Société Chimique de France

Sections régionales Occitanie-Méditerranée & Occitanie-Pyrénées

Chères et Chers collègues,

Les sections régionales Occitanie-Méditerranée & Occitanie-Pyrénées de la Société Chimique de France s'associent pour vous proposer une ½ journée scientifique « SCF d'Avenir » dont la 1ère édition aura lieu, dans un format virtuel, le **Jeudi 24 Juin 2021 de 14h à 17h30**.

Cet événement sera conjointement organisé par l'ensemble des deux bureaux régionaux, sénior et RJ. Il vise à donner l'occasion aux **nouveaux permanents, chercheurs et enseignants-chercheurs**, ainsi qu'aux **post-doctorants**, exerçant leur activité de recherche au sein d'un laboratoire localisé sur le périmètre géographique de l'une des deux sections régionales, de présenter leurs travaux de recherche, passés, présents ou futurs. Cette action a pour but de favoriser l'intégration de ces nouveaux acteurs dans nos communautés locales et régionales.

Cette journée est **gratuite et ouverte** à toutes et à tous. Pour vous connecter, utilisez le lien suivant :

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Nous sommes heureux de pouvoir vous proposer un programme de 9 intervenants comprenant 7 communications orales (15 min + 5 min discussion) et 2 conférences invitées (20 min + 5 min discussion). Les thématiques abordées seront diverses et donnent ainsi un aperçu de la richesse des champs disciplinaires traités sur nos territoires.

Bonne journée scientifique à toutes et à tous,

Les bureaux SCF Occitanie-Méditerranée & Occitanie-Pyrénées

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Société Chimique de France

Section régionale Occitanie-Méditerranée & Occitanie-Pyrénées

½ Journée SCF d'Avenir

Jeudi 24 Juin 2021 de 14h00 à 17h30

par visioconférence

14h00-14h05 Mot d'accueil
Crystalle CHARDET, Emmanuel GRAS

Session 1 Chairman : Lucas PAGES

14h05-14h25 Conférencier invité : **Gyorgy SZALOKI**, LHFA, Toulouse
Reactivity of Metal Complexes in Confined Environments

14h30-14h50 **Justine HARMEL**, CIRIMAT, Université de Toulouse, CNRS, Toulouse
Soft-chemistry approach for optimization of 2D-materials for electrochemical energy storage applications

14h50-15h10 **Francesco CALZAFERRI**, IBMM, UMR 5247 CNRS, Univ Montpellier, ENSCM, Montpellier
Non-nucleoside DNA methyltransferase inhibitors as therapeutic compounds and pharmacological tools for epigenetic reprogramming in cancer

15h10-15h30 **Lole JURADO**, LCC-CNRS, Université de Toulouse, CNRS, Toulouse
Single atom catalysts for hydroformylation reaction: a profitable alternative to conventional catalysts

15h30-15h50 **François-Xavier TOUBLET**, LCC-CNRS, Université de Toulouse, CNRS, Toulouse
Bio-active functional lipids: synthesis of terminal primary dialkynylcarbinamines

15h50-16h00 Pause

Session 2 Chairwoman : Crystalle CHARDET

16h00-16h20 **Carlos JARAVA-BARRERA**, LCC-CNRS, Université de Toulouse, CNRS, Toulouse
Selective Reductive Dimerization of CO_2 into Glycolaldehyde

16h20-16h40 **Chandramouli GHOSH**, IBMM, UMR 5247 CNRS, Univ Montpellier, ENSCM, Montpellier
Development of Covalent spCas9 inhibitors for gene editing regulation

16h40-17h00 **Mélissa DUMARTIN**, CEMES, Université de Toulouse, CNRS, Toulouse
Design and synthesis of artificial molecular machines: muscle & motors

17h00-17h25 Conférencier invité : **Renata MARCIA DE FIGUEIREDO**, ICGM, Montpellier
Towards the Total Synthesis of Tautomycetin

17h25-17h30 Clôture
Lucas PAGES, Sébastien ULRICH

Le réseau des chimistes

Reactivity of Metal Complexes in Confined Environments

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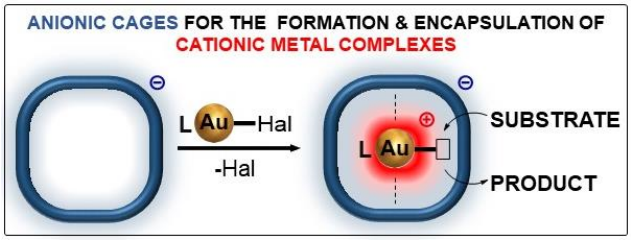
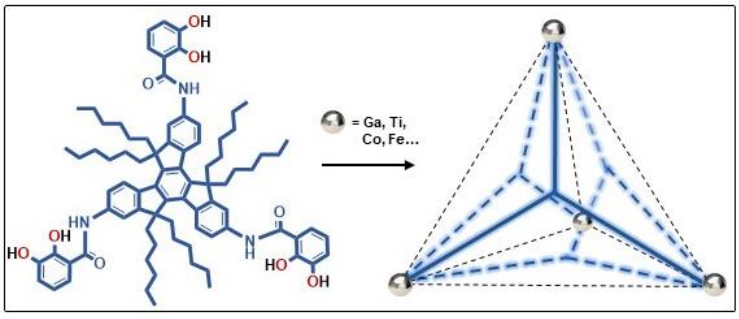
CONTEXT For a long time, supramolecular chemists have sought to reproduce enzymatic catalysis by using artificial cages as hosts. These cages have enabled the study of confinement effects in catalysis, which revealed a noticeable impact on both reaction rate and selectivity.[1] Recently, this concept has been developed towards organometallic chemistry, where the actual catalyst is an encapsulated metal complex. The potential of using anionic cages to form and encapsulate reactive gold complexes has been demonstrated.[2-4] However, due to poor synthetic accessibility, this concept has been limited to only one anionic cage (250 Å^3) and small model complexes (e.g. Me_3P-Au^+, 65 Å^3) with little catalytic relevance. In order to advance this concept towards catalytically relevant transformations, it is primordial to develop larger anionic cages.



OBJECTIVES In this context, the two main objectives of this project are: (1) Design, prepare and study new anionic supramolecular cages for catalytically relevant transition metal complexes, gold complexes in particular. (2) Develop the concept of transition metal catalysis in supramolecular cages: confinement-driven reactivity and selectivity. In the framework of the SCF d'Avenir, our initial results will be presented concerning the synthesis of novel anionic cages based on ligands such as cyclotricatechylene and truxene.



[1] Otte *ACS Catal.* **2016**, *6*, 6491.
[2] Reek et coll. *ChemCatChem* **2019**, *11*, 287.
[3] Scarso, Reek et coll. *J. Am. Chem. Soc*. **2011**, *133*, 2848.
[4] Bergman, Raymond, Toste et coll. *Science* **2015**, *350*, 1235.

Soft-chemistry approach for optimization of 2D-materials for electrochemical energy storage applications

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Energy storage is key in our daily life to power all our electronic tools as well as to store energy accumulated from intermittent sources such as wind and sun.[1] 2D materials are a material of choice for such application thanks to their highly accessible surface.

The role of chemistry in the optimization of material for energy application will be discussed through two examples. First, by using rational *soft chemistry* approach, we studied the synthesis and optimization of layered sodium transition metal-based oxides, with a general formula of Na_xMO_2 with specific metastable P-type structure for Na-ion batteries showing enhanced electrochemical storage properties.[2] Using co-precipitation techniques instead of the typical *solid-state* synthesis allows us to prepare various precursor in order to stabilize different targeted P-type lamellar oxides. (Fig. 1)

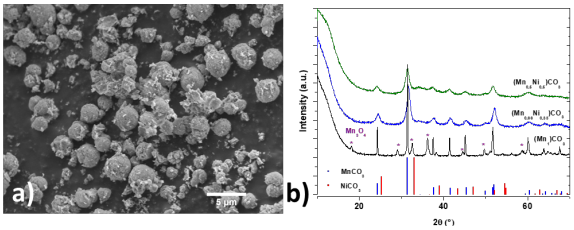

Figure 1. a) SEM image of $Mn_{0.5}Ni_{0.5}CO_3$ precursor prepared b) XRD pattern of a range of $Mn_{1-x}Ni_xCO_3$ precursors

In a second example, we will discuss how chemistry can help optimizaing another class of 2D-materials, Ti_3C_2 MXene, by modifying their structure in order to reach delamination into single or few layer sheets and therefore optimize their electrochemical performance. Recently, a study from our group reported on a molten salt synthesis of MXene material that allows, thanks to its termination group, enhanced electrochemical performance. This make them promising electrode materials for high-rate battery and hybrid devices such as Li-ion capacitor applications.[3]

In order to gain a better understanding at the nanoscale, a detailed study was conducted. We systematically studied and compared the performance of the pristine MXene to the treated delaminated ones in order to reach a higher specific surface area and a fast molecular transport of the ions. (Fig. 2)

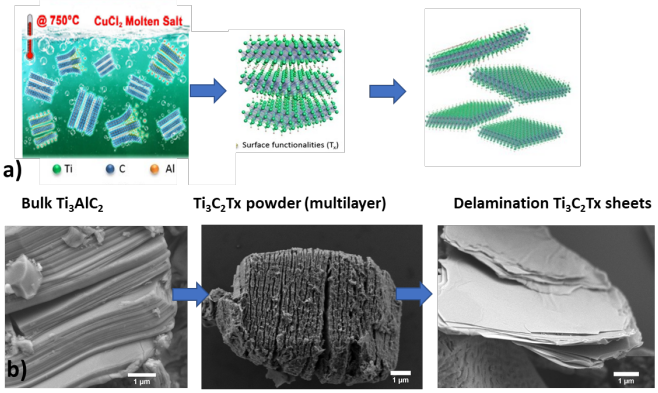

Figure 2. a) General scheme of the synthesis of delaminated MXene (adapted from [3,4]) b) SEM images of the corresponding samples

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1. P.Simon, Y. Gogotsi, Perspectives for electrochemical capacitors and related devices. Nat. Mater. 2020, 19, 1151–1163
2. C. Zhao, Q. Wang, Z. Yao, J. Wang, B. Sánchez-Lengeling, F. Ding, X. Qi, Y. Lu, X. Bai, B. Li, et al., Science 2020, 80, 370, 708-711.
3. Y. Li, H. Shao, Z. Lin, J. Lu, L. Liu, B. Duployer, P. O. Å. Persson, P. Eklund, L. Hultman, M. Li, K. Chen, X-H Zha, S. Du, P. Rozier, Z. Chai, E. Raymundo-Piñero, P-L Taberna, P. Simon and Q. Huang, Nat. Mater. 2020, 19, 894–899.
4. S. Yang, P. Zhang, F. Wang, A. G. Ricciardulli, M. R. Lohe, P. W. M. Blom, X. Feng, Angew. Chem. Int. Ed. 2018, 57, 15491.

Non-nucleoside DNA methyltransferase inhibitors as therapeutic compounds and pharmacological tools for epigenetic reprogramming in cancer

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DNA methylation is one of the main epigenetic mechanisms that regulate gene expression. The key players involved in this process are DNA methyltransferases (DNMTs) and DNA methylation pattern was shown to be altered in cancer cells [1]. In particular, hypermethylation of cytosines in CpG sites in tumour suppressor gene promoter regions silences their expression and favour tumour maintenance and proliferation [2]. Nucleoside DNMT inhibitors are currently used as anti-leukaemia treatment but show low stability and severe side effects due to their toxicity and their mechanism of action, *i.e.* incorporation in DNA. The use of non-nucleoside DNMT inhibitors could potentially bypass these drawbacks [3].

In our research for non-nucleoside DNMT inhibitors [4], our group has chemically optimised flavonoid compound firstly identified by enzymatic screening [5]. We showed that these 3-halo-3-nitroflavanones present interesting DNMT inhibition activities against the human catalytic DNMT3A isoform (DNMT3A-c) by a fluorescent-based assay. Moreover, their ability to inhibit cytosine methylation in cells was assessed by employing a cytomegalovirus promoter-controlled luciferase reporter gene transfected in KG-1 cell line. These data, together with compounds stability and cytotoxicity evaluation in KG-1 and HCT116 cells, provided 3-bromo-3-nitroflavanone as best candidate with increased potency compare to the control inhibitor. It showed (a) an EC_{50} of 3.2 ± 1.1 µM on *h*DNMT3A-c, (b) a 6-fold induction of luciferase in cells at 5 µM, (c) improved stability, and (d) no relevant cytotoxicity at the effective concentration.

Therefore, 3-bromo-3-nitroflavanones can be considered as interesting starting point towards epigenetic reprogramming of cancer cells, standing out as non-cytotoxic DNMT inhibitors that can be optimised to be envisaged as candidates for anticancer therapeutic agents. Current research is now directed to further increase compound stability and potency, and establish robust structure-activity relationships. Moreover, 3-bromo-3-nitroflavanones could pave the way for the development of interesting pharmacological tools to better understand the role of DNMTs in cancer through chemical biology strategies [6].

References

[1] Bestor TH *et al.* (1994) Dev Genet 15: 458-462.

[2] Baylin SB (2005) Nat Clin Pract Oncol 2 (S1): S4-S11.

[3] Lopez M *et al.* (2016) Adv Exp Med Biol: 431-473.

[4] Pechalrieu D *et al.* (2020) Eur J Med Chem 186: 111829.

[5] Ceccaldi A *et al.* (2011) ChemBioChem 11: 1337-1345.

[6] Pechalrieu D *et al.* (2020) 15: 952-961.

Single atom catalysts for hydroformylation reaction: a profitable alternative to conventional catalysts.

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Hydroformylation (HF) reaction is one of the most relevant homogeneously catalyzed industrial process; it produces aldehydes, from olefins and syngas (CO and H_2)[1, 2]. Aldehydes are widely employed in the production of chemicals such as surfactants or plasticizers. Conventional catalysts are composed by Co- or Rh-based complexes usually modified with phosphines and phosphites in the coordination sphere [1, 2]. Even if biphasic systems have been implemented in industry for HF of light α-olefinsn still the recovery from the reaction medium is the mayor concern of this approach. Rhodium single atom catalyst (SACs), have recently demonstrated to be a remarkable heterogeneous catalysts for HF[3].

This work focuses on the development of stable and active Co (I)-based SACs for HF. Owing to its two-dimensional structure, its ability to host other heteroatoms in its structure[4], support metals[5] and its low cost and straightforward preparation, graphitic carbon nitride is used as support. The rich pyridine-like nitrogen (see ***Fig 1***) can favor the metal absorption and its stabilization, thus, prevent them from leaching or sintering. Its ability to stabilize metal atoms was pointed out by the highly dispersed Rh atoms previously reached for Rh (III)-g-C_3N_4 (***Fig 2 (a)***). The addition of heteroatoms to the structure, typically boron, sulfur and phosphorus, can improve the stability of the metals supported on it. According to that and considering the use of phosphorus ligand in conventional HF catalysts, phosphorus-doped g-C_3N_4 as support is also considered in this study. The color change along with the shift to lower 2θ compared to g-C_3N_4 discerned by XRD for P-doped samples (*x*P-CN) proved the incorporation of P into g-C_3N_4 structure (***Fig 2(b)***). Additionally, the enhancement in the specific surface area of g-C_3N_4, from 5.4 to 7.8 $m^2 \cdot g^{-1}$, through P insertion is observed. Co-g-C_3N_4 prepared straightforwardly by impregnation of a Co (I) precursor is further tested in HF reaction of several olefins.

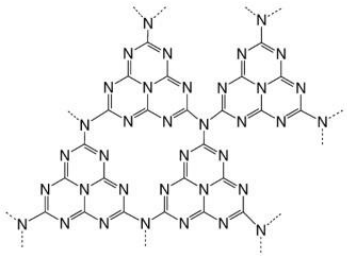

Fig 1. g-C_3N_4 network

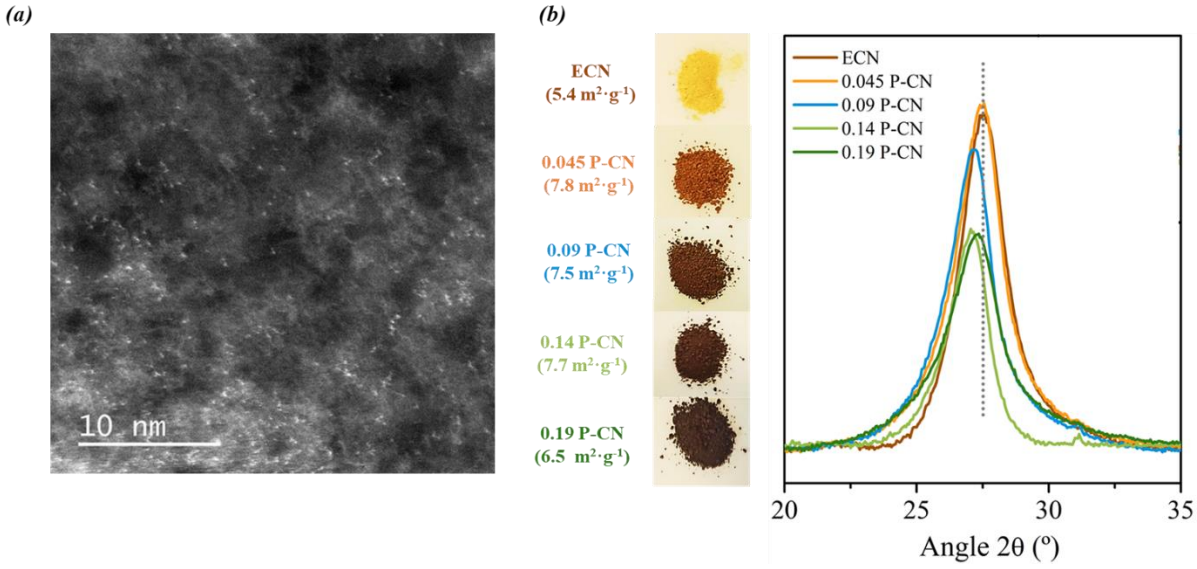

Fig 2. (a) TEM image of Rh-SAC and ***(b)*** Specific surface area and diffractograms of xP-CN (x=0-0.19)

1. M. Beller, B. Cornils, C. D. Frohning and C. W. Kohlpaintner, *J. of Mol. Catal A: Chemical*, 1995, **104**, 17-85.
2. D. M. Hood, R. A. Johnson, A. E. Carpenter, J. M. Younker, D. J. Vinyard and G. G. Stanley, *Science*, 2020, **367**, 542.
3. J. Amsler, B. B. Sarma, G. Agostini, G. Prieto, P. N. Plessow and F. Studt, *J. Am. Chem. Soc*, 2020, **142**, 5087-5096.
4. S. Kumar, M. B. Gawande, J. Kopp, S. Kment, R. S. Varma and R. Zbořil, *ChemSusChem*, 2020, **13**, 5231-5238.
5. Chen, Z.; Vorobyeva, E.; Mitchell, S.; Fako, E.; Ortuno, M. A.; Lopez, N.; Collins, S. M.; Midgley, P. A.; Richard, S.; Vile, G.; Perez-Ramirez, *J. Nat. Nanotechnol.* 2018, ***13***, 702-707

BIO-ACTIVE FUNCTIONAL LIPIDS: SYNTHESIS OF TERMINAL PRIMARY DIALKYNYLCARBINAMINES

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Summary:

Natural acetylenic products are scarce in Nature, due to the intrinsic chemical reactivity of the triple bonds, but constitute a singular biological potential deserving to be explored. Among known acetylenic natural products, lipidic alkynylcarbinols (LACs), such as (*S,E*)-icos-4-en-1-yn-3-ol (extracted from *Cibrochalina vasculum*) are particularly promising as antitumor agents.[1] Preliminary experimental works led to the design of unnatural lipidic dialkynylcarbinols (DACs, or "DACols"),[2] as highly cytotoxic agents against human HCT116 tumor cells (IC_{50} = 90 nM), two orders of magnitude more potent than the (*S,E*)-icos-4-en-1-yn-3-ol reference natural product.[3] On the basis of structural originality, the bioisosterism strategy was envisaged by substituting the hydroxyl group of DACols by an amino group in the corresponding DACamines (Fig. 1).

Few examples of functional propargylic primary amines are reported in the literature and the preparation of bis-propargylic versions, *i.e.* dialkynylcarbinamines (DACamines), is by itself a considerable challenge in organic synthesis. In addition, this structural modulation could lead to bio-inspired compounds with yet unexplored pharmacological properties. In this context, several pathways have been envisaged to obtain DACamine targets (with R = H or R ≠ H), such as reductive amination of a ketone precursor or nucleophilic addition to an *in situ*-generated imine. The most effective way to synthesize terminal primary DACamines (Fig. 1, R = H) is disclosed to rely on the *in situ* preparation of the *N*-Boc imine derivative from the RCH(NHBoc)($NBoc_2$) diaminal intermediate.[4] The final product, obtained as a hydrochloride salt, showed cytotoxic activity in the micromolar range on HCT116, U2OS and HAP1 cells.

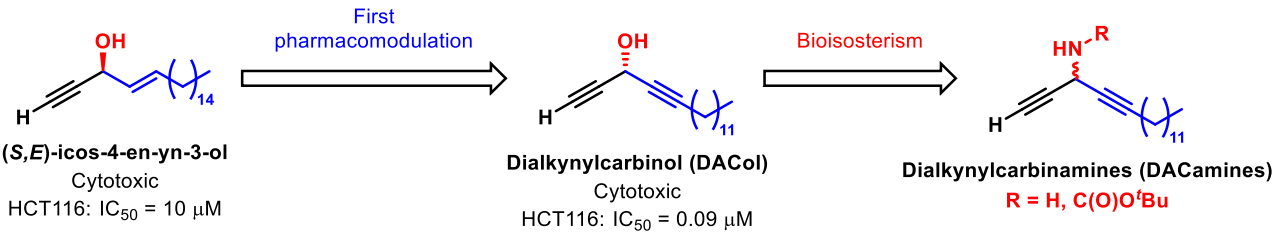

Fig. 1 Extended pharmacomodulation of natural alkenyl-alkynylcarbinol.

References:

1. Gunasekera, S. P.; Faircloth, G. T. *J. Org. Chem*. **1990**, *55*, 6223-6225.
2. El Arfaoui, D.; Listunov, D.; Fabing, I.; Oukessou, M.; Frongia, C.; Lobjois, V.; Samson, A.; Ausseil, F.; Ben-Tama, A.; El Hadrami, E. M.; Chauvin, R.; Genisson, Y. *ChemMedChem* **2013**, *8*, 1779-1786.
3. Listunov, D.; Joly, E.; Rullière, P.; Gaspard, H.; Bernardes-Genisson, V.; Genisson, Y.; Maraval, V.; Chauvin, R. *Synthesis* **2018**, *50*, 3114-3130, and references therein.
4. Kano, T.; Kobayashi, R.; Maruoka, K. *Angew. Chem. Int. Ed.* **2015**, *54*, 8471-8474.

Selective Reductive Dimerization of CO_2 into Glycolaldehyde

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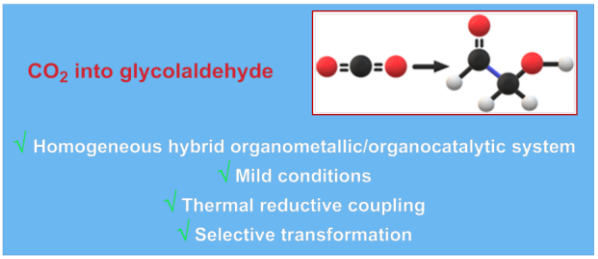
CO_2 is a stable, non-toxic, abundant molecule, and also a significant long-lived greenhouse gas in Earth's atmosphere. Its use as a starting material to obtain more complex C_n products is a sustainable alternative to the use of fossil fuels as C_n source. Additionally, if large scale use of CO_2 could be implemented in the future, CO_2 capture and utilization would be a way to mitigate CO_2 atmospheric concentration. However, CO_2 reductions to $C_{n>1}$ products are much less developed than to C_1 products due to the intrinsic difficulty of combining two individually challenging steps in a single process: CO_2 reduction and C−C bond formation. As a consequence, further developments of CO_2 utilization as the C_n source face two main issues: selectivity and limited scope of products.[1] Besides oxalate, acetate, and related products, most of the obtained compounds are highly reduced products: aliphatic hydrocarbons, olefins, and alcohols. Nevertheless, if one wants to use CO_2 as a sustainable C_n source, less reduced polyoxygenated compounds would be highly desirable because such compounds exhibit appealing molecular complexity.

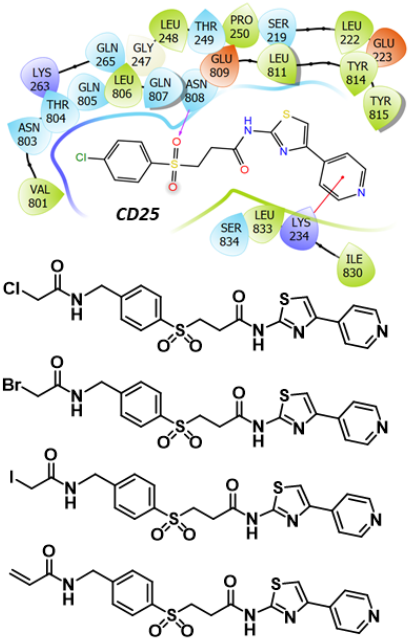
In the field of CO_2 reduction, hydrosilane and hydroborane reductants developed the reduction of CO_2 to the formaldehyde level with the selective generation of bis(silyl) and bis(boryl)acetal compounds. These reactive intermediates were proven particularly versatile for the synthesis of a large scope of different C_1 products.[2]

In this communication, we present the first catalytic system able to generate selectively glycolaldehyde from CO_2 in a two step strategy: 1) organometallic reduction of CO_2 into formaldehyde and 2) organocatalyzed C-C bond formation. Both carbon atoms of glycolaldehyde arise from CO_2 as proven by a labelling experiment with $^{13}CO_2$. [3]



References
[1] a) G. Prieto, *ChemSusChem* **2017**, *10*, 1056; b) F. Marques Mota; D. H. Kim, *Chem. Rev.* **2019**, *48*, 205.
[2]a) M. Rauch, G. Parkin, *J. Am. Chem. Soc.* **2017**, *139*, 18162, b) G. Jin, C. G. Werncke, Y. Escudié, S. Sabo-Etienne, S. Bontemps, *J.* Am. Chem. Soc. **2015***, 137*, 9563, c) X. Frogneux, E. Blondiaux, P. Thuéry, T. Cantat, *ACS Catal.* **2015**, *5*, 3983.
[3] D. Zhang, C. Jarava-Barrera, S. Bontemps, *ACS Catal*. **2021***,11*, 4568.

Research Title: Development of Covalent spCas9 inhibitors for gene editing regulation: CRISPR-associated nucleases (e.g., SpCas9) are RNA-guided DNA endonuclease that pair with guide RNA (gRNA) to recognizes the target DNA *via* a protospacer adjacent motif (PAM) sequence and base-pairing of the target DNA with gRNA. CRISPR-associated nucleases are being developed for numerous applications in biotechnology, biomedical research, and gene therapy. The need for precise dose and temporal control of CRISPR-associated nucleases in these applications has created a demand for inhibitory anti-CRISPR molecules. Dose and temporal controls, which are required of all therapeutic agents, are particularly important for SpCas9 as off-target effects, undesirable chromosomal translocations, and genotoxicity are observed at elevated levels and prolonged activity. We identified nuclease-based SpCas9 inhibitors CD25 with Kd: 500 nM as well as inhibitors that block all three enzymes (SpCas9, SaCas9, and Cpf1). In my postdoc tenure, I have improved the binding affinity of the cas9 inhibitor (CD25) by incorporating reactive warhead in the molecule. The modified CD25 can binds with spCas9 covalently in the binding pocket and exerts better cas9 inhibition, which can be useful to regulate the gene editing system. Our goal is to propel the development of therapeutic applications of genome editing technologies using chemical biology based approaches.



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Postdoctoral Researcher: Broad Institute of MIT & Harvard (USA)
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½ journée « SCF d'Avenir » – Région OCCITANIE

DESIGN AND SYNTHESIS OF ARTIFICIAL MOLECULAR MACHINES: MUSCLE & MOTORS

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Keywords: artificial molecular machines; mechanically interlocked molecules; rotaxane; molecular motors; organometallic compounds

Abstract: The field of artificial molecular machines (AMMs) – recognized in 2016 by the Chemistry Nobel Prize[1] – has provided the literature with a plethora of elegant and creative molecules over the past 40 years. A molecular machine can be described as an assembly of molecular components able to perform work – i.e. execute a task – when energy is added.[2] Beyond our ability to produce such complex molecules, the main challenge lies in programming these architectures so they can achieve a specific function.[3] Focusing on how to control movement to perform work, the field is evolving towards various applications. Notably developing new classes of materials based on redox-active molecular shuttles to be implemented in smart responsive materials. For this purpose, the use of molecular muscles able to induce large-amplitude contractile motions in response to an external stimulus could result in conformational changes if embedded in polymeric chains. Another current challenge resides in achieving controllable movement with individual molecular machines on surfaces in order to study the laws describing their motion. Which, eventually, could be harnessed, on a larger population of machines to be translated into macroscopic work. In this presentation will be discussed the design and synthesis two types of artificial molecular machines:

- An artificial molecular muscle (past work – postdoctoral research) exhibiting machine-like characteristics. It consists in a bistable [2]rotaxane actuated by a redox stimulus (**Figure 1a**) in which a long-range translational movement (i.e. of the mechanically interlocked ring) induces a large-amplitude orthogonal expansion or contraction.[4]
- Desymmetrized molecular motors (present and future work) to be studied on surface (**Figure 1b**). Through the functionalization by chemoselective cross-coupling of such Ru-complexes[5] we aim to generate a dipole moment on the rotor unit. Ultimately, we aim to study the motion of a series of such molecules (i.e. varying the dipole moments) at the single molecule scale on metallic surfaces when applying an electric field.

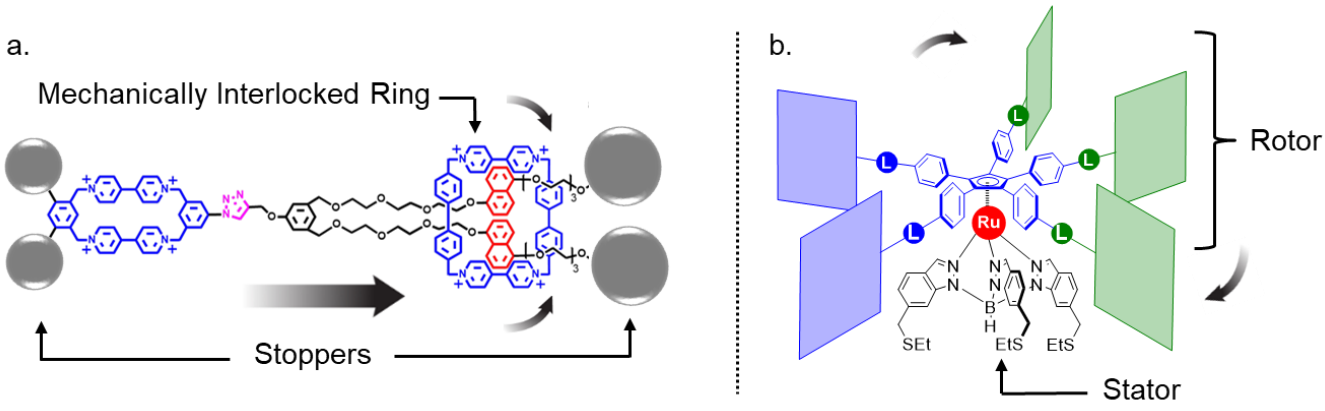

Figure 1. (a) Redox-controlled bistable [2]rotaxane (oxidized state). (b) Prototype of a desymmetrized molecular motor based on star-shaped ruthenium complexes.

References:

1. Feringa, B.L.; Sauvage, J.-P.; Stoddart, J. F., *Angew. Chem., Int. Ed.* **2017**, *56*, 11060−11125 (Nobel Lectures)
2. Erbas-Cakmak, S.; Leigh, D. A.; McTernan, C. T.; Nussbaumer, A. L., *Chem. Rev.* **2015**, *115*, 10081–10206
3. Balzani, V.; Credi, A.; Venturi, M., *Molecular Devices and Machines – A journey into the Nanoworld*, WILEY, **2006**
4. Dumartin, M.; Lipke, M. L.; Stoddart, J. F., *J. Am. Chem. Soc.* **2019**, *141*, 18308−183017
5. Erbland, G.; Abid, S.; Gisbert, Y.; Saffon-Merceron, N.; Hashimoto, Y.; Andreoni, L.; Guérin, T.; Kammerer, C.; Rapenne, G., *Chem. Eur. J.* **2019**, *25*, 16328−16339

Vers la Synthèse Totale de la Tautomycétine

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Le domaine de la synthèse totale de produits naturels constitue une source d'inspiration pour les chimistes organiciens. En effet, la plupart de ces molécules possèdent des activités biologiques prometteuses et sont, par conséquent, associées à des enjeux sociétaux. Par ailleurs, les produits naturels ont souvent des structures chimiques complexes et leur synthèse au laboratoire représente un réel défi.[1,2]

Un des axes de recherche développé par notre équipe consiste en la synthèse totale de produits naturels biologiquement actifs.[3] C'est dans ce contexte que nous nous sommes intéressés à la tautomycétine (TTN) (Figure 1), un polyketide naturel isolé en 1989 à partir de souches *Streptomyces griseochromogenes*. Ce produit naturel possède, en plus de sa structure chimique unique, des activités biologiques prometteuses. Nos efforts visant la première synthèse totale de ce produit naturel seront présentés et discutés.[4]

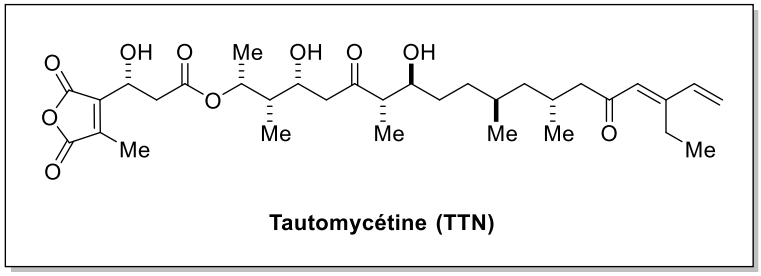

Figure 1. Structure de la Tautomycétine

[1] Pour un livre récent dans le domaine, voir: *Total Synthesis of Bioactive Natural Products,* 1st Edition by G. Brahmachari, Elsevier, **2019**. Voir également: *Molecules that Changed the World: A Brief History of the Art and Science of Synthesis and its Impact on Society* by K. C. Nicolaou and T. Montagnon, Wiley-VCH, **2008**.

[2] Pour une sélection de revues récentes, voir: a) K. C. Nicolaou, S. Rigol *Nat. Prod. Rep*. **2020**, *37*, 1404; b) L. Li, Z. Chen, X. Zhang, Y. Jia *Chem. Rev.* **2018**, *118*, 3752; c) D. J. Newman, G. M. Cragg *J. Nat. Prod.* **2016**, *79*, 629.

[3] a) L. Pantel *et al. Mol. Cell* **2018**, *70*, 83; b) M. Sarciaux, L. Pantel, C. Midrier, M. Serri, C. Gerber, R. M. de Figueiredo, J.-M. Campagne, P. Villain-Guillot, M. Gualtieri, E. Racine *J. Med. Chem.* **2018**, *61*, 7814; c) K. Spielmann, R. M. de Figueiredo, J.-M. Campagne *J. Org. Chem*. **2017**, *82*, 4737; d) S. Drissy-Amraoui, M. S. T. Morin, C. Crévisy, O. Baslé, R. M. de Figueiredo, M. Mauduit, J.-M. Campagne *Angew. Chem. Int. Ed.* **2015**, *54*, 11830; e) G. A. Zarate-Ruiz, R. M. de Figueiredo, G. Niel, J.-M. Campagne *Synlett* **2012**, *23*, 219.

[4] D. Pereira de Sant'Ana, C. de Oliveira Rezende Jr, J.-M. Campagne, L. C. Dias, R. M. de Figueiredo *J. Org. Chem*. **2019**, *84*, 12344.