EDSC
École Doctorale des Sciences Chimiques

Université de Strasbourg

JOURNEE DES DOCTORANTS EN CHIMIE 2023

Jeudi, 30 novembre 2023

Programme et Résumés

Collège Doctoral Européen
Campus de l'Esplanade

http://ed.chimie.unistra.fr/

AVANT-PROPOS

La Journée des doctorants en chimie en est à sa **17ème édition**.

Pour les doctorants déjà engagés dans le cursus doctoral, cette journée leur permet d'exposer leurs travaux de recherche.

Pour les doctorants de 1ère année, elle fait office de journée de rentrée et leur donne l'occasion :

- D'avoir un aperçu des recherches menées dans les laboratoires de chimie de l'Université de Strasbourg et du CNRS,
- De nouer des contacts avec les doctorants plus anciens, notamment ceux d'autres équipes et d'autres campus,
- De poser toutes les questions concernant le déroulement de la formation doctorale en chimie ainsi que l'après-thèse.

Je tiens à remercier toutes les personnes qui ont accepté de présenter leurs travaux de recherche lors de cette journée ainsi que celles qui ont fait des Journées précédentes un succès.

Mes remerciements vont tout particulièrement à Nathalie Kostmann pour sa contribution centrale dans l'organisation de la JDC 2023.

Gilles ULRICH

Directeur de l'EDSC

Journée des Doctorants en Chimie 2023

30 novembre 2023 - Amphithéâtre du CDE

PROGRAMME

	Programme de la matinée
8 h 00 - 8 h 20	**Ouverture** Exposé de rentrée de Gilles ULRICH, directeur de l'EDSC / Discussion avec les doctorants
8 h 20 - 8 h 30	**Présentation "programme de mentorat aux doctorant.es"** Exposé de Valérie CAPS et de Cécilia MENARD-MOYON
8 h 30 - 8 h 45	**Présentation "SCF-ALSACE"** Exposé de stéphane CHASSAING
8 h 45 - 8 h 55	**Présentation de l'Association ADDAL par Katia TOUAHRI** ***(doctorant UMR 7177)***
8 h 55 - 9 h 50	**Conférence** *" Advances in the field of bioelectrochemistry and surface enhanced IR spectroscopies for the study of the reaction of enzymes from the respiratory chain "* **Pr. Petra HELLWIG**
9 h 50 - 10 h 05	**Pause Café**
	Communications orales
10 h 05 - 10 h 25	**KARABIYIKLI Deniz**
10 h 25 - 10 h 45	**PIEJKO Maciej**
10 h 45- 11 h 05	**WERNER Emilie**
11 h 05 - 11 h 25	**ZIMMERMANN Joris**
11 h 25 - 11 h 45	**COURSEYRE Manon**
11 h 45 - 12 h 30	**Pause Repas**
12 h 30 - 12 h 50	**MOREIRA-PEREIRA Thiago**
12 h 50 - 13 h 10	**ROGNAN Charlou**
13 h 10 - 13 h 30	**CASAS Jaison**
13 h 30 - 13 h 50	**TEIXEIRA Michaël**
13 h 50 - 14 h 10	**PEPE Lucie**
14 h 10 - 14 h 20	**Pause Café**
14 h 20 - 14 h 40	**GOMMENGINGER Clément**
14 h 40 - 15 h 00	**MOGET Nicolas**
15 h 00 - 15 h 20	**HIRSCHLER Emilie**
15 h 20 - 15 h 40	**ZHANG Jinming**
15 h 40 - 16 h 00	**GOLUSHKO Andrei**
16 h 00 - 16 h 10	**Pause**
16 h 10 - 16 h 30	**DOUMI Iman**
16 h 30 - 16 h 50	**GAO Zhengfeng**
16 h 50 - 17 h 10	**ZHURAVLOVA Anna**
17 h 10 - 17 h 30	**SCHWOERER Célia**
17 h 30 - 17 h 50	**LOCQUET Pierre**

TITRES DES

COMMUNICATIONS ORALES

LISTE DES COMMUNICATIONS ORALES

(1) Development of Mechanochemical reaction conditions for Buchwald-Hartwig amination reaction
Deniz Karabiyikli, Dr Martine Schmitt, Dr Frédéric Bihel
Laboratoire d'Innovation Thérapeutique (UMR7200) Faculté de Pharmacie, 74 route du Rhin, 67401 Illkirch, cedex, FRANCE

(2) Solvent Polarity and Dispersion Forces under Vibrational Strong Coupling
Maciej Piejko, Bianca Patrahau, Kripa M. Joseph, Cyprien Muller, Eloïse Devaux, Thomas W. Ebbesen, Joseph Moran
University of Strasbourg, CNRS, ISIS and icFRC, 8 Allée Gaspard Monge, 67000 Strasbourg, France

(3) Metal/ADP complexes promote phosphorylation of ribonucleotides[1]
Emilie Werner[a], Silvana Pinna[a], Robert J. Mayer[a], and Joseph Moran[a]
[a] Institut de Science et d'Ingénierie Supramoléculaires, Université de Strasbourg & CNRS (UMR 7006), 8 Allée Gaspard Monge 67000 Strasbourg, France

(4) A Single Phosphorylation Mechanism in Early Metabolism – The Case of phosphoenolpyruvate[1]
Joris Zimmermann[a], Robert J. Mayer[a], and Joseph Moran[a]
[a] Institut de Science et d'Ingénierie Supramoléculaires, Université de Strasbourg, CNRS (UMR 7006), 8 Allée Gaspard Monge 67000 Strasbourg, France

(5) Immuno-PET imaging of the tumor-associated an6gen CD38 in the case of mul6ple myeloma
Manon Courseyre[1,2*], Rania Benazza[3], Oscar Hernandez[3], Sarah Cianferani[3], Yannick Guilloux[4], Michel Cherel[4], Tristan Martin[2], Alexandre Detappe[2], Aline Nonat[1]
[1] Équipe Synthèse pour l'Analyse (SYNPA), Ins>tut Pluridisciplinaire Hubert Curien (IPHC), CNRS UMR 7178, Strasbourg, France
[2] Laboratoire Nanotransla>onnel, Ins>tut de Cancérologie Strasbourg-Europe (ICANS), Strasbourg, France
[3] Équipe Spectrométrie de Masse BioOrganique (LSMBO), Ins>tut Pluridisciplinaire Hubert Curien (IPHC), CNRS UMR 7178,
Strasbourg, France
[4] Équipe Oncologie Nucléaire, Centre de Recherche en cancérologie et Immunologie Nantes Angers (CRCI2NA), Nantes, France

(6) Design and synthesis of 1,2,4-triazoles: structural exploration in the inhibition of GSK-3β for the treatment of Alzheimer's Disease
Thiago Moreira Pereira[1,3], Natalia Nadur[2], Angela de Simone[4], Elisa Uliassi[3], Maria Laura Bolognesi[3], Arthur Eugen Kümmerle[2], Martine Schmitt[1]
[1] Medicinal Chemistry Department, UNISTRA, Strasbourg, France
[2] Department of Organic Chemistry, UFRRJ, Rio de Janeiro, Brazil
[3] Department of Pharmacy and Biotechnology, UNIBO, Bologna, Italy
[4] Department of Drug Science and Technology, UNITO, Torino, Italy

(7) Design and Synthesis of Original N,S-containing Scaffolds to Access Complex Heterocycles
Charlou Rognan, Pierre Locquet, Nicolas Girard*, Mihaela Gulea*
Laboratoire d'Innovation Thérapeutique, LIT UMR 7200, Université de Strasbourg, CNRS, F-67000 Strasbourg

(8) Multidimensional Coordination Polymers based on the alloxazine core: Properties and Applications
Jaison Casas*(a), Dr. Abdelaziz Jouait[a], Pr. Sylvie Ferlay[a]
[a] Laboratoire de Synthèse et Fonctions des Architectures Moléculaires – UMR 7140

(9) Impact of Deep Eutectic Solvents on Metal-Organic Framework Synthesis and Properties
Michaël Teixeira[a], Renata A. Maia[a], Pauline André[a], Benoît Louis[b], Stéphane A. Baudron[a]
[a] UMR 7140, University of Strasbourg-CNRS, 4 rue Blaise Pascal, 67000 Strasbourg, France
[b] UMR 7515, University of Strasbourg-CNRS, 25 rue Becquerel, 67087 Strasbourg, France

(10) Quantum transport of informa2on in molecular open-quantum systems
Lucie Pepe
Laboratoire de Chimie Quantique de Strasbourg (LCQS) - Institut de Chimie de Strasbourg

(11) TBAF-Promoted Carbanion-Mediated Sulfonamide Cyclization of CF3-substituted N-allenamides: an Access to Fluorinated γ-Sultams

Clément Gommenginger[a], Yongxiang Zheng[a], Daniele Maccarone[b], Ilaria Ciofini[b] and Laurence Miesch[*a]

[a] Équipe de Synthèse Organique et Phytochimie, Université de Strasbourg, CNRS-UdS UMR 7177, 4, rue Blaise Pascal CS 90032, 67081 Strasbourg, France

[b] Chimie ParisTech, PSL University, CNRS, Institute of Chemistry for Life and Health Sciences, Chemical Theory and Modelling Group, F-75005 Paris, France

(12) Dévelopment of a new méthodology to access trifluoromethoxylated sulfoxides

Nicolas Moget, Jérémy Saiter, Armen Panossian, Gilles Hanquet*, and Frédéric Leroux[*]

LIMA - UMR 7042 - Université de Strasbourg, CNRS, Université de Haute-Alsace, Ecole Européenne de Chimie, Polymères et Matériaux (ECPM), 25 rue Becquerel, 67000 Strasbourg – France

(13) Use of chemical cross-link coupled to mass spectrometry for structural elucidation of a peptide complex with antimicrobial properties

Emilie Hirschler[1], Elise Glattard[2], Burkhard Bechinger[2], Emmanuelle Leize Wagner[1], Noelle Potier[1]

[1] Laboratoire de spectrométrie de masse des interactions et des systèmes, UMR 7140

[2] Laboratoire de biophysique des membranes et RMN, UMR 7177

(14) Operando X-ray photoelectron spectroscopy study of Ni/YSZ solid oxide cell cathode electrodes
during H2O electroreduction

J Zhang, M Barreau, D. Teschner, M. Haevecker and S Zafeiratos[*]

(15) Triarylamine-based macrocycle for tubular self-assembly: Towards supramolecular solenoid

Andrei Golushko, Andreas Vargas Jentzsch, Shoichi Tokunaga, Emilie Moulin, Nicolas Giuseppone

SAMS, Institute Charles Sadron, University of Strasbourg

(16) CuII-Dp44mT reactivity and selectivity towards biologically relevant thiols

Iman Doumi[a], Lukas Lang[b], Bertrand Vileno[a], Marcel Deponte[b], Peter Faller[a]

[a] Institut de Chimie (UMR 7177), University of Strasbourg – CNRS, 4 rue Blaise Pascal, 67000 Strasbourg, France.

[b] Fachbereich Chemie & Landesforschungszentrum OPTIMAS, RPTU Kaiserslautern, Erwin-Schrödinger Straße 54, D-67663, Kaiserslautern, Germany

(17) Graphene Oxide Conjugated with Antimicrobial Peptides Against Bacterial Infections

Zhengfeng Gao[1], Karahan Hüseyin Enis[1], Lucas Jacquemin[1], Oliver Chaloin[1], Yuta Nishina[2], Alberto Bianco[1]

[1] CNRS, Immunology, Immunopathology and Therapeutic Chemistry, UPR3572, University of Strasbourg, ISIS, 67000 Strasbourg, France

[2] Research Core for Interdisciplinary Sciences, and Graduate School of Natural Science and Technology, Okayama University, 3-1-1 Tsushima-naka, Kita-ku, Okayama 700-8530, Japan

(18) Highly sensitive and selective chemical sensing with functionalized 2D MoS2: a supramolecular approach

Anna Zhuravlova, Antonio Gaetano Ricciardulli, Dawid Pakulski, Adam Gorczyński, Adam Kelly, Jonathan N. Coleman, Artur Ciesielski, and Paolo Samorì

Université de Strasbourg, CNRS, ISIS, 8 allée Gaspard Monge, 67000 Strasbourg, France

(19) Captodative 2-cyanoenamides as innovative synthons to access original heterocyclic structures.

Célia Schwoerer, Pierre Hansjacob, Frédéric R. Leroux and Morgan Donnard[*]

LIMA – UMR 7042, Université de Strasbourg, CNRS, Université de Haute-Alsace, ECPM, 25 rue Becquerel, 67000 Strasbourg – France

(20) Toward the rebirth of the aromatic Cope rearrangement

Pierre Locquet[1], Emanuel Riguet[*,2] and Aurelien Blanc[*,1]

[1] Laboratoire de Synthèse et Réactivité et Catalyse, Institut de Chimie de Strasbourg, UMR 7177, 4 rue Blaise Pascal, Strasbourg, France

[2] Méthodologie en Synthèse Organique, Institut de Chimie de Reims, UMR 7312, Campus Moulin de la Housse, Reims, France

CONFERENCE

"Advances in the field of bioelectrochemistry and surface enhanced IR spectroscopies for the study of the reaction of enzymes from the respiratory chain"

Pr. Petra HELLWIG,
Chimie de la matière complexe (UMR 7140)

Advances in the field of bioelectrochemistry and surface enhanced IR spectroscopies for the study of the reaction of enzymes from the respiratory chain

Petra Hellwig and colleagues

Laboratoire de Bioélectrochimie et Spectroscopie, UMR 7140, Chimie de la Matière Complexe, Université de Strasbourg – CNRS 4, rue Blaise Pascal, 67081 Strasbourg, France ; hellwig@unistra.fr

Although the architectures of several membrane proteins in respiration as well as the basic chemical reactions have been described, the interactions on molecular level, the diversity and efficiency of the reaction mechanisms in bacterial systems, are under debate. Electrochemical and spectroscopic experiments will be presented that have been developed to study coupled electron and proton reactions, identify the contribution of individual amino acids, study the reactivity towards small molecules and, importantly, correlate it with the microenvironment of the cofactors. Th main projects will be presented:

1. Electrocatalytic studies on different membrane proteins from the respiratory chain, that demonstrate a different reactivity towards the substrate and the adaptation of the bacteria to the respective environment. [1, 2]
2. Surface enhanced IR spectroscopies (SEIRAS), that allow studies on the reactivity down to the picomolar level and on protein monolayers. Recent advances in the creation of ideal surfaces for SEIRAS will be given. [3-5]
3. Finally, the possibility to tailor nanostructures to enhance individual infrared signals will be demonstrated and the perspectives of these techniques for other fields of chemistry and biology discussed.[6]

Recent references

1. Safarian, S., Hahn, A., Mills, DJ., Radloff, M., Eisinger, ML., Nikolaev, A., Meier-Credo, J., Melin, F., Miyoshi, H., Gennis, RB., Sakamoto, J., Langer, JD., Hellwig, P., Kühlbrandt, W., Michel, H., Active site rearrangement and structural divergence in prokaryotic respiratory oxidases (2019) ***Science*** 366(6461):100-104.
2. Nikolaev, A., Safarian, S., Thesseling, A., Wohlwend, D., Friedrich, T., Michel, H., Kusumoto, T., Sakamoto, J., Melin, F., Hellwig P. (2021) ***Biochim Biophys Acta Bioenerg.*** 1862 148436.
3. Grytsyk, N., Santos Seiça, A.F., Sugihara, J., Kaback, H.R., Hellwig, P. 'Arg302 governs the pKa of Glu325 in LacY' (2019) ***Proc. Natl. Acad. Sci. U.S.A***. 116, 4934-4939.
4. Santos Seiça, A.F., Iqbal, M.H., Carvalho, A., Choe, J-Y., Boulmedais, F. and Hellwig, P. Study of Membrane Protein Monolayers Using Surface-Enhanced Infrared Absorption Spectroscopy (SEIRAS): Critical Dependence of Nanostructured Gold Surface Morphology (2021) ACS Sensors, doi.org/10.1021/acssensors.1c00238
5. Santos Seica, A.F., Schimpf, J., Friedrich, T., Hellwig, P. Visualizing the movement of the amphipathic helix in the respiratory complex I using a nitrile infrared probe and SEIRAS. (2020) FEBS Lett. 594(3):491-496.
6. Omeis, F., Santos Seica, A.F., Bernard, R., Javahiraly, N., Majjad, H., Moss, D., Hellwig, P., Following the Chemical Immobilization of Membrane Proteins on Plasmonic Nanoantennas Using Infrared Spectroscopy (2020) ACS sensors 5 (7), 2191-2197.

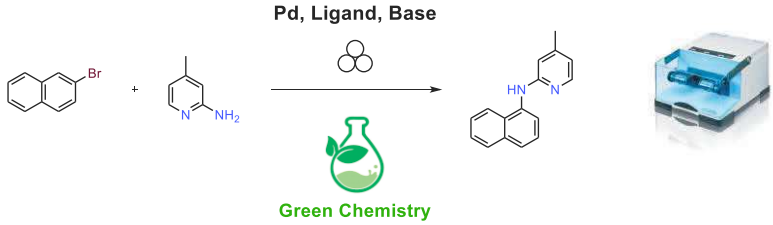
RESUMES DES

COMMUNICATIONS ORALES

Development of Mechanochemical reaction conditions for Buchwald-Hartwig amination reaction

Deniz Karabiyikli, Dr Martine Schmitt, Dr Frédéric Bihel
Laboratoire d'Innovation Thérapeutique (UMR7200) Faculté de Pharmacie, 74 route du Rhin, 67401 Illkirch, cedex, FRANCE
dkarabiyikli@unistra.fr, mscmitt@unistra.fr, fbihel@unistra.fr

Solvents are acknowledged to hold significant environmental impact, accounting up to 90% of the mass utilization in a given chemical reaction. As one of the largest users of organic solvents, the pharmaceutic industry, have made it a priority these last 20 years to make their production greener by the minimization, replacement, recycling or removal of said solvents[1].
In medicinal chemistry, transition metal catalysed coupling reactions play an important role by facilitating diverse bond formations[2]; such as the formation of an aromatic carbon-nitrogen bond through the Buchwald-Hartwig amination reaction[3]. However effective, these reactions necessitate the use of organic solvents, making them costly to the environment, and making the scale-up pharmaceutical manufacturing disadvantageous.
Mechanochemistry[4], is the discipline based on the use of mechanical energy generated through milling or grinding for chemical transformation. It has experienced a significant comeback thanks to its applicability to green chemistry[5]. Through avoiding the use of bulk solvents, solvent-free mechanochemical reactions provide safer reaction conditions for the environment and profitable conditions for industrial applications.
Although the use of various trans-metal catalysed reactions under mechanochemical reaction conditions have been thoroughly investigated[6], few published research can be found for Buchwald-Hartwig aminations [7–9]. The most notable example[8] uses liquid assisted grinding to prohibit the aggregation of the Palladium catalyst in the reactor, yet the agent used, a cyclic diene, is not well adapted to green chemistry.
In our lab, we are interested in using this relatively new technology for developing the right conditions for solvent-free Buchwald-Hartwig amination reactions. For this, we are using a previously well-studied catalytic system, under novel solvent-free reaction conditions, bringing a new perspective to our overall green chemistry endeavours.



(1) Kar, S.*; et al.* **2022**, *122* (3), 3637–3710.
(2) Magano, J. *; et al. Chem. Rev.* **2011**, *111* (3), 2177–2250.
(3) Ruiz-Castillo, P.; Buchwald, S. L. *Chem. Rev.* **2016**, *116* (19), 12564–12649.
(4) Do, J.-L.; Friščić, T. *ACS Cent. Sci.* **2017**, *3* (1), 13–19.
(5) Anastas, P.; Eghbali, N. *Chem. Soc. Rev.* **2010**, *39* (1),
(6) Kubota, K.; Ito, H.*Trends in Chemistry* **2020**, *2* (12), 1066–1081.
(7) Shao, Q.-L.; Jiang, Z.-J.; Su, W.-K. *Tetrahedron Letters* **2018**, *59* (23), 2277–2280.
(8) Kubota, K.*; et al*. *Nat Commun* **2019**, *10* (1), 111.
(9) Cao, Q.; *et al. Org. Biomol. Chem.* **2019**, *17* (7), 1722–1726.

Solvent Polarity and Dispersion Forces under Vibrational Strong Coupling

Maciej Piejko, Bianca Patrahau, Kripa M. Joseph, Cyprien Muller, Eloïse Devaux, Thomas W. Ebbesen, Joseph Moran

University of Strasbourg, CNRS, ISIS and icFRC, 8 Allée Gaspard Monge, 67000 Strasbourg, France

Presenting author's name and email address: Maciej Piejko, mpiejko@unistra.fr

---

Vibrational Strong Coupling (VSC) occurs when molecular vibrations hybridize with the modes of an optical cavity, an interaction mediated by vacuum fluctuations. VSC has been shown to influence the rates and selectivity of chemical reactions.[1,2] However, a clear understanding of the mechanism by which VSC exerts an influence on reaction rates remains elusive. Here we show that VSC affects the polarity of solvents, a parameter well-known to influence reactivity.[3] The strong solvatochromic response of Reichardt's dye (RD) was used to quantify the polarity of a series of alcohol solvents at visible wavelengths. We observed that by simultaneously coupling the OH and CH vibrational bands of the alcohols, the absorption maximum of Reichard's dye red-shifted by up to ~15.1 nm, corresponding to an energy change of 5.1 kJ·mol^{-1}. With aliphatic alcohols, the magnitude of the absorption change of RD was observed to be related to the length of the alkyl chain, molecular surface area, and polarizability. Therefore, we propose that dispersion interactions, which themselves originate from vacuum fluctuations, are fundamentally impacted under strong coupling, and are therefore critical to understanding how VSC influences chemistry.

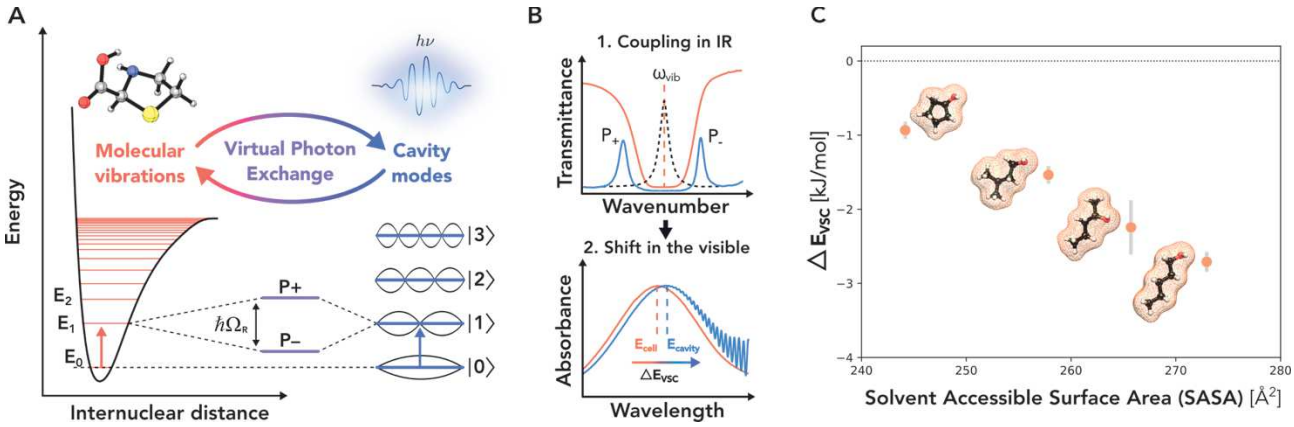


Figure 1. The effect of Vibrational Strong Coupling (VSC) reduces solvent polarity via modification of dispersion forces. (A) Schematic diagram showing the formation of hybrid light-matter states (polaritons, P+ and P-) from co-resonant vibrational and optical transitions inside an optical cavity via energy exchange mediated by vacuum field fluctuations. (B) Strong Coupling of solvent bands reduces the solvent polarity, which is measured using the $E_T(30)$ polarity parameter based on the molar transition energy of the intramolecular charge transfer band of Reichardt's dye in the visible range. (C) The VSC-induced alteration of polarity is proportional to the length of the solvent surface area and other parameters which correlate with dispersion interactions.

References:

(1) Thomas, A.; George, J.; Shalabney, A.; Dryzhakov, M.; Varma, S. J.; Moran, J.; Chervy, T.; Zhong, X.; Devaux, E.; Genet, C.; Hutchison, J. A.; Ebbesen, T. W., Ground-state chemical reactivity under vibrational coupling to the vacuum electromagnetic field. *Angew. Chem. Int. Ed.*, **2016**, *128*, 11634-11638. DOI: 10.1002/ange.201605504

(2) A. Thomas, Lethuillier-Karl, L.; Nagajaran, K.; Vergauwe, R. M. A.; Geogre, J.; Chervy, T.; Shalabney, A.; Devaux, E.; Genet, C.; Ebbesen, T.W., Tilting a ground-state reactivity landscape by vibrational strong coupling. *Science*, **2019**, *363*, 615-619. DOI: 10.1126/science.aau7742

(3) Piejko, M.; Patrahau, B.; Joseph, K.; Muller, C.; Devaux, E.; Ebbesen, T. W.; Moran, J. Solvent Polarity under Vibrational Strong Coupling, *J. Am. Chem. Soc.* **2023**, *145*, 13215-13222, DOI: 10.1021/jacs.3c02260

Metal/ADP complexes promote phosphorylation of ribonucleotides[1]

Emilie Werner,[a] Silvana Pinna,[a] Robert J. Mayer,[a] and Joseph Moran[a]

[a] *Institut de Science et d'Ingénierie Supramoléculaires, Université de Strasbourg & CNRS (UMR 7006), 8 Allée Gaspard Monge 67000 Strasbourg, France*

emilie.werner@etu.unistra.fr

Keywords: phosphorylation • adenine derivatives • catalysis • feedback • metabolism

Adenine derivatives are precursors to essential biomolecules such as cofactors and coenzymes. Famously, adenosine 5'-triphosphate (ATP), also known as life's universal energy currency, plays a central role in biochemistry by promoting polymerisation and phosphorylation reactions. However, it is unclear why and how adenine derivatives became central to metabolism. One hypothesis is that adenine derivatives were chemically best suited to promoting phosphoryl transfer. In this communication, we show that adenosine-5'-diphosphate (ADP) enables the non-enzymatic phosphoryl transfer from acetyl phosphate to other ribonucleotides and ribonucleosides in the presence of Fe^{III} or Al^{III} at room temperature in water. No other nucleoside diphosphates were found to promote the reaction. This work demonstrates how biomolecules can feed back into metabolic pathways, thereby strengthening or enlarging the chemical network. This system may represent an intermediary evolutionary stage between substrate-level[2-5] and enzymatic phosphorylation[6] (**Fig. 1**).

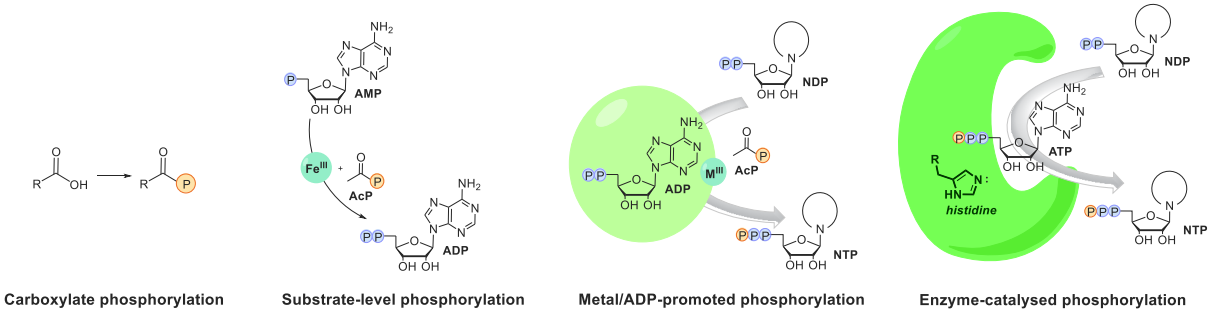


Fig 1. A plausible evolution of phosphorylation in protometabolism.

References

[1] Werner, E.; Pinna, S.; Mayer, R. J.; Moran, J.; *J. Am. Chem. Soc.* **2023**, *in press.*
[2] Maguire, O. R. *et al.* (2021): *Nat. Commun. 12* (1), 5517.
[3] Gibard, C. *et al.* (2018): *Nat. Chem. 10* (2), 212–217.
[4] Kitani, A. *et al.* (1995): *Bioelectrochemistry and Bioenergetics 36* (1), 47–51.
[5] Pinna, S. *et al.* (2022): *PLOS Biol. 20* (10), e3001437.
[6] Lascu, I. *et al.* (2000): *Bioenerg. Biomembr. 32* (3), 237–246.

A Single Phosphorylation Mechanism in Early Metabolism – The Case of Phosphoenolpyruvate[1]

Joris Zimmermann,[a] Robert J. Mayer,[a] and Joseph Moran [a]

[a] *Institut de Science et d'Ingénierie Supramoléculaires, Université de Strasbourg, CNRS (UMR 7006), 8 Allée Gaspard Monge 67000 Strasbourg, France*
joris.zimmermann@etu.unistra.fr

Keywords: Protometabolism • Carboxy-phosphorylation • PEP • Phosphoryl transfer • Mechanism

The emergence of protometabolism is thought to have arisen from self-organized reaction networks consisting of a small set of simple repeating reaction mechanisms that serve to accumulate key metabolites[2]. Within biological metabolism, phosphorylation helps drive nearly all anabolic pathways as well as biological polymerization. In the core of metabolism, two different types of phosphorylation reactions are found. Primarily, carboxylates are phosphorylated to acyl phosphates. However, phosphoenolpyruvate (PEP) – the metabolite with the most energetic phosphate bond – is synthesized by a different mechanism. Instead of phosphorylation of the carboxylate moiety of pyruvate, the enolate of pyruvate is generated within the enzyme, which subsequently undergoes direct phosphorylation (**Fig. 1A**). Interestingly, the hydrolysis of PEP, which corresponds to the reverse reaction, proceeds through an acylphosphate (**Fig. 1B**). We hypothesized that PEP formation via an enolate is the result of biological evolution, and that an ancient nonenzymatic pathway yielded PEP through the direct phosphorylation of the carboxylate of pyruvate followed by intramolecular transfer of the phosphoryl group. Here we demonstrate the plausibility of such a nonenzymatic phosphorylation mechanism, which corresponds to the reverse pathway of PEP hydrolysis. A single phosphorylation mechanism may have been sufficient to initiate biochemical networks.

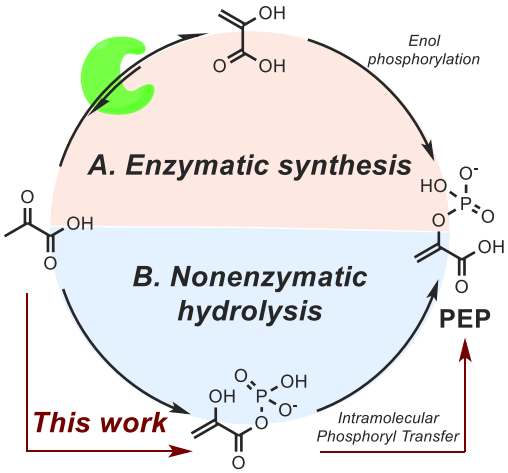


Fig 1. Enzymatic vs non-enzymatic phosphorylation of pyruvate to PEP.

References

[1] J. Zimmermann, R.J. Mayer, J. Moran; *in revisions*.
[2] K.B. Muchowska, S.J. Varma, J. Moran; *Chem. Rev*. **2020**,*120* (15), 7708–7744.

Immuno-PET imaging of the tumor-associated antigen CD38 in the case of multiple myeloma

COURSEYRE Manon,[1,2] BENAZZA Rania,[3] HERNANDEZ Oscar,[3] CIANFERANI Sarah,[3] GUILLOUX Yannick,[4] CHEREL Michel,[4] MARTIN Tristan,[2] DETAPPE Alexandre,[2] NONAT Aline,[1]*

1. Équipe Synthèse pour l'Analyse (SYNPA), Institut Pluridisciplinaire Hubert Curien (IPHC), CNRS UMR 7178, Strasbourg, France
2. Laboratoire Nanotranslationnel, Institut de Cancérologie Strasbourg-Europe (ICANS), Strasbourg, France
3. Équipe Spectrométrie de Masse BioOrganique (LSMBO), Institut Pluridisciplinaire Hubert Curien (IPHC), CNRS UMR 7178, Strasbourg, France
4. Équipe Oncologie Nucléaire, Centre de Recherche en cancérologie et Immunologie Nantes Angers (CRCI²NA), Nantes, France

* Correspondance : manon.courseyre@etu.unistra.fr

Abstract

Enhancing the detection of the Multiple Myeloma (MM) represents a critical challenge for optimizing its management. Current clinical imaging modalities of the MM patients rely mostly on positron emission tomography (PET) using non-specific radiotracers like ^{18}F-FDG. These radiotracers are employed to monitor the tumor activity[1]; however, in some cases, they fail to fix the plasma cell population because of low cellular proliferation and may lead to false negative results. Here, we seek to develop a novel immuno-PET radiotracer labeled with ^{64}Cu, targeting the tumor-associated antigen (TAA) CD38, in order to improve the monitoring of malignant myeloma cells. ^{64}Cu is an ideal radioisotope for this purpose due to its β^+ decay with high energy and long half-life ($t_{1/2}$ = 12.7 h)[2], providing logistical advantages that align well with the pharmacokinetic of the monoclonal antibody (mAb). To this point, bispidine chelators are promising pre-organized ligands for the formation of Cu (II) complexes, as highlighted their thermodynamic stability and excellent kinetic inertness in biological media[3,4]. This project focuses on the synthesis and characterization of bispidine-antibody conjugates allowing a specific detection of the TAA CD38 overexpressed at the surface of malignant MM cells. We have developed a series of labeled mAbs with varying degrees of labeling (DOL). In all cases, our conjugates effectively bind to the TAA CD38 on cancer cells. Thus, we present herein preliminary *in vitro* studies, which indicate a strong affinity and specificity of these conjugates to MM cells lines.

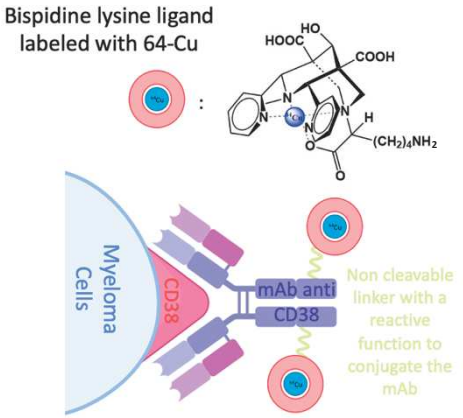


Figure 1: Structure of the mAb-bispidine immunoconjugate specifically targeting malignant MM cells.

Additionally, successful ^{64}Cu radiolabeling has also been achieved and *in vivo* studies are in progress. These promising results should lead to the first development of a novel ^{64}Cu bispidine complex targeted towards malignant MM cells.

Keywords

Bispidine, medical imaging, multiple myeloma, positron emission tomography

References

1. Zamagni, E. *et al.* Prognostic relevance of 18-F FDG PET/CT in newly diagnosed multiple myeloma patients treated with up-front autologous transplantation. *Blood* **118**, 5989–5995 (2011).
2. Wei, W. *et al.* ImmunoPET: Concept, Design, and Applications. *Chem. Rev.* **120**, 3787–3851 (2020).
3. Roux, A. *et al.* Bifunctional bispidine derivatives for copper-64 labelling and positron emission tomography. *Org. Biomol. Chem.* **15**, 1475–1483 (2017).
4. Ndiaye, D. *et al.* Unprecedented Kinetic Inertness for a Mn2+-Bispidine Chelate: A Novel Structural Entry for Mn2+-Based Imaging Agents. *Angewandte Chemie International Edition* **59**, 11958–11963 (2020).

Design and synthesis of 1,2,4-triazoles: structural exploration in the inhibition of GSK-3*β* for the treatment of Alzheimer's Disease

Thiago Moreira Pereira,[1-3] Natalia Nadur,[2] Angela de Simone,[4] Elisa Uliassi,[3] Maria Laura Bolognesi,[3] Arthur Eugen Kümmerle,[2] Martine Schmitt[1]

thm.pereira@hotmail.com; mschmitt@unistra.fr

[1]Medicinal Chemistry Department, UNISTRA, Strasbourg, France;
[2]Department of Organic Chemistry, UFRRJ, Rio de Janeiro, Brazil;
[3]Department of Pharmacy and Biotechnology, UNIBO, Bologna, Italy;
[4]Department of Drug Science and Technology, UNITO, Torino, Italy

Abstract

BACKGROUND: Currently 55 million people live with dementia worldwide with nearly 10 million new cases every year. Dementia results from a variety of diseases that affect the brain, and its most common form is the Alzheimer's disease (AD).[1] AD is driven by multiple deleterious factors, among them, the presence of insoluble filaments associated with Tau protein (p-Tau). GSK-3*β* inhibitors have shown promising results *in vivo*, emerging as a promising potentially disease-modifying therapeutic class for AD.[2] So, in this work, we aim to design, synthesize, and evaluate a new series of 1,2,4-trizole derivatives as GSK-3β inhibitors.
METHODS: The series **1** was proposed from alsterpaullone (**2**), through classic bioisosteric exchange of pyrrole by 1,2,4-triazole in **a**, and non-classical ring-opening in **b**. Based on molecular modeling studies, H-bond donnor/acceptor groups were proposed at positions 2, 3 and 4 of the ring **b**, aiming at making interactions with Lys85 and Asp200. Molecular docking analyses for **1a** indicated that the interaction prerequisites with the active site of GSK-3β were maintained, in the same way as **2**. The designed compound could make the main interactions with the ATP site (Asp133 and Val135), also directing ring **b** through Lys85 and Asp200 residues. The score value obtained for compound **1a** (score= 31.05) was quite similar to their direct prototype **2** (score= 32.39) (Fig 1).

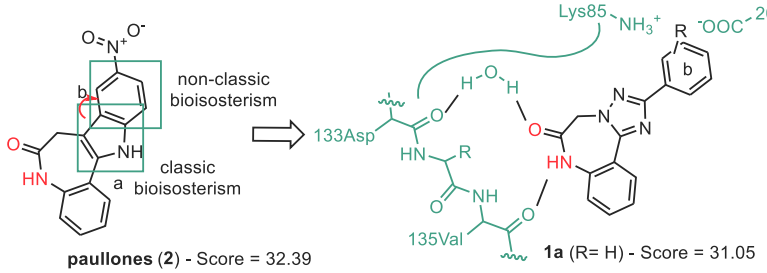
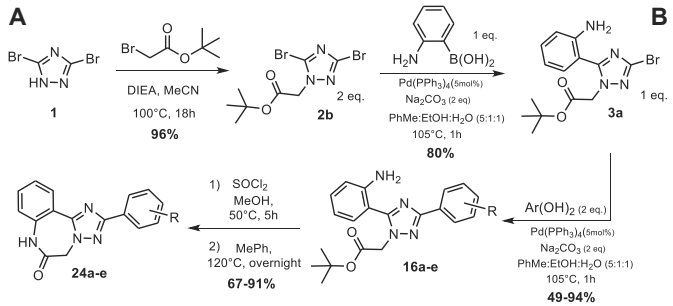


Figure 1. Design of the new series of GSK-3*β* inhibitors.

RESULTS: The synthesis of series **1** involved a first alkylation followed by two Suzuki reactions to introduce aromatic moieties on triazole core. In the last step, cpds **1a-j** were obtained in good to excellent yields after conversion of tert-butyric ester group to methyl ester with subsequent cyclization (Fig 2A). Preliminary evaluation of the inhibitory activity against GSK-3*β* was performed at 10 µM. Then, the IC_{50} of selected cpds (**1e-g**,**i**) were calculated. Cpd **1g** showed the best inhibitory profile (IC_{50} = 2.5µM) (Fig 2B). The results obtained are promising and the pattern of substitution of the aromatic moieties appeared to have an important role for the GSK-3*β* inhibition, as previewed by molecular modeling studies.

A



B

Cpd	R	%Inhibition @10 µM	IC_{50} [µM]
1a	H	42.3	-
1b	*p*-OMe	9	-
1c	*p*-COOMe	14.3	-
1d	*m*-OMe	15.2	-
1e	*m*-COOMe	52	44
1f	*p*-OH	49.7	15
1g	*m*-OH	71.2	2.5
1h	*p*-COOH	4	-
1i	*m*-COOH	42	21
1j	*p*-$CONH_2$	15.7	-

Figure 2. A - Scheme of Synthesis of proposed series **1**; **B –** Table of effects of compounds **1a-j** on GSK-3*β* activity

CONCLUSIONS: The synthetic route to obtain the designed compounds was successfully developed. Worthy of note, these compounds belong to a novel class of heterocycles and a new scaffold for the inhibition of GSK-3*β*. Encouragingly, the results of the inhibitory activity are promising, prompting further optimizations.

Acknowledgments

CAMPUS FRANCE and CAPES.

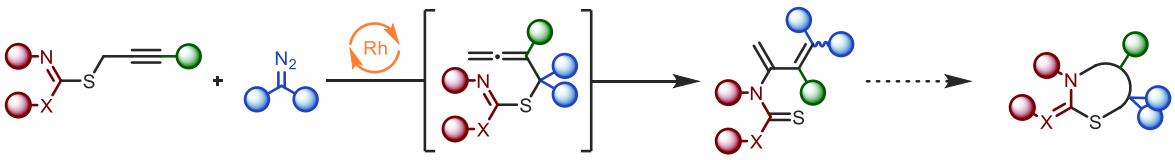
Design and Synthesis of Original N,S-containing Scaffolds to Access Complex Heterocycles

Charlou Rognan, Pierre Locquet, Nicolas Girard, Mihaela Gulea**
Laboratoire d'Innovation Thérapeutique, LIT UMR 7200,
Université de Strasbourg, CNRS, F-67000 Strasbourg
charlou.rognan@etu.unistra.fr, nicolas.girard@unistra.fr, gulea@unistra.fr

A large majority of bioactive molecules and pharmaceuticals contain at least one heterocycle in their structure.[1] *N,S*-heterocycles are represented in several drugs (i.e. Actos, Claforan, Seroquel),[2] however it is still need to extent the structural diversity of this class of compounds for therapeutic applications.

In this context, our group focus on the development of atom and step economic divergent synthetic strategies,[3] mainly based on metal-catalyzed domino reactions, to access new heterocyclic scaffolds bearing nitrogen and sulfur atoms with large molecular diversity.

Here we report a new domino sequence in which several carbon-carbon, carbon-nitrogen, and carbon-sulfur bonds are formed, leading to complex molecules from simple substrates. Starting from propargyl thioimidates and diazos compounds, the sequence involves a Rh-catalyzed Doyle-Kirmse reaction, followed by an unprecedent type of thio-Claisen rearrangement, and leads to original highly functionalized dienes. This methodology with a high atom economy offers the opportunity to vary more than three positions on the diene structure, giving access to a large molecular diversity. The reactivities of these dienes are under study to synthesize new *N,S*-heterocycles.



[1] Welsch, M. E.; Snyder, S. A.; Stockwell, B. R., *Curr Opin Chem Biol.* **2010,** *14*, 347–361.
[2] Scott, K. A.; Njardarson J. T., *Top. Curr. Chem.* **2018**, *376*, 5.
[3] Burke, M. D.; Schreiber S. L., *Angew. Chem. Int. Ed.* **2004**, *43*, 46–58.

Multidimensional Coordination Polymers based on the alloxazine core: Properties and Applications

Jaison Casas*[(a)], Dr. Abdelaziz Jouaiti[(a)], Pr. Sylvie Ferlay[(a)]
jaison.casas@unistra.fr
(a) Laboratoire de Synthèse et Fonctions des Architectures Moléculaires – UMR 7140

Keywords: Materials, Metal-Organic Frameworks, Redox activity, Alloxazine, Pillared Compounds.

Metal-Organic Frameworks (MOFs) are today well known for their porosity and their properties for adsorbing gas, delivering drugs, or storing energy[1]. A redox effect due to their metallic center or the redox active organic part of their structure allow interesting additional properties. One of the challenges today in this field is to propose new redox active core centered on their organic part which will contribute to their electron or ionic conductivities in the case of use in energy storage devices.

For these reasons, our laboratory focused on the use of the alloxazine a bio-inspired compound. Allowing the presence of three stable redox states[2] thanks to presence of the pteridine moiety (**Figure 1a**), this motif promoted as ligand can be a promising candidate for synthesizing new redox active MOFs.

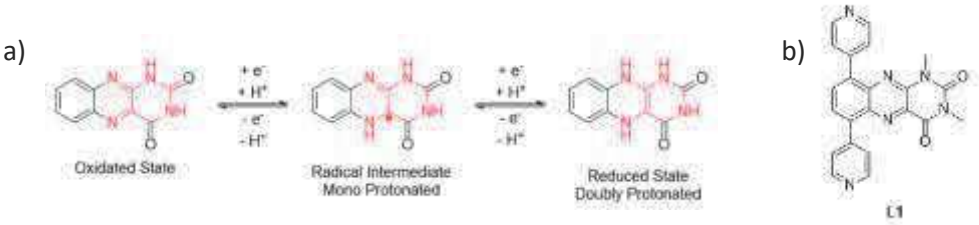
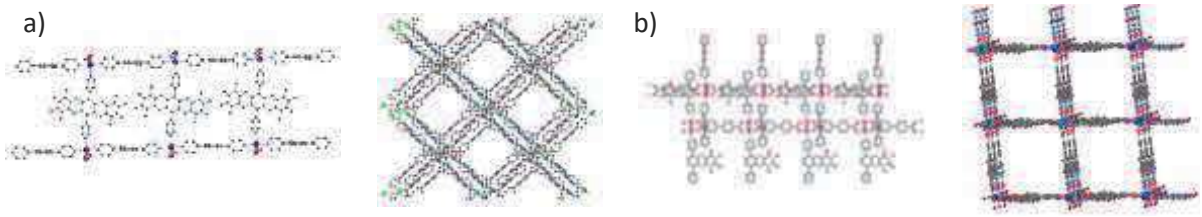


Figure 1 : *a) Oxidation states of the alloxazine core b) Redox active organic ligand containing an alloxazine core.*

We have successfully synthesized a large library of organic ligand favorizing the MOFs formation (**Figure 1b**), based on the alloxazine core. By combining them with a metal salt, mono and bidimensional (**Figure 2a**) coordination polymers containing the alloxazine core have been formed. Then by using, a three components strategy[3], by combining two different organic ligands and one metal salt, we have obtained bi and tridimensional Metal Organic Frameworks (**Figure 2b**).

The physico-chemical and electrochemical properties of these new MOFs have been studied in the solid state. They present a certain porosity allowing them to adsorb and release gas. Some of them have been also used as electrode materials in ionic batteries and their electrochemical behavior have been studied.



L1$_3$Co$_2$(NO3)$_2$ **L1**Co$_2$(NO$_3$)$_2$ **L1**BPDC$_2$Co$_2$ **L1**BPDC$_2$Co$_2$

Figure 2 : *a) Coordination polymers based on alloxazine core obtaining by the two component strategy b) MOFs based on alloxazine core obtaining by the three-components strategy (BPDC : 4,4'-BiPhenylDiCarboxylic acid).*

1. H. Furukawa, K. E. Cordova, M. O'Keeffe, and O. M. Yaghi, *The Chemistry and Applications of Metal-Organic Frameworks, Science,* **2013**, *341*, 6149. DOI : 10.1126/science.1230444
2. S. G. Mayhew, *The effects of pH and semiquinone formation on the oxidation-reduction potentials of flavin mononucleotide, Eur. J. Biochem.,* **1999**, *265*, 698-702. DOI: 10.1046/j.1432-1327.1999.00767.x
3. N. C. Burtch, and K. S. Walton, *Modulating Adsorption and Stability Properties in Pillared Metal-Organic Frameworks: A Model System for Understanding Ligand Effects*, *Acc. Chem. Res.,* **2015**, *48*, 2850-2857. DOI: 10.1021/acs.accounts.5b00311

Impact of Deep Eutectic Solvents on Metal-Organic Framework Synthesis and Properties

Michaël Teixeira [a], Renata A. Maia [a], Pauline André [a], Benoît Louis [b], Stéphane A. Baudron [a]

[a] *UMR 7140, University of Strasbourg-CNRS, 4 rue Blaise Pascal, 67000 Strasbourg, France*
[b] *UMR 7515, University of Strasbourg-CNRS, 25 rue Becquerel, 67087 Strasbourg, France*
michael.teixeira@etu.unistra.fr

Keywords: Metal-organic frameworks, Deep Eutectic Solvents, Porous materials, Crystal morphology

Deep Eutectic Solvents (DESs) represent an emerging class of solvents featuring some characteristics of their ionic liquid cousins - low vapor pressure, relatively wide liquid range, non-flammability and the ability to dissolve polar species - along with unique specificities, such as their limited toxicity and an improved biocompatibility [1]. Their use as media for the ionothermal preparation of Metal-Organic Frameworks (MOFs) has been recently explored, showing that not only DESs represent green and less toxic alternatives to solvents commonly used in the synthesis of these porous crystalline materials, but also that they may play different roles in the MOF construction [2]. Aiming at further investigating the potential of DESs for MOF synthesis and their impact on the properties of the materials, we are exploring their use for the preparation of prototypical MOFs as well as of new architectures [3-4]. For example, we have recently reported that the choline chloride/urea (1:2) DES and its analogue based on ethylene-urea can be used for the preparation of Mg-MOF-74 as well as of novel Ca-based MOFs. Interestingly, these mediums were shown to have an impact on the crystal morphology and textural properties, and were demonstrated to allow the preparation of otherwise water-sensitive materials [4]. These results and more recent efforts will be presented in this contribution.

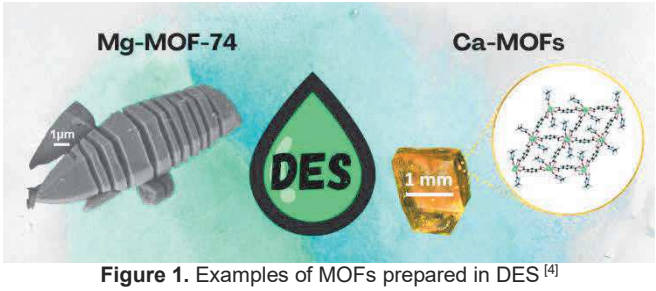


Figure 1. Examples of MOFs prepared in DES [4]

1. E. L. Smith, A. P. Abbott, K. S. Ryder, *Chem. Rev.*, **2014**, *114*, 11060.
2. a) E. R. Cooper, C. D. Andrews, P. S. Wheatley, P. B. Webb, P. Wormald, R. E. Morris, *Nature*, **2004**, *430*, 1012. b) R. A. Maia, B. Louis, S. A. Baudron, *CrystEngComm*, **2021**, *23*, 5016.
3. R. A. Maia, B. Louis, S. A. Baudron, *Dalton Trans.*, **2021**, *50*, 4145.
4. a) M. Teixeira, R. A. Maia, L. Karmazin, *CrystEngComm*, **2022**, *24*, 601. b) M. Teixeira, R. A. Maia, S. Shanmugam, B. Louis, S. A. Baudron, *Micropor. Mesopor. Mat.*, **2022**, *343*, 112148.

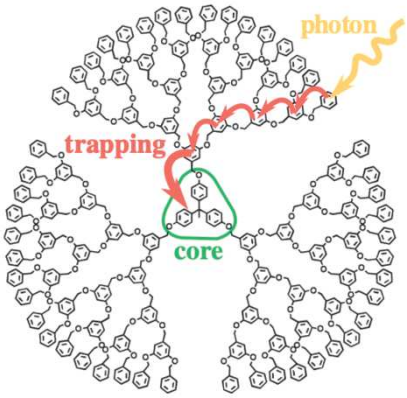
Lucie PEPE
2nd year PhD Student – Supervision: Saad Yalouz, Vincent Robert
Laboratoire de Chimie Quantique de Strasbourg (LCQS)
Institut de Chimie de Strasbourg

Abstract: Quantum transport of information in molecular open-quantum systems

In the biomimetic approach of developing Light-Harvesting Complexes (LHC) able of quantum transport of information, architectural considerations for an efficient exciton delocalization are required and can be theoretically explored using dendrimer models. In an extended star graph with peripheral defects and a core occupied by a trap, it has been recently shown that exciton-mediated energy transport from the periphery to the core can be optimized by a judicious choice of energy defects **[S. Yalouz et al. Phys. Rev. E 106, 064313 (2022)]**.

An extension of this work has been done by considering the exciton as an open quantum system perturbed by the presence of a dephasing environment. Simulating the dynamics using a Lindblad master equation, we observed a same type of quantum transport speedup when using the same initial optimal setting of energy defects (as long as the dephasing remains small enough). Nevertheless, once the strong dephasing regime is reached, the exciton transport gets hindered on the network.

These isolated- and open-dynamics results will be presented, together with a theoretical interpretation of the observed change in behavior, using the directed network formalism. In particular, the analytical form of the excitonic absorption time with this formalism will be recovered, and explanations of the strong dependence between this quantity and the size of the networks will be demonstrated.



TBAF-Promoted Carbanion-Mediated Sulfonamide Cyclization of CF_3-substituted *N*-allenamides: an Access to Fluorinated γ-Sultams

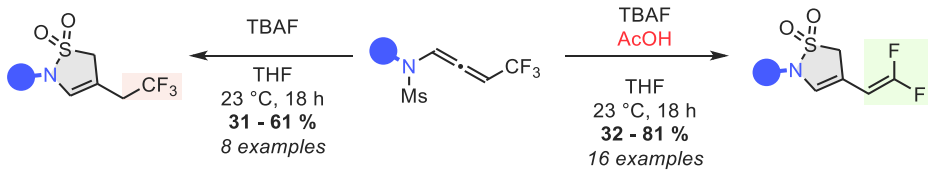
Clément Gommenginger[a], *Yongxiang Zheng*[a], *Daniele Maccarone*[b], *Ilaria Ciofini*[b] *and Laurence Miesch**[a]

[a] Équipe de Synthèse Organique et Phytochimie, Université de Strasbourg, CNRS-UdS UMR 7177, 4, rue Blaise Pascal CS 90032, 67081 Strasbourg, France [b] Chimie ParisTech, PSL University, CNRS, Institute of Chemistry for Life and Health Sciences, Chemical Theory and Modelling Group, F-75005 Paris, France

clement.gommenginger@etu.unistra.fr, lmiesch@unistra.fr

Since the discovery of sulfonamide antibacterials,[1] sulfonamides have played a key role in medicinal chemistry. The cyclic counterparts of sulfonamide compounds (sultams) display enhanced biological activities compared to their acyclic congeners.[2] Although not found in nature, these amide surrogates are considered privileged motifs that have found diverse applications in drug discovery. In view of our previous results on CF_3-substituted *N*-allenamides[3], we anticipated that deprotonation at the α-position of the sulfonyl moiety of *N*-sulfonyl-allenamides might initiate an anionic cyclization to produce cyclic sulfonamides.

N-mesyl based trifluoromethyl-*N*-allenamides were transformed into γ-sultams upon treatment with tetra-*n*-butylammonium fluoride (TBAF). Cyclic sulfonamides bearing an ene-*gem*-difluorinated tether could be obtained by addition of acetic acid to the ammonium salt, whereas TBAF alone provided the corresponding trifluorinated ethyl sultams. A combined experimental and computationnal mechanistic study suggested that this transformation involves a 5-*endo-dig* cyclization on the ene-ynamide generated *in situ*.[4]



[1] J. E. Lesch, The First Miracle Drugs: How the Sulfa Drugs Transformed Medicine, *Oxford University Press*, Oxford, 2007.

[2] Debnath, S.; Mondal, S. Sultams: Recent Syntheses and Applications: Sultams: Recent Syntheses and Applications. *Eur. J. Org. Chem*. 2018, *2018*, 933–956.

[3] (a) Zheng, Y.; Moegle, B.; Ghosh, S.; Perfetto, A.; Luise, D.; Ciofini, I.; Miesch, L. Copper-Catalyzed Synthesis of Terminal vs. Fluorine-Substituted *N* -Allenamides via Addition of Diazo Compounds to Terminal Ynamides. *Chem. Eur. J.* 2022, *28*, doi:10.1021/acs.orglett.1c01876. (b) Hourtoule, M.; Miesch, L. Regio- and Stereoselective Addition to Gem -Difluorinated Ene–Ynamides: Access to Stereodefined Fluorinated Dienes. *Org. Lett*. 2022, *24*, 3896–3900.

[4] C. Gommenginger, Y. Zheng, D. Maccarone, I. Ciofini and L. Miesch, TBAF-promoted carbanion-mediated sulfonamide cyclization of CF 3 -substituted N -allenamides: an access to fluorinated γ-sultams, *Org. Chem. Front.*, 2023, *10*, 4055–4060.

DEVELOPMENT OF A NEW METHODOLOGY TO ACCESS TRIFLUOROMETHOXYLATED SULFOXIDES

N. Moget, J. Saiter, A. Panossian, G. Hanquet,* and F. R. Leroux*
LIMA - UMR 7042
Université de Strasbourg, CNRS, Université de Haute-Alsace,
Ecole Européenne de Chimie, Polymères et Matériaux (ECPM), 25 rue Becquerel, 67000 Strasbourg - France

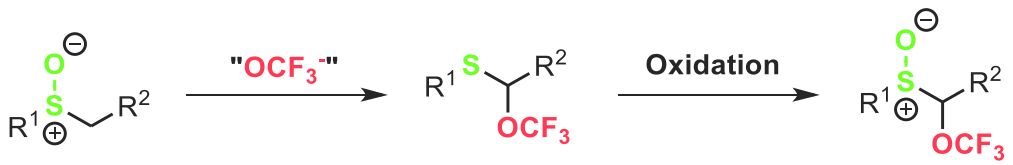
Email: nicolas.moget@etu.unistra.fr

The introduction of fluorinated groups on molecular targets has emerged as an important area of research in organic chemistry, with applications in material science, medicinal chemistry, and agrochemicals.[1] The substitution of a proton by a fluorinated group can lead to enhanced chemical stability, modified lipophilicity, altered pharmacokinetics and dynamics, and an overall improved biological activity.[2] The trifluoromethoxy moiety in particular can drastically increase the lipophilicity of a molecule relatively to a fluorine atom or a trifluoromethyl group.[3]

For the introduction of the OCF_3 group on stereogenic centers, we aimed at sulfoxides as substrates of choice, as they are easy-to-handle versatile chiral intermediates, which can be readily converted to various functional groups. They are known to have relatively high inversion energy barriers compared to many other types of organic molecules, making them attractive targets for this trifluoromethoxylation study.[4]

To obtain chiral compounds bearing the OCF_3 unit, a new method was thus investigated, namely the trifluoromethoxylation of sulfoxides *via* a Pummerer-type reaction followed by an oxidation to regenerate the sulfoxide functionality. Two different trifluoromethoxylating agents were used: trifluoromethyl *p*-toluenesulfonate (TFMS) is an air- and room temperature-stable oil and 2,4-dinitro-(trifluoromethoxy)benzene (DNTFB) is an inexpensive commercially available liquid. Both show great efficiency for the generation of the CF_3O^- anion.[5,6,7]

The synthesis of the trifluoromethoxylated sulfoxides as well as mechanistic insights into the reaction pathway will be presented.



References

1) S. Pazenok, D. Bernier, M. Donnard, G. Hanquet, A. Panossian, F. R. Leroux. **2022**. Modern Fluorine-Containing Agrochemicals. In PATAI'S Chemistry of Functional Groups, Z. Rappoport.
2) (a) C. Hansch, A. Leo, S. H. Unger, K. H. Kim, D. Nikaitani, E. J. Lien, *J. Med. Chem.* **1973**, *16*, 1207–1216. (b) L. Xing, D. C. Blakemore, A. Narayanan, R. Unwalla, F. Lovering, R. A. Denny, H. Zhou, M. E. Bunnage, *ChemMedChem* **2015**, *10*, 715–726.
3) F. R. Leroux, B. Manteau, J.-P. Vors, S. Pazenok, Beilstein *J. Org. Chem.* **2008**, *4*.
4) M. C. Carreño, G. Hernandez-Torres, M. Ribagorda, A. Urbano *Chem. Commun.*, **2009**, 6129–6144.
5) P. Tang, S. Guo, F. Cong, R. Guo, L. Wang, *Nature Chem.* **2017**, *9*, 546–551.
6) M. Lei, H. Miao, X. Wang, W. Zhang, C. Zhu, X. Lu, J. Shen, Y. Qin, H. Zhang, S. Sha, Y. Zhu, *Tetrahedron Lett.* **2019**, *60*, 1389–1392.
7) C. Bonnefoy, E. Chefdeville, A. Panossian, G. Hanquet, F. R. Leroux, F. Toulgoat, T. Billard, *Chem. Eur. J.* **2021**, *27,* 15986–15991.

Use of chemical cross-link coupled to mass spectrometry for structural elucidation of a peptide complex with antimicrobial properties

Emilie Hirschler[1], Elise Glattard[2], Burkhard Bechinger[2], Emmanuelle Leize Wagner[1], Noelle Potier[1]

1. Laboratoire de spectrométrie de masse des interactions et des systèmes, UMR 7140

2. Laboratoire de biophysique des membranes et RMN, UMR 7177

Antimicrobial peptides (AMPs) are a class of small, naturally occurring antimicrobial peptides. They are found in mammals, amphibians and insects as well as in humans [1].

These peptides form an integral part of their host's innate immunity, killing both Gram-negative and Gram-positive bacteria [2], enveloped viruses and fungi.

Magainins belong to this family of AMPs and are sourced from frog skin.

The peptides PGLa and Mag2, members of this Magainins family and both present in the skin of these amphibians, possess antimicrobial activity in their own right. Indeed, they intercalate at the membrane interface of foreign agents, causing membrane disruption and ultimately death.

Interestingly, a synergistic enhancement of this antimicrobial activity has been observed, with the formation of a heterodimeric complex [3].

The mechanism of interaction between the two peptides is not yet fully understood. In an attempt to shed light on this interaction, a chemical cross-linking approach coupled to mass spectrometry is used. Chemical cross-linking involves reacting a cross-linking agent with the peptides (Fig. 1). The cross-linking agent here reacts with the lysins (K) and covalently links these amino acids if they are sufficiently close in space. The cross-linked peptides are then analysed by mass spectrometry to obtain the proximity information.

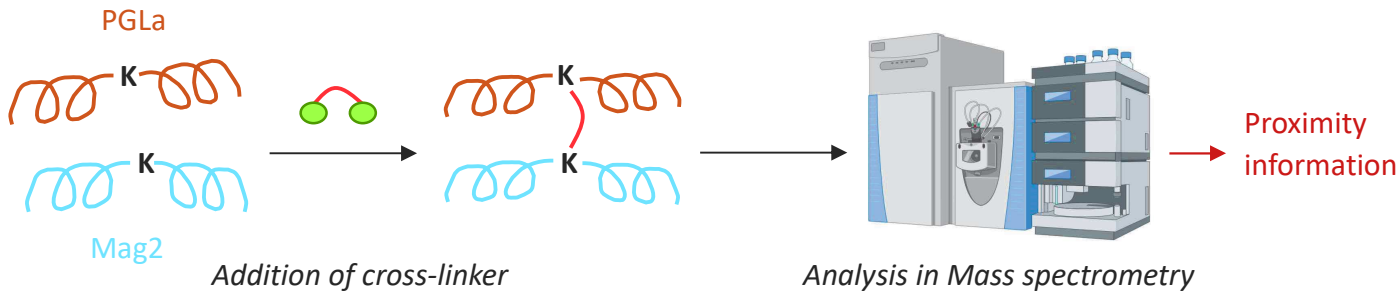


Fig. 1: Chemical cross-linking approach applied to the study of the two peptides, created using BioRender

Cross-liking experiments were performed either in a lipid medium consisting of 3:1 POPE/POPG vesicles or in a detergent medium with 0.025% dodecylmaltoside. The cross-linkers used were disuccinimidyl suberate and his hydrophilic homologue, bissulfosuccinimidyl suberate.

References:

1. Huan, Yuchen et al. “Antimicrobial Peptides: Classification, Design, Application and Research Progress in Multiple Fields.” *Frontiers in microbiology* vol. 11 582779. 16 Oct. 2020.

2. Ageitos, J M et al. “Antimicrobial peptides (AMPs): Ancient compounds that represent novel weapons in the fight against bacteria.” *Biochemical pharmacology* vol. 133 (2017): 117-138.

3. Bechinger, Burkhard et al. “Revealing the Mechanisms of Synergistic Action of Two Magainin Antimicrobial Peptides.” *Frontiers in medical technology* vol. 2 615494. 21 Dec. 2020.

Operando X-ray photoelectron spectroscopy study of Ni/YSZ solid oxide cell cathode electrodes during H_2O electroreduction

J Zhang, M Barreau, D. Teschner, M. Haevecker and S Zafeiratos*

Introduction

Solid oxide electrolysis cells (SOECs) are high temperature electrochemical devices that can efficiently convert electricity into chemical energy by reducing H_2O into H2, holds enormous potential in the transition to low-carbon energy systems.[1] Currently, the most commonly used SOEC cathode electrode is nickel mixed with yttria-stabilized zirconia (Ni/YSZ)[2]. Despite the fact that oxidation caused performance degradation of bulk NiO formation has been thoroughly investigated following postmortem electrode analysis, much less is known about the surface oxidation of nickel and its impact on the electrochemical performance. In this study, we employ synchrotron-based ambient pressure soft and hard X-ray photoelectron spectroscopies to analyze Ni/YSZ under open circuit and polarization conditions. Spectroscopic results are combined with the electrochemical characteristics of the cell recorded on line, allowing to correlate the surface chemical state with the electrocatalytic performance.

Materials and Methods

Combined AP-XPS, AP-HAXPES measurements were performed at the new CAT branch of the EMIL beamline at the synchrotron radiation facility BESSY II of the Helmholtz Zentrum Berlin. The samples were Ni/YSZ/Pt half-cells (Fig. 1a and 1b)[3]. Heating was performed from the rear side using an IR-laser. The electrochemical performance was evaluated by chronoamperometry and impedance spectroscopy (Fig. 1c) under H2O and H2O mixed with H2 at 780℃ and 1 mbar total pressure using a computer-controlled potentiostat.

Results and Discussion

Correlation of chronoamperometry, impedance spectroscopy depict the performance difference between Ni/YSZ electrodes that were slightly and substantially cells, but spectroscopic surface analysis did not show any discernible differences between them. This finding casts doubt on the widely held belief that nickel oxidation deteriorates the electrochemical performance. Depth profile photoemission measurements reveal clear differences in the NiO distribution between open circuit (O.C.) and polarization/electrolysis conditions, helping to elucidate the electrode performance. In particular, at O.C. the NiO component is more enhanced at the surface measurement (1.7 nm) indicating that it is located above metallic Ni^0 (Fig. 1d). On the contrary, during electrolysis the intensity of NiO and Ni^0 is similar in the two analysis depths suggesting that the two phases are homogenously distributed within the analyzed electrode volume (Fig. 1e). This can be explained by the presence of e^- and electrolysis products (H_2) that kept this part of the electrode in reduced state.

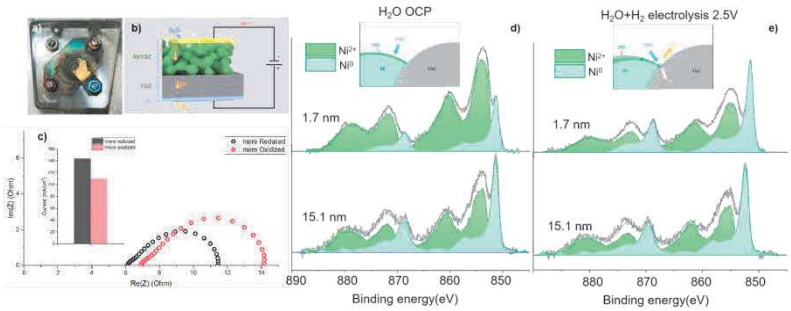


Figure 1. a) Miniature cell mounted on the spectrometer sample holder; b) schematic of the cell during H_2O electrolysis measurements; c) current density at experiments with various fuel and Ni surface oxidation; d) and e) *operando* Ni 2p AP-XPS and AP-HAXPES spectra in O.C. and H_2O electrolysis conditions.

References

1. A. Hauch, et al. Science 2020; 80, 370
2. S. Ovtar, et al. Nanoscale 2019; 11, 4394–4406.
3. D. Chen et al. Nano Energy 2022;101:107564.

Triarylamine-based macrocycle for tubular self-assembly: Towards supramolecular solenoid

Andrei Golushko, Andreas Vargas Jentzsch, Shoichi Tokunaga, Emilie Moulin, Nicolas Giuseppone

SAMS, Institute Charles Sadron, University of Strasbourg

e-mail: golushko@etu.unistra.fr

Triarylamines constitute a class of organic compounds known for their versatile properties in polymer science and organic electronics. The π-conjugated non-planar structure, strong electron-donating effect and low ionization potential make triarylamines desirable substrates in such areas as organic solar cells, organic light-emitting diodes (OLEDs) and nanoelectronics.[1,2] Previously, our research group reported the first triarylamine-based conjugated hexaaza[1_6]paracyclophane macrocycle, bearing six lateral amide functions.[3] The introduction of amide functionality made possible the self-assembly of macrocycles into tubular structures with delocalization of charge carriers achieved through bonds in the plane of the macrocycle and through space between macrocycles along the supramolecular stacks. Such multi-dimensional electronic delocalization portends the development of a new class of tubular assemblies with rich optoelectronic properties.

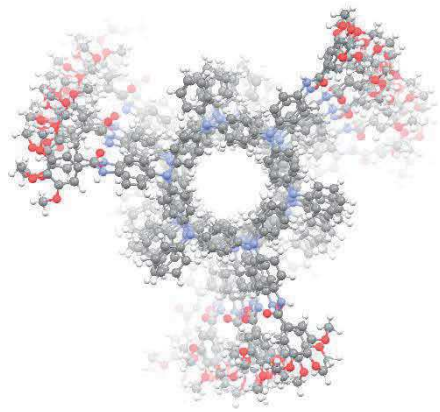


Figure 1. DFT-calculated tetrameric structure, formed by the macrocyclic hexaaza[1_6]paracyclophane trisamide.

To expand further the class of hexaaza[1_6]paracyclophane macrocycles, we designed and synthesized a triarylamine-based macrocycle with alternating lateral amide groups (Figure 1). The synthesis of this compound was achieved in 12 steps and its structure was confirmed by the means of spectroscopies (NMR, UV-vis, IR) and mass-spectrometry. The density functional theory calculations (DFT) at semi-empirical (PM6) and B3LYP levels of theory provided us with an insight into the geometry of macrocyclic monomer and self-assembled polymer. Calculated energies of the highest occupied and the lowest unoccupied molecular orbitals (HOMO and LUMO, respectively) expose the presence of closely lying and multiply degenerate energy states. Additionally, the binding energies for a range of guests within the tetrameric host were estimated in vacuum and solution, revealing a selective binding which is driven by a combination of C-H and van-der-Waals interactions.

References:

1. Wang, J.; Liu, K.; Ma, L.; Zhan, X. Triarylamine: Versatile Platform for Organic, Dye-Sensitized, and Perovskite Solar Cells. *Chem Rev* **2016**, *116* (23), 14675–14725

2. Moulin, E.; Armao, J. J.; Giuseppone, N. Triarylamine-Based Supramolecular Polymers: Structures, Dynamics, and Functions. *Acc Chem Res* **2019**, *52* (4), 975–983

3. Picini, F.; Schneider, S.; Gavat, O.; Vargas Jentzsch, A.; Tan, J.; Maaloum, M.; Strub, J.; Tokunaga, S.; Lehn, J.; Moulin, E.; Giuseppone, N. Supramolecular Polymerization of Triarylamine-Based Macrocycles into Electroactive Nanotubes. *J Am Chem Soc* **2021**, *143* (17), 6498–6504

Cu^{II}-Dp44mT reactivity and selectivity towards biologically relevant thiols

Iman Doumi[a], Lukas Lang[b], Bertrand Vileno[a], Marcel Deponte[b], Peter Faller[a]

[a] Institut de Chimie (UMR 7177), University of Strasbourg – CNRS, 4 rue Blaise Pascal, 67000 Strasbourg, France.
[b] Fachbereich Chemie & Landesforschungszentrum OPTIMAS, RPTU Kaiserslautern, Erwin-Schrödinger Straße 54, D-67663, Kaiserslautern, Germany
doumi@unistra.fr

Reactive oxygen species (ROS) are fundamental for many cellular functions such as redox homeostasis, regulation of transcription factors and signalling transduction[1,2]. However, high ROS levels are toxic because they can induce oxidative stress, which contributes to many pathologies such as cancer, cardiovascular disease, neurological disorders (i.e. Alzheimer's and Parkinson's disease).[2] Thus, the regulation of ROS is fundamental for cell survival. Intracellularly, thiol-containing molecules and proteins can be involved in the formation of ROS, as they are reducing agents hence a source of electrons for ROS production[3]. Furthermore, metal ions such Fe and Cu are very good catalyst in the reaction that brings the formation of hydroxyl radical, one of the most powerful oxidants between ROS[4]. In this frame, we were interested in thiols oxidation catalyzed by Cu-thiosemicarbazone(TSC) complexes used in anti-cancer therapies where the enhancement of ROS production is the desired outcome to induce cell apoptosis or necrosis[5]. Di-2-pyridylketone-4,4-dimethyl-thiosemicarbazone (Dp44mT) belongs to the class of α-N-heterocyclic TSCs and it has been proven to be cytotoxic in nM range in cell cultures[6]. Cu alone can catalyze the oxidation of thiols to disulfides in aerobic conditions with the production of ROS and Cu^{II}-Dp44mT causes the production of even more ROS (Fig.1)[7].

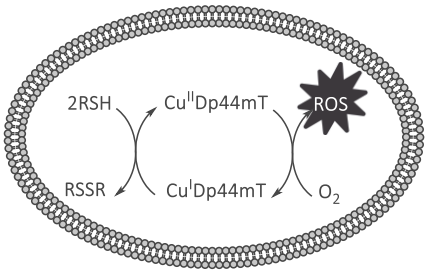


Figure 1. *Thiol reduction and ROS production catalyzed by Cu^{II}-Dp44mT in intracellular environment.*

In cells, there are different biological thiols at different concentration, therefore it is important to understand the reactivity and selectivity of Cu^{II}-Dp44mT with different thiols. Glutathione (GSH) is the most abundant thiol-bearing molecule intracellularly. Cysteine (Cys) is also present, but at a lower concentration (GSH to Cys ratio is approximately 10:1)[8]. Moreover, proteinogenic cysteinyl residues play an important role in many cellular functions such as catalysts in numerous enzymes and signal transducers. For these reasons, GSH, Cys and two model thiol-disulfide oxidoreductases glutaredoxin and thioredoxin were investigated in the presence of physiological relevant GSH concentration to explore the reactivity of Cu^{II}-Dp44mT compared to free Cu^{II}. By means of UV-Vis spectroscopy, EPR spin scavenging, and measurement of oxygen consumption, it has been assessed that Cu^{II}-Dp44mT oxidized thiols faster and it produced hydroxyl radicals faster than free Cu^{II}. Furthermore, Cu^{II}-Dp44mT is more reactive with Cys, but it is selective for GSH when the two thiols are present at physiological relevant concentration. Therefore, GSH protects Cys and Cys-residues against potential deleterious oxidation by Cu^{II}-Dp44mT. This investigation contributes to better understand the interaction between Cu^{II}-Dp44mT and mixtures of thiols in intracellular environment.

Keywords: ROS, oxidative stress, Cu^{II}-Dp44mT, thiols, GSH

[1] J. T. Hancock, R. Desikan, S. J. Neill, *Biochem Soc Trans* **2001**, *29*, 345.
[2] K. Jomova, R. Raptova, S. Y. Alomar, S. H. Alwasel, E. Nepovimova, K. Kuca, M. Valko, *Arch Toxicol* **2023**, *97*, 2499–2574.
[3] L. Moran, J. Gutteridge, G. Quinlan, *Curr Med Chem* **2001**, *8*, 763–772.
[4] U. Jungwirth, C. R. Kowol, B. K. Keppler, C. G. Hartinger, W. Berger, P. Heffeter, *Antioxid Redox Signal* **2011**, *15*, 1085–1127.
[5] Y. Lin, H. Betts, S. Keller, K. Cariou, G. Gasser, *Chem Soc Rev* **2021**, *50*, 10346–10402.
[6] D. B. Lovejoy, D. M. Sharp, N. Seebacher, P. Obeidy, T. Prichard, C. Stefani, M. T. Basha, P. C. Sharpe, P. J. Jansson, D. S. Kalinowski, P. V. Bernhardt, D. R. Richardson, *J Med Chem* **2012**, *55*, 7230–7244.
[7] E. Falcone, A. G. Ritacca, S. Hager, H. Schueffl, B. Vileno, Y. El Khoury, P. Hellwig, C. R. Kowol, P. Heffeter, E. Sicilia, P. Faller, *J Am Chem Soc* **2022**, *144*, 14758–14768.
[8] L. P. Osman, S. C. Mitchell, R. H. Waring, *Sulfur reports* **1997**, *20*, 155–172.

Graphene Oxide Conjugated with Antimicrobial Peptides Against Bacterial Infections

Zhengfeng Gao[1], Karahan Hüseyin Enis[1], Lucas Jacquemin[1], Oliver Chaloin[1], Yuta Nishina[2], Alberto Bianco[1]

[1]CNRS, Immunology, Immunopathology and Therapeutic Chemistry, UPR3572, University of Strasbourg, ISIS, 67000 Strasbourg, France
[2]Research Core for Interdisciplinary Sciences, and Graduate School of Natural Science and Technology, Okayama University, 3-1-1 Tsushima-naka, Kita-ku, Okayama 700-8530, Japan

Contact: z.gao@ibmc-cnrs.unistra.fr

The overuse or misuse of antibiotics has led to a fast-approaching “Post-antibiotic Era”. As a member of the graphene family materials, graphene oxide (GO) exhibits excellent properties including high biocompatibility [1]. Therefore, GO and GO-based composites have been widely explored as new antimicrobial substances. However, the antibacterial activity of GO is often limited by its negative charge and the limited ability to interact with bacterial membranes. To overcome these issues, GO-based antibacterial composites can be designed by combining GO with other molecules, such as antibacterial agents or polymers [2]. Compared with pristine GO, the antibacterial properties of GO-based composites are considered excellent, as reflected by faster sterilization and longer effects. Among the emerging agents for bacterial killing, antimicrobial peptides (AMPs) have been identified as potential alternatives to antibiotics, likely due to their significant advantages in terms of broad-spectrum antimicrobial activity and low probability to generate resistance. HHC36 peptide has already been proven to show superb bactericidal activity against both Gram-positive and Gram-negative bacteria [3]. To this end, a GO-based multifunctional antimicrobial platform was designed by combining AMPs. The designed GO multifunctional antimicrobial conjugate is expected to improve the antibacterial property of GO.

References

[1] Martín, C., Ruiz, A., Keshavan, S., Reina, G., Murera, D., Nishina, Y., Fadeel, B., Bianco, A., A Biodegradable Multifunctional Graphene Oxide Platform for Targeted Cancer Therapy. Adv. Funct. Mater. 2019, 29.
[2] O.N. Ruiz, K.A.S. Fernando, B. Wang, N.A. Brown, P.G. Luo, N.D. McNamara, M. Vangsness, Y. Sun, C.E. Bunker, Graphene oxide: a nonspecific enhancer of cellular growth, ACS Nano. 2011, 5.
[3] Chen, J.; Gao, M.; Wang, L.; Li, S.; He, J.; Qin, A.; Ren, L.; Wang, Y.; Tang, B. Z., Aggregation-Induced Emission Probe for Study of the Bactericidal Mechanism of Antimicrobial Peptides. ACS Applied Materials & Interfaces 2018, 10 (14), 11436-11442.

Highly sensitive and selective chemical sensing with functionalized 2D MoS_2: a supramolecular approach

Anna Zhuravlova, Antonio Gaetano Ricciardulli, Dawid Pakulski, Adam Gorczyński, Adam Kelly, Jonathan N. Coleman, Artur Ciesielski, and Paolo Samorì
Université de Strasbourg, CNRS, ISIS, 8 allée Gaspard Monge, 67000 Strasbourg, France
anna.zhuravlova@etu.unistra.fr

The substantial increase in pollutants from industrial and agricultural activities worldwide poses an important environmental challenge.[1] To address this issue, the development of novel robust and efficient chemical (nano)sensors is highly sought after. Low-dimensional materials such as nanoparticles, nanotubes and nanosheets present ideal scaffolds for chemical sensing due to the high surface-to-volume ratio and various interactions with the environment. [2] Among others, liquid-phase exfoliated two-dimensional transition metal dichalcogenides (e.g., molybdenum disulfide or MoS_2) are suitable candidates for chemical sensing thanks to their unique electrical characteristics and scalable processing.[2] In this work, we develop ultrasensitive and selective MoS_2-based sensors for heavy metal Co^{2+} ions via the covalent functionalization of defect-rich MoS_2 flakes with a specific receptor, i.e. 2,2':6',2''-terpyridine-4'-thiol. A continuous network is assembled by the healing of MoS_2 sulfur vacancies in a tailored microfluidic approach, which guarantees high control over the assembly of thin and large hybrid films. The Co^{2+} cations complexation represents a powerful gauge for low concentrations of cations which can be best monitored in a chemiresisitive ion sensor that features a 1 pM limit of detection, covers a broad concentration range, and exhibits high sensitivity combined with high selectivity towards Co^{2+} over K^+, Ca^{2+}, Mn^{2+}, Cu^{2+}, Cr^{3+} and Fe^{3+} cations. This general supramolecular approach based on highly specific recognition events can be adapted for sensing other analytes such as ions and (bio)molecules through the ad-hoc design of the specific receptor.[3] Overall, our work presents a versatile and effective strategy for developing advanced chemical sensors with broad applications in environmental monitoring.

References

[1] L. Yu, L. Sun, Q. Zhang, Y. Zhou, J. Zhang, B. Yang, B. Xu, Q. Xu, *Biosensors*, 12 (2022) 1096.
[2] R. Furlan de Oliveira, V. Montes-García, A. Ciesielski, P. Samorì, *Mater. Horiz.*, 8 (2021) 2685.
[3] A. Zhuravlova, A. G. Ricciardulli, D. Pakulski, A. Gorczyński, A. Kelly, J. N. Coleman, A. Ciesielski, P. Samorì, *Small*, (2023) 2208100.

Figures

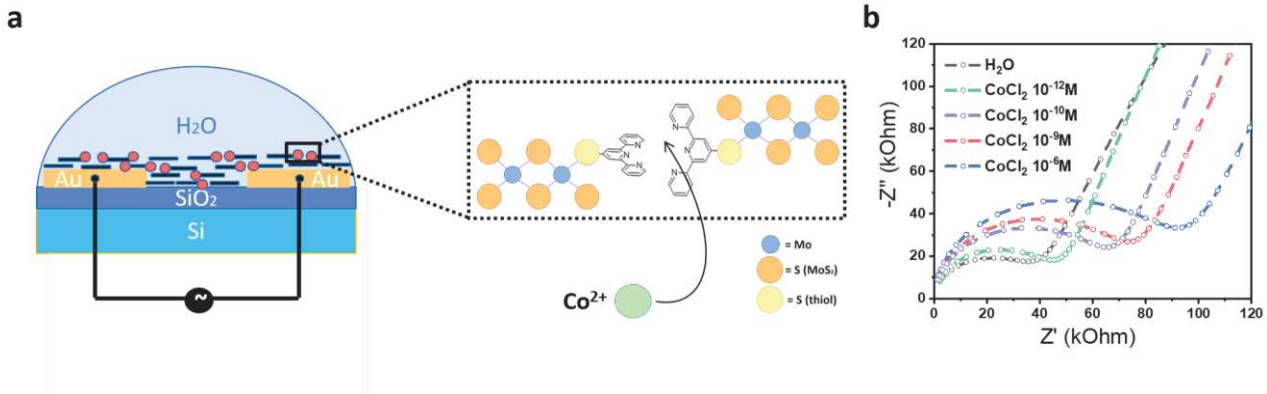
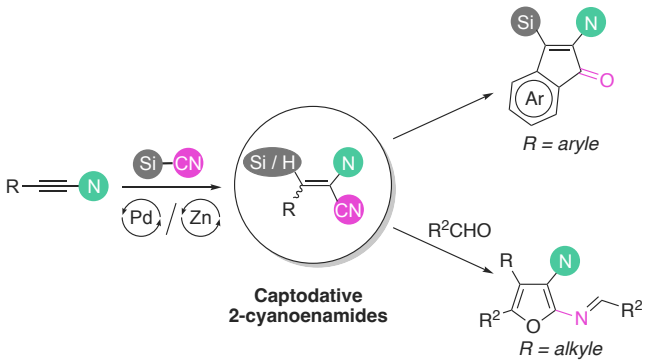


Figure 1: (a) Schematic representation of the device architecture. (b) Electrochemical impedance spectroscopy signal evolution upon Co^{2+} concentration increase.

Captodative 2-cyanoenamides as innovative synthons to access original heterocyclic structures.

*Célia Schwoerer, Pierre Hansjacob, Frédéric R. Leroux and Morgan Donnard**
LIMA – UMR 7042
Université de Strasbourg, CNRS, Université de Haute-Alsace
ECPM, 25 rue Becquerel, 67000 Strasbourg – France
Email: celia.schwoerer@etu.unistra.fr

Following the recent development for the synthesis of captodative 2-cyanoenamides in our group,[1] we have focused our attention on the very attractive reactivity of such unprecedented compounds to access new heterocyclic structures. In a first approach, access to the 2-amidoindenone scaffold was achieved by a very simple intramomecular Houben-Hoesch reaction between the nucleophilic aryl substituent and the nitrile function.[2] Various derivatives were afforded and could be valorized through iododesilylation, giving access to novel 3-substituted 2-amidoindenones.[3] In a second approach, we have started to investigate the synthesis of very rarely reported 2,3-diaminofurans *via* a domino reaction. The vinylsilane first goes through an electrophilic substitution with an aldehyde in the presence of a fluoride source.[4] The resulting alkoxide intermediate then cyclizes to form the furan ring. To this day, optimization of reaction conditions afforded the desired product in excellent yield and opened possibility to investigate the scope of the reaction. This methodology represents the first general and diversified access to 2,3-diaminofurans.



Access to various heterocyclic structures from the transformation of 2-cyanoenamides

References

[1] (a) P. Hansjacob, F. R. Leroux, V. Gandon, M. Donnard, *Angew. Chem. Int. Ed.* **2022**, *61*, e202200204; *Angew. Chem.* **2022**, *134*, e202200204. (b) P. Hanjacob, F. R. Leroux, M. Donnard, *Chem. Eur. J.* **2023**, *29*, e202300120.
[2] E. Campaigne, D. E. Mais, *J. Heterocycl. Chem.* **1975**, *12*, 267-271.
[3] C. Schwoerer, P. Hansjacob, F. R. Leroux, M. Donnard, *submitted manuscript.*
[4] Y. Sato, K. Hitomi, *J. Chem. Soc., Chem. Commun.*, **1983**, *170.*

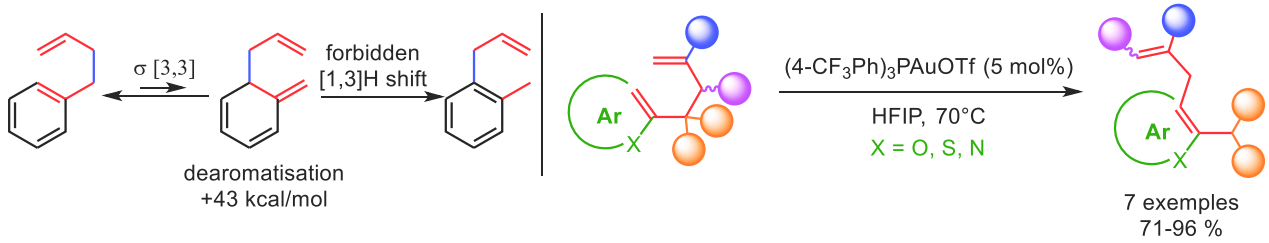
Toward the rebirth of the aromatic Cope rearrangement

Pierre Locquet (1), Emanuel Riguet* (2) and Aurelien Blanc* (1)

1) Laboratoire de Synthèse et Réactivité et Catalyse, Institut de Chimie de Strasbourg, UMR 7177, 4 rue Blaise Pascal, Strasbourg, France
2) Méthodologie en Synthèse Organique, Institut de Chimie de Reims, UMR 7312, Campus Moulin de la Housse, Reims, France

The Cope rearrangement, discovered in 1940 by Arthur C. Cope[1], is a powerful and well-studied pericyclic reaction involving a sigmatropic shift in a 1,5-hexadiene moiety. Yet, its aromatic version involving one of the alkenes within an aromatic ring has found to be very limited due to the impossibility to overcome thermodynamic and kinetic energetic barriers. Even if less than fifty papers[2] were consecrated to this reaction it has been theoretically studied and was performed using designed substrate under thermic condition[3].

Another way to achieve the rearrangement is the use of catalytic system in order to lower the energetic barrier and avoid high temperature. In this context, gold catalysis, especially Au^{I}, seems to be a perfect candidate due to its incredible π-acidity making it a strong carbophilic acid and has already shown activity in Cope rearrangement[4]. We thus demonstrated that, on an engineered substrate known to rearrange in thermic (> 110°C)[5], Au^{I} catalyst drastically decreased the activation barrier of the aromatic cope reaction. After optimization, we develop an efficient method using 5 mol% of $(4\text{-}CF_3Ph)_3PAuOTf$ in HFIP to perform the aromatic Cope rearrangement on various substrates in milder reaction conditions than the thermic one (74 - 96 %, 7 examples).



References

1) A.C. Cope, E.M. Hardy, *J. Am. Chem. Soc.,* 1940, 62, 2, 441
2) B.M. Tomiczek, A.J. Grenning, *Org. Biomol. Chem.*, 2021, 19, 2385
3) J. Barluenga, F. Azner, I. Gutiérrez, J.A. Martin, *Org. Lett.,* 2002, 4, 16, 2719
4) R.J. Felix, D. Weber, O. Gutierrez, D.J. Tantillo, M.R. Gagné, *Nat. Chem.*, 2012, 4, 405
5) M. Bos, E. Riguet, *Chem. Commun.*, 2017, 53, 4997