotherapeutic drugs [2,3].
We present here rationally designed lipid A analogues based on a monosaccharide structure that are active in binding MD-2/TLR4, thus activating or inhibiting LPS/TLR4 or DAMP/TLR4 signalling. We also present synthesis optimization of TLR4 modulators, with the aim of producing versatile synthetic intermediates and reducing the number of synthetic steps to efficiently scale the synthesis up for industrial purposes.



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Evidence of amino-thiadiazoles as innovative inhibitors of human glutaminyl cyclase, validated target for neurodegenerative disorders

Giusy Tassone[a], *Pasquale Linciano*[b], *Maria Paola Costi*[b], *Cecilia Pozzi*[a], *Stefano Mangani*[a]

[a]*Department of Biotechnology, Chemistry and Pharmacy – Department of Excellence 2018-2022, University of Siena, via Aldo Moro 2, 53100 Siena, Italy;* [b]*Department of Life Sciences, University of Modena and Reggio Emilia, Via Campi 103, 41125, Modena, Italy; e-mail: giusy.tassone@unisi.it*

Human glutaminyl cyclase (hQC) is a zinc-dependent enzyme belonging to the class of acyltransferases that catalyzes the intramolecular cyclization of the N-terminal glutaminyl or glutamyl of peptides and proteins into pyroglutamic acid (pGlu). This post-translational modification stabilizes and protects macromolecules from proteolytic degradation and assists them to develop the proper conformation [1]. However, since their tendency to rapidly aggregate, pGlu-modified peptides are highly neurotoxic, promoting the insurgence and progression of various neurodegenerative pathologies, such as Alzheimer (AD) and Huntington diseases (HD) [2,3]. Former studies have reported the upregulation of hQC in these neurodegenerative disorders, thus this enzyme represents an attractive target to develop novel drugs for these pathologies, still lacking effective treatments. In this study, we have investigated a series of molecules relying on the amino-thiadiazole core as new Zn(II)-binding moiety to probe their inhibition effects on hQC. This library of amino-thiadiazole derivatives was formerly developed by us to target the parasite enzyme, *Trypanosoma brucei* pteridine reductase 1 (*Tb*PTR1) [4]. Notably, these compounds showed a safe profile in a panel of early toxicity assay comprising cytotoxicity, mitochondrial toxicity, hERG toxicity, CYP isoforms, and Aurora B kinase. Thus, the amino-thiadiazole scaffold has a well-tolerated liability profile and it can be further explored for inhibitor development also towards other targets, such as hQC. For the present investigation, a set of twenty-four compounds have been selected from this library and tested towards hQC, leading to the identification of three inhibitors having K_i values in the high nM range. To unveil the binding mode of the most active compounds of this series, X-ray crystallography experiments have been performed using the hQC double mutant Y115E-Y117E (hQC-2X), formerly validated by us as soluble protein variant exploitable for drug discovery purposes [5]. The structural information achieved on the complexes of hQC-2X with fourteen amino-thiadiazole derivatives has allowed us to evaluate the structure-activity relationship of these inhibitors, obtaining key insights to evolve new hQC inhibitors based on this innovative Zn(II)-binding motif.

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Modulation of Ca^{2+}-ATPase transport activity by pharmacologically relevant compounds

Francesco Tadini-Buoninsegni, Patrick Severin Sfragano, Ilaria Palchetti

Department of Chemistry "Ugo Schiff", University of Florence, Via della Lastruccia 3-13, 50019 Sesto Fiorentino, Italy

The sarcoplasmic reticulum Ca^{2+}-ATPase (SERCA), belonging to the superfamily of membrane transport proteins known as P-type ATPases, is localized in the sarcoplasmic reticulum (SR) of muscle cells. The SERCA enzyme hydrolyzes one ATP molecule to transport two Ca^{2+} ions against their electrochemical potential gradient from the cytoplasm to the SR lumen. Ca^{2+} uptake in the SR lumen by SERCA plays an essential role in lowering cytoplasmic Ca^{2+} concentration and inducing muscle cell relaxation. Impaired SERCA function and regulation have been related to pathological conditions and several diseases with a wide range of severity. Therefore, SERCA represents an attractive target for the development of novel drugs with distinct therapeutic potential.
Here, we present a bioelectrochemical method based on a solid supported membrane (SSM) that has been used to investigate drug interactions with P-type ATPases [1]. The SSM, consisting of a hybrid alkanethiol/phospholipid bilayer supported by a gold electrode, is a convenient model system for a biological membrane. Membrane fragments/vesicles or proteoliposomes, incorporating the ATPase of interest, are adsorbed on the SSM surface and are subjected to a rapid concentration jump of a suitable substrate. The substrate concentration jump activates the ATPase and an electrical current is detected, which is related to charge movement across the ATPase [2,3].
In the present study SR vesicles containing SERCA were adsorbed on the SSM and activated by ATP concentration jumps. Following protein activation, a SERCA-related current signal was measured which was attributed to ATP-dependent translocation of Ca^{2+} ions across the vesicular membrane. The interaction of pharmacologically relevant compounds with SERCA was investigated. In particular, we analyzed the mechanism of action of some selected phytochemicals, i.e. demethoxycurcumin and gingerol that are known for their antioxidant, anti-inflammatory and anticancer properties. The SSM measurements indicate that such compounds affect Ca^{2+} translocation by SERCA and behave like activators or inhibitors of the SERCA enzyme. The identification of drugs that can modulate SERCA transport activity may represent an innovative approach to treat various diseases that are associated with SERCA dysfunction.

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Insulin loaded in liquid crystalline mesophases: effects on carrier structure and insulin stability

M. Pisani[a], *E. Giorgini*[b], *M. Parlapiano*[a], *P. Astolfi*[a]

[a]*Department SIMAU, Marche Polytechnic University, Ancona, Italy;* [b]*Department DISVA, Marche Polytechnic University, Ancona, Italy*

The loading of biomolecules, ranging from small drugs and peptide to proteins, in lyotropic liquid crystalline (LLC) nanosystems represents an efficient strategy for therapeutic drug delivery.[1,2] The amphiphilic nature of LLC vectors allows them to encapsulate both hydrophilic and hydrophobic molecules within the aqueous channels and the lipid bilayer, respectively. LLC matrices give 2-D and 3-D nanostructures with large surface areas and specific and controllable water channel sizes which provide a diffusion pathway for sustained and controlled release.
The aim of this work was to encapsulate insulin within LLC hexagonal and cubic mesophases (monoolein and oleic acid - GMO/OA and monoolein - GMO, respectively) to gain information on: i) changes in structure mesophases after insulin inclusion, ii) insulin structure when confined within the aqueous channels of 2-D and 3-D matrices and its tendency to misfolding or aggregation in confined space. To achieve this aim, SAXS and ATR-FTIR spectroscopy were used in combination and allowed to verify that the effect of confinement on insulin secondary structure was more pronounced when the protein was loaded in hexagonal phase (GMO/OA). In particular, the reduction of the α helix content in favor of the β-sheets one, upon heating, suggests that insulin confinement in a hexagonal structure symmetry could induce aggregation and, ultimately, fibrils formation.

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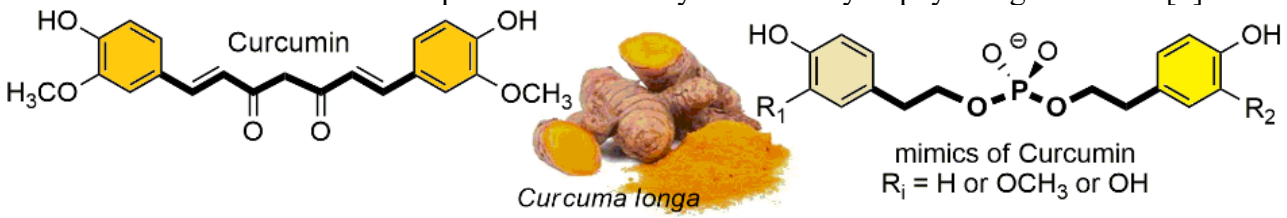
New curcumin mimics based on tyrosol scaffold: investigation of neuroprotective and anticancer activity

Valeria Romanucci[a], Marilena Giordano[a], Sara García-Viñuales[b], Danilo Milardi[b], Gaetano De Tommaso[a], Mauro Iuliano[a], Roberta Bernini[c], Rajesh Agarwal[d], Armando Zarrelli[a] and Di Fabio Giovanni[a]

[a]Department of Chemical Sciences, University of Napoli 'Federico II', Via Cintia, I-80126 Napoli, Italy; [b]Istituto di Cristallografia, Consiglio Nazionale delle Ricerche, Via Paolo Gaifami 18, 95126 Catania, Italy; [c]Department of Agriculture and Forest Sciences (DAFNE) University of Tuscia, Via S. Camillo De Lellis, 01100 Viterbo, Italy; [d]University of Colorado, Skaggs School of Pharmacy and Pharmaceutical Sciences, Aurora, CO 80045, USA

Natural products from different source organisms continue to inspire most drug leads for many diseases. On average, about half of the new drugs classified as small molecules approved by the FDA stem directly from natural sources or by the synthesis of analogues inspired by natural molecular motifs [1]. In the last few years, many reports have described the high therapeutic activity of curcumin (Figure), an active component of *Curcuma longa* (turmeric) with antioxidant, antibacterial, anti-inflammatory anticancer and neuroprotective activities [2]. Unfortunately, the potential utility of curcumin is limited because of its poor bioavailability and stability in physiological media [3].



To overcome these pharmacokinetic deficits, the synthesis of new curcumin mimics has been carried out taking advantages by an efficient solid phase strategy that provide the desired products in good yields and in short times. Several structure activity studies on cucurmin have well defined the structural key elements that are necessary to maintain its activity. In this frame, tyrosol-based phosphodiester dimers have been designed as curcumin mimics that retain the two aromatic rings with different hydroxyl substituents and the distance between them (Figure). In this work, we further investigate the neuroprotective and anticancer activity of new curcumin mimics based on tyrosol scaffold. The three tyrosol scaffolds [tyrosol (TYR), homo-vanillyl alcohol (HVA) and hydroxytyrosol (HDT)] have been previously investigated by MD simulation and ThT assay for their interesting neuroprotective activity [4]. The neuroprotective activity of new curcumin mimics tested by ThT assay confirmed the key role of HDT catechol function that confers a high inhibitor effect on Aβ aggregation to derivatives that contain it [5]. The anticancer activity evaluated on human pancreatic (PANC1), prostate (PC3), and colorectal (SW480), cancer cell lines reported a significant data for the derivative in which TYR and HVA units were linked by a phosphodiester bond. Interestingly, this mimic displays a strong growth inhibition and cell death efficacy for PC3 prostate cancer cells to non-effective findings in pancreatic cancer cells. In the light of these promising results on the first curcumin mimics based on tyrosol scaffold, an extension of the library is currently in progress.

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Modulation of Tau aggregation with natural coffee compounds

R. Tira, G. Viola, C. G. Barracchia, F. Parolini, F. Munari, M. Assfalg, M. D'Onofrio

Department of Biotechnology, University of Verona, Verona, Italy

Neurodegenerative diseases (NDs) are an ever-increasing threat to human life. A primary event in NDs is the misfolding, aggregation, and accumulation of specific proteins in neuronal cells, leading to cellular dysfunction, loss of synaptic connections, and brain damage. In Alzheimer's disease (AD), one of the pathological hallmarks is the presence of intracellular neurofibrillary tangles (NFTs) composed of "paired helical filaments" (PHFs) of hyper-phosphorylated Tau [1]. Tau is an intrinsically disordered protein, which transitions among multiple conformations.

The *in vitro* aggregation kinetics profile of Tau is well represented by a sigmoidal curve in which three phases are commonly observable: the lag-phase, the exponential-phase and the steady phase. Each of these sections of the aggregation process is characterized by structurally different intermediates, ranging from monomers and small oligomers to active nuclei, protofibrils and elongated fibrils [2]. These processes mimic aggregation events *in vivo*.

Mounting evidence suggests the possibility to perturb the dynamic interconversion of Tau among conformational states using small molecules, macromolecules, and nanoparticles to redirect the formation of neurotoxic aggregates. Coffee and coffee compounds are attracting interest in the field of neuro-inflammation and neuro-protection against oxidative-stress thanks to their bioavailability and ability to cross the Blood Brain Barrier [3]. Recent works demonstrate that some of these molecules, such as phenylindanes and other flavonoids, have the additional ability to inhibit Aβ and Tau protein aggregation [4]. Moreover, they suggested that coffee elements might have synergistic effects to produce the overall neuroprotective effect [5].

Relying on these promising perspectives, in our work we investigate the effects of selected coffee-derived bioactive molecules towards mitigation of Tau aggregation. Specifically, we study the kinetics of aggregation, the formation of prefibrillar aggregates and oligomers, the morphology of fibrils, and the conformational transitions of Tau in the presence of trigonelline, theobromine, and genistein. We are confident that this approach based on natural and readily available molecules is fundamental to give further possibilities in the Alzheimer's disease treatment.

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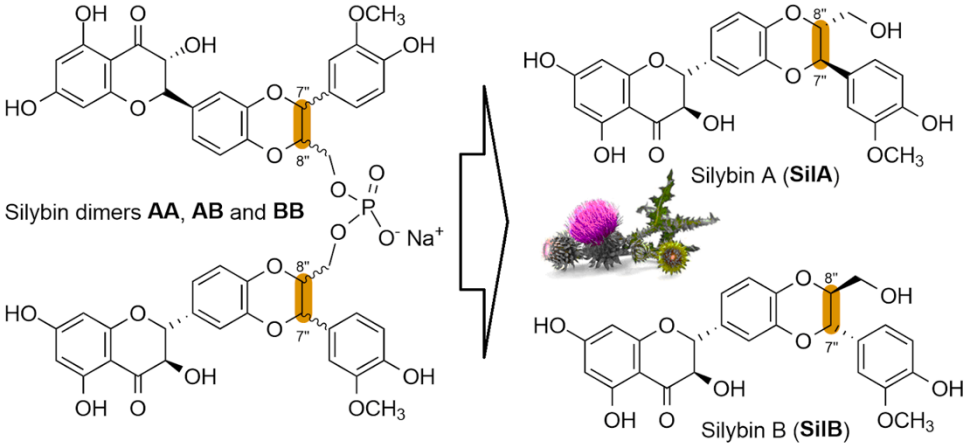
Phosphate-linked Silybin dimers: synthesis and investigation of biological activity

Rita Pagano[a], Valeria Romanucci[a], Domenica Capasso[b,c], Sonia Di Gaetano[b,d], Rita Russo[b], Armando Zarrelli[a] and Giovanni Di Fabio[a]

[a]Department of Chemical Sciences, University of Naples Federico II, Via Cintia 4, 80126 Naples, Italy; [b]CIRPEB, University of Naples "Federico II", Via Mezzocannone 16, 80134 Naples, Italy, [c]CESTEV, University of Naples "Federico II", Via De Amicis 95, 80145 Naples, Italy; [d]Institute of Biostructures and Bioimaging-CNR, Via Mezzocannone 16, Naples, 80134, Italy

The acclaimed ability of polyphenols to scavenge reactive oxygen species (ROS) is frequently cited to be the key property underlying the prevention and/or reduction of oxidative stress-related chronic diseases and age-related disorders. Today, however, there are many studies that suggest the implication of other properties in addition to the antioxidant capacity in their therapeutic activity [1,2]. In this frame, there is an increasing interest in dimeric flavonoids, and several reports highlighted their promising therapeutic values in the treatment of many diseases such as cancer, HIV, Alzheimer and malaria [3,4]. Recently, we have reported the synthesis of new silibinin dimers in which the two monomer units are linked through a phosphodiester bridge, with interesting structure-activity relationships related to their strong radical scavenger ability ($^1O_2$ and $HO^{\cdot}$) [5]. Silibinin is a diastereoisomeric mixture of two flavonolignans, namely silybin A and silybin B, in a ratio of approximately 1:1, extracted from the milk thistle seeds [*Silybum marianum* (L.) Gaertn.]. While there are many studies on the activity and/or mechanisms of action of natural silibinin, to date there are very few studies on the chirality-activity relationship.



As a deepening of our research efforts on these flavonolignan dimers, we herein report an efficient synthetic strategy to obtain silybin dimers in which the two monomer units are the pure diastereoisomers **SilA** and **SilB** linked through a 9"-9" phosphodiester bridge. The biological activity of the silybins (**SilA** and **SilB**) and new dimers (**SilAA**, **SilAB** and **SilBB**), in terms of antiproliferative effects and apoptosis induction, was evaluated on different human cancer cell lines and healthy cells, with the aim to evaluate their selectivity towards cancer over normal cells, to identify the best performed compound and to determine the structure-function relationship.

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Hybrid Porphyrin/DOPA-melanin Film as Versatile Biomaterial for Water Remediation

Massimiliano Gaeta, Matteo Barcellona, Maria Elena Fragalà, Alessandro D'Urso

Università degli Studi di Catania, Dipartimento di Scienze Chimiche, Viale Andrea Doria, 6, 95125-Catania Italy; e-mail: massimiliano.gaeta@unict.it

Water pollution, today, represents one of the most severe environmental issues. The rapid global population growth, the use of pesticides and fertilizers, the untreated human and industrial wastewater, have been determining a fast reduction of usable freshwater, which in turn implicates a forthcoming water-scarcity by 2050. Several efforts have been devoted to developing high-efficiency, low-cost, and eco-friendly materials for water remediation [1]. Inspired by adhesive proteins secreted by mussels for attachment to wet surfaces [2], melanin-like polymers have been successfully employed to provide highly resistant and adhesive biomaterials for the deposition of multifunctional films for water-remediation [1,3]. The robust adhesion to surfaces is related to an extensive network of covalent and noncovalent interactions due to phenolic hydroxyl/quinone groups based on DOPA. Indeed, the natural occurrence of melanin arises from enzymatic oxidation, operated by tyrosinase enzyme, of L-3,4-dihydroxyphenylalanine (L-DOPA) which leads to the deposition of melanin polymers [4].

Thus herein, we employ a porphyrin–spermine derivative, namely H2TCPPSpm4, in order to realize a new functionalized DOPA-melanin film. Indeed, by exploiting both *i)* the ability of H2TCPPSpm4 having primary and protonable amino groups prompt to react with melanin polymers; and *ii)* the adhesive properties of DOPA-melanins, we report a novel hybrid porphyrin/DOPA-melanin material able to form self-assembled film onto glass substrates through a viable synthesis in aqueous medium and at room conditions.

In particular, a small-scale commercial glass substrate -surface area about 3 square centimetres- was dipped in a not-stirred and aerated 0.5mM L-DOPA PBS buffer solution for some days. After two-week dipping, the glass substrate was coated by a quasi-homogeneous and porous dark melanin-like film also evidenced both from spectroscopic investigations and AFM surface morphology studies. The functionalised substrate was employed to remove methylene blue (MB), a common pollutant, from water revealing a high adsorption rate -more than 90%- in few hours of treatment. Afterwards, the adsorbed MB was either photodegraded by simulated solar irradiation or desorbed, bringing back the quasi-pristine hybrid melanin film. The restored composite substrate was reclaimed as dye-adsorbent showing an exceptional re-usability, for many adsorption cycles. These promising results illustrate the chance to realise a composite biomaterial for water-remediation with multi-purpose advantages: *i)* low-cost energy, self-assembled and biodegradable material; *ii)* high efficacy as dye-pollutant adsorbent; *iii)* recyclability; *iv)* potential scalability for real and practical application overcoming the expensive filtration process based on the most common adsorbent materials. Moreover, to our knowledge, no data concerning composite porphyrin/melanin films have been described so far.

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Hyaluronate–Carnosine conjugates: copper(II) complexes and antioxidant properties

Francesco Bellia[a], Valentina Greco[b], Valeria Lanza[a], Eleonora Bocchieri[a], Rosanna Inturri[c], Luciano Messina[c], Mariafiorenza Pulicetta[c], Susanna Vaccaro[c], Sebastiano Sciuto[b], Enrico Rizzarelli[a,b]

[a] *Istituto di Cristallografia, CNR, P. Gaifami 18, 95126 Catania, Italy;* [b] *Dipartimento di Scienze Chimiche, Università degli Studi di Catania, A. Doria 6, 95125 Catania, Italy;* [c] *FIDIA Farmaceutici S.p.A, Unità locale di Noto, Contrada Pizzuta, 96017 Noto, Italy*

Hyaluronic acid (Hy), is a polyanionic linear nonsulfated glycosaminoglycan (GAG) [1]. It is widely distributed throughout mammalian cells and tissues and its biomechanical and biochemical properties support its involvement in myriad physiological functions, including hydration and turgidity maintenance of tissue, extracellular matrix structure, regulation of innate immunity, and protection and lubrication of joints. Due to this versatility, Hy represents a promising bio-indicator of pathophysiology and inflammation, and has consequently been targeted for disease-specific diagnostics [2]. Moreover, the excellent biocompatibility makes Hy useful as a drug delivery system, to which pharmacologically active compounds can be covalently conjugated [3].
Carnosine (Car) is a multifunctional dipeptide widely distributed in several animal species [4]. The variety of physiological properties, including antioxidant, antiglycating, antiaggregant and metal binding abilities, account for the distribution in several tissues and the relative high concentration reached in many cerebral areas [5]. The promising role as a drug is limited by the rapid degradation in serum catalyzed by carnosinase. The bioconjugation of Car through the amino on the carboxylic groups has been proposed as a promising strategy to overcome this limitation [6].
Based on these data, a series of Hy-Car derivatives have been synthesized and patented by us in recent years [7], by using two different molecular weights (200 and 700 kDa) and different loading percentages of carnosine. All of them have been structurally characterized. The antioxidant property of the Hy-Car derivatives and that of their copper(II) complexes has been tested by using several assays and methodological approaches.

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The speciation of zinc complexes with chloroquine ligand

Daniele Vitone, Alessandra Barbanente, Fabio Arnesano

Department of Chemistry, University of Bari, via E. Orabona, 4, 70125 Bari, Italy

Chloroquine (CQ) is a first choice drug against several diseases, such as malaria and lupus, and has recently been used for the emergency treatment of COVID-19 [1]. Lysosomal targeting underlies the possible mechanism of action of CQ [2]. Considering that various pathogens, including SARS-CoV-2, use the endocytic pathway to invade host cells [3], CQ can inhibit pathogen entry through endosomal alkalinization. Other studies indicated that CQ can act as a Zn ionophore and that its cytotoxicity is enhanced by zinc [4]. Zn ions, which lie in lysosomes too, can block coronavirus replication by inhibiting RNA synthesis in vitro and Zn ionophores can stop the pH-dependent replication of these viruses in cell cultures [5]. Although the combination of CQ with Zn has shown some positive results for the treatment of COVID-19 [6], the authorization for the emergency use of this drug and hydroxychloroquine was revoked by FDA due to the high risk/benefit ratio [7]. Moreover, the NIH recommended against the use of CQ for COVID-19 except as part of clinical trials [8]. Hence we deemed of importance to investigate the coordination chemistry of CQ with the aim of obtaining mechanistic insights into the impact of CQ on Zn binding and intracellular distribution. Based on previous findings by Navarro et al. [9,10], we studied the effect of Zn salt additions on both purified CQ and its diphosphate form. The Zn complexes were characterized by solution NMR, ESI-MS, and X-ray absorption methods. The results showed that, depending on the pH and other solution conditions, CQ can bind Zn through different N donor atoms. The findings may lead to the optimization of prophylactic and therapeutic strategies against microbial infections.

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8-Hydroxyquinoline Hybrids Differentially Interact with α-Synuclein

I. M. M. Ahmed[a], F. Bellia[a], V. Oliveri[b], G. Vecchio[b]

[a]Istituto di Cristallografia, Consiglio Nazionale delle Ricerche, P. Gaifami 18, 95126 Catania, Italy; [b]Dipartimento di Scienze Chimiche, Università degli Studi di Catania, Viale A. Doria 6, 95125 Catania, Italy; e-mail: valentina.oliveri@unict.it

The association between protein aggregation and neurodegenerative diseases such as Parkinson's disease (PD) continues to be thoroughly discussed but poorly elucidated at a mechanistic level. Aggregation of alpha-synuclein (α-Syn) is one of the crucial events occurring during synucleinopathies such as PD. Hence, α-Syn has been seen as one of the leading and most compelling targets and is receiving a great deal of attention from researchers [1]. Nevertheless, there is no neuroprotective approach directed towards PD or other synucleinopathies so far. Preventing or reducing aggregation and cytotoxicity of α-Syn is one of the therapeutic strategies proposed but often the interaction of potential aggregation inhibitors and α-Syn is not studied in depth [1,2].
Numerous studies have shown that 8-hydroxyquinolines (HQs) provide neuroprotection in some neurodegenerative disorders [3,4]. Moreover, we have reported that the conjugation of HQs with sugars or other biological molecules could provide a new avenue to the identification of novel and important modulators of protein aggregation such as Aβ, a peptide involved in other neurodegenerative diseases [5,6].
This study comprehensively assesses the interaction ability and inhibitory properties of a series of HQ conjugates with cyclodextrin (CyD), trehalose (Tre), and carnosine (Car) in preventing α-Syn aggregation.
The interaction of α-Syn with HQ hybrids was studied by Native High-Resolution Mass Spectrometry (Native-HRMS), CD spectroscopy, and digestive enzyme studies. Moreover, the effects of HQ hybrids, that show a good interaction with α-Syn, were evaluated on the oligomerization and fibrillation process of α-Syn by Dynamic Light Scattering (DLS) and fluorescence measurements, respectively. Overall, CyD-HQ hybrids were the most effective compounds to interact with α-Syn and modulate its aggregation processes.

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Halogenation Dictates Architectures and Properties of Amyloid Peptides

Andrea Pizzi[a],Claudia Pigliacelli[a], Nicola demitri[b], Francesca Baldelli Bombelli[a], Pierangelo Metrangolo[a], Giancarlo Terraneo[a]

[a]Laboratory of Supramolecular and Bio-NanoMaterials (SupraBioNanoNLab), Department of Chemistry, Materials, and Chemical Engineering "Giulio Natta", Politecnico di Milano, via L. Mancinelli 7, 20131 Milano, Italy; [b]Elettra – Sincrotrone Trieste, S.S. 14 Km 163.5 in Area Science Park, 34149 Basovizza – Trieste, Italy

Besides pathological roles in many diseases, *e.g.*, Alzheimer's, Parkinson's, Creutzfeldt–Jakob, and Huntington's, amyloid peptide architectures have found many other non-biological applications such as forming highly ordered nanomaterials. Together with their biocompatibility and the ease of production, amyloidogenic peptides show a very versatile polymorphic behavior yielding a broad range of hierarchical structures, such as tapes, ribbons, fibers, nanoparticles, and nanotubes.
Subtle variations in the experimental conditions, peptide sequence or its chemical functionalization may impact the self-assembly pathway and, consequently, the resulting nanostructures.
Here we report that depending on the number, position, and nature of the halogen atoms introduced into either one or both phenylalanine benzene rings of the amyloid β peptide-derived core-sequences such as DFNKF (H_2N-Asp-Phe-Asn-Lys-Phe-COOH), KLVFF (H_2N-Lys-Leu-Val-Phe-Phe-COOH) and DSGYEV (H_2N-Asp-Ser-Gly-Tyr-Glu-Val-COOH; Figure 1), different architectures and properties are obtained in a controlled manner [1,2] .

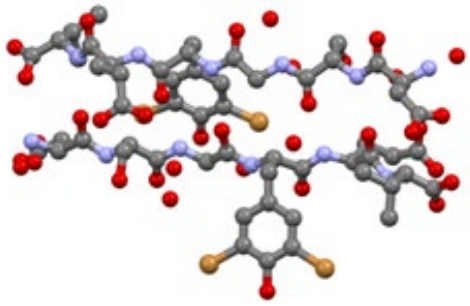

Figure 1. Crystal structure of DSGY(3,5-Br)EV. Asymmetric unit content showing two peptide strands and several water molecules

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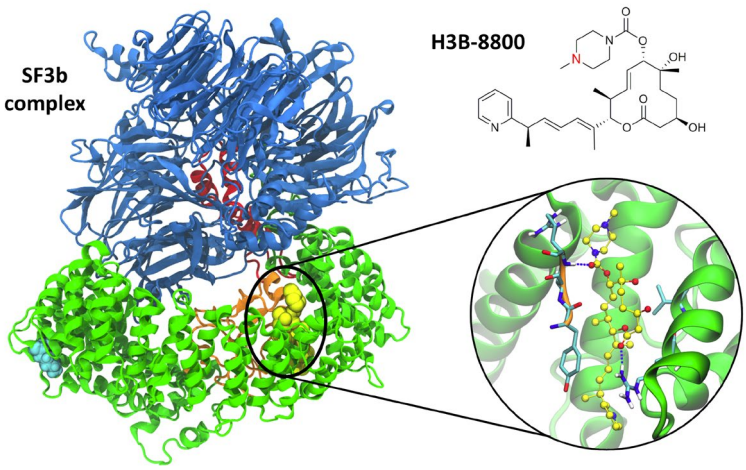
Small-molecule modulators of spliceosome-mutant cancers as a new therapeutic strategy against hematologic malignancies

Angelo Spinello[a], *Jure Borisek*[b], *and Alessandra Magistrato*[a]

[a]*CNR-IOM Democritos c/o International School for Advanced Studies (SISSA), via Bonomea 265, 34136 Trieste, Italy;* [b]*National Institute of Chemistry, Hajdrihova 19, 1000 Ljubljana, Slovenia*

Splicing of precursor messenger RNA, a key step in gene expression, is catalyzed by the spliceosome (SPL), a majestic multi-megaDalton ribonucleoprotein machinery. Mis-regulations of this fundamental biological process are responsible for up to 200 distinct diseases. Indeed, hotspot mutations in genes encoding splicing factors, such as SF3b, are detected at high frequency in samples from patients affected by hematologic malignancies. Among the known splicing modulators only H3B-8800, currently clinical trials, has shown a remarkable selectivity toward cancer cells bearing a mutated SF3b [1]. Recently, we have employed molecular dynamics simulations to obtain an atomic-level understanding of the functional dynamics of the SPL [2] and of the detailed mechanism of action exerted by distinct splicing modulators [3]. We are now applying state-of-the-art computational methods in order i) to shed light into the mechanism underlying the selectivity exerted by the H3B-8800 modulator towards spliceosome-mutant cancers, and ii) to unravel the structural basis for splicing mis-regulation caused by SF3b pathogenic mutations. This key information may pave the way toward the so-called "precision medicine", leading to drugs calibrated on specific patient's genetic profiles.



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Effects of sequence and base composition on the CD and TDS profiles of i-DNA

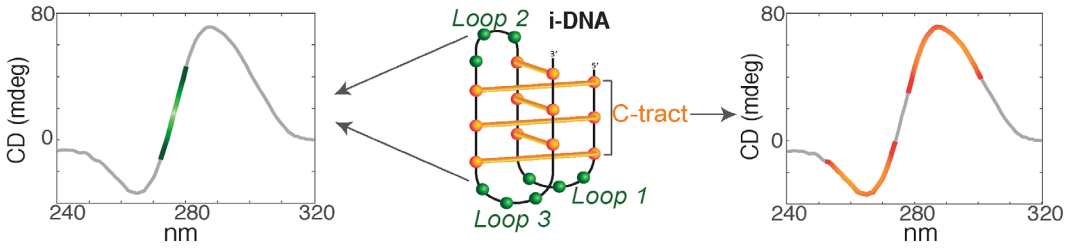
Nunzia Iaccarino[a], *Mingpan Cheng*[b,c], *Dehui Qiu*[b], *Bruno Pagano*[a], *Jussara Amato*[a], *Anna Di Porzio*[a], *Jun Zhou*[c], *Antonio Randazzo*[a], *and Jean-Louis Mergny*[b,c,d]

[a]*Department of Pharmacy, University of Naples Federico II, Via D. Montesano 49, 80131 Naples, Italy;* [b]*State Key Laboratory of Analytical Chemistry for Life Science School of Chemistry & Chemical Engineering, Nanjing University, Nanjing 210023, China;* [c]*ARNA Laboratory, Université de Bordeaux Inserm U1212, CNRS UMR5320, IECB 33607 Pessac, France;* [d]*Laboratoire d'Optique et Biosciences, École Polytechnique CNRS, INSERM, Institut Polytechnique de Paris 91128 Palaiseau, France*

I-motif DNA (i-DNA) is a non-canonical nucleic acid secondary structure which can form in cytosine-rich sequences [1]. Stabilized by acidic conditions *in vitro*, it is comprised of two parallel-stranded DNA duplexes held together by intercalated cytosine–cytosine$^+$ base pairs. In the last decade, i-motif arrangement has been widely investigated because of its presence in many regulatory regions of the genome, such as telomeres and promoters of oncogenes, being a desirable target for anticancer drugs [2].

i-DNA structures provide characteristic circular dichroism (CD) and UV thermal difference (TDS) spectra, whose profiles are affected by the intrinsic propensity of C-rich sequences to fold into different i-motif structures. In this investigation, we have analyzed the CD and TDS of 255 i-DNA-forming sequences by means of a powerful statistical tool, named Multivariate Analysis (MVA), which involves observation and analysis of a great number of variables at a time. Typically, MVA is used to find similarity and dissimilarities of multiple measurements and for this reason it is particularly suitable to study spectroscopic data that are of multivariate nature.

By using such approach, we were able to unveil very informative spectral bands, never considered to be relevant by the researchers working in this field, that showed to carry precious information about distinct i-DNA structural features such as the number of cytosines in the C-tracts and loops' length (see figure). The results of this study have been recently published [3].



Schematic representation of the i-DNA structure (in the middle) and relative CD spectral bands found to carry relevant structural information.

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Spectroscopic study on interactions of porphyrins and micro-RNA

Gabriele Travagliante, Massimiliano Gaeta, Roberto Purrello, Alessandro D'Urso.

Università degli Studi di Catania, Dipartimento di Scienze Chimiche, Viale Andrea Doria, 6, 95125 Catania, Italia; e-mail: travagliantegab@gmail.com

Porphyrins play a multitude of important biological roles such as catalysis, oxygen transport, electron and energy transfer [1]. These macrocycles, being an highly electronic system, show an intense absorption band in the 380–450 nm region called Soret band. When non-chiral substituents are present, porphyrins are achiral molecules therefore do not display any chiroptical signal. However, after interaction, with chiral molecules, an induced circular dichroism (CD) signal can be observed in the Soret absorption band region. This signal arises from chiral distortion of the porphyrin symmetry or intermolecular exciton coupling between at least two chirally oriented chromophores [1]. Although, several achiral cationic or anionic porphyrins have been studied as chiroptical probes to study the secondary structure of different biomolecules in aqueous solution, such as polynucleotides, polypeptides, proteins and so forth [2][3], there is a lack of studies regarding the noncovalent interaction of achiral porphyrins with micro-RNAs (miRNAs). The miRNAs are a class of small noncoding RNAs that regulate gene expression by base-pairing to mRNA targets, causing either target degradation or translational repression. MiRNAs play important roles in immunity response [4], haematopoiesis, developmental timing, cell death, cell proliferation and patterning of the nervous system [5].
Herein, we studied the supramolecular interactions between achiral porphyrins with miRNAs by using several spectroscopic techniques such as UV-Vis, Fluorescence, Resonance Light Scattering, Electronic Circular Dichroism (ECD) and CD-melting. In perspective, will be possible to use different porphyrins, as well as chiroptical probes, to stabilize (or destabilize) the miRNA's secondary structure by supramolecular interactions.

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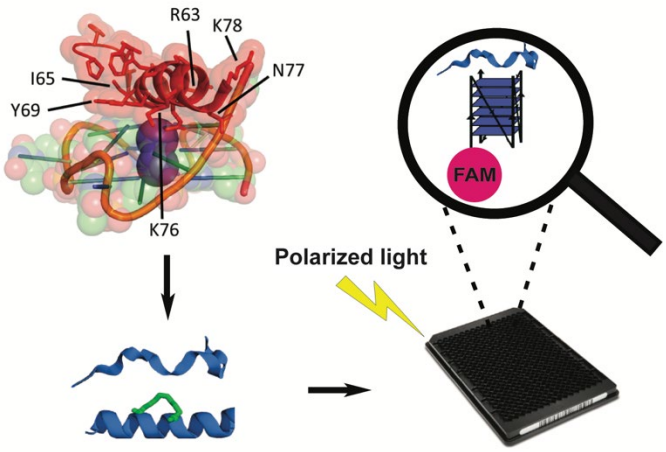
Identification of a short peptide that preferentially binds to the G-quadruplex structure in the c-MYC oncogene promoter

Anna Di Porzio[a], Aisling Minard[b,c], Danielle Morgan[d], Federica Raguseo[b], Denise Liano[b,c], Andrew G. Jamieson[d] and Marco Di Antonio[b,c]

[a] Department of Pharmacy, University of Naples Federico II, Via D. Montesano 49, 80131, Naples, Italy; [b] Imperial College London, Chemistry Department, Molecular Science Research Hub, 80 Wood Lane, W12 0BZ, London, United Kingdom; [c] Institute of Chemical Biology, Molecular Science Research Hub, 80 Wood Lane, W12 0BZ, London, UK; [d] School of Chemistry, University of Glasgow, G12 8QQ, Glasgow, United Kingdom

Besides the canonical double helix, there is increasing evidence suggesting that, under physiological conditions, DNA can also fold into various alternative arrangements such as G-quadruplexes (G4s) [1]. Sequences that form G4s are highly abundant and mostly occur in functional regions of the human genome [2]. The investigation of the biological processes regulated by G4-stabilization mainly relies on the use of small molecule ligands that can be applied in living cells and monitored in real-time. However, none of the compounds reported so far is selective for a specific G-quadruplex structure, or a small subset of G4s, over the ~700,000 available in the human genome. Therefore, selective tools are needed to unravel the biology behind an individual G4. In this work, we extracted the sequence of a short peptide from the crystal structure of the bovine DHX36 helicase bound to the G4 formed in the promoter region of the oncogene c-MYC and developed a fluorescence polarization assay to measure its binding affinity towards a small panel of parallel and non-parallel G4s. Interestingly, the peptide showed to preferentially bind (with nM affinity) to the c-MYC G-quadruplex, paving the way for developing a MYC-selective probe for disentangling the biological role of this particular G-quadruplex structure over the others [3].



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Talking about urease: how the grasp on the molecular aspects of this enzyme can help in counteracting its role in microbial pathogenesis and environmental issues

Luca Mazzei and Stefano Ciurli

Laboratory of Bioinorganic Chemistry, Dept. of Pharmacy and Biotechnology, University of Bologna, Italy

Urease is a Ni(II)-enzyme that plays a prominent role in the global nitrogen cycle by catalyzing the hydrolysis of urea to give ammonia and carbon dioxide [1]. The overall increase of pH associated with this reaction negatively affects both human health and the environment, therefore the development of urease inhibitors is necessary [1]. For this purpose, the knowledge of all steps of the catalytic mechanism at the molecular level is essential, but the very short lifetime of urea in the active site of urease has so far impeded this achievement.
In this work, a summary of the research carried out on urease in our laboratory is presented. First, the structural characterization of the urea binding mode in the active site of urease in the initial step of the catalytic mechanism was obtained by the determination of the X-ray crystal structure of the urease–urea complex in which the enzyme reactivity has been abolished by substituting a reactive Ni-bridging hydroxide with fluoride [2]. Additionally, the mobility of the active site flap, that covers the active site and plays a key role in the catalytic mechanism by switching from an *open* to a *closed* state, has been proved to be influenced by the pH through the determination of urease structures at different pH values [3]. Finally, the importance of the flap mobility for the catalytic mechanism was exploited to develop an alternative urease inhibition strategy based on the conformational blockage of the flap in an *open* state, that in turn prevents the urease-catalyzed urea hydrolysis from occurring. In this context, a structural and biochemical characterization for urease inhibition by transition metal ions such as Ag(I) [4,5] and Au(III) [6], as well as poly-hydroxylated aromatic molecules such as catechols [7,8], was carried out. These results constitute the basis for the design of new compounds as selective urease inhibitors with antibacterial applications.

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Uncovering the emergence of modern cells

Claudia Bonfio[a,b]

[a]*Department of Chemistry, Imperial College London, Molecular Sciences Research Hub, London W12 0BZ, United Kingdom;* [b]*Yusuf Hamied Department of Chemistry, University of Cambridge, Cambridge CB2 1EW, United Kingdom; e-mail: cb2036@cam.ac.uk*

The complexity of modern biochemistry suggests that a systems chemistry approach is required to understand and potentially recapitulate the intricate network of prebiotic reactions that led to the emergence of life. Early cells probably relied upon compatible and interconnected chemistries to link RNA, peptides and membranes. I'll describe networks of potentially prebiotic reactions in which the components of primitive cells could have spontaneously accumulated, interacted and yielded new species, which enabled the emergence of cells with increasingly advanced functionalities.

Exploring $\alpha_v\beta_5$-RGDechi15D peptide interactions on living cells surface using NUS/T1ρ-NMR methodologies

Clementina Acconcia[a], Biancamaria Farina[b], Maria Teresa Gentile[a], Sonia Di Gaetano[c], Domenica Capasso[d], Annarita Del Gatto[c], Antonella Paladino[e], Michele Saviano[f], Roberto Fattorusso[a], Laura Zaccaro[c] and Luigi Russo[a]

[a]Department of Environmental, Biological and Pharmaceutical Science and Technology, University of Campania - Luigi Vanvitelli, via Vivaldi 43, 81100 Caserta, Italy; [b]Advanced Accelerator Applications, a Novartis Company, via Vivaldi 43, 81100 Caserta, Italy; [c]Institute of Biostructures and Bioimaging-CNR, via Mezzocannone 16, 80134, Naples, Italy; [d]Interdepartmental Center of Bioactive Peptide, University of Naples Federico II, Via Mezzocannone 16, 80134 Naples, Italy; [e]Department of Science and Technology, University of Sannio, via Francesco de Sanctis, Benevento 82100, Italy; [f]Institute of Crystallography-CNR, via Amendola 122/O, 70126 Bari, Italy

Structural investigations of receptor-ligand interactions on living cells surface by high-resolution Nuclear Magnetic Resonance (NMR) are problematic due to their short lifetime, which often prevents the acquisition of experiments longer than few hours [1,2]. To overcome these limitations, we developed an on-cell NMR-based approach for exploring the molecular determinants driving the receptor-ligand recognition mechanism under native conditions. In particular, our strategy relies on the combination of high-resolution NMR data with Molecular Dynamics simulations and Molecular Docking studies. The key point of our methodologies is the application of Non Uniform Sampling (NUS) and T1ρ-NMR techniques to collect atomic-resolution structural and dynamics information on the receptor-ligand interactions using living cells, which can be used as conformational constraints in computational studies. This approach has been tested to describe the molecular determinants regulating the recognition process of the $\alpha_v\beta_5$-integrin/RGDechi15D complex [3,4]. This peptide is a selective cyclic molecule able to interfere with some relevant steps for tumor proliferation and progression and to decrease the formation of new vessels in endothelial cells. Our data demonstrate that the developed strategy represents an alternative in-cell NMR tool for studying, at atomic resolution, receptor-ligand recognition mechanism on the living cells surface.

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4-Amino-TEMPO loaded liposomes as EPR probes for detection of phospholipase A2 activity

Diego Alberti, Sabrina Elkhanoufi, Rachele Stefania, Simona Baroni, Silvio Aime and Simonetta Geninatti Crich

University of Torino, Department of Molecular Biotechnology and Health Sciences, Italy

Quantitative measurement of marker expression in diseased cells is still a topic of considerable interest and different methodologies are currently under intense scrutiny. Personalized medicine approaches require the development of fast, sensitive, and quantitative methods for the measurements of clinically relevant markers in order to propose the best treatment for each patient. This work aims at developing an in vitro diagnostic method based on Electron Paramagnetic Resonance (EPR) measurements of stable nitroxide radicals released from "EPR silent" liposomes. The liposome destabilisation and consequent radical release is enzymatically triggered by the action of phospholipase A2 (PLA2) present in the biological sample of interest. Liposomes composed of POPC:Cholesterol:DSPG:DSPE-PEG2000 (55:35:5:5 molar ratio) are prepared using the thin-film hydration method followed by extrusion. They are able to encapsulate ca. 15mM 4-Amino-TEMPO exploiting an ammonium sulphate gradient. Preliminary in vitro measurements demonstrated the high sensitivity and specificity of the method with a limit of detection (LOD) of PLA2 in physiological buffer (3.5 h 37 °C) of 6.7 U/L according to the most sensitive fluorescence assays (3 U/L) [1]. PLA2 is a large superfamily of proteins with a hydrolytic activity against phospholipids, which can selectively cleave fatty acid at the second position (sn-2) of phospholipid. PLA2 enzymes are found in all mammalian tissues including plasma and serum [2]. PLA2 has also been identified as a potential target of cancer therapy. They are excreted at the extracellular side of the plasma membrane and are overexpressed in a variety of tumors, e.g., up to 22-fold in prostate cancer [3]. Furthermore, it was also observed that plasma sPLA2 level increase in covid 19 patients with a concomitant dramatic depletion of plasma phospholipids concentration. The hydrolysis of phospholipids and formation of lyso phospholipids operated by PLA2 enzyme activity suggests its influence in progression of pathogenesis of covid 19 [4]. Therefore, a comprehensive assay system in which the activity of each of these PLA2s can be measured sensitively and selectively in biological samples is crucial to advancing the understanding of their respective roles in physiological and pathophysiological processes. Finally, the main objective is to overcome current limitations in the in vivo enzyme activity detection in a pathological tissue by Overhauser MRI.

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Towards the use of nanoparticles to redirect the aggregation of amyloidogenic proteins: study of the conformational transitions of protein tau at the nano-bio interface

Carlo Giorgio Barracchia, Franceca Munari, Francesca Parolini, Roberto Tira, Giovanna Viola, Mariapina D'Onofrio, Michael Assfalg

Department of Biotechnology, University of Verona, Italy

The abnormal deposition in the brain of misfolded protein fibrils is a hallmark event in many neurodegenerative disorders (NDs) [1,2]. The pathogenesis of these diseases remains unclear and the cures are currently lacking [3]. Perturbing the dynamics of these aggregation processes with small molecules, macromolecules, and nanoparticles (NPs) is a breakthrough in the field of research, offering the possibility to redirect the formation of neurotoxic aggregates [4,6].
NPs have emerged as attractive aggregation modulators and were found to either accelerate or inhibit fibrillogenesis, depending on their properties [3,7]. However, despite intense investigation, our understanding of how amyloidogenic proteins interact with NPs remains limited.
In our work, we focus on the protein tau, whose insoluble filaments are associated with Alzheimer's disease and several other disorders, collectively referred to as tauopathies. We combine biophysical techniques, such as circular dichroism and solution nuclear magnetic resonance spectroscopy, with biochemical methods to characterize the adsorbed protein molecules and the NP-induced conformational perturbations.
The collected data will serve to establish quantitative relationships between NPs features and protein conformational preferences, thereby providing the basis for the rational design of anti-amyloidogenic NPs.

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TOAC *vs*. Cys(MTSL): is Cys(MTSL) the best residue candidate for helical peptide spin labeling?

B. Biondi[a], G. Rocchio[b], V.N. Syriamina[c], A. Barbon[b], F. Formaggio[a,b], C. Toniolo[a,b], J. Raap[d], S.A. Dzuba[c]

[a] Institute of Biomolecular Chemistry, Padova Unit, CNR, 35131 Padova, Italy; [b]Department of Chemical Sciences, University of Padova, 35131 Padova, Italy; [c]Institute of Chemical Kinetics and Combustion, RAS, Novosibirsk 630090, Russian Federation; [d]Leiden Institute of Chemistry, Gorlaeus Laboratories, Leiden University, 2300 RA Leiden, The Netherlands

Site-directed spin labeling (SDSL) in combination with electron paramagnetic resonance (EPR) spectroscopy is a very effective biophysical method to analyze structure and dynamics of proteins in physiological conditions [1]. To evaluate the reliability in distance measurements of different spin labels, we designed and synthesized a 20-mer long model peptide and two analogs with a well-defined Aib-generated, stable α-helical structure. We introduced, at fixed separations (14 residues, about 2.2 nm), two α-amino acid residues of the helicogenic 2,2,6,6-tetramethylpiperidine-1-oxyl-4-amino-4-carboxylic acid (TOAC) or two S-(1-oxyl-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl)methyl (MTSL) groups conjugated to cysteines (Cys) in the sequence, respectively (Figure 1). The latter nitroxyl labeling methodology is by far the most widely utilized in protein investigations.

	peptide sequence
I	Ac-Aib-Lys-Aib-Ala-(Aib-Lys-Aib-Ala)$_3$-Aib-Ala-Aib-Lys-NH_2
II	Ac-Aib-Lys-**TOAC**-Ala-(Aib-Lys-Aib-Ala)$_3$-**TOAC**-Ala-Aib-Lys-NH_2
III	Ac-Aib-Lys-Aib-Cys(**MSTL**)-(Aib-Lys-Aib-Ala)$_3$-Aib-Cys(**MSTL**)-Aib-Lys-NH_2

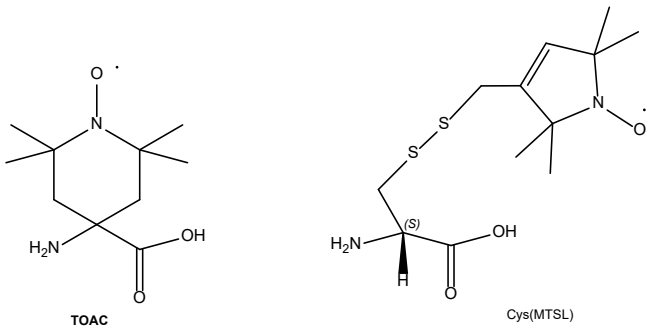

Figure 1. Peptide sequences and chemical structures of the TOAC and L-Cys(MTSL) spin labeled residues.

Through an in-depth conformational analysis (FT-IR absorption, CD and NMR), we confirmed a stable α-helical structure for all three peptides in different (water, methanol) environments.
Our detailed EPR analysis took advantage from both continuous-wave (CW) and double electron-electron resonance (DEER) experiments. The DEER data indicated a much narrower distance distribution for the TOAC-labeled peptide as compared with that of its MTSL-labeled counterpart. In the latter case, the experimental distance distribution exhibits two maxima which unambiguously point to the existence of two labeled conformers. We conclude that TOAC labels are much more rigid than MTSL labels, therefore providing more precise data on distance distributions in helical peptides.

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Thermally-driven membrane phase transitions enable content reshuffling in primitive cells

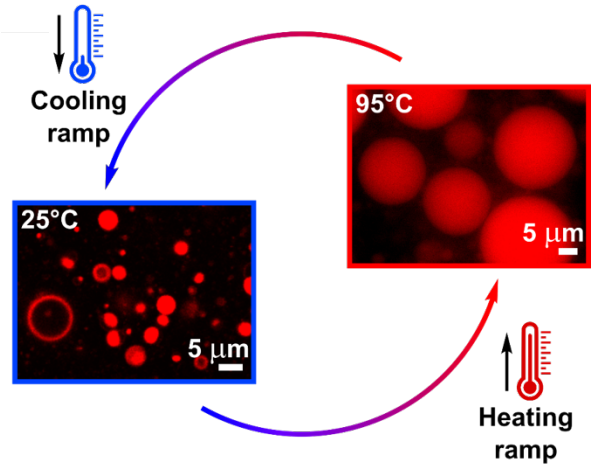
Roger Rubio-Sánchez[a], Derek O'Flaherty[b], Anna Wang[c], Francesca Coscia[d,e], Lorenzo Di Michele[f], Pietro Cicuta[a], Claudia Bonfio[d,g]

[a]Biological and Soft Systems, Cavendish Laboratory, University of Cambridge, Cambridge CB3 0HE, United Kingdom; [b]Department of Chemistry, University of Guelph, Guelph ON N1G 1Y4, Canada; [c]School of Chemistry, University of New South Wales, Sydney, New South Wales 2052, Australia; [d]Medical Research Council Laboratory of Molecular Biology, Cambridge Biomedical Campus, Cambridge CB2 0QH, United Kingdom; [e]Fondazione Human Technopole, Structural Biology Research Centre, Milan, Italy; [f]Department of Chemistry, Imperial College London, Molecular Sciences Research Hub, London W12 0BZ, United Kingdom; [g]Yusuf Hamied Department of Chemistry, University of Cambridge, Cambridge CB2 1EW, United Kingdom; e-mail: cb2036@cam.ac.uk

Self-assembling single-chain amphiphiles available in the prebiotic environment likely played a fundamental role in the advent of primitive cell cycles. However, the instability of prebiotic fatty acid-based membranes to temperature and pH seems to suggest that primitive cells could only host prebiotically-relevant processes in a narrow range of non-fluctuating environmental conditions.

We propose that membrane phase transitions, driven by environmental fluctuations, enabled the generation of daughter protocells with reshuffled content. A reversible membrane-to-oil phase transition accounts for the dissolution of fatty acid-based vesicles at high temperatures, and the concomitant release of protocellular content. At low temperatures, fatty acid bilayers reassemble and encapsulate reshuffled material in a new cohort of protocells. Notably, we find that our disassembly/reassembly cycle drives the emergence of functional RNA-containing primitive cells from parent non-functional compartments. Thus, by exploiting the intrinsic instability of prebiotic fatty acid vesicles, our results point at an environmentally-driven tunable prebiotic process, which supports the release and reshuffling of oligonucleotides and membrane components, potentially leading to a new generation of protocells with superior traits.

In the absence of protocellular transport machinery, the environmentally-driven disassembly/assembly cycle proposed herein would have supported protocellular content reshuffling transmitted to primitive cell progeny, hinting at a potential mechanism important to initiate Darwinian evolution of early lifeforms.



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Gold Nanoparticles as sensing probes for bacteria identification

C. M. Cafiero, L. Pasquato, P. Tecilla, P. Pengo

Dipartimento di Scienze Chimiche e Farmaceutiche, Università degli Studi di Trieste, Via Giorgieri 1, 34127 Trieste, Italy

Gold nanoparticles (AuNPs) have been regarded as optimal scaffolds for developing bacteria sensing platforms [1]. Indeed, the AuNPs surface can be easily functionalised with biomolecular recognition motifs, obtaining multivalent monolayers on the AuNPs with tailored bacteria-AuNPs affinity [2]. Our activity is focused on the development of an analytical method for bacteria identification using polymer-coated AuNPs as sensing elements [3]. Two sets of functionalised thiols (figure 1) have been designed and synthetised to modulate the hydrophobic properties of AuNPs surface and, consequently, the interactions between AuNPs and the bacterial cell wall. The first series of ligands (figure 1A) is composed by hydrogenated and fluorinated thiols with different chain length to achieve AuNPs with hydrophobic and hydrophilic domains of different morphologies [4,5]. In the second set of ligands (figure 1B) the presence of different peptide moieties is expected to enhance the site-specific interactions with the molecular patterns present on the bacterial wall.

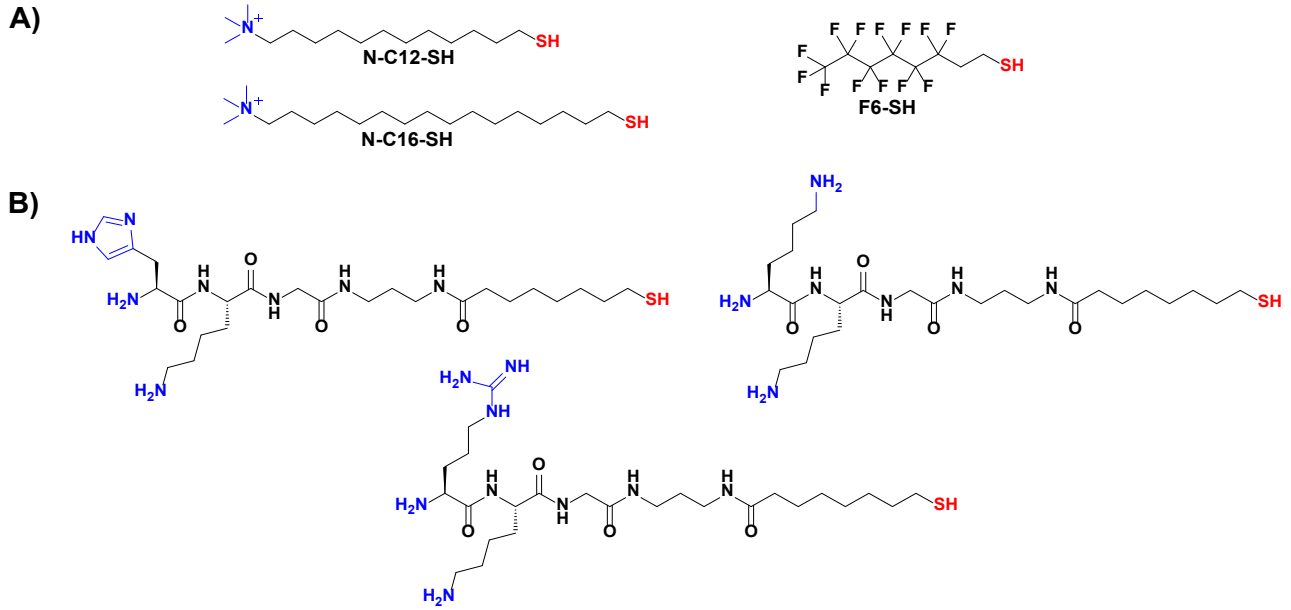

Figure 1. Two sets of functionalised thiols for water-soluble AuNPs preparation

Different anionic fluorescent polymers have been chosen to coat the AuNPs. These polymers will be released into solution upon interaction of the AuNPs-polymer composite with bacteria, providing fluorescence profiles dependant on the AuNPs-bacteria affinity and thus allowing the differentiation of bacteria strains.

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Impact of polystyrene nanoparticles on the structure and dynamics of biological macromolecules

Maria della Valle[a], Gianluca D'Abrosca[a], Marica Sassano[a], Luigi Russo[a], Carla Isernia[a], Roberto Avolio[b], Mariacristina Cocca[b], Maria Emanuela Errico[b], Gennaro Gentile[b], Gaetano Malgieri[a] and Roberto Fattorusso[a]

[a]*Departmennt of Environmental, Biological and Pharmaceutical Science and Technology, University of Campania – Luigi Vanvitelli, via Vivaldi 43, 81100 Caserta, Italy.*
[b]*Institute for Polymers, Composites and Biomaterials - CNR, via Campi Flegrei 34, 80078 Pozzuoli, Naples, Italy.*

The universal presence of micro- and nano-plastics and their unknown effects on the various biological systems are, to date, a significant concern. Plastic debris can be fragmented into smaller pieces by many physical and chemical processes, generating its own micro- and nano-plastics. Recently, this debris was shown to affect biota and to be gradually spreading through the food chain, becoming dangerous to humans [1].
In order to understand if nano-plastics (i.e polystyrene) may induce conformational changes that in turn inactivate biological macromolecules, we performed a structural and dynamical characterization of the human ubiquitin in the presence of polystyrene nanoparticles by using a multidisciplinary approach in which TEM (Trasmission Electron Microscopy) and CD (Circular Dichroism) data were integrated with high-resolution NMR (Nuclear Magnetic Resonance) methodologies. Overall, our data strongly indicate that the addition of polystyrene to the ubiquitin induces structural perturbations that activate aggregation processes.

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Helix coiled-coil formation in Glu/Lys peptides detected by EPR and CD

Elena A. Golysheva[a,b], Aimee L. Boyle[c], Barbara Biondi[d], Paolo Ruzza[d], Alexander Kros[c], Jan Raap[c], Claudio Toniolo[d,e], Fernando Formaggio[d,e], Sergei A. Dzuba[a,b]

[a]Novosibirsk State University, Novosibirsk 630090, Russian Federation; [b]V.V. Voevodsky Institute of Chemical Kinetics and Combustion, Novosibirsk 630090, Russian Federation; [c]Leiden Institute of Chemistry, Gorlaeus Laboratories, Leiden University, 2300 RA Leiden, The Netherlands; [d]Institute of Biomolecular Chemistry, Padova Unit, CNR, 35131 Padova, Italy; [e]Department of Chemical Sciences, University of Padova, 35131 Padova, Italy

Electron paramagnetic resonance (EPR) and circular dichroism (CD) spectroscopies were exploited for investigating the features of peptide aggregates formed by peptides rich in Glu and Lys [1]. This type of peptides is known to self-recognize and form helix coiled-coil heterodimers. We synthesized two Lys- or Glu-containing peptides and two analogs, each incorporating two paramagnetic TOAC residues (Figure 1) [2]. We then performed a three-dimensional structural investigation on the labeled peptides in the presence or absence of their unlabeled counterparts.

The TOAC spin-labels, replacing two Ala residues in each compound, are covalently and quasi-rigidly connected to the peptide backbone. They are known not to disturb severely the native structure, so that any conformational change can easily be monitored and assigned. Double electron-electron resonance (DEER, also known as PELDOR) is an EPR technique that enables the measurement of the intramolecular electron spin-spin distance distribution between two paramagnetic labels, within a length range of 1.5-8 nm. Therefore, this method allowed us to investigate the conformational changes occurring in our self-assembled systems, by analyzing the distance distributions between the well-defined unpaired nitroxide oxygen atoms.

In a phosphate buffer, the labeled Lys-analog was shown to form oligomers, but it produced coiled-coil heterodimers in the presence of the stabilizing, unlabeled Glu-peptide. DEER allowed also to detect differences between this peptide heterodimer and the Glu-labeled/Lys-unlabeled combination. Our CD analysis strongly support these conclusions. In particular, the conformations of the spin-labeled peptides are strongly influenced by the presence of their counterparts.

In summary, combined DEER/TOAC approach is a powerful tool to obtain accurate and reliable information about the conformation of helical peptides before and after their assembly into coiled-coil heterodimers.

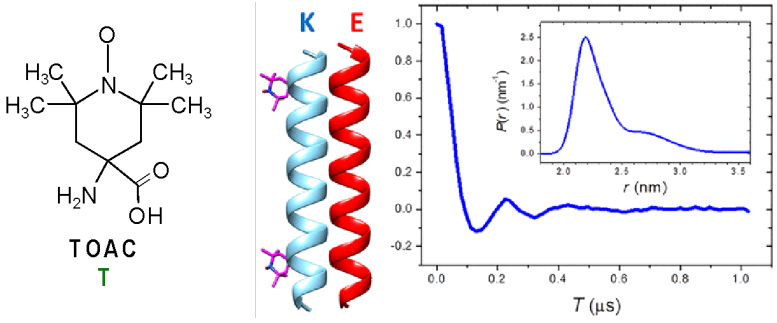

Figure 1. Amino acid sequences of the peptides used in this investigation (left), chemical structure of the paramagnetic α-amino acid TOAC (center), and example of a DEER signal and a distance distribution between labels (right).[2]

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SARS-CoV-2 M^{pro} inhibition by zinc ion: structural features and hints for drug design

Deborah Grifagni[a], *Vito Calderone*[a,b], *Stefano Giuntini*[a], *Francesca Cantini*[a,b], *Marco Fragai*[a,b] *and Lucia Banci*[a,b]

[a]*Magnetic Resonance Center (CERM), University of Florence, via Sacconi 6, Sesto Fiorentino, 50019 Italy;* [b]*Department of Chemistry "Ugo Schiff", University of Florence, via della Lastruccia 3, Sesto Fiorentino, 50019 Italy*

SARS-CoV-2 main protease (SARS-CoV-2 M^{pro}) is a cysteine protease that hydrolyses the viral polyproteins at several sites with a preference for the Leu-Gln(Ser, Ala, Gly) sequences [1,2]. The enzyme represents one of the main drug-target candidates for covid-19 syndrome because the large and deep pocket at the active site and its crucial activity for viral replication [3,5].
Here, we provide X-ray structural data on SARS-CoV-2 main protease in complex with the isolated Zn^{2+} ion. The comparison with the apo SARS-CoV-2 M^{pro} shows that residues involved in zinc binding are not affected by significant structural rearrangement upon zinc binding supporting the idea that the binding site is ready to accommodate the metal.
The interaction of SARS-CoV-2 M^{pro} with Zn^{2+} ion was also investigated by NMR. Moreover, zinc binding is able to inhibit protein activity, demonstrating that the zinc ion is capable of an efficient binding also in solution. These findings provide a solid ground for designing potent and selective inhibitors of SARS-CoV-2 M^{pro} suggesting that a zinc ion incorporated into suitable ligands interacting with additional sites at the protein surface can modulate the binding energy binding energy.

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Ubiquitin and its pivotal role in proteostasis: insights on interactions with proteins and drugs

Valeria Lanza, Danilo Milardi

Consiglio Nazionale delle Ricerche - Istituto di Cristallografia Via P. Gaifami 18, 95126 Catania, Italy; e-mail: valeria.lanza@cnr.it

Ubiquitin (Ub) is a major actor in protein homeostasis. Ub manages proteins turnover and, in turn, a plethora of regulatory pathways such as DNA damage and repair, cell cycle progression, apoptosis, receptor-mediated endocytosis, and signal transduction [1]. Alterations in Ub pathways often lead to pathological conditions. The Ub pathway involves an unusual combination of many specific enzymatic proteins that target nearly all short-lived and abnormal proteins for proteasomal degradation.

The study of the interaction of ubiquitin with proteins involved in misfolded diseases and with drug molecules is a promising approach for the design of new therapeutic strategies for many disorders [ref]. Here, we describe two examples of these interactions: i) with nerve growth factor and ii) amyloid beta peptide [2]. First, we highlighted the existence of a copper(II)-dependent association between Ub and NGF and indicated that the N-terminal domain of NGF was a valuable paradigm that recapitulated many traits of the full-length protein. Moreover we also demonstrated that Aβ40 binds Ub with a 1 : 1 stoichiometry and Kd in the high micromolar range [3]. The effects of drugs on ubiquitination pathway, has been also investigated and we reported how some molecules activate the ubiquitination pathway, as silibins.

The non-covalent interaction between small molecules and Ub may have relevant effects on the regulation of the upstream events of the UPS and pave the way to future in vivo studies addressing the role played by this drugs in the malfunction of proteome maintenance occurring in several pathologies.

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Structural insight into YAP-TEAD4 protein-protein interactions as target for cancer treatment

Ludovica Lopresti[a], *Cecilia Pozzi*[b], *Lorenzo Tagliazucchi*[c], *Domenico D'Arca*[b], *Gaetano Marverti*, *Maria Paola Costi*[c], *and Stefano Mangani*[a]

[a]*Dipartimento di Biotecnologie, Chimica e Farmacia, Università degli Studi di Siena, Siena, Italy;* [b]*Dipartimento Neurobiomet and* [c]*Dipartimento di Scienze della Vita, Università degli Studi di Modena e Reggio Emilia, Modena, Italy; e-mail: lopresti4@student.unisi.it*

The Hippo pathway is a signalling network which plays a key role in tissue homeostasis and organ size control, by regulating cell growth, proliferation and apoptosis. Once activated, the signalling transduction involves a core kinase-cascade, resulting in the phosphorylation, cytoplasmic retention and subsequent degradation of the Yes-associated protein (YAP). YAP is a DNA transcription co-activator without an intrinsic DNA binding domain, which, in its hypo-phosphorylated status, translocates into the nucleus and directly interacts with several DNA-binding partners. In mammalian cells, YAP primarily binds all four transcriptional enhancer associate domain (TEAD1-4) family members [1]. Since TEADs transcription factors are, in turn, unable to induce gene transcription, the interaction between YAP and TEAD is essential for the expression of Hippo pathway-downstream genes, involved in cell proliferation and apoptosis [2]. All four human TEADs (hTEADs) allocate an acylation binding site that is occupied by palmitic/myristic acid in physiological condition, but the influence of TEAD acylation on YAP:TEAD interaction is yet not fully understood [3]. Dysregulations of the Hippo pathway are associated with tumorigenesis, thus targeting YAP:TEAD interaction is an emerging, attractive therapeutic strategy in the oncology field [4]. To date, very few YAP:TEAD4 inhibitors have been reported and the development of new molecules targeting this protein complex remains challenging [5]. Structural information is missing and more work is necessary to contribute to function and ligand design.

Here, we report the development of reliable protocols for co-expression, co-purification and crystallization of the TEAD-binding domain (TBD) of human YAP (hYAP) (fragment 50-171) in complex with the C-terminal YAP-Binding Domain (YBD) of hTEAD4 (residues 217-434). Crystals of the hYAP-hTEAD4 complex were obtained using the microseeding crystallization technique, leading us to obtain the first structural characterization of the de-acylated state of this complex. The overall structure of de-acylated TEAD4 closely resembles that of the acylated protein in agreement with the biochemical and cellular assays of Mesrouze et al [3], assessing that acylation is not required for the interaction with hYAP, but it contributes to TEAD4 stability. However, some differences have been detected in the conformation of hYAP1 and in the orientation of its flexible N-terminal region.

Our investigation aims to the unveil the mechanisms regulating YAP:TEAD4 protein-protein interactions to support the rational design of new TEAD4 binder, preventing the formation of the complex.

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Targeting of telomeric repeat-containing RNA G-quadruplexes: from screening to biophysical characterization of a new hit compound

Simona Marzano, Nunzia Iaccarino, Antonio Randazzo, Bruno Pagano, Jussara Amato

Department of Pharmacy, University of Naples Federico II, Naples 80131, Italy

G-quadruplexes (G4s) are non-canonical nucleic acids secondary structures which emerged as very attractive targets in anticancer strategies. Indeed, guanine-rich tracts, potentially able to fold into G4s, are mainly found in telomeres and oncogene promoters [1,2]. Telomeres can be transcribed into RNA transcripts of telomeric repeats (TERRA), which also have a characteristic G-rich repeat sequence of r(5′-UUAGGG-3′) and form G4s [3]. Beside regulating telomerase activity and protecting chromosome ends from telomere degradation, TERRA G4s have been shown to take part in heterochromatin formation and homologous recombination [4,5]. Thereby, designing small molecules targeting TERRA G4s may represent a more valuable therapeutic strategy than targeting of their DNA counterparts.
Herein, to identify novel TERRA binders, we have employed a receptor-based virtual screening approach by using the G4-forming sequence 5′-UAGGGUUAGGGU-3′. From this screening, a total of 103 putative ligands were identified. Their ability to bind and thermally stabilize TERRA was then evaluated by means of circular dichroism spectroscopy, which allowed to select 6 candidates. Their affinity towards TERRA was then evaluated by fluorescence intercalator displacement (G4-FID) assay with thiazole orange. Interestingly, one out of the six compounds (B3H6) showed a significantly higher affinity compared to the other compounds, thus its TERRA *vs.* DNA G4s and TERRA *vs.* DNA/RNA duplex selectivity, was investigated through FID assays. Since B3H6 turned out to be a selective compound, it was also submitted to an ethidium bromide displacement assay, which demonstrated stacking interactions with the external G-tetrads. To further characterize B3H6 as promising ligand of TERRA, microscale thermophoresis experiments to determine the binding constant, and biological assays to evaluate its activity are ongoing in our laboratory.

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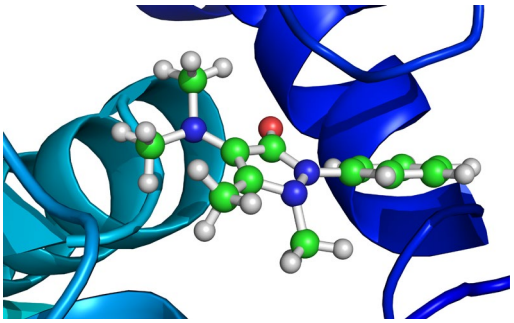
Aminopyrine activates the 20S proteasome and protects SH-SY5Y cells from amyloid toxicity

A. M. Santoro[a], V. Lanza[b], F. Bellia[a], D. Sbardella[b], G. R. Tundo[b], A. Cannizzo[c], G. Grasso[c], M. Arizzi[c], V. G. Nicoletti[d], S. Alcaro[e], G. Costa[e], A. Pietropaolo[e], G. Malgieri[f], G. D'Abrosca[f], R. Fattorusso[f], S. García-Viñuale[a], I. M. M. Ahmed[a], M. Coletta[b], D. Milardi[a]

[a]*Institute of Crystallography, CNR;* [b]*University of Rome Tor Vergata, Italy;* [c]*University of Catania, Italy;* [d]*BIOMETEC, University of Catania, Italy;* [e]*University Magna Graecia of Catanzaro, Italy;* [f]*University of Campania "Luigi Vanvitelli", Italy*

The proteasome is a multi-subunit enzyme responsible for the hydrolysis of many cytosolic proteins.[1] Accumulating evidence suggests that proteasome malfunction is normally associated with neurotoxic amyloid growth in the brain of patients affected by Alzheimer's Diseases (AD).[2] Therefore, proteasome activation is attracting increasing attention as a novel target in AD therapy. Pyrazolones are a class of synthetic drugs extensively employed as painkillers for more than a century. Inspired by recent reports pointing to pyrazolones as proteasome activators and attracted by the option to repurpose medicines and de-risk the drug development, we screened a small library of drugs by assaying their capacity to activate proteasome. Tube tests showed that aminopyrine activates proteasome through binding the α-ring surfaces and influencing its gating dynamics. Docking studies coupled with STD-NMR experiments showed that H-bonds and π-π stacking interactions between active pyrazolones and the enzyme play a key role in stabilizing the drug-target complex. Aminopyrine exhibits neurotrophic properties and protect differentiated human neuroblastoma SH-SY5Y cells from β-amyloid (Aβ) toxicity.



Our results point to aminopyrine as a neuroprotective proteasome activator and may pave the way to the development of new strategies for the treatment of AD.

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The monoamine oxidase inhibitor M30 as a multifunctional agent in the treatment of diseases related to metal dyshomeostasis

S. Scavo, V. Oliveri

Dipartimento di Scienze Chimiche, Università degli Studi di Catania, Viale A. Doria 6, 95125 Catania, Italy; e-mail: valentina.oliveri@unict.it

Neurodegenerative diseases, such as Alzheimer's Disease (AD), are multifactorial disorders, characterized by a variety of neurological symptoms, protein aggregation, oxidative stress, neurotransmission dysfunctions and metal dyshomeostasis [1]. In particular, copper dyshomeostasis and amyloid-beta (Aβ) represent key pathological features of AD [2].
Currently, several molecules with different mechanisms of action have been proposed for the treatment of AD. Among them, there is the class of 8-hydroxyquinolines (HQs), which can influence some potential causes responsible for neurodegeneration. An HQ derivative, known as M30, has shown some antineurodegenerative properties in animal models of Parkinson's disease and its properties have been attributed to its monoamine oxidase inhibitory action [3].
Herein, we demonstrate the ability of M30 to interact with copper ions and toxic species produced by copper-amyloid interactions through various experimental methods. In particular, the ability of M30 to suppress the protein aggregation and to inhibit the oxidation of ascorbate (ROS formation) induced by Cu(II) ions, both in the absence and in the presence of Aβ, were evaluated by UV-vis spectroscopy and circular dichroism (Figure 1). Overall, the obtained results suggest that M30 can act as a multifunctional agent, targeting and suppressing copper toxic species.

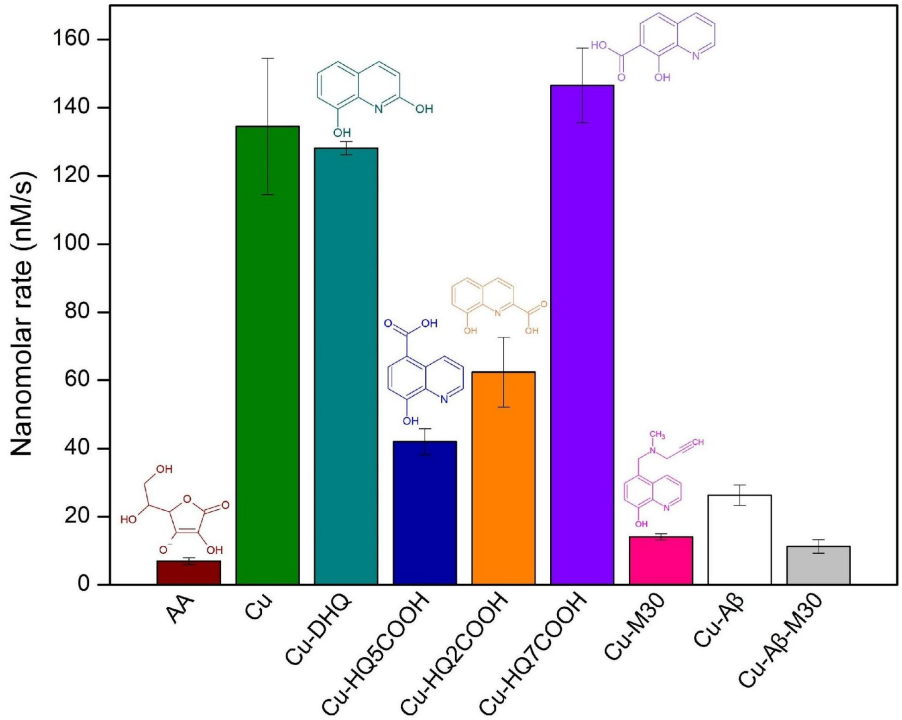

Figure 1. Initial oxidation rate of ascorbate (AA) alone and in the presence of Cu, Cu-complexes of HQs, such as M30, in the presence and in absence of Aβ.

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A novel iron(III)-based MRI contrast agent endowed with remarkable molecular and functional properties

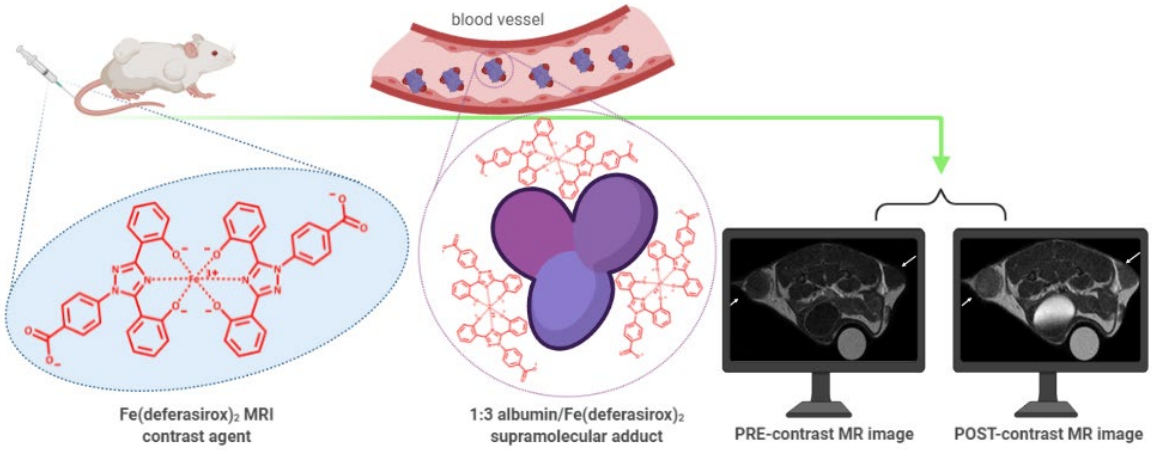
Lorenzo Palagi[a], *Enza Di Gregorio*[a], *Diana Costanzo*[a], *Rachele Stefania*[a], *Camilla Cavallotti*[b], *Martina Capozza*[a], *Silvio Aime*[a], *and Eliana Gianolio* [a]

[a]*Department of Molecular Biotechnology and Health Sciences, University of Torino,* [b]*CAGE Chemicals*

The search for alternatives to gadolinium-containing magnetic resonance imaging (MRI) contrast agents addresses the field of iron(III)-bearing species with the expectation that the use of an essential paramagnetic metal ion may avoid the issues raised by the exogenous gadolinium. Attention is currently devoted to highly stable Fe(III) complexes with hexacoordinating ligands, although they may lack any coordinated water molecule [1].

We found that the hexacoordinated Fe(III) complex with two units of deferasirox, a largely used iron sequestering agent [2], owns properties that can make it a viable alternative to Gd-based agents. Fe(deferasirox)$_2$ displays an outstanding thermodynamic stability, a high binding affinity to human serum albumin (three molecules of complex are simultaneously bound to the protein) and a good relaxivity that increases in the range 20-80 MHz. The relaxation enhancement is due to second sphere water molecules likely forming H-bonds with the coordinating phenoxide oxygens. A further enhancement was observed upon the formation of the supramolecular adduct with albumin. The binding sites of Fe(deferasirox)$_2$ on albumin were characterized by relaxometric competitive assays. Preliminary *in vivo* imaging studies on a tumor-bearing mouse model indicate that, on a 3 T MRI scanner, the contrast ability of Fe(deferasirox)$_2$ is well comparable to that one shown by the commercial Gd(DTPA) agent. ICP-MS analyses on blood samples withdrawn from healthy mice administered with a dose of 0.1 mmol/kg of Fe(deferasirox)$_2$ showed that the complex is completely removed in 24 h.

The herein reported relaxation efficiency, the overall biodistribution and excretion properties and the expected good biocompatibility of Fe(deferasirox)$_2$, make this system a promising candidate as an alternative to the Gd-based MRI contrast agents currently used in clinics. Furthermore, one may think of designing other systems based on the coordination cage of deferasirox with the introduction of substituents that may allow an improved control of the mobility of the second sphere water molecules, thus maintaining the interesting field-dependent properties shown by Fe(deferasirox)$_2$.



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Au(I) complexes installed on a self-assembled peptide scaffold efficiently catalyze intramolecular cyclization reactions.

Valentina Pirovano, Patrizia Brini, Elisabetta Rossi, Alessandra Romanelli

Università di Milano, Dipartimento di Scienze Farmaceutiche, via Venezian 21, 20133 Milano (Italy)

Supramolecular systems obtained upon self-assembly of short amino-acidic sequences are widely explored, since the discovery of the smallest self-assembled peptide (FF) in the core recognition motif of the beta amyloid peptide [1]. The ease with which these systems are obtained, due to the small size of the building blocks and robust synthetic protocols, strongly stimulated the research in this field. Applications of self-assembled systems based on small peptides range from electrochemical sensors to hydrogel scaffolds to support cell growth or to promote small molecule controlled release to the production of the superhydrophbic surfaces [2]. In addition, self-assembled peptides can be exploited as catalyst. One of the first examples of self-assembled peptide catalyst was reported by Stupp et al and refers to nanofibers formed by self assembled peptide amphiphiles that catalyze the hydrolysis of 2,4 -dinitro phenylacetate through an histidine residues [3]. The efficiency of the self-assembled system was related to the high density of catalytic sites exposed on the nanofiber surface.
In a different approach we explored the catalytic activity of phosphine-Au(I) complexes connected through a linker to the self-assembling dipeptide FF. The rigid structure of the self-assembled peptide offers a unique environment for the substrate subjected to the reaction. We here report the synthesis and the characterization of two FF-gold(I) chloride complexes and some preliminary examples of their catalytic activity in intramolecular cyclization reactions, figure 1[4].

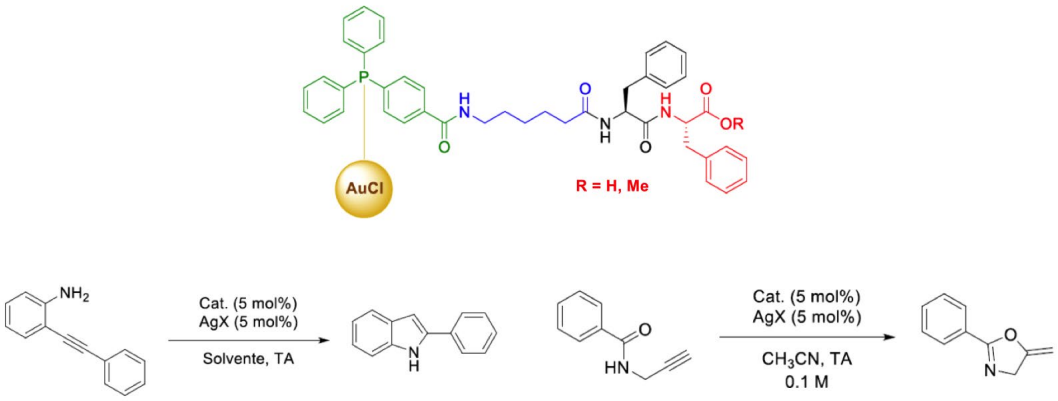

Figure 1: Representation of the catalyst in the monomeric form (top) and of the tested reactions (bottom).

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Paper-based electrochemical peptide nucleic acid (PNA) biosensor for detection of miRNA-492: a pancreatic ductal adenocarcinoma biomarker

Maria Moccia[a], Veronica Caratelli[b], Stefano Cinti[c], Biagio Pede[b], Concetta Avitabile[a], Michele Saviano[a], Anna Lisa Imbriani[d], Daniela Moscone[b], Fabiana Arduini[b]

[a]Institute of Crystallography, National Research Council, Via G. Amendola 122/O, 70126, Bari, Italy; [b]Tor Vergata University, Department of Chemical Science and Technologies, Rome, Italy; [c]University of Naples "Federico II", Department of Pharmacy, Via Domenico Montesano 49, 80131, Naples, Italy; [d]Biochemical Systems International S.p.a. Loc, Palazzo del Pero 23, 52100, Arezzo, Italy

Pancreatic ductal adenocarcinoma (PDAC) is considered one of the most lethal tumors, being responsible for 3% of all new cancer cases and 7% of all cancer-related deaths. It's a rare but lethal form of tumor, difficult to diagnose without performing an invasive procedure. The symptoms are rarely noticeable in its early stages and become evident only when cancer has become extensive or has already spread to other organs [1]. MiRNAs a class of small non coding RNAs, are known to be deregulated in PDAC patients, and recent studies have shown that they can be used as diagnostic and prognostic of the disease. The detection of miRNAs in samples acquired through minimally or non invasive procedures, such as serum, plasma, and saliva, can have a positive impact on the clinical management of these patients [2]. Herein, we reported the first paper-based electrochemical PNA biosensor for the detection of miRNA-492, which is suggested as biomarker for PDCA [3]. A sensitive and robust paper-based platform was designed employing an electrochemical sensor screen-printed on office paper and then engineered with a highly specific thiolated PNA as the recognition element. A signal on strategy was employed for miR-492 detection and the formation of PNA/miRNA-492 adduct was evaluated by monitoring the interaction between the positively charged ruthenium (III) hexamine with uncharged PNA and/or negatively charged PNA/miRNA-492 duplex by differential pulse voltammetry. The paper-based biosensor provided a linear range up to 100 nM, with a LOD of 6 nM. Excellent selectivity towards one- and two-base mismatches (1mM, 2mM) or scrambled (SCR) sequences was highlighted and the applicability for biomedical analyses was demonstrated, measuring miRNA-492 in undiluted serum samples.

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A Common Molecular Mechanism of Membrane Disruption by Intrinsically Disordered Proteins

Michele F.M. Sciacca[a], *Fabio Lolicato*[b], *Carmelo Tempra*[c], *Federica Scollo*[d], *Danilo Milardi*[a], *Antonio Raudino*[e], *Carmelo La Rosa*[e]

[a]*Istituto di Cristallografia, Sede Secondaria di Catania, Via P. Gaifami 18, I-95126, Catania, Italy;* [b]*Heidelberg University, Biochemistry Center, Heidelberg, Germany;* [c]*Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Prague, Czech Republic;* [d]*J. Heyrovský Institute of Physical Chemistry, Academy of Sciences of the Czech Republic, Prague, Czech Republic;* [e]*Department of Chemical Sciences, University of Catania, Viale A. Doria 6, 95125 Catania, Italy*

An increasing number of human diseases has been shown to be linked to aggregation and amyloid formation by intrinsically disordered proteins (IDPs). Amylin, amyloid-β, and α-synuclein are, indeed, involved in type-II diabetes, Alzheimer's, and Parkinson's, respectively. These proteins are thought to be toxic for cells because of their abnormal interaction with the cell membrane. Despite the correlation of the toxicity of these proteins at early aggregation stages with membrane damage, the molecular events underlying the process is quite complex to understand. Simpler model membranes (LUVs) have been used to study the early steps of membrane-protein interactions and their subsequent evolution. Phospholipid LUVs formed in water solution establish a chemical equilibrium between self-assembled LUVs and a small amount of phospholipids in water solution (CMC). In this study, we demonstrate the crucial role of non-vesicular lipids in the formation of lipid−protein complex, which enables an easy membrane insertion for amylin, amyloid-β, and α-synuclein. Experimental results from a variety of biophysical methods results reveal that this common molecular pathway in membrane poration is shared by amyloidogenic (amylin, amyloid-β, and α-synuclein) and nonamyloidogenic (rat IAPP, β-synuclein) proteins. Based on these results, we propose a "lipid-chaperone" hypothesis as a unifying framework for protein−membrane poration.

Identification of Phosphate-Containing Compounds as New Inhibitors of 14-3-3/ c-Abl Protein−Protein Interaction

Giusy Tassone,[a] Leire Iralde Lorente,[a] Letizia Clementi,[b] Lorenzo Franci,[c,d,e] Claire Munier,[f] Ylenia Cau,[a] Mattia Mori,[a] Mario Chiariello,[c,e] Adriano Angelucci,[b] Matthew Perry,[f] Cecilia Pozzi,[a] Stefano Mangani,[a] Maurizio Botta[a]

[a]Department of Biotechnology, Chemistry and Pharmacy, Department of Excellence 2018-2022, University of Siena, Siena, Italy; [b] Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy; [c] Istituto per lo Studio, la Prevenzione e la Rete Oncologica (ISPRO), Siena, Italy
[d] Department of Medical biotechnologies, Department of Excellence 2018-2022, University of Siena, Siena, Italy; [e] Consiglio Nazionale delle Ricerche, Istituto di Fisiologia Clinica, Siena, Italy; [f] Medicinal Chemistry, Research and Early Development, Respiratory, Inflammation and Autoimmune (RIA), BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden; giusy.tassone@unisi.it

Protein−protein interactions (PPIs) play a pivotal role in almost all cellular processes, classifying them as attractive targets for drug discovery. The modulation of PPIs through molecules acting as inhibitors or stabilizers is a promising strategy for the treatment of various human diseases, including cancer. The initial approach has been to modulate PPIs by the inhibition, although recently, new strategies based on PPI stabilization have appeared [1]. Human 14-3-3s are a family of seven protein isoforms (β, γ, ε, η, σ, τ, and ζ) that are implicated in a wide variety of cellular processes in which they recognize partner proteins through specific PPIs. 14-3-3s exploit their function as homo- or heterodimers that bind to their partner proteins in a phosphorylation-dependent manner [2]. Owing to their cellular role, aberrant 14-3-3 PPIs contribute to a wide variety of pathologies. c-Abl, a tyrosine kinase important for cell survival, proliferation, adhesion, and motility, is a 14-3-3 protein partner, specifically of the σ and ζ isoforms. The 14-3-3/c-Abl PPI is related to carcinogenesis, playing a pivotal role in the pathogenesis of chronic myeloid leukemia [3]. Previous studies have demonstrated that molecules able to disrupt this interaction improve the nuclear translocation of c-Abl, inducing apoptosis in leukemia cells [4]. Through an X-ray crystallography screening program, we have identified two phosphate-containing compounds, inosine monophosphate (IMP) and pyridoxal phosphate (PLP), as binders of human 14-3-3σ, by targeting the protein amphipathic groove [5]. Interestingly, they also act as weak inhibitors of the 14-3-3/c-Abl PPI, as demonstrated by NMR, SPR, and FP data. A 37-compound library of PLP and IMP analogues have been investigated using a FP assay, leading to the identification of three further molecules acting as weak inhibitors of the 14-3-3/c-Abl complex formation. The antiproliferative activity of IMP, PLP, and the three derivatives has been tested against K-562 cells, showing that the parent compounds have the most pronounced effect on tumor cells. PLP and IMP have also been effective in promoting the c-Abl nuclear translocation in c-Abl overexpressing cells. Further, these compounds have low cytotoxicity on human Hs27 fibroblasts. In conclusion, our data suggest that 14-3-3σ targeting compounds represent promising hits for the further development of drugs against c-Abl-dependent cancers [5].

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Metabolomics approach to identify putative anticancer metabolites against resistant cancer cells

Giovanna Valentino[a], Adriano Stinca[a], Teresa Troiani[b], Brigida D'Abrosca[a], Assunta Esposito[a], Antonio Fiorentino[a], Monica Scognamiglio[a]

[a]Dipartimento di Scienze e Tecnologie Ambientali, Biologiche e Farmaceutiche, Università degli Studi della Campania "Luigi Vanvitelli", Via Vivaldi 43, 81100 Caserta; [b]Oncologia medica, Dipartimento di Medicina di precisione, Università degli Studi della Campania "Luigi Vanvitelli", Italy; e-mail: giovanna.valentino@unicampania.it

A significant challenge in anticancer therapy is, nowadays, the ever-increasing occurrence of intrinsic and acquired drug resistance. This poses a serious limit to the currently available therapeutic approaches. Therefore, it is urgent to find chemotherapeutic agents to prevent or overcome this problem [1-3]. Plants are a possible source of such compounds. Plant specialized metabolites play, indeed, a key role in drug discovery due to high scaffold diversity, structural complexity and the vast number of metabolites [4-5]. Unfortunately, finding new active molecules from the crude extracts is a very long process due to the timescale and complexity of traditional methodologies that require different separation and isolation steps.

In this context, NMR-based metabolomics is a high-throughput approach which can allows to analyze a large number of samples in a very short time, providing the information on crude extract composition, simultaneously observing a wide range of metabolites belonging to different chemical classes. Furthermore, metabolites can be identified in mixture using various 2D-NMR experiments [6].

In this study, a number of Asteraceae species from Mediterranean area were investigated through NMR-based metabolomics paired with biological assays.

NMR-based metabolomics was used to chemically characterize the extracts, while biological assays performed towards a panel of resistant cancer cell lines were used to screen the biological activity of the extracts enriched in specialized metabolites obtained by SPE.

The integration of NMR-based metabolomics and bioactivity data of different extracts and fractions, with the help of different multivariate data analysis techniques made it possible to select the most promising extracts for further screening but also to hypothesize the metabolites potentially responsible for the activity.

This will allow to design a target isolation of the presumed active compounds, which can then be further explored to validate the biological activity and to understand the molecular mechanism.

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INDICE COMUNICAZIONI ORALI

Astolfi	Paola	TEC OR042
Atzori	Matteo	INO OR025
Audisio	Davide	ORG OR003
Avola	Tiziana	ANA OR086
Ayaz	Nazeeha	TEC OR027
Aye	Yimon	FAR KN005
Bacchiocchi	Riccardo	IND OR058
Baccolo	Giacomo	ANA OR034
Bach	Anders	FAR KN009
Badetti	Elena	ABC OR007
Baglio	Vincenzo	ELE OR57
Baglioni	Michele	FIS OR076
Baldassarre	Francesca	TEC OR041
Baldelli	Francesca	FIS OR067
Baldini	Laura	ORG OR087
Ballarotto	Marco	ORG OR019
Balliana	Eleonora	ABC OR002
Balsamo	Stefano Andrea	IND OR047
Bandiera	Tiziano	FAR KN011
Baratta	Mariafrancesca	FIS OR107
Barbanente	Alessandra	INO PZ008
Barbera	Vincenzina	TEC OR021
Barberis	Elettra	MAS OR005
Barbieri	Luisa	ABC OR054
Barbieri	Pierluigi	ABC OR058
Bardi	Brunella	FIS OR103
Barlocco	Ilaria	INO OR002
Barola	Carolina	MAS OR011
Baron	Marco	INO OR019
Barone	Laura	ANA OR114
Barreca	Marilia	FAR OR011
Bartella	Lucia	MAS OR010
Battista	Sara	ORG OR004
Battistuzzi	Gianantonio	CSB OR003
Begni	Federico	FIS OR088
Bella	Federico	IND OR036
Bellassai	Noemi	ANA OR068
Bellavita	Rosa	FAR OR042
Bellia	Francesco	CSB OR022
Bellina	Fabio	ORG OR069
Bellini	Marco	INO OR041
Belloni	Alessia	INO OR048
Bellotti	Denise	ANA OR087
Bellotto	Ottavia	CSB OR002
Benedetti	Michele	INO OR008
Bernardi	Anna	ORG PZ001
Bernes	Elisa	TEO OR017
Bernini	Roberta	ORG OR005
Bertani	Marco	TEO OR001
Bertinetti	Stefano	ANA OR060
Berto	Silvia	ANA KN010

Bertucci	Alessandro	ANA OR069
Bertuletti	Susanna	ORG OR117
Bertuzzi	Giulio	ORG OR108
Bettini	Simona	FIS OR080
Biagini	Denise	ANA OR035
Biagiotti	Giacomo	ORG OR027
Bianchera	Annalisa	TFA OR010
Bianchi	Federica	ANA OR076
Bianco Prevot	Alessandra	ANA IL005
Biancolillo	Alessandra	ANA KN004
Biasi	Pierdomenico	IND KN003
Biesuz	Raffaela	ANA OR123
Biffis	Andrea	INO OR022
Bifulco	Aurelio	TEC OR017
Biggio	Deborah	ANA OR115
Bigogno	Alessandra	ABC OR006
Bisag	Denisa	ORG OR118
Biscaglia	Francesca	FIS OR064
Bizzarri	Bruno Mattia	ORG OR020
Blangetti	Nicola	FIS OR111
Blasi	Davide	ORG OR028
Bloise	Ermelinda	TEC OR004
Bogialli	Sara	MAS KN003
Boldrini	Chiara Liliana	ORG OR080
Bollella	Paolo	ANA KN009
Bolognesi	Margherita	FIS OR049
Bonacchi	Sara	ELE OR11
Bonaccorso	Angela	TFA OR002
Bonfio	Claudia	CSB PZ002
Bonini	Andrea	ANA OR017
Bonini	Mauro	TFA IL003
Bonizzoni	Simone	ELE OR53
Bonomo	Matteo	ELE KN34
Bonomo	Matteo	IND OR039
Borella	Matteo	IND OR064
Bortolato	Tommaso	ORG OR109
Bossi	Alberto	ORG OR029
Bossi	Alessandra Maria	ANA OR070
Botla	Vinayak.	IND OR010
Braconi	Laura	FAR OR012
Branchini	Federica	DID OR001
Brandi	Jessica	ANA OR095
Brandiele	Riccardo	ELE IL31
Bretti	Clemente	ANA KN002
Brilloni	Alessandro	ELE OR67
Brufani	Giulia	ORG OR119
Brugnoli	Luca	TEO OR006
Brunelli	Andrea	ABC OR015
Brunetti	Leonardo	FAR OR009
Brunsveld	Luc	CSB KN003
Budroni	Marcello	FIS OR122

Buonsenso	Fabio	ORG OR033
Busato	Matteo	FIS OR094
Buscemi	Gabriella	ORG OR081
Cabri	Walter	IND KN002
Cademartori	Davide	ELE OR56
Caflisch	Amedeo	CSB KN006
Calà	Elisa	ANA OR063
Calabrese	Carla	IND OR024
Calandra	Pietro	ABC OR055
Calandra	Pietro	FIS OR085
Calcaterra	Andrea	ORG OR006
Calcio Gaudino	Emanuela	ORG OR120
Calgaro	Loris	ABC OR056
Calogero	Francesco	ORG OR121
Calvano	Cosima Damiana	ANA IL004
Calvini	Rosalba	ANA OR132
Calvino	Martina Maria	FIS OR118
Campagnolo	Filippo	INO OR024
Campanella	Beatrice	ANA OR116
Campiani	Giuseppe	FAR KN001
Campisciano	Vincenzo	ORG OR122
Campisi	Sebastiano	FIS OR034
Campisi	Sebastiano	IND OR014
Campitelli	Patrizio	INO OR037
Cannavacciuolo	Ciro	MAS OR009
Capone	Matteo	TEO OR015
Cappai	Rosita	ANA OR088
Caprioglio	Diego	ORG OR021
Capriotti	Anna Laura	ANA IL009
Caputo	Paolino	FIS OR040
Cara	Claudio	FIS OR105
Caratelli	Veronica	ANA OR134
Carbone	Daniela	FAR OR013
Cardoso Gomes	Guelber	TEO OR016
Carena	Luca	ANA OR061
Carmignani	Alessio	FIS OR099
Carpanese	Maria Paola	ELE OR48
Carpentieri	Maria Antonietta	DID OR002
Carucci	Cristina	FIS OR063
Caruso	Manfredi	TEC OR005
Casini	Angela	CSB KN005
Castiglione	Franca	TEC OR010
Casula	Luca	TFA OR011
Cataldo	Salvatore	ANA OR089
Catani	Martina	ANA PZ004
Catelli	Emilio	ANA OR064
Catto	Marco	FAR OR031
Cavalera	Simone	ANA OR096
Cavazza	Antonella	ANA OR025
Cavuoto	Denise	IND OR002
Cecchi	Teresa	DID OR010

Cecconi	Daniela	MAS OR001
Ceccucci	Anita	TEC OR045
Cefali	Manuel Amedeo	ABC OR059
Centomo	Paolo	INO OR033
Cerrato	Andrea	ANA OR097
Cerri	Luca	TFA OR012
Cesari	Cristiana	INO OR035
Chelazzi	David	FIS OR 129
Chenet	Tatiana	ANA OR026
Chiarcos	Riccardo	IND OR027
Chiarello	GianLuca	FIS OR030
Chino	Marco	INO OR032
Chiodo	Fabrizio	ORG OR007
Chirizzi	Cristina	FIS OR081
Ciacci	Luca	ABC OR003
Ciccola	Alessandro	ABC OR008
Cinti	Stefano	ANA OR071
Cioffi	Nicola	ANA IL010
Cipriano	Domenico	ABC OR045
Cirillo	Martina	ORG OR008
Clemente	Ilaria	FIS OR065
Cleto Bruzzese	Paolo	INO OR027
Colella	Marco	ORG OR022
Colella	Maria Francesca	FIS OR115
Collini	Elisabetta	FIS OR047
Colloca	Stefano	TFA IL002
Colozza	Noemi	ANA OR135
Comis	Silvia	ELE OR43
Condorelli	Marcello	FIS OR009
Consentino	Luca	IND OR015
Conte	Francesco	IND OR045
Contente	Martina	FAR OR018
Conti	Luca	INO OR023
Coralli	Irene	ANA OR077
Corbisiero	Dario	ORG OR023
Cordaro	Massimiliano	ORG OR024
Corinti	Davide	INO OR063
Corno	Marta	FIS OR101
Corradini	Danilo	ANA OR024
Corrente	Giuseppina Anna	FIS OR035
Corrieri	Matteo	ORG OR132
Cosentino	Ugo	DID OR015
Costa	Maria	DID OR003
Costanzo	Paola	ORG OR061
Cozzolino	Antonietta	IND OR028
Cristiano	Maria Chiara	TFA OR013
Cristina	Tealdi	ELE KN68
Crivellaro	Giovanni	ELE OR07
Crocetti	Letizia	FAR OR006
Cucinotta	Lorenzo	ANA OR003
Cupellini	Lorenzo	TEO PZ005

Curti	Claudio	ORG OR059
D'Ambrosio	Valeria	ABC OR022
D'Imperio	Nicolas	ORG PZ012
Da Pian	Marta	ORG OR034
D'Agata	Roberta	ANA OR117
Dai	Yasi	TEO OR018
Dal Bello	Federica	ANA OR028
Dall'Anese	Anna	INO PZ002
D'Alterio	Massimo Christian	INO OR004
D'Amato	Alfonsina	ANA OR105
Damiano	Caterina	INO OR016
Damin	Alessandro	FIS OR126
Danielis	Maila	IND OR005
D'Aria	Federica	FIS OR018
Darjazi	Hamideh	ELE OR72
Davighi	Maria Giulia	ORG OR010
de Araujo Lima e Souza	Giselle	TEC OR011
De Bon	Francesco	ELE OR16
De Bonis	Angela	FIS OR097
De Castro	Cristina	ORG OR011
De Ceglie	Cristina	ABC OR017
De Filpo	Giovanni	FIS OR082
De Gennaro	Gianluigi	ABC OR001
De Grazia	Gemma	ANA OR004
De Leo	Vincenzo	FIS OR019
De Luca	Chiara	ANA OR106
De Marchi	Fabiola	MAS OR008
De Santis	Roberto	FIS KN012
De Santis	Serena	TEC KN003
De Zotti	Marta	CSB OR001
Deganello	Francesca	INO OR039
Degli Esposti	Lorenzo	FIS OR021
Del Coco	Laura	INO OR061
Del Galdo	Sara	TEO OR022
Del Giudice	Alessandra	FIS OR053
Del Giudice	Daniele	ORG OR088
Del Grosso	Erica	ANA OR072
Della Pelle	Flavio	ANA KN011
Dell'Edera	Massimo	FIS OR113
Deng	Siyuan	TFA OR009
Desantis	Jenny	ORG OR012
Dettin	Monica	FIS OR096
Di Capua	Angela	ANA OR098
Di Carlo	Gabriella	FIS KN010
Di Carluccio	Cristina	ORG OR013
Di Carmine	Graziano	ORG OR035
Di Donato	Francesca	ANA OR036
Di Fidio	Nicola	IND OR053
Di Giulio	Tiziano	ANA OR018
Di Guida	Rossella	ORG OR014
Di Liberto	Giovanni	FIS OR028

Di Liberto	Giovanni	TEO PZ003
Di Maiolo	Francesco	TEO OR029
Di Maro	Mattia	ORG OR110
Di Maro	Salvatore	FAR OR039
Di Matteo	Paola	TEC OR025
Di Muzio	Simone	FIS OR071
Di Nardo	Fabio	ANA OR099
Di Noja	Simone	ORG OR031
Di Pietro	Maria Enrica	TEC OR012
Di Porzio	Anna	CSB OR029
Di Terlizzi	Lorenzo	ORG OR063
Dibenedetto	Carlo Nazzareno	FIS OR001
Dichiara	Maria	FAR OR021
Dichiarante	Valentina	TEC OR031
Dilonardo	Elena	TEC OR028
Dini	Danilo	ELE OR17
Dispenza	Clelia	TEC OR046
Distefano	Alessia	CSB OR009
Dogra	Raghav	ANA OR009
Domestici	Chiara	INO OR042
Donà	Lorenzo	TEO OR030
Donati	Greta	TEO PZ001
Donato	Paola Agata	ANA OR030
Donnarumma	Danilo	ANA OR118
Donnoli	Maria Irene	DID OR011
D'Onofrio	Mariapina	ORG OR009
Dozzi	Maria Vittoria	FIS KN009
D'Urso	Alessandro	CSB OR010
Econdi	Stefano	IND OR011
El Fadil	Dounia	ANA OR107
Elbaz	Lior	ELE KN55
Elkhanoufi	Sabrina	CSB OR008
Elliani	Rosangela	ANA OR005
Erba	Alessandro	TEO PZ002
Ermini	Elena	ORG OR036
Escolano Casado	Guillermo	FIS OR069
Esposito	Anna	ORG PZ014
Esposito	Germana	ORG OR037
Esposito	Roberto	INO OR020
Esposito	Rodolfo	FIS OR106
Esposito	Tiziana	TFA OR014
Espro	Claudia	TEC KN001
Estima Gomes	Manuela	TFA IL005
Fabbiani	Marco	FIS OR006
fabbri	Debora	ANA OR029
Fabiani	Laura	ANA OR019
Facchetti	Giorgio	INO OR031
Facchin	Alessandro	ELE OR35
Facchin	Alessandro	ELE OR51
Faginas-Lago	Noelia	TEO OR008
Fagiolari	Lucia	IND OR061

Fagnani	Francesco	INO OR007
Falco	Marisa	ELE OR62
Falletta	Ermelinda	IND OR048
Famulari	Antonino	INO OR062
Fanizza	Elisabetta	FIS OR014
Fanti	Federico	MAS OR004
Fasano	Valerio	ORG OR116
Fasolini	Andrea	IND OR040
Fasulo	Francesca	TEO OR009
Fattal	Elias	TFA IL001
Federico	Bella	TEC OR038
Felletti	Simona	ANA OR078
Fenti	Angelo	ABC OR009
Ferdeghini	Claudio	ORG OR032
Ferdinando Summa	Francesco	TEO OR023
Ferlenghi	Francesca	FAR OR019
Fermi	Andrea	INO OR045
Fermo	Paola	ANA IL006
Feroci	Marta	ELE KN045
Ferracane	Antonio	ANA OR006
Ferrari	Giorgio	IND OR065
Ferraro	Giovanni	FIS OR011
Ferrauto	Giuseppe	INO OR051
Ferrazzano	Lucia	ORG OR064
Ferrero	Luca	ABC OR005
Ferretti	Francesco	INO OR021
Fidaleo	Marco	TFA IL004
Filippin	Ilaria	TFA OR003
Fiorentini	Carlo	DID IL002
Fiorentino	Antonino	ABC OR034
Fiorenza	Roberto	IND OR016
Fiorito	Daniele	ORG OR060
Fischer	Peter	ELE KN06
Forchetta	Mattia	ORG OR082
Fornari	Fabio	ANA OR037
Fornasier	Marco	FIS OR016
Forni	Alessandra	FIS OR044
Fortino	Mariagrazia	TEO OR010
Fortunati	Alessia	ELE OR21
Foschi	Francesca	ORG OR123
Francesconi	Oscar	ORG OR089
Franchina	Flavio	ANA KN001
Franchino	Allegra	ORG OR067
Franco	Francesca	ORG OR076
Franzini	Roberta	ORG OR038
Frateloreto	Federico	ORG OR133
Freccero	Riccardo	INO OR069
Frosi	Ilaria	FAR OR017
Froudakis	George	FIS KN007
Funicello	Maria	ORG OR015
Gabas	Fabio	FIS OR058

Gaeta	Massimiliano	CSB OR021
Gaggero	Elisa	ABC OR035
Gaggiotti	Sara	ANA OR124
Gagliardi	Anna	IND OR049
Galantini	Luciano	FIS KN011
Galassi	Rossana	INO OR047
Galeotti	Marco	ORG OR039
Galletta	Micaela	ANA OR007
Galloni	Melissa Greta	IND OR017
Gambassi	Francesca	INO OR049
Garbarino	Gabriella	IND OR006
García Lascurain	P. Guzmán	ABC OR046
Garello	Francesca	INO OR054
Gaspa	Silvia	ORG OR070
Gatti	Lucrezia	ABC OR028
Gatto	Emanuela	FIS KN003
Gazzola	Silvia	ORG OR138
Gazzotti	Stefano	IND OR023
Gelain	Arianna	FAR OR014
Gelli	Rita	FIS OR052
Geninatti	Simonetta	INO OR084
Gentile	Luigi	FIS KN004
Gentili	Dario	ORG OR016
Gentili	Pier Luigi	FIS OR038
Gessner	Viktoria	INO IL001
Ghedini	Elena	IND OR070
Ghini	Veronica	CSB OR006
Ghini	Veronica	INO OR070
Ghirga	Francesca	ORG OR041
Giacalone	Francesco	ORG PZ007
Giambastiani	Giuliano	IND OR063
Giannetto	Marco	ANA OR073
Giedroc	David	INO IL003
Gilda Ritacca	Alessandra	TEO OR020
Gioiello	Antimo	FAR KN006
Giordana	Alessia	INO OR030
Giorgi	Silvia	IND OR057
Giorno	Lidietta	CSB OR004
Giovanni	Falcone	TEC OR044
Giovannini	Tommaso	FIS OR060
Girlando	Alberto	FIS OR090
Girolametti	Federico	ANA OR010
Giuffrè	Ottavia	ANA OR090
Giuliano	Elena	TFA OR017
Giurlani	Walter	ANA OR119
Giustiniano	Mariateresa	FAR PZ002
Gobbo	Pierangelo	ORG PZ004
Gobetto	Roberto	INO OR001
Gois	Pedro	FAR KN012
Golla	Manohar	IND OR029
Goracci	Laura	ORG OR042

Gori	Alessandro	TEC IL003
Gorla	Giulia	ANA OR120
Goti	Giulio	ORG OR083
Grattieri	Matteo	ELE OR18
Grigioni	Ivan	IND OR035
Groppo	Elena	FIS KN005
Gualandi	Andrea	ORG OR134
Gualandi	Isacco	ANA KN007
Gubitosa	Jennifer	FIS OR024
Guerra	Giulia	ABC OR036
Gugliuzza	Annarosa	ABC OR043
Guidoni	Leonardo	TEO OR013
Guidotti	Giulia	ABC OR021
Guidotti	Matteo	IND OR067
Gullifa	Giuseppina	ANA OR079
Guzman	Hilmar	ELE OR23
Hajareh Haghighi	Farid	INO OR066
He	Xiufang	ELE OR39
Hernandez	Simelys	IND OR034
Hessel	Volker	IND KN007
Hirsch	Anna	FAR KN008
Hmoudah	Maryam	IND OR071
Iaccarino	Nunzia	CSB OR027
Iammarino	Marco	ANA OR031
Ianni	Federica	FAR OR016
Illiano	Anna	ANA OR008
Illuminati	Silvia	ANA OR062
Impemba	Salvatore	INO OR052
Imperatore	Concetta	ORG OR043
Inaudi	Paolo	ANA OR044
Intagliata	Sebastiano	FAR OR028
Interino	Nicolò	ANA OR100
Irto	Anna	ANA OR091
Jacobson	Kenneth	FAR MD001
Joseph	Edith	ABC KN001
Jurinovich	Sandro	DID OR004
Kaveh	Moulaee	TEC OR035
Keserű	György	FAR KN002
Khalid	Shahid	ELE OR75
Koper	Marc	ELE KN19
Kuhnert	Nikolai	MAS PL003
La Nasa	Jacopo	ANA OR080
La Regina	Giuseppe	FAR OR004
La Tella	Roberta	ANA OR081
Labarile	Rossella	FIS OR015
Labate	Maria	ABC OR025
Lacarbonara	Giampaolo	ELE OR08
Lambruschini	Chiara	ORG OR040
Lamuraglia	Raffaella	ABC OR029
Lancellotti	Isabella	TEC OR018
Larisa	Lvova	TEC IL002

Laudadio	Gabriele	ORG PZ015
Laurati	Marco	FIS KN001
Laus	Michele	IND KN004
Lazzara	Giuseppe	ABC OR050
Leccese	Mirko	FIS OR102
Lenci	Elena	DID OR012
Lenci	Elena	ORG PZ009
Lenzi	Alessio	ANA OR108
Leonardo	Duranti	ELE OR49
Leone	Linda	INO OR005
Leonelli	Cristina	TEC OR016
Lesch	Andreas	ANA OR045
Li	Min	ANA OR121
Liccardo	Letizia	INO OR055
Licen	Sabina	ABC OR010
Licen	Sabina	ANA OR038
LiDestri	Giovanni	FIS OR002
Lipparini	Filippo	TEO OR025
Lippi	Martina	TEC OR033
Lisuzzo	Lorenzo	FIS OR072
Litti	Lucio	FIS OR078
Lo Porto	Chiara	FIS OR108
Lo Vecchio	Carmelo	ELE OR03
Locatelli	Marcello	ANA OR082
Lodesani	Federica	TEO OR031
Lodi	Giulia	ABC OR032
Loianno	Valerio	FIS OR086
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Lombardo	Marco	ORG OR135
Lopreside	Antonia	ANA OR074
Losi	Niccolo	ABC OR060
Lovison	Denise	INO OR056
Lucantonio	Stefania	IND OR060
Lucarini	Marco	ORG PZ005
Lucarini	Simone	FAR OR024
Lucenti	Elena	INO OR014
Lufrano	Ernestino	ELE OR65
Lunardon	Marco	INO OR072
Lupi	Michela	ORG OR136
Lupidi	Gabriele	ORG OR145
Luque	Rafael	IND KN006
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Macchia	Eleonora	ANA OR020
Magnaghi	Lisa Rita	ANA OR039
Magni	Mirko	ELE OR26
Mai	Antonello	FAR MD002
Maiuolo	Loredana	ORG OR074
Malacaria	Luana	ANA OR092
Malegori	Cristina	ANA KN005
Malferrari	Marco	ELE OR37

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Mancini	Alessandro	ABC OR061
Manfredi	Marcello	ANA OR109
Manfredi	Norberto	ORG OR084
Mangini	Anna	ELE OR66
Mangraviti	Domenica	ANA OR051
Mannias	Giada	INO OR075
Mantovani	Marco	ABC OR020
Manzoli	Maela	IND OR051
Marasco	Daniela	INO OR060
Marassi	Valentina	ANA OR101
Marchesi	Stefano	FIS OR110
Marchiò	Luciano	INO OR077
Marcì	Giuseppe	TEC OR029
Marcolin	Giampaolo	FIS OR043
Maresca	Giovanna	ELE OR74
Maria Squeo	Benedetta	ORG OR106
Mariani	Federica	ANA OR021
Mariconda	Annaluisa	INO OR068
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Marittimo	Nicole	ANA OR052
Marotta	Angela	TEC OR009
Martella	Daniele	IND OR031
Martelli	Giulia	ORG OR137
Martina	Bortolami	TEC OR040
Martini	Francesca	FIS OR048
Martí-Rujas	Javier	INO OR006
Maruccia	Elisa	ELE OR20
Marullo	Salvatore	ORG OR111
Marussi	Giovanna	ANA OR065
Marzo	Tiziano	INO OR011
Mascolo	Giuseppe	ABC OR037
Mascolo	Giuseppe	ABC OR038
Masi	Marco	ORG OR044
Massari	Serena	FAR OR036
Massaro	Arianna	TEO OR002
Massaro	Marina	ORG OR054
Mastrangelo	Rosangela	FIS OR074
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Mazzucato	Marco	ELE OR12

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Meninno	Sara	ORG PZ011
Merlo	Francesca	ANA OR110
Mero	Angelica	ORG OR112
Messa	Francesco	ORG OR072
Messina	Grazia	FIS OR007
Messore	Antonella	FAR OR038
Metrangolo	Pierangelo	ORG PZ003
Mezzetta	Andrea	ORG OR062
Mezzomo	Lorenzo	ELE OR63
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Migliore	Rossella	ANA OR093
Milanese	Chiara	FIS OR026
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Minella	Marco	ANA OR011
Minero	Claudio	ANA PL001
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Morillas Becerril	Lucía	ORG OR046
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Mura	Monica	FIS OR020
Muraglia	Marilena	FAR OR027
Murgolo	Sapia	ABC OR040
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Musella	Simona	FAR OR005
Musolino	Maria Grazia	IND OR037
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Mussini	Patrizia	ELE KN01
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Nardiello	Donatella	ANA OR012
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Pintus	Anna	INO OR044
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Piovano	Alessandro	IND OR025
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Pipitone	Giuseppe	IND OR022
Pippione	Agnese	FAR OR001
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Polo	Annalisa	FIS OR032
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Prati	Silvia	DID OR013
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Prosa	Mario	FIS OR084
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Ricci	Michele	ORG OR102

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Ricciarelli	Damiano	INO OR040
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Riva	Laura	TEC OR006
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Romanelli	Marco	TFA IL006
Romanucci	Valeria	CSB OR018
Romerio	Alessio	CSB OR014
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Rossano	Carmelina	IND OR056
Rossetti	Arianna	TEC OR043
Rossetti	Ilenia	IND OR050
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Rossi	Federico	FIS OR117
Rossi	Roberto	ORG OR095
Rossin	Andrea	INO OR036
Rossino	Giacomo	FAR OR022
Rosso	Francesca	IND OR062
Rotundo	Laura	ELE IL33
Rovaletti	Anna	TEO OR021
Roverso	Marco	ANA OR084
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Ruggieri	Silvia	INO OR010
Russina	Olga	FIS OR123
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Russo	Luigi	CSB OR007
Russo	Patrizio	ORG OR144
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Sabbatini	Simona	TEC OR008
Sabuzi	Federica	ORG OR103
Sacchetti	Annalisa	IND OR012
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Saielli	Giacomo	TEO OR011
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Salafia	Fabio	ANA OR032
Salerno	Tania	ANA OR055
Saliu	Francesco	ABC OR018
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Salvino	Rosachiara Antonia	FIS OR045
Salvitti	Chiara	INO OR009
Sanadar	Martina	TEC OR049
Sandri	Giuseppina	TFA OR019
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Sannino	Gennaro	ELE OR38
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Santino	Federica	ORG OR099
Santoro	Antonio	INO OR079
Santulli	Federica	INO OR028
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Sole	Roberto	IND OR007
Sologan	Maria	ORG OR105
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Terzi	Alberta	FIS OR017
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Tiboni	Mattia	TFA OR008
Tiecco	Matteo	ORG OR114

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Tocco	Davide	FIS OR054
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Vizza	Martina	ANA OR050
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Bellomo	Chiara	INO P0010
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Cecinato	Angelo	ABC P0025
Cecinato	Angelo	ABC P0026
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Cerri	Luca	TFA P0009
Cerveri	Alessandro	ORG P0024
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Cicchi	Stefano	ORG P0025
Cicco	Luciana	ORG P0026
Ciccola	Alessandro	ABC P0037
Ciccone	Lidia	FAR P0045
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Cipriano	Alessandra	FAR P0046
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Clemente	Mariangela	ORG P0027
Cofelice	Martina	FIS P0019
Cogliano	Tommaso	IND P0006
Colaiezzi	Roberta	INO P0020
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Consiglio	Giuseppe	TEC P0005
Consiglio	Giuseppe	TEC P0006
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Coppolino	Carmelo	ANA P0047
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Corradini	Danilo	ORG P0031
Corrente	Giuseppina Anna	FIS P0020
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Cressoni	Chiara	INO P0022
Croce	Lucia	ANA P0024
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De Beni	Eleonora	ABC P0009
De Castro	Federica	INO P0023
De Luca	Erik	INO P0024
De Santis	Serena	TEC P0007
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De Zotti	Marta	ORG P0035
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DellaLatta	Elisa	FIS P0022
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Di Pietro	Roberto	ANA P0011
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Di Vito Nolfi	Giuseppe	ORG P0043
Diego	Diego	CSB P0002
Dilauro	Giuseppe	ORG P0044
Dolla	Tarekegn	INO P0026
Donadio	Anna	INO P0086
Donato	Paola Agata	ANA P0048
Donato	Simone	IND P0008
Duro	Ida	MAS P023
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Fabbri	Lorenzo	ANA P0036
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Fabbri	Roberta	ORG P0112
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Faggiano	Antonio	ABC P0033
Fagiolari	Lucia	TEC P0008
Falgiani	Annamaria	ANA P0012
Fallica	Antonino Nicolò	FAR P0059
Fanizzi	P. Francesco	INO P0028
Farinini	Emanuele	ANA P0034
Fasano	V.	ORG P0045
Faverio	C.	ORG P0046
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Fermo	Paola	ABC P0005
Ferracane	Antonio	ANA P0049
Ferrara	Chiara	ELE P0005
Ferrauto	Giuseppe	INO P0029
Ferrone	Vincenzo	ANA P0050
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Giacomazzo	Gina	INO P0037
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Gigli	Matteo	INO P0038
Gili	Marilena	MAS P015
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Grassiri	Brunella	TFA P0018
Grassiri	Brunella	TFA P0019
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