GIFC 2024

XI EDIZIONE GIORNATE ITALO-FRANCESI DI CHIMICA
TORINO, 4-5 APRILE 2024

Organized by

the "Piemonte/Valle d'Aosta" and "Liguria" Sections of the
Società Chimica Italiana

and the Provence-Alpes-Côte d'Azur section of the
French Chemical Society

BOOK OF ABSTRACTS

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EdiSES

GIFC 2024: WELCOME TO TORINO!

Dear Colleagues,

we would like to thank you for your kind participation to the XI edition of the French-Italian Chemistry Days (*Giornate Italo-Francesi della Chimica*, GIFC 2024), organized by the *Piemonte/Valle d'Aosta* and *Liguria* Sections of the *Società Chimica Italiana* (SCI) and the *Provence-Alpes-Côte d'Azur* section of the *Société Chimique de France* (SCF).

GIFC 2024 just took place in Torino on 4–5 April 2024, hosted in the Chemistry Department of the University of Turin. We would like to thank the University of Turin, the University of Piemonte Orientale and Politecnico of Turin for their support.

This event is organized every two years alternately in the two countries: in 2002 in Juan-les-Pins, in 2004 in Genoa, in 2006 in Turin, in 2008 in Nice, in 2010 in Genoa, in 2012 in Marseille, and in 2014 in Turin, 2016 in Avignon, 2018 in Genoa and in 2022 in Toulon. Therefore, the French-Italian Chemistry Days represents a dynamic platform for interdisciplinary collaboration, fostering lasting connections among researchers in the *Piemonte/Valle d'Aosta* and *Liguria* regions and those in the *Provence-Alpes-Côte d'Azur* region, under the auspices of either SCI or SCF. Moreover, this event aims to facilitate enhanced scientific and cultural interaction at the European level.

Your participation to this event not only contributed to its success, but also aligned your research with cutting-edge developments in various chemical areas, including organic chemistry, bio-organic chemistry, physical and inorganic chemistry, chemical engineering, analytical and pharmaceutical chemistry, environmental chemistry, industrial chemistry, and materials chemistry.

During these days we have scheduled 4 prestigious plenary lectures, 4 invited speakers by the GIFC 2024 Organizing Committee, 38 oral presentations highlighting young researchers, and more than 80 posters.

This congress provided an excellent platform to showcase both advancement and innovation within the chemical sciences and it has been a great opportunity for all researchers, especially the PhD students who can live a truly educating and enriching experience, including prominent visibility throughout the event, and the opportunity to engage with leading researchers and professionals in the field.

We believe that your participation greatly enhanced the overall experience of the GIFC 2024 and contribute to the success of this collaborative initiative.

The GIFC 2024 organizing committee

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- Prof. Andrea Basso, University of Genova, SCI Liguria (Italy)
- Prof. Giuseppina Cerrato, University of Torino, SCI Piemonte/Valle d’Aosta (Italy)
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- Prof. Silvia Ronchetti, Polytechnic of Torino

GIFC2024 FINAL PROGRAM

Thursday, 4th April 2024			
Department of Chemistry, via Pietro Giuria 7, Aula Magna			
8:00	8:30	Welcome of the Participants	
8:30	9:00	Opening of the Day – Welcome Speech	
Chairs		Yoann Coquerel, Francesca Spyrakis	
9:00	9:40	Plenary lecture **Fabio Carniato, *University of Piemonte Orientale, Italy*** “Design and properties of nanoparticles for MRI diagnostic applications”	
9:40	10:20	Plenary lecture: Winner of the SCF Grand Prize **Ling Peng, CNRS and *Aix Marseille University, France*** “Self-assembling supramolecular dendrimers for biomedical applications”	
10:20	11.15	*Coffee Break and Poster Session 1 (posters 1-41)*	
Session 1: Organic and Bio-Organic Chemistry Aula Magna			*Session 2: Green Chemistry* Aula Disegno
Chairs		Giorgio Cevasco, Véronique Michelet	Giuseppina Cerrato, Gaelle Chouraqui
11:15	11:30	**Antoine Domain** ***Aix Marseille University, France*** “Enantioselective domino Michael/O-alkylation reaction for the control of both axial and central stereogenic elements”	
11:30	11:45	**Paul Guerin** ***Aix Marseille University, France*** “Enantioselective Pd(NHC)-catalyzed Kumada-Tamao-Corriu coupling: harnessing axial and planar chirality”	**Corentin Fournet** ***Aix Marseille University, France*** “Development of original catalysts without transition metals designed for hydrogenation reactions”
11:45	12:00	**Silvia Donoso** ***University of Genoa, Italy*** “α-Imino amidines: useful platforms for the synthesis of nitrogen heterocycles”	**Francesco Maria Raboni** ***University of Genoa, Italy*** “Glycerol-based oligomers, green building blocks for industry and cosmetic”
12:00	12:15	**Alexis Truchon** ***Université Côte d’Azur, France*** “Sequential Au- and Pd-catalyzed cyclization process: an efficient entry to polycyclic and polyfunctionalized cyclopropanes via 1,6-Enynes Prins-Type Cyclization/Cyclopropane C-H Activation”	**Carlotta Valle** ***University of Turin, Italy*** “Towards enological by-product-based biorefinery: a cascade approach disclosing comprehensive biomass valorization towards value added products”
12:15	12:30	**Martina Buccioli** ***University of Genoa, Italy*** “Study of an industrial reductive amination reaction: from batch to flow chemistry”	**Adrien Bonneau** ***University of Toulon, France*** “Zinc oxide development for wastewater treatment by photocatalytic degradation of the methylene blue dye”
12:30	13:45	*Lunch Buffet and Poster Session 1 (posters 1-41)*	
Session 3: Organic and Bio-Organic Chemistry Aula Magna			*Session 4: Material Chemistry* Aula Disegno
Chairs		Salvatore Baldino, Andrea Basso	Maela Manzoli, Silvia Ronchetti
13:45	14:00	**Matilde Arese** ***University of Turin, Italy*** “Post-industrial recycled polypropylene for automotive application: mechanical properties after thermal aging”	**Margherita Colombo** ***University Claude Bernard Lyon1, France*** “Multifunctional single-molecule magnets containing S-donor atoms”

14:00	14:15	**Louis Hospital** ***Aix Marseille University, France*** “Protease-activable di-alcoxyamine as contrast agent for MRI applications”	**Enrico Sartoretti** ***Politecnico of Turin, Italy*** “Mesoporous Pd/ceria-praseodymia catalysts for enhanced methane”
14:15	14:30	**Sara S. Y. Mohamed** ***Politecnico of Turin, Italy*** “Mesoporous silica microspheres containing tranexamic for hemostatic application”	**Titouan Beauzon** ***University of Toulon, France*** “Synthesis of photocatalytic cerium oxide: optimization using design of experiment”
14:30	14:45	**Marion Filliâtre** ***Aix Marseille University, France*** “Protease-activable prodrugs specific for Fibroblast Activation Protein”	**Emmanuela Di Giorgio** ***University of Genoa, Italy*** “Impact of stoichiometry and size on the persistent luminescence in $Cs_2(Na_{1-x}Ag_x)InCl_6:Mn^{2+}$ double perovskites”
14:45	15:00	**Sara Gariglio** ***University of Genoa, Italy*** “Exploiting spectroscopy and chemometrics for bloodstain dating in forensic chemistry”	**Yassine Elaadssi** ***University of Toulon, France*** “Cobalt ferrite $Co_xFe_{3-x}O_4$ as photocatalysis under visible light irradiation: experimental and theoretical approach”
15:00	15:15	**Keyu Mao** ***Université Côte d’Azur, France*** “ “Synthesis of azaborine heterocycles through ruthenium-catalyzed enyne metathesis ”	**Vyshnav Kannampalli** ***Aix Marseille University, France*** “Atomic layer deposition of the NiO_x using new precursors with different oxygen sources”
15:15	15:30	**Erwan Adriaenssens** ***Aix Marseille University, France*** “Study of a new mode of activation of alkoxyamines by radical addition leading to a cascade reaction”	**Neethu K. Varghese** ***University of Genoa, Italy*** “Electrochemical characterization of NiFe nanoparticles on colloidal CeO_2 for anion exchange membrane electrolysers”
15:30	15:45	**Andrea Messina** ***University of Genoa, Italy*** “Smart material: the surface functionalization of nanostructured *magnetorheological electrolytes* with the use of click-chemistry”	**Julio Cesar Fernandes Pape Brito** ***University of Piemonte Orientale, Italy*** “Kinetic study of sustainable preparation of organic-inorganic hybrid materials by grafting procedure”
15:45	16:25	***Coffee Break and Poster Session 1 (posters 1-41)***	
Chairs		**Yoann Coquerel, Enrica Gianotti, Paolo Oliveri**	
16:25	16:30	***PhD Thesis Award***	
16:30	16:45	**Guillaume Leseigneur, *Université Côte d’Azur, France*** “Detection, chirality and origin of extraterrestrial organic molecules in the context of the Rosetta and ExoMars space missions”	
16:45	17:00	**Pierfrancesco Maltoni, *University of Genoa, Italy*** “Design of magnetic ferrite nanostructures”	
17:00	17:15	**Andrea Fasano, *Aix Marseille University, France*** “Electrochemical investigations of the biodiversity of [FeFe] and [NiFe]-hydrogenases”	
17:15	17:30	**Eleonora Gianquinto, *University of Turin, Italy*** “*In silico* approaches for the design of innovative agents against emerging infectious diseases”	
Chairs		**Enrica Gianotti, Alain Burger**	
17:30	18:00	**Invited Speaker** **Chiara Lambruschini, *University of Genoa, Italy*** “From waste to resource: use of bio-based building blocks in organic synthesis”	
18:00	18:30	**Invited Speaker** **Julie Broggi, *Aix-Marseille University, France*** “Reductive reactions catalyzed by super electron donors”	

Friday, 5th April 2024			
8:30	9:00	**Welcome of the Participants**	
Chairs		**Paolo Oliveri, Yoann Coquerel**	
9:00	9:40	**Plenary Lecture** **Mario Barbatti, *Aix-Marseille University, France*** “Perspectives in Excited-State Dynamics for Modeling Photoprocesses”	
9:40	10:20	**Plenary Lecture** **Raffaella Boggia, *University of Genoa, Italy*** “Eco-efficient valorization of fishery side-streams”	
10:20	11:00	***Coffee Break and Poster Session 2 (posters 42-83)***	
		Session 5: Chemical Biology **Aula Magna**	***Session 6: Medicinal Chemistry*** **Aula Disegno**
Chairs		**Valentina Brunella, Andrea Basso**	**Alessandra Bianco Prevot, Giorgio Cevasco**
11:00	11:15	**Daniela Trisciuzzi** ***University of Bari, Italy*** “An integrated machine learning model to spot peptide binding pockets in 3D protein screening”	**Marta Falesiedi** ***University of Genoa, Italy*** “Combining repositioning and *de novo* synthesis of pyrazolo[3,4-*d*]pyrimidines to discover potet SIRT-2 inhibitors”
11:15	11:30	**Christian Cravotto** ***University of Avignon, France*** “Microwave-assisted extraction of phytochemicals from *Cannabis sativa* L. Inflorescenses with 2-methyloxolane”	**Chiara Vigato** ***University of Turin, Italy*** “Enhancement of the metabolic stability in 2-hydroxypyrazolo[1,5-a]pyridine scaffold-based inhibitors of human dihydroorotate dehydrogenase (hDHODH)”
11:30	11:45	**Zhenying Mei** ***Université Côte d’Azur, France* “** “Novel chitosan extraction from dung beetle and its potential application for the adsorption of cationic and anionic dyes”	**Carola Grondona** ***University of Genoa, Italy*** “Design and synthesis of new coumarin hybrids with antiproliferative activity against neuroblastoma cells”
11:45	12:00	**Francesca Cardano** ***University of Turin, Italy*** “Fluorescent nucleobases for bright PNA”	**Julie Lagouarde** ***Université Côte d’Azur, France* “** “Development of a magnetic colloid for blood flow recirculation”
12:00	12:15	**Zhancun Bian** ***Aix Marseille University, France*** “Bola-amphiphilic glycodendrimers target carbohydrate-binding proteins”	**Valeria Francesconi** ***University of Genoa, Italy*** “Exploiting the amino dihydrotriazine motif of Cycloguanil to develop novel anti-*Trypanosoma brucei* agents targeting folate enzymes”
12:15	12:30	**Mohamed El Ouardi** ***Aix Marseille University, France*** “Zinc vanadate photocatalyst for efficient degradation of Rhodamine B”	**Rachele Stefania** ***University of Piemonte Orientale, Italy*** “A novel PSMA-targeted probe for photodynamic therapy: synthesis and preclinical validation”
12:30	13:30	***Lunch Buffet and Poster Session 2 (posters 42-83)***	
Chairs		**Maela Manzoli, Véronique Michelet**	
13:30	14:00	**Invited Speaker** **Alain Burger, *University Côte d’Azur, France*** “Programmable fluorogenic probes for biology”	
14:00	14:30	**Invited Speaker: Winner of the SCI Grand Prize** **Giuseppina Cerrato, *University of Turin, Italy*** “New composites from waste materials for circular economy applications: innovative synthetic approaches and characterisation”	
Chair		**Francesca Spyrakis**	
14:30	14:45	***Poster Awards***	
14:45	15:00	***Closing Ceremony***	

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Session 2: Green Chemistry

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Session 4: Material Chemistry

Session 5: Chemical Biology

Session 6: Medicinal Chemistry

Posters

PLENARY LECTURES

Design and properties of nanoparticles for MRI diagnostic applications.

Fabio Carniato(1)*

(1) *Università del Piemonte Orientale, Dipartimento di Scienze ed Innovazione Tecnologica, V.le Teresa Michel 11, 15121 – Alessandria.*

Magnetic resonance imaging (MRI) is a noninvasive method employed for high-resolution visualization of internal tissue structures. Contrast in MR images can typically be improved by using paramagnetic complexes, which influence the longitudinal (T_1) relaxation times of nearby water molecules protons. MRI probes commonly used are based on Gd(III)-chelates, though they may have limitations in enhancing contrast performance, as indicated by their relaxivity parameter, particularly at clinical magnetic field strengths. Various approaches have been developed to enhance the efficacy of these probes, including anchoring or incorporating them into inorganic and organic matrices and this study presents three distinct examples based on i) silica nanoparticles,(1) ii) lanthanide fluorides,(2) and iii) paramagnetic nanogels(3).

i) In the first case, it was shown that silica nanoparticles with varied porosity and surface characteristics can influence the relaxometric behaviour of Gd-complexes anchored onto their surfaces. An optimized configuration was achieved through selective grafting of stable Gd(III) chelates onto the outer surface, providing direct accessibility to water molecules. A detailed characterization through specific relaxometric techniques gave information on both the dynamic mobility of the complex when attached to the silica and the exchange process of coordinated water molecule with bulk solution.

ii) The second example involves $NaGdF_4$ nanoparticles, coated on the surface by different organic ligands, as effective "positive" contrast agents in magnetic resonance imaging. A meticulous design of the coating was crucial for adjusting the relaxation properties, maintaining stability in aqueous suspension, and preserving the chemical integrity of the nanoparticles under physiological conditions.

iii) In the last case, the chemical and relaxometric properties of nanogels derived from chitosan, covalently modified with Gd(III) and Mn(II) chelates, have been elucidated. These novel nanogels present several benefits, including: i) higher relaxivity values compared to conventional contrast agents employed in clinical settings, ii) robust stability of the formulations in biological fluids, and iii) high biocompatibility.

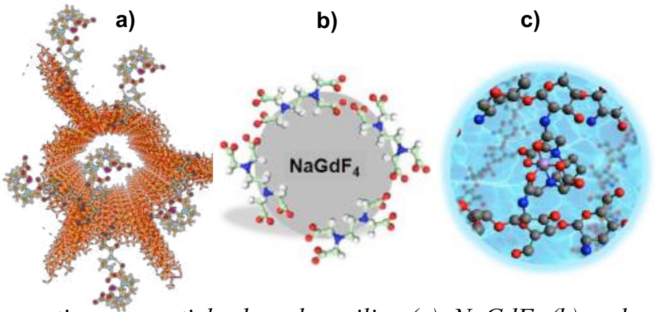

Figure 1: Paramagnetic nanoparticles based on silica (a), $NaGdF_4$ (b) and nanogels (c).

[1] F. Carniato, L. Tei, A. Arrais, L. Marchese, M. Botta, *Chem. Eur. J.*, **201**3, 19, 1421.
[2] F. Carniato, K. Thangavel, L. Tei, M. Botta, *J. Mater. Chem. B*, **2013**, 1, 2442.
[3] F. Carniato, M. Ricci, L. Tei, F. Garello, C. Furlan, E. Terreno, E. Ravera, G. Parigi, C. Luchinat, M. Botta, *Small*, **2023**, 19, 2302868.

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Self-assembling supramolecular dendrimers for biomedical applications

Peng L.[*]

Centre Interdisciplinaire de Nanoscience de Marseille, Aix-Marseille Université, CNRS, France

Dendrimers are ideal precision materials for elaborating nanomedicine by virtue of their well-defined structure, multivalent cooperativity and nanosize per se. We have pioneered modular and adaptive self-assembling supramolecular dendrimer nanosystems[1] for the delivery of anticancer drugs[2] and nucleic acid therapeutics[3] as well as imaging agents[4] for cancer detection and treatment. Remarkably, these supramolecular dendrimers are able to exploit the *in situ* tumor-secreted extracellular vesicles for effective delivery and deep penetration in tumor tissue, while overcoming tumor heterogeneity and dynamic evolution.[2a] Also, we have recently developed self-assembling dendrimer nanosystems against infectious diseases caused by antimicrobial resistant pathogens.[5] Our findings offer a fresh perspective for exploiting the advantageous features of supramolecular dendrimers to reach the ultimate goal of nanomedicine.

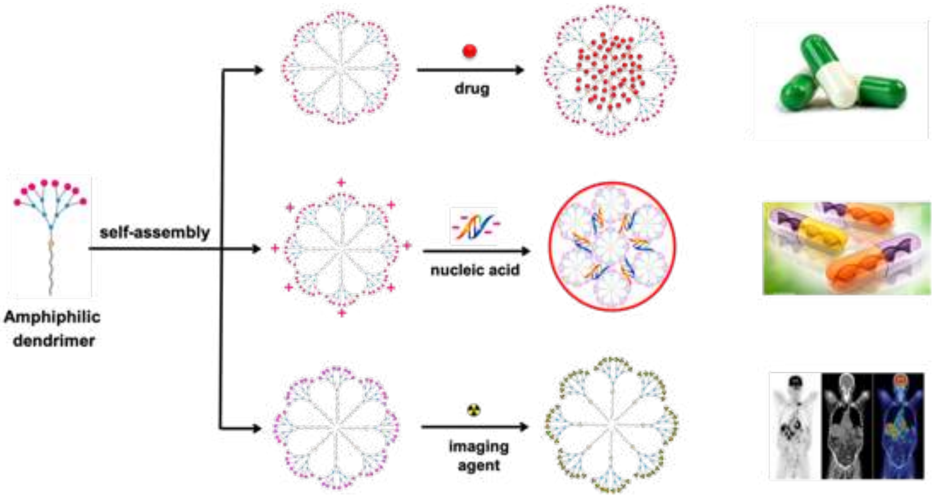

Figure 1 : Self-assembling supramolecular dendrimer nanosystems for the delivery of drugs, nucleic acid therapeutics and imaging agents.

References:

[1] Z. Lyu, L. Ding, A. Tintaru, L. Peng, *Acc. Chem. Res.* 2020, *53*, 2936-2946.

[2] a) Y. Jiang, et al, *Proc. Natl. Acad. Sci. U.S.A.* 2023, *120*, e2215308120; b) T. Wei, et al, *Proc. Natl. Acad. Sci. USA*, 2015, *112*, 2978-2983.

[3] a) J. Chen, et al, *Proc. Natl. Acad. Sci. U.S.A.* 2023, *120*, e2220787120; b) J. Chen, et al, *Acc. Mater. Res.* 2022, *3*, 5, 484-497.

[4] a) L. Ding, et al, *Adv Mater.* 2024, *36*, 2308262; b) L. Ding, et al, *Chem. Commun.* 2020, *56*, 301-304; c) P. Garrigue, et al, *Proc. Natl. Acad. Sci. USA,* 2018, *115*, 11454-11459.

[5] a) N. King, et al, *ACS Infectious Diseases*, 2024, *10*, 453-466; b) D. Dhumal, et al, *Nanoscale*, 2022, *14*, 9286-9296.

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Perspectives in Excited-State Dynamics for Modeling Photoprocesses

Barbatti M. (1,2)

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(2) Institut Universitaire de France, Paris, France

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Molecular excited electronic states are central to diverse fields, including biology, health, and technology. Upon photoexcitation, molecules are unequilibrated systems with multiple competing reaction pathways and time evolution from a few picoseconds to microseconds, depending on the processes involved. Moreover, they present highly complex electronic densities and often visit geometric conformations with multireference characters.

Mixed quantum-classical nonadiabatic dynamics help characterize these systems by providing insights into the physical-chemical phenomenon, delivering information for the deconvolution of experimental time-resolved data, and predicting properties before and after synthesis. However, these methods face challenges, including developing new functionalities, reliable research protocols, efficient computational methods, integration with experimental analysis, and a balanced description of the electronic correlation between states with different characters.

In recent years, my research group has proposed mixed quantum-classical nonadiabatic dynamics methods for treating open quantum systems, systems excited by incoherent light, and zero-point-energy leakage. We also created methodologies for propagating dynamics computing nonadiabatic couplings without wave functions and estimating the temperature of microcanonical quantum systems. I will overview some of these new approaches in this talk. I will also discuss case studies showing these methods in action.

Eco-efficient valorization of fishery side-streams

Boggia R[*]

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Recently, due to increased fish consumption, there has been a rise in the generation of side-streams within the fish supply chain, significantly contributing to global food waste. These side-streams, which encompass materials such as "unwanted catches, "by-catches" and non-edible parts like heads, scales, bones, or skin, represent between 20 to 80% of the original fish weight [1]. The Food and Agriculture Organization (FAO) estimates that approximately 35% of global fish production is lost or wasted annually, posing a significant economic and environmental challenges. Over the years, several conventional techniques have been employed to valorize fishery side-streams. Standard commercial products derived from fish leftovers involve e.g. the production of fish meal via wet pressing, fish oil through hydrophobic solvent extraction, and biofuel through esterification. However, most traditional processes for utilizing discarded fishery feedstocks are notably lacking in energy and resource efficiency, besides involving the use of various chemicals. The pressing need for transitioning production systems towards more environmentally friendly alternatives has prompted the EU Commission to develop and endorse the "Blue Growth," a strategic plan aimed at fostering sustainable growth in the marine and maritime sectors over the long term. This "blue transformation" also includes, among its primary objectives, enhancing the entire aquatic food chain to minimize loss and waste, thereby contributing to the attainment of the UN Sustainable Development Goals outlined in the Agenda 2030. Many research projects have been funded at European level, among them EcoeFISHent which is a project funded under the Horizon 2020 Program - Green Deal (Innovation Action, Grant agreement ID: 101036428) [2]. This project aims at promoting circular economy practices within the fishing sector with the peculiarity to revolve around handling and valorizing unsorted fishery biomasses.

The food chemistry research group of the University of Genoa participates to EcoeFISHent project focusing its activity on the set up of scalable extraction protocols to recovery and potentially valorise unsorted dehydrated biomasses coming from canned Yellowfin tuna processing and aquaculture sea bass and sea bream. The aim is their upcycling into high value bioactive compounds, such as proteins/peptides (e.g., gelatine, collagen, non-collageneous proteins and hydrolysed collagen peptides, hydrolysed peptides) fish oils and other bioactive metabolites to be exploited in the packaging, nutraceutical, and cosmetic sectors. Cascade flowcharts have been proposed to obtain high value bioactive compounds, according to the principles of green extraction [3], recovering also the intermediate co-products which have been evaluated for their potential further exploitation [4].

[1] Alfio VG, Manzo C, Micillo R. Molecules. 2021; 26(4):1002.
[2] https://ecoefishent.eu/
[3] Chemat F, Vian MA, Cravotto G. Green extraction of natural products: concept and principles. Int J Mol Sci. 2012;13(7):8615.
[4] Grasso F, Méndez-Paz D, Vázquez Sobrado R, Orlandi V, Turrini F, De Negri Atanasio G, Grasselli E, Tiso M, Boggia R. Gels. 2023;9(9):760.

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INVITED SPEAKERS

From waste to resource:

Use of bio-based building blocks in organic synthesis

Lambruschini C. (1)

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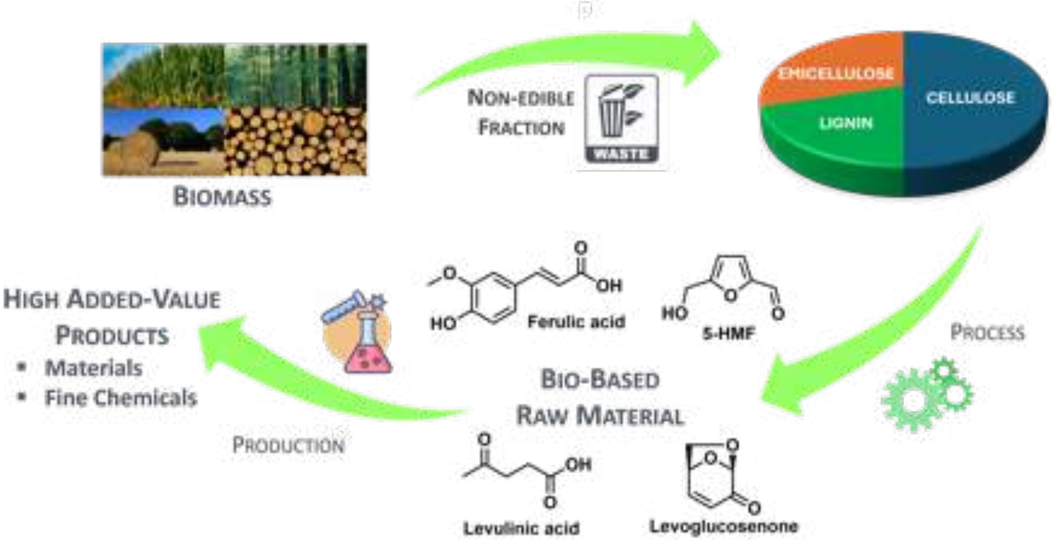
Nowadays organic chemistry can no longer ignore the need to be more sustainable and environmental-friendly. The development of processes that fulfill the principles of green chemistry might be a solution to the problem, but it is not enough, and it must be combined with the use of bio-based starting materials. In fact, one of the great challenges that organic chemists need to face is the shift from petrol-based starting materials to bio-based ones. To this aim the use of the non-edible biomass fraction is ideal and accomplishes the principles of bio-economy and circular economy. The processing of biomass provides small molecules, often highly functionalized, that can be exploited for the synthesis of high-added values compounds (e.g., active pharmaceutical ingredients, potential new drugs, nutraceuticals, monomers).[1]

Herein, will be presented results of our lab in the employment of levulinic acid, ferulic acid, levoglucosenone, and a derivative of 5-hydroxymethylfurfural as bio-based starting materials, also in combination with biocatalysis and multicomponent reactions.[2]



[1] *Polym. Chem.*, **2015**, 6, 4497-4559. / *Green Chem.*, **2014**, 16, 950-963

[2] *Org. Biomol. Chem.*, **2017**, 15, 9331-9351. / *Eur. J. Org. Chem.*, **2018**, 5445-5455. / *Molecules*, **2019**, 24, 2636. / *ACS Chem. Neurosci.*, **2019**, 10, 4462-4475. / *Org. Chem. Front.*, **2020**, 7, 380-398. / *Molecules*, **2021**, 26, 89. / *Eur. J. Org. Chem.*, **2021**, 1737-1749.

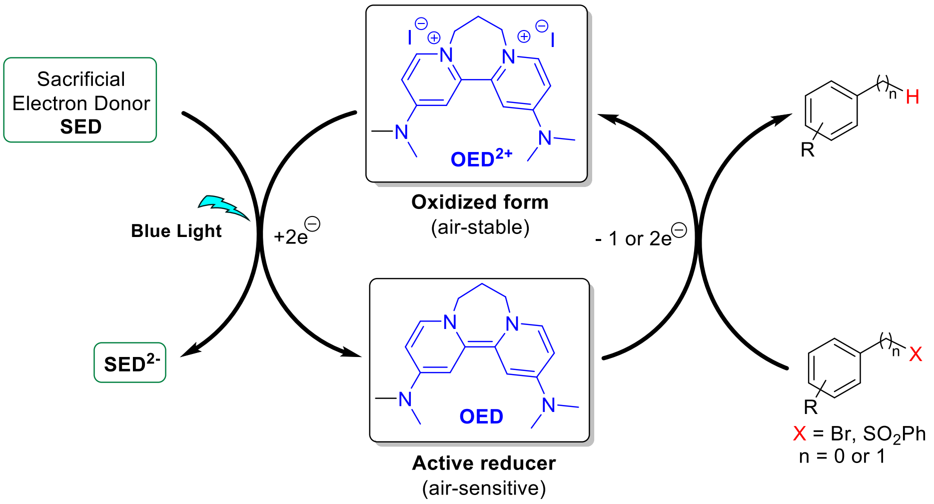
Reductive reactions catalyzed by super electron donors

Fall A., Moussounda Koumba T., Redon S., Vanelle P., **Broggi J.***

Aix Marseille Univ, CNRS, Institut de Chimie Radicalaire (ICR), Faculté de Pharmacie, 13005 Marseille, France.

Photocatalyzed reductive methodologies have emerged as a powerful strategy for the generation of original radical species under mild conditions.[1] Among the different photocatalysts explored, organic dyes have been used as an attractive alternative to transition metal complexes.[2] However, most of them present modest reduction potentials limiting their reactivity to the generation of radical intermediates from strong electron-deficient acceptors.

In the quest for innovative and selective reduction methodologies, super organic electron donors (OEDs) represent ideal eco-compatible and powerful reducing agents for the generation of radical or anionic species by single or double electrons transfers.[3,4] Nevertheless, OEDs were used in a stoichiometric amount. Therefore, we developed an OED-photocatalyzed reduction methodology where the active reducer **OED** is regenerated by electron transfers to its oxidized form **OED**$^{2+}$ using a sacrificial electron donor. This new photoredox catalytic system was applied to the reduction of functionals groups with low reduction potentials (sulfone, aryl halide and triflate) into radical or anionic intermediates. This photocatalytic system represents an unprecedented way to catalytically generate carbanions, including aryl anions.



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Programmable Fluorogenic Probes for Biology

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The central role of RNAs in numerous biological functions, such as coding, decoding, gene regulation, and expression, underscores the critical need to detect and localize them temporally and spatially within cells. While fluorescence microscopy stands as the preferred tool for observing living organisms, its application in nucleic acid studies has yet to reach its full potential. After a succinct review of current methodologies, I will delineate our approach, which revolves around the design and synthesis of programmable fluorogenic probes. Among the various solutions considered, we have developed an innovative and highly sensitive method. Proof of concept was demonstrated in *cellulo* for detecting oskar mRNA, further illustrating the compatibility of this approach with super-resolution imaging techniques.

From wastes to values: examples of different circular economy approaches

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The aim of this work is twofold: firstly, the valorization of the residual products of a transformation chain of organic urban waste, i.e., humic and fulvic acids, extracted from digestate (HAs and FAs, respectively) will be presented. HAs and FAs present oxygen-based functional groups allowing versatile adsorption on solid surfaces, thus selecting these it is possible to obtain multifunctional and nontoxic nanocomposites that could find application in agriculture, being capable of conducting multiple beneficial actions, including crop nutrition, plant stimulation and soil amendment [1a]. We used HAs and FAs to formulate nanohybrids with potential application in agronomy: in order to obtain a synergic co-release of plant-beneficial agents, we functionalized with HAs and FAs two inorganic matrices, hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$, HAp) and silica (SiO_2), in the form of nanoparticles. The former is a potential controlled-release fertilizer of P, with a still limited use due to its low solubility in neutral and/or alkaline soils [1b]. The latter contains almost no macronutrients, but many widespread crops are Si-accumulator and it is demonstrated the beneficial effect of Si in plant and soil, especially under environmental stress [1c].

Secondly, the abatement of unpleasant odors (the most disturbing pollutants and the main reason for air quality complaints in urban and industrial areas) will be considered. Odor emissions consist of various chemical components, some of which can be perceived at very low threshold levels and significantly harm mental/physical health even in very low amounts [2a]. Besides, nitrogen oxide (NOx) emissions represent one of the most hazardous air pollutants, causing both environmental and health problems, contributing to ground-level ozone, global warming, etc. Nowadays, many technologies are available to abate odors and NOx emissions : among them, photocatalysis employing TiO_2 under solar/artificial light has been thus widely applied [2b] and to overcome TiO_2 limitation, by extending its photo-response to the visible region (improving its photocatalytic performance), surface modification with noble metals nanoparticles (NPs) has been considered [2c]. Nevertheless, noble metals' high prices and resource shortage limit their applications : the employ of multiple noble metals-modified micrometric TiO_2-based photocatalysts, prepared by a cheap and sustainable approach based on the use of metal-enriched wastewaters (Ag, Au, Pt) from noble metals' extraction/processing will be presented.

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PhD THESIS AWARDS

Detection, chirality and origin of extraterrestrial organic molecules in the context of the Rosetta and ExoMars space missions

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Rosetta and ExoMars are two of the growing number of space exploration missions that delve into the molecular origins of life. Rosetta did so by looking at the chemical composition of a comet, one of the most pristine bodies, largely undisturbed since the birth of our Solar System more than 4.5 billion years ago. ExoMars will do so by looking for organic molecules on the red planet, a body that shared with Earth a similar early geological history, particularly during the time when life is supposed to have appeared on our planet.

One of the common analytical instruments onboard these two missions is a gas chromatograph coupled to a mass spectrometer (GC-MS), allowing for efficient separation and detection, respectively, of individual molecules within a sample. We revisit GC-MS data from the past Rosetta mission, and we bring an updated view of the chemical composition of the comet on which it landed [1,2].

In preparation for the future ExoMars mission, we focus on the detection of chiral molecules that are omnipresent in biology, such as amino acids and sugars. These molecules, that exist in two different forms that are mirror images of one another, are found in biology strictly in only one of these two configurations, which is an extremely useful property when looking to distinguish between biological and non-biological samples. Using chiral gas chromatography, we show a new, more indirect way of detecting possible extinct life on Mars using the lesser-known chirality of a few select hydrocarbons [3]. We then use this same protocol to assess the origin of these chiral hydrocarbons in meteorite samples.

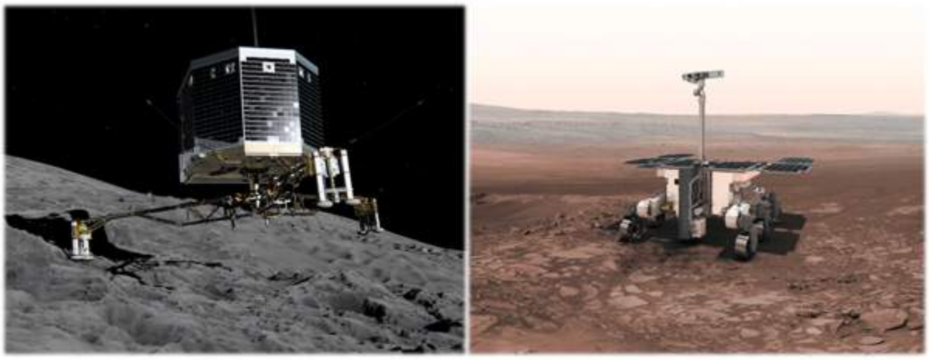

Figure 1 : Artist views of the Philae (Rosetta) and Rosalind Franklin (ExoMars) spacecrafts on a comet and Mars, respectively.

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Design of Magnetic Ferrite Nanostructures

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In the domain of magnetic nanomaterials, meticulous design considering both chemical and physical factors emerges as fundamental, [1]. By tailoring the composition, and crystal structure, researchers can finely tune the magnetic behavior, coercivity, and anisotropy. For instance, substituting diamagnetic cations like Al^{3+} for Fe^{3+} in ferrites enhances coercivity and tailors magnetic properties. Furthermore, physical properties such as particle size and shape, significantly influence magnetic response. Controlled synthesis of uniform and monodisperse nanoparticles is crucial for achieving desired magnetic functionalities. The interplay between different magnetic phases introduces complexity but also offers intriguing opportunities. Interface interactions between phases enable the development of advanced functionalities crucial for various applications including novel permanent magnets (Fig. 1). This thesis explores the role of magnetic interactions in ferrite nanoparticle systems, investigating both individual systems and assemblies. It reveals new sources of hysteresis bias unrelated to traditional exchange bias, highlighting the significance of dipolar interactions and morphological properties in influencing magnetic behavior. The study extends to assemblies of soft maghemite particles, demonstrating the possibility to tune interparticle interactions via control over surface coating, leading to collective behaviors such as superspin glass. Moreover, the research delves into the magnetic coupling in nanostructured bulk systems, revealing correlations between morphology and magnetic interactions. Strategies such as chemical doping and control over synthesis approaches are explored to tailor magnetic properties, showcasing the potential for developing permanent magnets with large coercivities. In conclusion, this study provides valuable insights into the intricate realm of magnetic interactions at the nanoscale, offering avenues for designing magnetic nanosystems with enhanced functionalities. [1]

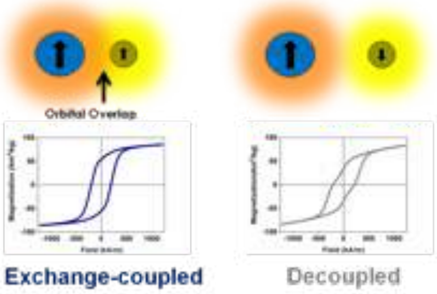

Figure 1: Example of magnetic nanoparticle systems comprising two magnetically coupled/decoupled phases.

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Electrochemical investigations of the biodiversity of [FeFe] and [NiFe]-Hydrogenases

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In Nature, the interconversion between H^+ and H_2 is catalysed by hydrogenases, enzymes with an inorganic active site that contains nickel or iron ions. The metal content of these active sites defines the [NiFe] and [FeFe]-hydrogenase families. Evolution has generated a large biodiversity within each of these two families, of which we have only scratched the surface in the last decade.

The biodiversity of hydrogenases is reflected in a wide range of catalytic properties, such as directionality (the ability to catalyse the reaction in one or both directions), reversibility (related to how much thermodynamic driving force is required to catalyse the reaction in either direction), and tolerance to inhibitors. The diversity of catalytic properties within the same family of hydrogenases indicates that structural features other than the active site control these properties.

We applied Protein Film Electrochemistry to study the catalytic properties of recently discovered hydrogenases, comparing them with the best-known enzymes. Using Site Directed Mutagenesis we looked at the effect of specific residues, sometimes very far from the active site, in controlling these properties.

We have studied the irreversible catalytic response of the [FeFe]-hydrogenase HydS from *Thermoanaerobacter marthranii* (Tam HydS) [1], and developed a kinetic model of the catalytic cycle [2] that allowed the comparison of the catalytic cycle of this enzyme with that of a well-known, reversible, hydrogenase. This investigation resulted in the identification of different parameters that influence the reversibility of the catalytic response [3]

The [FeFe]-hydrogenase from *Clostridium beijerinckii* (CbA5H) is the only O_2 tolerant [FeFe]-hydrogenase known so far. We elucidated the kinetic reasons behind the increased tolerance toward O_2 induced by the replacement of a residue 18 Å from the active site [4]. Intrigued by the similar catalytic response between CbA5H and the third hydrogenase from *Clostridium pasteurianum* (CpIII), belonging to a very poorly studied group of [FeFe]-hydrogenases, we have investigated the oxidative inactivation of CpIII and discussed it in terms of O_2 protection [5].

Regarding [NiFe]-hydrogenases, instead, we focused on two enzymes expressed by the same microorganism (*E. coli*) that have very different properties. We took advantage of the dimeric structure of their catalytic core to engineer a catalytically active chimeric complex made of two subunits, one from each hydrogenase. We could thus determine which subunit is responsible for each catalytic property, in particular directionality and sensitivity to the inhibitors CO and O_2 [6].

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In Silico Approaches for the Design of Innovative Agents against Emerging Infectious Diseases

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NB: Author who will be present should be written with bold and underlined characters

In this thesis, several *in silico* methods were applied to study target proteins for the design of antimicrobial agents. In the first application, a structure-based virtual screening pipeline was applied to identify candidates that were purchased and tested against a panel of isolated SBLs (CTX-M-15, KPC-2, AmpC) and MBLs (VIM-2 and NDM-1), and best inhibitors were further tested for synergistic activity with imipenem on clinical strains [1]. This pipeline yielded two MBL inhibitors with a 1,2,4-triazole-3-thione core, that were co-crystallized in NDM-1 and VIM-2 to determine their binding pose. Furthermore, a compound with a thiosemicarbazone core was identified as a modest SBL and MBL cross-class inhibitor, and potentiated imipenem activity when tested in clinical strains. The inhibition profile of 1,2,4-triazole-3-thione scaffold was further explored in a second publication [2], which reports four compounds with cross-class micromolar inhibition potency against relevant carbapenemases including two MBLs (IMP-1 and VIM-1) and a SBL (KPC-2).

A second topic involves the *in-silico* study of the interaction and the heme transfer process from human hemoglobin to the staphylococcal hemophore IsdB. A first paper on this project clarified computationally and experimentally several aspects of the IsdB-human hemoglobin interaction, among which the lack of selectivity between alpha and beta chain in hemoglobin, the preference of IsdB for the oxidized form of hemoglobin and the absence of cooperativity in the heme extraction process [3]. Further work was carried out to study the heme extraction process, where the heme transfer was simulated via multiple walkers well-tempered metadynamics. Here, interactions along the extraction process were characterized, and energetic local minima were identified through the path. Key residues participating in stabilizing local minima were identified and experimental data were added to confirm the key role of a specific residue in IsdB, namely Tyr444, in heme extraction from human hemoglobin.

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ORAL COMMUNICATIONS

Session 1: Organic and Bio-Organic Chemistry

Enantioselective Domino Michael/O-alkylation Reaction for the Control of Both Axial and Central Stereogenic Elements

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The enantioselective synthesis of chiral compounds containing multiple stereogenic elements *via* a single catalytic step from achiral precursors is a challenging process. Recently, some method emerged recently,[1] but only a few examples report the simultaneous control of both axial central stereogenic elements. Previously, we developed an organocatalyzed enantioselective domino Michael/*O*-alkylation reaction on various naphthol-derivatives, with the aim to obtain dioxa[6]helicenoids,[2] bearing helical and central chiralities with excellent diastereo- and enantioselectivity. Following this work, we propose a challenging extension of this reaction, starting from naphthol derivatives **1**, bearing either a C–C or a C–N bond displaying a low rotation barrier. These substrates underwent enantioselective dihydrofurannulation providing the desired dihydrofurans **2** bearing two stereogenic carbon atoms but also a configurationally stable C–C or a C–N bond, thanks to a high increase of the rotation barrier upon dihydrofurannulation.

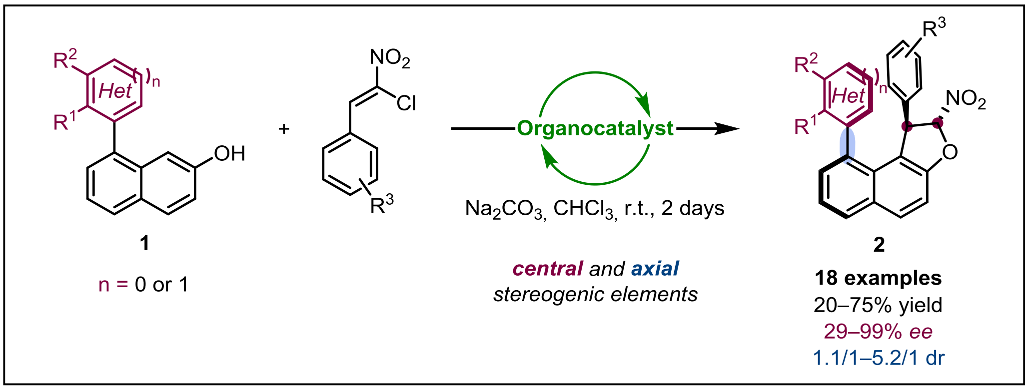

Figure 1: Diastereo- and enantioselective synthesis of biaryl compounds bearing axial and central chirality

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Enantioselective Pd(NHC)-catalyzed Kumada-Tamao-Corriu coupling: harnessing axial and planar chirality

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Palladium- and nickel-catalyzed Kumada-Tamao-Corriu couplings are widely used to synthetize biaryl compounds. Therefore, the development of chiral catalytic systems has attracted much attention to obtain enantioenriched biaryls.[1]

Since our laboratory has recently developed a new concept for the design chiral Pd(NHC) complexes (NHC = N-hetereocyclic carbene),[2] their potential was evaluated in the enantioselective Kumada-Tamao-Corriu coupling affording biaryl compounds containing an axis of chirality. In a thorough study, results were compared to the enantioselectivities obtained with other chiral NHC ligands reported in the literature. Moderate enantiomeric excesses were reached (up to 63% ee).[3]

This led us to conceive original transformations in which the enantiodetermining step will be different. Using cyclophanes as substrates,[4] appropriately designed, the cross-coupling reaction gives rise to planar chirality. After the optimizations of the reaction conditions and the structure of the chiral Pd(NHC) complex, up to 88% ee was reached. These results will be detailed, including the key factors such as the configuration stability but also the way to generate simultaneously an axis and a plan of chirality in a diastereoselective fashion.

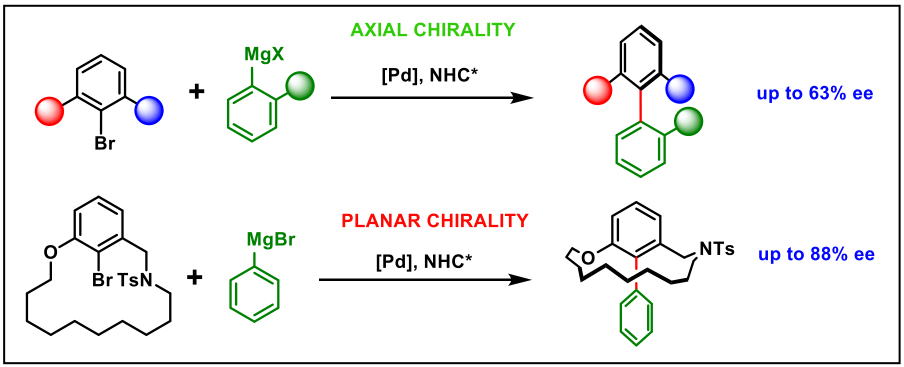

Figure 1 : Model reactions investigated with chiral Pd(NHC) complexes

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α-Imino amidines: Useful Platforms for the Synthesis of Nitrogen Heterocycle

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The synthesis of N-heterocycles is one of the most active areas due to their structures with extensi applications in the fields of organic, pharmaceutical and materials chemistry. In fact, the number novel N-heterocyclic moieties with significant physiological properties and promising applications medicinal chemistry is ever-growing [1].

Recently, we have studied the Ugi-type 3-component reaction between aldehydes, isocyanides a anilines, promotes by Graphene Oxide (GO) [2], to give α-amino amidines **1**. GO is not only able promoting the multicomponent reaction thanks to its Lewis and BrØnsted acid properties, but also converting **1** into the corresponding α-imino amidines **2** by oxidation of the C-N bond. The α-imi amidines **2** had never been reported in literature, though they can be considered useful synthet intermediates for further elaborations. For instance, we studied the intramolecular S$_E$Ar to gi substituted indolenines **3**, interesting structures present in several natural and pharmaceutical compoun [3]. All these processes have been optimized, studied and the one-pot protocol for the synthesis molecules **2** and **3** have been tested obtaining very satisfactory results [4].

Further studies for the transformation of **2** into different types of N-heterocycles are currently progress.

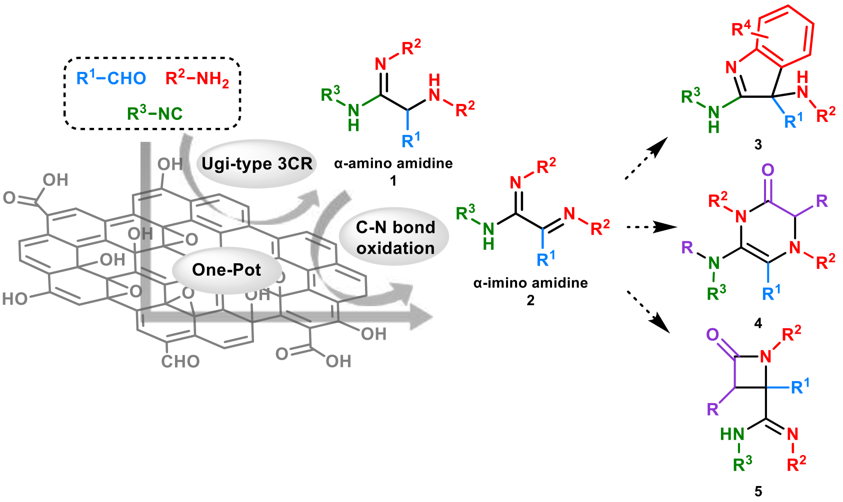

Figure 1 : Hightlights of the research

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Sequential Au- and Pd-catalyzed cyclization process: an efficient entry to polycyclic and polyfunctionalized cyclopropanes via 1,6-Enynes Prins-Type Cyclization/Cyclopropane C-H Activation.

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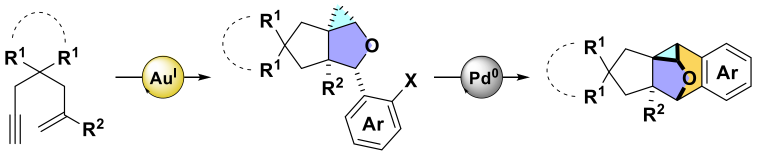
Despite their intrinsic value and the large representation of cyclopropane synthesis in the literature,[1] the direct functionalization of the latter remains an underexplored research area. In this context, we report a new efficient entry to polysubstituted cyclopropanes through a sequential process involving an Au-catalyzed Prins-type cyclization and a Pd-catalyzed cyclopropane C-H activation reactions. Considering our group's interest in atom-economical Au-catalyzed processes,[2] we showcased that the polycyclic heterocycles, potent for the C-H activation, would be obtained from easily accessible 1,6-enynes and *ortho*-halide arylaldehydes.[3] Under Pd optimized conditions, these intermediates were efficiently transformed into highly functionalized cyclopropanes in modest to excellent yields. The scalability of these reactions was notable, and mechanistic studies provided insights into the reaction pathways. Furthermore, post-functionalization steps underscored the synthetic versatility of this sequential transformation.[4]



$R^1 = CO_2R, -CH_2OC(CH_3)CH_2O-$
R^2 = Me, H   X = Cl, Br, I

- mechanistic & kinetics studies
- low temperature C-H activation
- highly substituted fused-cyclopropanes
- up to 96% yield

Figure 1: Sequential Au- and Pd-catalyzed process leading to polyfunctionalized cyclopropanes.

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Study of an industrial reductive amination reaction: from batch to flow chemistry.

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Reductive amination reactions play a very important role in pharmaceutical and medicinal chemistry thanks to the presence of many secondary amines among biologically active compounds. About a quarter of C−N bond-forming reactions in the pharmaceutical industry are performed via reductive amination.[1] This reaction is involved in the first step of a major synthetical route which leads to an important industrial API produced in Bioindustria L.I.M (AL), so it is significant to achieve high conversion, high yield and low impurities. To do that, the Design of Experiments (DoE), a solid chemometric and multivariate method, allows to study and define the interactions between the variables making a small number of experiments to evaluate many parameters.[2] Flow chemistry is a technique used in green chemistry to carry out chemical reactions in a more efficient and environmentally friendly manner compared to traditional batch processes and for these reasons it is the new goal for pharmaceutical companies.[3] The methodology reported in this contribution explains the use of DoE to optimize the operating conditions of this reductive amination reaction in batch, to further move to evaluate the applicability of the same reaction exploiting the in-flow technology (Figure1).

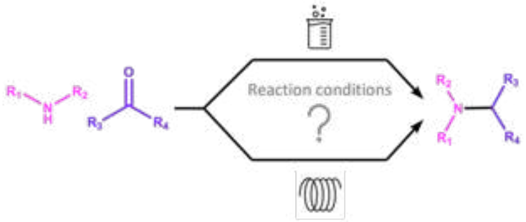

Figure 1 : Reductive Amination Reaction scheme

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Session 2: Green Chemistry

Development of original catalysts without transition metals designed for hydrogenation reactions

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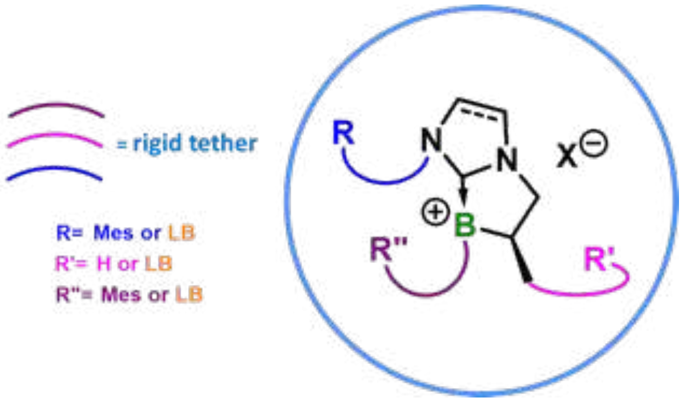
To answer the current societal issues, chemistry must imply a responsible approach by limiting its environmental impact, and by promoting green chemistry. This is one of the current challenges of chemists, and among the twelve principles of green chemistry; the field of catalysis holds a major place.

This project involves the development of modern tools for homogeneous catalysis based on original structures including a Lewis base and a Lewis acid. These platforms will be used in organic catalysis as Frustrated Lewis Pair (FLP) catalysts and their ability to activate small molecules.

Herein, we wish to disclose our efforts directed towards the synthesis of small molecules which will be used for the development, in a few steps, of a library of bifunctional and ambiphilic chiral main-group catalysts (see ***Scheme***). The design of these structures is based, on one hand, on a NHC skeleton previously developed in our group[1] and, on the other hand, on scaffold known in the literature to split the dihydrogen molecule.[2,3]



Scheme : Design of new original ambiphilic catalysts based on scaffolds known to split the dihydrogen molecule by a FLP-type process.

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Glycerol-based oligomers, green building blocks for industry and cosmetic

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Glycerol (GLO) is a versatile and useful molecule employed in many different areas, spanning from the applications as a lubricant in the textile industry to the production of materials that come in contact with food, pharmaceuticals, cosmetics or even human skin. GLO is a very interesting building block since it also fully incarnates the ideal of circular economy being a byproduct of biodiesel production.

In this work GLO was coupled with different biobased diacids (adipic, succinic, sebacic) to obtain small oligomers that could be a valid alternative to the petrol-derived polyethylene glycol (PEG) oligomers, widely used in the pharmaceutical industry, by being biodegradable and biocompatibile[1].

This work mainly focused on adipic acid containing oligomers, synthetized in neat conditions, using lipases as biocatalyst and the corresponding di-methyl ester to provide a better driving force by removal of methanol. Initially we optimized the synthesis: a small excess of GLO and the use of biocatalysis at very mild temperatures (40-60ºC) were crucial to achieve linear oligomers with a low branching degree (<30%)[2]. The oligomers were end capped at both ends with GLO to allow a further functionalization with fatty acids (FA) and/or small peptides. This second functionalization step was also done enzymatically. The long FA chains were used to modify the hydrophilic-lipophilic-balance (HLB) of the molecule, therefore enlarging the possible range of applications (spanning from emulsifying to wetting agents). N-Boc protected peptides were instead used to synthetize amphiphilic molecules, of interest for cosmetic applications as potential peptide-delivering vehicles[3].

The developed methodology is environmentally friendly and purification via column chromatography is not necessary. Conversions in the synthesis of the three main molecules, illustrated in *Fig.1,* are around 95%, furthermore all the compounds show promising properties, also highlighted by the HLB calculations[3].

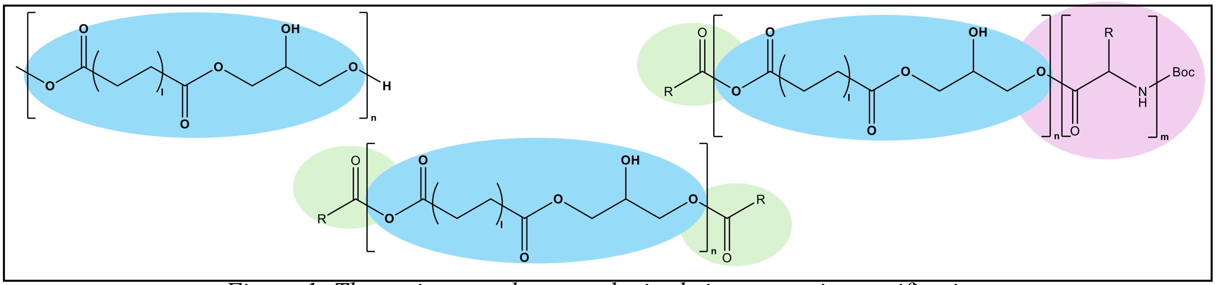

Figure 1: The various products synthetized via enzymatic esterification.

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Towards enological by-product-based biorefinery: a cascade approach disclosing comprehensive biomass valorization towards value added products

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One of the fundamental principles of the circular economy is waste minimization, aiming at transforming end-of-life products into resources for alternative purposes. This has led to an increased focus on agri-food waste valorisation. In particular, lignocellulosic biomasses have the potential to generate by-products that possess biological activity (*i.e.* secondary metabolites such as polyphenols) as well as biopolymers suitable for further conversion (*i.e.* cellulose, hemicellulose, pectins, lignin).

The wine industry is among the pillars of Italian agri-food sector. Still, it produces large amounts of by-products such as grape stalks, which are mostly disposed for a fee, thus representing an attractive negative-cost feedstock for biorefinery.

This work proposes a sequential biomass valorisation protocol featured by a multidisciplinary strategy, exploiting unconventional techniques and subcritical water as green solvent, where physical/chemical treatments work in synergy with biological ones. The early stage encompassed the sequential fractionation of grape stalks, achieving several product streams, enriched in polyphenols, hemicellulose and pectins, lignin and cellulose.

In detail, microwave (MW) heating [1] was exploited for the fractionation protocols to reach subcritical water conditions or enhance alkaline delignification [2]. Finally, the cellulose-rich residue from the cascade treatment was exploited as a fermentation substrate for the last step, producing lactic acid by harnessing suitably engineered *Clostridium thermocellum* strains (*Figure 1*). In particular, LL1111 (Δ*adhE, ldh*^{S161R}), an hyperproducer of lactic acid, [3] and LL1630, a mixed culture directly evolved from LL1111 characterized by a higher tolerance to lactic acid (up to 35 g/L) [4], were exploited.

Cascade pretreatments coupled with fermentation based on a cellulolytic microorganism can be considered a promising example of a biorefinery approach, having the advantage of allowing the full recovery of all the components contained in the agri-food waste it produces, aligning with the principles of Green Chemistry and Circular Economy.

Globally, this study represents a proof-of-concept of a 2nd generation biorefining process based on locally available biomass.

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Zinc oxide development for wastewater treatment by photocatalytic degradation of the methylene blue dye

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Heterogeneous photocatalysis is a recent technique employed in wastewater treatment in order to mineralize organic pollutants. For this purpose, zinc oxide-based catalysts depict an interesting and promising way [1] for degradation under sunlight compared to titanium oxide with a better visible light absorption [2].

Zinc oxide have been prepared according a eco-friendly green method. Metal precursors used were acetate and nitrate zinc. Plants present in the process allowed the formation and the self-assembling of ZnO during the crystal growth thanks to the expanded chemical family of polyphenol which act as reductants [3]. Two synthesis processes were tested: a hydrothermal method and a hotplate synthesis. Crystalline and organic matter-free compounds obtained after annealing were characterized with diffractive reflectance spectroscopy (DRS), X-ray diffraction, Fourier transform infrared spectroscopy (FTIR) and scanning electron microscopy (SEM). We tested the performance of the material based on its ability to oxidize methylene blue over time under simulated sunlight. The concentration of this pollutant has been determined using UV-visible spectroscopy by absorbance measurements.

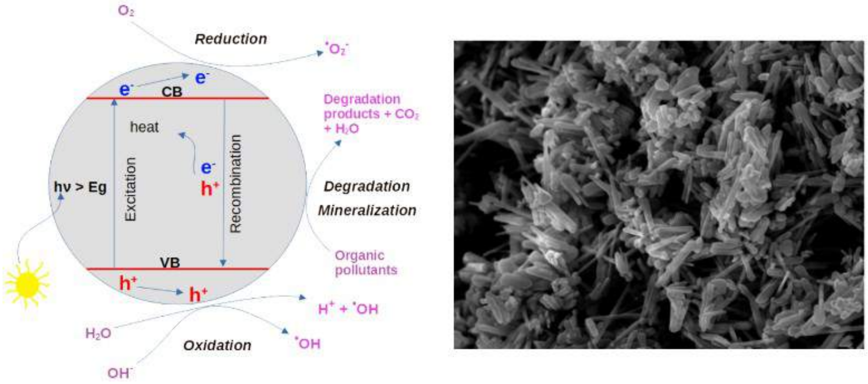

Figure 1 : Principle of heterogeneous photodegradation using plant-based ZnO

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Session 3: Organic and Bio-Organic Chemistry

Post-industrial recycled polypropylene for automotive application: mechanical properties after thermal aging

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Plastics have several vital functions in the economy and in our daily lives and they offer solutions to tackle a number of societal challenges. This includes its application as innovative lightweight materials in cars to save fuel and cut off the CO_2 emissions. However, the production, use, consumption and waste treatment of plastics is associated with several environmental problems and there is an urgent need to also tackle these issues.

In July 2023 the European Commission proposed a new regulation within the framework of the automotive industry, which is expected to have substantial environmental benefits, including an annual reduction of 12.3 millions tons of CO_2 emissions by 2035. The cited regulation focuses the attention on enhancing the circularity of the automotive sector, covering the design, production and end-of-life treatment of vehicles beyond setting a target about the recycled content: 25% of the plastic used to build a new vehicle will be required to come from recycling, of which 25% must be recycled from end-of-life vehicles1. This project arises from the need to build the rate of degradation of a polypropylene trim used on a vehicle as a result of aging processes due to environmental stress to which a component is subjected during the vehicle lifetime. Moreover, in this work, recycled materials are also considered with the aim of comparing their performance with the virgin ones and evaluate the substitution of the latter to increasingly embrace a green policy of the automotive industry. The materials selected for the study are PP from post-industrial origin and virgin PP filled with carbon black and talc at different concentrations, both for internal and external applications. The materials underwent two different types of thermal stress, a dry heat ageing and a thermal cycle ageing, according to the internal or external application of the vehicle. As regards the aging processes, all the materials tested showed an onset of degradation which did not affect the performance of the samples, indeed, they were shown to have good resistance to aging, not experiencing any decrease in mechanical properties or variations from a thermal point of view.

As regards the comparison between virgin and recycled PP, it can be stated that the characteristics are comparable.

Reference

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Protease-activable di-alcoxyamine as contrast agent for MRI applications

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Inflammatory diseases are a major burden in advanced countries. For instance, Chronic Obstructive Pulmonary Disease is the third cause of death in the world according to the World Health Organization.[1] Such diseases display overexpressed proteases carrying out extensive tissue damages, that can also be used as biomarkers for clinical diagnosis using molecular imaging. In order to lay anatomical images with improved contrast required for molecular imaging of proteolysis, Overhauser-enhanced Magnetic Resonance Imaging (OMRI) has been developed recently.[2,3] The aim is to benefit from this technology using nitroxydes released locally by protease-activated alcoxyamine as contrast agents to increase MRI contrast.

Therefore, using the specificity of those enzymes, the point is to design and synthesise a di-alcoxyamine that can undergo spontaneous homolysis in an inflammatory environment, and assess its ability to release nitroxides. The synthesis of such alcoxyamines has been carried out and its homolysis properties are currently assessed.

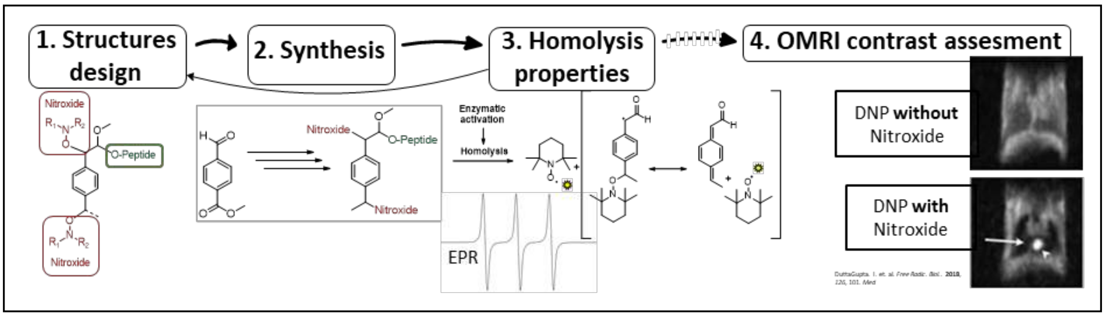

Figure 1 : organization of the steps to achieve OMRI contrast improvement

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MESOPOROUS SILICA MICROSPHERES CONTAINING TRANEXAMIC FOR HEMOSTATIC APPLICATION.

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Uncontrolled bleeding is considered one of the most common causes of potentially preventable death either in the military or the civilian field. Early bleeding management is considered vital to decrease the risk of mortality. For this purpose, a novel hemostatic material based on mesoporous silica microspheres (MSM) and loaded with tranexamic acid (TXA), an antifibrinolytic drug widely used to manage the excessive blood, was developed to be used during first-aid procedures. The main goal was to achieve a material with large pores (>15 nm) as they present better hemostatic performances, and able to release TXA within an hour, according to the CRASH-2 (Clinical Randomization of an Antifibrinolytic in Significant Hemorrhages-2) trial to achieve maximum efficiency.

MSM were synthesized under acidic conditions using Pluronic P123 as a template agent, TEOS as a silica precursor and mesitylene as a swelling agent. The obtained material was characterized by particles size ranging from 1.5 µm to 5 µm and average pore diameter of 25 nm. TXA was loaded (with a final content of 4.7 %w/w) through the incipient wetness impregnation method using water as a solvent. The XRD analysis revealed that TXA was distributed inside MSM in a non-crystalline form. The FT-IR analysis showed that TXA molecules were dispersed on the mesopore silica surface in the zwitterionic form.

A blood clotting time (BCT) test was performed to evaluate the hemostatic efficiency of the unimpregnated and impregnated sample. The results of the test showed that the clotting time was significantly shortened by both samples with respect to control. A hemolysis assay was carried out to evaluate the hemolytic activity of MSM. The result of the assay indicated that the sample presents good hemocompatibility.

Finally, a preliminary *in vitro* release test was performed to verify the possibility of a fast release of TXA from the microspheres. The test showed that the material was able to deliver TXA to the release medium within one hour, which makes this carrier suitable to control hemorrhages during emergencies as requested by the CRASH-2) trial.

In conclusion, the achieved results evidence that the proposed system is promising for the development of new topical hemostats suitable for bleeding control in emergency situations.

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Protease-activable prodrugs specific for Fibroblast Activation Protein

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Cancer is still a main cause of death worldwide, leading to one in six deaths which is nearly ten million per year, according to the World Health Organization (WHO). Many treatments are being developed to try to reduce the number of patients. With this in mind, we report a protease-activable alkoxyamine synthesis. As previously carried out, alkoxyamines are known to be molecules that spontaneously homolyse into two free radicals: a nitroxide and a highly reactive cytotoxic alkyl radical [1][2]. Four substrates were designed and synthesized to check spontaneous homolysis of dipeptidyl alkoxyamines, verified by EPR-kinetic experiments. Results showed an activity for cancer cells but no specificity. This led to the synthesis of the same molecule with two more amino acids, targeting Fibroblast Activation Protein (FAP), present in most of carcinomas. Enzymatic tests are currently under investigation for the biological part.

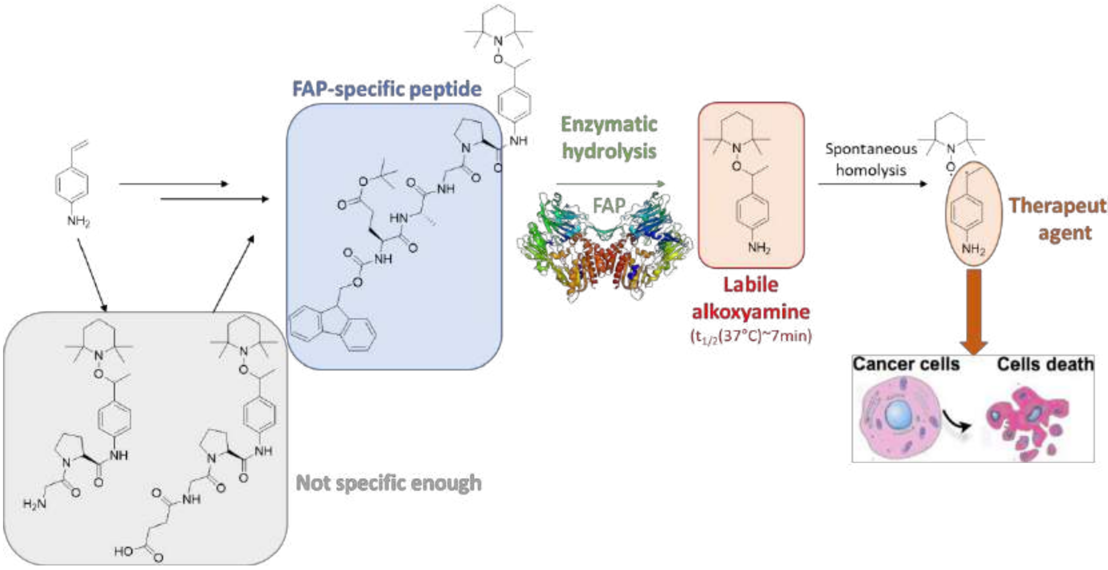

Figure 1: Target molecule synthesized and its mode of action

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Exploiting spectroscopy and chemometrics for bloodstain dating in forensic chemistry

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In a forensic context, non-destructive techniques are most desirable, due to the importance of preserving the specimens and to enable repeated analysis by all parts involved. For this reason, spectroscopies appear to be particularly attractive. By the way, the complex signals produced by those analytical techniques make it necessary to use chemometrics to extract useful information from the data.

An interesting topic in which spectroscopy and chemometrics can be exploited in forensic chemistry is the determination of time since deposition of bloodstains. Bloodstains dating may, indeed, represent a crucial evidence in resolving many cases of forensic interest. Even though this topic has been investigated with limited success since the 1960s, most studies focused on ultraviolet-visible (UV-Vis) spectroscopy, while few were conducted in the infrared spectral region, with only a handful concerning near-infrared (NIR) spectroscopy.

The final goal of the present work is to compare the performances of NIR spectroscopy for bloodstains dating with those of UV-Vis in the prospect of real-casework implementation. In pursuit of this goal, capillary blood was sampled and subjected to a 16-day aging, during which it was repeatedly analysed using both spectroscopic methods. Subsequently, chemometrics was applied to process the spectral data and independently assess the methods' performance. Classical preprocessing methods were used together with more targeted techniques (class centering) whose benefit was highlighted by principal component analysis (PCA). Lastly, partial least squares (PLS) regression models were computed to evaluate the effectiveness of both spectral methods in estimating the time elapsed since blood trace deposition. Comparable root mean square errors in prediction (RMSEP) were observed for both techniques, featuring an improvement with respect to the existing literature for NIR spectroscopy. Data fusion strategies for a multi-instrumental platform were also explored.

Subsequently, the effects of environmental conditions, light exposure and substrate on sample ageing were studied. Controlled ageing was carried out with the use of a climatic chamber and the ageing of samples deposited on cotton, polyblend fabric, metal and glass was followed for two weeks through NIR and Raman spectroscopies. Feasibility studies were also performed applying hyperspectral imaging for a contemporary identification and dating of bloodstains.

The results indicated that NIR spectroscopy integrated with adequate chemometric strategies deserves increased appreciation in forensic bloodstain dating.

Synthesis of Azaborine Heterocycles Through Ruthenium-Catalyzed Enyne Metathesis

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Azaborine heterocyclic compounds have attracted widespread attention in material science and biomedical research.[1] The enyne metathesis reaction has become an important tool for organic synthesis of multifunctional natural products and preparation of pharmaceuticals.[2] Although Schreiber and coworkers developed an effective boronic ester annulation using enyne metathesis,[3] this concept has never been extended to nitrogenated analogues. Therefore, a novel and green synthetic route for the preparation of functionalized polycyclic azaborine skeletons via a ruthenium-mediated ring-closing enyne metathesis transformation of alkynyl B-anthranilamide (aam) has been developed. In this context, B(aam) tethered enynes were engaged with Grubb catalyst to affordes the corresponding *exo*-cyclic compounds in good yields (25 examples, yields up to 89%).[3] This methodology was efficiently optimized and was performed in dimethyl carbonate[4] as green solvent: it provided a direct access to functionalized azaborine scaffolds displaying dienes, that may be useful for further functionalization such as Diels-Alder reaction. Preliminary results will be presented, scope and limitations as well as reaction on gram scale.

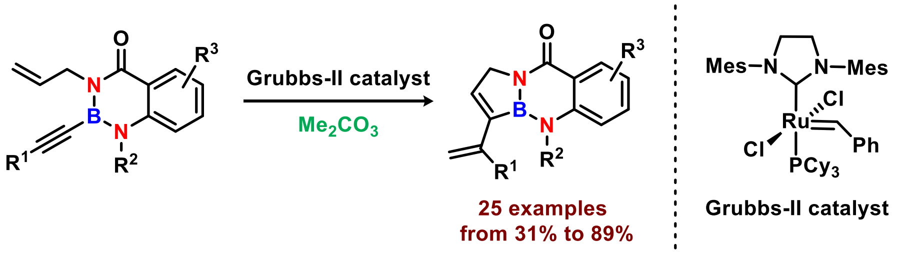

Figure 1: Ru-catalyzed enyne metathesis reaction

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Study of a new mode of activation of alkoxyamines by radical addition leading to a cascade reaction.

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For the past few decades, alkoxyamines, as well as their activation and homolysis mechanisms were investigated. In fact, their activation and usefulness in polymer chemistry, in biology and in materials science depend on the fragility of the C-ON bond, the type of formed radical and formed nitroxide. It is therefore necessary to adapt the activation mechanism according to the application in which we want to use alkoxyamines.

There are 3 main activation mechanism for alkoxyamines:

- Physical: Thermal activation, ultrasound, light activation, electrochemical activation, or electrostatic activation;
- Biological: By proteolysis (protonation, hydrolysis, solvent);
- **Chemical**: Protonation/deprotonation, chemical modification, non-covalent interactions, chemical oxidation, or **radical activation**.

In 2022, Chechik and al.[2] reported a new method for trapping short-lived radicals, based on a homolytic substitution reaction SH2′. This cascade reaction between radicals and alkoxyamines can be seen as a chemical activation mechanism. The presence of these molecules can reduce the rate of polymerization reaction. Using this methodology, different alkoxyamines were prepared in high yield. An investigation of homolysis kinetics as well as the efficiency of trapping radical was realized as a function of several parameters (temperature, concentration, type of radical and group on the allyl function).

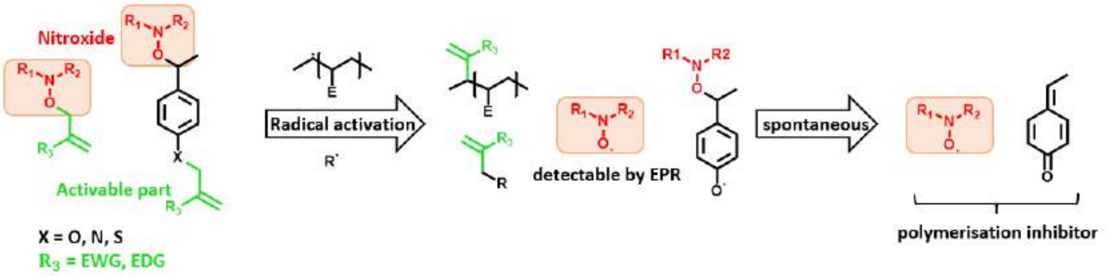

Figure 1: Principle of alkoxyamine activation by radical addition to an allyl.

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Smart Material: The Surface Functionalization Of Nanostructured *Magnetorheological Electrolytes With* The Use Of Click-Chemistry

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Today, more than ever, the interest in the reduction of pollution and waste, and in the displacement of fossil fuels is high. REMAP (Reusable Mask Patterning) [1] is a project funded by the European Union that wants to revolutionize the microfabrication sector (e.g. for advanced photovoltaic applications) by developing a greener surface patterning technique. REMAP's basic idea is to design so-called *magnetorheological electrolytes* (MREs) [2], fluids based on magnetic nanoparticles (NPs) and electrolytes that modify their apparent viscosity upon modulation of microstructured magnetic field gradients onto a substrate. Specifically, we are crafting the MRE properties to form infinitely reusable masks that would represent a huge step forward in the field of microfabrication with respect to standard lithography.

For the intended application we decided to create organic custom-made ligands that can be covalently bound to the surface of NPs using click-chemistry, to be able to drastically change the surface properties of NPs (*figure 1*). The synthetized ligand must fulfil the following key factors: i) high masking efficiency, ii) colloidal stability in aqueous media, and iii) fast redispersion of NPs in the absence of a magnetic field gradients.

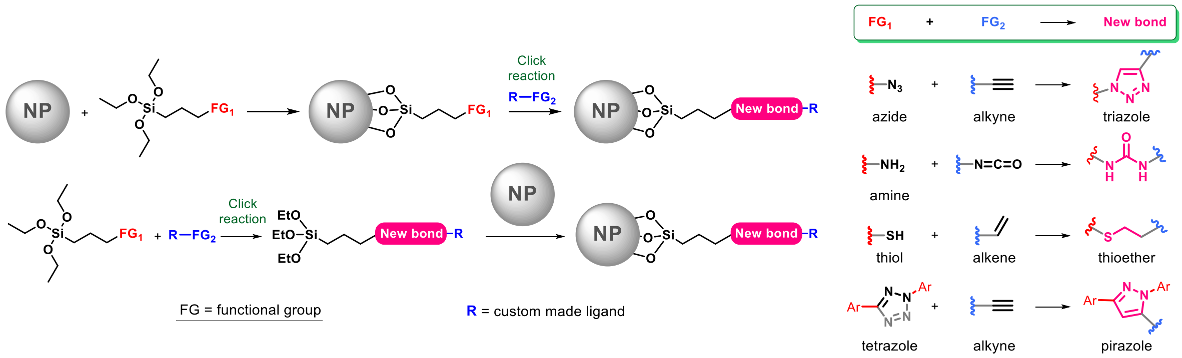

Figure 1 : Possible strategies and click reactions that can be used for the surface functionalization

Herein, we present the design and the synthesis of the organic ligands, and their application in the surface functionalization of NPs.

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[2] K. Shu., C. Wang, W. Li, T. Bussell, J. Ding, *Current Opinion in Electrochemistry,* 2020**,** *21*, 297-302

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Session 4: Material Chemistry

Multifunctional single-molecule magnets containing S-donor atoms

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The field of molecular magnetism has witnessed remarkable progress in the last decades, fuelled by the discovery of single-molecule magnets (SMMs).[1,2,3] Research into SMMs saw the introduction of lanthanide ions into these complexes thanks to their high spin and strong intrinsic magnetic anisotropy.[4,5] Some lanthanide ions also have very specific optical properties, since *f-f* transitions are forbidden by Laporte's rule. Among the diverse elements employed as ligands, sulphur stands out as a particularly intriguing coordinating atom due to its soft-donor character and its potential to impact both the magnetic and luminescent properties of metal complexes.[6] The aim of this work is to develop new SMMs based on Ln^{3+} ions and β-thioketonate ligands, and the study of the correlation between their structures and properties.[7] A new family of Ln^{3+} mononuclear complexes based on β-thioketonate ligands has been isolated as single crystals. Magnetic and photophysical properties of a complex have been studied and rationalized by *ab initio* calculations (Figure 1).

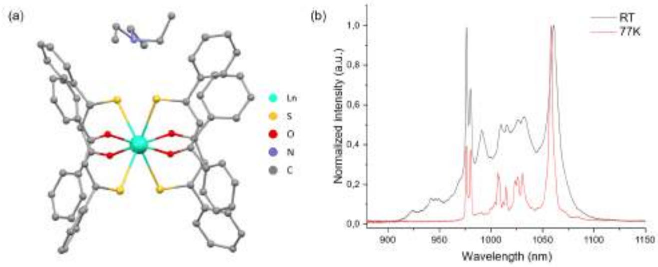

Figure 1: Cristal structure of $(Et_3NH)[Ln(L)_4]$ (L = 1,3-diphenyl-3-thioxopropan-1-one). H-atoms removed for clarity (a). Room and low temperature solid-state emission spectra of $(Et_3NH)[Yb(L)_4]$ (b).

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Mesoporous Pd/ceria-praseodymia catalysts for enhanced methane oxidation in dry and wet conditions

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Natural gas is currently considered a strategic fuel for Europe's energy transition, as a bridge solution in the path towards complete decarbonization. Nevertheless, unburned methane emissions associated with the use of this resource represent a critical issue, due to the high global warming potential of CH_4. In recent years, Pd/CeO_2 materials have proven to be effective catalysts for the abatement of methane through its total oxidation, thanks to the synergistic interactions between the noble metal and the redox support. Although these materials have already been extensively studied, further efforts are needed to limit the loss of activity at high temperature due to the PdO-Pd transition and the detrimental effects of water. In this perspective, recent studies proved that the introduction of a limited amount of Pr in the ceria support (10 at%) allows to obtain more active catalysts [1]. In the present work [2], three different synthesis routes were used to prepare high specific surface area mesoporous supports, consisting of pure CeO_2 and 10 at% Pr-doped ceria (Ce90Pr10). Nano-structured spheres were obtained with a microwave-assisted synthesis, dumbbell-like particles were produced through a urea-based hydrothermal method, and ordered mesoporous oxides were prepared by using SBA-15 as hard-template. The six materials were then impregnated with 2 wt% Pd and calcined at 500 °C. All the samples retained their high surface area after impregnation (75 – 110 m^2 g^{-1}), allowing a good dispersion of palladium. No significant structural or morphological differences were observed upon Pr doping, but a higher Pd oxidation state was induced by Pr-doped supports. All these catalysts exhibited similar activity in dry conditions, achieving almost complete CH_4 oxidation at 400 °C, with a really remarkable improvement with respect to analogous low surface area materials. A promoting role of Pr was instead noticed in wet conditions, thanks to its ability to counteract water-induced deactivation phenomena.

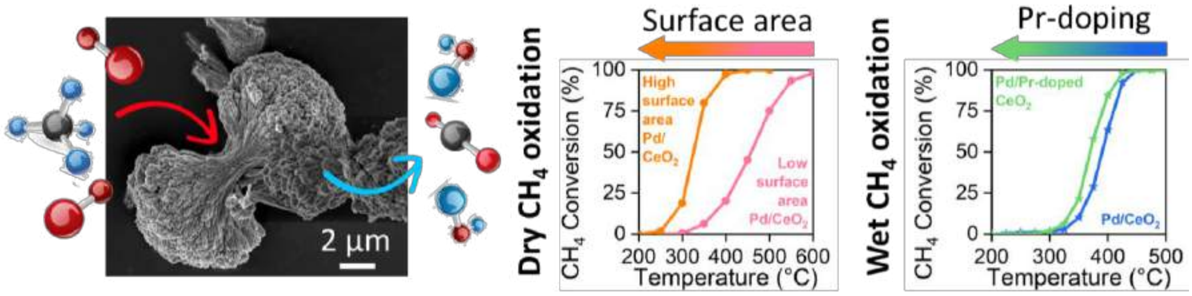

Figure 1 : FESEM image of a dumbbell-like structure in Pd/Ce90Pr10, with a scheme of the reaction; conversion curves illustrating the role of surface area and Pr doping on dry and wet CH_4 oxidation activity.

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Synthesis of photocatalytic cerium oxide: optimization using design of experiment

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Rapid progress in industrialization in recent years has led to an increase in the release of pollutants into the environment. This pollution mainly arises from the discharge of industrial waste and urban effluents into water bodies, posing a threat to both aquatic ecosystems and human beings.[1,2] Advanced oxidation through heterogeneous photocatalysis is one of the proven methods for the mineralization of refractory organic pollutants such as dyes, pharmaceutical residues, and pesticides.[3–6] The objective of this work is to synthesize innovative photosensitive composite materials based on metal oxides capable of achieving the complete mineralization of these compounds rapidly.

Modern developments in nanotechnology have allowed to improve the performance of photocatalytic and solar energy absorption processes owing to higher surface areas and efficient charge separation in semiconductor nanomaterials. Among the semiconductor studied, cerium oxides remain underexplored even though they could provide efficient visible-light absorbing photocatalysts. In our case, we want to synthesize a composite formed by two semiconductors, one of type p and one of type n, to create a p-n heterojunction and thus achieve superior photodegradation performance compared to the semiconductors taken separately. Cerium oxide is a good candidate as a n-type semiconductor, notably due to its stability at room temperature.

Currently, the key factors that could impact the synthesis of cerium oxide are still poorly understood. Therefore, we created a design of experiment to optimize the synthesis of cerium oxide, identify key factors influencing the synthesis, and understand the underlying mechanisms. Four factors will be studied: precursor concentration, surfactant concentration, surfactant nature, and the pH of the reaction medium. The aim is to comprehend the impact of these factors on the crystallinity, morphology, gap energy, and photodegradation performance of the synthesized oxides.

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Impact of stoichiometry and size on the persistent luminescence in $Cs_2(Na_{1-x}Ag_x)InCl_6:Mn^{2+}$ double perovskites

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Persistent Luminescence (PeL) is a peculiar type of luminescence where a material, after a proper activation (by X-rays, electrons, or ultraviolet/visible light), continues to emit radiation even for several hours once the excitation has ceased. PeL occurs due to the existence of metastable trap levels that can temporarily store the excitation energy. Most of the PeL materials (> 75%) are oxides; recently, PeL has been discovered in bulk halide double perovskites (HDPs) too. In particular, after UV activation, $Cs_2(Na_{1-x}Ag_x)InCl_6:Mn^{2+}$, in form of single crystals (SCs) have a red emission (~ 620 nm) that lasts for more than 1 hour [1-3]. Here, we explored the influence of stoichiometry and size on the PeL behaviour in HDPs. We synthesized different compositions of SCs pertaining to the $Cs_2(Na_{1-x}Ag_x)InCl_6:Mn^{2+}$ system. Then, we prepared the homologues in forms of micrometric and nanometric crystals (nanocubes - NCs and nanoplates - NPs). To gain inside this behaviour we carried different optical analyses: photoluminescence excitation, photoluminescence, PeL and thermoluminescence (10K to 300K; 300K to 450K). Our results showed how the PeL is strongly influenced by the materials size, *i.e.* PeL disappears from bulk to nano-structured samples (Figure 1). We hypothesise that this phenomenon is due to a different trap depth of bulk and nano samples.

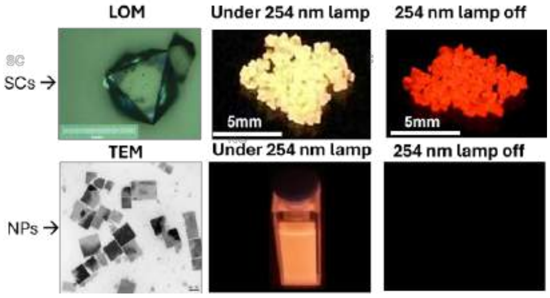

Figure 1. Different size impact PeL of $Cs_2(Na_{1-x}Ag_x)InCl_6:Mn^{2+}$: microscopies show morphologies (left), samples under 254 nm lamp (centre), samples when the 254 nm lamp is off (right).

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Cobalt ferrite $Co_xFe_{3-x}O_4$ as photocatalysis under visible light irradiation: experimental and theoretical approach.

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The precursors and the methods of $Co_xFe_{3-x}O_4$ particles synthesis have strongly influenced several parameters like particle size, crystallinity, morphology, and homogeneity [1]. Cobalt ferrite nanoparticles have been synthesized by a hydrothermal method using nitrates as precursors and characterized using X-ray diffraction (XRD), transmission electron microscopy (TEM), Mott-Schottky analysis, UV-visible diffuse reflectance spectroscopy and BET technique. The photocatalytic performance of the synthesized $Co_xFe_{3-x}O4$ nanoparticles was evaluated for the removal of Rhodamine B from water under visible light irradiation. The response surface methodology (RSM) based on the central composite design (CCD) model was used to evaluate the following set parameters: pH, dye concentration and catalyst weight and to optimize the RhB removal. The XRD and TEM analyses showed that the nanoparticles produced are single-phased with a nano-octahedral shape and a size less than 10 nm. UV-Vis spectrophotometry revealed distinct optical band gap values for $CoFe_2O_4$ and $Co_{1,5}Fe_{1,5}O_4$ of 2.32 eV and 2.01 eV, respectively. In addition, the developed $Co_xFe_{3-x}O_4$ powders showed remarkable efficiency in the photodegradation of an aqueous Rhodamine B (RhB) solution. The results showed that the pH of the solution was the most effective parameter for the photocatalytic removal of RhB by $Co_xFe_{3-x}O_4$. The optimum condition to achieve the highest photocatalytic degradation with minimum catalyst weight is obtained for a 6-ppm initial dye concentration, at pH 9. The predicted efficiency at the optimum condition is closed to 100% according to the experimental results. The experimental photodegradation efficiency of $Co_xFe_{3-x}O_4$ has been investigated and the RSM methodology allowed to optimize the photocatalytic RhB removal (100%) for a set of three experimental parameters.

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Atomic Layer Deposition of the NiO_x using new precursors with different oxygen sources

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NiO_x thin films have attracted tremendous attention owing to their outstanding chemical stability, good magnetic and catalytic properties[1]. Furthermore, the tuning resistance state of the NiO_x films with external electric field makes this as a potential candidate for memristor devices[2].

NiO_x thin films have been prepared by different deposition techniques, such as including physical vapor deposition (PVD), chemical vapor deposition (CVD), and atomic layer deposition (ALD). Among these, ALD is a more precise technique to grow thin conformal films with fine-tuning of both composition and thickness. However, ALD of NiO_x is not well developed yet. The commonly used nickel precursors for ALD process are $Ni(Cp)_2$, $Ni(MeCp)_2$, $Ni(EtCp)_2$, $Ni(dmamp)_2$, $Ni(dmamb)_2$, $Ni(acac)_2$, $Ni(apo)_2$, $Ni(dmg)_2$, $Ni(thd)_2$, and $Ni(amd)_2$ in combination with ozone, water, hydrogen peroxide, or oxygen plasma[1]. The major disadvantages associated with these precursors are low volatility, thermal instability, and poor reactivity or narrow ALD window. Some of these precursors are expensive or highly difficult to synthesize. The aforementioned difficulties indicate that developing an ALD recipe for the NiO_x using new precursors is pertinent. Our current work explores the possibilities of such a recipe.

In this work, we have investigated different Ni-precursors such as Ni-ketoiminates, specifically, $[Ni(ipki)_2]$,[3] and heterolyptic amidinate-based Nickel complex [(Ni(amd)X]. The [(Ni(amd)X] was provided by Air Liquide. These different precursors combined with different oxygen sources (H_2O and O_3) resulted in high-quality NiO_x thin films. The prepared thin films were subjected to morphological (SEM, TEM) and chemical investigations (XPS). The SEM and cross-sectional TEM studies indicate that the NiO_x films are uniform and exhibit a columnar morphology. The XPS analyses confirm the stoichiometry of NiO_x films. From the growth characteristics, it is found that the Ni precursors have a strong effect on the GPC. Similarly, the oxygen source affects GPC but it also influences the morphology of the layer leading to significant roughness variations (observed by X-ray Reflectivity and AFM). The use of H_2O can also result in a nucleation delay. After comprehensive optimization of the ALD process with [(Ni(amd)X] precursor, it has been possible to reach one of the highest growth rates of 1.3 Å/cy, with a wide temperature window (100 to 175 °C) with ozone. In this process, when the reaction temperature reaches 125°C, the films begin to exhibit polycrystallinity, and the crystallinity is enhanced with increasing deposition temperature (Fig.1). The same [(Ni(amd)X] precursor also reacted well with water, giving a GPC of 0.8 Å with a temperature window from 100 to 150 °C. With the use of Ni-ketoiminates, the growth rate could be enhanced considerably with a GPC of 0.48 Å in combination with O_3 at a higher temperature.

After the comprehensive study on the optimization of the NiO_x with three new precursor combinations, we further studied the optical and electrical properties of these films.

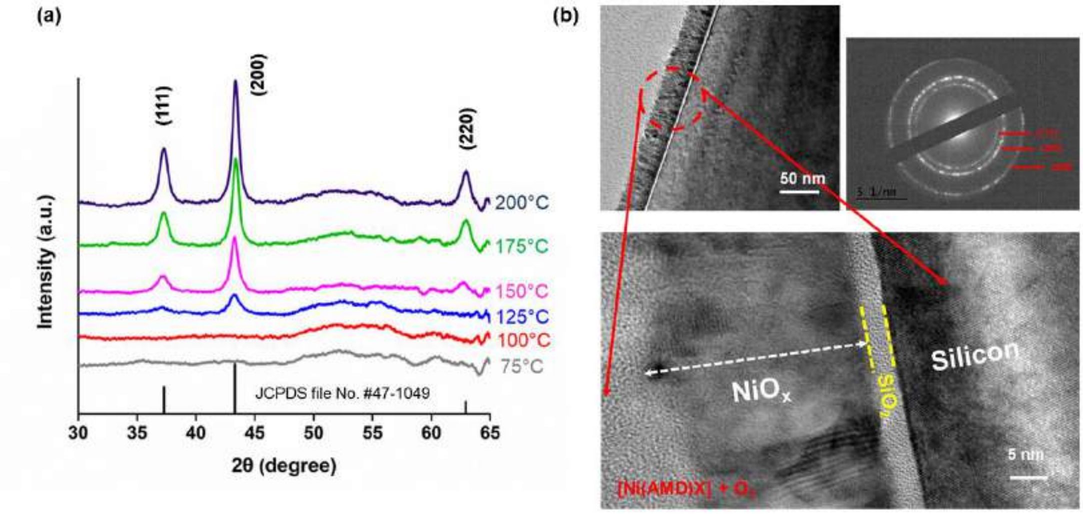

Fig 1. (a) XRD and (b) cross-sectional TEM of the NiO_x made by [(Ni(amd)X] and O_3 precursor combinations

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Chemistry Area:
☐Material Chemistry

11th Italian-French Chemistry Days
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April 4th-5th 2024

Electrochemical characterization of NiFe nanoparticles on colloidal CeO_2 for Anion Exchange Membrane Electrolysers

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Hydrogen is gaining momentum as a fuel of the future because it significantly reduces CO_2 emissions, has high energy density and versatility, and can be integrated easily with renewable energy[1]. Anion exchange membrane (AEM) electrolysis is an emerging technology which can produce hydrogen using non-expensive transition metal catalysts at high energy efficiency. NiFe class of catalysts have garnered significant attention due to their promising catalytic performances, cost-effectiveness, and relative abundance. These bimetallic catalysts, leveraging the synergistic properties of nickel and iron, have showcased their prowess, particularly in the oxygen evolution reaction (OER) segment of water splitting. In this study we evaluate Nickel and Iron nanoparticles dispersed on colloidal CeO_2 for their catalytic activity and performance for applications in AEM water electrolysis for water splitting reactions.

We synthesized catalysts with multiple Ni:Fe ratios on 30 weight percent commercial colloidal CeO_2 through chemical reduction method using $NaBH_4$. Morphological and structural properties of the catalysts are studied by using Scanning Electron Microscopy (SEM), Transmission Electron Microscopy (TEM) and XRD. N_2 Physisorption studies show a BET surface area in the range of 20-80 m^2/g. For electrochemical characterization, we conducted Cyclic Voltammetry (CV) for Oxygen Evolution Reaction (OER) in a rotating disc electrode setup using 1 M KOH electrolyte.

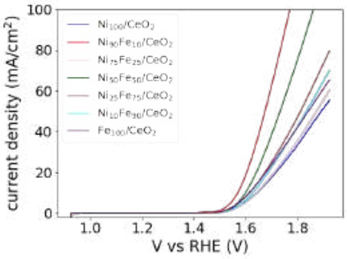

Figure 1 : The Linear Sweep Voltammetry measurements of NiFe/CeO_2 catalysts

Our results indicate that $Ni_{90}Fe_{10}/CeO_2$ has the highest catalytic activity among the catalysts with an overpotential of 329 mV at 10 mA/cm^2 current density. Tafel slope analysis shows lowest Tafel slope for $Ni_{90}Fe_{10}/CeO_2$ catalyst which suggests faster reaction kinetics and lower overpotentials higher current densities. Chronopotentiometry studies were conducted for 2 hours and all the catalysts were found to be stable. Nyquist plots and equivalent circuits show $Ni_{90}Fe_{10}/CeO_2$ catalyst has the lowest charge transfer resistance and higher efficiency compared to other compositions. These findings highlight the importance of Fe addition to improve the catalytic activity of Ni catalysts as well as the stability improvement provided by a catalyst support like colloidal CeO_2.

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Kinetic study of sustainable preparation of organic-inorganic hybrid materials by grafting procedure

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Organic-inorganic hybrid materials find many and important applications in different fields, such as catalysis, nanomedicine, electronics and many others. Generally, the synthetic approach used to prepare organic-inorganic hybrids is the grafting method, which allows the inorganic support to be functionalized with organic functionalities (Figure 1). The grafting procedure is usually performed in toluene, a toxic and non-renewable solvent [1,2,3]. In this work, we explored the use of renewable, cheap and non-toxic compounds, i.e. α-pinene, β-pinene, dimethyl carbonate, (+)-limonene and 2- methyltetrahydrofuran as solvents for a green grafting method. The kinetic of the grafting reaction between mesoporous ordered silica (MCM-41) and aminopropyltriethoxysilane (APTS) with pendant amino groups was followed by 1^{H} NMR spectroscopy at increasing time. This reaction is widely studied [4] and used to prepare hybrid heterogeneous catalysts with basic sites for many types of catalyzed reactions such as hydroformylation, Knoevenagel condensation, heterocyclic chemistry, cross-coupling reactions and many others.

Finally, the hybrids synthesized with the different solvents were characterized by FTIR spectroscopy and thermogravimetric analysis and compared to the same hybrid obtained using toluene as a solvent. Among all solvents, 2-methyltetrahydrofuran has revealed promising features for its use as solvent in grafting reactions both in terms of rapid kinetic of the grafting reaction and in terms of properties of the obtained hybrid with respect the hybrid obtained with toluene.

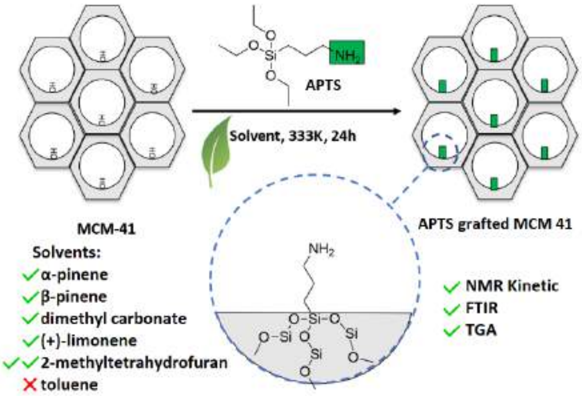

Figure 1. Green grafting procedure and characterization

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Session 5: Chemical Biology

AN INTEGRATED MACHINE LEARNING MODEL TO SPOT PEPTIDE BINDING POCKETS IN 3D PROTEIN SCREENING

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Peptide-protein interaction systems play a pivotal role to tackle the onset of several pathologies such as cancer and neurodegenerative diseases. The spread of machine learning and artificial intelligence likely changed the perspectives into peptide-protein molecular recognition although the identification and characterization of putative druggable peptide interacting cavities is still an open challenge. In this work, we present an innovative machine learning model based on Linear Discriminant Analysis (LDA) demonstrating to be highly predictive in detecting putative oligopeptide-binding regions [1].

Starting from a collection of 439 high-quality pockets derived from an *in house* dataset of peptide-protein crystallographic complexes previously investigated in terms of structural and energetic properties [2], three sets of well-established peptide-binding regions were selected through a Partitioning Around Medoids (PAM) clustering algorithm based on morphological and energetic 3D GRID-MIFs molecular descriptors. Next, LDA-based protocol implemented in BioGPS [3] automatically detected the best GRID-MIFs combination able to discriminate peptide binding cavities with respect to the empty ones. This classification model proved successfully to discern actual interacting peptide binding cavities from the rest of the protein partner returning AUC = 0.86 and early ROC enrichment at first 5% equal to 0.48. Noteworthy, LDA-based model has been successfully challenged on two external datasets of crystallographic peptide-protein complexes proving to be effective to the peptide drug discovery, including 3D protein virtual screening campaigns.

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Microwave-assisted Extraction of Phytochemicals from *Cannabis sativa* L. Inflorescences with 2-methyloxolane

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Abstract: In this study, 2-methyltetrahydrofuran, also known as 2-methyloxolane (2-MeOx) [1], was studied for phytochemicals extraction from *Cannabis sativa* L. inflorescences. Conventional dynamic maceration showed that 2-MeOx extracted a similar quantity of CBD (75.45 mg CBD/g matrix) compared to ethanol (77.71 mg) and hexane (75.09 mg). Additionally, using water-saturated solvent (2-MeOx 4.5% water) resulted in the highest recovery of CBD (81.30 mg CBD/g matrix) and polyphenols. Furthermore, 2-MeOx exhibited excellent recovery of hemp terpenes. We intensified the extraction process using microwave irradiation, which enhanced extraction efficiency and reduced extraction times. Response surface methodology was used to optimize microwave-assisted extraction (MAE) in batch by varying extraction time, microwave power, and solvent water content. Two optimized conditions yielded higher CBD compared to dynamic maceration: 86.76 mg CBD/g matrix (water 1.72%, power 1000 W, time 20 min) and 84.18 mg CBD/g matrix (water 3.65%, power 300 W, time 2 min). The feasibility of extraction and decarboxylation of dried inflorescences directly in the microwave reactor was also studied. However, microwave-assisted decarboxylation-extraction (MADE) with 2-MeOx resulted in less efficient decarboxylation of CBDA compared to ethanol. Finally, a new single-mode microwave reactor for flow extraction was tested. Approximately 75.48 mg CBD/g DM were extracted in flow with 2-MeOx (3.65% water) at 60 °C in 10 minutes. Further optimisation is required for flow-through MAE with 2-MeOx.

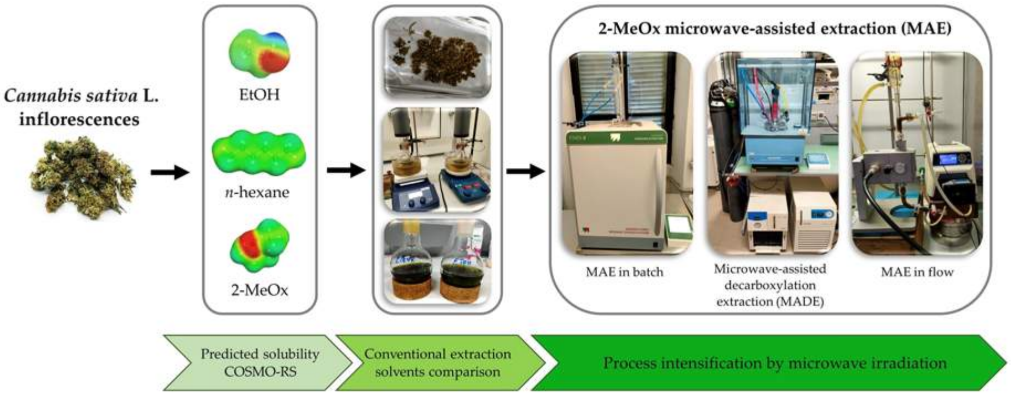

Figure 1: Graphical abstract

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Novel chitosan extraction from dung beetle and its potential application for the adsorption of cationic and anionic dyes

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The widespread use of organic dyes in various industrial sectors, including textiles, leather goods, and printing, has raised significant environmental concerns due to their persistence and potential toxicity [1]. Conventional methods of dye removal often fall short in efficiently and sustainably addressing this issue. There is a growing need for innovative solutions that not only remove dyes from wastewater but also align with the principles of sustainability and environmental responsibility. In this context, chitosan, a natural polysaccharide derived from chitin, has shown potential in dye removal [2]. The valorization of new sources of chitosan derived from insects, one of the most diverse and abundant groups of organisms on the planet, for dye removal offers an environmentally friendly and highly efficient alternative. Among them, dung beetles, produce chitin-rich exoskeletons as a part of their natural life cycle. In the current study, the focus is on evaluating the potential of chitosan from dung beetle, *Heteronitis castelnaui*, as an adsorbent for both cationic and anionic dyes. The research involves the extraction and characterization of chitosan from dung beetle sources using various analytical techniques, including FTIR, SEM, NMR, ash content, and deacetylation degree. The obtained chitosan was used to form hydrogels and then evaluated for its adsorption capacity through batch adsorption experiments using cationic dyes (methylene blue) and anionic dyes (methyl orange) as model pollutants. Furthermore, the kinetics of the adsorption process were analyzed using pseudo-first-order and pseudo-second-order models to understand the rate of adsorption. The maximum adsorption capacities were determined using Langmuir and Freundlich isotherm models, providing insights into the adsorption behavior.

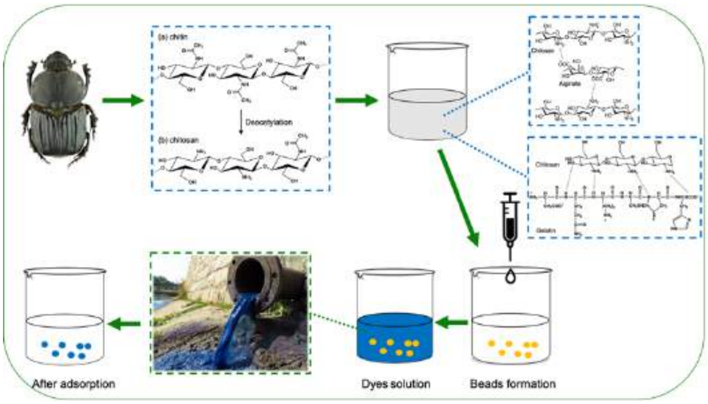

Figure 1 : Graphic

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Fluorescent nucleobases for bright PNA

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Peptide nucleic acids (PNA) play a pivotal role in chemical biology, easily interacting with DNA and RNA thanks for sharing the same nucleobase alphabet.[1,2] They have been already evaluated in antisense and antigene therapies, gene editing but also nucleic acid sensing and imaging.[2,3] The replacing of natural occurring nucleobases with emissive isomorphic analogues into PNA represents a unique strategy to impart intrinsic fluorescence while maintaining efficient paring aiming to overcome limitations of fluorophores' tagging.[4]

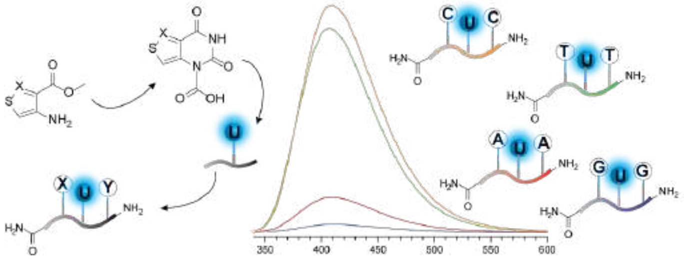

Figure 1: Emissive PNA.

Herein we present the complete studies of emissive thieno[3,4-*d*]pyrimidine nucleobases along with the successful synthesis of PNA short sequences incorporating a fluorescent base (Figure 1). Our studies confirm how the herein synthesized base is compatible for insertion into PNA sequences. Moreover, PNA optical properties have been analyzed varying the short sequences' composition to deeply understand the emissive traits in relation to the neighboring bases. These preliminary results highlight that a fluorescent analogue of Uracil can be easily used for PNA synthesis while conferring significant modular luminescence.

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Bola-amphiphilic glycodendrimers target carbohydrate-binding proteins

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Carbohydrates are the most abundant macromolecules in living organisms and play important roles in energy production, as structural materials and as signaling moieties.[1] Dendrimers are appealing scaffolds for creating carbohydrate mimics with unique multivalent cooperativity.[2,3] We report here bola-amphiphilic glycodendrimers bearing mannose and glucose terminals, and a hydrophobic thioacetal core responsive to reactive oxygen species.[4] They were synthesized using click chemistry, and their properties with regards to binding and targeting specific carbohydrate-binding proteins were studied. The peculiar bola-amphiphilic feature enabled stronger binding to lectin compared to the conventional amphiphile. In addition, these dendrimers were able to target mannose receptors and glucose transporters expressed on cell surface, facilitating their effective cellular uptake in microglia and astrocytes, respectively, as well as in cancer cells.[4] These bola-amphiphilic dendrimers therefore hold great promise for targeting carbohydrate-binding proteins and targeted drug delivery.

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Zinc vanadate photocatalyst for efficient degradation of Rhodamine B:

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The increase in industrial discharges into nature leads to pollution of the environment. Among these releases, those from the textile industry, loaded with dyes, are responsible for nuisances since most of them are toxic and not biodegradable. The use of synthetic dyes products (Rhodamine B as example) in our lives is getting more and more in progress, which became an issue and getting a considerable interest in the research area of organic pollutant removal for environmentalremediation.

In this context, via a soft chemistry method we succeeded in synthesizing zinc vanadate (ZnV), which is subsequently employed as an active photocatalyst for decomposing a model dye (RhB). The synthesized phase is characterized by X-ray diffraction, scanning electron microscopy, transmission electron microscopy coupled with energy dispersive spectrometry, Ultraviolet– Visible Diffuse Reflectance Spectroscopy and X-ray fluorescence spectroscopy. X-ray diffraction patterns showed characteristic peaks of zinc vanadate phase. Morphologically, ZnV was found to consist mainly of nanosheets, and in the point view of optical properties, the bandgap energy has been found to be 2.3eV.

The degradation was followed by UV-Visible spectrophotometry. RhB degradation efficiency of 97% was achieved for the optimal conditions of pH, photocatalyst mass, RhB concentration and irradiation time.

Keywords: Zinc vanadate, Photocatalyst, Rhodamine B, photodegradation.

Session 6: Medicinal Chemistry

Combining repositioning and *de novo* synthesis of pyrazolo[3,4-*d*]pyrimidines to discover potent SIRT-2 inhibitors

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Sirtuins (SIRTs) are a class of enzymes labelled as III histone deacetylases. In mammals, seven isoforms (SIRT-1 to SIRT-7) are known, and they seem to act as oncopromoters or oncosuppressors, depending on the sirtuin and the cancer type.[1] The discovery of sirtuins inhibitors (SIRTIs) has earned consideration not only for their possible application for cancer but also for diabetes, immune system clutters, and neurological illnesses. Recently, we applied a repurposing approach to our *in-house* library of pyrazolo[3,4-*d*]pyrimidines originally developed as Src and/or Abl kinase inhibitors. Two rounds of modelling studies and biological assay led us to the identification of a few SIRT-2 inhibitors.[2] In parallel, starting from the X-ray crystal structure of some of these ligands (*e.g.*, compounds **1**, **Figure 1**)[3] with SIRT-2, we carried out further *in silico* studies and individuated a family of derivatives potentially active as SIRTIs. The compounds have been synthesized and submitted to biological assays. Overall, we discovered a hit compound endowed with nanomolar activity towards SIRT-2. Biological data and structure-activity relationship evaluation will be discussed.

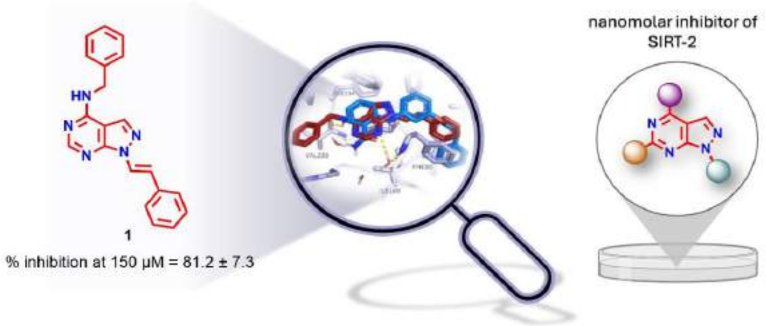

***Figure 1**: Structure, inhibitory activity towards SIRT-2 and docking pose of **1**, and general structure of the new generation of SIRT-2 pyrazolo[3,4-d]pyrimidine inhibitors.*

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Enhancement of the metabolic stability in 2-hydroxypyrazolo[1,5-a]pyridine scaffold-based inhibitors of human dihydroorotate dehydrogenase (*h*DHODH)

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Human dihydroorotate dehydrogenase (*h*DHODH), a pivotal enzyme in the *de novo* pyrimidine biosynthesis, stands as a validated target for the treatment of autoimmune diseases, solid tumors, and, more recently, acute myeloid leukemia (AML). By using a *non*-classic bioisosteric approach supported by structure-based drug design, we recently discovered **MEDS613**, a molecule 15-fold superior to **brequinar**, a known *h*DHODH inhibitor, in its cell-based *in vitro* potency. Unfortunately, **MEDS613** suffered from poor *in vitro* metabolic stability, thus limiting further preclinical studies.[1] This work discloses the process of identification of **MEDS613**'s propoxy chain metabolic soft spot, which allowed the design of the new *lead* structure **MEDS700**, a metabolically stable candidate (whose *h*DHODH binding mode has been elucidated by x-ray crystallography) with comparable, or even better, performance than **MEDS613** in terms of enzymatic inhibition, pro-apoptotic and pro-differentiating effects on AML cell lines (*Figure 1*). **MEDS700** represents a promising candidate for further steps into the drug development process, thus, before future *in vivo* toxicity/efficacy studies, the pharmacokinetics profile has been also outlined and here fully discussed.

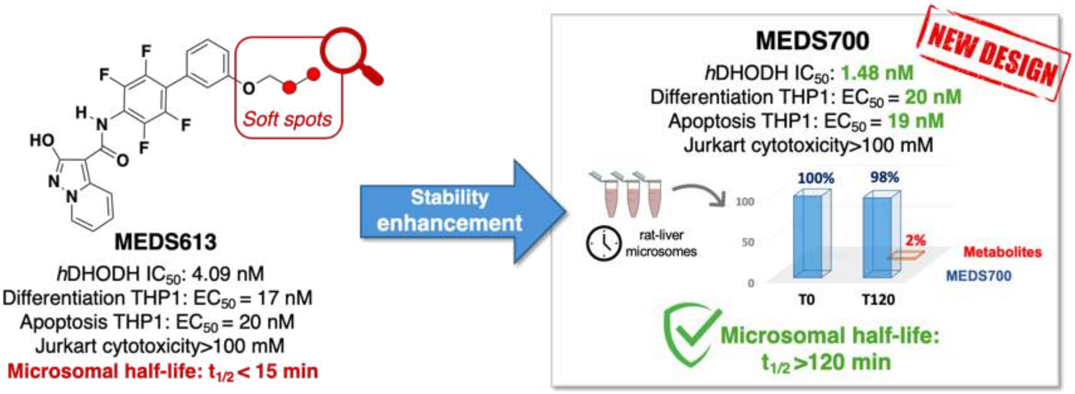

Figure 1: Optimization of MEDS613 metabolic soft spots with the design of MEDS700.

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Design and synthesis of new coumarin hybrids with antiproliferative activity against neuroblastoma cells

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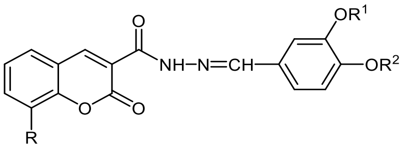
In order to identify new agents with anticancer activity, our research project is aimed at the design and synthesis of new hybrid molecules using the fragment-based strategy.

For this purpose, two naturally occurring scaffolds with antiproliferative and antioxidant properties, respectively, were combined. We synthesized new hydrazones of coumarin-3-carboxylic acid with aryloxy-substituted vanillin or isovanillin, obtaining a small library (16 compounds, Figure 1) throughout multistep synthesis.

The antioxidant properties of the compounds, were evaluated on the basis of their chemical structure by using *in vitro* DPPH colorimetric assay [1]. Furthermore, their anticancer activity was tested by MTT assay in a neuroblastoma (NB) cell line (HTLA-230) and in an etoposide-resistant one (HTLA-ER), selected by HTLA-230 [2]. Both the NB cell lines were treated for 48 h with increasing concentrations (2.5-30 μM) of the compounds. Most of the IC_{50} values showed an anticancer effect at low micromolar range (8-25 μM) with a similar trend in both NB cell populations.

Based on these results, it is possible to highlight some structure-activity-relationships useful for designing new compounds with better antiproliferative activity.

At the same time, further biological studies will be undertaken to identify the mechanisms of action of these new promising anticancer compounds.



R = H, OH, OCH_3
R^1 = CH_3, Ph, Bn, 4-F-Bn
R^2 = CH_3, Ph, Bn, 4-F-Bn

Figure 1: General chemical structure of the compounds ***1-16***

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Development of a magnetic colloid for blood flow recirculation

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During a brain stroke, blood clots in the vessels block the flow of blood and prevent oxygen supply to the brain. The success of the therapeutic treatment in the first few hours after stroke depends on the efficacy of the drug delivery to dissolve clots as fast as possible. Intravenous administration does not lead to rapid diffusion of the active substance to the clot due to the blood stagnation near to it.

Magnetic iron oxide nanoparticles (IONPs) can be highly effective to accelerate the transportation of drugs in blocked vessels. Our idea is to generate a collective rotation of the elongated IONPs aggregates using an oscillating magnetic field applied via external electric coils to generate a recirculation flow.

To achieve our therapeutic target, the first step was to develop non-toxic IONPs stable in physiological conditions. They were synthesized by co-precipitation and functionalized using PEGsilane. Characterization was carried out by dynamic light scattering, Fourier transform infrared spectroscopy, vibrating sample magnetometry, thermal gravimetric analysis and in vitro cytotoxicity assays confirming their biocompatibility.

The second step focuses on the behavior of the developed colloid under magnetic fields. First reversible aggregation results have been obtained, enabling micro-flow formation studies in an artificial vessel.

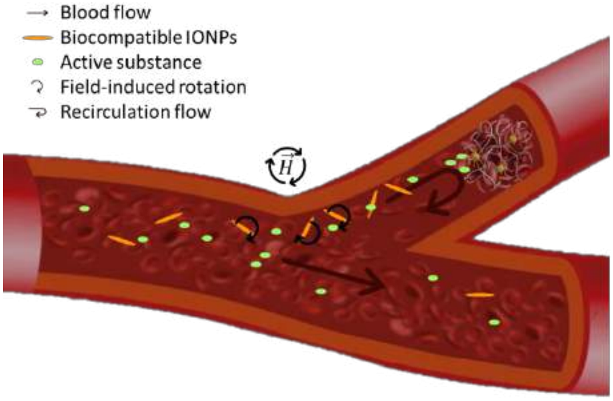

Figure 1 : Illustration of blood flow recirculation principle using biocompatible IONPs under field conditions to help the drug reach its target

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Exploiting the amino dihydrotriazine motif of Cycloguanil to develop novel anti-*Trypanosoma brucei* agents targeting folate enzymes

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Human African trypanosomiasis (HAT, also known as sleeping sickness) is a vector-borne parasitic infection caused by *Trypanosoma brucei* (*T.b.*). Despite the progress made to reduce its spread, to fully achieve the goal of eradicating the disease by 2030, there remains a critical requirement for enhanced disease tracking, intensified control efforts, and the development of innovative, safer, and more effective drugs.

A promising approach for the treatment of HAT aims to target the enzymes of folate metabolism, such as dihydrofolate reductase (DHFR) and pteridine reductase-1 (PTR1). Folates and pterins are essential cofactors for nucleic acid and protein biosynthesis. The antimalarial drug cycloguanil (Cyc) was found to target *Tb*PTR1 besides *Plasmodial* and *Trypanosoma* DHFR [1,2]. In the present study, we synthesized two novel series of compounds: (2-aminotriazino)benzimidazoles, where the amino triazino motif of Cyc is fused with a benzimidazole ring, and 2-guanidino benzimidazoles, as their open-ring and more flexible analogues.

The inhibitory activity of these compounds against *Tb*PTR1 and *Tb*DHFR, as well as against human DHFR, has been investigated to assess their selectivity for the protozoan enzymes. Furthermore, their cytotoxicity and antiparasitic effects were evaluated in cell-based assays. The crystal structures of both enzymes in complex with selected compounds have been solved, to elucidate the structural-activity relationship (SAR) of these two chemotypes that could be valorized for further drug development.

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A Novel PSMA-Targeted Probe for Photodynamic Therapy: Synthesis and Preclinical Validation

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Photodynamic therapy (PDT) is a procedure used in the clinic for the treatment of cancer and other diseases. PDT uses a photosensitiser (Ps) that can be activated by light for the production of reactive oxygen species (ROS), ultimately leading to cell death through necrosis and apoptosis. Silicon phthalocyanines (SiPcs) have exceptional physicochemical properties including their high singlet oxygen ($^1O_2$) quantum yield [1]. Here, to improve the specificity of SiPc in the treatment of prostate cancer, a PSMA (prostate specific membrane antigen) targeting ligand has been incorporated into both axial positions of SiPc, yielding the first axially bivalent PSMA-targeted PDT probe.

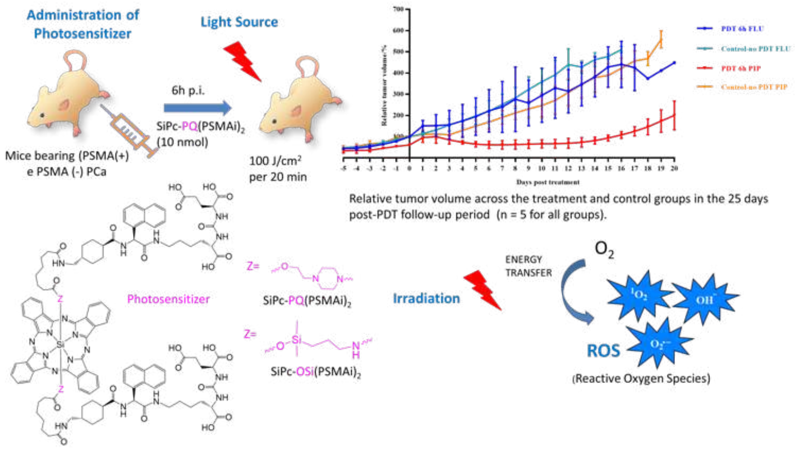

Figure 1: Chemical structure of SiPc-PQ(PSMAi)$_2$ and SiPc-OSi-(PSMAi)$_2$ and photodynamic therapeutic efficacy in vivo.

The PSMAi ligand (Glutamate-urea-lysine based binding motif) was attached to the central Si atom of Pc via an alkoxy (Si-O-C) or silyloxy (Si-O-Si) bond in order to compare and study their effectiveness, namely SiPcPQ(PSMAi)$_2$ and SiPcOSi(PSMAi)$_2$ (Figure 1). The UV–Vis absorption spectra of both conjugates acquired in water, showed an intense, well-defined absorption peak (Q-band) at 679–683 nm that strictly follows the Beer-Lambert law as a function of concentration, thereby indicating that the compound is essentially free from aggregation. Aggregation in water and limited solubility is a factor limiting the in vivo applications of most PCs. We studied the photophysical properties (singlet oxygen quantum yield Φ_Δ, fluorescence quantum yields Φ_F), the uptake specificity by PSMA-expressing PCa cells and the *in vitro* photodynamic-induced toxicity of the two new systems. The in *vivo* PDT treatment was performed with SiPc-PQ-(PSMAi)$_2$ that showed best results in vitro. This new PDT probe showed tumor growth delay and improved median survival in all PSMA (+) PC3-PIP tumors bearing mice.

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POSTERS

Methodological approach in the study of multi-material artefacts by the use of portable X-ray Fluorescence Spectrometry

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Obtaining reliable data through portable and non-invasive techniques is often a necessary condition in the study of Cultural Heritage. In fact, this study deals with the methodological approach adopted in the analysis of three reliquaries owned by Musée de Cluny (Paris, France) with which there is a consolidated collaboration. The main characteristic of these important medieval works lies in the variety of the materials they are made of: usually gilded metal decorated with glass, enamels, and gemstones as real pieces of jewellery [1]. Moreover, reliquaries are objects of cult that are sometimes carried in procession and exposed to the touch of the devout and they are often re-arranged over time or have been reproduced in copies. Elemental analysis allows the recognition of authentic parts and remakes and provides very useful information on production techniques and provenance of raw materials. Among other things, it allows comparisons to be made with other products of the same period but of different manufacture. The adoption of X-ray Fluorescence Spectrometry has enabled an accurate characterisation of artefact materials by exclusively non-invasive approach: different measurement conditions have been optimised over time to achieve data comparable with those presented in the literature concerning medieval jewellery [2]. The outcomes are of certain relevance given the lack of systematic diagnostic studies in the scientific literature specifically concerning materials of European late medieval anthropomorphic reliquaries [3]. The combination with optical microscopy allowed a characterisation of the appearance and the colours of the various surfaces investigated. The artefacts are all made of copper gilded with mercury amalgam, but some parts that can be attributed to later additions have been identified. Some elements detected in quantities in the glass are incompatible with medieval production and suggest they may be later substituted. Finally, precious stones as rock crystal, turquoise, zircons, and garnets were identified, in the last case with possible information about their provenance (India or Sri Lanka).

Decorative details of reliquary CI.1080

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Hierarchical zeolites by *top-down* and *bottom-up* approaches for a variety of applications

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Hierarchical zeolites, which exhibit a distinctive structure characterized by interconnected micropores and mesopores, are versatile materials that can overcome the typical issues related to microporous materials, including poor mass transfer, hindered diffusion, and strict selectivity of resulting products (Fig. 1). Typically, hierarchical porous materials can be obtained through *bottom-up* or *top-down* approaches. The former introduces dual porosity during synthesis, while the latter employs a post-synthetic step on a pre-existing microporous matrix. [1,2]

In this contribution, both approaches were applied to synthesize hierarchical porous materials with different properties. In detail: two commercial zeolites, HZSM-5 and Y (both with $SiO_2/Al_2O_3 = 80$) with a MFI and FAU structure respectively, and a natural clinoptilolite (HEU) were desilicated through a *top-down* approach using NaOH solutions at varying concentrations, to evaluate the treatment efficiency. In parallel, two different hierarchical SAPO-34 (CHA) were obtained through a *bottom-up* approach, using either non calcined MCM-41 or SBA-15, which serve as both Si source and mesoporogen. The synthesized hierarchical architectures were characterized by multi-technique approach using XRD, N_2 physisorption at 77K, TGA and FTIR spectroscopy of adsorbed probe molecules, to assess the nature, strength and accessibility of the acid sites.

The generated hierarchical zeolites hold potential applications in various fields, such as heterogeneous catalysis and as adsorbents toward cationic species in solution (i.e. metal ions), either individually or in combination, depending on the quantity of captured metal and its coordination state.

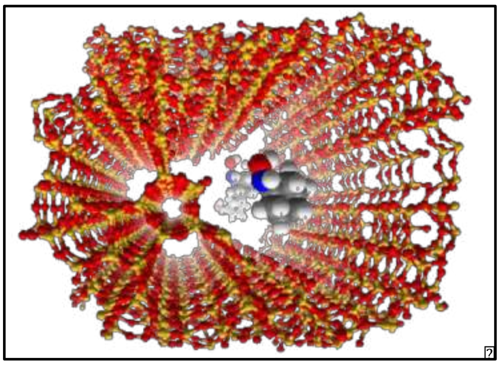

Figure 1: Graphical representation of a hierarchical zeolite.

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DFT simulation of FeOx/Au heterostructures: insights and relevance as electrochemical water splitting heterogeneous catalysts

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Nowadays there is a urge to transit from fossil fuels to clean energy sources: a crucial role in this process can be played by the oxygen evolution reaction (OER), hydrogen evolution reaction (HER) and oxygen reduction reaction (ORR) [1]. The main problem in the worldwide diffusion of the catalysts for these reactions is their high costs. The most efficient catalysts are in fact made of noble metals [2,3]. An alternative based on earth abundant metals would be needed and for this we propose and study FeOx /Au systems. The structure of supported FeOx layers is nonetheless still to be determined since a wide range of structures can be formed depending on the operating conditions (mainly the applied potential and the pH of the solution) [4,5].

In such framework, computational chemistry can play a relevant role in identifying conceivable structures based on Fe oxides and hydroxides with different oxidation numbers. Relevant structures have been fully analysed by considering their electron/magnetic properties and their relative stability at the operating conditions. The major interest is to establish the relationships between structure and properties in order to identify the active species taking part to the catalytic reactions.

The VASP code [6] has been used for calculations in combination with the DFT+U approach and PBEsol as functional since this computational set up guarantees a proper description of the transition metals centers and related (electro)chemical processes.

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SbnA as a target for the development of new antimicrobials towards *Staphylococcus aureus*

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Antimicrobial resistance (AMR) is the ability of bacteria to withstand treatments. In these conditions antibiotics can no longer inhibit the growth of bacteria. A high-priority bacterium to study is *Staphylococcus aureus,* which is resistant to many antibiotics and has developed different pathways to resist the majority of the known drugs [1].

Iron is a crucial nutrient for *S. aureus* to invade the host and cause infections. Human body can develop a mechanism called nutritional immunity (NI) to limit iron availability to bacteria. However, bacterial pathogens can counteract this by producing siderophores or by heme uptaking via hemophores. Siderophores can chelate iron with a high affinity and transport it to bacterial cells. Iron in hemoglobin is bound to heme and hemophores can scavenge heme groups from hemoglobin through the blood. The underlying mechanism of siderophore production is very complex and investigating the process in molecular scale is of particular interest [2].

We focus on SbnA enzyme which is a PLP-dependent protein involved in the biosynthesis of Staphyloferrin B (siderophore) by production of N-(1-amino-1-carboxy-2-ethyl)-glutamic acid (ACEGA). In this reaction O-Phospho-L-serine (OPS) and L-glutamate substrate enter the SbnA active site leading to conformational changes and the closure of the binding site and production of ACEGA [3]. We performed structure-based investigations to identify SbnA inhibitors as novel antimicrobials. In a first run of virtual screening (VS) we found phenyl maleic acid to be effective in the inhibition in the low micromolar range of SbnA. Then, using a modified version of phenyl maleic acid and ACEGA as templates, we performed additional VS using the Glide Virtual Screening Workflow (VSW) exploring many libraries including Enamine, Molport and Chembridge with a number of filters and pharmacophore restraints. This was followed by an induced-fit docking on top hits. The final selection resulted in almost 20 compounds. This will be followed by Molecular Dynamics simulations to check the stability of the compounds. Most promising molecules will be purchased and tested *in vitro* on the isolated protein and, if effective, on *S. aureus* cultures.

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An Electrochemical Study of Gold Complexes for Catalysis

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While the majority of gold-catalysed reactions underlines the carbophilic Lewis acid of gold(I),[1-4] several studies have shown these last twenty years the feasibility of Au(I)/Au(III) catalytic systems through the use of external oxidants.[5] This step opens up new prospects in the field of gold-based catalysis. Simultaneously, electrosynthesis is experiencing a major upsurge in interest among the scientific community: the direct use of electricity offers an economical, sustainable and safer alternative to conventional oxidising/reducing agents.[6] These methods are independently two powerful synthesis tools, both of which are undergoing a revival, and their combination could lead to new methodologies and new reactivities.[7]

In this context, a preliminary cyclic voltammetry study has been carried out on a range of gold complexes and ligands to determine their oxidation potentials. On the one hand, these data will potentially allow the *in situ* generation, the isolation and the characterisation of gold (III) complexes. On the other hand, it will also enable the development of new catalytic processes under electrochemical conditions.

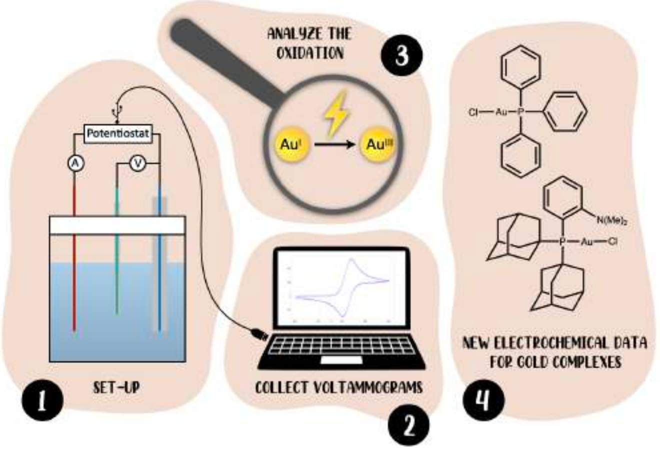

Figure 1: The different steps of the electrochemical study of gold complexes

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Online colorimetric measurement and timely dosage of hydrogen peroxide in a photo-Fenton process.

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The scale-up of a photocatalytic process for the removal of pollutants from water encompasses several relevant aspects, among them, the timely analytical control and the optimization of operational parameters, to maximize efficiency and minimize reagent consumption. Indeed, when running Advanced Oxidation Processes, reagents consumption represents one of the main costs; in the specific case of photo-Fenton processes, that rely on the generation of hydroxyl radicals through the reaction between hydrogen peroxide and Fe(II) ions, an excess of H_2O_2 could even hinder the pollutant degradation kinetics, making therefore its proper dosage a key issue.

The automation of H_2O_2 concentration control and dosage is therefore worth to be implemented, seeking for reliable, fast and cheap devices.

In this work the role of H_2O_2 dosage on the photo-Fenton degradation of paracetamol and caffeine (taken as model contaminants of emerging concern) was studied. A self-developed Arduino controlled automated device was employed for the online colorimetric measurement of H_2O_2 and for its dosage.

The kinetics of substrate degradation, organic carbon mineralization and H_2O_2 consumption were compared to define the most suitable H_2O_2 dosage procedure to maximize process efficiency.

The developed Arduino device also carried out the inline dissolved oxygen measurement, to verify any possible relationship between H_2O_2 consumption and the concentration of dissolved oxygen.

The development of an automated device for the online measurement and dosage of H_2O_2 provides a powerful tool for deepening the knowledge on the effect of H_2O_2 content on the efficiency of a photo-Fenton process, contributing to optimize the actual H_2O_2 concentration avoiding its depletion or excessive dosing.

The results obtained in the present work evidence two opposite trends for kinetics and overall H_2O_2 consumption when moving from single, stoichiometric H_2O_2 dosing approach to a fractioned dosing one. In fact, both substrate and DOC removal rates were higher when a single and stoichiometric H_2O_2 dose was added at the beginning of the process, while H_2O_2 consumption took advantage from small successive H_2O_2 addition as long as the previously added H_2O_2 was consumed before the following dose was added.

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Design and synthesis of INF195, a new NLRP3 Inflammasome Inhibitor with ex vivo cardioprotective effect

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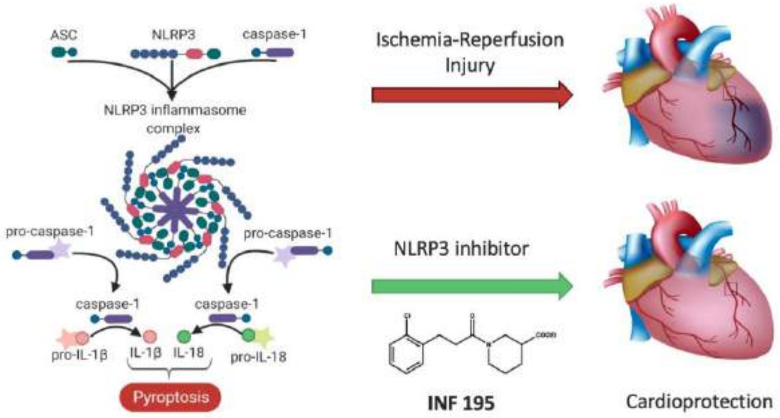
The NLRP3 inflammasome, a cytosolic multi protein complex involved in inflammatory processes, is emerging in the myocardial ischemia-reperfusion injury (IRI) framework, being engaged in both cell survival and damage [1-3].

In the search for novel NLRP3 inhibitors, we designed a series of compounds with the help of molecular docking techniques. The activity of the compounds was evaluated *in vitro* in human macrophages. One compound, INF195, was selected to investigate the cardioprotective properties [4]. We measured infarct size (IS) in isolated mouse hearts exposed to 30-minute global ischemia and then one-hour reperfusion, either in the absence or presence of different doses of INF195 (5, 10 or 20 μM). We also evaluated the production of the markers of NLRP3 activation, caspase-1 and IL-1β, measuring their concentrations in cardiac tissue homogenates. The results infer that heart pre-treatment with low doses of INF195, 5 and 10 μM, considerably reduce IS and IL-1β production, suggesting therefore that the activation of NLRP3 expressed in myocardial cells plays a role in IRI. Moreover, INF195 at low doses significantly reduced the infarcted area (the infusion at 5μM reduced IS from 64.8±1.9% to 38.1±1.3%). Overall, INF195 showed a promising cardioprotective effect worth of further studies.



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Enantioselective Synthesis of Benzopyrane Atropisomers

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Atropisomers are of utmost interest due to their prevalence in natural products,[1] but also for their biological relevance[2] and their numerous applications as chiral materials,[3] ligands[4] and organocatalysts.[5] Among them, biaryl and heterobiaryl atropisomers are the most common ones and many synthetic approaches are available.[6] Non-biaryl atropisomers constitutes another family of these axially chiral molecules with less synthetic approaches and consequently are less represented in the literature.[7] Within this family, the highly challenging enantioselective construction benzopyrane atropisomers still constitutes a daunting challenge of modern organic synthesis.[8]
Enantioselective halogenation reaction is a useful reaction for the production of atropisomers in enantioenriched form, *via* a dynamic kinetic resolution (DKR) of substrates presenting low enantiomerization barriers.[9] Therefore, we propose to exploit this approach for the atroposelective synthesis of axially chiral benzopyranes. While non-catalyzed version of the reaction has allowed to produce several examples of chiral benzopyranes in racemic form, encouraging enantiomeric excesses have been obtained with the use of a chiral phosphoric acid derivative and further investigations are currently undergoing in our laboratory.

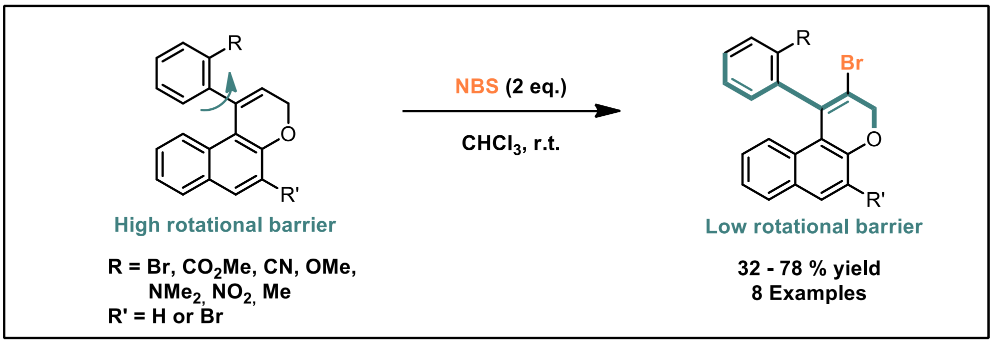

Figure 1 : Bromination reaction scheme

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MW-assisted Anisole Hydrogenation over Commercial Supported Catalysts

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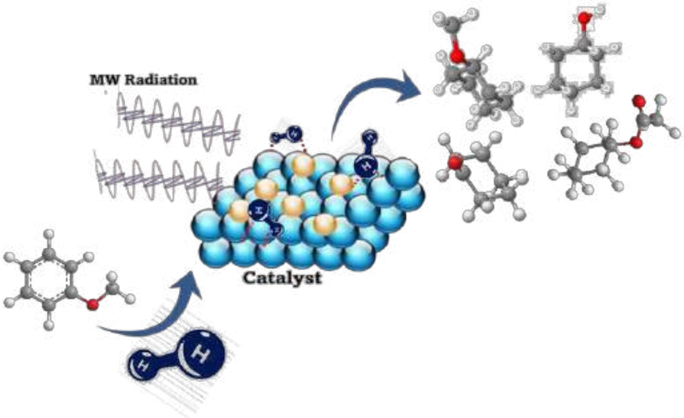

Figure 1: Anisole hydrogenation over bifunctional supported catalyst

Hydrogenations are among the best studied reactions as they are fundamental in petrochemical and coal chemistry, environmental industries, and fine chemicals production.[1] It is estimated that about 25 % of all chemical transformations involve at least one hydrogenation step. Starting from the first hydrogenation reaction of lignin-based chemicals carried out by Harris and Saeman,[2] most of the research aim to transforming monomers derived from lignin depolymerization through hydrogenation reactions. Currently, hydrogenations of lignin-based chemicals can be carried out using hydrogen gas or through the transfer hydrogenation (TH) route, using a H-source solvent (such as formic acid, isopropyl alcohol, or alkanes).[3] Biomass is constituted by lignocellulosic (LB) or non-lignocellulosic (non-LB) materials.[4] Considering lignocellulosic biomass, specifically the three main chemical components (cellulose, hemicellulose and lignin), only lignin has been rewarded less attention as for the bioconversion to biofuels, due to complex structure of the polymer,[5] despite it is characterized by a great amount of functional groups that are important active sites for further chemical modifications.

Among the various transition-metal-based catalysts, ruthenium and rhodium are mainly employed for hydrogenations of aromatics.[6,7]. This work aims to investigate the MW-assisted anisole hydrogenation in the presence of Ru or Rh catalysts with molecular H_2 and using an opportunely selected solvent. The conditions were optimised by reducing both the reaction time and temperature and using environmentally friendly and recyclable solvents to increase the sustainability of the process.

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Functionalization of levoglucosenone through Michael's reaction using microwave energy

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Biomass-derived chemicals and products are attracting more and more interest thanks to their renewable nature and the potential to reduce the carbon emissions derived from fossil fuels. In this work, an innovative synthetic protocol was for the synthesis of high added value bio-derivatives based on levoglucosenone (LGO) was developed. LGO was used as a Michael acceptor in conjugate addition reactions with malonates esters having an alkyl chain of varying length (R = Me, Et and Bu). For the first time the reaction was carried out in a microwave oven, in solventless conditions and using a heterogeneous inorganic catalyst with less impact than the usually employed KF/alumina[1]. The screening of four inorganic base catalysts: CaO, MgO, NaOH and K_2CO_3 showed that the most effective of all is calcium oxide. Subsequently, the reaction optimization was carried out via a Design of Experiment (DoE) approach considering three experimental parameters: reaction time (2 min, 8.5 min and 15 min), fixed microwave power (5 W, 13 W and 20 W) and the malonate equivalents (1 eq, 1.5 eq and 2 eq) in the reaction. The combination of microwave power and reaction time (20 W-2 min or 13W-15 min) appears to be the most significant parameter in determining the reaction rates. Different percentages of CaO were tested in combination with the previous experimental parameters with the best reaction conditions (conversion > 95%) that were obtained by using 10% w/w of the inorganic base[2]. Having found the optimal experimental conditions, replicates of the best synthesis were carried out and the products were purified by flash chromatography. The purification of the first adduct, made reacting LGO with dimethyl malonate (DMM-LGO), was the most challenging given the low ΔRf between LGO and DMM-LGO. Thanks to the amphiphilic nature of the LGO Michael adducts, the Hydrophilic-lipophilic balance (HLB) parameters were calculated using both the Griffin and Davies methods. The two interpretations agree on the lipophilic nature of diethyl malonate-levoglucosenone (DEM-LGO) and dibuthyl malonate-levoglucosenone (DBM-LGO) while values are at the interface for the DMM-LGO adduct. To validate these theoretical calculations, both water-organic solvent emulsion tests and contact angle analysis were conducted using different types of solvent (water, CH_2I_2, olive oil and DMSO) and different solid surfaces (glass, parafilm, tape and PTFE) to evaluate the material's properties. The optimization of the experimental conditions allowed a complete conversion of the LGO with isolated yields ranging from 85% to 91% for the three adducts.

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Asymmetric reduction of cyclic imines by Imine Reductase enzymes in non-conventional solvents

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Biocatalysis became a powerful tool for the synthesis of relevant high-added value molecules with excellent chemo-, stereo- enantioselectivities but also allow to perform greener chemical transformations. However, the low solubility of many organic substrates or products in aqueous solutions, commonly used in enzymatic reactions, often hampered the application of enzymes in synthesis, mainly because of substrate concentration restrictions. In this context, non-conventional solvents are acquiring increasingly relevance, and in recent publications, they were demonstrated to improve the yield and selectivity of enzymatic reactions in an economical, health-safe, and environmentally friendly manner.[1] In this field, Deep Eutectic Solvents (DESs) have rapidly emerged as a promising class of green reaction media.[2] In this work we report a successful example of non-conventional solvents used for the synthesis of cyclic chiral amines by bio-reduction of the starting cyclic imines.[3] The transformation was realized by means of a novel class of NADPH-dependant enzymes, namely Imine Reductases (IREDs). We performed the reduction of cyclic imines in a mixture of phosphate buffer/glycerol (50% v/v). Pyrrolidines, piperidines, and azepines were produced in good yields and excellent *S*-enantioselectivities (up to >99% *ee*). Also, the use of non-conventional solvents allows to increase the concentration of the starting material up to 100 mM. It is worth mentioning that applying a fed-batch strategy, we were able to work at mmol scale with 80% yield and excellent *ee,* which formally corresponds to a seven-fold use of the same enzyme. Our findings in terms of enantioselectivity, substrate scope and scalability will be presented.

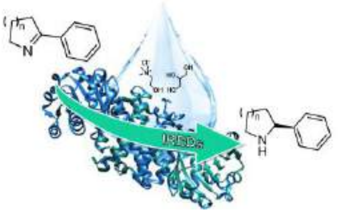

Figure 1: Enzymatic reduction of cyclic imines using IREDs in non-conventional solvents.

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Copper electrodeposition from a sustainable alkaline galvanic bath

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The deposition of copper is pivotal for the fabrication of integrated circuits and CIGS solar cells [1]. Copper thin films can be electrodeposited by the reduction of Cu^{2+} ions [2]. The state of the art is constituted by low efficiency acid baths due to hydrogen evolution, while alkaline baths use cyanide as a complexing agent, rising safety concerns [3]. We formulated and characterized a Cu alkaline bath for thin films electrodeposition, by exploiting alanine as complexing agent. By means of rotating disk electrode measurements, kinetic studies were carried out to have a better understanding of the deposition mechanism. These studies allowed us to acknowledge diffusion coefficients and adsorption constants at various temperatures, as well as the hydrodynamic radius of the coordination compounds.

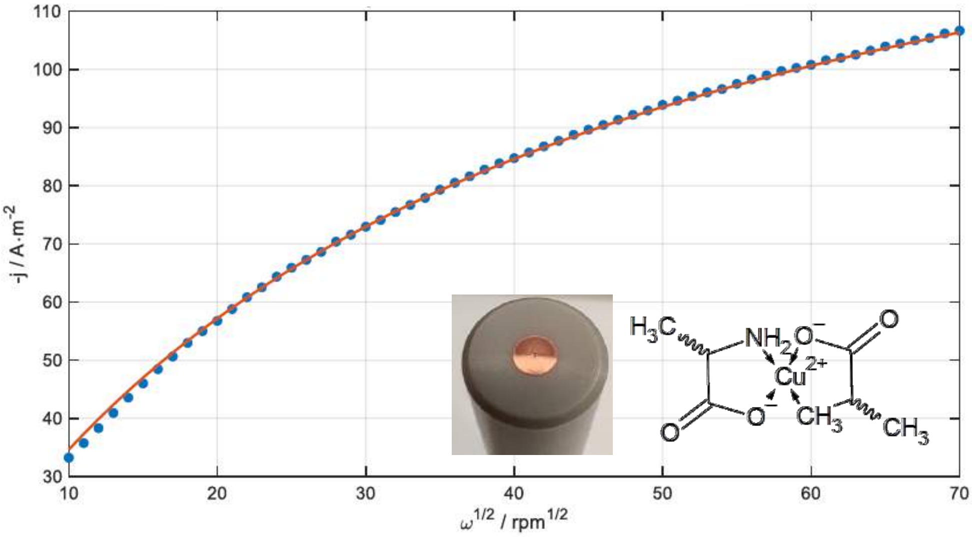

Figure 1 : Title(Times New Roman 10 + Italic)

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Application of Raman Spectroscopy for Bio-Fluid Spots Segmentation and Characterization on Cotton Supports

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Within the domain of forensic sciences, the detailed analysis of bio traces discovered at the scene of crimes emerges as a key topic[1]. This meticulous examination encompasses the study of various substances, such as body fluids, and can provide valuable insights into criminal investigations. By scrutinizing these biological traces, forensic experts can identify potential suspects, establish links between individuals and crime scenes, and unravel crucial details to reconstruct events accurately. This process involves employing advanced techniques like DNA analysis[2], serology, and toxicology to extract vital information that helps in piecing together the intricate puzzle of criminal cases[3]. Such scrutiny not only plays a pivotal role in solving crimes but also serves as a cornerstone in ensuring justice is upheld through scientific rigor and evidence-based conclusions. The analysis of these traces usually involves a sequence of extraction steps. These techniques can be optimised according to the unique characteristics of the trace being examined if it is possible in advance to establish its nature. This is also of particular importance since most of the aforementioned analytical methods are destructive and hamper the possibility of making counter-analyses or replicated measurements on samples that have been already analysed. Moreover, conventional diagnostic approaches to perform such preliminary discrimination do not allow the analyst to perform a significant profiling on the recovered evidence and evaluate the molecular composition beneath the sample surface. Therefore, the necessity to deconvolute the mixture components on the collected evidence is crucial in forensics since a partial, limited, unrepeatable examination of the traces jeopardizes the comprehensive characterization of crime evidence. Chemometric tools can aid in providing the two key requirements that must be fulfilled to allow this. Firstly, by means of a precise spot localization, with the aim of selecting only regions of the sample that can be associated with a biological residue instead of the support on which they are found. Secondly, through a correct spot characterization, differentiating the type of biological residue represented in the segmented spot.

Notably, Raman spectroscopy has emerged as a valuable technique for characterizing both biological fluids[4], whether in their desiccated or liquid states, on cotton-based supports[5]. Its proven efficacy underscores its significance in the realm of forensic investigations and with this work we intend to propose and assess its applicability for the preliminary scrutiny of biological traces on cotton supports. This has been carried out by applying a segmentation procedure, based on Soft Modelling of Class Analogy (SIMCA)[6] with the intent of selecting informative pixels that have a different spectral composition from the underlying support. Moreover, an assessment on the possibility of differentiating four of the most common biological fluids (i.e., blood, urine, saliva and sperm) has been conducted by comparing the segmented regions using Principal Component Analysis (PCA).

Author(s) acknowledge(s) support from the Project CH 4.0 under the MUR program "Dipartimenti di Eccellenza 2023-2027" (CUP: D13C22003520001)

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Lithium Carbenoid Mediated Manipulation of the Iminoisatin Scaffold: an Expeditious and Direct Access to New Highly Functionalized Indol-type Compounds

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The direct transfer of a reactive nucleophilic CH_2X or CHX_2 unit into an existing linkage enables the formal introduction of the moiety with the precisely defined degree of functionalization.[1] Upon the fine tuning of the reaction conditions governing the transformation, the initial homologation event can serve as the manifold for triggering unusual rearrangement sequences leading to complex architectures through a unique synthetic operation.[2]

Herein, we report the controlled manipulation of the iminoisatin scaffold via lithium carbenoid mediated insertion of a C1 unit, directly connected to the condensed ring. By properly selecting the carbenoid emploied in the protocol, a divergent synthesis of two different highly functionalized indol-type compounds is obtained.

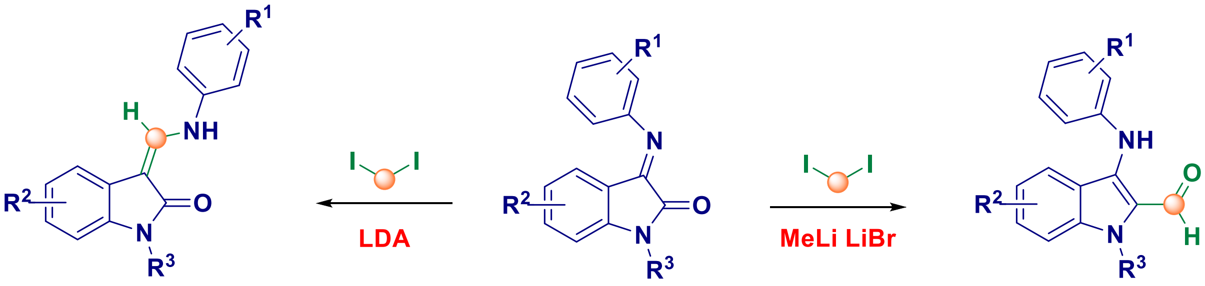

Figure 1: Lithium carbenoid mediated divergent synthesis of indol-type compounds

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Development of hydrogels with natural NADES-based extracts for cosmetic and pharmaceutical applications

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NADES (Natural Deep Eutectic Solvents) are emerging and promising green solvents for the extraction of bioactive compounds from botanical matrices. They show a wide polarity range, high solubilization strength for different compounds and present several advantages over classical solvents, such as biodegradability, absence of toxicity, sustainability, simple preparation and low cost. NADES can be easily obtained from solid naturally occurring molecules, hydrogen bond acceptors (HBAs) coupled with hydrogen bond donors (HBDs), forming supramolecular structures with very low melting points and high extraction efficiency. Their safety and intrinsic active properties allow to consider them functional ingredients of potential interest in the cosmetic and pharmaceutical fields [1].

In the present study, with the aim of developing simple, safe and active formulations, different NADES-based natural extracts (sage, citrus, and bergamot) were obtained, characterized and employed as ready-to-use ingredients (consisting of the NADES-based extractive itself) with antimicrobial and antioxidant properties, in combination with different natural polymeric systems (sodium ialuronate, xantan gum,carbossimetilcellulose, and hydroxyethylcellulose). The gelled systems were then investigated in regard to their rheological behavior and stability. From the results obtained, NADES-based extracts hydrogels could be considered efficient carriers of bioactive compounds, helpful in developing new natural, safe and bioactive hydrogel formulations with antimicrobial and antioxidant properties.

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Microwave-assisted reductive etherification of vanillin over Pd catalysts for the production of biomass-derived surfactants

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Among renewable feedstocks, lignocellulosic biomass is an attractive alternative to oil due to its abundance, low cost and renewability. Vanillin can be obtained through the depolymerization of the lignin fraction. The reductive etherification of the aldehyde group with aliphatic alcohols over heterogeneous Pd catalysts affords the corresponding ethers which can be further modified into bio-fuels, surfactants or fine chemicals, all relevant compounds in the chemical industry (Figure 1). A better understanding of the reaction mechanism is needed, since most of the literature focuses on Pd-based catalysts, and the acids sites of the support may play a role to promote etherification and hydrolysis [1,2]. Therefore, a tailored bifunctional catalyst would be required, considering that the acid sites also promote transesterification reactions and decomposition of the resulting ethers [1,3,4]. In this study Pd activity has been modulated through the addition of Au and a screening of the supports has been carried out to investigate catalyst acidity. Microwaves have been employed as unconventional heating method: as a result, carbon-based supports have shown to be prone to the formation of hot-spots leading to poor reproducibility of the process. Conversely, the use of alumina led to replicable and promising results, with conversions as high as 80% achieved over the Pd/Al_2O_3 catalyst (5 wt% Pd).

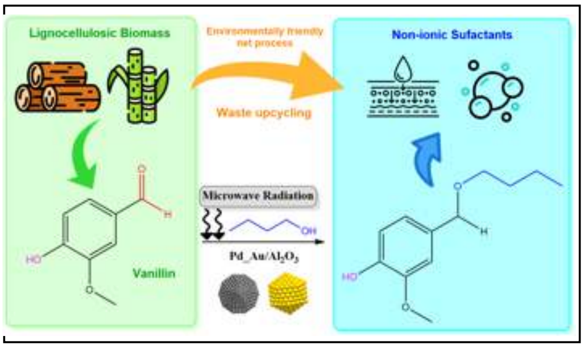

Figure 1: Schematic vanillin reductive etherification for the production of non-ionic surfactants.

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Synthesis and properties of highly contorted triphenylene–based multiple helicenes

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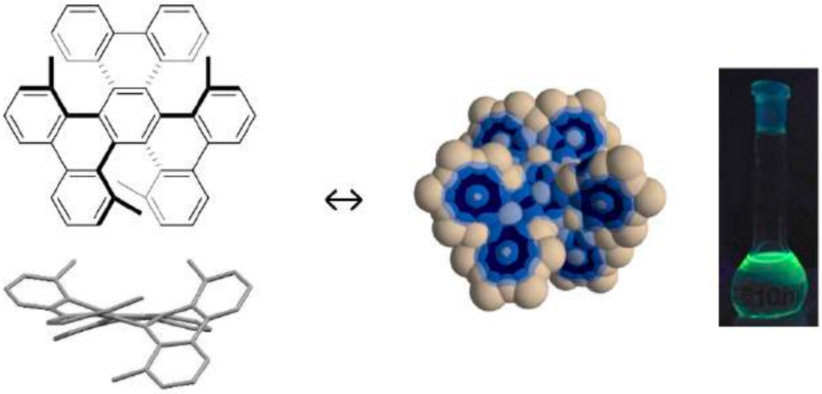
Polycyclic aromatic hydrocarbons (PAH) embedding a single π system are diverse by their size and shape. They have for long been considered as planar and rigid molecules, with only a few exceptions, for instance the helicenes, regarded as laboratory curiosities at the time of their discovery. This paradigm has gradually shifted, and nowadays it is well recognized that PAH are flexible and stretchable molecules. Thus, thousands of 3D curved PAH have been described in the last decade. Curvature in PAH can induce chirality[1] and largely affects their electronic properties. However, structure–property relationships have sparingly been examined for these molecules,[2,3] in part because the synthesis of series of comparable contorted PAH is a difficult task.

To tackle this problem, we have designed an original approach to access a series of tetrabenzotriphenylene–based multiple helicenes using aryne chemistry. Geometric factors and electronic properties in these molecules were determined and correlated (see illustration). This work establishes structure–properties relationships in this series of chiral PAH, which is expected to allow the rational design of other multiple helicenes with predicted properties.



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Synthesis of highly conjugated fluorophores by coupling the Ugi reaction with a $Pd^{(0)}$-catalyzed domino process and a final cyclo-aromatization.

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The synthesis of a novel class of heterocyclic fluorophores featuring the furo[2,3-*c*]isoquinoline main core has been developed. The two key steps of our synthetic strategy consist of an **Ugi 4-component reaction** coupled with a subsequent ***one-pot*** **Pd^0-catalyzed domino process** named **HSCA**, which stands for *Heck-Sonogashira-Cyclization-Aromatization*. This versatile combination successfully led to the synthesis of two generations of blue/green-fluorescent compounds(1,2). Considering the application potential of fluorescent organic small molecules(3), this approach has been recently employed to build new furoisoquinolines with an extended π-electron conjugation, with the aim to achieve a red-shift both in the absorption and the fluorescence bands (**Fig.1**).

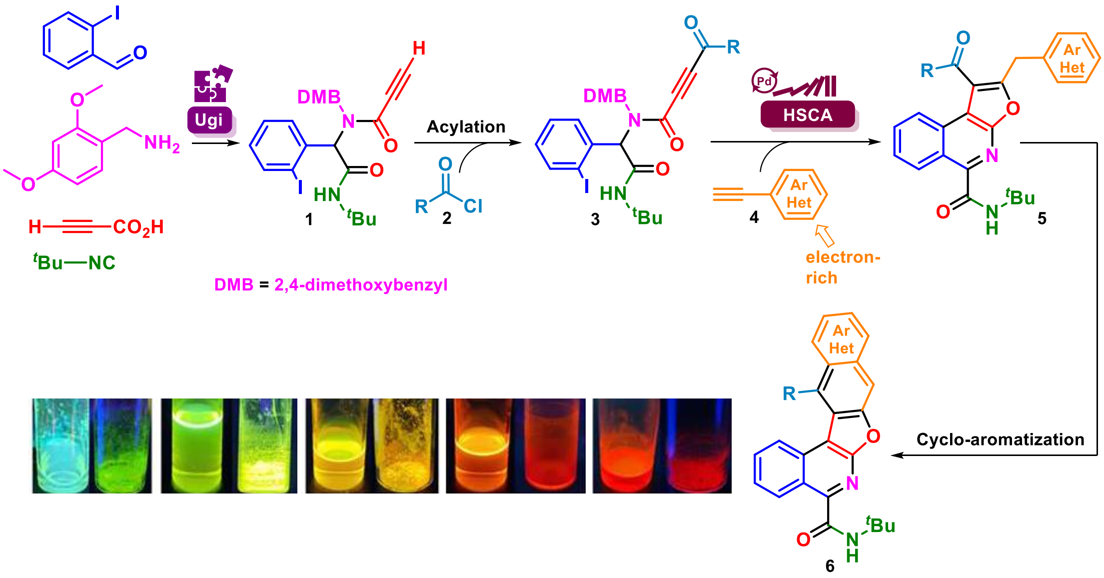

Figure 1 : the synthetic pathway to fused highly conjugated furo[2,3-c]isoquinolines ***6****.*

The structural complexity of the target molecules derives both from the acylation of **Ugi** product **1** to give **3**, and from the use of **electron-rich ethynyl arenes** **4** in the **HSCA**. Indeed, the resulting compounds **5** are able to increase the overall conjugation through a further cyclo-aromatization, resulting into fused highly conjugated furoisoquinolines **6**. These compounds, under UV excitation, exhibit an interesting fluorescence in solution and at the solid state ranging from the blue to the red region of the visible spectrum.

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Novel peptides as agonist of the FPR2 for treatment of ulcerative colitis

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The inflammatory bowel disease (IBD), Chron's disease and ulcerative colitis are among the idiopathic colorectal inflammatory disorders. As in other inflammatory processes, neutrophils migrate into inflamed tissue in response to chemotactic signals, stimulating various antimicrobial functions including ROS production, phagocytosis, and degranulation. The interruption of this process or the excessive recruitment of neutrophils can cause a dysregulation of the inflammatory process which hinders its resolution.

The Formyl Peptide Receptors (FPRs) are human G protein-coupled receptors located on neutrophils capable of binding specialized pro-resolving mediators and participating in the resolution process. The human FPR family constitutes FPR1, FPR2/ALX and FPR3.

The synthetic hexapeptide WKYMVm, an agonist of the FPR1 and FPR 2 receptors, showed a therapeutic effect against ulcerative colitis by blocking the decrease in body weight, colon shortening and mucosal destruction induced by DSS (in a model mice). In contrast, the FPR2-receptor was inhibited by the WRWWWW peptide, indicating the crucial role of this receptor in inflammatory pathology.

The aim of this study is to design and synthesize WKYMVm agonist/antagonist analogues, testing their binding capacity to the FPR2 receptor and their anti-inflammatory activity at different concentrations in vitro. Future development comprises their encapsulation in different liposomal formulations, investigation of their absorption and possible anti-inflammatory effects in a 2D CaCo2/HT29 and CaCo2/HT29-MTX culture model used in Crohn's disease study.

The novel synthesized peptides may represent useful therapeutic agents against chronic intestinal inflammation.

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Metal hydrides design and applications for energy

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The development of sustainable and efficient materials is nowadays the main objective to pursue a greener and more sustainable energy future.[1]

In the present work many examples of metal hydrides especially designed for different applications will be presented. The multiple use of hydrides in the energy field demonstrate how important are pioneer and basic research activities.

Firstly, the development of cheap and optimized alloys as solid-state hydrogen storage materials in the frame of the HyCARE project will be presented, to show how to tailor and develop materials from the lab-scale to a final large scale renewable energy storage prototype, and show how to develop and integrate metal hydrides, phase change materials and the industrial production of them.[2–4]

Secondly current research project on hydrogen purification will be introduced, where metal hydrides and hydrogen getters[5] are investigated to capture and release pure hydrogen from a contaminated stream coming from biomass treatment.

Thirdly, a brief hint will be shown on the EX-MACHINA project in which thermodynamics of metal hydrides and machine learning technique are studied and integrated to develop a large database and predict properties of interest.

Finally, a short overview of research activities on complex hydrides for battery materials will be presented, focusing on the study of solid-state electrolytes by mixing complex hydrides and metal halides.[6,7]

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Studies of Photosensitive mixed oxides Thin Films for high energy Radiation Detection.

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The aim of this work is to better understand the behavior of 'solid solution' materials under photon excitations of different energy ranges, specifically analyzing the exact role of fabrication conditions on luminescent properties in the visible range under UV, X-ray, and gamma excitations.
In this presentation, we highlight the significance of doping these MoO_4 or WO_4 hosts with small percentages of rare earth elements as it allows for the amplification and spectral control of emission, making it suitable for a wide range of scintillators, Figure 1. We chose the system based on oxyanions $Ce_{(2-x)}\,Sm_x\,(WO_4)_3$ due to their activity under photon flux. "These powders were synthesized using the coprecipitation method, as shown in Figure 2.

Research efforts also focus on the fabrication of thin films deposited through cathodic sputtering, we found that the chemical composition and microstructure are closely linked to adjustable sputtering parameters as working pressure, the O2/Ar ratio and sputtering power. These deposition parameters are the subject of in-depth studies to achieve the desired thin film based on the following composition x: $Ce_2\,(WO_4)_3$, $Ce_{1,5}\,Sm_{0,5}\,(WO_4)_3$, $Ce_1\,Sm_1\,(WO_4)_3$, $Ce_{0,5}\,Sm_{1,5}\,(WO_4)_3$, $Sm_2\,(WO_4)_3$.

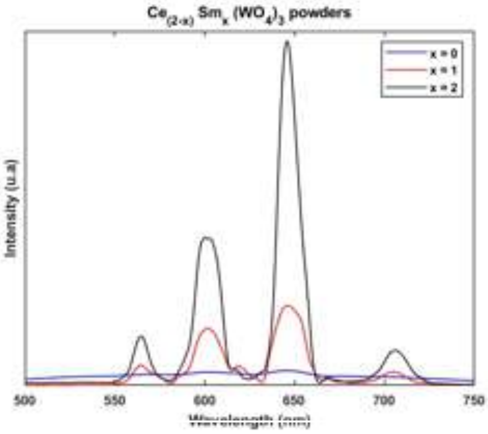

Figure 1: Spectrum of emission under UV excitation.

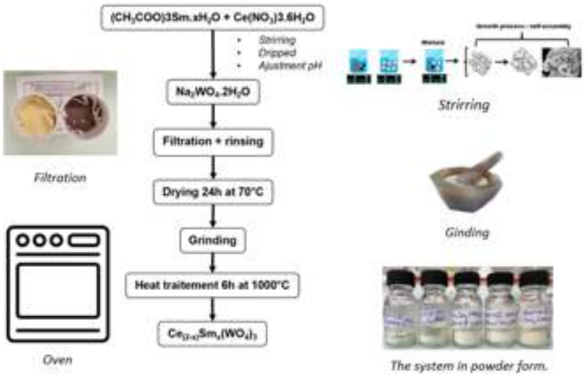

Figure 2: Synthesis by coprecipitation of $Ce_{(2-x)}\,Sm_x\,(WO_4)_3$.

Excitingly, promising results have been obtained from measurements of luminescent properties under UV and X-ray excitations for the Ce(2-x) Smx (WO4)3 system, which will also be presented.

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Monocrystalline nanowire transparent electrodes for photovoltaics

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Transparent electrodes play a crucial role in various optoelectronic devices such as solar cells, photodetectors, LEDs, and touch screens.

The efficiency of these devices relies heavily on the transparent electrodes' ability to transport electrons while maintaining excellent photon transparency with minimal absorption and reflection.

High-quality transparent electrodes are typically produced using energy-intensive methods, involving high temperatures and vacuum conditions, often rendering them incompatible with flexible substrates. Metal nanogrids emerged as a promising alternative to metal oxides such as indium tin oxide[1].

The large conductivity of metals allows efficient conduction of electrons, and the holes in the grid allow transparency.

The optoelectronic properties can be tuned by varying width and periodicity, making it a highly versatile architecture for transparent electrodes with unsurpassed performance.

Here I will present a new entirely bottom-up approach to making transparent electrodes using colloidal building blocks with nanometric dimensions. This approach aims to minimize environmental impact and cost, and enhance compatibility with flexible substrates.

Colloidal metal nanocubes are transferred by contact printing on a transparent substrate and then arranged in a grid pattern through nanoimprint lithography.

This is achieved by a pre-patterned flexible mold that pushes the nanocubes from their initial random position to the grid trenches present in the mold[1].

In the final step adjacent nanocubes are welded epitaxially to form a continuous (quasi)monocrystalline material.

Figure 1 shows the assembly of the nanogrids before welding on a 100 μm^2 area.

Face-to-face nanocubes’ orientation and proper filling of the grids on a larger scale are both fundamental parameters that still need to be optimized before the welding step, in order to successfully assemble monocrystalline nanowires.

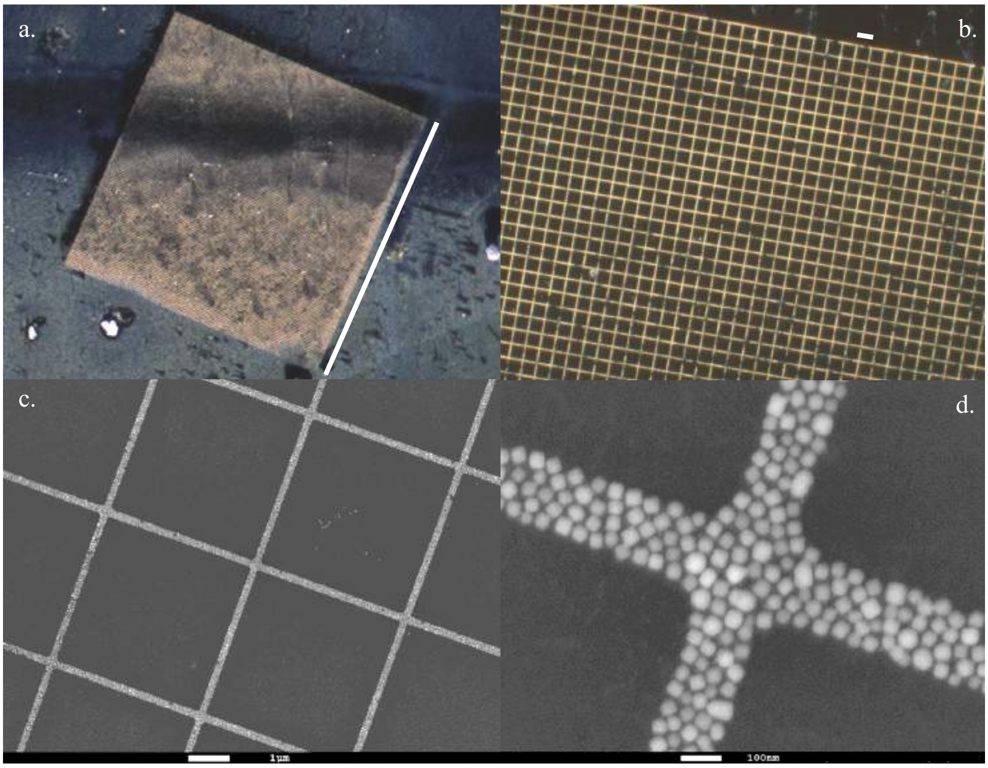

Figure 1: Ag nanocubes assembled in a grid structure (pitch=4µm, width=210nm) on a glass substrate[1,2]*:*

a. Stereo microscope (scale bar = 500µm)
b. Optical microscope (scale bar = 4µm)
c. SEM (scale bar = 1µm)
d. SEM (scale bar = 100nm)

[1] A. Capitaine, B. Sciacca et al., “Nanoparticle Imprint Lithography: From Nanoscale Metrology to Printable Metallic Grids,” ACS Nano, vol. 17, no. 10. American Chemical Society (ACS), pp. 9361–9373, May 12, 2023. doi: 10.1021/acsnano.3c01156.

[2] B. Sciacca et al., “Monocrystalline Nanopatterns Made by Nanocube Assembly and Epitaxy,” Advanced Materials, vol. 29, no. 26. Wiley, May 03, 2017. doi: 10.1002/adma.201701064.

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Evaluation of enzymatic activity and physical-chemical properties of new hydroxypyrazole inhibitors of *Plasmodium falciparum* dihydroorotate dehydrogenase and biochemical characterization of the recombinant protein

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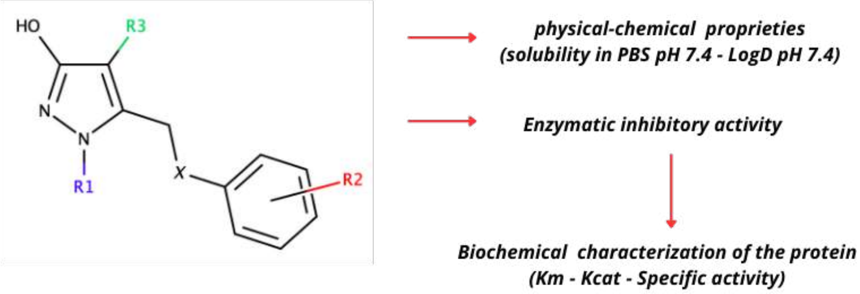
Malaria, caused by *Plasmodium falciparum* and transmitted by the Anopheles mosquito, represents one of the biggest infectious disease with a significative mortality and morbidity that kills millions of people every year. Currently, effective vaccines have not been developed yet and chemioterapy represents the main treatment. However, drug resistance is very common and new chemioterapic approaches have been identified. One of the most promising approaches is the targeting of the *Plasmodium falciparum* dihydroorotate dehydrogenase (*Pf*DHODH)[1]. DHODH is a ubiquitous flavine mononucleotide enzyme that rapresents the rate limiting step of *de novo* pyrimidine synthesis, acting the conversion of dihydroorotate (DHO) to orotate (ORO). This pathway is crucial to the survival of the parasite. While human cells have the capacity to employ the salvage pathway for acquiring pyrimidines, the Plasmodium species is limited to obtain pyrimidines exclusively through *de novo* synthesis.

The Medsynth group, an academic research team, previously published a work based on hydroxyazole scaffold-based *Pf*DHODH inhibitors[2]. In order to improve their activity, a new series of hydroxypyrazole inhibitors has been synthetized. Here we present the evaluation of their physical-chemical properties and the evaluation of their inhibitory activity on the recombinant *Pf*DHODH. This protein was firstly expressed and purified by the Department of Oncology and we present its biochemical characterization.



physical-chemical proprieties (solubility in PBS pH 7.4 - LogD pH 7.4)

Enzymatic inhibitory activity

Biochemical characterization of the protein (Km - Kcat - Specific activity)

Scaffold of the hydroxypyrazole pfDHODH inhibitors series.

[1] A. Singh, M. Maqbool, M. Mobashir, N. Hoda, Dihydroorotate dehydrogenase: a drug target for the development of antimalarials, Eur. J. Med. Chem. 125 (2017) 640-651.

[2] Pippione A.C., Sainas S., Goyal P., Fritzson I., Cassiano G.C., Giraudo A., et al. Hydroxyazole scaffold-based Plasmodium falciparum dihydroorotate dehydrogenase inhibitors: Synthesis, biological evaluation and X-ray structural studies. Eur J Med Chem. 163 (2019) 266–280.

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DNA detection via emissive naphthalenediimides intercalation

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In recent years, the use of emissive molecules for imaging has gained increased attention due to the unique features offered by fluorescence.[1] 1,4,5,8-Napththalenediimides (NDIs) are among the most versatile fluorophores explored throughout the last century.[2] In particular, this family of dyes has been employed in a large range of disciplines such as supramolecular chemistry, photovoltaics, ion-channels, catalysis through anion−π interactions, organic electronics and biological chemistry.[2] Bio-applications of NDIs are related to nucleic acids, lipid bilayer membranes and sensors for cells imaging.[3-5] Since 70s NDIs have been proposed as DNA intercalators due to their small size and flat profile which make them the suitable candidates for the accommodation between the base pairs in DNA duplex.[3] The combination of the traditional electron withdrawing imide-substitution with electron donor substituents in the core gives versatile push-pull chromophores.[6] The replacement of single group in the naphthalene moiety allows to modulate the optical and physical properties covering the whole visible spectra.[6] Instead, the variation of the imide edges has an effect on biological interactions and lipophilicity.

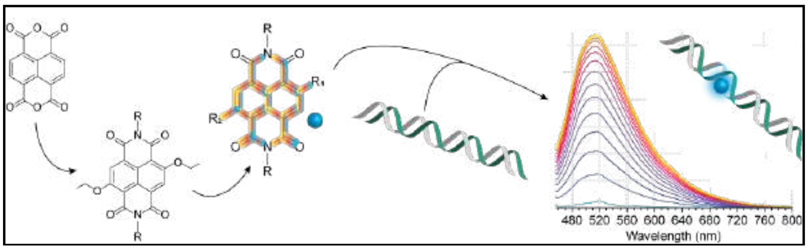

Figure 1 : Emissive DNA intercalating NDI.

Here we report NDIs decorated with various neutral and polar functionalities which prompt or facilitate the emissive NDIs intercalation in different commercially available DNA strands. The fluorescence modulation, signaling an effective intercalation, resulted to be driven by the crucial amphiphilic balance. A study on diverse substituent nature on the imide edges to fish out the most suitable candidate for the visualization of the nucleic acids in cells has been performed.

[1] Q. Shen, S. Wang, N. D. Yang, C. Zhang, Q. Wu, C. J. Yu, *J. Lumin*, **2020**, *225*, 117338.
[2] S. V. Bohosale, M. Al Kobaisi, R. W. Jadhav, P. P. Morajkar, *Chem. Soc. Rev.*, **2021**, *50*, 9845 – 9998.
[3] E. J. Gabbay, R. DeStefano, C. S. Baxter, *Biochem. Biophys. Res. Commun.*, **1973**, *51*, 1083 – 1089.
[4] D. Alonso Doval, A. Fin, M. Takahashi-Umebayashi, H. Riezman, A. Roux, N. Sakai, S. Matile, *S. Org. Biomol. Chem.*, **2012**, *10*, 6087.
[5] G.S. Khan, A. Shah, Zia-Ur-Rehman, D. Barker, *J. Photochem. Photobiol. B Biol.*, **2012**, *115*, 105 – 118.
[6] A. Fin, I. Petkova, D. Alonso Doval, N. Sakai, E. Vauthey, S. Matile, *S. Org. Biomol. Chem.*, **2011**, *9*, 8246.

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Comparison between SPE and QuEChERS extraction of emerging contaminants in Adamussium colbecki

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In recent years, research has substantiated the presence of emerging contaminants (ECs), known or assumed to cause harm to the environment, including in the ecosystem of remote regions, such as Antarctica. This unique environment, characterised by low temperatures, freezing water, and prolonged periods of darkness, reduces the degradation processes of contaminants, thus increasing the persistence of these chemicals [1]. Consequently, their accumulation or pseudo-persistence in the Antarctic environment may present various issues, such as mutagenicity, genotoxicity, reproductive and developmental disorders, and immune system disruption of various species [2]. To monitor marine contamination, bivalves are often utilized in the scientific literature [3]. These organisms are robust sentinels, due to their characteristics: they are filter feeders with limited mobility, posses wide spatial distribution, demonstrate tolerance to diverse environmental conditions, and are easily sampled [4]. Adamussium colbecki is one of the most common marine organisms on the Antarctic coasts. A. colbecki is a filter-feeding organism, that consumes phytoplanktonic suspensions, benthic diatoms, foraminifera, and general detritus and hence can accumulate ECs, especially those which are persistent, making it a reliable tool for environmental monitoring [3].

In this work, the bioindicator species A. colbecki was utilised to evaluate Antarctic contamination over the years. Certified reference material (CRM) was spiked with a known amount of ECs. Subsequently, the samples underwent two distinct pre-treatment procedures: solid-liquid extraction followed by solid phase extraction (SPE) and QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe) extraction. The resulting extracts were analysed using high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). The objective of the analysis was to evaluate the efficacy of the two different pre-treatment methodologies by comparing the matrix effect (ME%) and the recovery (R%) achieved by each technique. Analysis of the extract obtained after the SPE pre-treatment revealed that 5 compounds had acceptable ME (%) and R (%) (69%-79% and 79%-99%, respectively). Examination of samples subjected to pre-treatment with QuEChERS indicated that 8 compounds exhibited ME (%) and R (%) between 72% and 136% and 78% and 121%, respectively. These preliminary results indicate the potentialities of the latter procedure, characterised by higher eco-friendly characteristics and ease of use.

[1] Olalla, A. et al. (2020), Science of the Total Environment, 742, p. 140417.
[2] Bhardwaj, L. et al. (2018), Earth Systems and Environment, 2(1), pp. 35–54.
[3] Pizzini, S. et al. (2017), Chemosphere, 175, pp. 28–35.
[4] Pizzini, S. et al. (2015), Microchemical Journal, 121, pp. 184–191.

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New non-sulfonylurea NLRP3 inhibitors: discovery and selection of INF200, a 1,3,4-oxadiazol-2-one-based NLRP3 inhibitor

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The cytosolic multiprotein complex NLRP3, nucleotide-binding oligomerization domain leucine rich repeat and pyrin domain containing protein 3 inflammasome, plays an important role in the initiation and maintenance of the inflammation. Once activated and assembled, the NLRP3 inflammasome triggers the auto-proteolytic cleavage of pro-caspase-1 into the active caspase-1, converting the pro-inflammatory cytokines pro-interleukin (IL)-1β and pro-IL-18 into their active forms and causing pyroptotic cell death. An aberrant activation of NLRP3 inflammasome has been detected in chronic inflammatory diseases such as neurodegenerative, autoimmune, and cardiovascular diseases. The inhibition of the NLRP3 inflammasome activation represents an interesting new approach for the development of a new class of anti-inflammatory drugs. To date, the most studied NLRP3 inhibitor is MCC950, a disubstituted sulfonylurea derivative (figure 1). However, its *in vivo* use in humans has been limited due to hepatic toxicity.[1,2] Recent research has highlighted the key interactions of sulfonylurea inhibitors with the NACHT domain of the NLRP3 protein.[3] Inspired by this discovery, and through the use of computational techniques, we designed and synthesized a new series of compounds by replacing the sulfonylurea moiety with different heterocycles. The compounds were evaluated for *in vitro* ability to reduce IL-1β release and prevent NLRP3-dependent pyroptosis in human macrophages. The 1,3,4-oxadiazol-2-one derivative, **INF200**, showed the most promising results being able to prevent NLRP3-dependent pyroptosis triggered by LPS/ATP and LPS/MSU by 66.3 ± 6.6% and 61.6 ± 11.5% at 10 µM and to reduce IL-1β release with an IC_{50} of 16.6 ± 2.6 µM. **INF200** was tested in an *in vivo* model of high-fat-diet (HFD)-induced metaflammation in rats to evaluate its cardiometabolic effects. **INF200** proved able to reverse the unfavorable cardiometabolic dysfunction associated with obesity and to reduce systemic inflammation and anthropometric changes in HFD rats.[4]

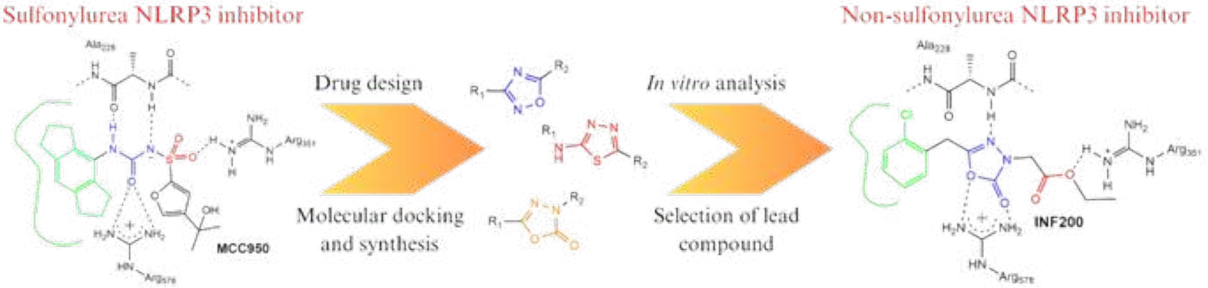

***Figure 1**. Structures of the investigated scaffolds and of the selected new NLRP3 inhibitor, **INF200**.*

[1] Swanson, K.V. et al. *Nat Rev Immunol*. 2019, **19**, 477–489.
[2] Blevins, H.M. et al. *Front Aging Neurosci*. 2022, **14**, 879021.
[3] Dekker, C. et al. *J. Mol. Biol*. 2021, **433**, 167309.
[4] Gastaldi, S. et al. *Eur. J. Med. Chem*. 2023, **257**, 115542.

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Exploring New Chemical Space in Drug Libraries via Gold Catalysis

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The great majority of medicinal chemistry-relevant structures tend to have a planar geometry.[1] Recently, in an effort to increase the molecular diversity in fragments libraries, a particular attention has been devoted to the three-dimensionality character of chemical structures.[2] However, synthesizing such original building blocks using a fast and efficient methodology remains a key challenge for an organic chemist. In another hand, driven by growing environmental concerns, the emergence of green chemistry induces the development of more sustainable synthesis methods. In this context, we focused on gold catalysis, which is known as a powerful tool for the synthesis of complex core structures according to atom-economical and green processes.[3] We developed an efficient and mild synthetic route for the preparation of functionalized polycyclic derivatives via gold-mediated transformations. Starting from simple substrates and depending on the reaction conditions, the specific reactivity of gold led to a divergent synthesis of various carbo- and heterocyclic scaffolds, with a high degree of molecular complexity.[4] By playing with and optimizing the conditions, we were able to reach selectively each structure. These building blocks represent privileged scaffolds in a search for increased molecular diversity of drug-candidate libraries.

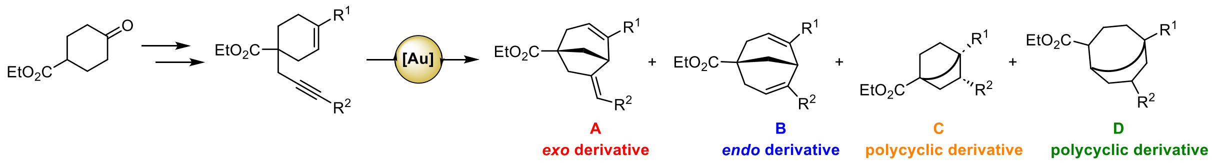

Figure 1 : Gold-catalyzed divergent synthesis of polycyclic derivatives

[1] Hamilton, D. J.; Dekker, T.; Klein, H. F.; Janssen, G. V.; Wijtmans, M.; O'Brien, P.; de Esch, I. J. P. *Drug Discovery Today: Technologies* **2020**, *38*, 77.

[2] (a) Lovering, F.; Bikker, J.; Humblet, C. *J. Med. Chem*. **2009**, *52*, 6752. (b) Lovering, F. *Med. Chem. Commun*. **2013**, *4*, 515. (c) Meyers, J.; Carter, M.; Mok, N. Y.; Brown, N. *Future Medicinal Chemistry* **2016**, *8*, 1753.

[3] (a) A. S. K. Hashmi, F. D. Toste, Eds.; Modern Gold Catalyzed Synthesis; Wiley VCH, **2012**. (b) F. D. Toste, V. Michelet Eds.; Gold Catalysis: An Homogeneous Approach; Imperial College Press: London, **2014**. (c) Z. Rappoport, J. F. Liebman, I. Marek, Eds.; John Wiley & Sons, **2014** (d) L. M. Slaughter, Ed.; Homogeneous Gold Catalysis. In Topics in Current Chemistry; Springer, **2015**.

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A sustainable approach for the synthesis of hydroxyapatite from eggshells

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Hydroxyapatite ($Ca_{10}(PO_4)_6(OH_2)$, HAp) is a biocompatible and biodegradable material, widely studied for biomedical applications as bioceramic in bone and dental implants and drug-carriers as well. Beyond these classical biomedical applications, HAp could also have a role in the ecological transition: its nanoparticles have been proposed as solid fertiliser, to promote a controlled release of P for more sustainable agronomy.[1]

Eggshells, which are composed of approximately 94% of $CaCO_3$, are an abundant and widespread waste and can be converted into different Ca-precursors to obtain HAp. Different synthetic approaches have been proposed (e.g. hydrothermal, wet precipitation, mechanochemical), but most of the reported studies involved thermal treatment at $T>600°C$.[2] This step requires high energy expenditure and produces a large amount of CO_2 from carbonate decomposition.

To reduce the environmental impact of HAp synthesis we decided to use ascorbic acid, a nontoxic and cost-effective reagent, to dissolve eggshell and trap the produced CO_2 as oxalate ions[3]. The composition, crystallinity and morphology of the obtained product were compared to HAp obtained by a classical precipitation method using $Ca(OH)_2$ or eggshell as Ca sources. We study the dissolution of the obtained HAp nanoparticles and results indicate that HAp obtained using eggshells and ascorbic acid is the most promising nanofertilizer, releasing a higher amount of P.

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[2] Arokiasamy p. et al., Ceram. Int. 2022, 48, 14959–14979
[3] Pastero, L.; Curetti, N.; Ortenzi, M.A.; Schiavoni, M.; Destefanis, E.; Pavese, A. Sci. Total Environ. 2019, 666, 1232–1244

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OXIDATIVE ANIONIC HOMO-FRIES REARRANGEMENT UNDER BENCH-TYPE AEROBIC CONDITIONS

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The development of new sustainable protocols which enable the use of aerobic/protic conditions in alkali-metal-mediated transformations has profoundly reshaped the conceptual chemistry of these highly polar organometallic reagents.[1] Our recent findings in this field disclosed that highly reactive alkyllithiums can efficiently promote chemoselective nucleophilic acyl substitution (S_NAc)[2] and regioselective metalation[3,4] reactions using deep eutectic solvents (DESs) or cyclopentyl methyl ether (CPME) as sustainable reaction media, working at room temperature, in the presence of moisture and air. Furthermore, we recently illustrated the beneficial active role of protic deep eutectic mixtures in the regioselective metalation/Fries rearrangement of *O*-aryl carbamates, as the commonly detrimental competitive protonolysis of the organolithium occurring in these reaction media prevents the formation of byproducts arising from multiple metalation steps.[5]

Motivated by our ongoing interest in extending the feasibility of organolithium reagents in unconventional sustainable solvents, we herein investigate the usefulness of bench-type conditions to promote the aerobic oxidation of benzylic anions generated from *O*-tolyl carbamate derivatives upon a metalation-Fries rearrangement sequence. Kinetic studies and mechanistic insights into the formation of dianionic species will be also discussed.

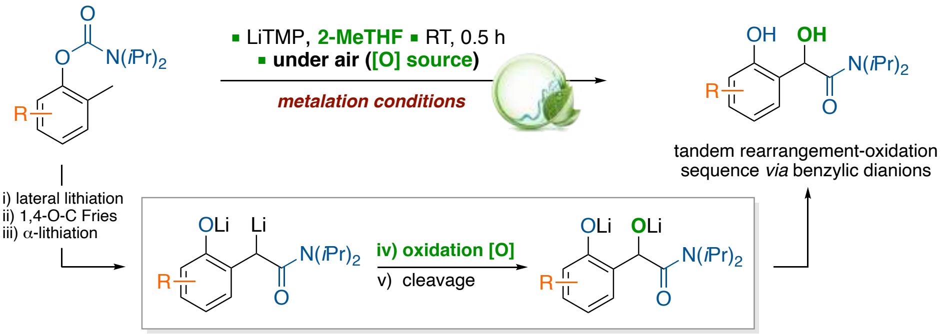

***Figure 1**: one-pot oxidative anionic homo-Fries rearrangement.*

[1] a) F. M. Perna, P. Vitale, V. Capriati, *Curr. Opin. Green Sustain. Chem.* **2021**, *30*, 100487; b) S. E. Garcia-Garrido, A. Presa Soto, E. Hevia, J. García-Álvarez, *Eur. J. Inorg. Chem.* **2021**, *2021*, 3116 – 3130; c) J. García-Álvarez, E. Hevia, V. Capriati, *Chem. Eur. J.* **2018**, *24*, 14854 – 14863.

[2] S. Ghinato, D. Territo, A. Maranzana, V. Capriati, M. Blangetti, C. Prandi, *Chem. Eur. J.* **2021**, *27*, 2868 – 2874.

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Gold-Catalyzed One-Pot Cycloisomerization/Nucleophilic Addition/Rearrangement of Pyrrole Carbaldehyde Derivatives

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The use of gold catalysis as a tool in organic synthesis is a promising approach that has been emerging in the past decade.[1] Some of the important work in this area includes the gold-catalyzed addition/cyclization reaction to 3-alkoxy-benzoisochromenes that was developed by the Grela group.[2] Considering our group's interest in atom-economical Au-catalyzed processes,[3] we have envisioned building on this reactivity, inspired by studies on C→O rearrangement in presence of a Lewis acid conducted by Harrity's group.[4] Recent studies by our group,[5] building on these two studies, extended the reactivity to nucleophilic aromatic derivatives to allow for a gold-catalyzed orthogonal tandem reaction to access carbocyclic ketones on naphthalene. The present study focuses on extending this cyclization-rearrangement reactivity to pyrrole derivatives, which have been shown, unlike previous substrates, to be diastereoselective. Studies have been conducted to optimize the gold-catalyzed conditions for this type of substrate, followed by scoping using modified substrates and different nucleophiles.[6] Finally, given the interesting property of diastereospecificity of the reaction on pyrrole carbaldehyde derivatives, enantioselective versions of the transformation were also envisioned.

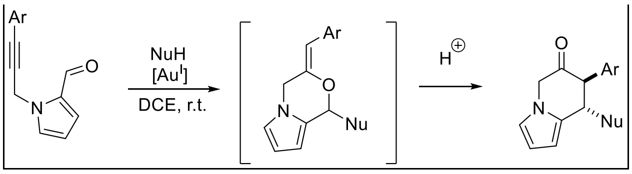

Figure 1 : Gold-catalyzed cyclization/rearrangement of pyrrole derivatives.

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Exploitation of the whole unsorted tuna side streams: extraction of valuable proteins within EcoeFISHent project

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The fishery production has grown dramatically over the past few years, and as a result, disposing of the side streams that are produced has become a major environmental and economic problem to solve [1].

One of the main objectives of EcoeFISHent, a project of the Horizon 2020 Program–Green Deal (G.A. ID 101036428) [2], consists in the valorization of rejected and underused biomass coming from the fish supply chain and the sustainable extraction of high-value bioactive molecules with potential applications in nutraceutical and cosmetic industries, following the "zero-waste" concept according to the 12th Sustainable Development Goal (SDG) [3].

Many investigations are being conducted on the enzymatic extraction of proteins from fish biomasses, but almost no research has paid attention to the exploitation of unsorted, non-separated fishery biomasses.

The authors suggest a scalable method in order to recover valuable proteins starting from samples of unsorted mixed raw (crude) tuna scraps [4], which had previously been dehydrated using an industrially patented process [5] that improves the logistics of managing highly perishable biomass by reducing its volume and stabilizing it microbiologically, while also avoiding the laborious sorting step of tuna side streams.

All the protein fractions namely, non-collagenous proteins (NCs and ALKs), gelatin (G), and hydrolyzed gelatin/collagen peptides (HGPs) were recovered in the proposed single cascade flowchart. After their isolation/purification, the protein extracts have been stabilized by different dehydrations (lyophilizing, oven-drying and spray-drying). The so obtained products were characterized in terms of proximate analysis, FTIR/molecular structure, amino acid composition, and CIELab color. Moreover, as regards G and HGPs, further analyses concerning rheological properties and antioxidant activity were performed in order to assess their potential applicability in different fields such as biomaterials, nutraceuticals and cosmetics.

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Investigation on sustainable technologies for Olive Mill Wastewaters

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The olive mill wastewaters (OMW) represent a significant by-product of the olive oil extraction process. These waters are rich in organic compounds, including polyphenols, lipids, proteins, and carbohydrates, giving them potential value as a resource[1]. However, the disposal or management of OMW poses a critical challenge with significant environmental and agricultural repercussions. Currently, many regions allow the spreading of OMW onto the soil as a disposal method; nevertheless, this practice presents several problems. OMW has a high COD and organic matter content, which can increase nutrient loads in soil and groundwater bodies, leading to contamination issues. Additionally, the presence of phytotoxic and antimicrobial compounds, such as polyphenols, can harm plants and the surrounding ecosystem[2]. Consequently, there is an urgent need to develop sustainable alternatives for the treatment and utilization of OMW to mitigate the environmental and agricultural risks associated with its management. This research aims to address this challenge by exploring innovative methodologies for the extraction, purification, and concentration of compounds of interest from OMW to produce biopesticides and biofertilizers for use in agriculture.

Among the possible approaches that can be adopted, there is an initial pretreatment, which involves acidifying the OMW to increase the sedimentation rate of suspended solids, thus facilitating the removal of these solids and making the water easier to process. Another possible approach is the filtration of the OMW using membrane separation processes, which not only removes suspended solids but also purifies the waters from high molecular weight organic compounds and concentrates compounds of interest such as polyphenols. In this context, three different nanofiltration membranes and one reverse osmosis membrane have been tested. The performances of the membranes, in terms of retention of salts and polyphenols, were studied thanks a lab scale stirred cell. To gain most of the performance of the two types of membranes, it was decided to couple a dialysis process (nanofiltration membrane) that promotes the washing of the OMW and therefore the recovery of polyphenols onto the permeate stream, with a concentration process (reverse osmosis membrane) that allows the reduction of the volumes of water obtained from dialysis and therefore the concentration of polyphenols. At the same time, however, part of the salts that dialysis cannot retain are concentrated, and therefore, to remove them, solvent extraction and a separation treatment on resin are interesting. Both processes allow the separation of salts from phenolic compounds, which can then be lyophilized and used as a matrix for subsequent treatments. One of these is an enzymatic lipophilization, which consents the esterification of polyphenols, now lipophilic and hence no longer soluble in water but in organic solvents. This process is in its early stages but is promising as it can be used to create a suitable matrix for the formulation of a biopesticide composed of an active ingredient consisting of acylated polyphenol, possibly dissolved in an organic solvent, dispersed and thus diluted in an aqueous phase.

This research is funded by Agritech Project (PNRR), National Center for Technology in Agriculture.

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Study of influence of organic matter and inorganic ions on soybean peroxidase activity: from the lab to real applications

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Bioremediation methods have become very attractive for environmental applications, and specific enzymes-based treatments offer several advantages as high catalytic capacity with milder reaction conditions, production of nontoxic compounds, and environmental friendliness.

Several studies have been published on the use of peroxidases for the remediation of both synthetic and real aqueous matrices containing organic contaminants. However, a relative limited number of research are devoted to study the influence of dissolved organic matter on the activity of these enzymes or to define the influence of inorganic ions and ionic strength.

With the purpose to explore these aspects and to better evaluate the effective possibility to exploit peroxidases for real application in fresh and sea water, in this work we subjected soybean peroxidase (SBP) to various activity tests in deionized water and in aqueous matrices containing humic acids or salts (a mixture of NaCl, NaBr and other salts simulating sea water according to the ASTM D1141-98 standard procedure). As shown in Figure 1, the enzymatic activity decreases as function of humic acid concentration (from 25 to 100 ppm) while it seems enhanced by the increase in the ionic strength of the solution (from 0 to 2M), in particular by addition of NaBr. These trends are also maintained when studying the reaction between SBP and target contaminants as dyes (methyl orange) or chlorinated molecules (2,4,6-trichlorophenol and 2,4-dichlorophenol).

These preliminary results are in agreement with previous studies which hypothesize that the organic matter could inhibit peroxidases efficiency by acting as competitive substrates [1] and suggest a possible use of bio-remediation also for contaminated sea water [2].

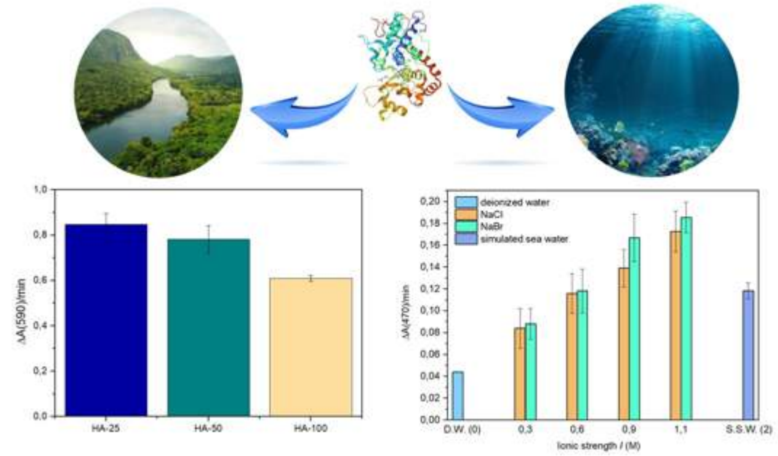

Figure 1: SBP activity test results. Left: SBP activity as function of humic acid concentration (DMAB/MBTH/H_2O_2 system); right: SBP activity as function of ionic strength (Guaiacol/H_2O_2 system)

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Development of a novel catalytic methodology for the synthesis of cyclic ethers with potential anticancer applications

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Sodwanones, triterpenoids isolated from the marine sponge *Axinella weltneri*, have been reported to inhibit the hypoxia-inducible factor 1 (HIF-1)[1], a target scarcely explored in the context of therapy-resistant cancers.[2] They feature a cyclohexane-oxepane subunit, which is known to exhibit interesting cytotoxic properties[3], attached to a variety of eastern fragments. Despite their promising biological activities[4], very few synthetic approaches have been reported so far, due to their structural complexity. Herein, we report an efficient biomimetic synthetic methodology, to access a wide range of oxepane derivatives.

Most of the developed strategies to obtain seven membered-ring cyclic ethers rely on the cyclization *via* the addition of hydroxy functions on an electrophilic site (epoxides, allenes, activated olefins,…), mediated by stoichiometric amount of Lewis acids such as boron trifluoride etherate.[5] This work focused on the development of a novel Lewis acid based catalytic methodology, starting from di-epoxidized monoterpene derivatives (*i.e.* geraniol and nerol). The use of Lewis superacids such as bismuth (III) triflates, at only 1 mol%, triggers an epoxide-opening cascade reaction, leading to various cyclic ethers, among them several oxepane derivatives (Figure 1). Applied to more complex sesquiterpenes, this methodology would allow access to a wide range of cyclohexane-oxepane derivatives, analogs of the western fragments of sodwanones, that will be evaluated for their biological properties, notably against HIF-1.

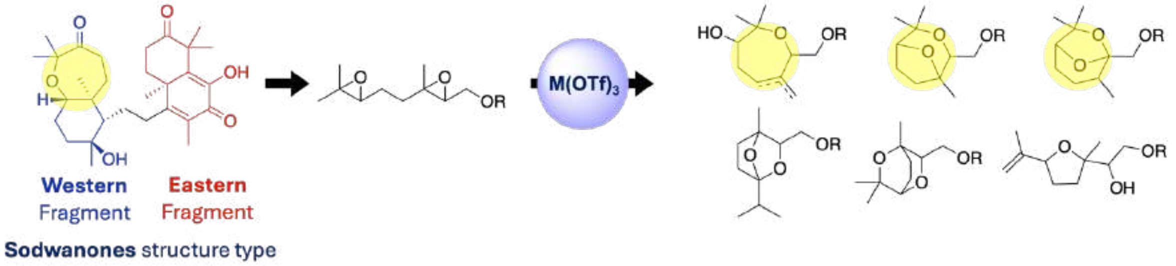

Figure 1: General overview of the obtained structures

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Hydroxide ion mobility in anion exchange ionomers

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The effective hydroxide ion mobility in anion exchange membranes is an important phenomenological parameter, which is key for electrochemical applications, because it is related to the ion conductivity of the membrane and thus the Ohmic drop of the device.

The effective hydroxide ion mobility can be calculated from the ionic conductivity and the water uptake of the membranes. We have compiled many hydroxide ion mobility data from our own measurements and from available literature data. We show that linear relations can be written between the ion mobility and the square root of the ion concentration, which have similarities with classical Kohlrausch laws for dilution of weak electrolytes.

The percolation threshold and tortuosity of the membranes can be deduced from the universal law and a renormalization equation, respectively; they are discussed from the point of view of membrane composition and ion mobility-ionomer structure relationships. [1]

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Biocatalytic routes for the synthesis of N-acyl amino acids

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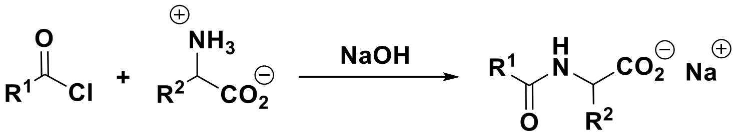
Surfactants are chemical compounds that due to hydrophilic and hydrophobic moieties reduce surface tension after concentration at the interface.

Mainly, the raw materials for their synthesis have petrochemical origin. However, extraction and using of oil is not environmentally friendly, it causes serious damage to various ecosystems. Environmental legislation and governmental restrictions as well as low toxicity, high biodegradability and high efficiency led to increasing of the surfactants production from renewable raw materials.

Amino acid-based surfactants are mild surfactants, that have aroused strong interest in the last twenty years because of their properties and possibility to use raw materials of animal or agricultural origin[1].

The most common reaction for mild surfactants production is Schotten-Baumann aminolysis (*Scheme 1*), carried out in water at low temperature.

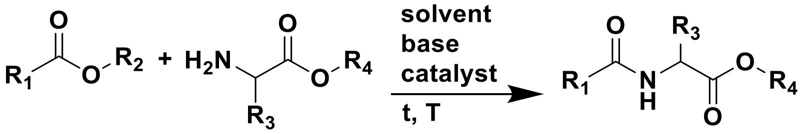


Scheme 1: Schotten-Baumann aminolysis

The most significant disadvantage of this process is the not environmentally production of acyl chlorides. For their formation, toxic reagents are used ($SOCl_2$, $COCl_2$, PCl_3, $POCl_3$, PCl_5) in stoichiometric quantities[2].

Catalytic alternatives led to improve atom economy and, also, to minimize environmental impact. Biocatalytic approaches make it possible to use biodegradable and nontoxic wild-type and engineered enzymes in different type of chemical reactions[5].

Instead of environmentally unfriendly acyl chlorides in enzymatic amide formation (*Scheme 2)* due to catalytic mechanism fatty acid esters were used as the acyl donor.



Scheme 2: Enzymatic amide formation

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Looks can be deceiving: not just chalk in chalk. Analysis of the materials of *Madonnari* art by XRPD and ATR-FTIR

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The characterisation of painting materials is a very special aspect aimed at a greater understanding of the painting technique adopted, the definition of different types of workability and the durability of the artwork. This last feature is the peculiarity of *Madonnara* art: a particular *ephemeral category of street art* that entails the use of materials not intended to last over time. The study first involved the professionalism of curators and artists involved in the *Arte Madonnara* Festival, conceived in 1973 in Grazie di Curtatone (Mantua, Italy), where a 24-hour international art competition takes place annually [1]. Usually, these street paintings are realised on the cobbles or asphalt, nevertheless there is an increasing intention to use mobile substrates, consequently, can be preserved and musealised. Within this research, for the first time, both home-made materials, reclaimed materials and commercial 'chalks' used by some *Madonnari* artists were investigated. The techniques adopted were X-ray Powder Diffraction (XRPD) and Attenuated Total Reflection Fourier Transform Infrared Spectroscopy (ATR-FTIR) (Fig. 1), here combined because providing complementary information. XRPD detected inorganic components, in which the diffractometric patterns obtained can be traceable to crystalline phases. ATR-FTIR enabled the identification of organic dyes and pigments together with any other organic components such as modifiers and stabilisers. The result was a great heterogeneity observed in commercial pastels in which several fillers other than chalk were identified such as barite, kaolinite, calcite, and talc. Also, a certain variety occurred for the different dyes and pigments identified. Moreover, the prevailing minerals of the recovered materials and the composition of the home-made pastels were defined, which were matched by considerations of ease of colour application then related to composition [2].

Figure 1 : ATR-FTIR analysis of red chalk.

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Synthesis and characterization of TI_3C_2 MXene heterojunctions for enhanced photocatalytic properties in hydrogen photoproduction

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The hydrogen production can be performed in different ways: electrolysis, thermo-splitting, and photo-splitting. [1] The methods just mentioned use different types of energy to decompose water into hydrogen and oxygen, even though the efficiencies are really different. Indeed, the efficiencies of these systems are generally 70% when electricity is used, 40% when heat is used, and about 0,5% when light is the source of energy. With the idea of developing efficient green processes to produce hydrogen, among the quoted mechanisms photolysis results be a very interesting and feasible option since harvesting solar energy would directly produce H_2. The efficiency of the technology is still very low, due to several factors that depend on the reaction itself and for the catalyst used.

The work performed during this master thesis was therefore devoted to producing and characterizing MXene (Ti_3C_2) [2] to use it as a cocatalyst in possible combination with other synthesized semiconductors for an enhanced photocatalytic heterojunction. This material shown a 2D structure and is also interesting the presents of many functional groups that can be tuned by changing the synthesis. It exhibits absorption in the visible spectrum, boasts conductivity comparable to metals, and maintains an ideal Fermi level for hydrogen production when interacting with water.

In this study, the synthesis of this compound was always executed starting using Ti_3AlC_2 as precursor, trying different etching processes. Different semiconductors were also synthesized paying particular attention to different factors such as energy gap, the position of valence and conduction band, and sustainability aspects. All the heterojunctions between semiconductors and MXene were formed with the same calcination method (450°C for 4h in air). All the synthetize materials were then characterized with XRD, SEM and UV-Vis analyses.

In the end, the photocatalytic performances of the materials were tested for the production H_2 by using different LED source (characterize by different wavelengths) to evaluate the performances.

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Theoretical study of the reaction mechanism and solvent effect in the reaction between $LiCH_2SiMe$ and *N*-benzoylpirrolydine

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A theoretical side-by-side study with the department's organic chemistry laboratory was conducted on the conversion of non-activated amides to α,β-unsaturated ketones using $LiCH_2SiMe_3$.[1] The use of two different solvents, THF and CPME, resulted in the formation of two distinct products, with high stereoselectivity. The purpose of this study is to elucidate the unknown reaction mechanism in the two different solvents using DFT calculations. Because lithium tends to form aggregates in solution[2], we tried to perform different model situations that represent our reagent, from the monomeric to dimeric structures, to take into account the solvation effect on the complex (Figure 1). The two-layer ONIOM method was used to study the dimeric structures. In addition to the calculation of the same reaction carried out in the two aforementioned solvents, studies were also performed in water because the reaction was experimentally quenched with water. This study provides valuable insights into the reaction mechanisms of acyl nucleophilic substitution and emphasizes the need for further investigation to fully understand the role of the solvent and the equilibrium between different reaction products.

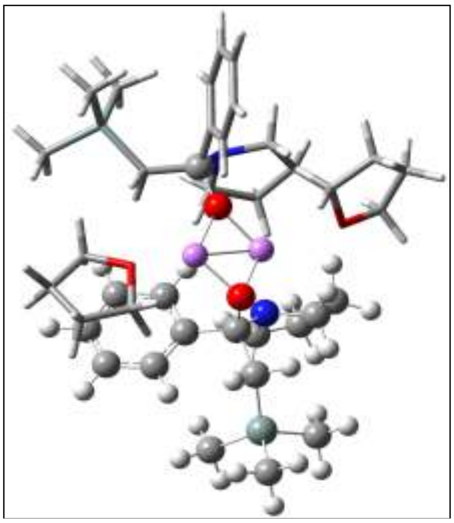

Figure 1 : Dimeric structure of the initial complex. The different visualization choices, tube and ball and sticks, correspond to the low and high level of calculation using ONIOM method, respectively.

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Self-assembling dendrimer nanosystems effectively decrease drug affinity to hERG channel for overcoming cardiotoxicity

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Cardiotoxicity is a leading cause of drug failure or drug withdrawal from market, with hERG-related cardiotoxicity accounting for over 70% of such cases [1]. Overcoming or reducing hERG binding to mitigate cardiac toxicity is therefore of paramount importance for drug development. Nanotechnology-based drug delivery has been extensively applied to reduce drug toxicity and promote drug efficacy [2]. However, there is little research on nanotechnology-based drug delivery to reduce hERG-related cardiotoxicity. Here, we report the use of self-assembling dendrimer nanosystems for drug encapsulation [3-5] to effectively reduce hERG-binding related cardiotoxicity. Specifically, the self-assembling amphiphilic dendrimer nanosystems efficiently loaded the antimalarial drug chloroquine, the anticancer agent doxorubicin, and the NUPR1 inhibitor ZZW-115, all three drug molecules having high hERG affinity. Indeed, the binding affinities of these molecules to hERG were reduced by 3 to 10 times when they were encapsulated within the dendrimer nanomicelles. Importantly, the drug-loaded dendrimer nanosystems also reduced the in vivo toxicity of the free drugs while enhancing their in vivo therapeutic activity through passive targeting of disease lesions via the enhanced permeability and retention (EPR) effect. This study highlights the potential of the self-assembling dendrimer nanosystems to overcome and reduce the hERG-binding and related cardiotoxicity, offering a new perspective in drug development for safe and efficacious treatment.

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Chemo-enzymatic routes from levoglucosenone to sustainable terpolyesters

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The need to develop more sustainable chemicals and materials for mitigating the effects of climate change is a pressing challenge for mankind. The research of innovative materials based on by-products can be a solution to convert waste into value therefore reducing the impact of industrial processes. For example, the use of the cellulose-derived monomer levoglucosan (LGA) for the synthesis of terpolymers has recently been reported[1].

In this work, novel terpolyesters based on the levoglucosenone-derived diol HO-LGOL were developed. HO-LGOL is similar to LGA and it's difficult to polymerize because of its secondary hydroxyl groups. In comparison with previous works, in the enzymatic polycondensation experiments the traditionally used reaction solvent diphenyl ether (DPE) was substituted with Cygnet 2.0, a green solvent derived from Cyrene (also obtained by cellulose pyrolysis and subsequent hydrogenation). The family of Cygnets solvents offers sustainable and safe alternatives to toxic aprotic dipolar organic solvents such as NMP and DMF[2] in applications such as enzymatic polymerizations[3] and membrane casting[4]. Cygnet 2.0 is beneficial because it provides a suitable reaction environment for the enzyme and allows the complete solubilization of the monomers, enhancing the greenness of the synthesis.

Terpolymerizations were conducted using α-ω diols of different lengths and dimethyl adipate as monomers in addition to HO-LGOL using the lipase B from *Candida antarctica* (CaLB) as the biocatalysts. Regarding polymerization, different monomers and various molar ratios were tested to investigate and find the best possible combination. Between 12-44% HO-LGOL was incorporated into the polymer chain, indicating a good monomer incorporation. Reaction yields ranged from 20 to 59%, while the obtained M_n values were between 1.3 and 3.1 kDa, showing the formation of oligomeric polymer chains. Thermal analyses of the materials exhibited interesting T_g values, between -50 and 16 °C, highlighting how the different incorporation of HO-LGOL can significantly alter the thermal and physical properties of the polymers.

In conclusion, bio-based monomers have been successfully polymerized to create interesting terpolyesters with a significant HO-LGOL incorporation and a range of different T_g values, utilizing enzymes as the catalysts and Cygnet 2.0 as a green reaction solvent.

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[2] Alves Costa Pacheco, A. et al. *ChemSusChem* **2016**, *9* (24), 3503–3512.
[3] Warne, C. M. et al. *Green Chemistry Letters and Reviews* **2023**, *16* (1), 2154573.
[4] Milescu, R. A et al. *ChemSusChem* **2021**, *14* (16), 3367–3381.

Diversity-oriented synthesis of pyrazole and pyrimidine compounds as novel antimalarial agents

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Push-pull alkenes refer to substituted alkenes bearing one or two electron-donating groups at one end of the double bond and one or two electron-accepting groups at the other end. Due to their unique electron distribution, push-pull alkenes can react with both electrophilic and nucleophilic species and therefore represent versatile synthons in organic synthesis [1]. In particular, ketene *N,S*- and *S,S*-acetals are representative classes of push-pull olefins widely used as for the preparation of heterocycle derivatives [2]. Recently, we reported a stepwise synthetic procedure for the preparation, through ketene *N,S*-acetal intermediates, of novel 5-anilinopyrazoles **1** (Figure 1) endowed with antimalarial activities [3]. To further extend the structure-activity relationships (SARs) of these compounds, we designed and synthesized the highly functionalized pyrazoles **2** and pyrimidines **3** (Figure 1). These compounds were prepared through a versatile synthetic procedure which involved the isolation of ketene *S,S*-acetals **A**, their functionalization to *N,S*-acetals **B**, followed by cyclization with hydrazine or guanidine.

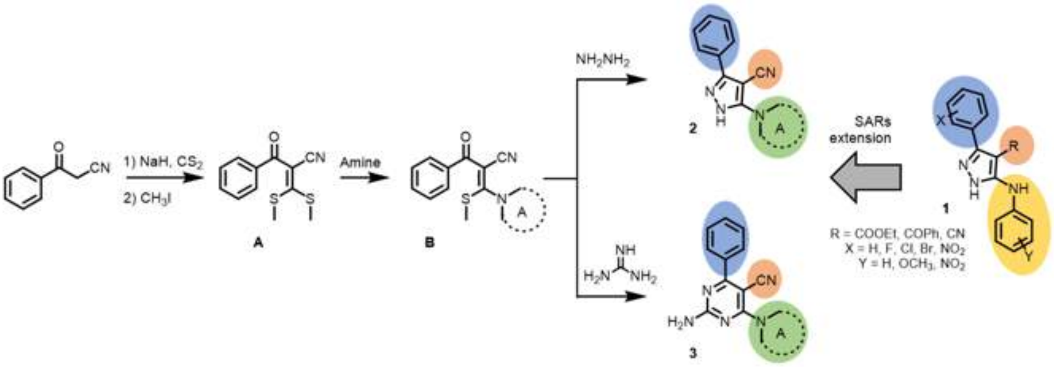

*Figure 1: Structure of previously reported pyrazoles **1** and synthesis of novel heterocyclic compounds **2** and **3**.*

Selected derivatives **2** and **3** showed significant activity against D10 and chloroquine-resistant W2 *Plasmodium* strains without cytotoxic effect on normal fibroblast cells.

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[3] Lusardi, M. *et al.*, *Molecules* **2023**, *28*, 1712.

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Hybrid materials for the adsorption removal of dyes from water

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The problem of environmental pollution is well-known by the scientific community. In these last years, it is estimated that 7 x 10^5 tons of toxic wastewater containing dyes are produced every year. Dyes are known for their low biodegradability, high solubility in water and toxicity in the environment. Therefore, it is necessary to find a strategy for the removal of these pollutants from wastewater. The removal of organic molecules from water media through adsorption on solid sorbents deserved a lot of attention in the last years. An ideal adsorbent should remove in a short time high quantities of dyes and should be inexpensive, regenerable and reusable. Different materials, for instance carbons, zeolite, clays, polymers are used to this purpose, but the class of hybrid organic-inorganic silica materials is deserving increasing interest for their peculiar adsorption performances [1].

Among the class of hybrid silicas, Swellable Organo-Modified Silicas (SOMS) possess the peculiar ability to swell, thus expanding their volume, when in contact with organic solvents. The swelling property gives SOMS more enhanced adsorption performances towards organic moieties in water, including dyes, if compared to inorganic or organic-grafted silicas [2]. SOMS are synthesized by a base-catalysed sol-gel process of bis(trimethoxysilylethyl)benzene that possesses an aromatic ring linked to the silicon atom by an ethyl group. SOMS can also be functionalized with a quaternary amino group, which gives a positive surface charge to the final material (QA-SOMS) [3]. These materials will be used for the removal of dyes from water by adsorption, considering their promising performances.

Moreover, different mesoporous silicas (SBA-16 type) were synthesized and functionalized with organic groups to perform a comparison in adsorption performances.

The characterization of the materials was made through a multi-technical investigation (elemental analysis, XRD, FT-IR, ss-NMR, DLS, Z-Potential) to obtain morphological, textural, and chemical information. Finally, the adsorption kinetics, isotherm, pH-effect, and reutilization towards dye molecules were tested for the materials synthesised, in particular for SOMS which resulted to be the most promising adsorbent (Figure 1).

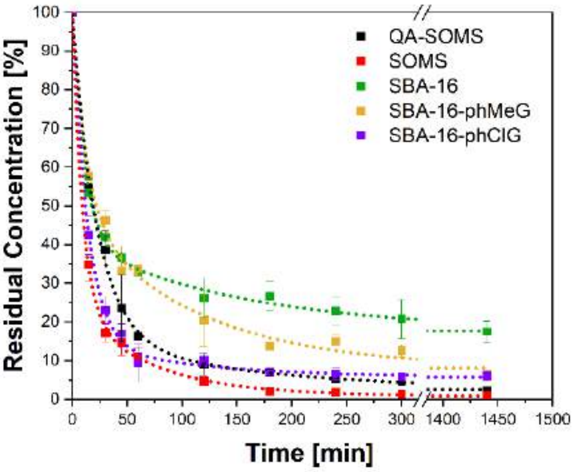

Figure 1: Adsorption kinetics of a 100 ppm solution of crystal violet by SOMS, QA-SOMS and mesoporous silica SBA-16 both organo-functionalized (SBA-16-phClG and SBA-16-phMeG) and not (SBA-16).

[1] J. Guo et al., *Separation and Purification Technology*, **2024**, *330*, 125480.
[2] V. Miglio et al., *J. Phys. Chem. C*, **2024**, *128*, *5*, 2179–2189.
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ALD of Ternary Silicides as Efficient Catalysts for Water Photooxidation

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Silicon is a well-known semiconductor, whose abundance and stability make it the most widely used material in the electronics industry. Among all the applications, the position and the width of its band gap make it also suitable for photoelectrochemical devices, specifically for the water-splitting reaction. However, due to the poor stability and efficiency of silicon in aqueous solutions, protective and catalytic layers are necessary. Currently, Pt and IrO_2 are considered the best catalysts for HER and OER reactions, but they are rare and critical materials.[1] Therefore, research on affordable, abundant and efficient catalytic materials is crucial. In this context, the research on affordable, abundant, and efficient catalytic materials has become crucial. Our group recently optimized the Atomic Layer Deposition (ALD) of TiO_2 as an efficient protective layer[2] and tested innovative ALD precursors for the synthesis of NiO_x, which shows good catalytic properties in alkaline media[3]. From the combination of these two non-critical materials, we obtained a new class of promising cost-effective co-catalysts for water photo-oxidation. The $Si/TiO_2/NiO_x$ system was annealed through rapid thermal processing in a reductive atmosphere, resulting in the formation of a chemically stable $Si_7Ti_4Ni_4$ alloy, in the shape of nanoparticles (figure 1b). A patent was filed for this development.[4] The nanostructured particles enhance the active surface area of the electrode and reduce the charge recombination rate, leading to a remarkable improvement in the onset potential of the oxygen evolution reaction (figure 1c).

However, the catalytic mechanism is not yet well understood and a photoelectrochemical activation of the catalyst is needed to improve the photoanode performance. Therefore, we are investigating different deposition combinations of the two oxide layers and trying to understand the correlation between the material structure and the photoelectrochemical results. The presence of a SiO_x interlayer between the substrate and the catalyst might allow us to obtain a metal-insulator-semiconductor system, which can improve the effective barrier height and the degree of band bending near the Si surface, and as a result, increase the photocurrent.[5]

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Activated alkoxyamine conjugated nanoparticles as antibacterial agents for plants

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Global trade and climate changes facilitate both, "migration" and colonisation of our shores by new types of bacteria coming from other continents. The EU has chosen to ban the use of antibiotics to control plant bacterial diseases with the aim to limit the emergence and the spreading of antibiotic resistant strains. The curative fight against plant bacteria will allow the conquering of new territories leading to dramatic changes in economics, cultures, landscape and ecology.

To circumvent the issues of anti-bacteria drugs, we envision a strategy relying on the development of a new nano-system based on the controlled *in situ* generation of Reactive Oxygen Species (ROS) as weapon. This versatile family of inorganic nanoparticles conjugated with radical initiators (alkoxyamines) envisioning a controlled generation of ROS bases on the activation of nanoparticles by external stimuli such as magnetic field (*Fig. 1*).

We synthetize alkoxyamine linked to gallic acid[1] and possessing phosphoric acid function. The gallic acid is the vector for the bacteria and the phosphonic acid will be linked to the nanoparticles (*Fig. 2*). X. fastidiosa[2] (X.f.) have been chosen here as a model bacteria in order to demonstrate the proof of the concept in vitro and in vivo plants.

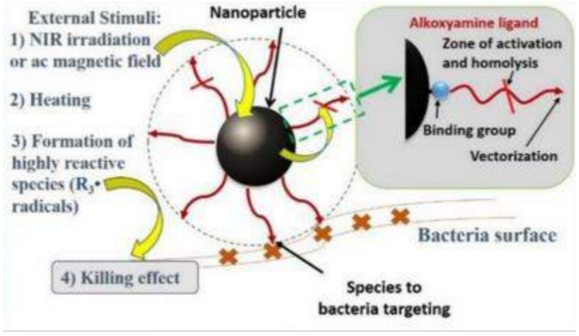

Figure 1 : The aim idea of the project

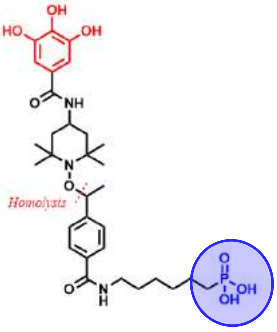

Figure 2 : Alkoxyamine with bacterium vector

[1] S. A. Lee, et al., PLOS ONE, 2020, 15.
[2] K. Schneider, et al., Proceedings of the National Academy of Sciences, 2020, 117, 9250.

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Scaling up synthesis and *in vivo* evaluation of MEDS433: a promising preclinical candidate targeting AML

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Human Dihydroorotate Dehydrogenase (*h*DHODH) is a validate drug target associated with the metabolism of cancer cells. It is an important regulator of the *de novo* biosynthesis of pyrimidines and it has emerged as a new target able to induce cellular differentiation. In particular, extensive studies have shown that AML (Acute Myeloid Leukemia) cells are very sensitive to the inhibition of this enzyme: the cells undergo to a condition of pyrimidine starvation that leads to the differentiation and then apoptosis of leukemic cells [1].
In recent years, the MedSynth Research group developed a novel class of *h*DHODH inhibitors based on hydroxypyrazolo[1,5-a]pyridine scaffold and MEDS433 is emerged as a potent pro-apoptotic agent in AML cells [2]. The MEDS433 high potency on isolated enzyme (IC_{50} *h*DHODH 1.2 nM) is translated into powerful effects at the cellular level. Considering the encouraging results obtained, MEDS433 stands out as the most favorable candidate for advancement into the preclinical development phase.
Since integrate more sustainable approaches in early drug development stages is crucial for maximizing benefits, one of the objectives of this work is to optimize the synthetic scheme prior to the clinical trial authorization to prevent the need for future modifications and avoiding the necessity for GMP reassessment and additional clinical trials in an advanced phase. As a result, a more practical synthesis of MEDS433 in multi-gram quantities has been achieved and allowed the obtainment of promising *in vivo* efficacy, pharmacokinetic and toxicity data of the drug candidate.

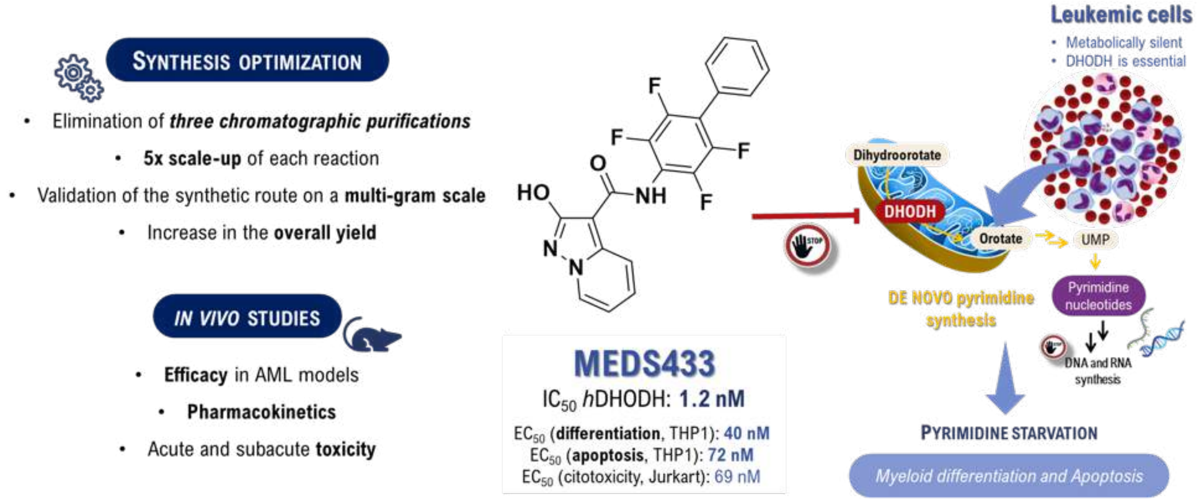

Figure 1: Key highlights of MEDS433 synthesis optimization and its biological activity.

[1] Sykes et al., 2016, Cell 167, 171–186.
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The role of 8-hydroxyquinoline-2-carboxylic acid in coordination and medicinal chemistry: case study in coordination of vanadium(IV/V)

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8-Hydroxyquinolines (8-HQs) belong to an interesting class of heterocyclic compounds showing moderate metal-binding abilities. In the last decades, 8-hydroxyquinolines and their derivatives attracted attention since they seem to be useful structures for the design of new drug candidates [1]. 8-Hydroxyquinoline-2-carboxylic acid (8-HQA) shows interesting features, such as biological activity and pronounced coordination abilities. The study of the interaction between 8-HQA and biologically relevant metal ions could be interesting to understand its role in the body. In recent years the 8-HQA has been studied in combination with different metal ions, in particular $Fe^{2+/3+}$ [2], and MoO_4^{2-} [3]. Nevertheless, the interaction between the 8-HQA and the oxovanadium(IV) and oxidovanadium(V) is still unexplored. The study of the speciation of this system in aqueous solution could expand the knowledge about the complexing abilities of the 8-HQA ligand and the chemistry of vanadium(IV/V) metal complexes. Vanadium ions possess interesting chemical and biological properties. Vanadium(IV) and vanadium(V) represents the most relevant oxidation states and are able to form coordination compounds with ligands such as metabolites, amino acid, and biomolecules [4]. Anyway, the aspects governing the redox conversion, the stability of vanadium coordination complexes, their biological activity and bioavailability are not yet fully understood. The interconversion between the two considered oxidation states and their different behavior in biological media represent an attractive case of study [5]. Specifically, the interaction of oxovanadium(IV) and dioxidovanadium(V) with 8-hydroxyquinoline-2-carboxylic acid (8-HQA) was assessed. A multi-technique approach was adopted to describe the speciation of the two metal oxo-cations with 8-HQA in aqueous solution. Potentiometric and UV/Vis spectrophotometric titrations were performed in combination with voltammetric experiments, EPR and NMR to investigate the system. Considering oxovanadium(IV), oxidation of the metal ion was observed leading to instability of the complexes at alkaline pH. Experiments excluding oxygen were conducted to explore the systems in the oxidation sensitive region. Combining the information obtained from all the different techniques, it was possible to achieve a good grade of knowledge about the chemistry of the systems. The main species formed in the solutions at various pH values were identified and the stability constants of the complexes were estimated.

Acknowledgements: This contribution is based upon work from COST Action CA18202, NECTAR − Network for Equilibria and Chemical Thermodynamics Advanced Research, supported by COST (European Cooperation in Science and Technology).

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Physicochemical characterization of chitin extracted from Black Soldier Fly Larvae at different growth stages

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In recent years, biopolymers have been widely used in many fields. The search for new sources of biopolymers and biomaterials has led to an increased focus on production and extraction processes, especially from natural and renewable sources. In this field, chitin is one of the most widely used biopolymers, and it consists of units of N-acetyl-2amino-2deoxy-D-glucopyranose and 2-amino-2-deoxy-D-glucose in pyranose form and linked to each other by 1-4 glycosidic bonds with an acetylation degree greater than 60%. [1]

Currently chitin is extracted from different animal and vegetable sources such as crab shells, mushrooms, and yeasts. These sources are subject to seasonality, moderately long growth times and maintenance of specific conditions; for these reasons, the potential of insect such as Hermetia Illucens (Black Soldier Fly or BSF) has been investigated. This insect is able to grow on a wide variety of organic materials and does not require special environmental conditions.In addition, BSF can be used as a means of reusing household organic waste, reducing the environmental impact during the farming phase. [2]In the AIWTUC – EUROSTAR project: “An innovative way to use Chitin: from Organic Waste to functional fabrics”, the chitin was obtained from BSF larvae and was characterized by Infrared Spectroscopy, X-Ray Diffractometry, solid-state Nuclear Magnetic Resonance (^{13}C CPMSNMR) and thermogravimetric analysis. These characterizations were conducted to investigate the molecular parameters of the extracted chitin such as acetylation degree % (DA%), crystallinity (CrI%), allomorphic form (α, β, γ form) and presence of residual impurities. All these parameters are fundamental for determining the fields of application.

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The synthesis of novel organic fluorophores using new isocyanides in the GBB three-component reaction

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Novel structural modifications of already known fluorescent compounds have been explored. The introduction of the isocyanide group on 1,8-naphthalimide[1] and coumarin-based[2] cores allowed us to perform a Groebke-Blackburn-Bienaymé reaction (GBB)[3],[4] in order to obtain potentially fluorescent complex heterocyclic molecules **5a** and **5b** (*Fig.1)*

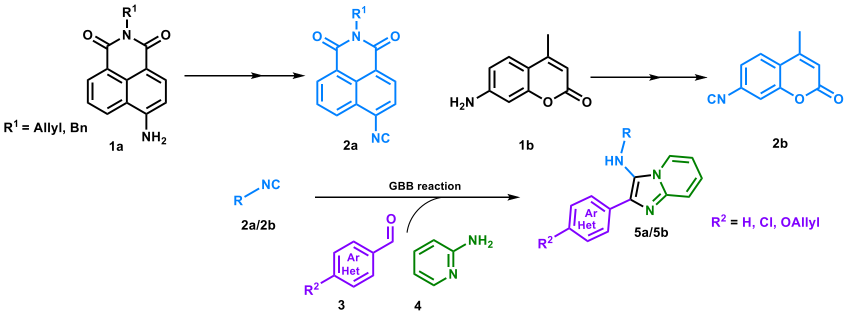

Figure 1: Synthesis of GBBR adducts with 1,8-naphthalimide and coumarin-based isocyanides.

The synthesis of the isocyanides has been deeply investigated, also from the perspective of fluorescence. This led to a deeper understanding of the structure-photophysical properties that are related to the nature of the functional group (-NH_2, -NHCOH, -NC). Aware of the significant relevance of organic fluorophores, we decided to pursue our set goal following the synthetic pathway above represented. The optimization of the GBB-3CR, also from a green chemistry perspective, allowed us to synthesize some of our target molecules.

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Turn on the light in mitochondria with a pyrazolo-pyridine-2-ol based probe: rational design of first environmentally sensitive fluorosteric *h*DHODH inhibitor

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Receptor target fluorescent probe is an imaging technique used to study and understand biological processes in live organisms. Typically, the core structure of these probes involves three key elements: the biological ligand, the linker, and a fluorophore.[1] After this modulation, however, the change in the pharmacological and physiochemical properties of the original ligand can be a significant drawback. To avoid these issues, one potential and innovative strategy involves merging the concepts of biological target and fluorescent probe, resulting in the design of a *biologically active fluorescent ligand.* [2]
To develop this concept, we decided to investigate pyrazolo[1,5-a]pyridin-2-ol, a small heterocycle characterized by strong intrinsic emission in the blue region. With the aim of achieving a useful fluorescent probe for biological applications, several series of compounds were developed and studied, with the final goal of shifting the emission profile from the blue to red region. Here we present a comprehensive analysis of the explored fluorescence properties of this probe and, *as a proof of concept* of the designed technology, a first biological application obtained through the development of the first ever designed fluorosteric *h*DHODH inhibitor.

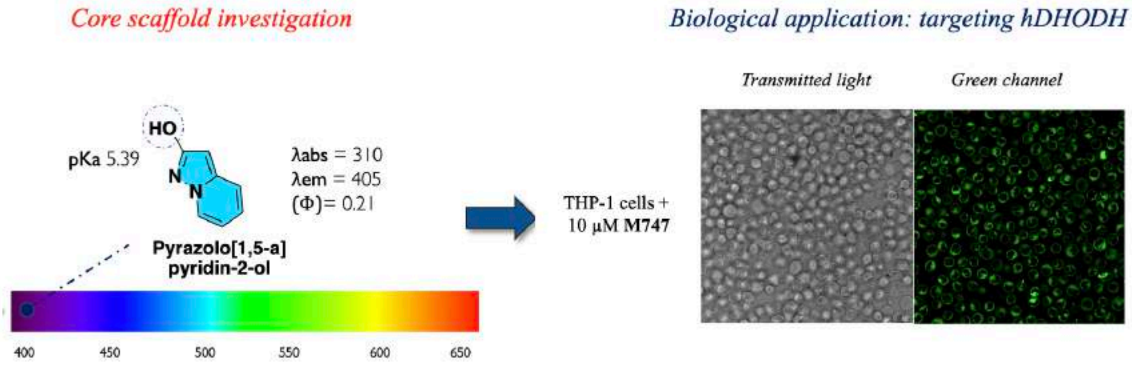

Figure 1: Structure of the investigated pyrazolo[1,5-a]pyridin-2-ol and first biological application of the developed fluorescence probe.

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Optimization of Progesterone Encapsulation Using Ball-Milling Kneading with β-Cyclodextrin and Nanosponges: Characterization, Release Profile, and Biological Activity Evaluation

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New technologies are being explored to efficiently encapsulate bioactive compounds and drugs without incurring significant time and yield losses. In this study, we compared the encapsulation of progesterone, a lipophilic hormone used in hormone replacement therapy, using kneading techniques with β-cyclodextrin (β-CD) and Nanosponges (specifically, βNS-CDI 1:4 and 1:8). Various ratios of β-CD, nanosponges, and progesterone were tested, and evidence from FTIR, TGA, DSC, and encapsulation efficiency analyses revealed complete drug encapsulation even at a 1:1 ratio. These findings indicate that all the drug was encapsulated within the nanosponges and β-CD.

Dialysis studies (using a 1KDa cut-off) demonstrated that the complexes exhibited a faster and more gradual release profile compared to the free drug, with slight differences among them. Evaluation of the complexes' efficacy against the MCF-7 cell line, in comparison to physical mixtures, highlighted the significant influence of proper complexation on effectiveness. This study underscores the importance of optimizing the encapsulation process depending on the drug and suggests ball-milling kneading as a promising method for complex formation.

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Synthesis of chiral amines by a chemoenzymatic one-pot tandem protocol

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Multistep one-pot synthetic protocols are an emerging and attractive field in organic chemistry, since the development of these synthetic strategies allows to produce chemicals in compliance with criteria of more sustainable and green processes.[1] One-pot and/or tandem reactions are a strategic tool when it is not possible to isolate highly reactive or transient species. In this context, the combination of chemical and biocatalytic transformations represents a valuable alternative to traditional approaches. In this context, our preliminary investigations revealed the possibility to synthesize chiral amines by means of a chemoenzymatic tandem protocol which combines the reactivity of organolithium reagents with the enzymatic asymmetric reduction of cyclic imines, generated *in situ* in the first step of the reaction (Figure 1). Compared to the previously reported operating conditions,[2] promising results have been obtained performing the addition of PhLi to 5-bromovaleronitrile under sustainable conditions, using a greener solvent such as cyclopentyl methyl ether (CPME), at room temperature and under air, within a short reaction time. The bioenzymatic transformation is then realized by means of a novel class of NADPH-dependant enzymes, namely Imine Reductases (IREDs), which have been recently employed for the asymmetric reduction of chiral imines under sustainable conditions.[3] Preliminary results will be discussed.

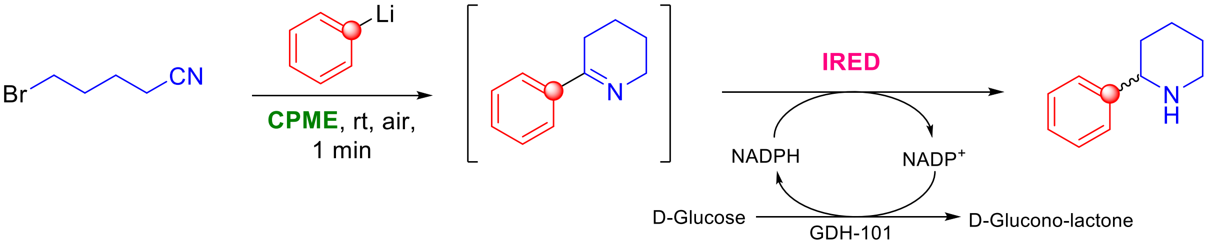

Figure 1: Chemoenzymatic tandem protocol to synthesize chiral amines.

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Difluoromethyltrimethylsilane (TMSCHF$_2$): a valuable and versatile donor of CHF$_2$ moiety under nucleophilic regime

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The selective insertion of a difluoromethyl unit into an organic compound profoundly regulates the chemico-physical properties of the resulting scaffold. The commercially available and experimentally convenient difluoromethyltrimethylsilane (TMSCHF$_2$) is proposed as a valuable and versatile donor of the CHF$_2$ moiety under nucleophilic regime to various electrophiles and, nowadays, it represents the first-choice reagent for difluoromethylation in both academic and industrial research.

We rationalized the possible and convenient develop of a direct, one step, methodology for the installation of a difluoromethyl motif into an electrophile levered on the use of TMSCHF$_2$ proving to be an effective protocol for synthesizing difluoromethyl ketones via the homologation of variously functionalized Weinreb amides. Uniformly high-yields, excellent tolerance to sensitive functionalities and retention of the stereochemical informations are observed.[1]

Difluoromethyltrimethylsilane (TMSCHF$_2$) proved its versatility also in the case of iso(thio)cyanates, allowed the access to the unprecedented α,α-difluoromethyl oxo- and thio-amides with high chemocontrol and substrate scope[2], and in the case of non-carbon electrophiles (Sn, Ge, Si, Au, S, Se, Te) furnishing in high yields the bench-stable analogues.[3]

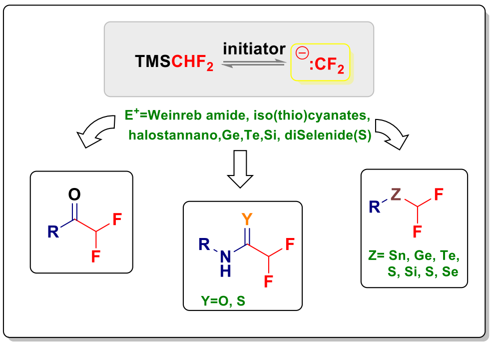

Figure 1 : Difluoromethylation of a variety of Electrophiles.

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First-Principles Anharmonic IR and Raman Spectra of Materials: Fermi Resonance in Dry Ice

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We introduce a computational tool for the quantum-mechanical simulation of anharmonic infrared and Raman vibrational spectra of materials [1]. The approach, implemented in the CRYSTAL software [2], stems from Taylor's expansion of the potential energy surface (PES) on the basis of normal modes up to cubic and quartic terms. The PES can be sampled with four different numerical schemes at the level of density functional theory (DFT). Anharmonic states are obtained by solving Shrödinger's nuclear equation with either the vibrational self-consistent field (VSCF) or vibrational configuration interaction (VCI) methods. Nuclear quantum effects are thus fully accounted for [3]. Infrared intensities are computed numerically through a Berry phase approach or analytically through a coupled-perturbed (CP) approach. Raman intensities are computed analytically via the CP approach.
A variety of anharmonic features of vibrational spectra of materials can be simulated, including band shifts, combination bands, overtones, resonances (first-order Fermi, second-order Darling–Dennison), and hot bands. We showcase the effectiveness of the approach on the description of a first-order Fermi resonance (FR) in CO_2 dry ice: a challenging test-case given that the FR occurs in the Raman spectrum, requires NQEs, and involves two- and three-mode couplings [4]. Fundamental mechanistic differences with respect to the well-known FR in molecular CO_2 are addressed. This application represents the first quantum-mechanical, periodic description of FR in dry ice.

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Highly Active Ni/Al_2O_3 based catalysts for RWGS reaction

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The accelerated growth of the world population and industrialization are the problems faced by humanity which will enhance the demand for energy. This results in the increasing levels of CH_4 and CO_2 in the atmosphere of the Earth[1]. To face this problem, it is necessary to develop more efficient catalysts for the CO_2 consuming reactions as well as dry reforming of methane (DRM) and reverse water-gas shift (RWGS) reactions. In the DRM reaction, carbon dioxide (CO_2) and methane (CH_4), two of the major greenhouse gases, will react together and produce a mixture of carbon monoxide (CO) and hydrogen (H_2). These gases (CO and H_2) can be used to produce a variety of valuable chemicals and liquid fuels[2]. During the RWGS reaction, CO_2 reacts with hydrogen and is converted to CO and water. This CO can be further converted to various versatile products through the syngas routes[3]. Aluminium oxide is the most popular support for synthesis metal catalysts. It has a large specific surface area due to a well-developed powder pore structure. Al_2O_3 exists in various forms such as- α-, β- and γ-Al_2O_3. However, for catalytic applications, α and γ-Al_2O_3 are usually more interesting[4].

In this work, we synthesized catalysts based on Al_2O_3 modified with nickel nanoparticles (Ni NPs). The synthesis of Al_2O_3 is carried out using a facile method based on sol synthesis by aluminium nitrate precipitation. Ammonium carbonate solution was added dropwise to an aqueous solution of aluminium nitrate till it reached a pH of 8 at room temperature to obtain a white precipitate of $Al(OH)_3$. Then the solution was heated to obtain a boehmite sol. For synthesis of the Ni NPs, a green synthetic route was used with the addition of glucose for the reduction of the Ni NPs. The Ni NPs were mixed with the boehmite sol and dried in the oven at 100°C in air or by the freeze-drying to retain the initial porosity and to increase their specific surface area. Ni-NPs/Al_2O_3 catalysts with different Ni NPs loadings were prepared, namely 18.7%, 9.4% and 4.7%.

RWGS and DRM reactions were performed with all the catalysts at 450 ºC and 600 ºC with N_2, CO_2, H_2 and N_2, CO_2, CH_4 mixtures, respectively. Products were analyzed with a gaschromatograph (GC, Agilent 7820A). The catalysts were characterized by N_2 physisoprtion at 77 K (Micromeritics, ASAP 2020 Plus) to calculate the specific surface area, by powder diffraction to identify the Ni crystalline state. In addition, some magnetic measurements were done to evaluate further catalyst developments. Both Al_2O_3 and Ni/Al_2O_3 catalysts showed a high specific surface area (e.g. 298 m^2/g). In RWGS we were able to obtain a CO_2 conversion of 30-35% and a H_2 conversion of 45-55%.

The research fellowship is funded by the project «Network 4 Energy Sustainable Transition – NEST » under the National Recovery and Resilience Plan (NRRP) by the NextGenerationEU.

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An *in situ* thermogelling injectable formulation for Glioblastoma treatment

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Glioblastoma (GBM) is the most aggressive and frequent brain tumor in adults with a median survival of only 15 months[1]. The poor prognosis of GBM lies its infiltrative nature, a strong cellular heterogenicity and its resistance to current therapies. The standard treatment consists of a maximum safe surgical resection followed by radiotherapy and concomitant chemotherapy with oral Temozolomide (TMZ)[2]. In this contest, a gel-based drug delivery system, applicated in the tumor resection cavity after surgery, may reduce the incidence of recurrences in the time gap between surgery and chemoradiation with a controlled drug release. Thermogelling injectable formulations are liquid solutions before injection, which rapidly form a gel when at physiological temperature. In the current study, gel-forming systems were developed with a crosslinking reaction between chitosan, a cationic polysaccharide, and an anionic β-cyclodextrin, sulfobutylether-β-cyclodextrin (SBE- β -CD, Captisol®). Chitosan is an appetible nano-carrier, since it is a natural biopolymer, biodegradable, mucoadhesive, and easily sensible to chemical modifications. Anti-GBM cancer agents (such as Olaparib, Ibrutinib, Topotecan, and Bindarit) were complexed in SBE-β-CD (molar ratio of 1:1.2, SBE-β-CD /drugs), and ionic gelation reactions of chitosan with SBE-β-CD was followed. The ability to gel *in situ* was permitted by the addition of Pluronic® F-127, a thermosensitive polymer. All gels were characterized for their physico-chemical and functional properties. *In vitro* release studies of the selected gels in artificial cerebrospinal fluid were also conducted. Finally, this method may be representing a novel alternative on a challenging field of brain drug delivery.

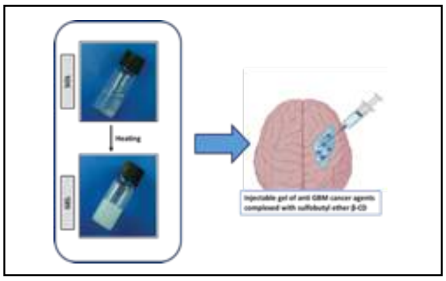

Figure 1: Schematic representation of the sol-gel transition of thermogelling injectable formulations.

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Stereocontrol of N-Linked Non-Biaryl Atropisomers

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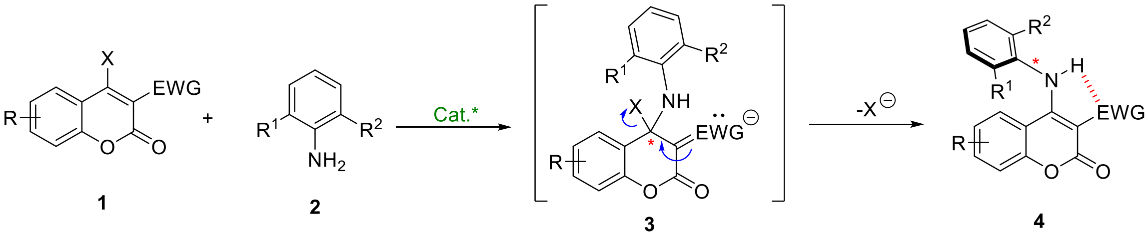
Axially chiral compounds have received considerable interest from the chemical community due to their great success in the development of chiral ligands or organocatalysts in asymmetric synthesis.[1] They have also recently become increasingly prevalent in drug discovery, with many atropisomers currently undergoing clinical trials.[2] Among the various structural motifs encountered in biologically active compounds and pharmaceuticals, diarylamines and their related structures are particularly widespread,[3] but their atroposelective synthesis remains a difficult task. The difficulties in obtaining configurationally stable diarylamines is mainly due to the fact that in such structures, unlike classical atropisomers, the rotation is possible around two bonds, which grants low barriers to enantiomerization via concerted bond rotations.[4] Herein, we aimed to develop an atroposelective synthesis approach for axially chiral diarylamines, via an organocatalyzed aza-Michael addition-elimination between coumarins **1** and sterically hindered aniline **2**. The elimination step will afford axially chiral arylamines **4** with establishment of an intramolecular hydrogen-bond, granting high barriers to enantiomerization.



EWG= NO_2,CHO,
SO_2R, CO_2R
X= Cl, Br, I

Centrally chiral
intermediate

Scheme 1: synthesis of configurationally stable diarylamines.

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Enantioselective Synthesis of Benzothiophenes Atropisomers

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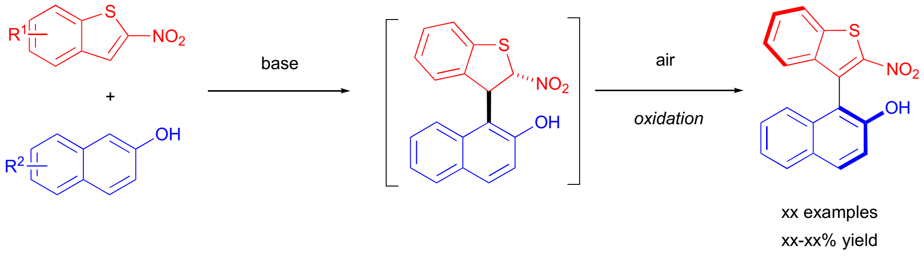
Nonracemic axially chiral molecules gather significant interest across a broad range of chemists owing to their myriad applications as chiral ligands, organocatalysts, and materials, as well as their biological significance. Among these, biaryl atropisomers are the most prevalent, with numerous synthetic approaches available.[1] In sharp contrast, the substantially more arduous enantioselective synthesis of atropisomeric heteroaryl structures remains a formidable challenge in modern organic synthesis, particularly those featuring a five-membered heterocycle.[2] Within this category, the enantioselective synthesis of thiophene atropisomers has been rarely addressed.[3] Herein, we present a metal free, C–H activation protocol for the direct coupling between 2-naphthol derivatives and 2-nitrothiophenes giving rise, in the presence of a base, to the desired benzothiophene atropisomers, after smooth oxidation of the dihydrobenzothiophene intermediate under air. Enantioselective version using a chiral organocatalyst allowed to reach 66% *ee*.



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In-depth analysis on the structure/properties relationship of g-C_3N_4 based nanoarchitectures.

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Graphitic carbon nitride (g-C_3N_4), a polymeric 2D layered graphene-like metal-free semiconductor, has emerged as a challenging material due to its exceptional properties like thermal and chemical stability, non-toxicity, tunable band gap and visible light activity, and, mostly, due to its environmentally friendly and sustainable properties. For this, many applications, including degradation of pollutants, photocatalysis for hydrogen production, carbon dioxide reduction, water splitting, solar light-driven photo-redox catalysis, photoelectric conversion have been developed [1]. However, some well-known g-C_3N_4 drawbacks are worthy of mention, including the high recombination rate of the photoinduced electron–hole pairs, the chemical inertness itself, the poor charge carrier mobility, the low specific surface area. For these reasons, nowadays, many efforts are devoted to overcome the aforementioned limitations [2], either by establishing g-C_3N_4/g-C_3N_4 or g-C_3N_4/graphene metal-free homo/hetero-junctions or g-C_3N_4 /inorganic semiconductors and/or metals, etc.. hybrid materials. In this contribution, porous g-C_3N_4 nanoarchitectures are obtained by a facile and effective in situ synthesis method, that entailed the thermal treatment of different melamine (M) and urea (U) precursor mass ratios. The role of the precursors on morphology and structure, was analysed by means of many characterization techniques, including HRTEM, FESEM, X-ray diffraction, UV-visible and FTIR with Density Functional Theory (DFT) calculations, using the CRYSTAL code [3]. It will be shown that the complex structure of g-C_3N_4 systems can be described as a mixture of highly condensed g-C_3N_4 domains embedded in a less condensed “melon-like” framework [4]. Some more samples obtained from different melamine (M) and urea (U) precursor mass ratios combine the advantage of high thermal stability and significant reaction yields, which are due to melamine action and the greatly improved surface area and short migration paths, which are due to urea action, thus providing the suitable conditions for charge transfer within the interfaces, which could be effective for photocatalytic performance.

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Design of metallic materials for biocompatible applications

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With the increasing life expectancy the need for biomaterials, and implants in particular, has risen. Even though the materials used today as hard tissue replacements showcase good short-term properties, they tend to fail long term because of not sufficient corrosion resistance, release of cytotoxic elements, difference between the elastic moduli of the implant and the human bone, and poor resistance in biofilm formation on their surfaces. [1]

Titanium (Ti) has gained great popularity in the field because of its exceptional properties and bioinerteness. Although promising materials, Ti and its alloys, do not exhibit optimal surface properties, such as wettability and topography, and they have high Young moduli, compared to that of the human bone.

Designing new β-Ti alloys and engineering their surfaces is of great importance, as it allows to achieve the desired interaction with the body eliminating the unwanted side effects, namely poor osteointegration, reduction of bone mass, biofilm formation and implant related infections. [2]

In this work, two low Young modulus β-Ti alloys were chosen to be studied, Ti-24Nb-4Zr-8Sn (%wt) (Ti2448) and Ti-45Nb (%wt) (Ti45Nb). Apart from their low moduli (45GPa and 64GPa respectively), these alloys do not contain toxic elements, in comparison with Ti6Al4V, the most commercially used alloy in biomedical applications.

The alloys were prepared by arc-melting in argon atmosphere and the ingots were remelted 7 times to ensure all elements were fully melted. The two alloys underwent different homogenization heat treatments, Ti2448 at 900°C for 30min and was allowed to cool naturally in ambient air, whereas Ti45Nb at 1000° for 24h and was quenched in water afterwards. SEM and XRD analysis were carried out to access the microstructure and the crystallinity of the two alloys.

The surfaces of two the β-Ti alloys were hydrothermally treated to create a nanopatterned surface. These features are a promising way to achieve the desired implant surface-cell interaction, as osteoblast adhesion onto the surface. Following the modification treatments, studies on the hemo- and bio-compatibility of the surfaces were carried out using hemolysis assays (HA) and simulated body fluids (SBF).

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Synthesis and relaxometric characterization of Fe(III) complexes and their supramolecular adducts

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All the FDA-approved contrast agents (CAs) are Gd(III)-based complexes (GBCAs) and they are used in 40% of the tens of millions of Magnetic Resonance Imaging scans performed each year. Recently, concerns regarding geopolitical, environmental and clinical impacts have spurred interest in exploring alternative CAs, notably those utilizing endogenous ions like Fe(III). Initial studies suggest that Fe(III) chelates, administered at higher doses than GBCAs, exhibit comparable efficacy in typical clinical settings. However, understanding the mechanisms underlying water proton relaxation enhancement by Fe(III) complexes and their structural features is still nascent.[1,2] In this study, we investigated Fe(III) complexes with derivatives of EDTA functionalized on the acetic arms with one (EDTA-BOM) or two (EDTA-BOM$_2$) benzyloxymethyl groups. The objective is to explore the effects of ligand modification on the overall efficacy (relaxivity, r_1) of these systems for contrast enhancement. In fact, an increase in the relaxivity of these probes is expected because of the elongation of the molecular thumbling, provided by the increasing molecular mass. Moreover, the lipophilic nature of the BOM substituents allows non-covalent interaction with different substrates (β-cyclodextrin, poly-β-cyclodextrin and human serum albumin), which can further increase their efficacy. For these reasons, we present the ^{1}H and ^{17}O NMR relaxometric characterization of these two novel complexes and their supramolecular adducts, for which we also investigated their thermodynamic stability, kinetic inertness and redox behavior.

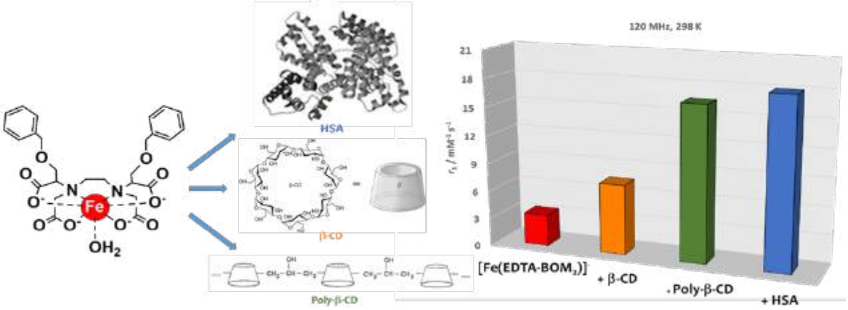

Fig. 1. Schematic representation of some of the investigated systems and their r_1 values (120 MHz, 298 K).

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Water reactivity on Schreibersite: a reservoir for prebiotic living phosphorus

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Phosphorus is an element of primary importance for all living creatures, being present in many biological activities in the form of phosphate (PO_4^{3-}). However, there are still open questions about the origin of this specific element and on the transformation which allowed it to be incorporated in biological systems. The most probable source of prebiotic phosphorus is the intense meteoritic bombardment during the Archean era, few million years after the solar system formation, which brought tons of iron-phosphide materials (schreibersite) on the early Earth crust.[1] It was recently demonstrated that by simple wetting/corrosion processes from this material various oxygenated phosphorus compounds are produced.[2] In the present work, the wetting process of schreibersite (Fe_2NiP) was studied by computer simulations using density functional theory, with the PBE functional supplemented with dispersive interactions through a posteriori empirical correction (D*0).[3,4,5] Therefore, the two stable (110) and (001) Fe_2NiP surfaces were used simulating different water coverages, from which structures, water binding energies and vibrational spectra have been predicted. The computed (ana-)harmonic infrared spectra have been compared with the experimental ones, thus confirming the validity of the adopted methodology and models (see Figure 1).[6,7] Moreover, water reactivity was inspected in several possible deprotonation reactions, also increasing the number of water molecules in order to lead to the formation of phosphonic and phosphoric acids and their corresponding deprotonated forms.

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Additive free microwave assisted direct C-H amination of benzoxazole by supported copper(I) catalyst

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Among nitrogenous heterocyclic compounds 2-aminoazoles, especially 2-aminobenzoxazoles, possess high relevance due to their biological and pharmaceutical activities.

Selective C-N bond formation of benzoxazoles is usually performed by reactions as Buchwald Hartwig or Ullmann and Goldberg couplings but still some disadvantages are needed to be solved for better agreement with green chemistry criteria. Thus, developing greener and simpler methodologies, the direct amination of aromatic C–H bonds is regarded as a more powerful alternative.

Many transition metals had been exploited as catalysts, however Copper use has risen thanks to its low cost, high functional group tolerance, high environmental abundance and safety, and low overall toxicity. [1], [2]

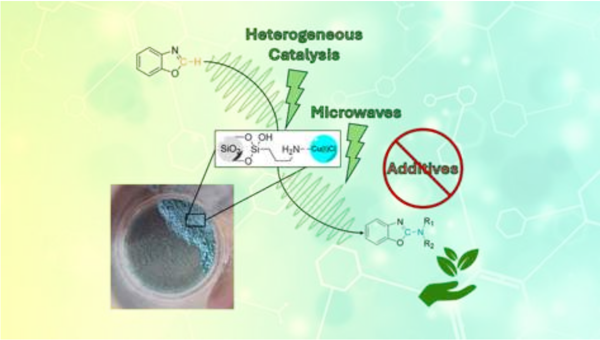

Figure 1 : Graphical representation of microwave assisted C-H amination of benzoxazole

Successfully examples of benzoxazole selective C-H amination are reported in literature, however they usually show limits such as the use of stoichiometric amount of an acid or base as a promoter, non-greener peroxide oxidants or solvents, pre-functionalised amino-reactants as well as high temperature.

The aim of the present work is the optimization of a simple, efficient and green direct C-H amination which avoids the use of any acidic, basic or oxidant additive. The reaction was proved to take advantage from microwave irradiation and excellent results were achieved in presence of a silica supported Cu(I) catalyst. The catalyst allowed a convenient isolation of the final product, and a simple procedure for catalyst regeneration was exploited to reuse the catalyst up to height times without losing catalytic activity.

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ION conducting Materials for Electrochemical Energy Technologies (ION-MEET)

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The ION-MEET project objective is to strengthen the collaboration in research and training between internationally recognized teams in the Mediterranean area to make advances in the field of energy storage and conversion devices (alkali-ion batteries, fuel cells FC and water electrolyzers WE) based on solid-state ion conductors (SICs).

Developing all-solid-state batteries is the holy grail of battery research especially for safety, which is paramount from the customer point of view. The project tackles this problem by:
i) synthesis of solid polymer electrolytes: investigation of various types, mostly single-alkali-ion conducting polymers, where the counter-anion is grafted on the polymer chain;
ii) high performance electrodes for alkali-ion batteries: study of electrode materials with a reduced environmental impact based on nickel and the ligand benzenetetramine (BTA), high voltage cathodes, based on Ni-Mn spinels, mixed with polymer to increase the redox stability and nanostructured anodes including nano-Si, Si/C or Sn/C nanocomposites with very high insertion capacities;
iii) electrodes compatible with solid polymer electrolytes, containing less critical raw materials (CRM) and more eco-friendly components based on biochar, an eco-friendly material that can be produced from renewable sources like protein-rich waste biomass;
iv) post-mortem analysis and recycling to directly produce cathode materials.

Developing of more sustainable MEA (membrane electrode assembly) components for hydrogen FC and WE, avoiding critical raw materials (CRM) and focusing on renewable green ones, is a clear trend. The main lines for the development of innovative core components are:
i) stable and highly conducting ionomers (cationic and anionic), including hybrid materials, for membranes and electrodes, synthesized from biomass exploiting sustainable methods;
ii) exploitation of biomass resources for the preparation of biochar electrodes. Nanostructured catalytic electrodes with optimized ink formulation using carbonaceous materials doped with different heteroatoms and ionomers as main components of the catalyst layer;
iii) life-cycle and degradation analysis by accelerated degradation tests and multiscale numerical analysis based on big data and neuronal network approaches.

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Study on pyrolysis kinetics of a commercial polymeric waste mix

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Pyrolysis is a promising thermochemical process that offers a valuable route to mitigate plastic waste pollution by converting carbonaceous feed materials into valuable products. The process is well-known and studied in literature but real waste materials, with high variability and heterogeneity in composition, are rarely used. The diffusion of bigger scale plants is still very limited because of the process complexity, therefore gaining knowledge over the influence of feed composition on products yield and distribution will help to make the process more flexible and predictable, encouraging its diffusion [1]. The aim of this work has been to gain insight into the mechanisms of pyrolysis of real waste materials by studying composition and decomposition kinetics of a commercial waste polymer mix.

To study the mechanisms of pyrolysis different model-free approaches (e.g. Kissinger, Flynn-Wall-Ozawa and Kissinger-Akahira-Sunose models) were applied to results of Thermogravimetric Analysis (TGA) [2]. The tests were run at different scanning speed and were also performed on pure components of the mix, to have a comparison and to obtain information of the influence of additives and impurities. Composition of the mix was studied with Fourier-Transform Infrared Spectroscopy (FT-IR) and Differential Scanning Calorimetry (DSC). A commercial polymeric waste mix (Bluair®) mainly made of polyolefins was used as main subject in this work.

All the tests run lead to identifying the main components of the waste mix studied, TGA studies provided valuable information on pyrolysis, and they allowed to investigate kinetics, activation energies and mechanisms of this process. TGA can be useful in a preliminary study of pyrolysis plant setup or vice versa to evaluate the attitude of a waste mix to be used as feedstock for an already existing process.

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Innovative carbon nitride material for CEC removal

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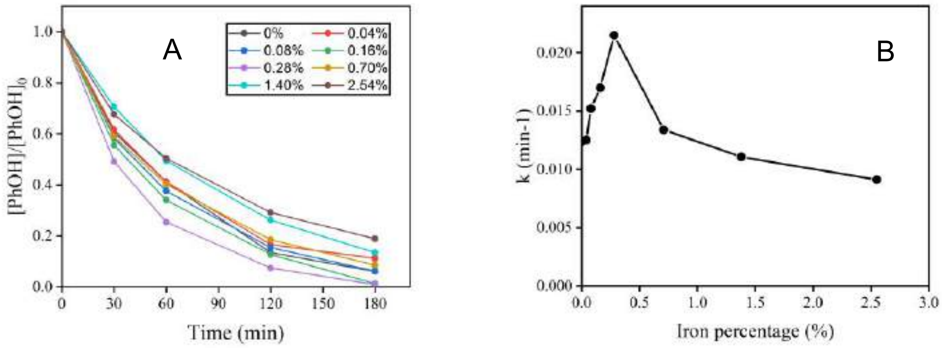

Figure 1. (A) PhOH degradation and (B) reaction kinetic constants by g-C_3N_4 with different iron content (expressed as the percentage of Fe m/m in the initial mixture with melamine). Conditions: UVA light and pH_0 = 7.0.

The removal of contaminants of emerging concern in water represents a challenge for the sustainable development of societies, where advanced oxidation processes are the main method for their abatement. In this work focus is concentrated on the synthesis of carbon nitride (g-C_3N_4) based materials, added with iron to obtain synergistic effects on degradation. g-C_3N_4 is an emerging photocatalyst with a honeycomb structure, where metals can be complexed between heptazine units through coordinations with 6 nitrogen atoms [1]. In this way, it is possible to introduce iron metal centers to extend Fenton reactions at neutral pH, otherwise compromised at pH > 4 for iron precipitation [2]. At the same time, the UVA irradiation of carbon nitride allows the production of H_2O_2 in situ, which can be used for Fenton reactions, through the reduction of dissolved oxygen by excited conduction electrons of the semiconductor.

The synthesis of the photocatalyst was carried out by adding $FeCl_3{\bullet}6H_2O$ to melamine through a thermal polycondensation reaction carried out under anoxic conditions at a temperature of 500°C, followed by exfoliation with sonication for 1 h. The quantitative transfer of iron in the structure was confirmed by determining the content from thermal decomposition treatments of the materials. The photocatalytic performance was evaluated by measuring phenol (PhOH) 100 µM degradation under UVA irradiation, with a fixed amount of photocatalyst of 1.65 g L^{-1} at initial pH = 7.0. When needed, H_2O_2 1.0 – 25 mM was also employed.

Studies at different iron concentrations, reported in figure 1, have shown that content of 0.28% m/m iron is optimal for the reduction of PhOH in the absence of external H_2O_2 (75% degradation of PhOH 0.1 mM in 1 h under UVA light irradiation for Fe-g-C_3N_4, whereas with

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Synthesis of spiroindolenines through a one-pot multistep process mediated by visible light

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Diversity-Oriented Synthesis (DOS) plays a key role in organic synthesis, especially in providing an expansive exploratory space for pharmaceutical lead discovery and creating biologically active molecules.[1] This study highlights the importance of the spiroindolenine framework, which is commonly found among biologically active compounds. The synthetic strategy employed involves a one-pot four-step reaction leading to the synthesis of 2-amino 3,3' spiroindolenines **3**, using tertiary amines, electron-rich anilines and isocyanides as starting materials. This process has many advantages, such as simplicity of operations during the work-up phase, rapid construction of molecular complexity and absence of photocatalyst. The synthetic pathway begins with the oxidation of tertiary amines, such as N-aryl tetrahydroisoquinolines, resulting in the formation of iminium ions **1**. Subsequently, a three-component Ugi-type reaction involving an electron-rich aniline, an isocyanide and the iminium ion takes place. The oxidation of the Ugi-type product **2** induces a spontaneous cyclization reaction. A crucial aspect of this synthesis is the selective oxidation of the C-N bond, achieved through blue LEDs (451 nm) irradiation and bromotrichloromethane ($BrCCl_3$) as the oxidizing agent.[2] The photochemical approach has been explored and optimized leading to the creation of a small library of spiroindolenines **3**.

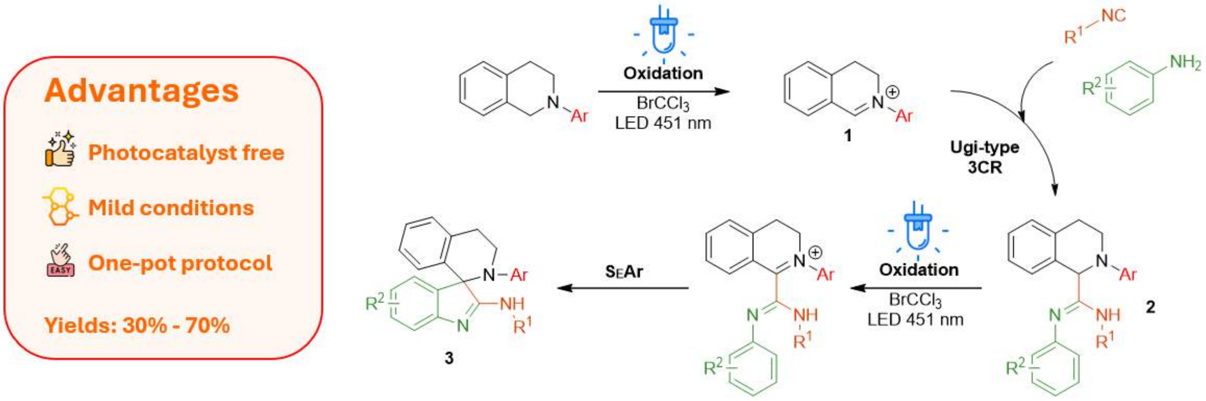

Figure 1: Four step one-pot synthesis of 2-amino 3,3' spiroindolenines

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Chalcogen bond and anion-π interactions in telluronium-dicyanoaurate salts

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Chalcogen bond, as the other σ and π hole interactions like halogen bond, pnictogen bond etc, has revolutionized the interpretation of supramolecular chemistry of main group elements and, more recently, also of transition metals.[1] These weak but directional interactions are opening worlds in some sense parallel to that of the heavily studied hydrogen bond. In these worlds, these new instruments of crystal engineering are opening new routes for applications in fields like catalysis or material properties. [2] Tellurium derivatives, especially in the case of the cationic trisubstituted telluronium salts (with tellurium(VI) oxidation state) demonstrate a strong tendency to form very strong chalcogen bond interactions, that have been also used for catalysis and anion recognition.[3] In this work, we synthesize and characterize two telluronium salt of dicyanoaurate, with the aim of checking the possibility for Au(I) centres to be chalcogen bond acceptor. The resulting interactions in the solid state have been studied with a series of computational methods (QTAIM analysis, MEP surface and NCI plot for example) to access the nature and the strength of each contribution.[4] The results would be interesting for the comprehension of the nature of charge assisted chalcogen bond and the possibilities of gold derivatives in the field of supramolecular chemistry.

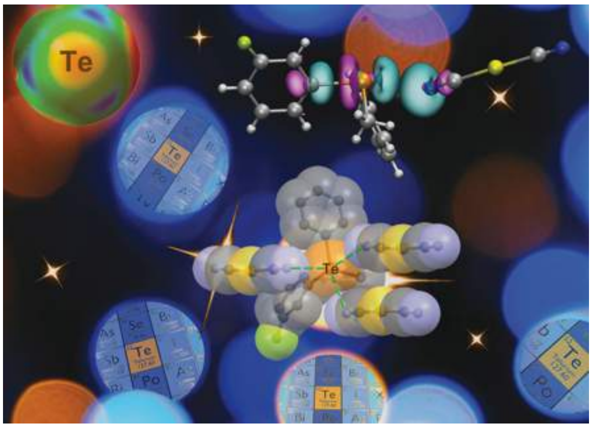

Figure 1 : interactions between a telluronium molecule and dicyanoaurate anion

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Nanocrystalline cellulose from different sources as bio-filler for sustainable rubber composites

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In the last few decades nanocellulosic materials have received increasing interest due to their great strength, high surface area and good renewability. The integration of nanocellulose into polymer matrices has the potential to enhance the performance attributes of the material and increase its sustainability. [1-2] Furthermore, the surface of cellulose can undergo various chemical modifications to enhance the interaction between the filler and the matrix. [2]

The final aim of this project is to produce polymer-based composite materials containing chemically modified nanostructured cellulose, which could enhance the mechanical and barrier proprieties of the polymeric matrix. In this perspective, different cellulosic materials (i.e., hemp pulp, microcrystalline cellulose and microfibrillated cellulose) were treated under different hydrolysis conditions in order to obtain cellulose crystals with nanoscale dimensions (CNC), as shown in Figure 1. The starting materials and the extraction products were chemically characterized via Infrared Spectroscopy (FT-IR) and X-ray diffraction analysis (XRD), while the morphology of the samples was investigated via Transmission Electron Microscopy (TEM). The extracted material was then oxidized through a TEMPO-mediated reaction in order to introduce carboxylic groups on the nanocrystals surface, which can serve as a basis for subsequent functionalization or crosslinking reactions.

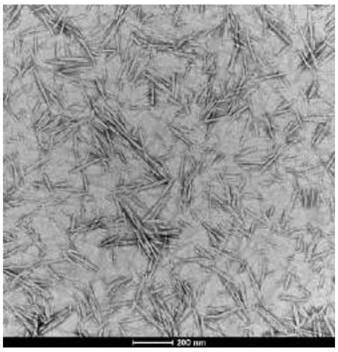

Figure 1: Hemp-derived cellulose nanocrystals (CNC)

This study was carried out within the MadABio project – funded by European Union – Next Generation EU within the PRIN 2022 PNRR program (D.D.1409 - 14/09/2022 Ministero dell'Università e della Ricerca).

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Photophysics of a nucleic acid-protein interaction model depends on solvation dynamics: an experimental and theoretical study

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1. *Scuola Superiore Meridionale, Napoli, 80138, Italy.*
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A molecular description of the interplay between nucleic acids (NA) and proteins is vital to understand the most basic processes of life, from DNA replication to protein expression and synthesis. Isolation of transient NA-protein complexes in their biological conformation is a challenging task: a promising technique for this goal is to induce *in vivo* NA-protein crosslinking (NPCL) by femtosecond-stimulated UV laser pulses.[1] The photo-addiction of phenylalanine to thymine results an exemplificatory reaction of such a class of crosslinking and the photocyclization of 5-benzyluracil (5BU) to 1,2-indaneuracil has been proposed as a model reaction for studying the mechanism of NPCL.[2] In this context, we present a combined experimental and theoretical study of the ground-state conformational equilibrium and the photophysics of 5BU in methanol,[3] exploiting the framework of the DFT and TD-DFT.[4] We performed an *ab initio* molecular dynamics (AIMD), adopting the ADMP[5] method and an hybrid QM/MM ONIOM[6] partition scheme enforcing non-periodic boundary conditions[7]. We recorded the UV absorption spectrum in methanol solution and simulated the band shape from TD-DFT analysis of the AIMD trajectory, finding a good agreement between experiments and simulation. The simulated absorption spectrum, calculated on such ensemble, allowed to give a molecular interpretation of the experimental UV-Vis lowest energy band, involved also in the induced photo-reactivity upon irradiation. In particular, the first two excited states both contribute to 5BU lowest energy absorption. Moreover, as main result, the nature and brightness of such electronic transitions is strongly influenced by 5BU conformation and the microsolvation of its heteroatoms. Our study suggests a dependence of NPCL on the surrounding environment and remarks the importance of AIMD and an accurate treatment of the solvent to understand the photophysics of this model system; it also may serve as a starting point for a non-adiabatic treatment of the photoinduced evolution of the system in the excited state.

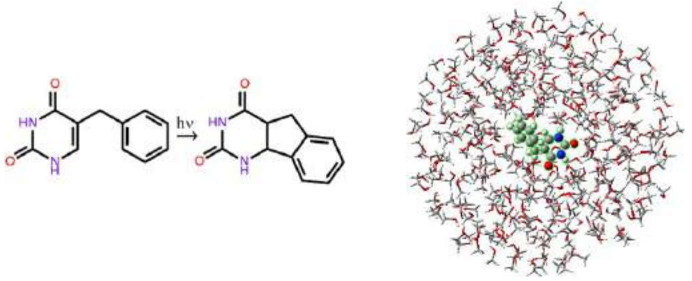

Figure 1 : The photocyclization of 5BU (left) and A snapshot from the AIMD of 5BU in methanol (right).

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Multinuclear and multifrequency NMR study of the interactions between Ln^{III} ions complexes and fluoride anions

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Contrast-enhanced Magnetic Resonance Imaging (MRI) has revolutionized the modern radiodiagnostic field, as it significantly improves the accuracy of diseases diagnosis. Most of MRI contrast agents (CAs) in clinical use are octadentate macrocyclic Gd(III) chelates with one metal-bound water molecule (q) in fast chemical exchange with the bulk. Such coordination cage grants the high stability and inertia properties required for *in vivo* applications, making Gd-based CAs among the safest drugs on the market. Recently, a new MRI CA has been approved, Gadopiclenol^{TM}[1], that is a heptadentate Gd(III)-complex with q = 2 and double efficiency compared to conventional CAs, which allows to decreasing the administered dose with equal efficacy. However, many bis-hydrate chelates form ternary complexes with anions (carbonate, phosphate, citrate etc..) following the displacement of one or both water molecules [2]. Here, we investigate the interaction between the fluoride anion and two negatively charged Ln(III)-complexes with similar structure but different hydration states (see *Figure 1*), with the aim of determining how the nature of the ligand affects the water substitution. For this purpose, a combination of high- and low-resolution NMR techniques in the frequency and time domains has been employed, which allows an in-depth characterization of the kinetics and thermodynamics of the fluoride binding event. In particular, fast-field cycling relaxometry (^{1}H longitudinal relaxation rates vs B_0), ^{17}O transverse relaxation rates vs temperature and high-resolution NMR measurements (^{19}F NMR) were performed on the paramagnetic Gd(III) and diamagnetic Y(III) complexes, respectively. This approach allowed us to gain insights into the binding affinity, thermodynamics and kinetics associated with the chemical exchange of water molecules with fluoride anions.

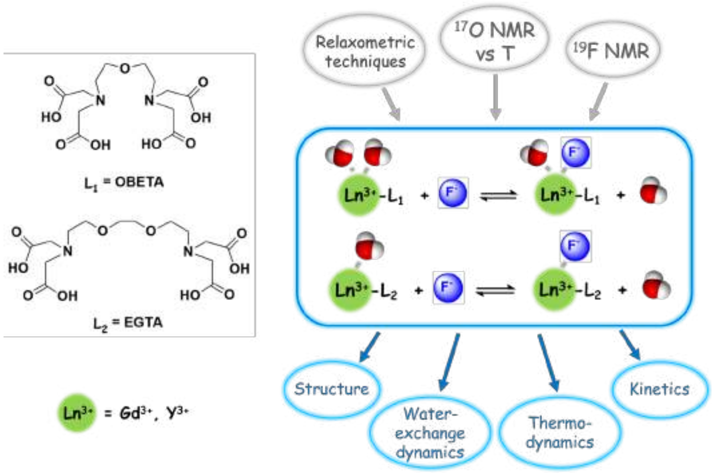

Figure 1: Low-field and high-field NMR techniques used to study the interactions between Ln(III)-OBETA/EGTA complexes and fluoride anions.

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NHC-catalysed atroposelective desymmetrisation of *N*-aryl maleimides

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In the field of enantioselective organocatalysis, if the control of central chirality is an area of increasing expertise, the same cannot be said for axial chirality, found in a large class of compounds in which a restricted rotation around a single σ bond results in the existence of two enantiomers, called atropisomers.[1] If significant advances have been made in the last few years for the simultaneous control multiple centers of chirality,[2] or multiple Csp^2–Csp^2 stereogenic axes;[3] the control of non-adjacent two or more different chirality elements in a single operation still remains a high synthetic challenge.[4] This lock is bigger when central chirality is combined with configurationally more labile pentatomic axially chiral Csp^2–N frameworks.

In this context, we recently demonstrated under NHC-catalysis the reactivity of chiral azolium dienolates in (4+2) annulation reactions for the atroposelective desymmetrization of prochiral *N*-arylmaleimide derivatives. [5] This one-step atroposelective *de novo* formation of 6-members ring leads to the formation of 3 C–C bonds and up to 6 elements of chirality, including two challenging remote-controlled C–N axes in the pentatomic series. Moreover, the easy base-induced transformation of the chiral *bis*-succinimide precursors allows to prepare the initially planned N-aryl phthalimide atropisomers with excellent retention of enantiopurity.

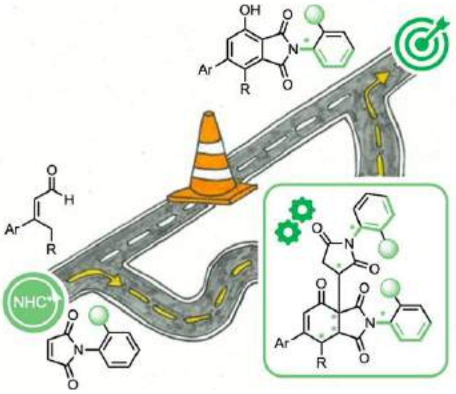

Figure 1: En route to original C–N atropisomers

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Conductive Polymeric Nanocomposite Based On Carbonaceous Fillers For Integrated Metal-Free Cabling And Sensing

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In recent years, the aim to develop new classes of multi-functional materials to reduce component complexity and enhance their recyclability has become one of the main driving forces in several industrial applications. The extraordinary electrical properties of carbonaceous graphene-based fillers, such as graphene nanoplatelets (GNPs) and carbon nanotubes (CNTs), lead to a big interest in the production of a new class of nanocomposites with both excellent mechanical properties and innovative electrical behaviours [1].

In particular, when the graphene-based filler concentration is below a critical value, called the percolation threshold, the electrical properties of these composites are dominated by the insulating polymer matrix and the material acts as an insulator. However, if the filler concentration is above the percolation threshold, the formation of a three-dimensional conductive network leads to a change in the electrical properties of the nanocomposite, and the material acts as a conductor [2].

Concerning this class of materials, an interesting and promising technology consists in the functionalization by laser treatment of nanocomposites, in which the filler concentration is below the percolation threshold. The interaction between the material and the laser beam leads to the formation of a V-shaped track where the filler concentration is locally above the percolation threshold resulting in a local electrical conductivity [3]. This innovative type of laser-functionalized nanocomposites could pave the way for a new technology for the production of metal-free electrical circuits and sensors. This could revolutionize product design, prototyping and production techniques used nowadays and will lead to several advantages, as follows: 1. weight loss of complex components for automotive and other industries; 2. reduction of production steps and production materials; 3. easier recyclability.

In our research, we used a CO2 laser to obtain conductive tracks on polypropylene-based nanocomposites. Three different compositions filled with GNPs and graphene oxide (GO) percentages between 2.5 and 4.0 wt% were tested. Across all compositions, a linear correlation between track length, electrical resistance and resistivity values lower than 2 ohm/sq, was observed. This promising result allows us to further optimize this technology by developing new types of nanocomposites using different polymer matrices, including recycled polymers, and different types of nanocarbons, including environmentally friendly fillers like biochar.

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[3] Cesano F. et al., Carbon (2013), 63-71. 10.1016/j.carbon.2013.04.066

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“Exploiting arginase 2 intrinsic dynamics for designing selective inhibitors endowed with antitumoral activity”

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Arginase (L-arginine ureahydrolase, or amidinohydrolase; ARG), is a binuclear manganese metalloenzyme that catalyzes the hydrolysis of L-arginine to form the amino acid L-ornithine and urea. ARG is an homotrimeric protein present in two different isoforms: ARG1 and ARG2. ARG1 is localized in the cytoplasm and mainly expressed in the liver and is responsible for detoxification of ammonia in the urea cycle, whereas ARG2 has been found predominantly in the mitochondria and is primarily linked to the generation of polyamine [1]. Both enzymes metabolize the amino acid most strongly depleted in tumour microenvironment (TME), namely free L-arginine [2], which is required by proliferating cells.

Recently, it has been reported that the ARG2 pathway is a means by which Regulatory T cells (Tregs) regulate inflammation in tissues. Furthermore, ARG2 reduced the survival and proliferation of $CD8^+$ T-cells, impacting anti-tumour immune responses. Thus, arginine metabolism via ARG2 is an immunoregulatory pathway implemented by Tregs in human tissues with significance for both autoimmunity and cancer, which makes ARG2 a relevant pharmacologic target [2].

Despite several inhibitors have been published so far, most of them lack activity and/or selectivity, likely because of the binding site similarity [1]. The goal of our project is to design and develop new inhibitors, likely able to specifically target ARG2, exploiting its different cellular localization, or exploiting the different binding site dynamics. It is indeed well known that very similar proteins can behave quite differently in terms of intrinsic dynamics, and, consequently, of ligand binding [3]

Here, we have applied computational methods to analyse in detail, and compare, the dynamics of ARG1 and ARG2 pockets, looking for possible difference to be exploited in drug design. We have applied extended standard molecular dynamics (MD) simulations and analysed them to highlight the binding site behaviour along the trajectories. In particular, we have performed root mean square fluctuation and essential dynamics analyses to identify the most flexible residues lining the binding site, we have tracked the pocket volume adjustment and the behaviour of waters in the pocket.

We found that crucial residues indeed show a different intrinsic dynamic that might be exploited for the design of more selective inhibitors.

[1] Pudlo et al., 2016, doi.org/10.1002/med.21419
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[3] Gossen et al., 2021, doi.org/10.1021/acsptsci.0c00215

The development of hypoxia-activated PROTACs to selectively degrade BRD4 in hypoxic cancer cells

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Proteolysis targeting chimeras (PROTACs) are bifunctional molecules comprising a ligand for a protein of interest (POI) attached to a ligand for an E3 ligase. They function by inducing degradation of the POI through the ubiquitin-proteasome system. However, the cellular effects of degrading a whole protein are profound, making strategies to target protein degradation to a given location or context essential.[1] This approach will reduce on-target dose-limiting toxicity, enhancing the therapeutic window for the use of PROTACs against a wide range of POIs. Hypoxia (conditions of lower-than-normal oxygen) is a characteristic of solid tumours that conveys poor patient prognosis, but the chemically reducing conditions found in hypoxia allow it to be targeted with pro-drugs. We have previously applied this strategy to HDAC inhibitors, demonstrating selective activation of the pro-drug in a tumour *in vivo*.[2]

To enable context dependent activation of PROTACs, we have developed a series of hypoxia-activated PROTACs (HAP-TACs). To achieve this, we employed a bioreductive group, never applied before, to mask key features of either a cereblon- or VHL-recruiting PROTAC, rendering them inactive in normal oxygen concentrations (normoxia, 21% O_2). In hypoxia, the bioreductive group releases the active E3 ligase ligand enabling degradation of the POI (Figure 1). As a proof-of-principle, we have applied this strategy to the degradation of BRD4. Our HAP-TACs are stable in normoxic conditions, but release the active PROTAC in hypoxia, leading to selective degradation of BRD4 when oxygen levels are reduced below 2%. As the bioreductive group is attached to the cereblon or VHL E3 ligase ligand, this strategy is applicable to any PROTAC that recruits these E3 ligases. This work, therefore, provides an exciting avenue for the development of HAP-TACs, for a range of targets, increasing the likelihood of success in the clinic.

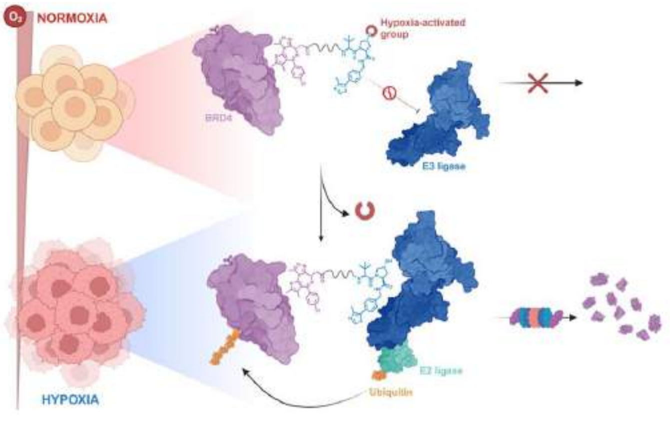

Figure 1 : The principle of hypoxia-activated PROTACs

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Integration of Lateral Flow nanoMIP Assay with Gold Silica Nanoparticles for Enhanced Point-of-Care Diagnostics

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In the ever-evolving panorama of immunodiagnostics, where various strategies aim to improve versatility, robustness, and cost-effectiveness[1], the advancement of molecular imprinting technology, particularly through the solid-phase synthesis of nanoparticles (nMIPs), has led to their emergence as highly efficient mimics of natural receptors [2]. Although the current state-of-the-art applications predominantly employ nMIPs for tasks such as molecular separation, sensing, and controlled release, their adoption as primary recognition elements in diagnostics remains limited.

This study presents a novel approach to lateral flow immunoassay (LFIA) diagnostics, aiming to reshape point-of-care testing (POCT) by minimizing reliance on biomolecules.

A simple method for fabricating a new composite material is proposed, which combines the molecular recognition properties of nMIPs with the optical properties of the metallic nanoparticles for biosensing[3][4]. Gold nanoparticles are well-known for their optical power and are widely used in LFIA due to their unique properties[3]. A highly selective nMIPs was prepared to target Bovine Immunoglobulin G and was incorporated in a novel composite material by conjugating with core-shell Au-SiO2 nanoparticles, using a simple synthetic approach for optimal integration[6].

The material structure was studied using transmission electron microscopy, UV-visible spectroscopy, and dynamic light scattering. Then, the hybrid nanomaterial was evaluated as a new probe candidate to be used in the colorimetric LFIA analytical platform, confirming its suitability.

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Initial design of pyrazole-based small molecules towards CDK20 inhibition

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CDK20 – also known as CCRK – is a serine-threonine protein kinase, expressed in a wide variety of tissues. Although its biological role is not fully understood, it has been linked to the rise of different tumors, like HCC and medulloblastoma(1). Given that lack of information, no inhibitors are approved to this date and CDK20 has been recognized as an understudied target(2). Therefore, an *in-silico* driven approach has been implemented in order to discover new scaffolds able to interact with CDK20, to provide initial hits for the future development of inhibitors. With no crystal structure available for the protein, a structure computed by AlphaFold (already exploited in other studies(3)) has been used to evaluate several combinatorial libraries of putative pyrazole-based CDK20 inhibitors. From these initial guesses, through the use of molecular docking, we narrowed the selection to three different chemotypes of pyrazole-based small molecules, that were then synthesized and tested in biological assays. Each step of the process – from the conceptualization to the synthesis – was continuously updated in an iterative fashion.

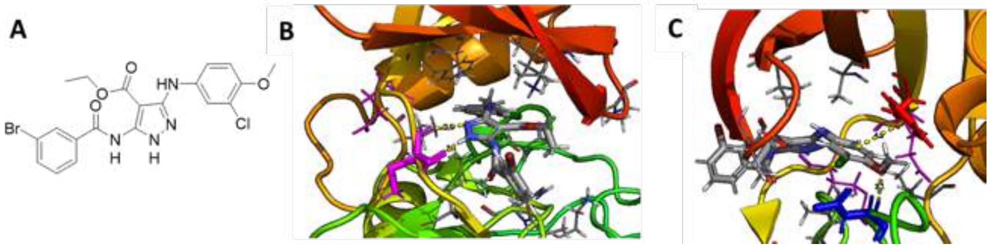

Figure 1: A) Structure of a selected compound; B) and C) Computed interactions (H-bond and π-stacking) between the molecule and specific peptides found in the catalytic region of the enzyme.

MTT assays performed on the compounds provided a wide variety of results. While the link between computed docking scores and inhibiting potency was only partially confirmed, the most promising molecules recorded IC_{50} values in the low micromolar range, showcasing the potential of these scaffolds to be further optimized towards CDK20 inhibitors.

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(2) Essegian D *et al., Cell Rep Med.* 2020 Oct 20;1(7):100128
(3) Feng Ren *et al.*, *Chem. Sci.*, 2023,14, 1443-1452

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New material Pegda-based as adsorbent for lithium from wastewater LIBs solutions.

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During the last few years, the demand for lithium has increased exponentially due to environmental regulation and technological transition, this high rate of demand has made lithium part of row critical material list and therefore is considered a limited element. Many methodologies are available for the recovery of lithium but most of them present disadvantages related to huge amounts of precipitating agent or the large use of organic solvent for extraction, moreover, they are inefficient when lithium concentration in the leaching solution is too low [1].
In this way, the ionic imprinting technique could be an innovative approach because it could be directly applicable to the leaching solutions.

This work presents an original approach to obtaining selective adsorbent materials for lithium from diluted solutions. These ionic imprinted polymers (IIPs) are based on the application of linear bi-functional monomers as polyethylene glycol diacrylate (PEGDA) that can spontaneously cyclopolymerize and give structures that are mimics of pseudo crown ethers able to stabilize cations thanks to the so-called macrocyclic effect [2]; in this way, the use of real crown ethers is avoiding.

To evaluate the validity of this strategy the experimental part focused on the effects of different molar ratios of PEGDA: Li (I), as a result, we obtained at last a capacity of about 0.190 mg/g with the highest selectivity towards lithium. To improve this capacity different reaction solvents (DMSO and water) and leaching solutions (basic and acidic ones) are explored and tested. Results show a general increase of binding capacity when the amount of basic leaching solution is progressively higher this allowed us to obtain an improvement in the capacity up to 1.70 mg of lithium adsorbed for each g of IIP.

[1] Alessia, A., Alessandro, B., Maria, V. G., Carlos, V. A. & Francesca, B. Challenges for sustainable lithium supply: A critical review. *J Clean Prod* **300**, 126954 (2021).

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In silico analysis of the potential interaction of legacy and novel per-fluoro alkyl substances (PFAS) with specific human proteins

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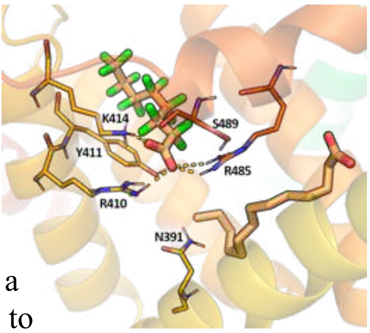

Over the last decades the spread of PFAS applicability rapidly grew, while the research on their side effects on environmental impact and human health slowly followed [1-2]. Indeed, because of their little intermolecular interactions with both polar and apolar substances [3], poly- and perfluorinated compounds possess high industrial applicability but also high bio-accumulability potential. This project aim to explore the possible interaction, by means of *in silico* methodologies, of a representative set of PFAS with transporters and receptors known to be targeted by the most famous PFOA and/or PFOS. We started from a small library of 26 PFAS: 13 carboxylic acids (e.g. PFOA), 6 sulfonic acids (e.g. PFOS), 3 newly formulated ether carboxylic acids (GenX, ADONA, cC6O4), 2 fluorotelomer alcohols and 2 perfluorinated alkanes, to include both legacy PFAS widely studied in scientific literature and new, scarcely reported ones. To further evaluate the effect of chain-protein interaction we included the last group, perfluorinated alkanes with no functional groups, as a mean to evaluate the proteophilic nature[4] of these chemicals.

We considered four proteins' families: organic anion transporters (OATs), expressed mainly in the kidney, fatty acids binding proteins (FABPs), expressed throughout the body, human serum albumin (HSA), and other thyroid hormone transporters (e.g. TTR and TBG), which act as a buffer system for extrathyroidal T4 levels. Protein-PFAS interactions have been simulated by means of molecular docking, applying an induced fit approach to allow for the mobility of proteins' binding sites, especially in the case of FABPs and HSA. Then, specific complexes were submitted to MD simulations to verify the ligand stability and the reliability of the predictions. The binding of PFOA and cC6O4 to bovine serum albumin (BSA) has been experimentally evaluated through dialysis equilibrium experiments showing lower binding probability of legacy PFAS compared to novel ones. Preliminary results showed overall higher affinities for medium length, straight molecules (PFOA, PFOS) than shorter and more branched ones, like novel PFAS, as for instance cC6O4.

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[4]. Lanza H.A. et al., *Environmental Toxicology and Chemistry*, **2017,** https://doi.org/10.1002/etc.3726

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The therapeutic potential of PIN-1 inhibition: new agents and strategic approaches

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The peptidyl-prolyl cis-trans isomerase PIN-1 is an important regulator of cellular processes. It is known for its unique ability to specifically identify and catalyse the isomerisation of the phosphorylated serine/threonine-proline motif (pSer/Thr-Pro) in proteins, which affects the function of the target protein. Overexpression of PIN-1 is observed in various cancers, where it acts as a modulator of key cancer-promoting signalling pathways. Despite extensive preclinical studies to identify PIN-1 inhibitors, only all-trans retinoic acid (ATRA) in combination with arsenic trioxide (ATO) has so far found clinical application [1]. The authors, that have already contributed to the discovery of one of the most potent and advanced PIN-1 inhibitors (KPT 6566), [2] here develop new inhibitors using two different approaches: on the one hand, a bioisosteric approach led to the design of ATRA analogues, resulting in compounds with potency similar to ATRA; on the other hand, a screening of the MEDSynth library identified some 3-hydroxy-1H-pyrazole-4-carboxylic acid derivatives as potential inhibitors, and some of them showed promising inhibition at 10 µM concentration. Further studies focusing on the binding mode of the most promising derivatives will lead to the design and synthesis of new compounds for both series. Theoretical design, computational studies, synthesis, SAR, and biological assays of new compounds are presented and discussed.

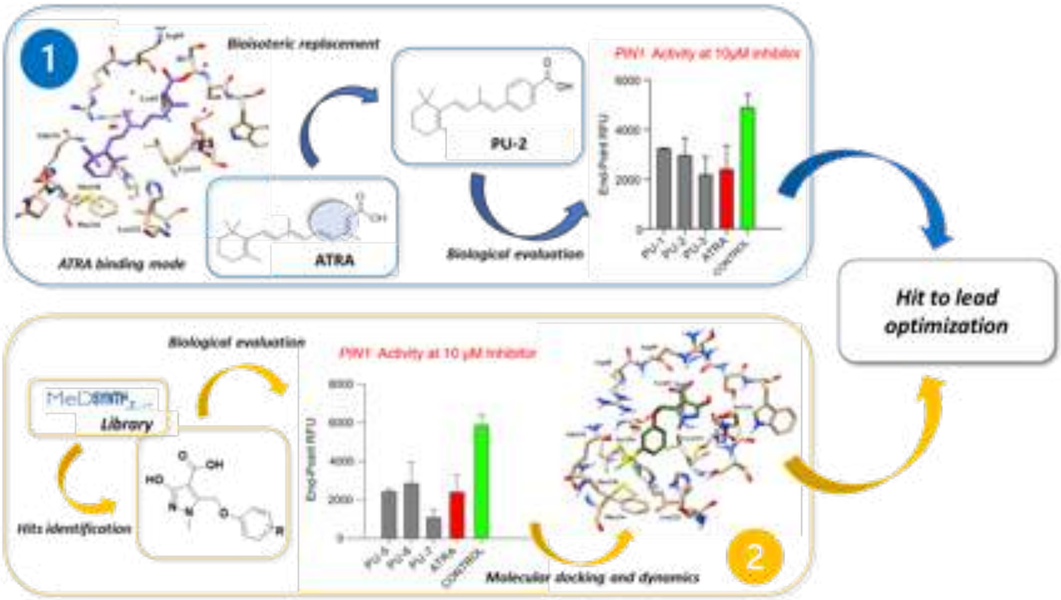

Figure 1: The two approaches using in hits identification.

[1] Siyu He. *et al. J. Med. Chem.* **2023**, *66*, 9251-9277 [2] Campaner, E. *et al.*, *Nat Commun*. **2017**, *8*, 15772

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