

International School of Chemistry: Chemistry for everyday life

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Chemistry for everyday life

Dear Participant! Welcome to the 2020 web edition of the Camerino Summer School!

This year the COVID19 pandemic has largely devastated our world causing a painful and not yet ended chain of illness and death along its progressive diffusion all over the Earth. As a minor, but important, collateral effect of the pandemic, all university institutions and research centers worldwide have suffered a lot and our PhD students have not been able to carry out research in their laboratories for several months. Most of them will not be able to participate in any face-to-face training activities in 2020.

In this frame, we do believe it is important to give them an opportunity that they may no longer have during their training course: attend webinars given by top-level scientists, be able to interact scientifically and, if they want, even present a small contribution in front of them.

For this reason, we have decided to organize a web edition of the Camerino summer school, one of the oldest School in Chemistry currently held in Italy, with a long-lasting tradition and high reputation in the international scientific community. The School this year has been named as the **International School of Chemistry “Chemistry for everyday life”** and has been thought and assembled as a general school of chemistry dedicated to present the views of a group of outstanding speakers delivering lectures on some of the **Global challenges facing mankind** and, therefore, affecting the everyday life of all of us with a genuine multidisciplinary approach where the word Chemistry is inflected through some of the hottest and actual topics like Health, Energy, Environment, Green economy and Innovative materials.

Hopefully, we anticipate a friendly atmosphere of the School with our young participants actively involved in stimulating discussions with the lecturers, flash-presentations and abstract submissions (3 ECTS will be assigned to the participant on the request) and able to bring back home a sound memory of an excellent vocational training path.

Lecturers



Silvio Aime - Università degli Studi di Torino
Chemistry for the design of MRI diagnostic probes



Matthias Beller - Leibniz-Institut für Katalyse
Chemistry & Catalysis - Key Tools for a Sustainable Society



David Cole-Hamilton - EaStCHEM, University of St. Andrews
The Role of Chemists and Chemical Engineers in a Sustainable World



Luisa De Cola - University of Strasbourg
Imaging and sensing with metal complexes



Vy M. Dong - UC Irvine
Choose your own adventure in metal-hydride catalysis



Paul J. Dyson - EPFL, Lausanne

Catalytic transformations of natural and synthetic waste into sustainable chemicals



Odile Eisenstein - CNRS Montpellier

Solvent role on organometallic reaction



Christian Hartinger - University of Auckland

With Metal-based Pharmacophores and Bioactive Ligands Towards Multitargeted Anticancer Agents



Evamarie Hey-Hawkins - University of Leipzig
Switchable Catalysts



Patricia Horcajada - Institute IMDEA Energy, Madrid
Biomedical and environmental interest of Metal-Organic Frameworks



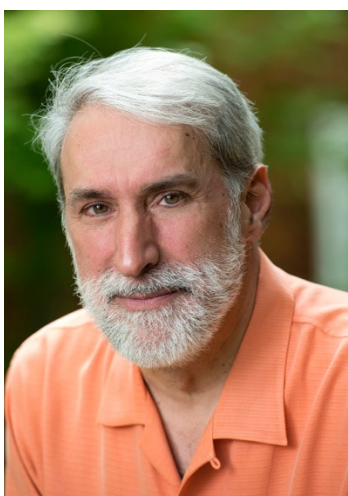
Jean-Marie Lehn - ISIS, Université de Strasbourg
Perspectives in Chemistry: From Supramolecular Chemistry towards Adaptive Chemistry



Nicolai Lenhert - University of Michigan
The nitrogen cycle: enzymes and mechanism



Bruce H Lipshutz - UC Santa Barbara
Synthetic Organic Chemistry in Water; It's Our Future



Daniel G. Nocera - Harvard University
Renewable fuel and food for the everyday life of the poor



Robin Perutz - University of York

The second coordination sphere matters in organometallic chemistry



Maurizio Prato - Università degli Studi di Trieste

Carbon Nanostructures in Energy and Biomedicine Applications



Alessandra Sanson - ISTECCNR, Faenza

Chemistry and Materials towards a real solar decarbonisation



Omar Yaghi - UC Berkeley
Reticular Chemistry and Harvesting Water from Desert Air

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TIMETABLE

September 1st

2.30 pm
Jean Marie Lehn
Perspectives in
Chemistry: From
Supramolecular
Chemistry towards
Adaptive Chemistry

3.45 pm
David Cole
Hamilton The Role
of Chemists and
Chemical Engineers
in a Sustainable
World

5 pm
Silvio Aime
Chemistry for the
design of MRI
diagnostic probes

6.15 pm
FLASH
PRESENTATION

September 2nd

2.30 pm
Omar Yaghi
Reticular Chemistry
and Harvesting
Water from Desert
Air

3.45 pm
Luisa De Cola
Imaging and
sensing with metal
complexes

5 pm
Bruce H. Lipshutz
Synthetic Organic
Chemistry in Water;
It's Our Future

6.15 pm
FLASH
PRESENTATION

September 3rd

2.30 pm
Robin N. Perutz
The second
coordination
sphere matters in
organometallic
chemistry

3.45 pm
Maurizio Prato
Carbon
Nanostructures
in Energy and
Biomedicine
Applications

5 pm
Vy M. Dong
Choose your own
adventure in metal-
hydride catalysis

6.15 pm
FLASH
PRESENTATION

September 4th

2.30 pm
Paul J. Dyson
Catalytic
transformations
of natural and
synthetic waste
into sustainable
chemicals

3.45 pm
Patricia Horcajada
Biomedical and
environmental
interest of Metal-
Organic Frameworks

5 pm
Matthias Beller
Chemistry & Catalysis
- Key Tools for a
Sustainable Society

6.15 pm
FLASH
PRESENTATION

September 5th

2.30 pm
Christian Hartinger
With Metal-based
Pharmacophores
and Bioactive
Ligands Towards
Multitargeted
Anticancer Agents

3.45 pm
Evamarie
Hey-Hawkins
Switchable Catalysts

5 pm
Daniel G. Nocera
Renewable fuel
and food for the
everyday life of the
poor

6.15 pm
FLASH
PRESENTATION

September 6th

2.30 pm
Odile Eisenstein
Solvent role on
organometallic
reaction

3.45 pm
Alessandra Sanson
Chemistry and
Materials towards
a real solar
decarbonisation

5 pm
Nicolai Lenhert
The nitrogen cycle:
enzymes and
mechanisms

6.15 pm
FLASH
PRESENTATION

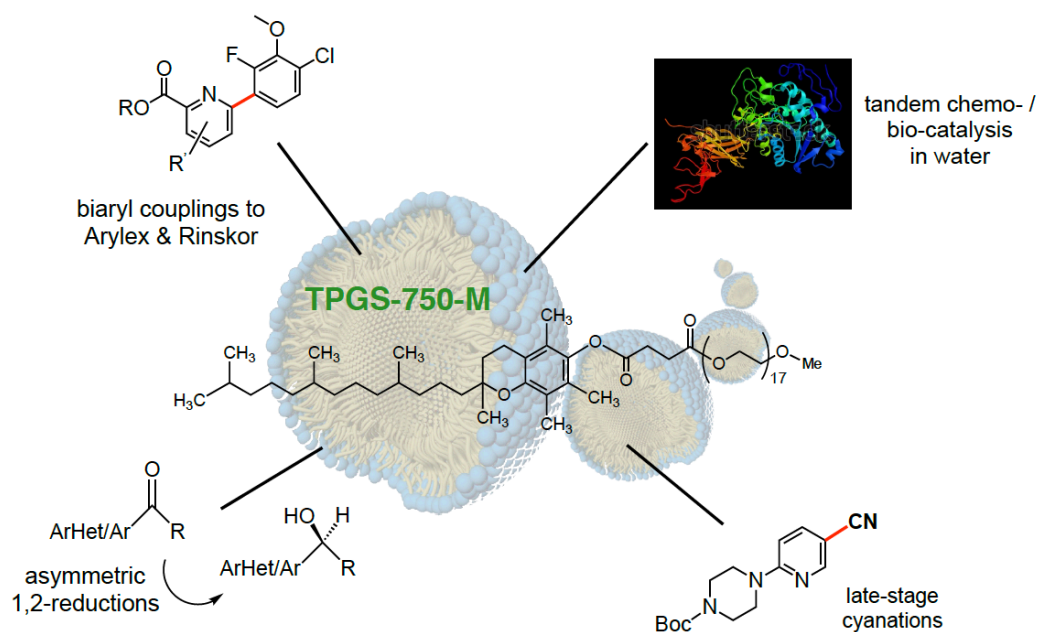
Synthetic Organic Chemistry in Water. It's Our Future

Bruce H. Lipshutz

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Modern organic chemistry, and synthesis in particular, as currently practiced is not sustainable. Hence, new technologies that address several important, representative reactions from both the synthetic and environmental perspectives will be presented, as illustrated below. Each is enabled using a tailor-made, environmentally benign surfactant such as TPGS-750-M that self-aggregates into nanoreactors of the proper size and shape to accommodate substrates and catalysts to maximize yields. Reactions all take place in water under mild conditions, typically between rt and 45 °C. For transition metal catalyzed processes, especially those involving precious and endangered metals such as Pd, catalysts that function at the ppm level of the metal have been developed. The combination of chemo- and bio-catalysis used in tandem reactions in water will also be discussed.



all reactions in water between 0 and 45 °C

[Click here to enter text.](#)

Reviews: Lipshutz, B. H.; Ghorai, S.; Cortes-Clerget *Chem. Eur. J.* **2018**, *24*, 6778 (*The Hydrophobic Effect Applied to Organic Synthesis: Recent Synthetic Chemistry "in Water"*); Lipshutz, B. H. *J. Org. Chem.* **2017**, *82*, 2806 (Perspective).

With Metal-based Pharmacophores and Bioactive Ligands Towards Multitargeted Anticancer Agents

Christian G. Hartinger

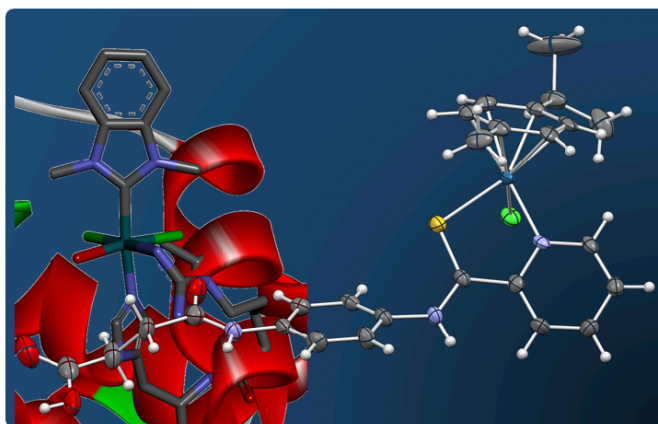
School of Chemical Sciences, University of Auckland, 23 Symonds Street, Auckland 1010, New Zealand. <http://hartinger.auckland.ac.nz>, c.hartinger@auckland.ac.nz.

Keywords: Anticancer Bioorganometallics, Compound Design, Mode of Action Studies

Resistance to chemotherapeutics, whether intrinsic or acquired, is a major limitation in the treatment of cancer patients. This represents an opportunity for metal-based compound design considering the unique properties of metal complexes and often non-conventional modes of action. One of our research directions is the development of organometallic, multitargeted anticancer agents, in which we often combine bioactive ligand systems with metal center to create a synergistic effect [1-4]. By developing new bioanalytical methods, we aim to improve our understanding of the fate of such metal-based anticancer agents in a biological environment, especially at the molecular level.

In this lecture, I will particularly focus on the design of multitargeted organometallics, the selection of the ligands and studies on their reactions with biomolecules [5]. The impact of the nature of the ligands on the biological properties of the organometallic anticancer agents will be discussed. Bioanalytical data helps us to gain a deeper understanding of the modes of action and to assess the impact of the structure on the bioactivity.

Financial support by the University of Auckland, Cancer Research Trust NZ and the Royal Society of New Zealand (Marsden Fund) is gratefully acknowledged.



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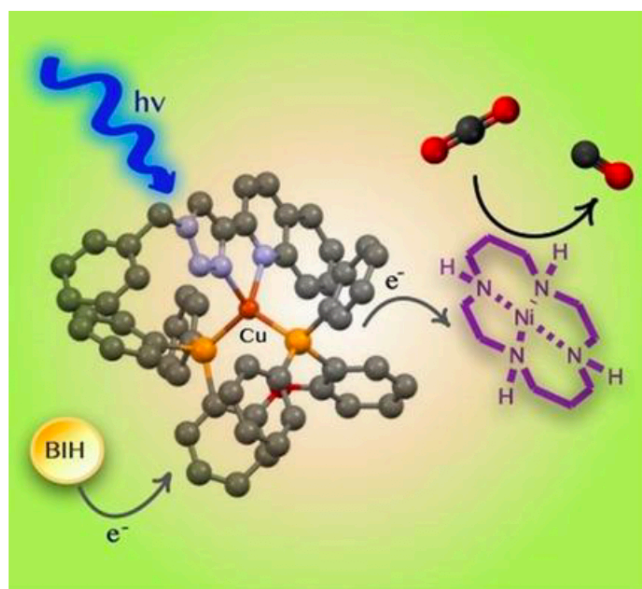
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A fully earth abundant system for the photocatalysis of CO₂ through visible light

Lisa-Lou Gracia, Luisa Luci, Cecilia Bruschi, Prof. Dr. Letizia Sambri, Dr. Patrick Weis, Dr. Olaf Fuhr, Dr. Claudia Bizzarri

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Many research efforts have been carried on for decades in order to achieve an artificial photosynthetic system. Although nature reduces carbon dioxide into carbohydrates and biomass, in artificial photosynthesis, researchers aim at a direct photoreduction of CO₂, employing photocatalytic systems.¹ To overcome the kinetic and thermodynamic stability of CO₂, heterogeneous as well as homogeneous systems have been developed^{2a,b}. In this work³, the synthesis and full characterisation of four new heteroleptic Cu^I complexes are reported, which can work as photosensitizers. The complexes bear a bulky diphosphine (DPEPhos=bis[(2-diphenylphosphino)phenyl] ether) and a diimine chelating ligand based on 1-benzyl-4-(quinol-2'yl)-1,2,3-triazole. Their absorption has a relative maximum in the visible-light region, up to 450 nm. Thus, their use in photocatalytic systems for the reduction of CO₂ with blue light in combination with the known catalyst [Ni^{II}(cyclam)]Cl₂ was tested. This system produced CO as the main product through visible light ($\lambda = 420$ nm) with a TON up to 8 after 4 hours. This value is in line with other photocatalytic systems using the same catalyst. Nevertheless, this system is entirely noble-metal free. The new Cu^I photosensitizers show new perspectives for the development of more efficient and sustainable systems.



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- 3 Lisa-Lou Gracia, Luisa Luci, Cecilia Bruschi, Letizia Sambri, Patrick Weis, Olaf Fuhr, Claudia Bizzarri, *Chem. Eur. J.* 2020, **26**

Novel Ir-Cp* Complexes as Homogeneous and Heterogenized Water Oxidation Catalysts

Chiara Domestici, Francesco Zaccaria, Leonardo Tensi, Roberto D'Amato, Ferdinando Costantino, Cristiano Zuccaccia, Alceo Macchioni

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Nowadays the conversion of solar energy into fuel by artificial photosynthesis is certainly one of the most crucial and challenging goals in scientific research.^[1] For the solar fuel production to be advantageous from an economic and environmental point of view, an abundant and cheap reagent that can be oxidized, providing electrons and protons for the reductive production of fuels, is needed. Water is largely identified as a most promising candidate, even though its oxidative reaction is thermodynamically and kinetically demanding. For these reasons, the development of efficient water oxidation catalysts (WOCs) is crucial in the framework of constructing an artificial photo(electro)synthetic apparatus for the production of solar fuels.^[2] Over the last years, huge efforts have been devoted to developing efficient WOCs based both on earth-abundant and noble metals. Generally, the latter exhibit better performances especially, but not only, in terms of durability. Therefore, rather than their replacement with earth-abundant elements, research is moving towards the minimization of the precious metals according to the “noble metal atom economy” principles.^[3] The first possible strategy is exploring heterogeneous WOCs, in which the noble metal centers are diluted in a suitable material providing high accessibility of the active centers.^[4] The second one is developing homogeneous WOCs, which ideally guarantee the totality of active sites and the possibility of rational ligand design.^[5] Finally, homogeneous WOCs bearing proper ancillary ligands can be heterogenized onto a suitable support, gaining additional advantages in terms of recyclability and recoverability.^[6] Herein, we show an exemplifying comparison between homogeneous and heterogenized systems, by exploring the catalytic activity of two novel Ir-Cp* complexes, bearing EDTA and EDTMP as ancillary and anchoring ligands and their TiO₂-supported analogues in WO driven by NaIO₄.

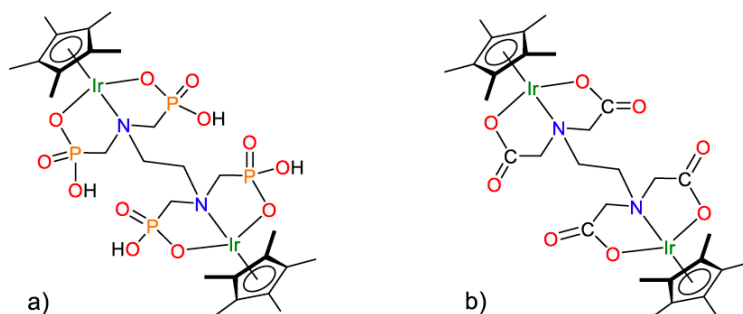


Figure 1. Sketch representations of the dinuclear Ir-complexes bearing EDTMP (a) and EDTA (b) ligands.

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TREATMENT AND VALORIZATION OF OLIVE MILL'S RESIDUES: INTEGRATION OF FENTON-LIKE OXIDATION AND MEMBRANE PROCESSES

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Olive oil extraction is one of the utmost traditional agroindustrial activities in the Mediterranean region. Data from the last decade show that the European Union is responsible, on average, for nearly 70% of the worldwide production [1]. Depending on the extraction process employed, wastewaters generated by this industry – known as olive mill wastewaters (OMW) – may represent >50% of the total water inputs. As water becomes scarcer, it is of vital importance to prioritize wastewater treatment and reuse, as to maintain the sustainability of natural and urban water cycles [2].

Management of OMW is a complex subject due to its typically high organic load and polyphenolic fraction, responsible for the antibacterial activity and phytotoxic properties. In addition, solid and semi-solid sub-products (such as olive stones and olive pomace) also require specific handling, encompassing additional operational difficulties and added costs for producers.

The Fenton reagent is an advanced oxidation process that relies on the ability of Fe^{2+} to decompose H_2O_2 into highly reactive and non-selective hydroxyl radicals, capable of mineralizing a wide range of pollutants at moderate operational conditions of temperature and pressure (room temperature and atmospheric pressure). The development of heterogeneous catalysts, where the catalytically active phase is anchored in a solid matrix, has been the focus of researchers for many years, as it tackles some of the constraints associated with the homogeneous process (e.g. downstream handling of iron-rich sludges) [3].

Our research is focused at the simultaneous valorization of solid organic waste as catalysts' supports, which would be used for the Fenton-like treatment of OMW, in the same agro-industrial activity, and recovery of water by permeable membranes – Fig. 1. In a perspective of circular and sustainable economy, the treated OMW and recovered water could potentially be reused for crops irrigation or machinery washing, thus reducing the environmental footprint of the process.

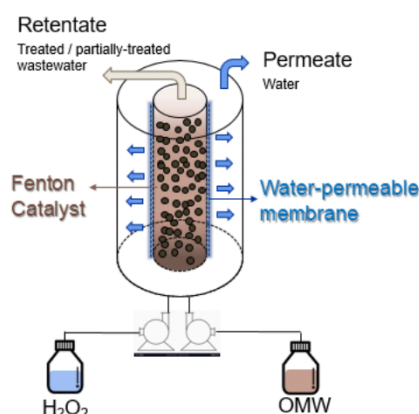


Fig. 1 Schematic representation of the reactor assembly proposed.

Several catalysts have been prepared with different supports (e.g. olive stones, tree pruning), methods of synthesis (carbonization, hydrothermal carbonization, etc.), activation

conditions, and also different properties regarding the active metallic phase (metal nature and loading, doping agents, etc.). The main goal is to develop catalytically active and stable catalysts for the Fenton-like oxidation of OMW.

Experiments have shown that synthesized catalysts from organic sub-products are able to decompose polyphenolic compounds (TPh) commonly present in OMW, remaining catalytically active after several cycles and only showing residual metal leaching levels. The oxidation of such compounds was found to be key for the abatement of the toxic character of the effluent, as proven by the linear relationship between the phenolic content and *Vibrio fischeri* bacteria inhibition (used as toxicity indicator).

Preliminary results with diluted OMW highlighted the ability of the synthesized catalysts to drastically reduce the toxic character of the effluent (60% TPh removal), also oxidizing 40% of the initial organic load (as chemical oxygen demand) and making the effluent colorless (according to industrial wastewater discharge legislation). Further studies will focus on the implementation of the proposed membrane-reactor assembly and tests in continuous flow operation, if feasible with raw OMW.

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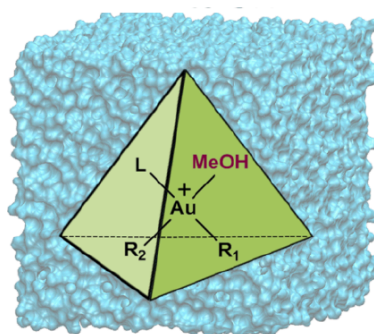
Metal-Organic Cages [(Ga₄L₆)¹²⁻] as Catalysts: Computational Evaluation of Au(III) / C-C Reductive Elimination

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Self-assembled metallocupramolecular coordination cages represent one of the most interesting developments in supramolecular host design.¹ The design of metal-organic cages (MOCs) offering cavities is highly desired since they can become catalysts for chemical transformations.² They were initially inspired in biological processes, but new man-made microenvironments based on organic ligands and metal atoms have been developed.

Here, we will present our computational studies on the origin of supramolecular catalysis based on a [(Ga₄L₆)¹²⁻] metal-organic cage by means of theoretical methods. A combination of several computational techniques, ranging from pure quantum mechanics to force fields were employed. The C-C bond formation by reductive elimination from a Au(III) complex is analyzed trying to disclose the origin of the catalytic behavior. The effects of microsolvation and encapsulation are evaluated.³ Moreover, the observation that modifying the phosphine size (PEt₃ vs PMe₃) the reaction rate is significantly modified will be also addressed.⁴ Overall, the analysis of the reaction in solution and the reaction in the metallocage will provide clues on the origin of catalysis.



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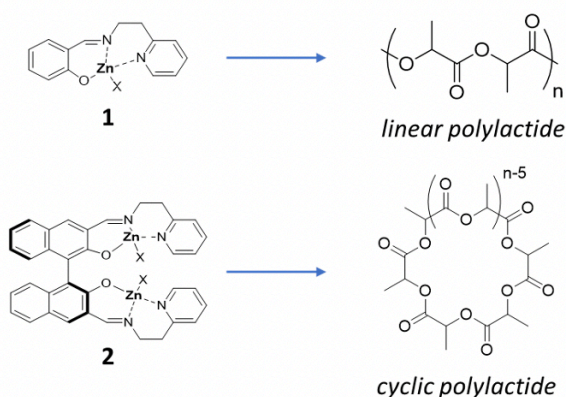
Financial support acknowledgment: Projects n° CTQ-2017-87889.

Switching between linear and cyclic polylactides with mono or bimetallic zinc complexes

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Plastic pollution has become one of the most pressing environmental issues: the production of disposable plastic objects is overwhelming our ability to manage it. Every year about 8 million tons of plastic waste escapes into the oceans and currently the idea of a world without plastic would seem a pure utopia, given the daily use we make of it.¹ A valid alternative could be the use of bioplastics, such as polylactic acid (PLA) which is biodegradable, biocompatible and of natural origins.² The physico-chemical properties of this polymer can change according to its microstructure and topology. In particular, cyclic polylactide shows a higher glass transition temperature and a lower viscosity than linear polylactide, with the same molecular weight.³ In this work, two zinc-based complexes with phenoxy-imine-pyrimidine ligands were successfully synthesized. They were used in the polymerization of *rac*-lactide, thus showing different and interesting behaviours.



The monometallic complex **1** turned out to be very active, showing a TOF of about 11000 h⁻¹ at room temperature and managed to give only linear polylactide with good control of the molecular weight. The analogous bimetallic complex **2** managed to give exclusively cyclic polylactide, placing itself as the most active catalyst to give this product.

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ZIRCONIUM METAL-ORGANIC FRAMEWORKS CONTAINING A BISELENOPHENE LINKER: SYNTHESIS, CHARACTERIZATION AND LUMINESCENT PROPERTIES

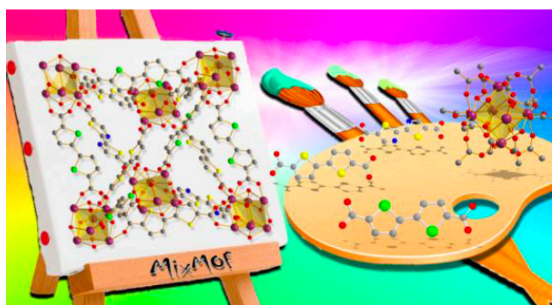
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Metal-Organic Frameworks (MOFs) are a class of nanoporous materials that, in recent years, have gained great attention for their widespread application in several field of materials science (catalysis, luminescence, gas storage and separation). MOFs have an extraordinary versatility in their design achieved through a tailored combination of organic linkers and inorganic metallic nodes. This characteristic gives to MOFs unique advantages, including control of their pore size, high specific surface areas^[1] and the possibility to include suitable functional groups on their linkers' skeleton.^[2] In this work, the bicyclic ditopic linker 2,2'-biselenophene-5,5'-dicarboxylic acid (H_2SpSp) specifically designed for MOFs construction has been synthesized and fully characterized. Then, the corresponding zirconium MOF $[Zr_6O_4(OH)_4(SpSp)_{3.8}Cl_{4.4}]$ (**1**) has been prepared. The crystallographic analysis has revealed that this MOF is isostructural with its bithiophene and bithiazole analogues. The biselenophene MOF family has been enlarged through the preparation of three new mixed-linker MOFs containing biselenophene (H_2SpSp), bithiophene (H_2ThTh) and bithiazole (H_2TzTz) linkers together: the two double-mixed samples $[Zr_6O_4(OH)_4(SpSp)_{2.6}(ThTh)_{1.3}Cl_{4.2}]$ (**2**) and $[Zr_6O_4(OH)_4(SpSp)_2(TzTz)_{1.8}Cl_{4.4}]$ (**3**), as well as the triple-mixed $[Zr_6O_4(OH)_4(SpSp)_{1.6}(ThTh)_{1.2}(TzTz)_{1.4}Cl_{3.6}]$ (**4**) compound. **1-4** have been tested for luminescent applications; they are featured by emission at wavelengths falling in the blue-green visible region under UV irradiation. The results will be presented.^[3]



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Antimicrobial-loaded calcium phosphate nanoparticles as a potential new therapy for cystic fibrosis-related infections.

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Cystic fibrosis (CF) is a progressive, genetic disease that causes persistent lung infections and limits the ability to breathe over time. It is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) protein that regulate chloride ions secretion and sodium ions balance.[1] Mutations of the CFTR gene affecting chloride ion channel function lead to an hypersecretion of thick mucus difficult to clear. The over-production of this mucus makes the lungs susceptible to recurrent and persistent bacterial infections.[2] The aim of this work consists in the preparation of biocompatible and biodegradable calcium phosphate inorganic nanoparticles (CaP-NPs) functionalized with antibiofilm and antimicrobial peptides to treat CF, in order to improve the current treatment of this disease that involves the use of drugs via inhalation routes (oral or nasal). The advantages of using NPs for the peptides delivery are several: (i) co-localization of biomolecules with synergistic therapeutic actions, and (ii) peptides protection against early degradation. In this work, peptides were added in the reaction mix to obtain an encapsulation of the molecules into the one-pot synthesis of CaP,[3] or by a post synthesis surface functionalization. The materials characterization was performed by UV-Vis Spectrometry, High-performance liquid chromatography (HPLC), Thermogravimetric analysis (TGA), Attenuated total reflectance (ATR) and Dynamic Light Scattering (DLS).

A promising new therapeutic formulation based on biodegradable CaP-NPs functionalized with selected antibiofilm and antimicrobial peptides was achieved in order to potentially impair biofilm formation and microorganism vitality as well as to lower the drug resistance phenomenon in the treatment of CF related infections.

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ACKNOWLEDGMENTS

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Investigating the Electrochemical Behavior of the *Physalis peruviana* using with cyclic voltammetry and squar wave voltammetry methods

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Abstract: The aim of this study is to evaluate the antioxidant and the antimicrobial effect of *Physalis peruviana*. Also We have investigated atioxidan capacity *Physalis peruviana* using with cyclic voltammetry and squar wave voltammetry methods. Effect of pH and some metal on the antioxidant capacity has been studied (Cu^{2+} , Ca^{2+} , Cd^{2+} , Co^{2+} and Zn^{2+}). The kinetic data were extracted from cyclic voltammograms with the help of digital simulation. The homogeneous and heterogeneous rate constants were estimated by comparing the experimental cyclic voltammetric responses with the digital simulated results.

Keywords: Antioxidant , Electrochemical, Cyclic Voltammetry, digital simulation.

I. INTRODUCTION

Physalis peruviana, a plant species of the genus *Physalis* in the nightshade family Solanaceae, has its origin in Peru. The plant and its fruit are commonly called Cape gooseberry, goldenberry, golden berry, Pichuberry or physalis, among numerous regional names It has been cultivated in England since the late 18th century, and in South Africa in the Cape of Good Hope since at least the start of the 19th century. Widely introduced in the 20th century, *P. peruviana* is cultivated or grows wild across the world in temperate and tropical regions.

II. METHODS AND RESULTS

We have investigated antioxidant capacity *Physalis peruviana* using with cyclic voltammetry and squar wave voltammetry methods. The kinetic data were extracted from cyclic voltammograms with the help of digital simulation. The homogeneous and heterogeneous rate constants were estimated by

comparing the experimental cyclic voltammetric responses with the digital simulated results.

III. CONCLUSION

The reduction of *Physalis peruviana* is pH independent and occurs at very high potentials, which means that it can be studied only at pH values higher than 5.50. The use of buffer electrolyte in a mixed acetonitrile/water solvent proved very convenient for preventing strong adsorption of the analyte on the electrode surface and enabling better repro- ducibility and sensitivity. Adsorptive linear sweep square wave voltammetry permitted accurate quantification of *Physalis peruviana* in commonly used pharmaceutical drugs in the micromolar range after a very simple and rapid sample treatment. Good precision was obtained .This electroanalytical method can be used for determination of thera- peutic doses of *Physalis peruviana* in biological fluids if coupled with high performance liquid chromatog- raphy (HPLC) with electrochemical detection.

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Development of UHTCMCs via Water-based Powder Slurry Infiltration and Polymer Infiltration and Pyrolysis for Extreme Environments

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Keywords: UHTCMC, PIP, Carbon fibres, microstructure, high temperature properties, polycarbosilane.

Advanced materials able to withstand in extreme environments are always of great interest in aerospace field. Ultra-high temperature ceramic matrix composites (UHTCMCs) are novel materials which can overcome the main limitations of currently used CMCs (C/C and C/SiC), showing higher temperature capability and ablation resistance. Potential applications for these materials are leading edges and thermal protection systems (TPSs) for Earth re-entry or hypersonic vehicles and rocket nozzles for propulsion. We explore the manufacturing of carbon fibre reinforced ZrB₂-enriched composites via water-based slurry infiltration coupled with Polymer Infiltration and Pyrolysis (PIP) technique. UHTC matrix is added to 0/0°, 0/90° and 2D carbon fibre preforms by slurry infiltration and represents 20-30 vol% of the final material. Several infiltrations with a commercial SiC precursor (allylhydrido polycarbosilane SMP-10 from Starfire Systems, Inc.) followed by curing and pyrolysis reduced the porosity from ~40% to less than 10%. Microstructural features and mechanical properties, including bending strength, elastic and shear modulus, were analyzed. Oxidation resistance in air up to 1650 °C was investigated.

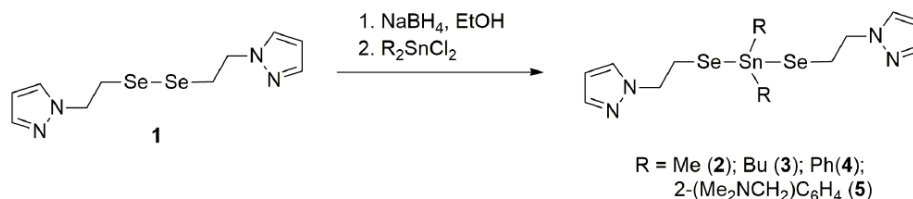
TIN(IV) BIS(ORGANOSELENOLATES): SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY

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Over the past decades, organoselenium and organotin compounds were investigated for their biological properties, e.g. antibacterial, antifungal or antiproliferative activity.^[1,2] In addition, pyrazole based compounds were shown to be important in medicinal chemistry as antibacterial, antifungal or antitumor agents as well.^[3] Therefore, the combination of these structural elements is expected to result in a new class of compounds with biological properties.

Our current studies are focused on the synthesis and structural characterization of new diorganotin(IV) compounds with organoselenolato ligands based on pyrazole (pz) functionalities. The starting diorganodiselenide (pzCH₂CH₂)₂Se₂ (**1**) was obtained by reacting the corresponding organic bromide with freshly prepared Na₂Se₂. Cleavage of the Se–Se bond with NaBH₄, followed by the reaction with R₂SnCl₂ (R = Me, Bu, Ph, 2-(Me₂NCH₂)C₆H₄) in a 2:1 molar ratio gave the target compounds (Scheme 1),^[4] which were investigated by multinuclear NMR spectroscopy (¹H, ¹³C, ⁷⁷Se and ¹¹⁹Sn) and mass spectrometry.



Scheme 1. Synthesis of the diorganotin(IV) complexes

The starting diorganodiselenide **1** and the tin compounds **2** and **5** were screened for their antiproliferative activity against the murine colon carcinoma C26 cell line. The obtained results show that the presence of tin in the molecule did not bring any improvement of the activity, nonetheless all the compounds have a better activity than the standard drug, 5-fluorouracil.

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Sensing of mercury(II) in aqueous solutions by luminescent bipyrazolate-based zinc(II) MOFs

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Waters contamination by mercury is one of the current global concerns, due to its high toxicity even at low concentrations. Spread in the environment by anthropogenic activities, this heavy metal can accumulate in the human body through the food chain, leading to heart or cardiovascular diseases, cognitive or motion disorders, renal failures. Among the approaches to detect or remove heavy metals from water, adsorption has shown to be economic and effective. The traditional adsorbents deeply investigated in this field, such as nano-sized metal oxides, layered metal sulfides, activated carbons, or graphene oxides, have shown not negligible limitations (slow adsorption kinetics, limited selectivity, poor regeneration) [1]. Hence, the development of advanced porous materials for heavy metal sensing or sequestration is highly desirable. Metal-organic frameworks (MOFs) [2], crystalline materials with 3D open frameworks built up by the self-assembly of metal ions and organic linkers *via* coordination bonds, are promising candidates [3], due to the versatility of their structural and functional properties, granted by the vast library of nodes and spacers.

To obtain a luminescent sensor for Hg^{2+} in aqueous solutions, we prepared the bipyrazolate-based MOFs $\text{Zn}(\text{C}_2\text{BPz})$ (**i-Zn**) and $\text{Zn}(\text{C}_2\text{BPz}) \cdot n\text{DMF}$ (**ni-Zn**) [$\text{H}_2\text{C}_2\text{BPz}$ = 1,2-bi(pyrazol-4-yl)-ethyne; DMF = dimethylformamide], featuring a triple bond in the ligand skeleton. The two materials possess a 3D porous network with 1D square (**ni-Zn**) or rhombic channels (**i-Zn**) (Figure 1), though the empty volume is significantly different (55 vs. 22%), due to the interpenetration about the triple bond present in **i-Zn**. Both MOFs show high thermal stability in air [at least up to 450 °C and 490 °C for **ni-Zn** and **i-Zn**, respectively]. Upon suspension in water under ambient conditions, **ni-Zn** interconverts into **i-Zn** in 1 day, while **i-Zn** is stable for at least 15 days. Preliminary trials carried out upon suspending **i-Zn** in HgCl_2 aqueous solutions demonstrated the gradual **i-Zn** to **ni-Zn** transformation upon Hg^{2+} and Cl^- adsorption (XRF and PXRD evidence), with a rate dependent on the metal salt concentration. Juxtaposing UV-Vis absorption, fluorescence emission and fluorescence excitation spectroscopy allowed to unveil a key difference in fluorescence emission by the two MOFs at *ca.* 470 nm upon excitation at 365 nm. This occurrence allows to

discriminate among the two materials, *i.e.* to easily detect the **i-Zn** to **ni-Zn** transformation prompted by Hg^{2+} adsorption, making this system promising as a luminescent sensor for this heavy metal.

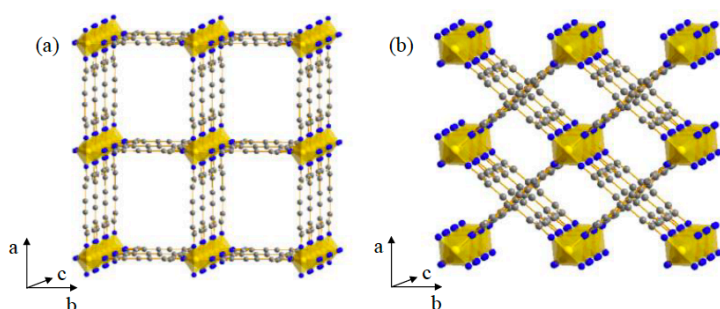


Figure 1. Portion of the crystal packing of a) **ni-Zn** and b) **i-Zn** viewed in perspective along [001].

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Antifungal imidazolyl compounds as ligands in antitumoral neutral cyclometalated Pt(II)-complexes

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Antifungal agents Clotrimazole (CTZ) and Bifonazole (BFZ) are prescribed against mycotic infections like athlete's foot, vulvovaginal and oropharyngeal candidiasis, between others.¹ Due to the high efficiency and the unremarkable side effects of CTZ,² this drug has been tested against other diseases: Sickle cell disease, Malaria (*Plasmodium*), Chagas (*Trypanosoma cruzi*) and Cancer.

In order to enhance the biological activity or modify the mechanism of action of the platinum drugs, the synthesis of new Pt(II)-complexes bearing ligands with biological activity themselves could be a good strategy. Only two examples of Pt(II) complexes containing CTZ and none with BFZ have been described. $K_2[PtCl_4(CTZ)_2]$ was tested against *Trypanosoma cruzi*³ and, later, the *cis*- and *trans*- complexes with formula $[PtX_2(CTZ)_2]$ (X= Cl, I) showed activity against six tumor cell lines (prostate, pancreas, breast, colon between others) although both complexes showed lower cytotoxicity than cisplatin.⁴

Motivated by these studies we design and synthesized the first family of neutral cyclometalated Pt(II)-complexes containing CTZ and BFZ (See Figure 1) and we tested their activity as antibacterial and antitumoral agents. The Pt(II)-complexes were characterized in solution and in solid state and present luminescence in the cyan-green hue.

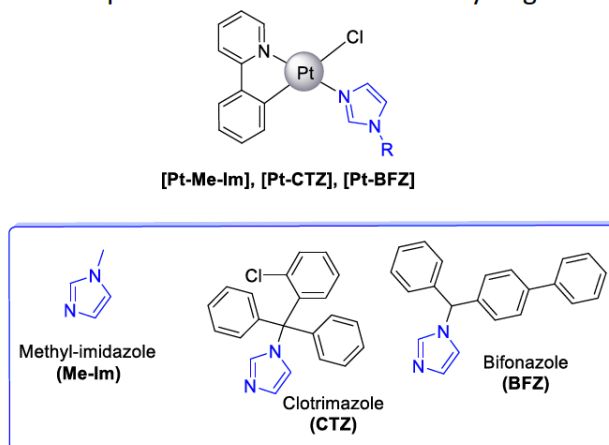


Figure 1.- Pt(II) complexes bearing imidazolyl-antifungal ligands.

The cytotoxic activity of the complexes was evaluated in lung adenocarcinoma (A549) and colon adenocarcinoma (SW480) cells. In both cell lines **[Pt-MeIm]** and **[Pt-BFZ]** are four or two fold more cytotoxic than cisplatin and all the complexes interact with double stranded DNA, a commonly identified cellular target for Pt(II) complexes.⁵ In addition, apoptosis studies revealing that the death mechanism is not mediated by caspases.

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Photoactivation of Dual Antibacterial and Anticancer Activities of New Luminescent 2-Benzoazole-Phenolato Cycloplatinated(II) Complexes.

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One of the common challenges faced by chemotherapy patients are bacterial infections due to inherent cancer immunodeficiencies, neutropenia, disruption of mucosal barriers¹ being those caused by Gram-positive bacteria (including multidrug resistant (MDR) strains) the most common infections.² In this context, the development of new compounds provided with antibacterial and antitumour activities that can be easily modulated by photoactivation could be an interesting approach in combating bacterial infections in cancer chemotherapy patients. Three neutral cycloplatinated(II) complexes of the type [Pt(dmba)(L)] (dmba = *N,N*-dimethylbenzylamine- $\kappa N, \kappa C$; L = 2-(benzo[d]oxazol-2-yl)-phenolato- $\kappa N, \kappa O$ **1**, 2-(benzo[d]thiazol-2-yl)-phenolato- $\kappa N, \kappa O$ **2**, and 2-(1-methyl-1H-benzo[d]imidazol-2-yl)phenolato- $\kappa N, \kappa O$ **3**) (Figure 1) were synthesized and characterized. The effect of the 2-benzoazole-phenolato hemilabile N⁺O ligand in both their anticancer and antibacterial activities in the dark and upon blue light irradiation was evaluated.

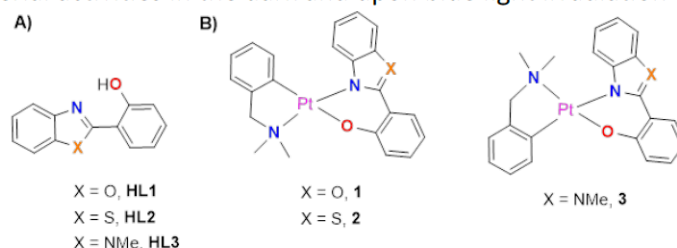


Figure 1. A) Pro-ligands HL and **B)** Pt(II) complexes.

Complexes **1** and **2** are photoreactive under blue light irradiation. Noteworthy, the antibacterial activity of complex **2** against pathogenic Gram-positive bacteria strains is photopotentiated being the phototoxic index (PI) = 15 for MRSA *Staphylococcus aureus*.

Regarding anticancer activity, all the Pt(II) complexes are more cytotoxic than cisplatin in all the tested cell lines and are able to overcome the cisplatin resistance in A2780cis cancer cells. Again, the antitumor activity of compounds **1** and **2** is increased upon blue light irradiation in human lung A549 cancer cells. Regrettably, the biological activity of complex **3**, which is active in both bacteria and cells, is not photopotentiated with blue light. The three luminescent complexes are localized in the cytoplasm as it was observed by confocal microscopy and inductively coupled plasma mass spectrometry (ICP-MS). Flow cytometric experiments confirmed that the present complexes induced ROS-independent cell cycle arrest at G2/M phase and apoptosis-mediated death in lung cancer cells.

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Encapsulation of Arsenoplatin-1 within the ferritin nanocage

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Arsenoplatin 1 (AP-1) belongs to a novel class of metallodrugs containing a $\text{PtAs}(\text{OH})_2$ core with a square planar Pt(II) and a five coordinate As(III) geometry (Figure 1A). It is very stable in solution and it has a promising activity in drug-resistant cancer cell lines¹. The activity of **AP-1** can be further improved by using a nanocarrier. Ferritin nanocages have attracted intense interest as protein drug delivery systems. In fact, they have been already used to encapsulate a variety of drugs and biologically active substances². In the present work, it was chosen to encapsulate **AP-1**. The **AP-1**-encapsulated Aft was prepared following the alkaline pH procedure (Figure 1B) previously used to produce cisplatin-encapsulated Aft³. Uv-Vis spectroscopy confirmed the successful encapsulation, while ICP-OES measurements allowed to calculate the exact amount of **AP-1** present in the Aft nanocage. The X-ray structure of **AP-1**-encapsulated Aft was also solved and revealed that, upon reaction with ferritin, an $[\text{AP-1} \cdot \text{Cl}]$ fragment binds the protein. Then, the biological activity of **AP-1**-loaded Aft was tested on cancer cell lines and compared to that observed in normal ones. The results clearly indicated that **AP-1** is more toxic when encapsulated in the Aft nanocage and that the presence of the cage improve its selectivity since tumor cells are more sensitive compared to normal cells.

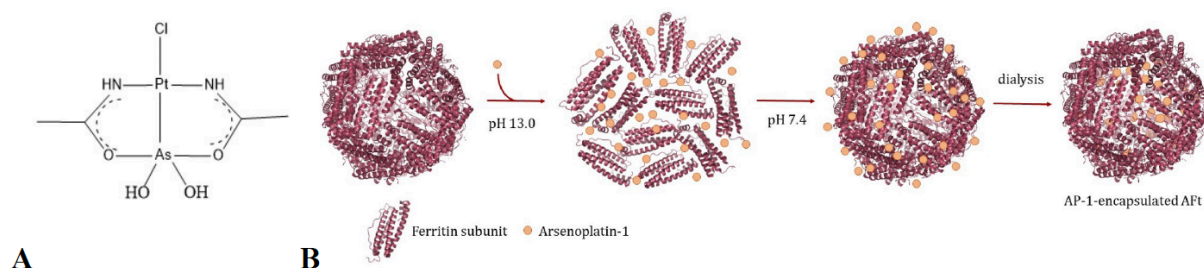


Figure 1. Structure of AP-1 (A). Schematic representation of the alkaline pH procedure (B).

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Homogeneous monomeric and dimeric salen Fe(III) catalysts for biodiesel synthesis

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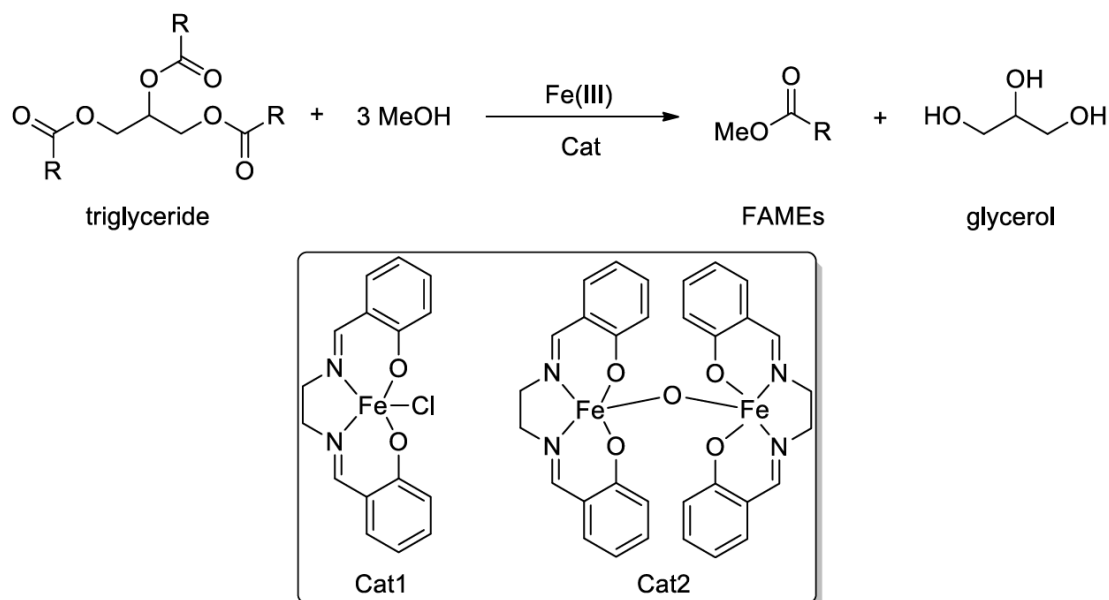
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The continuous and increasing consumption of energy and the constant decrease of non-renewable feedstocks are the driving forces that have led academic and industrial research towards the development of more eco-sustainable products, processes, and technologies.

In this framework, vegetable oils and lignocellulosic materials are important renewable feedstocks to produce biochemicals and biofuels.¹ From the transesterification of triglycerides with methanol, it is possible to obtain a mixture of fatty acid methyl esters (FAMES) ready to be used as biofuel in existing diesel engines.²

Recently we reported catalytic esterification and transesterification of levulinic acid and methyl levulinate promoted by monomeric and μ -oxo dimeric salen Fe(III) complexes Cat1 and Cat2 (in Scheme 1).³ Here we report preliminary results for FAMES synthesis promoted by the same catalysts. The effect of free acidity on the reaction yield was investigated for both catalysts, and complete conversion was achieved with Cat2 under optimized conditions ($T = 160^\circ\text{C}$, $t = 2$ h, MeOH/oil molar ratio: 10, cat. loading 0.1% mol_{Fe}/mol_{oil}).



Scheme 1 – Salen Fe(III) catalyst for biodiesel synthesis

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Studying the Effectiveness of Lithium Zincates Species in Michael Addition Reactions: Synthetic and Structural Insights

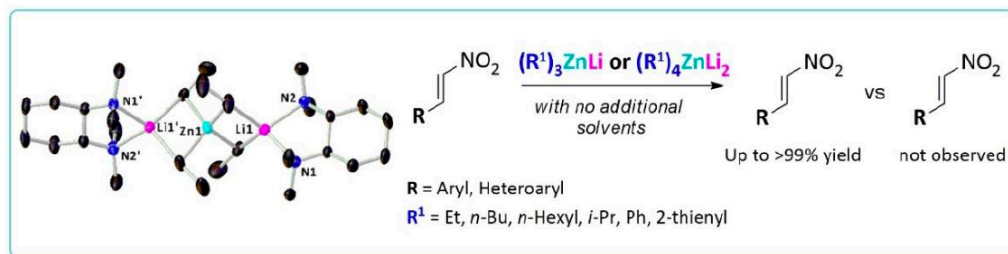
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The conjugate addition of organometallics to nitroalkenes provides a useful method for nitro-alkylation. This type of addition is much pursued in organic synthesis as the nitro group can be easily transformed into various functional groups including carbonyl derivatives by the Nef reaction, amines by reduction, nitriles, imines by other transformations.^[1] While 1,4-conjugated additions of organozinc reagents (R_2Zn and $RZnX$) have been extensively studied,^[2] applications of alkali-metal zincates in fundamental organic transformations are still in their infancy.^[3] These type of reagents show unique, synergistic chemical characteristics which cannot be replicated by their monometallic (organolithium/organozinc) counterparts. Furthermore, the replacement of the vinylic nitro group by an alkyl group remains a complication encountered when nitrostyrenes are reacted with dialkylzinc compounds in the absence of a Lewis acid.^[4] In our recent work we demonstrated that under optimized reaction conditions, 0 °C and with no additional solvents, Michael additions promoted by aliphatic and aromatic organozincates take place with high regio- and chemoselectivity providing the expected nitroalkanes in yields up to >98%, and with no replacement of the vinylic nitro group by the alkyl group.^[5]



Based on these findings, the necessity to develop an enantioselective version of this transformation became important. In order to develop an enantioselective reaction, a chiral ligand is known to be necessary. In this case, we thought to create a chiral lithium zincate using two different approaches: harnessing the deprotonative capability of the tetraorganozincate species towards mobile protons like the ones present in amino alcohols and using a co-complexation approach between the corresponding lithium alkoxide of the ligand employed and an organozinc compound. In this communication, isolation of key intermediates as well as structural and synthetic aspects will be discussed.

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Nano-bio systems for water remediation

<https://isc.unicam.it/>A. Brioli¹, M. Blosi¹, I. Zanoni^{1,2}, S. Orrelli¹, S. Albonetti³, and A.L. Costa¹¹: Institute of Science and Technology for Ceramics, National Research Council, Via Granarolo 64, Faenza (Italy)²: Clinical Unit of Occupational Medicine, Department of Medical and Surgical Sciences, University of Trieste, Via della Pietà 2/2, 34129 Trieste, Italy³: Dipartimento di Chimica Industriale "Toso Montanari", University of Bologna, viale del Risorgimento 4, 40136 Bologna, Italy**Abstract**

We present the development of a novel nano-bio catalyst usable in downstream treatment of industrial wastewater remediation. We combined the potentialities of *Chlorella Vulgaris* microalgae with the photocatalytic properties of TiO₂ NPs, in order to investigate unexplored synergistic effects which will enable the innovation of the algal remediation technology toward a more promising cost-effective balance consistent with its industrial implementation. We started from non-living *C. Vulgaris*, which keeps the absorption properties of the living microalgae, but greatly enhancing its processability. *C. Vulgaris* biomass was coupled with TiO₂ NPs with an optimized colloidal process and with different TiO₂/*C. Vulgaris* weight ratios. The hybrid nanosols were then dried by means of a spray freeze drying (SFD) technique, able to produce highly reactive granules [1]. A widespread physicochemical characterization of the nano-bio catalysts (DLS, ELS, BET, FESEM, FTIR, ICP-OES, UV-VIS) supported the preparation process and the performances evaluation in terms of Cu²⁺ absorption and photocatalytic activity. The results exhibited greatly enhanced heavy metal absorption, pointing out a positive synergistic interaction between *C. Vulgaris* and TiO₂. The preliminary results pave the way for the integration of such nano-bio catalysts into water remediation systems. Tests are ongoing on living microalgae doped with TiO₂, where the metabolic activity could emphasize new application perspectives.

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Square planar vs. trigonal bipyramidal molecular geometry in organometallic Pt(II) anticancer complexes bearing glycosylated nitrogen ligands: synthesis, characterization and solution behaviour

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Cancer is one of the primary causes of the death in the world. In 2018 more than 1.700.000 cases have been registered in the USA with more than 600.000 deaths,¹ making urgent to find valid therapies to contrast the disease. In this frame, platinum-based drugs (over all cisplatin, carboplatin and oxaliplatin) have assumed a prominent role in chemotherapeutic treatments, despite the occurrence of severe issues (side effects and drug resistance) which limit their effects. In recent years, our research group proposed several organometallic Pt-complexes as anticancer agents bearing sugar-based ligands.² In fact, it is well known that the presence of a sugar fragment in the coordination sphere of the complex could enhance the selectivity of the drug, due to the increased “hunger” of cancer cells for carbohydrates (Warburg effect).³ Among the proposed molecules, there are five-coordinate Pt(II) complexes in which glucose fragments are linked to the metal through nitrogen-based ligands (**1Pt** in **Figure 1**).⁴

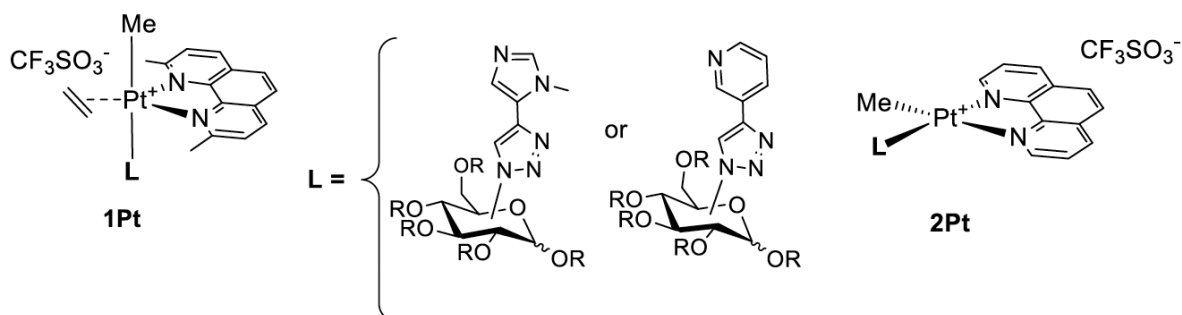


Figure 1

Such library of compounds showed to be more active than cisplatin whereas no selectivity was observed. Solution studies in organic and mixed water-organic solvents showed that the sugar ligand was quickly substituted by solvent molecules probably due to the strong trans-effect exercised by the methyl group. On this basis the related family of square-planar compounds **2Pt** (in **Figure 1**) has been synthesized and characterized. Preliminary investigations disclose that **2Pt** compounds are more inert toward ligand substitution, preserving the glucose-ligand. The biological activity of the compounds will be tested on the cell panel used for **1Pt** along with the study of the interaction with model biomolecules, to obtain useful structure-activity relations between the two libraries.

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Synthesis and characterization of new chiral ionic liquids tweezers from isomannide and isosorbide.

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Ionic Liquids (ILs) are organic salts with a melting point lower than 100°C. Their unique properties have attracted a lot of attention in the last twenty years.^{1,2} Chiral Ionic Liquids (CILs), a subclass of these compounds featuring an asymmetric moiety, have found application in chiral chromatography, enantioselective separations, asymmetric synthesis and as chiral solvents.³⁻⁵ To be employed as chiral selector, a CIL must possess a chiral structure endowed with functional groups able to establish enantioselective interactions with chiral or prochiral substrates. An additional desirable feature is the employment of low-cost starting materials and synthetic procedures for the preparation of such CILs. For these reasons, the majority of CILs derive from the chiral pool, which offers enantiomerically pure, readily available and cheap starting materials.

Among the compounds belonging to the chiral pool, isomannide and isosorbide (**Figure 1**) have received a great deal of attention:⁶⁻

⁹ they are renewable, inexpensive and commercially available chiral compounds derived from the dehydration of sorbitol and mannitol, which are waste products formed during the processing of corn oil and are obtained as by-products from the starch industry.¹⁰

Starting from these compounds, we synthesized eight new CILs with a vaulted structure. The ionic group of these derivatives, unlike the previous CILs of isomannide and isosorbide,⁶⁻⁹ is located far from the isohexide bicyclic skeleton. The synthesized CILs were characterized by studying their thermophysical properties and through a stereochemical investigation by electronic circular dichroism (ECD) spectroscopy. TGA analysis showed a higher thermal stability of Tf₂N (T_{start5%} from 348 to 363°C) CILs than the corresponding iodide salts (T_{start5%} from 192°C to 223°C). This thermal stability gain due to the halide-bistriflimide anion exchange was not observed before for this kind of CILs. Moreover, the here proposed Tf₂N CILs are by far the most stable isohexide-based ionic liquids prepared up to now.^{9,10} To conclude, a theoretical conformational analysis suggested the possible use of the isohexide derivatives as tweezers-type hosts in recognition processes toward different kinds of guests.

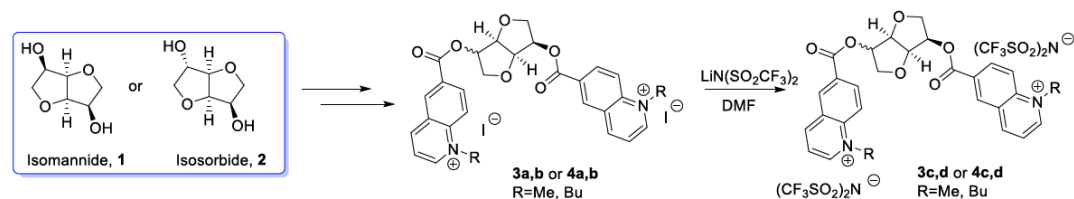


Figure 1-New CILs from isomannide and isosorbide.

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Amide Functionalized 3D Co(II) and Zn(II) Metal Organic Frameworks as catalysts for Benzyl Alcohol Oxidation and C-C Coupling reactions

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Abstract:

Two new 3D metal-organic frameworks (MOFs) $[\text{Co}(\text{1}\kappa\text{N}; 2\kappa\text{O}^{\text{O}'}-\mu\text{-L})_2]_n \cdot 4n(\text{DMF}) \cdot 1.5n(\text{H}_2\text{O})$ (**1**) and $[\text{Zn}_2(\text{1}\kappa\text{N}; 2\kappa\text{O}-\mu\text{-L})_2(\kappa\text{O}^4-\mu_4\text{-BTC})]_n \cdot 3n(\text{DMF}) \cdot 2n(\text{H}_2\text{O})$ (**2**) were synthesised using pyridyl amide functionalized benzoic acid (**HL**) [$\text{L} = 4\text{-(pyridin-4-ylcarbamoyl)benzoate}$; $\text{BTC} = \text{benzene-1,3,5-tricarboxylate}$]. They were meticulously characterized by conventional methods and their structures were elucidated by single crystal X-ray diffraction analyses. MOFs were found to act as a heterogeneous catalyst in benzyl alcohol oxidation and C-C bond formation model reactions (Fig. 1). MOF **1** exhibited decent catalytic activity in the solvent-free microwave-assisted oxidation of benzyl alcohol to benzaldehyde. On the other hand, MOF **2** in spite of having redox inactive Zn(II) site also displayed such alcohol oxidation, which is explicated by DFT calculations. Furthermore, MOF **2** exhibited good catalytic activity in sonochemical Knoevenagel condensation of benzaldehyde and malononitrile (yields up to 94%) and in the Henry C-C coupling reaction of benzaldehyde with nitroethane in water (yields > 99%), showing noticeable diastereoselectivity towards the *syn* isomer. The recyclability of catalysts was also examined.

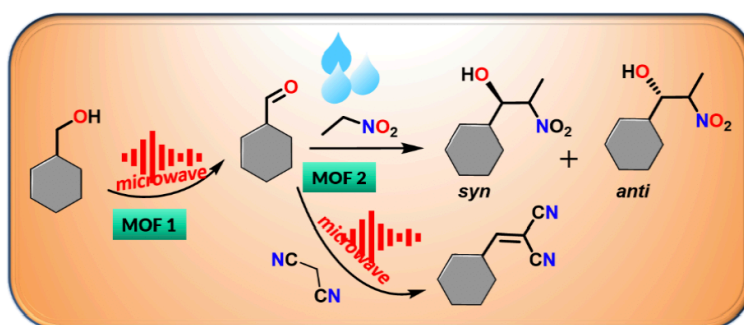


Fig. 1. Catalytic activity of MOFs 1 and 2.

Acknowledgements:

A. Paul acknowledges financial support from FCT and IST through "DL/57/2017", (Contract no. IST-ID/197/2019)

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Asymmetric reduction of cyclic imines by a new hybrid catalyst based on an iridium/ Vancomycin system

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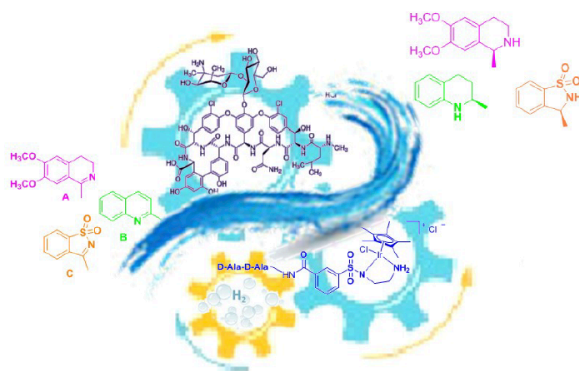
Abstract

The so-called hybrid catalysts, derived from the combination of transition metal catalysts embedded within a biological environment have recently risen up as a promising approach able to merge the attractive properties of both metal-based catalysis and biocatalysis^[1]. Dalbapeptides, such as vancomycin, teicoplanin, ristocetin, are variously substituted heptapeptides whose antibiotic activity stems from their binding to the D-Ala-D-Ala dimer of peptidoglycan precursors thus resulting in the inhibition of cell wall biosynthesis. In this system, indeed, the source of chirality is due to the presence of the aminoacidic chain, but also from the atropoisomerism of their structure. This interaction is marked by such a low dissociation constant ($K_D = \sim 10^{-17}$ M) that makes dalbapeptides an innovative option to the classical biotin/(strept)avidin second sphere coordination system^[2,3].

In this context, aminoethylbenzenesulfonamide ligands functionalized with the D-Ala-D-Ala dimer at different positions of the phenyl ring were employed for the synthesis of the hybrid catalysts in association with an iridium centre leading to reductases applied to the asymmetric transfer hydrogenation of cyclic imines.

An encouraging 48% (*S*) e.e. was obtained in the asymmetric reduction of the salsolidine precursor using the *meta*-hybrid system in NaOAc 0.1 M buffer at pH 5.

In the case of the most demanding isoquinoline substrates, the *meta*-hybrid system afforded the product in an outstanding 71% (*S*) e.e. in the reduction of quinaldine. This result was obtained by increasing the vancomycin/catalyst ratio to 4:1, underlining the great impact of the second sphere in inducing chirality to the system^[4].



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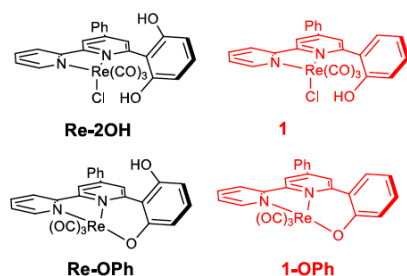
MOLECULAR CATALYSTS WITH INTRAMOLECULAR Re-O BOND FOR ELECTROCHEMICAL REDUCTION OF CARBON DIOXIDE

Laura ROTUNDO,¹ Carlo NERVI,¹ Roberto GOBETTO,¹ Gerald MANBECK,² Dmitry POLYANSKY,² Etsuko FUJITA²

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The utilization of CO₂ via electrochemical reduction represents a promising approach toward production of added value chemicals or fuels using intermittent renewable energy sources. Most electrocatalytic studies in this field focus primarily on the catalyst/substrate interaction in homogeneous solution. The concept of local proton source applied to the electrochemical reduction of CO₂¹ has been extended not only to the Mn-bpy system, but also to the Re-bpy complexes.^{2,3} Recently we studied the effect of the two OH functionalities on *fac*-Re(pdbpy)(CO)₃Cl³ (**Re-2OH**), (pdbpy = 4-phenyl-6-(phenyl-2,6-diol)-2,2'-bipyridine). The intermediate **Re-OPh** (Scheme 1) is proposed to be produced after the first 1e⁻ reduction. However, its identity was not corroborated by other experimental techniques and its precise effect on catalysis remained unclear. In order to shed light on the fundamental aspects of



Scheme 1. Chemical sketches of **Re-2OH**, **Re-OPh**, **1** and **1-OPh**.

this electrochemical mechanism and to provide additional spectroscopic evidence for phenolate coordination to the metal, a novel complex bearing a single hydroxyl group instead of two, namely *fac*-Re(pmbpy)(CO)₃Cl (pmbpy = 4-phenyl-6-(2-hydroxy-phenyl)-2,2'-bipyridine), **1**, has been synthesized⁴ (Scheme 1). The corresponding intermediate **1-OPh** has been isolated via Controlled Potential Electrolysis and subsequently characterized. We demonstrated that in the case of Re bipyridine-type complex, the formation of this relatively stable Re-O bond and a preference for phenolate-based reactivity with CO₂ slightly inhibit the electrocatalytic reduction of CO₂ to CO, resulting in a low TON value of 9 for **1**, even in the presence of phenol as proton source.

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User-friendly analytical methods for metabolomics applications to unconventional biological matrices

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Whole blood, serum and plasma are well established specimens in clinical studies aiming to discover new biomarkers linked to pathologies, or to identify the impairment of metabolic cycles due to the effect of external agents, including food, drugs and supplements. However, their sampling requires the presence of specialized personnel, it is invasive and could adversely affect the participation of volunteers to the study. Nowadays unconventional biological matrices (e.g. saliva or exhaled breath condensate) can be collected in a non-invasive manner and have thus attracted increasing attention in the field of metabolomics.

Derivatization reactions for both GC-MS and LC-MS analysis of these biological media are in general necessary to address specific classes of compounds, with the drawbacks of time-consuming sample preparation, mostly the handling of toxic derivatization agents and the loss of simultaneous determination of multiple classes of analytes.

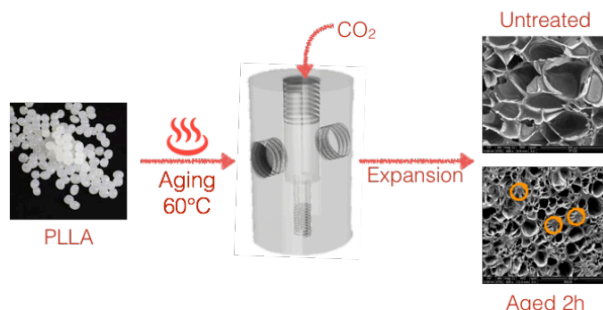
Here, two straightforward analytical approaches developed at CNR-ICCOM and based on (i) headspace solid-phase microextraction coupled with gas chromatography-mass spectrometry for the analysis of volatile organic compounds, and (ii) liquid chromatography-diode array detection for the quantification of small organic metabolites, will be presented. Both methods are suitable for the simultaneous determination of more than 20 compounds and do not require any derivatization step. The validated procedures have been applied to the analysis of saliva, exhaled breath condensate and cell culture media to address specific metabolic questions.

Influence of crystal nucleation on foamability of poly(L-lactic acid)

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Bio-based and biodegradable plastics are becoming increasingly important in industry as environmentally benign substitutes of plastics derived from fossil resources. Among all the bio-based polymers, poly (L-lactic acid) (PLLA) is the most frequently used. PLLA is a thermoplastic polyester, biocompatible and derived from renewable resources. It is used in a variety of industrial fields, which mainly include films for packaging or agriculture, or biomedicine, as 3D printing, or for production of foams. Besides being used for tissue engineering and medical implants, PLLA foams have several additional applications such as thermal and sound insulation in construction and food packaging industry. Unfortunately, the use of chemical blowing agents leads to an exothermic reaction which makes the whole process and the final cell structure hard to be controlled. Then research focused on physical blowing agents like CO₂. The use of supercritical CO₂ as physical blowing agent in foaming PLLA, influences the crystalline properties of the polymer since it can swell and plasticize polymers, leading to a depression of their glass-transition temperature (T_g). This depression in T_g of the polymer, leads to an increase in the chain mobility and then to an easier reorganization of polymer chains, which results in a faster crystallization of the polymer. Literature data clarify how aging of glassy PLLA allows formation of crystal nuclei which enhances/accelerates subsequent crystallization at temperatures above the glass transition by reducing the energy barrier needed to create new surfaces. The same enhancement in surface free energy is expected to apply also for nucleation of bubbles in foaming, where crystals, or any other solid surface, may promote bubble nucleation and their subsequent growth. The large advantage of homogeneous nuclei, compared to existing crystals, is the absence of initial crystallinity, which, coupled with their very high density per unit volume, should provide an enormous number of sites for bubble growth.

This knowledge leads us to study the influence of crystal nucleation in glassy PLLA on its foaming properties, to improve them.

The influence of aging of glassy poly (L-lactic acid) (PLLA) on foaming efficiency and foam morphology is detailed in this contribution.

Glassy PLLA aged for 0.5, 2 and 4 hours has been foamed with supercritical CO₂. Study on density of the foams demonstrated how increasing the aging time and, consequently, the number and the density of homogeneous nuclei, the foam density decreases. At the same time, study on the morphology of the foams confirmed the formation of surfaces able to promote bubble nucleation.

This leads to the conclusion that aging glassy PLLA can be an efficient method to improve the expansion ratio of the polymer.

Sensing the temperature generated by self-assessed photothermal agents in ex-vivo experiments via lanthanide doped luminescence nanothermometers

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Lanthanide doped nanoparticles due to their peculiar electronic configuration and temperature-dependence optical properties,¹ have the ability to be implemented as luminescent nanothermometers. Luminescent nanothermometers enable temperature readouts in a plethora range of applications.² Here, we explore the self-assessing properties of Ho, Tm:KLu(WO₄)₂ nanocrystals, synthesized via novel solvothermal methodology, to sense the temperature in an *ex-vivo* application. These nanocrystals can be excited with near infrared light (808 nm), located at first biological window (I-BW), and emit at the third biological window (III-BW), where scattering and absorption from biological tissues are both reduced, allowing for thermal sensing at high penetration depths.^{3,4} Upon this excitation wavelength, these nanocrystals can generate simultaneously photoluminescence and heat, which allows their applications as nanothermometers and as photothermal agents in the III-BW, *i.e.* self-assessed photothermal agents.⁵ The intensity ratio among the emissions of these nanocrystals located at 1.45 μm , 1.8 μm and 1.96 μm , attributed to the $^3\text{H}_4 \rightarrow ^3\text{F}_4$ and $^3\text{F}_4 \rightarrow ^3\text{H}_6$ electronic transitions of Tm³⁺ and $^5\text{I}_7 \rightarrow ^5\text{I}_8$ electronic transition of Ho³⁺, displayed a maximum thermal sensing of 0.33% K⁻¹ and photothermal conversion efficiency of around 45%. For the *ex-vivo* application, tested in a chicken breast, the nanocrystals achieved their self-assessing properties at a maximum penetration depth of 2 mm.

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Asymmetric Synthesis of Chiral Primary Amines by Addition of Highly Polarized Organometallic Compounds to *N*-*tert*-Butanesulfinyl Imines in Deep Eutectic Solvents

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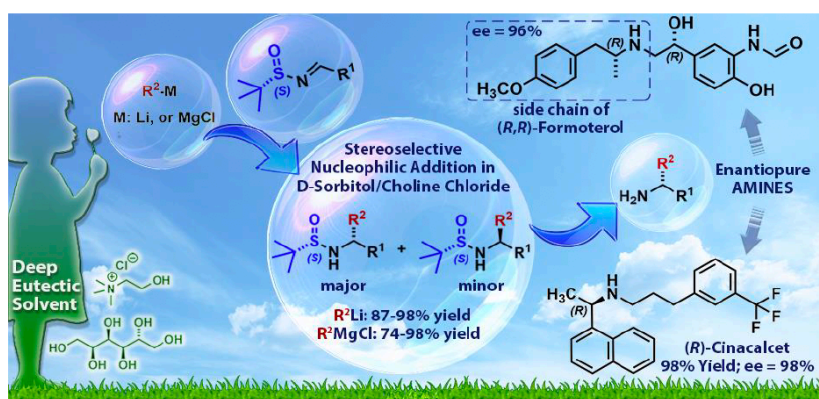
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Recent contributions from Hevia and García-Álvarez¹ and by our group² have shown that reactions of simple/functionalized organolithium compounds can be smoothly performed in unconventional reaction media at room temperature (RT), under air, and competitively with protonolysis. Building on these findings, we described the nucleophilic addition promoted by both Grignard and organolithium reagents to enantiomerically pure Ellman imines³ **1** in D-sorbitol/choline chloride eutectic mixture, at RT and under air and provided the diastereomeric sulfinamides in very good yields (74 – 98%) but low dr. The two diastereomers, however, could always and easily be and deblocked to the corresponding enantioenriched free amines in high yield (98%). In this communication, we report the results of the application of this methodology for the preparation of enantioenriched primary amines **3**, side-chain of (*R,R*)-Formoterol and the pharmaceutically relevant (*R*)-Cinacalcet, in three steps. The chemo- and diastereoselectivity of these addition reactions was discussed and assessed by ¹H NMR analysis.⁴



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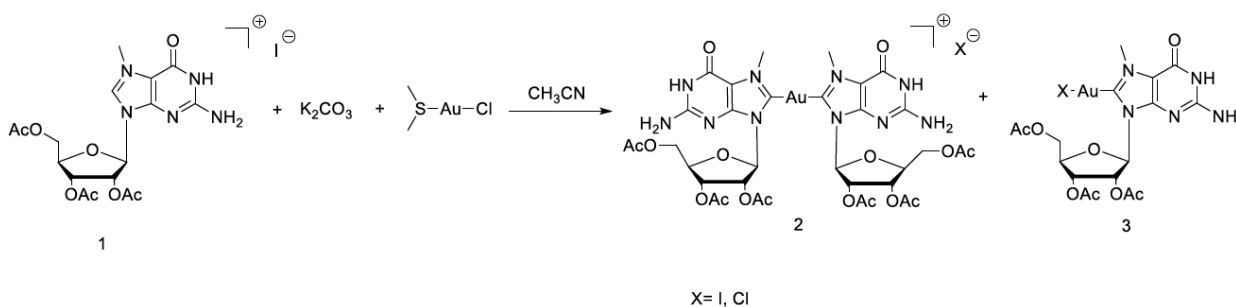
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NEW GOLD COMPLEXES BASED ON GUANOSINE

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Combining a strong σ -donor character and tunability from the modification of the side chains, N-heterocyclic-carbenes (NHCs) are excellent candidates as ligands for metallocenes^[1]. Recently, *Wragg et al.* have described how a series of gold NHCs interact with DNA telomeres stabilising G-quadruplex, in addition to inhibiting thioredoxin reductase, whose mediation for cytotoxicity has been reported earlier^[2,3]. Following our work with purine bases, we examined the formation of gold NHCs based on guanosine, aiming for obtain complexes able to induce molecular recognition via base pairing. In this communication, we will discuss synthetic strategies and report our preliminary studies.



Scheme 1 - Reaction of direct metalation

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MANGANESE (DI)TRIAZOLYLIDENE COMPLEXES: SYNTHESIS, CHARACTERIZATION AND REACTIVITY

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Mesoionic carbenes, especially those derived from 1,2,3-triazoles, are an interesting subclass of N-heterocyclic carbene ligands that have advanced to prominent class of ligands in catalysis. Surprisingly, in contrast to noble metals, mesoionic 1,2,3-triazolylidenes (Trz) are almost unexplored as ligands for first-row transition metals, with only rare examples reported in the literature.^[1] Recently, our group demonstrated the preparation of two rare examples of Mn complexes bearing trz ligands.^[2] Here in we present the synthesis of bimetallic Mn(0) and monometallic Mn(I) complexes with chelating or bridging mesoionic di(1,2,3-triazolylidene) ligands (**1** and **2**, Figure 1). All complexes have been fully characterized by NMR, IR spectroscopy, cyclic voltammetry, and in some cases by crystal X-ray diffraction. To study the reduction processes of complex **2**, spectroelectrochemistry and DFT calculations were performed. Reactivity of complexes **1** and **2** were also tested using Br₂ and MeI or phosphine ligands in the presence and absence of visible light.

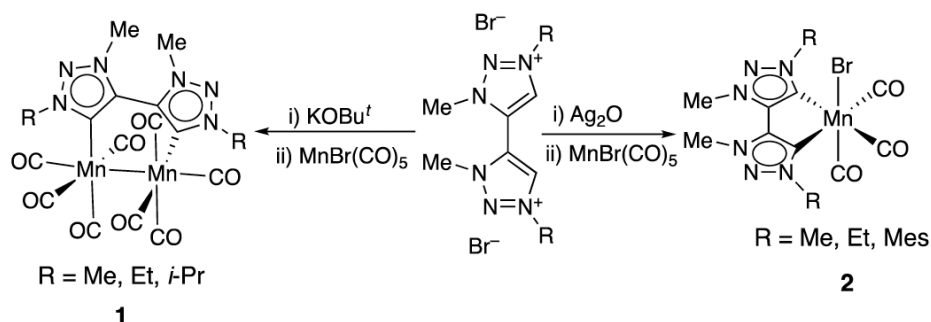


Figure 1. Synthesis of Mn(0) and Mn(I) complexes with chelating or bridging Trz

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Photoelectrocatalytic Hydrogen Evolution in Thin Films

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Hydrogen is a promising renewable fuel and an industrially important gas. Cobalt bis(benzenedithiolate) catalysts are adept at catalyzing proton reduction to hydrogen. Immobilizing these molecular catalysts on a surface combines the advantages of molecular catalysts with the advantages of heterogeneous catalysis. Cobalt bis(dithiolbenzene) catalysts have been physisorbed on to graphitic surfaces, such as thin films of reduced graphene oxide, and used for electrocatalytic hydrogen production. Specifically, this work uses Cobalt bis(dichlorodithiolbenzene) which has been shown to physisorb well and have high activity. This work explores photoelectrocatalytic hydrogen production in a thin film. Thin films of reduced graphene oxide, photosensitizer, and catalyst are dropcast onto a glassy carbon electrode and evaluated for photoelectrocatalysis of hydrogen. Organic dyes are used as photosensitizers, using visible light to provide high energy electrons for this reaction. Synthesis and optimization of these reduced graphene oxide, catalyst, photosensitizer systems will be described. Photoelectrocatalytic hydrogen production will be evaluated.

A Force Field for Halogenated Active Pharmaceutical Ingredients

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The discovery of a new active pharmaceutical ingredient (API) that is effective for a specific disease is a very costly and time-consuming process. Many interesting APIs in development pipelines fail to reach the market because of problems that have a negative impact in the production and performance of a drug, such as low solubility, polymorphism, and incompatibilities with excipients. For example, low solubility often implies a low bioavailability, and polymorphism, the ability of a molecule to adopt more than one crystal structure, frequently leads to differences in physical properties that hinder the production of drugs with highly reproducible performance.

Molecular dynamics (MD) simulations have become increasingly more familiar to pharmaceutical developers as a powerful tool to rationalize and forecast the properties of prospective APIs that are critical for an a priori evaluation of negative impacts on production and performance. A critical aspect of the use of MD simulations is the development of force fields that are able to accurately capture the energetic (e.g. lattice energy) and structural (e.g. unit cell dimensions) characteristics of an as large as possible class of substances. Here we describe the parameterization and validation of a force field suitable for halogenated molecules, based on the study of three marketed APIs (Figure 1): triclosan, (b) chlorzoxazone and (c) clioquinol

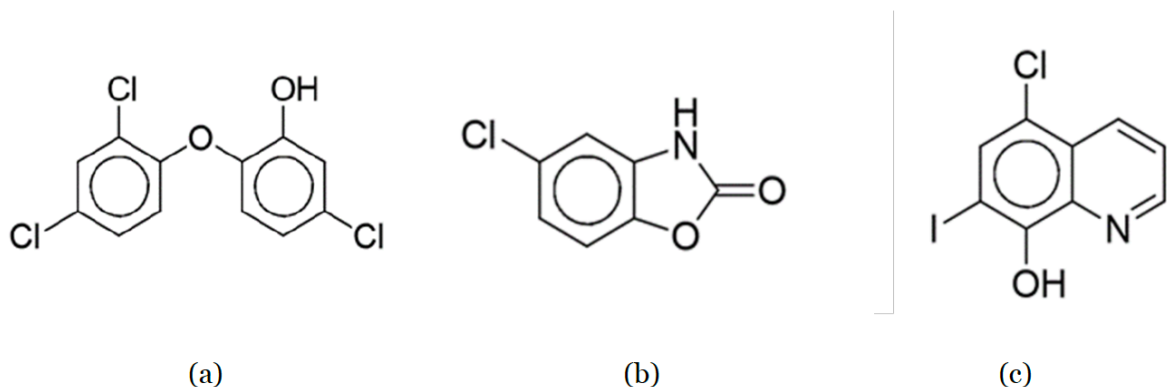


Figure 1. Halogenated APIs selected to develop this work: (a) triclosan, (b) chlorzoxazone and (c) clioquinol.

Synthesis and Catalytic Activities of a Zn(II) Based Metallomacrocyclic and a Metal-Organic Framework towards One-pot Deacetalization–Knoevenagel Tandem Reactions under Different Strategies: A Comparative Study

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Abstract

Solvothermal reactions between a pyridine based amide functionalized dicarboxylic acid, 4,4'-((pyridine-2,6-dicarbonyl)bis(azanediyl))dibenzoic acid (H_2L), and zinc(II) nitrate in absence and presence of base produced the binuclear metallomacrocyclic compound $[Zn_2(L)_2(H_2O)_4] \cdot 2(H_2O) \cdot 6(DMF)$ (**1**) and the metallomacrocyclic based two dimensional MOF $[Zn_5(L)_4(OH)_2(H_2O)_4]_n \cdot 8n(DMF) \cdot 4n(H_2O)$ (**2**), respectively. Compound **1** bears two tetrahedral Zn(II) centres, whereas the 2D framework **2** includes a penta-nuclear Zn(II) cluster as secondary building block unit, with two of the metal cations assuming a tetrahedral type geometry and the remaining three an octahedral type one. These compounds heterogeneously catalysed the tandem deacetalization–Knoevenagel condensation reactions carried out under conventional heating, microwave irradiation or ultrasonic irradiation (Figure 1). Comparative studies show that ultrasonic irradiation (final product yield of 99% after 2h of reaction time) provides the most favourable method (e.g., microwave irradiation leads to a final product yield of 91% after 3h of reaction time). Moreover, the catalysts can be reused at least for five consecutive cycles without losing activity significantly.

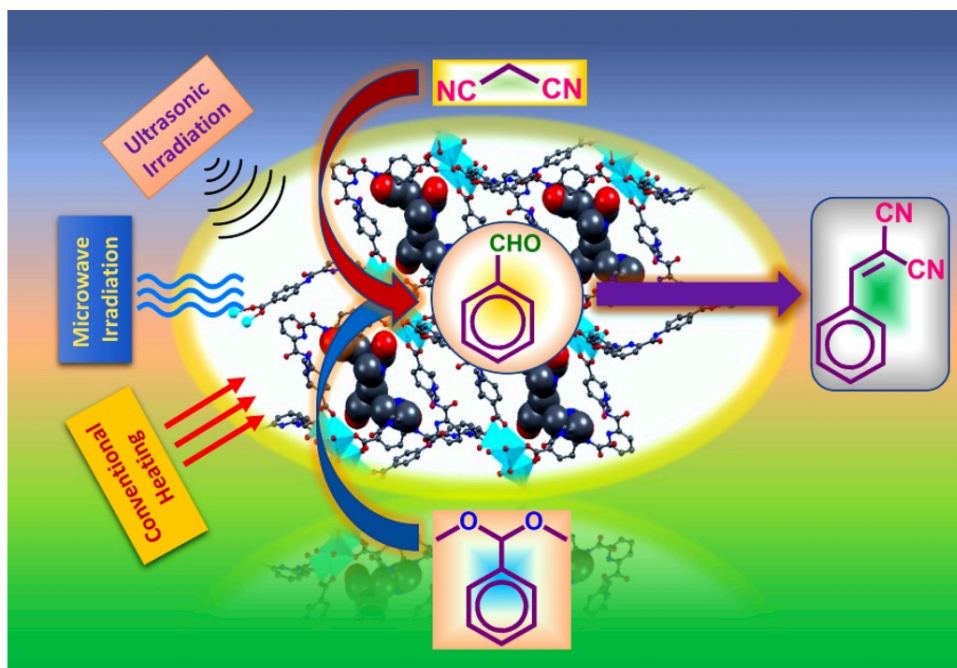


Figure 1: One-pot tandem deacetalization-Knoevenagel reactions catalyzed by **1** and **2** using conventional heating, microwave and ultrasonic methods.

Sustainable route in the preparation of polymeric membranes using dimethyl isosorbide (DMI) as a sugar-based solvent from biomass

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Keywords: Sustainable membranes, Dimethyl isosorbide (DMI), Green solvent, Inversion phase.

Membrane processes was considered a green technology according to Processes Intensification Strategy [1] but at the same time, the preparation of membranes required the use of toxic solvents such as N, N-dimethylformamide (DMF) or N-methyl-2-pyrrolidone (NMP). These substances may pose several issues for both human health and environment. The replacement of these solvents with new chemicals from biomass valorisation, according the Green Chemistry approach, represent the new goal for producing membranes [2]. The objective of this work is to study, for the first time, the effects of dimethyl isosorbide (DMI) as a new sugar-based solvent, for the preparation of polyethersulfone (PES) and poly(vinylidene fluoride) (PVDF) membranes [3]. A predictive investigation on the possibility of using DMI as a solvent for both polymers was carried out by the Hansen and Hildebrand solubility parameters and the relative energy difference. The evaluation of thermodynamic was determined by the phase diagram as reported in figure 1a and the kinetic study was evaluated in term of viscosity. Polymeric membranes were prepared by induced phase separation (VIPS) and non-solvent induced phase separation (NIPS) techniques. The different exposure time to humidity, pore size without the need of any pore forming additive were investigated. The results showed a pore size in the range of micro and ultrafiltration and a spongy and finger-like morphology by scanning electron microscopy (SEM) for PVDF and PES membranes, respectively (figure 1b). The membranes obtained also a good mechanical resistance and properties, like water permeability, comparable to the membranes prepared with traditional solvents.

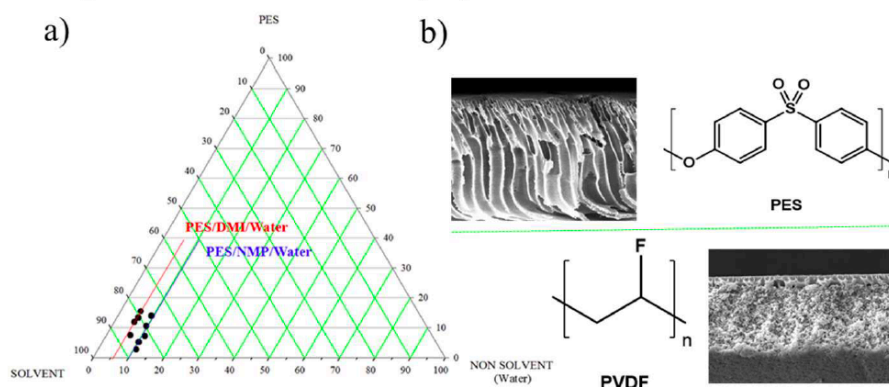


Figure 1. Diagram of a) PES membranes and SEM of b) PVDF and PES membranes.

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Hydrothermal Pre-treatment of Waste Activated Sludge (WAS)

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The increasing worldwide energy consumption, higher energy requirements for future, exhaustion of fossil fuel-based resources and global warming have led to the application of renewable sources like biomass to meet energy demands. In a vision of Circular Economy, valorisation of secondary biomass and waste can offer a sustainable way to obtain more useful products like fuels and chemicals either directly or indirectly. This work utilizes wastewater sludge biomass produced from civil and industrial wastewater treatment plants. The total wastewater sludge production in terms of dry solids is approximately 13 Mt across the European Union. With an increase in the number of wastewater treatment plants and stringent effluent discharge rules, sludge production rate is expected to rise. Traditional technologies are focused on sludge disintegration and minimization. However, sludge biomass contains significant concentration of organic carbon which on pre-treating could be valorised into bioproducts. Here hydrothermal pre-treatment tests are carried out on dewatered sludge samples at different operating conditions. It is intended to maximize the solubilisation of organic carbon in the aqueous phase and a reduction in the total solid sludge mass after pre-treatments.

Blue emitting boron difluoride compounds of 2-(imidazo[1,5-a]pyridin-3-yl)phenols and their hydrogenated derivatives

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Boron containing compounds proved to be a highly promising class of building blocks for optoelectronic materials; specifically, boron dipyrromethene (BODIPY) derivatives¹ show relevant fluorescence properties and have found applications in several fields, including optoelectronic materials like OLEDs² which are becoming more and more important in various everyday technologies.

Alongside, imidazo[1,5-a]pyridines are a class of heterocyclic compounds whose photochemical properties have been widely explored, especially due to large Stokes shift and high quantum yields they usually show. Furthermore, there are numerous publications on luminescent transition metal compounds based on imidazo[1,5-a]pyridines. We also reported on fluorescent zinc(II)³ and silver(I)⁴ complexes with these ligands, while more recently we investigated the emissive properties of some tetrahydro(imidazo[1,5-a]pyrid-3-yl)phenols⁵

With these premises, we prepared a series of boron difluoride compounds of 2-(imidazo[1,5-a]pyridin-3-yl)phenols, obtained by reacting our imidazo[1,5-a]pyridines with $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (Figure 1), in order to combine the properties of these two classes. Herein, we report the fluorescent behavior of these species, which have been widely characterized both in solution and in solid state.

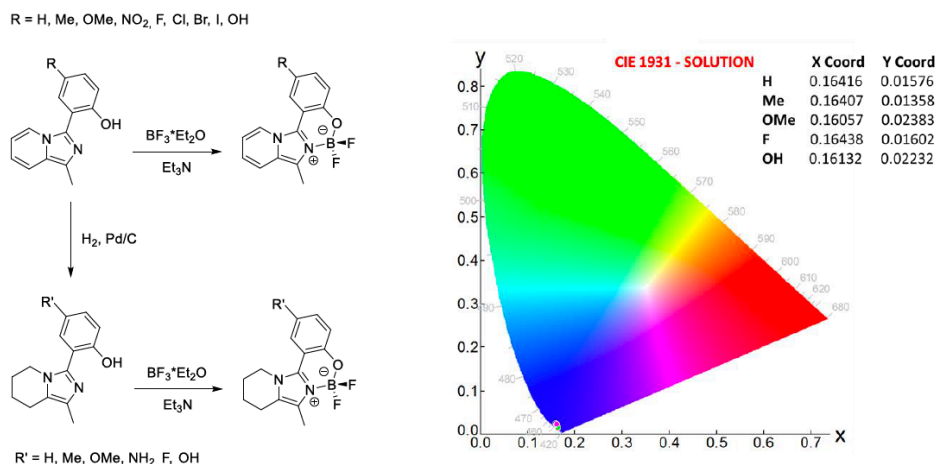


Figure 1: Synthesis of the compounds object of this study and CIE 1931 chromaticity plot for the emission in solution (5×10^{-5} M CH_2Cl_2) of the hydrogenated species.

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Asymmetric transfer hydrogenation of Ketones promoted by a well-defined Manganese pre-catalyst supported by chiral aminophosphines

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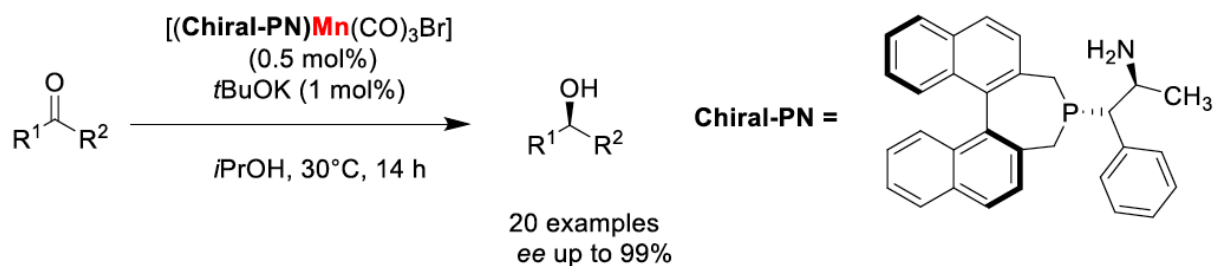
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Abstract

Chiral alcohols are highly valuable synthetic intermediates for the production of pharmaceutical, agrochemical and fine chemical products. As a result, asymmetric reduction of ketones by direct hydrogenation (ADH) or hydrogen transfer (ATH) catalyzed by organometallic complexes has been intensively investigated. ATH represents an efficient and appealing approach since it uses alcohols, or an azeotropic mixture of formic acid and triethylamine, as solvent and reducing agent, and avoids therefore the use of pressurized hydrogen gas. Although noble metals have proven to be particularly efficient for this class of transformation,^[1] and for this reason are still widely used, this field of research has recently met a significant shift towards the use of earth-abundant, inexpensive and more environmentally friendly first row transition metals such as Fe, Co and Mn.^[2]

In this context, we have developed a catalytic system based on commercially available chiral amino-phosphines, in combination with $\text{Mn}(\text{CO})_5\text{Br}$ for the asymmetric reduction of ketones, using isopropanol as hydrogen source.^[3] With the most selective ligand, the corresponding manganese complex was synthesized, fully characterized and implemented in ATH. A series of ketones (20 examples) was hydrogenated in the presence of 0.5 mol% of the manganese pre-catalyst at 30 °C. All the results will be detailed in the present communication.



Carbon Nanodots in photoinduced electron transfer systems

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Carbon nanodots (CNDs) are newcomers in the large family of carbon-based nanomaterials.^{1–3} This nanomaterial consists on quasi-spherical 0D nanoparticles composed essentially of carbon, oxygen and hydrogen. CNDs have unique properties such as low toxicity, water solubility, rich redox chemistry, wide light absorption and emission and high chemical and photo-stability. These properties make CNDs interesting multifunctional nanomaterials useful for many applicative areas that range from the bio-applications to the opto-related ones.^{4,5}

In our research group we have focused on the rational design of CNDs conceiving a synthetic protocol that serves for the production of nanoparticles with selected properties.^{6,7} This protocol is essentially based on the rational selection of the CNDs precursors in order to introduce specific features in the final nanoparticle structure. The first type of CNDs synthesis conceived in our labs was focused on the production of doped carbon nanodots since doping represents a good way to enhance the emissive properties of these nanoparticles.^{8–11} By the control and optimization of the synthetic parameters, using a microwave assisted hydrothermal process and N-rich precursors, ethylene diamine (EDA) and L-arginine (Arg), nitrogen doped CNDs (NCNDs) were successfully obtained with the desired/designed doping and enhanced emissive properties.

Recently these nanoparticles resulted interesting building blocks for photoinduced electron transfer systems when coupled to porphyrin molecules.^{12,13} Such results inspired us on the expansion of the study of such electron transfer systems investigating novel NCNDs hybrids with optically active molecules. Current efforts were especially devoted to the study of multi-chromophore systems in which our nanoparticles could act as electron transfer bridge between dyes.^{14,15}

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MECHANISTIC STUDY OF THE HECK REACTION: β -HYDRIDE ELIMINATION ASSISTED BY DEPROTONABLE P-N LIGANDS

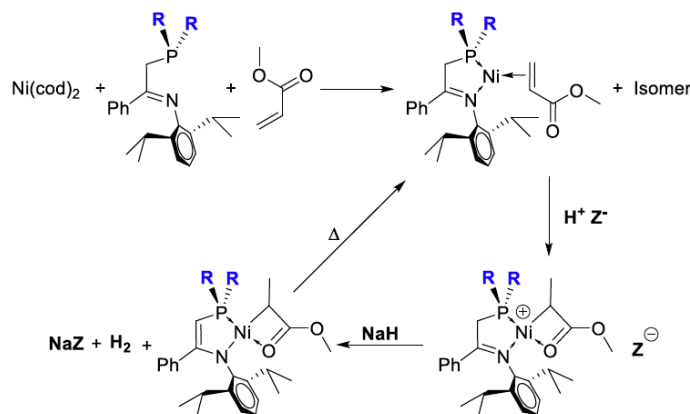
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To ensure a sustainable society, it is necessary the development of new catalysts, not just either more selective or efficient but cheaper. In this sense, the preparation of organic molecules has led to sustained interest in methods based on homogeneous catalysts, particularly in the development of ligands which can be tuned to specific needs.

The properties of a metal complex as a whole are the result of the interaction between the metal centre and its surrounding ligands. In traditional approaches, the steric and electronic properties of the ligands are used to control the performance of the catalyst, which play a spectator role, because the reactivity takes place at the metal centre. Recent new approaches, deviate from this concept, make use of more reactive (actor) ligands, that can play an active role in the elementary bond activation steps in a catalytic cycle [1,2]. The central idea is that the metal and the ligand can cooperate in a synergistic manner, and their interplay facilitates the chemical process [3].

Thus, we have been investigating the Heck reaction using Nickel complexes stabilized with phosphine-imine ligands which turn out not to have a spectator function, but they play a very important role in the catalytic system, particularly in the third step of the process: β -hydride elimination based induced. It was discovered that during this last step, the relatively acid character of the P-N ligands makes them easier to be deprotonated by a base. Subsequently, the β -hydride elimination is produced on account of the movement of the proton from the organic fragment back to the ligand (Scheme 1). For that aim, a model was studied.



Scheme 1

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DESIGN AND SYNTHESIS OF HOLE TRANSPORTING MATERIALS FOR PEROVSKITE SOLAR CELLS

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Perovskite solar cells (PSCs) are one of the emerging technologies in the field of photovoltaics. [1] Hole transporting materials (HTMs) play essential roles in improving the device performances; their main task is to capture the hole formed after light absorption in the perovskite layer and transport it to the cathode. The goal of this study was to synthesize new, cheaper and more stable organic HTMs than Spiro-OMeTAD, an organic molecule showing the best performances in PSC devices to date. [2] Organometallic reactions were used to form new carbon-carbon and carbon-nitrogen bonds to assemble different molecular fragments in simple way; in particular, we used palladium catalyzed Suzuki-Miyaura and Buchwald-Hartwig cross-couplings to prepare two new HTMs (HTM1 and HTM2, see figure 1). These compounds were then used to study how small structural modifications may affect the performance of the resulting PSCs.

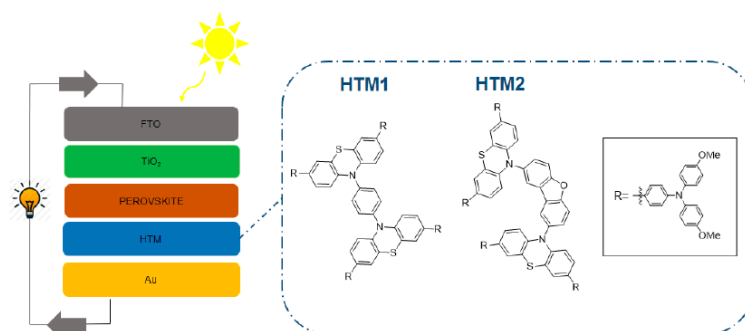


Figure 1: HTM1 and HTM2 synthesized

Acknowledgements (We thank Regione Toscana (« ARIADNE» project, POR-FESR 201 2020) for financial support.

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NOVEL TWO-DIMENSIONAL BASED MEMBRANES FOR ENHANCED WATER DESALINATION VIA MEMBRANE DISTILLATION

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Abstract: This work focuses on new advanced two-dimensional materials-based membranes for highly productive and efficient water desalination^{1,2}.

A special study is dedicated to the effects of exfoliated few-layers graphene and other transition metal dichalcogenides (TMDs) such as telluride bismuth on the productivity-efficiency trade-off in membrane distillation. The integration of inorganic and organic materials in unique systems enables outstanding functions unlikely reachable in single pristine materials³⁻⁶. Here, experiments carried out under different operating conditions - temperature, flow rate and salt concentration - are examined and discussed, while relationships between exfoliated few-layer materials and membrane properties are assessed. The experimental outputs indicate an important increase in mass transfer, thereby resulting in enhanced trans-membrane flux as compared to the pristine and other 2D-materials-based PVDF membranes.

Stable waterproofness and controlled resistance to scaling and thermal polarization are observed with time, whereas a noteworthy efficiency is estimated from both the energetics and salt rejection points of view, respectively.

This work yields interesting insights about the attractive role of 2D materials in membranes designed for an eco-sustainable membrane process, which supports the water reuse within a wider circular economy context.

ACKNOWLEDGEMENTS

We acknowledge financial grant from 'the Italian Ministry of Foreign Affairs and International Cooperation' within the framework of the Great Relevance International Project Italy (MAECI)-China (NSFC) 2018-2020 - New Materials, with particular reference to Two-dimensional systems and Graphene (2DMEMPUR).

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Rhenium-Catalyzed Reduction of Carboxylic Acids with Hydrosilanes

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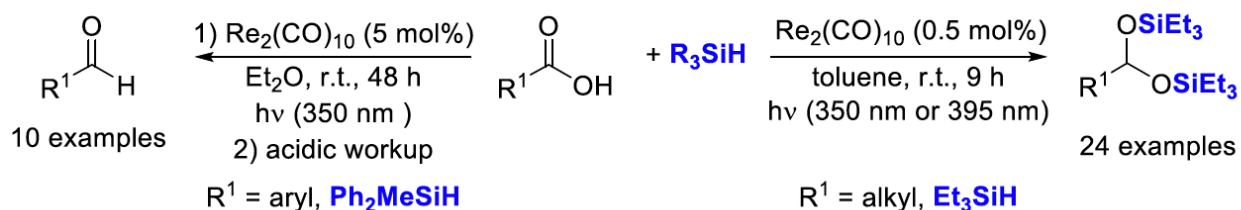
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Because of their essential role as organic synthons, simple and direct methods to produce aldehydes are highly required. The reduction of carboxylic acids, which is a common transformation, is one of the classical methods for the formation of aldehydes. However, due to the higher reactivity of aldehyde products with respect to acid precursors, the direct reduction of carboxylic acids to aldehydes is generally tedious and the formation of alcohols due to excessive reduction is difficult to avoid.^[1]

We reported recently that $\text{Re}_2(\text{CO})_{10}$ efficiently catalyzes the direct reduction of various carboxylic acids under mild conditions (rt, irradiation 350 or 395 nm). While aliphatic carboxylic acids were readily converted to the corresponding disilylacetals with low catalyst loading (0.5 mol %) in the presence of Et_3SiH (2.2 equiv), aromatic analogues required more drastic conditions ($\text{Re}_2(\text{CO})_{10}$ 5 mol %, Ph_2MeSiH 4.0 equiv) to afford the corresponding aldehydes after acid treatment.^[2]



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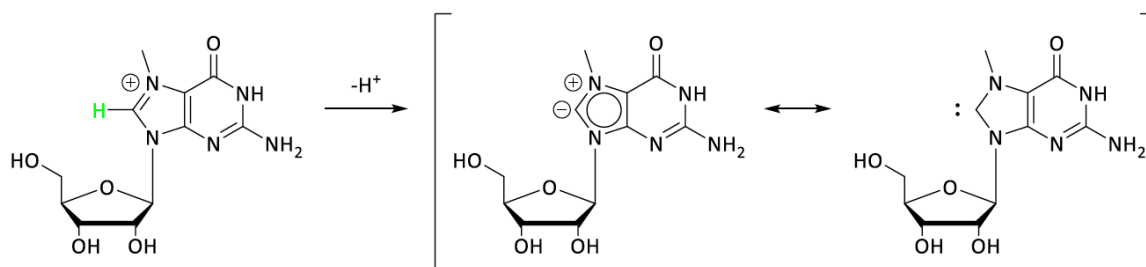
mRNA CAPS: C-H OXIDATIVE ADDITION OF 7-METHYLGUANOSINE TO PLATINUM(0) AND ANTIPROLIFERATIVE ACTIVITY

Maria Inês P. S. Leitão,¹ Federico Herrera,² Ana Petronilho¹

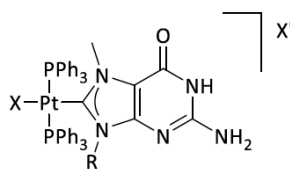
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The formation of 7-methylguanosine (7-MeG) at 5' end of mRNA in eukaryotes is a fundamental step in transcription.^[1-4] Once methylated, 7-methylguanosine, the so-called mRNA cap 0, acquires a positive charge due to the quaternization of N7, and the corresponding C8-H becomes exchangeable. This reactivity has been attributed to the transient formation of an ylide and the corresponding N-heterocyclic carbene (NHC; Scheme 1).^[5,6] In line with this, the reaction of 7-MeG with Pt(0) precursors yields the corresponding C-H oxidative addition product, a hydride-Pt(II) NHC complex (Scheme 2).



Scheme 1. Formation of ylide for 7-methylguanosine.



R = Tri-*O*-acetylribose, Ribose, CH₃
X = H, Br
X' = Cl, I

Scheme 2. Platinum(II) NHCs bearing guanosine or guanine as co-ligands.

Following our preliminary results with nucleoside based NHCs for anticancer activity,^[7] we examined the antiproliferative activities of the mRNA cap 0 derivatives and our results will be discussed in this communication.

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Heterogenization of Cu(I)-DAPTA complexes on carbon materials for the synthesis of 1,2,3-triazoles

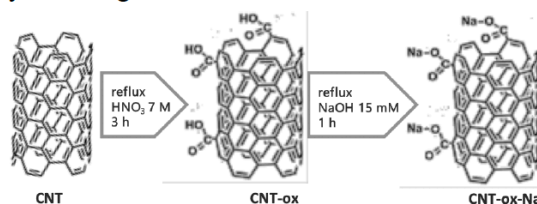
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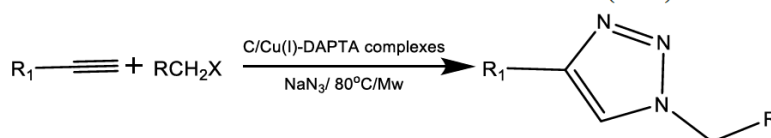
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The Cu(I)-DAPTA halide complexes were synthesized according to the literature¹ and were immobilized on three different carbon materials (activated carbon and multi-walled carbon nanotubes) with three different surface treatments (shown in Scheme 1, pristine; oxidized with nitric acid-ox; and oxidized with nitric acid and afterwards with NaOH-oxNa) according to previous publications.²⁻⁷ The immobilized complexes on the carbon materials were used as recyclable catalysts for the synthesis of disubstituted triazoles (Scheme 2), as in literature.^{8,9} The heterogenization process was more efficient on carbon nanotubes treated with nitric and sodium hydroxide. Moreover, the reaction was performed under MW irradiation for 15 min at lower temperature (80 °C) with a catalyst loading of 0.5 mol %.



Scheme 1. Functionalization of carbon nanotubes (CNT).



Scheme 2. Preparation of 1,2,3-triazoles using C/Cu(I) complexes.

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Synthesis of new catechol-*O*-methyltransferase stabilizers

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KEYWORDS: *Catechol-O-methyltransferase, Cancer, Structure-based drug design, chemical synthesis, Stabilizers*

ABSTRACT: Catechol-*O*-methyltransferase (COMT) is an enzyme responsible for the *O*-methylation of catechol substrates, such as catecholamines and catechol estrogens (CE). Considering its physiological functions and polymorphic activity, several studies associated COMT with the pathogenesis of several neurological disorders, cardiovascular diseases, and hormone-dependent cancers [1]. In fact, the major CE metabolites, 2- and 4-hydroxyestrone, are carcinogenic in peripheric tissues and it has been demonstrated that lower COMT activity increases the risk of developing hormone-dependent diseases. However, 2-methoxyestradiol, a 2-hydroxyestradiol metabolite originated by COMT-mediated methylation, exhibited antitumor properties. Hence, the main goal of this work is to develop new COMT stabilizers, to maintain or increase COMT activity with potential clinical interest. For this, we prepared triazolopyrimidine derivatives, through the Biginelli reaction using 3-amino-1,2,4-triazole instead of urea [2], which can be considered catechol bioisosteres with the potential to bind/stabilize the enzyme. To select the compounds with a higher potential to bind COMT, we performed an *in silico* screening using molecular docking (AutoDock Tools) and studied the pharmacokinetics using predictive models (pkCSM and SwissADME). The most relevant molecules were synthesized and their stabilizing properties were evaluated using recombinant human COMT lysates, followed by an MTT cytotoxicity assay in N27 cell lines [3]. Overall, the selected compounds displayed stabilizing effects on COMT activity, and no marked cytotoxicity was observed. To sum up, these findings can be useful for crystallographic studies, thermal stability assays and structure-activity relationship studies.

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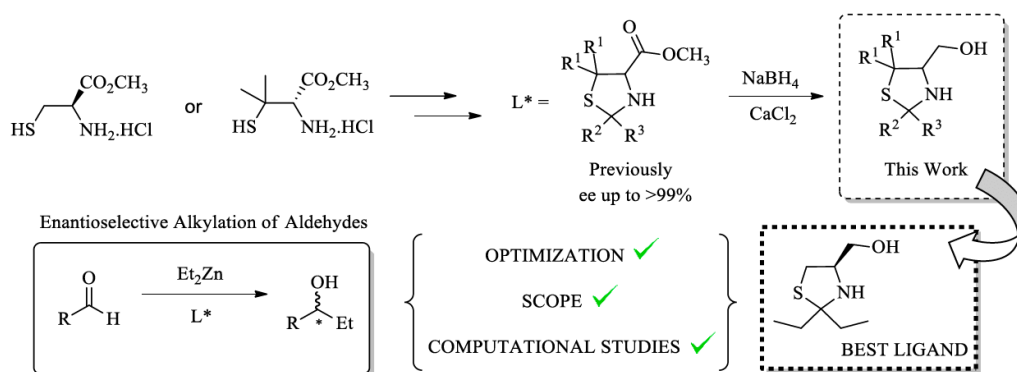
Thiazolidine-Based Amino Alcohols with Opposite Stereochemistry: Catalytic and Computational Analysis of their Behaviour as Ligands in Enantioselective Alkylation Processes

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The addition of alkylzinc species to aldehydes is a well-known strategy in organic chemistry for the obtention of secondary alcohols. The combination of the low reactivity of diethylzinc and a chiral ligand enables the synthesis of these alcohols in a stereoselective manner, creating precursors or even species with important applications in fine and medicinal chemistry.¹

Our recent interest in studying the catalytic properties of chiral thiazolidines has been revealing them as remarkable ligands for the enantioselective ethylation of aldehydes, namely the ones with an ester group linked to the C4 of the heterocyclic ring.² The extensive study of amino alcohol type ligands in this reaction prompted us to modify the thiazolidine core in order to obtain the hydroxymethyl derivatives, Scheme 1. A ligand screening was made, using L-cysteine and D-penicillamine as starting materials, allowing the preparation of thiazolidines with opposite stereochemistry at C4. Surprisingly, some hydroxymethylated L-cysteine derivatives led to better *ee* values than the corresponding esterified thiazolidines, inverting the usually verified tendency. With the best β -amino alcohol thiazolidine excellent conversions and enantioselectivities were obtained at 0 °C, after only 6 hours, and its scope was studied with a wide range of aromatic, heteroaromatic and aliphatic substrates. Resorting to computational calculations at the DFT level of theory, the mechanism of the reaction with this type of ligands was analyzed, in order to rationalize the observed enantioselectivities. The obtained results for the catalytic and computational studies will be disclosed in this communication.



Scheme 1

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Sulfonic acid functionalized silica nanoparticles: Design and Catalytic Application

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The development of new technologies for producing energy and chemicals from biomass, the most abundant and renewable carbon source in the world has become an important area of research in order to fill the gap between energy demand and petroleum availability [1].

Acid catalysis is one of the most important areas of catalysis and has been widely used in many sectors of chemical manufacturing [2]. Acid-catalysis are essential processes in the valorization chain of biomass (or biomass components) for food, fuel and chemical industries. As one of the top bio-based platform molecules, levulinic acid (LA) is a precious intermediate for the synthesis of several valuable chemicals [3,4]. Alkyl levulinates (ALE) also exhibit similar properties to biodiesel including low toxicity, high lubricity, flash point stability and moderate flow properties under low temperature conditions, making them special molecules to be used as cold flow improvers in biodiesel and as oxygenate fuel additives [5].

Furfural, a natural precursor derived from biomass (e.g. catalytic hydration of sugars and the hemicellulosic pentose fractions of biomass such as cornstalks and corncobs oat and peanut husks, and other agricultural surpluses) has been emphasised as an important building block for value added chemicals and versatile fuel additives.[6-8]

In this work silica nanoparticles (SiO₂NPs) were covalently functionalized with aryl-sulfonic acid groups (SO₃H-) through post-grafting methodologies. The chemical and structural characterization of the SO₃H-SiO₂NPs, carried out by elemental analysis (EA), X-ray photoelectron spectroscopy (XPS) and Fourier transform infrared spectroscopy (FTIR), confirmed the success of the organosulfonic functionalization procedures. The produced SO₃H-aryl-SiO₂NPs have demonstrated to be promising catalysts for catalytic esterification of LVA with propanol (with excellent activity and stability > 83.2% yield after 10 cycles, 2h reaction) and aldol condensation reaction of furfural with 3-methylfuran with excellent catalytic activity, stability and reusability for 7 catalytic cycles (without loss of activity) under mild reaction conditions.

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Disclosing the Interaction between CO and Alkylated Ti^{3+} Species: Direct Insight into Ziegler-Natta Catalysis

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Ziegler-Natta catalysts are multicomponent hierarchical systems used in olefin polymerization. Despite the fact that they are in use since middle of 20th century, there are still questions about active sites that has to be answered [1]. In the industry CO is used to quench polymerization reaction when it runs too fast, approaching critical levels for the plant safety [2]. The quenching effect is explained as due to the reversible coordination of CO to the titanium active sites. For this reason, CO quenching has been also used to determine number of active sites by evaluating CO consumption [3]. However, no direct evidence for CO coordination to Ti^{3+} sites and insertion into Ti-R bonds has been ever reported.

In this work CO was employed as a probe molecule at different temperatures to characterize the active sites in model Ziegler-Natta catalyst using FT-IR spectroscopy. For the first time CO coordinated to alkylated Ti^{3+} sites and the Ti-acyl species formed upon the subsequent insertion of CO into the Ti^{3+} -alkyl bond were detected (Figure 1). Moreover, the industrial ethylene polymerization conditions were mimicked by dosing CO was along with ethylene (1:1 molar ratio). The results show that polymerization reaction starts immediately but it stops as soon CO coordinates to Ti^{3+} sites. These results indicate that FT-IR spectroscopy is a powerful tool characterizing the Ti active sites in Ziegler-Natta catalyst, even under working conditions [4].

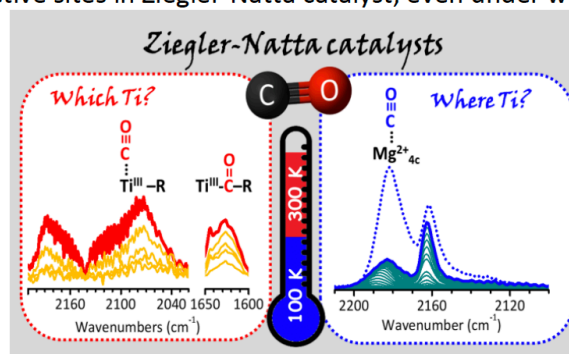


Figure 1 FT-IR spectroscopy of CO adsorbed at 100K and 300K on the $\text{MgCl}_2/\text{TiCl}_4$ catalyst

Acknowledgement: This work is part of DPI research program, Project #813 MULTIPOL

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Metal-organic frameworks with rod secondary building units: knowledge database, exceptional patterns, electrical conductivity and breathing phenomenon

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Metal-organic frameworks (MOFs) with rod secondary building units (SBUs) are a subclass of highly stable MOFs. Rod SBU consists of metal coordination centers, which coordination polyhedra are connected by functional groups of ligands (e.g. carboxylate, hydroxyl) into an one-periodic chain (Fig. 1a). Presence of rod SBUs predetermines both high stability of the frameworks and the anisotropy of their properties along rods and in perpendicular directions. Using the topological methods implemented in ToposPro (<https://topospro.com>) we have completely classified topologies, pore space properties, and flexibility of about 2000 MOFs with rod SBUs. We have found that the number of different directions for rods varies from 1 to 3. We studied in detail the peculiar structures with three different orientations of rods and proposed a route for their designing [1]. An extensive list of correlations between composition and topology of the 2000 MOFs was established and stored in the knowledge database (Fig. 1b) [2].

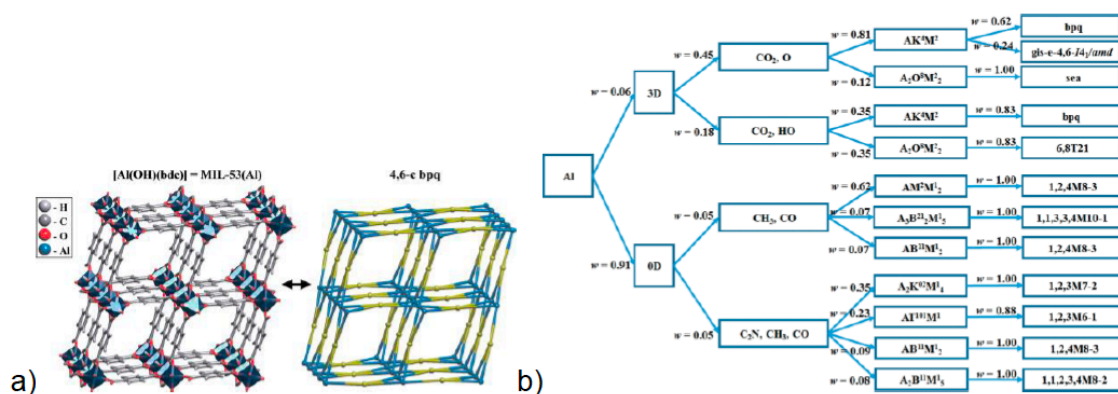


Figure 1. (a) Coordination network (left) and the corresponding underlying net of the **bpq** overall topology in the crystal structure of MIL-53. (b) Frequency pattern tree for aluminum-organic compounds and the descriptors: Network Periodicity → Ligand Composition → Coordination Formula → Overall Topology.

Tuning the excited state of transition metal complexes: toward new and cheaper photocatalysts

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The importance of harnessing the power of light was pointed out by the Italian chemist Giacomo Ciamician in 1912 [1]. He was the first to envision a world relying totally on solar energy, where the chemical industry of the future would have played a crucial role, thanks to the production of new substances without fossil fuel consumption. Nearly 100 years after Ciamician's words, harvesting solar energy and exploiting it for synthetic purposes is still one of the greatest challenges of our days, and it is among the most intriguing and complex fields in chemistry as well. In this regard, transition metal complexes with polypyridyl ligands gained attention in the scientific community for their extraordinary photophysical and photochemical properties.

The first model complex was $\text{Ru}(\text{bpy})_3^{2+}$, where the 2,2'-bipyridine (bpy) ligands offer the suitable electronic structure to induce metal-to-ligand (MLCT) electronic transitions, resulting in efficient absorption of visible light [2]. Moreover, the nature of the metal atom allows for spin-orbit coupling, which changes the excited state spin manifold from singlet to triplet (inter-system crossing). Singlet and triplet states of Ru^{2+} are long lived, granting more chance for a single-electron transfer to occur; triplet states may activate molecular oxygen as well, making photo-driven oxygen addition to organic compounds possible. Thus, second and third row transition metals have been investigated as suitable candidates for photocatalysis: $\text{Ru}(\text{II})$ and $\text{Ir}(\text{III})$ complexes with polypyridyl and cyclometalating ligands were characterised and used as photocatalysts on lab scale organic syntheses [3]. However, one of the main drawbacks for a large scale and a routine use of these complexes is the cost of the metal, as well as the difficulty to retrieve it at the end of the reaction. To lower the cost of the photocatalyst, the use of cheaper first row transition metals is a favourable choice; however, non-radiative deactivation can occur more easily with respect to $\text{Ru}(\text{II})$ and $\text{Ir}(\text{III})$ complexes, resulting in short-lived excited states with consequent reduction of their photocatalytic activity.

We propose several strategies to employ in order to tune the excited state properties and lifetimes of transition metal complexes, focusing mainly on the nature of the ligands and their coordination geometry around the metal. We underline the main characteristics that ligands should feature in order to improve the photophysics on the metal centre, thus making the design of new transition metal catalysts easier and more effective.

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New Cu(I) Complexes of Bis(pyrazol-1-yl)acetate Ligands Functionalized with an NMDA Receptor Antagonist with Cytotoxic Activity

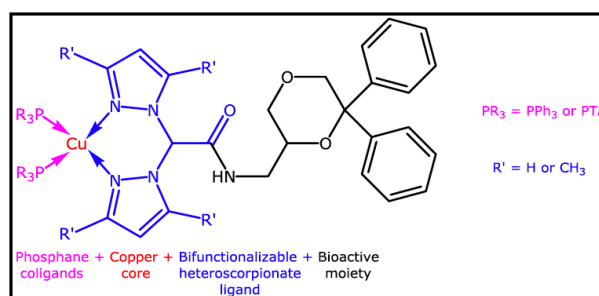
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Among transition metals, copper is one of the most versatile elements to obtain metal-based drugs, due to the wide structural variability, biologically accessible redox properties and bioavailability.¹ In the attempt to find potential Cu-based antitumor agents, our efforts have been recently focused on the design and synthesis of copper compounds of bis(azoly)acetate heteroscorpionate ligands of general formula [(az)₂CH(COOH)], where az = pyrazole, 3,5-dimethylpyrazole and 1,2,4-triazole.^{2,3} Cu(I) compounds have been synthesized employing bis(pyrazol-1-yl)acetic acid (LH), bis(3,5-dimethylpyrazol-1-yl)acetic acid (L²H) and the same ligands conjugated with the NMDA receptor antagonist (6,6-diphenyl-1,4-dioxan-2-yl)methanamine (L^{NMDA} and L^{2NMDA}). The selection of an NMDA antagonist for the coupling with LH and L²H has been suggested by the observation that NMDA receptors are expressed and play a role in several types of cancer models. Phosphanes as coligands (triphenylphosphine, PPh₃, and 1,3,5-triaza-7-phosphaadamantane, PTA) have also been used in order to stabilize the Cu(I) centre in the +1 oxidation state.

All the new complexes have shown a significant antitumor activity on a panel of human tumor cell lines of different histology, with cisplatin-sensitive, cisplatin-resistant or multi-drug-resistant phenotype. Their half maximal inhibitory concentration (IC₅₀) values have been in the low- and sub-micromolar range and, in general, significantly lower than that of cisplatin. Interestingly, the fact that all the complexes have proved to be significantly more active than cisplatin even in three-dimensional (3D) spheroids of H157 and BxPC3 cancer cells has increased the relevance of the *in vitro* results.⁴



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Flowsheet Optimization for the Isolation of Recombinant STEAP1 from *Komagataella pastoris* Bioreactor Cultures

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Keywords: Bioreactor, Characterization, Chromatography, *Komagataella pastoris*, STEAP1

Abstract (2500 characters, with spaces)

The Six-Transmembrane Epithelial Antigen of the Prostate (STEAP) family of proteins share a six-transmembrane domain and intracellular N- and C- termini, although differ in cellular functions and expression patterns [1]. Based on amino-acid sequence, transmembrane topology, and cellular localization, it was suggested that STEAP1 could act as transporter, being involved in cellular communication and in stimulation of cell growth by increasing the levels of ROS [2-5]. Also, STEAP1 seems to contribute to maintaining metal homeostasis, oxidative stress response, cell-cell communication, proliferation, invasion and apoptosis [1, 6]. Considering that no expression is detected in normal cells but it is mainly over-expressed in the cell membrane of prostate cancer (PCa) cells, STEAP1 has been pointed as an attractive biomarker and immunotherapeutic target [1, 6-9]. In fact, several studies have shown that over-expression of STEAP1 enhances cancer cell proliferation and contributes to tumour development and aggressiveness [2, 8, 10, 11]. Although STEAP1 is linked to PCa, the determination of a high-resolution structure of the protein, as well as the mechanisms underlying its function remains elusive. Our goal was to isolate the STEAP1 protein in a single fraction with a high degree of purity. We evaluated the fraction capacity of typical hydrophobic matrices (Octyl, Phenyl and Butyl-Sepharose) on crude lysates obtained from *Komagataella pastoris* X-33 Mut⁺ mini-bioreactor cultures. Since the ionic strength affects the interaction between the hydrophobic domains of STEAP1 and chromatographic matrices, we thoroughly analysed the effect of salt concentration upon protein elution. Interestingly, STEAP1 was fully retained onto Butyl-Sepharose matrix, using only 50 mM (NH₄)₂SO₄ as binding buffer. In less hydrophobic matrices this interaction was partial (Phenyl) or inexistent (Octyl). The Butyl support also provided a selective elution of STEAP1 throughout a linear gradient from 10 mM Tris to H₂O. Both buffers were supplemented with 0.1 % SDS to mimic the protein's native environment. Size exclusion chromatography allowed to obtain a monodisperse sample of STEAP1. In this work, we established a procedure for the purification of recombinant STEAP1 with a considerable purification yield, using a combination of traditional hydrophobic techniques. These results will prompt us to gather a detailed functional and structural characterization of STEAP1.

Acknowledgements

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CO₂ REDUCTION WITH FORMATE DEHYDROGENASE MIMETIC COMPOUNDSM.A. Bento,*^{1,2} Luísa Maia,² P.N. Martinho.¹¹BioISI, Faculdade de Ciências, Universidade de Lisboa, Campo Grande, 1749-016 Lisboa, Portugal; ²LAQV, REQUIMTE, NOVA School of Science and Technology, Campus de Caparica, Portugal; *marcosben31@hotmail.com

Currently, carbon dioxide (CO₂) is one of the greenhouse effect gases that exceeded its balanced limit in Earth's atmosphere. The increasing levels of this gas in our environment, due to an uncontrolled use of fossil fuels, resulted in a climate change that can have irreversible and dramatic effects in our planet. In recent years scientists started investigating new solutions to tackle this problem for example by capturing and converting CO₂ in other chemicals that can have some economical value.[1-2] This conversion can be made using electrochemical and photochemical approaches, like electroreduction and photoreduction by inorganic catalysts, some of them based on natural metalloenzymes.[3] In this work, we report the synthesis and activity of inorganic catalysts inspired on molybdenum-dependent formate dehydrogenases (FDH) enzymes.

FDH catalyzes the reversible oxidation of formate (HCOO⁻) to CO₂ and its active site holds a molybdenum (Mo) atom coordinated by the *cis*-dithiolene group of two pyranopterin cofactor molecules and a sulfido group. (Figure 1) [4] Our strategy to mimic the FDH active site is the preparation of molybdenum compounds with *cis*-dithiolene groups. The ability of these complexes to convert CO₂ is also tested.

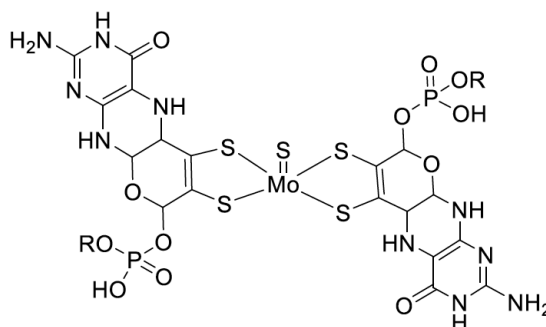


Figure 1: Molybdenum center of formate dehydrogenase active site; R=guanosine monophosphate.

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Acknowledgments

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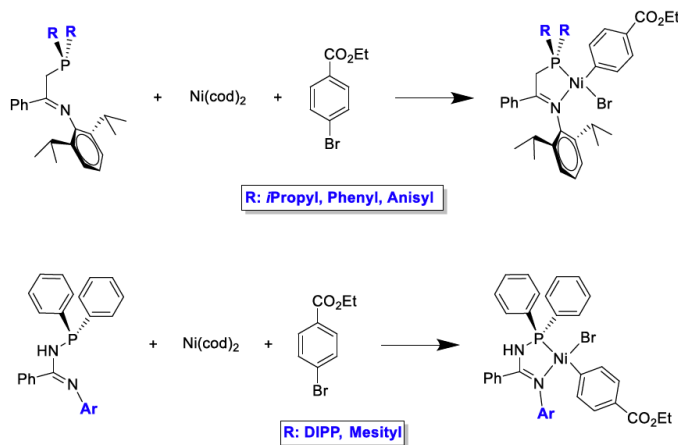
The Nickel-Catalyzed Heck Reaction: Studies on the Oxidative Addition Reaction using Hybrid Phosphine-Imine Ligands.

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Palladium compounds are extremely efficient catalysts for the Heck reaction, one of the most widely used tools for selective C-C bond.¹ However, in recent years there is a growing interest in replacing costly noble metal catalysts for more abundant first-row transition elements. Nickel is the most obvious replacement for Palladium in the Heck reaction, since both elements share many similar chemical features that are critical for the process.² Furthermore, Ni can activate certain substrates (e. g., unreactive aryl sulfonates or chlorides) much more readily than Pd, which suggests that Ni Heck catalysts could represent much more than a cheaper replacement for Pd. In spite of this, very few examples of Ni-catalyzed Heck reactions have been reported. The reasons behind the apparently lower catalytic capacity of Ni complexes in this specific reaction are poorly understood.³

This capacity of Ni to activate challenging substrates encourage us to develop some studies about the oxidative addition reaction with this metal. The key tools so as to accomplish this aim are the use of hybrid iminophosphine ligands. These Ni complexes stabilized by iminophosphine ligands have the ability to undergo both migratory insertion of olefins and β -hydride elimination. Additionally, we recently reported their prowess to perform oxidative addition reactions of substrates of type 4-haloacetophenone, affording isolable complexes.⁴ Thus, we tried to go further investigating the oxidative addition reaction of ethyl 4-bromobenzoate to a source of Ni(0) using iminophosphine ligands as stabilizing agents.

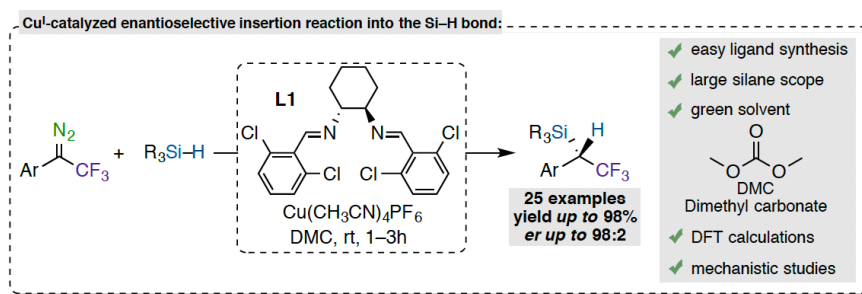


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Asymmetric Cu^I-Catalyzed Insertion Reaction of CF₃-Diazo Compounds into Si–H Bonds and Tandem Desilylative Defluorination

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The asymmetric Cu-catalyzed insertion reaction of CF₃-diazo compounds into the silicon–hydrogen bond will be presented.¹ The use of CF₃-diazo compounds in asymmetric insertion reactions remains underdeveloped. Our aim was to develop a cost-effective catalytic system, based on a copper salt and a chiral ligand to efficiently catalyze the Si–H insertion reaction under mild conditions in dimethyl carbonate as the solvent. This reaction represents a major step in many structures leading to natural compounds, biologically active molecules, and drugs. The optimization of this transformation will be detailed, followed by the scope of the insertion reaction with a wide range of silanes. Excellent yields have been obtained, together with high enantioselectivities for 25 chiral organosilanes. In order to understand the mechanism and the chiral induction, a detailed study has been performed. Isotopic studies, Hammett correlations, scrambling experiments, and DFT studies led us to propose a mechanism for this insertion reaction. Derivatizations of organosilanes to increase their potential in synthetic organic chemistry will also be detailed.



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Recent advances in Capillary Ion Chromatography (CIC) for food safety analytical controls

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Ion Chromatography has almost substituted classical methods for the determination of ionic and ionizable compounds, not only in environmental applications, but also in food and drugs safety fields. Moreover, the use of capillaries provide high sensitivity and selectivity and minimize eluent consumption, making CIC a simple, fast and “Green” technique [1].

For official food controls purpose, our laboratory developed and validated, in agreement with decision No. 657/2002/EC and EU Regulation No. 1333/2008, different methods for the determination of food additives, by using CIC. In particular, nitrates and nitrites were determined in several matrices (meat, fish, cheese, vegetables, fruits, feed, etc.), with good validation parameters, such as recovery (ranging from 93% to 105%), precision (CV% 2.66% and 3.40%), linearity ($R^2 > 0.999$), detection limits in matrix (1.2 and 0.68 mg/L) [2,3]. Another analytical procedure was developed and validated for the determination of sulfite, a well-known food allergen, in wine, modifying the distillation-titration official method, substituting the final titration with CIC determination. The values obtained for precision (1.5%), recovery percentage (97.8%) and measurement uncertainty (11.6%) resulted satisfactory. In beverage and liquid dietary supplements, a preliminary method for the determination of benzoates and sorbates was developed with good results in terms of selectivity (see fig1). Other possible future applications include polyphosphates, polyols, acidity regulators, flavour enhancers, gelling and firming agents.

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CIC for determination of food additives

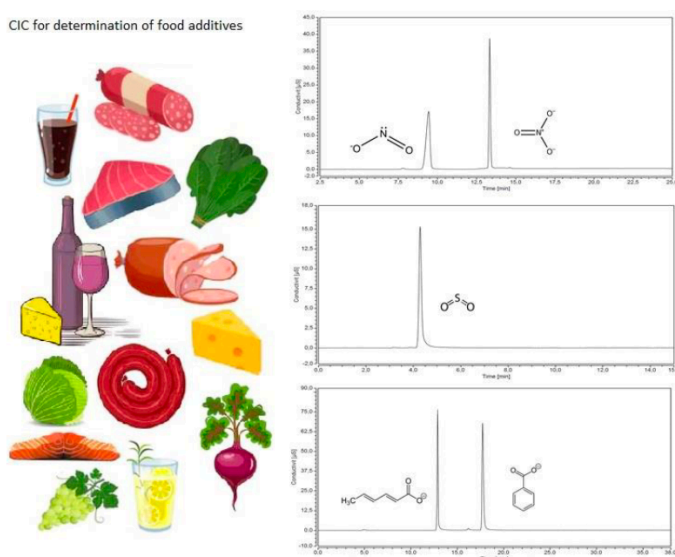


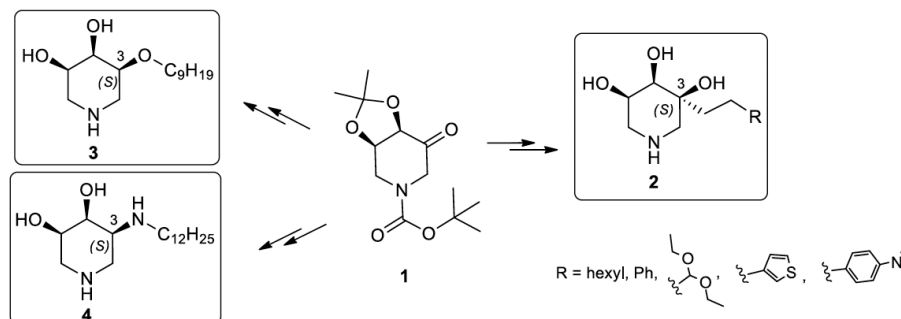
Fig.1 Chromatograms of standard samples for (1) nitrite and nitrate (2) sulfur dioxide (analyzed as sulfate) and (3) sorbate and benzoate

Highly stereoselective synthesis of alkylated “all cis” trihydroxypiperidines and their congeners from a carbohydrate derived ketone

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Alkylated trihydroxypiperidines are known to be potent inhibitors of lysosomal enzymes and potential pharmacological chaperones for the treatment of Gaucher Disease (GD).^[1] The glycomimetic moiety ensures affinity towards the enzyme while the alkyl chain may improve cell permeability. In particular, remarkable chaperoning activity for β -glucocerebrosidase, the enzyme responsible for GD, was recently found for 2-alkyl trihydroxypiperidines mimicking the D-glucose configuration and bearing alkyl chains ranging from 8 to 12 carbon atoms.^[2] This project aims to access “all cis” trihydroxypiperidines and congeners substituted at C-3 (Scheme 1), which mimic the D-galactose configuration, through functionalization of ketone **1** derived from inexpensive D-mannose^[3] by employing three different synthetic strategies. i) The addition of lithium acetylides^[4] to **1**, followed by the reduction of triple bond and deprotection of Boc and acetonide groups, allowed to access C-3 diversely functionalized compounds **2** with high yield and complete diastereoselectivity towards the (*S*)-configured newly formed stereocenter. ii) The Williamson reaction performed on the 3-(*S*)-configured alcohol in turn obtained by diastereoselective reduction of ketone **1**,^[3] provided ether **3**. iii) A reductive amination reaction on **1** with dodecyl amine afforded, after deprotection, the amino azasugar **4** with complete diastereoselectivity towards the (*S*)-configured newly formed stereocenter.^[3] All the synthesized azasugars were screened as inhibitors for lysosomal enzymes and the most promising inhibitors will be tested as pharmacological chaperones (PCs) for LSD.



Scheme 1. Strategies to afford “all cis” trihydroxypiperidines and congeners substituted at C-3.

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Scalable TiO₂-based nanoparticles synthesis approach

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TiO₂ is the most investigated semiconductor for clean-up application; due its high photoactivity, high chemical and photochemical stability, high oxidative efficiency and low production cost. In particular, nanosized TiO₂ demonstrated improved performances with respect to its bulk counterpart thanks to its extremely high surface-to-volume ratio and the size-dependent band gap of nanosized semiconductors allows tuning the red-ox potentials to achieve selective photochemical reactions. There are many strategies to synthesize TiO₂ NPs[1], the final properties of the synthesized NPs depends on the synthetic technique, nature of the precursors and the reaction conditions [2-4]. In particular, the photoactivity of TiO₂ NPs is strongly dependent on its crystalline phase. Indeed, the anatase phase has been generally regarded as the most photoactive crystalline phase of TiO₂. Most of the investigated reported synthetic approaches need high reaction temperatures and/or single or multiple post-synthesis calcination steps at a temperatures higher than 300° C to promote crystallization in anatase phase.[5] [6, 7] in this work a new scalable and low costs synthetic approach for TiO₂ nanoparticles is reported. In particular is used a precipitation method starting from TiOSO₄ react with a base NH₄HCO₃. After the purification, the product was thermally treated in oven in the range between 2 and 24 h. Interestingly a mild thermal treatment promotes a progressive transition of the pristine brookite phase toward anatase crystalline structure, as a function of the duration of the thermal. Structural properties, such as the specific surface area and nanoparticles size are also affected by the heat treatment time. Consequently, the photocatalytic performance of TiO₂ nanostructures, evaluated by the degradation of the model molecule, Methylene Blue (MB), showing a progressive increase for the photocatalyst obtained after prolonged heat treatment.[8]

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Increasing sustainability in organic solar cells fabrication through the synthesis of polymer-based water-processable blend nanoparticles

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Organic photovoltaic (OPV) technology has been intensively investigated over the last decades as an intriguing alternative for electrical power generation. Even if recently the power conversion efficiencies have been increased, its market penetration is still limited by some drawbacks making expensive their industrial production, as in particular the use of huge amount of halogenated and aromatic solvents, which are toxic and harmful (1,2). Three main strategies have been developed in order to increase the sustainability of the active layer production processes: (i) using other organic solvents that are less harmful for human life and environment; (ii) functionalization of donor and acceptor structure with polar groups and so the use of less hazardous solvents as methanol; (iii) production of polymer-based water-processable nanoparticles (WPNPs). We have focused our attention on this latter strategy because, in addition to reduce halogenated wastes, it allows the control of the final film morphology and the optimization of the interpenetrating electron donor/acceptor networks ensuring good performances in the final device (3,4,5). Particularly, our research group developed the preparation of polymer-based WPNPs using amphiphilic rod-coil block copolymers (ABCPs), bearing a rigid block and a hydrophilic flexible segment. Thanks to these features, ABCPs are able to self-assemble through miniemulsion method generating organized nanostructures under specific conditions. The hydrophilic flexible block works as surfactant and assures the colloidal suspension stability interacting with aqueous medium (6,7). Also, it interacts with the electron-acceptor material (n-type), leading to the formation of pre-aggregated domains, suitable to achieve the charge percolation into the final device (8,9). We synthesized a well-known low band-gap polymer PTB7, in order to connect it to a tailored segment of P4VP producing a new ABCP, the PTB7-*b*-P4VP. We tested its capability to self-assemble in aqueous medium to produce nanoparticles, both neat and in blend with fullerene derivatives. The obtained WPNPs were characterized by dynamic light scattering (DLS) and UV-Vis spectroscopy, deposited in films topologically characterized by atomic force microscopy (AFM) to confirm the compactness of the obtained active layer. Now we will employ them as active layers for the fabrication of sustainable OPV devices.

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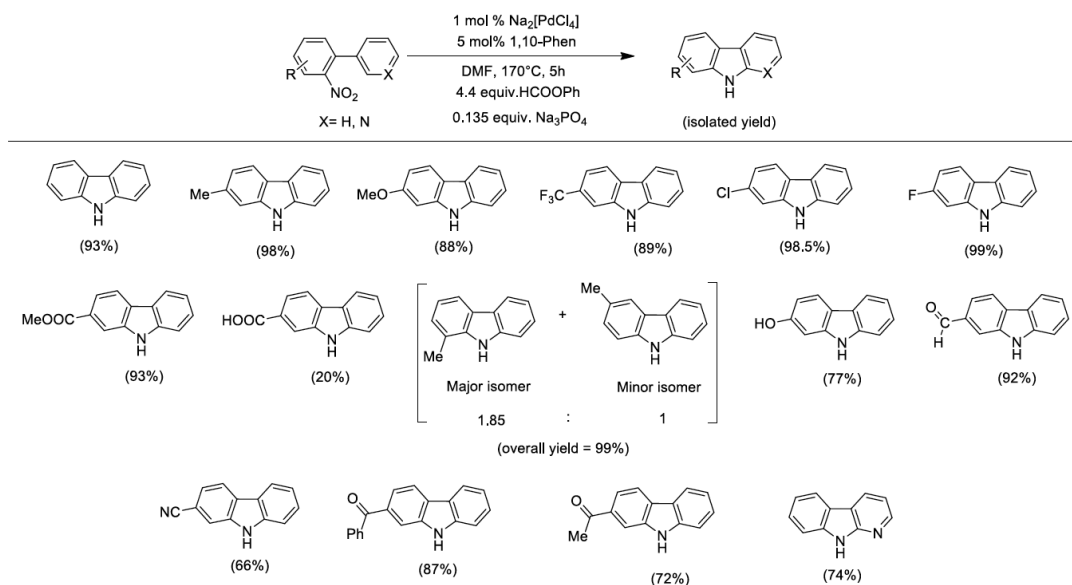
Pd/Phen Catalyzed Synthesis of Carbazoles by Reductive cyclization of 2-Nitrobiaryls: Use of Formate Esters as CO Surrogates

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Palladium complexes with phenanthroline ligands are so far the most effective catalysts for the reductive cyclization of nitroarenes by carbon monoxide to yield a variety of N-heterocyclic compounds.^[1] Despite the high efficiency of many of these reactions, they have not become of widespread use. This is mainly attributed to the need for pressurized CO (requiring specific safety measures). In the aim of turning this kind of reaction into a “general tool” for the synthetic chemist, we developed a procedure based on the use of phenyl formate as an *in situ* source of CO. The reaction can be performed in a glass pressure tube, a cheap equipment accessible to every laboratory. Our previous work was mainly focused on the synthesis of indoles^[2] and oxazines.^[3] However, the application of the previously optimized procedure to the reductive cyclization of 2-nitrobiphenyls to produce carbazoles afforded only moderate yields even under harsher conditions and higher catalyst loadings. Here we report an improved catalytic system and its application to the synthesis of several carbazoles (Scheme 1). In addition, a mechanistic study is in progress to find out whether the metal plays a role in the cyclization step or its role is confined only to deoxygenation of 2-nitrobiphenyl.



Scheme 1. Scope of the reductive cyclization of 2-nitrobiaryls to carbazoles using HCOOPh as CO source.

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Calorimetry as a Tool to Investigate Polymorphism in Organic Compounds

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Polymorphism is a common phenomenon in organic compounds, which consists in the ability of a molecule to crystallize in different packing arrangements. The structural differences between polymorphs are often accompanied by significant changes in physical and chemical properties (e.g. solubility, dissolution rate, fusion and decomposition temperature, etc.). The control of polymorphism is, therefore, a key aspect in the production of materials, such as active pharmaceutical ingredients (APIs), that need to be obtained with highly reproducible properties. A critical aspect within this scope is the assessment of the relative stability of the various polymorphic forms that may coexist under a given set of ambient conditions. A good indicator of that stability hierarchy is the standard molar enthalpy of transition between forms, $\Delta_{\text{trs}}H_{\text{m}}^{\circ}$, which reflects their difference in lattice energy, and can be experimentally determined from enthalpy of solution measurements.¹ Quite often, however, the amount of each polymorph available during development stages is insufficient for the application of common solution calorimetry techniques that typically require samples of more than 100 mg per experiment.¹

The present work describes a novel electrically calibrated solution calorimetry cell (Fig. 1a), that requires samples of only 1-10 mg, and was specifically designed for a Thermal Activity Monitor (TAM) calorimeter (Fig. 1b). The accuracy and precision of the system was tested, based on the measurement of the standard molar enthalpy of solution of KCl in water. The apparatus was then used to determine the standard molar enthalpy of transition between the two known polymorphs of 4'-hydroxyacetophenone (HAP), at 298.15 K, from measurements of their standard molar enthalpies of solution in DMSO. The obtained result was in excellent agreement with a previously reported value measured in ethanol using ~7 times larger amounts of sample and solvent. The fact that the two HAP polymorphs are easily prepared and such good agreement was observed between results from two considerably different calorimetric techniques and solvents, suggests that HAP can be proposed as benchmark system for the validation of solution calorimetry measurements or force field predictions on the relative enthalpic stability of organic polymorphs.



(a)



(b)

Fig. 1 (a) Calorimetric cell developed in this work. (b) Thermal Activity Monitor (TAM) instrument used in the experiments.

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Size, shape and phase modulation of plasmonic copper sulphide nanocrystals

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Abstract

Self-doped copper sulphide Cu_{2-x}S nanocrystals (NCs) are semiconductor near infrared absorbing (NIR) plasmonic materials explored in a wide variety of applications such as catalysis, energy conversion, sensing and biomedicine. Due to their stoichiometry-, size- and shape- dependent properties, the NCs design is crucial to yield high performances devices. Indeed hexagonal-faceted NC structure has been used as solar cell electrodes, $\text{Cu}_{1.94}\text{S}$ NCs as cathodes in all-vanadium redox flow batteries, $\text{Cu}_{1.8}\text{S}$ nanospheres as photoactive agents in photodynamic (PDT) and/or photothermal (PTT) therapy, CuS nanotubes as electrochemical sensors and hollow CuS as chemical storage and drug delivery vectors. Among the synthetic approach, colloidal synthesis by hot-injection offers a toolbox of macroscopic thermodynamic parameters that together with microscopic chemical considerations such as precursor reactivity, ligand binding strengths, valence of metal precursors, can provide a fine control of the NC features. However, within the wide range of Cu_{2-x}S NC preparatory approaches available, there is still the lack of *a priori* rationalization of the impact of the synthetic procedure in defining the characteristics of NC. The aim of my work is to fill this gap. By means of systematic investigation of Cu_{2-x}S NCs, prepared under different experimental conditions, I want to outline how the combination of precursors/ligands, their molar ratios shape the final geometry, size, composition and thus crystalline structure and optical properties. Hard-Soft-Acid-Base theory allows to qualitatively predicting the intermediate complex/monomer stability and ligands binding to NC surface, for the kinetic and thermodynamic control of nucleation and growth, with electron affinity of ligand coordinating groups also affecting the plasmonic properties. This study wants to offer through an in-depth and generalized comprehension of the synthetic mechanism, practical guideline for controlling Cu_{2-x}S NC size, shape, phase and plasmonic properties for future applications.

Mechanistic Studies on the Photocatalytic Reduction of CO₂ using a Dinuclear Xanthene-Bridged Rhenium(I) Complex

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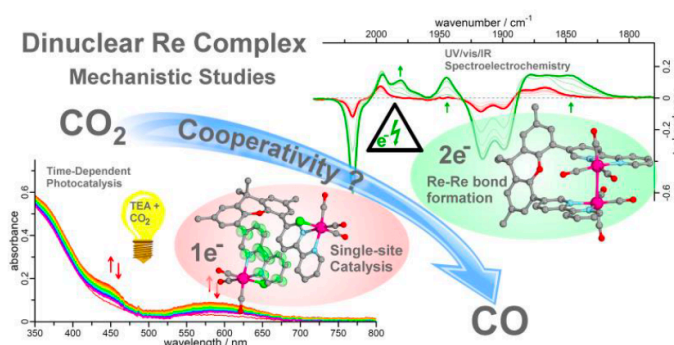
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The reduction of CO₂, one of the most prominent anthropogenic greenhouse gases, into usable C1 building blocks by means of photocatalysis is a very appealing process. In the early 1980's Lehn *et al.* reported for the first time on the successful reduction of CO₂ to CO using (bpy)Re(CO)₃Cl (bpy = 2,2'-bipyridine).^[1] Since then, many mechanistic studies have been pursued.^[2]

We recently discovered an unexpected wavelength dependency of this well-known catalyst, leading to new mechanistic insights: irradiation with wavelengths >450 nm results in an increased catalytic activity during the photocatalytic CO₂ reduction – although the complex hardly absorbs energy in this spectral region. As a result, an alternative reaction pathway involving a dimeric Re-Re species is presented, suggesting the beneficial effect of two closely oriented rhenium centers.^[3]

Consequently, a new homobimetallic xanthene-bridged rhenium(I) complex was synthesized and thoroughly characterized. Time-dependent catalytic and spectroscopic experiments as well as UV/vis/IR spectroelectrochemical measurements and chemical reduction experiments accompanied by (TD-)DFT calculations were performed to shed light on the reactivity towards CO₂, with a focus on the elucidation of cooperative reaction pathways.^[4]

These insights will not only improve the understanding of this class of catalyst, but also guides further design strategies of dinuclear metal complexes for the activation of small molecules.



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MW-assisted synthesis of zirconia: is it a valuable way to obtain a working catalyst?

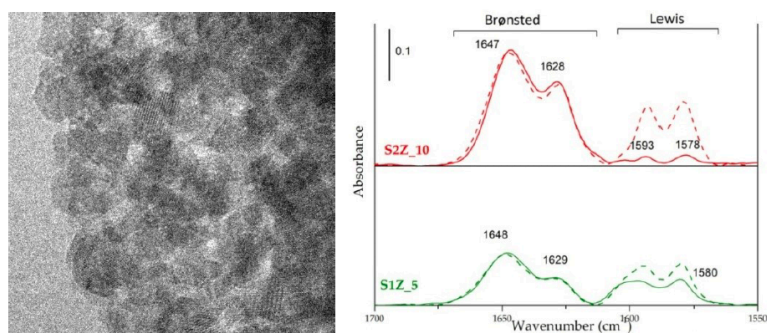
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Zirconia (ZrO_2) has found application in various technological fields, because of its interesting physical and chemical properties. In particular, in heterogeneous catalysis ZrO_2 has been used in many reactions as both metal catalysts' support and pure catalyst. [1]

Microwave (MW)-assisted processing can help to overcome disadvantages of common synthetic techniques by reducing reaction time, improving yield and leading the preparation of nanoparticles with an homogenous distribution of both shape and dimensions. [2] Here, we proposed a new and quick procedure to obtain zirconia: MW-assisted sol-gel synthesis, followed by MW-assisted calcination. The product obtained is almost totally tetragonal ZrO_2 , as confirmed by different techniques (PXRD, HR-TEM, Raman and FT-IR spectroscopies).

Sulfated zirconia (SZ) and Nickel-promoted zirconia have been obtained using the same synthetic procedure. Surface functionality and acidity of these materials have been investigated using CO and 2,6-dimethylpyridine (2,6-DMP) as probe molecules. [3,4]



On the left HR-TEM image of $t\text{-ZrO}_2$, on the right FT-IR spectra of adsorption/desorption of 2,6-DMP on different SZ samples.

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PYRIDINE-2,6-BIS(1H-1,2,3-TRIAZOL-4-YL): A SELECTIVE CHELATING UNIT FOR MINOR ACTINIDE EXTRACTION FROM RADIOACTIVE WASTES

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One of the most important scientific, and social challenges that humanity faces today is to manage the huge amounts of nuclear wastes accumulated in the last 70 years and to make, nuclear energy as sustainable as possible.¹ Currently, the PUREX (Plutonium and URanium EXtraction) process is used worldwide to recover Pu and U from the spent fuel while the remainder of the waste contains the minor actinides (MAs) that account for most of the long-term radiotoxicity.² Interestingly the recovery of the MAs and their separation from Lanthanides would allow to re-use them in novel nuclear fuels thus closing the Nuclear Fuel Cycle. Soft-donor ligands are known to interact more strongly with trivalent actinide ions, An (III), rather than with trivalent lanthanide ions, Ln (III). In the last few years, we have been exploring different chelating units based on nitrogen ligands and found that the “clicked” pyridine-bis-triazole unit is rather effective and selective in An/Ln extraction from simulated nuclear wastes. We performed the synthesis of both hydrophilic and lipophilic ligands based on pyridine-bis-triazole unit (Fig. 1). They both show ability to effectively and selectively separate An from Ln even at very high nitric acid concentration and in the presence of other fission products. In parallel we also seek for the synthesis and the study of the possible degradation products identified upon radiolysis of the ligands. In this way we will be able to test the efficiency and feasibility of the entire separation process.

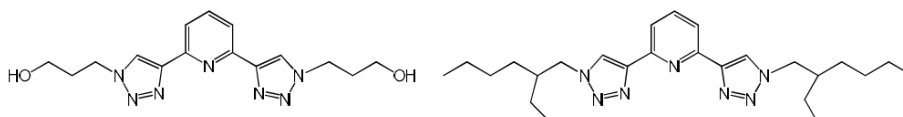


Figure 1. The hydrophilic (left) and lipophilic (right) versions of the pyridine-bis-triazole ligands studied

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An application of computational chemistry methods to study interactions of psychoactive compounds with suitable 5-HT receptors

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Computational chemistry approaches were applied to investigate physico-chemical properties of seven selected psychoactive compounds: DMT, MDMA, LSD, PSILOCYBIN, Mescaline, Fluoxetine and Sertraline. The simulations were performed on basis of Density Functional Theory [1]. The Becke three-parameter hybrid-exchange functional [2] and 6-311+G(d,p) [3] basis set were applied. The metric and electronic structure description was further used to prepare models for docking studies. The investigated compounds were docked to three serotonin receptors: 5-HT_{1B}, 5-HT_{2A} and 5-HT_{2B} [4] and the analysis of the ligand-receptor interactions was performed. The obtained theoretical results were compared with experimental data available.

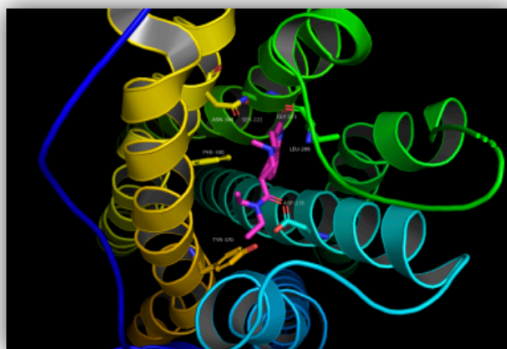


Figure: The LSD molecule docked to the 5-HT_{1B} receptor.

Acknowledgments

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Microsolvation of histidine – an investigation of intermolecular interactions using AIM and SAPT approaches

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Abstract

Histidine is an interesting amino acid because of its rich tautomeric properties [1]. The main aim of our research was an investigation of histidine in its three protonation states (HIP, HIE and HID), microsolvated with one to six water molecules [2]. The simulations were performed in the gas phase and with solvent reaction field (PCM model and water used as a solvent) within the density functional theory (DFT) framework [3,4]. The metric parameters analysis reveals the presence of intra- and intermolecular hydrogen bonds in the studied complexes. The Atoms in Molecules (AIM) [5] theory was employed to determine the impact of solvation on the charge flow within the histidine. The Symmetry-Adapted Perturbation Theory (SAPT) [6] interaction energy analysis was applied to examine the stability of the microsolvation clusters.

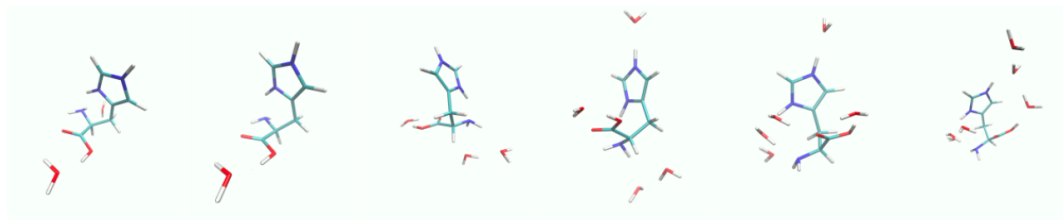


Figure. Histidine HIP form microsolvation models (with 1-6 water molecules).

Acknowledgments

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Understanding the hydration process of gypsum plaster using a combined approach of diffraction and phase contrast tomography:

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Gypsum plaster is developed industrially from calcium sulfate hemihydrate ($\text{CaSO}_4 \cdot 0.5 \text{H}_2\text{O}$) with a hydration process. Gypsum plaster is also called plaster of Paris and is one of the most widely used hydraulic binder in the construction industry. The reason why studying the dynamic of plaster hydration is that it is related to the properties and the structure of the final material, the one that is used in constructions. The state of the art in this field is quite arid and a complete understanding of the precise kinetic steps and spatial relationship between phases during the hydration process is still missing.

Some of the precedent works have investigated the hydration process of calcium sulfate hemihydrate using nuclear magnetic resonance (NMR), measurement of ultrasonic activity and also 3-Dimensional submicrometric simulations [1]. Performing *in-situ* experiments with a combined approach of powder diffraction and phase contrast tomography aims, for the first time, at the acquisition of a complete dataset able to give both crystallographic and spatial information. Powder diffraction reveals the phases that dominate the hydration process, and phase contrast tomography enables a 3-Dimensional reconstruction of the sample showing the spatial and volumetric relationship present.

A multi-technical approach appears indeed to be appropriate to provide quantitative and morphological insights about this system. Moreover, this first-of-a-kind experiment in the field of constructions shows a very promising tool that contributes to answer the long-standing question about the reactivity of hydraulic binders.

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Encapsulation of a Porous Organic Cage into the Pores of a Metal–Organic Framework for Enhanced CO₂ Separation

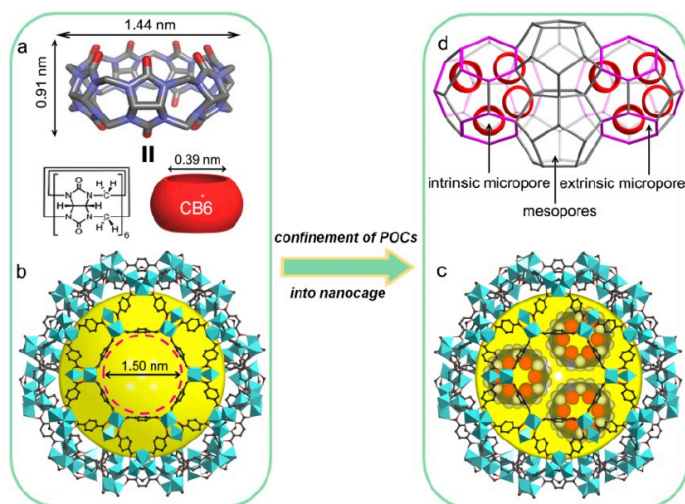
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We present a facile approach to encapsulate functional porous organic cages (POCs) into a MOF by an incipient-wetness impregnation method. Porous cucurbit[6]uril (CB6) cages with high CO₂ affinity were successfully encapsulated into the nanospace of Cr-based MIL-101 (Scheme 1). The encapsulated CB6 amount is controllable. Importantly, as the CB6 molecule with intrinsic micropores is smaller than the inner mesopores of MIL-101, more affinity sites for CO₂ are created in the resulting CB6@MIL-101 composites, leading to enhanced CO₂ adsorption and CO₂/N₂, CO₂/CH₄ separation performance at 1 bar. This POC@MOF encapsulation strategy provides a facile route to achieve POC-based materials for various potential applications.^[1]



Scheme 1: Illustration of the host-in-host concept for creating functional hybrid materials by the incorporation of cucurbit[6]uril (CB6) into Cr-based MIL-101. Schematic views of a) porous CB6 molecule; b) mesoporous cage with hexagonal windows in MIL-101; c) CB6 in the larger cage of MIL-101; d) CB6 being doped into the larger cages in MIL-101 while leaving the smaller cages empty. Hexagonal windows in pink colour.

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New insights into the products of the reaction of dirhodium tetraacetate with proteins: unusual structural features in the adduct with lysozyme

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The interaction of the cytotoxic¹ paddlewheel dirhodium complex $[\text{Rh}_2(\mu\text{-O}_2\text{CCH}_3)_4]$ with the model protein hen egg white lysozyme has been investigated. X-ray structures indicate that under the investigated experimental conditions $[\text{Rh}_2(\mu\text{-O}_2\text{CCH}_3)_4]$ in part breaks down and extensively reacts with the protein. A Rh center coordinates the imidazole ring of the side chain of His15. Dimeric Rh-Rh units with Rh-Rh distances equal to 2.3 and 3.3 Å are bound to the side chain of Asp18 and to the C-terminal carboxylate, respectively. These data, which are supported by replicated structural determinations,^{2,3} shed light on the reactivity of dirhodium tetracarboxylates with proteins, providing useful information for the design of new Rh-containing biomaterials⁴ with an array of potential applications ranging from catalysis to medicinal chemistry.

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The world of protein-ligand interactions – Computational, biophysical and structural characterization of vanadium-based complexes

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Keywords: Vanadium and medicinal chemistry, Human Serum Transferrin (HTF), Hen Egg White Lysozyme (HEWL), X-ray crystallography, Small Angle X-ray Scattering (SAXS), Computational methods

Vanadium (V) is an important element with several known biological functions.¹ The therapeutic use of inorganic and organic vanadium-based ligands has been also suggested as insulin-enhancer, anti-cancer and anti-parasitic agents as widely described in the literature. The coordinated ligands are particularly important as these can improve the absorption and possibly the transport and uptake of vanadium to the cells reducing the dose necessary for producing the same effect.^{2,3,4,5}

The first X-ray protein-V^{IV} structure was obtained by soaking a vanadium picolinate complex with HEWL. The 1.28 Å resolution structure (beamline ID29, ESRF) shows a V^{IV}O(pic)₂ adduct covalently bound to the COO⁻ moiety of the side chain of the Asp52 residue (Figure 1). A relatively long V(IV)=O bond distance (~1.82 Å) was obtained (theoretical value: ~1.60 Å). However, EPR and DFT experiments confirm the presence of V(IV). We propose that the long V^{IV}=O bond was due to the exposure of the crystal to the intense X-ray beam which induce a progressive reduction of V(IV) to V(III). This was confirmed by analysis of several sub-sets of the collected data.³

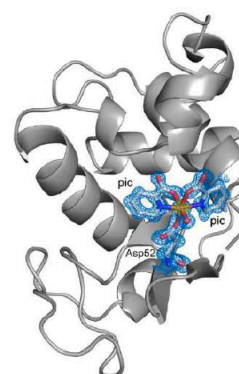


Figure 1 – Overall representation of the HEWL-V^{IV}O(pic)₂ structure.

Next, we extended our investigations to other proteins and V-based complexes. HTF, a metal ion blood carrier, was used to confirm the protein-ligand binding by SAXS. Three datasets – native apoHTF, apoHTF-V^{IV}OSO₄ and apoHTF-NaV^{VO}₃ – were collected at beamline BM29 (ESRF) revealing that the binding of both compounds – particularly vanadate(V) – induce a partial closing of apo-HTF even if less pronounced than the one observed in the holo-HTF sample.⁵

To further characterize such interactions, a 1.34 Å resolution HEWL-V^{IV}OSO₄ soaked structure was obtained at beamline BM30A (ESRF). The structure reveals the presence of three metal adducts next to Asp52, Asp87 and Leu129 with different occupancies and geometries. Importantly, the detected V^{IV}=O bond distances suggest the presence of V^{IV} species and, currently, theoretical calculations are being performed in order to confirm it.⁶

In conclusion, X-ray crystallography is a powerful technique to gain valuable insights on protein-ligand interactions at the atomic level. Properly complemented by other computational and biophysical methods, such insights could be relevant to accurately evaluate the pharmacokinetics of the V-based compounds contributing for their potential application as safe drugs.

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Luminescent carbon dots: insights on an environmentally friendly facile synthetic approach

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Carbon-based luminescent nanoparticles, namely carbon dots (CDs), are emerging as greener, low cost and potentially more biocompatible alternatives to inorganic semiconductor quantum dots in a broad range of applications, such as optoelectronic devices, solar cells, photocatalytic devices and sensors [1]. Here, a cost effective bottom-up synthetic approach is employed, based on a suitable amphiphilic molecule as carbon precursor, i.e. cetylpyridinium chloride (CPC), to prepare CDs upon treatment of CPC with concentrated NaOH solutions under mild reaction conditions. The investigated method allows obtaining, in a one-pot procedure, both water-dispersible CDs (W-CDs) and oil-dispersible CDs (O-CDs), emitting in the green-yellow region of the visible spectrum [2], being the O-CDs characterized by a higher photoluminescence quantum-yield (PLQY). The study provides original insights on the chemical reactions involved in the process of carbonization of CPC, finally proposing a reliable mechanism that accounts for the formation of the O-CDs in an aqueous system. Moreover, the formation of blue-emitting molecular fluorophores during the reaction is highlighted, and their contribution to the overall PL emission of the O-CDs is evaluated. The ability to discriminate the contributions of the different species, allows to properly single out the O-CDs emission. Moreover, the preparative conditions have been investigated in order to further increase the efficiency of the synthetic approach, towards a fast preparation of brightly green-emitting CDs, dispersible in various common organic solvents. In particular, a mild heating of the reaction mixture, at 70°C, has been demonstrated able to dramatically decrease the very long reaction time (i.e. from tens of hours to days, depending on the concentration of the added NaOH solution) required to obtain the O-CDs at room temperature, allowing to obtaining O-CDs in only 20 min, preserving their morphological and optical properties.

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Cu-As-(Sb, Ni) systems: Determination of phase diagrams

The project will focus on the physico-chemical properties of copper (Cu) mined from sulfosalt minerals, such as tetrahedrite, tennantite, and enargite. These ores are characterised by high concentrations of arsenic (As), nickel (Ni), and antimony (Sb). Despite being the earliest produced alloy, the characteristics of Cu-As-(Ni, Sb) based alloys are still poorly understood, and no phase diagrams of such ternary alloys exist; consequently, material characteristics of such alloys are widely unknown. The project will take advantage of the infrastructures, experience and synergies at the Università degli Studi di Genova (UNIGE) to achieve the following objectives:

- 1) *Build phase diagrams:*
 - a) investigate the phases of each alloy and identify yet unknown phases with desirable properties;
 - b) understand initial phase formation, stability, and changes in alloys over the passage of time at different temperatures;
 - c) explain and predict specific material behaviour during thermomechanical treatment.
 - d) understand the effects of Ni and Sb addition on pristine/parent Cu-As alloys.
- 2) *Create a base for new applications and less pollution:* Cu-As based alloys have superior ductility and corrosion resistance than pure copper, and other copper alloys. The project will provide the data for Cu-As-(Ni, Sb) alloys to
 - a) enable new, exciting applications in material engineering;
 - b) find modern-day uses for them, and, consequently;
 - c) reduce processing cost and pollution since As, Sb, Ni would not need to be removed from mined sulfosalt minerals;
- 3) *Provide the data base for urgent research questions in prehistory:* Cu-As-(Ni, Sb) alloys are the oldest alloys used. As basic data such as phase diagrams are still missing, the alloys' behaviour and properties are still poorly understood. The project will provide the data needed to
 - a) Assess the earliest metal technologies in prehistory;
 - b) Explain the adaption, recycling and final disregard of Cu-As alloys c. 2000 BCE.

The project applies an interdisciplinary approach by combining X-ray diffraction (XRD), differential thermal analysis (DTA), differential scanning calorimetry (DSC), metallographic and chemical analysis (via SEM-EDXS and optical microscopy) of Cu-As alloys for building phase diagrams. Reference alloys of Cu-As and low percentages of 1-5 wt.% of metals and metalloids such as Ni or Sb, will be prepared and their phase transitory properties evaluated. Focus will be placed on the copper rich corner of the Cu-As-(Ni, Sb) ternaries systems. Since As is highly toxic and carcinogenic, appropriate protection and care will be applied while handling it.

The project will be carried out under the supervision of Prof. P. Manfrinetti, one of the main Italian experts in the field with over 30 years of experience in the building of phase diagrams also with As, Sb, Cu, and Ni, and to characterize their crystal structures. The project builds on the experienced researcher's (ER) experience gained and the data achieved during her previous MSCA fellowship at the Université Bordeaux Montaigne, where she focused on the loss of arsenic in binary Cu-As alloys during recycling activities, as well as on out-of-equilibrium phase diagrams and basic mechanical properties of Cu-As alloys (IEF-Fellowship no. 656244).¹

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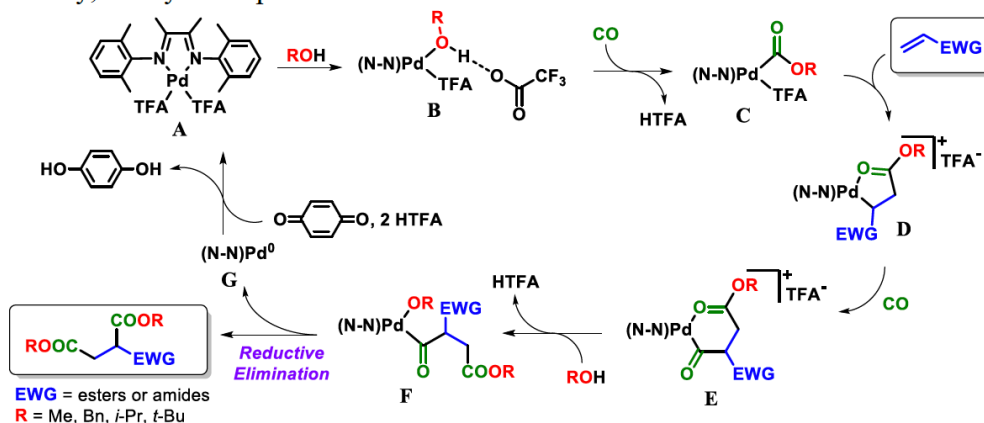
PALLADIUM CATALYZED BIS-ALKOXYCARBONYLATION OF VARIOUSLY SUBSTITUTED ALKENES

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Despite the considerable progress made so far in the field of alkoxy carbonylation of alkenes,^[1] the carbonylation of olefins bearing an electron-withdrawing group (EWG) conjugated to the carbon-carbon double bond has not been widely developed and remains a major challenge. This is probably due to the lower coordination ability of the olefinic bond and the possible interaction of the functional group of the alkene with the catalyst, resulting in low reactivity of these substrates.^[2] After the excellent results achieved in the field of the bis-alkoxy carbonylation of internal olefins,^[3] we recently described the first bis-alkoxy carbonylation of electron-deficient alkenes.^[4] Using variously substituted acrylates and acrylic amides as substrates, 2-alkoxy carbonyl and 2-carbamoyl succinates were obtained respectively, with yields up to 98%.



Scheme 1. Proposed mechanism for the bis-alkoxy carbonylation of olefins.

The aryl α -diimine palladium (II) catalyst **A** is able to promote the carbonylation of both the β - and the generally non-reactive α -positions of electron-poor alkenes, under mild reaction conditions (4 bar of CO at 20 °C). The reaction proceeds with various alcohols as nucleophiles, using *p*-benzoquinone as an oxidant and *p*-toluenesulfonic acid as an additive. DFT calculations allowed us to clarify the key steps of the proposed catalytic cycle, depicted in Scheme 1.^[5] Notably, our computations have shown that the formation of the succinate is associated with a reductive elimination reaction in the palladium complex **F** and not with an alcoholysis, as always suggested by the literature for analogous processes.^[6]

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GREEN OXIDATION OF N-OCTANOL OVER GOLD SUPPORTED CATALYSTS

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Introduction. Currently supported gold is a remarkable catalyst for oxidation of alcohols from biomass conversion products in the liquid phase with high activity, high selectivity and better resistance to deactivation than Pt and Pd. However, it must be stressed that the catalytic activity of gold is strongly sensitive to many factors, such as gold dispersion, preparation method, nature of the support, Au-support interface etc., therefore this research topic is still open to further study.

n-Octanol is often used for comparative studies of catalytic activity in oxidation of alcohols, as a convenient model of primary alcohols of long chain. However, very few studies where mild conditions have been applied for the efficient and selective liquid phase oxidation of *n*-octanol using gold supported catalysts.

Our group investigated Au/M_xO_y/TiO₂ catalysts, where M_xO_y = La₂O₃ or CeO₂, in oxidation of *n*-octanol with molecular oxygen as an environmental friendly alternative way to stoichiometric amounts of inorganic oxidants, which generate abundant waste. It has been found the formation of the active surface responsible for the catalytic properties is strictly dependent on the modifying additives used for better metal-support interaction and as a tool for transforming and stabilizing gold species. However, the effect of metal load in a combination of pretreatment atmosphere in such catalytic systems has deserved much less attention.

In the light of this, the purpose of this work is a study of the influence of gold amount, support nature and pretreatment atmosphere on their catalytic performance for selective oxidation of *n*-octanol under mild conditions.

Catalyst preparation. Unmodified and modified with lanthanum or cerium oxides titania (TiO₂, La₂O₃/TiO₂ and CeO₂/TiO₂) were used as supports. The nominal Au loading were 0.5 and 4 wt%. Au NPs were made from HAuCl₄·3H₂O by deposition-precipitation with urea followed by vacuum drying at 80 °C for 2 h.

Catalytic tests. Catalytic tests in *n*-octanol oxidation were studied using catalyst samples either without treatment or after pretreatment during 1 h at 300°C in H₂ or O₂ atmosphere. Reaction conditions were: 0.1 M *n*-octanol in *n*-heptane, no base added, atmosphere pressure and T = 80 °C with a molar ratio *n*-octanol/Au = 100 for 6 h. Reactants and products were analyzed in a Varian 450 GC.

Characterization methods. Catalysts were characterized by BET, EDX, XRD, STEM HAADF, H₂-TPR, CO₂-TPD, XPS methods.

Results and Discussion. The results showed that the gold content, support nature and the pretreatment atmosphere significantly affect catalytic properties of gold catalysts. The order of catalytic activity depended on the support nature for all treated samples, as follows: Au/La₂O₃/TiO₂ > Au/CeO₂/TiO₂ > Au/TiO₂.

The catalytic activity enhanced with the increase of gold loading in the samples with hydrogen pretreatment, while after the oxidative pretreatment of the catalysts the opposite dependence of the activity with the gold content was found. This catalytic behavior was explained by a change in the surface concentration of monovalent gold ions, which seemed to be the active sites.

Density functional theory (DFT) simulations confirmed that the gold cationic sites play an essential role in *n*-octanol adsorption. The most active catalyst, 0.5% Au/La₂O₃/TiO₂, pretreated in oxidative atmosphere, reached 63% conversion of the alcohol, in 6 h, with 63% selectivity to ester and had the highest surface concentration of monovalent gold ions.

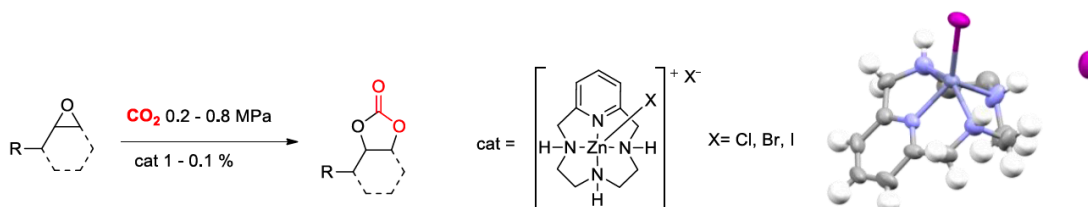
Acknowledgments. The authors would like to thank Laura Pascual, Susana Martinez Gonzalez, Grigory Mamontov, Daria Pichugina, Nadezhda Nikitina, Mario H. Fariás and Nina Bogdanchikova for valuable help in characterization of catalysts and results interpretation.

New zinc (II) halide complexes of Pyridine-containing Ligands as stand-alone efficient catalysts for cycloaddition of CO₂ to epoxides for cyclic carbonates production

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The exponential increase of carbon dioxide (CO₂) emission in the atmosphere is becoming an alarming problem which threaten the whole environment [1]. For this reason, many researchers are focused on developing catalytic systems for the reutilization of carbon dioxide as a feedstock for chemical production. One attractive prospective is the cycloaddition of CO₂ to epoxides to produce cyclic carbonates which find application in many fields as high-boiling non-toxic solvents, electrolytes for batteries and as intermediates for further transformations [2]. In this transformation, the thermodynamic stability of carbon dioxide, which has limited its employment as chemical, is compensated by the use of high energy starting materials such as epoxides [3]. The mechanism of this transformation is nowadays largely known, requiring a combination of a Lewis acid and a nucleophile often represented respectively by a metal ion and onium salts [4]. In our work we present a series of monometallic zinc (II) halide complexes of pyridine-containing ligands able to catalyze such transformation even without the employment of any added co-catalyst such as onium salts (**Scheme 1**). These complexes possess an uncommon square-pyramidal geometry, as confirmed by single-crystal XRD, with one halide atom coordinating the metal at the top of the pyramid and the other placed outside the coordination sphere (**Figure 1**). We suggest that the latter act as the nucleophile for substrate activation nullifying the addition of any onium salt. Early results are encouraging in terms of conversion of substrates and selectivity towards cyclic products.



Scheme 1 – General reaction scheme and condition

Figure 1 – Structure of Pc-L ZnI₂

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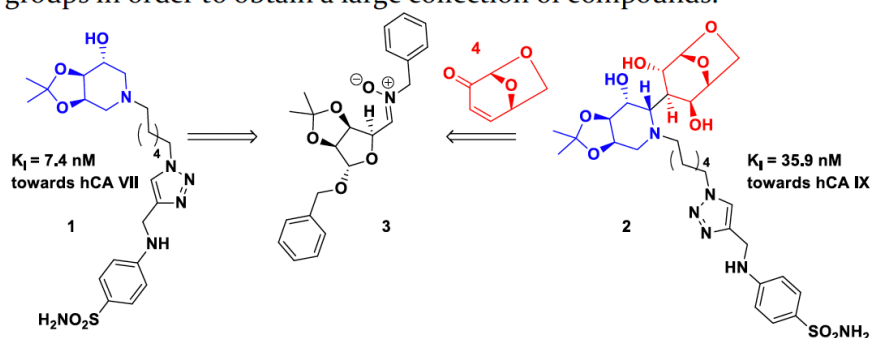
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Glycomimetic based approach toward selective carbonic anhydrase inhibitors

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The human (h) expressed carbonic anhydrases (CAs, EC 4.2.1.1) play important roles both in physiological processes and in various pathologies. The synthesis of selective inhibitors of human carbonic anhydrases (hCAs) is of paramount importance to avoid side effects derived from undesired interactions with isoforms not involved in the targeted pathology and was partially addressed by combining the sulfonamide group^[1], responsible for interaction with the enzyme active site, with a sugar moiety (the so-called “sugar approach”^[2]). Since glycomimetics are considered more selective than the parent sugars in inhibiting carbohydrate-processing enzyme, we explored the possibility of further tuning the selectivity of hCAs inhibitors by combining the sulfonamide moiety with a sugar analogue residue. In particular, we report the synthesis of two novel hCAs inhibitors **1** and **2** which feature the presence of a piperidine iminosugar, originated by reductive amination of a carbohydrate-derived nitrone **3**, and an additional carbohydrate moiety derived from levoglucosenone (**4**)^[3]. Levoglucosenone (**4**) is a small highly functionalized compound produced by pyrolysis of cellulose-containing urban and industrial residual materials such as waste paper^[4]. Biological assays revealed that iminosugar **1** is a very strong and selective inhibitor of the central nervous system (CNS) abundantly expressed hCA VII ($K_I = 7.4$ nM) and showed a remarkable selectivity profile towards this isoform. Interestingly, the presence of levoglucosenone in glycomimetic **2** imparted a strong inhibitory activity towards the tumor associated hCA IX ($K_I = 35.9$ nM). In this way, other potential CAs inhibitors will be synthesized with iminosugar fragment, levoglucosenone and different functional groups in order to obtain a large collection of compounds.



Scheme 1. Iminosugar and levoglucosenone fragments in hCAs novel inhibitors allow the tuning of selectivity towards different isoforms

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Cocrystallization, high pressure/low temperature behaviour and vapochromism in a family of aurophilic copper-gold supramolecular networks.

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The synthesis and conception of coordination polymers and supramolecular networks based on gold(I) complexes used as metallo-ligands (especially dicyanoaurate) is an established procedure to obtain materials with exciting properties: phosphorescence, non-linear optical behaviour, vapochromism and non-classical response to temperature and pressure [1-2]. However, the appearance of these solid-state properties is often connected to the manifestation of aurophilic interaction. The Au(I)⋯Au(I) interaction, an attraction between closed shell d¹⁰ metal centres, is a relativistic effect that has a strength comparable to that of classical hydrogen bond [3]. Therefore, the study of new functional materials based on gold(I) properties must encourage the formation of these contacts in the crystal environment. We prepared, by a judicious choice of chelating ligands and balance in coordination equilibria [4], a series of 12 new coordination polymers or supramolecular networks based on dicyanoaurate anion and copper complexes presenting aurophilic interactions. The choice of copper as metal centre to connect to [Au(CN)₂]⁻ makes the synthesis particularly predictable due to the Jahn-Teller effect in the case of Cu(II), and the appearance of Cu(I) compounds due to redox effect of specific ligands will be commented. These compounds have been tested for vapochromism, and their behaviour in presence of ammonia has been interpreted with Raman, Ir and Uv-Vis absorption spectroscopy. On the same time, the response to temperature (T= 100-420 K) and pressure (P= 0.1-1.5 GPa) of {Cu(bipy)₂[Au(CN)₂]}[Au(CN)₂] (bipy =2,2'-bipyridine), a prototypical bimetallic aurophilic supramolecular network, has been investigated. Both the dependence of structural and reticular parameters to thermal and compression stimuli has been studied, and a phase transition at 1.2 GPa has been revealed. Moreover, we investigated the possibility to modulate the structural behaviour with the cocrystallization with other d¹⁰ metal tectons, and we demonstrate the possibility to obtain inclusion compounds with the presence of Hg(CN)₂ with a 3D weakly interacting framework still presenting Au⋯Au contacts.

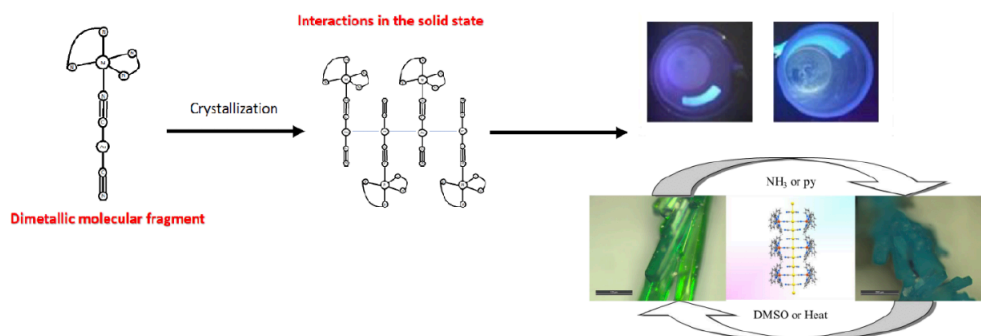


Figure 1. The supramolecular aggregation of dimetallic fragments through aurophilic interaction during the crystallization creates the correct crystal environment for luminescence and vapochromism.

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Keywords: Aurophilic interactions; vapochromism; cocrystals; high pressure/low temperature

Eco-friendly method for keratin extraction from poultry feathers and direct electrospinning to obtain keratin-based bioplastic

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The rapid urbanization and intensification of the anthropogenic activities have led to production of various kinds of waste, which were accumulated in the ecosystem increasing the environmental pollution. In particular, meat market, slaughterhouse and wool industry generate millions of tons of keratin-rich waste biomasses every day ^[1]. Among them poultry feathers are the most abundant ^[2] and the common disposal strategies involve their landfill and incineration ^[3].

The high amount of keratin present in the poultry feathers and the peculiar properties of this protein have attracted the interest of many researchers in the last few years, but a simple, cheap, environmentally sustainable and industrially applicable extraction method has not yet been developed ^[4].

My PhD project is focused on the development of a method for keratin extraction from poultry feathers and direct electrospinning of the extracted solution, without further purification, in a one pot process. The aim is to obtain keratin-based bioplastic materials for food packaging and biomedical applications.

We used a microwave assisted extraction process which exploits a coaxial dipole antenna to apply microwaves directly inside the extraction medium. The advantage of this technology, successfully used in our lab [5] [6], is that it can be easily scaled up at industrial level. We used acetic acid as extraction solvent, because it is inexpensive, eco-friendly [7] and allows the direct electrospinning of the extract without purifying the solution. The effect of extraction time (2 and 5 h) and different solvent/feathers ratio (1:75 and 1:150) on the extraction yield was investigated and the composition of the extracted solution was determined analysing the amino acid, peptide and protein contents. The extracted keratin solution was then blended with gelatin and 3-(glycidyloxypropyl)trimethoxysilane and used to prepare keratin-based bioplastics by direct electrospinning. This work is in progress and the first electrospinning experiments, varying applied voltage (35 and 50 KV) and gelatin concentration (10 and 20 %w/w) have been successful. The mechanical and barrier properties of the keratin-based electrospun obtained will be investigated by tensile test and water permeability, respectively. A morphological characterization will be performed using scanning electron microscopy. Moreover, the thermal behaviour of these materials will be studied through thermogravimetric and calorimetric analysis.

Acknowledgments

This work has been performed in the framework of the **KERAPACK** project. This European project aims to develop a novel material, based on keratin extracted from poultry feathers, which can be used in manufacturing process, in particular in the packaging area.

Controlled Synthesis of Pd^{II} and Pt^{II} Supramolecular Copolymer with Sequential Multiblock and Amplified Phosphorescence

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Supramolecular copolymers constitute a fundamental new class of functional materials attracting burgeoning interest, but examples that display phosphorescence and long-lived excited states are rare. Herein, we describe the synthesis of sequential phosphorescent multi-block supramolecular copolymers in one and multiple dimensions using pincer Pt^{II} and Pd^{II} complexes as building blocks by manipulating out-of-equilibrium self-assemblies via the living supramolecular polymerization approach. Doping a small amount of Pt^{II} complexes (2 mol%) into the Pd^{II} assemblies significantly boosted the emission efficiency and radiative decay rate constant ($\Phi_{\text{em}} = 3.7\%$, $k_r = 1.8 \times 10^4 \text{ s}^{-1}$ in Pd^{II} assemblies; $\Phi_{\text{em}} = 76.2\%$, $k_r = 58.6 \times 10^4 \text{ s}^{-1}$ in Pt^{II}-Pd^{II} co-assemblies), which is ascribed to an external heavy-atom spin-orbital coupling effect arising from the doped Pt^{II} complex with a delocalized $^3[\text{d}\sigma^* \rightarrow \pi^*]$ excited state. The findings on Pt^{II} and Pd^{II} supramolecular copolymers with controlled sequences and greatly enhanced phosphorescence efficiencies open the door to new photofunctional/responsive luminescent metal-organic supramolecular materials.

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Wan, Q.; To, W.-P.; Chang, X.; Che, C.-M. Controlled Synthesis of Pd^{II} and Pt^{II} Supramolecular Copolymer with Sequential Multiblock and Amplified Phosphorescence. *Chem* **2020**, 6, 945-967.

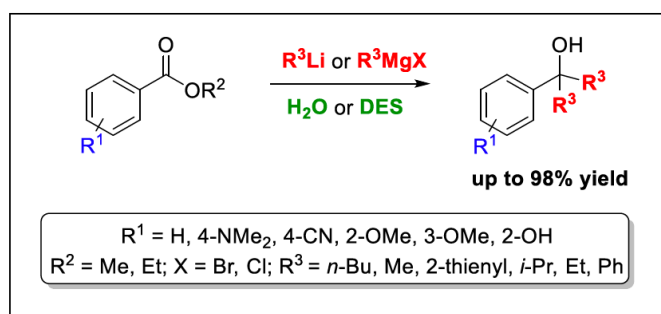
Direct Synthesis of Tertiary Alcohols via Addition of Highly Polarized Organometallic Compounds to Aryl Esters in Unconventional Reaction Media

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The addition of highly polarized organometallic compounds of s-Block Elements to imines, carbonyl and carboxylic acid derivatives is among one of the most important carbon-carbon bond-forming reaction in synthetic organic chemistry. Although the majority of approaches making use of Grignard and organolithium reagents still rely on restricted reaction conditions [rigorously aprotic and anhydrous volatile organic compounds (VOCs), inert atmospheres, often low temperatures], recent contributions from our^{1–5} and other^{6,7} research groups have seen the progressive flourishing of organometallic synthetic strategies developed in protic, nontoxic, biodegradable and cheap non-conventional solvents like water and the so-called Deep Eutectic Solvents (DESS), and under aerobic conditions.⁸

Building on these findings, in this communication we disclose that tertiary alcohols can be straightforwardly obtained by reacting organolithiums or Grignard reagents with aryl esters in unconventional solvents. Working “on water” or in DESS, at room temperature (RT, 25 °C) and under air, conversion was quantitative after short reaction times (5 sec), and tertiary alcohols could be isolated in very good yields (up to 98%) and with a broad substrate scope. The few studies reported on this topic have shown that the nucleophilic addition of Grignard reagents to esters in VOCs, at low temperature, always led to mixtures of mono- and bis-addition products.⁹ The application and utility of the described protocol was additionally demonstrated by the multistep synthesis of functionalized trityl thioethers starting from trityl alcohols, which are known to display a selective inhibition of human Eg5 and anti- cancer properties.



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Mn and Fe Polynuclear Complexes with O,N-Donor Ligands and Their Catalytic Activity Towards Oxidative Functionalization of Alkanes

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Following our interest in the study of polynuclear complexes with O,N-donor ligands [1], with potential application as catalysts in the oxidation and amidation of cyclohexane under mild conditions, we have synthesized novel mixed-valent manganese compounds: $[\text{Mn}^{\text{II}}\text{Mn}^{\text{III}}(\text{H}^n\text{BuDEA})_2(^n\text{BuDEA})_2(\text{EBA})_4]$ (**1**) (Figure 1, left), $[\text{Mn}^{\text{II}}\text{Mn}^{\text{III}}(\text{H}^n\text{BuDEA})_2(^n\text{BuDEA})_2(\text{DMBA})_4]$ (**2**), $[\text{Mn}^{\text{II}}\text{Mn}^{\text{III}}(\text{H}^n\text{BuDEA})_2(^n\text{BuDEA})_2(^t\text{BuAA})_8]$ (**3**) and $[\text{Mn}_3^{\text{II}}\text{Mn}_8^{\text{III}}\text{O}_4(\text{OH})_2(^n\text{BuDEA})_6(\text{DMBA})_8]$ (**4**), through reactions of manganese(II) chloride and/or Mn(0) with *N*-butyldiethanolamine and 2-ethylbutyric (for **1**), 2,2-dimethylbutyric (**2** and **4**) or *tert*-butylacetic (**3**) acids in methanol (MeOH) or dimethylformamide (DMF). Another synthesis attempt of **2** resulted most likely in $[\text{Mn}_7^{\text{II}}\text{Mn}_4^{\text{III}}\text{O}_6(\text{H}^n\text{BuDEA})_2(^n\text{BuDEA})_2(\text{DMBA})_8]$ (**2b**). The same methodology resulted in novel iron(III) compounds too: $[\text{Fe}^{\text{III}}_3\text{O}(\text{DMBA})_6(\text{MeOH})_3]\text{Cl}\cdot\text{MeOH}$ (**6**), $[\text{Fe}^{\text{III}}_3\text{O}(\text{DMBA})_6(\text{H}_2\text{O})_3]\text{Cl}\cdot 3\text{DMF}$ (**7**) and $[\text{Fe}^{\text{III}}_{22}\text{O}_{14}(\text{OH})_4(^n\text{BuDEA})_6(^t\text{BA})_{20}](\text{NO}_3)_2\cdot 10\text{H}_2\text{O}$ (**8**), *via* reactions of iron(III) chloride or nitrate with H_2^tBuDEA (**6** and **8**) or H_2^tBuEA (**6** and **7**) and HDMBA (**6** and **7**) or isobutyric acid (**8**) in MeOH or DMF.

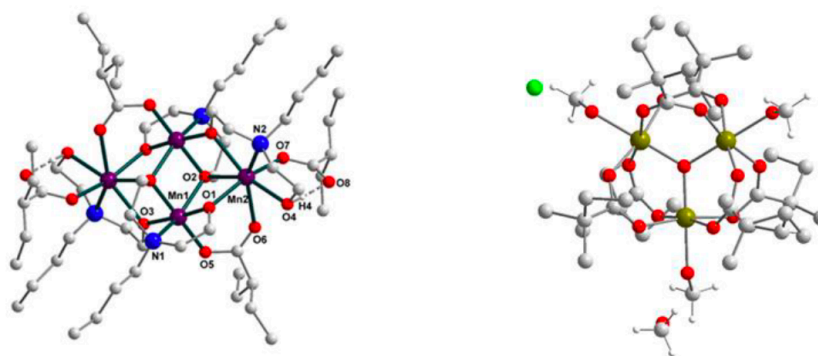


Figure 1. X-Ray crystal structure of $[\text{Mn}^{\text{II}}_2\text{Mn}^{\text{III}}_2(\text{H}^n\text{BuDEA})_2(^n\text{BuDEA})_2(\text{EBA})_4]$ (**1**) [H atoms are omitted for clarity] (left); X-Ray crystal structure of $[\text{Fe}^{\text{III}}_3\text{O}(\text{DMBA})_6(\text{MeOH})_3]\text{Cl}\cdot\text{MeOH}$ (**6**) [color scheme: Fe, green; Cl, light green; O, red; C, gray; H, white; H atoms of carboxylic acid are omitted for clarity] (right).

Compounds **1-3**, **4/2b** exhibited catalytic activity towards oxidation of cyclohexane in acetonitrile for systems having TBHP as oxidant and the iron one (**6**) (Figure 1, right) for both H_2O_2 and $^t\text{BuOOH}$ systems (yielding the highest TON of 237). No catalytic activity was reported for systems using *m*CPBA and no oxidative halogenation took place in the studied conditions. Compounds **1** and **8** do not possess catalytic activity regarding amidation of cyclohexane with benzamide in toluene using DTBP as oxidant.

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Mesoporous silica coated plasmonic nanoparticles for biomedical application

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In the last years, new multifunctional nanovectors have been studied and developed for biomedical applications, especially in cancer diagnosis and therapy. In this regards, plasmonic nanoparticles (NPs) can be successfully employed as contrast agents in early and accurate diagnosis and, in photothermal therapy (PTT) for cancer treatment. PTT produces cell or tissue thermal ablation by means of a PTT agent (PTTA) able to convert light absorbed by a laser source into locally released heat[1].

For clinical applications, the human tissues, as well as water and endogenous cellular components (i.e. hemoglobin and melanin) are considered to be transparent to photons in the near infrared (NIR) region, therefore additional therapeutic advantages are expected to come from the use of PTTA able to absorb laser light in this energy region. Also, improvement in terms of depth of penetration and concomitantly in limited invasiveness of laser-light induced therapies can be anticipated. Here, organic capped plasmonic Cu_{2-x}S NPs, synthesized by means of hot injection approach, and Au NPs, obtained by thermal reduction in organic solvent, have been encapsulated into a hydrophilic mesoporous silica shell ($\text{Cu}_{2-x}\text{S}@MSN$ and $\text{Au}@MSN$).

Cu_{2-x}S NPs, characterized by a plasmonic absorption in the NIR region (second biological window 1000-1350 nm), can be potentially used as PTTA, while Au NPs, can be exploited as promising X-ray contrast agent[2]. The as synthesized NPs, dispersed in volatile organic solvent, have been firstly mixed with water solution of cetyltrimethyl ammonium bromide (CTAB) to provide an efficient functionalization of the NPs and their phase transfer in the aqueous medium. Then, mesoporous silica shell has been grown in a biphasic system consisting of an aqueous base solution with CTAB at a concentration above the critical micelle concentration, where the NPs are dispersed, and ethyl acetate, in the presence of tetraethoxysilicate (TEOS). The high solubility of TEOS in the organic phase and its slow hydrolysis and condensation at the water/ethylacetate interphase, result in a homogenous coverage of the NPs with a mesoporous silica shell, templated by CTAB micelle. The experiments have been devoted to identify the reaction conditions most suited to provide high yield of core-shell structures, while preserving the plasmonic properties of the NPs.

A preliminary NP surface treatment with long alkyl chain surfactant has been demonstrated able to improve the yield of core-shell structures, while low base concentration (NaOH 5mM) and reaction temperature (40°C) have been found suitable to preserve the plasmonic properties.

Core-shell $\text{Cu}_{2-x}\text{S}@MSN$ and $\text{Au}@MSN$ nanostructures with a good colloidal stability in aqueous solution, sizes less than 100 nm, suitable for *in vitro* and *in vivo* experiments, and retained plasmonic properties have been successfully obtained (Figure 1).

SnO₂-based composite anodes for high energy density LIBs

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Since their development, rechargeable Li-ion batteries (LIBs) quickly became the devices of choice for powering portable electronics and for the ever rising electric (EVs) and hybrid (HEVs) vehicles. With the advancement of technology, high energy density materials are required to satisfy the new energetic needs ¹. The present work proposes three SnO₂-based composites (SnO₂/TiO₂, SnO₂/C, and C-coated SnO₂ nanorods) with high experimental capacities (1411 mAh/g for bare SnO₂) compared to standard graphite (372 mAh/g), as possible replacements for the latter ².

Structural and morphological characterizations were achieved through X-ray Diffraction spectroscopy and Scanning Electron Microscopy, respectively. Electrochemical characterization involved galvanostatic cycling, cyclic voltammetry, rate capability, GITT and PEIS, in order to study the behavior of the materials upon cycling and evaluate the internal resistances associated to the processes involved. All analyses have been performed by employing 1M LiPF₆ in EC:DMC 1:1 + 2% VC electrolyte.

All materials were found to display high average specific capacity values (> 750 mAh/g) over prolonged cycling at high current densities, with improved cycling stability and good coulombic efficiencies.

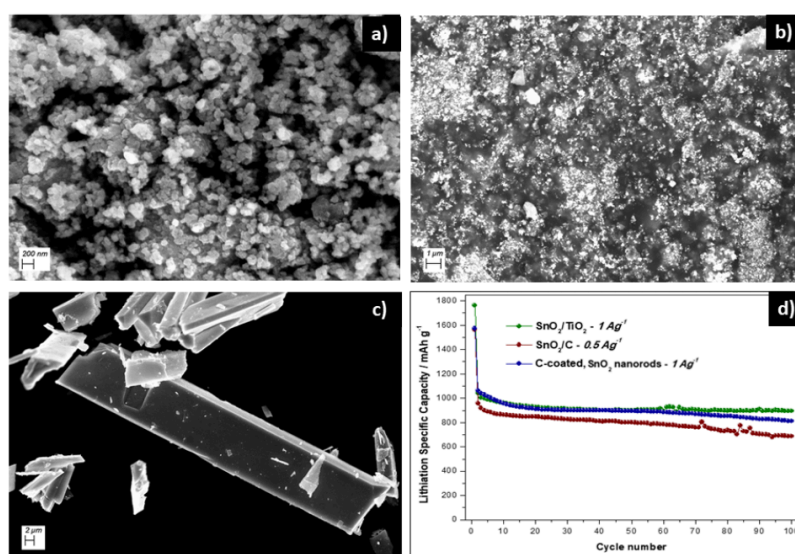


Figure 1. SEM images of a) SnO₂/TiO₂, b) SnO₂/C and c) C-coated SnO₂ nanorods; d) Cycling performance of the three composites.

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SOLVATE INFLUENCE ON IRON(III) SCO COMPLEXES

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With the need to produce materials that store information at the molecular level with increased capacity the spin crossover (SCO) is still a growing field since its relevance ranges from the role of metal ions in biology to magnetic device applications. SCO candidate compounds can be found among a limited group of $3d^4$ – $3d^7$ transition metal ions, such as Fe(III).^[1] The effect of the solvent in the lattice of the complex plays an important role in the cooperativity and hysteric transitions due to the intermolecular bonds formed (π -stacking, hydrogen-bonding and van der Waals interactions).^[2] The enhancement of the SCO cooperativity mediated by these interactions may also strongly depend on the geometry and electronic structure of the anions and solvent molecules, which should impose appropriate packing favoring significant elastic interactions. The influence of the solvent molecules included in the crystal packing on the SCO properties has already been documented for many different systems, but such changes are rare for mononuclear complexes.^[3]

We present the synthesis and characterisation of mononuclear Fe(III) Schiff base complexes that crystallise with different solvates in the crystal lattice. The study of the solvate effect and the influence on the magnetic properties of the compound is also investigated.

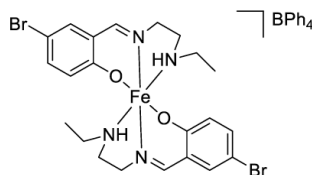


Figure 1: Mononuclear salEn Fe(III) Schiff base complex with BPh₄⁻ as anion.

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INTERACTION OF VANADIUM(IV) SPECIES WITH UBIQUITIN: A COMBINED INSTRUMENTAL AND COMPUTATIONAL APPROACH

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One of the most interesting and promising application of the vanadium chemistry is the development of V-based potential drugs.¹ Despite vanadium compounds exhibit a wide variety of pharmacological properties, like anti-diabetic and anti-tumor, their mechanism of action is not fully known.

Once the metallodrug is administered, in the blood and cellular environment several chemical processes can occur such as ligand exchange, complexation and/or, in several cases, redox reactions. In all these biotransformations, proteins play a central role, both for the high affinity toward specific metals and their large concentration in the biological environment. In light of these assumptions, the study of how a metal species interacts with proteins is fundamental.

In this work, the interaction of V^{IV}O²⁺ ion and some of its bis-chelated pharmacologically active complexes formed by pyranones (maltol, kojic acid), pyridinones (dhp and L-mimosine) and acetylacetone with ubiquitin (Ub) was characterized through EPR (Electron Paramagnetic Spectroscopy), ESI-MS (ElectroSpray Ionization – Mass Spectrometry), and computational (docking and DFT) methods.² Ub is a small regulatory protein, ubiquitous in all the eukaryotes, which contains only few potential binding donors, including the N-terminal Met1 (S donor) and His68 (N donor) as well as five carboxylates belonging to Asp and six to Glu residues (O donors). Since Ub is commercially available with a high level of purity and its amino acid sequence is known in detail, it has been considered as a good model for studying metallodrugs–protein binding.

The combined application of experimental and computational techniques allow to characterize the metallodrug-protein interaction. In particular, ESI-MS allows the determination of the number of moieties (VOL⁺ or VOL₂) bound to the protein, EPR helps distinguish the type of residues involved in the coordination (Asp/Glu or His), and docking/QM calculations allow the prediction of the specific residues interacting with V and provide the 3D structure of the binding site.

This study can open new avenues in the characterization of complex systems, such as those containing metal species and proteins, and presents an alternative approach to the X-ray analysis (often not possible) or NMR determination (not easily applicable for paramagnetic ions).

Finally, the data presented could pave the way for a rational design of new pharmacologically active compounds, highlighting a series of features that must be tuned to optimize the interaction strength with the target protein(s).

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Study of rubber compounds with recycled rubber obtained by different methods

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The most common way to eliminate rubber wastes is to deposit them in a landfill: these stocks represent a serious problem for the environment (fire danger) and for people's health (rodents, mosquitoes and other plagues).¹ Different methods have been developed in order to overcome this situation: however, because of the inherent structure network of rubber compounds, the strength of sulfur/rubber bonds (vulcanization process) and the different formulation, the recycling is currently a challenge.² Several grinding, ultrasonic, biological, chemical, thermomechanical and thermochemical devulcanization processes have been studied:³ the latter ones are the most used in industry. These two methods are different: in the thermomechanical process, the material is submitted to high shear strain, at a controlled pressure and temperature, stretching the network of the rubber and some additives, such as oils or reclaiming agents, can help the devulcanization stage.⁴ The thermochemical process involves the use of chemical agents that break C-C or S-S bonds. Devulcanizing chemical agents could be disulfides, hydroxides, chlorinated hydrocarbons or thiol-amine reagents.⁵ Starting from this consideration, two compounds realized with rubber waste previously treated with thermomechanical and thermochemical devulcanization processes have been characterized and their properties have been evaluated in a chemical, physical-mechanical and applicative view.

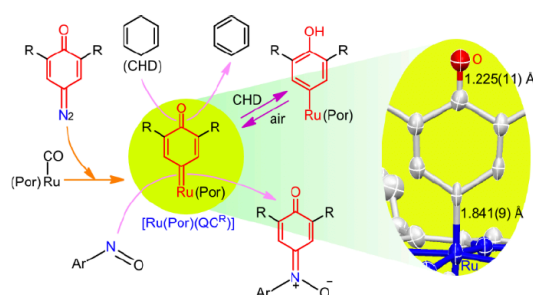
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Metal Quinoid Carbene Complexes: From Bonding to Catalysis

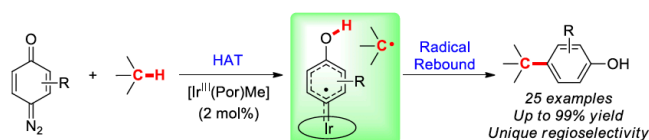
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Reactivity study of novel metal carbene complexes can offer new opportunities in catalytic carbene transfer reactions as well as in other synthetic protocols. Metal complexes with quinoid carbene (QC) ligands are assumed to be key intermediates in a variety of catalytic QC transfer reactions developed in recent years. To better understand metal-QC species, we synthesized and characterized a series of Ru(II) porphyrins containing axial QC ligands. The QC ligands exhibit quinonoid structure in both solid and solution states and feature redox non-innocent property. Notably, these Ru-QC complexes display dual reactivity toward carbene transfer reactions with nitrosoarenes (ArNO) and hydrogen atom transfer (HAT) reactions with weak C(sp³)-H and X-H bonds. Detailed mechanistic studies on these reactions have also been undertaken.



Based on the HAT reactivity of metal-QC species, we further developed a synthetic protocol of Ir(III)-catalyzed intermolecular QC insertion reaction into C(sp³)-H bonds which passes through a stepwise radical mechanism and affords C-H arylation products. This methodology is efficient for activated hydrocarbons (down to 40 min reaction time, up to 99% yield, up to 1.0 g scale). Mechanistic studies support the proposed radical mechanism and that the electrophilic Ir(III) center plays a key role in facilitating the radical rebound step.



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STRETCHING-INDUCED PHASE TRANSITION OF THE BUTENE-1/ETHYLENE RANDOM COPOLYMER

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The stretching-induced phase transition from tetragonal form II to hexagonal form I and the corresponding evolution of crystallite orientation were studied for the butene-1/ethylene random copolymer with 1.5 mol% ethylene by using a combination of tensile test and in situ wide angle X-ray diffraction. Three orientation pathways were distinguished for II-I phase transition, including the phase transition accomplishing within off-axis oriented crystallites (pathway 1), the phase transition with simultaneous formation of highly oriented crystallites (pathway 2), and the phase transition occurring within the highly oriented crystallites already formed (pathway 3). Except for the fact that phase transition kinetics can be significantly accelerated during stretching [1-2], we also found that the kinetics of II-I transition was correlated with the macroscopic mechanical response, which exhibits a strong dependence on orientation. In orientation pathway 1, the triggering of phase transition corresponds to the mechanical yielding in orientation pathway 1. More interestingly, the kinetics of subsequent transition exhibits the identical dependence with stress. However, in orientation pathways 2 and 3, appearance of the highly oriented crystallites substantially alters transition kinetics, which is tentatively associated to the stress bearing by the inter-stack tie chains.

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THE LOW LYING DOUBLE-EXCITON STATE OF CONJUGATED DIRADICALS INCLUDING OLIGOACENES AND CYCLACENS: A COMPUTATIONAL INVESTIGATION

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Conjugated diradicals with a singlet ground state have received remarkable attention owing to their potential applications in optoelectronic devices.[1] A distinctive character of these systems is the location of the double-exciton state, a low lying excited state dominated by the doubly excited H,H→L,L configuration, which may influence optical and other photophysical properties. In this contribution we investigate this specific excited state, for a series of recently synthesized conjugated diradicals and also for oligoacenes and cyclacenes.

The simplest quantum-chemical model to describe a diradical includes two electrons in two orbitals (2e-2o). The double-exciton state emerges as one of the two singlet excited states from a full configuration interaction (CI) within the 2e-2o model. A reliable prediction of its excitation energy is however challenging because of correlation effects and generally MCSCF + CASPT2 or similarly correlated methods are required. However, double excitations can be recovered from TDDFT calculations also with the spin-flip (SF) scheme [2] and, for systems with well localized *Broken Symmetry* (BS) frontier molecular orbitals (FMOs), TDUDFT calculations can be used to predict the excitation energy of the double-exciton state since this excited state is described in terms of singly excited configurations.[3]

The results of the calculations indicate the presence of a low lying double exciton state for all the investigated systems, in particular for long oligoacenes displaying large diradical character (y_0) and cyclacenes formed with an even number of fused rings. The quality of computed results is assessed considering diradical and multiradical (N_{FOD}) descriptors, and the excited state wavefunction composition for the investigated systems.

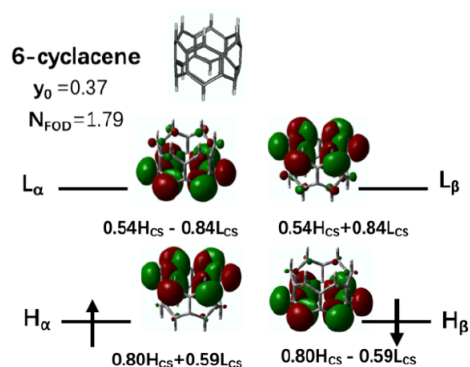


Figure 1. BS FMOs of 6-Cyclacene. Linear combination of the BS orbitals in terms of closed-shell (CS) orbitals, along with y_0 (PUB3LYP/6-31G*) and N_{FOD} (TPSS/def2-TZVP, $T_{\text{el}} = 5000\text{K}$) are presented.

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KETO-IMINE Cr(III)-COMPLEXES FOR HIGHLY PERFORMING POLYOLEFINS

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This study is part of a wider project which aims at designing, synthesizing and characterizing a series of Cr-based catalysts for the synthesis of polyolefins having functional properties.^[1] Two Cr(III)-complexes have been synthesized, reacting the same keto-imine ligand with CrCl₃(THF)₃ (complexes A and B). In complex A the ligand is coordinated to chromium, while in complex B the ligand has been covalently bound to the metal, by deprotonating the ligand with *n*BuLi during the synthesis of the complex.

The two Cr(III)-complexes, in combination with an aluminum alkyl, were tested in the homopolymerization of ethylene and norbornene, employing different reaction conditions (solvent, Al-activator, Al/Cr ratio, temperature). The obtained polymers were characterized in terms of thermal properties, crystallinity and molecular weight. Both complexes exhibited a moderate reactivity towards ethylene, to give a polyethylene with high molecular weight and melting temperature, while they were found to be very active towards norbornene, affording a semi-crystalline diheterotactic polynorbornene.

Figure 1a shows the hypothetical structure of the two Cr(III)-complexes, which however is not supported by X-ray diffraction data due to the impossibility of obtaining suitable single crystals. To fill this gap and, more important, to elucidate the nature of the active sites, the physicochemical properties of the two complexes before and after the addition of the Al-activator were investigated by spectroscopic methods. In particular, ATR-IR spectroscopy gives information on the Cr-ligand bonds, while transmission UV-Vis spectroscopy (**Figure 1b**) gives information on the Cr oxidation state and geometry of the complexes.

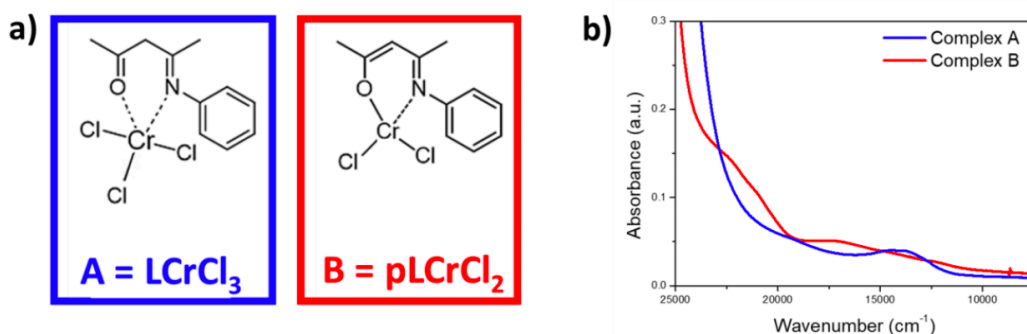


Figure 1. Hypothetical structures (part a) and UV-Vis spectra in chloroform solution (part b) of the two Cr(III)-complexes.

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Model studies of ion channel gating by Atomic Force Spectroscopy and High-Resolution NMR on synthetic phospholipidic bilayers and iron-storing proteins

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Ion channels are pore-forming proteins, present on the membranes of cells, that allow the selective movement of ions across membranes ^[1]. Given their important biological role, precise inhibition or activation of a distinct type of ion channel is crucial in medicine and in neurobiological research. To achieve the control over the ion channels, drugs ^[2] are widely used, as well as optogenetics ^[3]: a recent and revolutionary technology which uses light to control light-gated ion channels. However, both methods suffer limitations: drugs reach their targets very slowly and are not selective for one type of channel over another, while the type of light required for optogenetics (at high frequency wavelength) is poorly penetrating into the tissues and can produce radicals and hence toxic side effects ^[4]. To overcome these limitations, the noMAGIC project (Noninvasive Manipulation of Gated Ion Channel) intend to develop a new generation of ion channels that can be controlled *in vivo*, by non-harmful stimuli, e.g. magnetic field (MF) which is deeply penetrating into tissues. The strategy is to engineer the small and robust viral K⁺ channel by connecting it with a suitable sensor domain: upon perception of the stimulus (MF), the sensor undergoes a conformational change which is transmitted to the pore gate, activating or inactivating the passage of ions. In this case the sensor domain will be the iron-storing protein ferritin. The movement of ferritin, which is induced by an external magnetic field, will gate the pore. Ferritin consists of a mineral core of hydrated ferric oxide, and a multi-subunit protein shell that encloses the former: 24 protein subunits self-assemble in a roughly spherical cage with an outer diameter of approximately 12 nm and an inner cavity of 7–8 nm ^[5]. In the frame of the noMAGIC project, an in-depth characterization of ferritins has been carried out by Atomic Force Microscopy (AFM). In particular ferritins from *Pyrococcus furiosus* and from *Humanized Archaeoglobus fulgidus* have been studied. The results of the morphological analysis, carried out by AFM in fluid with various imaging buffers, sample concentration and substrate functionalization, showed that the holo-ferritin is more stable than the apo- form, and that the self-assembly equilibrium is not always shifted toward the 24-mer, and strongly concentration dependent.

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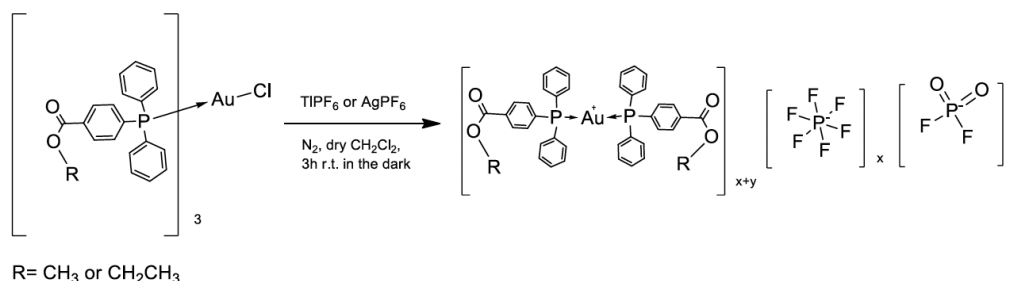
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Synthesis of tris- and bis-phosphane gold(I) complexes. Spectroscopic evidences of hydrolysis in solution of the hexafluorophosphate counterion.

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Tris-phosphane gold(I) complexes are well characterized in the solid state but in solution they may be subjected of ligand dissociation reaction or chemical equilibria, making difficult their complete characterization.^[1] Recently our research group synthesised four coordinated phosphane gold(I) chloride complexes by starting from the 4-(diphenylphosphino)benzoic acid and its methyl or ethyl esters.^[2] The most intriguing aspect for these complexes is the dynamic behavior in solution. As in example, the $[(4\text{-COOMe-Ph})\text{Ph}_2\text{P}]_3\text{AuCl}$ exhibits at room temperature two large ^{31}P NMR resonances at 31 and 24 ppm in CDCl_3 which converge at 32 ppm at -55°C in CDCl_3 . With the aim to have additional information about the behavior in solution of the tris-phosphane gold(I) cation we substituted the Cl^- anion with the less coordinating PF_6^- (scheme 1). The reaction's product resulted to be the bis-phosphane gold(I) complexes with PF_6^- and another anion containing phosphorous whose ^{31}P NMR signal falls at -18 ppm as a triplet. This latter was attributed to the PO_2F_2^- anion and its formation may be explained by the hydrolysis of PF_6^- due to the presence of adventitious water. The direct metathesis of $[(4\text{-COOMe-Ph})\text{Ph}_2\text{P}]_2\text{AuCl}$ with one equivalent of AgPF_6 gave the same results.



Scheme 1. Reaction scheme of the $[(4\text{-COOR-Ph})\text{Ph}_2\text{P}]_3\text{AuCl}$ complexes ($\text{R} = \text{Me}, \text{Et}$) with TIPF_6 or AgPF_6

In all the tris- or bis-phosphane gold(I) compounds metathesis reactions, the ^{31}P NMR showed resonances in the 38-36 ppm range in CDCl_3 which are consistent with the $[(4\text{-COOR-Ph})\text{Ph}_2\text{P}]_2\text{Au}^+$ species and a triplet at -18 ppm ($^1J_{\text{P-F}} = 979 \text{ Hz}$) and a septet at -143 ppm ($^1J_{\text{P-F}} = 708 \text{ Hz}$), attributed to the PO_2F_2^- and the PF_6^- species respectively.^[3] According to these results, the composition of the mixtures in solution was unraveled. The presence of weakly coordinating anions privileges the formation of bis phosphane gold(I) complexes whose ^{31}P NMR chemical shifts were attributed as the ones at the highest chemical shift (36-38 ppm). Reasonably, the tris-phosphane gold(I) complexes falls around 30-32 ppm which is in the same range of the monophosphane gold(I) compounds.

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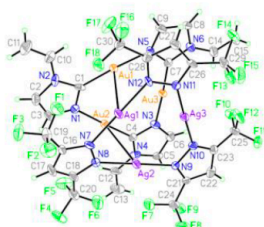
Stacked Coinage Metals Trinuclear Cyclic *versus* Mixed Metal Trinuclear Cyclic Products.

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In the past few years the synthesis and characterization of new coinage metals heterometallic complexes has received much attention due to their unique catalytic and optoelectronic properties.^{1,2} It has been demonstrated that these properties arise from Au(I)-Ag(I) or Au(I)-Cu(I) metallophilic interactions, as well as due to the reduced symmetry of the heterometallic complexes with respect to the homometallic precursors.² Thus, the mechanism leading to the formation of new heterobimetallic complexes likely proceeds to an initial π -acidic/ π -basic interaction³ between homometallic Au(I) and Ag(I) or Cu(I) cyclotrimers, which can be followed by metal and, sometimes, ligand exchanges. However, from this first step π -acidic/ π -basic interaction many paths may be consequently attained depending on the nature of the cyclotrimers.⁴ In general, depending on the reactant, the breaking of the starting intermolecular metallophilic interactions is observed to give rise to compounds where the starting triangular metal framework may be broken as well as it may be conserved.^{2,4,5} The reactivity observed in these studies is often “product favorite”, with the isolation of the products in stoichiometric yield. It is reasonable to assume that the preferred path is governed by a fine tuning of all the weak interactions involved in the solid and in solution states of the cyclotrimers, so that the substituent on the ligands makes the difference in the reactivity. In a previous work the reactivity of homometallic imidazolate or carbenate gold(I) and 3,5-diphenylpyrazolate silver(I) cyclotrimers afforded to mixed metal dimer of trimers units where the metal framework was Au₂Ag or Ag₂Au depending on the stoichiometric ratio.⁵ In this work we attempted to synthesize new π -acidic/ π -basic adducts starting from Au(I) imidazoles and Ag(I) or Cu(I) pyrazolates homometallic cyclotrimers, starting from cyclotrimers with different substituents on the bridging ligand to evaluate the effect of these latter on the π -acidic/ π -basic interaction and on the final fate of the reaction. Surprisingly, some reaction did not afford to the heterobimetallic cyclotrimers but to the stacking compounds. In figure, the X-ray crystal stacked structure of the 1-vinylimidazolate gold(I) with the 3,5-(CF₃)₂-pyrazolate silver(I) cyclotrimers.



Antimicrobial-loaded calcium phosphate nanoparticles as a potential new therapy for cystic fibrosis-related infections.

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Cystic fibrosis (CF) is a progressive, genetic disease that causes persistent lung infections and limits the ability to breathe over time. It is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) protein that regulate chloride ions secretion and sodium ions balance.[1] Mutations of the CFTR gene affecting chloride ion channel function lead to an hypersecretion of thick mucus difficult to clear. The over-production of this mucus makes the lungs susceptible to recurrent and persistent bacterial infections.[2] The aim of this work consists in the preparation of biocompatible and biodegradable calcium phosphate inorganic nanoparticles (CaP-NPs) functionalized with antibiofilm and antimicrobial peptides to treat CF, in order to improve the current treatment of this disease that involves the use of drugs via inhalation routes (oral or nasal). The advantages of using NPs for the peptides delivery are several: (i) co-localization of biomolecules with synergistic therapeutic actions, and (ii) peptides protection against early degradation. In this work, peptides were added in the reaction mix to obtain an encapsulation of the molecules into the one-pot synthesis of CaP,[3] or by a post synthesis surface functionalization. The materials characterization was performed by UV-Vis Spectrometry, High-performance liquid chromatography (HPLC), Thermogravimetric analysis (TGA), Attenuated total reflectance (ATR) and Dynamic Light Scattering (DLS).

A promising new therapeutic formulation based on biodegradable CaP-NPs functionalized with selected antibiofilm and antimicrobial peptides was achieved in order to potentially impair biofilm formation and microorganism vitality as well as to lower the drug resistance phenomenon in the treatment of CF related infections.

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