



Journées Grand Sud-Ouest de la Société Chimique de France

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Phytochemical screening and pharmacological properties of African mustard extracts

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Recently, special attention has been paid to *Brassica* species as one of the excellent sources of nutrients and health-promoting phytochemicals responsible for the prevention and treatment of several chronic diseases (inflammation, Alzheimer and diabetes). The current study aimed to assess the phytochemicals as well as their pharmacological properties in different African mustard extracts by butanol and water. The phytochemical investigation of extracts using HPLC-DAD and GC-MS revealed the presence of a large number of phytoconstituents such as 3',5'-dihydroxyflavone, 7-hydroxyflavone, phenoxodiol, pinostilbene hydrate, propane, 1-isothiocyanato-3-(methylthio)- and n-hexadecanoic acid^{1 2}. Biologically, the two mustard extracts demonstrated a promising potential anti-xanthine oxidase and anti-inflammatory activities. At 50 mg/ml, the aqueous extract reduced xanthine oxidase activity by 24%, while the buthanolic extract lowered anti-inflammatory activity by 23,7%.

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Zwitterionic polyamide membrane with anti-biofouling properties

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Bio-fouling is a phenomenon common to all filtration membranes with protein-rich solution. This problem affects the filtering properties of the membranes making them almost inefficient over time. In this work we have modified polyamide membranes to reduce the biofouling. The membranes used here are polyamide membranes obtained from piperazine (PIP) and Benzene-1,3,5-tricarbonyl chloride (TMC) deposited on a commercial polyethylene sulfone (P-PT) support.¹ These membranes were then modified by interfacial polymerization with polymers from polyethylene glycol (PEG) and zwitterionic molecules such as sulfobetaine.^{2,3} The estimate of the fouling membranes was carried out by the filtration of a solution of bovine serum albumin (BSA). We obtained for the reference polyamide membrane a NaCl retention of 50% and a fouling of 39%. The filtration results obtained for the membranes modified with PEG and sulfobetaine, showed an increase of 30% of the fouling resistance as well as an increase of 18% of the retention compared to the reference polyamide membrane.

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Towards a sustainable transformation of N₂: simultaneous activation of N₂ and H₂ by a metal center

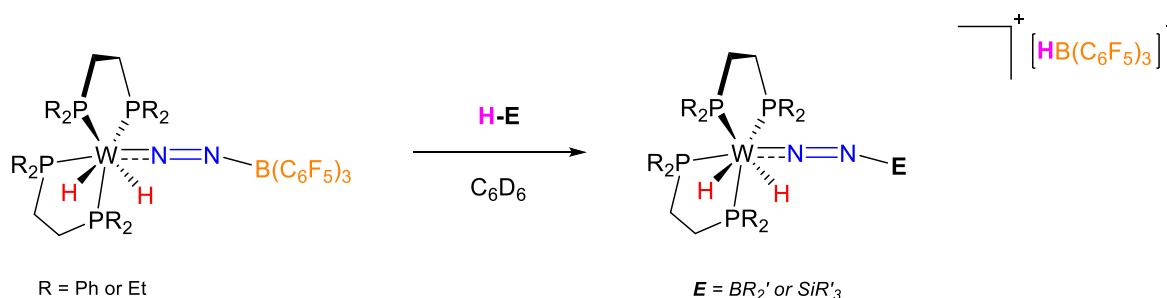
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Atmospheric N₂ is the primary source of all nitrogen atoms present on earth, but the inertness of this molecule prevents its use as a direct nitrogen source in the biosphere and in industry. Nowadays, N₂ reduction to NH₃ is achieved through the Haber-Bosch (HB) process, a highly energy-demanding and fossil fuel-dependent process. If most of the ammonia produced is devoted to the manufacture of fertilizers, 10–20% are used for the synthesis of more valuable nitrogen-containing chemicals. The formation of C-N, Si-N and B-N bond, under mild conditions, via N₂ activation bypassing the HB process is the key step in the synthesis of high-valued N-containing molecules and remains a long-term and challenging target in chemistry.^[1]

Inspired by the recent chemistry of "Frustrated Lewis Pairs", our team (SMAc) is currently working on the development and study of cooperative activation methods of N₂ by complexes combining an abundant and non-toxic transition metal (W or Mo) and the strong Lewis acid B(C₆F₅)₃.^{[2], [3]} Preliminary studies have shown that such complexes were able to activate simultaneously nitrogen and dihydrogen, leading to the formation of dinitrogen metal hydrides. This work presents the reactivity of these complexes towards small molecules such as hydro-silanes or -boranes, Lewis bases, and CO₂.



Scheme 1. “Frustrated Lewis Pair” activation of hydro-silanes and boranes at a dinitrogen-dihydride metal complex.

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Borinic acid vitrimers: synthesis and applications

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Vitrimers are a new class of polymer which were introduced by Dr. Leibler *et al.* in 2011. They define vitrimers as “a polymer network that can change its topology while maintaining the constant number of chemical bonds”.¹ They are characterized by their ability to combine the properties of thermoplastics (reusability) and thermosets (superior thermo-mechanical properties and chemical resistance) due to a chemical network incorporating covalent dynamic cross-links. Transesterification reactions with boronic esters in vitrimers has already been described taking advantage of the exchange properties of the B-O bonds which are switchable without catalyst.² Nowadays, Sun *et al.* described polymers with borinic acids monomers, however there is no example of borinic acid vitrimers.³ Borinic acids offer the possibility to obtain new materials with interesting properties as hydrolytic stability, fluorescence, etc. The main goal of the project is to develop new functionalized borinic acid compounds which can be used for vitrimers as cross-linker (Strategy A – Figure 1) or monomer (Strategy B – Figure 1) thanks to a divergent strategy. Non symmetrical borinic acid bearing an alkyne has been synthesized as a key compound and copper-catalyzed alkyne-azide cycloaddition (CuAAC) has been applied to obtain borinic acid monomers and bis-borinic acids.

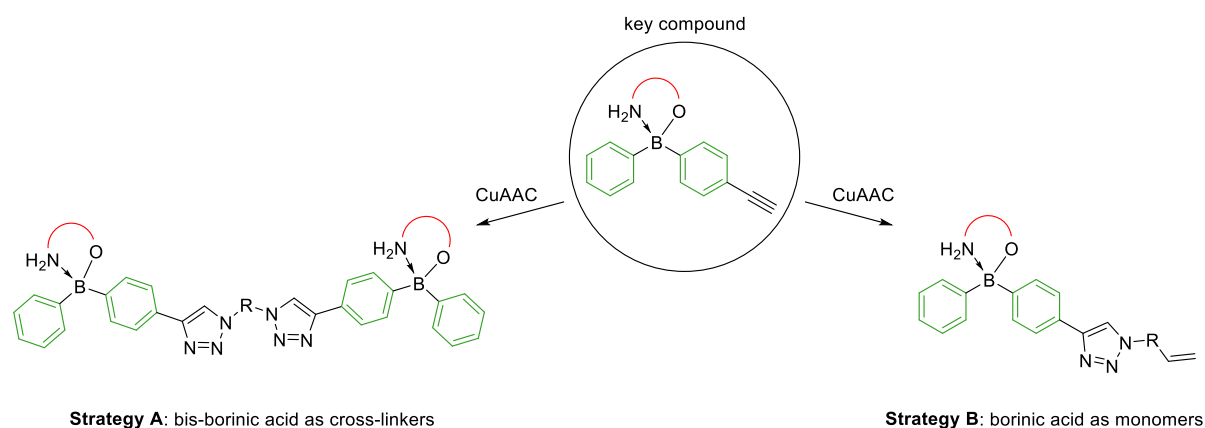


Figure 1 - Bis-borinic acid linkers (strategy A) and borinic acid monomers (strategy B) for vitrimers synthesis

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Détection du glyphosate par inhibition enzymatique

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Les pesticides sont des substances chimiques largement utilisées en agriculture pour protéger les cultures et les semences avant et après la récolte. Ils ont apporté des bénéfices économiques importants depuis leur mise sur le marché. En même temps, leur généralisation a créé de sérieux problèmes liés à leurs effets sur l'environnement et sur la santé humaine¹. En raison de son efficacité à tuer les mauvaises herbes avec un coût modéré, le glyphosate est l'un des pesticides les plus utilisés au monde. Bien qu'il soit considéré moins toxique par rapport aux autres pesticides chimiques, le glyphosate a suscité la préoccupation publique en raison de son utilisation massive conduisant à sa détection ainsi que ces résidus dans les eaux de surfaces². Depuis nos connaissances, aucun système de détection efficace et peu coûteux de glyphosate n'est actuellement disponible. Un tel système, qui permettrait de détecter la contamination sur place et en temps réel, est nécessaire de toute urgence pour alerter les autorités locales et sensibiliser la population.

Dans cette optique, nous étudions le potentiel de développement d'une méthode rapide, peu coûteuse et écologique pour surveiller la contamination des eaux de surface par le glyphosate. Le principe de détection est basé sur l'inhibition de l'activité de deux enzymes, l'exonucléase I (Exo I) et la T5 exonucléase (T5 Exo) par le glyphosate. Ces deux enzymes digèrent les oligonucléotides en séquences plus courtes jusqu'aux mononucléotides. En présence du glyphosate dans le milieu réactionnel, l'activité des deux enzymes est inhibée et la digestion est retardée. En utilisant le SYBR Gold comme sonde de fluorescence, la détection du glyphosate est réalisée par spectroscopie de fluorescence : puisque la digestion enzymatique est freinée, l'intensité de fluorescence de la sonde augmente avec des quantités croissantes en glyphosate, ce qui indique la perte de la digestion enzymatique en présence de ce contaminant. Dans les conditions optimales, cette méthode permet la détection spécifique et reproductible du glyphosate dans une gamme de linéarité entre 100 et 500 μM , ce qui ouvre la voie à la détection éventuelle du glyphosate dans des matrices réelles à des limites de détection plus appropriées.

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Synthetic approaches for Cathepsin S inhibitors and fluorinated analogues

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Atherosclerosis is responsible for a large part of cardiovascular events and causes more than 19 million deaths each year.¹ The detection of « unstable » plaques, which will evolve and are likely to break down is therefore a major current issue in the prevention of such cardiovascular accidents.

Positron emission tomography (PET) represents an extremely promising imaging technique for their detection since it allows an in vivo non-invasive visualization of atheromatous plaques which will be qualitatively defined through selective targeting.²

Cathepsin S belongs to the cysteine protease family and recent studies have shown that these proteases are overexpressed in the above-mentioned cardiovascular pathologies. More precisely, its expression has been specifically identified in human atherosclerotic lesions and not in healthy arterial segments.³ Identification of atheromatous lesions by PET might thus be investigated in vivo by labelling of Cathepsin S with radiofluorinated inhibitors.

Our project aims to synthesize such fluorinated analogues of Cathepsin S inhibitors, especially LHVS **Fig.1**. This Leucine derivative compound exhibits the required properties for building a relevant library of analogues: a very good inhibition constant (K_i) of 5nM for Cathepsin S as well as an excellent selectivity. We will present our recent synthetic efforts in the generation of a library of such fluorinated analogues, including ones featuring new scaffold variations.

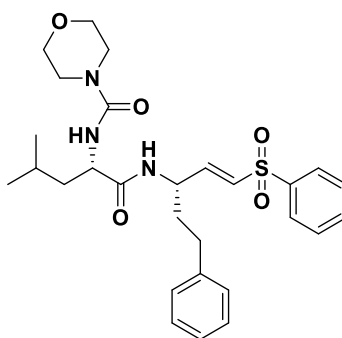


Fig. 1 LHVS a lead toward fluorinated Cathepsin S inhibitors

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Novel, tunable boron-based luminescent compounds incorporating NHC moieties

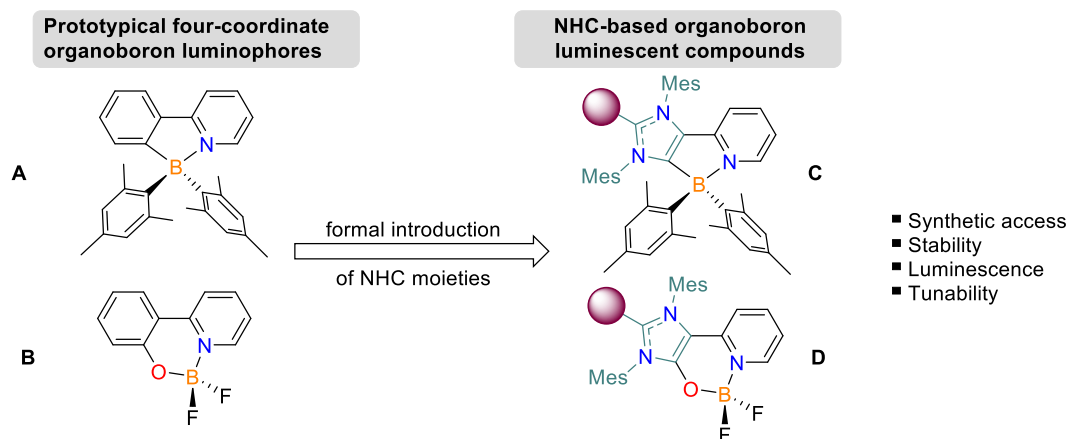
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Thanks to their high luminescence intensity and quantum yields associated with a remarkable chemo- and photo-stability, four-coordinate organoboron compounds are promising light-emitting materials and have been the subject of intense research efforts over the last two decades with numerous practical applications including organic light-emitting diodes (OLEDs), photo-responsive materials, sensors or bio-imaging.¹ These boron-bridged compounds have in common a π -conjugated structure formed by aryl or heteroaryl groups, which can be decorated/modified for desirable properties.

In view of the outstanding benefits brought by the use of N-heterocyclic carbenes (NHCs) ligands in photoluminescent complexes and materials,² we devised to incorporate various NHC moieties into luminescent organoboron compounds. Starting from the two prototypical luminescent compounds **A** and **B**, our strategy thus consists in the formal replacement of the aryl groups of the chelate by imidazolyl-based NHCs units leading to the new classes **C** and **D**, in which the C4-position (abnormal carbene) is linked to the boron atom and the C2-position (normal carbene) is available for further derivatization.



In this communication, we will present the routes towards new luminescent species **C** and **D** employing either a classical organic synthesis or the “organometallic” strategy recently developed in our group.³ The characterization and preliminary studies of their luminescent properties will be also discussed.

This work was supported by CNRS Emergence@INC2022 grant NHC_Lumen. A. R. thanks Erasmus+ mobility program for Master 2 fellowship.

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Spin crossover in bis[hydrotris(1,2,3-triazol-1-yl)borate]iron(II): bulk studies, thin films and application

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Nanoscale spin-crossover thin films capable of undergoing reversible switching between their low-spin and high-spin electronic configurations with markedly different physical properties are excellent candidates for various technological applications¹.

Herein we report a detailed study on the physical and spin-state switching properties of bis[hydrotris(1,2,3-triazol-1-yl)borate]iron(II) ($[\text{Fe}(\text{HB}(1,2,3\text{-tz})_3)_2]$ or **1**) both in bulk powder and in thin film form. Synthesis of the complex in a form of dodecahydrate (**1**·12H₂O) was reported earlier by Jenkins *et al.*² The anhydrous $[\text{Fe}(\text{HB}(1,2,3\text{-tz})_3)_2]$ complex, obtained *via* dehydration of the dodecahydrate, undergoes structural phase transitions upon the first heating in the 303–493 K range followed by reversible, gradual spin crossover upon further thermal cycling, with a transition temperature of $T_{1/2} = 373$ K (Fig. 1a). The compound is capable of sublimation that allowed us to obtain thin films with thicknesses in the range of 20–180 nm on various substrates by means of vacuum thermal evaporation. The obtained films retain the gradual character of spin crossover (Fig. 1a), independently on thickness, and exhibit a high endurance upon thermal cycling and long-term storage in ambient air conditions. As the thermal spin transition is accompanied by a drastic change of the optical properties of the films (in particular in the UV spectral domain), we have shown that these films can considerably enhance the thermorefectance properties of surfaces on a wide temperature range. Using this appealing property, we have experimentally demonstrated that the thin films of **1** can be used as a high-performance temperature sensor, probed by optical reflectivity, for mapping and measuring the surface temperature on Joule-heated metallic microwires (Fig. 1b). As such, these molecular thin films open an opportunity for their application in microscale thermometry.

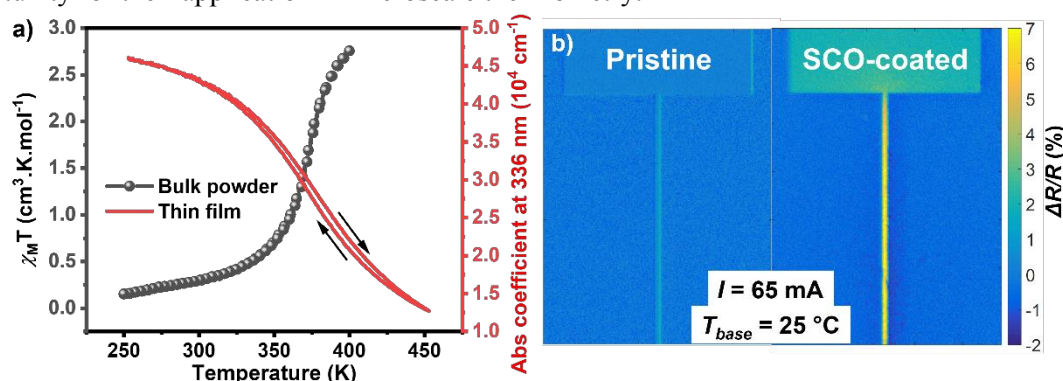


Figure 1. Temperature dependence of magnetic (bulk) and optical (thin film) properties of **1** (a); Optical reflectivity change maps of Joule-heated microwire: both pristine and SCO-coated (b).

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Aptasensors for the detection of emerging contaminants: development of an electrochemical platform

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This work is part of a four-years research project, which aims at the development of a sensitive and selective electrochemical aptasensor as an analytical strategy to detect, *in situ* and in real time, contaminants (pesticides and drugs) in water.

In this context, the objective of my work is the development of the transducer to be integrated in the electrochemical platform to eventually achieve efficient aptasensing. The approach we do investigate shall provide electrodes of high specific surface area and enable the controlled covalent grafting of the selected aptamer.

Two strategies have been chosen to functionalize carbon electrode surfaces: either the use of conducting polymers or the deposition of self-assembled peptides.

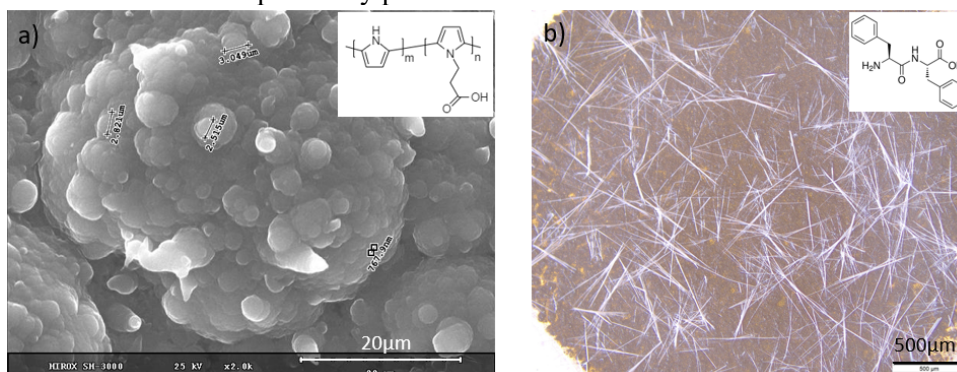
The first approach is focused on the electropolymerization of pyrrole¹ with suitable functional groups allowing the covalent grafting of the aptamer.

The second one is based on the self-assembly of diphenylalanine (FF)² dipeptide in order to obtain a stable coating on the electrode surface.

The two strategies were developed in parallel to determine strengths and limitations of both approaches. Several aspects were taken into account in our study: the conditions to form stable structures, the achievement of homogeneous coatings on carbon electrodes, the electrochemical properties, the wettability and the possibility to perform the covalent grafting of aptamers.

Several techniques were employed to reach these aims: optical microscopy, scanning electron microscopy (SEM), cyclic voltametry (CV), contact angle, X-ray photoelectron spectroscopy (XPS), infrared spectroscopy (FTIR).

Our main results on the development and characterization of the electrochemical platform based on polypyrrole and FF will be comparatively presented here.



a) SEM of polypyrrole electropolymerized on carbon electrode and b) optical microscopy of FF fibers on carbon electrode.

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Mechanochemical development of sydnone derivatives: how to make sydnones rock !

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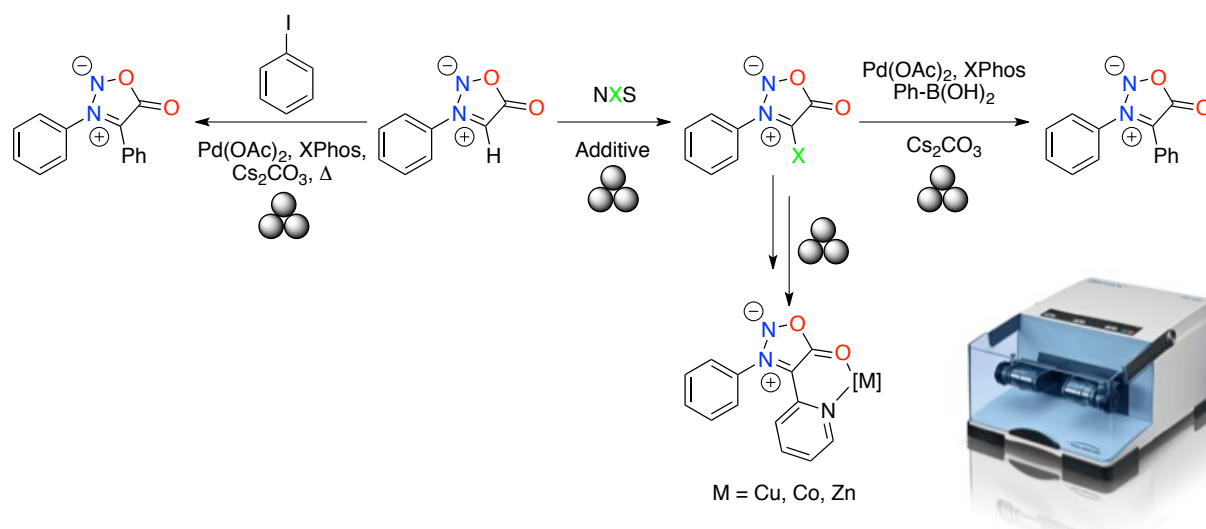
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Sydnones are mesoionic compounds largely studied over the past decades for their biological activity and their propensity to undergo 1,3-dipolar cycloaddition reactions. Sydnone compounds are usually synthesized from *N*-substituted amino acids by nitrosation and cyclization.¹ Our team is focusing its expertise on the development of synthetic methodologies by mechanochemical activation for the production of high value molecules.²

Hence, we developed two straightforward methods to obtain *N*-substituted amino acids from anilines and a subsequent one-pot two-step sequence to obtain sydnones. To go further, a sydnone functionalized with a pyridine was used as a ligand in coordination complexes.³

More recently, we demonstrated that sydnones could be efficiently halogenated by ball-milling. Corresponding halo-sydnones could be subsequently used in palladium-catalyzed cross-coupling mechanochemical reactions. In parallel, direct mechanochemical C-H activation of sydnones allowed to obtain arylated sydnones.



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Reactivity of a Cationic Mo(VI) Pentahydride Complex towards C=X (X = O, N, S) Bond Reduction

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The chemistry of molybdenum polyhydride complexes containing mono and bidentate phosphine ligands has been the subject of significant investigations, notably due to the ability of such species to support mixed coordination modes associating η^2 -H₂ ligands and hydride ligands. By contrast, the reactivity of these species towards common small molecules still has to be explored and understood.

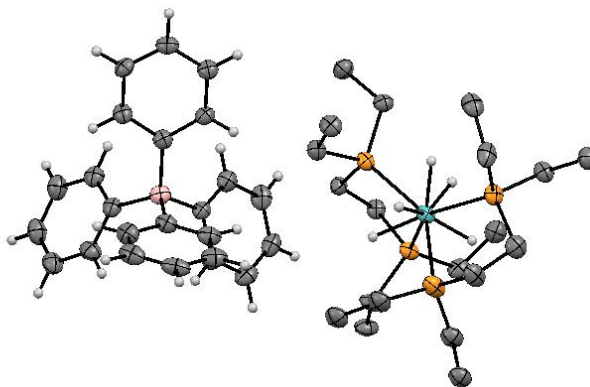


Figure 1. Molecular structure of the cationic pentahydride molybdenum complex, [MoH₅(depe)₂][BPh₄].

In this communication, two parallel preparations of a rare 9-coordinate cationic pentahydride Mo(VI) complex will be reported and its various reductive reactivities towards small molecules (CO₂, CS₂, CO, C₂H₄) described. Further work towards the development of catalytic systems relying on the use of such polyhydride derivatives will be discussed.



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Urea-based foldamer catalyst for C-C bond forming in asymmetric Michael reaction : a DFT investigation

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Bioinspired urea-based oligomers that fold with high fidelity (foldamers (**F**)) have been proven¹ as robust alternatives to metal based asymmetric catalysis, able to catalyze challenging C-C bond forming reactions with high enantioselectivity, and loadings as low as 1:10000 chiral catalyst/substrates molar ratios. However, studies developed at the atomistic level are necessary to understand the characteristics and function of the foldamers as catalysts. A DFT based Global Optimization procedure has been performed to find the low lying molecular arrangement in the conjugate addition of dimethylmalonate (**M**) to (1E)-3-methyl-1-nitrobut-1-ene (**N**) (see Figure below). It was found that **N** prefer the second site as H-bond donor, and **M** the first site. The interactions stabilizing the system are mainly electrostatic and noncovalent, with a set of Van der Waals interactions well defined between **N** and the phenyl group in **F**. Further investigations have been made in the Transition States, and the enantiomer **R** was predominant over the enantiomer **S**, which is coincident with the experimental observations. The enantiocontrol is identified to be related with specific geometrical parameters of the catalyst. These results rationalize the structure-properties relationship of the catalyst, and present for the first time a conclusive identification of its function. Further improvements to the catalytic properties of **F**-like foldamers are now possible.

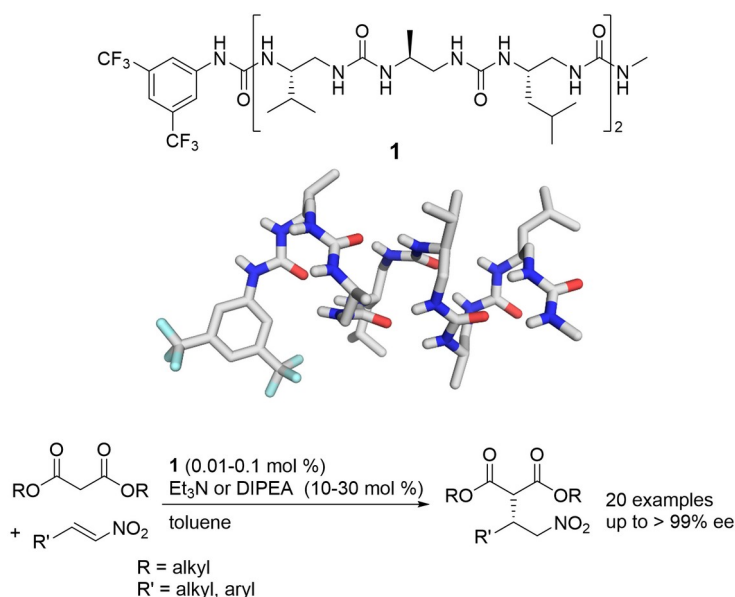


Figure 1. Representation of the foldamer and the substrates under study in our investigation.

¹ *J. Am. Chem. Soc.* **2017**, 139, 36, 12524–12532



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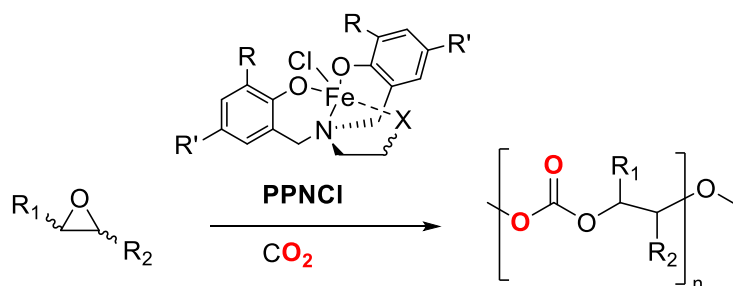
Preparation of green polycarbonates by a copolymerization of CO₂ with epoxides

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The emission of carbon dioxide (CO₂) in the atmosphere increased during the past two hundred years.^[1] The variation of this concentration has a significant effect on the environment and increases the global warming. At the same time, CO₂ is a non-toxic, abundant, cheap carbon and oxygen source.^[2] In this context, this molecule has become valuable for the synthesis of various chemicals.^[1] The copolymerization of CO₂ with epoxides to produce polymeric carbonate is an advantageous option for the utilization of CO₂.^[1] These polycarbonates are described as biopolymers for their biodegradability but also for the transformation of waste into wealth.^[2] Metal catalysis has a central importance for this copolymerization.^[3] However, the aim is to replace toxic heavy metals such as chromium and cobalt by using active catalysts composed of green metals. In this work, we wish to present our results concerning the development of new iron based homogeneous catalysts for the CO₂/epoxide copolymerization using cyclohexene oxide as a substrate for the first catalytic screening. Preliminary tests on biobased epoxides such as limonene oxide will also be presented.



PPNCI : Bis(triphenylphosphoranylidene)ammonium chloride

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Journées Grand Sud-Ouest de la Société Chimique de France

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Photo-release of Nitric Oxide in Ruthenium Complexes for Potential Biological Application

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Cutaneous wound infections are a global issue with millions of infected patients and costly treatments each year. The development of biofilm, aggregated communities of bacteria, causes delay in wound healing and bacterial resistance towards numerous antimicrobials.

The synthesis of a new generation of antimicrobials is crucial, as 75% of them currently under clinical trials are simply derivatives of already known and used ones, which most probably will not have significant roles in combating bacterial resistance. [1]

Nitrosyl ruthenium (Ru-NO) complexes have shown efficiency as donors of nitric oxide (NO[•]), known as a key mediator in biofilm dispersal, and whose controlled release is responsible for antibacterial activity. [2]

Herein, we propose to develop light controlled Ru-nitrosyl complexes with an efficient, local and targeted NO[•] production, as “non-traditional” antimicrobial agents with wound healing activity. [3] A library of Ruthenium-nitrosyl complexes with ligands of various photo-physical properties will be synthesized and characterized. Antimicrobial spectrum will then be determined on several Gram (+) and Gram (-) bacterial strains, after preliminary tests such as the determination of the maximum non-toxic concentration.

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Journées Grand Sud-Ouest de la Société Chimique de France

11-12 Juillet 2022, Toulouse

Production et caractérisation de pigments par des bactéries marines pour l'éco-conception des OLEDs

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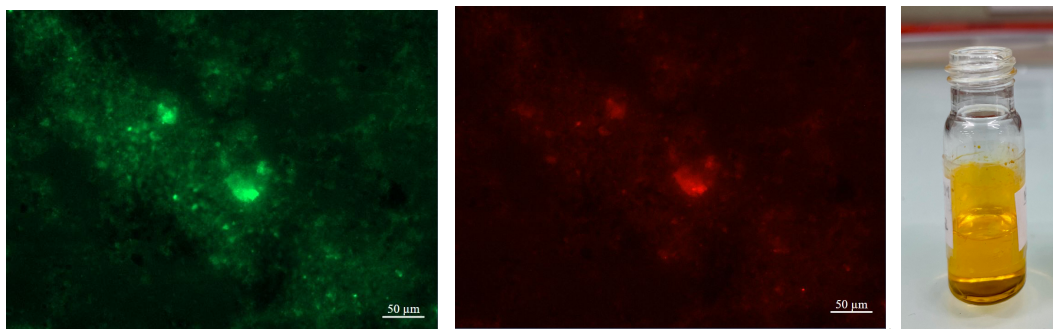
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Les caroténoïdes, au-delà de leurs bienfaits sur la santé humaine et animale, de par leur caractéristique structurale, sont également dotés de propriétés de semi-conducteurs. Sous tension, ces semi-conducteurs organisés en une structure multicouche peuvent présenter une électroluminescence. Ces molécules organiques peuvent ainsi substituer les semi-conducteurs minéraux dans la fabrication de transistors, de cellules photovoltaïques ou de diodes électroluminescentes organiques « Organic light-emitting diodes (OLEDs) » [1].

Les propriétés photo-électroniques du bêta-carotène, le caroténoïde naturel le plus courant, ont été mises en évidence offrant une utilisation potentielle de ce pigment dans les dispositifs photo-électriques [2, 3]. L'utilisation de matériaux bio-sourcés, tels que les pigments microbiens, permettra une écoconception des OLEDs afin de réduire leur impact environnemental.

Dans ce contexte, nous nous intéressons aux micro-organismes environnementaux, producteurs de caroténoïdes.



Emission de la lumière verte et rouge (microscope à épifluorescence) par une suspension bactérienne marine, productrice de pigments jaunes.

Après la sélection de micro-organismes pigmentés à partir de biofilms bactériens naturels, nous avons entrepris de stratégies d'optimisation des performances des souches microbiennes ainsi que les études des propriétés photo-électroniques et anti-oxydantes de pigments obtenus.

L'objectif principal consiste à mettre en évidence l'intérêt de souches microbiennes et particulièrement leurs pigments en vue de l'exploitation de ces molécules dans les dispositifs photo-électriques.

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Journées Grand Sud-Ouest de la Société Chimique de France

11-12 Juillet 2022, Toulouse

***Vitis vinifera* stem part: chemical profile and biological potential**

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Vitis vinifera is an herbaceous plant cultivated in different regions of the world. Diverse studies have demonstrated the pharmacological and therapeutic effects of the grapevine plant such as antioxidant, anticancerous, and antidiabetic [1]. Furthermore, numerous bioactive compounds have been reported in the grape plant, such as resveratrol, caftaric, coumaric acid, flavanol, and dihydroflavanol glycosides [2]. The purpose of our study is the investigation of the chemical composition as well as the therapeutic potential of the grape stem part. Two extraction methods were performed in this study: Maceration and Accelerated Solvent Extraction (ASE) using organic solvents of increasing polarity (cyclohexane, dichloromethane, ethyl acetate, methanol, and H₂O). The chemical analysis of the obtained extracts was performed by the GC-MS technique, and the phenolic content was determined by the TPC method. For the biological analysis, several *in vitro* assays were performed (antidiabetic, antialzheimer, and cytotoxic activity). The GC-MS analysis of the volatile profile of the stem extracts has led to the identification of 36 compounds among them seven were identified for the first time in the grape plant (decane, 3-methyl-, 2,3-dimethyldecane, pentadecane, phthalic acid, di(2-propylpentyl) ester, hydracrylic acid, nonanoic acid, and 2,2'-methylenebis(6-tert-butyl-4-methylphenol). Concerning the biological analysis, results have shown that the ethyl acetate extract (EtOAc) obtained by maceration has demonstrated significant potential regarding anti-alzheimer (IC₅₀ = 14.1 µg/mL), antidiabetic (IC₅₀ = 13.4 µg/mL), and cytotoxic with HCT-116 (IC₅₀ = 12.5 µg/mL).

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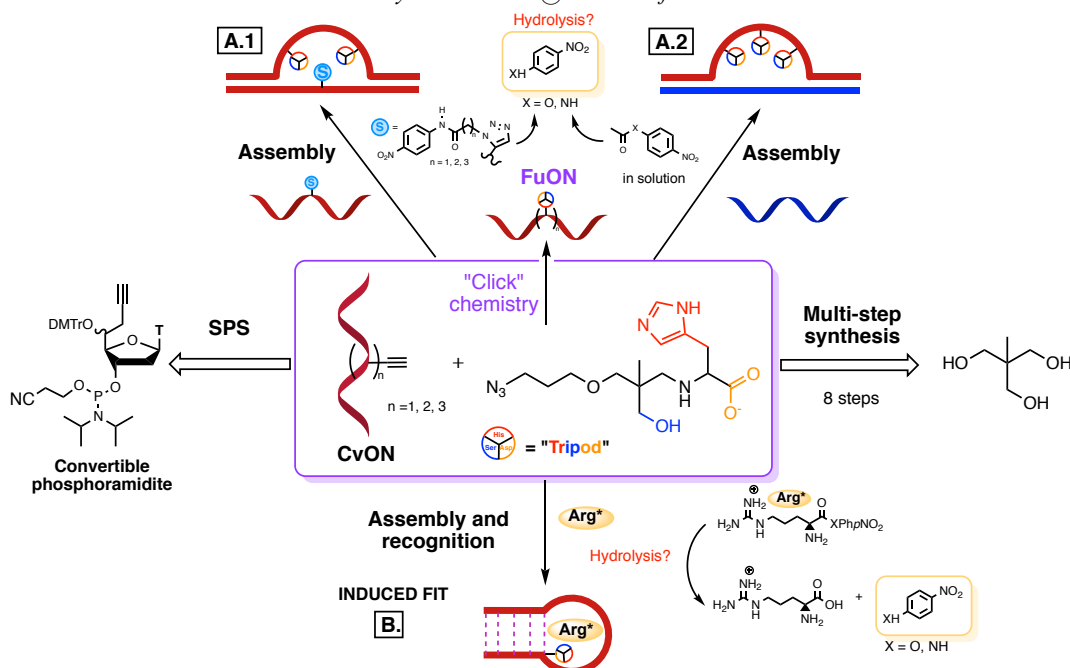
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Serine Protease Mimics: a New Approach through Functionalized Oligonucleotides

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The chemical hydrolysis of the amide bond is mainly performed in harsh conditions. Yet, in Nature, the ubiquitous peptide bond is quite easily hydrolyzed thanks to serine proteases bearing a catalytic triad composed of three cooperative amino acids (aspartate, serine and histidine), found within the catalytic site of the enzyme.¹ The goal of our project is the rational design of nucleic mimics capable of performing this hydrolysis by means of functionalized oligonucleotides (FuON), that are covalently modified to expand their catalytic repertoire towards protease-like DNA catalysts.²

A library of FuON bearing amino acid side chains-like residues was obtained using “click” chemistry between two partners: a **convertible oligonucleotide (CvON)** synthesized using a convertible alkyne phosphoramidite *via* solid phase phosphoramidite approach, and a tri-functionalized azide building block (“**Tripod**”- Figure).³

With carefully designed sequences and thanks to oligonucleotides’ ability to self-assemble, the obtained FuON were arranged into flexible secondary structures (such as bulges or hairpins) by the use of a pertinent modified (or not) complementary strand. The catalytic properties of those DNA catalysts were then evaluated with chromogenic ester or amide substrates, presented either on the complementary strand of the FuON (A.1) or free in solution (A.2) to study turn-over possibility. We are also working on aptamer sequences in order to ally recognition and catalytic properties to construct an aptazyme able to perform the specific hydrolysis of a fluorogenic amide or ester substrate (B).

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Journées Grand Sud-Ouest de la Société Chimique de France

11-12 Juillet 2022, Toulouse

Preliminary study of aging of rhum agricole : impact of barrel state on the rum chemical profile

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“Rhum Agricole” is a spirit made from fresh and pure sugar cane juice. It must be differentiated from the molasses-based rum called industrial rum widely produced in the Spanish and English-speaking islands in the Caribbean. The “Rhum Agricole” from Martinique has been granted the “Appellation d’Origine Contrôlée” (AOC) designation since November 1996. According to the AOC regulation the rum must be aged in oak cask during at least 3 years to be called “Rhum vieux”. Compared to the rum made from molasses, studies regarding the “Rhum Agricole” are currently difficult to be found. Specific data is needed to understand the events occurring during the aging process in the tropical climate of Martinique. A first study was conducted to follow the physicochemical features (dry extract, color intensity, volatile organic and total phenolic compounds) of rum in used barrels. The results were compared to those obtained with new barrels. These preliminary data will help us define the better physicochemical markers of rum aging. Another study in progress based on a three-year aging trial, will allow us to compare the chemical and sensorial profile of rum from new and once-used barrels. The sample will be subjected to chromatographic analysis (LC-DAD-MS and GC-MS)¹ and inductively coupled plasma analysis². The antioxidant activity will be also defined³. These research studies are aimed at giving relevant information to the master blender so that the aging practices could be improved.

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Journées Grand Sud-Ouest de la Société Chimique de France

11-12 Juillet 2022, Toulouse

Cell culture, wet spinning and 3D printing with carbohydrate supramolecular hydrogels

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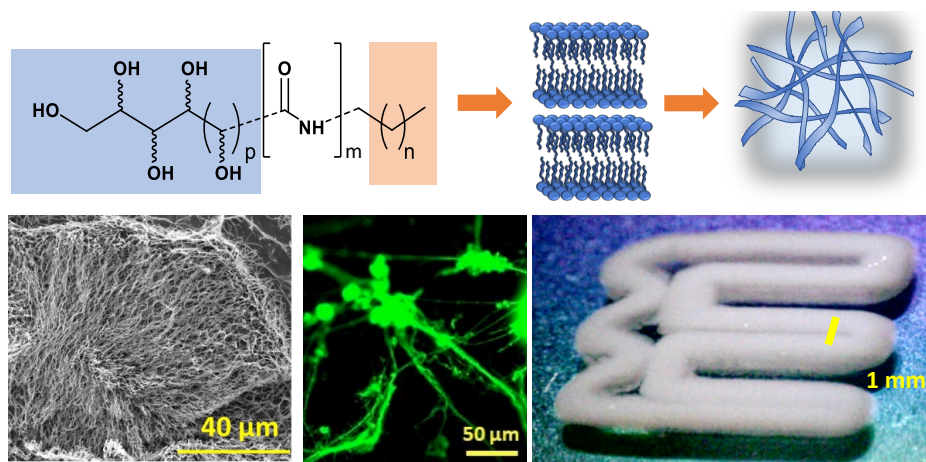
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Supramolecular low molecular weight hydrogels are formed by the self-assembly of small non-polymer molecules. These hydrogels are generally fragile and as such, they are not often considered for cell culture applications and 3D printing. However, they are pure molecules, which helps to create reproducible structures. Also the very low modulus of these hydrogels may be favorable for the culture of cells from soft tissues such as neurons. Finally, the microstructure of the fibers may affect the cell morphology and fate and may guide the cell extensions. We show that hydrogels based on only these small molecules can be used successfully as scaffold for neuron and mesenchymal stem cell culture¹.



We are also developing different gelation methods such as wet spinning² or 3D printing³ to build more complex and precise gel architectures with various gelators. These methods involve a solvent-water exchange. In some conditions, radially organized supramolecular fibers are observed revealing the mixing phenomenon that occurs at the solvent-water interface². In 3D printing, thanks to the very fast self-assembly of the molecules during water-solvent exchange and a very fast setting of the ink, well-resolved patterns are obtained. Also, by changing only the length of the molecular gelator, we got either sacrificial or persistent gels. Imbrication of these gels followed by the spontaneous dissolution of the sacrificial gel gives self-standing molecular gel architectures with channels³.

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[3] F. Andriamiseza et al., 3D Printing of Biocompatible Low Molecular Weight Gels. *J. Coll. Interf. Sci.* **2022**, 617, 156–170.



Journées Grand Sud-Ouest de la Société Chimique de France

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Recyclable Polymeric Nano-reactors Applied to Aqueous Biphasic Hydrogenation Reactions

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Convergent syntheses of core-crosslinked polymeric micelles, made by controlled radical polymerization in water using a trithiocarbonate transfer agent [R₀-SC(S)SP_r] (RAFT technique and PISA strategy), are presented. The amphiphilic block copolymers are composed of a polystyrene core, functionalized with 4-(diphenylphosphino) styrene as ligand, and a poly(1-methyl-4-vinylpyridinium iodide) polyelectrolytic shell (Figure). The self-assembled micelles were further cross-linked at the hydrophobic end by diethylene glycol dimethacrylate.¹

With the objective to use these structures as nano-reactors in aqueous biphasic catalysis, the phosphine ligands were used to anchor a rhodium(I) precursor into the micelles and the resulting objects were applied to the catalytic hydrogenation of water insoluble substrates with excellent recyclability and negligible leaching.²

Furthermore, rhodium nanoparticles could be synthesized and maintained well dispersed into these polymeric structures, leading to a second class of nano-reactors, which were applied to the catalytic hydrogenation of acetophenone, styrene and 1-octene under aqueous biphasic conditions.³

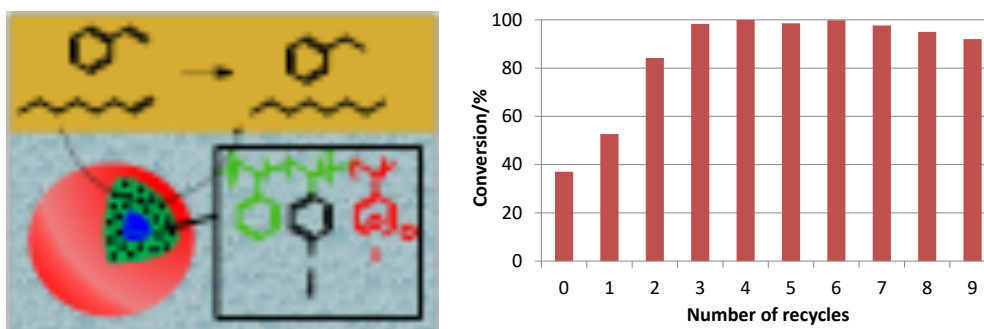


Figure. Schematic view of the nano-reactors and their catalytic applications (left), and example of results obtained for a recycling test in Rh-catalyzed styrene hydrogenation (right).

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Journées Grand Sud-Ouest de la Société Chimique de France

11-12 Juillet 2022, Toulouse

En route to *carbo*-diphosphinines as putative macro-aromatic bridging ligands: Synthesis of a *carbo*-1,4-dihydro-1,4-dithiophosphinine

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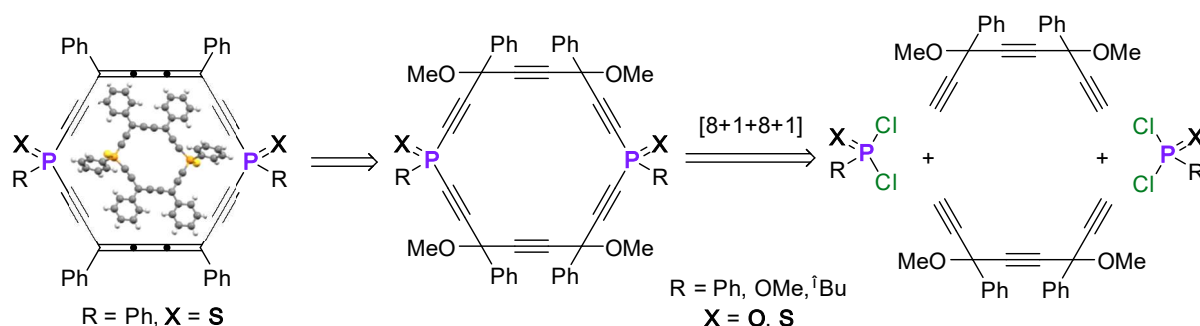
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While phosphinines have long been experimentally studied, in particular for the purpose of P-coordination chemistry, ring *carbo*-mers thereof have only been calculated.¹ Considering the synthesis efficiency of centrosymmetric *carbo*-benzenes,² centrosymmetric ring *carbo*-mers of 1,4-diphosphinines can be envisaged as "reasonable" experimental targets for their potential behavior as aromatic bridging P,P-ligands. To obviate the issues of the P,P-aromatization step, ring *carbo*-mers of non-aromatic 1,4-dihydro-1,4-diphosphinines have been first targeted.

Inspired by a report on the synthesis of a parent dihydro-1,4-diphosphinines,³ a first example of *carbo*-1,4-dihydro-dithiophosphinine and related macrocyclic acetylenic phosphanes with different substituents and oxidation states were synthesized. Their preparation was achieved by a quite efficient and general method involving a tetracomponent [8+1+8+1] macrocyclization reaction with up to 48 % yield. After a final reductive elimination step with SnCl₂/HCl, hexaphenyl-*carbo*-1,4-dihydro-dithiophosphinine was produced with 20 % yield and was fully characterized by NMR, HRMS, IR, UV, electrochemistry, single crystal X-ray diffractometry. Selected results on this new series of carbon-rich phosphorous-containing macrocycles will be disclosed.



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Journées Grand Sud-Ouest de la Société Chimique de France

11-12 Juillet 2022, Toulouse

Artificial Water Channels for Membrane Distillation

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In the field of sea water desalination, energy friendly processes which are easier to implement as compared to reverse osmosis need to be considered. Particularly in systems of decentralized fresh water production. One such interesting option would be membrane distillation (MD) with porous polymer membranes and hydrophobic hybrids, which are thoroughly described in the literature ^[1]. MD is a process based on a vapor pressure difference whereby hydrophobic membranes (polymers and ceramics) are used. Membrane distillation presents interesting features namely low operating temperature, low hydrostatic pressure and resistance to membrane fouling. However, one major drawback limiting its industrial application is the low permeate flux leading to higher energy consumption. As such, this work aims at developing novel hybrid polyvinylidene fluoride (PVDF) membranes incorporating amphiphilic molecules known as Artificial Water Channels (AWCs). Artificial Water Channels are synthetic mimics of biological water channel proteins, aquaporins which therefore allow them to replicate the latter's characteristic features. These include the possibility of combining high water permeability with high water/solute selectivity along with higher processability and stability compared to protein channels ^[2]. The presence of AWCs within the polymer matrix creates selective pathways through which water can flow freely, thus accelerating the permeate flux. In this study our focus has been on determining a hybrid PVDF membrane incorporating AWCs with improved permeate flux as compared to its reference membrane. Our efforts have been oriented towards three PVDF polymer grades with different molecular weights (MWs), namely 180 000, 275 000 and 530 000 g/mol and the variation of the concentration by mass of AWCs (0.025, 0.05, 0.075 and 0.1 Wt%) within each system. Water permeability tests have been performed on the prepared membranes using a dead end filtration setting. These tests have allowed for the identification of one reference membrane and of its hybrid membrane. A water permeability of 75.29 L.m⁻².h⁻¹.bar⁻¹ was attained for the hybrid membrane prepared using 16 Wt% PVDF-530 000 g/mol and incorporating 0.05 Wt% AWCs while its corresponding reference membrane demonstrated a water permeability of 30.65 L.m⁻².h⁻¹.bar⁻¹. The MD performances of both membranes were investigated using a 35 g/L aqueous NaCl solution. The hybrid membrane yielded a NaCl rejection of 97.56% and its reference membrane a rejection of 88.27%.

1

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Gd³⁺/ Poly(ethylene oxide)-*b*-poly(acrylic acid-*co*-vinylphosphonic acid) hybrid polyionic complexes for MRI contrast agents : influence of the charged block composition on physical properties.

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Magnetic resonance imaging (MRI) is one of the most common non-invasive medical imaging techniques for detecting a variety of diseases. In order to increase image resolution and get more information from this method, so-called contrast agents (CAs) are used. CAs most often contain metal atoms (e.g. Gd³⁺) that shorten longitudinal T1 relaxation time, making the MRI image brighter. The main limitation of the use of Gd³⁺ is its toxicity and bioaccumulation in the body. We focus on the preparation of gadolinium-based CAs with anionic-neutral double hydrophilic block copolymers (DHBCs), by simply adding metal ion to the polymer to spontaneously obtain micelle-like nanostructures called hybrid polyionic complexes (HPICs) (Fig.1a). After first reports on Gd³⁺/poly(ethylene oxide)-*b*-poly(acrylic acid) (PEO-*b*-PAA) HPICs,¹ we here consider vinylphosphonic acid as AA comonomer in reversible addition-fragmentation chain transfer (RAFT)-derived PEO-*b*-P(AA-*co*-VPA) DHBCs with different compositions of the AA/VPA block (Fig.1b). HPICs were obtained for all compositions, their stability was tested at different pH values. Relaxation values and other physicochemical characteristics were determined (Fig.1c-e). It was found that using pure PAA as the ionizable block gave the highest relaxation values but at the same time the lowest stability at low pH. In contrast, the use of VPA, gave higher stability, but lower relaxation.

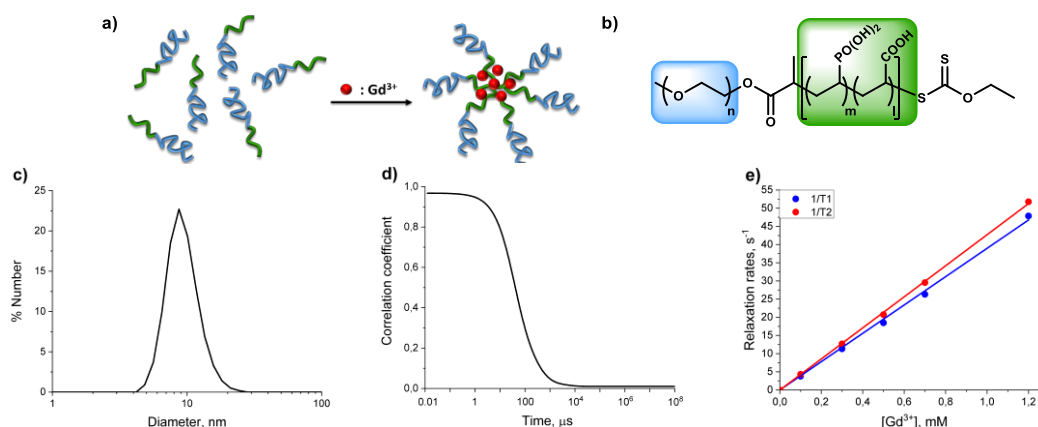


Figure 1. (a) Schematic representation of HPICs formation by adding Gd³⁺ to the DHBCs. (b) Chemical structure of the DHBCs with neutral (blue) and ionizable (green) blocks. (c) Typical number-averaged diameter distribution, and (d) correlogram measured by DLS experiment. (e) Plot of relaxation rates of a HPICs

To conclude, a compromise between the colloidal stability of Gd³⁺-based HPICs, in particular at low pH, and an acceptable level of relaxivity properties can be reached by varying the AA/VPA composition of the DHBC.



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11-12 Juillet 2022, Toulouse

Rhodium(II) complexes and catalytic carbene transfer for small ring synthesis

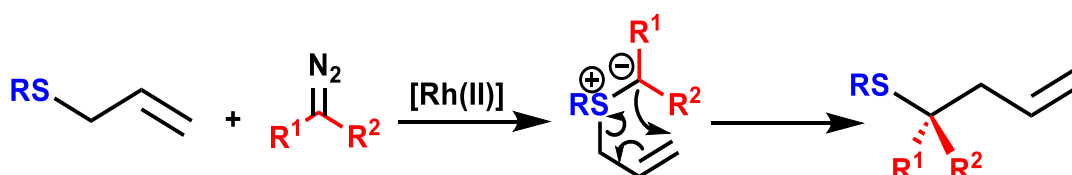
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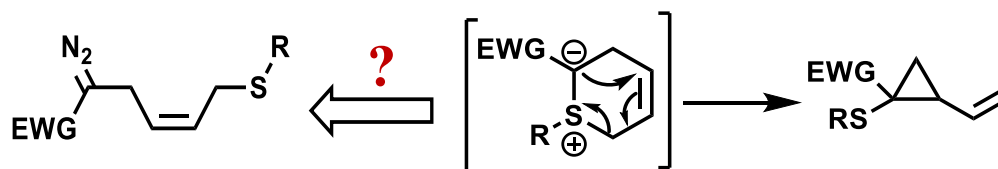
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Vinylcyclopropanes (VCP) are constituting a class of small ring containing molecules that can be found in natural products (monoterpene) as well as in medicinal chemistry (antifungal compounds). Besides, most importantly VCP are showing a wide range of applications in organic synthesis as versatile synthons. They are especially useful building blocks to access complex molecular structures through cycloaddition chemistry.¹

Although cyclopropanation of a double bond appears as the most straightforward approach to cyclopropane. However, selectivity issue arises to access VCP from conjugated dienes. Interested in ylide formation by carbene transfer reaction, we envisaged that intramolecular Doyle-Kirmse reaction might provide an alternative access to VCP.² Our first results in this direction will be described.



Scheme 1. Doyle-Kirmse reaction



Scheme 2. Toward VCP through intramolecular Doyle-Kirmse reaction

[1] Y. Gao, Y. Mao, Z. Miao *Org. Lett.*, **2022**, *24*, 3064.

[2] H. Ishibashi, M. Okada, H. Nakatani, M. Ikeda, Y. Tamura *J. Chem. Soc., Perkin Trans. 1*, **1986**, *10*, 1763.



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Hybrid polymeric micelles stabilized by ferric cations: Structural investigation and Photo-Fenton Performance

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Recently, hybrid organic–inorganic nanomaterials based on polymers have attracted great attention, and show outstanding potential to combine different properties in one material.^{1,2} Hybrid polyionic complexes (HPICs) micelles are organic-inorganic nano-assemblies which are complexed by double hydrophilic block copolymers and multivalent metal ions. Following previous work,^{3,4} here we developed a strategy for iron-based HPICs micelles and investigated their potential as catalysts for the Fenton reaction. The formation of HPICs nanostructure from the complexation in aqueous solution of a double hydrophilic block copolymer PEO_{5k}-b-PAA_{3.2k} with Fe³⁺ was successfully demonstrated by means of UV-vis, FT-IR, DLS and TEM. The hybrid polyionic complex obtained by this simple self-assembly process has a core-shell structure and is chemically stable in the pH range of 3 to 7 with a core composition is strongly correlated to the pH of the solution. The Photo-catalytic activity of these nanostructures is evaluated through the degradation of naphthol blue black induced by a Photo-Fenton process. The kinetic of degradation with this nanocatalyst is slightly slower than in traditional homogeneous Fenton reaction (as expected with such hybrid architecture). Chemical and colloidal stabilities as well as the recyclability of the HPIC nanocatalyst are largely improved opening new opportunities for recoverable photocatalysts.

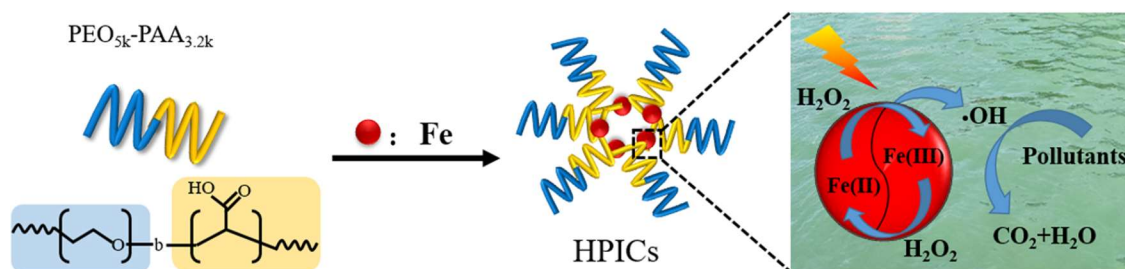


Figure 1: Schematic diagram of the synthesis and catalytic mechanism of HPICs.

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- [2] Nabiyan. A, Max. J, Schacher. F. H, *Chem. Soc. Rev.* **2022**, 51, 995.
- [3] Frangville. C, Li. Y, Bilotey. C, et al. *Nano Lett.* **2016**, 16, 4069.
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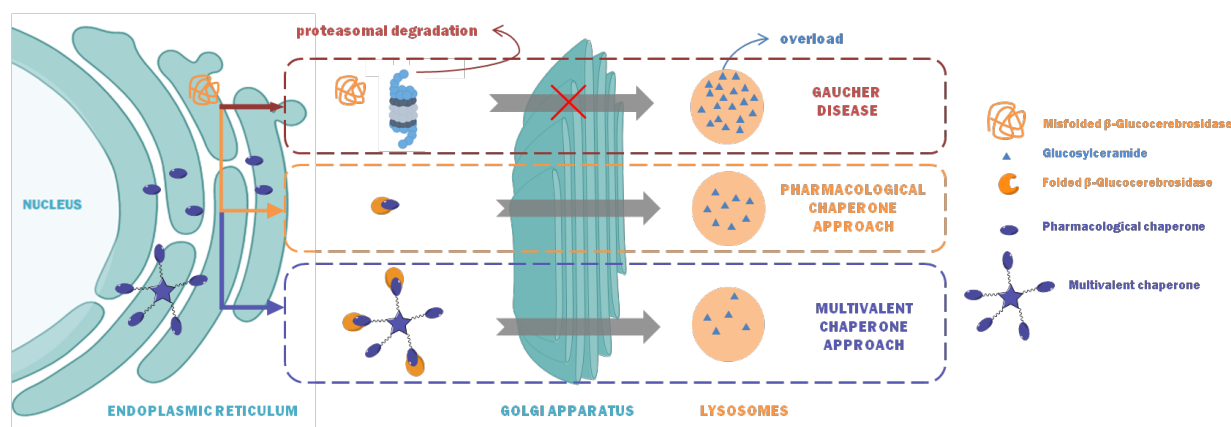
Synthesis of dendrimer-based multivalent pharmacological chaperones against Gaucher disease

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Gaucher disease (GD) is a rare disease but yet the most common among lysosomal disorders. The disease is caused by the enzyme β -Glucocerebrosidase (GCase) misfolding, leading to a lack of GCase hydrolytic activity and resulting to accumulation of glucosylceramide in lysosomes. The most common, type 1 GD, is characterized by bone involvement and hepatosplenomegaly whereas neurological disorders are present in types 2 and 3. Two strategies are currently used for symptomatic treatment: enzyme replacement therapy and substrate reduction therapy.¹ Pharmacological chaperone therapy is an innovative strategy consisting in the use of small molecules which bind specifically to the enzyme. It allows the proper folding and stabilization of GCase helping its trafficking to lysosomes where it exerts its hydrolytic activity.² To date, there is no pharmacological chaperone marketed for GD because of their lack of selectivity towards the GCase or their lack of efficiency *in vivo*.



This project aims to develop a multivalent approach by generating new series of multivalent scaffolds with several pharmacological chaperones. The multivalent effect is the significant increase in ligand affinity for its receptor by incorporating several copies of an identical motif on the surface of a multivalent template. Several multivalent chaperones of GCase have already been described in the literature.³ In order to allow efficient grafting of the pharmacophores on the surface of multivalent platforms, click chemistry, CuAAC and SPAAC, approaches will be used. Clickable iminosugars analogues were prepared. Moreover, original dendrimers carrying 6 or 12 activated alkynes units have been prepared to allow grafting of the pharmacophores in the absence of copper salt (in collaboration with Dr. C.-O. Turrin, LCC, Toulouse). Then, those compounds were evaluated for their cytotoxicity, their inhibitory activity on GCase, their multivalent effect and finally their chaperone effect.

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PEGylated SMIL coatings to limit protein adsorption in capillary electrophoresis

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Capillary electrophoresis (CE) is one of the best ways to analyse intact proteins due to its high resolution and low sample consumption. When the separation efficiency is only controlled by axial diffusion, the theoretical plates number for a protein should be theoretically around 1 million for an hydrodynamic radius of typically 3 nm. However, experimentally, this value generally dropped to a few thousand theoretical plates due to surface adsorption onto the capillary wall. To prevent this phenomenon, Successive Multiple Ionic-polymer Layer (SMIL) capillary coatings were found to be able to reduce protein adsorption. Recently, a methodology was proposed to quantify the residual adsorption of proteins on capillary coating by determining their retention factor (k). This quantification can be obtained by measuring the separation efficiency of the proteins at different separation voltages and by using a theoretical modelling of the separation efficiency in electrochromatography. By this way, it is possible to rank the performances of coatings relatively to their ability to limit protein adsorption, and independently of the migration times and electroosmotic mobilities.

In the literature, it is known that polyethylene glycol (PEG) has antifouling properties against bacteria and proteins, for instance in marine environments. In the present study, different commercial polycations were PEGylated using either EDC/NHS or click chemistry coupling reactions with different molar ratios (from 0% to 20%) and different PEG lengths (1kDa, 5kDa). Compared to neutral coatings, SMIL coating can be constructed by simple flushes of the capillary without chemical bonding onto the capillary wall. The aim was to investigate the impact of polycation PEG grafting used in the last layer of a 5-layer SMIL coating on the limitation of protein adsorption in CE. For that, residual protein retention factor k was systematically determined for the separation of a mixture of 4 model intact proteins (Trypsin Inhibitor (TI), Myoglobin (Myo), Ribonuclease A (RNase A) and Lysozyme (Lyz)) in 2 M acetic acid background electrolyte. SMIL capillary coatings were composed of 5 polyelectrolyte layers terminating by the PEGylated polycation. The 4 first layers were composed of poly(diallyldimethyl ammonium chloride) (PDADMAC) as polycation and poly(styrenesulfonate) (PSS) as polyanion. The selected polycations for the last layer were polyallylamine (PAH), polyethyleneimine (PEI), ϵ -poly-L-Lysine (ϵ PLL) and α -poly-L-Lysine (α PLL).

Before PEGylation, the best separation performances were obtained with PAH on the last layer. Using a PEGylated polycation as the last layer strongly impacted the electroosmotic mobility (EOF) in the case of 5kDa chains from -45 Tiselius unit (for the unmodified polycation) to -5 TU (for the 20% mol PEG modified polymer). The detection order of the proteins is reversed (positive polarity) compared to non-PEGylated SMIL (negative polarity). PEGylated SMIL becomes de facto a new way to built in neutral capillary coating by simple capillary flushes. On the contrary, PEGylated SMILs with 1kDa latera chains only slightly impacted the EOF (decrease of about -5 TU in the EOF). As for the k values PAH polycation grafted with 1kDa PEG chains led to SMIL coating with lower k value (5.31×10^{-2} vs 6.84×10^{-2}) and higher peak resolution (3.56 ± 0.35 vs 4.34 ± 0.06 for the Myo / RNase pair) than for the unmodified PAH last layer. The decreased migration time led to lower peak resolution (2.17 ± 0.03), but to even lower k value (4.8×10^{-2}). Blood analysis or monoclonal antibodies (mAb) characterization will benefit from those modifications. For CE or CE-MS analysis, better peak resolution, lower adsorption, and control of eof through 5kDa PEG density (without any modifications of the BGE) will lead to better separations and better understanding of therapeutic monitoring.