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Book of Abstracts

Substrate-aggregate/gold photocatalyzed alkylynative cyclization of ortho-ethynyl-tosylanilines to indoles

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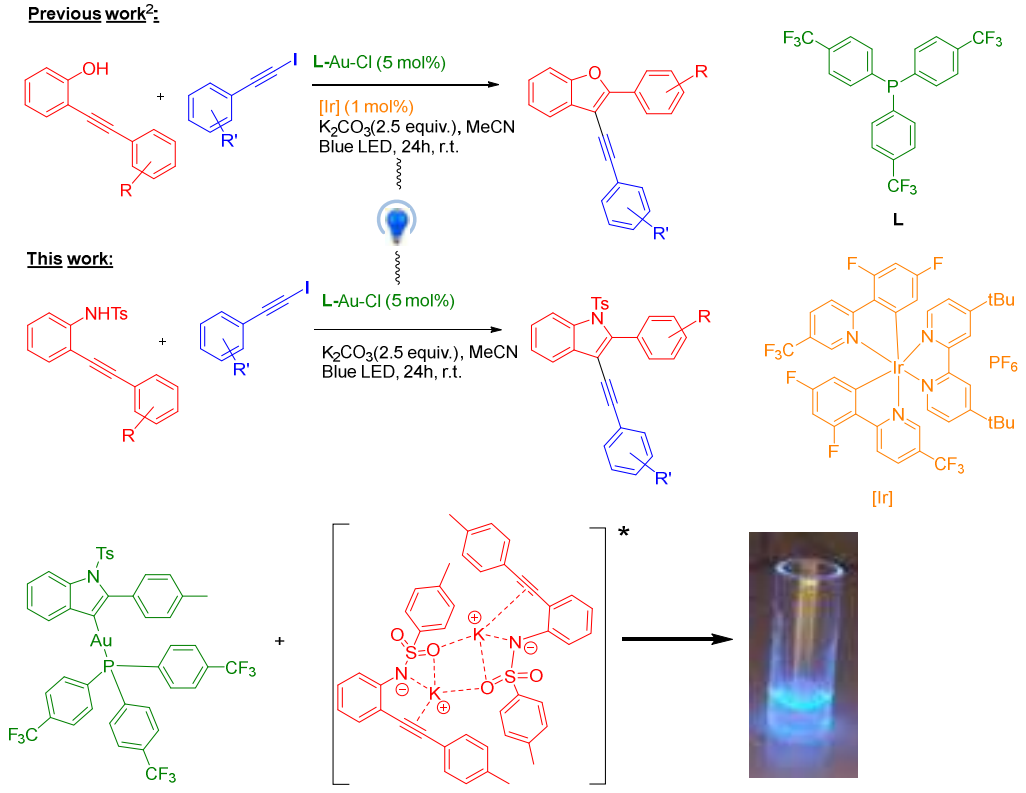
Gold(I) complexes can hardly perform oxidative additions with alkynyl and aryl halides in cross-coupling reactions due to a high Au(I)/Au(III) redox potential[1] and this issue remains challenging nowadays . Within this context, our team developed in 2019 a methodology employing an iridium photosensitizer to excite a vinyl-gold(I) complex and achieve an alkylynative cyclization of ortho-alkynylphenols to benzofuranes through the oxidative addition of alkyne iodines[2]. Thereafter we explored the formation of tosylated indoles. Interestingly, we observed that the photosensitization efficiently occurred without an exogenous photocatalyst. Through our research, we found that the potassium salt of ortho-ethynyl-tosylaniline can act as a photoactive aggregate, capable to trigger the photosensitization of the vinylgold intermediate and achieve the cross-coupling reaction.



Acknowledgments: Fen Zhao for the scope and the post-functionalization, Dr. Héloïse Dossmann (IPCM) for the modeling part, Dr. Vincent Corcé (IPCM) for his support during the mechanistic study and particularly the photophysical experiments, Pr. Ludovic Jullien, Dr. Thomas Lesaux and Dr. Agathe Espagne (ENS Ulm) for the photochemical study of the mechanism.

[1] Hopkinson, M., N.; Tlahuext-Aca, A.; Glorius, F. *Acc. Chem. Res.* **2016**, *49,* 2261-2272.

[2] Xia, Z.; Corcé, V.; Zhao, F.; Przybylski, C.; Espagne, A.; Jullien, L.; Saux, T. L.; Gimbert, Y.; Dossmann, H.; Mouriès-Mansuy, V.; Ollivier, C.; Fensterbank, L. *Nat. Chem.* **2019**, *11* ,797–805.

Design of Selective Inhibitors of Serine Protease involved in inflammatory processes by Dynamic Combinatorial Chemistry on Folded Peptidic Scaffolds

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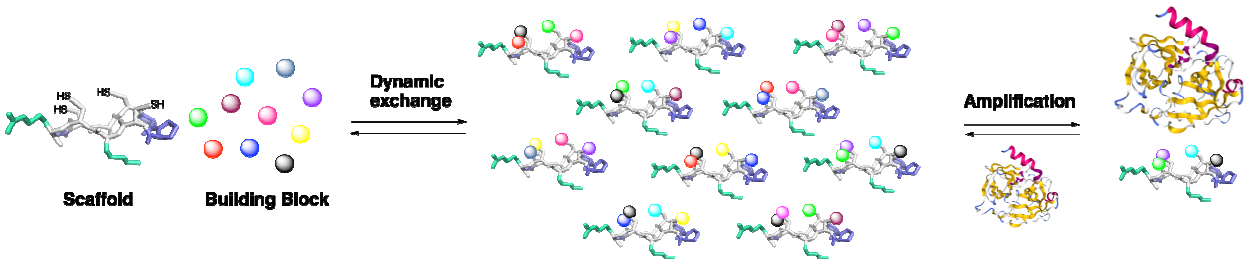
Dynamic combinatorial chemistry (DCC) has demonstrated its efficiency to identify ligands for biological targets[1]. This strategy relies on a mixture of small molecules that can react reversibly with each other under physiological conditions. This is leading to a dynamic chemical library (DCL) where the products are in equilibrium and can interconvert with each other. Molecular recognition between a biological target and a member of the DCL will shift the equilibrium of the library and the ligand with the highest affinity will be amplified[1–3].

We are currently exploiting this strategy in order to graft amino acids side-chain functionalities on a well-ordered peptide scaffold.

Derived from proteins, small peptides are attractive and underexploited compounds that can closely reproduced their specific side chain arrangement. They incarnate the simplest protein mimicry. When removed from their biological context, they failed to adopt their bioactive conformation affecting their affinity for their targets. Strategies have been developed to overcome this phenomenon[4–6] but structural information are needed and cycles of optimization often required represent a challenging step of the process to obtain a nanomolar affinity hit.

With our innovative strategy, we are hoping to overcome those limitations applying DCC to drive the identification of ligands that can selectively distinguish between several serine proteases involved in inflammatory processes.



Acknowledgments: Roba Moumné, Chahrazade El Amri, Emmanuelle Sachon, Claudia Bich and SU Mass Spectrometry platform.

[1] R. Huang, I. K. H. Leung, *Molecules* **2016**, *21*, DOI 10.3390/molecules21070910.
[2] A. Herrmann, J. Li, P. Nowak, S. Otto, *J. Am. Chem. Soc.* **2013**, *135*, 9222–9239.
[3] M. Mondal, A. K. H. Hirsch, *Chem. Soc. Rev.* **2015**, *44*, 2455–2488.
[4] T. A. Hill, N. E. Shepherd, F. Diness, D. P. Fairlie, *Angew. Chemie - Int. Ed.* **2014**, *53*, 13020–13041.
[5] Y. H. Lau, P. De Andrade, Y. Wu, D. R. Spring, *Chem. Soc. Rev.* **2015**, *44*, 91–102.
[6] J. A. Wells, C. L. McClendon, *Nature* **2007**, *450*, 1001–1009.

Flow Chemistry Processes for the Catalytic Functionalization of Biomass Derivatives

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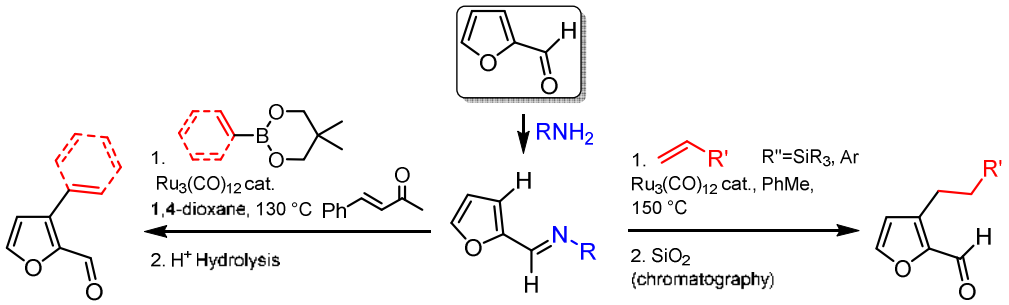
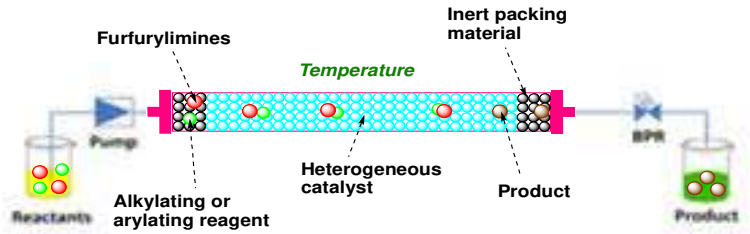
Furfural is one of the most promising bio-based products and is obtained by dehydration of lignocellulosic biomass from both agricultural residues and dedicated crops[1]. It has a strong potential as a renewable platform for the sustainable production of fine chemicals[2]. In particular, the direct functionalization of furfural by C-H activation is an emerging area that is the focus of many research efforts.

The team of Dr. J. Oble and Prof. G. Poli (IPCM) has recently developed methods for the functionalization of furfural-derived imines at the C-3-position by alkylation, arylation and alkenylation [3,4]. These processes are based on the use of a homogeneous catalyst [Ru3(CO)12] at high temperatures (130-150 °C).



In collaboration with the Dr. J. Blanchard and the Dr. C. Louis (LRS), specialized in surface functionalization and heterogeneous catalysis, our current objective is to transpose these C-H activation reactions **from batch to continuous flow** mode using a **heterogeneous catalysis** [5] in order to combine both the advantages of flow chemistry with those of heterogeneous catalysis by grafting the ruthenium complex onto a solid support (such as oxide supports or polymers). The catalyst is covalently immobilized on the support by ligand exchange on a pre-functionalized support with a linker carrying a chelating ligand.



[1] a) Hoydonckx, H. E.; Van Rhijn, W. M.; Van Rhijn, W.; De Vos, D. E.; Jacobs, P. A. *Furfural and derivatives.* In *Ullmann's Encyclopedia of Industrial Chemistry*; Wiley-VCH Verlag GmbH & Co. KgaA: Weinheim, Germany, 2000; Volume 16, pp. 285. b) Mariscal, R.; Maireles-Torres, P.; Ojeda, M.; Sádaba, I.; López Granados, M. *Energy Environ. Sci.* **2016**, *9*, 1144.

[2] Yan, K.; Wu, G.; Lafleur, T.; Jarvis, C. *Renew. Sustain. Energy Rev.* **2014**, *38*, 663. b) Bohre, A.; Dutta, S.; Saha, B.; Abu-Omar, M. M. *ACS Sustain. Chem. Eng.* **2015**, *3*, 1263.

[3] Pezzetta, C.; Veiros, L. F.; Oble, J.; Poli, G. *Chem. Eur. J.* **2017**, *23*, 8385.

[4] Siopa, F.; Ramis Cladera, V-A.; Afonso, C. A. M.; Oble, J.; Poli, G. *Eur. J. Org. Chem.* **2018**, 6101.

[5] Miura, H.; Wada, K.; Hosokawa, S.; Inoue, M. *ChemCatChem.* **2010**, 2, 1223 – 1225.

Mechanistic study of dual catalysis involving hypercoordinated silicon compounds

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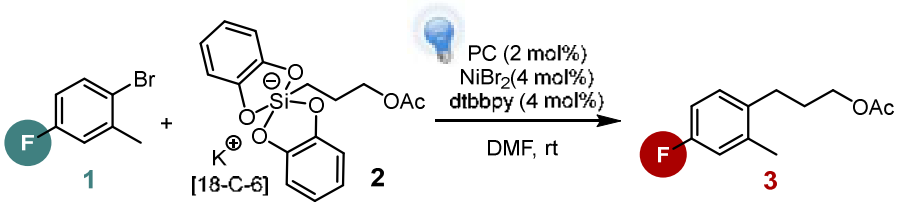

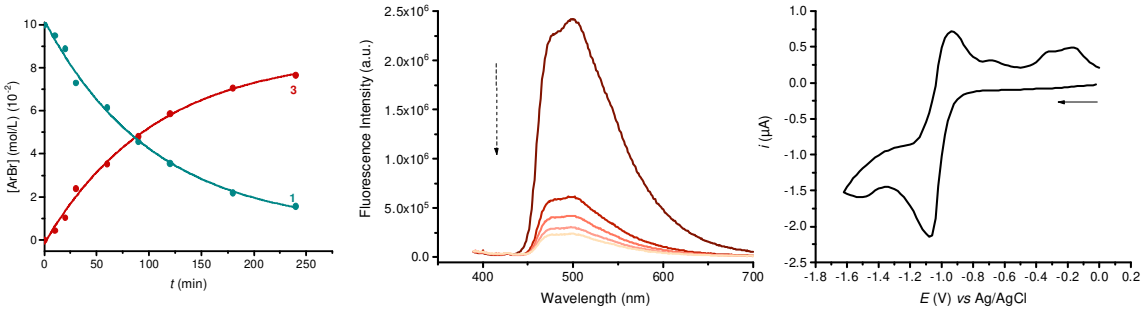

Dual catalysis involving photoredox and Ni-catalyzed cross coupling for carbon-carbon bond formation has been considerably developed during the last decade.[1] Several pathways have been proposed suggesting that either a Ni(I)/Ni(III) or a Ni(0)/Ni(II)/Ni(III) mechanism could be considered and DFT calculations supported the former.[2] However, to our knowledge no experimental study of the whole mechanism for this kind of reaction has been performed.

This project aims at studying the mechanism of dual catalyzed C-C bon formations with silicates as radical precursors. To do so, we combined electrochemistry, NMR, spectroscopy, conductometry and photophysical experiments with micro-kinetics and DFT calculations to provide a complete overview of the reaction mechanism.

Investigations of the Ni-based catalytic cycle prove that the oxidative addition of aryl halides proceeds with the bipyridine-ligated Ni^0 complex, the resulting $ArNi^{II}Br$ is catalytically competent and constitutes the resting state for the catalyst. Moreover, we showed that this complex is able to trap a free radical generated under thermal conditions and the resulting Ni(I) complex is an efficient catalyst for this coupling reaction. We therefore demonstrated that a self-sustained Ni(0/II/III) cycle is operative.

Concerning the Ir catalytic cycle, quenching experiments between the excited photocatalyst $^*Ir^{III}$ and silicates proved the efficiency of the radical formation and several experiments have been done to discriminate between SET and EnT. The detailed analysis of by-products formation clearly demonstrated that two radicals are involved in the process. This result led us to propose a revised catalytic cycle for Ni and micro-kinetics are currently performed to assess this revised mechanism.

Acknowledgments: We thank ANR-17-CE07-0018 HyperSilight for financial support.

1 V. Corcé, L.-M. Chamoreau, E. Derat, J.-P. Goddard, C. Ollivier, L. Fensterbank, *Angew. Chem. Int. Ed.* **2015**, 54, 11414-11418.

2 O. Gutierrez, J.-C. Tellis, D.- N. Primer, G.-A. Molander, M.-C. Kozlowski, *J. Am. Chem. Soc.* **2015**, 137(15), 4896-4899.

Hybrid polyoxometalates as a way to build memory devices

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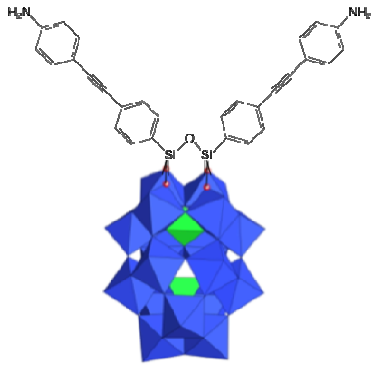

Fig. 1 – post-functionalized Dawson type

Polyoxometalates (POMs) are nano-scaled metal-oxides, with general formula $[X_xM_PO_Y]^{n-}$ (X = P, Si, M = Mo (VI), W (VI), V (V), Nb (VI)), considered as promising electron reservoirs. In the application research process, lacunary POM (where a metal center is eliminated thanks to a controlled pH), can be considered as a keystone since they enable functionalization and post-functionalization, via Sonogashira cross-coupling. Starting from Keggin, $[XM_{12}O_{40}]^{n-}$, and Dawson, $[XM_{18}O_{62}]^{n}$, platforms we developed a wide variety of post-functionalized POMs aiming for different nanostructuration, from chromatic gels to hierarchical and self-assembled macro structures to surface immobilization.[6,7,8,9]

This presentation will be focused on Dawson-type hybrids used for memory devices application. In this work, hybrid POMs are composed of two organic arms ending with amino moieties. In situ generated diazonium functions have been activated by the application of a determined current, allowing the system to be covalently grafted to an Indium Tin Oxide (ITO) substrate. Aiming for multilayers, the determination of the thickness by AFM and SEM-FEG has been a primordial axis of research before sending the substrates to Singapore for physical characterization. On NTU side, gold plots are deposited on the POM layer to be used as top-electrodes and memory tests are run. Finally we obtained a system where Write Once Read Many (WORM) memory type is obtained. [10,11]

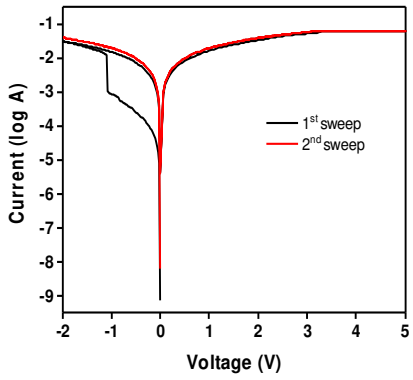

Fig. 2 – WORM type memory

Acknowledgments: Sorbonne University, Nanyang Technological University, Commissariat à l'énergie atomique et aux énergies alternatives

[6] C. Rinfray, G. Izzet, J. Pinson, S. G. Derouich, J.-J. Ganem, C. Combellas, F. Kanoufi and A. Proust, *Chem. Eur. J.* **2013**, *19*, 13838-13846.

[7] Y. Ben M'Barek, T. Rosser, J. Sum, S. Blanchard, F. Volatron, G. Izzet, R. Salles, J. Fize, M. Koepf, M. Chavarot-Kerlidou, V. Artero and A. Proust, *ACS Appl. Energy Mater.* **2020**, 3, 1, 163-169.

[8] M. Segado Centellas, M. Piot, R. Salles, A. Proust, L. Tortech, D. Brouri, S. Hupin, B. Abécassis, D. Landy, C. Bo and G. Izzet *Chem. Sci.* **2020**, *11*, 11072-11080.

[9] R. Salles, B. Abécassis, E. Derat, D. Brouri, A. Bernard, Q. Zhang, A. Proust, C. Desmarets and G. Izzet, *Inorg. Chem.* **2020**, *59, 4*, 2458-2463.

[10] F. Volatron, J.-M. Noël, C. Rinfray, P. Decorse, C. Combellas, F. Kanoufi and A. Proust, *J. Mater. Chem. C* **2015**, *3*, 6266-6275.

[11] K. Qian, V. C. Nguyen, T. Chen and P. S. Lee, *J. Mater. Chem. C* **2016**, *4*, 9637-9645.

Rhodium-Catalyzed Asymmetric Transfer Hydrogenation/Dynamic Kinetic Resolution of 3-Benzylidene-Chromanones

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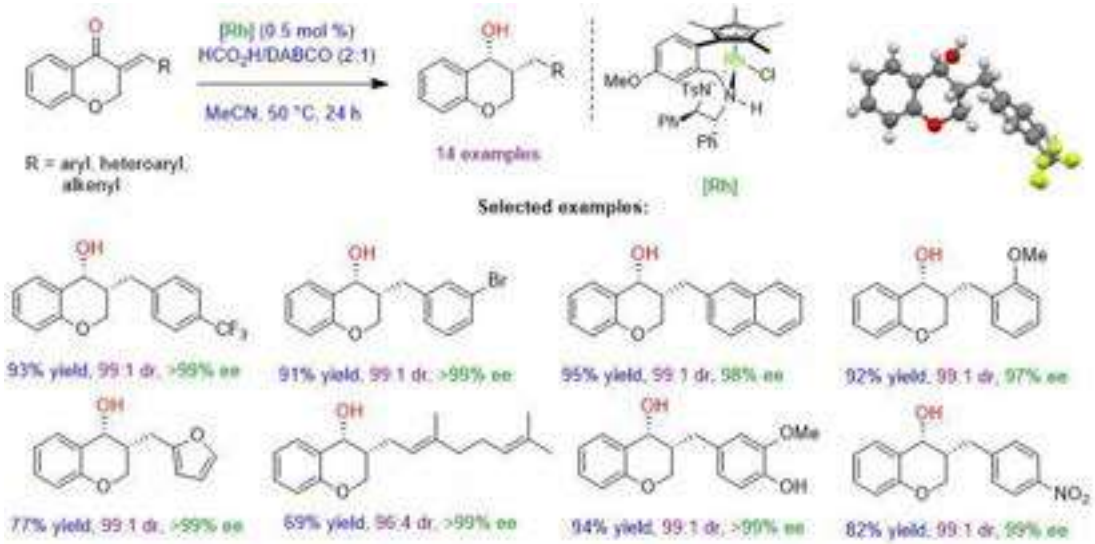
Homoisoflavonoids are a widespread family of molecules, naturally occurring in plants, which possess a promising set of biological activities. Among those, benzyl chromanols are a promising family that could be accessed through a key step of asymmetric transfer hydrogenation combined with a dynamic kinetic resolution process (ATH/DKR).[12] Continuing our interest in asymmetric transfer hydrogenation (ATH),[13] we developed a straightforward access to enantiomerically enriched *cis*-3-benzyl-chromanols from (*E*)-3-benzylidene-chromanones through a Rh-catalyzed asymmetric transfer hydrogenation. This transformation allowed the reduction of both the C=C and C=O bonds and the formation of two stereocenters in high yields with excellent levels of diastereo- and enantioselectivities (up to >99:1 dr, up to >99% ee) in a single step through a dynamic kinetic resolution process using a low catalyst loading and HCO_2H/DABCO as the hydrogen donor. This efficient and straightforward catalytic route provides access to synthetically useful chromanol derivatives and valuable chroman pharmacophores as well and tolerates a broad range of functionalities.[14]



[12] For selected reviews a) Noyori, R.; Tokunaga, M.; Kitamura, M. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 36. b) Samec, J. S. M.; Bäckvall, J.-E.; Andersson, P. G.; Brandt, P. *Chem. Soc. Rev.* **2006**, *35*, 237. c) Foubelo, F.; Nájera, C.; Yus, M. *Tetrahedron: Asymmetry* **2015**, *26*, 769. d) Barath, E. *Synthesis* **2020**, *52*, 504. e) Pellissier, H. *Tetrahedron* **2011**, *67*, 3769. f) Molina Betancourt, R.; Echeverria, P.-G.; Ayad, T.; Phansavath, P.; Ratovelomanana-Vidal, V. *Synthesis* **2021**, *53*, 30 and cited references.

[13] For selected recent references a) Zheng, L.-S.; Férard, C.; Phansavath, P.; Ratovelomanana-Vidal, V. *Chem. Commun.* **2018**, *54*, 283. b) He, B.; Zheng, L.-S.; Phansavath, P.; Ratovelomanana-Vidal, V. *ChemSusChem* **2019**, *12*, 3032.c) Zheng, L.-S.; Phansavath, P.; Ratovelomanana-Vidal, V. *Org. Lett.* **2018**, *20*, 5107. d) He, B.; Phansavath, P.; Ratovelomanana-Vidal, V. *Org. Lett.* **2019**, *21*, 3276. e) Westermeyer, A.; Guillamot, G.; Phansavath, P.; Ratovelomanana-Vidal, V. *Org. Lett.* **2020**, *22,* 3911

[14] Molina Betancourt, R.; Phansavath, P.; Ratovelomanana-Vidal, V. *Org. Lett*. **2021**, 23, 1621.

Hybrid Nanomaterials

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In this research project by functionalizing inorganic nanoparticles by coordination complexes, we aim to obtain new hybrid nano-objects carrying physicochemical properties that are not present (or almost absent) in their building blocks. The aim is to obtain either a synergy of the properties of these bricks expressed by the hybrid, or to express a molecular property on the scale of the (nano-) material. The first part of the project focused on the study of the improvement of the magnetic properties of superparamagnetic maghemite nanoparticles (NPs), given the critical role of these systems in biomedicine and in ultra-high density data storage [15]. The surface of these NPs was functionalized by condensation of Co (II) complexes (solvated cations and coordination complexes), which induced a significant increase in the magnetic anisotropy of the NPs and therefore in their coercive field and their blocking temperature while maintaining a stable colloidal system.

The second part of the project targets other properties. By associating luminescent CdSe nanoplatelets (NPLs) with chiral (para) magnetic coordination complexes, we aim to self-assemble NPLs into chiral and magnetic stacks. The coordination complexes will make it possible to control the chirality of the stacks in the first place, but also, given the magnetic nature of the metal center and the cooperativity of the optical properties observed in the stacks of NPLs, to induce in the nanosystem what we call magneto chiral dichroism. This phenomenon could be at the origin of the homochirality of the living world on Earth, and its application in metamaterials would pave the way for magneto-optical applications [16].

15 a) "Magnetic recording media" Fuji Electric review **2011**, *57*, 2. b) L.H. Reddy, J.N. Arias, J. Nicolas,; P. Couvreur, *Chem. Rev.* **2012**, *112*, 5818-5878.

16 a) G. L. J. A. Rikken and E. Raupach, *Nature*, **2000**, *405*, 932–935. b) B. L. Feringa, *Science*, **2001**, 292, 2021–2022

Peptide mimics of the thrombospondin C-terminal binding domain: Analysis of their therapeutic potential to trigger immunogenic death of cancer cells targeting the TSP1-CD47 axis

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Summary. Our team recently developed PKHB1, a serum-stable peptide-mimic of the TSP1 C-terminal domain able to induce caspase-independent cell death in refractory chronic lymphocytic leukemia (CLL).[i] PKHB1-induced cell death in CLL depends on a Ca^{2+} influx regulated by signaling of PLCG1, a molecule which overexpression correlates with CLL progression.[ii] In the present thesis the therapeutic potential of PKHB1 against different types of cancer, including T-cell acute lymphoblastic leukemia (T-ALL), breast, colon, pancreas, and lung cancer was assessed.[iii-vi] PKHB1 induced caspase-independent cancer cell death, which could be pharmacologically inhibited by impairing PLCG1-related Ca^{2+} signaling in all cases. PKHB1 was not toxic to human or murine peripheral blood mononuclear cells, nor to cells coming from mice primary or secondary lymphoid organs. In immunocompetent mice, PKHB1 reduced the growth of T-ALL and breast cancer tumors and promoted immune cell recruitment to the tumor site. This was explained by immunogenic cell death induction after PKHB1 treatment, demonstrated by measurement of high levels of danger-associated molecular patterns production, prevention of tumor establishment by prophylactic vaccination, and mechanistical *ex vivo* experiments using co-cultures of PKHB1-killed cells, dendritic cells, and T cells. Therapeutic vaccination with PKHB1-killed cells had a strong activity against established tumors and led to cancer remission and long-term immunological memory, proving PKHB1-based therapies relevant for cancer treatment. Moreover, optimization of PKHB1 potency using a homotrimerization approach was assessed in the present work. A scan of primary amine methylations in PKHB1 sequence led to the discovery of PKT16, a more soluble peptide with similar structure and activity that was used to develop a homotrimer, $[PKT16]_3$. This homotrimeric peptide was ten times more potent than PKHB1 to induce Ca^{2+}-regulated cell death in CLL and lung cancer cell lines, proving that structural modifications can improve the potency of TSP1 mimetic peptides.[vii]

Acknowledgments:

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[i] Denèfle et al., *Journal of Medicinal Chemistry*, **2016**, *Vol. 59 (18)*, 8412-8421.

[ii] Martínez-Torres et al., *Plos Medicine*, **2015**, *Vol. 12 (3)*, e1001796.

[iii] Uscanga-Palomeque, Gómez-Morales, Calvillo-Rodríguez, et al., *Cancer Science*, **2019**, *Vol. 110 (1)*, 256-268.

[iv] Martínez-Torres et al., *Journal of Oncology*, **2019**, *Vol. 2019 (ID 9852361)*, 1-11.

[v] Calvillo-Rodríguez, Gómez-Morales, et al. (to send for publication to *Journal for Immunotherapy of Cancer*), **2021**.

[vi] Gómez-Morales, Calvillo-Rodríguez, et al. (to send for publication to *Bioorganic and Medicinal Chemistry*), **2021**.

[vii] Denèfle, Pramil, Gómez-Morales, et al. *Journal of Medicinal Chemistry*, **2019**, *Vol. 62 (17)*, 7656–7668.

Molecular information ratchet based on cyclodextrin [2]rotaxane

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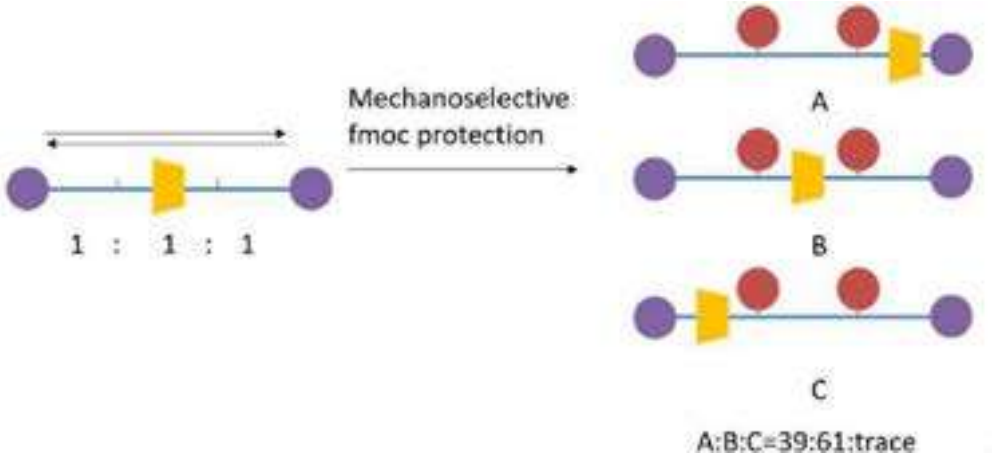
Molecular machines,[17] defined as an assembly of a discrete number of molecular components designed to perform mechanical-like movements as a consequence of external stimuli,[18] have drawn attention of the scientific community. Although various examples of small molecular machines have been described,[19] the regulation of the unidirectional movement remains a challenge.
Information ratchets[20] are a general class of mechanism in which an energy barrier is regulated on a potential energy surface in order to directionally drive the Brownian particle distribution away from equilibrium. Therefore, creating molecular information ratchet is crucial to reach unidirectional movement of molecular machines. Cyclodextrins[21] could be good candidates for this system because of their asymmetric cone-like shape and chiral cavity.
Herein, we describe a permethylated cyclodextrin [2] rotaxane which can perform ratcheting motion. The rotaxane is composed of three equivalent stations separated by two secondary amines as reactive sites that can react with Fmoc derivatives. During the Fmoc-protection a kinetic bias resulting in a non-statistical distribution between the three possible mechano-isomers was observed. This bias can be rationalized by the asymmetry of the CD that favors the reaction when the amine is facing the secondary rim rather than the primary rim. Different factors controlling the ratcheting mechanism, such as solvent, reaction temperature and reactivity of the Fmoc derivatives were investigated and will be presented.



Acknowledgments:

[17] Sundus Erbas-Cakmak, David A. Leigh, Charlie T. McTernan, Alina L. Nussbaumer, *Chem. Rev*. **2015**, *115*, 10081
[18] Vincenzo Balzani, Alberto Cerdi, Françisco M. Raymon, J. Fraser Stoddart; *Angew. Chem. Int. Ed.* **2000**, *39*, 3348-3391.
[19] Liang Zhang, Vanesa Marcos, and David A. Leigh, *PNAS*. **2018**, *115*, 9397–9404. D. Leigh et al., *Nature* **2016**, *534*, 235; B. L. Feringa, *J. Am. Chem. Soc.* **2006**, *128*, 5127.
[20] Astumian, R. D. ; Derényi, I. *Eur. Biophys. J.* **1998**, *27*, 474-489. Parmeggiani, A. ; Jülicher, F. ; Ajdari, A. ; Prost, *J. Phys. ReV. E.,* **1999**, *60*, 2127-2140. Parrondo, J. M. R. ; De Cisneros, B. *J. Appl. Phys. A*, **2002**, *75*, 179-191.
[21] A. Harada, *Acc. Chem. Res.* **2001**, *34*, 456.

Digital humanities and construction of scientific disciplines: the history of chemistry in the 18th century through the prism of encyclopedias and dictionaries.

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Digital humanities is a new computational approach that brings new perspectives to many fields of research. The purpose of my thesis is to see to wich extent digital humanities can bring new results in the history of chemistry.

First, we established a corpus of about a hundred volumes of dictionaries and encyclopedias, from the first *Dictionnaire de Richelet* (1680), known as the first french dictionary, to the *Encyclopédie Méthodique de Chimie* (1815). The corpus includes other French dictionaries, including the *Dictionnaire de l'Académie française* (1794), the *Encyclopédie* of Diderot and D'Alembert (1751 - 1765), and the *Dictionnaire de Chymie* of Macquer (1766). The corpus includes successive reprints too, throughout the 18th century.
Secondly, we collected the digitizations of these dictionaries on Gallica and Google Books. Then, we ocerized these ancient texts, in order to approach as much as possible the original texts. We used the Transkribus software, which uses artificial intelligence technology. Transkribus allows us to create our own recognition models, suitable for character fonts of the end of the 17th century. Getting these texts is the first step to build a database.
The forwarding step consists in structuring these texts, using Python scripts, to reproduce the structure of dictionaries. This enriched database (consisting of XML files) will allow us to study the evolution of the chemical nomenclature, taking into account the revolution of the chemical vocabulary in 1787 by Antoine Lavoisier and his companions.

The formatting of these data by visualization processes, will then bring new elements about the constitution of chemistry as a discipline in the 18th century, through numerical methods.

Pressure-Induced Conversion of Paramagnetic FeCo square Complexes into molecular switches

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In the last decades, More and more researchers have shown their interests in the discrete cyanide-bridged heterometallic complexes which display reversible ETCST transition triggered by external stimuli such as temperature, light and pressure. Here ETCST stands for intermetallic Electron Transfer Coupled to Spin Transition on one metal site. Up to now, most of these studies focused on the thermally activated or light-induced ETCST process, and pressure study on these discrete molecular analogues of Prussian Blues still remains rare in the literature. However pressure is also a powerful external stimuli for switching the magnetic and optical properties of these systems, as pressure is expected to stabilize the diamagnetic heterometallic pair whose volume is significantly smaller as that of the high-spin one.

In this context, we have investigated a family of FeCo square complexes, $\{[Fe(X)(CN)_3]_2[Co(Y)_2]_2\}^{2-}$(X=Tp（Tp= Hydrotris(1-pyrazolyl)borate）/Tp*(Tp*=hydrotris(3,5-dime-thylpyrazol-1-yl)borate),Y=vbik/bik(vbik= Bis(1-vinylimidazol-2-yl)ketone),bik= Bis(1-methyl-2-imidazolyl)ketone). These squares can be trapped in a paramagnetic state when crystallized at high temperature from mother solution.[22] The application of moderate pressure can convert the paramagnetic complexes into diamagnetic ones which undergo subsequently the thermally-induced ETCST transitions with hysteresis. Interestingly, the compressed complexes can display an anomalous ETCST transition: greater is the pressure, wider the hysteresis[23] as the picture depicted. In order to further understand the structure-properties relationship compounds under pressure, we are studying the effects of ligands, counter-anions and solvents on the intermolecular interactions of the compressed complexes, as well as their related ETCST behavior.

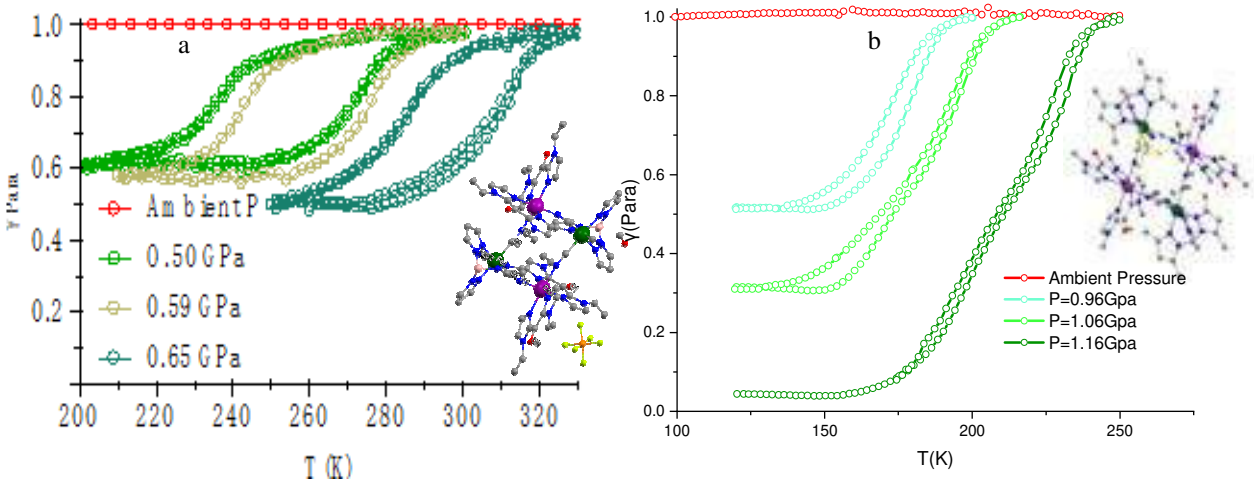

Fig: Thermal variation of the paramagnetic $\{[Fe^{III}_2Co^{II}_2\}$ molar fraction γ_{para} in 1 under various hydrostatic pressures
a: $\{[Fe(tp)(CN)_3]_2[Co(Vbik)_2]_2\}(PF_6)_2{\cdot}2CH_3OH$; b: $\{[Fe(tp^*)(CN)_3]_2[Co(bik)_2]_2\}(BF_4)_2{\cdot}XACN$

Acknowledgments: Oversea Study Program of Guangzhou Elite Project.

[22] De, Siddhartha et al, *RSC Adv.*, ***2016***,*21*,17456-17459.
[23] Yanling Li et al, *Angewandte Chemie Int. Ed.*, ***2020***, *132*, 17425-17429.

Radical Addition of SF_5Cl to cyclopropenes: Synthesis of (Pentafluorosulfanyl)cyclopropanes

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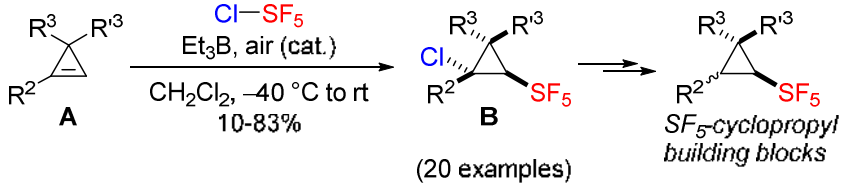
Cyclopropanes lie among the top ten most common rings in drugs approved by the Food and Drug Administration.[1] Incorporation of a cyclopropane in a lead compound can result in an increase in selectivity toward the desired target and improved pharmacokinetic properties making it more likely to become a marketed drug.[2]

Regarding the number of newly approved drugs, fluorinated compounds come up as top players representing a third of approved pharmaceuticals and agrochemicals.[3] Among them, molecules containing "emergent fluorinated motifs" turned out to be interesting targets for the design of new bioactive compounds. The pentafluorosulfanyl group (SF_5), belongs to this new category. Indeed, it excels the hegemonic trifluoromethyl group in terms of electronegativity, lipophilicity, steric demand and metabolic stability.[4]

Thus far, synthetic efforts have mainly focused on the synthesis of (hetero)aromatic SF_5 compounds.[5] Hence the need for the design of new aliphatic building blocks containing SF_5 moiety. The most general conditions in this regard are the radical addition of SF_5Cl on alkenes or alkynes triggered by Et_3B in the presence of O_2 as a radical initiator.[6]

Herein, we report our results on the chloropentafluorosulfanylation of diversely substituted cyclopropenes **A** and the subsequent manipulation of the carbon-chlorine bond in adducts **B** to access diversely substituted SF_5-cyclopropyl building blocks.



R^3 = CO_2Alkyl, CH_2OAc, Ph; R'^3 = H, CO_2Me, CH_2OAc

R^2 = Alkyl, $(CH_2)_nOTBDPS$, $(CH_2)_2OBz$, CH_2OBn, CH_2NPhth

Acknowledgments: Financial support from the ANR (DEFIS project, ANR-17-CE07-0008) is gratefully acknowledged.

[1] R. D. Taylor, M. MacCoss, A. D. G. Lawson, *J. Med. Chem.* **2014**, *57*, 5845-5859.
[2] T. T. Talele *J. Med. Chem.* **2016**, *59*, 8712-8756.
[3] M. Inoue, Y. Sumii, N. Shibata, *ACS Omega* **2020**, *5*, 10633-10640.
[4] Emerging Fluorinated Motifs: Synthesis, Properties and Applications, D. Cahard, J.-A. Ma Eds.; Wiley-VCH, 2020.
[5] P. R. Savoie, J. T. Welch *Chem. Rev.* **2015**, *115*, 1130-1190.
[6] S. Aït-Mohand, W. R. Dolbier *Org. Lett.* **2002**, *4*, 3013-3015.

Multifunctional hetero-poly-metallic architectures

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The design of functional molecular materials has attracted a great deal of attention in recent years. Among these, our interest is focused on polynuclear metal complexes that exhibit photophysical, magnetic or switching properties but also on their ability to achieve multifunctionality. In line with this goal, we adopt a supramolecular approach that consists in using functional metallic complexes as building blocks. This method is advantageous as it affords variations in synthetic parameters and the properties of the building blocks are well established. Most interestingly, their incorporation within a single molecular framework may contribute to synergistic effects.[24]

Our strategy essentially relies on cyanide- and oxalate-based coordination chemistry. It allows a great control over connectivity and topology, and promotes magnetic as well as photo-magnetic properties. Another two key building blocks are trinuclear complexes, LnCuCo and $LnCo_2$ (Ln = Gd, Tb, Dy), that feature high-spin molecule, single-molecule magnet or luminescent properties. In collaboration with Dr. Moritz Malischewski (Freie Universität Berlin), we have developed five different families of hetero-poly-metallic architectures.[25] Here, we report the synthesis of hetero-tetra-metallic complexes and hetero-tri-metallic dendrimers. The magnetic and the photophysical properties are also investigated.

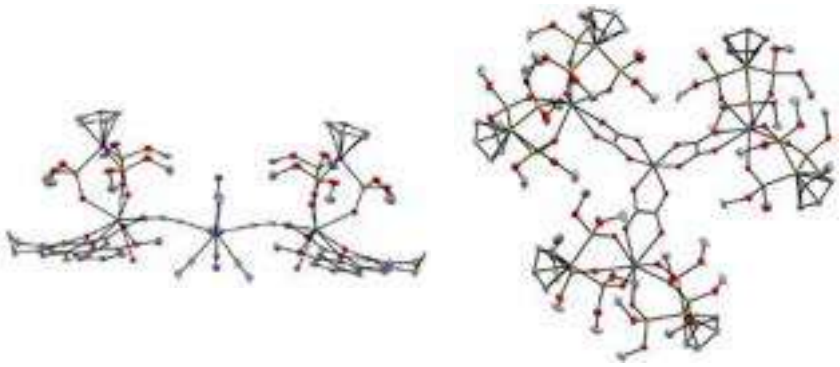

Figure 1. X-ray structure of the hetero-tetra-metallic complex $Mo(LnCuCo)_2$ and the hetero-tri-metallic dendrimer $CrLn_3Co_6$ (solvent molecules and hydrogen atoms have been omitted for clarity).

Acknowledgments:

[24] V. Balzani, A. Juris, M. Venturi, S. Campagna, S. Serroni, *Chem. Rev.*, **1996**, *96*, 2, 759–834
[25] I. Suzana, J. Forte, M. Malischewski, V. Marvaud, *Manuscript in preparation*
I. Suzana, S. Rupf, F. Rahman, B. Klemke, E. Rousset, V. Marvaud, M. Malischewski, *Manuscript in preparation*

Chemoenzymatic synthesis of glycosphingolipid analogues and biological evaluation of their anticancer activities

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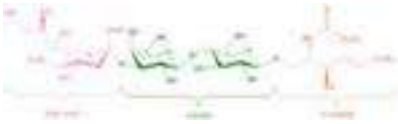
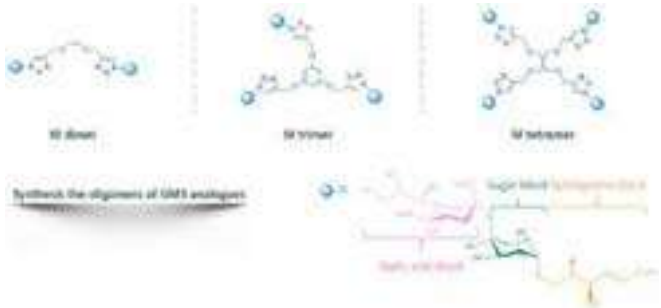
Glycosphingolipids (GSLs) are ubiquitous components on animal cell membranes and exposed on the outer surface of cell membranes. Ganglioside GM3, the first and simplest member in the metabolic series of a GSLs family, contains sialic acid, lactose and ceramide. GM3 has a strong impact on the occurrence and development of human cancer. GM3 is not only overexpressed in several types of cancer but also inhibits tumor cell growth through anti-angiogenesis or motility. In particular, the effect of GM3 on EGFR signalling is essential for cancer.[26] Previously our laboratory prepared a series of GM3 analogues, among them, several compounds display interesting activity against tumour growth. In the present study, we would like to improve the biological activity of this type of the compounds by using the multivalency effect. We screened out mannose-containing analogues with better anti-tumor activity from the previously synthesized GM3 analogues,[27] and further synthesized mannose-containing analogues oligomers, in order to study their antitumor activities and search new leading compounds for cancer therapy.



Structure of ganglioside GM3

At first, the sialic acid was activated as sialyl xanthate form. Then the lipid precursor azidosphingosine was synthesized from the commercially available D-(+)-galactose. Finally, the mannose bearing a free 6-OH residue was prepared by enzymatic hydrolysis, as the enzyme CRL (Candida rugosa) is specific for removing acetyl group at C-6 position. Further α-sialylation reaction and conjugation with lipid precursor were performed. After several steps of manipulations, the mannose-containing analogues were synthesized. we firstly synthesized novel mannose-containing GM3 analogues by enzymatic hydrolysis and chemical procedures. Next, conjugation of mannose-containing analogues to multivalent skeleton through the click reaction was carried out. At last, dimer, trimer and tetramer containing mannose analogues were synthesized.



Acknowledgments:

[26] S. Hakomori, Y. Zhang, *Chem. Biol.* **1997**, *4*, 97-104.
[27] C. Zheng, H. Guan, Y. Liu, Z. Li, T. Bavaro, M. Terreni, M. Sollogoub, J. Xu, Y. Zhang, *Eur. J. Med. Chem.* **2019**, *165*, 107-114.

Design and study of anti-oxidant inorganic complexes mimicking the superoxide dismutase (SOD)

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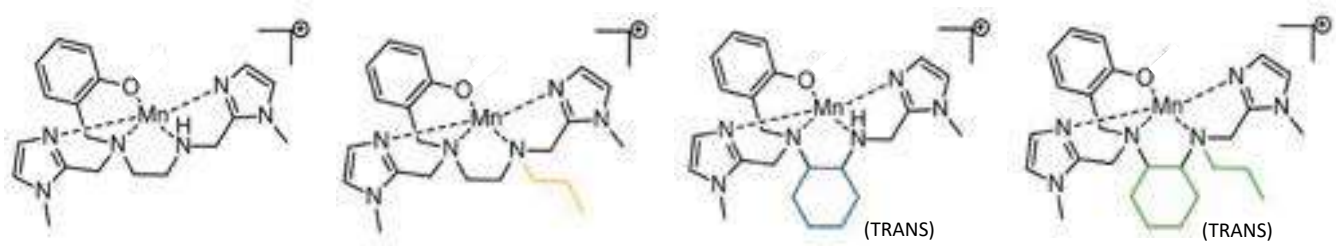
Superoxide Dismutases (SODs) are metalloenzymes involved in the cellular antioxidant defenses. They regulate the concentration of the superoxide anion, a reactive oxygen species (ROS).[28] It has been shown that SOD defenses are weakened in intestinal epithelial cells of patients suffering from inflammatory bowel diseases (IBDs).[29] The resulting increase in ROS amount, leading to oxidative stress, may contribute to the pathogenesis in IBDs. Low-molecular weight complexes, mimicking SOD activity may be promising antioxidant metallodrugs for the treatment of IBDs. The research conducted in Policar's group has led to the development of the manganese complex Mn1 that has shown anti-oxidant and anti-inflammatory activities in intestinal LPS-stressed epithelial cells, an inflammation model mediated by oxidative stress.[30] However, Mn1 is very flexible compared to the native SOD and is prone to metal-assisted dissociation in cells. Indeed, metal exchanges might occur between the manganese center and metal ions present in the biological environment. Aiming at improving the bioactivity of this SOD mimic, three new MnSOD mimics derived from Mn1 have been designed. Their structure includes additional cyclohexyl and propyl groups. In one hand, by rigidifying the ligand structure, the cyclohexyl group may provide a compact and preorganized coordination cavity to encapsulate the manganese ion and thus may improve the kinetic inertness of the complexes . In the other hand, the lipophilic propyl group may avoid any deprotonation issue during the subsequent speciation studies.



We have assessed the potential of new SOD mimics derived from Mn1 to demonstrate higher intrinsic SOD activity, higher lipophilicity and improved kinetic inertness in the cellular environment. Very interestingly, the new Mn1 derivatives were shown to provide anti-inflammatory effects in intestinal LPS- stressed epithelial cells at lower doses than Mn1 and are hence more efficient SOD mimics.

Acknowledgments: Martha Zoumpoulaki (LBM), Géraldine Gazzah (LBM), Jean Bouvet (LBM), Sylvie Demignot (CRSA)

[28] Yuewei Sheng et al., « Superoxide Dismutases and Superoxide Reductases », *Chemical Reviews* 114, nº 7 (9 avril 2014): 3854-3918, https://doi.org/10.1021/cr4005296.

[29] Laurens Kruidenier et al., « Differential Mucosal Expression of Three Superoxide Dismutase Isoforms in Inflammatory Bowel Disease », *The Journal of Pathology* 201, nº 1 (septembre 2003): 7-16, https://doi.org/10.1002/path.1407.

[30] Emilie Mathieu et al., « A Cell-Penetrant Manganese Superoxide Dismutase (MnSOD) Mimic Is Able To Complement MnSOD and Exerts an Antiinflammatory Effect on Cellular and Animal Models of Inflammatory Bowel Diseases », *Inorganic Chemistry* 56, nº 5 (6 mars 2017): 2545-55, https://doi.org/10.1021/acs.inorgchem.6b02695.

Multifunctional gold nanoparticles for bio-applications

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Cancer is one of the most important causes of death in the world with a number of diagnosed cancers which is rising rapidly. Currently, the main therapeutic approaches used to treat cancer are surgery, chemotherapy and radiotherapy. In this context, it is desirable to develop highly efficient systems that first selectively target cancerous tissues and then, once localized in the tumor, can be remotely activated to induce a local cytotoxic effect.

Over the past few years, gold nanoparticles (AuNPs) have emerged as interesting candidates in the biomedical field because of their unique optical and physical properties.[31] Besides their biocompatibility and stability at physiologic pH, AuNPs can be functionalized by numerous agents (polymers, ligands, drugs, DNA, proteins, peptides, …) which can provide them suitable applications for targeting, treatment of cancer cells and even imaging.[32,33,34]

Our goal project is to develop a core-shell like nanoparticles which will allow the treatment via chemo, photo and radio-therapy by targeting especially cancer cells. A gold core was selected for its well-established strong absorbance (X-rays and IR) suitable for radiotherapy or for induced local hyperthermia.

On the other and, the shell selected is a modified polysaccharide: carboxymethyl-dextran (CM-dextran), interesting for its biocompatibility, its furtivity and its easy degradation in the body. The key point is the presence of reactive carboxylic acids in this derivative which opens an easy functionalization by a wide range of molecules of interest (targeting peptides, drugs, fluorophores…).

[31] D. Astruc, M-C Daniel, *Chem. Rev.*, **2004**, 104, 293-346
[32] W. Chen *et al.*, *Adv. Mater.*, **2016**, 28, 8567-8585
[33] S. Her, D.A. Jaffray, C. Allen, *Adv. Drug Delivery Rev*., **2017**, 109, 84-101
[34] O.S. Muddineti *et al*., *Int. J. Pharm*., **2015**, 484, 252-267

Thermal and sigmatropic rearrangements involving (cyclopropyl)vinyl azides: Synthesis of pyridines and cycloheptadienes

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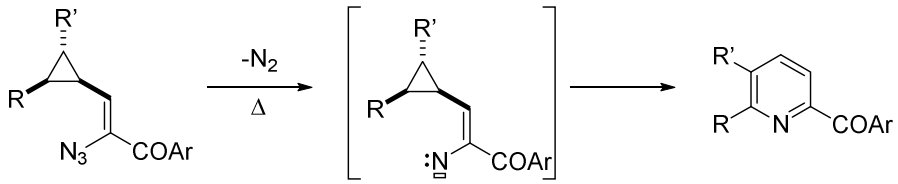
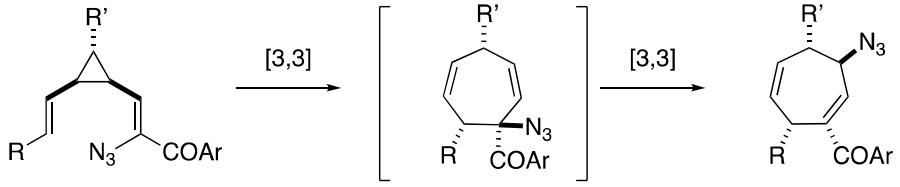
Vinyl azides display a versatile reactivity since these compounds can behave as nucleophiles, electrophiles or even radical acceptors.[35] These vinyl azides blocks have found many applications in the synthesis of nitrogen-incorporating molecules and nitrogen heterocycles in particular. [36]

We have investigated the reactivity of diversely substituted (cyclopropyl)vinyl azides **A** in thermal rearrangements which proceed through (cyclopropyl)vinyl nitrene intermediates **B** to afford substituted pyridines **C** after aromatization.[37]



A **B** **C**

During the course of our investigations, we have discovered that (2-vinylcyclopropyl)vinyl azides **A'** undergo a [3,3]-sigmatropic Cope rearrangement under mild conditions.[38] The resulting allylic azide intermediates **D** subsequently isomerize into highly functionalized seven-membered rings **E** through a [3,3]-sigmatropic rearrangement.[39]



A' **D** **E**

Acknowledgments: T. A. thanks the MESRI for a grant.

[35] (a) J. Fu, G. Zanoni, E. A. Anderson, X. Bi, *Chem. Soc. Rev.* **2017**, *46*, 7208–7228 ; (b) H. Hayashi, A. Kaga, S. Chiba, *J. Org. Chem.* **2017**, *82*, 11981–11989.

[36] B. Hu, S. G. DiMagno, *Org. Biomol. Chem.* **2015**, *13*, 3844–3855.

[37] K. Isomura, H. Kawasaki, K. Takehara, H. Taniguchi, *Heterocycles* **1995**, *40*, 511–514.

[38] (a) T. Hudlicky, R. Fan, J. W. Reed, K. G. Gadamasetti, *Org. React.* **2004**, *41*, 1–133; (b) S. Krüger, T. Gaich, *Beilstein J. Org. Chem.* **2014**, *10,* 163–193.

[39] (a) A. Gagneux, S. Winstein, W. G. Young, *J. Am. Chem. Soc.* **1960**, *82*, 5956–5957; (b) A. S. Carlson, J. T. Topczewski, *Org. Biomol. Chem.* **2019**, *17*, 4406–4429.

Lewis Acids and Bases Encapsulated in the Cavity of Cyclodextrins

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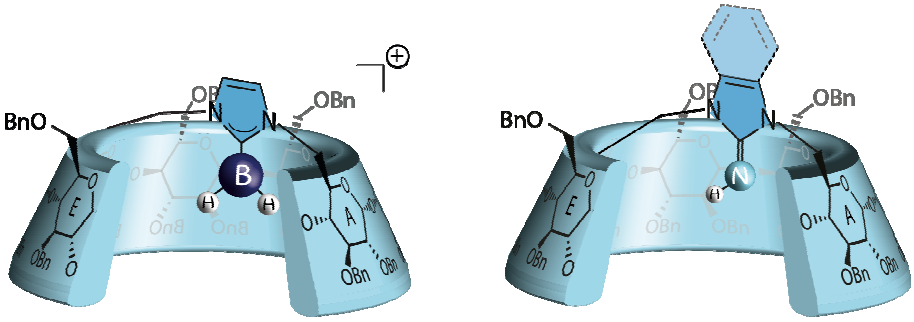
Cyclodextrins (CDs) have been studied for many years as platforms for selective catalytic reactions. The bridging of CDs with a N-heterocyclic carbene (NHC) ligand leads to a rigidification and a deformation of the cavity, conferring them a helicoidal chirality.[40,41] The presence of the NHC moiety allows the formation of diverse metallic complexes pointing inside the cavity. Several reactions involving coinage metals (Cu, Ag, Au) have been described and showed great regio- or enantio- selectivities towards hydroboration,[42] cycloisomerization[41] and alkoxycyclization[43] reactions. The synthesis of novel cyclodextrins encapsulating Lewis acids and bases should allow the access to new catalytic reactivities for those macromolecules. We synthetized encapsulated superbases,[44] and studied their Lewis and Brønsted-Lowry basicities. We also turned our interest towards borenium ions for which interest has grown during the past few years.[45] The protection brought by the cavity of the cyclodextrin allowed us to form the elusive NHC–BH_2^+ borenium ion that was thought, until proved otherwise, to be non-isolable.[46]



First encounter of NHC–BH_2^+ borenium ion

Encapsulated superbases

Acknowledgments: Dr. Lucile Anthore-Dalion and Dr. Thibault Cantat collaborators of the ANR CaSPair.

[40] M. Guitet, P. Zhang, F. Marcelo, C. Tugny, J. Jiménez-Barbero, O. Buriez, C. Amatore, V. Mouriès-Mansuy, J.-P. Goddard, L. Fensterbank, Y. Zhang, S. Roland, M. Ménand, M. Sollogoub, *Angew. Chem. Int. Ed.* **2013**, *52*, 7213 – 7218.
[41] P. Zhang, C. Tugny, J. Meijide Suárez, M. Guitet, E. Derat, N. Vanthuyne, Y. Zhang, O. Bistri, V. MourièsMansuy, M. Ménand, S. Roland, L. Fensterbank, M. Sollogoub, *Chem* **2017**, *3*, 174 – 191.
[42] P. Zhang, J. Meijide Suárez, T. Driant, E. Derat, Y. Zhang, M. Ménand, S. Roland, M. Sollogoub, *Angew. Chem. Int. Ed.* **2017**, *129*, 10961 – 10965.
[43] C. Tugny, N. del Rio, M. Koohgard, N. Vanthuyne, D. Lesage, K. Bijouard, P. Zhang, J. Meijide Suárez, S. Roland, E. Derat, O. Bistri-Aslanoff, M. Sollogoub, L. Fensterbank, V. Mouriès-Mansuy, *ACS Catal.* **2020**, *10*, 5964 – 5972.
[44] R. Kunetskiy, S. Polyakova, J. Vavřík, I. Císařová, J. Saame, E. Roos Nerut, I. Koppel, I. Koppel, A. Kütt, I. Leito, I. Lyapkalo, *Chem. Eur. J.* **2012**, *18*, 3621 – 3630.
[45] a) C. Chen, J. Li, C. Daniliuc, C. Mück-Lichtenfeld, G. Kehr, G. Erker, *Angew. Chem. Int. Ed.* **2020**, *59*, 21460 – 21464. b) Y. Liu, B. Su, W. Dong, Z. Li, H. Wang, *J. Am. Chem. Soc.* **2019**, *141*, 8358 – 836. c) W. Piers, S. Bourke, K. Conroy, *Angew. Chem. Int. Ed.* **2005**, *44*, 5016 – 5036.
[46] B. Inés, M. Patil, J. Carreras, R. Goddard, W. Thiel, M. Alcarazo, *Angew. Chem. Int. Ed.* **2011**, *50*, 8400 – 8403.

Functionalization of silicon substrates with Polyoxometalates

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Summary:
Polyoxometalates (POMs) are anionic nanosized oxo-clusters formed by early transition metals in their highest oxidation state. Besides their large diversity of structures, they provide appealing redox properties as they can be successively and reversibly reduced, making them good candidates as redox mediators or electron reservoirs.[47] Immobilization of POMs onto electrodes (Si, ITO) have been previously studied using hybrid POMs bearing organic tethers.[48] To go further in the POM/substrate study, we propose to integrate photoreducible POMs monolayers into nanoelectronics. Indeed, assembling these POMs on a surface is a way of controlling the surface charge through irradiation with UV light, and this phenomenon can be used to design an optically gated transistor. However, the electrical properties of the resulting device will depend on the assembly quality and the POMs stability on surface is not to be neglected. Monolayers of NH_2/NH_3^+-terminated alkyl chains SAMs on oxide-free silicon substrates were thus prepared via thermal hydrosilylation and post-functionalization.[49] (nBu$_4$N)$_3$[PMo$_{12}$O$_{40}$] POM and the corresponding one- and two-electrons reduced species were chemically synthesized[50] prior to adsorption onto the modified Si substrates. Emphasis will be given on the surface characterization and understanding of the immobilized POM photoreduction property using different techniques. Some preliminary results of electrical characterization of a pseudo-MOSFET prototype device[51] will also be presented.

Fig. 1: Towards a POMs-based field effect transistor

Acknowledgments: PhD advisors, Irina IONICA, Miltiadis ALEPIDIS, Antoine MICHE, Milana Cherie THOMAS, Yves Jean CHABAL

[47] (a) Izzet, G; Volatron, F; Proust, A, *Chem. Rec.* **2017**, 17, 250-266. (b) Song, YF; Tsunashima, R, *Chem. Soc. Rev.* **2012**, 41, 7384-7402.
[48] (a) Volatron, F; Noël, JM; Rinfray, C; Decorse, P; Combellas, C; Kanoufi, F; Proust, A, *J. Mater. Chem. C*. **2015**, 3, 6266-6275. (b) Ben M'Barek, Y; Rosser, T; Sum, J; Blanchard, S; Volatron, F; Izzet, G; Salles, R; Fize, J; Koepf, M; Chavarot-Kerlidou, M; Artero, V; Proust, A, *ACS Appl. Energy Mater.* **2020**, 3, 163-169.
[49] Seitz, O; Fernandes, PG; Mahmud, GA; Wen, HC; Stiegler, HJ; Chapman, RA; Vogel, EM; Chabal, YJ, *Langmuir.* **2011**, 27, 7337-7340.
[50] Artero, V; Proust, A, *Eur. J. Inorg. Chem.* **2000**, 2393-2400.
[51] Cristoloveanu, S; Bawedin, M; Ionica, I, *Solid-State Electronics.* **2016**, 117, 10-36.

Photolabelling coupled to mass spectrometry to understand antimicrobial peptide DMS-DA6 interaction with bacterial membranes at the molecular level

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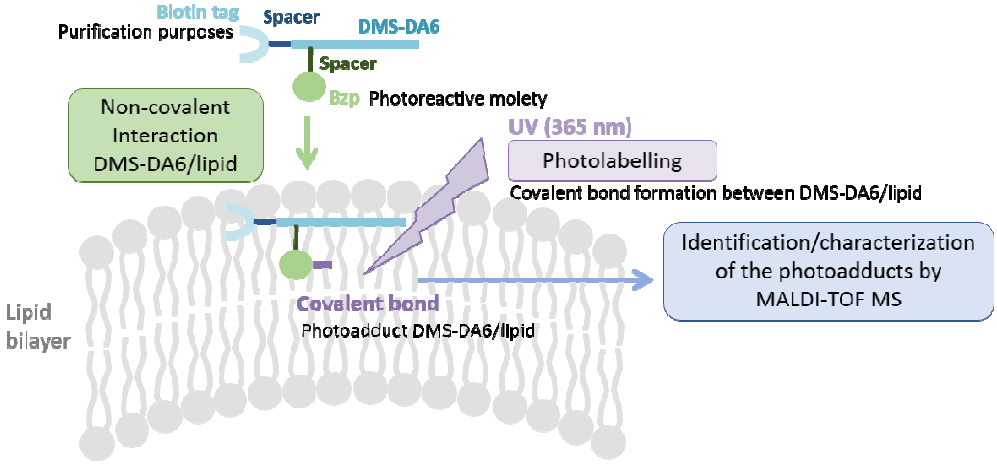
Antimicrobial peptides (AMPs) are part of the innate immune response that is effective against bacteria. AMPs cross the bacterial cell-wall, before inserting into membrane bilayers under different pore formation mechanisms. Among AMPs, DMS-DA6 is a 26 residues cationic peptide (sequence: GVWGIAKIAGKVLGNILPH VFSSNQS-CONH2) from the Dermaseptin family. Our work aims to understand the interactions of DMS-DA6 with membranes at the molecular level, using an approach coupling photolabelling to mass spectrometry (MS).

To this end, we synthesized a photoreactive DMS-DA6 containing a benzophenone (Bzp) as the photoreactive moiety and a biotin tag for purification purposes. Under UV irradiation, the photoreactive DMS-DA6 can form a covalent bond with interacting partners. We compared photolabelling yields for various photoreactive analogues of DMS-DA6. These analogues contain different linkers between the N-terminus of the peptide and the biotin tag, or between the Bzp and the peptide backbone and the Bzp moiety is introduced at different positions in the peptide sequence.

Modifications of the DMS-DA6 sequence with different substitution/insertion/deletion were also investigated, taking care to maintain an amphipathic α helix structure and the antibacterial properties of the initial DMS-DA6.

In this work, we show that the yield of photolabelling could be improved by judicious positioning of the Bzp label on the hydrophobic side of the α helix. Intact peptides/lipids photoadducts have been identified or not, depending on the position and the length of the spacer between the peptide backbone and the Bzp moiety. A longer and more flexible spacer led to the observation of intact photoadducts whereas shorter arms led to more constrained and less stable photoadducts which rapidly fragment via retro-Paterno Büchi reactions, leading to lower mass species. This spontaneous fragmentation is very informative and can be used to assess the depth of insertion of the peptide in the membrane bilayer.

Finally, MS analysis revealed a peculiar behaviour of the DMS-DA6 peptide sequence in the MALDI-TOF reflector negative ions mode in which the peptide did not appear at the expected m/z of the [M-H]- deprotonated ion but with a mass shift of +1 Da. Moreover, in source fragmentation occurs at the peptide bond between the asparagine N15 and the isoleucine I16, leading to the so-called δ-cleavage classically observed in CID experiments of peptide anions. Taking advantage of such fragmentation occurring directly at the MS level in the negative ions mode could be interesting in case of low amount of material impairing MS/MS analysis for further characterization or de novo sequencing of natural antimicrobial peptides.



Selective functionalization of furfural and its derivatives

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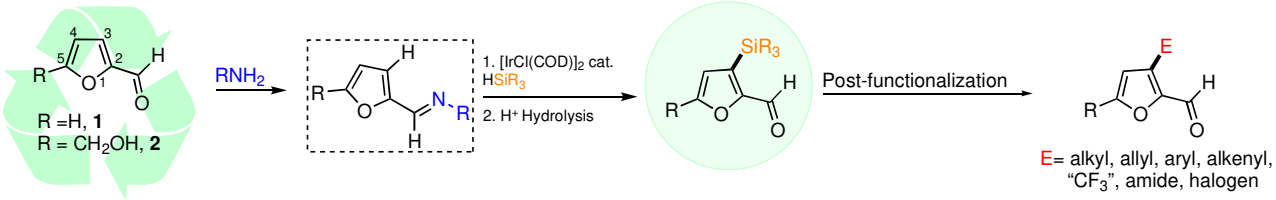
In order to develop an ever more eco-compatible synthetic chemistry, it is nowadays essential to synthesize intermediates and added-value chemical compounds starting from substrates derived from biomass rather than those from fossil resources. Furfural **1** and 5-(hydroxymethyl)furfural (HMF) **2** are among the most promising bio-based molecules.[1] Obtained by dehydrating lignocellulosic biomass from agricultural residues and dedicated crops, these molecules have great potential as renewable platforms for the sustainable production of fine chemicals.[2]

In particular, the direct functionalization of furfural, without prior modification of the redox state of the aldehyde function, by selective C–H activation[3] is an emerging field that is attracting considerable interest. In this contest, our team has recently developed protocols for functionalizing furfural-derived imines at the 3-position by ruthenium-catalyzed alkylation,[4] arylation[5] and acylation.[6]

Herein, we disclose a directed C3–H silylation of furfural derivatives under iridium catalysis. This new selective functionalization is achieved on furfuryl imines with triorganosilanes or organodisilyloxysilanes in the presence of a hydride scavenger. This transformation gives access to even more versatile platforms that can be further functionalized using the C(sp^2)–Si bond as handle. Post-functionalizations through TM-catalyzed cross-coupling reactions[7] or Brook-type rearrangements[8] are investigated; especially through fluoride anion activation. Discovery of these reactivity, as well as optimizations and scopes of these methods will be described.



[1] Mika, L.T.; Cséfalvay, E.; Nemeth A. *Chem. Rev.* **2018,** *118*, 505.
[2] Liu, B.; Zhang, Z. H. *ChemSusChem* **2016**, *9,* 2015.
[3] Roudesly, F.; Oble, J.; Poli, G. *J. Mol. Catal. A. Chem.* **2017**, *426*, 275.
[4] Pezzetta, C.; Veiros, L. F.; Oble, J.; Poli, G. *Chem. Eur. J.* **2017**, *23*, 8385.
[5] a) Siopa, F.; Ramis Cladera, V-A.; Afonso, C.; Oble, J.; Poli, G. *Eur. J. Org. Chem.* **2018**, 6101.b) Ravasco, J. M. J. M.; Monteiro,
C. M.; Siopa, F.; Trindade, A. F.; Oble, J.; Poli, G.; Simeonov, S. P.; Afonso, C. A. M. *ChemSusChem* **2019**, *12*, 4629.
[6] Sala, R.; Roudesly, F.; Veiros, L. F.; Broggini, G.; Oble, J.; Poli, G. *Adv. Synth. Catal.* **2020**, *362*, 2436.
[7] Cheng, C.; Hartwig, J. F. *Chem. Rev.* **2015**, *115*, 8946.
[8] Curpanen, S.; Poli, G.; Oble, J.; Perez-Luna, A. *Eur. J. Org. Chem.* **2021**, 7, 1055.

Enantioenriched allylsilanes: preparation through S_N2' catalyzed addition of Grignard reagents

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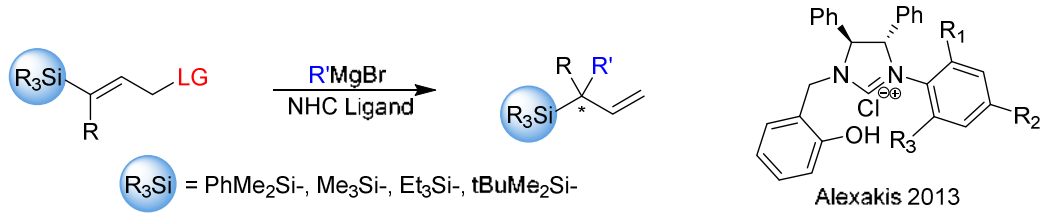
Allylsilanes are very useful and versatile structures extensively used in organic synthesis with a large number of applications on it.[i] Their bench-stability and easy-handling along with their low toxicity and functional group tolerability, allow them to occupy a unique place in the armory of the organic chemist.

As useful building blocks (they can undergo a great variety of silicon transformations such as cross-coupling reactions, ring-closing and cross-metathesis processes), its synthesis has been deeply investigated and several reliable reaction protocols have been developed for its preparation. These molecules have raised particular interest as convenient intermediate reagents to perform stereo-selective and -control C-C bond formations (addition of allyl patterns to electrophiles as carbonyl groups or imines),[ia,ii] representing a complementary method to the enolate based aldol reaction.

Since Hayashi and Kumada reported the first preparation of enantioenriched allylsilanes in 1982,[iii] many other synthetic strategies had been developed based in Pd-catalysis, Claisen rearrangement, Asymmetric Allylic Alkylation (AAA) or Asymmetric Allylic Silylation (AAS) methods among others.

However, the increasing demand of these molecules and the lack of an established method that allow to access optically active allylsilanes with good regio- and enantio-selectivity, bearing tertiary and quaternary stereogenic centers, big substrate scope and large variation of the silicon moiety, encourage us to develop a new synthesis strategy.

Based on previous results published by Alexakis *et al.*,[iv] we focused our method in a Cu-free AAA of Si-substituted allylic electrophiles with Grignard reagents in the presence of chiral N-Heterocyclic Carbene (NHC) ligands.



Acknowledgments:

[i] (a) C. E. Masse, J. S. Panek, *Chem. Rev.* **1995**, *95*, 1293-1316, (b) I. Fleming, A. Barbero, D. Walter, *Chem. Rev.* **1997**, *97*, 2063-2192, (c) L. Chabaund, P. James, Y. Landais, *Eur. J. Org. Chem.* **2004**, 3173-3199.
[ii] J. A. Marshal, *Chem. Rev.* **2000**, *100*, 3163-3185.
[iii] (a) T. Hayashi, M. Konishi, H. Ito, M. Kumada, *J. Am. Chem. Soc.* **1982**, *104*, 4962-4963, (b) T. Hayashi, M. Konishi, M. Kumada, *J. Org. Chem.* **1983**, *48*, 279-281.
[iv] (a) O. Jackowski, A. Alexakis, *Angew. Chem. Int. Ed.* **2010**, *49*, 3346-3350, (b) D. Grassi, C. Dolka, O. Jackowski, A. Alexakis, *Chem.: Eur. J.* **2013**, *19*, 1466-1475.

Benchmarking of Oxygen Evolution Catalysts on Porous Nickel Supports

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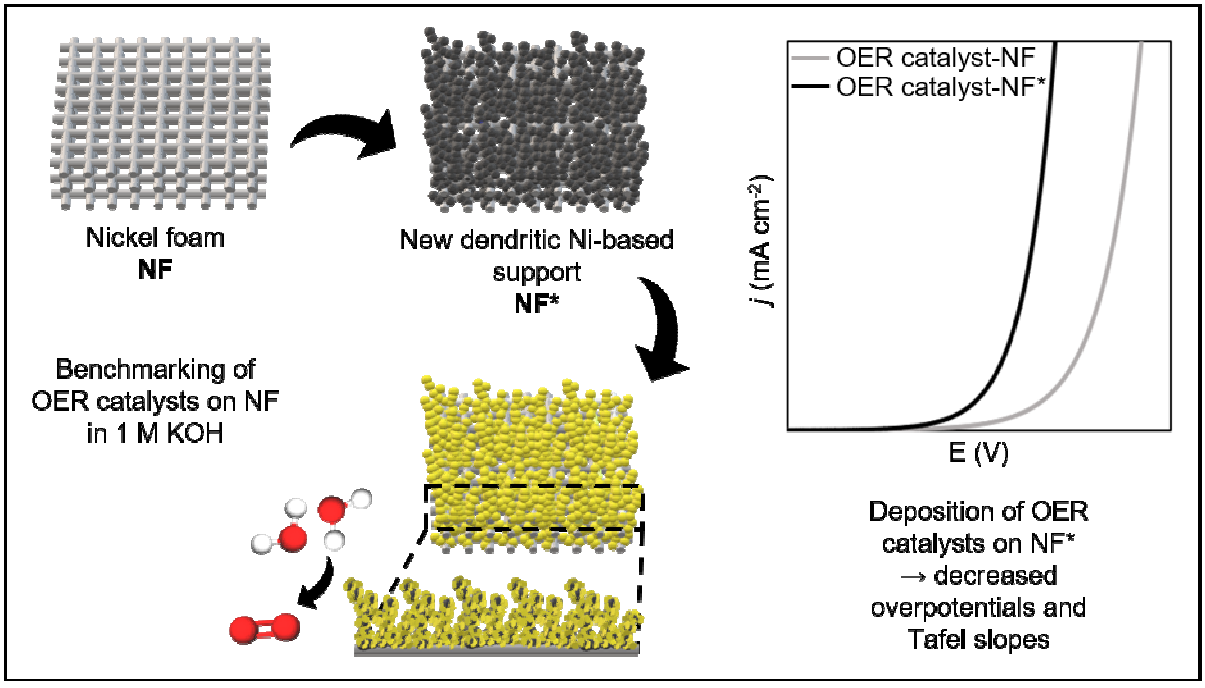
Summary

Active and inexpensive oxygen evolution reaction (OER) electrocatalysts are required for energy efficient electrolysis applications. Objective comparison between OER catalysts has been blurred by the use of different supports and methods to evaluate performance. We selected nine highly active transition-metal-based catalysts and describe their synthesis using a porous nickel foam and a new Ni-based dendritic material as the supports. We designed a standardised protocol to characterise and compare the catalysts in terms of structure, activity, and stability. Therefore, we highlight the most active anode materials and provide an easy way to increase the geometric current density of a catalyst by tuning the porosity of its support. [1]



[1] A. Peugeot, C. Creissen, D. Karapinar, H. Ngoc Tran, M. Schreiber, M. Fontecave, *Joule*, **2021**, doi.org/10.1016/j.joule.2021.03.022

Development of one-pot procedures for the preparation of conjugated trienes through sulfone- and π-allylpalladium chemistry

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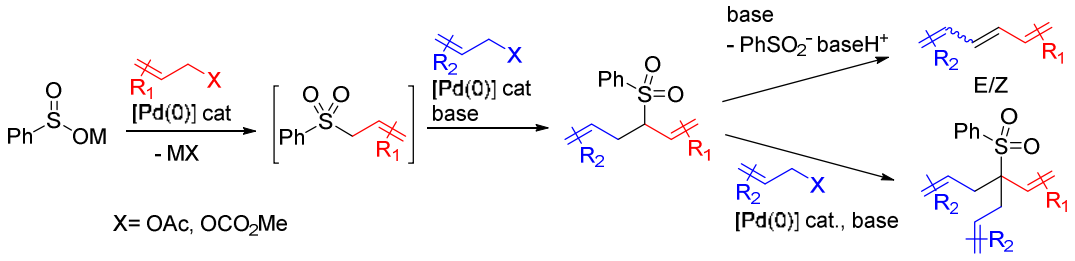
Sulfones are versatile synthetic intermediates in organic chemistry because of their high stability.[53] Molecules possessing a sulfone unit have many applications in synthetic chemistry,[54] with three main reactions concerned within this project. The first one is a Tsuji-Trost sulfonylation with π-allylpalladium complexes from sulfinates,[55] the second one is a Tsuji-Trost allylation from deprotonated allylsulfones[56] and the third one is a 1,2-elimination reaction to form conjugated polyenes. This last reaction is possible from sulfones that contain β-hydrogen and is due to the fact that sulfonyl groups are also good leaving groups.[57] Although each of these transformations has been independently reported, the combined use of these reactions in a domino or one-pot process is, to the best of our knowledge, unknown.

Our goal is to find conditions allowing the combination of these reactions by palladium-catalyzed domino sequences. We found out that under Pd(0)–catalysis, allylcarbonates and allylacetates react with sodium benzenesulfinate to generate allylsulfones, which are subsequently allylated with another molecule of allylcarbonate or allylacetate to afford 3-phenylsulfonylhexa-1,5-dienes (monoallyl product) in one-pot. We also discovered that with similar conditions, the one-pot triple allylation sequence can afford 3-phenylsulfonyl-3-allyl-hexa-1,5-dienes coming from the diallylation of the allylsulfone obtained after the first step of the sequence. Optimization, scope and limitation of these methods will be shown.



Acknowledgments: China Scholarship Council for funding

[53] For a selection of examples, see: (a) Julia, M.; Nel, M.; Saussine, L. *J. Organomet. Chem.* **1979**, *181*, C17; (b) Deeming, A. S.; Russell, C. J.; Hennessy, A. J.; Willis, M. C. *Org. Lett.* **2014**, *16*, 150−153.

[54] (a) Trost, B. M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 107; (b) Liu, N.-W.; Liang S.; Manolikakes G. *Synthesis*, **2016**, *48*, 1939.

[55] (a) Katsuhiko, I.; Taku, Y.; Hiroshi, K. *Chem. Lett.* **1981**, 1357; (b) Felpin, F.-X.; Landais, Y. *J. Org. Chem.* **2005**, *70*, 6441.

[56] (a) Trost, B. M.; Schmuff, N. R.; Miller, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 5979-5981. (b) Tsuji, J.; Shimizu, I.; Minami, I.; Ohashi, Y.; Sugiura, T.; Takahashi, K. *J. Org. Chem.* **1985**, *50*, 1523; (c) Minami, I.; Ohashi, Y.; Shimizu, I.; Tsuji, J. *Tetrahedron Lett.* **1985**, *26*, 2449.

[57] (a) Arnould, D.; Chabardes, P.; Farge, G.; Julia, M. *Bull. Soc. Chim. Fr.* **1985**, 130. (b) Chabardes, P.; Decor, J. P.; Varagnat, J. *Tetrahedron* **1977**, *33*, 2799; (c) Alam, M. S.; Koo, S. *Synth. Commun.* **2018**, *48*, 247-254.