Merck Young Chemists' Symposium 2021

Book of Abstracts

Rimini (IT)
Hotel Continental

22-24 November 2021

Società Chimica Italiana
Gruppo Giovani

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Welcome to the 20th edition of the ***Merck Young Chemists' Symposium*** (***MYCS***), formerly also known as *SAYCS* and *MEYCS*.

This international conference is organized by the Young Group of *Società Chimica Italiana* (***SCI Giovani***) and the National Interuniversity Consortium of Materials Science and Technology (***INSTM***) with the financial support from *Merck* and several other sponsors, that you will meet during the conference.

The symposium covers all the disciplines of Chemistry, aiming to connect young researchers, inspire new ideas, and potentially trigger new collaborations. With the contributions of our five invited plenary speakers, and the international environment guaranteed by the presence of people coming from 6 different countries, we truly hope that you will all enjoy this great event with us. For this 20th anniversary, we are extremely honored to host you in an in-person conference. We have worked hard to organize this meeting with the exceptional number of 250 participants, keeping as a priority the respect of Covid-19 preventive measures. Thank you for the great trust shown towards *SCI Giovani*, *Merck* and all our supporters. Enjoy the conference and have a nice stay with us!

Elena Lenci
SCI Giovani Coordinator

Merck Young Chemists' Symposium 2021

Rimini (IT) – November 22-24 2021

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Optical and electrochemical point-of-care sensors as tools for precision medicine

Claudio Parolo

[a] Barcelona Institute for Global Health (ISGlobal), Calle Rosselló 132, 08036, Barcelona, Spain
[b] Catalan Institute of Nanoscience and Nanotechnology (ICN2), Campus UAB, 08193, Barcelona, Spain
[c] University of California Santa Barbara, Department of Chemistry and Biochemistry, Santa Barbara, 93106, United States
E-mail: claudio.parolo@isglobal.org

The COVID-19 pandemic has made clear how our society needs low-cost and easy-to-use diagnostic devices to tackle most of current healthcare problems. These types of devices are generally defined as point-of-care sensors. For decades, classic lateral flow assays [1] and electrochemical sensors have provided excellent analytical capabilities at the point of care, allowing for example the diagnosis of pregnancy in less than 15 minutes or the monitoring or glucose levels in real-time. However, those technologies in their basic forms fail to address the needs of precision medicine. Here we present how the introduction of novel concepts in those well-known technologies allows to obtain sensors that retain the low cost and ease of use, while provide excellent analytical performance, such as the use of untreated blood samples [2] or the continuous monitoring of a protein biomarker directly inside a urinary catheter [3].

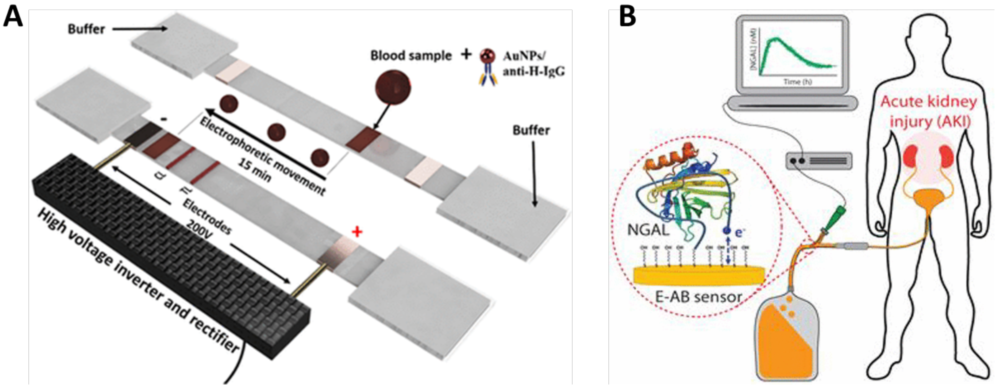

Figure 1: A) The integration of electrophoresis capabilities into lateral flow assays allow the use of untreated blood samples [2]. B) The use of aptamers that undergo a binding-induced conformational change as bioreceptors in electrochemical sensors makes possible the real-time and continuous monitoring of protein biomarkers [3].

[1] C. Parolo, A. Sena-Torralba, J.F. Bergua, E. Calucho, C. Fuentes-Chust, L. Hu, L. Rivas, R. Álvarez-Diduk, E.P. Nguyen, S. Cinti, D. Quesada-González, and A. Merkoçi, *Nature Protocol* **15** (2020) 3788-3816
[2] A. Sena-Torralba, R. Alvarez-Diduk, C. Parolo, H. Torné-Morató, A. Müller, and A. Merkoçi, *Analytical Chemistry* **93** (2021) 3112-3121
[3] C. Parolo, A. Idili, G. Ortega, A. Csordas, A. Hsu, N. Arroyo, S. Ferguson, J.P. Wang, and K. W. Plaxco, *ACS Sensors* **5** (2020), 7, 1877–1881

Chemical challenges in energy technologies – A perspective from an under-35 chemist

Federico Bella

[a] Department of Applied Science and Technology, Politecnico di Torino, Corso Duca degli Abruzzi 24, 10129-Turin, Itay
[b] National Interuniversity Consortium of Material Science and Technology (INSTM), Via Giuseppe Giusti 9, 50121-Florence, Italy
E-mail: federico.bella@polito.it

The global energy and environmental context clearly highlights the need for new technologies capable of guaranteeing the conversion of renewable sources and the storage of the produced energy in a sustainable, safe and geographically balanced way. Chemical technologies are the basis of many of these strategies and international decision-makers, being aware of them, have begun to promote suitable funding initiatives.

In this scenario, the main challenges that chemists need to consider at the academic research level are the following:

- the use of sustainable, abundant and recyclable (or reusable) materials when fabricating energy devices at a large-scale;
- the integration of energy conversion and storage devices, stopping working in separate communities;
- the redesign of industrial chemistry processes in a sustainable way, targeting the low-impact production of solar fuels;
- create medium-scale laboratories in universities to ensure a more credible scalability of the proposed technologies.

In this plenary talk I will give an overview on the main trends in this field, with a special focus on what is studied at the Electrochemistry Group @PoliTO and on how it impacted on my career since 2013, when I joined MYCS conference for the first time as a PhD student.

[1] F. Bella, G. Griffini, J. P. Correa-Baena, G. Saracco, M. Grätzel, A. Hagfeldt, S. Turri, and C. Gerbaldi, *Science* **354** (2016) 203-206.
[2] F. Bella, L. Porcarelli, D. Mantione, C. Gerbaldi, C. Barolo, M. Grätzel, and D. Mecerreyes, *Chem. Sci.* **11** (2020) 1485-1493.
[3] T. N. Huan, D. A. Dalla Corte, S. Lamaison, D. Karapinar, L. Lutz, N. Menguy, M. Foldyna, S. H. Turren-Cruz, A. Hagfeldt, F. Bella, M. Fontecave, and V. Mougel, *Proc. Natl. Acad. Sci. USA* **116** (2019) 9735-9740.

This research project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (grant agreement no. 948769, project title SuN$_2$rise).

Upscaling vegetable biopolymers with water-based methods into materials for packaging

Giovanni Perotto

Smart Materials, Istituto Italiano di Tecnologia, Via Morego 30, 16163-Genova, Italia
E-mail: giovanni.perotto@iit.it

The possibility of using vegetable macromolecules, with minimal processing, as source of materials capable of substituting plastics in packaging is a very compelling goal to mitigate the environmental issues associated conventional plastics. Furthermore, the possibility to use byproducts and waste from inedible parts of plants or discarded fruits and vegetables, will generate new value from resources that otherwise will be discarded, while at the same time it will also eliminate the controversy associated with the use of foodstuff (e.g. corn, sugars) to produce plastic alternatives such as starch-based plastics, PLA or PHAs. Lots of research was done on chemically modified cellulose (e.g. cellulose acetate) or on the use of lignocellulose biomass as natural filler, but in this talk we will update on our work on the fabrication of biocomposites made entirely from vegetable macromolecules. A mild hydrolysis carried out only in water, was developed to produce vegetable-based freestanding films from different vegetables. We were able to correlate the thermo-mechanical properties with the composition and morphology using a combination of techniques: solid state NMR, FTIR, SEM, confocal microscopy, dynamic mechanical thermal analysis and Time Domain NMR. We studied and verified the biodegradability of the final material and the preservation of plant-derived properties such as color and antioxidant properties. This knowledge allowed us to devise new fabrication techniques, such as hot embossing to obtain complex shapes and to study the materials as mulches for agricultural applications. The proposed production process was studied by Life Cycle Analysis, and compared to traditional plastics and bioplastics like HDPE, PET, PLA and starch. The vegetable biocomposites were more competitive than traditional plastics in terms of global warming potential and cumulative energy demand, and were more competitive than PLA in their water scarcity index.

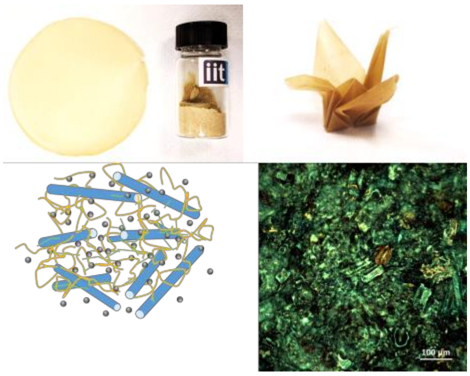

Figure 1: carrot bioplastic films from dried carrot pomace. Origami obtained by plasticization of the material. Schematic depicting the interaction with water and film structure as observed by confocal microscopy.

[1] G. Perotto, L. Ceseracciu, R. Simonutti, U. C. Paul, S. Guzman-Puyol, T.-N. Tran, I. S. Bayer, and A. Athanassiou, *Green Chemistry* **20** (2018) 894-902.
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Smart materials for the conservation of built Heritage

Lucia Toniolo

[a] *Department Chemistry, Materials and Chemical Engineering "Giulio Natta", Politecnico di Milano, Piazza Leonardo da Vinci 32, 20133 Milano, Italy*
E-mail: lucia.toniolo@polimi.it

Although stone can be considered one of the most stable materials used in structures and buildings since prehistoric times, it is well known that they are subjected to natural weathering and deterioration phenomena, potentially leading to dangerous, severe and sometimes rapid effects. Marbles and limestones, e.g., have been extensively used in historical architecture and sculptures owing to their good microstructural and mechanical properties, workability and durability and overall aesthetic quality. Nevertheless, the conservation of historical marbles in outdoor urban conditions is a very difficult task, moreover in rather aggressive and polluted environment.

From the scientific literature, it is clear that the protection strategy for stone surfaces should be directed to avoid water absorption by the porous microstructure and, at the same time, to grant an eventual effective drying of the stone; with climate and air quality changing, the priority challenge will be to protect the surfaces against the attack of CO2 and NOx and microbiological pollutants.

The contribution proposes an overview of the constraints and requirements for a correct approach to the conservation of remarkable, sometimes unique, architectural surfaces and the history of use and implementation of materials and methodologies for conservation. It will focus on the strategies based on nanostructured materials and methods, with a particular emphasis for protective treatments based on the use of SiO2, TiO2, ZnO and Ag nanoparticles to confer superhydrophobic, self-cleaning and antifouling properties to surfaces.

[1] Price, C. A., & Doehne, E. (2011). Stone conservation: an overview of current research. Getty Conservation Institute, Getty Publications, LA, USA.
[2] Toniolo, L., & Gherardi, F. (2018). The protection of marble surfaces: The challenge to develop suitable nanostructured treatments. In: Advanced materials for the conservation of stone, Karapanagiotis, I., & Hosseini, M. Eds. Springer, Cham pp. 57-78.
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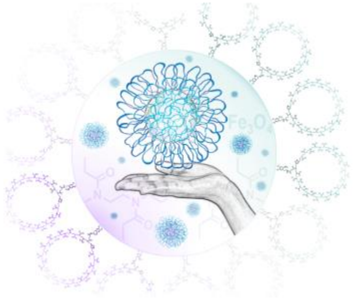
Topological Evolution of Bioinert and Functional Polymer Interfaces

Edmondo M. Benetti

Polymer Surfaces Group, Department of Chemical Sciences, University of Padova, via Marzolo 1, 35122 Padova (Italy)
E-mail: edmondo.benetti@unipd.it



The application of cyclic polymers in surface functionalization enables an extremely broad modulation of interfacial physicochemical and functional properties, surpassing the attractive characteristics provided by commonly applied, linear polymer "brushes".

This is valid on macroscopic, inorganic surfaces, where chemically inert, cyclic polymer brushes provide an enhanced steric stabilization of the interface and a superlubricious behavior [1-4]. Alternatively, when cyclic brushes form shells on inorganic nanoparticles (NPs), their highly compact and ultradense character make them impenetrable and long-lasting shields, which extend the stability of NP dispersions and hinder any interaction with serum proteins [5,6].

The steric and conformational constraints introduced during cyclization additionally affect the characteristics of polymer assemblies when these feature a functional character. This is the case for polymer interfaces that are chemically designed to actively interact with proteins present in the medium, or, alternatively, which respond to a chemical stimulus by a significant change in their properties.

The augmented effective intramolecular repulsion between polymer segments within cyclic macromolecules does not only determine a higher excluded-volume effect and enhanced solvation, but it additionally leads to an increment in electrostatic repulsive forces when the polymers are ionizable, and provides an increased exposure of functional groups enabling a more efficient binding of biological entities [7,8]. On the one hand, the amplified responsiveness of cyclic polyelectrolyte brushes broadens the tuning potential for interfacial properties on "smart" surfaces, providing a new molecular design for responsive materials. On the other hand, the increased availability of functions on cyclic brush-bearing surfaces indicates that an enhancement in reactivity towards biological entities can be generalized to different polymer chemistries. If this hypothesis was validated, cyclic polymer assemblies could not only be applied as extremely efficient bioinert surfaces, but they could also act as synthetic supports for biological recognition, improving the performance of nanomedical devices and biosensors.

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Novel liposomes as levodopa nanocarriers for the treatment of Parkinson disease

Elena Allegritti,[a] Sara Battista,[a] María Luisa González Rodríguez,[b] and Luisa Giansanti[a]

[a]*Dipartimento di Scienze Fisiche e Chimiche, Università degli Studi dell'Aquila, Via Vetoio 1, 67100 - L'Aquila, Italy*
[b]*Departamento de Farmacia y Tecnología Farmacéutica, Universidad de Sevilla, Calle Profesor García González 2, 41012 – Sevilla, Spain*
E-mail: elena.allegritti@graduate.univaq.it

Parkinson disease (PD) is a progressive disease of the central nervous system and affects 1% of the population; it is characterized by the loss of dopaminergic neurons in the substantia nigra, resulting in low dopamine concentration. The presence of the blood-brain barrier (BBB) hampers the delivery of dopamine to the brain while levodopa (L-DOPA, Figure 1a), a precursor, can reach the target site. However, high doses of pro-drug must be administered to patients to reach the minimum therapeutic concentration because less than 3% of given L-DOPA gets to the brain. Moreover, it is easily oxidized thus becoming inactive [1]. Despite these limitations, L-DOPA remains the most effective therapy in the treatment of the disease. Therefore, there is a need to develop new strategies that are able to extend and control the release of this pro-drug.

Liposomes, which are sphere-shaped vesicles, could be suitable carriers. Besides being biocompatible, their structure gives them the ability to load antioxidant molecules together with L-DOPA in order to prevent its oxidation and to retard the progression of PD. Furthermore, liposomes have gained attraction since they can deliver drugs to the brain by intranasal administration: this approach grants a direct access to the brain circumventing the need to cross the BBB [2].

Based on these premises, L-DOPA and natural antioxidants (*L*-ascorbic acid and quercetin, Figure 1a) were included in mixed liposomes formulated with a saturated natural phospholipid and structurally related synthetic surfactants (Figure 1b) to investigate the effect of the composition on the properties of the final vesicles.

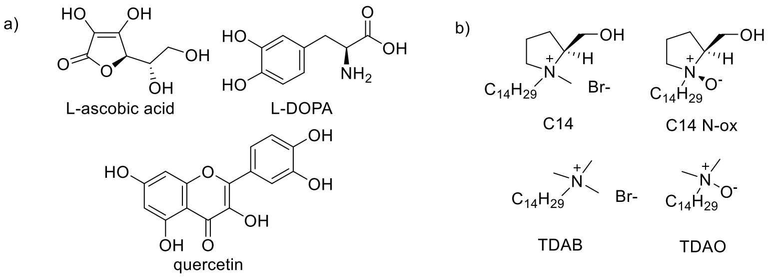

Figure 1: a) L-DOPA and natural antioxidants; b) synthetic surfactants

[1] W. Poewe, A. Antonini, J. C. M. Zijlmans, P. R. Burkhard, and F. Vingerhoets, *Clin Interv Aging* **5** (2010) 229-238.
[2] S. Hong, K. T. Oh, H. Choi, and S. Lim, *Pharmaceutics* **11** (2019) 540-557.

Potential CDC20 inhibitors: synthesis and biological evaluation of Apcin analogues

Dario Telese,[a] Carla Boga,[a] Gabriele Micheletti,[a] Joseph Durante,[a] Natalia Calonghi,[b] and Giorgia Simonetti[c]

[a] Department of Industrial Chemistry 'Toso Montanari', University of Bologna, Viale Del Risorgimento 4, 40136-Bologna, Italy
[b] Department of Pharmacy and Biotechnologies, University of Bologna, Via Irnerio 48, 40126-Bologna, Italy
[c] IRCCS Scientific Institut of Romagna for the Study and the Cancer treatment (I.R.S.T.), Via Piero Maroncelli, 40, 47014-Meldola (FC), Italy
E-mail: dario.telese2@unibo.it

The research of compounds able to inhibit the interaction between APC/C and CDC20 has strongly emerged gaining a great deal of interest in recent years as useful tool for the design of CDC20 inhibitors, [1] providing a therapeutic window in multiple human malignancies. [2] Recently it has been discovered a new molecule called Apcin, which binds to CDC20, inhibiting the anaphase promoting complex into cells afflicted by AML (acute myeloid leukemia). In this context we planned the synthesis of a series of Apcin analogues **5** in Figure 1, characterized by an amino aza-heterocycle moiety (in blue), bounded to a trichloroethyl group (in green) in turn functionalized to a group (in red) inserted through nucleophilic substitution to the precursor **4**.
[3] Preliminary biological tests were carried out on the compounds obtained towards a panel of solid and hematological cancer cell lines.

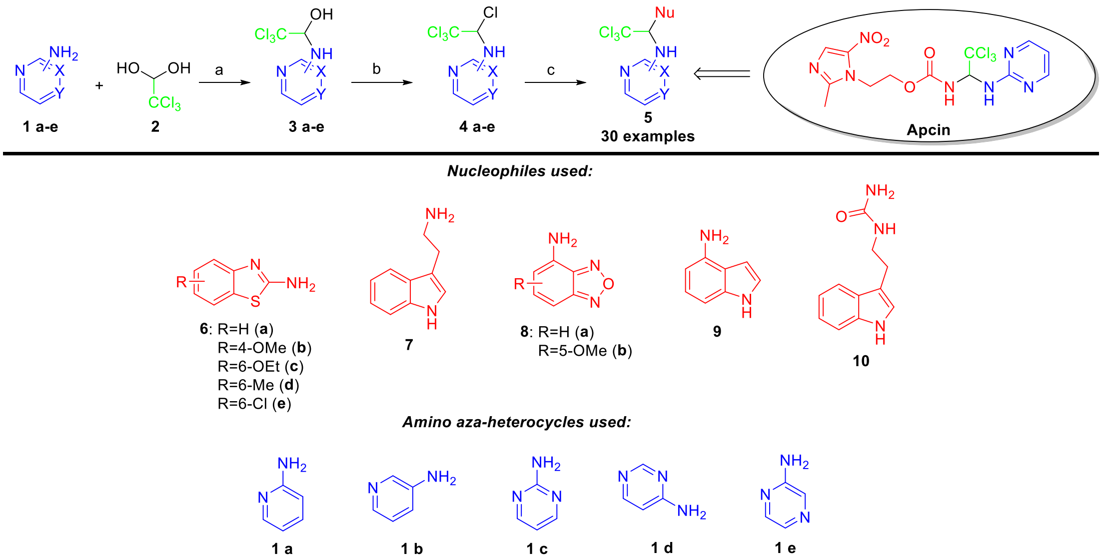

Figure 1: Synthesis and *building blocks* of Apcin analogues. Reaction conditions: a) THF, MW, 90°C, 3.5 h; b) $SOCl_2$, N_2, THF, r.t., 2 h; c) NuH, THF, MW, 70°C, 5-8 h.

[1] P. Huang, X. Le, F. Huang, J. Yang, H. Yang, J. Ma, G. Hu, Q. Li and Z. Chen, *J. Med. Chem.* **63** (2020) 4685-4700.
[2] Y. Gao, B. Zhang, Y. Wang, and G. Shang, *Oncol. Rep.* **40** (2018) 841-8.
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Synthesis and Evaluation of Novel Anti-Cancer Metastatic Drugs that Disrupt Cancer-Stromal Cell Communication

Daniela Carbone

Dipartimento di Scienze e Tecnologie Biologiche Chimiche e Farmaceutiche (STEBICEF),
Università degli Studi di Palermo, Via Archirafi 32, 90123 Palermo, Italy
E-mail: daniela.carbone@unipa.it

Extracellular vesicles (EVs) are key players in intercellular communication, under both healthy and pathological conditions, including the induction of pro-metastatic traits by hijacking stromal cells (e.g., mesenchymal stromal cells (MSCs)) in the pre-metastatic niche [1]. Upon endocytosis, cancer-derived EVs within late endosomes enter the nucleoplasmic reticulum, *via* a tripartite complex formed by the proteins VAP-A (in the outer nuclear membrane), ORP3 and late endosome-associated Rab7 (the VOR complex hereafter), and transport EV cargo (proteins and nucleic acids) to the nucleoplasm, where they alter the fate of target cells [2]. The nuclear transfer of EV cargo and subsequently the pro-metastatic activity of cancer EVs is inhibited by the antifungal agent itraconazole (ICZ), which binds to ORP3 and blocks VOR complex formation [3]. In the effort to find a new smaller novel chemical entity that mimics ICZ, we rationally designed and synthesized a novel compound (PRR851), which proved effective in inhibiting the nuclear transfer of EV cargo and subsequently the pro-metastatic activity of colon cancer EVs. Compared to ICZ, PRR851 elicited a rather superimposable set of interactions with VOR complex, comprising both polar and hydrophobic contacts (Figure 1), but the absence of moieties that inhibit other non VOR-related targets suggests that PRR851 should have a clinically more favorable toxicity profile, which is consistent with lack of cytotoxicity up to 10 μM and no evidence for general toxicity in mice exposed to 100 and 200 mg/Kg. In addition, to confirm the molecular target, PRR851 was biologically evaluated as fluorescent probe and the results indicated that it inhibits the binding of Rab7 to ORP3/VAP-A complex, resulting in the suppression of the pro-metastatic morphological transformation of cancer cells and their migratory properties. Based on these considerations, applications in cancer and/or in virology, where endosomal compartments are involved, could be developed.

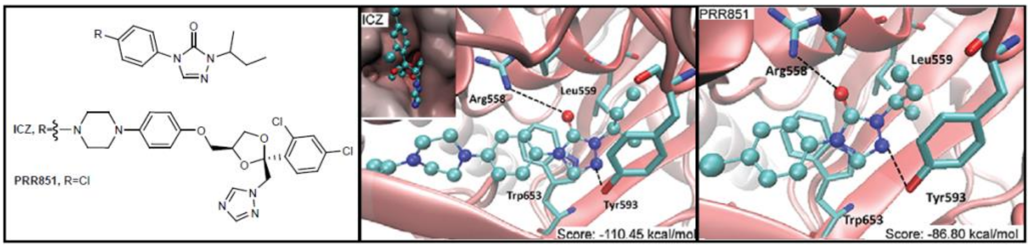

Figure 1: Chemical structures and docking simulations for ICZ and its derivative PRR851 within the VOR complex.

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Synthesis of fluorinated polymers for drug/gene delivery and ^{19}F-MRI imaging

Carola Romani, and Alessandro Volonterio

Dipartimento di Chimica, Materiali e Ingegneria Chimica “Giulio Natta, Politecnico di Milano, via Mancinelli 7, 20131-Milano, Italy
E-mail: carola.romani@polimi.it

The development of polymeric non-viral vectors for gene delivery has gained great attention in the last years, due to their potentiality to overcome the cytotoxicity and the non-biodegradable nature of the golden standard nowadays present in literature (i.e., Polyethylenimine (PEI) based polymers and Polyamidoamine (PAMAM))[1].

However, transfection efficiency remains the principal obstacle of these kind of systems [1,2].

Advancement of controllable polymerization and macromolecular functionalization techniques paved the way to the development of more controllable and engineered structures [1-3].

In this work, investigation of perfluorinated transfecting agents as smart imaging tools for ^{19}F magnetic resonance imagining (^{19}F-MRI) gave the possibility to synthesize a library of 10 novel multifunctional building blocks, characterized by specific and proper functional groups, showing a single or two different fluorine signal, with closer chemical shift, suitable for imaging purposes.

The coupling of these fluorinated building blocks to polymeric structures will permit to obtain functional macromolecular systems for novel tunable platform for multimodal imaging and therapeutic products for gene/drug delivery; in this scenario, functionalization of commercial PAMAM of generation 2 (G2) and 4 (G4) was performed choosing three multifunctional building blocks from the developed library (Figure 1).

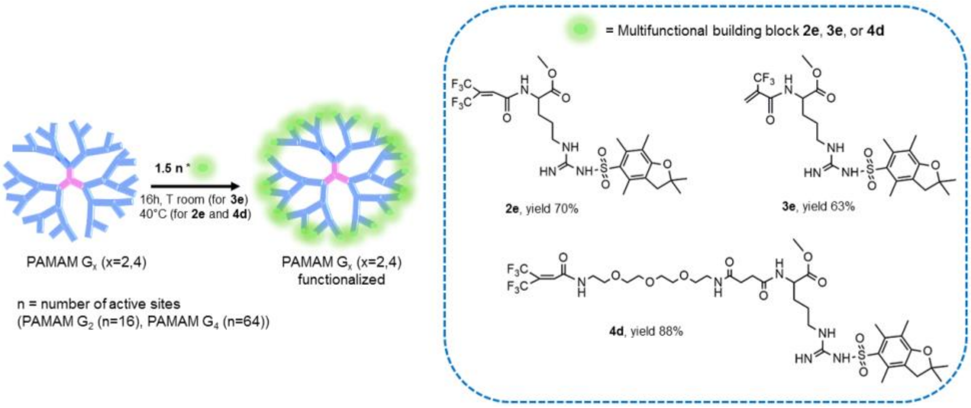

Figure 1: Graphic representation of PAMAMs functionalization reaction.

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Gadolinium doped Carbon Nanodots for MRI applications

Michele Cesco,[a] Lucia Cardo,[a] Marta Martinez-Moro,[a] Lydia Martinez-Parra,[a] and Maurizio Prato[a,b]

[a] *Carbon Nanobiotechnology Laboratory, CIC biomaGUNE, Donostia-San Sebastián, Spain.*
[b] *Department of Chemical and Pharmaceutical Sciences, INSTM UdR Trieste, Università degli studi di Trieste, Trieste, Italy*
Email: mcesco@cicbiomagune.es

Magnetic Resonance Imaging (MRI) is a widely used non-invasive medical imaging technique to visualize the inner part of human body. Carbon Nanodots (CNDs) are a new class of fluorescent small-carbon nanomaterials with particle sizes of less than 10 nm [1]. The strong fluorescence and low toxicity of CNDs make them attractive materials for a variety of biomedical applications, such as biosensing and bioimaging. Recently, gadolinium-doped CDs have emerged as a new generation of nanoprobes as imaging agents. Gadolinium MRI agents function by catalytically relaxing water tissues protons through dipolar interaction. We have produced amorphous carbon-based nanodots of 6-8 nm doped with Gd(III) (Gd-CNDs). They can be used as multi-modal imaging agents for Magnetic Resonance Imaging (MRI) and theragnostic applications. Generally, our Gd-CNDs are obtained by fast solvothermal treatment of one amino acid (i.e alanine, arginine, tryptophan, a linking coordinating unit (i.e. EDTA) and $GdCl_3$ in water using a focused microwave synthesiser. Whilst this approach allows fast screening of several combinations of precursors and reaction conditions, it also presents one main drawback concerning the isolation of one homogenous material from unwanted side products. Therefore, we focus on combining gel electrophoresis and HPLC techniques to reveal the presence of different populations of material and identify/isolate only those containing gadolinium. In here we present the example of one of our Gd-CNDs, as negatively charged amorphous particles with size around 7 nm (by TEM and AFM) and able to incorporate around 10% of Gd. The material also presents nice absorption in the UV-Visible region and the excitation-depending emission profile that is well known for CNDs in general [2]. Our purification strategy allowed the isolation of two distinct population of material, with similar size and morphology, and both containing gadolinium. However, their IR profiles are significantly different and XPS analysis shows that Gd (III) is involved in different types of Gd-O bonds, suggesting that the metal is incorporated within the Gd-CNDs in more than one coordination environment. Remarkably, our Gd-CNDs present a longitudinal relaxivity (r1) of 3-7 $mM^{-1}\ s^{-1}$, which is comparable with or higher than r1 of contrast agents currently employed in diagnostics (i.e. Magnevist, 3.40 $mM^{-1}\ s^{-1}$).

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Ruthenium (II) polypyridyl complexes as promising light-responsive antimicrobials agents

Gina Elena Giacomazzo,[a] Luca Conti,[a] Alessio Mengoni,[b] Camilla Fagorzi,[b]
Patrik Severin Sfragano,[a] Barbara Valtancoli,[a] and Claudia Giorgi [a]

[a] *Department of Chemistry “Ugo Schiff”, University of Florence, via della Lastruccia 3, 50019 Sesto Fiorentino, Italy*
[b] *Department of Biology, University of Florence, via Madonna del Piano 6, 50019 Sesto Fiorentino, Italy*
E-mail: ginaelena.giacomazzo@unifi.it

Multidrug resistance of bacterial pathogens is a major health concern worldwide and the widespread use of antibiotics over the last decades has determined the emergence of drug-resistant populations of microorganisms which have become an important cause of death [1]. Therefore, there is an urgent need for the development of new and effective antimicrobial agents.

In this scenario, ruthenium (II) polypyridyl complexes represent an attractive class of compounds due to their unique chemical-physical repertoires, structural diversity and redox properties which provide a unique opportunity for designing effective antibacterial agents. Moreover, modulation of ancillary ligands on ruthenium (II) complexes allows to obtain both photostable sensitizers, whose activation promotes the production of reactive oxygen species, and photoactivable complexes capable to release bioactive molecules following irradiation with low-energy visible light.

The two approaches, named respectively antimicrobial photodynamic therapy (aPDT) and photoactivated chemotherapy (PACT), are compared presenting two different classes of ruthenium (II) polypyridyl complexes: one capable to produce an oxidative stress on gram positive bacteria strains [2], the other capable to release bioactive drugs through oxygen independent mode of action.

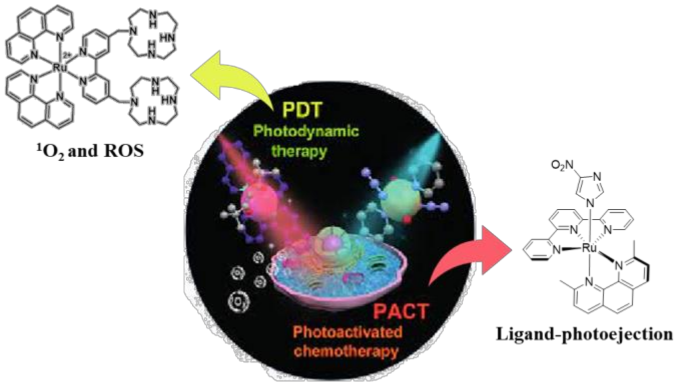

Figure 1: Different ruthenium scaffolds for two different antimicrobial mode of action.

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Native mass spectrometry-directed identification of novel disruptors of the LPS transport system

Francesco Fiorentino,[a,b] Jani R. Bolla[b] Carol Robinson,[b] Dante Rotili[a] and Antonello Mai[a]

[a] Department of Drug Chemistry & Technologies, Sapienza University of Rome, P. le A. Moro 5, 00185-Rome, Italy
[b] Department of Chemistry, University of Oxford, South Parks Road, OX1 3QZ-Oxford, UK
E-mail: f.fiorentino@uniroma1.it

Native mass spectrometry (nMS) is a biophysical method that allows the study of protein-protein interactions (PPIs), protein-ligand interactions, subunit architecture, and stoichiometry [1]. Here we developed a nMS-based approach to gain insights on the modulation and disruption of the lipopolysaccharide (LPS) transport protein LptH.

The presence of LPS in the outer membrane (OM) is essential for membrane stability and protection of Gram-negative bacteria. The LPS transport (Lpt) complex is responsible for LPS translocation from the inner membrane to the OM (Fig. 1a) [2]. Among the Lpt proteins, the periplasmic LptA forms an oligomeric bridge connecting the two membranes. Thus, a promising strategy for antimicrobials drug discovery relies on the design of PPI disruptors targeting LptA. In the multidrug-resistant opportunistic pathogen *P. aeruginosa*, the orthologue of LptA is called LptH and forms dimers in solution [3]. Using nMS we quantified the monomer-dimer equilibrium of LptH (Fig. 1b) and assessed the potency and efficacy of the antimicrobial peptide thanatin and small molecule disruptors, obtaining new information on their structure-activity relationships (Fig. 1c-d). This approach led to the discovery of new quinoline-based hit compounds representing the basis for the development of novel LPS transport inhibitors.

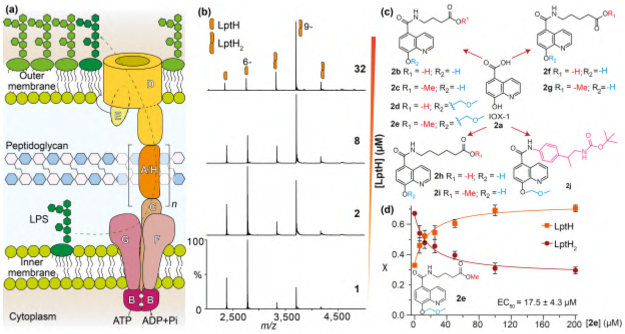

Figure 1: (a) Representation of the Lpt system showing the LptB$_2$FG-(LptA/H)$_n$-LptDE multiprotein complex. (b) nMS of LptH at increasing concentrations showing the transition from monomer to dimer. (c) Structures of the quinoline derivatives employed in this study. (d) Plot of monomer (orange) and dimer (red) mole fraction (χ) as a function of compound concentration and relative quantification of EC$_{50}$ and E$_{max}$.

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Buffer modification workflow for the resolution of phosphocholine-containing lipid isomeric mass overlaps in negative ionization mass spectrometry

Andrea Cerrato, Chiara Cavaliere, Carmela Maria Montone, Susy Piovesana, and Anna Laura Capriotti

Dipartimento di Chimica, Università degli Studi di Roma La Sapienza, Piazzale Aldo Moro 5, 00185, Rome, Italy
E-mail: andrea.cerrato@uniroma1.it

Lipidomics, once considered a branch of metabolomics, has nowadays gained its proper analytical approaches that differ significantly from routinary methods for metabolomics [1]. Shotgun mass spectrometry (MS) and liquid chromatography coupled to MS (LC-MS) are the foremost techniques for lipidomics analyses, either in targeted or untargeted fashion. In untargeted lipidomics, the structural information is highly dependent on the analytical methods [2], and data processing and lipid identification by software programs are toughened by a large number of adducts and several isomeric mass overlaps [3]. Buffer modification workflows (BMW) are based on the use of unlabeled and stable-isotopically labeled buffer modifiers (e.g., $^{14}NH_4^+$ and $^{15}NH_4^+$), which significantly facilitate feature annotation.

For the first time, a BMW approach is presented specifically for phosphocholine-containing polar lipids (PCLs), e.g., phosphatidylcholines and sphingomyelins. The approach is based on the simultaneous use of AcOH and d_3-AcOH in the chromatographic buffers, given the well-known ability of PCLs of forming acetate adducts through their quaternary ammonium group. For data processing, a customized workflow on Compound Discoverer was specifically set up for the purpose. The proposed methodology was optimized by Box-Behnken design of experiments, and the overall performance were compared to several standard metabolomics- and lipidomics-based approaches. The optimized methodology was applied to the characterization of human plasma samples, a commonly analyzed yet of great complexity matrix, resulting in 135 PCLs correctly annotated and extracted from the raw datasets.

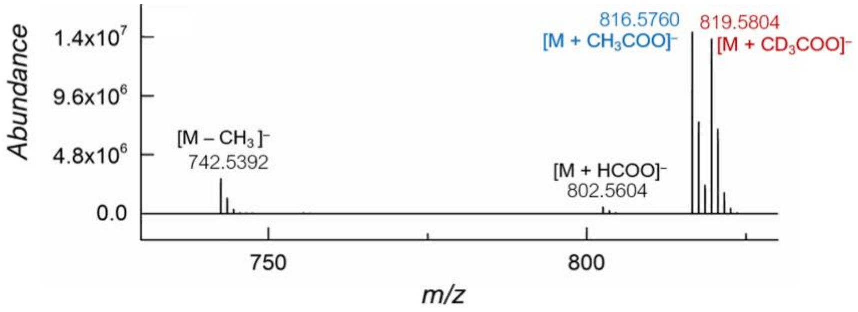

Figure 1: MS spectra obtained for standard PC(16:0/18:2) by BMW

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Synthetic nitrogenated analogues inspired by honokiol as hypoglycemic and antiobesity agents

Claudia Sciacca,[a] Nunzio Cardullo,[a] Vera Muccilli [a] and Corrado Tringali[a]

[a] *Dipartimento di Science Chimiche, Università degli studi di Catania, V.le A. Doria 6, 95125-Catania, Italy*
E-mail: claudia.sciacca@phd.unict.it

Obesity is a metabolic disorder resulting from an excessive accumulation of body fat. It is considered a risk factor for chronic diseases and disabilities such as cardiovascular diseases, cancer, osteoarthritis, and hypertension [1]. Moreover, the incidence of obesity is frequently associated with type 2 Diabetes mellitus, a metabolic disorder characterized by insulin hormone dysfunction. Several strategies have been developed for the inhibition of the enzymes involved in metabolic diseases. Pancreatic lipase is a key enzyme responsible for the hydrolysis of 50–70% of triglycerides and free fatty acids, and its inhibition is used to reduce obesity. α-Amylase is a carbohydrate hydrolyzing enzyme, and its inhibition is currently a strategy to manage hyperglycemia. Although with several undesired side effects, Orlistat and Acarbose are presently employed as pancreatic lipase and α-amylase inhibitors. Thus, the search for inhibitors with minor or absent undesired effects is of great importance.

Some natural polyphenols have been reported as inhibitors of the digestive enzymes [2,3], involved in metabolic disorders. The present work aims to synthesize nitrogenated analogues inspired by honokiol and evaluate their biological properties to obtain new potential therapeutical agents. The synthetic strategy involves: i) borylation of aminophenol, ii) Suzuki-Miyaura cross-coupling reaction, iii) reaction of allylation, and iv) subsequent Claisen rearrangement. As the first biological screening, the new compounds were evaluated for their *in vitro* inhibitory activity against α-amylase and pancreatic lipase enzyme, with promising results.

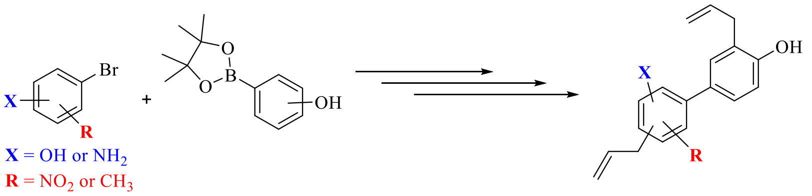

Figure 1: Synthetic strategy.

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On the effect of the stationary phase chemistry and the composition of the mobile phase on retention and selectivity of cannabinoids under normal phase conditions

Simona Felletti,[a] Alessandro Buratti,[a] Chiara De Luca,[a] Federica Pellati,[b] Virginia Brighenti,[b] Yannick Krauke,[c] Svea Stephan,[c] Kate Monks,[c] Martina Catani,[a] and Alberto Cavazzini[a]

[a] *Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, via Borsari 46, 44121, Ferrara, Italy*
[b] *Department of Life Sciences, University of Modena and Reggio Emilia, Via G. Campi 103, 41125 Modena, Italy*
[c] *KNAUER Wissenschaftliche Geräte GmbH, Hegauer Weg 38, 14163 Berlin*
E-mail: fllsmn1@unife.it

Due to the progress decriminalization of recreational cannabis and the growing interest in hemp and cannabis products, in the last years much effort has been devoted to investigating the biological and pharmacological activity of cannabinoids in order to ensure consumer safety. However, only 20% of natural occurring cannabinoids (or phytocannabinoids) is currently available as a certified reference material and new cannabinoids are continuously being discovered [1].

The purification of cannabinoids, especially from hemp extracts, could be very challenging due to the presence of a large number of components (such as terpenes, waxes, other cannabinoids, etc.), many of them with similar chemical structure. This points the attention on the need of fast, efficient and cost-effective methods for the isolation and purification of cannabinoids, especially from plant materials [2].

In this field, preparative liquid chromatography (LC) and multicolumn countercurrent chromatography (MCC) are the most employed technique for industrial purification of cannabinoids. However, a deeper understanding of the fundamentals of cannabinoids retention is required for the selection of the optimal combination of mobile phases and column chemistries.

In this work, the effect of the stationary phase polarity on retention, separation and selectivity of five different neutral phytocannabinoids, namely CBD, CBC, CBG, CBN and Δ9-THC, has been investigated on four 150×4 mm polar columns packed with 5 *μ*m particles under normal phase (NP) isocratic elution conditions.

Results, obtained in an analytical scale, indicate that NP chromatography could be very promising if applied to large scale separations and purifications of cannabinoids, when compared to RP chromatography, due to fast analysis, low backpressure, high selectivity and high sample solubility.

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Eco-friendly hydrogels and glues from soy proteins and polyphenols

Rita Argenziano

Department of Chemical Sciences, University of Naples “Federico II”, Via Cintia 4, I-80126 Naples, Italy
E-mail: rita.argenziano@unina.it

Soy proteins isolates (SPI), the main industrial waste in soybean processing, are of particular interest for implementation of natural adhesives since they are cost-effective and easy to handle, but they show low strength and poor water resistance. On this basis, the present work was aimed to improve the adhesive properties of soy proteins by use of natural polyphenols and polyphenol rich water extracts.

Initially, it was shown that SPI thermal denaturation is critical to get adhesiveness as evaluated by a simple test involving application of the adhesive on wood specimens that are then pressed together and soaked in water. Caffeic acid (CA) and its methyl ester, gallic acid and chlorogenic acid (CGA) were evaluated as additives. SPI was dissolved in water at 10% w/w and taken at 85°C for 1 h, then the polyphenol was added at 28 mM and the resulting mixture taken to 50°C and to pH 9. These conditions were expected to favor oxidation of o-diphenols to o-quinones that can be entrapped by nucleophilic residues of the protein with formation of a network [1]. Development of a green chromophore typical of benzacridines from oxidative coupling of CGA with lysine provided evidence for an effective interaction for SPI/CGA [2].

Water resistance of wood specimens glued with the polyphenol/SPI proved higher (> 22 days for CGA/SPI) compared to that obtained using SPI alone (1 day). In addition, shear strength of polyphenol/SPI wood specimens was higher than 2.07±0.70 kgcm^{-2} obtained for Urea/SPI previously described [3] with values up to 3.21±0.19 kgcm^{-2} in the case of CA/SPI. Determination of amount of free SH and NH_2 groups on the final material as lyophilized powder by Ellman’s reagent and o-phthalaldehyde (OPA) reagent assay indicated the substantial involvement of these groups in the formation of cross-linking between polyphenols and SPI.

To assess the potential of these materials for biomedical applications in wound treatment, agarose/SPI gel was prepared starting from agarose water solution and adding thermally denaturated SPI at 1:2 w/w ratio. Then the obtained solution was cooled in a petri dish and immersed in 10 mM water solution at pH 9 of the appropriate polyphenol. The resulting gel obtained from CGA with agarose/SPI showed a green color, due to the formation of benzacridine systems, indicating the reaction of CGA with lysine residues of proteins present inside the preformed gel. The cytocompatibility of these gels is currently under assessment.

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Fluorination of dopamine and its polymerization behaviour

Giorgio Rizzo, and Francesco Babudri

Dipartimento di Chimica, Università degli studi di Bari Aldo Moro, Via E. Orabona 4, 70126, Bari
E-mail: giorgio.rizzo@uniba.it

Dopamine, also known as 2-(3,4-dihydroxyphenyl)ethylamine, has attracted great interest in material sciences, since its polymerization reaction is a non-enzymatic spontaneous process in aqueous solutions in mild conditions. Since polydopamine (PDA) is composed by different monomer and oligomer moieties, further complicated by supramolecular interactions and highly influenced by the reaction conditions, its deep characterization is impossible and its structure is still under debate. All the intermediates create a dark brown branched polymer exhibiting a high number of hydrogen donor and acceptor units and aromatic rings held together by covalent and π-π stacking.[1] PDA finds applications in metal chelating and reducing properties, ultrathin coatings and in adhesives.[2] In particular, PDA and related dopamine-rich proteins are responsible for the exceptionally high adhesion of marine creatures, such as mussels (*Mytilus spp.*). We focused on the chemical modification of dopamine through selected chemical reactions involving fluorine atoms addition. Fluorine is a well known substituent able to dramatically modify the hydrophobic/hydrophilic behaviour of a molecule or a surface. [3] The presence of a perfluoroalkyl pendants is mandatory when an increase of water repulsion is desired as, for instance, in the design of new stronger underwater adhesives. Fluorinated dopamines still maintain their unique ability to polymerize in the typical PDA structure. Electrochemistry showed that polymerization preserves the hydroxyl residues, making PDA a new bioderived material for high tech applications in the field of water-resistant, hydrophobic materials. This fine chemistry on dopamine could shed light on the true mechanisms of polymerization through the study of chemical environments of fluorine atoms specifically included in the molecule.

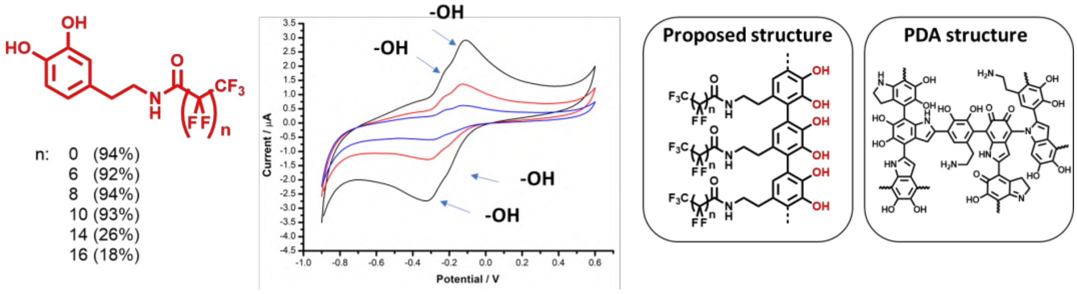

Figure 1: Study on the effect of fluorination on the final PDA structure. Cyclovoltammetry suggests a polymerization pathway in which -OH are maintained.

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Coated SuperParamagnetic Iron Oxide Nanoparticles (SPIONs) as versatile support for the heterogenization of organometallic complexes

Roberta Colaiezzi, Andrea Lazzarini, Andrea Di Giuseppe, Marcello Crucianelli

Department of Physical and Chemical Sciences, University of L'Aquila, Via Vetoio (COPPITO 1-2), 67100, L'Aquila, Italy
E-mail: roberta.colaiezzi@graduate.univaq.it

Magnetic iron oxide nanoparticles (NPs) have shown great potential as recyclable magnetic nanocatalysts, as well as information storage materials, in adsorption /separation processes and biomedical applications. In the field of catalytic research, the importance of the recyclability of a heterogeneous catalyst is an aspect that is arousing much interest in the scientific community [1]. Superparamagnetic silica-coated iron oxide nanoparticles (SPION) 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 to optimizing the thickness of the silica layer. A comprehensive set of characterization techniques was employed to reveal the characteristics of the catalyst. We are currently developing a procedure for the heterogenization of organometallic complexes based on Schiff bases containing Mo in the organic binder, shown in Figure 1. For this reason, the efficiency of the coating is essential to provide a tailored anchor point for the phase. activates the catalyst. The oxidation of cis-cyclooctene with tert-butyl hydroperoxide in the presence of SPION was used as a reaction probe to verify the possible reactivity of the coated NPs, as such, and the efficacy 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 by modifications of the magnetic core. The olefin oxidation reaction was used for catalytic tests, which showed high yields and selectivity, as well as good recyclability.

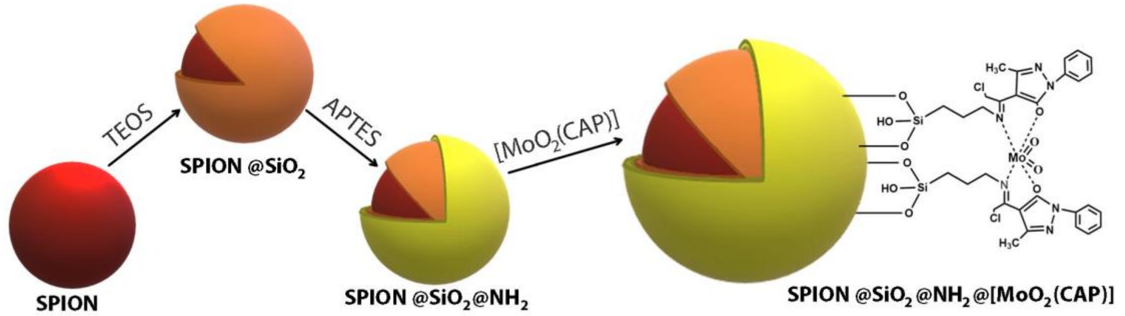

Figure 1: synthetic procedure of the heterogeneous catalysts

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Divergent synthesis of functionalized β-amino ketones through gold/Selectfluor partnership

Vincenzo Marsicano,[a,b] Antonio Arcadi,[a,c] and Véronique Michelet [b]

[a] *Dipartimento di Scienze Fisiche e Chimiche, Università degli Studi di L'Aquila, Via Vetoio, 67100-Coppito (AQ), Italy*
[b] *Institut de Chimie de Nice, UMR 7272 CNRS, Université Côte d'Azur, Parc Valrose, Faculté des Sciences, 06100-Nice, France*
[c] *Dipartimento di Ingegneria e Scienze dell'Informazione e Matematica, Università degli Studi di L'Aquila; Via Vetoio, 67100-Coppito (AQ), Italy*
E-mail: vincenzo.marsicano@univaq.it

Gold catalysis has undoubtedly widened the range of organic architectures accessible from simple starting materials such as alkynes. Nevertheless, certain transformations are still not accessible, especially those involving changes in the oxidation state of the metal. A significant improvement in the field has been done through the association of gold with other reactive partners, such as Selectfluor [1]. In partnership with Selectfluor, gold can easily promote the formation of C-C and C-heteroatom bonds, with a special focus on C-F bonds. The possibility to easily introduce fluorine atoms into organic molecules is of great appeal in the fields of organic and medicinal chemistry, due to the multiple properties of organofluoride compounds [2].

Following our recent report on the regioselective hydration of *N*-propargyl phthalimides [3], the association of gold catalysis with Selectfluor was exploited to divergently generate three distinct chemical entities from the same *N*-propargyl phthalimide starting material through the "functionalized hydration" strategy. Herein we report the results of such investigation.

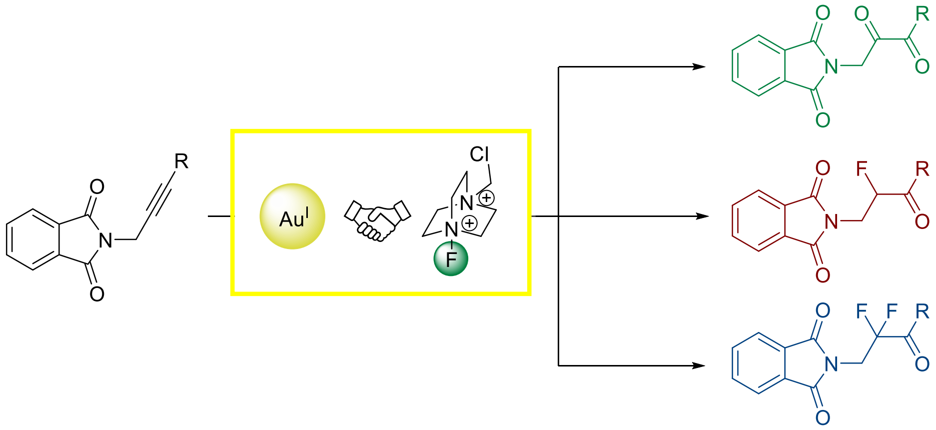

Figure 1: Scaffolds obtained through the gold/Selectfluor partnership.

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HLADH activity and recyclability: a kinetic approach

Alice Vetrano,[a] Francesco Gabriele,[a] Nicoletta Spreti,[a] Laura Goracci,[b] and Raimondo Germani[b]

[a] Dipartimento di Scienze Fisiche e Chimiche, Università degli studi dell'Aquila, Via Vetoio–Coppito, 67100-L'Aquila, Italy
[b] Dipartimento di Chimica, Biologia e Biotecnologie, Università degli studi di Perugia, Via Elce di Sotto 8, 06123-Perugia, Italy
E-mail: alice.vetrano@graduate.univaq.it

Horse liver alcohol dehydrogenase (HLADH) is a broadly specific enzyme that catalyzes the reversible oxidation of a wide range of both primary and secondary alcohols to their corresponding aldehydes and ketones with the simultaneous conversion of the cofactor. The reaction mechanism and the kinetics of the enzyme have been extensively characterized and studied already in the second half of the twentieth century. However, oxidoreductases are still today the most commonly applied biocatalysts, after hydrolases, for the synthesis of active pharmaceutical intermediates and fine chemicals on both academic and industrial scale [1].

In this work we studied the kinetic parameters of the free enzyme with respect to both the substrate, as is usually performed, and the cofactor, as previously reported by Dalziel [2]. The enzymatic assay of the oxidation and reduction reactions was performed on three classes of alcohols and on the respective carbonyl compounds, i.e., cyclic, benzyl and alkyl. The kinetic profiles were reported in Figure 1 as function of the cofactor concentration.

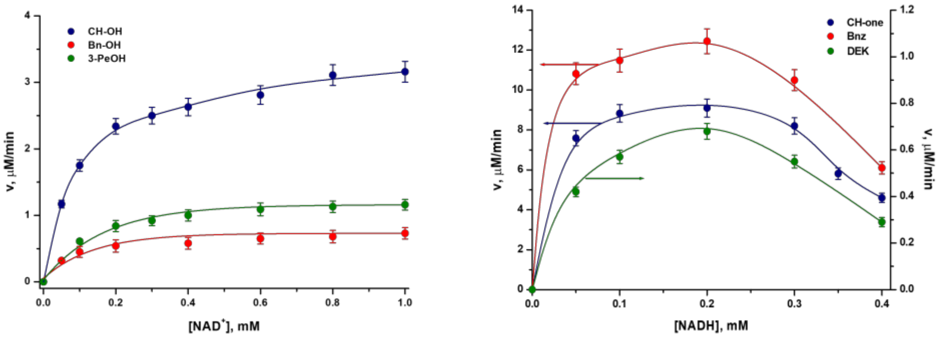

Figure 1: Kinetics of HLADH towards three different alcohols (left) and the corresponding carbonylic compounds (right).

All the reduction reactions do not follow Michaelis-Menten trend and show a maximum of activity at 0.2 mM of NADH; to explain this particular behavior modeling studies are underway. After such kinetic characterization, the enzyme was immobilized inside alginate beads in order to evaluate its stability (both operational and thermal) and to improve the recyclability of the biocatalyst.

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Oxidative copper-catalyzed reactions of aromatic benzylamino derivatives for the synthesis of fluorescent compounds

Marta Papis, Francesca Foschi, and Gianluigi Broggini

Dipartimento di Scienza e Alta Tecnologia, Università degli Studi dell'Insubria, Via Valleggio 9, 22100-Como, Italy
E-mail: mpapis@studenti.uninsubria.it

Transition metal-catalyzed processes under oxidative conditions have received significant attention from the scientific community due to the possibility to form new bonds using non-activated compounds as substrates [1]. Furthermore, copper-catalyzed reactions have proved to be a smart alternative to the well-known versatility demonstrated by palladium [2].

Herein we present our results on the development of a new protocol for the direct synthesis of polycyclic products bearing a benzoxazole or a benzimidazole moiety starting from benzylamino derivatives.

The dimerization of the aminophenol substrates followed by cyclization to oxazole rings allowed selective access to the tetracyclic products using a catalytic amount of CuCl combined with (diacetoxyiodo)benzene. The cascade process which leads to 5*H*-oxazolo[4,5-*b*]phenoxazine compounds was proven to be general and regiospecific involving three C-H functionalization steps.

Replacement of the starting amino-phenols with the structural and electronic analogues *N,N'*-dibenzyl-1,2-benzendiamines under the standard conditions didn't provide tetracyclic fused-ring products, although giving rise to a dimerization process with formation of a five-membered ring.

The actractiveness of this type of compounds is remarkable due to their emitting properties. Measurements in solution showed that both the dimeric compounds exhibit fluorescent emission with λ_{em} variable in a wide range.

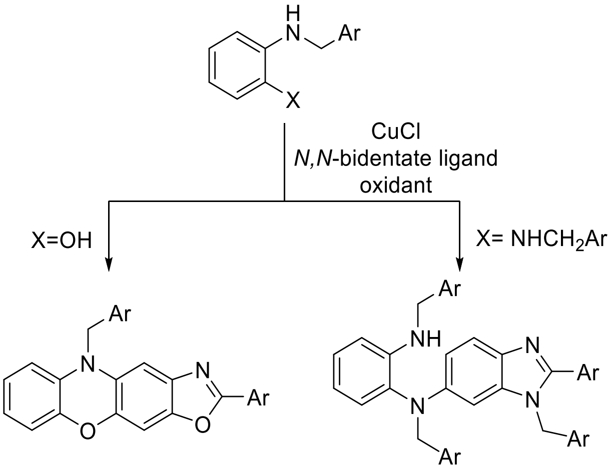

Figure 1: Dimerization/cyclization of aromatic benzylamino derivatives.

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A new approach for the synthesis of 1-aryl-2-aminopropanes

Camilla Loro,[a] Gianluigi Broggini,[a] and Giovanni Poli [b]

[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*
E-mail: cloro@uninsubria.it

Over the last two decades, hydroamination procedures involving the functionalization of a carbon-carbon double bond are strongly attractive processes. In this field, *O*-allyl carbamates showed a wide typology of chemical behavior at intra- and intermolecular level. For example, Shi and coworkers have 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]. Following our interest in alkene difunctionalization, we have now developed an acid mediated decarboxylative arylation/hydroamination reaction of *O*-allyl carbamates defining a direct synthesis of *N*-substituted phenethylamine derivatives. These latter have been widely studied in the last years for their value as scaffolds for a variety of applications in the fields of organic, bioorganic, and medicinal chemistry [3]. This procedure involved a Friedel-Crafts alkylation on the terminal position of the allylic cation in a cascade process for the double functionalization of C3 synthons that is so far unknow in the literature.

More specifically, in the presence of $Cu(OTf)_2$ as additive, *O*-allyl carbamates behaved as C3-1,2-dication equivalents allowing the generation of 1-aryl-2-aminopropanes through a selective anti-Markovnikov hydroamination pathway (Figure 1). The detailed mechanism of these transformations will be discussed in detail.

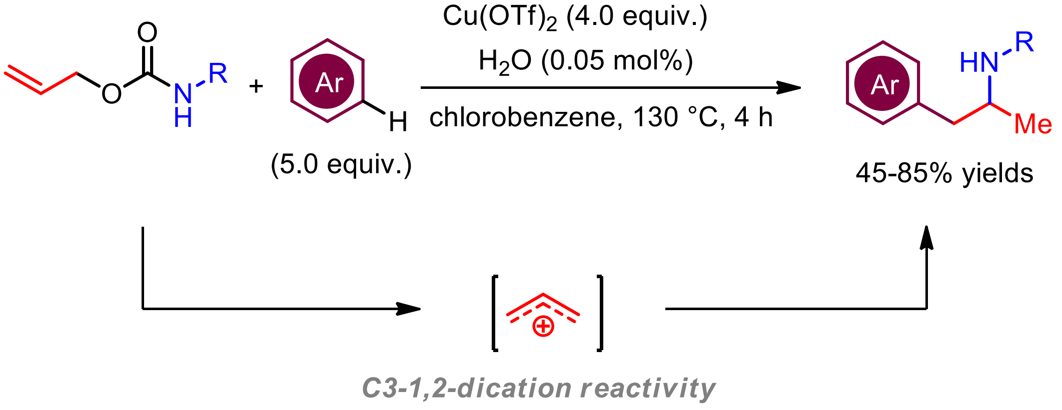

Figure 1: Arylation/hydroamination procedure.

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Study of the synthetic approach influence in Ni/CeO_2 catalyst for methane dry reforming reaction

Marco Pizzolato,[a] Francesca Langiano,[a] Michela Signoretto,[a] Elena Ghedini,[a]
Federica Menegazzo,[a] Alessandro Di Michele,[b] and Giuseppe Cruciani[c]

[a] Dipartimento di Scienze Molecolari e Nanosistemi, Università Ca' Foscari and INSTM RUVe consortium, Via Torino 155, 30172-Venezia, Italy
[b] Dipartimento di Fisica e Geologia, Università degli Studi di Perugia, Via Pascoli 1, 06123-Perugia, Italy
[c] Dipartimento di Fisica e Scienze della Terra, Università degli Studi di Ferrara, Via Saragat 1, 44122-Ferrara, Italy
E-mail: marco.pizzolato@unive.it

Methane dry reforming (MDR) is a promising process for syngas production through the valorization of two of the main Greenhouse gases [1]. Despite the high endothermicity, it can be coupled with Solid Oxide Fuel Cells to achieve a synergistic effect between the two processes. The catalyst plays a key role in this reaction as it should encourage syngas formation by limiting coke deactivation. This work focusses the attention on the effects of different synthetic approaches in the activity and stability of nickel-based catalysts [2]. To deeply investigate how the synthetic approach influences the reaction pathway, Ni/CeO_2 catalysts were prepared using three different routes: incipient wetness impregnation, co-precipitation and nitrate combustion synthesis. The fresh and spent catalysts were characterized via N_2-physisorption, AAS, TPR, XRD, CO_2-TPD, RAMAN spectroscopy and SEM techniques to understand the morpho-physical features of the materials and to identify the causes of catalysts deactivation. The catalysts were tested for MDR at the temperature of 700 °C.

The catalyst prepared via incipient wetness impregnation showed the highest degree of deactivation reaching only 10% H_2 yield after 20h on stream. Co-precipitation and nitrate combustion synthesis showed higher stability, achieving 40% H_2 yield after 28h on stream. The catalytic activity can be well explained by the characterization performed on the catalysts: an opportune synthetic approach capable to ensure higher metal dispersion and stronger interaction with the support is mandatory for the stability of the catalyst towards coking and deactivation.

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The twelve principles of green chemistry translation guide for palladium catalyzed cross coupling reactions

Tommaso Fantoni,[a] Sara Bernardoni,[a] Alexia Mattellone,[a] Giulia Martelli,[a] Lucia Ferrazzano,[a] Paolo Cantelmi,[a] Dario Corbisiero,[a] Alessandra Tolomelli,[a] Walter Cabri, [a] Federica Vacondio,[b] Francesca Ferlenghi,[b] and Marco Mor [b]

[a]Department of Chemistry "Giacomo Ciamician", Alma Mater Studiorum, Via Selmi 2, 40126-Bologna, Italy
[b]Department of Food and Drug Sciences, University of Parma, Parco Area delle Scienze 27/a, 43124-Parma, Italy
E-mail: tommaso.fantoni3@unibo.it

Catalysis is one of the main alternatives to classical stoichiometric chemistry for carbon-carbon bond formation at industrial level. However, a modern approach cannot avoid the inclusion of green elements from the beginning of the process design. In 1998, Anastas and Wagner introduced The Twelve Principles of Green Chemistry, with the main target to inspire the development of industrial chemical synthesis. The most important cross coupling reactions found a fertile environment in the pharmaceutical segment and, among them, palladium catalyzed reactions, are nowadays by far the most versatile ones. Our research group proposed a translation guide of the twelve principles for catalysis, in order to facilitate the development of green methodologies for the pharmaceutical industry [1]. In addition, we optimized a sustainable Heck-Cassar-Sonogashira (HCS) protocol in a green solvent/base blend with the consequent recycling and recovery of the catalyst to minimize the Process Mass Intensity (PMI) and increase the Turnover Number (TON) of the process. The protocol was then successfully applied to the telescoped synthesis of Erlotinib, an oral antitumor drug, that requires a Sonogashira reaction step in the synthesis [2,3].

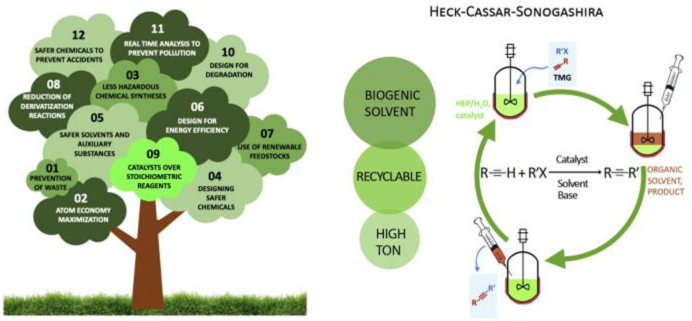

Figure 1: Twelve Principles of Green Chemistry (left); Heck-Cassar-Sonogashira general recycling protocol (right).

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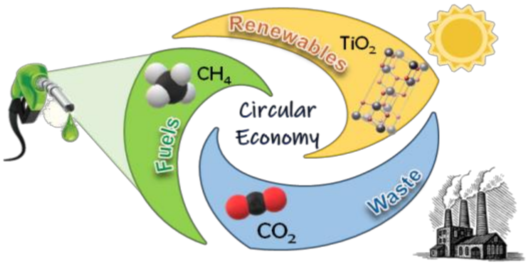
Effects of SiO_2-based scaffolds in TiO_2-photomediated CO_2 reduction

Giulia Forghieri[a], Danny Zanardo[a], Elena Ghedini[a], Federica Menegazzo[a], Alessandro Di Michele[b], Giuseppe Cruciani[c], Michela Signoretto[a]

[a] *CATMAT Lab, Department of Molecular Sciences and Nanosystems, Ca' Foscari University Venice and INSTM-RU Venice, Via Torino 155, 30172 Venezia Mestre, Italy*
[b] *Department of Physics and Geology, University of Perugia, Via Pascoli, 06123 Perugia, Italy*
[c] *Department of Physics and Earth Science, University of Ferrara, Via Saragat 1, 44122 Ferrara, Italy*
E-mail: giulia.forghieri@unive.it

The process of CO_2 photo-reduction has emerged as appealing opportunity to upgrade a waste gas into valuable fuels or chemicals, due to mild reaction conditions and the possibility to use sunlight as energy source [1]. Amongst the several semiconductors (SC) materials considered, titanium dioxide (TiO_2) is one of the most popular material used as catalyst for this reaction, being abundant, cheap, photo-stable and non-toxic, but also having poor activity, owed to fast charge carrier recombination and its wide band gap (3-3.3 eV), resulting in effective photo-activity only in the UV region [2]. The proposed strategies to overcome these issues are surface modification with a co-catalyst, visible-light sensitizing and scaffolding of the active phase. The use of transparent and porous materials has been proposed to favour reagent adsorption and only recently to promote light scattering as mean to increase photo-activity of the dispersed catalyst [3]. While the effectiveness of mesoporous scaffolds in improving CO_2 photo-conversion has already gained attention, no macroporous materials have yet been successfully applied or reported, to the best of our knowledge. In this study, we report a comparison of the effect of micro- and nano-structured silica on the photocatalytic performance of TiO_2 over CO_2 photo-reduction. A benchmark TiO_2 was supported on a macroporous SiO_2, mesoporous SBA-15 and non-porous SiO_2 spheres. The materials were tested both for CO_2 photo-reduction and as CO_2 capture-and-conversion hybrid systems. The SBA-15-supported system was the most performant.

Figure 1. Convertion of waste CO_2 to high-value resources



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Design of foldamers to achieve controllable chemical reactions

Matteo Pollastrini, Giulia Marafon, and Alessandro Moretto

Dipartimento di Scienze Chimiche, Università degli Studi di Padova, via Marzolo 1, 35131-Padova, Italy
E-mail: matteo.pollastrini@phd.unipd.it

The *de novo* design of synthetic highly stable enzymes, able to catalyze a broad range of chemical reactions in variable conditions, is a great challenge which requires the development of programmable and finely tunable artificial tools.

In recent years, chemists developed protein secondary structure mimics to achieve some desirable features of proteins. Such non-natural oligomers, so called foldamers, can adopt highly stable and predictable architectures and have extensively demonstrated their attractiveness for widespread applications in fields from biomedical to material science [1].

Foldamer science was more recently considered to provide original solutions to the *de novo* design of artificial enzymes. The modular nature of foldamers at the covalent level enables the exploration of new moieties and new geometries for sets of reactive side chains [2].

In this communication we report our progress in this field, where foldamers are accurately designed to achieve chemical consequences in virtue of their primary and secondary structures. In particular, we made use of helical foldamers to run the hydrolysis of esters [3], and the formation of “hard to achieve” intramolecular C-C bonds.

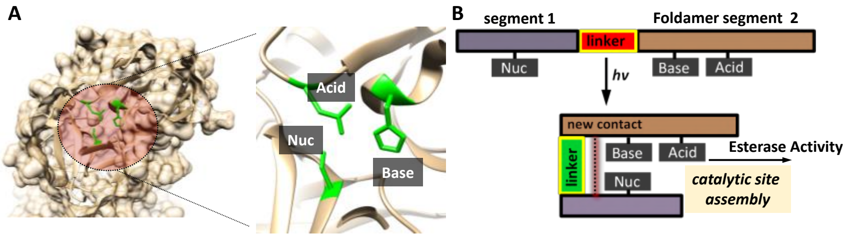

Figure 1: An example of our work. **A**: The catalytic action of serine peptidases depends on the interplay of a nucleophile, a general base and an acid. In the classic trypsin family this catalytic triad is composed of serine, histidine and aspartic acid residues. According to the chymotrypsin X-ray diffraction structure, the geometric relationship of Asp^{102}, His^{57} and Ser^{195} led to the hypothesis that His^{57} assists in relocating the proton from Ser^{195} to Asp^{102} in a charge relay mechanism. **B**: Our approach to achieve the light-induced in situ assembly of a catalytic triad of reactive side chains – Ser, His and Asp – in a photo-responsive helical foldamer. In our strategy, two peptide segments are connected by a switchable linker which allows the conformation of the foldamer to be reorganised simply by irradiation with UV-light and allows assembly of the catalytic site.

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Nanostructured TiO_2 as anode material for potassium batteries

Lucia Fagiolari, Federico Giraldo, Sabrina Trano, Daniele Versaci, Julia Amici,
Carlotta Francia, Silvia Bodoardo and Federico Bella

Department of Applied Science and Technology, Politecnico di Torino, Corso Duca degli
Abruzzi, 24, 10129-Turin, Italy
E-mail: lucia.fagiolari@polito.it

The development of solar energy conversion technologies energy must be coupled with efficient storage systems or solar fuels generators (like NH_3). Nowadays, the most known batteries are lithium-ion ones (LIBs), that allowed the great success of portable electronic devices in the last decade. However, the low natural abundance of lithium threatens the further development of LIBs; consequently, the research moved toward post-lithium batteries, such as potassium-ion systems (PIBs) [1].

Due to the large atomic radius of potassium, some electrode materials that are commonly used in Li-ion systems are not suitable for potassium batteries. Thus, anode and cathode materials that can tolerate the intercalation/deintercalation of K^+, without suffering from the reorganization energy, are needed [2].

Herein, we report the use of TiO_2, in the form of both nanoparticles (NP) and nanotubes (NT), as anode material for PIBs. TiO_2 NPs afforded a quite stable specific capacity, with a 87.4% retention efficiency after 200 charge/discharge cycles, when KFSI in DME was used as electrolyte. The Coulombic efficiency (CE) was remarkably high (> 98%), starting from the first cycles, suggesting the high reversibility of the insertion reaction. TiO_2 NTs were synthesized by anodic oxidation of a Ti foil, in both the amorphous and the anatase phase and by varying the anodization time. In the best case, the specific capacity was 75 μAh/cm^2, with a retention efficiency of 86.4% after 200 cycles and a CE of 98%.

This preliminary work paves the way to a further development of nanostructured TiO_2 as anode material in the PIB field.

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Dye-catalyst photosystems for the photoelectrochemical water oxidation

Cristina Decavoli,[a] Norberto Manfredi,[a] Chiara Liliana Boldrini,[a] Vanira Trifiletti,[b] Sally Luong,[b] Oliver Fenwick,[b] and Alessandro Abbotto[a]

[a] Department of Materials Science, Milano – Bicocca Solar Energy Research Center – MIB-Solar and INSTM Milano-Bicocca research unit, University of Milano-Bicocca, Milano, Italy
[b] School of Engineering and Material Science (SEMS), Queen Mary University of London, London, UK
E-mail: c.decavoli@campus.unimib.it

To overcome the intense use of fossil fuels, clean and affordable alternatives using the solar radiation as energy source are a real option. In this scenario, dye-sensitized photoelectrochemical cells (DS-PEC) play a significant role. They can mimic the nature generating solar fuels like hydrogen and oxygen through sun-driven water splitting.

The strategic center of the device is the photosensitizer which collects the solar radiation and converts it into the hole/electron couple. In recent years, organic dyes have gained much attention in this field due to their easy synthesis and tuning, low cost, and abundance of precursors [1]. The other important element in DS-PEC is the water oxidation catalyst (WOC) who fastens the water-splitting reaction. Unlike the dye, that is chemically bonded to the surface of the electrode, the WOC, typically a ruthenium complex, can be dissolved in the solution where the electrode is immersed or anchored to its surface. However, in both cases the possibility of charge recombination between the catalyst and the semiconductor electrode is high and thus the decrease in efficiency. A development for DS-PEC is the synthesis of a single molecule, composed by the union of these two essential elements. In this way, it is possible to keep the catalyst away from the electrode surface and ensure a faster charge transfer.

Here, I present a new way to connect these two elements in an integrated dye-catalyst photosystem through the formation of a stable non-conjugated covalent bond between a proper designed organic dye and a ruthenium-based benchmark WOC. These systems have been investigated in oxygen evolution through solar-driven water-splitting, showing interesting faradaic efficiencies, thus opening new perspectives for the development of efficient molecular dyads based on metal-free dyes for water splitting in DS-PEC [2].

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ZIF-derived Fe-N-C catalysts for oxygen reduction reaction in alkaline membrane fuel cells

Williane Freitas,[a] Alessandra D'Epifanio,[a] Ernesto Placidi,[b] and Barbara Mecheri [a]

[a] *Department of Chemical Science and Technologies, University of Rome Tor Vergata, 00133-Rome, Italy.*
[b] *Department of Physics, Sapienza University of Rome, Piazzale Aldo Moro 2, Rome 00185-Rome, Italy.*
E-mail: williane.freitas@uniroma2.it

Alkaline membrane fuel cells (AEMFCs) have been seen as strong technological candidates in the transition to a sustainable economy since these devices can generate electrical energy at low or zero pollutant emissions. However, the scarcely availability, high-cost and low durability of Platinum Group Metals (PGMs) for the oxygen reduction reaction (ORR) at the cathode side of these cells, still hampers their applicability pointing out PGM-Free materials as suitable candidates [1,2]. Metal Zeolitic Imidazolate Frameworks (ZIFs) represents a promise and scalable alternative to obtain atomically dispersed M-N-C active sites in PGM-Free catalysts. These materials consist of metal-centered joined by organic linkers to form large networks of crystalline nature [3]. In this work, a zinc-based ZIF was synthesized at room temperature and used as template to incorporate iron (II) ions to obtain the iron-nitrogen-based precursor, which was combined with a functionalized carbon support to synthesize a series of Fe-N-C catalysts through wet impregnation and pyrolysis steps in argon atmosphere. Synthesis of ZIF precursor was confirmed by FTIR, XRD and TGA analysis. Tailoring synthesis parameters allowed obtaining electrodes with a high accessible active sites and ORR activity, as indicated by X-ray photoelectron spectroscopy and, cyclic voltammetry with rotating ring disk electrode. We found that increase in pyrolysis temperature led to higher ORR activity which can be ascribed to higher formation and exposure of the Fe- and N-based active sites.

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Photocatalytic removal of organic contaminants and mercury from aqueous solutions

Elisa Gaggero,[a] Paola Calza,[a] Erica Bertozzi,[a] Maria Cristina Paganini,[a] Erik Cerrato,[a] and María-José López-Muñoz[b]

[a] Department of Chemistry, Università degli Studi di Torino, Via Pietro Giuria 7, 10125-Torino, Italy
[b] Department of Chemical and Environmental Technology, ESCET, Universidad Rey Juan Carlos, C/Tulipán s/n, 28933- Móstoles, Madrid, Spain
E-mail: elisa.gaggero@unito.it

A critical challenge for the 21st century is the water crisis resolution. Rapid growth in human population, urbanization, the increase in areas dedicated to agriculture and climate change are some of the main causes of the scarcity of clean water supplies, making this issue of primary concern. Nowadays, potentially toxic elements (PTEs) and contaminants of emerging concern (CECs) are conveyed to the environment by multiple routes and targeted actions to treat contaminated water are required. CECs include a wide range of organic molecules, all sharing a poor removal during the conventional wastewater treatment plants, which results in their introduction in the environment [1]. PTEs, as arsenic, mercury, lead and cadmium, are ubiquitous and persistent and may be toxic to biota even at low concentrations; they can bioaccumulate in fish and biomagnified in the food chain with consequent negative health effects in humans [2]. In the last decades, heterogeneous photocatalysis based on transition metal oxide semiconductor nanomaterials has been widely developed finding application in the abatement of organic pollutants and in the removal and recovery of a variety of metal ions from aqueous matrices [3]. However, the photocatalytic efficiency of the most used semiconductors, such as ZnO and TiO_2 is limited by very poor response to visible light. In order to efficiently utilize solar energy, different strategies such as anion and cation doping, surface deposition and instauration of heterojunctions have been developed.

In this study, ZnO-based photocatalysts with enhanced absorption on the visible region were tested for the degradation of organic pollutants and for the removal of mercury. In the first case, high oxidation potential of $^{\bullet}OH$ radicals, generated after the photoexcitation of the semiconducting materials and the formation of electron-hole charge carriers, is exploited. In the latter case, the reduction of metallic ions by the photogenerated electrons occurs, with subsequent metal deposition on photocatalyst surface. The performance of the photocatalysts were compared and assessed changing the operating conditions in terms of irradiation source, pH and photocatalyst's concentration.

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New biodegradable complexes as catalysts for photo Fenton-like processes at neutral pH

Prisco Prete,[a] Antonino Fiorentino,[a] Luigi Rizzo,[b] Antonio Proto,[a] and Raffaele Cucciniello[a]

[a] Dipartimento di Chimica e Biologia "Adolfo Zambelli", Università degli Studi di Salerno, Via Giovanni Paolo II 132, 84084 – Fisciano (SA), Italy
[b] Dipartimento di Ingegneria Civile, Università degli Studi di Salerno, Via Giovanni Paolo II 132, 84084 – Fisciano (SA), Italy
E-mail: pprete@unisa.it

Fenton and photo Fenton processes are among the most effective advanced oxidation processes (AOPs) in industrial and urban wastewater treatment and disinfection. However, they are still not feasible for full-scale applications due to the need of a strongly acidic pH to ensure the solubility of ferric ions. Therefore, different approaches have been proposed to cope with this issue, including the use of heterogeneous and homogeneous catalysts for (photo) Fenton-like processes. In heterogeneous (photo) Fenton-like processes a solid catalyst is used in place of Fe^{2+}, while in homogeneous processes iron or other transition metal cations can be used in combination with chelating agents to form soluble complexes even at neutral pH. [1]

Thus, in the last years, following the benign-by-design approach and the Green Chemistry Principles, [2] new ligands from renewable resources have been presented in literature.

Herein, copper and iron iminodisuccinate (IDS) complexes (Cu-IDS and Fe-IDS) were synthetized, characterized, and applied as catalysts for (photo) Fenton-like processes performed at neutral pH.

Both catalysts were preliminary tested as catalysts in (photo) Fenton-like processes for the degradation of phenol as a model compound. Encouraging results were obtained in photo Fenton-like processes, which were more efficient than other AOPs.

Then, feasibility of these processes was assessed using photo Fenton-like process catalyzed by Cu-IDS for the disinfection of urban wastewater, and photo and solar photo Fenton-like catalyzed by Fe-IDS for the treatment of an olive mill wastewater. The former, was proven to be effective disinfection process, (complete inactivation of *E. coli* after 10 min.) [3] and the latter resulted as a valuable option for pretreatment of the industrial wastewater, enhancing its biodegradability (BOD/COD ratio) from 0.16 up to 0.50, thus making it suitable for a further biological treatment.

[1] P. Prete, A. Fiorentino, L. Rizzo, A. Proto, and R. Cucciniello, *Curr. Opin. Green Sustain. Chem.* **28** (2021) art. no. 100451.
[2] R. Cucciniello, and P. T. Anastas, *Curr. Opin. Green Sustain. Chem.* **31** (2021) art. no. 100528.
[3] A. Fiorentino, R. Cucciniello, A. Di Cesare, D. Fontaneto, P. Prete, L. Rizzo, G. Corno, and A. Proto, *Water Res.* **146** (2018) 206-215.

OR27

One-pot synthesis of TiO2-rGO photocatalysts for the degradation of groundwater pollutants

Stefano Andrea Balsamo[a], Roberto Fiorenza[a], Marcello Condorelli[a], Roberta Pecoraro[b], Maria Violetta Brundo[b], Francesca Lo Presti[a], and Salvatore Sciré[a]

[a] Department of Chemical Sciences, University of Catania, Viale A. Doria 6, 95125 Catania, Italy
[B] Department of Biological, Geological and Environmental Science, University of Catania, Via Androne 81, 95124 Catania, Italy
E-mail: stefano.balsamo@phd.unict.it

A non-conventional approach to prepare titanium dioxide-reduced graphene oxide (TiO_2-rGO) nanocomposites based on solar photoreduction is here presented [1]. The standard hydro-solvothermal synthesis of the TiO_2-rGO composites requires high temperatures and several steps, whereas the proposed one-pot preparation allows to obtain the photocatalysts with a simple and green procedure.

The TiO_2-rGO catalysts were tested in the solar photodegradation of a widely adopted toxic herbicide (2,4-Dichlorophenoxyacetic acid, 2,4-D), obtaining the 97% of degradation after 3 h of irradiation. The as-prepared TiO_2-rGO composites were more active compared to the same photocatalysts prepared through the conventional thermal route. The structural, optical, and textural properties of the composites, determined by Raman, Photoluminescence, Fourier Transform InfraRed (FTIR), UV-vis diffuse reflectance (DRS) spectroscopies and N_2 absorp-tion-desorption measurements, showed as the solar irradiation favours the reduction of graphene oxide with higher efficiency compared to the thermal-driven synthesis. Furthermore, the possible toxicity of the as-synthesized composites was measured exposing nauplii of microcrustacean Artemia sp. to solutions containing TiO_2-rGO.

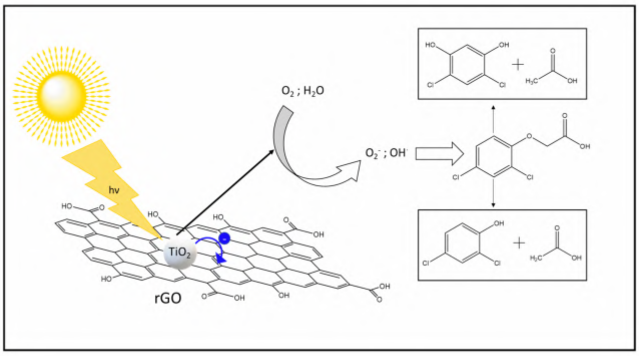

Figure 1: Proposed preparation and degradation path mechanism

The good results in the 2,4-D degradation process and the easiness of the TiO_2-rGO synthesis allow to consider the proposed approach a promising strategy to obtain performing photocatalyststs.

[1] S.A. Balsamo, R. Fiorenza, M. Condorelli, R. Pecoraro, M. V. Brundo, F. Lo Presti and S. Sciré, *materials* **14(20)** (2021) art. no. 59398.

New biodegradable complexes as catalysts for photo Fenton-The water-energy nexus in a drinking water supply system

Francesco Arfelli[a], Luca Ciacci[a], Fabrizio Passarini[a,b]

[a]Department of Industrial Chemistry "Toso Montanari", University of Bologna, viale del Risorgimento 4, 40136 Bologna, Italy; [b]Interdepartmental Centre of Industrial Research "Renewable Resources, Environment, Sea and Energy", University of Bologna, via Angherà 22, 47922 Rimini, Italy.
Email: francesco.arfelli3@unibo.it

Water sustainability is a topic of global interest mainstreamed by the United Nations that, in the "2030 Agenda for Sustainable Development", inserted "Clean water and sanitation" between the SDGs [1]. The balance between drinking water supply and demand implies the investment of resources aimed at optimizing the management of water sources and requires a detailed knowledge of the techniques and operations involved in a drinking water supply system (DWSS). Accordingly, the study consists in the application of the Life Cycle Assessment (LCA) methodology to the DWSS located in the Romagna territory, with the aim to analyze the system as a whole and to compare, from an environmental perspective, different production alternatives related to three water sources (dam water, RD; surface water, SW; and groundwater, GW) and two treatment technologies (conventional and ultrafiltration). This work required the identification and quantification of the main water and energy flows through the Material Flow Analysis (MFA), allowing to provide considerations about the interlinkages and reciprocal dependencies between the two resources (*water-energy nexus*) in the local context. Despite electricity is essential for drinking water supply, the water sector is responsible for a limited portion of the regional electricity consumption (about 0.5% of the total generated).

Results are reported as a function of 1m^3 of delivered drinking water and following a *cradle-to-gate* approach. The chosen impact assessment method is ReCiPe 2016 [2]. Despite the influence of the dam infrastructure, the best environmental performances are observed for RD water treated through the conventional technology. Both GW and SW, being them treated in conventional or ultrafiltration plants, resulted in higher impacts. Electricity and aluminum sulfate, which is employed as coagulating agent, resulted the main contributors to the observed values. SW associated processes, instead, are highly influenced by the management of the treatment residues. Afterwards, it is confirmed that decreasing the dependency on electricity produced by fossil sources, the environmental impacts observed are remarkably reduced, especially for the global warming category. The LCA and the nexus analysis are confirmed essential tools to drive companies in addressing environmental-friendly solutions, especially in the field of water sustainability, which represents one of the most urgent challenges to face in the coming years.

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Adsorption of emerging contaminants from water: the role of graphene oxide 'defects'

Sara Khaliha[a], T. D. Marforio[b], A. Kovtun[a], S. Mantovani[a], N. Boulanger[c], V. Palermo[a], M. Calvaresi[b], A. V. Talyzin[c], M. Melucci[a]

[a]Institute of Organic Synthesis and Photoreactivity (CNR-ISOF), Bologna, Italy
[b]Alma Mater Studiorum - UNIBO, Department of Chemistry 'G. Ciamician', Bologna, Italy
[c]Umeå University, S-90187-Umeå, Sweden
E-mail: sara.khaliha@isof.cnr.it

In the last years, academic and industrial interest has been increasingly focused on water treatments, especially for what concerns the removal of "emerging contaminants" (ECs),[1] in order to answer to the recently renovated Drinking Water Directive EU2020/2184, which introduces new limits and safety approaches to water management. Current water treatment technologies are not efficient in the removal of most of these contaminants from drinking water and new materials and technologies are required to face this challenge. Graphene-based materials have shown great potential for water purification purposes due to the high surface area and multiple interactions pathways with a vast range of organic molecules. In particular, graphene oxide (GO) has shown high performance in the removal of some ECs [2], despite the fact that the mechanism driving the adsorption selectivity and efficiency is not completely known. Aiming at a deeper insight on such issues, here we investigate GO nanosheets with tailored number of surface "defects" (i.e. holes and vacancies), and different superficial oxygenated groups ratio. Defect-rich graphene oxide (dGO), synthesized by explosive thermal exfoliation of graphite oxide followed by reoxidation using Hummers method was studied together with less-defective graphene types synthesized by Hummers and Brodie methods (hGO and bGO respectively).[3] These GO nanomaterials were used as sorbents of selected ECs in tap water, including drugs and dyes. Their adsorption performances were rationalized by molecular dynamic (MD) simulations, kinetic and isotherms study and compared to those of Granular Activated Carbon (GAC), the industrial sorbent benchmark.

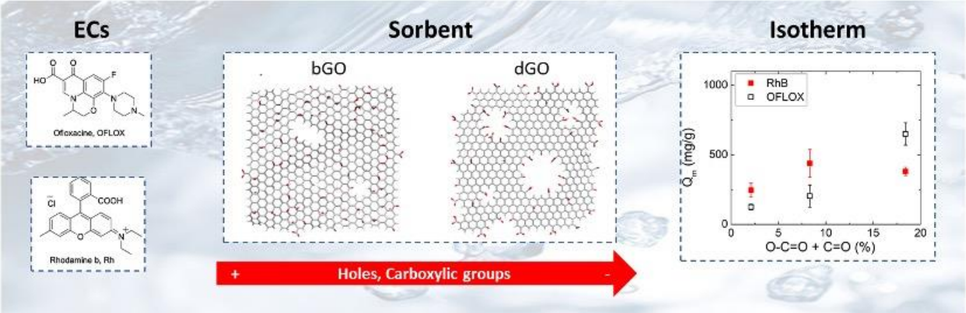

Figure 1: Adsorption of ECs (i.e. Ofloxacin and Rhodamine) on Graphene Oxide.

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[2] Wang, J.; Wang, S., *Journal of Environmental Management* 182 (2016), 620-640
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Synthesis and fast purification of functionalized graphene oxide for water treatment

Mantovani Sebastiano,[a] Sara Khaliha,[a] Laura Favaretto,[a] Cristian Bettini,[a] Antonio Bianchi,[a] Alessandro Kovtun,[a] Massimo Zambianchi,[a] Massimo Gazzano,[a] Barbara Casentini,[b] Vincenzo Palermo,[a] and Manuela Melucci[a]

[a]Institute of Organic Synthesis and Photoreactivity (CNR-ISOF), Via Piero Gobetti 101, 40129-Bologna, Italy
[b]Water Research Institute (CNR-IRSA), Via Salaria Km 29,300 C. P, 10-00015, Italy
E-mail: Sebastiano.mantovani@isof.cnr.it

Covalent modification of graphene oxide (GO) is a widely exploited strategy to tailor the surface of graphene and enable new applications [1]. In recent years, a plethora of modified GO have been synthetized as specific sorbent materials for water remediation [2]. However, scale-up methods optimization to produce modified GO is required to guarantee large amount of the materials and reproducible batch purity levels. Here we report a microwave (MW) accelerated synthesis combined with microfiltration (MF) on commercial hollow fiber modules for facile and high efficiency purification. The procedure was optimized on the synthesis of polyethyleneimine (PEI) modified GO nanosheets that was then used for the removal of arsenic, lead and selected organic emerging contaminants from tap water [3].

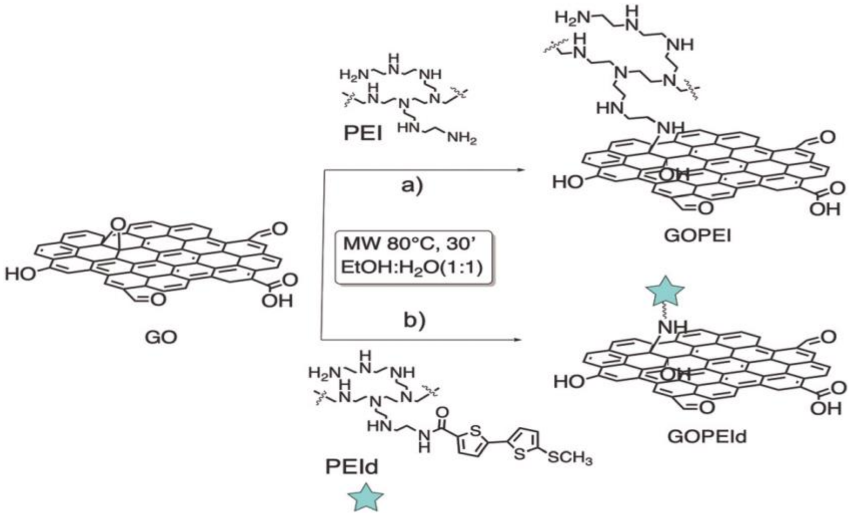

Figure 1: Synthetic pathways to GOPEI and GOPEId.

[1] C. Backes, and C. Alonso, *2D Mater.* **7**, (2020) 022001.

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Antiproliferative bioactives from blueberry-peels valorization: harnessing natural deep eutectic solvents and enabling technologies

Giorgio Grillo,[a] Veronika Gunjević,[a,b] Kristina Radošević,[b] Ivana Radojčić Redovniković,[b] and Giancarlo Cravotto[a]

[a] Dept. of Drug Science and Technology, University of Turin, Via P. Giuria 9, 10235 Turin, Italy
[b] Dept. of Biochemical Engineering, Laboratory for Cell Culture Technology and Biotransformations, Faculty of Food Technology and Biotechnology, University of Zagreb, Pierottojeva ulica 6, 10000 Zagreb, Croatia
E-mail: giorgio.grillo@unito.it

Waste reduction via reuse and recycling is one of the main principles of the circular economy [1]. The food industry produces large amounts of waste and by-products, source of dramatic environmental pollution, possessing significant concentration of bioactive metabolites. In particular, blueberry-peels (BP) possess a dramatic antioxidant activity, mainly due to their exceptional concentration of anthocyanins. The beneficial health effects of dietary anthocyanins derive from strong antioxidant activity, leading to anti-inflammatory, antiproliferative and neuroprotective activity.

Interest in bioactive phytochemicals and sustainable processes is the driving force behind this study on two novel green extraction methods, aiming to recover anthocyanins from BP [2]. Five natural deep eutectic solvents (NaDES) have been tested for extractions, adopting conventional benchmark, monitoring eutectic systems shelf-life as well. The most promising NaDES was tested for microwave (MAE)- and ultrasound-assisted extractions (UAE), describing the related kinetics. MAE and UAE.

The antiproliferative activity of the products was determined by a Cell Proliferation Assay on human tumor HeLa (human cervical adenocarcinoma) cells and human skin HaCaT (normal human keratinocyte) cells. Nonconventional extracts exhibited strong antiproliferative activity that was much greater than that of their conventionally extracted analogues. The presented study demonstrated the synergistic effects of enabling technologies together with green solvents application. Hence, an antiproliferative agent can be recovered from a food industry residual biomass.

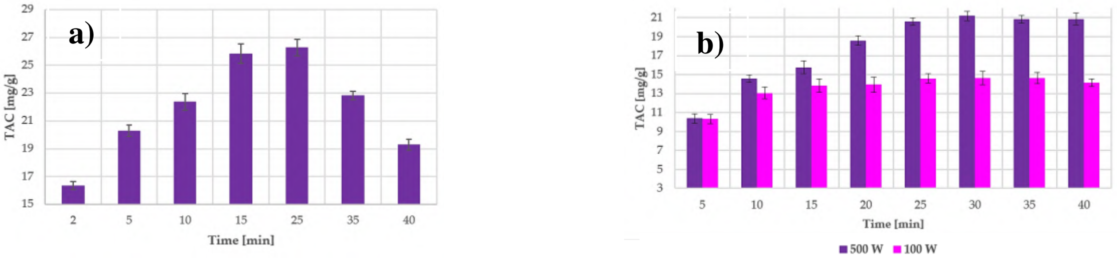

Figure 1: Total anthocyanin content (TAC) trend during: a) MAE; b) UAE at different powers (100W and 500W). Results are expressed as average values ± SD.

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Keta-functionalized nitroolefins and indoles as useful building blocks for the one-pot synthesis of polysubstituted carbazoles

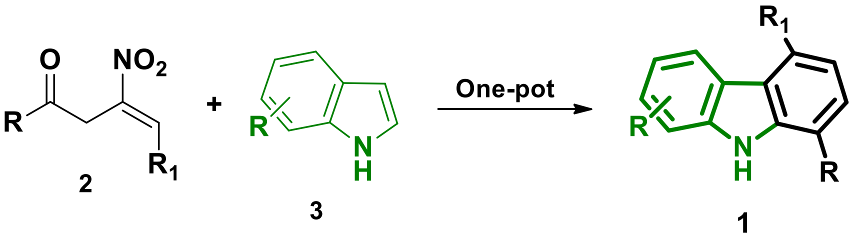
Benedetta Bassetti,[a], Gabriele Lupidi,[a] and Alessandro Palmieri [a]

[a] *Green Chemistry Group, School of Science and Technology, Chemistry Division, University of Camerino, Via S. Agostino n. 1, 62032 Camerino (MC), Italy*
E-mail: benedetta.bassetti@unicam.it

Carbazoles (**1**) represent one of the most important class of nitrogen-containing heterocycles. They are present in a wide range of natural products and pharmaceuticals because of their antimicrobial, anti-inflammatory, anticancer and antiviral activity. Furthermore, carbazoles find application in material sciences as photoconductors, light-emitting diodes (LEDs), and as components in photovoltaic devices and solar cells [1].

Thanks to their versatility, the interest in these compounds has grown extensively in the last decades and considerable efforts have been directed to the optimization of their synthesis, which is mainly based on the derivatization of pre-existing scaffolds or on the ex-novo synthesis of carbazole systems starting from proper precursors [2].

In this context, and taking into account our experience using functionalized nitroolefins [3], we developed a new one-pot synthesis of polysubstituted carbazoles (**Figure 1**) 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 to afford the title targets (**1**).



I Step: TFE, r.t., 8 h
II Step: 1.2 g/mmol Amberlyst™15, 2-MeTHF, 100 °C (MW), 3 h

Figure 1: Synthesis of polysubstituted carbazoles

[1] (a) Caruso, A.; Ceramella, J.; Iacopetta, D.; Saturnino, C.; Mauro, M. V.; Bruno, R.; Aquaro, S.; Sinicropi, M. S.; *Molecules,* **2019**, 24, 1912; (b) Grazulevicius, J.V.; Strohriegl, P.; Pielichowski, J.; Pielichowski, K.; *Prog. Polym. Sci.,* **2003**, 28, 1297.

[2] (a) Aggarwal, T.; Sushmita and Verma, A. K.; *Org. Biomol. Chem.*, **2019**, 17, 8330; (b) Roy, J.; Jana, A. K.; Mal, D.; *Tetrahedron*, **2012**, 68, 6099.

[3] (a) Ballini, R.; Gabrielli, S.; Palmieri, A.; *Current Organic Chemistry,* **2010**, 14, 65; (b) Palmieri, A., Gabrielli, S., Chiurchiù, E.; *Adv. Synth. Catal.*, **2019**, 361, 630.

Steps in the journey toward green solid phase peptide synthesis (GSPPS)

Alexia Mattellone,[a] Giulia Martelli,[a] Paolo Cantelmi,[a] Chiara Palladino,[a] Dario Corbisiero,[a] Tommaso Fantoni, Alessandra Tolomelli,[a] Marco Macis,[b] Antonio Ricci,[b] Walter Cabri,[a] and Lucia Ferrazzano[a]

[a] P4i Lab, Department of Chemistry, Alma Mater Studiorum University of Bologna, Via Selmi 2, 40126-Bologna (Italy).
[b] Innovation and Development¸Fresenius kabi iPsum, via San Leonardo 23, 45010-RO, Italy.
E-mail: alexia.mattellone2@unibo.it

The success of peptides in several therapeutic areas is directly related to the availability of reliable synthetic techniques that allowed medicinal chemists to better explore this molecular space. Nowadays, several technologies can be used for the synthesis of pharmaceutical grade polypeptides, but solid-phase peptide synthesis (SPPS) is still playing a central role in this context.[1]

The main components of SPPS wastes in the upstream process are solvents (80-90% of waste) and the most widely used is *N,N*-Dimethylformamide (DMF) which is reprotoxic. Piperidine is the main popular base for Fluorenylmethyloxycarbonyl (Fmoc) removal. Since itis employed to produce drug intermediates, its sale is regulated by strict controls. For these reasons, we explored greener alterantives for solvent and base. First, we identified *N*-octyl pyrrolidone (NOP) as the best candidate. NOP showed good performances in terms of swelling, coupling efficiency and low isomerization generating peptides with very high purity. A mixture of NOP with 20% dimethyl carbonate (DMC) allowed a decrease in solvent viscosity, making the mixture suitable for the automated solid-phase protocol.[2] Then, we have investigated the use of alternative bases with good greenness scores that are able to efficiently deprotect the Fmoc moiety without interfering with the SPPS of the growing peptide. We evaluated deprotection time, racemization ratio, dibenzofulvene trapping and aspartimide formation comparing Diethyltrimethylenediamine (DEAPA) and piperidine in NOP and DMF. DEAPA proved to be an efficient base for Fmoc removal in SPPS upstream processes.

Based on these considerations, Aib-enkephalin and linear octreotide were successfully synthesized to test the designed methodologies achieving the same results than DMF and piperidine. In these experiments, NOP, DMC and DEAPA could be easily recovered by direct distillation from the process waste mixture. The process mass intensity (PMI), being reduced by 63–66%, achieved an outstanding value representing a clear step forward in achieving green SPPS. [3]

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[3] G. Martelli, P. Cantelmi, C. Palladino, A. Mattellone, D. Corbisiero, T. Fantoni, A. Tolomelli, M. Macis, A. Ricci, W. Cabri and L. Ferrazzano, *Green Chem.*, (2021), Advance Article

A case study of CO_2 aerosol reactions: the efficient conversion of styrene oxide to carbonate in microdroplets conditions

Caterina Rovegno,[a,b] Daniele Urbani,[a,b] Eleonora Polo,[a] Alessandro Massi,[b] and Paolo Dambruoso[a]

Caterina Rovegno and Daniele Urbani equally contributed to this research.

[a] Institute for the Organic Synthesis and Photoreactivity of the Italian National Research Council, Area della Ricerca di Bologna, Via P. Gobetti, 101 – 40129 – Bologna (Italy)
[b] Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Via L. Borsari, 46 – 44121 Ferrara (Italy)
E-mail: caterinarovegno11@gmail.com

Great attention has been recently paid by the scientific community to microdroplets reactions, because this innovative methodology can prompt a relevant acceleration [1] to valuable transformations. There are many reported examples of homogeneous liquid phase, and two phases liquid-liquid reactions in inert gas atmosphere that led to successful syntheses. The physical and physico-chemical phenomena which take place within the microdroplets or at their interface with gas are able to explain the obtained results [2]. Moreover, the promising results of the recently reported [3] water TPPS-mediated $^1O_2$ aerosol photochemical selective oxidation of sulfide to sulfoxide in air pave the way for the extension of this new approach to many biphasic gas-liquid transformations.

In this stimulating scenario we exploited this innovative paradigm to study the microdroplets conversion of styrene oxide to styrene carbonate in CO_2 atmosphere mediated by potassium iodide/triethylene glycol (KI/TEG) complex (Fig. 1).

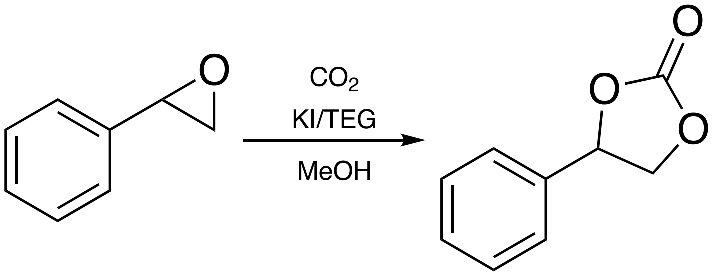

Figure 1: Scheme of the model reaction.

We herein present the study of this model reaction by comparing ordinary bulk *vs* microdroplets reaction at various temperatures and conditions, highlighting the positive effects of microdroplets conditions on reaction rates.

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Eco-friendly production of biodiesel catalyzed by selective and recyclable metal nanoparticles

Ambra M. Fiore, Maria Michela Dell'Anna, Giuseppe Romanazzi, and Piero Mastrorilli

DICATECh, Polytechnic University of Bari, Via Orabona 4, 70125-Bari, Italy
E-mail: ambramaria.fiore@poliba.it

Biomasses are a useful source to produce energy and chemicals. The production of biofuel deriving from animal fats, vegetable oils and so on had an increasing scientific interest in the last few years [1]. Several advantages are linked to the strategy of using renewable sources as fuels, such as reduction of CO, unburned hydrocarbon emissions, no production of sulphur compounds and other substances which cause an increase of the smokescreen. On the other hand, biodiesel deriving from vegetable oils cannot be use directly in industrial applications due to its high viscosity, autopolymerisation, high amount of unsaturation which makes it sensitive to oxidative processes.

With the aim to set up new environmentally friendly synthetic methods to be performed under mild and sustainable conditions with high efficiency, herein we report the synthesis and characterization of two polymers supported Ni(II) and Pd(II) complex respectively as Ni-POL and Pd-NPs. They were obtained by co-polymerization of Ni(AAEMA)$_2$ (AAEMA$^-$ = deprotonated form of 2-acetoacetoxyethyl methacrylate) and Pd(AAEMA)$_2$ with suitable co-monomer and crosslinker. Only Ni-POL was then calcinated at 300 °C under N$_2$ yielded polymer supported Ni (0) nanoparticles (Ni-NPs) [2]. The synthesised nano-catalysts were tested in the upgrade of fatty acid methyl esters (FAMEs) deriving from waste cooking oil (WCO) showing different selectivity. Two different mild reaction conditions were performed by using H$_2$ and NaBH$_4$ as reducing agents. Pd-NPs and Ni-NPs results active and recyclable for seven and five catalytic runs, respectively. They were fully characterized by SEM, IR and elemental analysis before, during and after several catalytic runs.

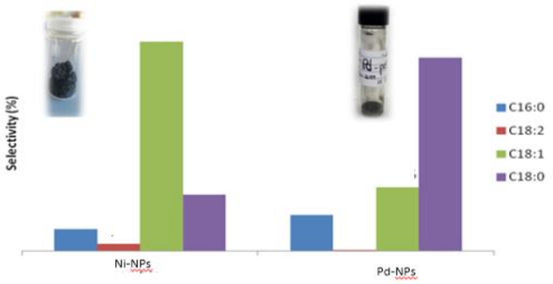

Figure 1: Selectivity of nano-catalysts for biodiesel production.

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Visible light-driven α-functionalization of enol silyl ethers via arylazo sulfones

Lorenzo Di Terlizzi, Ivana Cola, Carlotta Raviola, Maurizio Fagnoni and Stefano Protti

PhotoGreen Lab, Department of Chemistry, Università degli Studi di Pavia, Viale Taramelli 12, Pavia, 27100, Italy.
E-mail: lorenzo.diterlizzi01@universitadipavia.it

The structural motif of α-aryl ketones or esters is commonly present in both natural and artificial bioactive products. As for the preparation of these derivatives, in the last decade, several protocols exploiting the photoredox catalyzed α-arylation of enol acetates and silyl ethers by aryl diazonium salts have been proposed as mild and promising alternatives to traditional transition-metal catalyzed cross-coupling reactions [1]. Recently, we focused on the photoreactivity of arylazo sulfones, ($ArN_2SO_2CH_3$), that are yellow to orange bench-stable compounds bearing a dyedauxiliary group (DG = $-N_2SO_2CH_3$) which imparts both colour and photoreactivity to the molecule [2].

We present herein a visible light-driven protocol for the synthesis of α-aryl ketones and α-arylazo esters under photocatalyst- and metal-free conditions by using arylazo sulfones as the arylating agents and enol silyl ethers or ketene silyl acetals as the coupling partners. The reaction is performed upon visible light irradiation (λ = 456 nm) in mixed organic/aqueous solvent and in the presence of a buffering agent ($NaHCO_3$)m [3].

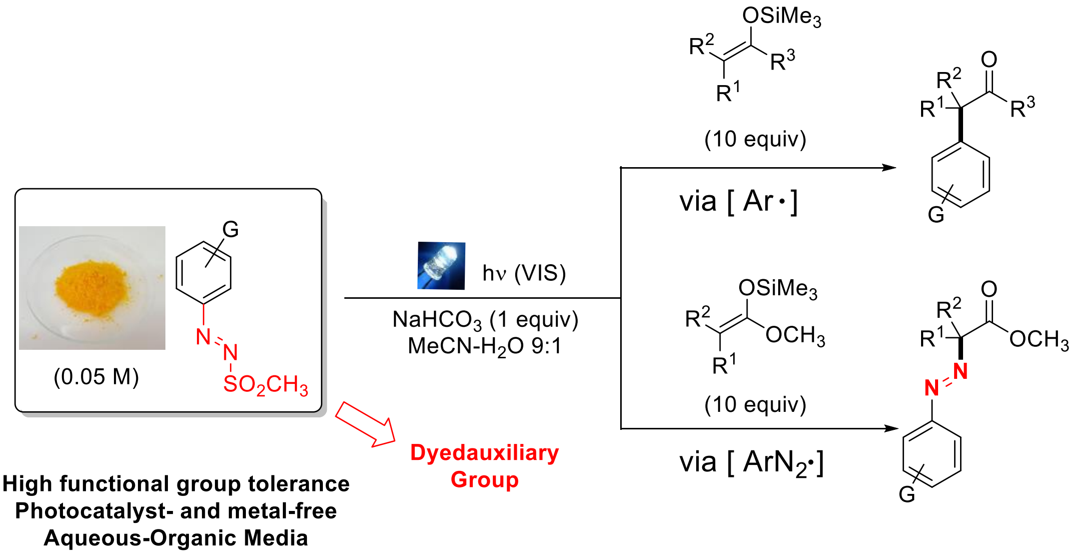

Figure 1: Light-driven α-functionalization of ketones and esters via arylazo sulfones.

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Liquid crystalline networks for bioinspired artificial muscles and actuators

Simone Donato,[a,b] Daniele Martella,[a,c] Diederik Sybolt Wiersma,[a,b,c] Cecilia Ferrantini,[a,e] and Camilla Parmeggiani[a,c,d]

[a] European Laboratory for Non-linear Spectroscopy (LENS), University of Florence, Via Nello Carrara 1, Sesto Fiorentino (FI), Italy
[b] Department of Physics and Astronomy, University of Florence, Via Sansone 1, Sesto Fiorentino (FI), Italy
[c] Istituto Nazionale di Ricerca Metrologica (INRIM), Strada delle Cacce 91, Torino (TO), Italy
[d] Department of Chemistry "Ugo Schiff", University of Florence, Via della Lastruccia 3, Sesto Fiorentino (FI), Italy
[e] Department of Experimental and Clinical Medicine, University of Florence, Largo Giovanni Alessandro Brambilla 3, Firenze (FI), Italy
E-mail: donato@lens.unifi.it

Liquid Crystalline Networks (LCNs) are among the best candidates, within smart materials, for applications from the medical field to robotics, given their ability to act in response to an external stimulus (light, temperature, etc.) [1]. In this communication, we will show the design and synthesis of new molecules to improve the material force development, that for the current mixture is of 70 mN/mm^2 under illumination at a power of 1.5 W/mm [2]. Therefore, a new cross-linker palette possessing bulky substituents (trimethyl and dimethyl) in the aromatic cores have been prepared and used for the preparation of LCNs. Ideally, the introduction of different substituents will decrease the interactions among a LC molecule and its nearest neighbors thus leading to a reduction in the amount of energy to be supplied to obtain the force development. These materials can be applied for the realization of smart actuators able to perform different movement as torsion up to their folding into helical structures. Such deformation is of particular interest for applications in the field of milli- and micro-robotics, as it simulates movements performed by animals (e.g. octopus tentacle) or plant (e.g. plant tendril) organs, the most important source of inspiration for the development of advanced soft robotics.

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Just tape, a candle, and oil: design and fabrication of a home-made stretchable tape that prevents ice adhesion

Marco Carlotti, Ilaria Cesini, and Virgilio Mattoli

Center for Smart Materials Interfaces, Istituto Italiano di Tecnologia, Viale Rinaldo Piaggio 34, 56025, Pontedera, Italy
E-mail: marco.carlotti@iit.it

Unwanted icing has major safety and economic repercussions on human activities, affecting means of transportation, infrastructures, and consumer goods. Compared to the common deicing methods in use today, intrinsically icephobic surfaces can decrease ice accumulation and formation without any active intervention from humans or machines. However, such systems often require complex fabrication methods and can be costly, which limits their applicability.

In this study, we report the preparation and characterization of a series of slippery lubricant-infused porous surfaces (SLIPSs) realized by impregnating with silicone oil a candle soot layer deposited on double-sided 3M adhesive tape.

Despite the use of common household items, these SLIPSs showed anti-icing performance comparable to other systems described in the literature (ice adhesion < 20 kPa) and a good resistance to mechanical and environmental damages.

To improve the overall performances, we explored several design solutions involving surface functionalization of the inner pores and the use of fluorinated lubricants.

The use of a flexible and functional substrate as tape allowed these devices to be stretchable without suffering significant degradation and highlights how these systems can be easily prepared and applied anywhere needed. In addition, the possibility of deforming the substrate can pave the way for the application of SLIPS technology in mechanical ice removal methodologies, drastically incrementing their performance.

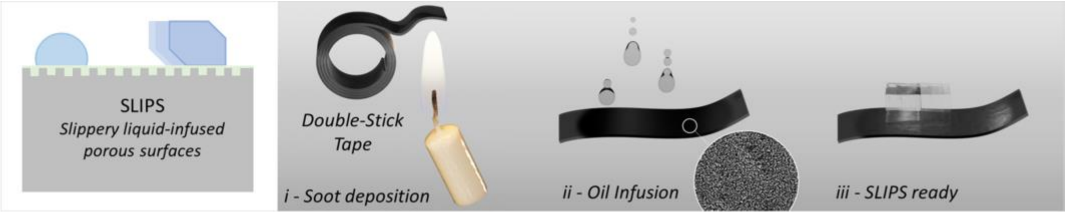

Figure 1: Cartoon showing the working principle and the fabrication procedure of SLIPS on tape.

Metal-triggered peptide hydrogel: synthesis, characterization and application in water treatment and food spoilage detection

Anna Fortunato and Miriam Mba

Department of Chemical Science, University of Padova, via Marzolo 1, 35131, Padova, Italy
E-mail: anna.fortunato.1@studenti.unipd.it

In light of the cost, biocompatibility, availability, structural variety and supramolecular behavior of peptides, the design of new peptide-based supramolecular hydrogels capable of achieving a chosen function is very active [1]. Among supramolecular interactions, the metal-ligand one has emerged as an important tool to modulate the self-assembly, but its employment to form peptide-based supramolecular metallogels with new properties and applications is almost unexplored.

Herein we report the design, synthesis, characterization and application of a pentapeptide, covalently linked to a pyrene moiety. The effect of different metals on gelation ability, morphology, mechanical and optical properties have been studied.

Global food waste and water pollution are far-reaching problems with tremendous ethical, environmental and financial costs. Our hydro-metallogels showed new properties due to the presence of the metal that allowed us to address the aforementioned problems. Cu-mediated metallo-hydrogels showed colorimetric changes in the presence of amines, which allowed us to use them in food freshness monitoring. Furthermore, the Zn-mediated hydro-metallogel showed good dye adsorption abilities. The removal efficiency for methylene blue (MB) solution was 89% in 20 minutes and 100% in less than 4 hours, highlighting a possible employment for the treatment of water in textile industries [2].

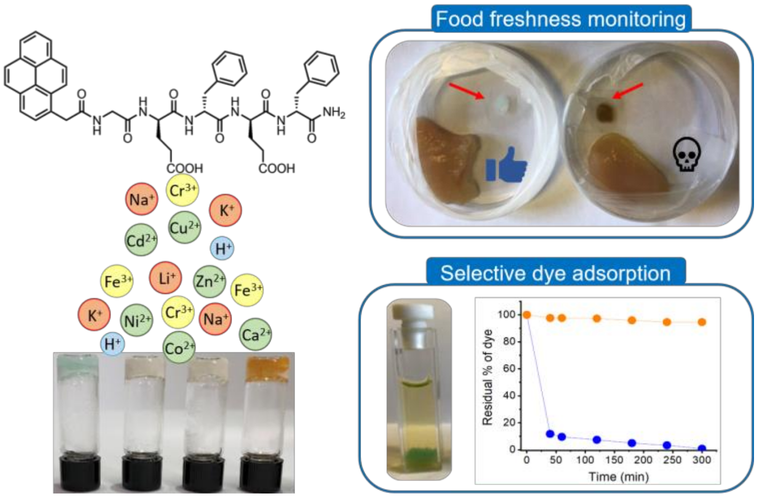

Figure 1: left, structure of compound and image of gelled sample; right, (top) colorimetric response of Cu gel when exposed to meat; (bottom) image of cuvette containing Zn-xerogel upon dye absorption of MB mixed with MO and the residual concentration over time of MB (blue dots) and MO (orange dots).

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Porphyrin self-assembly as a versatile strategy to realise innovative hybrid material for energetic and environmental applications

Massimiliano Gaeta, Matteo Barcellona, Gabriele Travagliante, Maria Elena Fragalà, Roberto Purrello, and Alessandro D'Urso

Dipartimento di Scienze Chimiche, Università degli Studi di Catania, Viale Andrea Doria 6, 95125-Catania, Italy
E-mail: massimiliano.gaeta@unict.it

Chemists have been fascinated by the challenging syntheses of nature-inspired systems to design supramolecular complexes. In fact, over the last decades, a fascinating development in chemistry is the construction of nanomaterials from small building blocks by self-assembly of porphyrinoids [1]. However, these molecules hide manifold trouble; even if the peripheral charged groups make these macrocycles water-soluble, nevertheless, porphyrins remain mainly hydrophobic molecules, preserving the well-known tendency to aggregate. This "dichotomy" is worthy of special attention because (*i*) it plays a central role in the non-covalent syntheses and (*ii*) in conjunction with inorganic -or polymeric- structures to arrange quite complex hybrid composite materials for environmental applications. Therefore, in this communication, we intend to describe some interesting cases.

For instance, from an energetic point of view, polyaromatic membranes, such as sulphonated polyetheretherketone (sPEEK), can be considered as a low-cost alternative to PFSA (*i.e.,* Nafion™) based membranes, for portable fuel cell applications. In order to improve the characteristics of membranes based on bare sulphonated polymer, composite membranes based on sPEEK and porphyrins were widely investigated for real portable applications [2].

Recently, a growing interest is arising in the degradation of antibiotics by heterogeneous photocatalysis using suspended TiO_2 nanoparticles. With the attempt to increase the photocatalytic efficiency of TiO_2, we decided to functionalize it with porphyrins. Thus, we tested the photocatalytic efficiency of the TiO_2-porphyrin system to degrade, in water, oxolinic acid and oxytetracycline, two of the most extensively used antibiotics in aquaculture [3].

Finally, inspired by adhesive proteins secreted by mussels for attachment to wet surfaces, we obtained hybrid porphyrin/DOPA melanin-like films as an easy-to-scale and reusable device to remove high concentrations of dye-pollutant from water.

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3D printed microstructures handling by ultra-conformable freestanding polymeric membranes

Frank den Hoed,[a,b] Andrea Ottomaniello,[b] Marco Carlotti,[b] Omar Tricinci,[b]
Patrizio Raffa,[a] and Virgilio Mattoli[b]

[a] *Department of Chemical Engineering, University of Groningen, Nijenborgh 4, Groningen, The Netherlands*
[b] *Center for Materials Interfaces, Instituto Italiano di Tecnologia, Viale Rinaldo Piaggio 34, 56025 Ponedera PI, Italy*
E-mail: f.m.den.hoed@rug.nl

With the introduction of 2-photon lithography, it has become possible to fabricate detailed 3D structures with sub-micrometer precision. To widen the prospect of potential applications, we have overcome an important limitation of the current 2PP technology: the lack of post-fabrication handling possibilities. Our method exploits thin, ultra-conformable parylene films as freestanding supports for microstructures. These separate the microstructures from the flat support used for 2PP and allow, by a simple and elegant method, to wrap arrays of structures around geometrically complex shapes, a previously very difficult challenge.

The method follows from previous work by our group on conformable freestanding capacitors based on polyvinyl formal films instead of parylene. [1] The preparation of the substrate films for this work, involves chemical vapor deposition of the parylene dimer resulting in a polymerized coating on top of a glass or silicon support (Fig. 1). After fabrication of 3D structures, the coating delaminates from the glass coating by slow immerging in water under an angle and light pulling. From there, we could transfer the floating film to a new support such as a thin needle. Since the films are so thin (<400 μm), they strongly attach to the new support due to vanderwaals-forces. In this project, we have exploited the possibilities and limitations of the new microstructure handling technique, shown its ultra-conformability, fabricated in-air floating membranes with structures on top and, as a follow up of previous work from our group [2], developed a structure pattern that can retain air on a curved surface.

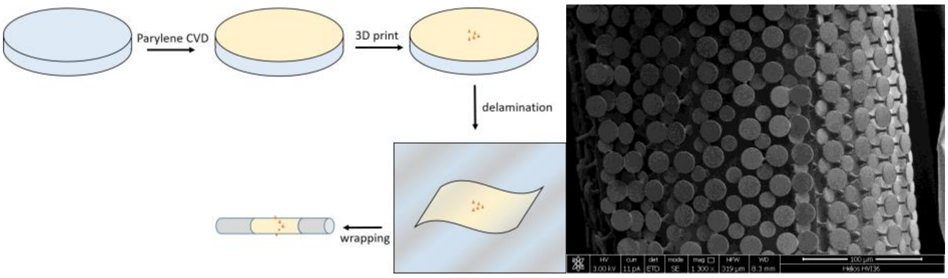

Figure 1: Overview of method (L), SEM of transferred structures around a wire(R).

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2-Alkyl piperidine-based derivatives as potential tools against Schistosomiasis

Sara Rossi, Sandra Gemma, Giuseppe Campiani

Dipartimento di Biotecnologie, Chimica e Farmacia, Università degli Studi di Siena, via Aldo Moro 2, 53100, Siena, Italy
E-mail: rossi115@student.unisi.it

Schistosomiasis is a widely spread and overlooked tropical disease, which counts an impressive growth in yearly infections among the tropical and subtropical areas. The high morbidity and mortality characterize the socioeconomical impact of this endemic disease. Chronic and acute Schistosomiasis is caused by a parasitic trematode of the genus Schistosoma, who's life cycle is complex and involves an intermediate host for completion. The transmission occurs through contact with contaminated water and symptom onset can occur after months or years from the primary infection. The main clinical manifestations are a consequence of the host immune response to the Schistosoma eggs deposited in the tissues, and include granulomatous inflammation and fibrosis in the infected tissues. The current medical treatment and prevention relies on the use of Praziquantel which is only effective on adult stage parasite, therefore multiple cycles of treatment are necessary. Furthermore, the threat of drug-resistant parasites represents a risk, for these reasons the research for a valid alternative is of the utmost importance. The piperidine derivative perhexiline is an anti-anginal drug which has proved to be effective against various stages of *S. mansoni* life cycle as a racemic mixture of R-(+) and S-(-) [1]. In order to explore the antischistosomal activity of the single enantiomers a stereoselective synthesis of this lead compound has also been designed [2]. The interesting results obtained prompted us to develop appropriate synthetic approaches for the preparation of further piperidine-based derivatives with the aim of exploring the structure-activity relationships.

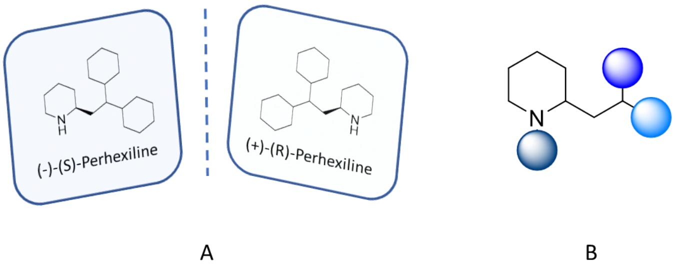

Figure 1: (-)-(S)- and (+)-(R)-Perhexiline (A), 2-alkyl piperidine derivatives common scaffold (B).

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Fingerprint-patterned liquid crystalline elastomers as active cell culture substrates and smart coatings

Bruno Grandinetti,[a,b] Marta Rojas,[a] Danqing Liu,[c] Daniele Martella,[a,h] Silvia Querceto,[d,e] Cecilia Ferrantini,[e] José Manuel Pioner,[e] Chiara Tesi,[e] Dick Broer,[c] Diederik Sybolt Wiersma,[a,b,h] Corrado Poggesi,[a,e] Leonardo Sacconi,[a,g] and Camilla Parmeggiani[a,f]

[a] European Laboratory for Non Linear Spectroscopy, Università degli Studi di Firenze, 50019-Sesto Fiorentino (Italy)
[b] Department of Physics and Astronomy, Università degli Studi di Firenze, 50019-Sesto Fiorentino (Italy)
[c] Department of Chemical Engineering and Chemistry, Eindhoven University of Technology, 5612AZ-Eindhoven (The Netherlands)
[d] Department of Molecular and Developmental Medicine, Università degli Studi di Siena, Istituti Biologici S. Miniato, 53100-Siena (Italy)
[e] Department of Experimental and Clinical Medicine, Università degli Studi di Firenze, 50134-Firenze (Italy)
[f] Department of Chemistry "Ugo Schiff", Università degli Studi di Firenze, 50019-Sesto Fiorentino, (Italy)
[g] National Institute of Optics, National Research Council, 50019-Sesto Fiorentino (Italy)
[h] Istituto Nazionale di Ricerca Metrologica (INRiM), 10135-Torino (Italy)
E-mail: grandinetti@lens.unifi.it

Liquid crystalline elastomers (LCEs) are shape-changing materials that have proved to be good candidates for the design of biomedical implants and devices, thanks to their stimulability, tunable properties and biocompatibility. LCEs are also an example of cell-instructive materials: the anisotropy of their network has been shown to drive cell alignment, which positively affects functionality in different lines [1–2]. Moreover, these materials have been studied in the fabrication of responsive coatings [3]. In this contribution, the latest advances in the use of LCEs in the field of tissue engineering will be reviewed. The communication will focus on the preparation and characterization of responsive fingerprint-patterned surfaces, originated by self-assembly of chiral nematic LC molecules, and on their effect on cell growth and functionality (Figure 1). The research leading to these results has received funding from Ente Cassa di Risparmio di Firenze, grant n. 2020/1583.

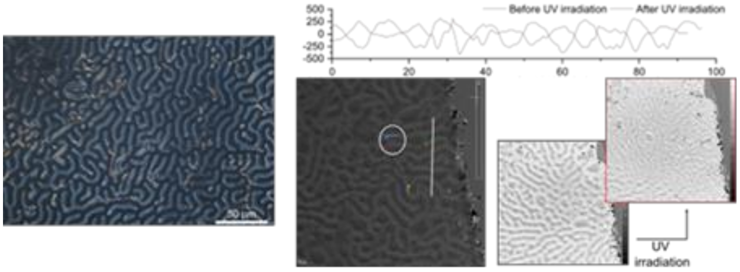

Figure 1: A fingerprint-patterned surface.

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Poly-lipoic acid-based nanoparticles as a new biocompatible therapeutic tool for delivering active molecules

Lucía Morillas-Becerril,[a] Regina Tavano,[b] Chiara Castellani,[c] Annalisa Angelini,[c] Emmanuele Papini[b] and Fabrizio Mancin[a]

[a] Dipartimento di Scienze Chimiche, Università degli studi di Padova, via Marzolo 1, Padova, I-35131, Italy
[b] Dipartimento di Scienze Biomediche, Università degli studi di Padova, via U. Bassi 58/B1, Padova, I-35131, Italy
[c] Dipartimento di Scienze Cardio-Toraco-Vascolari e Sanità pubblica, Università degli studi di Padova, via Giustiniani 2, Padova, I-35128, Italy
E-mail: lucia.morillasbecerril@unipd.it

Studies on the delivery of active molecules to target tissues with nanosystems have experienced a renaissance in the last years. Indeed, this approach can be of particular interest to deal with complex disease.[1] However, controlling tissue distribution, accumulation, persistence and clearance in vivo of nanosystems is still a challenge.[2] In this study, we present an innovative approach to produce biocompatible, degradable and stealth polymeric nanoparticles based on poly-lipoic acid, stabilized by PEG-ended surfactant. Taking advantage from the well-known thiol induced polymerization of lipoic acid, non-toxic nanovectors made by a solid cross-linked polymeric matrix of lipoic acid monomers were prepared and loaded with active species with a one-step protocol. Biological studies demonstrated a high stability in the biological media, the virtual absence of "protein" corona in biological fluids, absence of acute toxicity in vitro and in vivo, complete clearance from the organism and a relevant preference for short term accumulation in the heart of rodents.[3] These features candidate these nanoparticles as a promising tool in the medical field.

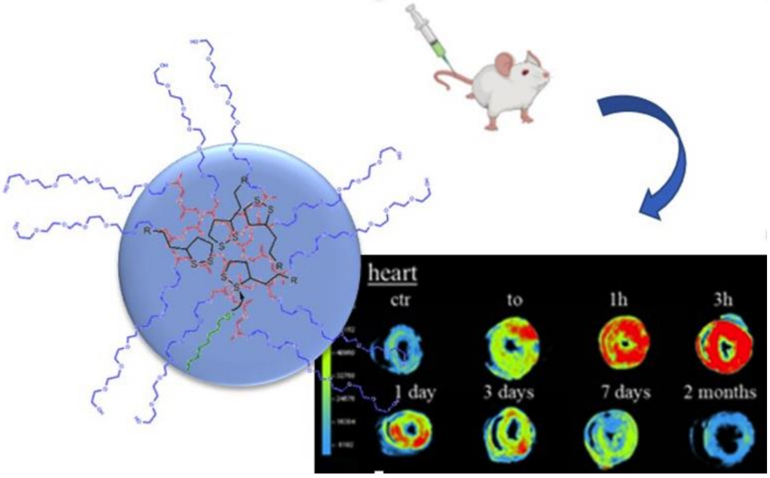

Figure 1: Poly-lipoic acid-based nanoparticles and their in vivo accumulation in rodents.

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Recent advances in lateral flow assay technique

Fabio Di Nardo, Simone Cavalera, Matteo Chiarello, Thea Serra, Laura Anfossi, and Claudio Baggiani

Department of Chemistry, University of Torino, Via Pietro Giuria 5, 10127-Torino, Italy
E-mail: fabio.dinardo@unito.it

The Lateral Flow Immunoassay (LFIA) is by far one of the most successful analytical platforms to perform the on-site detection of target substances (figure 1). LFIA can be considered as a sort of lab-in-a-hand and, together with other point-of-need tests, has represented a paradigm shift from sample-to-lab to lab-to-sample aiming to improve decision making and turnaround time. The features of LFIAs made them a very attractive tool in clinical diagnostic where they can improve patient care by enabling more prompt diagnosis and treatment decisions. The rapidity, simplicity, relative cost-effectiveness, and the possibility to be used by nonskilled personnel contributed to the wide acceptance of LFIAs. As a consequence, from the detection of molecules, organisms, and (bio)markers for clinical purposes, the LFIA application has been rapidly extended to other fields, including food and feed safety, veterinary medicine, environmental control, and many others [1].

The adequate analytical sensitivity, together with versatility and good usability, made LFIA the most commercially available point-of-care diagnostic format. This is also because in contrast to other promising paper-based analytical platforms that mainly remain as laboratory prototypes, LFIA devices easily enter into real-life applications with a high market penetration mainly because they do not need extensive upgrades to become an end-user device. The wide acceptance of LFIA devices also played an eminent role in the use of the platform for the detection of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in the current pandemic situation, as we can still notice and as extensively reported in the literature [2].

In this communication, an overview on the LFIA technique will be given, as well as recent advances proposed by our research group.

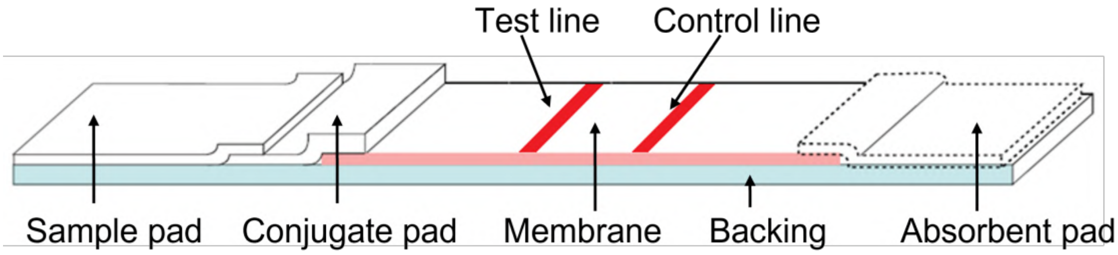

Figure 1: Scheme of a typical LFIA strip.

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2D merged paper-based devices for fast electrochemical detection of metals in different matrices

Antonella Miglione,[a] Ritamaria Di Lorenzo,[a] Sonia Laneri,[a] Michele Spinelli,[b]
Angela Amoresano,[b] and Stefano Cinti[a,c]

[a] *Dep. of Pharmacy, University of Naples Federico II, Via Domenico Montesano 49, 80131-Naples, Italy*
[b] *Dep. of Chemical Sciences, University of Naples Federico II, Via Cintia 21, 80126-Naples, Italy*
[c] *Interuniversity Center for Studies on Bioinspired Agro-Environmental Technology (BAT Center), University of Naples Federico II, 80055-Naples, Italy*
E-mail: antonella.miglione@unina.it

In recent years, the electroanalytical field has exploited great advantages in using paper-based analytical tools. The well-known properties of paper, such as abundance, affordability, lightness and biodegradability, combined with features of printed electrochemical sensors, have enabled the development of sustainable devices that drive (bio)sensors beyond the state of the art [1]. The ability of paper to autonomously filter/purge/react with target species make these devices powerful in establishing point-of-need tools, even if the word “paper” might be general; in fact, the mainly adopted paper-based substrates are often chromatographic and office ones [2]. They are characterized by main features (and drawbacks): chromatographic paper is well-established for storing reagents/treating samples, but the sensitivity compared to traditional screen-printed is lower (due to porosity), while office paper represents a sustainable alternative to plastic (with similar sensitivity), but its porosity is not enough to load reagents. Our idea is to exploit all the paper-based substrates, utilizing different combination of substrates, to overcome these limitations and take full advantage of all the benefits associated with their use. We applied our research towards the detection of metal ions in two different matrices, namely copper and nickel. Exposure to metals involves, depending on the case, risks or benefits for humans. Copper is an essential metal that plays a crucial role in various biochemical reactions and significant changes in its serum levels could reflect pathological disorders. Additionally, metals are also commonly found in cosmetic products in which they can cause serious skin problems and allergies: nickel is one of the most common allergens that can cause contact dermatitis or eczema. Due to their relevance on human health, the adoption of portable and easy-to-use devices represent a valid and effective alternative to existing analytical methods that usually require time-consuming procedures, skilled personnel and sophisticated equipment. Herein, we obtained a novel architecture by combining sustainable and robust electrochemical strips, screen-printed on different substrates (paper and polyester), and chromatographic paper to 1) store the reagents, 2) collect real sample and 3) pre-concentrate the analyte of interest. The novel sensing platforms have allowed to obtain very low limits of detection for both metals, working with small amount of real matrices (including serum, cream and gel), and the accuracy of these methods has been evaluated by comparing those with ICP-MS measurements.

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Bio-responsive and electroactive graphene inks for the manufacturing of ink-jet printed amperometric electrodes

Alessandro Silvestri,[a] Alejandro Criado,[a] Fabrizio Poletti,[b] Faxing Wang,[c] Pablo Fanjul-Bolado,[d] María B. González-García,[d] Clara García-Astrain,[a,e] Luis M. Liz-Marzán,[a,e,f,g] Xinliang Feng,[c] Chiara Zanardi,[b,h] and Maurizio Prato[a,g,i]

[a] Center for Cooperative Research in Biomaterials (CIC BiomaGUNE), Basque Research and Technology Alliance (BRTA), 20014 Donostia-San Sebastián, Spain
[b] Department of Chemical and Geological Sciences, University of Modena and Reggio Emilia, 41125 Modena, Italy
[c] Faculty of Chemistry and Food Chemistry and Center for Advancing Electronics Dresden (cfaed) Technische Universität Dresden, 01062 Dresden, Germany
[d] Metrohm DropSens, S.L. Vivero Ciencias de la Salud, C/Colegio Santo Domingo de Guzmán s/n, 33010 Oviedo (Asturias), Spain
[e] Centro de Investigación Biomédica en Red, Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), 20014 Donostia-San Sebastián, Spain
[f] Department of Applied Chemistry, University of the Basque Country, 20018 Donostia-San Sebastián, Spain
[g] Ikerbasque, Basque Foundation for Science, 48013 Bilbao, Spain
[h] Institute of Organic Synthesis and Photoreactivity, National Research Council of Italy, 40129 Bologna, Italy
[i] Department of Chemical and Pharmaceutical Sciences, Universitá Degli Studi di Trieste, 34127 Trieste, Italy
E-mail: asilvestri@cicbiomagune.es

With the advent of flexible electronics, the old fashioned and conventional solid-state technology will be replaced by conductive inks combined with low-cost printing techniques [1]. Graphene is an ideal candidate to produce conductive inks, due to its excellent conductivity and zero band gap [2]. The possibility to chemically modify graphene with active molecules opens up the field of responsive conductive inks [3]. Herein we present a bio-responsive, electroactive and inkjet-printable graphene ink. The ink is based on graphene chemically modified with selected enzymes and an electrochemical mediator, to transduce the products of the enzymatic reaction into an electron flow, proportional to the analyte concentration. A water-based formulation was engineered to be respectful with the enzymatic activity while matching the stringent requirements of inkjet printing. The versatility of the system was demonstrated by modifying graphene with various oxidoreductases, obtaining inks with selectivity toward glucose, lactate, methanol, and ethanol. We used the electroactive ink to manufacture electrodes by inkjet printing, demonstrating its efficient electrochemical performance, as well as a proof-of-concept application in biosensing..

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Graphene field effect transistors for neurotransmitter monitoring

Cecilia Wetzl,[a] Alejandro Criado Fernández,[b,a] Elisabet Prats,[d] Sergi Brosel,[d]
Anton Guimerà,[d] and Maurizio Prato,[a,c]

[a] CIC biomaGUNE, Paseo Miramón, 182, 20014 San Sebastián, Guipúzcoa, Spain.
[b] Universidade da Coruña, Centro de Investigacións Científicas Avanzadas (CICA), Rúa As Carballeiras, A Coruña, Spain.
[c] Department of Chemical and Pharmaceutical Sciences, University of Trieste, Piazzale Europa, 1, 34127 Trieste, Italy.
[d] Institut de Microelectrónica de Barcelona (IMB-CNM, CSIC), Campus Universitat Autónoma de Barcelona, 08193-Bellaterra, Barcelona, Spain.
E-mail: cwetzl@cicbiomagune.es

In the recent years, graphene field effect transistors (FETs) emerged as promising electronic platform to perform biosensing. These devices show several interesting features as amplification capability, low sensitivity to environmental interferences and ease miniaturization that make them suitable to develop innovative bioelectronic platforms [1]. The employment of graphene as FETs channel material provides some crucial properties for device fabrication as biocompatibility, flexibility as well as the possibility of introducing specific receptor onto the device surface. This last point is one of the main challenges in building such biosensors, as the immobilization strategy must preserve the electronic properties of the device while anchoring the receptor at a controlled distance from the surface. In fact, the sensitivity of the device is strongly dependent on the distance between the receptor and the device [2].

The aim of our project is to create a highly sensitive and selective device for neurotransmitter monitoring combining the graphene FETs technology with an aptameric recognition system, previously employed in neurotransmitter sensing [2]. To achieve the controlled modification of the graphene surface, we designed a hindered maleimide aryl diazonium salt and studied different reduction methodologies as thermal, electrochemical, and reducing agents mediated reduction. The grafting of a maleimide moiety enables the fast bioconjugation of a serotonin-selective aptamer by further thiol-ene chemistry.

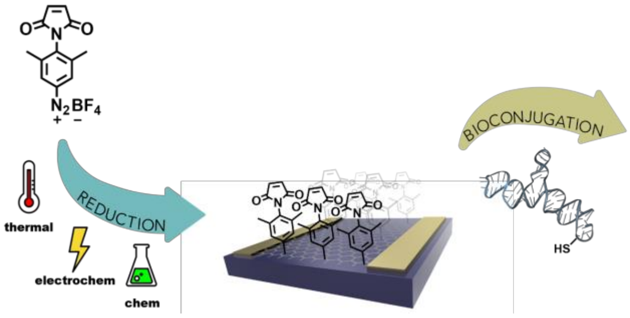

Figure 1: Schematic representation of graphene FET functionalization strategy.

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Paper-based multiplexed colorimetric device for the simultaneous detection of salivary biomarkers

Tania Pomili,[a,b] Paolo Donati,[a] and Pier Paolo Pompa[a]

[a] Nanobiointeractions&Nanodiagnostics, Istituto Italiano di Tecnologia (IIT), Via Morego, 30 – 16163 Genova (Italy)
[b] Department of Chemistry and Industrial Chemistry, University of Genova, Via Dodecaneso, 31 – 16146 Genova, Italy
E-mail: tania.pomili@iit.it

Point-of-care tests (POCTs) have recently gained enormous success in the healthcare system, due to the possibility to perform near-patient tests with real-time results. In the wide range of fabrication substrates, paper appears to be very promising, since it may be easily folded to form suitable microchannels, enabling fine control of the flow of the biological samples [1]. Most of the current paper-based POC devices provide the detection of a single target analyte, such as the Covid-19 rapid antigen test. Multiplexed analysis, on the other side, enables the identification, in one single analysis, of different parallel biomarkers or a combination of them, providing a better clinical value of the test [2]. Furthermore, the integration of nanoparticles (NPs) in POCT, can improve the device performance, and stability. In particular, noble metal NPs could be exploited for both their tunable plasmonic properties and their nanozyme activities. The remarkable sensitivity of NPs integrated in POCT enables detecting biomarkers in non-invasive fluids, where the concentrations are even hundreds of times lower than those in blood [3].

In the present work, we describe the development of a monolithic and fully integrated paper-based device for the simultaneous detection of three prognostic biomarkers in saliva. The pattern of the proposed multiplexed device is designed with a central sample deposition zone and three identical arms, each containing a pre-treatment and a test zone. Its one-step fabrication is realized by CO_2 laser cutting, providing remarkable parallelization and rapidity (ca. 5 sec/device). The colorimetric detection is based on the sensitive and selective target-induced reshaping of plasmonic multibranched gold NPs, which exhibit a clear spectral shift (and blue-to-pink color change) in case of above-physiological concentrations of the three salivary biomarkers. A rapid and multiplexed naked-eye or smartphone-based readout of the colorimetric response is achieved within 10 minutes. A prototype kit for POCT testing is also reported, providing robustness and easy handling of the device.

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Peptide bond formation using unprotected N - carboxyanhydrides under green chemistry conditions

Federica Santino, Rossella Petruzzelli, Junwei Zhao, Elisa Boanini, Luca Gentilucci

Department of Chemistry “G. Ciamician”, University of Bologna, via Selmi 2, 40126, Bologna, Italy
E-mail: federica.santino2@unibo.it

Peptide bond forming reactions are fundamental to the synthesis of peptides and peptidomimetics. Unfortunately, the chemistry of the peptide bond rouses much concern in terms of economic cost, environmental impact, and production of wastes, especially toxic organic solvents. In a Green Chemistry perspective, we reconsidered the use of unprotected N-carboxy anhydrides (NCAs) of standard α-amino acids under minimal liquid-assisted grinding (LAG) conditions. NCAs are very attractive in peptide synthesis for their simplicity and atom economy.

Indeed, the molecular bulk of these N-protected/C-activated bidentate reactants remains with the newly formed peptide. However, the NCAs are prone to polymerization, a formidable obstacle to the development of mechanochemical conditions. Nevertheless, polymerization can be prevented by operating under controlled basic conditions. In this work, we described peptide bond forming reactions from NCAs and amino partners by LAG in amalgam with nanocrystalline hydroxyapatite (HAp) powder as a bio-compatible, reusable inorganic base.

The experiments supported the combination of HAp and the green solvent γ-valerolactone, and highlighted the importance of NCAs’ purity and crystallinity, as studied by NMR, SEM, and XRD. The efficacy of the procedure was assessed by the synthesis of the 13-mer cytotoxic peptide PTP7.

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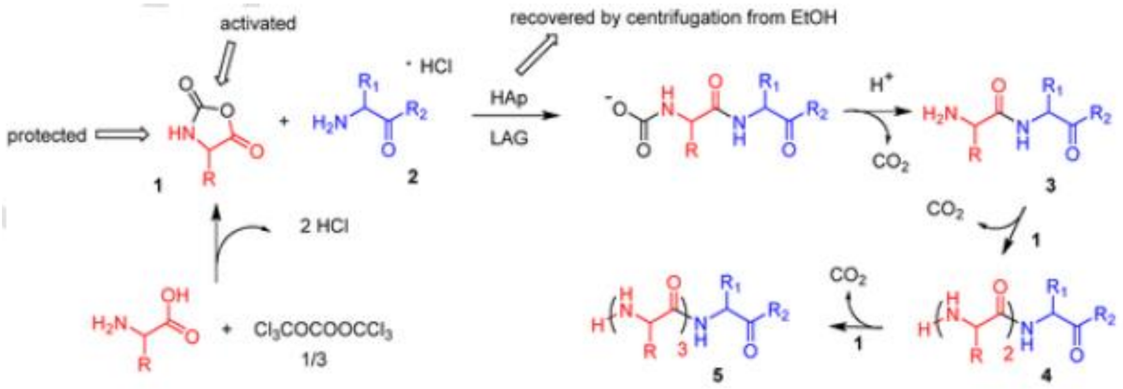


Figure 1: Synthesis of the NCAs and peptide bond formation in the presence of HAp.

Synthesis and biological evaluation of novel Hydantoin-based peptidomimetics

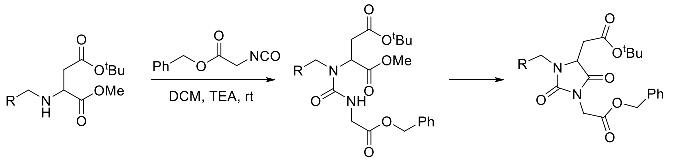
Alessio M. Caramiello, Prof. Dr. Alessandro Sacchetti and Prof. Dr. Alessandro Volonterio

Dipartimento di Chimica, Materiali e Ingegneria Chimica "G.Natta",Politecnico di Milano, Via Mancinelli 7, 20131, Milano (MI), Italy
E-mail: alessiomaria.caramiello@polimi.it

Peptidomimetic compounds have almost overcome peptide and peptide-derived drugs because they offer better transport properties, resistance to enzymatic cleavage/degradation and even to immune response.

Among many different molecules, we knew that we needed an easily accessible β-turn mimetic scaffold able to target PPIs in the hot-spot region and that this scaffold should offer virtually unlimited screening possibilities due to its ease of modification.

We then demonstrated [1] that the chemical structure needed to achieve the previously mentioned benefits was a molecule containing an hydantoin core. This scaffold showed to be very important since it can be properly functionalized, allowing the molecule to adapt to a wide range of kinetically and thermodynamically accessible conformations, that can subsequently mimic selected secondary protein structures. The target of our study is Insulin Degrading Enzyme (IDE), involved in the degradation of insulin and other amyloidogenic substrates. By modulation of the action of this enzyme, it is possible to open new therapeutic strategies to treat many IDE-dependent pathologies (like diabetes and Alzheimer's disease) [2].



isolable intermediate, in excess base undergoes a 5-membered ring closure

Scheme 1: Key step for the formation of the hydantoin core

The synthetic sequence for our hydantoins implies the formation of an isocyanate that will react with an amine to form a urea. This urea is the key intermediate for the preparation of the hydantoin core, since it is involved in an intramolecular cyclization in basic conditions. The key step for its preparation is reported in Scheme 1. We synthesized different derivatives after having optimized this cyclization, then we took inspiration from the literature [3] to design a new class of antimicrobial agents. We performed different experiments to determine all the molecules' structural properties and we want to perform biological studies to establish their effectiveness.

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Bridged bicyclic endoperoxides: from natural compounds to synthetic analogues active against *P. falciparum* strains

Roberta Ibba,[a] Stefano Federico,[a] Simone Brogi,[b] Stefania Butini,[a] Sandra Gemma,[a] and Giuseppe Campiani[a]

[a] *Department of Biotechnology, Chemistry and Pharmacy, Università degli Studi di siena, via Aldo Moro 2, 53100, Siena, Italy*
[b] *Department of Pharmacy, Università degli Studi di Pisa, via Bonanno 6, 56126, Pisa, Italy*
E-mail: roberta.ibba@unisi.it

Malaria is an infectious, haematological disease caused by the Plasmodium parasite, five species of which are known to infect humans. *P. falciparum* causes the most threatening infections with high mortality and morbidity rates. Artemisinins are antimalarial natural compounds extracted from sweet wormwood which constitute the first line treatment for *P. falciparum* malaria according to WHO guidelines [1]. Dihydroartemisinin (1, Figure 1) is an endoperoxide-based natural product, which is highly effective against clinically relevant *P. falciparum* strains responsible for human malaria. Plakortin (2) is a natural antimalarial endoperoxide which shares with artemisinin the antimalarial mechanism of action but is endowed with a less complex molecular scaffold. Endoperoxides were proved to cause the death of the parasite by the release of a toxic carbon radical, generated by a Fe^{II}-induced reductive activation of endoperoxides nucleus [2].

Since several years our group is engaged in the discovery of synthetic endoperoxides as low-cost and accessible alternatives to natural artemisinins and plakortins. Here we describe the discovery of a novel series of bridged bicyclic endoperoxides (3) as synthetic analogues of the natural endoperoxide plakortin. Suitable and upfront synthetic procedures for the preparation of bicyclic endoperoxides have been established. The peroxides presented here are potent antiplasmodials with favourable resistance index toward chloroquine-resistant *P. falciparum* strains.

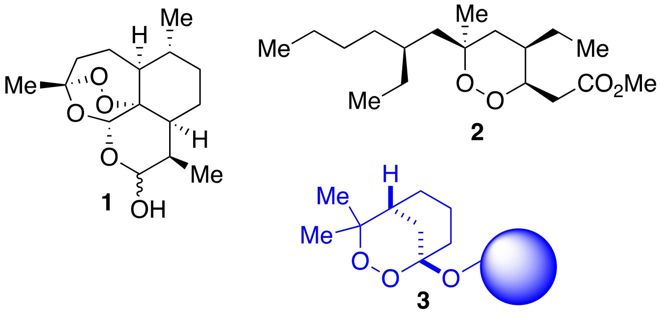

Figure 1: Natural products dihydroartemisinin (1) and dihydroplakortin (2) and general structure of the bridged bicyclic endoperoxides (3).

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Development of indoline-based HDAC6 inhibitors for the treatment of Idiopathic Pulmonary Fibrosis

Gabriele Carullo,[a] Stefania Butini,[a] Sandra Gemma,[a] Simone Brogi,[b] Peter Bradding,[c] Antje Prasse,[d] David W. Christianson,[e] and Giuseppe Campiani[a]

[a] Dipartimento di Biotecnologie, Chimica e Farmacia, Università di Siena, Via Aldo Moro 2, 53100, Siena, Italy
[b] Dipartimento di Farmacia, Università di Pisa, Via Bonanno 6, 56126, Pisa, Italy
[c] Department of Respiratory Sciences, University of Leicester, UK, Institute of Lung Health and NIHR Leicester BRC-Respiratory, LE5 4PW Leicester, U.K.
[d]Klinik für Pneumologie, Medizinische Hochschule Hannover, Hannover 30625, Germany
[e]Roy and Diana Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104-6323, United States.
E-mail: gabriele.carullo@unisi.it

Idiopathic pulmonary fibrosis (IPF) is an interstitial lung disease characterized by a progressive-fibrosing phenotype. Nowadays, only two drugs, pirfenidone and nintedanib are availbale for IPF treatment [1]. IPF has been associated with aberrant HDAC6 activity [2]. In this frame, a series of novel *h*HDAC6 inhibitors, having low inhibitory potency over *h*HDAC1 and *h*HDAC8 have been synthesized as potential tools for IPF treatment. Their inhibitory potency was combined with low *in vitro* and *in vivo* toxicity. Structural analysis of the lead compound by x-ray analysis and structure−activity relationship studies contributed to the optimization of the binding mode of the new molecules. The best-performing analogues were tested for their efficacy in inhibiting fibrotic sphere formation and cell viability, proving their capability in reverting the IPF phenotype. The most promising tools were also validated in a human lung model of TGF-β1-dependent fibrogenesis [3].

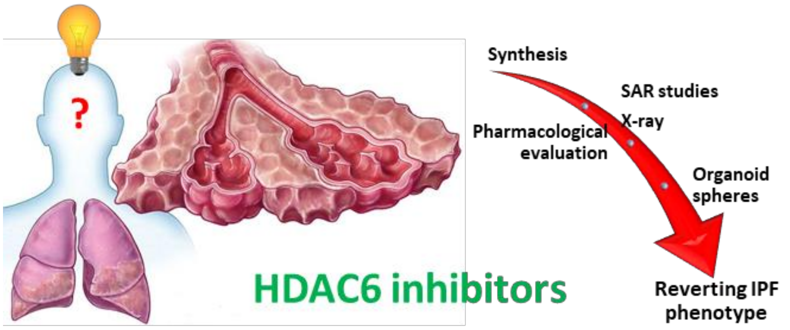

Figure 1: Discovery of novel HDAC6 inhibitors for IPF treatment

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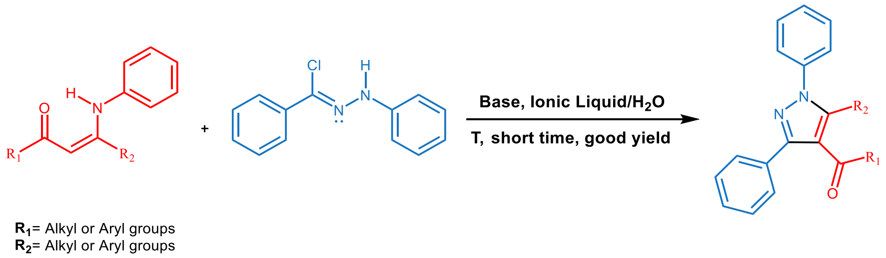
Eliminative 1,3-dipolar cycloaddition for the regioselective synthesis of 1,3,4,5-tetrasubstituted pyrazoles

Vincenzo Algieri,[a] Fabrizio Olivito,[a] Cristina Algieri,[b] Antonio Jiritano,[a] Matteo Antonio Tallarida,[a] Loredana Maiuolo,[a] Paola Costanzo,[a] Salvatore Nesci,[b] and 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, 40064 - Ozzano dell'Emilia (BO), IT.*
vincenzo.algieri@unical.it

Pyrazoles are five-membered aromatic heterocycles composed of two adjacent nitrogen atoms and three carbons. 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. Generally, the pyrazoles synthesis leads to the formation of mixtures of regioisomers [2] 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. Furthermore, the obtained pyrazoles were subjected to preliminary studies to evaluate their antioxidant activity through the Uv/Vis spectrophotometry with DPPH and ABTS assays. In addition, pyrazoles were tested on the opening phenomenon of the mitochondrial permeability transition pore showing interesting biological activity.

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Performance improvement in the purification of a bioactive peptide through Multicolumn Countercurrent Solvent Gradient Purification (MCSGP) process

Chiara De Luca,[a] Simona Felletti,[a] Desiree Bozza,[a] Giulio Lievore,[a] Alessandro Buratti,[a] Massimo Morbidelli,[b] Marco Macis,[c] Antonio Ricci,[c] Walter Cabri,[c,d] Alberto Cavazzini,[a] and Martina Catani[a]

[a] Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Via L. Borsari 46, 44121 Ferrara, Italy
[b] Department of Chemistry, Materials and Chemical Engineering Giulio Natta, Politecnico di Milano, via Mancinelli 7, 20131 Milan, Italy
[c] Fresenius Kabi iPSUM srl, I&D, Via San Leonardo 23, 45010 Villadose (Rovigo), Italy
[d] Department of Chemistry Giacomo Ciamician, Alma Mater Studiorum-University of Bologna, Via Selmi 2, 40126 Bologna, Italy
E-mail: dlcchr@unife.it

Pharmaceutical products, including peptides, must satisfy very strict purity specifications, because of quality and safety reasons. Therefore, the necessity to operate one or more purification steps to obtain high quality drugs is indisputable. Critical impurities chemically very similar to the target product are generated during the synthesis and are generally removed by means of preparative single-column chromatographic techniques (=batch methods) [1]. Batch methods struggle to separate completely the peptide of interest from other groups of impurities, because of their similarity and of high loading of sample processed in preparative conditions, which cause peaks overlapping. The typical situation encountered in these cases is the so-called center-cut separation, where the target elutes as intermediate between two other groups of impurities less and more retained respectively. The direct consequence of this apparently insurmountable overlapping is a yield-purity trade-off, a limit intrinsic to batch chromatography according to which it is possible to obtain either high purity or high recovery of the peptide of interest, depending on whether the overlapping windows are collected or not. This trade-off leads to drawbacks in the overall economy of the process. Multicolumn chromatographic processes, operating in continuous and countercurrent mode, can alleviate this limitation by performing internal recycling of the overlapping portions of the chromatogram [2]. The technique used in this research is twin-column Multicolumn Countercurrent Solvent Gradient Purification (MCSGP), which has been applied to the purification of an industrial crude of a bioactive decapeptide. It has been demonstrated that MCSGP leads to promising results, including a remarkable improvement in process performance (up to 6 times higher) from the point of view of recovery, productivity and solvent consumption, with respect to the corresponding batch run. The automation of the process on industrial scale would lead to great reproducibility which would reflect in improved consistency in product quality.

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OR56

Developing novel classes of protein kinase CK1δ inhibitors by fusing [1,2,4]triazole with different bicyclic heteroaromatic systems

Ilenia Grieco,[a] Maicol Bissaro,[b] Davide Benedetto Tiz,[a] Daniel I. Perez,[c] Conception Perez,[c] Ana Martinez,[c,e] Sara Redenti,[a] Elena Mariotto,[f] Roberta Bortolozzi,[b] Giampietro Viola,[f,g] Giorgio Cozza,[h] Giampiero Spalluto,[a] Stefano Moro,[b] , and Stephanie Federico[a]

[a] *Dipartimento di Scienze Chimiche e Farmaceutiche, Università degli Studi di Trieste, Via Licio Giorgieri, 1, 34127, Trieste, Italy;*
[b] *Molecular Modeling Section (MMS), Dipartimento di Scienze del Farmaco, Università degli Studi di Padova, via Marzolo 5, 35131, Padova, Italy;*
[c] *Centro de Investigaciones Biological, CSIC, Ramiro de Maetzu 9, 28040, Madrid, Spain;*
[d] *Instituto de Quimica Medica, CSIC, Juan de la Cierva 3, 28006, Madrid, Spain;*
[e] *Centro de Investigacion Biomedica en Red en Enfermedades Neurodegenerativas (CIBERNED), Instituto Carlos III, 28031, Madrid, Spain;*
[f] *Dipartimento di Salute della Donna e del Bambino, Laboratorio di Oncoematologia, Università di Padova, 35131, Padova, Italy;*
[g] *Istituto di Ricerca Pediatrica (IRP), Corso Stati Uniti 4, 35128, Padova, Italy;*
[h] *Dipartimento di Medicina Molecolare, Università degli Studi di Padova, Via U. Bassi 58/B, 35131, Padova, Italy.*
E-mail: ilenia.grieco@phd.units.it

Protein kinase CK1δ is an attractive target for several pathological conditions comprising neuroinflammatory and neurodegenerative diseases [1]. A promising scaffold for the development of ATP competitive kinase inhibitors is represented by 5,6-fused heteroaromatic systems that emulate the adenine ring of ATP. In particular, series of [1,2,4]triazolo[1,5-*c*]pyrimidines (TP) and [1,2,4]triazolo[1,5-*a*][1,3,5]triazines (TT) were developed as ATP-competitive CK1δ inhibitors and a structure activity relationship has been outlined. Molecular docking studies revealed that the free amino group at the 5- and 7- positions of the TP and TT, respectively, and the 3-hydroxyphenyl or 3,5-dihydroxyphenyl moiety at the 2- position of both scaffolds are able to interact with key residues of the CK1δ ATP-binding pocket. The 5-(7-amino-5-(benzylamino)-[1,2,4]triazolo[1,5-*a*][1,3,5]triazin-2-yl)benzen-1,3-diol, the most potent compound of the developed series (IC_{50} = 0.18 μM), showed an intermediate ability to passively cross the blood-brain barrier in a parallel artificial membrane permeability assay (PAMPA). In addition, it displayed a great selectivity in kinome and resulted no toxic against normal cell lines at a concentration of 10 μM. Thus, it represents a promising hit compound to develop more potent and selective derivatives useful to investigate CK1δ therapeutic implications [2].

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Untargeted characterization of medium- and short-sized antioxidant peptides from soybeans

Carmela Maria Montone, Chiara Cavaliere, Andrea Cerrato, Susy Piovesana, and Anna Laura Capriotti

Department of Chemistry, University of Rome “La Sapienza”, Rome (Italy)
E-mail: carmelamaria.montone@uniroma1.it

Soybeans (Glycine max) are an excellent source of dietary proteins and peptides with potential with many potential health benefits in reducing chronic diseases such as obesity, cardiovascular disease, insulin-resistance/type II diabetes, certain type of cancers, and immune disorders. Using different approaches, many soy bioactive peptides that have a variety of physiological functions such as hypolipidemic, anti-hypertensive, and anti-cancer properties, and anti-inflammatory, antioxidant, and immunomodulatory effects have been identified [1].

Here, a comprehensive characterization of medium-sized and short peptides (two to four amino acids) obtained from simulated gastrointestinal digestion was presented. Two different analytical approaches were employed for peptide characterization, namely a common peptidomic analysis for medium-sized peptides and a suspect screening analysis for short peptides, employing an inclusion list of exact m/z values of all possible amino acid combinations. Moreover, fractionation by preparative reversed-phase liquid chromatography was employed to simplify the starting protein hydrolysate. Six fractions were collected and tested for antioxidative activity by an innovative antioxidant assay on human gastric adenocarcinoma AGS cell lines. The two most active fractions (2 and 3) were then characterized by a peptidomic approach and database search, as well as by a suspect screening approach, in order to identify potential antioxidant amino acid sequences. Some of the peptides identified in these two fractions have been already reported in the literature for their antioxidant activity.

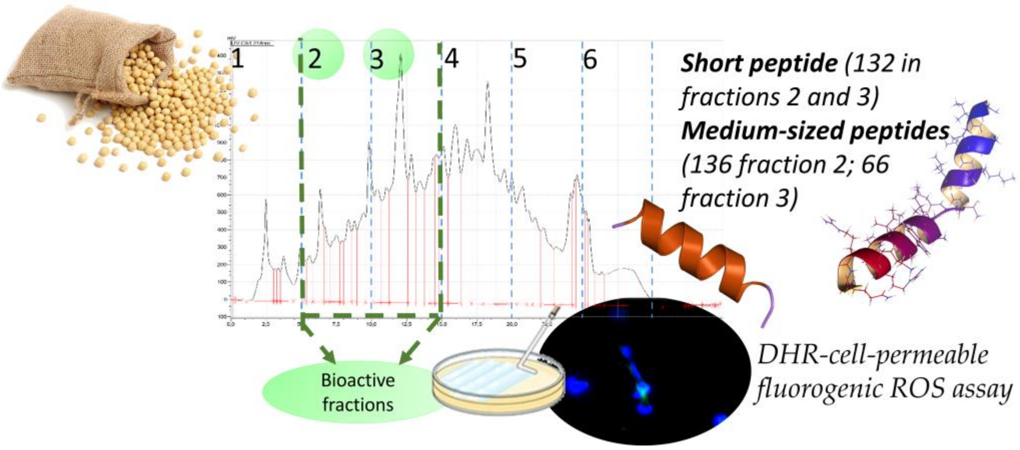

Figure 1: The two most active fractions (2 and 3) for antioxidant activity

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An easy way for the simultaneous hydrolysis, pre-concentration, and chemical stabilization of crocetin from saffron powder

Lucia Palumbo,[a] Serena Fiorito,[a] Francesco Epifano,[a] Chiara Collevecchio,[a]
Fabio Cardellini,[b] Maria Bastianini,[b] Roberto Spogli,[b] and Salvatore Genovese [a]

[a]*Dipartimento di Farmacia, Università degli studi "G. d'Annunzio" Chieti - Pescara, Via dei Vestini 31, 66100-Chieti Scalo (CH), Italy*
[b]*Prolabin & Tefarm Srl, Via dell'Acciaio 9, 06134-Perugia, Italy*
Email: lucia.palumbo@unich.it

Crocetin is the main apocarotenoid extracted from *Crocus sativus*. The most of properties of saffron are ascribed to crocetin and its diester with gentiobiose, known as crocin-1 (Figure 1). It is nowadays well established to act as valuable and powerful nutraceutical, especially in the prevention and management of metabolic disorders in humans, myocardial dysfunctions, neurological disorders, and associated syndromes [1]. With the aim of its selective concentration by means of extractions from saffron powder aqueous solutions in the heterogeneous phase, we report herein that some synthetic clays, like zinc hydroxy chloride, magnesium aluminium hydroxy chloride, magnesium aluminium hydroxy acetate, and zinc aluminium chloride are not only able to selectively retain crocetin in the solid phase, but also to lead to its hydrolysis from its digentiobyosil ester (crocin) in nearly quantitative yield and to its chemical stabilization (e.g. oxidation) over time. This phenomenon was assessed by HPLC analyses after desorption of crocetin from the respective support, evaluating its degradation along a period of 30 days. The method we set up could represent a good mean to obtain pure crocetin from saffron powder, preserving in the meantime its chemical properties for a concrete exploitation for food, pharmaceutical, and cosmetic purposes.

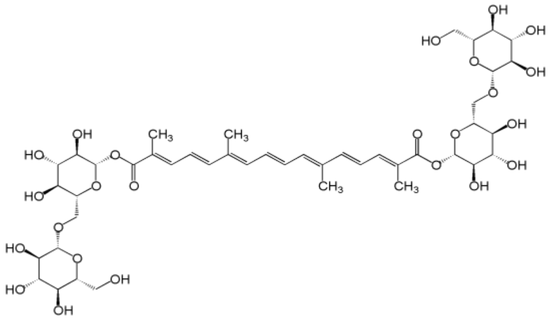

Figure 1: Chemical structure of crocin-1.

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Interfacing and boosting artificial cells with biological systems

Silvia Holler,[a] and Martin Michael Hanczyc,[a,b]

[a] Department of Cellular, Computational and Integrative Biology (CIBIO), University of Trento,
Via Sommarive 9 Trento, 38123, Italy
[b] Chemical and Biological Engineering, University of New Mexico, MSC01 1120, Albuquerque,
NM, 87131-0001, USA
E-mail: silvia.holler@unitn.it

Liquid chemical droplets possess, when pushed away from equilibrium, life-like behaviors such as fission, fusion, movement and chemotaxis. Chemotaxis, the directed motion in response to external gradients, is an important process in living systems. *Dictyostelium,* for instance, uses its pseudopodia to sense cAMP gradients, find its source and survive during starvation. Some artificial systems are also capable of this chemotactic activity. Decanol droplets, when placed in a high pH solution containing surfactants, are able to 'sense' salt gradients and move towards the starting salt source.

These droplet-based chemotactic systems when interfaced with biological systems can act as transporters and move cargo such as hydrogel alginate capsules containing living cells [1], cells survive the transport and proliferate again in the site where the chemotaxis ends. This system is efficient to transport bacteria (*B. subtilis, E. coli*), yeast (*S. cerevisiae*) and eukaryotic cell. The interesting thing is that, when we transported mammalian cell lines (H460, H1299, A549, HEK293T and HS68), we discovered that some lung cancer cell lines release surfactants only when placed in the hydrogel capsules [2]. These surfactants establish the interface between the encapsulated cells and the droplet and also support the chemotaxis of the droplet. Because of this, the droplet-mediated transport system is selective for living cells that produce biosurfactants. This is an example of how the integration of artificial life and biological life could be designed where the systems augment each other and function together as a unit. In this case the living system produces the surfactants that the droplet needs for cargo transport and the artificial system provides the transport for the otherwise sessile mammalian cells. Future applications of droplet-based cell handling that is able to distinguish between cells based not only on viability but cell type, developmental stage or other quantifiable traits can be considered.

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Amorphous nanostructures based on calcium phosphates: biological relevance and physico-chemical investigation

Rita Gelli, Francesca Ridi, and Piero Baglioni

Dipartimento di Chimica “Ugo Schiff” & CSGI, Università degli Studi di Firenze, Via della Lastruccia 3, 50019-Sesto Fiorentino, Italia
E-mail: rita.gelli@unifi.it

Amorphous calcium phosphate-based materials (ACP), together with their crystalline counterpart, represent the main inorganic components of human body, where they are present in several locations and fulfill a great number of functions (Figure 1) [1]. The investigation of their formation and features in bio-relevant media is of outmost importance, as it could contribute to unravel the *in vivo* formation mechanisms and to drive the design of tailored materials for biomedical applications. Among the different scenarios in which ACPs are present in our body, we focused our attention on synthetic analogs of amorphous magnesium-calcium phosphate nanoparticles (AMCPs) present in mammalians' gut [2] and calciprotein particles (CPPs) which form upon the complexation of amorphous CaP and the protein Fetuin-A in serum [3]. We studied their formation in conditions reproducing to a certain extent the *in vivo* milieu, aiming at relating the physico-chemical findings with the physiological and pathological role of these amorphous CaP-based nanostructures. For AMCPs, we inspected the effect of pH and Mg^{2+} on the lifetime of the amorphous phase, and we investigated how simulated intestinal fluids and bio-relevant proteins affect their formation and the features. For CPPs, their stability and crystallization processes at different Fetuin-A concentration and in the presence of stabilizing ions were inspected. As a general approach, these inorganic/hybrid nanostructures were prepared and characterized by means of a multi-technique approach including electron microscopy, X-rays diffraction, infrared spectroscopy, thermal analysis, light scattering and turbidimetry, which allowed us to obtain a comprehensive physico-chemical overview of the systems.

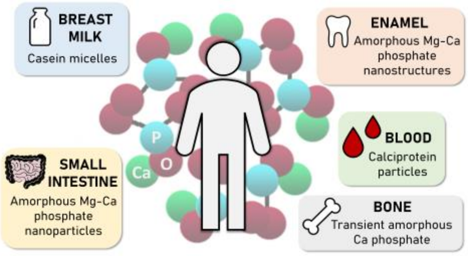

Figure 1: Sketch of the different scenarios of ACP in human body.

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The complex molecular architecture of olefin-based multiblock copolymers by chain shuttling technology

Gaia Urciuoli,[a,c] Antonio Vittoria,[a,c] Salvatore Costanzo,[b,c] Claudio De Rosa,[a,c] Roberta Cipullo,[a,c] Nino Grizzuti,[b,c] Vincenzo Busico,[a,c] and Finizia Auriemma[a,c]

[a] Department of Chemical Sciences, University of Naples Federico II, Complesso Monte Sant'Angelo, via Cintia 21, 80126-Napoli, Italy
[b] Department of Chemical, Materials, and Industrial Engineering, University of Naples Federico II, P.le Tecchio 80, 80125-Napoli, Italy
[c] Dutch Polymer Institute (DPI), P.O. Box 902, 5600 AX-Eindhoven, the Netherlands
E-mail: gaia.urciuoli@unina.it

Olefin block copolymers (OBCs) are high-performance materials that combine apparently conflicting properties such as elastic behavior, low density, high melting temperature, and high mechanical resistance. OBCs, and in particular ethylene-based OBCs (EOBCs), are obtained through the chain shuttling process and feature alternating crystallizable hard blocks constituted by polyethylene (HDPE) and amorphous soft blocks constituted by random ethylene/α-olefin copolymers [1].

Given that in the chain shuttling process growing-chain transfers occur between active metal centers, a reactor blend of non-uniform chains with differences in block length and number of blocks/chain is obtained. In addition to the intrinsic polydispersity of these systems, it should also be considered that the presence of both hard crystallizable blocks and soft amorphous blocks results in a complex interplay between microphase separation and crystallization.

To address the complexity of these systems and to expand their field of application, it is necessary to grasp what is the effect of the different operating parameters in the chain shuttling copolymerization on the microstructure, on phase separation, and on the final properties through the setting up of characterization pathways [2].

In particular, rheological measurements and transmission electron microscopy can help to shed light on the critical role of polydispersity, molecular mass, and dimension and distribution of blocks on the phase behavior of these intriguing multiblock copolymers.

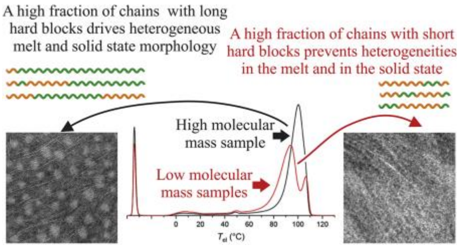

Figure 1: Influence of the distribution of block molecular mass on solid-state behavior for ethylene-based multiblock copolymers (adapted from [2]).

Acknowledgement: This research forms part of the DPI research program, project #817.

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Surface-stabilization of ultrathin gold nanowires for application as capacitive sensors for flexible electronics

Veronica Vetri Buratti,[a] Mirko Maturi,[a] Annalisa Bonfiglio,[b] Letizia Sambri,[a] and Mauro Comes Franchini[a]

[a] *Department of Industrial Chemistry "Toso Montanari", University of Bologna, Viale Risorgimento 4, 40136 Bologna, BO, Italy.*
[b] *Department of Electrical and Electronic Engineering, University of Cagliari, Via Marengo, 09123 Cagliari, CA, Italy.*
E-mail: veronica.vetri2@unibo.it

In the last few decades, the combination of the good mechanical properties of polymeric matrices with the peculiar aspects of nanostructured materials gained the attention of the scientific community for the development of innovative multifunctional nanocomposite [1]. This study reports a completely novel investigation focused on the synthesis and the surface stabilization of ultrathin gold nanowires (AuNWs) for the manufacturing of strain sensors after formulation with polydimethylsiloxane (PDMS) matrices. In order to avoid the formation of collapsed structures, AuNWs are stabilized with a thiolated ligand, through the formation of lipophilic self-assembled monolayers (SAMs) onto gold surfaces. The successful preparation of gold nanostructure is verified by TEM (Figure 1), ^{1}H-NMR and UV-VIS characterizations. The use of AuNWs loaded ultrathin PDMS films is evaluated for its application as capacitive sensors in flexible electronics.

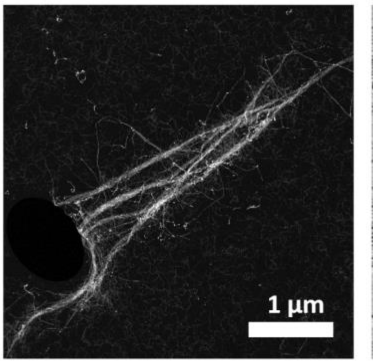

Figure 1: TEM characterization of AuNWs.

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Improving the gelation ability by inserting fluorine atoms

Paolo Ravarino, Nadia Di Domenico, Demetra Giuri, and Claudia Tomasini

Dipartimento di Chimica “Giacomo Ciamician”, Alma Mater Studiorum Università di Bologna, Via Selmi 2, 40126, Bologna, Italy
E-mail: paolo.ravarino2@unibo.it

In the design of a new low-molecular-weight (LMW) gelator, a few guidelines should be followed. Among them, the insertion of moieties able to form weak bonds like H-bonds and hydrophobic interactions is a common strategy.

However, predicting if a molecule can form a gel is not straightforward. Among all the possible weak interactions, π-π stacking plays a pivotal role in governing the gelation process [1]. As halogen atoms usually enhance π interactions and allow the formation of additional weak bonds [2], their insertion on aromatic rings is another strategy to improve the gelling ability of a molecule.

In this work, we present three molecules, sharing the same scaffold with a different number of fluorine atoms on a phenyl ring: Boc-^{D}Phe(F_n)-^{L}Oxd-OH (**F0**: n = 0; **F1**: n = 1; **F2**: n = 2). The molecule **F2** has already been probed to form gels with the addition of glucono-δ-lactone (GdL) [3]. These molecules were tested for the formation of hydrogels at 0.5% w/V concentration under different conditions (figure 1): in EtOH:H_2O mixture in 3:7 ratio (samples **1**-**3**), in iPrOH:H_2O mixture in 3:7 ratio (samples **4**-**6**), in H_2O with GdL to slowly reduce the pH (samples **7**-**9**), and in H_2O with the addition of calcium ions (samples **10**-**12**).

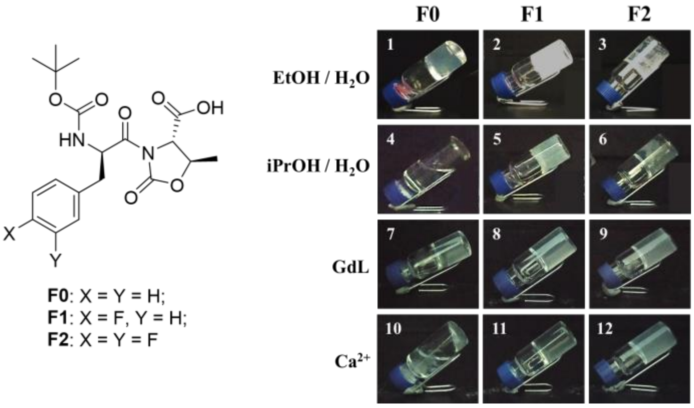

Figure 1: Left: chemical structure of the three gelators synthesised; right: gelling outcomes of the three molecules tested with different methodologies.

Most of the gels display a broad range of transparency in the visible region. This property is very useful for biomedical and optical applications.

Finally, the absence of fluorine atoms on **F0** prevents the formation of stable gels under several conditions, suggesting that the fluorine atoms play an important role in the gelation ability of these molecules.

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Peptide-based gelators for the preparation of functional supramolecular materials

Demetra Giuri,[a] Claudia Tomasini,[a] and Dave Adams[b]

[a] Dipartimento di Chimica “Giacomo Ciamician”, Alma Mater Studiorum, Università di Bologna,
via Selmi 2, 40126 Bologna, Italy
[b] School of Chemistry, University of Glasgow, Glasgow, G12 8QQ, U.K.
E-mail: demetra.giuri2@unibo.it

Low-Molecular-Weight Gelators (LMWGs) are a versatile class of compounds able to self-assemble into supramolecular materials (like gels) thanks to non-covalent interactions. Peptide derivatives are ideal candidates as LMWGs because they are often biocompatible and can be effectively synthesized and functionalized.

The tunability of the gelator structure and of the conditions used for the gelation process (concentration, solvent, trigger) allows the preparation of a class of materials with different mechanical properties, morphology and structural features, that result in different applications.

Our gelators proved to be particularly useful in the absorption of pollutant from aqueous solutions and in their photo-degradation *in situ* (Figure 1a), when combined with catalysts such as TiO_2 nanoparticles [1]. We also obtained composite hybrid materials useful for biomineralization studies: in presence of calcium and carbonate ions, the gelation of one of our compounds occurs with the contemporary formation of $CaCO_3$ crystals (Figure 1b) [2]. This gelator was recently added inside calcium phosphate cements, to provide structural reinforcement with its self-assembled fibrous network (Figure 1c), expanding the use of LMWGs in biomaterials for bone regeneration.

Mixing different LMWGs provides opportunities to further increase the tunability of these systems, achieving materials with improved or unusual properties. We recently reported a multicomponent gel where the gelling component aligns in a magnetic field, affecting the crystal growth of the second component, and resulting in anisotropic crystals being formed [3].

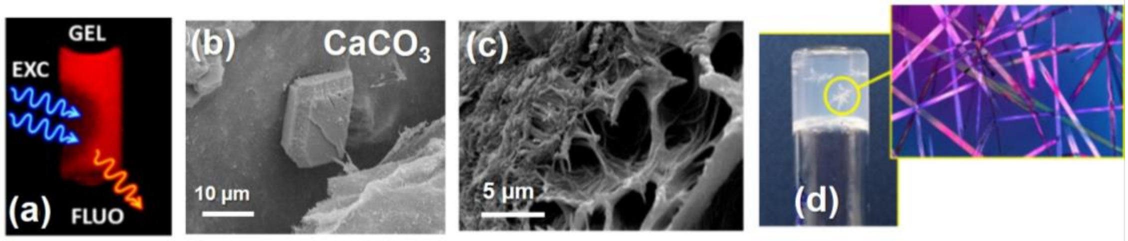

Figure 1: Schematic representation of the materials described.

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Multi-replica biased sampling for chirality switching mechanism in nanomaterials

Mariagrazia Fortino, Gioacchino Schifino, and Adriana Pietropaolo

Dipartimento di Scienze della Salute, Università di Catanzaro, Viale Europa, 88100 Catanzaro, Italy
E-mail: mariagrazia.fortino@unicz.it

Asymmetric nanomaterials are constantly gained a significant interest due to the possibility of getting tunable chiral signatures. In this background, asymmetric π-conjugated polymers are attracting considerable interest in view of their light-dependent torsional reorganization around the π-conjugated backbone, which determines peculiar light-emitting properties. More specifically, polyfluorene derivatives are of wide interest in the field of organic electronics, because their typical photo-induced helix-sense switching (twisted-coplanar transition), enabling a specific molecular response after light-irradiation.

Inspired by the interest in designing asymmetric frameworks with tunable photoelectronic properties, a computational framework able to enhance the sampling of the torsional conformational space and, at the same time, to estimate ground to excited-state free energy differences has been recently proposed. This scheme is based on a combination of Hamiltonian Replica Exchange Method (REM) [1], parallel bias metadynamics (PBMetaD) [2] and free-energy perturbation theory (FEP) [3] and it has been applied on a pentamer of 9,9-dioctylfluorene by biasing multiple torsions.

We found that, upon irradiation, our simulation strategy predicts ground and excited state free-energy surfaces, together with absorption and emission spectra, showing a nice agreement with the experiments.

The proposed simulation scheme, which combines advanced simulation techniques including REM, PBMetaD and FEP theory, allowed us to enhance the sampling of a switchable conjugated polymers and to estimate the free-energy gap between ground and excited states. This is a general scheme that can be used to predict large-scale rearrangements occurring upon light-irradiation and it allow designing new system with enhanced chiral signature. We conclude broadening our view towards future challenges on prospecting modern simulation protocols tunable for optimizing the design of chiral nanomaterials.

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Innovative packaging materials from fish chitinolytic biowastes

Jessica Costa

Department of Biotechnology, Chemistry and Pharmacy, University of Siena, Via Aldo Moro 2, 53100-Siena, Italy
E-mail: jessica.costa2@unisi.it

More than 350 million tons of plastics are produced in the world every year. Packaging, particularly food packaging is one of the largest application fields for plastics. However, the accumulation of huge amounts of plastic waste in the environment leads to development and application of eco-friendly materials, such as bioplastics obtained from renewable resources. Chitosan is a biopolymer originated from the deacetylation of chitin, the second most abundant natural polysaccharides behind cellulose. The main industrial source of biomass for chitin production is the waste of marine food production, particularly the exoskeleton of crabs, lobsters and shrimps. Chitosan has received considerable attention for food packaging applications due to its particular physicochemical features, biodegradability, non-toxicity, biocompatibility, good film-forming properties, intrinsic antioxidant and antimicrobial activity and chemical stability [1]. The FISH4FISH project involves the production of active and sustainable packaging material based on chitinolytic derivatives, using fish biomass waste. Marine biowastes were used to obtained chitin and its deacetylated form, chitosan. The chitooligosaccharides (COS), which have greater antimicrobial activity compared to chitosan, were obtained using the hydrolytic activity of chitinase immobilized on magnetic nanoparticles and chitosan beads [2]. In order to improve the antioxidant, antimicrobial, UV-shielding and mechanical properties of the new packaging, the lignin nanoparticles coated with COS were incorporated in the preparation as active biofiller [3]. The innovative packaging is able to enhance fish shelf life, and in the end of its life, it can be used as fertilizer and microbial preservatives for plants.

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Smart sensors based on cyanine dyes with acidichromic and hydrophobic-to-hydrophilic switching response

Maria Laura Alfieri

Department of Chemical Sciences, University of Naples Federico II, via Cintia 4, 80126-Naples, Italy
E-mail: marialaura.alfieri@unina.it

In recent years cyanine dyes, featuring peculiar chromophoric and fluorescence properties, outstanding biocompatibility and low toxicity to living systems, have largely been exploited as biological reporters and in other technological applications. In this frame, inspired by $\Delta^{2,2'}$-bibenzothiazine photochromic and acidichromic chromophore of red human hair pigments trichochromes, a new class of cyanine dyes termed trichocyanines was designed in which a highly tunable cyanine-type chromophore was implemented using the benzothiazine nitrogen as the acceptor moiety at high basicity allowing for a marked bathochromic shift even at slightly acidic pHs. Starting from this background, new red hair-inspired 1,4-benzothiazine-based scaffolds are disclosed herein, built upon a modular D-π-A architecture *via* condensation of the easily accessible 3-phenyl-2*H*-1,4-benzothiazine with indole-3-carboxaldehyde [1] or glyoxal [2]. The cyanines thus obtained were characterized as 2*Z*-((1H-indol-3-yl)methylene)-3-phenyl-2*H*-1,4-benzothiazine) (**1**) and 2*Z*,2'*Z*-(1,2-ethanediylidene)bis(3-phenyl-2*H*-1,4-benzothiazine) (**2**) respectively, by complete spectral analysis. In both cases, a reversible acidichromic behaviour with a marked bathochromic shift upon acidification, was observed on various fabrics, paper, polylactic acid films or alginate hydrogels as well as on thin films of the cyanine exposed to acid/basic vapors and proved reversible over several cycles [1,2].

Noteworthy, the acidichromic behavior of cyanine **2** was associated to a remarkable hydrophobic-to-hydrophilic switch, that was probed in a filter permeability experiment [2]. Other applications that are presented for the cyanine **2** include the use as pH sensor paper for visual assessment of pHs below 0 and devices for monitoring food freshness, *e.g* detection of volatile amines generated by fish spoilage or pH changes associated to milk deterioration [2].

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Chiroptical study of the aggregation modes of chiral diketopyrrolo[3,4-*c*]pyrrole dyes in solution and thin films

Gianluigi Albano,[a] Francesco Zinna,[b] Maria Annunziata M. Capozzi,[a] Gennaro Pescitelli,[b] Angela Punzi,[a] Gianluca Maria Farinola,[a] and Lorenzo Di Bari[b]

[a] *Dipartimento di Chimica, Università degli Studi di Bari "Aldo Moro", Via Edoardo Orabona 4, 70126-Bari, Italy*
[b] *Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via Giuseppe Moruzzi 13, 56124-Pisa, Italy*
E-mail: gianluigi.albano@uniba.it

Organic π-conjugated systems have acquired a prominent role in optoelectronics and nanotechnology applications [1]. Their intrinsic physicochemical properties can be finely modulated for the desired application not only by chemical structure modifications, but also by controlling their organization in the solid state at different hierarchal levels, from the first-order supramolecular arrangement to the nano/mesoscale. A crucial aspect is the possibility of different local domains: the same molecular system may undergo competing aggregation pathways during film fabrication, leading to polymorphic aggregated phases (kinetic *vs.* thermodynamic states), each featuring different optoelectronic properties [2].

Instrumental techniques able to characterize aggregation states at multiple hierarchical levels are fundamental for clarifying the structure-property relationships of such systems. Chiroptical spectroscopies, and in particular electronic circular dichroism (ECD), play a central role in the elucidation of the aggregation modes of chiral π-conjugated systems, providing valuable information about the first level of supramolecular organization at the nanometre scale for both solution and solid state, often complementary to that given by microscopic techniques [3].

Here we synthesized a family of structurally related 1,4-diketo-3,6-dithienylpyrrolo[3,4-c]pyrrole (DPP) dyes (**Figure 1**), functionalized with inexpensive chiral groups from natural sources. ECD measurements on these chiral dyes were performed in different conditions of solution aggregation and thin films, in order to provide unique information about their first level of supramolecular organization.

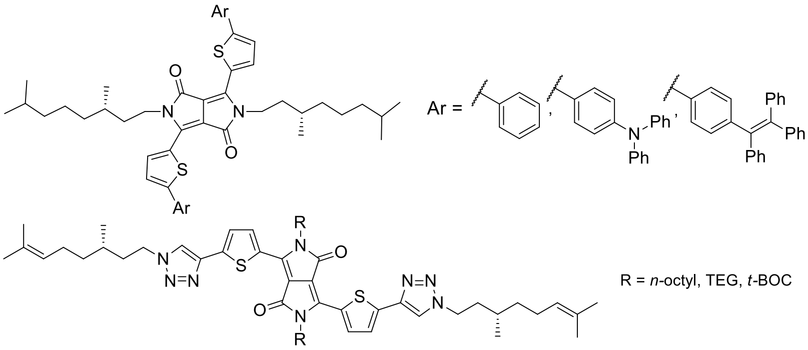

Figure 1: Chemical structures of chiral DPP dyes investigated in this work.

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Polydopamine encapsulation of *Rhodobacter sphaeroides* for energy transduction

Rossella Labarile,[a,b] Danilo Vona,[a] Gabriella Buscemi,[a,b] Maria Varsalona,[a,b]
Matteo Grattieri,[a,b] Gianluca Maria Farinola[a] and Massimo Trotta[b]

[a] Dipartimento di Chimica, Università degli Studi di Bari Aldo Moro, via Orabona 4, 70125-Bari, Italy
[b] CNR-IPCF Institute for Physical-Chemical Processes, via Orabona 4, 70125-Bari, Italy
E-mail: rossella.labarile@uniba.it

In Bio-electrochemical systems, living and metabolically active microorganisms can be used for the sustainable production of energy. The direct electron transfer couples the microbial metabolism with external charge transport and requires the intimate contact between the bacterial cell membrane and the electron acceptor surface.

The membrane of the caroteinodless mutant strain of the photosynthetic purple non sulfur bacterium *Rhodobacter (R.) sphaeroides* R26 was coated with a melanin-like material to improve the interface between electrodes and photosynthetic microorganisms.

Polydopamine (PDA), a bioinspired polymer produced by the self-polymerization of dopamine in mild condition was selected for its biocompatibility and its adhesive properties. The coating, obtained by introducing dopamine monomers into the growth medium of *R. sphaeroides* [1, 2] does not interfere with the proper cell growth and allows the satisfactory electronic communication with the glassy carbon electrodes.

Electrochemical characterization was performed to investigate the electronic behavior of these biohybrids, unveiling that the polymer layer on the bacterial cells does not hinder the diffusion of the mediator and its capability to react at the electrode surface. The effects of dopamine concentration on the light-induced photoresponse of the biohybrid systems will be discussed and compared to bare bacteria.

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Rapid and direct photocatalytic C(sp^3)–H acylation and arylation in flow

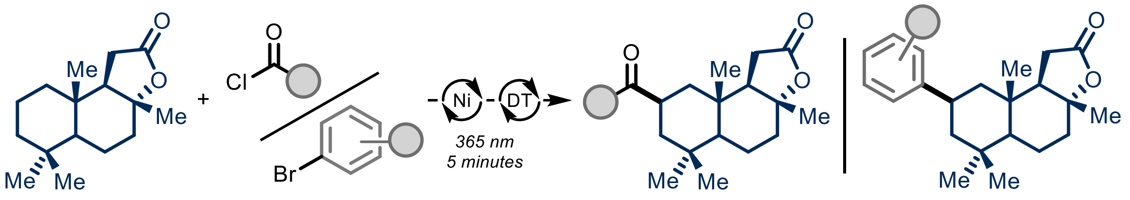
Daniele Mazzarella,[a] Antonio Pulcinella,[a] Loïc Bovy,[a] Rémy Broersma,[b] and
Timothy Noël[a]

[a] Van't Hoff Institute for Molecular Sciences, University of Amsterdam
Science Park 904, 1098 XH, Amsterdam, The Netherlands
[b] Signify Research, High Tech Campus 7, 5656 AE Eindhoven, The Netherlands
E-mail: d.mazzarella@uva.nl

The merger of direct photocatalytic C–H functionalization methods with transition metal catalysis has recently showed tremendous potential for enabling the construction of carbon–carbon and carbon–heteroatom bonds starting from abundant and generally inert substrates [1]. Nonetheless, these methods are still plagued by the requirement of prolonged reaction times, generally 12 to 48 hours, as the C–H abstraction is usually the rate determining step (RDS), leading to difficult-to-scale reaction conditions.

We wondered whether we could expand the breadth of direct photocatalytic C–H functionalization reactions to the nickel-catalyzed direct acylation of unfunctionalized C(sp^3)–H bonds. Moreover, to face the drawback of extended reaction times, we speculated that the use of a continuous-flow environment in combination with high photon flux light sources, would provide an intense and uniform irradiation over the entire reaction mixture. This would substantially accelerate the overall reaction and grant scalable reaction conditions [2].

Herein, we report a photocatalytic procedure that enables the acylation/arylation of unfunctionalized alkyl derivatives in flow [3]. The method exploits the ability of the decatungstate anion to act as a hydrogen atom abstractor and produce nucleophilic carbon-centered radicals that are intercepted by a nickel catalyst to ultimately forge C(sp^3)–C(sp^2) bonds. Owing to the intensified conditions in flow, the reaction time can be reduced from 12-48 hours to only 5-15 minutes. Finally, kinetic measurements highlight how the intensified conditions do not change the reaction mechanism but reliably speed up the overall process.



- Good Selectivity - Fast Process - Easily Scalable

Figure 1: Fast photocatalytic C(sp^3)–H acylation and arylation in flow.

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Effects of substitutional and interstitial nitrogen(N)-doping on the photocatalytic activity of ZnO(100)-ATiO$_2$(101) heterojunction: a DFT study

Ida Ritacco,[a] Lucia Caporaso,[a] and Matteo Farnesi Camellone[b]

[a] Dipartimento di Chimica e Biologia "Adolfo Zambrelli", Università degli Studi di Salerno, Via Giovanni Paolo II 132, 84084, Fisciano (SA), Italia
[b] CNR-IOM Consiglio Nazionale delle Ricerche – Istituto Officina dei Materiali, c/o SISSA, via Bonomea 265, 34136, Trieste (TS), Italia
E-mail: iritacco@unisa.it

Understanding the mechanism of the heterojunctions is fundamental in order to generate systems with high photocatalytic power. To this aim, we have theoretically investigated the effects of substitutional, interstitial and mixed nitrogen(N) doping, both in absence and presence of oxygen vacancies (Ov), on the electronic and structural properties of the wurtzite (ZnO) and anatase (ATiO$_2$) heterojunction by means of Density Functional Theory (DFT). Our structural analysis provides a key information on the nature of the interaction between these two non-polar surfaces, showing that the substitutional N doping is favored in TiO$_2$ region while the interstitial N doping prefers the ZnO portion of the heterojunction and the energy required to generate substitutional (interstitial) N-doped sites decreases(increases) farther from the interfacial zone. In addition, both at low and high N dopants concentrations, the photocatalytic activity of the system increases compared to the undoped heterojunction [1]. In fact, substitutional and interstitial N-doped sites improve the visible light adsorption of the heterojunction due to the introduction of gap states. These states, which act as deep electronic traps, improve the charge separation delaying electron-hole recombination [2]. Furthermore, the N-dopants presence facilitates the Ov formation causing a decrease in the formation energy (E_{FORM}) of the vacancy. Finally, we have shown that the band alignment of the N-doped models, compared to the undoped system, is not affect neither by the N presence nor by the N concentration nor by the presence of oxygen vacancies. Therefore, the N-doped sites are useful in order to generate the higher energy gap states, which presence increases the photocatalytic activity of the system delaying electron-hole recombination. For these reasons, photocatalytic processes can be improved by using the following strategy: N-doped heterojunction with oxygen vacancies.

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Decatungstate-mediated C(sp³)–H heteroarylation via radical-polar crossover in batch and flow

Luca Capaldo,[a] Ting Wan,[a] Gabriele Laudadio,[a] Alexander V. Nyuchev,[b] Juan A. Rincón,[c] Pablo García-Losada,[c] Carlos Mateos,[c] Michael O. Frederick,[d] Manuel Nuño,[e] and Timothy Noël[a]

[a] Van 't Hoff Institute for Molecular Sciences (HIMS), University of Amsterdam, Science Park 904, 1098 XH-Amsterdam, NL
[b] Department of Organic Chemistry, Lobachevsky State University of Nizhny Novgorod, Gagarina Avenue 23, 603950-Nizhny Novgorod, RU
[c] Centro de Investigación Lilly S.A, .Avda. de la Industria 30, 28108-Alcobendas-Madrid, ES
[d] Small Molecule Design and Development, Eli Lilly and Company, 46285-Indianapolis, US
[e] Vapourtec Ltd., Park Farm Business Centre, IP28 6TS-Bury St Edmunds, UK
E-mail: l.capaldo@uva.nl

Photocatalytic hydrogen atom transfer (HAT) is witnessing an ever-growing interest from the synthetic community as a versatile strategy for the late-stage functionalization of C(sp^3)−H bonds. In this activation mode, the excited state of a photocatalyst can be conveniently exploited to cleave directly such strong bonds to obtain nucleophilic C-centered radicals. Amongst the different HAT photocatalysts, the decatungstate anion (DT, $[W_{10}O_{32}]^{4-}$) has proven to be an ideal candidate owing to its unique selectivity, robustness and ease of preparation. Despite several manifolds to forge C−C, C−F, and C−O bonds have been reported [1], only few examples demonstrate the formation of C−N bonds.

To expand the scope of C(sp^3)−N bond forming reactions using HAT photocatalysis, we envisioned that an unprecedented combination of a DT-induced HAT event with an oxidative radical–polar crossover (RPC) step might overcome this challenge [2]. More specifically, we surmised that subsequent oxidation of C-centered radicals generated via HAT would lead to carbocations, which can be conveniently trapped with N-heteroaryl-based nucleophiles, thus establishing the targeted carbon–nitrogen bond.

In this contribution, we show the development of an efficient DT-mediated heteroarylation of C(sp^3)−H bonds through the merger of HAT and RPC (Figure 1), thus demonstrating a new reactivity mode for this widely used HAT photocatalyst [3].

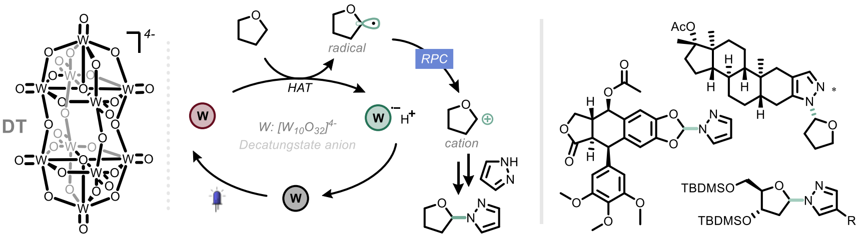

Figure 1

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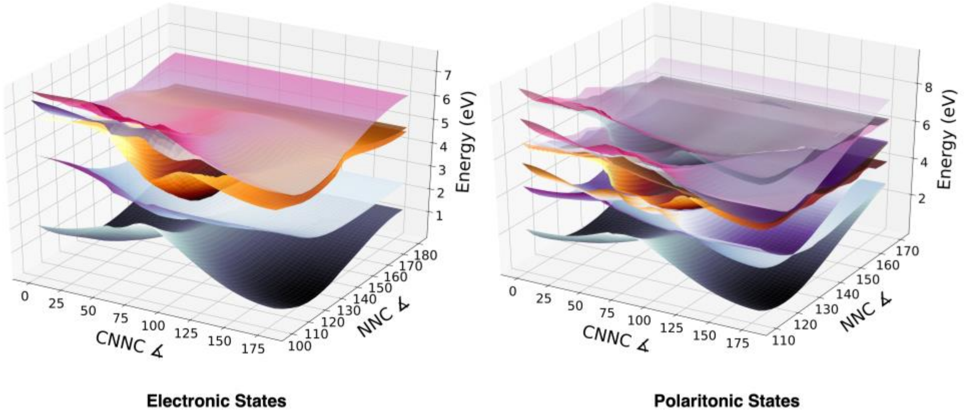
Controlling photochemical reactions through strong light-molecule coupling

Jacopo Fregoni[a,b,1], Giovanni Granucci[c], Maurizio Persico[c] and Stefano Corni[b,d]

[a] *Dipartimento di Scienze Fisiche, Informatiche, Matematiche "FIM", Università degli studi di Modena e Reggio Emilia, 41125-Modena, Italy*
[b] *Istituto di Nanoscienze "S3", Consiglio Nazionale delle Ricerche, 41125-Modena, Italy*
[c] *Dipartimento di Chimica e Chimica Industriale, Università di Pisa, 56124-Pisa, Italy*
[d] *Dipartimento di Scienze Chimiche "DiSC", Università degli studi di Padova, 35131-Padova, Italy*
E-mail: jacopo.fregoni@uam.es

Strong coupling between molecules and light can be achieved in resonant cavities, giving rise to hybrid light-molecule states (polaritons). In these systems, light does not act only as an external driving to trigger photochemical processes, but it is actively involved in modifying photochemical properties. As such, polaritonic chemistry[1] is emerging as a compelling and non-conventional approach to manipulate photochemical reactions. To provide the conceptual tools for interpreting polaritonic chemistry results, we firstly introduce the basic theoretical tools of strong coupling needed to interpret polaritonic chemistry photoreactions. We show examples of quenching of photochemical processes, efficient photoprotection[2] and selective enhancement of photoisomerization reactions[3]. Through our results, we disclose the potential of polaritonic chemistry to control photochemical reactions at the nanoscale.

Figure 1: Electronic (left) and polaritonic (right) potential energy surfaces for the two reactive coordinates (proper dihedral CNNC and piramidalization angle NNC) of the azobenzene molecule..



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[1] Current affiliation: *Departamento de materia condensada "IFIMAC", Universidad Autónoma de Madrid, 28049-Madrid, Spain*

Photocatalytic cross-dehydrogenative coupling of aryl-glycine mediated by mesoporous graphitic carbon nitride (mpg-CN) in green solvents: a route to indole-decorated non proteinogenic amino-acid

Lorenzo Poletti, Graziano Di Carmine, Daniele Ragno, Alessandra Molinari, Alessandro Massi, and Olga Bortolini

Department of Chemical, Pharmaceutical and Agricultural Sciences (DOCPAS), Università degli Studi di Ferrara, Via L. Borsari 46, 44121-Ferrara, Italy
E-mail: lorenzo.poletti@edu.unife.it

In recent years, the mass production of consumer goods has led to an improvement in living conditions, but this caused an excessive growth of waste and contaminants. In order to limit the production of toxic by-products to humans and environment, modern chemistry has revised its position within society, accentuating efforts to develop new methodologies in a more sustainable perspective. The main challenge is to apply in the best way the principles of "green chemistry" while maintaining high production of key compounds in the pharmaceutical, energy and materials sectors [1]. In this spirit, this work leads to the development of a methodology for the synthesis of key intermediates in the pharmaceutical sector [2], which are non-proteinogenic amino acids with indolic scaffold, under eco-sustainable conditions (Figure 1). The use of light as activation energy, which is a clean and renewable energy source, combined with the use of a heterogeneous, metal-free and recyclable photocatalyst such as mesoporous carbon nitride (mpg-CN) brings several benefits to the synthesis of these compounds.

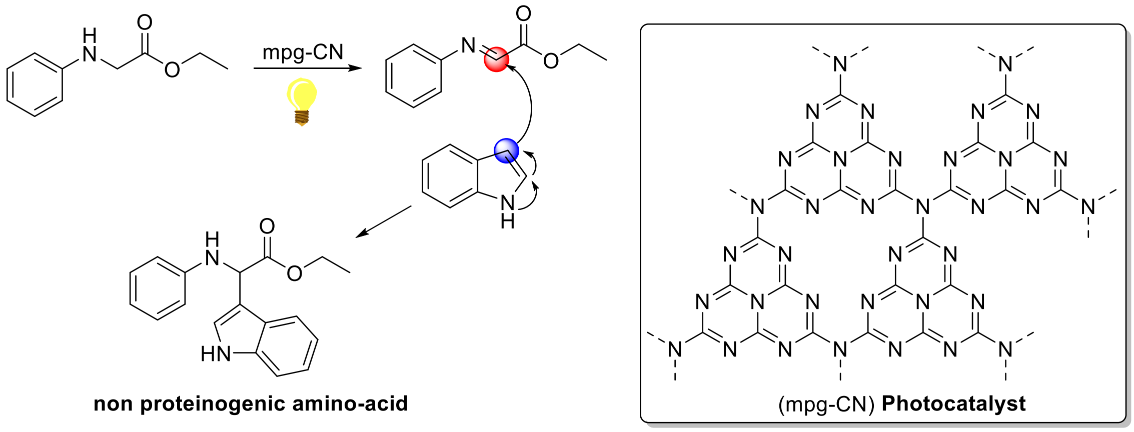

Figure 1: General scheme of the photocatalyzed reaction.

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Cytotoxic effects of 5-Azacytidine on Primary Tumour Cells and Cancer Stem Cells from Oral Squamous Cell Carcinoma: an *in vitro* FTIRM analysis

Valentina Notarstefano,[a] Alessia Belloni,[a] Chiara Pro,[a] Giulia Orilisi,[b] Riccardo Monterubbianesi,[b] Vincenzo Tosco,[b] Hugh J. Byrne,[c] and Elisabetta Giorgini[a]

[a] *Department of Life and Environmental Sciences, Università Politecnica delle Marche, via Brecce Bianche, 60131-Ancona, Italy*
[b] *Department of Clinical Sciences and Stomatology, Università Politecnica delle Marche, via Tronto 10/a, 60126-Ancona, Italy*
[c] *FOCAS Research Institute, Technological University Dublin, 13 Camden Row, Dublin 8, D08 CKP1, Ireland*
E-mail: v.notarstefano@univpm.it

In the present study [1], primary Oral Squamous Cell Carcinoma cells (OSCCs) and Cancer Stem Cells (CSCs) from human biopsies were investigated by an *in vitro* Fourier Transform InfraRed Microscospectroscopy (FTIRM) approach coupled with multivariate analysis, to assess the cytotoxic effects of the hypomethylating agent 5-azacytidine (5-Aza). OSCC is an aggressive oral tumoral lesion, usually diagnosed in advanced stages, causing poor prognosis with low success rates of surgical, radiation and chemotherapy treatments. OSCC may recur after chemotherapy, and patients may develop refractoriness to some drugs: this may be ascribable to the presence of CSCs niches, responsible for cancer growth, chemoresistance and metastasis.

The spectral information from FTIRM was correlated with cytotoxicity tests and image-based cytometry. The spectral multivariate (Fig. 1) and univariate analyses let identify markers that clearly highlighted the demethylation of DNA, followed by the re-activation of transcription and DNA conformational changes, and, finally, to cell death through apoptosis. Moreover, the results suggest a different mechanism of action between OSSC and CSC cells, with a possible enrichment of a drug-resistant subpopulation and a reversion of the demethylating effects of 5-Aza on OSCCs. Since no information on the onset of a chemoresistance to 5-Aza in OSCC has been reported yet, this peculiar aspect will be further investigated by a single-cell Raman Microspectroscopy approach.

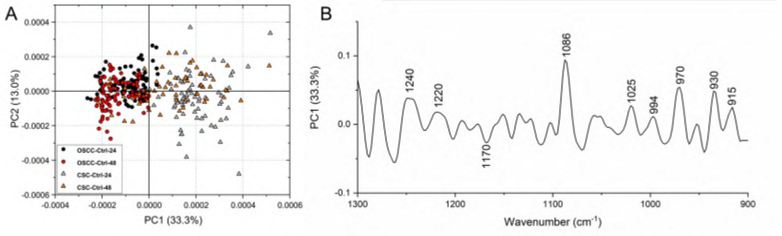

Figure 1: PCA scores plot (A) and corresponding PC1 loading (B) calculated for OSCC and CSC control cells in the 1300-900 cm^{-1} spectral region.

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The thermodynamic stability of miRNAs might influence their biological activity

Gabriele Travagliante,[a] Massimiliano Gaeta,[a] Salvatore Alaimo,[b] Alfredo Ferro,[b] Roberto Purrello,[a] and Alessandro D'Urso[a]

[a] Dipartimento di Scienze Chimiche, Università degli Studi di Catania, Viale Andrea Doria, 6, 95125-Catania, Italia
[b] Dipartimento di Medicina Clinica e Sperimentale, Università degli Studi di Catania, Italia c/o Dipartimento di Matematica e Informatica, Università degli Studi di Catania, Viale Andrea Doria, 6, 95125-Catania, Italia
E-mail: travagliantegab@gmail.com

Mature micro-RNAs (miRNAs) are a class of small non-coding RNAs that regulate gene expression by base-pairing to mRNA targets, causing either target degradation or translational repression, and they are involved in many physiological and pathological processes.

MiRNAs can explore several secondary structures when found in solution as single-stranded molecules and it is hypothesized that such conformations may have biological consequences as this may affect their activity and selectivity toward the targets [1].

To elucidate the possible relation between the thermodynamic stability of miRNAs and their biological activity the attention was focused on miRNA sequences which differ only for few bases but have different targets, to demonstrate that not only the sequence determines the specific function of miRNA.

MiR-337-3p lends itself as the perfect case study to investigate the energy constraints and the thermodynamic profile of miRNA conformations as this microRNA is variant in bats compared to all other mammals. In fact, miR-337-3p in bats and humans differs only by two nucleotides, but it is predicted to regulate a distinct spectrum of gene targets [2].

Indeed, we investigated by Electronic Circular Dichroism (ECD) and ECD-melting experiments the secondary structures and the thermodynamic stability of human and bat miR-337-3p. Our spectroscopic studies revealed that the two sequences can adopt in solution different conformations with distinct stability. Finally, the two miRNA sequences were modified, out of the seed region, to change the stability of the secondary structures adopted. Our findings suggest that miRNAs secondary structures and their thermodynamic stability are related to biological function, in perspective further investigation will be performed to see if higher (or lower) thermodynamic stability of miRNAs can increase (or decrease) the target efficiency.

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In search of P-bearing species in astronomical environments: the reaction between CH_2NH and the CP radical

Silvia Alessandrini,[a] Francesca Tonolo,[a] and Cristina Puzzarini[b]

[a] Scuola Normale Superiore, Piazza dei Cavalieri 7, 56126-Pisa, Italy
[b] Dipartimento di Chimica "G. Ciamician", Alma Mater Studiorum – Università di Bologna, Via Francesco Selmi 2, 40127-Bologna, Italy
E-mail: silvia.alessandrini@sns.it

The interstellar medium (ISM) is nowadays established as a chemically diverse environment, containing several interstellar complex organic molecules (iCOMs) among which, for example, benzonitrile, ethanolamine and, propylene oxide. However, even if new molecules are constantly discovered, several puzzling questions remain on the elemental abundances of the ISM and on the possible reaction pathways for the formation of iCOMs in the cold and sparse conditions of the ISM. In this context, the abundance of P-containing molecules in the ISM is a wide-open topic considering that phosphorus is an important biogenic element, but very few (and simple) P-bearing species have been detected in the ISM like, PH3, CP, CCP, PO and, HCP. Therefore, there is room to hypothesize the presence of exotic P-bearing species in the ISM, such has those obtainable from the reaction between the CP radical and methanimine CH_2NH, both detected in the carbon-rich circumstellar shell IRC+10216. The accurate investigation of the reactive potential energy surface reported in ref. [1] has revealed a reaction mechanism between CH_2NH and CP that can occur --- from an energetic point of view --- even in the harsh conditions of the ISM. The major products of this path are E- and Z-2-phosphanylidyneethan-1-imine and N-(phosphaneylidynemethyl)methanimine as schematically reported in Figure 1. These products are consistent with species already detected in the ISM obtained from similar gas-phase reactions, like CH_2NH+OH or CH_2NH+CN. Since these atypical P-bearing species have not been spectroscopically characterized yet, the corresponding rotational spectroscopic constants have been obtained by means of ad-hoc computational approaches, providing initial parameters for an experimental characterization of the three species that will then allow for a potential observation of these molecules in the ISM.

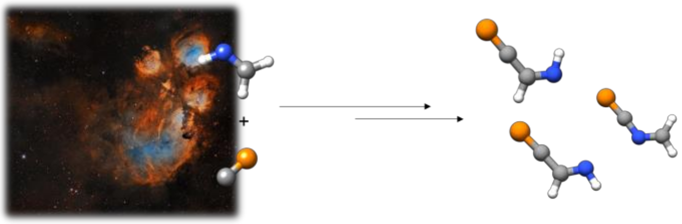

Figure 1: Schematic representation of the reaction CH_2NH+CP occurring in astrochemical conditions.

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The quest for a plausible formation route of formyl cyanide in the Interstellar Medium: a state-of-the-art quantum-chemical and kinetic approach

Francesca Tonolo,[a,b] Jacopo Lupi,[a] Cristina Puzzarini,[b] and Vincenzo Barone[a]

[a] Scuola Normale Superiore, Piazza dei Cavalieri 7, 56126-Pisa, Italy
[b] Department of Chemistry "Giacomo Ciamician", University of Bologna, via F. Selmi 2, 40126-Bologna, Italy
E-mail: francesca.tonolo@sns.it

The extreme conditions of the interstellar medium (ISM) pose strong limitations on the feasibility of chemical reactions in the gas phase, with the formation pathways of the detected molecules being often unknown. Aiming at their disclosure and understanding, new reaction mechanisms need to be investigated from both thermochemical and kinetic points of view. While energetic studies allow for deriving possible accessible pathways, only the determination of accurate reaction rates can confirm which formation routes can indeed occur. These in turn provide useful information in view of rationalizing the molecular abundances observed in interstellar clouds.

This talk will address a suggested and validated effective mechanism for the formation of formyl cyanide (HCOCN) in the ISM [1]. The search for possible precursors was based on relative abundances in the Sagittarius B2 region, where formyl cyanide was detected, and led to the selection of CN, formaldehyde, and acetaldehyde. Guided by state-of-the-art electronic and kinetic computations, an accurate characterization of feasible mechanisms starting from the C-attack of the CN radical on formaldehyde as well as on acetaldehyde, and/or the abstraction of a hydrogen atom of formaldehyde by the CN radical has been carried out. The solution of a master equation including the different reaction channels showed that the very low pressures characterizing the ISM permit to reach the final products, even in the presence of very stable intermediates. Under these conditions, the reaction of formaldehyde with CN is faster than that of acetaldehyde with CN, whereas the situation is reversed at higher pressures (where collision stabilization plays a role).

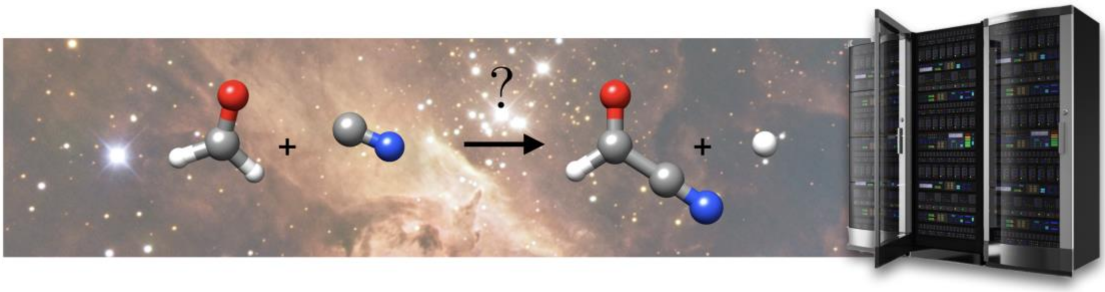

Figure 1

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Thiol-coated gold nanoparticles as supramolecular receptors for NMR chemosensing

Andrea Cesari, Giordano Zanoni, Daniele Rosa-Gastaldo, Federico Rastrelli and Fabrizio Mancin

Dipartimento di Scienze Chimiche, Università di Padova, via Marzolo 1, 35131-Padova, Italy
E-mail: andrea.cesari@unipd.it

Sensing methodologies for the identification and quantification of target analytes in complex mixtures relies on the indirect response of a sensor, produced as a consequence of a modification in its physico-chemical properties. The reliability of output signal must be guaranteed by the selectivity of the sensor and is then quantified by using proper standards compounds, if available. Differently, with NMR-based chemosensing a full spectrum of target analytes is produced and extracted from that of non-bound analytes. Several techniques have been proposed for this purpose, such as diffusion-ordered spectroscopy (DOSY) and magnetization transfer experiments (STD) [1]. In this context, "nanoparticle-assisted NMR chemosensing" combines these techniques with the recognition abilities of monolayer-protected gold nanoparticles (AuNPs). The reduced molecular motion of bulky nanoparticles offers a way to transfer magnetization to the interacting analytes and promotes efficient spin diffusion, crucial in saturation transfer experiments [2]. Moreover, the easiness of preparation of AuNPs capped with the desired thiols pave the way to virtually detected any class of analytes.

In this communication our last results will be reported, aimed to investigate the structure-affinity relationships between analytes/AuNP and their influences on the sensing performances of relevant biomarkers down to μM concentrations.

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Facile purification method for $CsPbBr_3$ nanocrystals and application in light-emitting diodes

Manuela De Franco,[a,b] Matilde Cirignano,[a,b] Tullio Cavattoni,[b] Sergio Fiorito,[b] Houman J. Bahmani,[b] Mirko Prato,[c] and Francesco Di Stasio [b]

[a] *Dipartimento di Chimica e Chimica Industriale, Università degli Studi di Genova, Via Dodecaneso 31, 16146 Genoa, Italy*
[b] *Photonic Nanomaterials group and* [c] *Materials Characterization Facility, Istituto Italiano di Tecnologia, Via Morego 30, 16163 Genoa, Italy*
E-mail: manuela.defranco@iit.it

Since their discovery in 2015 [1], colloidal all-inorganic lead halide (CsPbX3, where X is the halide X= Cl, Br, I) perovskite nanocrystals (NCs) have been extensively researched as an exciting class of semiconductor materials for optoelectronics. Lead halide perovskite NCs are characterized by remarkable properties such as tunable emission, narrow emission band (full-width-half-maximum, FWHM < 19 nm), and near-unity photoluminescence quantum yield (PLQY), which could lead to highly efficient color-pure devices for application in displays and illumination [2].

Surface chemistry plays a fundamental role to increase functional lifetime and optoelectronic properties. A major challenge is the NCs isolation and purification due to the labile nature of the surface ligands, which combined with the ionic character of the colloidal core, induces instability during the NCs classical washing process [3]. Therefore, a protocol of ligand exchange reaction is employed to replace the native ligands with a new ligand which can stabilize the NCs and increase the optical properties. Nevertheless, the electrical properties of the material as an ensemble in film form are affected by the presence of excesses of organic molecules that can act as an insulator causing electrical stress in the neighbors NCs with the consequent damaging and performances decreasing. Therefore, an additional purification protocol is developed and implemented, that is based on the precipitation of by-products and furthers impurity avoiding any NCs degradation.

The overall devices efficiency, which is indicated by the external quantum efficiency (EQE) increases 4 times after the careful formulation of the purification process where the maximum EQE reached is 8.9%. Furthermore, the LEDs architecture engineering has also been explored in terms of hole transport materials and related thicknesses to obtain enhanced performances.

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Doped ceria systems at non-ambient conditions: effect of T and P on their structural and transport properties

Sara Massardo,[a] Davide Marchelli,[a] Cristina Artini,[a,b] Marcella Pani,[a,c] and Maria Maddalena Carnasciali[a,d]

[a] DCCI, Dipartimento di Chimica e Chimica Industriale, Università degli Studi di Genova, Via Dodecaneso 31, 16146-Genova, Italy
[b] CNR-ICMATE, Via De Marini 6, 16149-Genova, Italy
[c] CNR-SPIN, Corso Perrone 24, 16152-Genova, Italy
[d] INSTM, Genova Research Unit, Via Dodecaneso 31, 16146-Genova, Italy
E-mail: sara.massardo@edu.unige.it

Doped ceria oxides are promising electrolytes for Solid Oxide Fuel and Electrolysis Cells (*SOFCs* and *SOECs*, respectively) that work in the intermediate temperature range. In the present compounds, the insertion of a small amount of trivalent rare earth ions (RE^{3+}) into the fluorite-like (F) structure of pure ceria causes the occurrence of a solid solution in which Ce^{4+} ions are randomly replaced by RE^{3+} ions, and not associated oxygen vacancies are free to move through the lattice, making the $Ce_{1-x}RE_xO_{2-x/2}$ systems good oxygen ions conductors. When the dopant amount increases ($x>x_{max}$), the F-based solid solution is no longer stable and different structural scenarios may occur, mainly depending on the difference in size between the Ce^{4+} and RE^{3+} ions [1]. However, the highest values of ionic conductivity are always reached well below the x_{max} compositional limit, since C phase nanoclusters (where C is the RE_2O_3 typical structure of the smallest lanthanides) that trap oxygen vacancies grow within the F matrix with increasing x, thus affecting the ionic conductivity of the system. In the last few years, our research group undertook a comprehensive study on differently doped ceria systems at non-ambient conditions. In particular, a high-pressure x-ray diffraction study was performed to evaluate the capability of doped ceria oxides to tolerate deformations, and so to evaluate their possible use in portable *SOFCs*, in which they are employed in the form of thin films that experience strain [2]. Moreover, a high temperature study was performed on different doped ceria systems to verify their structural stability at the typical *SOFCs* working temperatures, and μ-Raman spectroscopy resulted to be a technique of choice for the study of the present systems, since it allows to detect the presence of C-phase defect clusters growing in the F matrix even at the nanoscale [3]. To date, our research group is also performing a low temperature μ-Raman study on the present compounds, to increase the resolution of Raman spectra. In fact, previous studies performed at room temperature on these systems, suggested the presence of hardly detectable Raman modes, partially hidden underneath the main signals, which could be revealed by lowering the temperature of the system, thus providing additional structural information on this class of compounds. Comparative results from the analyses performed will be given.

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Interfacial charge transfer process between lead halide perovskite and a novel triphenylamine/phenothiazine-based hole transport material: a first-principles study

Carmen Coppola,[a,b] Adriana Pecoraro,[c] Ana Belén Muñoz-García,[c] Rossella Infantino,[a,d] Riccardo Basosi,[a,b,d] Adalgisa Sinicropi,[a,b,d] and Michele Pavone[e]

[a] *Dipartimento di Biotecnologie, Chimica e Farmacia, Università degli Studi di Siena, 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] *Dipartimento di Fisica "Ettore Pancini", Università degli Studi di Napoli "Federico II", Comp. Univ. Monte Sant'Angelo, Via Cintia 21, 80126-Napoli, Italy*
[d] *Istituto di Chimica dei Composti OrganoMetallici (ICCOM), Consiglio Nazionale delle Ricerche (CNR), Via Madonna del Piano 10, 50019-Sesto Fiorentino, Italy*
[e] *Dipartimento di Scienze Chimiche, Università degli Studi di Napoli "Federico II", Comp. Univ. Monte Sant'Angelo, Via Cintia 21, 80126-Napoli, Italy*
E-mail: carmen.coppola@student.unisi.it

The last decade has seen an unprecedented rapid interest in lead halide-based perovskite solar cells (PSCs) within the solar energy community thanks to promising photoconversion efficiencies climbing up to 25% [1]. In spite of their flexibility, ease of fabrication, tunability and lightweight, large-scale PSCs production is still hindered by the lack long-term stability of PSC devices, which is partly related to perovskite/hole transport material (HTM) interface properties [2]. As a matter of fact, the perovskite/HTM structural and electronic features remain not fully understood yet [2], especially for HTMs different from the well-established but labile spiro-OMeTAD.

In this context, this contribution dissects the structural and the electronic properties of a recently designed phenothiazine and triphenylamine-based HTM (HTM1) [3] when interacting with the (001) surface of the parent perovskite $CH_3NH_3PbI_3$ (MAPI) from the computational point of view. To this end, we employ state-of-the-art Density Functional Theory (DFT) methods as implemented in the SIESTA software.

Besides evaluating HTM1/MAPI interaction energies, we compute the driving force for the hole injection from the two possible surface terminations of MAPI (001), i.e. the PbI_2- and the MAI-terminations.

The present study provides new insights into the charge transfer process involving triphenylamine-based molecules, a crucial aspect to design more efficient HTMs and, hence, to improve PSC performances in the near future.

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Carbon nanostructures decorated with Cerium Oxide as multi-functional electrocatalysts for CO_2 conversion

Miriam Moro,[a] Giovanni Valenti,[a] Tiziano Montini,[b] Lucia Nasi,[c] Michele Melchionna,[b] Giovanni Bertoni,[c] Marcella Bonchio,[d] Paolo Fornasiero,[b] Francesco Paolucci [a] and Maurizio Prato [b]

[a] Dep. of Chemistry "Giacomo Ciamician", University of Bologna, Via Selmi 2, 40126-Bologna, Italy
[b] University of Trieste, Dep. of Chemical Science, Center of Excellence of Nanostructured Material (CENMAT), Trieste, Italy
[c] CNR-IMEM Institute, Parco area delle Scienze 37/A, 43124-Parma, Italy
[d] University of Padova, Via F. Marzolo 1, 35131-Padova, Italy
E-mail: miriam.moro2@unibo.it

The electrocatalytic reduction of CO_2 is a captivating strategy for the conversion of CO_2 into useful fuels. The design of new electrocatalysts that reduce CO_2 in a selective and efficient fashion is a key step for future exploitation of this technology. Here we present how the combination of different building blocks in a single nanostructure might be a good strategy to achieve a good selectivity in the CO_2 reduction process.

Combining the unique physico-chemical properties of functionalized nanomaterials (such as carbon nanotubes and carbon nanohorns) and nanocrystalline cerium dioxide (CeO_2) we revealed faradaic efficiency for formic acid production as high as 55% at an overpotential as low as 0.02V in acid solutions. These performances have been possible by the formation of partially reduced ceria ($Ce^{4+/3+}O_{2-x}$) responsible of an increased CO_2 adsorption and a more efficient electron transfer at the surface [1]. In the nanocomposite, the carbon nanostructures are used as support and they have a fundamental role in to counteracting the insulating effect of oxide nanoparticles and promoting the generation of Ce^{3+} sites [2]. In particular, the nanohorns have a unique conical geometric, where the nano-tips terminals act as "electron collector", increasing the charge mobility [3]. We demonstrated that the interconnections between various components are fundamental for the efficient CO_2 reduction to formic acid and opens new possibilities in the design of optimized electrocatalytic materials.

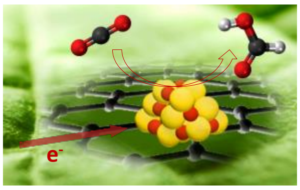

Figure 1: Schematic CO_2 reduction into formic acid on MWCNT@CeO_2

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Trivalent metal-EDTA ionic liquids: a novel approach for redox flow battery electrolytes

Luca Guglielmero,[a,b] Angelica Mero,[a] Andrea Mezzetta,[a] Felicia D'Andrea,[a]
Christian Silvio Pomelli,[a] and Lorenzo Guazzelli[a]

[a] Dipartimento di Farmacia, Università di Pisa, Via Bonanno 6, 56126-Pisa, Italia
[b] Dipartimento di Ingegneria dell'Energia, dei Sistemi, del Territorio e delle Costruzioni,
Università di Pisa, Largo L. Lazzarino, 56122-Pisa, Italia
E-mail: luca.guglielmero@gmail.com

Ethylenediaminetetracetic 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 and offers interesting perspectives from an electrochemical point of view and as innovative electrolytes for redox flow batteries [1,2].

In this context, a new simple and highly performing synthetic approach 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 [3] has been proposed and successfully tested. The complementary solubility characteristics imparted by the [BMIM] and the [TOMP] cations made possible a first investigation of the influence of solvent environments on metal-EDTA complexes redox behavior [3]. The excellent solubilities shown by both [BMIM] and [TOMP] ILs series, in aqueous and non-aqueous environment respectively, in conjunction with their good electrochemical properties, suggest this new class of redox active ILs as promising electrolytes for both water- and organic solvent-based redox flow batteries [3].

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WO_3-$BiVO_4$ photoanodes: influence of the nanostructuring of the WO_3 underlayer

Chiara Nomellini, Annalisa Polo, Maria Vittoria Dozzi, and Elena Selli

Department of Chemistry, Università degli Studi di Milano, Via Golgi 19, 20133-Milano, Italy
E-mail: chiara.nomellini@unimi.it

Given the abundance of water and the inexhaustibility of solar irradiation, the possibility to produce hydrogen through photoelectrochemical (PEC) water splitting is a promising choice. Tungsten trioxide (WO_3) and bismuth vanadate ($BiVO_4$) are two of the most studied photocatalysts for the water oxidation reaction. When these two materials are combined, a synergistic effect is obtained, due to the formation of a heterostructure with an extended visible light harvesting capability and an increased separation of the photoproduced charges [1]. Further beneficial effects on the PEC performance of the composite can be achieved by controlling the morphology of the photoelectrodes.

In this work, a nanostructured WO_3 photoanode characterized by a nanoflake-like (NF) morphology has been prepared along with its corresponding heterojunction (WO_3 NF-BV). At the same time, WO_3 and WO_3-$BiVO_4$ electrodes displaying a flat morphology and the same tungsten oxide thickness were also prepared, in order to investigate the effects of WO_3 nanostructuring on the PEC performance of the photoanodes. Incident Photon to Current Efficiency (IPCE) analyses (Fig. 1a) evidence that the flat heterojunction exhibits low PEC efficiency especially below 420 nm, due to the activation of a detrimental recombination path [2]. The nanostructured heterojunction presents instead growing efficiencies in the UV range and overall higher IPCE values also under visible light. As shown in Fig. 1b, the nanostructured photoanode presents a 3-fold higher charge separation efficiency with respect to that of the flat heterojunction.

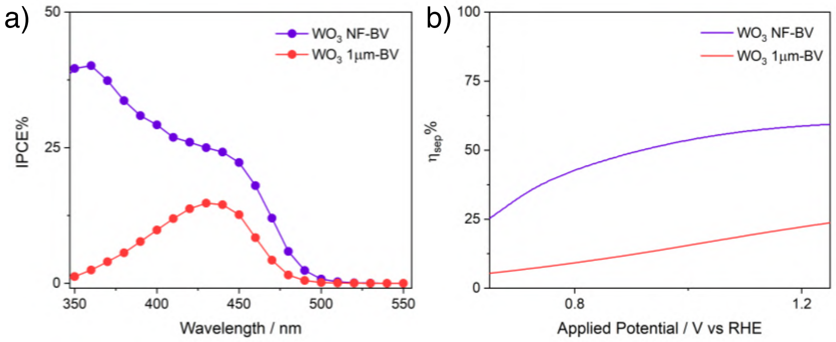

Figure 1: (a) back-side Incident Photon to Current Efficiency (IPCE) at 1.23 V vs RHE in 0.5 M Na_2SO_4 and (b) charge separation efficiency η_{sep} of the nanostructured (WO_3 NF-$BiVO_4$) and flat (WO_3 1μm-$BiVO_4$) heterojunction.

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Copper molybdo-tungstate photoanodes for photoelectrochemical solar energy conversion

Annalisa Polo, Maria Vittoria Dozzi, Ivan Grigioni, and Elena Selli

Department of Chemistry, Università degli Studi di Milano, Via Golgi 19, 20133-Milano, Italy
E-mail: annalisa.polo@unimi.it

$CuWO_4$ has emerged as a promising ternary oxide semiconductor for solar light conversion via photoelectrochemical (PEC) water splitting thanks to its relatively narrow band gap (2.3 eV) and high stability in an alkaline environment. However, its efficient use as a photoanode material is prevented by a severe intrinsic charge recombination which strongly limits the observed PEC performance, as recently demonstrated by a combined photochromic and transient absorption spectroscopy study in the fs–ns timescale [1,2].

To address this fundamental issue, we propose an effective partial Mo^{6+} for W^{6+} substitution strategy resulting in $CuW_{1-x}Mo_xO_4$ electrodes with a high optical transparency, prepared through deposition onto fluorine-doped tin oxide (FTO) glass substrates according to a recently developed time-saving aqueous solution-based technique. A thorough optimization study of both the film thickness in the wide 250-700 nm range and the extent of the Mo^{6+} for W^{6+} substitution allowed us to identify a *ca.* 250 nm thick $CuW_{0.5}Mo_{0.5}O_4$ film with a 1:1 W:Mo molar ratio as best performing electrode material exhibiting a highly improved photoactivity compared to pure $CuWO_4$ (Figure 1a), thanks to both the more extended visible light absorption and the greatly enhanced separation of photogenerated charge carriers.

The optimal properties of the $CuW_{0.5}Mo_{0.5}O_4$ photoactive layer were then exploited by coupling it with $BiVO_4$ and WO_3, two well-established metal oxide photocatalysts, in either a $FTO/CuW_{0.5}Mo_{0.5}O_4/BiVO_4$ or a $FTO/WO_3/CuW_{0.5}Mo_{0.5}O_4/BiVO_4$ heterojunction system, both clearly providing a superior performance compared to the individual components over the entire investigated spectral range (Figure 1b).

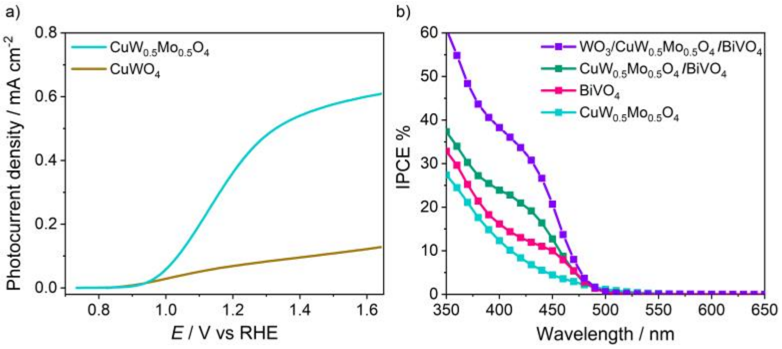

Figure 1: a) Linear sweep voltammetry (LSV) and b) Incident photon to current efficiency (IPCE) at 1.23 V *vs.* RHE, in 0.1 M K_3BO_3 electrolyte solution.

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Catalytic Transfer Hydrogenation of Methyl Levulinate with Alcohols: Batch vs Continuous Gas-Flow Conditions

Riccardo Bacchiocchi,[a] Tommaso Tabanelli,[a] Emilia Paone,[b] Rosario Pietropaolo,[b] Paola Blair Vásquez,[a] Fabrizio Cavani,[a] and Francesco Mauriello[b]

[a] Dipartimento di Chimica Industriale "Toso Montanari", Alma Mater Studiorum - Università di Bologna, Viale Risorgimento 4, I-40136 Bologna, Italy
[b] Dipartimento DICEAM, Università degli Studi di Reggio Calabria "Mediterranea", Loc. Feo di Vito, I-89122 Reggio Calabria, Italy
email: riccardo.bacchiocchi@unibo.it

Levulinic acid (LA) and its esters (e.g. methyl levulinate, ML) are polyfunctional molecules that can be obtained from lignocellulosic biomass. Nowadays, due to their potentials as chemical intermediate the most common strategy for their valorization is the chemical reduction in order to obtain valuable compounds [1]. In particular, LA (or its esters) can be reduced through catalytic transfer hydrogenation (CTH) to γ-valerolactone (GVL) with the Meerwein-Ponndorf-Verley (MPV) mechanism. This approach uses organic molecules (e.g. alcohols) as hydride transfer agent (H-donor), in order to reduce a molecule containing a carbonyl group. An efficient MPV reduction can take place over ZrO_2 due to the presence of both Lewis acid and basic sites of suitable strength over the catalyst's surface [2].

The performances of synthesized ZrO_2 (120 m^2/g) catalyst in the CTH of ML, using MeOH or EtOH as solvents/H-donor molecules under batch conditions, were found to be inefficient in GVL production. Instead, 2-PrOH is by far the most effective in the production of GVL (selectivity higher than 80% at 250°C). Interestingly, at the same conditions (2-PrOH and 250°C), the results obtained by feeding ML under continuous gas-flow conditions over ZrO_2 showed a complete ML conversion for more than 300 min of time-on-stream, promoting the formation of GVL with an excellent yield (80%). Surprisingly, also EtOH shows similar behavior allowing to achieve GVL yield of around 60-70%. In contrast, using MeOH selectively promote the alcoholysis and/or transesterification reactions, with a very low average GVL yield (4%). In conclusions, the performance of ZrO_2 catalyst in the CHT of ML with different alcohols was investigated under both batch and continuous gas-flow conditions. The CTH ability of alcoholic solvents is the main driving force for the transformation of methyl levulinate into GVL, which changes in the order 2-PrOH > EtOH ≫ MeOH. In the liquid phase (batch) using 2-PrOH, a very high selectivity (>80%) to GVL was observed, whereas the continuous gas-flow approach allows us to obtain complete levulinate conversion and very high GVL yield (>70%) with both 2-PrOH and EtOH (or bio-EtOH) as H-donor.

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Photocatalytic reforming of glycerol for hydrogen and chemicals production

Pio Gramazio, Valeriia Maslova, Andrea Fasolini, Stefania Albonetti, and Francesco Basile

Department of Industrial Chemistry "Toso Montanari", Alma Mater Studiorum – University of Bologna, Viale del Risorgimento, 4, 40136 Bologna, Italy
E-mail: pio.gramazio2@unibo.it

In recent years there have been intensive efforts toward the development of novel technologies for the production of H_2 from renewable resources, mainly water and biomass [1]. Among these, glycerol is one of the feasible feedstocks that is produced in large amounts as by-product of transesterification for biodiesel production. Glycerol can be utilized as substrate in the reaction of Photo-reforming, by employing TiO_2 as catalyst and producing H_2 and solar fuels *via* an efficient, technologically-simple, ecologically-benign and potentially low-cost process [2]. In the present work, a study on the photo-reforming of glycerol under base-free ambient and anaerobic conditions was carried out by investigating both the effect of TiO_2 semiconductor synthetic pathway and the noble metal co-catalyst addition. Inverse microemulsion mediated lab-made TiO_2 was compared with commercial TiO_2 powders, namely Cristal ACTiV DT-51 and Degussa P25 [2], [3]. Several characterizations were carried out by XRD, nitrogen physisorption, TEM and UV-vis reflectance analyses. By tuning the reverse microemulsion-based synthesis condition, nanosized TiO_2 particles of anatase and rutile crystalline phase were obtained. The resulted nano-oxides were found to have smaller average crystalline size, higher surface area and narrower band gap than the commercial ones, P25 and DT-51. Lab-made TiO_2 rutile revealed higher H_2 production when bare supports were compared. Moreover, these sample was also used as supports for platinum nanoparticles prepared by two different methods: incipient wetness impregnation and deposition-precipitation. The latter one, showed smaller and more homogeneously distributed metal nanoparticles, compared to the Pt-Nps obtained by the classical impregnation method, resulting in encouraging H_2 evolution. Despite that, employing classical impregnation on rutile lead to the formation of more homogeneous, disperse and smaller Nps, and consequently a better H_2 production was obtained. Nevertheless, P25-based materials outperformed the other types of titania supports in H_2 production. Concerning the liquid products, P25, lab-made anatase and rutile-based catalysts exhibited higher production rates of glycolaldehyde, while DT-51 based ones showed slightly greater productivity to glyceraldehyde than glycolaldehyde.

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Continuous-flow methyl methacrylate synthesis over Gallium-based bifunctional catalysts

Tommaso Tabanelli,[a,b] Jacopo De Maron,[a] Francesco Basile,[a] Nikolaos Dimitratos,[a] Pedro J. Maireles-Torres,[c] Enrique Rodriguez-Castellón,[c] and Fabrizio Cavani[a]

[a] Dipartimento di Chimica Industriale "Toso Montanari", Alma Mater Studiorum Università di Bologna, Viale Risorgimento 4, I-40136 Bologna, Italy
[b] Consortium INSTM, Research Unit of Bologna, Via G. Giusti 9, I-50121 Firenze, Italy
[c] Departamento de Química Inorgánica, Cristalografía y Mineralogía (Unidad Asociada al ICP-CSIC), Universidad de Málaga, Avenida Cervantes 2, E-29071 Málaga, Spain
E-mail: tommaso.tabanelli@unibo.it

Methyl methacrylate (MMA), with a production scale of around 4.8 Mt/year in 2020, is the monomer for polymethyl methacrylate manufacture [1]. The state of art in MMA production is the Alpha process which employs formaldehyde (FA) for the hydroxy-methylation/dehydration of methyl propionate (MP), the latter produced by ethylene hydroformylation in presence of methanol (MeOH). Even if a commercial process is not yet available, MP may be obtained from bio-based 1,2-propanediol [2] and therefore it remains the most promising starting material for a sustainable MMA manufacture. However, the storage of anhydrous FA (known carcinogen) should be avoided in favor of a one-pot approach which consists in its *in-situ* production by MeOH dehydrogenation. Few authors investigated the heterogeneously catalyzed reaction between MeOH and MP in the gas-phase, but most of them recognized the importance of catalysts possessing both basic and redox properties: the former is required to activate MP to nucleophilic attack on FA by abstraction of an acidic α-proton, the latter is needed to promote the dehydrogenation of MeOH. For these reasons, we investigated a series of heterogeneous catalysts ranging from MgO to Ga_2O_3, including two mixed oxides (Mg/Ga/O, with a Mg/Ga atomic ratio of 10 and 20 respectively). Interestingly, the presence of Ga not only greatly enhances catalyst dehydrogenating properties at lower temperatures leading to higher yields in FA and H_2 but also allows to limit the main parasites reaction like ketonization (negligible if compared to the results obtained with pure MgO) and H-transfer reaction. In this way, much higher MMA selectivity and productivity (expressed as Kg/h of MMA divided by Kg of catalyst) were achieved. Finally, combining characterization technics and catalytic results as function of reaction temperature, time factor and reagents molar ratio we were able to determine the reaction scheme and minor/major reaction pathways, and assess structure-activity relationships [3].

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Comparison study between new green coating and benchmark products for the protection of frescoed surfaces

Raffaella Lamuraglia,[a,c] Andrea Campostrini,[a,b] Alessia Artesani,[a]
Elena Ghedini,[c,d] Federica Menegazzo,[c,d] Michela Signoretto,[c,d] and Arianna Traviglia [a]

[a] Center for Cultural Heritage Technology, Istituto Italiano di Tecnologia, Via della Libertà, 12, 30175 - Marghera (VE), Italy;
[b] Dipartimento di Chimica "Giacomo Ciamician", Alma Mater Studiorum Università di Bologna, Via F. Selmi 2, 40126 - Bologna, Italy;
[c] Dipartimento di Scienze Molecolari e Nanosistemi, Università Ca' Foscari Venezia, via Torino 155, 30170 - Venezia Mestre, Italy;
[d] INSTM RUVe, via Torino 155, 30170 - Venezia Mestre, Italy;
E-mail: raffaella.lamuraglia@iit.it

This study reports the assessment of a new green coating for the protection of frescoes exposed outdoor, combining the antimicrobial and antifungal activities of chitosan biopolymer with the bacteriostatic and hydrophobic features of silver nanoparticles (Ag^+ NPs) [1,2]. The protective surface properties of the new formulation were compared with those of commercial products (i.e. Paraloid B72 ® and Proconsol ®) used by restorers for consolidation and protection interventions on wall paintings and stone materials. The coatings have been tested on *ad hoc* prepared mock-ups, investigating chemical and colorimetric stability, hydrophobicity, water vapor permeability and surface morphological variations, before and after artificial ageing. Since the conservation environment is closely related to the conservation conditions of frescoes, the multi-analytical methodology and the ageing protocol (i.e. temperature, light irradiation and rainfall simulation) of this study were developed specifically, starting from the conservation conditions of the archaeological site of Aquileia, considered as a case study. The results of this comparative work demonstrated that the new green coating gives the frescoed surface a good hydrophobicity and permeability to water vapor. These are important characteristics for guaranteeing the breathing of the wall and for avoiding stagnant water, and thus trigger further forms of degradation [3]. Furthermore, compared to the commonly used Paraloid B72 ® and Proconsol ®, the new formulation showed a limited variation of color, it did not make the surface glossy, and a good chemical stability after artificial ageing, as demonstrated by the lack of chemical modifications in the FTIR-ATR spectrum. The developed formulation is promising for the protection of frescoes exposed outdoor and for minimizing the progression of surface degradation. The antimicrobial and antifungal properties of the excipients will be tested in future studies, in order to provide a complete overview on the new formulation.

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Novel potential multitarget compounds for treatment of Type 2 Diabetes

Artasensi A.[a], Angeli A.[b], Lammi C.[a], Supuran C.[b], Vistoli G.[a], and Fumagalli L.[a]

[a] Department of Pharmaceutical Sciences “Pietro Pratesi”, University of Milan, Via Mangiagalli 25, I-20133 Milan, Italy;
[b] Department of Pharmaceutical Sciences “NEUROFARBA”, University of Florence, Via Ugo Schiff 6, 50019 Sesto Fiorentino, Florence, Italy.
E-mail: angelica.artasensi@unimi.it

The term diabetes describes a group of metabolic disorders characterized and identified by the presence of hyperglycemia in the absence of treatment. The heterogeneous etiopathology includes defects in insulin secretion, insulin action, or both, and disturbances of carbohydrate, lipid, and protein metabolism.

These dysregulations certainly cause micro and macro-vascular damages that lead to serious chronic complications such as blindness, renal failure, and diabetes-accelerated atherosclerosis [1]. Since diabetes has a multifactorial nature, it has to be approached not as a single disorder but rather as an interconnected combination of risk factors and complications. Thus, multi-target drugs which could reduce hyperglycemia and concomitantly inhibit the progression of complications may be a valuable therapeutic option for the management of this chronic condition [2].

To find new antidiabetic compounds, repurposing and morphing approaches were applied on WB-4101, a well-known adrenergic ligand.

Computational molecular docking demonstrated that WB-4101 can fit into the pockets of two enzymes that can be exploited in the antidiabetic therapy, namely Dipeptidyl Peptidase IV (DPP IV) and Carbonic Anhydrase II (CA II), even if it lacks some required interactions.

To satisfy these needs, we designed different WB-4101 derivatives, also corroborated by computational investigations. In such new derivatives the amine moiety has been morphed as well as the methoxy groups, and a sulfonamide function has been inserted to fulfill the lacking interactions.

Furthermore, computational and pharmacological investigations were performed also on CA V, a mitochondrial Carbonic Anhydrase isoform involved in glucose metabolism [3].

This work allowed us to extend our knowledge about structural requirements needed to bind DPP IV and CA II/V. Moreover, two newly synthesized derivatives, compound **XI** and **XII** exhibited a satisfactory nanomolar potency towards the targeted enzymes.

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New-generation self-immolative spacers for fast and controlled release of bioactive molecules

Alberto Dal Corso

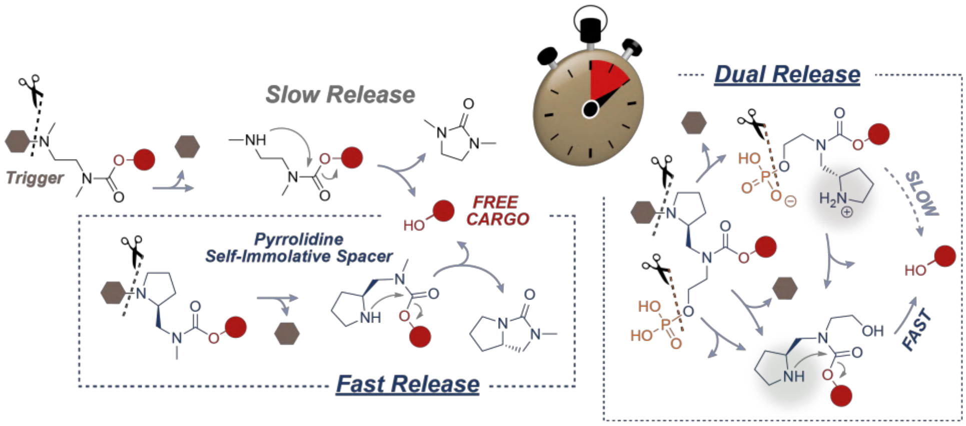
Università Degli Studi Di Milano, Dipartimento di Chimica, via Golgi 19 - 20133 Milano, (I)
E-mail: alberto.dalcorso@unimi.it

Self-immolative (SI) spacers are covalent constructs capable of undergoing a spontaneous disassembly starting from a stable and inactive state, in response to specific stimuli [1].

The growing interest in the generation of stimuli-responsive devices has led to the widespread application of SI spacers in different areas, including synthetic and analytical chemistry, material sciences, and medicinal chemistry, especially in the context of prodrugs, antibody-drug conjugates, and several other drug-release strategies.

We have recently described a novel SI spacer, based on a pyrrolidine scaffold, that is able to release different types of anticancer drugs (possessing either a phenolic or secondary and tertiary hydroxyl groups) through a fast cyclization mechanism involving carbamate cleavage. The high drug release efficiency obtained with this spacer was found to be beneficial for the in vitro cytotoxic activity of protease-sensitive prodrugs, compared with a commonly used spacer of the same class [2].

In light of these promising data, novel derivatives of the pyrrolidine-based SI spacer have been designed and synthesized, either to further accelerate the degradation mechanism or to develop a first-in-class SI spacer for dual-controlled release [3].
These results expand the repertoire of degradation machineries and are instrumental for the future development of highly efficient delivery platforms.



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OR93

Hydroxypyridinones for the treatment of iron overload

Rosita Cappai, Guido Crisponi and Valeria Nurchi

*[a] Dipartimento di Scienze della Vita e dell'Ambiente, Università degli Studi di Cagliari, SS554
Bivio per Sestu, 09042-Monserrato, Italy
E-mail: cappai@unica.it*

In the modern age, the exposure to metal ions is increasing and so their effects on humans. Metal ions can play conflicting roles in the body: essential, toxic, or some essential can be toxic depending on concentration. For instance, iron is an essential element for many metabolic functions in the body but, when in excess, it becomes toxic producing hydroxyl radicals that react quickly with biological molecules, including proteins and DNA. Iron overload in humans can be caused by genetic disorders in the absorption (hemochromatosis) or by blood transfusions (treatment of β-thalassemia).

The use of chelating agents for the treatment of metal overload has been one of the best therapeutic strategies. Over the last decades, deferoxamine (DFO), Deferiprone (DFP) and Deferasirox (DFX) have been approved as Fe^{3+} chelating drugs. Our group have extensively explored the family of 3-hydroxy-4-pyridinones (3,4-HPs), a family of *N*-heterocyclic chelators with a hydroxyl group in *ortho* to a ketone group yielding a five-membered ring chelates where metal ion is coordinated by two oxygen donor atoms. Hexadentate 3,4-HPs have been specifically investigated to fulfill the metal coordination by formation of 1:1 M^{3+}-ligand complexes with improved thermodynamic stability and bio targeting capacity [1].

We present hexadentate (KC18) and tetradentate (KC21) 3,4-HPs containing respectively two and three 3,4-HP moieties *N*-attached to the carboxylic groups of a backbone and their iron complexes in comparison with other 3,4-HPs derivatives previously studied [2].

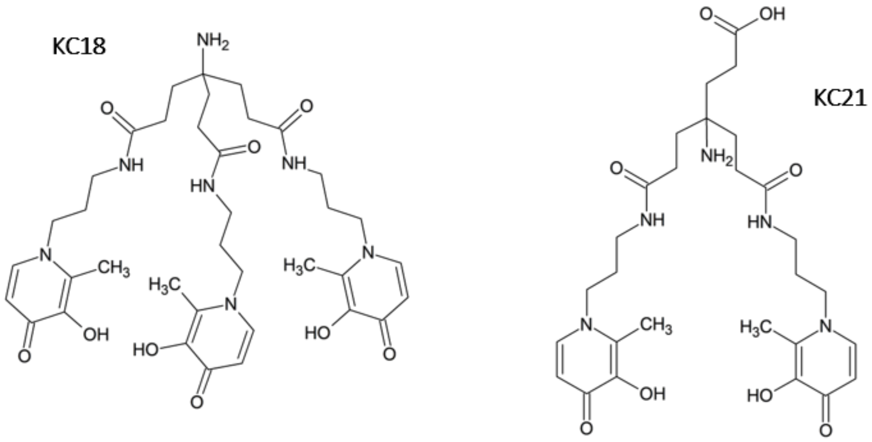

Figure 1: Structures of hexadentate 3,4-HP (KC18) and tetradentate 3,4-HP (KC21)

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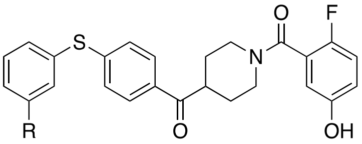
Synthesis and biological evaluation of diaryl-sulfide benzoylpiperidine derivatives as reversible and potent MAGL inhibitors

Giulia Bononi,[a] Giacomo Tonarini,[a] Giulio Poli,[a] Marco Macchia,[a] Flavio Rizzolio,[b] Filippo Minutolo,[a] Carlotta Granchi,[a] and Tiziano Tuccinardi[a]

[a] Department of Pharmacy, University of Pisa, Via Bonanno Pisano 6, 56126-Pisa, Italy
[b] Department of Molecular Sciences and Nanosystems, Ca' Foscari University, 30123-Venezia, Italy
E-mail: giulia.bononi@phd.unipi.it

Monoacylglycerol lipase (MAGL) is a cytosolic serine hydrolase which represents one of the most interesting enzymes of the endocannabinoid system (ECS). MAGL is the major contributor to the hydrolysis of brain 2-arachidonoylglycerol, an endocannabinoid neurotransmitter involved in many pathological processes, such as cancer progression. MAGL is upregulated in aggressive cancer cells, where it promotes tumor aggressiveness, invasiveness and proliferation. So, by inhibiting MAGL it is possible to develop new potential anti-cancer agents. Thus, we aimed to develop new reversible MAGL inhibitors by optimizing the benzoylpiperidine-based MAGL inhibitors previously discovered by my research group. Among this chemical class, three new potent diaryl-sulfide benzoylpiperidine MAGL inhibitors were identified: compounds **1a-c** (Figure 1) [1].



1a-c

a: R = CF_3; **b**: R = Cl; **c**: R = OCF_3.

Figure 1: Structures of compounds **1a-c**.

Compounds **1a-c** proved to be among the most potent reversible MAGL inhibitors (IC_{50} values ranging from 1.26 to 1.86 nM). Moreover, they are selective towards fatty acids amide hydrolase (FAAH), another important enzyme of the ECS. Furthermore, in antiproliferative assays **1a-c** exhibited IC_{50} values ranging from 0.32 to 10 μM in series of cancer cell lines. In conclusion, the newly developed diphenylsulfide benzoylpiperidines **1a-c** are potent, selective and reversible MAGL inhibitors which may be used as perspective anti-cancer agents.

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Towards the identification of new potential anticancer agents: exploration of the chemical space around RC-106

Roberta Listro,[a] Giacomo Rossino,[a] Alessio Malacrida, [b] Mariarosaria Miloso, [b] and Simona Collina[a]

[a] Dipartimento di Scienze del Farmaco, Università degli studi di Pavia, Via Taramelli 12, 27100-Pavia, Italy
[b] Experimental Neurology Unit, Università degli studi di Milano Bicocca, Via Cadore 48, 20900-Monza, Italy
E-mail: roberta.listro01@universitadipavia.it

Cancer is one of the major causes of death in world. Particularly, orphan tumors such as Glioblastoma (GB) and Multiple Myeloma (MM) still represent an important unmet medical need with inadequate treatment options. In the search for new agents acting on multiple pathways and/or innovative targets, our group recently identified RC-106**,** a pan-Sigma Receptor (pan-SR) modulator endowed with proteasome inhibition activity. This compound showed antiproliferative activity towards GB and MM human cell lines and a good pharmacokinetic profile [1].

Starting from this evidence, the chemical space around RC-106 was investigated in an effort to discover new active compounds potentially useful in cancer treatment.

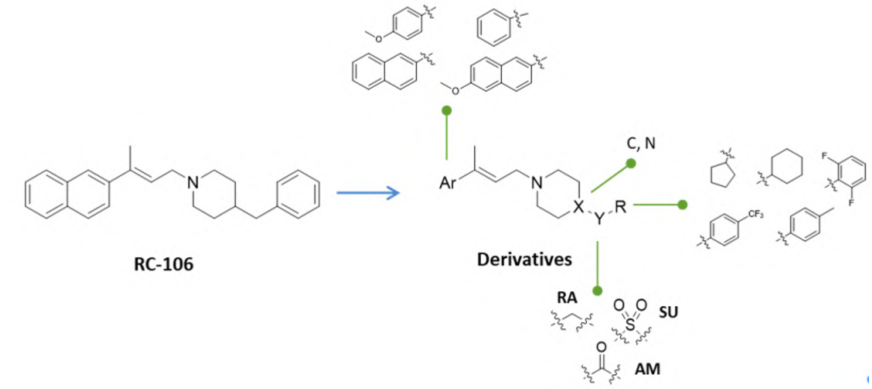

Figure 1: Structure of hit compound RC-106 and its derivatives.

A library of new 65 derivatives was designed, the drug-like properties of each compounds evaluated in silico and lastly synthesized applying a combinatorial approach, through amidation, sulfonilation and reductive amination [2].

The MTT test, trypan blue cell viability and proteasome inhibition assays evidenced that three new derivatives showed higher activity against MM with respect to RC-106 and a good efficacy in inhibiting proteasome. Further studies to investigate on a possible synergic mechanism between SR and proteasome are ongoing.

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Bitopic Sigma 1 Receptor (S1R) modulators: novel tools to study ligand binding and receptor oligomerization at molecular level

Giacomo Rossino,[a] Marta Rui,[a] Pasquale Linciano,[a] Daniela Rossi,[a] Massimo Boiocchi,[b] Marco Peviani,[c] Elena Poggio,[c] Daniela Curti,[c] Dirk Schepmann,[d] Bernhard Wünsch,[d] Mariela González-Avendaño,[e] Ariela Vergara-Jaque,[e] Julio Caballero,[e] and Simona Collina[a]

[a] Department of Drug Sciences, Università degli Studi di Pavia, Via Taramelli 12, 27100 Pavia, Italy
[b] Centro Grandi Strumenti, Università degli Studi di Pavia, via Bassi 21, 27100 Pavia, Italy
[c] Department of Biology and Biotechnology "L. Spallanzani", University of Pavia, Via Ferrata 9 - 27100 Pavia, Italy
[d] Institute of Pharmaceutical and Medicinal Chemistry, University of Münster, Correnstraße 48, 48149 Münster, Germany
[e] Center for Bioinformatics and Molecular Simulation, Universidad de Talca, 1 Poniente, 1141 Talca, Chile
E-mail: giacomo.rossino@unipv.it

Sigma 1 Receptor (S1R) is a ligand-operated chaperone involved in many important biological processes, and for this reason is considered a promising therapeutic target. Despite significant pharmacological investigation over the past decades, S1R remains an enigmatic target with many unanswered questions [1]. Capitalizing our experience in the design and evaluation of S1R modulators, we envisaged a novel series of bitopic ligands (Figure 1) as versatile chemical tools to investigate binding processes, allosteric modulation, and oligomerization mechanisms. These bivalent molecules, which are based on our in-house developed S1R agonist (*R*)-RC-33 [2], have been prepared in enantiopure form and subjected to a preliminary biological evaluation, while *in silico* investigations helped to rationalize the results. Compound **7** was identified as the most promising (K_i = 2.6 ± 0.6 nM) and represents the first bivalent S1R ligand endowed with low nanomolar affinity reported thus far. Its high affinity is possibly due to its ability to stabilize the open conformation of the receptor by binding simultaneously the occluded primary binding site and a peripheral site on the cytosol-exposed surface, as suggested by computational analyses. These findings pave the way to new S1R ligands with enhanced activity and/or selectivity which could also be used as probes for the identification of the elusive allosteric site(s).

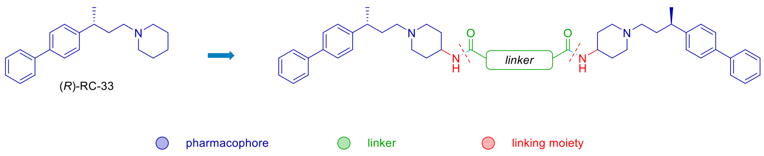

Figure 1: Model compound (*R*)-RC-33 and general structure of bitopic S1R ligands.

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Evidence of destabilization of the human Thymidylate Synthase (hTS) dimeric structure induced by the interface mutations

Ludovica Lopresti,[a] Giusy Tassone,[a] Matteo Santucci, Lorenzo Tagliazucchi, [b] Maria Paola Costi, [b] Cecilia Pozzi, [a] and Stefano Mangani [a]

[a]Dipartimento di Biotecnologie, Chimica e Farmacia, Università degli Studi di Siena, Siena, Italy
[b]Dipartimento di Scienze della Vita, Università degli Studi di Modena e Reggio Emilia, Modena, Italy
E-mail: lopresti4@student.unisi.it

Thymidylate synthase (TS) is an essential enzyme of the folate metabolic pathway. TS is an obligate homodimer that catalyzes the reductive methylation of 2'-deoxyuridine-5'-monophospate (dUMP) to 2'-deoxythymidine-5'-monophospate (dTMP), using N^5,N^{10}-methylenetetrahydrofolate (mTHF) as cofactor. TS provides the only *de novo* source of dTMP required for DNA biosynthesis, thus, its inhibition arrests cell replication and induces apoptosis in rapidly dividing cells, a phenomenon known as "thymineless death" [1]. human TS (hTS) represents a validated target for anticancer chemotherapy and inhibitors targeting the enzyme active site are currently in clinically use, but they have limited efficacy for the onset of drug resistance due to TS overexpression [2]. Indeed, hTS acts as translation repressor of its own mRNA (TS-mRNA). Despite the TS-mRNA binding site on hTS is still uncharacterized, the experimental evidence suggests the implication of the hTS dimer interface in hTS-mRNA recognition and binding [2]. Thus, among the new strategies to block hTS activity without triggering drug resistance mechanisms, there is the disruption of its homodimer quaternary assembly. In this work, we have generated and investigated a set of hTS interface variants aiming to perturb the stability of the homodimer, providing key information for the rational design of interface-targeting inhibitors. Residues in positions 62, 198, and 251, facing themselves on the partner subunit, have been mutated into charged residues, through site direct mutagenesis. The new interface variants have been characterized by circular dichroism (CD) thermal denaturation and kinetic analyses, and X-ray crystallography. The effective destabilization of the variants quaternary structure has been demonstrated by their decreased melting temperature with respect to the wild-type enzyme and by the structural evidence showing a slight opening of the hTS homodimer [3]. The interactions of the new variants with the physiological substrate dUMP and its analogue FdUMP have been further explored. The introduced point mutations result in the loss of enzymatic activity [3]. The identification of effective protein-protein inhibitors is challenging, thus our variants having a more accessible interface represent a useful tool exploitable for mechanistic studies and for the development of innovative interface-targeting compounds.

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Oxylipins as inflammatory biomarkers to understand the evolution and severity of COVID-19

Denise Biagini,[a] Paolo Oliveri,[b] Maria Franzini,[c] Tommaso Lomonaco,[a] Silvia Ghimenti,[a] Andrea Bonini,[a] Federico Vivaldi,[a] Lisa Macera,[c] Laurence Balas,[d] Thierry Durand,[d] Camille Oger,[d] Jean-Marie Galano,[d] Fabrizio Maggi,[e] Alessandro Celi,[f] Aldo Paolicchi,[c] and Fabio Di Francesco[a]

[a] Department of Chemistry and Industrial Chemistry, University of Pisa, Italy; [b] Department of Pharmacy (DIFAR) University of Genova, Italy; [c] Department of Translational Research on New Technologies in Medicine and Surgery, University of Pisa, Italy; [d] Institut des Biomolécules Max Mousseron (IBMM), UMR 5247, University of Montpellier, CNRS, EBNSCM; [e] Department of Medicine and Surgery, University of Insubria, Italy; [f] Department of Surgery, Medicine, Molecular Biology, and Critical Care, University of Pisa, and Respiratory Medicine Unit, Pisa Hospital, Italy

E-mail: denise.biagini@dcci.unipi.it

Over 200 million reported cases and over 4 million deaths have been globally ascribed to the ongoing coronavirus disease (COVID-19) pandemic. About 15% of COVID-19 cases are severe and require hospitalization for oxygen supplementation, and 3–5% of these need admissions to the intensive care unit (ICU) for ventilation support. A critical care triage that prioritizes patients for intensive care, thus rationing limited ICU resources, is strongly required. Immune-inflammatory markers, which come from both cytokine and oxylipin storms, represent potential candidates as physiological prediction scores. Oxylipins are bioactive lipids generated from both ω-3 and ω-6 polyunsaturated fatty acids (PUFAs) through enzymatic (e.g., prostanoids, epoxy and hydroxy fatty acids) and non-enzymatic (e.g., isoprostanes) oxidation reactions. During the course of inflammation, oxylipins switch from pro-inflammatory effectors to both anti-inflammatory and specialized pro-resolving lipid mediators (SPM), which could lower the inflammatory response and even promote its resolution. In the present work, a very powerful analytical platform, based on micro-extraction by packed sorbent (MEPS) coupled to liquid chromatography-tandem mass spectrometry (UHPLC-ESI-MS/MS) [1], was proposed for the determination of 60 plasmatic oxylipins in COVID-19 patients. A chemometric approach was employed to compare inflammatory metabolites coming from both cytokine and oxylipin storms between ICU and non-ICU patients. Unlike cytokines, oxylipins provided such a clear separation between ICU and non-ICU patients, when considered in a multivariate way by principal component analysis (PCA). Moreover, the presence nearby the ICU-cluster of subjects who would have ended up in ICU from 1 to 4 days after the oxylipin quantitation, suggested a potential predictive role of our panel of lipid mediators. A multivariate ROC curve was obtained by application of the UNEQ class-modelling strategy [2], thus showing an area under the curve equal to 0.92. As far as we know, our observational study is the first one to report on an inflammatory response dysfunction discriminating between ICU- and non-ICU patients.

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Theoretical study of Cu(II)-thiosemicarbazone complexes reduction mechanism in cellular environment

Alessandra Gilda Ritacca,[a] Enrico Falcone,[b] Peter Faller,[b] and Emilia Sicilia[a]

[a] Dipartimento di Chimica e Tecnologie Chimiche, Università della Calabria, Rende, 87036, Italy
[b] Institut de Chimie (UMR 7177), Université de Strasbourg-CNRS, 4 rue Blaise Pascal, 67000 Strasbourg, France
E-mail: a.ritacca@unical.it

In the field of anticancer drugs, copper compounds are considered a good alternative to conventional chemotherapeutic metallo-drugs, like cisplatin. In fact, they are less toxic than Pt(II)-complexes because copper is an essential metal ion already present in human body [1]. Currently, an intense pharmacological research is focusing on the therapeutic actions of Cu(II)-thiosemicarbazones (TSCs). They possess antitumor properties via different proposed mechanisms, most of them including the production of reactive oxygen species (ROS). TSCs have not only anticancer activity but are also antimicrobial and antifungal [2]. Such activity is often improved when they are applied in complexes with metal ions. Recently, it has been reported that there is a correlation between the cytotoxicity and the stability of different Cu(II)-TSCs against physiological concentrations of metallothioneins (MT) and glutathione (GSH), two strong cysteine-containing metal ligands, that have the potential to reduce Cu(II) and to deactivate the pharmacological action [3]. To understand such correlation, we studied two representative Cu-TSCs, Cu(II)-Dp44mT and Cu(II)-3AP (figure 1), by using a quantum-chemical approach. In particular, it was experimentally reported that reduction of Cu(II) to Cu(I) and dissociation of Cu(I) from TSC occurs quickly only for Cu(II)-3AP complex, whose catalytic ROS production is therefore stopped, while the reduction of Cu(II)-Dp44mT is slower but dissociation does not occur. Hence, ROS production is not stopped. The aim of the present work was to compare the properties of the Cu(II)-TSCs and to establish the most reliable mechanism of Cu(II) reduction and the eventual GSH assisted Cu(I) release. DFT computational exploration, together with the experimental findings, help to study the different stability of the Cu(II)-TSCs in presence of typical cytosolic concentrations of GSH and to obtain information about the diverse behavior displayed by such complexes towards thiol rich molecules. The results of this investigation could help in rationalizing the correlation of reduction process and anticancer activity of Cu(II)-TSCs, that would help to improve the anticancer activity of these compounds in the future.

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Scaffold repurposing of an in-house chemical library toward the identification of new CK1δ inhibitors

Eleonora Cescon,[a] Giovanni Bolcato,[b] Stephanie Federico,[a] Maicol Bissaro,[b] Alice Valentini,[b] Maria Grazia Ferlin,[b] Giampiero Spalluto,[a] Sturlese Mattia,[b] and Stefano Moro[b]

[a] Dipartimento di Scienze Chimiche e Farmaceutiche, Università degli Studi di Trieste, Via L. Giorgieri 1, 34127, Trieste, Italy
[b] Dipartimento di Scienze del Farmaco, Università degli Studi di Padova, Via Marzolo 5, 35131, Padova, Italy
E-mail: eleonora.cescon@phd.units.it

Protein kinase CK1δ (Casein Kinase 1 isoform δ) has proved to be an important and innovative target since mutations and deregulation of its expression and activity are linked to the development of several neurodegenerative disorders including Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS) [1,2]. Currently, there are no available drugs for this molecular target and reported CK1δ inhibitors rarely bring together potency, selectivity and ability to reach the CNS, thereby encouraging the development of new CK1δ inhibitors.

This study aims to identify new compounds with innovative scaffolds able to interact with the protein kinase by a dual approach *in silico/in vitro*. A docking-based virtual screening (DBVS) was performed on an in-house chemical library that was previously designed and synthesized for other molecular targets. A pharmacophore-driven filtering process applied to all the docking poses led to the identification of two promising candidates that share the pyrrolo[3,2-*f*]quinolinone moiety (**Figure 1**).

These compounds have a novel scaffold in the landscape of CK1δ inhibitors and an activity in the micromolar range. The work can, therefore, be seen in the scaffold repurposing logic and the selected molecules are a promising starting point to develop new potent CK1δ inhibitors [3].

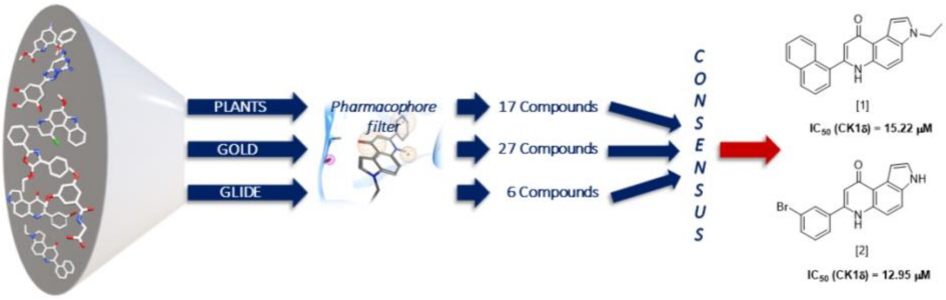

Figure 1: Workflow for hit compound identification trough docking-based virtual screening and pharmacophore filter. Selected compounds were tested on CK1δ with biochemical assays and showed an activity in the micromolar range.

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Unrevealing the antimicrobial properties of calcitermin and its peptide derivatives

Denise Bellotti,[a] Magdalena Rowińska-Żyrek,[b] and Maurizio Remelli[a]

[a] Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, via L. Borsari 46, 44121-Ferrara, Italy
[b] Faculty of Chemistry, University of Wrocław, ul. F. Joliot-Curie 14, 50383-Wrocław, Poland
E-mail: blldns@unife.it

Thanks to the broad spectrum of activity and scarce attitude to induce antimicrobial resistance, antimicrobial peptides (AMPs) represent a rational chance to overcome the current drug-resistance crisis. Among several uncharacterized molecules that contribute to the overall antimicrobial activity of human nasal fluid, a 15-residue antimicrobial peptide named calcitermin (VAIALKAAHYHTHKE) has been identified [1].

Calcitermin contains a metal-binding domain with three alternated histidine residues (His9, His11 and His13) and the free terminal amino and carboxyl groups. Based on our preliminary studies, it exhibits an improved microbicidal activity when Zn^{2+} or Cu^{2+} ions are present in the culture medium. Additionally, calcitermin His-to-Ala mutants – where each histidine residue is replaced with one alanine – have different metal coordination modes, resulting in significant changes of the antimicrobial properties [2].

These promising results prompted us to focus on calcitermin derivatives where the peptide structure is modified in order to confer higher proteolytic stability. The first task of this work consists of a careful evaluation of the enzymatic stability of native calcitermin in human plasma. Afterwards, C- and/or N- terminal modifications have been introduced to possibly obtain calcitermin derivatives resistant to proteases [3]. Changes in the peptide backbone, and in particular the N-terminus protection, can affect the calcitermin metal-binding behaviour and therefore further investigations on the metal interaction with the synthesized protected peptides have been performed, in order to connect the antimicrobial activity of calcitermin with the complex-formation ability. The characterization of metal complexes has been performed by means of several techniques, including potentiometry, high-resolution mass spectrometry, NMR, UV-Vis, circular dichroism and EPR. The obtained results will allow us to propose and design new therapeutic antimicrobial strategies based on calcitermin derivatives and their metal complexes.

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Glycerol carbonate as alkylating agent: an innovative way to benzodioxanes

Gabriele Galletti,[a] Tommaso Tabanelli,[a,b] Carlo Giliberti,[a] Rita Mazzoni,[a]
Raffaele Cucciniello,[c] and Fabrizio Cavani[a]

[a] Dipartimento di Chimica Industriale "Toso Montanari", Università di Bologna, Viale Risorgimento 4, 40136-Bologna, Italy
[b] Consortium INSTM, Research Unit of Bologna, Via G. Giusti 9, I-50121 Firenze, Italy
[c] Dipartimento di Chimica e Biologia "Adolfo Zambelli", Università degli Studi di Salerno, Via Giovanni Paolo II 132, 84084-Fisciano (SA), Italy
E-mail: gabriele.galletti5@unibo.it

Organic carbonates are a promising class of molecules which feature several interesting characteristics in terms of reactivity, biodegradability and safety, and find applications in many different fields. In this framework, glycerol carbonate (GlyC) comes out as a noteworthy compound, displaying a good solvency, low toxicity and versatile reactivity given by the presence of both a free hydroxyl group and a cyclic carbonate moiety [1].

Recently, our group has investigated the effectiveness of GlyC as alkylating agent in the reaction with aromatic molecules, such as catechol, finding out a peculiar reaction mechanism which brought, in basic catalysis, to the production of 2-hydroxymethyl-1,4-benzodioxane (HMB). This molecule is a key intermediate for several APIs such as antidepressant (e.g. Doxasozin), antihypertensive and antithrombic drugs. In the synthesis we reported (Figure 1), a slight excess of GlyC is reacted with catechol in the presence of a basic catalyst (both homogeneous and heterogeneous catalysts were proven to be effective) in solventless conditions, and it is possible to obtain HMB with high yields in relatively short times. Interestingly, the main side product obtained is the HMB isomer with the 7 terms heterocyclic ring, an intermediate for the synthesis of calone analogues, involved in the production of fragrances [2].

Considering the application of HMB in the pharmaceutical field, a reaction protocol focused on the stereoselective synthesis of this product has also been investigated.

Finally, the study has been extended to substituted catechols, like 4-methylcatechol.

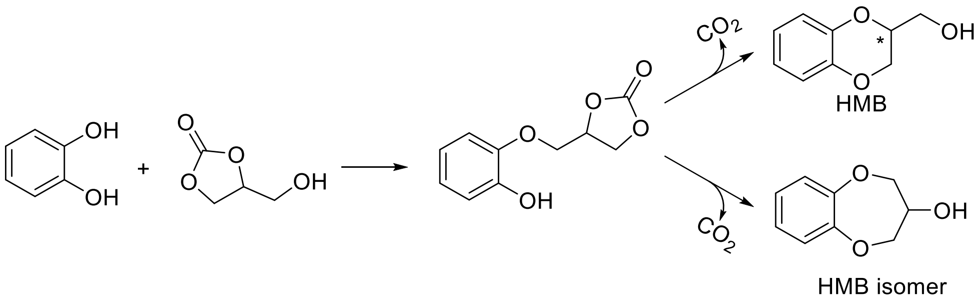

Figure 1: Reaction between catechol and GlyC.

[1] P. P. Pescarmona, *Current Opinion in Green and Sustainable Chemistry,* **29** (2021) art. no. 100457.
[2] T. Tabanelli, C. Giliberti, R. Mazzoni, R. Cucciniello, and F. Cavani, *Green Chem.* **21** (2019) 329-338.

Renewable polymers: conversion, synthesis, applications

Fabrizio Olivito, Vincenzo Algieri, Paola Costanzo, Antonio Jiritano, Matteo Antonio Tallarida, Loredana Maiuolo, and Antonio De Nino

Department of Chemistry and Chemical Technologies, University of Calabria, 87100-Rende (CS), Italy
E-mail: fabrizio.olivito@unical.it

In recent years there has been a growing interest in the conversion, synthesis and applications of renewable chemicals and materials. Polymers represent a class of compounds with a continuous growth of production and applicability that expands in different sectors. They may be of natural or synthetic origin, but today many efforts are being made to substitute fossil or synthetic reagents with renewable starting materials [1]. Biomass derived compounds represent high value platform chemicals for industrial or chemical purposes. Cellulose is one of the most exploited natural polymers. The hydrolysis is the common way for its conversion to obtain bio-based materials. Polyurethanes are a class of synthetic polymer that have been studied and employed from decades with applications that fall back into everyday life [2]. Catalysis can be conducted in a more sustainable approach respect to the classic methodologies. Cellulose-derived polyols have a large applicability for the production of new bio-based polyurethanes [3]. Bio-based polymers and composites represent the materials of the new era respecting the environment for a sustainable world (Figure 1).

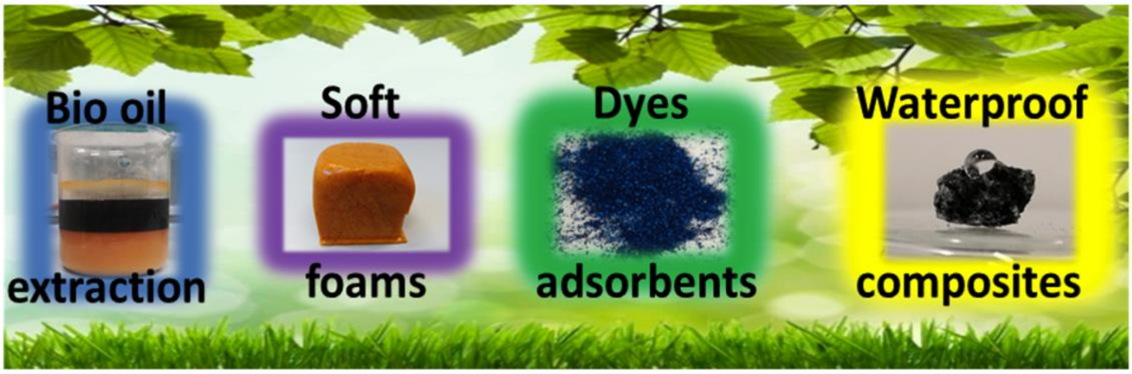

Figure 1: Some examples of renewable materials.

[1] I. Romeo, F. Olivito, A. Tursi, V. Algieri, A. Beneduci, G. Chidichimo, L. Maiuolo, E. Sicilia, and A. De Nino, *RSC Adv.* **10** (2020), 34738-34751.
[2] A. De Nino, F. Olivito, V. Algieri, P. Costanzo, A. Jiritano, M.A. Tallarida, and L. Maiuolo. *Toxics*. **9** (2021), 186-101.
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Deep eutectic solvents (DESs): a green approach for C-C bond reactions

Costanza Papucci,[a] Massimo Calamante,[a] Lorenzo Zani,[a] Gianna Reginato,[a] Alessandro Mordini[a]

[a] CNR-ICCOM Via Madonna del Piano 10, 50019, Sesto Fiorentino, Italy
E-mail: costanza.papucci@iccom.cnr.it

Deep eutectic solvents (DESs) are emerging green solvents for the most common organic reactions. DESs are two or more phase-immiscible solid mixtures, with a lower melting point than the melting point of its single pure components [1].

C-C bond construction is a central and ubiquitous issue for organic chemistry.

Cross coupling reactions are commonly employed as efficient and useful organocatalyzed reactions for the formation of new C-C bond [2]. In particular, recently, C-H activation and C-C oxidative coupling, which not involved organometallic reactants, are the new subject of numerous recent studies in organic chemistry for their more ecofriendly approach [3].

The modern challenge is to match this ecofriendly approach with the employment of more sustainable reaction media. Our challenge was examined new possible application of DES for alternative synthetic strategies, not yet investigated.

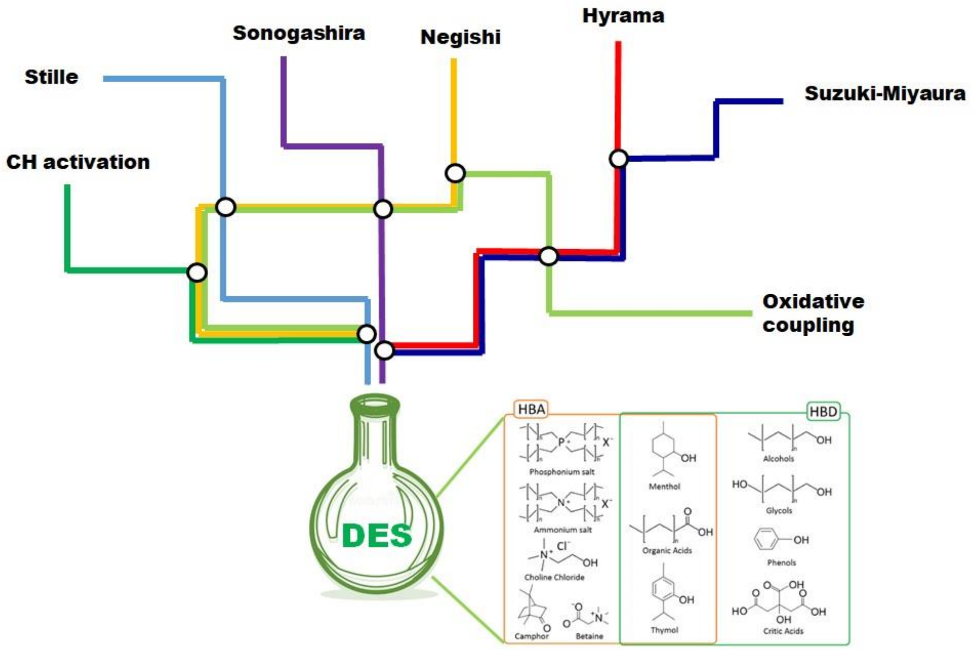


Figure 1: Common cross coupling reactions employable in DESs.

[1] A.P. Abbott, G. Capper, D.L. Davies, R.K. Rasheed, V. Tambyrajah, *Chem. Commun.*, **2003**, 70-71.
[2] L.-C. Campeau, N. Hazari, *Organometallics*, **2019**, *38*, 3.35.
[3] T. Tian, Z. Li, C.-J- Li, *Green Chem.*, **2021**, *23*, 6789-6862.

Valorisation of food industry wastes by exploiting green solvents

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] *Dipartimento di Farmacia, Università degli Studi di Pisa, via Bonanno Pisano 6, 56126 Pisa, Italy*
E-mail: angelica.mero@phd.unipi.it

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 and circular economy, the full exploitation of biomass food waste and its recycle into a new chain of value via the development of sustainable and green process are of primary importance[1],[2]. In this study, green solvents such as natural deep eutectic solvents (NADESs) and bio based-ionic liquids (bio-ILs) have been employed for the valorization of different food industry wastes (i.e. chestnut shell, cherry pomaces). More in details, choline chloride, betaine or L-proline-based DESs 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 HPLC analyses and the polyphenols content was assessed by colorimetric assays. Then, cholinium glycinate bio-IL has been successfully employed for the fractionation of the lignocellulosic residue obtained after polyphenols extraction. 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 thermal gravimetric 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.

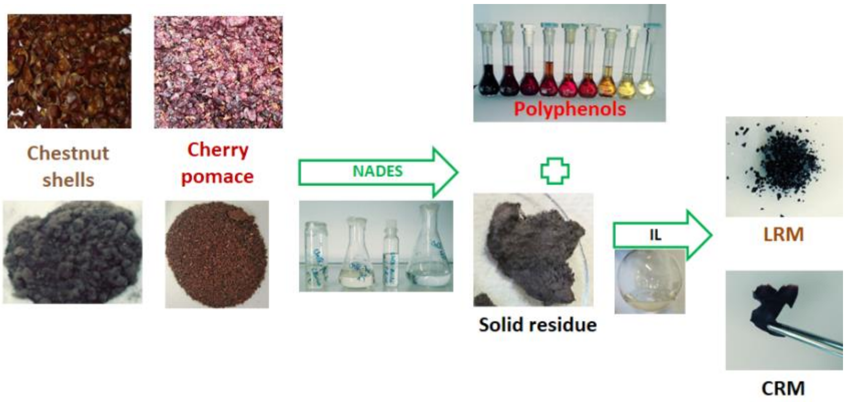


Figure 1: Valorisation process of chestnut shells and cherry pomace.

[1] P. Gullón, B. Gullón, A. Romaní, G. Rocchetti, and J. M. Lorenzo, *Trends in Food Science & Technology* **101** (2020), 182-197.
[2] E. S. Morais, A. M. da Costa Lopes, M. G. Freire, C. S. R. Freire, J. A. P. Coutinho, and A. J. D. Silvestre, *Molecules* **25** (2020), 3652.

Flow-based biocatalyzed redox reactions for the synthesis of bioactive compounds

Francesca Annunziata,[a] Martina L. Contente,[b] Raffaella Gandolfi,[a] Paola Conti,[a]
Cecilia Pinna,[b] Andrea Pinto,[b] and Lucia Tamborini[a]

[a] Department of Pharmaceutical Sciences, University of Milan, Via Mangiagalli 25, 20133 Milan, Italy
[b] Department of Food, Environmental and Nutritional Sciences, University of Milan, Via Celoria 2, 20133 Milan, Italy.
E-mail: francesca.annunziata@unimi.it

Biocatalysis and flow chemistry are ideal partners for accessing novel chemical spaces and define efficient and sustainable synthetic tools with high level of intensification [1]. Biocatalytic redox reactions are very attractive because they often occur with high regio- and stereo-selectivity under mild and environmentally friendly conditions. The aim of our work was to develop greener and scalable routes for the synthesis of high value chemicals, using both whole cells and isolated enzymes.

i) Enantioselective reduction of β-ketonitriles: Immobilized whole cells of *Rhodotorula rubra* MIM 147 have been exploited in a fully automated system for the enantioselective synthesis of β-hydroxynitriles starting from β-ketonitriles. We selected a natural deep eutectic solvent (NADES) made by choline chloride/glucose as a co-solvent and as a source of glucose, fundamental for the cofactor regeneration. The optimized protocol allowed the isolation of a key building block for the synthesis of the antidepressant drug duloxetine, *i.e.*, (*S*)-3-hydroxy-3-(thiophen-2-yl)propanenitrile, in 80 minutes of residence time with >90% conversion and >99% e.e. and resulted to be versatile for the enantioselective reduction of different β-ketonitriles.

ii) Oxidation of tyrosol to hydroxytyrosol: Tyrosol (Ty) and hydroxytyrosol (HTy) are valuable dietary phenolic compounds present in olive oil and wine and possess a range of biological effects [2]. The availability of gram amounts of pure Ty, HTy, their metabolites and derivatives is highly appealing for a deep biological evaluation. In this context, we performed the oxidation of easily accessible Ty using a free tyrosinase from *Agaricus bisporus* in presence of oxygen and ascorbic acid. The aqueous flow stream was then extracted in-line with ethyl acetate and the aqueous layer, containing the biocatalyst and the excess of ascorbic acid, was recirculated to improve the overall efficiency in a self-sufficient closed-loop system. Furthermore, an in-line purification for the collection of pure HTy was designed. Then, a bioreactor packed with an immobilized acyltransferase from *Mycobacterium smegmatis* (MsAcT) was used to produce acetate derivatives [3]. With this modular set up, HTy was obtained with an isolated yield of 75%, whereas the acetate metabolites showed yields up to 80% in 10 minutes.

[1] L. Tamborini, P. Fernandes, F. Paradisi, and F. Molinari, *Trends Biotechnol.* **36** (2018), 73-88.
[2] A. Karkovíc Markovíc, J. Toríc, M. Barbaríc, and C. Jakobušíc Brala, *Molecules* **24** (2019), 2001.
[3] M. L. Contente, S. Farris, L. Tamborini, F. Molinari, and F. Paradisi, *Green Chem.* **21** (2019), 3263-3266.

Computational study of the interaction between dicationic ionic liquids based on imidazole and CO_2

Guelber Cardoso Gomes, Claudio Ferdeghini, Lorenzo Guazzelli, and Christian Silvio Pomelli

Dipartimento di Farmacia, Università di Pisa, Via Bonanno Pisano 12, 56126-Pisa, Italy
E-mail: g.cardosogomes@studenti.unipi.it

Ionic liquids (ILs) gain a high relevance in the last decades and have been extensively studied as alternatives solvents due to their properties such as negligible vapor tension, thermal and chemical stability, and the possibility to recycle [1]; A promising application of ILs is for CO_2 capture [2]. In this context, we use the molecular dynamics technic to determine the stability of the IL-based on the two imidazolium rings connected by a xylene spacer with ortho (Figure1a), meta (Figure1b), and para (Figure1c) isomers with bromide, tungstate (Figure1d), and tungstate combined with the CO_2 anions. The program XTB [3] was used for the simulation, a total of 2ns of production was made with a 1fs step and the coordinate was saved every 100fs, with a total of 2000 points.

Using molecular dynamics is found that the system based on WO_4^{2-} anion are more stable than those with the Br^- anion. These calculations demonstrate that the presence of the WO_4^{2-} anion creates strong ionic bonds between the cation and the anion leading to stable ionic pairs. Is also observed that the system with the CO_2 is stable, meanly on the meta system, the CO_2. For this system, is also observed the interaction between the WO_4^{2-} and the cation, however, is also observed that the CO_2 interacts with the tungstate and oxygen atom, this interaction creates a structure with lower energy. This result demonstrates that the system with tungstate presents a stable IL and present interesting interaction with CO_2, which can be a good clue to the functionality of this compound.

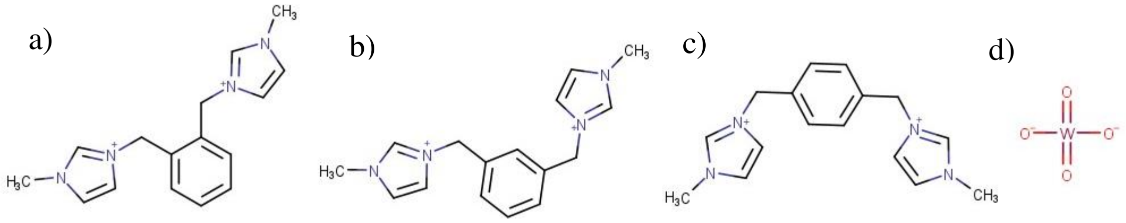


Figure 1: Structure a) orto; b) meta, c) para and d) tungstate anion.

[1] D. D. Patel, and J. M. Lee, *Chem. Rec.* **12** (2012) 329–355.
[2] M. Ramdin, T. W. De Loos, and T. J. H. Vlugt, *Ind. Eng. Chem. Res.* **51** (2012) 8149–8177.
[3] C. Bannwarth, E. Caldeweyher, S. Ehlert, A. Hansen, P. Pracht, J. Seibert, S. Spicher, and S. Grimme, *Wiley Interdiscip. Rev. Comput. Mol. Sci.* **11** (2021) 1–49.

Linear dicationic ionic liquids: synthesis and thermal study

Claudio Ferdeghini, Andrea Mezzetta, Christian Silvio Pomelli, and Lorenzo Guazzelli

Dipartimento di Farmacia, Università degli studi di Pisa, Via Bonanno Pisano 6, 56126, Italy
E-mail: c.ferdeghini@phd.unipi.it

Because of their properties, ionic liquids have captured the interest of several researches as a possible solution toward the development of more sustainable chemicals and processes [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, due to their rather recent discovery, DILs have been less studied than their monocationic counterparts, and potential, scope and field of application still need to be defined.

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 reaction is the main route for preparing ILs and DILs and has been already used to create a wide variety of structures. In the DILs case, several features can be changed such as the cationic moiety and the type of anion, but also the internal spacer which can be appropriately selected between simple alkyl chains or (poly)functionalized ones.

In the present work, various families of DILs with different length of the spacer and different cationic head groups have been synthesized (Figure 1). The thermal stability and thermal behavior of these compounds have been investigated to ascertain the range of possible applications. Interestingly, differences in their degradation pathways as a function of the length of the internal linker have been observed.

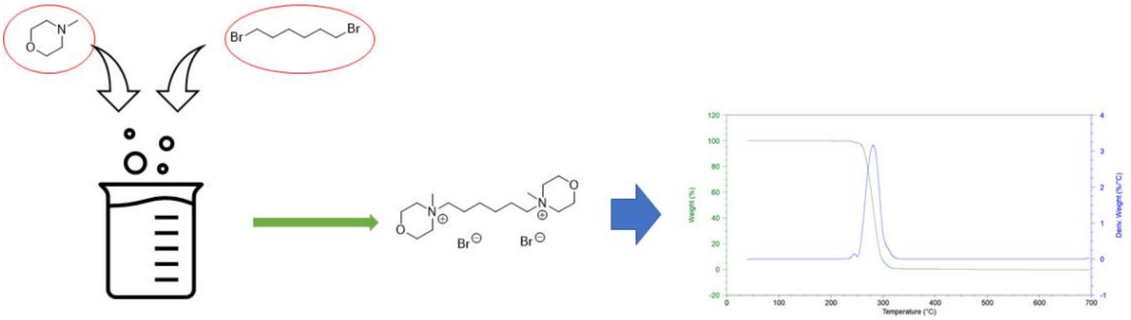


Figure 1: Synthesis and thermal stability study of DILs.

[1] G. Cevasco and C. Chiappe, *Green Chem.* **16** (2014) 5 2375-2385.
[2] L. Guglielmero, A. Mezzetta, L. Guazzelli, C. S. Pomelli, F. D'Andrea, and C. Chiappe, *Front. Chem.* **6** (2018) 1-16.

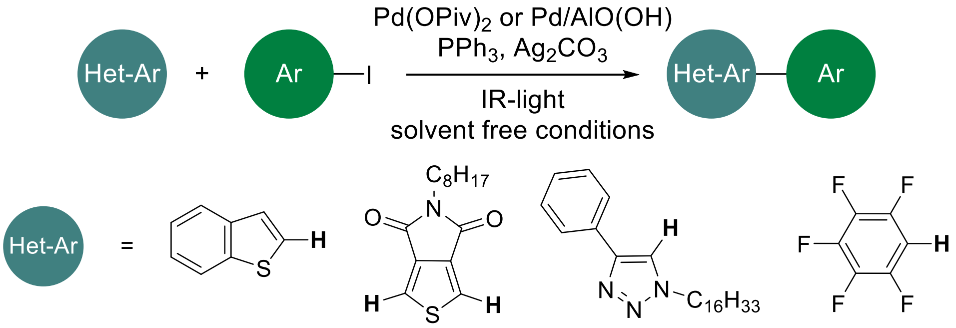
Infrared assisted Pd-catalyzed direct(hetero)arylation in solvent free conditions

Gianfranco Decandia,[a,b] Gianluigi Albano,[a] Nicola Zappimbulso,[a]
Maria Annunziata Macella Capozzi,[a] Angela Punzi,[a] and 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, Dipartimento di Chimica, Via E. Orabona 4, 70126 Bari, Italy*
E-mail: gianfranco.decandia@uniba.it

The direct C-H bond activation is the most convenient choice for the formation of the (hetero)aryl-aryl motif: it eliminates the need of the preliminary preparation of air- and moisture-sensitive, expensive, and toxic organometallic reagents used in other cross couplings reactions [1]. Recently, innovative and more environmentally friendly protocols for direct arylation have been explored: they include the use of more sustainable solvents, such as water, or even the absence of solvent [2].

This study combines the advantages of direct arylation with those of infrared (IR) heating [3], making it possible to achieve high yields in a short time, avoiding the formation of undesired byproducts and making workup easier. In particular, the coupling of different (hetero)aryls with electron-rich and electron-poor aryl iodides has been successfully performed, affording yields as high as 87% in just fifteen minutes reaction.



Scheme 1: General scheme of the direct arylation couplings.

[1] R. D. Kimbrough. *Environ. Health Perspect.* **14** (1976) 51–56.
[2] A. Punzi, N. Zappimbulso; G.M. Farinola. *European J. Org. Chem.* **2020(22)** (2020) 3229–3234.
[3] N. Zappimbulso, M.A.M. Capozzi, A. Porcheddu, G.M. Farinola; A. Punzi. *ChemSusChem* **14** (2021) 1363–1369.

Valorization of chestnut wood fiber as a clean and largely available source of ellagic acid and lignin via a rational and tunable deep eutectic solvent-based processing

Federica Moccia

Department of Chemical Sciences, University of Naples “Federico II”, Via Cintia 4, I-80126 Naples, Italy
E-mail: federica.moccia@unina.it

Deep eutectic solvents (DES) are emerging as efficient, sustainable, and cost effective alternatives to conventional solvents for the recovery of functional compounds from natural sources. We report herein three different DES-based extraction procedures for the recovery of antioxidant molecules from chestnut wood fiber (CWF), one of the main byproducts of the tannin extraction process from wood [1] (Figure 1).

First, a mild protocol was developed using a choline chloride (ChCl)/tartaric acid DES at 50 °C, for 90 min. Ellagic acid (EA) was identified as the only low molecular weight phenolic component of the extract. In other experiments, harsher conditions were explored involving treatment of CWF with ChCl-based DESs at 120 °C for 8 h, which afforded a solid sample characterized by high phenolic content and antioxidant properties, and containing guaiacyl-syringyl lignin along with EA. Based on these results, a sequential two-step DES-based treatment of CWF was eventually designed, allowing to selectively obtain both a EA-enriched and a EA-free, lignin-enriched sample, with an overall 50% w/w of the starting CWF dissolved. In particular, a 2.3% w/w yield of EA was achieved, which is significantly higher than those reported in the case of DES-based processing of other agricultural wastes. The proposed tunable, straightforward, and eco-friendly approach may allow to fully exploit CWF as a green, cheap and easily accessible source of high-value products.

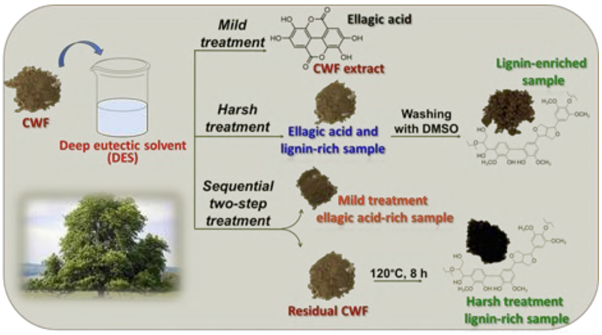


Figure 1: Representation of the DES-based treatment of CWF developed.

[1] L. Panzella, F. Moccia, M. Toscanesi, M. Trifuoggi, S. Giovando, and A. Napolitano, *Antioxidants* ,**8** (2019), E84.

A novel robust and easily regenarable anilato-based 3D MOF used for CO_2 uptake and separation

Noemi Monni,[a,b,c] Eduardo Andres-Garcia,[b] Katia Caamaño,[b] Víctor García-López,[b] Juan Modesto Clemente-Juan,[b] Mónica Giménez-Marqués,[b] Mariangela Oggianu,[a,c] Enzo Cadoni,[a] Guillermo Mínguez Espallargas,[b] Miguel Clemente-León,[b] Eugenio Coronado[b] and Maria Laura Mercuri[a,c]

[a] Dipartimento di Scienze Chimiche e Geologiche, Univeristà degli Studi di Cagliari, SS 554 Bivio per Sestu, 09042-Monserrato, Italy
[b] Instituto de Ciencia Molecular, Universidad de Valencia, Catedratico José Beltran 2, 46980-Paterna, Spain
[c] INSTM, Cagliari Unit, Via Giuseppe Giusti, 9, 50121-Firenze, Italy
E-mail: noemi.monni@unica.it

The development of systems able to capture CO_2 from the atmosphere and/or gas mixtures is of paramount importance both for environmental and industrial applications. In this context, Metal Organic Frameworks (MOFs) are the optimal candidates because of their intrinsic porosity and fine tunability. By combining the properly designed organic linker, 3,6-N-ditriazoyil-2,5-dihydroxy-1,4-benzoquinone (trz_2An), with Co^{II} ions, a novel 3D ultramicroporous MOF with high CO_2 uptake capacity and separation efficiency (CO_2/N_2 and CO_2/CH_4 gas mixtures) was obtained.[1] This material, one of the first examples of a 3D anilato-based MOF containing the trz_2An linker, enables the selective entrance of CO_2, but not of molecules with larger kinetic diameter such as N_2 or CH4, due to its 3D ultramicroporous structure with channels with an affinity for CO_2 molecules. The adsorption study revealed that *i)* the MOF presents a remarkable carbon dioxide uptake, above 20% in weight; *ii)* CO_2 adsorptive separation is successfully performed in CO_2:N_2 and CO_2:CH_4 gas mixtures, exhibiting high selectivity in a large operation range; *iii)* regeneration is easily achieved at mild conditions.

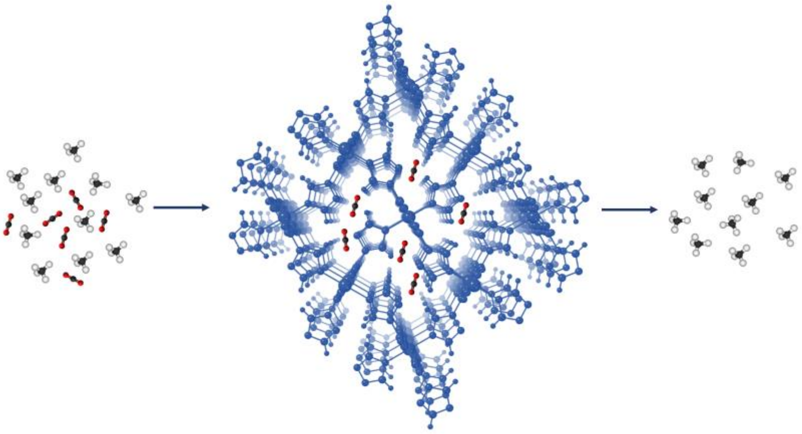


Figure 1: Scheme of gas separation of a CO_2/CH_4 mixture achieved by the use of the novel anilato-based MOF.

[1] N.Monni, E. Andres-Garcia, K. Caamaño, V. García-López, J. M. Clemente-Juan, M. Giménez-Marqués, M. Oggianu, E. Cadoni, G. Mínguez Espallargas, M. Clemente-León, M. L. Mercuri and E. Coronado, submitted to *Journal Mater.Chem. A* (2021)

Silicon-based fluorescent platforms for copper(II) detection in water

Mariangela Oggianu,[a,c] Cristiana Figu,[b] Vito Lippolis,[a] Carla Cannas,[a,c] Claudia Caltagirone,[a] Enzo Cadoni,[a] Maria Laura Mercuri[a,c] and Francesco Quochi[b]

[a] Dipartimento di Chimiche e Geologiche, Università degli Studi di Cagliari, ss 554 Bivio per Sestu, I-09042 Monserrato (CA), Italy
[b] Dipartimento di Fisica, Università degli Studi di Cagliari, Complesso Universitario di Monserrato, I-09042 Monserrato (CA), Italy
[c] INSTM, Cagliari Unit, Via Giuseppe Giusti, 9, Firenze, I-50121, Italy
E-mail: mariangela.oggianu@unica.it

A fundamental study on silicon-based fluorescent platforms for detection of trace metal ions in aqueous environment is herein presented. Fluorescein isothiocyanate (FITC) was covalently linked to APTES (3-aminopropyltriethoysilane)-prefunctionalized silicon substrates *via* thiourea formation to realize silicon-based on-chip devices integrating both recognition and fluorescent units. The obtained hybrid heterostructures exhibited high sensitivity and selectivity towards copper(II), a limit of detection compatible with the recommended upper limits for copper in drinking water, and good reversibility using a standard metal–chelating agent. The fluorophore–analyte interaction mechanism at the basis of the reported fluorescence quenching was also investigated [1].

The herein presented sensing architecture allows for, in principle, tailoring of the selectivity towards other metal ions by proper fluorophore selection, and provides a favorable outlook for integration of fluorescent chemosensors with silicon photonics technology.

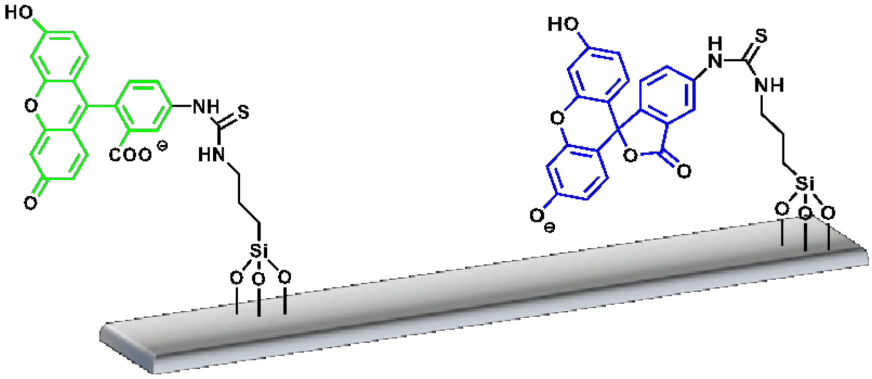


Figure 1: Schematic representation of the fluorescent silicon chips.

[1] Oggianu, M., Figus, C., Ashoka-Sahadevan, S., Monni N., Marongiu, D., Saba, M., Mura, A., Bongiovanni, G., Caltagirone, C., V., Lippolis, V., Cannas, C., E Cadoni, Mercuri, ML. and Quochi, F. *RSC Advances 11(*2021), 15557–15564.

Liposome@PDA microspheres for the removal of methylene blue from aqueous solutions

Anna Maria Maurelli,[a] Vincenzo De Leo,[a] Fabio Lupone, [a] Chiara Ingrosso,[b,c] Angela Agostiano,[a,c] and Lucia Catucci[a]

[a] *Department of Chemistry, University of Bari "Aldo Moro", Via Orabona 4, 70126 Bari, Italy*
[b] *CNR-IPCF, Institute for Physical and Chemical Processes, Bari unit, via Orabona 4, 70126 Bari, Italy*
[c] *National Interuniversity Consortium of Materials Science and Technology (INSTM)*
E-mail: anna.maurelli@uniba.it

Polydopamine (PDA) is a mussel-inspired polymer which arises from the self-polymerization of dopamine hydrochloride (DA) in slightly alkaline conditions, and it has been demonstrated to be an excellent adsorbent material for several kinds of pollutants [1]. We prepared PDA coated liposomes, hereinafter called "Liposome@PDA microspheres", and explored their adsorption capacity in aqueous solutions by using methylene blue (MB) as a model cationic compound for pollutants.

Liposomes were prepared by extrusion method using membranes with a porosity of 200 nm. Then, they were coated with PDA by inducing the self-polymerization of DA in a buffer alkaline aqueous solution and exploiting the template effect induced by the presence of liposomes. TEM and DLS analysis were used to monitor PDA growth over time, while the polymerization yield was evaluated exploiting the decrease of the peak of absorption of the DA at 280 nm. The capability of our systems to remove the MB from the water was then evaluated in terms of adsorption capacity (q_t) [2] changing the process parameters.

Since the considered adsorption process involves mainly the contribution of electrostatic interactions [1], the effect of the pH on the process was investigated. We found that our systems keep the highest adsorption capacity at pH = 8.0. This evidence can be explained considering the change of the charge of the PDA layer at different pH values. ζ-potential measurements show a positive charge of the systems at pH = 3 and a progressively more negative charge with increasing pH values. Fixed the pH values to 8, the effect of the MB and Liposome@PDA concentrations on the q_t was studied.

The adsorption capacities obtained in this study are higher than several ones reported in literature for similar PDA based absorbent materials, with removal efficiencies up to 96%. Moreover, it is possible to sediment the Liposome@PDA microsphere with a centrifuge in less than a minute. This can be useful in the optic of an easy and low-cost remotion of the adsorbent material from the treated water.

Finally, kinetic and thermodynamic studies were conducted. Results show that the process follows a pseudo-second order kinetic model and well fit a Langmuir isotherm model. Moreover, the process seems to be spontaneous and endothermic in the realized experimental conditions

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Photodegradation of ibuprofen using CeO_2 nanostructured materials

Maryam Hmoudah,[a,c] Noemi Gallucci,[a,b] Eugenie Martinez,[d] Martino Di Serio,[a]
Luigi Paduano,[a,b] Giuseppe Vitiello,[b,e] and Vincenzo Russo [a,f]

[a]Department of Chemical Sciences, University of Naples Federico II, Naples, Italy.
[b]CSGI, Center for Colloid and Surface Science, Sesto Fiorentino, Italy.
[c]Department of Chemical Engineering, An-Najah National University, Nablus, Palestine.
[d]University of Grenoble Alpes, CEA, LETI, Grenoble, France.
[e]Department of Chemical, Materials and Production Engineering, University of Naples Federico II, Naples, Italy.
[f]Åbo Akademi, Laboratory of Industrial Chemistry and Reaction Engineering, Turku, Finland.
E-mail: maryam.hmoudah@unina.it

Water is a vital resource for all life beings on earth. Nowadays, pharmaceutical compounds occurrence in drinking water is growing due to the booming pharmaceutical industrialization and dramatic increase in the global population[1]. Ibuprofen (IBP) ($C_{13}H_{18}O_2$) is one of the most common pharmaceutical products that can be found in wastewater[2]. It is a non-steroidal anti-inflammatory drug and is also considered an emerging pollutant that may contaminate surface and underground water[3]. Different water treatment technologies are employed nowadays to mitigate the presence of these pollutants in water bodies. Photodegradation using nanomaterials is considered one of the most sustainable and cheap technologies that can be used in water purification. In this study, the photodegradation efficiency of CeO_2 nanostructured materials towards ibuprofen was assessed under UV irradiation. CeO_2 nanoparticles (NPs) were prepared through wet-chemical synthesis and characterized by XRD, XPS, TEM, DLS, and UV-Vis DRS techniques. The photodegradation activity of the synthesized CeO_2-NPs was compared to the commercial Aeroxide TiO_2-P25. Moreover, the photodegradation performance of CeO_2-NPs was investigated under different operational parameters, namely, air flow rate, stirring rate, temperature, catalyst bulk density, and ibuprofen solution initial concentration. Reusability of CeO_2-NPs and kinetic modeling were also addressed. The characterization results confirmed the successful synthesis of CeO_2-NPs. It was also found that the performance of Aeroxide TiO_2-P25 is slightly better than that for CeO_2-NPs. The goodness of the kinetic modeling of the experimental data was proven through the estimated kinetic parameters, together with the statistical information. On the other hand, reusability and stability tests showcased the sustainability of these NPs.

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Hydrofluorochromism: towards white-light emitting Ag clusters

Giacomo Romolini,[a] Cristina Martín,[b] Eduard Fron,[a] Didier Grandjean,[c]
Loredana Latterini,[d] Maarten Roeffaers,[e] and Johan Hofkens,[a]

[a] Department of Chemistry, Molecular Imaging and Photonics, KU Leuven, Leuven, Belgium
[b] Departamento de Quìmica Fìsica, Universidad de Castilla-La Mancha, Albacete, Spain
[c] Laboratory of Solid State Physics and Magnetism, KULeuven, Leuven, Belgium
[d] Department of Chemistry, Biology and Biotechnology, Nano4Light, Università degli Studi di Perugia, Italy
[e] cMACS, Department of Microbial and Molecular systems, KU Leuven, Leuven, Belgium
E-mail: giacomo.romolini@kuleuven.be

Microporous frameworks, possessing cages and pores of molecular size, can be used as efficient scaffolds to synthesize, confine and stabilize luminescent metal clusters. These clusters are fabricated by thermal treatment [1], UV-irradiation [2], or X-ray irradiation [3] via a self-assembly approach. In general, metal clusters have attracted increasing attention in the field of optoelectronics, e.g., light-emitting diodes, chemical sensors, etc., owing to inherent unique optical properties, outperforming those of traditional phosphors. In view of this, we recently synthesized luminescent silver clusters (AgCLs) presenting outstanding photophysical properties inside SAPO-42 molecular sieve, isostructural with zeolite A. Although AgCLs have the same structure as in zeolite A, they exhibit significantly different photoluminescence in SAPO-42, regardless of the amount of silver loading. However, the optical properties are strongly influenced by hydration, unveiling the hydrofluorochromism effect. Subsequently, this feature offers room to fine-tune their emission color over the entire visible range, with the possibility to obtain a remarkable single-phase white light LED.

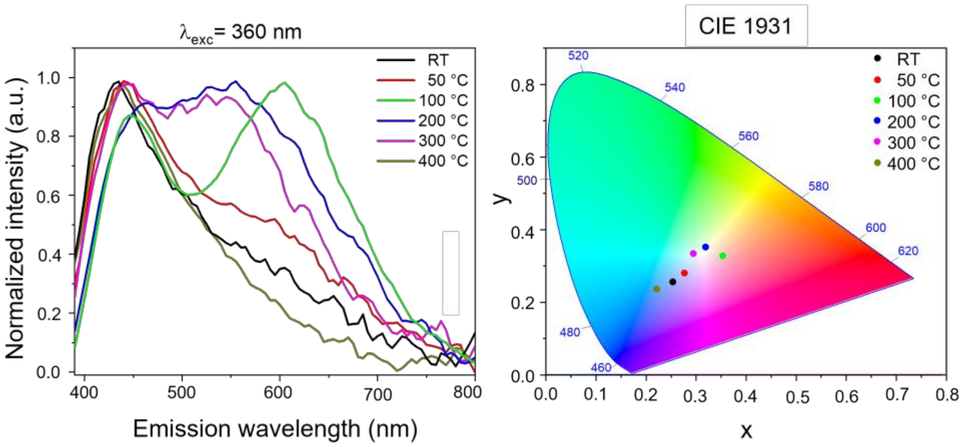

Figure 1: AgCLs@SAPO-42 (*left*) hydration dependent emission spectra and (*right*) their 1931 CIE coordinates, both at 360 nm excitation.

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Versatile Adhesive Polydopamine for enanched Biohybrid Photoanodes with Photosynthetic Microorganisms

Gabriella Buscemi[a,b], Rossella Labarile[a,b], Danilo Vona[a], Pinalysa Cosma[a,b], Angela Agostiano[a,b], Massimo Trotta[b], Gianluca M. Farinola[a], and Matteo Grattieri[a,b]

[a] Department of Chemistry, University of Bari "Aldo Moro", via E. Orabona 4 Bari, 70125, Italy;
[b] National Research Council, IPCF-CNR, via E. Orabona 4 Bari, 70125, Italy
E-mail: gabriella.buscemi@uniba.it

Photosynthetic microorganisms have a versatile metabolism that allowed using sunlight to oxidize various organic compounds. With the intent to mimic their natural processes, many attempts were made to exploit the ability of energy storage and energy conversion into chemical or electrical energy using biohybrid electrochemical systems. Such approaches allow developing an eco-friendly and scalable technology based on self-repairing biocatalysts where sunlight is utilized as primary green energy source [1]. In the application of living organisms in bioelectronic devices, the challenging aspect is related to the electrochemical interface between biotic and abiotic domains. Various approaches can be applied, such as layer by layers techniques to entrap whole cell onto electrodes surfaces or the use of conductive material to burst electronic communication [2].

In this context, we combined a versatile polymer, polydopamine (PDA), with the purple bacteria *Rhodobacter capsulatus* as biocatalyst. Polydopamine, containing both catechol and amine groups, is a biocompatible polymer presenting similar characteristic to the adhesive plaque of mussel byssus, suitable for confinement and protection of biomacromolecules [3]. PDA can be obtained by oxygenic self-assembly polymerization of dopamine in water or by electro-polymerization. Moreover, the tunable conductive properties and the key feature of being adhesive onto a variety of surfaces make this material suitable for bioelectrochemical devices. Here, we report a biohybrid photoanode obtained by a one-step immobilization of the living whole cells into PDA matrix, while entrapping a quinone-based redox mediator. The presented approach enabled to convey a more stable adhesion of the biocatalyst onto the electrode overtime, while improving and stabilizing the electrochemical response.

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New theoretical and computational models for the simulation of vibrational spectra

Marco Mendolicchio, Julien Bloino, and Vincenzo Barone

Scuola Normale Superiore, Piazza dei Cavalieri 7, 56126-Pisa, Italy
E-mail: marco.mendolicchio@sns.it

Spectroscopies, such as infrared and Raman, are powerful tools for the investigation of the physical-chemical properties of molecular systems, providing detailed information related to the structure and dynamics. However, experimental spectra are characterized by several intertwined effects which can make their interpretation challenging without the support of computational models. Such models are required to obtain accurate predictions of the transition energies and intensities leading to line-shapes directly comparable to experiment. Despite the unquestionable success of static structure-property relationships and of the basic rigid-rotor / harmonic-oscillator (RRHO) model to introduce dynamic effects, accurate results, directly comparable with experiment, can be obtained only employing more refined models, including anharmonic effects. Among the possible methods employable for the inclusion of anharmonic effects in the simulation of vibrational spectra, the second-order vibrational perturbation theory (VPT2) [1] offers a good balance between accuracy and computational cost, giving the possibility to target even medium-to-large systems. Historically, different formulations of VPT2 have been proposed based on the type of molecules (linear, symmetric, spherical, or asymmetric rotors) [2]. However, a unified theory is the first step to build a versatile computational platform able to support other types of coordinates (e.g., internal) and to combine perturbational and variational calculations. This contribution focuses on the extension of the standard VPT2 approach for Abelian groups to non-Abelian groups without employing specific equations for two- or three-fold degenerate vibrations [3]. In fact, all the degeneracy issues are properly handled in order to derive the customary spectroscopic signatures of non-Abelian groups (e.g., *l*-type doubling). In particular, the results for frequencies are equivalent to those delivered by previous conventional implementations (including accidental resonance contributions), but we are now able to compute also intensities for both IR and Raman spectra without any need of using complex algebra. The whole procedure has been implemented in our general engine for vibro-rotational computations beyond the RRHO model and has been validated for different levels of electronic structure computations.

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Ligand exchange on perovskite nanocrystals for LED fabrication

Matilde Cirignano

Istituto Italiano di Tecnologia, Via Morego 30, 16163-Genova, Italy
Dipartimento di Chimica e Chimica Industriale, Università degli Studi di Genova, Via Dodecaneso 31, 16146-Genova, Italy
E-mail: matilde.cirignano@iit.it

Colloidal semiconductor nanocrystals (CSNCs) are among the most investigated nanomaterials thanks to their desirable optoelectronic properties [1], which make them suitable for applications in light emitting technologies. Generally, CSNCs are stabilized by long chain ligands (as oleylamine and oleic acid) which produce solubility in non-polar solvents and prevent their aggregation. However, these long alkyl chain ligands can impede carrier mobility within thin films made by nanocrystals [2]. Therefore, the development of ligand exchange processes has been studied to replace the long-chains with shorter ones leading to improved functionality of CSNCs in device applications. Solution-phase procedures for ligand exchange on perovskite's nanocrystals have been widely studied [3]; yet, this is not the case for the solid-phase ones. The solid-phase ligand exchange is at the base of the layer-by-layer approach that allows to increase the thickness of the emissive material's film while maintaining a homogeneous drafting. This method is of great interest in the field of Light Emitting Diode fabrication and Photovoltaics. Here, some preliminary results of solid-phase ligand exchange on $CsPbBr_3$ NCs are reported, using solvents with strategic polarity so as to avoid NCs dissolution or damaging.

The preparation of cubic-shaped $CsPbBr_3$ NCs is performed following a hot-injection procedure; film fabrication is made by spin-coating as well as the solid-phase ligand exchange that requires specific concentrations of exchanging ligand solutions. Spectrofluorometer measurements show a significant increase after the exchange comparable to the liquid-phase procedure, leading to a 100% of PLQY in film.

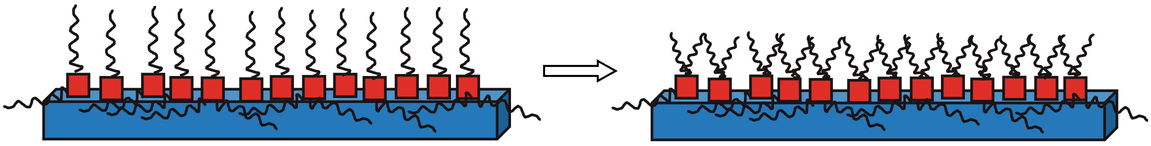

Figure 1: Solid-phase ligand exchange.

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The “LEGO bricks” approach for accurate equilibrium structures on top of DFT computations

Alessio Melli,[a,b] Francesca Tonolo,[a,b] Vincenzo Barone,[a] and Cristina Puzzarini[b]

[a] Scuola Normale Superiore, Piazza dei Cavalieri 7, 56126-Pisa, Italy
[b] Dipartimento di Chimica “Giacomo Ciamician”, Università di Bologna, Via Selmi 2, 40126-Bologna, Italy
E-mail: alessio.melli@sns.it

In the evaluation and interpretation of stereo-electronic, thermodynamic, and spectroscopic properties of isolated molecules, the accurate determination of their equilibrium structure is a mandatory step [1]. If the considered system is small and semi-rigid, the results obtained using state-of-the-art computational techniques can be compared with those issuing from the most sophisticated experimental results [1]. However, considering larger and/or more flexible systems, cheaper yet accurate approaches still need to be defined.

Within this context, the double-hybrid rev-DSD-PBEP86 functional already delivers remarkable results [2], which can be further improved by means of a “LEGO bricks” model. The foundation of this approach is the idea that a molecular system can be considered as formed by different smaller fragments (i.e. the “LEGO bricks”), whose accurate semi-experimental equilibrium geometries are available. To join the different “LEGO bricks”, we relied on: (i) the template molecule approach to account for the changes occurring when going from the smaller fragment to the larger molecular system and (ii) the linear regression model to correct the linkage between the fragments. Finally, we tested our results by comparing them to semi-experimental structures (when available) and experimental rotational constants (which straightforwardly depend on the equilibrium geometry). The deviations on bond lengths, angles and semi-experimental equilibrium rotational constants improved from 3 mÅ, 0.2° and 1% at the rev-DSD level to 1 mÅ, 0.1° and 0.2%, respectively.

The molecular systems considered are the ones obtained by addition/elimination reactions of nucleophilic unsaturated radicals (e.g., CN, C_2H, phenyl) to alkenes, imines, and aldehydes. For several of these systems, the rotational spectra have been investigated, but no accurate structural determinations are available. The main outcome of our study is the reliability, robustness, and accuracy of this novel approach.

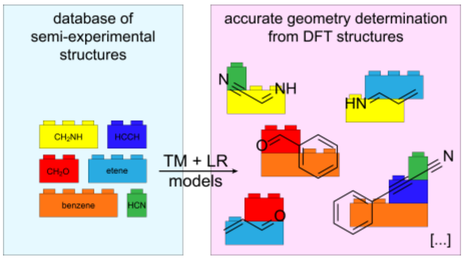

Figure 1: Graphical representation of the “LEGO bricks” approach.

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Structural studies and *in crystallo* reactivity of the dirhodium tetracarboxilate/protein adducts

Domenico Loreto,[a] Anna Esposito,[b] Annalisa Guaragna,[b] and Antonello Merlino*[a]

[a] Dipartimento di Scienze Chimiche, Università degli Studi di Napoli "Federico II", Via Cinthia 21, 80126-Naples, Italy
[b] Dipartimento di Ingegneria Chimica, dei Materiali e della Produzione industriale, Università degli Studi di Napoli "Federico II", P.le V.Tecchio 80, 80125-Naples, Italy
E-mail: domenico.loreto@unina.it

Paddlewheel dirhodium tetracarboxylates are a class of bimetallic compounds with a widespread catalytic activity, that can be used for the development of artificial metalloenzymes [1-2]. The metal complexes *cis*-$Rh_2(AcO)_2(TFA)_2$ and $Rh_2(AcO)(TFA)_3$ (AcO^-= acetate ion; TFA^-=trifluoroacetate ion) have been synthetized and their interaction with the model protein bovine pancreatic ribonuclease (RNase A) has been studied in solution and at solid state. The results have been compared with those previously obtained studying the interaction of $Rh_2(OAc)_4$ with the same protein [3]. The comparison reveals that the metal ligands do not play a significant role in directing the interaction between the metal complexes and the examined protein: the dirhodium center coordinates the side chain of His residues at the axial site. Since all the three dirhodium complexes retain the bimetallic core upon interaction with RNase A, the reactivity of the $Rh_2(OAc)_4$/RNase A adduct with imidazole and glycine has been studied at solid state. Notably, contrarily to the expectations, both imidazole and glycine replace an acetate ligand of the dirhodium center while they do not displace the solvent molecule at the axial site (Figure 1).

Overall, these data offer interesting insights into the interaction of dirhodium tetracarboxylates with proteins and into the reactivity of dirhodium tetracarboxylate/protein adducts, providing useful indications for the design of new Rh-containing biomaterials with potential applications in the field of catalysis.

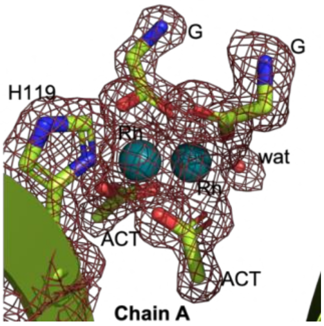

Figure 1: Product of the reaction of glycine (G) with the dirhodium tetracetate/RNase A adduct at crystal state.

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Multi-line Pt-based lateral flow device for colorimetric measurement of antioxidant levels in saliva

Anna Scarsi,[a,b] Deborah Pedone,[a] and Pier Paolo Pompa[a]

[a] Nanobiointeractions & Nanodiagnostics, Istituto Italiano di Tecnologia (IIT), Via Morego 30, 16163-Genova, Italy
[b] Department of Chemistry and Industrial Chemistry, University of Genova, Via Dodecaneso 31, 16146-Genova, Italy
E-mail: anna.scarsi@iit.it

Total Antioxidant Capacity (TAC), the complete pattern of antioxidant molecules fighting free radicals within the body, represents a fundamental biomarker for monitoring the health status of the organism [1]. To date, several assays to measure TAC are commercially available [2]. However, their application is often limited by inaccuracy, time- and cost-consuming procedures, and invasiveness [2]. To address this, we developed an innovative detection scheme exploiting the peroxidase enzyme-like properties of 4 nm platinum nanoparticles (PtNPs), combined with biologically relevant radical probes (hydroxyl radicals), for an accurate and rapid (5 minutes) assessment of the body TAC. 3,3',5,5'-tetramethylbenzidine (TMB) is used as chromogenic probe, allowing the naked-eye evaluation of the total antioxidant content of the sample [3]. Furthermore, we developed a multi-line Pt-based lateral flow device, relying on three sequential test lines with increasing concentrations of Pt nanozymes. Saliva sample flows along the device, first encountering TMB and then the detection zone, coloring a number of blue lines that is proportional to the level of antioxidants. This non-invasive colorimetric nanosensor provides a rapid, easy, and naked-eye discrimination of the body TAC (Figure 1).

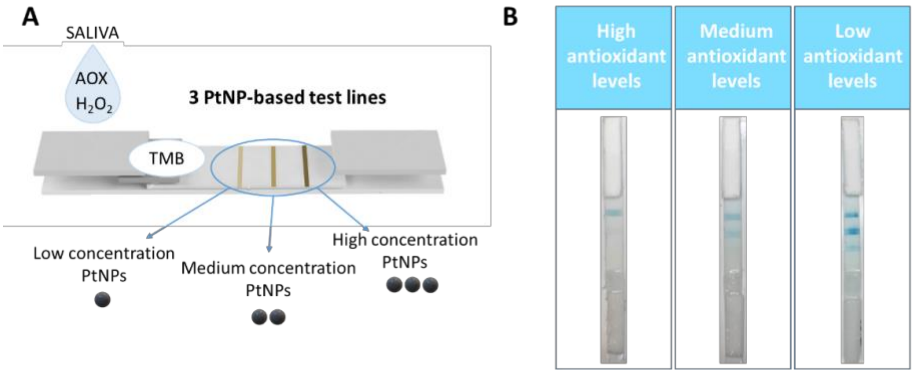

Figure 1: (A) Scheme of the multi-line Pt-based lateral flow device. (B) Representative pictures of three devices used to determine the antioxidant levels of three saliva samples.

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Polyamine receptors as fluorescent chemosensors for anti-inflammatory nonsteroidal drugs in aqueous media

Giammarco Maria Romano,[a] Liviana Mummolo,[b] Matteo Savastano,[a] Patrizia Rossi,[c] Paola Paoli,[c] Luca Prodi,[b] and Andrea Bencini[a]

[a] Dipartimento di Chimica "Ugo Schiff", Università degli Studi di Firenze, Via della Lastruccia 3, 50019-Sesto Fiorentino, Firenze, Italy
[b] Dipartimento di Chimica "Giacomo Ciamician", Università degli Studi di Bologna, Via Selmi 2, 40126-Bologna, Italy
[c] Dipartimento di Ingegneria Industriale, Università degli Studi di Firenze, Via di S. Marta 3, 50139-Firenze, Italy
E-mail: giammarcomaria.romano@unifi.it

In the last few years, the interest in the development of new sensing systems for certain consumer drugs, such as non-steroidal anti-inflammatories drugs (NSAIDs), has progressively increased. Indeed, their wide use and release in the environment, which is still often poorly regulated, can lead to a continuous consumption from living beings, with possible long term toxic effects [1,2]. Here we report two fluorescent receptors, L1 and L2, constituted by a triamine chain and two anthracene signalling units, as optical probes for ketoprofen (KP). Binding and sensing properties of the receptors and their Zn(II) complexes have been studied in aqueous media by coupling potentiometric, ^{1}H NMR, UV-Vis spectrophotometric and fluorescent emission measurements. Potentiometric titrations have shown that both receptors can interact with the substrate to form 1:1 adducts, stabilized by charge-charge and hydrogen bonding interactions between the protonated triamine chain of the receptors and the carboxylate group of KP. This hypothesis has been also confirmed by an X-ray crystal structure of the adduct between the diprotonated form of L2 and KP. In contrast, ^{1}H NMR measurements have pointed out that the anthracene units seem do not interact with aromatic groups of the substrate. However, at pH 7 the interaction gives rise to an increase of the fluorescence emission of both L1 and L2. Indeed, binding of KP induces a translation of the acidic proton from the central nitrogen of the monoprotonated triamine chain to a benzylic amine group, inhibiting the PET process.

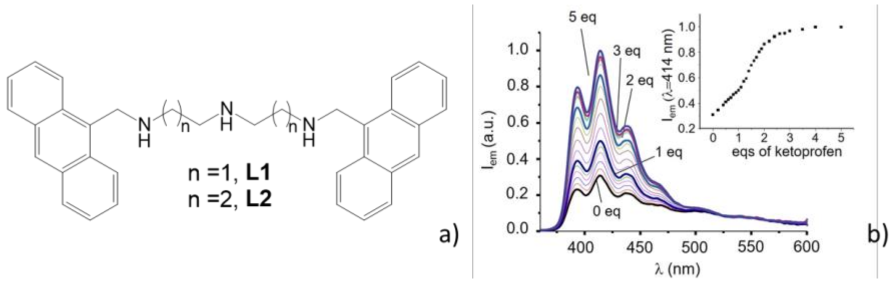

Figure 1: a) Structure of the receptors. b) Fluorescence emission spectra of L1 and (inset) emission intensity at 414 nm in the presence of increasing amounts of KP.

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Graphene-based electrochemical platforms for the detection of biomarkers in complex matrices

Fabrizio Poletti,[a] Barbara Zanfrognini,[b] Alessandra Scidà,[b] Alessandro Kovtun,[b] Manuela Melucci,[b] Emanuele Treossi,[b] Vincenzo Palermo,[b,c] and Chiara Zanardi[a,b]

[a]Department of Chemical and Geological Sciences, Università degli Studi di Modena e Reggio Emilia, via G. Campi, 103, 41125-Modena, Italy
[b]Institute for the Organic Synthesis and Photoreactivity, Consiglio Nazionale delle Ricerche, Via P. Gobetti 101, 40129-Bologna, Italy
[c]Chalmers University of Technology, Department of Industrial and Materials Science, SE-412 96-Gothenburg, Sweden
E-mail: fabrizio.poletti@unimore.it

Graphene and its related materials (GRM) have been largely employed for the realization of electrochemical devices which can accurately measure biomarkers of physiological interest, allowing a personalized approach to fitness goals and health monitoring. In this presentation, we report the advantages in the use of GRM for the realization of feasible enzymatic biosensors for the detection of glucose and lactate from the human sweat. On the one hand, the oxidized moieties already present on graphene oxide (GO) were exploited to achieve covalent functionalization of the nanomaterial with chitosan, thus increasing the amount of enzymes stably anchored on the electrode surface [1]; strenuous electrochemical tests on a flow of solution (Fig.1a) demonstrated the stable anchoring of the enzyme, allowing the realization of efficient biosensors in terms of sensitivity, limit of detection, linear range, repeatability, and reproducibility, which are required conditions for the use in specific applications. On the other hand, these same oxidized moieties were used for the realization of wearable platforms entirely made of GRM [2] (Fig. 1b) for the detection of NADH, a cofactor of several enzymes, even including lactate dehydrogenase, outperforming commercial devices. These new, unfunctionalized electrodes are obtained on flexible plastic and textile supports, opening new possibilities in the development of biosensors and smart fabrics.

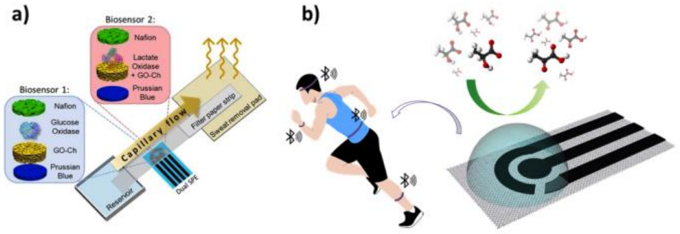

Figure 1: a) biosensor for glucose and lactate detection in a capillary flow device [1]; b) all-graphene electrode on textile and application for lactate detection during training [2].

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PCR-free hepatitis B virus whole genome determination by electrogenerated chemiluminescence

Pavlos Nikolaou,[a] Salvatore Petralia,[b] Alessandra Zanut,[a,c] Giovanni Valenti,[a] Sabrina Conoci,[d] Luca Prodi,[a] and Francesco Paolucci[a]

[a] Department of Chemistry “Giacomo Ciamician”, University of Bologna, Via Selmi 2, 40216-Bologna, Italy
[b] Dipartimento di Scienze del Farmaco e della Salute, University of Catania, Viale Andrea Doria 6, 95125-Catania, Italy
[c] Department of Chemical and Biomolecular Engineering, New York University, 6 Metrotech, Brooklyn, NY-11201 USA.
[d] Dipartimento di Scienze Chimiche, Biologiche, Farmaceutiche ed Ambientali, University of Messina, Viale Ferdinando Stagno d’Alcontres, 31, 98168-Messina, Italy
E-mail: pavlos.nikolaou2@unibo.it

Electrochemiluminescence or Electrogenerated Chemiluminescence (ECL) is an electrochemical technique with a simple instrumentation which is based on a luminescent phenomenon, produced from an electron-transfer reaction taking place on the surface of the electrode and yielding light-emitting excited states. The most know luminophores/coreactant system in aqueous media is tris(2,2’-bipyridine) ruthenium(II) ($[Ru(bpy)_3]^{2+}$)/tri-n-propylamine with important analytical application in commercial assays for the detection of biomarkers [1,2]. According to World Health Organization (WHO) Hepatitis B Virus (HBV) is the main problem of the infection of 257 million people. An ECL-based and also PCR-free sensor is developed for the determination of the double-standed DNA of HBV (ds-DNA). The ds-DNA of HBV has been immobilized and remained anchored between two monoclonal oligonucleotide chains probes (P1 and P2), thus the same time the triplex formation is created via Hoogstern H-bonds (Figure 1) [3]. The ECL-active molecule $[Ru(phen)_2dppz]^{2+}$ it can be remained intercalated in the ds-DNA according to the π-π* stalking intercalation -dppz. The ECL-based sensor is tested in a range from 0-1 copies μL^{-1} obtaining a limit of detection of 0.06 copies μL^{-1} which is much more sensitive, comparing it with other techniques.

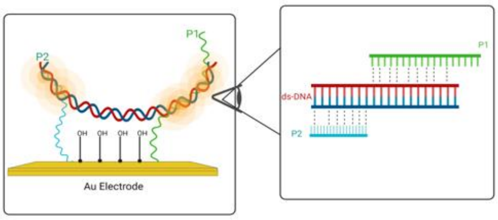

Figure 1: Immobilization of specific probes and triplex formation between ds-DNA of HBV and P1, P2 probes.

[1] A. Zanut, A. Fiorani, S. Rebeccani, S. Kesarkar and G. Valenti, *Anal. Bioanal. Chem.* **411** (2019) 4375-4382.
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Selective recognition of adenine derivatives by a dimeric, uracil-based receptor

Stefano Volpi,[a] Sasa Korom,[a] Martina Neri,[a] and Roberto Corradini[a]

[a] Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università degli studi Parma, Parco Area delle Scienze 17/A, 43124, Parma, Italy.
E-mail: stefano.volpi@unipr.it

The research in the field of artificial nucleobases has encompassed the synthesis of compounds that can simultaneously recognize the Watson-Crick and Hoogsteen domains of purine targets, taking inspiration from the T-AT and C$^+$-GC triplets observed in triple helical oligonucleotides [1]. According to this strategy, we reasoned to design the dimeric receptor **1** (Figure 1a)**,** in which two uracil units are arranged on a naphthalene scaffold to bind adenine derivatives by triplex-like base pairing. This compound was tested in the complexation of 9-ethyl adenine (9-Et-A) by a series of H^1 NMR titrations (CDCl$_3$, 50°C), estimating an association constant (K_a) of $4 \cdot 10^5$ M^{-1}. The monomeric compound **2** (Figure 1b) bound instead 9-Et-A with $K_a = 58$ M^{-1}, suggesting a high cooperation between the uracil units of **1**. The chemical shift perturbations observed during the course of the titrations, in combination with NOESY experiments, evidenced a structural rearrangement for **1** to form triplex-like motifs with its target (Figure 1a). A CDCl$_3$ solution of this receptor was also able to sequester 40% of adenosine from D$_2$O forming of an insoluble 1/1 complex at the interphase, at contrary to what observed for the monomeric control compound **2**. A precipitate with the same composition was formed when a mixture of all the four ribonucleosides was present in the D$_2$O layer, demonstrating the selectivity of **1** for adenosine.

In the future, **1** is planned to be included as a nucleobase into peptide nucleic acids (PNAs), to be used as tools for the detection of point mutations on relevant oncogenes in plasma (i. e. liquid biopsy) [2]. Strategies for the connection of **1** to the backbone of PNA oligomers are currently under evaluation in our lab.

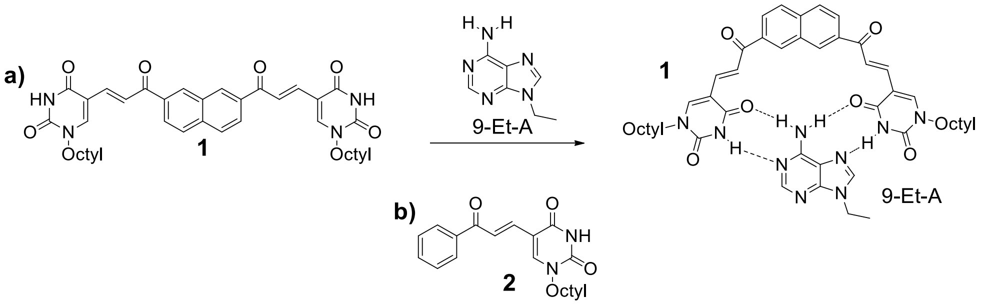

Figure 1: **a)** The dimeric receptor **1** presented in this work undergoes a structural rearrangement to bind 9-Et-A. **b)** Receptor **2** used as monomeric control compound.

[1] K. R. Fox, T. Brown, and D. A. Rusling, *DNA-targeting Molecules as Therapeutic Agents; The Royal Society of Chemistry* Ed. M. J. Waring (2018) 1–32.
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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.
E-mail:costanza.leonardil@unife.it

In recent years, chiral cyclopropenimines have been coming to light as effective Brønsted base orgacatalysts in enantioselective reactions by HOMO activation of pronucleophiles with high pKa values [1]. An unprecedented strategy for the immobilization of chiral 2,3-bisaminocyclopropenium salt (pre-catalyst) onto polystyrene and silica supports is presented together with a suitable procedure for the conversion into the corresponding cyclopropenimine superbase bifunctional catalysts [2]. The activity and recyclability of polystyrene- and silica-supported cyclopropenimines were initially tested under batch conditions in a model Michael addition detecting comparable efficiencies but a superior stability of the latter heterogeneous catalyst (5 cycles, accumulated TON of 27.1).

The preferred silica-supported cyclopropenimine behaved very similarly to the soluble counterpart in the reaction of glycine imine with different Michael acceptors (48-92% yield; 60-98% ee) and it could be utilized for the first time as packing material for the fabrication of fixed-bed mesoreactors (pressure-resistant stainless-steel columns). Continuous-flow experiments were performed with satisfactory long-term stability (24 h on stream) with unaltered conversion efficiency and enantioselectivity.

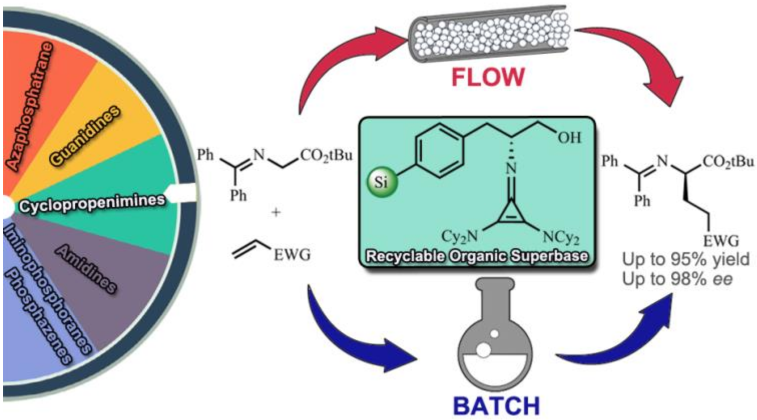

Figure 1: Supported cyclopropenimine catalyst in model Michael reaction in heterogeneous phase

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Role of His residues in tau-inspired copper peptides with redox catalytic behaviour

Silvia Gentili,[a] Fabio Bontempo,[a] Alessia Caruso,[a] Olga Iranzo,[b] and Matteo Tegoni[a]

[a] Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco Area delle Scienze 11A, 43124-Parma, Italy
[b] CNRS Centrale Marseille, Institut des Sciences Moléculaires de Marseille, Aix Marseille Université, 52 Av. Escadrille Normandie Niemen, 13013-Marseille, France
E-mail: silvia.gentili@unipr.it

The study of metal ions/peptide adducts that promote oxidative stress phenomena is of major importance, since these processes eventually lead to the degradation of biological tissues and neuronal death. The main feature of these systems relies on the presence of multiple histidine residues, well-known metal binding sites. This is the case of tau protein, a biomolecule strongly related to Parkinson's Disease [1].

The fragment R3 of tau contains a His-His tandem site that was found to promote the reduction of Cu(II) to Cu(I), mainly through the formation of stable Cu(I)/R3 adducts. By accommodating copper in both oxidation states, the His-His site provides an active catalyst for reactions that activate oxygen, such as catechol oxidation [2,3].

Several neuropeptides, actually, contain other His residues beyond those of the His-His dyad (e.g. β-amyloid). While the speciation and the reactivity of copper(II) bound to the His-His motif are relatively well known, the role of a third histidine residue remains unclear. With this in mind, we have designed four tau-inspired peptide sequences that bear a His-His tandem site and one additional His in positions -2, -4 and -6 (Figure 1).

In this communication, we will discuss the speciation of copper(II) adducts with these peptides, and their reactivity towards the oxidation of 4-methylcatechol (MC).

P-Ctrl	Ac-GWKAASAGAI***HH***KPG-NH_2
P-His(-2)	Ac-GWKAASAG***H***I***HH***KPG-NH_2
P-His(-4)	Ac-GWKAAS***H***GAI***HH***KPG-NH_2
P-His(-6)	Ac-GWKA***H***SAGAI***HH***KPG-NH_2

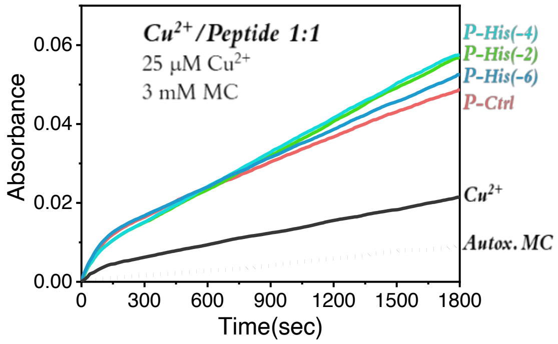

Figure 1: Amino acidic sequences of the tau-inspired peptides (left) and reactivity of their Cu(II)-complexes towards 4-methylcatechol oxidation (right).

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Chemoenzymatic stereodivergent synthesis of all the stereoisomers of the 2,3-dimethylglyceric acid ethyl ester

Francesco Presini, Simona D'Aprile, and Pier Paolo Giovannini

Dipartimento di Scienze Chimiche, Farmaceutiche ed Agrarie, Università degli Studi di Ferrara,
via Luigi Borsari 46, 44121-Ferrara, Italy
E-mail: francesco.presini@edu.unife.it

The 2,3-dimethylglyceric acid, constitutes the acyl and/or the alcoholic moiety of many bioactive natural esters. We will describe a chemoenzymatic methodology which gives access to all the four possible stereoisomers of the 2,3-dimethylglyceric acid ethyl ester. The racemic ethyl α-acetolactate, produced by *N*-heterocycle carbene (*N*HC)-catalyzed coupling of ethyl pyruvate and methylacetoin has been employed as the starting material [1]. The racemic mixture has been resolved through (*S*)-selective reductions, promoted by the acetylacetoin reductase (AAR) affording the resulting ethyl (2*R*,3*S*)-2,3-dimethylglycerate [2]; the isolated remaining (*S*)-ethyl α-acetolactate has been successively treated with baker's yeast to obtain the corresponding (2*S*,3*S*) stereoisomer. *syn*-2,3-Dimethylgliceric acid ethyl ester afforded by reducing the *rac*-α-acetolactate with $NaBH_4$ in the presence of $ZnCl_2$ was kinetically resolved through selective acetylation with lipase B from *Candida antarctica* (CAL-B) and vinyl acetate to access to (2*S*,3*R*) stereoisomer. Finally, the (2*R*,3*R*) stereoisomer, has been prepared by C3 epimerization of the (2*R*,3*S*) stereoisomer recovered from the above kinetic resolution, achieved through the TEMPO-mediated oxidation, followed by the reduction of the produced ketone with $NaBH_4$. The resulting 2,3-dimethylglicertate enriched in the (2*R*,3*R*) stereoisomer was submitted to stereospecicific acetylation with vinyl acetate and CAL-B in order to separate the major stereoisomer.

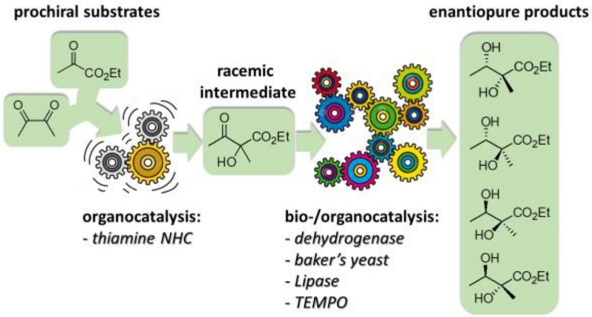

Figure 1: Schematic representation of the whole chemoenzymatic synthesis.

The entire procedure, allowed to obtain the four enantiopure stereoisomers of the ethyl 2,3-dihydroxy-2-methylbutyrate with the following overall yields: 42% for the (2*R*,3*S*), 40% for the (2*S*,3*S*), 42% for the (2*S*,3*R*) and 20% for the (2*R*,3*R*).

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Boosting selectivity in indole oxidation by Mn-porphyrin catalysis

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

[a] Dipartimento di Scienze Chimiche, Università degli Studi di Napoli "Federico II", Via Cintia 21, 80126-Napoli, Italia
[b] Istituto di Biostrutture e Bioimmagini, Consiglio Nazionale delle Ricerche, Via Mezzocannone 16, 80134-Napoli, Italia
E-mail: linda.leone@unina.it

The oxygenated derivatives of indole have gathered significant interest in different areas of research and industry [1]. Although 2-oxindole is a stable and commercially available molecule, obtaining 3-oxindole is quite difficult due to the high susceptibility of this compound to spontaneous oxidation. The synthetic strategies developed to access the 3-oxindole scaffold usually involve post-oxidation indole assembly rather than the direct oxygenation of indole, as the latter typically provides multiple products [2].

Here, we present indole oxidation catalyzed by a synthetic peptide-porphyrin mini-enzyme, namely Mn-MC6*a. This catalyst is able to regioselectively promote indole oxidation at the C3 position, upon activation of hydrogen peroxide.

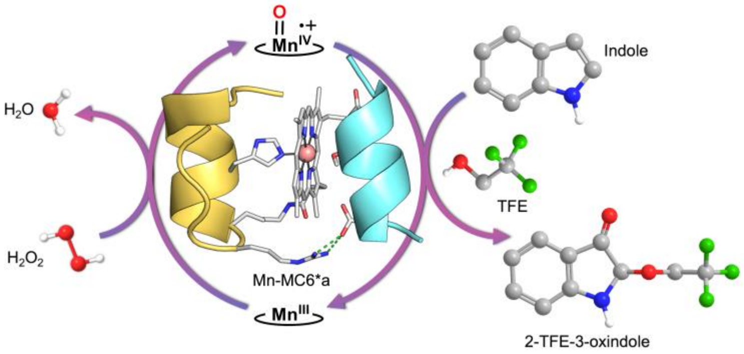

Figure 1. Reaction scheme of catalytic indole oxidation promoted by Mn-MC6*a

Interestingly, the presence of 2,2,2-trifluoroethanol (TFE) as a cosolvent, required for driving peptide folding and enhancing the catalytic performances of Mn-MC6*a, allowed us to shed light on the observed selectivity. TFE actively participates in the reaction, by capturing a highly reactive indole oxidation product. Indeed, we were able to isolate 2-(2',2',2'-trifluoroethoxy)-3-oxindole (2-TFE-3-oxindole) as a solvent-trapped 3-oxindole derivative, which may represent a useful starting material for subsequent transformations. Furthermore, we propose a possible reaction mechanism, by evaluating the effect of indole substitutions and of different cosolvents on the reaction outcome.

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Fe(III)-MimochromeVI*a as a catalyst for the development of functional nanomaterials

Emilia Renzi, Alessandra Esposito, Rocco di Girolamo, Marco Chino, Angela Lombardi, and Flavia Nastri

Dipartimento di Scienze Chimiche, Università degli Studi di Napoli "Federico II", via Cintia 21, 80126-Napoli, Italy
E-mail: emilia.renzi@unina.it

The synergic integration between nanotechnology and biocatalysis grants with the possibility of engineering functional nanomaterials with interesting application in industrial and biotechnological fields. In this area, gold nanomaterials (AuNMs) provide a high enzyme loading, due to the large surface area-to-volume ratio, possess a versatile surface chemistry as well as tunable sizes and shapes. Anisotropic AuNMs, such as nanorods (AuNRs), are characterized by a plasmon-related optical response, dependent upon their aspect ratio, which is an intriguing feature in building optical devices and biosensors [1]. In this context, the conjugation of AuNMs with artificial miniaturized heme-proteins, known as *Mimochromes* (MCs), enables the construction of versatile nanomaterials. Indeed, recent studies on Fe(III)-MCs proved the successful anchoring of these artificial biocatalysts on gold nanosurfaces, such as nanoparticles, while retaining structural properties and catalytic potential [2].

Herein we report the behaviour of the synthetic mini-peroxidase Fe(III)-MimochromeVI*a (FeMC6*a) when conjugated to AuNRs, by focusing on the relationship between the gold nanomaterial shape and the enzyme structural/functional properties. The covalent attachment of FeMC6*a on AuNRs was carried out by click chemistry, using the strain-promoted azide-alkyne cycloaddition (SPAAC, **Figure 1**).

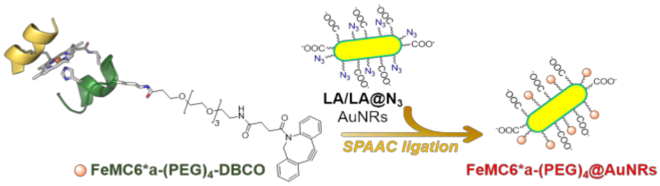

Figure 1: Schematic representation of the conjugation strategy to assemble FeMC6*a-(PEG)$_4$@AuNRs nanoconjugate.

The prepared nanoconjugate was thoroughly characterized by means of several analytical techniques (such as UV-Vis-NIR spectroscopy, transmission electron microscopy and circular dichroism). The catalytic properties of the resulting nanomaterial were evaluated using model oxidation reactions, which revealed that FeMC6*a-(PEG)$_4$@AuNRs is catalytically active. All the results demonstrate that the artificial metalloprotein FeMC6*a can be firmly anchored on AuNRs, thus offering new opportunities for the development of innovative materials with applications in biosensing and biocatalysis.

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Effect of stabilizers on gold supported nanoparticles in 4-nitrophenol reduction to 4-amminophenol

Alessia Ventimiglia, Eleonora Monti, and Nikolaos Dimitratos

Dipartimento di Chimica Industriale "Toso Montanari", Alma Mater Studiorum University of Bologna, Viale del Risorgimento 4, 40136-Bologna, Italy
E-mail: alessia.ventimiglia3@unibo.it

4-nitrophenol (4-NP) is a phenolic derivative that has different uses, as the production of insecticides, synthetic dyestuffs and leather manufacture [1]. These compounds enter the industrial effluents from chemical plants and companies, where they are used for agricultural treatments, subsequently discharging them into the waterways. The main problem is that 4-NP has been classified as a carcinogenic and mutagenic compound, causing skin diseases [2]. Consequently, its removal from wastewater is fundamental for human health. This can be done using different processes, such as physical, chemical and biological, which however have specific limitations and challenges to overcome. The catalytic reduction of 4-NP to 4-aminophenol (4-AP) with $NaBH_4$ using gold supported nanoparticles (Figure 1) seems to be a promising routes for a sustainable transformation of 4-NP: in particular, 4-AP is a product that shows several applications in various sectors: it can be used for slubbing photographic films in black and white, as a corrosion inhibitor, as a drying agent, but its most promising use is in the pharmaceutical sector: it is, in fact, an important intermediate in the synthesis of paracetamol.

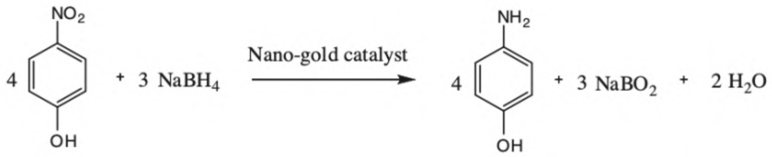

Figure 1: Scheme of 4-NP reduction with $NaBH_4$ using Nano-gold catalysts.

In this work sol-immobilization technique was used to synthesize Au nanoparticles supported on active carbon. Because the particle size of the nanoparticles influences the catalytic activity for this reaction [3], the materials were synthesized varying the quantity of stabilizer agent, that is polyvinyl alcohol (PVA), respect to Au. All the materials obtained were characterized by ultraviolet-visible (UV-vis) spectroscopy, dynamic light scattering (DLS), x-ray diffraction (XRD) and transmission electron microscopy (TEM) imaging. These materials were then tested in the 4-NP to 4-AP reduction reaction to evaluate their catalytic activity and the influence of the stabilizer.

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Aquivion® PFSA-based spray-freeze dried composite materials for the conversion of furfuryl alcohol to levulinates

Alessandro Allegri,[a] Michele Offidani,[a] Andrea Brigliadori,[b] Ilaria Zanoni,[b]
Giuseppe Fornasari,[a] and Stefania Albonetti[a,b]

[a] *Department of Industrial Chemistry "Toso Montanari", Alma Mater Studiorum - Università di Bologna, Viale Risorgimento 4, 40136 Bologna, Italy*
[b] *ISTEC-CNR, Institute of Science and Technology for Ceramics, National Research Council, Via Granarolo 64, 48018 Faenza, Italy*
E-mail: alessandro.allegri2@unibo.it

Fluorinated acid polymers like Aquivion® PFSA have attracted interest from the scientific community in recent years for their unique and interesting properties, such as superacidity and high thermal and chemical resistances. Despite these most promising characteristics, its solubility, high cost and low accessibility of the acid sites are of hindrance in the direct application of Aquivion® PFSA as a catalyst.[1] In this work, it has been evaluated the possibility of preparing composite Aquivion® PFSA-based materials with different supporting oxides, such as silica, titania, and zirconia, by means of spray-freeze drying,[2] and they have been tested in the conversion of biomass derived furfuryl alcohol to isopropyl levulinate, a promising platform molecule for the production of chemicals and fuels.

A range of innovative Aquivion® PFSA-based spray-freeze dried composite materials were prepared following the patented protocol,[2] varying the oxidic phase therein contained and studying the effect of the calcination. The oxides tested were commercial titania (Degussa P25), commercial silica (Ludox HS-40) and tetragonal zirconia synthesized following the procedure reported in literature.[3] The materials were characterized by means of SEM, TGA and BET, then tested as catalysts in the conversion of furfuryl alcohol to isopropyl levulinate in a 2-propanol solution.

All the samples displayed a significant, albeit different, activity in the studied reaction. Studying the produced species in the reaction mixture at different reaction times and temperatures by means of GC-MS provided insight on the different intermediates produced and the associated reaction pathways (Scheme 1), as well as the influence of the reaction conditions, especially the water content, on the outcome.

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

Marta Stucchi,[a] Daniela Meroni,[a] Claudia L. Bianchi,[a] and Laura Prati[a]

[a] *Dipartimento di Chimica, Università degli Studi di Milano, Via Camillo Golgi, 19, 20133 Milano, Italy*
E-mail: marta.stucchi@unimi.it

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 (Figure 1a). The addition of a small amount of Au nanoparticles (as low as 0.5% wt.) synthesized by sol-immobilization produced a strong synergistic effect not only improving the activity of the photo-catalyst but also modifying the final product distribution (Figure 1b). 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-TiO_2 also leads to synergistic photochromic effects under UV irradiation that, to the authors' best knowledge, have never been previously reported.

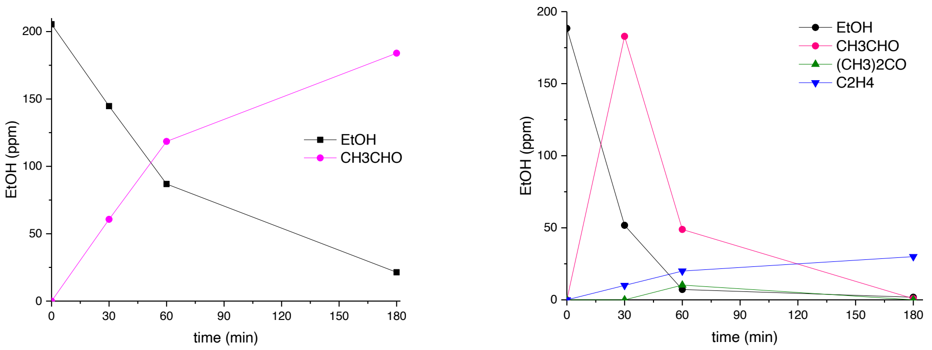

Figure 1: EtOH UV photo-oxidation by Ag-TiO_2 and by 0.5%Au/Ag-TiO_2.

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Exceptional ORR catalytic activity of Pt_xY nanoalloys prepared by Laser Ablation in Liquid

Brandiele Riccardo, Vincenzo Amendola, Christian Durante

Dipartimento di Scienze Chimiche, Università degli Studi di Padova, Via Marzolo 1, 35131 Padova
riccardo.brandiele@unipd.it

An innovative synthesis method for Pt_xY alloy NPs is Laser Ablation in liquid (LAL). The main problem of the LAL is the control of the NP size distribution. The size and composition properties of the obtained particles are influenced by the experimental conditions, which include the laser frequency, the beam wavelength or the different solvents. In this work, LAL of Pt-Y NPs was performed by focusing the pulses of a Nd-YAG laser on a bimetallic Pt_3Y target. Pt_xY NPs were synthetized in ethanol (PtY-E), a mixture of ethanol and NaCl solution (PtY-E_NaCl) and acetone (PtY-A). PtY-E NPs solution was further irradiated (PtY-E_IRRx) in different conditions. TEM images of PtY-E NPs show three different size distribution picked at 4.08 nm, 18.37 nm and 47.76 nm, and the NPs exhibit a metal Pt_3Y core and a carbon shell. The alloyed component was evaluated by XPS analysis, which confirmed a Pt-Y ratio of *c.a.* 3, corresponding in literature to the most active alloy [1]. The Y alloy content was 21 % for the sample synthetized in ethanol. The XRD analysis show a mixture of Pt_3Y and Pt_2Y and the absence of Pt pure phases. The best performing catalysts is PtY-E_A_IRR1, which shows, a $E_{1/2}$ = 0.943 V vs. RHE and a Mass Activity higher than 1000 A g^{-1}. The high electrochemical performance are connected to the good NPs distribution and dimension obtained with the irradiation treatment and to the shell removal obtained with the acid treatment [2,3].

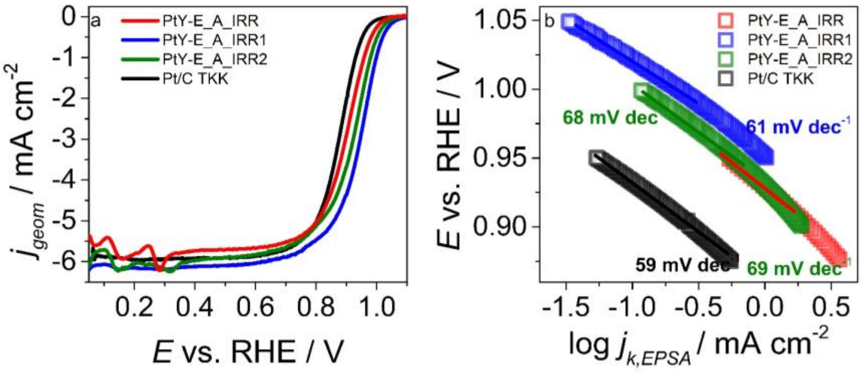

Figure 1 : Electrochemical characterization for Pt and Pt_xY catalysts after the acid treatment a) LSV with RDE recorded at 20 mV s^{-1} and 1600 rpm in O_2 saturated $HClO_4$ solution. b) Tafel plots limited to the kinetic region, the current is normalized by the $EPSA_{CO}$

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De novo design of a type 2 copper metalloenzyme for the production of value-added chemicals

Salvatore La Gatta, Gianmattia Sgueglia, Marco Chino, Flavia Nastri, and Angela Lombardi

Dipartimento di Scienze Chimiche "Paolo Corradini", Università degli Studi di Napoli Federico II,
Via Cintia 21, 80126-Napoli, Italia
E-mail: salvatore.lagatta@unina.it

The oxidative degradation of recalcitrant polymeric substrates, as polysaccharides, catalyzed by lytic polysaccharide monooxygenases (LPMOs, figure 1a), may represent the first step for the valorization of waste chemicals and for their reconversion into second-generation biofuels [1].

LPMOs contain type 2 copper site, composed of two histidine residues: a N-terminal histidine, donating both the N-terminal amino group and the Nδ imidazole nitrogen in a chelating fashion, while the other is bonded to the copper through the Nε imidazole nitrogen. This peculiar active site is known as Histidine Brace (figure 1b) and is the heart of the activity displayed by LPMOs [2].

Reproducing the catalytic features of these enzymes in de novo designed protein scaffolds can be important for structure-function relationship studies, but also for the development of efficient enzymes useful in waste treatment.

Here we present the de novo design, synthesis, and preliminary characterization of miniLPMO (figure 1c), a de novo designed protein with a Histidine Brace copper-binding site. MiniLPMO binds copper with a Histidine Brace-like motif, as confirmed by UV-Vis spectroscopy, and stabilizes copper-oxygen complex under mild conditions. Finally, miniLPMO shows oxidase activity, similar to natural LPMOs.

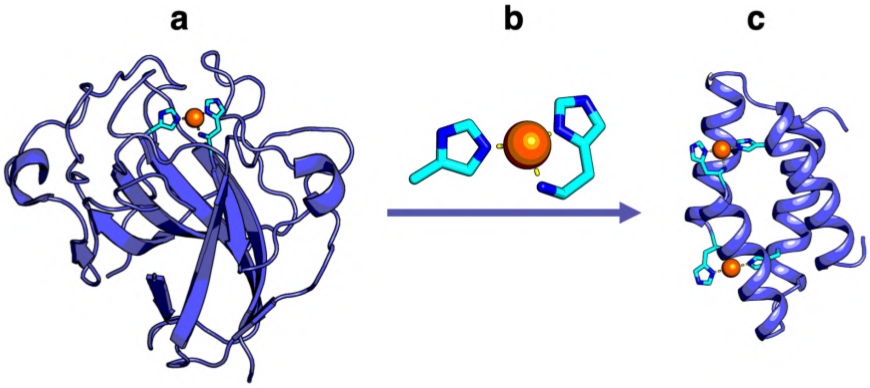

Figure 1: a) Structure of LPMO (PDB ID: 4mah). b) Histidine Brace sticks representation. c) De Novo Designed Scaffold (PDB ID: 1qp6) engineered with Histidine Brace copper-binding site.

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Microemulsion synthesis of TiO_2 nano-spheres and their application as supports in the aqueous phase reforming of glycerol

Andrea Fasolini, Erica Lombardi, Tommaso Tabanelli, and Franceso Basile

Dipartimento di Chimica Industriale "Toso Montanari", Alma Mater Studiorum – Univeristà di Bologna, Viale del Risorgimento 4, 40136-Bologna, Italy
E-mail: andrea.fasolini2@unibo.it

Glycerol is an interesting bio-derived molecule that has been intensely studied in the last years due to its high availability as by-product of the bio-diesel production process. Within the different approaches for glycerol valorization, the Aqueous Phase Reforming reaction (APR) represents a valuable pathway to obtain liquid products and hydrogen, with selectivities depending on the reaction conditions and catalyst employed [1]. Catalysts for APR are usually bifunctional systems, since the support is participating in the reaction pathway in presence of an active metal; the most used systems are VIII group metals supported on oxides. Among APR catalysts investigated in literature, Pt supported on TiO_2 has rose little attention [2]. Nevertheless, the acidic moieties of titania could be beneficial to glycerol APR. In this study an innovative microemulsion technique was used to prepare titanium dioxide that were subsequently impregnated with Pt to produce a bifunctional catalyst [3]. The optimization of the microemulsion technique led to the obtainment of small and regular TiO_2 nano-spheres which displayed high surface area. In addition, it also led to a homogeneous morphology of the TiO_2 nanospheres, as the microemulsion micelles acted as microreactors. This provided a higher density of weak acid sites, compared to commercial TiO_2. When impregnated with Pt, applied to glycerol APR and compared with a commercial TiO_2 support, the microemulsion synthetized titania gave increased hydrogen selectivity and glycerol conversion. This was related to an improved catalytic activity toward consecutive dehydrogenation reactions. The latter was provided by an enhanced cooperation between the acid sites of the support and Pt nanoparticles. Finally, a reaction mechanism for the Pt/TiO_2 synthetized by microemulsion was drawn from the results obtained in glycerol APR and by reactions with intermediates.

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Flash communications

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FL02	Degnet Melese DEREJE
FL03	Lucrezia COMPARINI
FL04	Angela DI SOMMA
FL05	Marco SIRIGNANO
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FL29	Mariangela GIANCASPRO

Rational design of improved *Sm*HDAC8 inhibitors

Luca Pozzetti, Stefania Butini, Sandra Gemma, and Giuseppe Campiani

Department of Excellence of Biotechnology, Chemistry and Pharmacy, University of Siena, Via Aldo Moro 2, 53100, Siena, Italy
E-mail: luca.pozzetti@student.unisi.it

Schistosomiasis is a neglected tropical disease caused by the parasites of the genus *Schistosoma* that affects almost 240 million people in the world. To date, the only approved treatment for this disease relies only on Praziquantel [1].

With the aim to increase the therapeutic options and to overcome the threat of drug resistance, our research group focused on a new possible target, namely *Schistosoma mansoni* histone deacetylase 8 (*Sm*HDAC8), a class I zinc-dependent HDAC expressed in all the stages of the parasite life cycle. Recent studies demonstrated both the importance of this enzyme for the parasite homeostasis and some crucial aminoacidic differences between the human and parasite isoforms, thus making *Sm*HDAC8 a promising target for drug discovery [2].

Previous work, started from a virtual screening of our in-house database, allowed us to identify two main core structures, characterized by the presence of a zinc chelating moiety coupled to different cap groups, that were able to impair parasites viability and to affect different aspects of the worm's homeostasis *in vitro* by inhibiting *Sm*HDAC8 [3]. These promising results, despite a low selectivity profile over human orthologues, prompted us to rationally design and to computationally assess novel compounds able to selectively target the parasite's HDAC isoforms, thus paving the way for the development of improved antischistosomal agents.

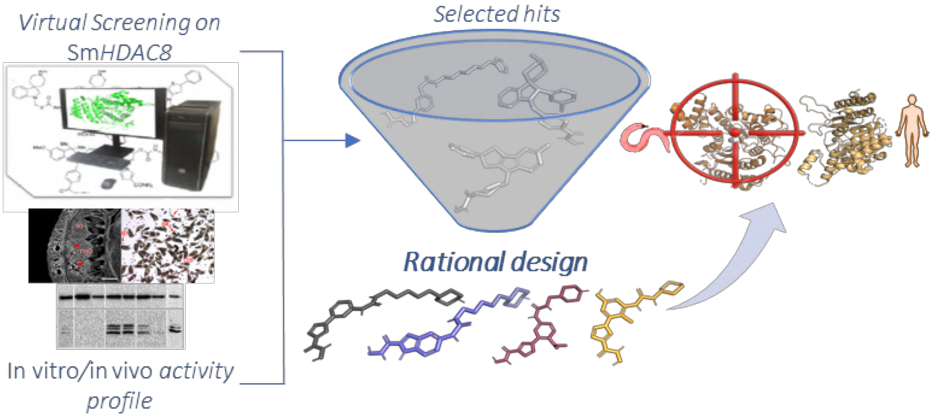

Figure 1: Rational design of improved inhibitors of *Sm*HDAC8.

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Polymethine dyes incorporated in NIR fluorescence emissive organic nanocarriers: PLGA and HSA

Degnet Melese Dereje,[a] Crlotta Pontremoli,[a] Cosmin Stefan Butnarasu,[b] Maria Jesus Moran, [a] Claudia Barolo, [a] Sonia Visentin[b], and Nadia Barbero [a]

[a] Department of Chemistry, NIS Interdepartmental and INSTM Reference Centre, University of Torino, 10125 -Torino, Italy
[b] Department of Molecular Biotechnology and Health Science University of Torino,10135 -Torino, Italy
E-mail: degnetmelese.dereje@unito.it

Strong absorbance on NIR and excellent photochemical properties of polymethine dyes make them excellent probe in the theranostics application. Even if squaraines and cyanines are characterized by high molar absorption coefficients, remarkable brightness, fluorescence and photostability in organic media [1], poor chemical and aqueous solubility, medium cytotoxicity, and short blood circulation half-life in physiological conditions limits their wide application [2]. In this context, the incorporation of these dyes inside multi-functional nanoparticles (NPs) is extremely important to prevent the formation of dye aggregates in aqueous environment and protect the photophysical characteristics.

Poly(lactide-co-glycolide) (PLGA) has attracted considerable attention due to its physicochemical properties: biodegradability and biocompatibility, FDA and EMA approval in drug delivery systems for parenteral administration, well described versatile formulations and methods of production adapted to various types of hydrophilic or hydrophobic molecules, possibility of sustained release, and versatility in functionalization to target nanoparticles to specific organs or cells. Nanoparticles made of albumins garnered interest recently as carriers to encapsulate hydrophobic drugs. Compared to other NPs, the super biodegradable and biocompatible albumin NPs are less toxic and easier to make, simply by self-assembly or by water-in-oil emulsion methods followed by crosslinking with glutaraldehyde [3].

The present work deals with the design of albumin and PLGA NPs for the incorporation of several polymethine dyes with different structural features. NPs-dye complexes have been characterized by means of DLS, SEM, UV-Vis and fluorescence spectroscopy. They exhibit excellent optical properties and remarkable photostability.

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Development of new anti-diabetic small molecules acting as GLP-1 secretagogue

Lucrezia Margherita Comparini, Lisa Giannessi, Federico Dani, Sebastiano Di Pietro, and Mauro Pineschi*

Department of Pharmacy, University of Pisa, Via Bonanno Pisano 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, it 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 enhancement of GLP-1 pathway is an established mechanism to treat diabetes and obesity. Several peptide agonists, close in structure to native GLP-1, are now in the market [1]. Such peptides have high costs, an administration route which is normally by injection and several adverse side effects such as nausea. 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 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 [2a-c]. We now report the chemical diversification of the library of compounds with an emphasis on late stage manipulations.

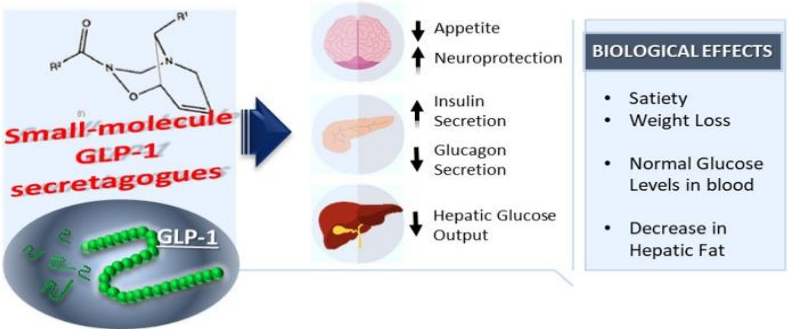

Figure 1: Biological effect of GLP-1.

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A comparative study of the inhibitory action of berberine derivatives on the *E. coli* protein FtsZ

Angela Di Somma,[a,b] Carolina Canè,[a] Maria Maddalena Cavalluzzi,[c] Giovanni Lentini,[c] and Angela Duilio[a,d]

[a] Department of Chemical Sciences, University of Naples "Federico II", 80126 Napoli, Italy
[b] National Institute of Biostructures and Biosystems (INBB), 00136, Roma, Italy
[c] Department of Pharmacy–Pharmaceutical Sciences, University of Bari Aldo Moro, 70126 Bari, Italy
[d]CEINGE Biotecnologie Avanzate, 80145, Naples, Italy
E-mail: angela.disomma@unina.it

Since antiquity, medicinal plants have been serving as the largest biochemical and pharmaceutical living stores for treating human diseases. The genus *Berberis* is an excellent source of drugs used in herbal medicine particularly to address the problem of antimicrobial multiresistance. The important properties associated with this genus are mainly due to the presence of berberine, a modified alkaloid with a benzyltetrahydroisoquinoline structure [1].

Berberine performed antibacterial effects by developing activity against Gram-negative and Gram-positive bacteria, affecting DNA duplication, RNA transcription, protein synthesis and the integrity of the cell surface structure. However due to its adverse effects, several studies have been addressed to the development of different synthetic berberine analogues with the aim to enhance its beneficial effects.

Recently, we prepared and screened a series of berberine analogues using the molecular simplification approach to identify functional analogues possibly endowed with better properties and easier synthetic access. Molecular docking simulations suggested FtsZ, a bacterial tubulin homolog responsible for the Z-ring formation during cell division, as a possible target of berberine analogues [2].

In this work we investigated the effective ability of different berberine analogues to inhibit recombinant *E. coli* FtsZ thus impairing celle division. All the tested compounds were able to inhibit the GTPase activity of FtsZ by both competitive and non competitive mechanisms. Among others, compounds 6·HBr and 9·HBr displayed a significant inhibition of the enzymatic activity of FtsZ. Moreover, fluorescence spectroscopic analyses were carried out in order to evaluate the stability and the dissociation constant of their complexes with FtsZ.

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A^3coupling reaction and hydroamination reaction catalyzed by silver(I) and gold (I) N-heterocyclic carbene complexes

Marco Sirignano,[a] Annaluisa Mariconda,[b] and Pasquale Longo[a]

[a] Dipartimento di Chimica e Biologia (DCB), Università degli Studi di Salerno, Via Giovanni Paolo II 132I, 84084-Fisciano (SA), Italy
[b] Dipartimento di Scienze, Università degli Studi della Basilicata, Viale dell'Ateneo Lucano 10, 85100-Potenza (PT), Italy
E-mail: msirignano@unisa.it

N-functionalized compounds (amines, enamines, imines, and amide) are key products for the synthesis of interesting pharmaceutical molecules, in fact they have found application as antibacterial, anticancer, antimalarial and in the treatment of neurodegenerative diseases [1].

The most attractive strategies for the synthesis of these class of compounds are the multicomponent reaction (MCR) and the addition of amine moiety to C-C multiple-bond (hydroamination), either catalyzed by transition metal complexes.

The action of the catalyst is fundamental for the formation of C-N bond to overcome the high active barrier subsequent by the repulsion among the alkyne or alkene and the nucleophilic amine [2].

In this context *N*-heterocyclic carbene (NHC) complexes of silver and gold have been show the ability to catalyze many organic transformations such as A^3 (aldehyde, amine, and alkyne-MCR) reaction to lead propargylamines and hydroamination reaction to produce imines [1,3].

Herein, we report the synthesis, the characterization, and the catalytic activity in A^3 coupling and hydroamination reactions of new silver(I) and gold(I) complexes containing unsymmetrical *N*-heterocyclic carbene ligands with different substituents on the backbone (Figure 1).

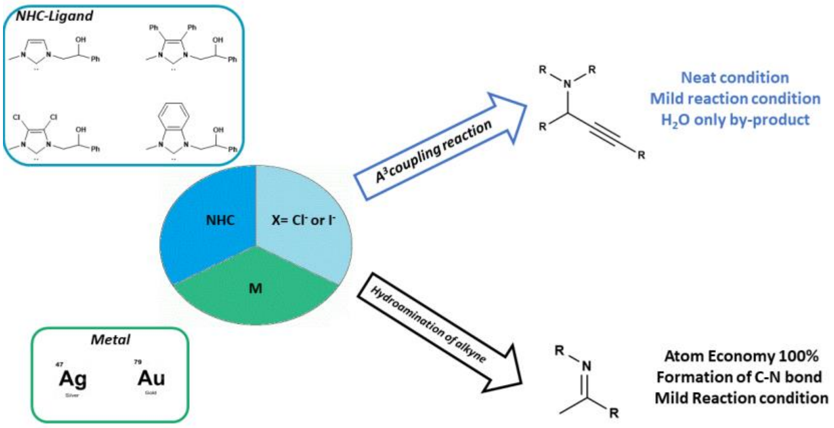

Figure 1: Reaction catalyzed by silver and gold NHC complexes.

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

Francesco Bartoli,[a,b] Hamish A. Miller,[a] Maria Vincenza Pagliaro,[a] Marco Bellini,[a] Andrea Marchionni,[a] Jonathan Filippi,[a] Laura Capozzoli,[a] Lorenzo Poggini,[a] and Francesco Vizza[a]

[a] Istituto di Chimica Dei Composti Organometallici ICCOM-CNR, Via Madonna del Piano 10, 50019 -Sesto Fiorentino, Italy
[b] Dipartimento Di Biotecnologie, Chimica E Farmacia, Università di Siena, Via Aldo Moro 2 53100-Siena,Italy
E-maill: francesco.bartoli@iccom.cnr.it

Hydrogen economy is becoming more feasible in recent years due to technological progresses in materials development, which also lowering the manufactoring costs, making hydrogen even more competitive.

Here we report PGM (Platinum Group Metal) free catalysts for anion exchange membrane electrolyser, based on [1] nickel-molybdenum alloys and [2] iron oxide-hydroxide: $MoNi_4$:$MoO_{x\text{-}3}$/Ni_{foam} for the cathode and Fe-$MoNi_4$:$MoO_{x\text{-}3}$/Ni_{foam} for the anode (Figure 1), using H_2O as abundant and renewable source of H_2.

Tests carried out in complete AEM (anion exchange membrane) electrolyzer demonstrate improved performances, showing very good stability during the time with a current loading of 500 mA/cm^2 for 2 week at 60 °C, maintain a potential around 1.8 V. Scaling-up the electrodes is the current focus, going from 5 to 78.5 cm^2,and then carry out test in appropriate electrolyzer.

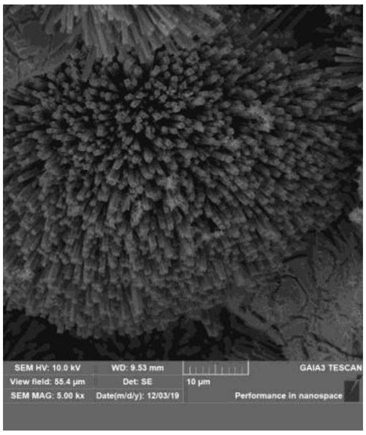

Figure 1: SEM image of $MoNi_4$:$MoO_{x\text{-}3}$/Ni_{foam}.

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An overview on Li-mediated ammonia production

Anna Mangini, Lucia Fagiolari, Julia Amici, Carlotta Francia, Silvia Bodoardo, and Federico Bella

Department of Applied Science and Technology, Politecnico di Torino, Corso Duca degli Abruzzi 24, 10129 - Turin, Italy
E-mail: anna.mangini@polito.it

Electrochemical N_2 reduction reaction (E-NRR) is studied as a sustainable and renewable energy-based process to replace the well-established Haber-Bosch process (HB) for NH_3 production. Ammonia, one of the top-3 chemicals produced worldwide, is at the base of fertilizers synthesis and a viable green energy carrier, since it is easier transportable and safer than H_2. Operating in harsh conditions (at least 450 °C - 200 atm), the HB process is responsible of about 1% of the global greenhouse gas emissions (about 400 Mtons/year of CO_2 are released) [1]. Even using “green” or “blue” H_2, the HB process is viable only in huge centralized plant and would reach no more than 40% energy efficiency, remaining highly energy-consuming [1]. Thus, to reach independence from fossil energy sources, it is quite urgent to find a sustainable process working in mild conditions and driven by abundant even if discontinuous renewable energy sources.

Li_3N is the only stable nitride of alkali metals and its formation is thermodynamically favored also in ambient conditions. Li-mediated NRR has recently demonstrated promising results, both in continuous systems with Li^+ ions and a proton donor in the same cell, and in discontinuous processes involving Li_3N formation and subsequent protonation into NH_3. In the first setup, E-NRR carried out in aqueous or ethanol environments has been proposed and a recent study demonstrated a Faradaic efficiency (FE) of around 30% [2], far greater than that of standard E-NRR. In the second approach, cell design is similar to that of Li-air batteries and shows an intriguing possibility, i.e. to avoid the main competitive reaction (hydrogen reduction reaction); in this way, it is possible to reach FE higher than 60% [3].

This poster gives an up-to-date overview of Li-N_2 electrochemical systems for NH_3 synthesis.

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Polymer electrolytes for potassium batteries in the SYNERGY project framework

Sabrina Trano, Matteo Gandolfo, Lucia Fagiolari, Julia Amici, Carlotta Francia, Silvia Bodoardo, and Federico Bella

Department of Applied Science and Technology (DISAT), Politecnico di Torino, Corso Duca degli Abruzzi 24, 10129-Turin, Italy
E-mail: sabrina.trano@polito.it

SYNERGY European project aims to strengthen the scientific and technical competences at the involved Portuguese institutions (PT Cluster) in the field of energy harvesting and micropower management, as a key component towards self-sustainable smart platforms on flexible substrates.

Among the most in-vogue electrochemical energy technologies, the contribution from Politecnico di Torino also includes the development of advanced materials for potassium-based batteries. In this contribution, we present our recently started work focused on polymer electrolytes to replace unsafe and unstable liquid-state systems.

Indeed, the high reactivity of alkali metals, like lithium and potassium, also interfacing with electrolytes, causes the unavoidable creation of the SEI layer, which is very likely to be fragile and heterogenous, causing the dendrites formation and eventually the failure of the cell. Gel polymer electrolytes (GPE) have been already proven to suppress dendrites growth thanks to their higher shear modulus [1]. A BMA-co-PEGDA UV-cured system incorporating a plasticizer is here fully characterized and proposed as gel-polymer electrolyte for potassium-based batteries, showing outstanding ionic conductivity, excellent capacity retention in lab-scale cell prototypes and very good performances for more than 500 cycles.

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This project has received funding from the European Union's Horizon 2020 Research and Innovation programme (grant agreement No. 952169, project title: SYNERGY).

FRET resonance energy transfer for dye-sensitizer solar cells (DSSC)

Rossella Infantino,[a,b] Alessio Dessì,[b] Daniele Franchi,[b] Gianna Reginato,[b] Lorenzo Zani,[b] Massimo Calamante,[b] and Alessandro Mordini,[b]

[a] Department of Biotechnology, Chemistry and Pharmacy, University of Siena, Via Aldo Moro 2, 53100-Siena, Italy
[b]Institute of Chemistry and Organometallic Compounds (CNR-ICCOM), Via Madonna del Piano 10, 50019-Sesto Fiorentino, Italy
E-mail: rossella.infantino@student.unisi.it

Förster resonance energy transfer (FRET) is based on dipole-dipole coupling between two different molecules or molecular fragments separated by a short distance, one of which is able to transfer its energy to the other by means of a non-radiative mechanism.

The goal of this study is to demonstrate the physics of FRET effect between two bound organic fragments within the structure of an organic DSSC (Dye-Sensitized Solar Cell) sensitizer. In fact, if the light energy absorbed by the donor (or antenna) moiety gets transferred to the acceptor dye through FRET, it is possible to broaden the light absorption profile of the resulting device, possibly improving its performances [1]. The right choice of the fragments is driven by the good overlap between the emission and the absorption spectra of the compounds. We examined the possibility of designing a new covalent antenna-dye system with a completely organic structure (Figure 1), connecting the two units with a "azide-alkyne cycloaddition" reaction at the end of our route. We selected a typical metal-free DSSC dye characterized by a D-A-π-A (Donor-Acceptor-π-spacer-Acceptor) architecture, while as the antenna we employed a benzothiadiazole scaffold decorated with thiophenes bearing different substituents. In this communication, we will report recent progresses on the synthesis of this new covalent construct, and on its spectroscopic characterization

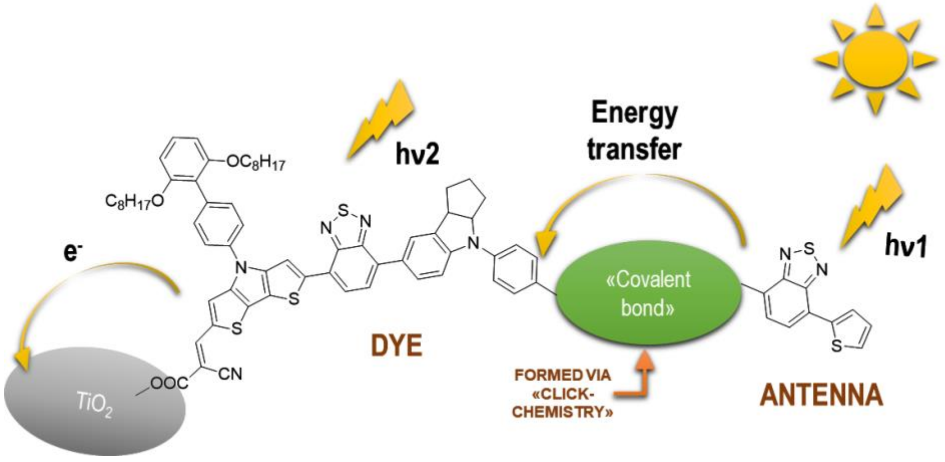

Figure 1: Schematic representation of FRET effect in dye-antenna system.

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Geopolymer based supports for the removal of organic and inorganic pollutants from water matrices

Michele Castiglioni,[a] Luca Rivoira,[a] Irene Ingrando,[a] Stefano Calanni,[a] Karine Goulart,[b] Renata Botti,[b] Giorgia Franchin,[b] Paolo Colombo,[b] and Maria Concetta Bruzzoniti,[a]

[a] *Chemistry Department, Università degli Studi di Torino, Via Pietro Giuria 7, 10125, Torino, Italy*
[b] *Industrial Engineering Dept. University of Padova, Via Marzolo 9, 35131, Padova, Italy*
E-mail: michele.castiglioni@unito.it

Geopolymers (GPs) are aluminosilicate-based materials, characterized by -Si-O-Al-O- chains. Because of their green properties (i.e. low temperatures synthesis, industrial and agricultural waste feedstocks, etc.) and excellent physicochemical properties (i.e. high mechanical strength, resistance to low and high temperatures, limited backpressures, etc.), GPs can be considered as adsorbents for environmental friendly applications, such as the removal of pollutants from waters.

Moving from the above-mentioned assumptions, in this work adsorption properties of several GPs, characterized by different shapes and structures, towards glyphosate (a well-known herbicide with toxic effects against environment and human beings) and heavy metals (As, Pb, Ni, Cd, Se, Cr) in water matrices are presented.

To highlight the possible interaction mechanisms, the contribution of selected synthesis parameters was investigated, in particular: i) GPs shape (spheres, powdered and 3-dimensional printed supports); ii) functionalization with specific agents, that were supposed to enhance the interaction towards pollutants (i.e. magnetite, zeolites and commercial activated carbons with anion-exchange properties, etc.); iii) templating agents employed for the synthesis or the printing (e.g. bentonite and PEG1000).

GPs were preliminary characterized by specific surface area/pore volume measurements.

Results showed that tested GPs have good adsorption performances towards glyphosate (removal rates up to 45% for sorbents modified with both active carbons and zeolite), as well as for heavy metals (up to 97%).

This study confirms the potential use of GPs towards the removal of glyphosate and metals from water matrices, in view of their potential use for water treatments.

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Synthesis of new bio-based hybrid materials for water purification

Monica Rigoletto, Enzo Laurenti, and Paola Calza

Dipartimento di Chimica, Università degli Studi di Torino, Via Pietro Giuria 7, 10125 Torino, Italy
E-mail: monica.rigoletto@unito.it

Nowadays the development of green approaches for environmental treatments, together with the concept of circular economy, is becoming more and more important.

For water restoration, a consistent part of scientific research is focusing on the use of biopolymers (such as alginate, cellulose or chitosan) as sustainable adsorbent materials for pollutants, alternative to activated carbon. Biopolymers are very abundant in nature and can often be recovered from waste. Therefore, advantages in using these biological macromolecules are their low cost, high biodegradability, and the possibility to exploit naturally present functional groups and to modify them chemically in order to modulate their properties.

It is even more interesting to make these materials also capable of degrading contaminants by exploiting synergistic interactions with photocatalysts, enzymes or both.

Previous results showed as hybrid systems containing photocatalytic oxides and soybean peroxidase (SBP) immobilized on silica monoliths or on polymeric fibers are able to degrade dyes and recalcitrant organic pollutants [1,2]. But enzymatic activity strongly decreased after immobilization and the support had to be removed from water and managed at the end of the reaction since it is not biodegradable.

Therefore, in this work we synthesize bio-based and reusable alginate hydrogels containing both SBP previously bounded to cellulose obtained from agricultural waste, and TiO_2 or ZnO (pristine or doped with Ce). These metal oxides, when irradiated with simulated or real solar light, induce photocatalytic degradation of pollutants and production of hydrogen peroxide, which is necessary to activate the enzymatic action. The synergistic action between the enzymatic oxidation catalyzed by SBP and the photocatalytic process led to a faster and complete degradation of the studied molecules. Moreover, both the oxides and the cellulose-SBP components remain trapped into the hydrogel, permitting their reuse for several reaction cycles.

These preliminary results are part of a larger project, whose final goal is to obtain and test waste-derived materials easy to make, use and reuse, working across a broad spectrum of water contaminants, activated by the sun, safe and sustainable.

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Development of sustainable and green methodologies for homogeneous gold(I) catalysis

Filippo Campagnolo,[a] Jacopo Segato,[a] Diego Sorbelli,[b] Alessandro del Zotto,[a]
Leonardo Belpassi,[bc] Paola Belanzoni,[b] 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.

E-mail: campagnolo.filippo@spes.uniud.it

Gold(I) complexes of general formula [L-Au+…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, the Meyer–Schuster rearrangement of 1-phenyl-2-propyn-1-ol via 4-endo-dig cyclization and the methoxylation of alkynes.

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 [3]. This complete rationalization of the counterion effect allowed us to: 1) develop a highly efficient methodology under solvent-, silver-, and acid-free conditions and 2) replace traditional volatile organic solvents with more eco-friendly ones.

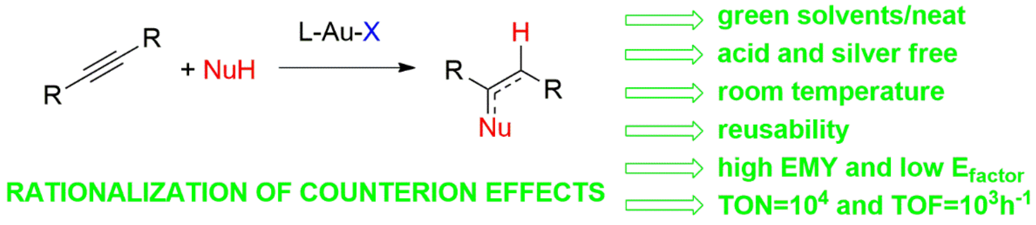

Figure 1: Global scheme depicting the aim of the project

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

Francesca Gambassi, Maria Cristina Cassani, Daniele Nanni, Ilaria Ragazzini, and Barbara Ballarin

Industrial Chemistry Department 'Toso Montanari', Alma Mater Studiorum Bologna University, Viale del Risorgimento 4, 40136-Bologna, Italy
E-mail: francesca.gambassi2@unibo.it

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 electrochemical applications. The novel material was fully characterized using several complementary techniques. Synchrotron X-ray diffraction data analysis, in particular, revealed that this MOF, labelled Cu-YBDC 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) [1].

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. The particular morphologic conformation of Cu-YBDC is also imaged by means of SEM.

Moreover, the surface electrochemical properties of this novel functionalized material are investigated as sensor for nitrite by CV techniques.

The new Cu-YBDC MOF, it is immobilized on a glassy carbon electrode by drop-casting (GC/Cu-YBDC). Afterward, GC/Cu-YBDC was treated with $HAuCl_4$ and the direct electro-deposition of Au nanoparticles was obtained (GC/Au/Cu-YBDC). The performance of both electrodes towards nitrite oxidation was tested and it was found that GC/Au/Cu-YBDC exhibited the best electrocatalytic behavior [2].

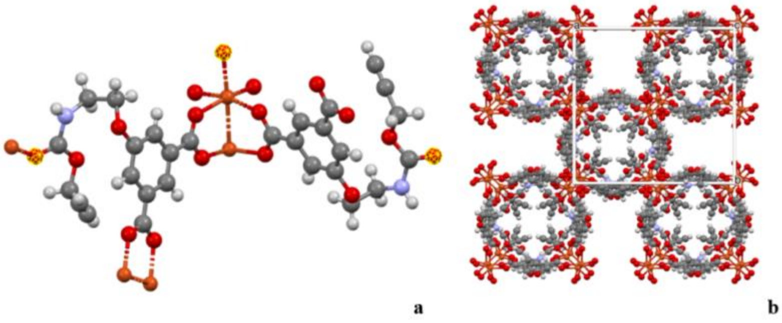

Figure 1: The paddlewheel moiety of Cu(II)-MOF (a). The MOF complex netwotk (b).

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Study of new water-soluble polythiophenes as photo-active layer in polymeric photovoltaic devices

Debora Quadretti,[a] Massimiliano Lanzi,[a,b] Martina Marinelli,[a] and Elisabetta Salatelli[a]

[a] Department of Industrial Chemistry "Toso Montanari", University of Bologna, Viale Risorgimento 4, 40136 Bologna, Italy
[b] INSTM-National Interuniversity Consortium of Materials Science and Technology, Via Giusti 9, 50121 Firenze, Italy
E-mail: debora.quadretti2@unibo.it

Due to the fast decrease of fossil resources and the growing trend towards renewable energies, several studies have been conducted in order to exploit solar energy as an alternative source. To make this possible using eco-friendlier techniques, latest researches have been focused on the development of bulk heterojunction organic solar cells (BHJ) based on water-soluble polymeric photoactive layers processable from green solvents (i.e. water and alcohols).

In this study the two water-soluble components of the BHJ photo-active blend, i.e. poly{3-[6-(tributylphosphonium)-hexyl]-thiophene-2,5-diyl bromide} ($PT6buP^+$) and malonodiserinolamide fullerene (C_{60}-Ser), have been synthesized [1] and tested in a photovoltaic device as electron-donor (ED) and electron-acceptor (EA) materials, respectively. The photovoltaic properties of the ionic homopolymer have been compared with those of a water-soluble double-cable copolymer, i.e. poly[3-(6-tributylphosphonium)-hexylthiophene]bromide-*co*-3-(6-fullerenylhexyl)thiophene] ($P[(T6buP^+)$-*co*-(T6F)]), which is easily synthesizable and combines solubility in polar solvents with improved optical properties [2].This material bears both ED-EA units in the polymer structure and the ionic moiety of side chain is the same of the homopolymer.

The synthetized materials have been characterized with spectroscopy techniques, thermal analyses and have been tested in photovoltaic devices in order to evaluate the efficiencies determined by the two types of blend. The obtained results (PCE: 3.11% for $P[(T6buP^+)$-*co*-(T6F)] vs. 2.29% for $PT6buP^+$:C_{60}-Ser) are very promising for the future research on greener organic photovoltaic solar cells.

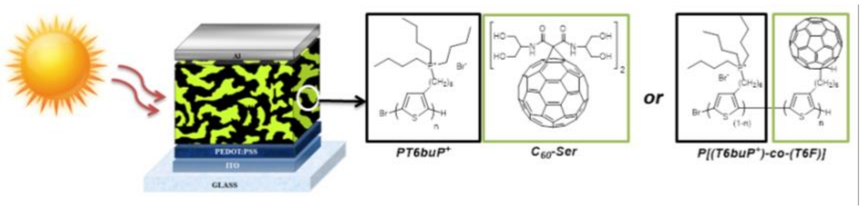

Figure 1: Scheme of two tested photo-active layers for BHJ solar cell.

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New approaches in the synthesis of furan-based diepoxy monomers

Angela Marotta,[a] Pierfrancesco Cerruti,[b] Alice Mija[c] and Veronica Ambrogi[a,b]

[a] Dipartimento di Ingegneria Chimica dei Materiali e della Produzione Industriale (DICMaPI),
Università degli studi di Napoli Federico II, p.le Tecchio 80, 80125-Naples, Italy
[b] Istituto per i Polimeri Compositi e Biomateriali (IPCB), Consiglio Nazionale delle Ricerche
(CNR), Via Campi Flegrei 34, 80078-Pozzuoli (NA), Italy
[c] Institut de Chimie de Nice (ICN), Université Côte D'Azur, Parc Valrose 28 avenue Valrose,
06108-Nice Cedex 2, France
E-mail: angela.marotta@unina.it

In consideration of the concerns about the lack of petrochemical resources and their associated environmental risks, it is mandatory to research and develop new building blocks and synthetic routes respectful towards the environment.

Furanic molecules, bio-derived compounds bearing an aromatic moiety, are valuable building blocks that can substitute petrol-derived molecules. For example, it is already proved that 2,5-furandicarboxylic acid (FDCA) is an excellent substitute of terephtalic acid in the production of polyesters with improved barrier properties. FDCA may also be a substitute of Bispehol A in the production of high-quality epoxy resins but its epoxidation requires long reaction time and hazardous reactants and solvents [1]. Therefore, the achievement of epoxy resins from FDCA monomers through simple, scalable and low environmental and human health impact protocols still represent a challenge.

In this work, two innovative synthetic routes are proposed in order to obtain the diglycidyl ester of furan (BOFD, Figure 1).

The first one involves FDCA glycidylation with epichlorohydrin (mimicking the consolidated route for glycidylation of Bisphenol A), while the second one is based on the transesterification of dimethyl 2,5-furandicarboxylate (DM-FDCA) in the presence of glycidol. The chemical structures of the obtained monomers following both procedures were validated by ^{1}HNMR, ^{13}CNMR, and FTIR spectroscopies, proving the feasibility of these new routes [2].

More efforts are now devoted to further improve the yield of reaction, through the selection of more efficient catalyst.

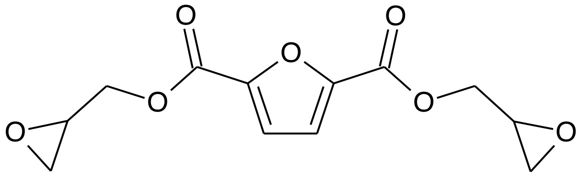

Figure 1: Chemical structure of diglycidyl ester of furan (BOFD).

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Antibacterial activity of ZnO nanorods on electrospun polyethersulfone fibers

Matteo Barcellona,[a] Mario Salmeri,[b] Giulia Ognibene,[c] Alessandro D'Urso,[a]
Gianluca Cicala,[c,d] and Maria Elena Fragalà[a,d]

[a] Dipartimento di Scienze Chimiche, Università degli Studi di Catania, Viale Andrea Doria, 6, 95125-Catania, Italy
[b] Dipartimento di Scienze Biomediche e Biotecnologiche, Università degli Studi di Catania, Torre Biologica via S. Sofia, 97, 95123-Catania, Italy
[c] Dipartimento di Ingegneria Civile ed Architettura, Università degli Studi di Catania, Viale Andrea Doria, 6, 95125-Catania, Italy
[d] Consorzio INSTM UdR, Università degli Studi di Catania, Viale Andrea Doria, 6, 95125-Catania, Italy
E-mail: mb.barcellona@gmail.com

The designing and realization of a smart-material must include a fast and easy synthesis, mild condition process, low-cost reagents, and as possible unharmful. It was evaluated the synergy of polymeric and ceramic properties of a composite material to achieve improved features.

In this work, zinc oxide (ZnO) nanorods (NRs) were grown on polyethersulfone (PES) by Chemical Bath Deposition (CBD). The growing conditions were opportunely tuned in the attempt to reach better deposition efficiency. The post-seeding annealing emerges to be a crucial step of the whole deposition process. Scanning Electron Microscopy (SEM) and Thermogravimetric Analysis (TGA) techniques supported the study of the composite synthesis and optimization.

The antimicrobial activity of the PES/ZnO mats has been evaluated on both positive and negative grams bacteria strains. The reduction of bacteria concentration can be followed by Optical Density at 600 nm (OD_{600}) and residual bacteria concentration expressed in Colony Forming Unit per milliliter (CFU/mL).

Among the numerous antimicrobial mechanisms that can take place, the cytotoxicity of zinc cations (Zn^{2+}) has been examined. In particular, the Zn^{2+} leaching from the ZnO surface was detected functionalizing a glass slide with the H_2T_4 porphyrin, which is able to coordinate the Zn^{2+} cations and express UV-Vis spectroscopic variations after the complexation [1].

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Synthesis of water-soluble hybrid nano-materials and their application in biomedical field

Giorgia Gullo, Eleonora Vaioli, and Franca Bigi

Department of Chemistry, Life Sciences an Environmental Sustainability, Università degli Studi di Parma,
Parco Area delle Scienze 17/A, 43124 – Parma, Italy
E-mail: giorgia.gullo@unipr.it

A clinical approach for the treatment of superficial cancer is the photodynamic therapy (PDT), 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 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 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*, the combination of PS and AuNP has been proposed, taking into account that under X-ray irradiation, havy elements increase the dose absorbed and then delivered to surrounding tissues and that also PS can increase the ROS production [2]. A further strategy recently published is the incorporation of PS and AuNPs into liposomes [3], 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 water soluble (4-hydroxyphenyl)porphyrin (THPP) functionalized with three polyethylenglycole chains was synthetized and the covalent binding on stabilized gold nanoparticles was studied using different thiol-ending linkers.

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The search for IDE activity modulators: new perspectives for therapeutic potentials in Alzheimer's disease

Alessia Distefano, Valentina Oliveri, and Giuseppe Grasso

Dipartimento di Scienze Chimiche, Università degli Studi di Catania, Viale Andrea Doria 6,
95125-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 inactive closed state (IDE_c) and the active open state (IDE_o), as well as in different oligomeric forms which are in equilibrium in solution. In particular, the monomeric variant of IDE (R767) is able to degrade Insulin although it has a depletion in C-region [2].

Allosteric modulation of the enzyme inducing IDE_o can be carried out both by large substrates, *i.e.* insulin, or by small molecules interacting with the IDE exosite. Moreover, as compared to large substrates, small molecules can also regulate IDE activity towards other substrates.

In this perspective, the search for small molecules modulating IDE activity can have potential therapeutic applications in the above-mentioned diseases. For this reason, we have tested L-carnosine as a possible activator of IDE. This small molecule shows a more significant neuroprotective activity against the toxic oligomeric form of $A\beta_{1-42}$ than the enantiomer D-carnosine [3].

In this respect, with the aim to investigate the IDE-carnosine interaction, Surface Plasmon Resonance (SPR) technique was applied to fully assess the effect of L-carnosine on the IDE-insulin interaction. In addition, Dynamic Light Scattering (DLS) measurements were performed to examine about the possible role of L-carnosine in conformational change/oligomerization of IDE.

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Electrochemiluminescent biosensor on BDD electrode

Claudio Ignazio Santo,[a] Andrea Fiorani,[b] Yasuaki Einaga,[b] Giovanni Valenti,[a] and Francesco Paolucci[a]

[a] Department of Chemistry "G. Ciamician", University of Bologna, Via Selmi 2, 40126 Bologna, Italy
[b] Department of Chemistry, Keio University 3-14-1 Hiyoshi, Yokohama 223-8522, Japan
E-mail: claudioignazio.santo@unibo.it

Biomarkers such as proteins, hormones, nucleic acids are biological indicators with a key role in identifying human body function variations. Electrochemiluminescence (ECL) became a leading technique in their detection for early diseases diagnosis, also thanks to high signal to noise ratio of the technique, due to the absence of a light source. ECL is a luminescent phenomenon generated by an electrochemical reaction [1]. In the commercial ECL-based immunoassays the biomarkers are detected after their immunorecognition through the creation of a labelled sandwich immunoassay attached onto magnetic microbeads. Beads are attracted to the working electrode surface using a magnet and ECL signal acquired after potential application (see scheme below). However, one of the main disadvantages of ECL in aqueous solutions is high potential necessary to produce light (typically 1.4 V), that could cause some modifications on the electrode surfaces (gold, platinum) and the generation of bubbles from water oxidation [2]. In the last years, few researchers focused their attention on the application of novel electrode materials in order to overcome those problems.

Herein, we will show the ECL application of Boron Doped Diamond electrode to beads-based immunoassay. BDD electrode exhibits superior properties, such as the fast reaction rate for the charge transfer reaction, wide potential window, low background current, high sensitivity, and high chemical stability. Thanks to its electrochemical stability, BDD allows to activate reactions that occur at high potentials without problems of the water oxidation [3]. It proved more suitable for ECL study at high oxidation potential.

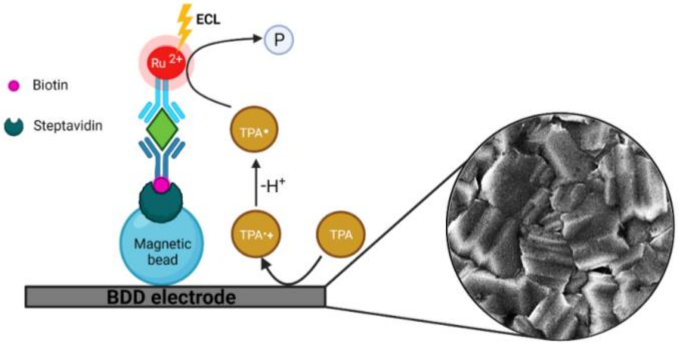

Figure 1: Schematic representation of bead-based electrochemiluminescent biosensor on BDD electrode.

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A Flower-Like Paper-Based Electrochemical Device for the Detection of Pesticides

Veronica Caratelli,[a] Greta Fegatelli,[a] Danila Moscone[a] and Fabiana Arduini[a,b]

[a] *Department of Chemical Science and Technologies, University of Rome Tor Vergata, Via dela Ricerca Scientifica, 00133-Rome, Italy*
[b] *Sense4Med s.r.l., Via Renato Rascel 30, 000128-Rome, Italy*
E-mail: veronica.caratelli@uniroma2.it

Pesticides are largely used at worldwide level to improve the food production, fulfilling the needs of the global population, which is increasing year by year. Although persistent pesticides (e.g. DDT) have been replaced with less persistent ones, contamination of food, soil and water by pesticides remains an issue of public concern. To better manage this problem, EU sets regulations for a sustainable employment of pesticides by promoting the adoption of Integrated Pest Management (Directive 2009/128/EC). In this overall scenario, the detection of pesticides in liquid and aerosol solutions at low concentrations (ppb level) is required to accomplish the regulatory aspect and to preserve the health of environment and human being. Herein, we propose a flower-like origami paper-based device for the detection of several classes of pesticides by combining different enzyme-inhibition biosensors.

This device was developed by integrating two different office paper-based screen-printed electrodes and multiple filter paper-based pads to load enzymes and enzymatic substrates. The versatile analysis of different pesticides was carried out by folding and unfolding the filter paper-based structure, without any addition of reagents and any sample treatment (e.g. dilution, filtration, pH adjustment) [1]. The paper-based platform was employed to detect paraoxon, 2,4-dichlorophenoxyacetic acid and glyphosate at ppb level by exploiting the capability of these different types of pesticides to inhibit butyrylcholinesterase, alkaline phosphatase and peroxidase enzymes respectively. The degree of inhibition, correlated to the quantity of pesticides, was chronoamperometrically evaluated, monitoring the enzymatic activity in the absence and in the presence of pesticides by using a portable potentiostat. To improve the sensitivity, the paper-based electrodes were modified with carbon black nanoparticles in the case of platforms for 2,4-dichlorophenoxyacetic acid and glyphosate detection or carbon black decorated with Prussian blue nanoparticles for the detection of paraoxon. The detection of pesticide5 in gas phase was performed using a commercial portable nebuliser (SIMBR aerosol system) and the LOD obtained was 30 ppb, 10 ppb and 2 ppb, respectively for 2,4-D, glyphosate and paraoxon.

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A rapid and simple method for fatty acids profiling by UHPLC-HRMS/MS in hemp inflorescence

Sara Elsa Aita, Andrea Cerrato, Carmela Maria Montone, and Susy Piovesana

Department of Chemistry, Sapienza University of Rome, Piazzale Aldo Moro 5, 00185, Rome, Italy
E-mail: saraelsa.aita@uniroma1.it

Industrial hemp (Cannabis sativa L.) is a versatile herbaceous crop. This fast-growing plant has recently seen a resurgence of interest because of its multi-purpose applications: it is indeed a treasure trove of phytochemicals and a rich source of both cellulosic and woody fibers. Equally highly interested in this plant are the pharmaceutical and construction sectors, since its metabolites show potent bioactivities on human health [1]. As such, a detailed characterization of the composition of this plant could help future research to further exploit the beneficial effects of hemp compounds on the human health. Among the many compounds of hemp, fatty acids represent an interesting class of minor components, which has been overlooked so far. In this work [2], an untargeted approach based on liquid-chromatography coupled to a high-resolution mass spectrometry and a dedicated structure-based workflow for raw data interpretation was employed for the characterization of fatty acids from hemp inflorescences. A simple method, without any chemical derivatization, was developed for extraction and characterization of fatty acids leading to the tentative identification of 39 fatty acid species in the five hemp samples. A quantitative analysis on the untargeted data was initially performed, using peak areas as surrogate of analyte abundance for relative quantitation. Five fatty acids resulted the most abundant in all hemp samples, with ca. 90% of the total peak area. For these compounds a targeted quantitative method was validated, indicating that the most abundant ones were linolenic acid (1.39–7.95 mg g-1) and linoleic acid (1.04–7.87 mg g-1), followed by palmitic acid (3.74–6.08 mg g-1), oleic acid (0.91–4.73 mg g-1) and stearic acid (0.64–2.25 mg g-1).

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Optimization of supercritical CO_2 oil extraction from waste of tomatoes paste production

Chiara Cavagnero,[a,b] Marco Micera,[a,b] Riccardo Destefano[a], Alfonso Botto[a] and Guido Viscardi,[b]

[a] Exenia group S.r.l. Via Carlo Borra 47, 10064 Pinerolo (TO), Italy
[b]Department of Chemistry, Università degli Studi di Torino, via P. Giuria 7, 10125 Torino, Italy
E-mail: chiara.cavagnero@unito.it

This work is intended to present a food waste material revaluation project from the food industry using supercritical carbon dioxide ($scCO_2$) as a green solvent to obtain high added value compounds. Nowadays the food industry wastes are estimated to be around 90 million tons every year [1], most of them are converted in energy, however they still contain high added value chemical compounds. This study aim is to optimize the extraction of those valuable compounds with a green extraction method without using organic solvents and following an experimental design. The research was conducted next Exenia Group, an Italian company working with $scCO_2$ since 1995; in these years it had dealt with many different $scCO_2$ application fields: from pasteurization to supercritical fluid extraction (SFE). Exenia Group is set on the research and development of new $scCO_2$ industrial applications, feasibility studies and processes optimization. The literature shows that tomatoes seeds and peels, coming from the tomatoes paste production industry, contain carotenoids such as lycopene and β-carotene, that can act as quencher of free radicals [2]. For the oil rich in lycopene extractions, an experimental design has been worked out to evaluate possible interactions among process variables. A D-optimal design with two quantitative variables (pressure and temperature) and two qualitative variables (raw material batch and CO_2 flow) has been applied. After an analysis of the plot of normalized determinant and inflation factors, it has been possible to establish the best compromise between experiments number and model explained variance. Eighteen experiments plus six repetitions have been performed. Twenty-four experiments were available to estimated 13 variables with 9 degrees of freedom. $Oil (g) = 14.15 + 2.85X_1(^{**}) + 0.08X_2 + 1.55X_3(^{*}) + 3.03X_4(^{**}) + 0.89X_1X_2 + 0.41X_1X_3 + 1.12X_1X_4 + 0.53X_2X_3 + 1.77X_2X_4(^{*}) - 0.32X_3X_4 + 0.01X_{12} + 0.12X_{22}$ Residual standard deviation: 2.63; % explained variance: 71.93. The experimental variability was acceptable with a pooled standard deviation of 2.70 (11 d.o.f, not significantly different from the residual standard deviation – no lack of fit). The linear terms for the variables pressure (X_1), flow (X_3) and time (X_4) were significant. The temperature-time interaction (X_2X_4) was also significant. The linear terms showed that higher oil extraction yields were achieved at higher pressure and higher flow rate and mainly with batch B. To understand the interaction that occurs between the variable temperature and batch the response surface has been analyzed.

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Biomimetic receptors for carbohydrates: a promising tool for the development of drug delivery systems

Francesco Milanesi,[a,b] Nastassja Burrini,[a] Roberta Giaquinto,[a] Marzia Cirri[a] and Oscar Francesconi [a]

[a] Department of Chemistry, University of Florence, Via della Lastruccia 3-13, 50019-Sesto Fiorentino, Italy
[b] CERM, University of Florence, Via Sacconi 6, 50019-Sesto Fiorentino, Italy
E-mail: francesco.milanesi@unifi.it

Targeting specific sites is a major challenge in precision medicine. Most of the current anticancer drugs are not able to differentiate between healthy and cancer cells and these led to undesired side effects. Glycosylation on cell surface is an important fingerprint in cancer cells; in some tumors, high-mannose type oligosaccharides are over-expressed and they represent an attractive therapeutic target to tune anticancer drugs [1]. Biomimetic receptors, small abiotic molecules capable of recognizing carbohydrates by non-covalent interactions under physiological conditions, are a promising tool to cope this issue [2]. Indeed, decorating an anticancer drug-containing nanovesicle with a biomimetic receptor for mannosides (**Figure** 1) could tune drug releasing only in highly mannosilated cancer cells [3]. In this study we present the development and characterization of niosomes functionalized with biomimetic receptors for mannose-targeted antitumoral drug delivery.

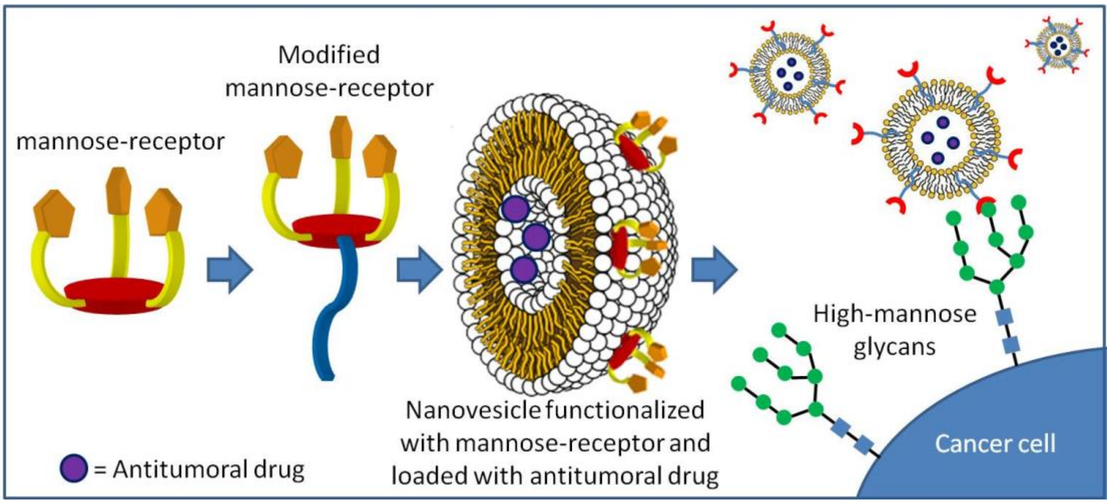

Figure 1: Design of decorated niosomes.

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N-adamantyl-antranil amide derivatives: new selective ligands for the CB2 receptor

Giovanni Graziano,[a] Pietro Delre,[b] Jose Manuel Brea,[c] Francesca Carofiglio,[a] Francesca Intranuovo,[a] Claudia Gioè,[d] Maria Majellaro,[d] Orazio Nicolotti,[a] Nicola Antonio Colabufo,[a] Carmen Abate,[a] Maria Isabel Loza,[c] Eddy Sotelo,[d] Giuseppe Felice Mangiatordi,[b] Marialessandra Contino,[a] Angela Stefanachi*[a] and Francesco Leonetti[a]

[a] Department of Pharmacy-Pharmaceutical Sciences, University of the studies of Bari "Aldo Moro", via E.Orabona 4, 70125-Bari, Italy
[b] CNR – Institute of Crystallography, Via Giovanni Amendola, 122/O, 70126-Bari, Italy
[c] Center for Research in Molecular Medicine and Chronic Diseases (CIMUS), University of Santiago de Compostela, Av. Barcelona, 15782-Santiago de Compostela, Spain
[d] Department of Organic Chemistry, Faculty of Pharmacy, University of Santiago de Compostela (CIQUS), C/ Jenaro de la Fuente s/n, 15782-Santiago de Compostela, Spain
E-mail: giovanni.graziano@uniba.it

The endocannabinoid system is essentially composed by endocannabinoids that bind to the two G-protein-coupled receptors (GPCR): CB1R and CB2R. CB1 receptors are highly expressed in the central nervous system (CNS), where its activation leads to unwanted psychotropic effects, whereas CB2 receptors are predominantly, although not exclusively, concentrated in the cells of the immune system. In the last decade, several studies have shown that the CB2R is overexpressed in activated CNS microglia cells, in disorders based on an inflammatory state such as neurodegenerative disorder, neuropathic pain, and in cancer cells [1,2]. For this reason, the anti-inflammatory, and the immune-modulatory actions of CB2 ligands can be a catchy therapeutic option for these diseases. Supported by computational studies, we focused our attention on the design and the synthesis of new CB2 selective modulators. The main difficulties we have faced in the design of selective ligands were due to the high homology between the two receptors [3]. We rationally designed and synthesized, new N-adamantyl-antranil amide derivatives (Figure 1) and we evaluated them for their affinity and selectivity profile towards CB2R. Several compounds showed good affinity values towards CB2R and selectivity with respect to the CB1R subtype. For the compounds showing the best pharmacodynamic profiles, activity studies are ongoing to better understand their pharmacological potential.

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Covalent inhibition mechanism of SARS-CoV-2 Main protease by Ebselen-like inhibitors: a computational study

Angela Parise,[a,b] Isabella Romeo,[a] Nino Russo,[a] and Tiziana Marino[a,]

[a] *Dipartimento di Chimica e Tecnologie Chimiche, Università della Calabria, Via Pietro Bucci,*
87036 Arcavacata di Rende, CS, Italy
[b] *Institut de Chimie Physique UMR8000, Université Paris-Saclay, CNRS, 91405 Orsay, France*
E-mail: angela.parise@unical.it

Antiviral drugs for the management of human coronavirus infections represent a serious challenge in current global efforts to counter the serious consequences of the spread of COVID-19 syndrome. Coronavirus genome encodes several structural proteins including the glycosylated spike S-protein that acts as a major inducer of host immune responses. The viral genome also encodes several nonstructural proteins including RNA-dependent RNA polymerase (RdRp), coronavirus main-protease (Mpro) and papain-like protease (PLpro) [1]. Considering that Mpro is only found in the virus rather than in the host cell, this protein represents an interesting target for the development of new promising anti-coronavirus therapeutic agents. The inhibition mechanism of the main protease (Mpro) of SARS-CoV-2 by ebselen (EBS) and its analog with a hydroxyl group at position 2 of the benzisoselenazol-3(2H)-one ring (EBS-OH) was studied by using a density functional level of theory. Preliminary molecular dynamics simulations on the apo form of Mpro were performed taking into account both the hydrogen donor and acceptor natures of the Nδ and Nε of His41, a member of the catalytic dyad [2]. The knowledge of the inhibition mechanism of Mpro by the small protease inhibitors EBS or EBS-OH can enlarge the possibilities for designing more potent and selective inhibitor-based drugs to be used in combination with other antiviral therapies.

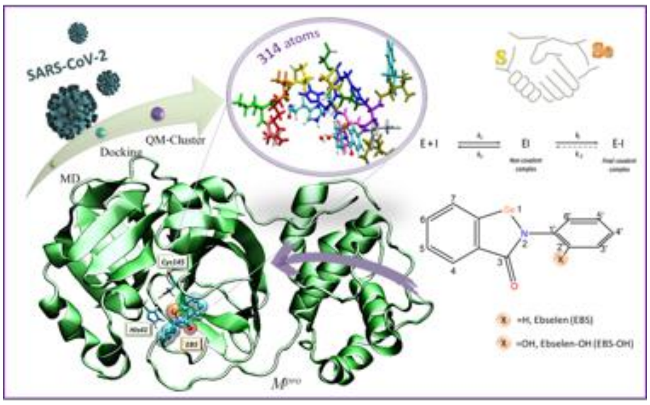

Figure 1: Mpro cartoon representation, QM-cluster model used for DFT calculations and Ebselen-like inhibitor structures.

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Broadly applicable hydrogel fabrication procedure for mechanobiology investigation

Veronica Torresan,[a] Alessandro Gandin,[a] Lorenzo Ulliana,[b] Tito Panciera,[b]
Anna Citron,[b] Stefano Piccolo,[b] and Giovanna Brusatin,[a,c]

[a] *Dipartimento di Ingegneria Industriale, Università degli studi di Padova, Via Marzolo 9, 35131 Padova (PD), Italy*
[b] *Dipartimento di Medicina Molecolare, Università degli studi di Padova, via Ugo Bassi 58/B, 35131, Padova (PD), Italy*
[c] *INSTM, Via Giuseppe Giusti 9, 50121, Firenze (FI), Italy*
E-mail: veronica.torresan@phd.unipd.it

Mechanobiology represents a merging field between materials science, chemistry, physics and biomedicine, that in the recent years has raised increasing interest to investigate the effects of mechanical signals on cell behavior and to understand cell mechanics. [1] This is fundamental for tissue engineering and regenerative medicine. A great limitation in this field remains the lack of fundamental understanding of the interaction between the material and cells. In this regard, hydrogels have emerged as essential tool for mechanobiology investigations thank to their capability to mimic the natural tissue in term of stiffness and adhesiveness. On the other hand, synthesis and functionalization of these tools are quite difficult for a biological laboratory related to the lacking of material science expertise.

Here, we optimized materials designed as 2D substrates for mechanobiology investigation based on Polyacrylamide (PAA) and 8-arm polyethylene glycol (PEG).

In particular, regarding PAA based hydrogel, we optimized the functionalization with adhesive proteins overcoming the low conjugation efficiency of previous protocols [2] and we optimized the throughput of the synthesis. We introduced the N-hydroxyethyl acrylamides (HEA) in the PAA formulation to make available the -OH coupling with fibronectin, a natural adhesive protein of the extracellular matrix. Finally, we developed an easily, tunable and degradable system in which not only the stiffness is finely modulated, but also the density of the adhesive sites, using 8-arm Norbornene terminated polyethylene glycol (PEG) as macromer. In particular we optimized a system [3] in which it's possible tuning the stiffness from <1 kPa to >20 kPa and the concentration of adhesive site from 0.5 mM to 3 mM, using a YAP/TAZ mechanosensors as universal mechanical rheostat.

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Emissive 2D Mn - based hybrid metal halides

Marta Campolucci,[a,b] Sophia Victoria Ochoa Meza,[a] Emanuela Sartori,[a,b]
Liberato Manna,[b] Federico Locardi,[a,b], and Maurizio Ferretti,[a]

[a] *Dipartimento di Chimica e Chimica Industriale, Università degli Studi di Genova, Via Dodecaneso 31, 16146, Genova, Italy*
[b] *Nanochemistry Department, Istituto Italiano di Tecnologia, Via Morego 30, 16163 Genova, Italy*
E-mail: marta.campolucci@edu.unige.it

Starting from the well-studied ABX_3 (A = $CH_3NH_3^+$, Cs^+; B = bivalent metal cation, X = Cl^-, Br^-, I^-) perovskite, new derivates can be obtained with the partial or full substitution of the A and B cations with different metal ions [1]. The introduction of larger or smaller cations in the A site favors the formation of polymorphs of a lower dimensionality (2D or 0D). To date, one of the most promising strategy to tune and confer excellent optoelectronics is the insertion of an organic cation instead of an inorganic one. These structures are called "hybrid metal halides" [2]. Promising compounds can be obtained starting from the emissive Mn-based stoichiometries $AMnX_3$. $CsMnBr_3$ is a lead-free and red-emitting compound with a PLQY of 54% [3].

Here, we present the recent results achieved in the preparation of a new emissive 2D Mn-based hybrid metal halide as single crystals. Starting from the reported synthesis of $CsMnBr_3$, the Cs^+ cation was progressively substituted with the butylammonium BA cation ($C_4H_{12}N^+$) leading to a new phase, presenting an interesting orange emission. The obtained sample crystallizes in orthorhombic system and present the BA_2MnBr_4 stoichiometry; the crystal structure consists of monolayers of connected $[MnBr_6]$ octahedra stacked by two BA^+ forming. The synthesis used is based on the dissolution of the precursors ($MnCO_3$ and BABr) in an acid media (HBr), followed by the slow solvent evaporation. The characterization of these materials is made using techniques such as XRD, FTIR, DTA-TG coupled with GC-MS, ABS, PLE, PL.

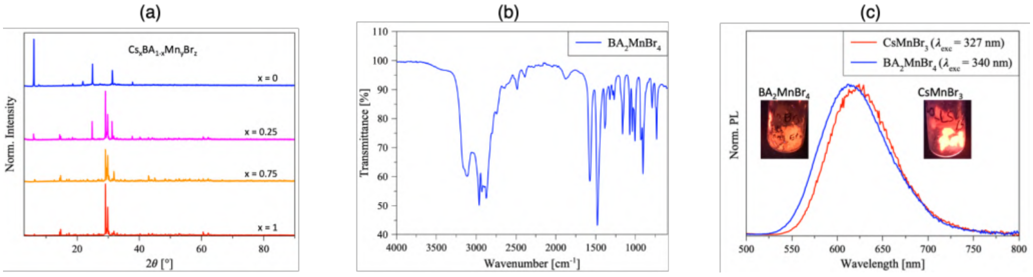

Figure: (a) Experimental powder patterns of the samples with $Cs_xBA_{1-x}Mn_yBr_z$ composition, with increasing amount of BA. (b) FTIR spectra of BA_2MnBr_4. (c) PL spectra with images under UV lamp (λ = 365 nm) of crystals' $CsMnBr_3$ and BA_2MnBr_4.

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Electrochemistry and ECL of novel polycyclic aromatic derivatives of Benzo[rst]pentaphene

Lorenzo Ripani[a], Xiushang Xu[b], Akimitsu Narita[b], and Massimo Marcaccio[a]

[a] *Department of Chemistry "G. Ciamician", University of Bologna, Via Francesco Selmi 2, Bologna, Italy*
[b] *Department of Chemistry, Okinawa institute of science and technology, Okinawa, Japan*
E-mail: lorenzo.ripani2@unibo.it

Planar and curved polycyclic aromatic hydrocarbons (PAHs) constitute a large class of organic molecules with an extended and delocalized π-system that provides interesting properties for optoelectronic [1] and energy storage applications [2]. In the framework of our recent work on corannulene oligomerization [3], we investigated a series of benzo[rst]pentaphene (BPP) derivatives which, in principle, could lead to an extension of the aromatic π-system through an anodic oligomerization on the electrode followed by an electrochemically induced cyclodehydrogenation reaction.

In this study, we report the electrochemical characterization by cyclic voltammetry of a family of pristine and mesitylene substituted mono- and dimeric BPP. The presence of bulky and non-linear side groups, as mesitylene (Mes), provides a more stable electrochemical behavior. Furthermore, the photophysical properties of BPP and its derivatives have been investigated by electrochemiluminescence (ECL) and spectro-electrochemistry.

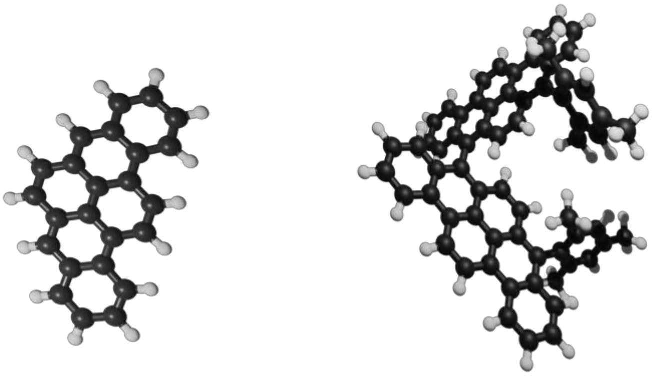

Figure 1: Molecular structures of benzo[rst]pentaphene (BPP) and substituted dimer of BPP.

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Colloidal $Cu_{2-x}S$ nanocrystals: size, shape and phase modulation

Mariangela Giancaspro,[a] Teresa Sibillano,[b] Francesca Panzarea,[a] Cinzia Giannini,[b], Silvia Schmitzer,[a] Fabio Vischio,[a,c] Nicoletta Depalo,[c] Angela Agostiano,[a,c,d] Maria Lucia Curri,[a,c,d] Marinella Striccoli,[c] and Elisabetta Fanizza[a,b]

[a] *Chemistry Department, Università degli studi di Bari Aldo Moro, Via Orabona 4, 70126-Bari, Italy*
[b] *CNR-Istituto di Cristallografia (CNR-IC), Via Amendola, 122/O, 70126-Bari, Italy*
[c] *CNR-Istituto per i Processi Chimico-Fisici (CNR-IPCF), SS-Bari, Via Orabona 4, 70126-Bari, Italy*
[d] *National Interuniversity Consortium of Materials Science and Technology (INSTM), Italy*
E-mail: mariangela.giancaspro@uniba.it

Self-doped copper sulphide $Cu_{2-x}S$ nanocrystals (NCs) are p-type semiconductors with fascinating near infrared (NIR) plasmonic properties beneficial in a wide variety of applications such as catalysis, energy conversion, sensing and biomedicine [1,2]. Due to their stoichiometry-, size- and shape- dependent properties, the NCs design is essential for producing high performances devices. Even though progress in controlling geometry and optical properties has been made in $Cu_{2-x}S$ NCs synthesis by hot injection, unexpected sizes and shapes and broad polydispersity still represent critical problems. This work aims to address such limitations giving an insight into the influence of reactants on $Cu_{2-x}S$ NCs size, shape and phase modulation.

Various conventional copper precursors (i.e. CuCl, $CuCl_2$, $Cu(AcAc)_2$, $Cu(AcO)_2$), sulphur reactants (i.e. S_8, tert-dodecanthiol (tDT) or dibuthyldisulfide (DBDS)) and coordinating solvents (oleic acid, OA and oleylamine, Olam) have been used to prepare $Cu_{2-x}S$ NCs by hot injection method. A systematic morphological, structural, and spectroscopic analysis of $Cu_{2-x}S$ NCs samples have been carried out.

The $CuCl > CuCl_2 > Cu(AcO)_2 > Cu(AcAc)_2$ order of reactivity directly affect the rate of monomer release controlling the size and shape monodispersity. While the type of counterions, balanced by the ligand composition, has been proven to define the final NC shape when S_8 is used as sulfur precursor, in the case of alkanethiol, the formation of hexagonal monodispersed thin NPLs is templated by hexagonal discotic micellar structures of chloride Cu-tDT liquid crystalline phase. The intrinsic poor reactivity of organosulphur, injected in situ provides the djurlite $Cu_{1.94}S$ whereas S_8, decomposed ex situ in coordinating reducing solvent, has led to digenite $Cu_{1.8}S$ NCs [3]. Overall, this work has effectively contributed to the fundamental understanding of the complex mechanism responsible for the formation of $Cu_{2-x}S$ NCs, providing a valuable toolbox, to achieve NCs with controlled structural and morphological characteristics.

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Poster presentations

PO01	Filomena TEDESCO
PO02	Lorenza DESTRO
PO03	Jacopo TRICOMI
PO04	Anna FONTANA
PO05	Ruggero ROSSI
PO06	Alessandro PAPA
PO07	Francesca CLEMENTE
PO08	Giulia DAVIGHI
PO09	Debora PRATESI
PO10	Michela PUXEDDU
PO11	Jessica SEBASTIANI
PO12	Desirée PECORA
PO13	Valentina LAZAZZARA
PO14	Carolina CANÈ
PO15	Giuliana PREVETE
PO16	Gabriele PIRODDA
PO17	Lilia LONGO
PO18	Valentina PETRELLI
PO19	Chiara PORTOLANI
PO20	Maurizio CHIMINELLI
PO21	Tommaso LORENZETTO
PO22	Andrea DI VERA
PO23	Angela MALARA
PO24	Mariacristina BIANCO
PO25	Luca RIVOIRA
PO26	Francesca TUNIOLI
PO27	Saul SANTINI
PO28	Chiara SARTI
PO29	Martina NERI
PO30	Lapo RENAI
PO31	Alice CANTALUPI
PO32	Alessandro MONARI
PO33	Luca FIORE
PO34	Stefano CRESPI
PO35	Alessandra CICOLELLA
PO36	Angelo GIORDANO
PO37	Fabio DE STEFANO
PO38	Rosarita D'ORSI
PO39	Luca LAZZARIN
PO40	Gioacchino SCHIFINO
PO41	Manuel IMPERATO
PO42	Alessia BELLONI
PO43	Fabio BUONSENSO
PO44	Matteo ATZORI
PO45	Sebastiano TIEULI

Short synthesis of 2-oxopiperazine scaffolds for non-peptide α-helix mimetics

Filomena Tedesco, Elena Lenci, and Andrea Trabocchi

Dipartimento di Chimica "Ugo Schiff", Università degli Studi di Firenze, Via della Lastruccia 3-13, 50019-Sesto Fiorentino, Italy
E-mail: filomena.tedesco@unifi.it

Protein-protein interactions (PPIs) are involved in numerous biological processes and their dysregulation is observed in a multitude of pathological conditions, such as infections, cancer, diabetes. Thus, the development of molecules able to target PPIs is of interest for the development of novel therapeutic agents. Since a high percentage of PPIs are mediated by α-helical structure at the interacting surface, several research groups have developed α-helix mimetics, such as foldamers and peptoids, capable of replacing the essential conformational components of helices (Figure 1a) [1,2].

Our research group has focused the attention on the design and synthesis of novel peptidomimetics inhibitors of the SARS-CoV-2 ACE-2/Spike interaction. In particular, after the optimization of a synthetic strategy reported in the literature [3], using L-Phe and Gly amino acids precursors, we have synthetized two differently functionalized 2-oxo-piperazine scaffolds, with good yields (Figure 1b). These building blocks, showing optimal drug-like properties, will be used to develop oligomeric structures as potential inhibitors to be screened against the SARS-CoV-2 Spike protein.

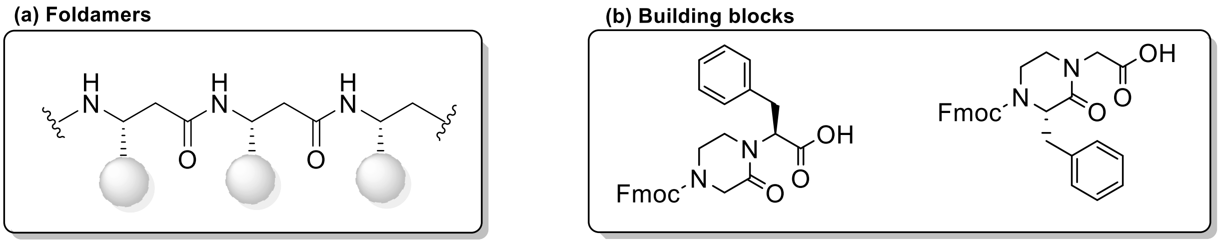

Figure 1: a) Schematic representation of foldamers; b) Building blocks 2-oxo-piperazine.

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Expedient approach to type II PKI by sequential condensation and MW-assisted Suzuki coupling

Lorenza Destro,[a] Luca Mologni,[b] Valentina Crippa,[b] Giovanni Marzaro,[c] and Alfonso Zambon [a]

[a] Department of Chemical and Geological Sciences, University of Modena and Reggio Emilia,
Via Campi 103, 41125 Modena, Italy
[b] Department of Medicine and Surgery, University of Milan-Bicocca, 20900 Monza, Italy.
[c] Department of Pharmaceutical and Pharmacological Sciences, University of Padova
via F. Marzolo 5, 35131 Padova - Italy
E-mail: lorenza.destro@unimore.it

FLT3 and RET protein kinases (PKs) are often concomitantly activated in acute myeloid leukemia (AML), a type of blood cancer with poor prognosis and limited therapeutic options[1]. Our current research aims at the development of dual inhibitors of RET and FLT3 that could meet the medical needs of the large portion of AML patients showing abnormalities in both these proteins.

We identified as starting scaffold a specific Type II chemotype of Protein Kinase Inhibitors (PKIs), enticing an aromatic pyrazole linked to a urea moiety. This scaffold has been shown to confer therapeutic efficacy against specific targets PKs [2,3]; first generation tool compounds have already shown interesting activities against both proteins. We are thus in a favorable position to develop dual inhibitors able to act on both FLT3 and RET, and to study the structural features that drive the selectivity of the chemotype for those of kinases.

In order to access efficiently the chemical space of our inhibitors, we designed an expedient synthetic route enticing a limited number of high yielding steps with little purification issues. The main diversity points of the scaffold are introduced late in the synthetic line, in order to limit the number of exclusive reactions needed for each analogue.

Key to this route is a MW-assisted Suzuki cross-coupling on the problematic benzo-urea scaffold, which reduces the number of reactions needed to synthesize analogues of g. The introduction of this new synthetic protocol allowed us quick access to a number of target analogues, enriching our library and allowing us to investigate in depth the chemical space of our RET/FLT3 inhibitors.

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Working in the puzzling world of G-Protein Coupled Receptors (GPCRs): the case of β-Adrenergic Receptors (β-ARs)

Jacopo Tricomi,[a] Athanasios Papakyriakou,[b] Ugo Cavallaro,[c] Jillian Baker,[d] and
Barbara Richichi[a]

[a] Department of Chemistry "Ugo Schiff", University of Florence, Via della Lastruccia 3-13,
50019, Sesto Fiorentino (FI), Italy
[b] Institute of Biosciences & Applications "Demokritos", Νεαπόλεως 27, 153 41, Athene, Greece
[c] European Oncological Institute (IEO), Via Ripamonti 435, 20141 Milan, Italy
[d] School of Life Sciences, University of Nottingham, Nottingham NG7 2RD, UK
E-mail: jacopo.tricomi@unifi.it

β-adrenergic receptors (β-ARs), comprising three subtypes (β1/β2/β3-ARs), are members of the G-protein-coupled receptors (GPCRs) that mediate a wide range of catecholamine-induced physiological responses. Recent reports proved that β-ARs, mainly β2- and β3-ARs, are significantly overexpressed in multiple tumor types and the levels of β-ARs correlate with disease stage and prognosis [1]. β-ARs signaling is involved in boosting many important aspects of malignant phenotype, thus, opening a new area of oncological research called 'Neurobiology of cancer' [2]. The widespread distribution of β-ARs in the human body makes the identification of selective ligands able to modulate β-ARs signaling a sought-after goal. However, drug discovery must deal with several issues associated to the pharmacology and the structural properties of β-ARs [3]. Indeed, the structural plasticity of β-ARs (i.e., they adopt different conformations within active/inactive states), and the limited availability of X-ray crystal structures complicate the study of the pharmacological properties of the β-AR ligands. Then, the ligand-directed signaling, namely the ability of β-AR ligands to direct the signaling toward one pathway or another according with the state and the conformation of the receptor they bind, makes also challenging the selection of the proper *in vitro* models to study the binding and the functional activity of the ligands. This communication reports on our approach to move forward in β-AR ligands drug discovery. In particular, we describe our efforts in the identification of selective chemical tools either for the study of pharmacology and the biological effect in model diseases of β-ARs. In doing so, the identification of new molecular entities enables exploring in-depth the ligand space around the previously reported ligands, leading to further structural clues for β-AR activity/selectivity.

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Discovery of azetidine-2-one as new cap group for the development of selective HDAC6/8 inhibitors

Anna Fontana,[a] Simone Brogi,[b] Sandra Gemma,[a] Lucia Altucci,[c] Stefania Butini,[a] and Giuseppe Campiani [a]

[a] *Department of Biotechnology, Chemistry and Pharmacy, University of Siena, 53100 Siena, Italy;*
[b] *Department of Pharmacy, University of Pisa, 56126 Pisa, Italy;*
[c] *Department of Precision Medicine, University of Campania "Luigi Vanvitelli", 80138 Naples, Italy.*
E-mail: a.fontana5@student.unisi.it

Histone deacetylases (HDACs) are promising therapeutic targets for the treatment of cancer and rare diseases due to their involvement in the onset of several pathophysiological pathways [1]. Recently, considerable efforts have been directed toward the development of isoform-selective HDAC inhibitors (HDACis) to limit the side-effects associated to the therapy with pan-HDACis [2]. Taking into account the beneficial effect deriving from simultaneous, and selective, inhibition of the isoforms 6 and 8, we focused on the research of dual acting small molecules [3]. To this end, we reasoned that azetidin-2-one, being a privileged scaffold in medicinal chemistry, could represent an innovative and druggable cap-group. Thus, we have developed a new set of compounds (**1a-i**, Fig.1), having an appropriately functionalized azetidin-2-one core, that showed selectivity toward *h*HDAC6/8 over the *h*HDAC1 isoform as resulted from the enzymatic studies. These data were corroborated by thorough structure−activity relationship studies, computational studies and western blotting analysis. These latter studies demonstrated the engagement of the target enzymes at the cellular level (Fig. 1). The data collected so far highlighted a promising potentiality of these compounds to behave as useful pharmacological tools.

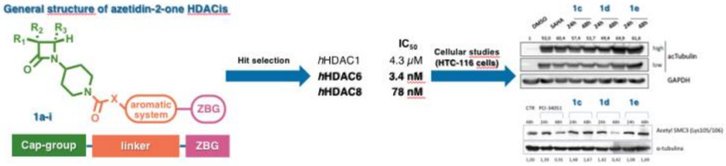

Figure 1: Discovery of new selective HDAC6/8 inhibitors.

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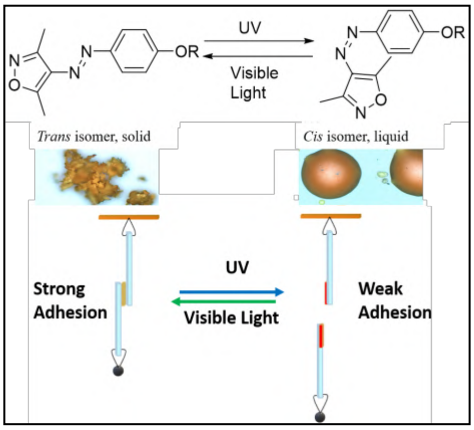
New azo based polymers for light-responsive adhesives

Ruggero Rossi[a], Daniele Martella[a,c], Benedetto Pizzo[d], Camilla Parmeggiani[a,b]
and Antonella Salvini[b]

[a]*European Laboratory for Non Linear Spectroscopy, Università degli studi Firenze, Sesto F.no, Italy*
[b]*Department of Chemistry "Ugo Schiff", Università degli studi di Firenze, Sesto F.no, Italy*
[c]*Istituto Nazionale di Ricerca Metrologica (INRiM), Torino, Italy*
[d]*Institute for the Bioeconomy (CNR-IBE), Italian National Research Council, Sesto F.no, Italy*
E-mail: rossir@lens.unifi.it



Light-responsive polymers are currently the best answer to many technological questions, from the biomedical field to the adhesive world. Looking at this second research field, reversible adhesion between different surfaces play a crucial role in many technological application and requires the use of solvents or thermal treatments to remove the adhesive. However, these solutions are not adequate for certain environments (e.g. underwater) or materials (e.g. glass). In this communication, we present an alternative approach based on photoresponsive compounds which have been tested as photoreversible adhesives. The proposed solution should lead to a series of advantages because light stimulus is less aggressive than heat, it can be localized, remotely controlled, and it is cheap. With this aim, we synthesized and characterized different formulations containing an arilazoisoxazolic moiety which presents a UV light induced photoisomerization around the azoic chromophore.

During the isomerization the adhesive strength of the formulation can be tuned up to obtain a complete debonding of the two glasses. We demonstrated how the insertion of an arylazoisoxazolic moiety in a polymeric matrix allows for a significant increase in the adhesive strength as well as a better photoresponsivity than the corresponding monomer [1]. Moreover, the polymer is also easier to spread as a thin film thus more suitable for application on different surfaces. The same photoresponsive moieties will be inserted in Liquid Crystaline Elastomers (LCE) systems to prepare artificial cardiac tissues. Those new formulations could show a more efficient conversion of light into mechanical energy comparing to azobenzene based materials.

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Development of novel optimized FAAH inhibitors as tools for neuroinflammatory conditions

Alessandro Papa,[a] Fabrizio Vincenzi,[b] Alessio Lodola,[c] Sandra Gemma,[a] Katia Varani,[b] Marco Mor,[c] Stefania Butini,[a] and Giuseppe Campiani [a]

[a] Department of Biotechnology, Chemistry and Pharmacy, DoE Department of Excellence 2018-2022, University of Siena, via Aldo Moro 2, Siena-53100, Italy
[b] Department of Translational Medicine, University of Ferrara, via Fossato di Mortara 17-19, Ferrara-44121, Italy
[c] Dipartimento di Scienze degli Alimenti e del Farmaco, Università degli Studi di Parma, Parco Area delle Scienze 27/A, I-43124-Parma, Italy
Email: alessandro.papa@student.unisi.it

Fatty acid amide hydrolase (FAAH) is a membrane-bound enzyme that *in vivo* controls content and biological activity of *N*-arachidonoylethanolamine (AEA) and other relevant bioactive lipids, termed endocannabinoids (ECs), which act as cannabinoid receptor type 1 and type 2 ligands. The 3D structure of FAAH shows its homodimeric nature, characterized by multiple channels for the simultaneous access to both membrane and cytosolic cell compartment [1]. Augmentation of endocannabinoid (EC) tone through FAAH inhibition is a valuable therapeutic approach to enhance anti-inflammatory and anti-nociceptive effects CB1 and CB2 mediated [2]. Taking inspiration from our previous work we rationally designed a new library of carbamate-based FAAH inhibitors embedding ionizable functions for improving water solubility compared to previous analogues, while maintaining nanomolar inhibition potency towards the enzyme. In-depth computational studies, coupled with specific enzymatic assays allowed rationalizing the observed enzyme inhibition properties for the developed compounds. Selected analogues were effective in reducing oxidative stress by preventing the production of reactive oxygen species (ROS) in neuronal cells. Compounds toxicity was evaluated on fibroblast murine cell line and astrocytes, while solubility was determined by HPLC.

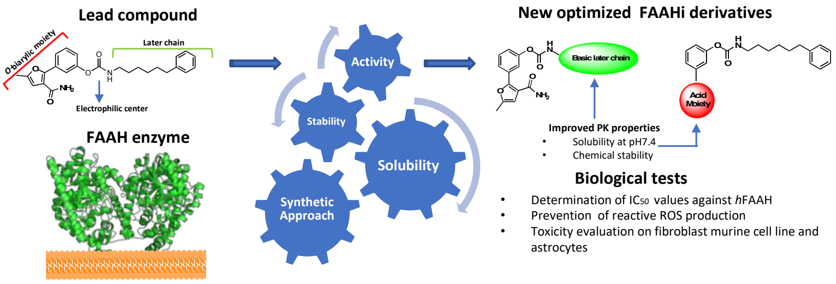

Figure 1: rational approach in the development of novel optimized FAAH inhibitors.

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PO07

Synthesis of new substituted trihydroxypiperidines and evaluation of their activity towards lysosomal β-galactosidase

Francesca Clemente, Maria Giulia Davighi, Macarena Martínez-Bailén, Camilla Matassini, Andrea Goti, Francesca Cardona

Dipartimento di Chimica “Ugo Schiff” DICUS, Università di Firenze, Via della Lastruccia 3-13,
50019 Sesto Fiorentino, Italia
E-mail: francesca.clemente@unifi.it

Pharmacological chaperones (PCs) are small compounds able to rescue the activity of mutated lysosomal enzymes favoring their correct folding in the endoplasmic reticulum and facilitating its translocation to the lysosomes when used at subinhibitory concentration. Nitrogen-containing glycomimetics such as aza- or iminosugars are known for their crucial role in glycosidase and glycosyltransferase inhibition. More recently, aza- and iminosugars became attractive as potential therapeutic agents toward lysosomal storage disorders (LSDs), following the observation of their counter-intuitive effect in enhancing the enzyme activity, thus acting as PCs [1]. In particular, defective activity of lysosomal β-galactosidase (β-gal), which is responsible for the hydrolytic removal of a terminal β-galactose residue from several glycoconjugates, leads to two different LSDs, the sphingolipidosis GM1-gangliosidosis and the Mucopolysaccharidosis IVB [2].

A series of variously substituted trihydroxypiperidine azasugars with different substitution patterns on the piperidine nucleus were synthesized (Figure 1) and their activity against β-gal was tested in order to carry out a structure activity relationship (SAR) study for the identification of new potent β-gal PCs. All the new compounds were achieved with efficient and stereoselective synthetic approaches starting from low cost D-mannose [3].

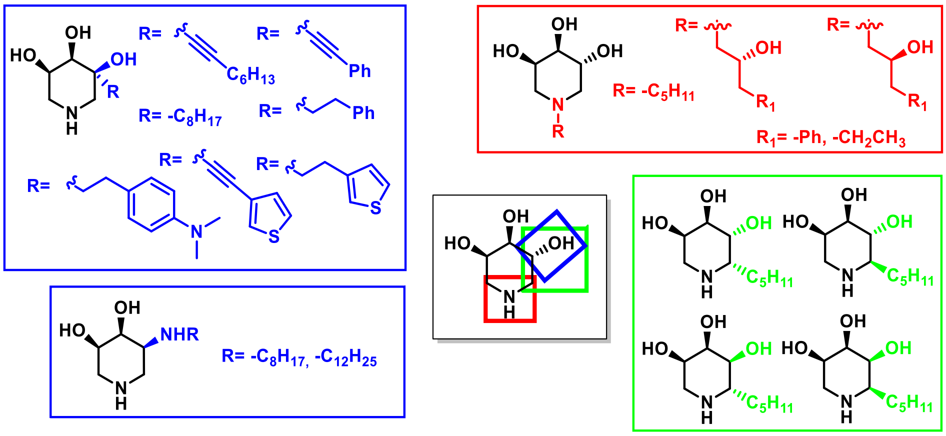

Figure 1: New differently substituted trihydroxypiperidine azasugars.

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Photoswitchable GCase inhibitors

Maria Giulia Davighi, Francesca Clemente, Camilla Matassini, Martina Cacciarini, Francesca Cardona, and Andrea Goti

Department of Chemistry 'Ugo Schiff', University of Firenze, via della Lastruccia 3-13, 50019 Sesto Fiorentino (FI), Italy
E-mail: mariagiulia.davighi@unifi.it

Pharmacological Chaperones therapy (PCT) is emerging as promising therapeutic approach for the treatment of lysosomal storage disorders (LSD). Gaucher disease, the most common LSD, is caused by deficiencies in the activity of β-glucocerebrosidase (GCase), the enzyme which hydrolyses glucosylceramide to ceramide and glucose. GCase malfunctioning resulted in the accumulation of lysosomal glucosylceramide, ultimately leading to organ disfunction. Pharmacological Chaperones (PCs) are small molecules able to recover the enzymatic activity when used at sub-inhibitory concentration [1], acting as reversible inhibitors of the enzyme and thus minimizing side effects. Nitrogenated glycomimetics, such as aza- and iminosugars, are known to behave as PCs for Gaucher disease. The aim of this project is the development of a novel collection of stimuli responsive azasugars connecting a trihydroxypiperidine to light-sensitive [2] functionalities such as dihydroazulene and azobenzene. The incorporation of a photoswitchable linker to an azasugar aims at a structural change of the PCs within time and therefore at modulating its binding affinity after it has entered the lysosome and helping the replacement of the PCs by glucosylceramide. The half-life of the light sensitive compounds has been investigated by UV-Vis and NMR spectroscopy. The inhibitory and chaperoning activity of all the compounds and their corresponding irradiated forms were evaluated towards the enzyme GCase. We also investigated the importance of azasugar skeleton in the inhibitory activity and the role of the scaffold through the comparison with some other reference compounds. The evaluation of cell viability for the synthetized compounds together with a thermal stabilization study will be reported.

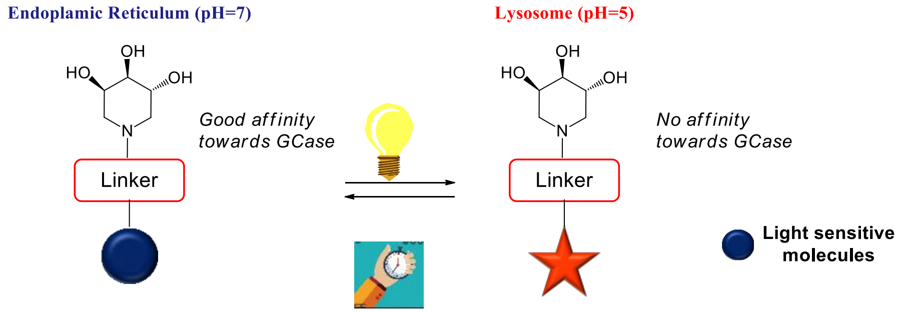

Figure 1: Structures of light sensitive compounds.

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Value added chemicals from biomass: stereocontrolled synthesis of 4-aminosugars from cellulose

Debora Pratesi,[a] Camilla Matassini,[a] Rolando Spanevello,[b] Francesca Cardona,[a] and Andrea Goti[a]

[a] Dipartimento di Chimica 'Ugo Schiff', Università degli Studi di Firenze, via della Lastruccia n. 3-13, Sesto Fiorentino (FI) 50019, Italy.
[b] Instituto de Química Rosario, Facultad de Ciencias Bioquímica y Farmacéuticas, Universidad Nacional de Rosario, CONICET, Suipacha 531, S2002LRK Rosario, Argentina.
E-mail: debora.pratesi@unifi.it

Pyrolysis is one of the most promising technologies for using biomass. In particular, the pyrolysis of cellulose, as well as of urban and industrial residual materials containing cellulose (such as waste paper), leads to the formation of levoglucosenone (**1**), a small molecule which may be used for the synthesis of biologically relevant compounds [1]. Allyl cyanate to isocyanate rearrangement reactions of glycals have recently been reported to afford aminosugars under metal free conditions and with complete stereocontrol [2]. We therefore envisaged that this innovative strategy could be applied to levoglucosenone-derived allyl alcohols **2** and **3**. These compounds were synthesized and transformed into the corresponding carbamates **4** and **5**, precursors of the required allyl cyanate for the rearrangement. The process involves three steps, which are usually performed in one-pot: the initial dehydration of the carbamate to the corresponding elusive cyanate is followed by spontaneous [3,3]-sigmatropic rearrangement to the isocyanate, which is conveniently trapped with a nucleophile (*O*- or *N*-nucleophiles) to afford the final products **6** and **7**. The rearrangement allows to install a nitrogen functionality at C-4. After dihydroxylation of the double bond and opening of the 1,6-bridge it will be possible to obtain 4-aminosugars in a stereocontrolled manner.

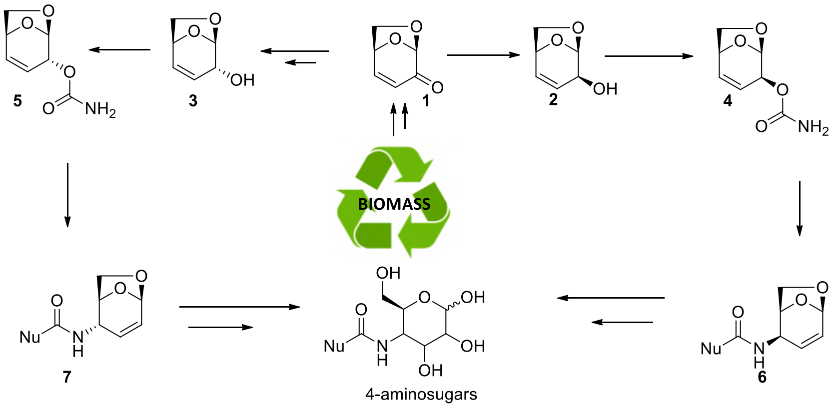

Figure 1: Synthesis of 4-aminosugars through allyl cyanate/isocyanate rearrangement.

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Discovery of novel pyrrole derivatives as anti-glioblastoma and anti-chronic myeloid leukemia agents

Michela Puxeddu,[a] Giuseppe La Regina,[a] Antonio Coluccia,[a] Ernest Hamel,[b] Te Liu,[c] Romano Silvestri,[a] and La Regina, G[a]

[a] Laboratory affiliated to Istituto Pasteur Italia — Fondazione Cenci Bolognetti, Dipartimento di Chimica e Tecnologie del Farmaco, Sapienza Università di Roma, Piazzale Aldo Moro 5, 00185, Rome, Italy;
[b] Molecular Pharmacology Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, Frederick National Laboratory for Cancer Research, National Cancer Institute, National Institutes of Health, Frederick, 21702, Maryland, United States;
[c] Shanghai Geriatric Institute of Chinese Medicine, Shanghai University of Traditional Chinese Medicine, 365 South Xiangyang Road, 200031, Shanghai, China.
E-mail: michela.puxeddu@uniroma1.it

Long-term survivors of glioblastoma multiforme (GBM) are at high risk of developing second primary neoplasms, including leukemia. For these patients, the use of classic tyrosine kinase inhibitors (TKIs), such as imatinib mesylate, is strongly discouraged since this treatment causes a tremendous increase of tumour and stem cell migration and invasion. We aimed to develop agents useful for the treatment of patients with GBM and chronic myeloid leukemia (CML) using an alternative mechanism of action from the TKIs, specifically based on the inhibition of tubulin polymerization. [1]

(4-(Thiophen-3-yl)-1-(p-tolyl)-1H-pyrrol-3-yl)(3,4,5-trimethoxy-phenyl)methanone (RS5645) and (1-(4-fluorophenyl)-4-(pyridin-4-yl)-1H-pyrrol-3-yl)(3,4,5-trimethoxyphenyl)methanone (RS5893) derivatives, as planned, not only inhibited tubulin polymerization, but also inhibited the proliferation of both GMB and CML cells, including those expressing the T315I mutation, at nanomolar concentrations. In in vivo experiments in BALB/cnu/nu mice injected subcutaneously with U87MG GBM cells, RS5645 significantly inhibited tumour growth, tumorigenesis, and angiogenesis.

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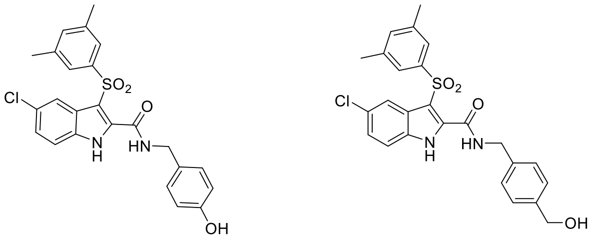
PO11

Novel class of norovirus inhibitors

Jessica Sebastiani,[a] Jana Van Dycke,[b] Michela Puxeddu,[a] Giuseppe La Regina,[a] Eloise Mastrangelo,[c] Jelle Matthijnssens and Romano Silvestri[a]

[a] Laboratory affiliated to Istituto Pasteur Italia, Fondazione Cenci Bolognetti, Dipartimento di Chimica e Tecnologie del Farmaco, Sapienza Università di Roma, Piazzale Aldo Moro 5, 00185, Rome, Italy
[b] Laboratory of Virology & Chemotherapy, Department of Microbiology, Immunology & Transplantation, Rega Institute for Medical Research, KU Leuven, University of Leuven, 3000 Leuven, Belgium
[c] CNR, Biophysics Institute, Università degli Studi di Milano, 20122 Milano, Italy
E-mail: jessica.sebastiani@uniroma1.it

Human noroviruses (HuNoVs) are the most common cause of viral gastroenteritis resulting in ~219,000 deaths annually. The current therapy consists merely of supportive supplementation with oral rehydration salts (ORS). There are still no antivirals or vaccines to treat and/or prevent HuNoV infections. An efficacious anti-norovirus drug that could be used as a prophylactic or to treat HuNoV infections is urgently needed. A large-scale antiviral drug screening, which included ~1000 drug-like small molecules from our compound library, allowed to identify the compound **1** (figure 1). The 3-((3,5-dimethylphenyl)sulfonyl)-5-chloroindole-N-(phenylmethanol-4-yl)-2.carboxamide (**1**) showed a good activity against the MNV replication with an EC50 of 0.5 ± 0.1 μM. Starting from the derivate **1**, we designed and synthesized a set of 10 analogs of which a compound showed an improved potency/selectivity (EC50 0.2 ± 0.1 μM) against MNV; good activity was also observed against the HuNoV GI replicon (EC50 1.2 ± 0.6 μM) [1]. Time-of-drug-addition studies revealed that analog **2** (figure 1) acts at a time point that coincides with the onset of viral RNA replication. Resistance development is a major obstacle in antiviral therapy, and almost all active antiviral agents have shown to select for resistance mutations. To assess whether resistant variants to compound 6 would easily arise, we passaged the virus passaged in the presence of compound 6 up to 30 consecutive times. After reverse engineering S131T and Y154F as single mutations into the MNV backbone, we did not find a markedly compound 6^{res} phenotype [1]. In this study, we present a class of novel norovirus inhibitors with a high barrier to resistance and in vitro antiviral activity.



1 **2**

Figure: Chemical structure of compound **1** and **2**.

[1] J. V. Dycke, M. Puxeddu, G. La Regina, E. Mastrangelo, D. Tarantino, J. Rymenants, J. Sebastiani, M. Nalli, J. Matthijnssens, J. Neyts, R. Silvestri, and J. Rocha-Pereira, *Pharmaceuticals* **14** (2021) art. no. 1006.

Discovery of new PLpro inhibitors against SARS-CoV-2

Desirèe Pecora,[a] Friedericke Hucke,[b] Eloise Mastrangelo,[c] Mario Milani,[c]
Marianna Nalli,[a] Giuseppe La Regina,[a] J.J. Bugert,[b] and Romano Silvestri[a]

[a]*Department of Drug Chemistry and Technologies, Sapienza University of Rome, P.le Aldo Moro 5, I-00185-Rome, Italy*
[b]*Institute of Microbiology, Munich, Germany*
[c]*Biophysics Institute, CNR, Via Celoria 26, I-20133, Milano*
E-mail: desiree.pec@gmail.com

There is an urgent need of effective drugs for the treatment of the SARS-CoV-2 infection. Remdesivir (Veklury®), a nucleotide analogue, is the only drug that was approved by FDA on October 22nd, 2020, for certain COVID-19 patients.

We performed virtual screening studies of a proprietary compound library of >6000 molecules against conserved SARS-CoV-2 enzymes, namely papain-like protease (PLpro), 3C-like proteinase (3CLpro) e RNA-dependent RNA polymerase (RdRp).

In these preliminary docking studies, we identified compounds with EC_{50} values in low micromolar range of concentration in cell viability assay in VeroE6 cells against SARS-CoV-2-mucIMB and SARS-CoV2-mucIMB-CB (alpha variant) strains. In particular, compound RS2523 inhibited SARS-CoV-2 PLpro with IC_{50}= 27 μM and SARS-HCoV-OC43 strain with IC_{50}= 4.30 μM. Compound **RS2523** was selected as a lead compound for optimization studies.

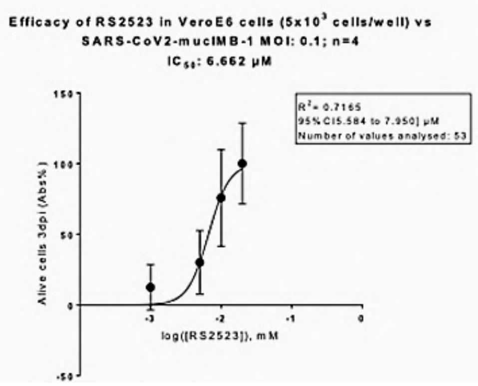


Figure 1: IC_{50} values of RS2523 against SARS-CoV-2-mucIMB-1 in infected cells.

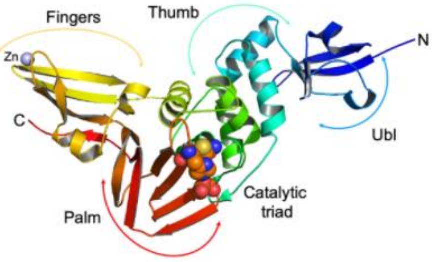


Figure 2: Structure of PLpro of SARS- CoV2 [1].

[1] J. Osipiuk, SA. Azizi, S. Dvorkin, M. Endres, R. Jedrzejczak, K. A Jones, S. Kang, R. Youngchang Kim, V. G Lisnyak, S. L Maki, V. Nicolaescu, C. A Taylor, C. Tesar, Y. Zhang, Z. Zhou, G. Randall, K. Michalska, S. A Snyder, B. C Dickinson, A. Joachimiak, *Nat Commun.* **12** (2021) 743.

Metabolomic approach for understanding grapevine communication mediated by volatile organic compounds

Valentina Lazazzara,[a] Sara Avesani,[a,b,c] Michael Oberhuber,[b] Peter Robatscher,[b] and Michele Perazzolli,[a,c]

[a] Plant pathology and applied microbiology, Research and Innovation Centre, Fondazione Edmund Mach, Via E. Mach 1, 38098 San Michele all'Adige, Italy
[b] Laboratory for Flavours and Metabolites, Laimburg Research Centre, Laimburg 6, Pfatten (Vadena), 39040 Auer (Ora), Italy
[c] Center Agriculture Food Environment (C3A), University of Trento, Via E. Mach 1, 38098 San Michele all'Adige, Italy
E-mail: valentina.lazazzara@fmach.it

Plants can produce a wide variety of volatile organic compounds (VOCs), which play a crucial role in the interaction with other organisms and the regulation of plant responses against stresses. Different modes of action against phytopathogens have been attributed to biogenic VOCs, such as induction of plant resistance and direct inhibition of pathogen growth. In particular, the amount of some biogenic VOCs was higher in downy mildew-resistant compared with susceptible grapevine genotypes upon inoculation with *Plasmopara viticola*. Thus, biogenic VOCs indicate a possible involvement in the grapevine resistance mechanisms against this pathogen. This work aims at identifying the metabolic response of VOC-treated grapevine leaves and the potential activation of VOC-mediated resistance mechanisms. Susceptible grapevine leaf disks were treated with pure biogenic VOCs or with water as control. Functional and transcriptional analyses confirmed that two VOCs reduced downy mildew severity and increased expression level of defense-related genes in susceptible leaf disks. An untargeted metabolomics approach was applied using ultra-high pressure liquid chromatography-high resolution-quadrupole-time of flight-mass spectrometry (UHPLC-Q-TOF-MS) analysis to clarify the mechanisms of action of VOCs and the response of VOC-treated leaf disks. Preliminary results revealed marked differences occurred between VOCs-treated and control samples, indicating a clear metabolic response of receiver plants in response of biogenic VOCs. Principal component analysis (PCA) discriminated samples according to the time point and VOC treatment. Further data analyses will help to improve knowledge on the plant defense mechanisms activated by biogenic VOC.

The antimicrobial peptide Mag-2 interacts with the membrane protein BamA impairing the correct folding of *E. coli* membrane proteins

Carolina Canè,[a] Antonio Moretta,[c] Luigi Paduano,[a] Domenico Cavasso,[a] Angela Duilio [a,d] and Angela Di Somma[a,b]

[a] *Department of Chemical Sciences, University of Naples "Federico II", 80126 Napoli, Italy;*
[b] *National Institute of Biostructures and Biosystems (INBB), 00136, Roma, Italy;*
[c] *Department of Sciences, University of Basilicata, 85100, Potenza, Italy;*
[d] *CEINGE Biotecnologie Avanzate, 80145, Naples, Italy*
E-mail: carolina.cane@unina.it

Most studies performed so far for the investigation of the mechanism of action of Antimicrobial Peptides (AMPs), including Magainin-2 (Mag-2), on bacterial cells were principally focused on their membranolytic effects. Recent findings indicated alternative and non-lytic modes of action for different AMPs, suggesting the possible occurrence of specific intracellular targets opening up the way to a detailed description of their effects at the molecular level.

Particularly, the possible exploitation of AMPs as new antibacterial drugs is strictly related to a clear definition of each step of their intracellular action, such as the cell penetration mechanism and/or the identification of the specific intracellular target(s) [1].

In this work, we elucidated the mechanism of action of Mag-2 using biochemical and spectroscopic techniques. Functional proteomics studies demonstrated the interaction of the peptide with *E. coli* outer membrane proteins, particularly BamA belonging to the BAM complex. In Gram-negative bacteria, the BAM complex is responsible for the folding and insertion of nascent β-barrel Outer Membrane Proteins (OMPs) in the outer membrane [2].

Docking predictions and fluorescence spectroscopy analyses confirmed the interaction of Mag-2 with recombinant BamA, suggesting formation of a stable complex with a favourable dissociation constant. Moreover, dynamic light scattering investigations displayed a reduction of BamA hydrodynamic radius in the presence of the peptide, confirming the occurrence of the Mag-2/BamA complex.

[1] A. Di Somma, C. Avitabile, A. Cirillo, A. Moretta, A. Merlino, L. Paduano, A. Duilio and A. Romanelli, *BBA- Gen. Subj.* **1864.7** (2020) art. no. 129606.
[2] Doyle, Matthew T. and Harris D. Bernstein. *Nature commun.* **10.1** (2019) 1-13.

Bactericidal effects of resveratrol-loaded glycosylated liposomes on *Staphylococcus aureus* and MRSA

Giuliana Prevete,[a,b] Marco Mazzonna,[b] Enrica Donati,[b] Francesca Mariani,[b]
Giulia Cappelli,[b] Cecilia Bombelli,[c] and Giovanna Mancini[b]

[a] Department of Chemistry and Technology of Drug, Sapienza University of Rome, P. le A. Moro 5, 00185 Rome, Italy
[b] CNR- Institute for Biological Systems (ISB), Area della Ricerca di Roma 1, Via Salaria km 29,300, 00015 Monterotondo, Italy
[c] CNR- Institute for Biological Systems (ISB), Secondary Office of Rome c/o Chemistry Department, Sapienza University of Rome, P. le Aldo Moro 5 00185 Roma, Italy.
E-mail: giuliana.prevete@uniroma1.it

Liposomes have unique characteristics of biocompatibility, versatility and simplicity of preparation, making them excellent candidates for drug delivery. These nanosystems can allow the release of drugs to target cells, reducing the dosage and avoiding healthy tissues and organs; moreover, due to their ability to fused with bacteria and to improve antibiotics activity, they hold the potential to overcome multi-drug resistance in bacterial infections [1].

Here we report the targeted delivery of *trans*-resveratrol (RSV), a Quorum Sensing Inhibitor, to two strains of resistant and biofilm forming bacteria, *Staphylococcus aureus and* Methicillin-Resistant *Staphylococcus aureus* (MRSA). RSV was encapsulated in cationic glycosylated liposomes formulated with 1,2-dioleoyl-*sn*-glycero-3-phosphocoline (DOPC), cholesterol (chol) and one glycoamphiphile featuring a galactosyl, mannosyl or glucosyl moiety, previously synthesized and used in our laboratory to target bacteria and biofilms (Figure 1) [2,3]. In fact, the synthetic glycolipids are able to increase liposomes specificity toward lectins, a class of non-enzymatic sugar-binding proteins involved in cellular recognition and adhesion, and sugar-protein transporters located on the outer membrane of bacterial cells.

All the glycosylated formulations showed a hydrodynamic size around 100 nm, a good homogeneity, positive zeta potential and good RSV Entrapment Efficiency (EE%).

Bactericidal activity of liposomes was evaluated by determining the Minimal Inhibitory Concentration (MIC) and the Minimal Bactericidal Concentration (MBC) on the in vitro grown bacteria.

[1] M. Ferreira., M. Ogren, J. N. R. Dias, M. Silva, S. Gil, L. Tavares, F. Aires-da-Silva, M. M. Gaspar, and S. I. Aguiar, *Molecules* **26** (2021) art. no. 2047.
[2] I. Francolini, L. Giansanti, A. Piozzi, B. Altieri, A. Mauceri, and G. Mancini, *Colloids and Surfaces B: Biointerfaces*, **181** (2019) 632-638,
[3] S. Aiello, L. Pagano, F. Ceccacci, B. Simonis, S. Sennato, F. Bugli, C. Martini, R. Torelli, M. Sanguinetti, A. Ciogli, C. Bombelli, and G. Mancini, *Colloids and Surface A: Physiochemical and Engineering Aspects,* **617** (2021) art. no. 126321

The synthesis, characterization, and catalytic properties of novel gold(I) complexes bearing alkylated PTA ligands

Gabriele Pirodda,[a] Paolo Sgarbossa,[a] and Andrea Biffis,[b]

[a]Dipartimento di Ingegneria Industriale, Università degli Studi di Padova, via Marzolo 9, 35131 – Padova, Italy; [b]Dipartimento di Scienze Chimiche, Università degli Studi di Padova, via Marzolo 1, 35131 – Padova, Italy
E-mail: gabriele.pirodda@unipd.it

Organophosphines are among the most common ancillary ligands used in organometallic chemistry, owing to their ability to stabilize low metal oxidation states and their capacity to influence both the steric and electronic properties of the metal center upon coordination. The monodentate, adamantane-like phosphine PTA (1,3,5-triaza-7-phosphaadamantane) and its derivatives have been the subject of interest over the last two decades due to their relatively small cone angle (103°) and the availability of nitrogen atoms for further functionalization. This, together with their chemical and thermal stability as compared to PMe_3 and PEt_3, which are sterically similar yet are known to oxidize easily and spontaneously ignite in air, makes them attractive ligands for use in synthesis and catalysis [1]. With these factors in mind and considering the variety of reactions catalyzed by gold(I) phosphine complexes [2], we synthesized various different gold(I) long chain-N-alkylated PTA complexes (Scheme 1) bearing alkyl, aryl, and fluoroalkyl substituents. The complexes were subsequently used as pre-catalysts in model addition reactions, such as the hydroarylation of alkynes and the cyclopropanation of alkenes. The effect of both the alkyl side chain and the counterion on the solubility and reactivity in different solvents is analyzed. Furthermore, the stability of the ligands and the resultant complexes is evaluated.

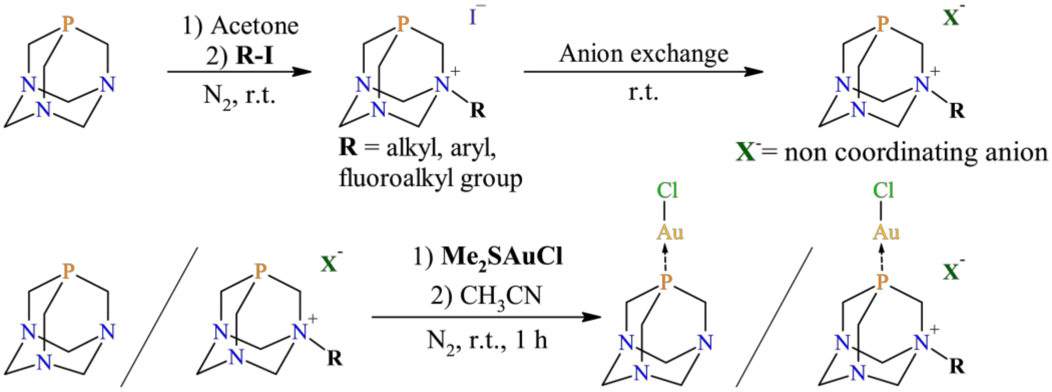


Figure 1: Synthesis of N-alkylated PTA ligands and their relative gold(I) complexes.

[1] A.D. Phillips, L. Gonsalvi, A. Romerosa, F. Vizza, M. Peruzzini, *Coord. Chem. Rev.* **248** (2004) 955-993
[2] Z. Li, C. Brouwer, C. He, *Chem. Rev.* **108** (2008) 3239-3265

Biochar based catalysts for biomass valorization

Lilia Longo, Sebastiano Tieuli, Federica Menegazzo, Elena Ghedini, and Michela Signoretto

Dipartimento di Scienze Molecolari e Nanosistemi, Università Ca' Foscari Venezia, and INSTM RUVe consortium, Via Torino 155, 30172-Venezia, Italia
E-mail: lilia.longo@unive.it

The thermochemical decomposition of biomass in absence of oxygen, named pyrolysis, leads to solid (biochar), liquid (bio-oil) and gaseous (bio-gas) products. Biochar is a carbonaceous material that, after activation, displays several interesting features to be used as support for metal nanoparticles dispersion [1]: high porosity and superficial area, great stability to high temperatures and coke, and modulable superficial functional groups, which can be tuned depending on the biomass precursor nature (i.e., vegetal or animal) strongly influencing the catalytic performances.

The study here presented is an investigation of different biochars from different biomasses, with particular focus on the possible catalytic applications. For this purpose, hazelnut shells, artichoke wastes, rice husks, and tannery by-products have been chosen: the choice of these biomasses is related to the massive amount of production of these feedstocks in Italy. Another key aspect in biomass selection is the chemical composition: hazelnut, artichoke and rice are principally made of lignin, cellulose, and hemicellulose in different ratios, while tannery wastes are mainly composed by collagen and tanning agents (tannins).

Biochars have been consequently characterized: FT-IR, pH, elemental analysis, and temperature programmed desorption have been accomplished to characterize the chemical composition and the surface functional groups. N_2 physisorption and SEM microscopy have been carried out to obtain information about the morphology of the materials. Moreover, the activation process has been study to improve the surface area and porosity: specifically physical activation has been conducted and compared, with CO_2 and steam as activating agents. Elemental analysis reported several differences between biochars, showing a very high and appealing quantity of nitrogen in tannery biochar. It has been noticed that, depending on the original biomass, some biochars (hazelnut shells and rice husks derived), display a microporous structure and noteworthy superficial areas (200-300 m^2/g), which can be increased to higher values (700-800 m^2/g) after the activation process. Other biochars (i.e., tannery waste derived), despite not showing any porosity after pyrolysis, can reach promising values of surface area and a wider pore distribution, related to the activating agent.

Preliminary studies of the synergic effects of the support with a metallic active phase, (i.e., Pd), have been studied, evaluating the properties of the catalysts and the activity in hydrogenation reactions on model molecules (benzaldehyde and 5-hydroxymethylfurfural).

[1] J.L. Santos, P. Maki-Arvela, A. Monzòn, D.Y. Murzin, M. A. Centeno, *Appl. Catal. B. Environ.* **268** (2020) 118423.
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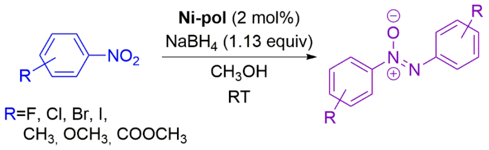
Urchin-like Ni-nanoparticles for reduction of nitroarenes towards azoxyarenes under mild conditions

Valentina Petrelli,[a] Ambra Maria Fiore,[a] Giuseppe Romanazzi,[a] Darya Nefedova,[a] Maria Michela Dell'Anna,[a] Cristina Leonelli,[b] Cecilia Mortalò,[c] and Piero Mastrorilli[a]

[a]DICATECh, Politecnico di Bari, via Orabona, 4, Bari-70125, Italy
[b]Dipartimento di Ingegneria "Enzo Ferrari", Università di Modena e Reggio Emilia, via P. Vivarelli 10, Modena-41125, Italy
[c]CNR-ICMATE, Istituto di Chimica della Materia Condensata e di Tecnologie per l'Energia, Corso Stati Uniti 4, Padova-35127, Italy
E-mail: valentina.petrelli@poliba.it

Azoxyarenes have gained considerable research attention due to their versatile applications as dyes and pigments, reducing agents, analytical reagents, food additives, chemical stabilisers, polymer inhibitors, and liquid crystal displays [1].

Traditional industrial preparations of azoxyarenes are achieved by diazotisation but the process is costly and environmentally unfriendly, due to the formation of unstable intermediates and harsh conditions. An alternative synthetic approach for azoxyarenes is either the reduction of nitro compounds or the oxidation of amines. In both cases, the formation of the azoxy derivatives is accomplished through the condensation of intermediate reaction products. However, the possible formation of different reaction products renders very challenging to control the reaction towards the selective formation of the azoxyarenes opening important research issues. Herein, with the aim to replace noble metals with earth abundant first-row transition metals, and continuing our studies on metal-containing polymers to be used as heterogenous active catalysts [2], we were able to prepare a innovative Ni-pol catalyst. TEM analyses in STEM mode on Ni-pol showed that, within the polymeric matrix, homogeneously distributed Ni NPs are formed, and they have a very unusual morphology such as an urchin-like shape. Next, by using $NaBH_4$ as a reducing agent under very mild reaction conditions, Ni-pol has been proven to be a highly selective catalyst for the reduction of a variety of structurally different nitroarenes towards their corresponding azoxyarenes (Figure 1). Finally, recovery and reuse of the catalytic system has been also investigated demonstrating good recyclability of **Ni-pol** (up to 5 runs) without appreciable Ni leaching, loss of activity and selectivity as well as Ni NPs agglomeration.



Wide substrate scope
(more than 20 examples)
Isolated yields up to 99%
Selectivities up to 100%
Recyclability up to 5 runs

Figure 1: Scheme of reaction.

[1] Y. Dai, C. Li, Y. Shen, T. Lim, J. Xu, Y. Li, H. Niemantsverdriet, F. Besenbacher, N. Lock and R. Su, *Nat. Commun.* **9** (2018) 1–7 and reference therein.
[2] A. M. Fiore, D. Nefedova, G. Romanazzi, V. Petrelli, M. Mali, C. Leonelli, C. Mortalò, M. Catauro, P. Mastrorilli and M. M. Dell'Anna *Macromol. Symp.* **395** (2021) 2000195.

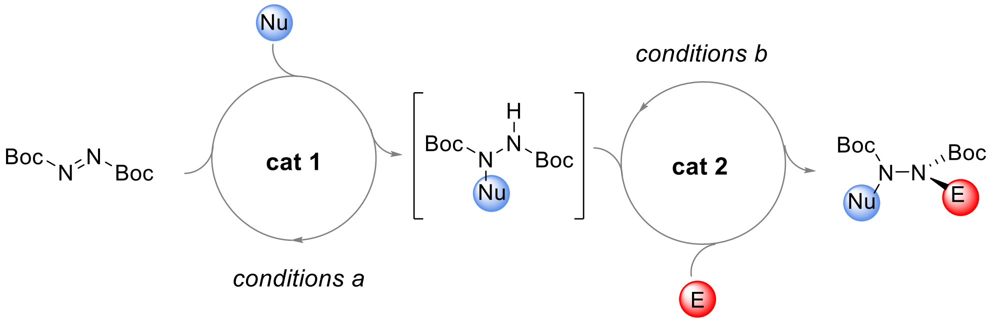
Synthesis of chiral tetrasubstituted hydrazines as novel N-N atropisomers

Chiara Portolani, Giovanni Centonze, Paolo Righi, and Giorgio Bencivenni

Department of Industrial Chemistry “Toso Montanari”, Alma Mater Studiorum-University of Bologna, Viale del Risorgimento 4, 40136-Bologna, Italy
[a] INSTM, Via Giusti, 9 – 50121 Firenze
E-mail: chiara.portolani2@unibo.it

Atropisomerism is an intensively pursued area since the disciplines where axial chirality is influential are numerous, starting from pharmaceutical industries, as well as its wide application for catalysis and synthesis. While the first and most studied class of atropisomers derives from biaryls backbones connected by C-C bonds, several non biaryls structures and C-X atropisomers (with X=N, O, S) have been developed [1]. In this well explored scenario, atropisomerism deriving from an X-X axis is totally underdeveloped, with only few examples of asymmetric synthesis [2]. This research is based on the development of an asymmetric route to achieve novel N-N atropisomers. While the N-N bond is shorter than a C-C bond and the lone pairs contribute to restrict the rotation, the synthesis is challenging because N-N is a relatively weak bond, deplanarization can occur and the energy barriers are typically quite low.

The hypothesis is to obtain a tetrasubstituted hydrazine starting from di-*tert*-butyl azodicarboxylate and adding bulky substituents to inhibit the rotation. DFT calculations on this kind of substrates indicate that the energy barrier is high enough to allow atropisomerism ($\Delta G^{\ddagger}_{rot}$>30 kcal mol^{-1}), and kinetic analysis confirmed that these compounds exist as atropisomers. Preliminary results show that a good enantio- and diastereoselection can be obtained with both an auto-relay and a sequential relay multicatalytic one-pot approach, affording stable N-N atropisomers.



Nucleophile (Nu) Electrophile (E)

Auto-Relay: cat 1 = cat 2; conditions a = conditions b
Sequential Relay: cat 1 ≠ cat 2; conditions a ≠ conditions b

Figure 1 General scheme of the synthesis of tetrasubstituted hydrazines.

[1] J. K. Cheng, S. Xiang, S. Li, L. Ye, and B. Tan, *Chem. Rev.* **121** (2021) 4805-4902.
[2] G. J. Mei, J. J. Wong, W. Zheng, A. A. Nangia, K. N. Houk, and Y. Lu, *Chem.* **7** (2021) 1–15.

Photocatalytic dimerization of enallenes for the synthesis of taxanes analogues

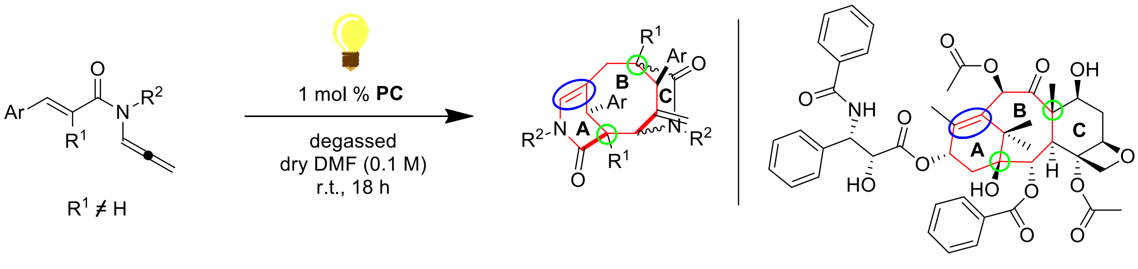
Maurizio Chiminelli, Andrea Serafino, and Giovanni Maestri

Department of Chemistry, Life Sciences and Environmental Sustainability, Università degli Studi di Parma, Parco Area delle Scienze 17/A, 43124-Parma, Italy
E-mail: maurizio.chiminelli@unipr.it

Photoredox catalysis with transition metal complexes is a green and innovative way to achieve new reaction pathway in synthetic organic chemistry. This approach relies on the ability of a catalyst upon photoexcitation with visible light to engage in electron or energy transfer processes with organic substrates, which would be otherwise inert to the radiation [1].

In this work, acylallenamides have been investigated as an interesting and original building block to induce visible-light promoted cascades. These molecules are characterized by the presence of an amide bound to the allenic moiety. Desired substrates were mainly synthesized performing an Heck coupling between an acrylate and an aryl halide or via Wittig reaction between an aryl aldehyde and a bromoacetate. The resulting cinnamoyl ester is then hydrolysed, chlorinated, and eventually reacted with a secondary propargyl amine. Finally, the desired allenamides were synthesized through a based-catalysed isomerization of the corresponding enynes. These substituted allenamides can selectively undergo a complex dimerizing cascade when reacted in the presence of an Ir (III) photocatalyst and visible light.

This original reactivity has several significant features: the cascade led to the formation of four new C-C bonds in one step, making it one of the longest sequences promoted by light reported to date; it led to the formation of a fused tricycle with the presence of an eight – member ring flanked by two lactams one; the unusual central medium – sized ring is enriched by the presence of two, congested, all – carbon quaternary stereocenters at his headbridging positions. Moreover, this complex scaffold is very interesting due to the analogy with taxanes structures, a class of compounds widely used as chemotherapy agents.



R^1: methyl, propyl, phenylethynyl
R^2: Bn, PMB, cyclopropyl, $-CH_2CN$, $-4-F-C_6H_4$
Ar: *p*-Cl, *p*-OMe, *p*-nBu

YIELD: 31 - 64 %

TAXOL

Figure 1: Photocatalytic reaction and structural analogies with Taxol.

[1] C. K. Prier, D. A. Rankic, and D. W. C. MacMillan, *Chem. Rev.* **113** (2013) 5322 – 5363.

New sitosterol-based designer surfactants for catalysis in water

Tommaso Lorenzetto, Fabrizio Fabris, and Alessandro Scarso

Dipartimento di Scienze Molecolari e Nanosistemi, Università Ca' Foscari Venezia, Via Torino 155, 30172-Mestre Venezia, Italy
E-mail: tommaso.lorenzetto@unive.it

Micellar catalysis is a well-established field of research exploiting surfactants and their property of generating supramolecular aggregates in water. These assemblies act as nanoreactors, allowing to solubilize organic lipophilic molecules in water and to perform traditional organic transformations without the need of common organic solvents, thus achieving efficiently greener synthetic routes [1]. Apart from classic surfactants, the present-day environmental awareness has spurred the introduction of designer surfactants making micellar catalysis a real option in synthetic organic chemistry. These molecules, introduced by Lipshutz some years ago [2], are new amphiphiles specifically designed and developed for catalytic applications in water, some currently commercially available.

In this contribution, we propose the development of new designer surfactants comprising a rigid extended hydrophobic portion based on β-sitosterol, a naturally occurring compound, connected to a polyoxoethylene chain, linked by an ether bond. The proposed amphiphilic compounds represent a minimalistic approach with respect to Lipshutz's third generation of designer surfactants [3] due to the lack of a spacer between polar and apolar units. The properties of these novel amphiphiles allowed to achieve Pd-catalyzed cross-coupling reactions in water under mild conditions, playing a fundamental role in modern synthetic organic chemistry. In order to better understand the aggregation properties of these amphiphiles, critical aggregation concentration (C.A.C.) in water was investigated by NMR analyses and the performances in catalysis were compared to those of commercially available surfactants as benchmarks.

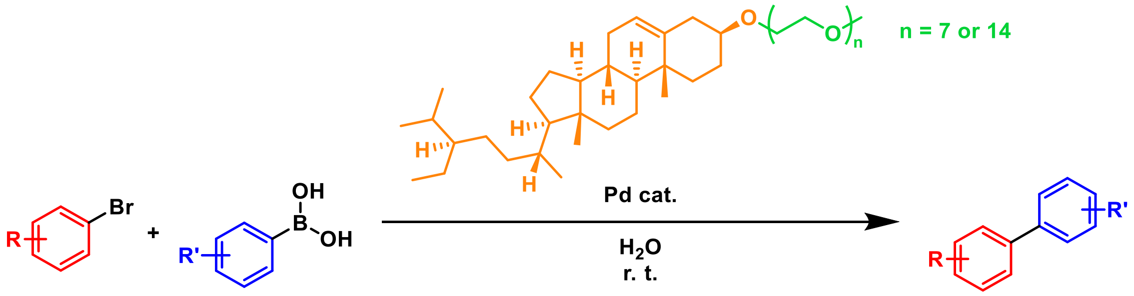


Figure 1: β-Sitosterol-based designer surfactants catalyzed Suzuki-Miyaura Pd-catalyzed cross-coupling reactions in water.

[1] G. La Sorella, G. Strukul, and A. Scarso, *Green Chem.* **17** (2015) 644-683.
[2] T. Lorenzetto, G. Berton, F. Fabris, and A. Scarso, *Catal. Sci. Technol.* **10** (2020) 4492-4502; B. H. Lipshutz, and S. Ghorai, *Aldrichimica Acta* **41** (2008) 59-72.
[3] P. Klumphu, and B. H. Lipshutz, *J. Org. Chem.* **79** (2014) 888-900.

Quick microwave-assisted reactions for tunable luminescent carbon quantum dots

Andrea Di Vera,[a] Adolfo Speghini,[b] and Patrizia Canton[a]

[a] Dipartimento di Scienze Molecolari e Nanosistemi, Università Ca' Foscari di Venezia, Via Torino 155, 30172 Venezia, Italia.
[b] Dipartimento di Biotecnologie, Università degli studi di Verona, Strada Le Grazie 15, 37134 Verona, Italia.
E-mail: andrea.divera@unive.it

Carbon quantum dots (CQDs) are fascinating luminescent materials that boosted research studies in the past 10 years due to their intriguing properties [1]. Low toxicity and cost coupled with valuable optical properties make CQDs a suitable candidate for the design of many different applications, ranging from solar technologies and optical sensors to photocatalysis and biological implementation.

The interest in those materials increased during years in terms of scientific publications dealing with a variety of approaches for CQDs production [2]. For example, the syntheses of these materials have been developed using different techniques such as, just to cite a few, solvothermal treatments, microwave assisted synthesis, ultrasound reactions and many others. The choice of the reaction conditions heavily influences the nature of the final quantum dots regarding both optical and chemical properties. One of the most promising way to obtain CQDs is the microwave technology due to extremely quick and facile reaction procedure that can be positively impact price and time production [3].

The study here reported, is based on the strategy of reagent engineering to synthesize, by microwave-assisted reactions, highly luminescent CQDs having tunable fluorescence. Different combinations of weak organic acids with o-phenylenediamine are exploited to modulate the organic functional groups on the CQDs surface and tuning the energy band gaps. A variety of emissive species has been obtained, confirming the effective influence of the chemical composition on the luminescent features. The optical and morphological properties have been investigated with a particular focus on the relationship between size, reactivity, and luminescence behaviors.

The most promising compounds have been employed for the preparation of luminescent composite materials based on polymeric matrices (polymethyl methacrylate), achieving high emission features in solid state. The design of plastic materials with valuable optical responses can be a useful tool for the preparation of modern and innovative devices.

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Production and characterization of hybrid nanofibers for functional coatings

Angela Malara,[a,b] Antonio Fotia,[c] Lucio Bonaccorsi,[a,b] and Patrizia Frontera[a,b]

[a] *Department of Civil, Energy, Environment and Material Engineering, Mediterranea University of Reggio Calabria, Via Graziella Loc Feo di Vito, Reggio Calabria, 89134, Italy*
[b] *Consorzio Interuniversitario per la Scienza e la Tecnologia dei Materiali (INSTM), Firenze, 50121, Italy*
[c] *Department of Information Engineering, Infrastructures and Sustainable Energy, Mediterranea University of Reggio Calabria, Via Graziella Loc Feo di Vito, Reggio Calabria, 89134, Italy*
E-mail: angela.malara@unirc.it

Nanofibers manufacturing by electrospinning is regarded a well-assessed process to produce one-dimensional nanostructures. The unique properties and physicochemical features, such as large surface area, mechanical strength, surface functionality, flexibility and shape adaptability are only few of the characteristics that make nanofibers interesting for traditional and new applications [1].

The synthesis by electrospinning is a very simple, scalable, and inexpensive technique, which allows obtaining different morphologies, such as dense, hollow and core-shell fibres. Indeed, the fabrication of materials with a nanoscale structure is of great interest because of the manifold applications in many different fields such as in the environmental sector, in the catalysis, in biomedical applications, in sensor devices, and in the sustainable exploitation of energy [1, 2].

In this study, innovative materials based on hybrid polymer-zeolite nanofibers were produced and tested. In particular, porous materials were embedded in the polymeric nanofibers and their performance, especially in terms of water uptake adsorption and mechanical strength, were evaluated. The obtained composite materials showed interesting properties, whose further investigation might have a great role for a number of applications, especially as coatings for water adsorption systems driven by low temperature heat sources [3], the so-called waste thermal energy.

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Study on solution equilibria in the Sn^{2+}-H_2O-F^- system through potentiometry using GE, Fluoride Ion-Selective and Sn(Hg) amalgam electrodes

Mariacristina Bianco and Ermanno Vasca

Dipartimento di Chimica e Biologia "Adolfo Zambelli", Università degli Studi di Salerno, Via Giovanni Paolo II, 132 84084-Fisciano (SA), Italy
E-mail: mariacristinabianco1@gmail.com

Relatively easy oxidation of Sn(II) to Sn(IV) makes solution equilibria, involving the metal in the oxidation state +2, very difficult to study.

The ion Sn^{2+} gives, in aqueous solution, a strong acid hydrolysis, widely studied through specific techniques, including potentiometry [1]. Although most of the authors agree on the speciation model, depending on the experimental concentration of tin(II), the numerical values of the stability constants seem not consistent.

The available data, on hydrolysis of Sn^{2+}, have so far been interpreted assuming the existence of mononuclear species $SnOH^+$, $Sn(OH)_2$ and $Sn(OH)_3^-$ at low concentrations of tin(II) (< 0.5 μM), while, at higher metal concentrations polynuclear species predominate, probably one or more among $Sn_2(OH)_2^{2+}$, $Sn_2(OH)_3^+$ and $Sn_3(OH)_4^{2+}$ [2].

Of considerable importance are the species that Sn(II) forms with halides, and in particular, binary complexes with fluoride, SnF_2, widely used in the cosmetic industry and, specifically, in toothpaste formulations as a source of fluoride, whose adsorption on dental enamel is favoured by the presence of Sn^{2+} ions.

Ternary species formed by Sn^{2+} with hydroxide and some halides, Br^- and Cl^- have also been reported, while, up to now, studies concerning the formation of mixed ternary species Sn^{2+}, OH^-, F^- are absent [3].

In this work the study of the formation equilibria of mixed Sn^{2+}-OH^--F^- complexes by potentiometric titrations of hydrolysed tin solutions with NaF solutions, monitoring $[H^+]$, $[Sn^{2+}]$ and $[F^-]$, simultaneously, using glass membrane electrode (GE), tin amalgam electrode and fluoride ion-selective electrode (ISEF), respectively, is reported. The formation of the different complexes is also investigated by NMR techniques.

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Removal of organic and inorganic contamination from municipal landfill leachate through low-cost and eco-friendly sorbents

Luca Rivoira, Michele Castiglioni, Clara Castiglioni Minischetti, and Maria Concetta Bruzzoniti

Department of Chemistry, Università degli Studi di Torino, Via Pietro Giuria 5, 10125, Torino
E-mail: luca.rivoira@unito.it

Despite the use of landfills for the disposal of urban wastes is nowadays avoided, many sites are still active today, not counting those plants which were closed less than thirty years ago, which requires special maintenance. Among these attentions, the management of the leachate is one of the most important. Leachate is defined by Italian Legislative Decree no. 36 of 13 January 2003 as a wastewater characterized by the presence of organic and inorganic pollutants (whose concentration depends on several environmental factors and on the life phase of the landfill), deriving from biological and physicochemical processes that originate inside landfills, mainly following water infiltration.

Due to the presence of these toxic substances, and in compliance with current legislation, purification methods have been developed aimed at reducing both organic and inorganic contamination. Among them, adsorption techniques are the most common.

Based on the above-mentioned assumptions, the aim of this work was to test economic and green adsorbents in the removal of organic and inorganic contaminants in a municipal landfill leachate, located in the Piedmont area.

Two types of supports were studied: i) biochars, materials deriving from the combustion of biomass, only recently studied for pollutant removal applications, and ii) zeolites. In detail, six biochars deriving from different plant feedstocks and heat treatments (gasification and pyrolysis) were considered, as well as two zeolites, a chabasite of natural origin and a synthesized 13X molecular sieve.

For all the sorbents, the removal yield of heavy metals, ammonium and organic content (measured as color) was studied, due to their toxic effect to human beings and to the environment. The effect of sorbent dose (0.5, 1.5 and 3.5 g in 50 mL of leachate) on pollutant removal efficiency was also investigated.

Results showed that the biochar produced by gasification from pine, beech and hazel wood exhibited the highest removal efficiency for metal and color (more than 80% yield for Fe), while it was not able to remove ammonium. On the contrary, the two zeolites showed removal yields greater than 50% for NH4+, regardless of the activation solution tested (NaCl or NaOH).

Finally, the physicochemical properties of biochars and the previously obtained removal yields were treated through a principal component analysis (PCA), in order to highlight possible correlations and to understand how biochar intrinsic properties could influence the retention of target pollutants.

Graphene composites for advanced drinking water treatment

Francesca Tunioli,[a] Sara Khaliha,[a] Burcu Saker Onar,[b] Marjan Hezarkhani,[b]
Barbara Casentini,[c] and Manuela Melucci[a]

[a] Istitute of Organic Synthesis and Photoreactivity (ISOF-CNR), via Gobetti 101, 40129-Bologna, Italy
[b] Nanotechnology Research and Application Center, Sebanci University, Orta Mh. Üniversite Cd. 27/1, 34956-Instanbul, Turkey
[c] Water Research Institute (IRSA-CNR), via Salaria Km 29,300 C. P., 10-00015-Roma, Italy
E-mail: francesca.tunioli@isof.cnr.it

The so called “emerging contaminants” (ECs), such as pharmaceuticals, cosmetics, pesticides and polyfluoroalkyl substances (PFAS) are increasingly found in tap water [1], calling the urgent development of new treatment technologies. Graphene based materials have shown great potential for water purification due to their high surface area and their adsorption properties, promoted by multiple interactions pathways with organic molecules and metal ions [2]. Here, we report on the adsorption properties of graphene oxide (GO), reduced GO (rGO) and graphene nanoplatelet (GNP) obtained from waste tires (Nanografen Co). We tested the adsorption selectivity and efficiency of these nanomaterials towards several organic molecules and metals, including PFAS and arsenic. In addition, we report on the preparation and performance of composites based on the combination of graphene related materials with natural polymers, including alginate (ALG), polylactic acid (PLA) and polycaprolactone (PCL), aimed at the combination of filtration (through the porous polymer structure) and adsorption (through graphene component). PLA and PCL-graphene membranes were prepared by core-shell electrospinning method and alginate-graphene hydrogel beads by ionotropic gelation method.

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Development of a fast, effective, easily applicable analytical method to determine SGARs in tawny owl samples

Saul Santini,[a] Chiara Sarti,[a] Cristian Marinelli,[b] Laura Sposato,[b] Tania Martellini,[a] and Alessandra Cincinelli[a]

[a] Dipartimento di Chimica "Ugo Schiff", Università degli Studi di Firenze, Via della Lastruccia 3-13, 50019-Sesto Fiorentino, Italy
[b] ANALYTICAL Food, Via Orcagna 70, 50121-Firenze, Italy
E-mail: saul.santini@unifi.it

Anticoagulant rodenticides (AR) are pesticides widely used in agriculture and in the control of urban rodents. AR can be divided into first generation (FGAR) and second generation (SGAR) compounds; the latter show greater toxicity, accumulation and persistence, resulting lethal to animals in a single feed due to the greater affinity to binding sites in the liver. In addition to attracting rodents, baits can also attract other animal species causing accidental or intentional poisoning. AR inhibits vitamin K, which is an important cofactor in the blood coagulation process [1]. Other less common clinical symptoms due to accidental exposure of animals to AR are: tarry blood and bleeding gums, difficulty breathing, weakness, lethargy, vomiting, seizures, bruising, abdominal distention and pain [2].

The challenge of this research is to develop a fast, effective and easily applicable analytical method to determine SGARs in tawny owls and apply it to 17 samples from different European countries. The analysis focused on Bromadiolone, Difethialone, Brodifacoum, Flocoumafen and Difenacoum.

In order to develop an analytical method, particular attention should be paid to the very low concentration at which these organic compounds occur in the biota samples, the complexity of the matrix and the high amount of lipid content. Extraction and clean-up/preconcentration represent the most critical steps in the analytical process and play a key role in maximizing analyte recovery and minimizing the matrix effect.

To this aim, a method for the SGARs analysis in Tawny owl livers has been developed starting from a previous study by Vandenbrouke et al., 2008 [3]. The analytical parameters of the method were evaluated by adding SGAR standards and labeled Bromadiolone at different concentrations in 1g wet weight of chicken liver. The precision data, relative standard deviations (RSD), for the analytical method were calculated for 4 spike levels with 3 repetitions. The limit of detection (LOD) and limit of quantification (LOQ) were assessed by replicate (n = 5) analysis of the procedure and calculated from Signal to Noise Ratio (S/N). To investigate the matrix effect on linearity, the slope and intercept of the calibration curve were statistically compared with those obtained from the analyses of the standard solutions in matrix extracts.

Finally, recoveries were also evaluated.

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The influence of in-amphorae vinification on the molecular profile of Sangiovese and Cabernet Franc

Chiara Sarti,[a] Tania Martellini,[a] Laura Sposato,[a,b] Susanna Pucci,[c] Gaia Meoni,[d]
Cristian Marinelli,[b] Leonardo Tenori,[a,e] Claudio Luchinat,[a,e] Rodorico Giorgi,[a,f]
Saul Santini,[a] and Alessandra Cincinelli[a,f]

[a] *Department of Chemistry "Ugo Schiff", University of Florence, Via della Lastruccia 3, 50019-Sesto Fiorentino, Italy*
[b] *ANALYTICAL S.R.L., Via Orcagna 70, 50121-Florence, Italy*
[c] *Department of Soil Science and Plant Nutrition (DISPAA), University of Florence, P.le delle Cascine 28, 50144-Florence, Italy*
[d] *Giotto Biotech s.r.l., Via Madonna del Piano 6, 50019-Sesto Fiorentino, Italy*
[e] *Magnetic Resonance Center (CERM), University of Florence, Via L. Sacconi 6, 50019-Sesto Fiorentino, Italy*
[e] *CSGI, University of Florence, Via della Lastruccia 3, 50019-Sesto Fiorentino, Italy*
E-mail: chiara.sarti@unifi.it

A quality wine is the result of a good balance of different factors, including oxidation processes, esterification and hydrolysis reactions, which can influence the volatile fraction of phenolic compounds, contributing critically to the determination of the final complex aroma and consumer preferences.

Chemical and physical changes during the process are strictly dependent on the slow and continuous oxygen diffusion, spontaneous clarification, and CO_2 elimination [1]. These aspects are closely linked to the materials used in winemaking processes such as stainless steel, wood, cement, terracotta; in fact, the permeability of the tank can influence the micro-oxygenation processes and, consequently, the final quality of the wine [2,3].

In the last decade, some winemakers have therefore re-evaluated the role of micro-oxygenation provided by the porosity of terracotta in the fermentation and ageing phases, resulting in the need for further chemical investigation into the potential and limitations of this technique. The volatile profile of the wine was analyzed by solid-phase headspace microextraction coupled with gas chromatography-mass spectrometry, and the percentages of volatile compounds in Sangiovese and Cabernet Franc vinified in stainless steel containers and in amphorae over time were compared.

The results showed that vinification in amphora improves the aromatic components of Cabernet Franc wine, while there is no substantial difference for Sangiovese wine. A metabolomic approach was also attempted for the first time and NMR analysis showed a difference between the spectra of samples vinified in amphora compared to those vinified in stainless steel, suggesting a potential new approach to obtain significant traceability.

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Heptadentate trensal-type ligands for lanthanides coordination and separation

Martina Neri, Giulia Bonfant, Alex Falco, Matteo Tegoni, and Luciano Marchiò

Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università degli Studi di Parma, Parco Area delle Scienze, 17/A, 43124-Parma, Italy
E-mail: martina.neri@unipr.it

One of the most important challenges of the modern era is to close the life-cycle of electronic materials that are dominant in today's economy. Rare-earth metals (REEs) are precious for wind and solar energy, electric and hybrid vehicles considering that they are essential components of high-performance magnets. A peculiar neodymium–iron–boron (Nd–Fe–B) permanent magnet of e-vehicles, e-scooters and e-bikes typically contains 28–35 wt% REEs (Pr, Nd, Tb, and Dy) which means that the recovery and recycling of REEs from magnetic waste may represent an important strategy for addressing the issue related to their high supply risk [1].

In the present work, we designed specific ligands that take into account the little and subtle differences between the chemical properties of the lanthanides, such as ionic radius or coordination numbers (Figure 1) with the aim to recovery one specific REE over another [2,3]. A set of known or new heptadentate N/O ligands (trensal family, H_3trensal = 2,2',2''-Tris(salicylideneimino)triethylamine) were prepared, starting from a central triethylamine scaffold functionalized with aromatic hydroxylamines (N/O donor), imine (N donor) or phenoxy (O donor) groups. The different moieties of these ligands allow to modify the chemical-physical properties of REE complexes such as the solubility in various solvents. We focused on Neodymium and Dysprosium rare-earth metals and studied the different structures that these two metals build with the same ligand. At a further level, the lipophilicity of the ligands can be also modified by including specific hydrophilic or hydrophobic moieties (for example with halogen atoms I>Br>Cl).

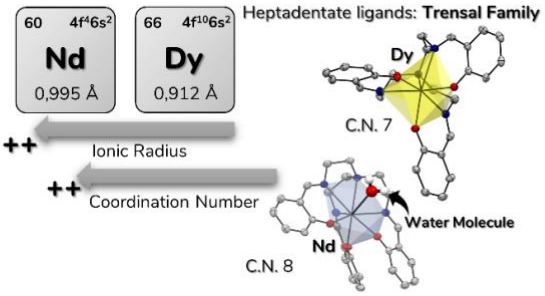

Figure 1: Different coordination numbers and complexes of Nd and Dy metals with trensal-type ligands.

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Improving the annotation of post-prandial metabolites in human urine samples from an untargeted LC-MS-based bilberry-blueberry intervention study by Feature-Based Molecular Networking

Lapo Renai,[a] Marynka Ulaszewska,[b] Massimo Del Bubba,[a] and Justin J.J. van der Hooft[c]

[a] Department of Chemistry "Ugo Schiff", University of Florence, Via della Lastruccia 3, 50019 Sesto Fiorentino, Italy
[b] IRCCS "San Raffaele" Hospital, Center for Omics Sciences, Proteomics and Metabolomics Facility (ProMeFa), Via Olgettina, 60, 20132 Milan, Italy
[c] Bioinformatics Group, Wageningen University, 6708 PB Wageningen, the Netherlands
E-mail: lapo.renai@unifi.it

The annotation process is a main bottle-neck in liquid chromatography-mass spectrometry (LC-MS) based untargeted metabolomics, due to the complexity of the metabolome and the high-dimensional and heterogeneous set of ionized metabolites occurring in biological samples [1]. In this context, Molecular Networking (MN) represents an efficient tool for the rapid formation of several molecular families within complex mixtures, by grouping molecular and pseudo-molecular ions according to their structural relationships [2]. This research aims to extend the annotation coverage of metabolites occurring in human urine samples from an already published intervention study on bilberry (*V. myrtillus*) and blueberry (*V. corymbosum*) intake [3], combining LC-MS standard feature detection tools with MN, i.e. Feature-Based Molecular Networking (FBMN). By this approach, using the GNPS infrastructure including public spectral libraries, 66 additional potential marker of berries intake were annotated, increasing the annotation coverage of the 45% compared to the previous research, and the structures of fifteen additional metabolites were hypothesized by spectral analysis. Moreover, several molecular families of the phase II (e.g. glucuronidated and sulfated phenolics) and phase I (e.g. phenylpropionic acids) metabolism were identified by longitudinal correlation analysis. We expect that our approach will greatly assist in disentangling the microbial and human biotransformations of food-derived metabolites.

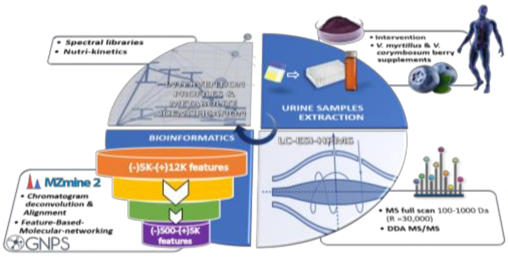

Figure 1: Graphical workflow of the experimental steps followed in this study.

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Investigation of inorganic arsenic content in Italian rice samples before and after cooking

Alice Cantalupi, Mario Casali, Erika Fantozzi, and Cinzia Simonelli

Laboratorio di Chimica, Merceologia e Biologia Molecolare, Centro Ricerche sul Riso, Ente Nazionale Risi, Strada per Ceretto 4, 27030 Castello d'Agogna (PV), Italy
E-mail: a.cantalupi@enterisi.it

Arsenic (As) is a metalloid naturally present in the environment and produced by anthropogenic activity. This element in trivalent or pentavalent inorganic form (As-i) is a hazardous pollutant for human health. In fact, it is easily absorbed and accumulated in tissues and body fluids. Several evidences led the International Agency for Research on Cancer (IARC) to classify it as a Group I carcinogen [1].

Rice is one of the foods that most easily accumulates As-i. Indeed, this cereal has the ability to take up and accumulate toxic metals, such as As, thus becoming a major source of human intake [2]. For this reason, the European community established maximum levels of As-i in rice and some of its derived products by Regulation (EU) 2015/1006, which amends Regulation (EC) 1881/2006.

The following study proposes an investigation on the content of As-i in rice before and after cooking in excess of water, in order to examine its behavior during the preparation by the consumer.

14 samples of Italian varieties with two different milling degree (milled and brown rice), parboiled and not, were selected. The determinations were carried out on samples before cooking and after cooking in excess of water (1:10 rice to water) for an average time of 15 minutes; the obtained cooked samples were dried in oven (85°C for 12-14 hours), left to cool and finely milled.

Analyses were performed by Atomic Absorption Spectroscopy with Hydride Generation (HGAAS) after acid extraction with 0,28 mol/l HNO_3 (according to UNI CEN/TS 16731:2014). The values of As-i were reported at a relative humidity value of 14%, to allow a comparison of collected data.

For non parboiled samples, the results for milled rice showed that the As-i in cooked rice decreased about 66-67%. Meanwhile in brown rice the decrease is more than 80%. Instead, parboiled rice showed a percentage decrease of As-i between 40 and 65%.

This shows that the cooking process actually results in a decrease in As-i content. Furthermore, the high temperature and pressure treatment of parboiling already leads to a first loss in the As-i of the samples, resulting to a minor content of this pollutant in parboiled rice.

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Novel electro-analytical approach for the detection and discrimination of cannabinoids in real samples extracts

Alessandro Monari,[a] Gabriele Bevini,[a] Barbara Zanfrognini,[b] Chiara Zanardi,[a,b] Giorgia Foca,[c] and Alessandro Ulrici,[c] Laura Pigani,[a]

[a] Dep. of Chemical and Geological Sciences, University of Modena and Reggio Emilia, via Campi 103, 41125-Modena, Italy
[b] Institute of Organic Synthesis and Photoreactivity (ISOF), National Research Council (CNR), Via P. Gobetti 101, 40129-Bologna, Italy
[c] Dep. of Life Sciences, University of Modena and Reggio Emilia, via Amendola 2, 42122-Reggio Emilia, Italy
E-mail: alessandro.monari@unimore.it

Cannabinoids are terpenophenolic compounds of great interest which have been extensively investigated due to their important pharmacological properties. Phytocannabinoids are cannabinoids derived from Cannabis sativa L; among them, trans-Δ^9-tetraidrocannabinol (THC) is widely known for its psychoactivity while cannabidiol (CBD), which is non-psychoactive, is known for its neuroprotective, anti-inflammatory and analgesic characteristics. Marijuana and hashish, referred as recreational Cannabis, are illicit products possessing high THC levels and low CBD levels, while some fiber-type Cannabis products (including those known as "Cannabis light") have been recently legalized in many countries. This type of products present on the market are growing exponentially, urging the need of an accurate controls to meet specific regulations. The determination of cannabinoids in real samples and the determination of THC/CBD ratio is performed with the use of chromatographic techniques; however, the non-portable instrumentation, the consuming sample preparation and the long analysis time don't allow for their use in in-situ analysis. As promising alternatives to these techniques in allowing a real-time and fast cannabinoid screening, electrochemical sensors have been receiving considerable interest, thanks to their low cost, handiness and miniaturization possibility [1]. In fact, THC, CBD and their natural acidic precursors (i.e. THCA and CBDA) are electroactive, due to the oxidation of the phenolic group, that makes them good candidates for electrochemical analysis. This work was then focused on the development of sensors exploiting the electroactivity of cannabinoids to perform qualitative and quantitative analysis even in real matrices extracts. Among all the electrodic materials tested, screen printed electrodes (SPEs) modified with carbon black (CB) showed very promising results [2]. The sensor ability to recognize various Cannabis samples has been investigated coupling voltammetric techniques to chemometric data analysis. Initial experiments have been developed in aqueous/methanol mixtures containing THC or CBD and both; then measurements have been performed on real samples represented by extracts of different types of cannabis. The electrochemical procedure proposed lead to excellent results, allowing the discrimination between samples with different CBD-THC content.

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A printed microfluidic wearable sensor for cortisol monitoring in sweat: preliminary results

Luca Fiore,[a] Vincenzo Mazzaracchio,[a] Aristi Serani,[a] Laura Fabiani,[a] Danila Moscone,[a] and Fabiana Arduini[a,b]

[a] *Department of Chemical Science and Technology, University of Rome "Tor Vergata", Rome, Italy*
[b] *Sense4Med S.r.l., Italy*
e-mail: luca.fiore@uniroma2.it

Monitoring biomarker levels in sweat samples is becoming increasingly relevant. Cardiovascular disease (CVD) is one of the main causes of death worldwide, according to the World Health Organization (WHO) [1]. Psychosocial stress is said to be a key cause of CVD [2]. Stress is becoming a global issue that impacts people's behavior. Cortisol, commonly known as the stress hormone, is a significant component in the psychobiology of the stress response and its detrimental health consequences [3]. In recent years, an increasing interest in the development of wearable biosensors grew up. Electrochemical methods provide analytical tools for the determination of cortisol due to their properties such as high sensitivity, easiness to use, and cost-effectiveness. Herein, we describe the development of a miniaturized microfluidic wearable immunosensor for real-time monitoring of cortisol in sweat. The device consists of low-cost fabricated screen-printed electrodes (SPE), fabricated on a polyester substrate, for the amperometric detection of the analyte combined with the microfluidic platform including a paper-based pad in which all the reagents needed to carry on the measurement were pre-loaded. The immunosensor was conceived as a direct competitive immunoassay using acetylcholinesterase-cortisol conjugate measuring the enzymatic by-product thiocholine at the screen-printed electrode modified with carbon black/Prussian blue (CB/PB-SPE). CB/PB-SPEs were overnight incubated with 4 μL-drop of anti-cortisol monoclonal antibody designed to selectively bind cortisol. After the immobilization process, the sensors were incubated for 30 min with 20 μL of BSA solution (3% w/v) for blocking the free active sites of the working electrode surface, to avoid non-specific adsorption. After the incubation, the excess of BSA was removed by washing with 0.5 mL of PBS. Then, the sensors were incubated with 15 μL of a solution containing enzyme-labeled cortisol (fixed amount) and cortisol (increasing concentrations) for 90 min, hence removing the excess by washing with 0.5 mL of PBS. Finally, amperometric detection was carried out by dropping 70 μL of acetylthiocholine solution 10 mM, applying a potential of 0.3 V for 130 seconds. The linearity was observed in the range comprised between 5 to 150 ng/mL of cortisol described by the following equation $y= -0.0004x + 0.1080$, $R^2= 0.945$.

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Phenylimino indolinone: a green light responsive t-type photoswitch exhibiting negative photochromism

Stefano Crespi,[a] Nadja A. Simeth,[a] Mariangela Di Donato,[b] Sandra Doria,[b] Charlotte N. Stindt,[a] Michiel F. Hilbers,[c] Ferdinand L. Kiss,[a] Ryojun Toyoda,[a] Sammo Wesseling,[a] Wybren Jan Buma,[c] Ben L. Feringa,[a] and Wiktor Szymański[a]

[a] *Stratingh Institute for Chemistry, University of Groningen, Nijenborgh 4, 9747AG Groningen, The Netherlands*
[b] ICCOM-CNR, via Madonna del Piano 10, 50019 Sesto Fiorentino, Italy
[c] *Van 't Hoff Institute for Molecular Sciences, University of Amsterdam, Science Park 904, 1098 XH Amsterdam, The Netherlands*
E-mail: s.crespi@rug.nl

Imines are photoaddressable motifs useful in the development of new generations of molecular switches, but their operation with low energy photons and control over isomer stability remain challenging. Based on a computational design, we developed Phenylimino Indolinone (PIO), a green-light addressable T-type photoswitch, showing negative photochromism. The isomerization behavior of this photoactuator of the Iminothioindoxyl (ITI) class was studied using time-resolved spectroscopies on time scales from femtoseconds to steady-state, and by quantum chemical analyses. The understanding of the isomerization properties and substituent effects governing these photoswitches opens new avenues for the development of novel T-type, visible-light addressable photoactuators based on C=N bonds.

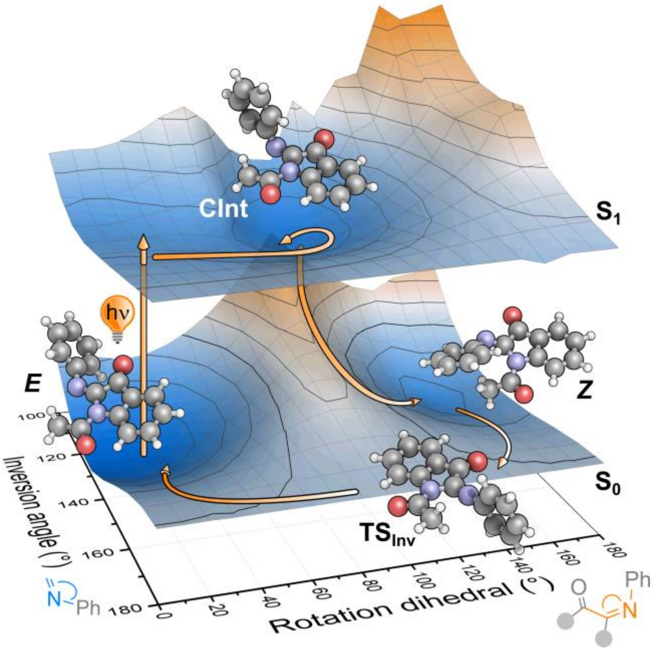

Figure 1: The full rotational cycle of unsubstituted PIO (SF-BH&HLYP/cc-pVDZ).

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Oriented microstructures in polyethylene-syndiotactic polypropylene di-block copolymers induced by epitaxial crystallization

Alessandra Cicolella, Claudio De Rosa, Rocco Di Girolamo, Giovanni Talarico, and Miriam Scoti

Dipartimento di Scienze Chimiche, Università degli Studi di Napoli Federico II, Via Cintia, 80126-Napoli, Italy
E-mail: alessandra.cicolella@unina.it

Crystallization and phase separation in the melt in semicrystalline block copolymers (BCPs) compete in defining the final solid state structure and morphology. In crystalline-crystalline di-block copolymers the sequence of crystallization of the two blocks plays a definitive role.

In this work we show that the use of epitaxial crystallization on selected crystalline substrates allows achieving a control over the crystallization of the blocks by inducing crystal orientations of the different crystalline phases and a final control over the global morphology. A sample of polyethylene-block-syndiotactic polypropylene (PE-b-sPP) block copolymer has been synthesized with a stereoselective living organometallic catalyst and epitaxially crystallized onto crystals of two different crystalline substrates p-terphenyl (3Ph) and benzoic acid (BA) [1].

The epitaxial crystallization on both substrates produces formation of highly ordered morphologies with crystalline lamellae of sPP and PE highly oriented along one direction. However, the epitaxial crystallization onto 3Ph should generate a single orientation of sPP crystalline lamellae highly aligned along one direction and a double orientation of PE lamellae, whereas BA crystals should induce high orientation of only PE crystalline lamellae. Thanks to the use of the two selective substrates, the final morphology reveals the sequence of crystallization events during cooling from the melt and what is the dominant event that drives the final morphology. The observed single orientation of both crystalline PE and sPP phases on both substrates, indeed, indicates that sPP crystallizes first onto 3Ph defining the overall morphology and PE crystallizes after sPP in the confined inter-lamellar sPP regions. Instead, PE crystallizes first onto BA defining the overall morphology and sPP crystallizes after PE in the confined inter-lamellar PE regions.

This allows discriminating the different crystalline phases and defining the final morphology, which depends on which polymer block crystallizes first on the substrate. This work also shows that the use of epitaxial crystallization and the choice of suitable substrate offer a mean to produce oriented nanostructures and morphologies of block copolymers depending on the composition and the substrates.

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Crystallization behavior of propylene-ethylene copolymers synthesized with heterogeneous Ziegler/Natta catalysts as a tool to reveal the molecular structure.

Angelo Giordano, and Claudio De Rosa

Dipartimento di Scienze Chimiche, Università degli Studi di Napoli "Federico II", Complesso Monte S. Angelo, Via Cintia, 80126-Napoli, Italy
E-mail: angelo.giordano@unina.it

A study of the crystallization properties and polymorphic behavior of samples of propylene-ethylene isotactic copolymers (iPPEt) prepared with heterogeneous Ziegler-Natta catalysts is reported. Generally, copolymerization with Ziegler-Natta catalysts produces a mixture of macromolecules characterized by a different composition and a non-uniform distribution of the comonomeric units along the chains. This results in a complex structure of the macromolecules with the presence of segments of chains rich in propene that may crystallize as isotactic polypropylene (iPP) and segments richer in ethylene that may crystallize as polyethylene (PE). The crystallization of the α and γ forms of iPP from the propene-rich segments depends on the length of the regular propene sequences [1] and, therefore, the relative amount of the two polymorphs may give information about the length of the crystallizable segments and shed light on the molecular structure and architecture of these copolymers.

iPPEt copolymers of different ethylene concentrations have been crystallized from the melt at different temperatures. All samples crystallize as mixtures of the α and γ forms and the amount of *γ* form increases with increasing crystallization temperature and ethylene concentration. The maximum amount of γ form that develops for each sample of iPPET copolymers is much lower than that obtained in analogous samples of iPPEt copolymers of similar ethylene concentration prepared with metallocene catalysts, which are characterized by a uniform composition and an ideal random distribution of comonomers along the chains [2]. This different crystallization behavior indicates that in the Ziegler-Natta iPPET copolymers the length of crystallizable propene sequences is much longer than in the metallocene copolymers. This, in turn, indicates that in Ziegler-Natta iPPEt samples most of the defects are segregated in more irregular portions of the chain connected to more regular and long segments that crystallize in the α form. These results allow concluding that some fractions of Ziegler-Natta iPPEt copolymers are characterized by chains with a "blocky" structure, consisting of regular isotactic sequences chemically linked to more irregular sequences.

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Crystallization of propene-pentene isotactic copolymers: further evidence of the double role of comonomers on the crystallization behavior of isotactic polypropylene

Fabio De Stefano, Claudio De Rosa, Miriam Scoti, Rocco Di Girolamo, Giovanni Talarico, and Anna Malafronte

Dipartimento di Scienze Chimiche, Università di Napoli "Federico II", Complesso Monte S. Angelo, Via Cintia, 80126-Napoli, Italy
E-mail: fabio.destefano@unina.it

A study of the crystallization from the melt of random propene-pentene isotactic copolymers (iPPC5) is presented. All samples with pentene concentration in the range 0.5-11 mol% crystallize from the melt at any crystallization temperature in α and γ forms of isotactic polypropylene (iPP). For pentene concentration higher than 10-11 mol%, the trigonal δ form becomes favored and the sample with the highest pentene content of 12.4 mol% crystallizes from the melt in mixtures of α form and trigonal δ form [1].

The data of the maximum amount of γ form that develops from the melt in iPPC5 copolymers have been compared with those of copolymers of iPP with ethylene, butene and hexene and of stereodefective samples of iPP containing only *rr* stereodefects, reported in the literature [2,3]. These data give evidence of the general view of the crystallization behavior of iPP, which is based on the definition of a dual role played by defects, the interruption effect that shortens the regular isotactic propene sequences and favors crystallization of γ form, and the effect of inclusion of defects into the crystalline unit cell of α and γ forms, which favors crystallization of the polymorphic form that better accommodate the defect into crystals at low cost of conformational and packing energy. The relative efficiency of the two effects depends on the type and size of the defect.

Different relationships between the maximum amount of γ form and the average length of regular propene sequences have been obtained for the different copolymers and steroirregular iPPs, according to the different type and size of defects and the different efficiencies of their interruption and inclusion effects. The different relationships are a result of the equilibrium between these two effects achieved by each defect and confirm that the crystallization of γ form of iPP is a perfect indicator of the length of regular propene sequences and may provide very detailed information on the molecular structure of iPP.

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Towards application of kraft lignin in organic electronics

Rosarita D'Orsi,[a] Bilge Kahraman,[b,c] Yasin Kanbur,[b,d] Mihai Irimia Vladu,[b] Niyazi Serdar Sariciftci,[b] and Alessandra Operamolla[a]

[a] *Department of Chemistry and Industrial Chemistry, University of Pisa, via Giuseppe Moruzzi 13, 56127, Pisa*
[b] *Linz Institute for Organic Solar Cells (LIOS), Physical Chemistry, Johannes Kepler University Linz, Altenberger Str. Nr. 69, 4040 Linz, Austria*
[c] *Department of Material Science and Nanotechnology Engineering, TOBB ETU University, Söğütözü, Söğütözü Cd. No:43, 06510 Çankaya/Ankara Turkey*
[d] *Department of Chemistry, Karabük University, Baliklarkayasi Mevkii, 78050 Karabük, Turkey*
E-mail: rosarita.dorsi@dcci.unipi.it

Cellulose, hemicellulose and lignin are the main components of lignocellulosic biomass. In particular, lignin is a waste product of cellulose industry with limited large-volume usefulness. Lignin is a biopolymer whose structure and properties critically depend on its natural origin and isolation procedure. Therefore, it displays variable properties that limit its straightforward use in materials science. Some of the newest applications of lignin include its use in materials as an additive or filler, as a copolymer former or as an aromatic feedstock [1,2]. Conversely, data or information about the use of lignin as an active material in the organic electronic field is scarce: its poor solubility in common solvents and broad distribution of molecular weight limit the use of this material in the development of devices, which usually require polymers with highly regular and definite molecular structure [3]. In this communication, we describe the deposition of kraft lignin films by spin-casting. Solubility, absorption, and deposition conditions of two types of lignin were studied and optimized to investigate their performance as solid-state gate dielectric in organic field effect transistors (OFETs). We describe further work done towards lignin fractionation to achieve more definite lignin structures.

Figure 1: Application and study of Kraft lignin in organic electronics.

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Hybrid sensitizers for solar energy conversion

Luca Lazzarin, and Enzo Menna

Dipartimento di Scienze Chimiche, Università degli Studi di Padova, Via Marzolo 1, 35131-Padova, Italy
E-mail: luca.lazzarin@studenti.unipd.it

Over the past decade, an increasing attention has been paid to the development of new classes of photosensitizing agents for solar, photovoltaics and photocatalysis [1]. In particular, the research has been focused on the sustainability and low-cost of photoactive components and, for dye-sensitized solar cell (DSSC), on the replacement of expensive and polluting Ru-based complexes with metal-free organic dyes [2]. Moreover, recent investigations have highlighted advantages of graphene-based hybrid dyes [3].

In this study, "Donor-π-Acceptor" dyes grafted on a reduced graphene oxide (rGO) matrix are presented and characterized. Further photoelectrochemical analysis of the performance of the cell based on this new material will follow, giving an idea of the photoactive behavior in a DSSC.

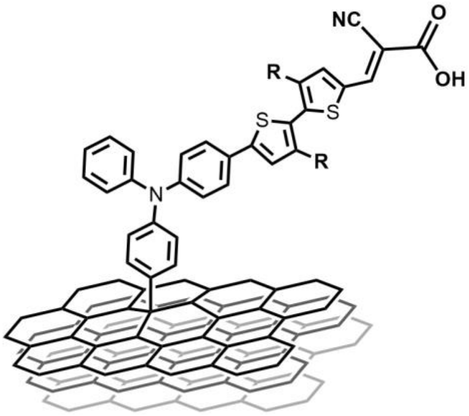

Figure 1: rGO functionalized with a Donor-π-Acceptor system

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Symmetry breaking in self-assembled $TPPS_4$ porphyrin aggregates

Gioacchino Schifino,[a] Mariagrazia Fortino,[a] Luigi Monsù Scolaro,[b] and Adriana Pietropaolo[a]

[a] Dipartimento di Scienze della Salute, Università di Catanzaro, Viale Europa, 88100 Catanzaro, Italy
[b] Dipartimento di Scienze Chimiche, Biologiche, Farmaceutiche e Ambientali, Università degli Studi di Messina, V.le F. Stagno D'Alcontres 31, Vill. S. Agata, 98166 Messina, Italy
E-mail: gioacchino.schifino@studenti.unicz.it

In recent years, the dynamical symmetry-breaking event involving the generation of a chiral supramolecular structure starting from achiral constituents has attracting considerable interest for the development of advanced chiral materials. In this background, the spontaneous self–organization of achiral π-conjugated molecules has gained significant attention due to their versatile optical and electronic properties. Specifically, meso-tetrakis(4-sulfonatophenyl)porphine ($TPPS_4$) have shown great ability to self-assemble into chiral supramolecular structures. The conformation of porphyrin frameworks can be witnessed by the four torsional pyrrole dihedral angles having values approaching ± 5 degrees in all four cases, together with the side chains phenyl rings. However, self-assembly interactions may lead to structural deviations generating instantaneous asymmetry that can be propagated along the whole supramolecular structure. Motivated by the interest in designing new chiral material and to investigate the symmetry-breaking event occurring during the formation of chiral aggregates starting from achiral $TPPS_4$ monomers, enhanced sampling simulations have been performed on $TPPS_4$ in its monomeric, dimeric, trimeric and tetrameric forms (Figure 1). Specifically, the free-energy profiles as a function of the pyrrole improper torsions of the porphyrin ring have been reconstructed for all the $TPPS_4$ aggregates allowing us to evaluate how the symmetry of $TPPS_4$ supramolecular system can be modified by increasing the aggregate dimension.

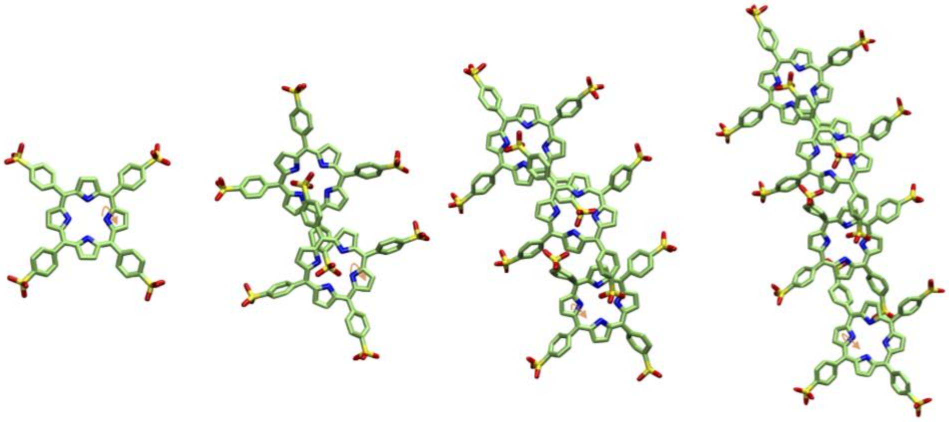

Figure 1: The monomer, dimer, trimer and tetramer of the $TPPS_4$ system conformations disclosed from enhanced sampling simulations.

Design of molecular qubits based on metal-organic paramagnets

Manuel Imperato,[a,b] Matteo Boniburini,[b] Alessio Nicolini,[b] and Andrea Cornia[b]

[a] Department of Physics, Informatics and Mathematics, University of Modena and Reggio Emilia, Via G. Campi 213/A, 41125-Modena, Italy.
[b] Department of Chemical and Geological Sciences, University of Modena and Reggio Emilia & INSTM, Via G. Campi 103, 41125-Modena, Italy.
E-mail: manuel.imperato@unimore.it

Quantum technologies exploit the quantum properties of matter to develop new functional tools and devices. The core of this approach is the quantum bit (qubit), the quantum version of the classic binary bit. Classical bits exist in one of two states, 0 or 1, whereas qubits can be placed into a quantum superposition of their two constituent states, thus simultaneously accessing multiple states [1]. The coherence time, which describes the lifetime of the superposition state before it collapses into one of its constituent classical states, is the most important figure of merit of a qubit. Among the physical realizations of qubits are magnetic molecules prepared through molecular chemistry. Simple metal-organic paramagnets with a single unpaired electron (S = ½), like vanadium(IV) complexes, can exhibit sufficiently long coherence times to allow quantum operations. Decoherence is mainly induced by electron−electron and electron−nuclear spin−spin interactions, which can be controlled by chemical design [2]. However, other desirable properties for a molecular qubit are chemical and thermal stability, good processability and a functionalizable structure. For this reason, our current goal is to design new molecular qubits based on robust, neutral macrocyclic complexes of transition metals with O donors, which contain no nuclear spins. We recently optimized the synthesis of H_2L (Fig. 1), a pre-organized tetradentate proligand containing two fused β-diketones [3]. H_2L was characterized by 1D and 2D ^{1}H-NMR spectroscopy, but the interpretation of the spectra was complicated by the occurrence of keto-enol tautomerism. To obtain unambiguous structural data we prepared the cobalt(II) complex of L^{2-}. Crystals suitable for X-ray diffraction were obtained from THF/*n*-hexane solution by adding an excess of pyridine (py) to complete the octahedral coordination geometry of the metal. Surprisingly, the product has a dinuclear structure and its molecular formula is $[Co_2(L)_2(py)_4]$. This new compound was characterized by UV-Vis-NIR, FT-IR/ATR and ^{1}H-NMR spectroscopies. We are currently working on the challenging synthesis of oxovanadium(IV) complex [VO(L)], which is expected to act as a qubit. Despite repeated attempts, only a noncrystalline green solid was obtained so far, which however has the correct metal-to-ligand ratio (1:1) as well as the characteristic bands of VO^{2+} in its UV-Vis-NIR and FT-IR/ATR spectra.

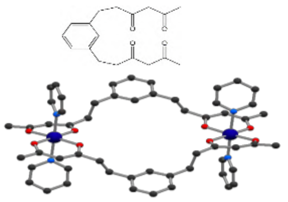

Figure 1. ***Structures of H_2L (above) and $[Co_2(L)_2(py)_4]$ (below). Color code: dark blue, Co; red, O; blue, N; black, C. Hydrogen atoms are omitted for clarity.***

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PON2 silencing to evaluate the effectiveness of Cisplatin treatment in OSCC cells by FTIRM analyses

Alessia Belloni[a], Valentina Notarstefano[a], Alessia Salvucci[b],
Roberto Campagna[b], Graziana Spinelli[b], Davide Sartini[b], Elisabetta Giorgini[a],
and Monica Emanuelli[b]

[a] *Department of Life and Environmental Science, Università Politecnica delle Marche, Via Brecce Bianche, 60131 Ancona, Italy.*
[b] *Department of Clinical Sciences, Università Politecnica delle Marche, Via Tronto 10/a, 60126 Ancona, Italy.*
E-mail: a.belloni@pm.univpm.it

The resistance and recurrence to chemotherapy treatments showed by some types of cancer is one of the main concerns in cancer therapy. Oral Squamous Cell Carcinoma (OSCC) is one of these; it has been demonstrated that its cancer stem cells (CSCs) play a crucial role in the refractoriness to Cisplatin, and hence, this finding makes them the main target of this therapy [1]. Another strategy to counteract the inconvenience of resistance could be represented by the targeting of PON2 gene which expresses the paraoxonase-2 enzyme: this gene, that is naturally involved in protecting cell damage against reactive oxygen species (ROS), seems to be able to defend cancer cells by the toxicity induced by Cisplatin, with the same mechanism [2,3]. In this study, after PON2 silencing, OSCC cells were treated with Cisplatin at different concentrations and time points: a molecular and spectroscopic approach was exploited to evaluate the effectiveness of silencing and the response of silenced OSCC cells to Cisplatin. Cell samples were analyzed by FTIRM spectroscopy, and the spectral data were submitted to univariate and multivariate analyses to detect eventual changes among the main biological macromolecules (Figure 1).

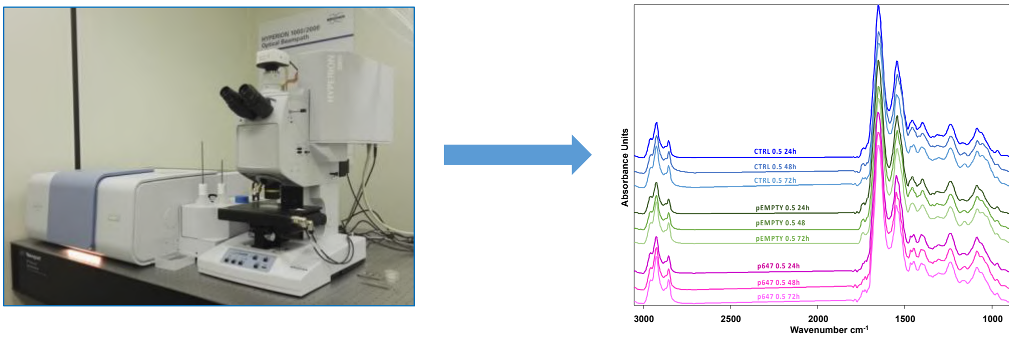

Figure 1: FTIRM spectrometer (left) and Average Absorbance spectra extracted from OSCC samples (right): control group (CTRL, blue), OSCC transfected by an empty plasmid (pEMPTY, green) and OSCC transfected with plasmid 647 coding shRNAs targeting PON2 (p647, pink) at three different time points (24, 48, 72 hours of treatment with Cisplatin [0,5 *μ*g/ml]).

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Enantiomerization barrier of 1-[2-(2-methyl-2-methoxycarbonylacetamido) benzenesulfonyl]-1h-pyrrole studied by enantioselective dynamic HPLC, classical off column technique and computational approach

Fabio Buonsenso,[a] Roberto Cirilli,[b] Romano Silvestri,[a] and Marco Pierini [a]

[a] Dipartimento di Chimica e Tecnologie del Farmaco, "Sapienza, Università di Roma", Piazzale Aldo Moro 5, 00185, Rome, Italy
[b] Istituto Superiore di Sanità, Centro Nazionale per il Controllo e la Valutazione dei Farmaci, Viale Regina Elena 299, 00161, Rome, Italy
E-mail: fabio.buonsenso@uniroma1.it

Many commonly used drugs are chiral compounds. As known, drugs' enantiomers are certainly characterized by identical physicochemical properties, but can differ in their pharmacokinetics, pharmacodynamics and toxicity. In connection with this, interest in chiral analysis and evaluation of stereolability of biologically active compounds has grown significantly in recent years. In this work, the stereochemical analysis of the chiral heterocyclic compound 1-[2-(2-methyl-2-methoxycarbonylacetamido) benzenesulfonyl]-1h-pyrrole [1] was carried out through the aid of two different analytical approaches: 1) kinetic batchwise studies monitored by enantioselective HPLC (eHPLC) technique; 2) kinetic on-column studies monitored by Dynamic enantioselective High Performance Liquid Chromatography (D-eHPLC). The chromatographic analyses were carried out by the commercially available Chiralcel OJ column. The study also covered the effects arising from the modification of the mobile phase, with variations concerning kind and polarity of the employed solvents, as well as the transition from normal to reverse phase, in presence or not of organic modifiers, such as triethylamine (TEA) and trifluoroacetic acid (TFA). All the resulting dynamic chromatograms were analysed by means of the home-made computer program *Auto-DHPLC-y2k*. Analysis of the obtained experimental data made it possible to achieve kinetic and thermodynamic information relevant to the enantiomerization/racemization process of the heterocyclic compound under consideration. [2,3] Finally, as the conclusive step of the investigation, the possible mechanisms responsible for the observed enantioisomerizations have been inquired by computational study.

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Magneto-Chiral Dichroism in Chiral Molecules and Magnets

Matteo Atzori,[a,b] Ivan Breslavetz,[a] Angela Perez Valentin,[c] Kévin Paillot,[b] Elizabeth Hillard,[c] Patrick Rosa,[c] Andrea Caneschi,[d,b] Roberta Sessoli,[d,b] Geert Rikken,[a] and Cyrille Train[a]

[a] Laboratoire National des Champs Magnétiques Inteses, CNRS & Université Grenoble Alpes, 25 Rue de Martyrs, 38042, Grenoble, France
[b] Consorzio Interuniversitario Nazionale per la Scienza e Tecnologia dei Materiali INSTM, Via Giusti, 9 50121 Firenze, Italy
[b] Centre de Recherche Paul Pascal, CNRS & Université de Bordeaux, 115 Avenue du Dr Albert Schweitzer, 33600, Pessac, France
[c] Dipartimento di Chimica "Ugo Schiff", Università degli Studi di Firenze, Via della Lastruccia 3, 50019 Sesto Fiorentino, Firenze, Italy
E-mail: matteo.atzori@lncmi.cnrs.fr

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 contribution 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 $\mathrm{Mn^{II}}$ and $\mathrm{Cr^{III}}$ ions [3], the key-role of spin-orbit coupling in driving MChD signals in a single-chain magnet based on tetragonally distorted $\mathrm{Mn^{III}}$ ions [4] and the strong MChD observed for a chiral $\mathrm{Yb^{III}}$-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 $\mathrm{Ni^{II}}$ complexes [6].

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N-doped porous carbon from leather solid waste for application in sustainable lithium batteries

Sebastiano Tieuli, [a] Michela Signoretto, [a] Somayeh Taghavi,[a] Pejman Salimi,[b,c]
Remo Proietti Zaccaria,[b] Riccardo Pasquale,[d] Massimiliano Silvestri[e]

[a] *CATMAT Lab, Department of Molecular Sciences and Nanosystems, Ca' Foscari University Venice and INSTM RU of Venice, via Torino 155, I-30172 Venezia, Mestre, Italy*
[b] *Istituto Italiano di Tecnologia, via Morego 30, Genova 16163, Italy*
[c] *Department of Chemistry and Industrial Chemistry, University of Genova, via Dodecaneso 31, I-16146 Genova, Italy*
[d] *GSC GROUP S.P.A., Via dell'industria, 5, 36054 Montebello Vic.no, Vicenza Italy*
[e] *Pasubio S.p.A., II Strada 38, 36071 Arzignano, Vicenza Italy*
E-mail: sebastiano.tieuli@unive.it

Lithium-ion batteries (LIBs) are considered as the most popular energy storage system for portable electronic devices and transportation applications [1]. However, LIBs still face several challenges, particularly in electrodes' capacity, stability, and cost; which play a crucial role in a battery efficiency. Although the conventional electrode such as graphite as the anode part in commercial batteries possesses several advantages, it could not meet the future needs of the battery industry. The graphite has a limited theoretical gravimetric capacity of 372 mAh g^{-1}, poor diffusion kinetics of lithium, and it relies heavily on fossil fuel-based precursors and harsh or energy-intensive synthesis [2]. In this scenario, biochar (solid fraction of pyrolysis process) represents an attractive alternative either from an economic or electrochemical point of view.

In the present study, metals-free leather shaving waste has been considered as a bio-waste precursor to produce carbonaceous material, and to design anode for the half-cell application. The structure of pyrolyzed waste (biochar) was engineered with physical activation method, based on steam. A deep investigation of the physical/chemical properties of obtained carbon compared with the electrochemical performance of electrode has been the goal of the study.

The results showed that due to the spontaneous presence of doping heteroatoms such as N, S and O in the waste material, together with the high surface area, the electrochemical response of the activated biochar resulted in a high initial specific capacity of 1500 mAh g^{-1} at 0.1 A g^{-1}. Moreover, the electrode has shown very high Li-ions storage capacity over cycling showing a specific discharge capacity of 635 mAh g^{-1} after 500 charge and discharge cycles at 0.5 A g^{-1}.

In view of the promising performance observed in this work for the electrode derived from leather solid waste and the chemical/physical features of synthesized carbon material, an application of it could also be found in fuel cells, and supercapacitors.

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Sponsors presentations

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SP05	Anna TESTOLIN (DE NORA)

Merck Life Science

Roberto Pascucci

Sales Manager – Academia Italy - Merck Life Science
E-mail: roberto.pascucci@merckgroup.com

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Simona Trabace[a], Jacopo Bonanomi [b]

[a] *R&D – Researcher*
[b] *R&D – Team Leader*

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Sustainability and Greener Alternatives

Manuela Vacatello

Research Technology Specialist for Chemistry at Merck Life Science
E-mail: manuela.vacatello@merckgroup.com

At Merck Life Science we offer more than 300,000 products that support 1 million customers, and how we make, distribute, and enable the use and disposal of those products can have a large and meaningful impact on the environment.

Our sustainability goals an initiatives will be presented together with some of our greener alternatives for Chemistry to also help our customers be more sustainable, as our bio-renewable solvent Cyrene and its applications in Organic Chemistry [1] and Material Science [2], micellar catalysis, non-precious metal catalysts and other solutions to reduce chemical consumption and waste.

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From the laboratory to the publishing industry: how a chemist can shape the scientific knowledge

Marta Meazza

Elsevier, Oxford, United Kingdom
E-mail: m.meazza@elsevier.com

The talk will focus on the journey from research chemist to scientific editor, with a specific focus on the Tetrahedron journals' series and the newly launched Gold Open Access journal Tetrahedron Chem. In this talk I will outline the skills and expertise needed for this role, including the daily tasks and routine, and the typical life cycle of a manuscript following submission.

In 2018, Elsevier relaunched its free e-learning platform Researcher Academy [3]. The e-learning modules take you through the different phases of the research cycle – from the beginnings of research preparation, through the publishing process, all the way to demonstrating impact.

[1] https://researcheracademy.elsevier.com/

De Nora: a century of innovation towards a sustainable future

Anna Testolin

Industrie De Nora SpA, Via Bistolfi 35, 20134, Milano (MI)
E-mail: anna.testolin@denora.com

De Nora is an Italian multinational company, global provider of innovative technologies and solutions and is recognized as a partner of choice for important industrial electrochemical processes.

Since its foundation in 1923, De Nora has been driven by the philosophy of continual improvement and today is the world's largest supplier of high-performing catalytic coatings and insoluble electrodes for electrochemical and industrial applications, and a leading supplier of equipment, systems and processes for water disinfection and filtration. De Nora's technologies are recognized as a high-value enabler that facilitates transformation processes for many industrial applications: chemistry, water purification, electronics, energy storage, infrastructural corrosion protection, and many others.

De Nora is committed to developing unconventional solutions to achieve the energy transition to decarbonization, the green hydrogen economy, and clean water for everyone. In this context, one of the Company's current focuses is Alkaline Water Electrolysis (AWE) and the development of advanced anodes and cathodes to produce green hydrogen.

Including production facilities, sales offices, and technical support, De Nora has 24 locations in 12 countries around the world, with 4 R&D centers in Italy, the United States, and Japan (2 sites). This widespread presence allows the company to effectively serve customers in 119 countries throughout the world. De Nora currently holds about 350 patent families, with over 3000 territorial extensions. More than 1,650 employees work together with passion and enthusiasm, sharing knowledge and experience, for a sustainable future.

List of Participants

AITA Sara Elsa	UniROMA1	saraelsa.aita@uniroma1.it	**FL21**
ALBANO Gianluigi	UniBA	gianluigi.albano@uniba.it	**OR68**
ALESSANDRINI Silvia	SNS	silvia.alessandrini@sns.it	**OR77**
ALFIERI Maria Laura	UniNA	marialaura.alfieri@unina.it	**OR67**
ALGIERI Vincenzo	UniCAL	vincenzo.algieri@unical.it	**OR54**
ALLEGRI Alessandro	UniBO	alessandro.allegri2@unibo.it	**OR132**
ALLEGRITTI Elena	UnivAQ	elena.allegritti@graduate.univaq.it	**OR01**
ANNUNZIATA Francesca	UniMI	francesca.annunziata@unimi.it	**OR106**
ANNUNZIATO Giannamaria	UniPR	giannamaria.annunziato@unipr.it	-
ARFELLI Francesco	UniBO	francesco.arfelli3@unibo.it	**OR28**
ARGENZIANO Rita	UniNA	rita.argenziano@unina.it	**OR11**
ARTASENSI Angelica	UniMI	angelica.artasensi@unimi.it	**OR91**
ATZORI Matteo	CNRS	matteo.atzori@lncmi.cnrs.fr	**PO44**
BACCHIOCCHI Riccardo	UniBO	riccardo.bacchiocchi@unibo.it	**OR87**
BALSAMO S. Andrea	UniCT	stefano.balsamo@phd.unict.it	**OR27**
BARCELLONA Matteo	UniCT	mb.barcellona@gmail.com	**FL16**
BARTOLI Francesco	UniSI	francesco.bartoli@iccom.cnr.it	**FL06**
BASSETTI Benedetta	UniCAM	benedetta.bassetti@unicam.it	**OR32**
BELLA Federico	PoliTO	federico.bella@polito.it	**PL02**
BELLONI Alessia	UnivPM	a.belloni@pm.univpm.it	**PO42**
BELLOTTI Denise	UniFE	blldns@unife.it	**OR101**
BENASSI Alessandra	UniPV	alessandra.benassi01@universitadipavia.it	-
BENETTI Edmondo Maria	UniPD	edmondo.benetti@unipd.it	**PL05**
BIAGINI Denise	UniPI	denise.biagini@dcci.unipi.it	**OR98**
BIANCO Mariacristina	UniSA	mariacristinabianco01@gmail.com	**PO24**
BONFIO Claudia	ISIS Strasbourg	claudia.bonfio@gmail.com	-
BONONI Giulia	UniPI	giulia.bononi@phd.unipi.it	**OR94**
BRANDIELE Riccardo	UniPD	riccardo.brandiele@unipd.it	**OR134**
BUONSENSO Fabio	UniROMA1	fabio.buonsenso@uniroma1.it	**PO43**
BUSCEMI Gabriella	UniBA	gabriella.buscemi@uniba.it	**OR116**
CAMPAGNOLO Filippo	UniUD	155682@spes.uniud.it	**FL12**
CAMPOLUCCI Marta	UniGE	marta.campolucci@edu.unige.it	**FL27**
CANÉ Carolina	UniNA	carolina.cane@unina.it	**PO14**
CANESCHI Andrea	UniFI	andrea.caneschi@unifi.it	-
CANTALUPI Alice	Ente Risi	a.cantalupi@enterisi.it	**PO31**
CAPALDO Luca	Univ. Amsterdam	l.capaldo@uva.nl	**OR72**

CAPPAI Rosita	UniCA	cappai@unica.it	**OR93**
CARAMIELLO A. Maria	PoliMI	alessiomaria.caramiello@polimi.it	**OR51**
CARATELLI Veronica	UniROMA2	veronica.caratelli@uniroma2.it	**FL20**
CARBONE Daniela	UniPA	daniela.carbone@unipa.it	**OR03**
CARDOSO GOMES Guelber	UniPI	g.cardosogomes@studenti.unipi.it	**OR107**
CARIOLA Alice	UniBO	alice.cariola2@unibo.it	-
CARLOTTI Marco	IIT	marco.carlotti@iit.it	**OR38**
CARULLO Gabriele	UniSI	gabriele.carullo@unisi.it	**OR53**
CASTIGLIONI Michele	UniTO	michele.castiglioni@unito.it	**FL10**
CAVAGNERO Chiara	UniTO	chiara.cavagnero@unito.it	**FL22**
CERRATO Andrea	UniROMA1	andrea.cerrato@uniroma1.it	**OR08**
CESARI Andrea	UniPD	andrea.cesari@unipd.it	**OR79**
CESCO Michele	CIC biomaGUNE	michele.cesco96@gmail.com	**OR05**
CESCON Eleonora	UniTS	eleonora.cescon@phd.units.it	**OR100**
CHIMINELLI Maurizio	UniPR	mauriziochiminelli@gmail.com	**PO20**
CICOLELLA Alessandra	UniNA	alessandra.cicolella@unina.it	**PO35**
CINTI Stefano	UniNA	stefano.cinti@unina.it	-
CIRIGNANO Matilde	IIT	matilde.cirignano@iit.it	**OR118**
CLEMENTE Francesca	UniFI	francesca.clemente@unifi.it	**PO07**
COLAIEZZI Roberta	UnivAQ	roberta.colaiezzi@graduate.univaq.it	**OR13**
COMPARINI Lucrezia Margherita	UniPI	lucrezia.comparini@phd.unipi.it	**FL03**
COPPOLA Bartolomeo	PoliTO	bartolomeo.coppola@polito.it	-
COPPOLA Carmen	UniSI	carmen.coppola@student.unisi.it	**OR82**
COSTA Jessica	UniSI	jessica.costa2@unisi.it	**OR66**
CRESPI Stefano	Univ. Groningen	s.crespi@rug.nl	**PO34**
CURSARO Ilaria	UniSI	ilaria.cursaro@student.unisi.it	-
D'ORSI Rosarita	UniPI	rosarita.dorsi@gmail.com	**PO38**
DA PIAN Marta	Elsevier	marta.dapian@gmail.com	-
DAL CORSO Alberto	UniMI	alberto.dalcorso@unimi.it	**OR92**
DAVIGHI Maria Giulia	UniFI	mariagiulia.davighi@unifi.it	**PO08**
DE FRANCO Manuela	IIT	manuela.defranco@iit.it	**OR80**
DE LUCA Chiara	UniFE	dlcchr@unife.it	**OR55**
DE STEFANO Fabio	UniNA	fabio.destefano@unina.it	**PO37**
DECANDIA Gianfranco	UniBA	gianfranco.decandia@uniba.it	**OR109**
DECAVOLI Cristina	UniMIB	c.decavoli@campus.unimib.it	**OR23**
DEL GIUDICE Daniele	UniROMA1	Daniele.delgiudice@uniroma1.it	-
DEN HOED Frank	Univ. Groningen	f.m.den.hoed@rug.nl	**OR41**
DEREJE D. Melese	UniTO	degnetmelese.dereje@unito.it	**FL02**

DESTRO Lorenza	UniMORE	lorenza.destro@unimore.it	**PO02**
DI NARDO Fabio	UniTO	fabio.dinardo@unito.it	**OR45**
DI SOMMA Angela	UniNA	angeladisomma@unina.it	**FL04**
DI TERLIZZI Lorenzo	UniPV	lorenzo.diterlizzio1@universitadipavia.it	**OR36**
DI VERA Andrea	UniVE	andrea.divera@unive.it	**PO22**
DISTEFANO Alessia	UniCT	distefano-alessia@libero.it	**FL18**
DONATO Simone	UniFI	donato@lens.unifi.it	**OR37**
FAGIOLARI Lucia	PoliTO	lucia.fagiolari@polito.it	**OR22**
FANTONI Tommaso	UniBO	tommaso.fantoni3@unibo.it	**OR19**
FARINOLA Gianluca	UniBA	gianlucamaria.farinola@uniba.it	-
FASOLINI Andrea	UniBO	andrea.fasolini2@unibo.it	**OR136**
FELLETTI Simona	UniFE	fllsmn1@unife.it	**OR10**
FERDEGHINI Claudio	UniPI	claudioferdeghini@gmail.com	**OR108**
FERELLA Francesco	INFN	francesco.ferella@lngs.infn.it	-
FIORE Ambra M.	PoliBA	ambramaria.fiore@poliba.it	**OR35**
FIORE Luca	UniROMA2	luca.fiore@uniroma2.it	**PO33**
FIORENTINO Francesco	UniROMA1	f.fiorentino@uniroma1.it	**OR07**
FONTANA Anna	UniSI	a.fontana5@student.unisi.it	**PO04**
FORGHIERI Giulia	UniVE	giulia.forghieri@unive.it	**OR20**
FORTINO Mariagrazia	UniCZ	mariagrazia.fortino@unicz.it	**OR65**
FORTUNATO Anna	UniPD	anna.fortunato.1@studenti.unipd.it	**OR39**
FREGONI Jacopo	Uni. Madrid	jacopofregoni@gmail.com	**OR73**
FREITAS Williane	UniROMA2	williane.freitas@uniroma2.it	**OR24**
GABBININ Lorenzo	Olon	LGabbini@olonspa.it	-
GAETA Massimiliano	UniCT	massimiliano.gaeta@unict.it	**OR40**
GAGGERO Elisa	UniTO	elisa.gaggero@unito.it	**OR25**
GALLETTI Gabriele	UniBO	gabriele.galletti5@unibo.it	**OR102**
GAMBASSI Francesca	UniBO	francesca.gambassi2@unibo.it	**FL13**
GELLI Rita	UniFI	rita.gelli@unifi.it	**OR60**
GENTILI Silvia	UniPR	silvia.gentili@unipr.it	**OR127**
GIACOMAZZO G. Elena	UniFI	ginaelena.giacomazzo@unifi.it	**OR06**
GIANCASPRO Mariangela	UniBA	mariangela.giancaspro@uniba.it	**FL29**
GIORDANO Angelo	UniNA	angelo.giordano@unina.it	**PO36**
GIRIBALDI Francesco	Merck	francesco.giribaldi@merckgroup.com	-
GIURI Demetra	UniBO	demetra.giuri2@unibo.it	**OR64**
GRAMAZIO Pio	UniBO	pio.gramazio2@unibo.it	**OR88**
GRANDINETTI Bruno	UniFI	grandinetti@lens.unifi.it	**OR43**
GRAZIANO Giovanni	UniBA	giovanni.graziano@uniba.it	**FL24**
GRIECO Ilenia	UniTS	ilenia.grieco@phd.units.it	**OR56**

GRILLO Giorgio	UniTO	giorgio.grillo@unito.it	**OR31**
GUERRA Gaetano	UniSA	gguerra@unisa.it	-
GUGLIELMERO Luca	UniPI	luca.guglielmero@gmail.com	**OR84**
GULLO Giorgia	UniPR	giorgia.gullo@unipr.it	**FL17**
GUZMAN Paulina	PoliMI	paulina.guzman@polimi.it	-
HMOUDAH Maryam	UniNA	maryam.hmoudah@unina.it	**OR114**
HOLLER Silvia	UniTR	holler.silvia@gmail.com	**OR59**
IBBA Roberta	UniSI	roberta.ibba91@gmail.com	**OR52**
IMPARATO Claudio	UniNA	claudio.imparato@unina.it	-
IMPERATO Manuel	UniMORE	88864@studenti.unimore.it	**PO41**
INFANTINO Rossella	UniSI	rossella.infantino@student.unisi.it	**FL09**
KHALIHA SARA	CNR	sara.khaliha@isof.cnr.it	**OR29**
LA GATTA Salvatore	UniNA	salvatore.lagatta@unina.it	**OR135**
LABARILE Rossella	UniBA	rossella.labarile@gmail.com	**OR69**
LAMURAGLIA Raffaella	UniVE	raffaella95@msn.com	**OR90**
LAZAZZARA Valentina	Fond. E. Mach	valentina.lazazzara@fmach.it	**PO13**
LAZZARIN Luca	UniPD	luca.lazzarin@studenti.unipd.it	**PO39**
LENCI Elena	UniFI	elena.lenci@unifi.it	-
LEONARDI Costanza	UniFE	costanza.leonardi@unife.it	**OR126**
LEONE Linda	UniNA	linda.leone@unina.it	**OR129**
LISTRO Roberta	UniPV	roberta.listro01@universitadipavia.it	**OR95**
LONGO Lilia	UniVE	lilia.longo@unive.it	**PO17**
LOPRESTI Ludovica	UniSI	lopresti4@student.unisi.it	**OR97**
LORANDI Francesca	UniPD	francesca.lorandi@unipd.it	-
LORENZETTO Tommaso	UniVE	tommaso.lorenzetto@unive.it	**PO21**
LORETO Domenico	UniNA	domenico.loreto@unina.it	**OR120**
LORO Camilla	UniINSUBRIA	cloro@uninsubria.it	**OR17**
MALARA Angela	UniRC	angela.malara@unirc.it	**PO23**
MANGINI Anna	PoliTO	anna.mangini@polito.it	**FL07**
MANTOVANI Sebastiano	CNR	sebastiano.mantovani@isof.cnr.it	**OR30**
MARCHESI Stefano	UniUPO	stefano.marchesi@uniupo.it	-
MAROTTA Angela	UniNA	angela.marotta@unina.it	**FL15**
MAROTTA Ludovica	UniSI	ludovica.marotta@student.unisi.it	-
MARSICANO Vincenzo	UnivAQ	vincenzo.marsicano@univaq.it	**OR14**
MARTINELLI Angelo	UniPV	angelo.martinelli01@universitadipavia.it	-
MASSARDO Sara	UniGE	sara.massardo@edu.unige.it	**OR81**
MATTELLONE Alexia	UniBO	alexia.mattellone2@unibo.it	**OR33**
MAURELLI Anna Maria	UniBA	anna.maurelli@uniba.it	**OR113**

MAZZARELLA Daniele	Univ. Amsterdam	d.mazzarella@uva.nl	**OR70**
MEAZZA Marta	Elsevier	m.meazza@elsevier.com	**SP04**
MELLI Alessio	SNS	alessio.melli@sns.it	**OR119**
MENDOLICCHIO Marco	SNS	marco.mendolicchio@sns.it	**OR117**
MERO Angelica	UniPI	angelica.mero@phd.unipi.it	**OR105**
MIGLIONE Antonella	UniNA	antonella.miglione@unina.it	**OR46**
MILANESI Francesco	UniFI	francesco.milanesi@unifi.it	**FL23**
MOCCIA Federica	UniNA	mocciafederica@gmail.com	**OR110**
MONARI Alessandro	UniMORE	alessandro.monari9@gmail.com	**PO32**
MONCELSI Giulia	Elsevier	m.moncelsi@elseviier.com	-
MONNI Noemi	UniCA	noemi.monni@unica.it	**OR111**
MONTONE C. Maria	UniROMA1	carmelamaria.montone@uniroma1.it	**OR57**
MORILLAS BECERRIL Lucia	UniPD	lucia.morillasbecerril@unipd.it	**OR44**
MORO Miriam	UniBO	miriam.moro2@unibo.it	**OR83**
MORSELLI Davide	UniBO	davide.morselli6@unibo.it	-
NERI Martina	UniPR	martina.neri@unipr.it	**PO29**
NIKOLAOU Pavlos	UniBO	pavlos.nikolaou2@unibo.it	**OR124**
NOMELLINI Chiara	UniMI	chiara.nomellini@unimi.it	**OR85**
NOTARSTEFANO Valentina	UnivPM	v.notarstefano@univpm.it	**OR75**
OGGIANU Mariangela	UniCA	mari.oggianu@gmail.com	**OR112**
OLIVITO Fabrizio	UniCAL	fabrizio.olivito@unical.it	**OR103**
PALAZZOTTI Deborah	UniPG	deborah.palazzotti@studenti.unipg.it	-
PALUCCI Benedetta	CNR	benedetta.palucci@scitec.cnr.it	-
PALUMBO Lucia	UniCH	lucia.palumbo5@gmail.com	**OR58**
PAONE Emilia	UniRC	emilia.paone@unirc.it	-
PAPA Alessandro	UniSI	Alessandro.papa@student.unisi.it	**PO06**
PAPIS Marta	UniINSUBRIA	marta.papis@libero.it	**OR16**
PAPUCCI Costanza	CNR	costanza.papucci@gmail.com	**OR104**
PARISE Angela	UniCAL	angela.parise@unical.it	**FL25**
PAROLO Claudio	ICN2	claudio.parolo@gmail.com	**PL01**
PASCUCCI Roberto	Merck	roberto.pascucci@merckgroup.com	**SP01**
PECORA Desirèe	UniROMA1	pecora.1699809@studenti.uniroma1.it	**PO12**
PEROTTO Giovanni	IIT	giovanni.perotto@iit.it	**PL03**
PETRELLI Valentina	PoliBA	valentina.petrelli@poliba.it	**PO18**
PETROSILLI Laura	UniMi	laura.petrosilli@unimi.it	-
PIRODDA Gabriele	UniPD	gabriele.pirodda@unipd.it	**PO16**
PIZZOLATO Marco	UniVE	marco.pizzolato@unive.it	**OR18**
POLETTI Fabrizio	UniMORE	fpoletti@unimore.it	**OR123**
POLETTI Lorenzo	UniFE	lorenzo.poletti@edu.unife.it	**OR74**

POLLASTRINI Matteo	UniPD	matteo.pollastrini@studenti.unipd.it	**OR21**
POLO Annalisa	UniMI	annalisa.polo@unimi.it	**OR86**
POMILI Tania	IIT - UniGE	tania.pomili@iit.it	**OR49**
PONTE Fortuna	UniCAL	fortuna.ponte@unical.it	**-**
PORTOLANI Chiara	UniBO	chiara.portolani2@unibo.it	**PO19**
POZZETTI Luca	UniSI	luca.pozzetti@student.unisi.it	**FL01**
PRATESI Debora	UniFI	debora.pratesi@unifi.it	**PO09**
PRESINI Francesco	UniFE	francesco.presini@edu.unife.it	**OR128**
PRETE Prisco	UniSA	pprete@unisa.it	**OR26**
PREVETE Giuliana	UniROMA1	giuliana.prevete@uniroma1.it	**PO15**
PROTTI Stefano	UniPV	proste07@unipv.it	**-**
PUXEDDU Michela	UniROMA1	michela.puxeddu@uniroma1.it	**PO10**
QUADRETTI Debora	UniBO	debora.quadretti2@unibo.it	**FL14**
RAVARINO Paolo	UniBO	paolo.ravarino2@unibo.it	**OR63**
REBECCANI Sara	UniBO	sara.rebeccani2@unibo.it	**-**
RENAI Lapo	UniFI	lapo.renai@unifi.it	**PO30**
RENZI Emilia	Un iNA	emilia.renzi@unina.it	**OR130**
RIGOLETTO Monica	UniTO	monica.rigoletto@unito.it	**FL11**
RIPANI Lorenzo	UniBO	lorenzo.ripani2@unibo.it	**FL28**
RITACCA A. Gilda	UniCAL	a.ritacca@unical.it	**OR99**
RITACCO Ida	UniSA	iritacco@unisa.it	**OR71**
RIVOIRA Luca	UniTO	luca.rivoira@unito.it	**PO25**
RIZZO Giorgio	UniBA	giorgio.rizzo.1000@gmail.com	**OR12**
ROMANI Carola	PoliMI	carola.romani@gmail.com	**OR04**
ROMANO G. Maria	UniFI	giammarcomaria.romano@unifi.it	**OR122**
ROMOLINI Giacomo	KU Leuven -UniPG	giacomo.romolini@kuleuven.be	**OR115**
ROSSI Ruggero	UniFI	rossir@lens.unifi.it	**PO05**
ROSSI Sara	UniSI	rossi115@student.unisi.it	**OR42**
ROSSINO Giacomo	UniPV	giacomo.rossino@unipv.it	**OR96**
ROVEGNO Caterina	CNR	caterinarovegno11@gmail.com	**OR34**
SANTINI Saul	UniFI	saul.santini@unifi.it	**PO27**
SANTINO Federica	UniBO	federica.santino2@unibo.it	**OR50**
SANTO Claudio Ignazio	UniBO	claudioignazio.santo@unibo.it	**FL19**
SARTI Chiara	UniFI	sarti_chiara@yahoo.it	**PO28**
SCARSI Anna	IIT - UniGE	anna.scarsi@iit.it	**OR121**
SCHIFINO Gioacchino	UniCZ	gioacchino.schifino@studenti.unicz.it	**PO40**
SCHLICH Michele	UniCA	michele.schlich@unica.it	**-**
SCIACCA Claudia	UniCT	claudia.sciacca@phd.unict.it	**OR09**

SEBASTIANI Jessica	UniROMA1	jessica.sebastiani@uniroma1.it	**PO11**
SEPICH Silvia	Merck	silvia.sepich@merckgroup.com	-
SILVESTRI Alessandro	CIC biomaGUNE	asilvestri@cicbiomagune.es	**OR47**
SIRIGNANO Marco	UniSA	msirignano@unisa.it	**FL05**
STUCCHI Marta	UniMI	marta.stucchi@unimi.it	**OR133**
TABANELLI Tommaso	UniBO	tommaso.tabanelli@unibo.it	**OR89**
TEDESCO Filomena	UniFI	filomenated96@gmail.com	**PO01**
TELESE Dario	UniBO	dario.telese2@unibo.it	**OR02**
TESTOLIN Anna	De Nora	anna.testolin@denora.com	**SP05**
TIEULI Sebastiano	UniVe	sebastiano.tieuli@unive.it	**PO45**
TONIOLO Lucia	PoliMI	lucia.toniolo@polimi.it	**PL04**
TONOLO Francesca	SNS	francesca.tonolo@sns.it	**OR78**
TORRESAN Veronica	UniPD	veronica.torresan@phd.unipd.it	**FL26**
TORTORELLA Sara	Molecular Horizon	sara@molhorizon.it	-
TRANO Sabrina	PoliTO	sabrina.trano@polito.it	**FL08**
TRAVAGLIANTE Gabriele	UniCT	travagliantegab@gmail.com	**OR76**
TRABACE Sara	Olon	strabace@olonspa.it	**SP02**
TRICOMI Jacopo	UniFI	jacopo.tricomi@unifi.it	**OR03**
TRIVERI Alice	UniPV	alice.triverio1@universitadipavia.it	-
TUNIOLI Francesca	CNR	francesca.tunioli@isof.cnr.it	**PO26**
URCIUOLI Gaia	UniNA	gaia.urciuoli@unina.it	**OR61**
VACATELLO Manuela	Merck	manuela.vacatello@merckgroup.com	**SP03**
VENTIMIGLIA Alessia	UniBO	alessia.ventimiglia3@unibo.it	**OR131**
VETRANO Alice	UnivAQ	alice.vetrano@graduate.univaq.it	**OR15**
VETRI BURATTI Veronica	UniBO	veronica.vetri2@unibo.com	**OR62**
VOLPI Stefano	UniPR	stefano.volpi@unipr.it	**OR125**
WETZL Cecilia	CIC biomaGUNE	cwetzl@cicbiomagune.es	**OR48**

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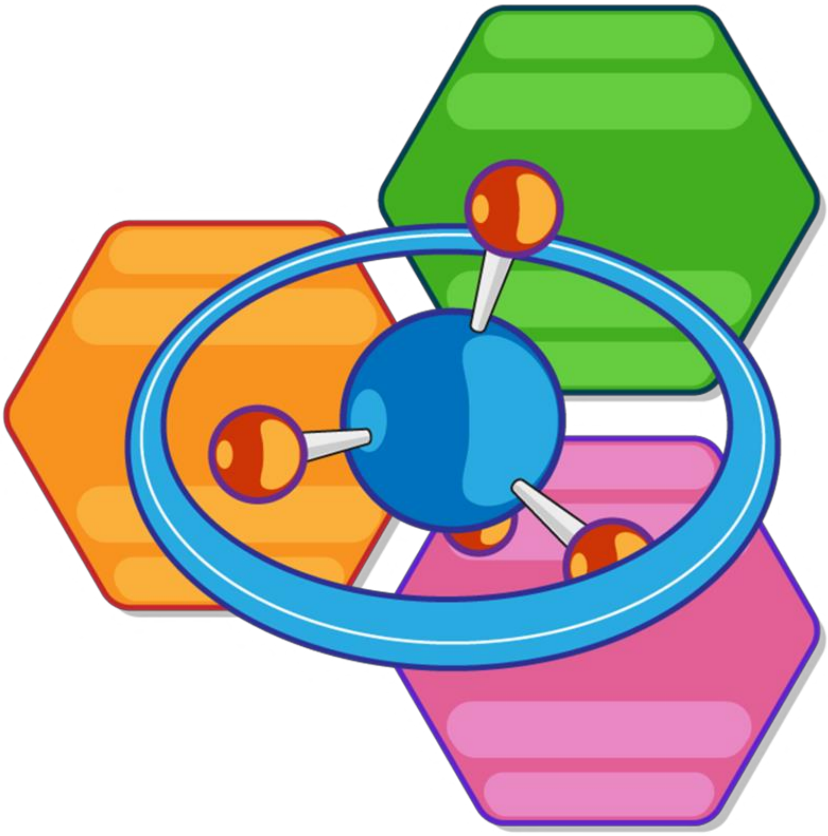

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