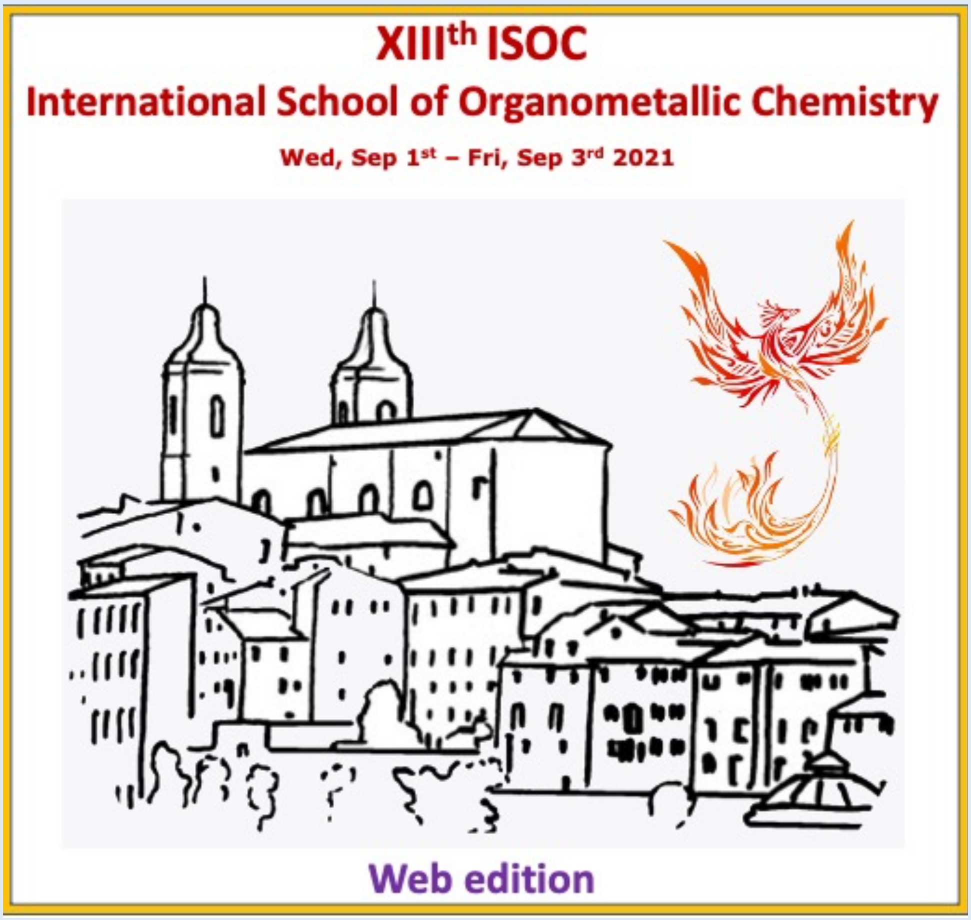
13th INTERNATIONAL SCHOOL OF ORGANOMETALLIC CHEMISTRY

SUMMER SCHOOL
Camerino, Italy
01-03 September 2021
https://isoc.unicam.it



Interdivisional Group of Organometallic Chemistry

New Directions and Perspectives on Organometallic Chemistry

Title New Directions and Perspectives on Organometallic Chemistry
13th edition of the International School of Organometallic Chemistry, University of Camerino,
Web edition, Camerino, 1-3 September 2021
ISBN 9788867680528

Sponsored by University of Camerino

UNICAM
Università di Camerino
1336

Università di Camerino

INTRODUCTION

New Directions and Perspectives on Organometallic Chemistry

The ISOC series is the most important school on organometallic chemistry at the European level, organized by Camerino University under the auspices of EuCheMS (the European Association for Chemical and Molecular Sciences) and the Interdivisional Group of Organometallic chemistry of the Italian Chemical Society. The aim is to encourage the presence of young researchers and Ph.D students both from University and Industry, including those not directly involved in organometallic research projects, in order to bring together young researchers and distinguished European scientists as a contribution to the important goal of increasing the transfer of knowledge at a high level between different European countries and different generation of scientists.

The 13th edition of ISOC will deal with fundamental principles to their use in novel applications, with a specific focus on the role of organometallic chemistry in finding solutions to many of the major societal challenges in the 21st century: from the development of sustainable energy solutions to the mitigation of climate change, from the synthesis of effective therapeutics to the production of new materials ranging from novel polymers to nanomaterials, from the generation of industrial feedstocks to the remediation of the environment. The scientific community is increasingly being stimulated to tackle problems of practical interest and the society will undoubtedly rely on advances made in the field of organometallic chemistry.

SCIENTIFIC PROGRAMME

Timetable

Wednesday 1 September	Thursday 2 September	Friday 3 September
14:40-15:00 **Welcome greetings**		
15:00-16:00 **Prof. Gratzel Michael** *Molecular photovoltaics and artificial photosynthesis*	15:00-16:00 **Prof. Gansäuer Andreas** *How can one activate titanocenes for catalytic radical chemistry? From electro- to photochemistry*	15:00-16:00 **Prof. Cramer Nicolai** *Catalytic Enantioselective C-H Functionalization - The Transition to 3d-Transition-Metals*
16:00-17:00 **Prof. Llobet Antoni** *Molecular anodes for green and sustainable energy applications*	16:00-17:00 **Prof. Kozuch Sebastian** *Understanding Kinetics through the Energy Representation*	16:00-17:00 **Prof. Reiser Oliver** *Copper makes the difference: Visible light driven transformations using Cu(I)- or Cu(II)-complexes as photocatalysts*
17:00-19:00 **Flash-presentations**	17:00-18:00 **Prof. Anna Trzeciak** *Formation and catalytic activity of palladium nanoparticles in C-C cross-coupling reactions*	17:00-18:00 **Prof. Ingrid Montes Gonzalez** *An overview of Ferrocene derivatives: synthesis, characterization, and applications*
	18:00-19:00 **Flash-presentations**	18:00-18:15 **Conclusions**

ORGANIZING COMMITTEE

Prof. Augusto Cingolani
Honorary President of ISOC

Prof. Claudio Pettinari
Chair

Prof. Fabio Marchetti
Co-chair

Prof. Riccardo Pettinari

Prof. Corrado Di Nicola

Prof. Marino Petrini

Prof. Enrico Marcantoni

Prof. Alessandro Palmieri

Dr. Serena Gabrielli

Dr. Alessia Tombesi

SCIENTIFIC COMMITTEE

Prof. Walter Baratta
Prof. Andrea Biffis
Prof. Piergiorgio Cozzi
Prof. Enrico Marcantoni
Prof. Carlo Nervi
Prof. Alceo Macchioni
Prof. Maria Valeria D'Auria
Prof. Claudio Pettinari
Prof. Fabio Ragaini
Prof. Gianna Reginato
Prof. Renata Riva

SPEAKERS

Prof. Nicolai Cramer **Ecole Polytechnique Fédérale de Lausanne**

Catalytic Enantioselective C-H Functionalization - The Transition to 3d-Transition-Metals

Prof. Andreas Gansäuer **University of Bonn**

How can one activate titanocenes for catalytic radical chemistry? From electro- to photochemistry

Prof. Michael Gratzel **Ecole Polytechnique Fédérale de Lausanne**

Molecular photovoltaics and artificial photosynthesis

Prof. Antoni Llobet **ICIQ Institute of Chemical Research of Catalonia**

Molecular anodes for green and sustainable energy applications

SPEAKERS

Prof. Ingrid Montes Gonzalez **University of Puerto Rico-Rio Piedras Campus**

An overview of Ferrocene derivatives: synthesis, characterization, and applications

Prof. Oliver Reiser **University of Regensburg**

Copper makes the difference: Visible light driven transformations using Cu(I)- or Cu(II)-complexes as photocatalysts

Prof. Anna Trzeciak **University of Wrocław**

Formation and catalytic activity of palladium nanoparticles in C-C cross-coupling reactions

Prof. Sebastian Kozuch **Ben-Gurion University of the Negev**

Understanding Kinetics through the Energy Representation

ABSTRACTS OF LECTURES

Lecture of 1 September 2021, h 15.00-16.00

Molecular Photovoltaics and Artificial Photosynthesis

Michael Graetzel

School of Chemistry, Ecole Polytechnique Fédérale de Lausanne , Lausanne, Switzerland,
E-mail: michael.graetzel@epfl.ch

Learning from the concepts used by green plants photosynthesis, we have developed molecular photosystems affording efficient solar light harvesting and conversion to electricity and fuels.[1] Solar cells using dyes, semiconductor quantum dots or perovskite pigments as light harvesters have emerged as credible contenders to conventional silicon cells. Dye sensitized solar cells (DSCs) were the first to use a three-dimensional mesoscopic junction for solar electricity production. The power conversion efficiency for DSC's is currently 15.1% in direct sunlight and 35% in ambient light. DSCs are simple and inexpensive to manufacture and they possess unique practical advantages including flexibility and transparency. These features along with excellent long-term stability have fostered first commercial applications large scale industrial production. DSCs have engendered the advent of perovskite solar whose rapid efficiency rise from 3% to over 25% has stunned the photovoltaic community. Due to their exceptional performance, they are presently being intensively investigated as one of the most promising future PV technology. We have applied these fundamentally new concepts to realize highly efficient generation of hydrogen and reduction of carbon dioxide to ethylene and ethanol by sunlight using water as electron source/ mimicking fuel generation by natural photosynthesis.

Figure 1 Electric car charging statio, powered by dye sensitized solar cell panels near Villa-Saint-Pierre, Switzerland.

[1] http://lpi.epfl.ch

Lecture of 1 September 2021, h 16.00-17.00

Molecular Anodes for Green And Sustainable Energy Applications

Antoni Llobet

Institute of Chemical Research of Catalonia (ICIQ), Barcelona Institute of Science and Technology (BIST), Av. Països Catalans 16, E-43007 Tarragona, Spain and Departament de Química Universitat Autònoma de Barcelona, Cerdanyola del Vallès, E-08193 Barcelona, Spain.
E-mail: allobet@iciq.cat

The replacement of fossil fuels by a clean and renewable energy source is one of the most urgent and challenging issues our society is facing today, which is why intense research has been devoted to this topic recently. Nature has been using sunlight as the primary energy input to oxidize water and generate carbohydrates (a solar fuel) for over a billion years. Inspired, but not constrained by nature, artificial systems[1] can be designed to capture light and oxidize water and reduce protons, CO_2 or other compounds to generate useful chemical fuels and feedstocks. In this context, this contribution will describe the preparation of efficient molecular water oxidation catalysts both in homogeneous phase and confined into solid conductive or semiconductive supports. Further the nature of the anchoring strategy on the performance of these molecular (photo)anode will be further discussed as well their implications for the generation of solar fuels.[2]

[1] (a) Berardi, S.; Drouet, S.; Francàs, L.; Gimbert-Suriñach, C.; Guttentag, M.; Richmond, C.; Stoll, T.; Llobet, A. *Chem. Soc. Rev.*, **2014**, *43*, 7501-7519. (b) Matheu, R.; Ertem, M. Z.; Gimbert-Suriñach, C; Sala, X.; Llobet, A. *Chem. Rev.* **2019**, *119,* 3453–3471. (c) Matheu, R.; Garrido Barros, P.; Gil Sepulcre, M.; Ertem, M. Z.; Sala, X; Gimbert-Suriñach, C; Llobet, A. *Nat. Rev. Chem.* **2019,** *3,* 331–341.

[2] (a) Creus, J.; Matheu, R.; Llobet, A. et al., *Angew. Chem. Int. Ed.* **2016,** *55*, 15382-15386. (b) Matheu, R.; Gray, H. B.; Brunschwig, B. S.; Llobet, A; Lewis, N. S. et al., *J. Am. Chem. Soc.* **2017**, *139,* 11345-11348. (c) Garrido-Barros, P.; Gimbert-Suriñach, C.; Llobet, A. et al., *J. Am. Chem. Soc.* **2017**, *139,* 12907–12910. (d) Hoque, Md. A.; Gil-Sepulcre, M.; Llobet, A. et al. *Nat. Chem.* **2020**, *12*, 1060–1066. (e) Schindler, D.; Gil-Sepulcre, M.; Llobet, A.; Würthner, F. *Adv. Energy Mater*. **2020**, 2002329. (f) Gil-Sepulcre, M.; Llobet, A. et al. *J. Am. Chem. Soc.* **2021**, *143*, 11651–11661.

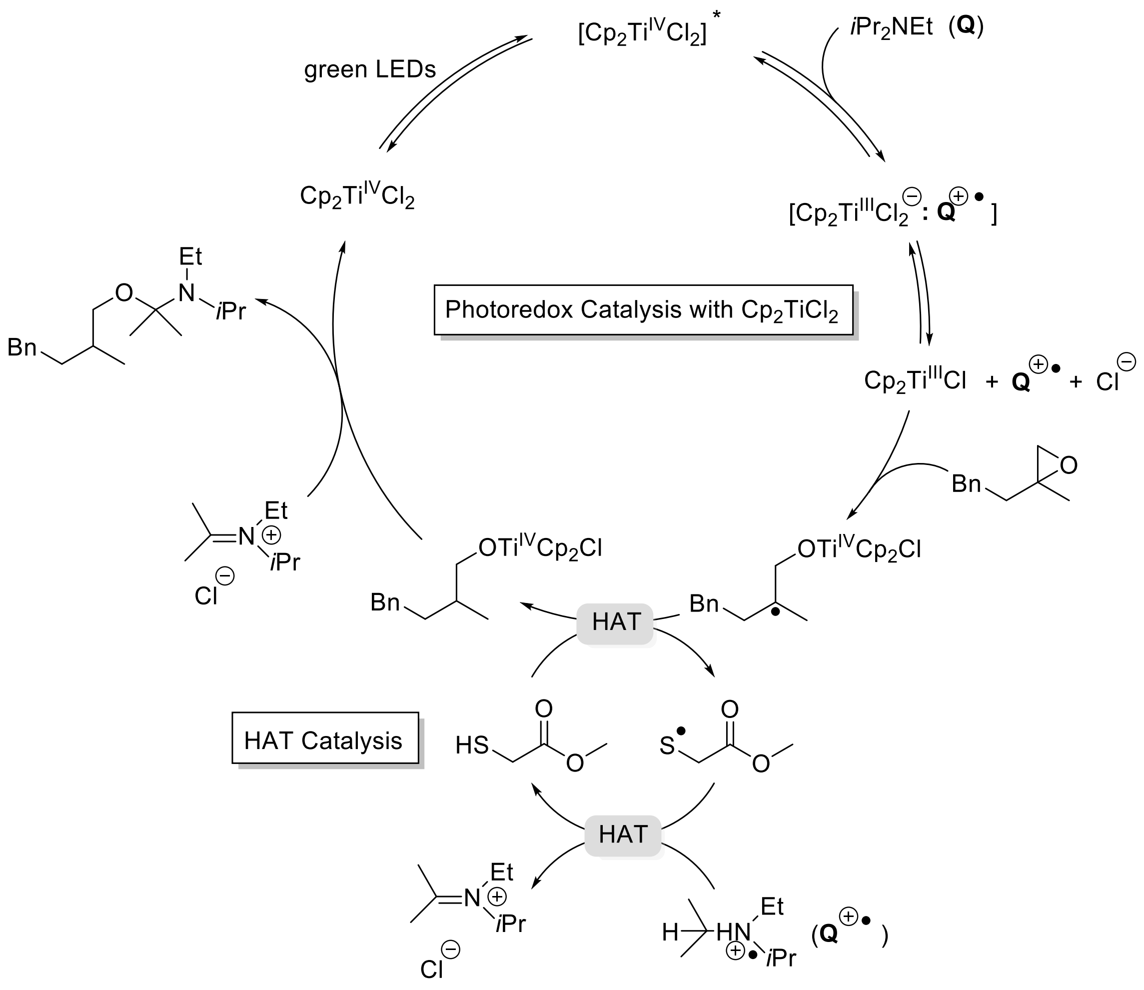
Lecture of 2 September 2021, h 15.00-16.00

How Can One Activate Titanocenes for Catalytic Radical Chemistry? From Electro- to Photochemistry

Andreas Gansäuer

Kekulé-Institute for Organic Chemistry, Gerhard-Domagk-Str. 1, 53121 Bonn
E-mail: andreas.gansaeuer@uni-bonn.de

In this talk, it will be shown how epoxides can be used as substrates in catalytic radical chemistry with titanocene complexes as catalysts. Key-aspects are the concepts of oxidative additions and reductive eliminations in single electron steps and the tuning of the catalysts' properties for efficient catalysis. It will be shown how the insights gained can be used to activate the catalysts by electrochemistry and photochemistry.



Lecture of 2 September 2021, h 16.00-17.00

Understanding Kinetics through the Energy Representation

Sebastian Kozuch

Department of Chemistry, Ben-Gurion University of the Negev, Beer-Sheva 841051, Israel.
E-mail: kozuch@bgu.ac.il

With the development of computational tools the calculation of reaction pathways for catalytic systems has become a routine job. But still, a missing link between the calculated reaction profile and the kinetics of a catalytic cycle makes it impossible to resolve the basic question: What makes for a good catalytic cycle?

With the aid of the energy span model[1–6] we will be able to calculate the TOF (turn-over frequency) and TON (turn-over number) of catalytic cycles from their energy representation in a simple, physically correct and elegant manner. In this way we can seamlessly bridge experimental and computational outcomes of catalytic cycles, explain their efficiency, and even suggest improvements.

[1] Solel, E.; Tarannam, N.; Kozuch, S. Catalysis: Energy Is the Measure of All Things. *Chem. Commun.* **2019**, *55*, 5306–5322.

[2] Kozuch, S. Taking the k out of kinetics https://www.chemistryworld.com/opinion/taking-the-k-out-of-kinetics/3010619.article

[3] Kozuch, S. Steady State Kinetics of Any Catalytic Network: Graph Theory, the Energy Span Model, the Analogy between Catalysis and Electrical Circuits, and the Meaning of "Mechanism." *ACS Catal.* **2015**, 5242–5255.

[4] Kozuch, S.; Martin, J. M. L. "Turning Over" Definitions in Catalytic Cycles. *ACS Catal.* **2012**, *2*, 2787–2794.

[5] Kozuch, S. A Refinement of Everyday Thinking: The Energetic Span Model for Kinetic Assessment of Catalytic Cycles. *WIREs Comput. Mol. Sci.* **2012**, *2*, 795–815.

[6] Kozuch, S.; Shaik, S. How to Conceptualize Catalytic Cycles? The Energetic Span Model. *Acc. Chem. Res.* **2011**, *44*, 101–110.

Lecture of 2 September 2021, h 17.00-18.00

Formation and Catalytic Activity of Palladium Nanoparticles in C-C Cross-Coupling Reactions

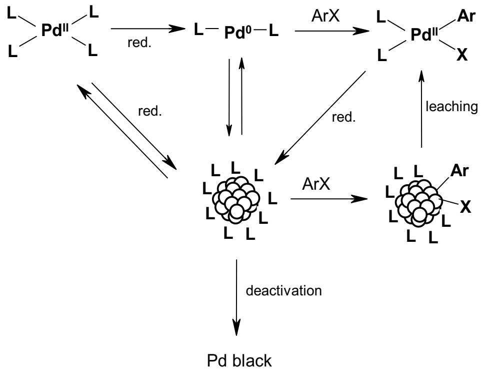
Anna M. Trzeciak

Faculty of Chemistry University of Wrocław, F. Joliot-Curie 14, 50-383 Wrocław, Poland.
E-mail: anna.trzeciak@chem.uni.wroc.pl

Palladium nanoparticles, Pd NPs, play an important role as catalysts of C-C cross-coupling reactions leading to valuable organic products used as pharmaceuticals or agrochemicals. An attractive feature of Pd NPs immobilized on organic or inorganic supports is their potentially easy recovery and recycling after the catalytic process. In this case, adequately designed polymeric support stabilize Pd NPs against agglomeration due to interactions with functional groups of polymer. The promising properties of highly porous MOFs (Metal Organic Frameworks) as supports for Pd NPs should be also mentioned.

The high catalytic activity of Pd NPs, often higher than that of Pd complexes, can be related to the high surface-to-volume ratio and availability of many metal centers for substrates activation. There are many examples of palladium catalytic systems in which Pd NPs formed *in situ* presented higher activity than the pre-formed ones. This significantly facilitates the preparation of a catalyst, which can be introduced to the reaction mixture as a Pd(II) precursor. Transformation of Pd(II) to Pd NPs can be easily monitored using TEM, XPS or XRD methods.

Catalytic reaction can occur on the surface of Pd NPs following a heterogeneous pathway. However, under catalytic conditions solubilization of Pd NPs can proceed as a result of their reaction with substrates, for example with aryl halide. Consequently, the size of Pd NPs decreases and Pd(II) complexes appearing in solution can participate in the catalytic process according to the homogeneous mechanism. Thus, the final catalytic activity can be explained by cooperation of different forms of palladium (Scheme 1).



Scheme 1 Different forms of Pd present in the catalytic system during C-C cross-coupling.

[1] Trzeciak, A. M.; Augustyniak, A.W, *Coord. Chem. Rev.*, **2019**, *384*, 1-20.
[2] Jia, Ch.-J.; Schuth, F., *Phys. Chem. Chem. Phys.,* **2011**, *13*, 2457-2487.
[3] Ananikov, V.P.; Beletskaya, I.P., *Organometallics*, **2012**, *31*, 1595-1604.

Lecture of 3 September 2021, h 15.00-16.00

Enantioselective C-H Functionalization. The Transition to 3d-Transition-Metals

Nicolai Cramer

EPFL, SB, Institute of Chemistry and Chemical Engineering, Laboratory of Asymmetric Catalysis and Synthesis
BCH4035, 1015 Lausanne, Switzerland.
E-mail: Nicolai.cramer@epfl.ch

Advances in organic chemistry are of importance for modern society and synthesizing tailored molecules in high purity is critical for many industries. In addition, important production requirements of sustainability and timeliness have been raised. Of particular relevance is the efficient production of enantiopure compounds due to their unique properties. The catalytic direct and enantioselective functionalization of carbon-hydrogen (C-H) bond is well suited. The organic ligands surrounding the central transition-metal atom of the catalysts are the key contributors to boost reactivity and selectivity of the underlying reactions. The design and development of novel enabling ligands systems is vital for success and represents one of your central research goals.[1] My presentation will cover some of our recent developed tools for enantioselective carbon-hydrogen bond activations using 3d-transition-metals[2] such as cobalt,[3] nickel[4] and iron.[5] We point towards the future potential of these cheap metals in the production of relevant small molecules (Figure 1).

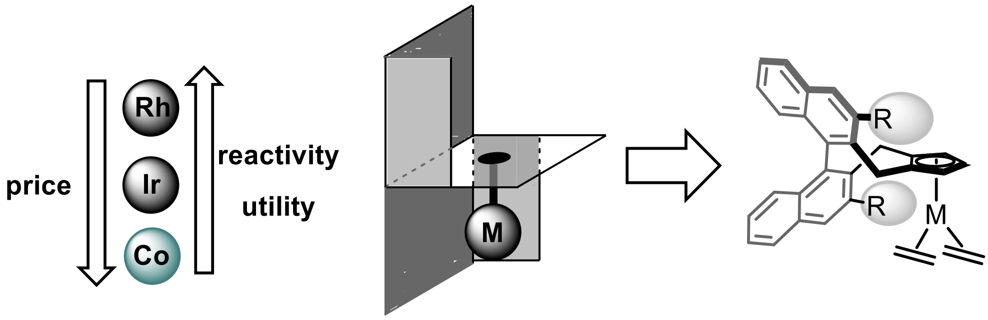


Figure 1

[1] (a) Ye, B.; Cramer, N. *Acc. Chem. Res.* **2015**, *48*,1308; (b) Mas-Roselló, J.; Herraiz, A. G.; Audic, B.; Laverny, A.; Cramer, N. *Angew. Chem. Int. Ed.* **2021**, *60*, 13198.
[2] Woźniak, Ł.; Cramer, N. *Trends Chem.* **2019**, 1, 471.
[3] (a) Ozols, K.; Jang, Y.-S.; Cramer, N. *J. Am. Chem. Soc.* **2019**, *141*, 5675; (b) Ozols, K.; Onodera, S.; Wozniak, L.; Cramer, N. *Angew. Chem. Int. Ed.* **2021**, *60*, 655.
[4] Braconi, E.; Cramer, N. *Angew. Chem. Int. Ed.* **2020**, *59*, 16425.
[5] Braconi, E.; Götzinger, A. C.; Cramer, N. *J. Am. Chem. Soc.* **2020**, *142*, 19819.

Lecture of 3 September 2021, h 16.00-17.00

Copper Makes the Difference: Visible Light Driven Transformations Using Cu(I) or Cu(II)-Complexes ss Photocatalysts

Oliver Reiser

Institut für Organische Chemie, Universität Regensburg, 93053 Regensburg, Germany.
E-mail: Oliver.Reiser@ur.de

/Synthetic organic chemistry undertakes great efforts to develop new catalytic transformations that utilize greener reagents and avoid stoichiometric additives. In this regard, visible-light photoredox catalysis offers a unique activation mode of molecules, which is serving as an alternative to many thermal transition-metals catalyzed reactions. The vast majority of photoredox catalyzed processes capitalizes on heavy metals namely, Ru(II) or Ir(III)-complexes which can serve as single electron oxidant or reductant in their photoexcited states. As a low cost-alternative, organic dyes are also frequently used photocatalysts but suffer in general from lower photostability. Copper based photocatalysts are rapidly emerging, offering not only economic and ecologic advantages, but in addition are able to interact with substrates beyond electron transfer via inner sphere mechanisms, which has been successfully utilized to achieve challenging transformations. Moreover, the combination of conventional photocatalysts with copper(I) or copper(II) salts allows a most efficient merger of photoredox and transition metal based catalysis.

Selected synthetic applications from our laboratory, highlighting the complementary opportunities of copper and iridium based photocatalysts, will be discussed.

[1] Abderrazak, Y.; Bhattacharyya, A.; Reiser, O. *Angew. Chem. Int. Ed.* **2021**, Early View; doi: 10.1002/anie.202100270: Visible-Light-Induced Homolysis of Earth-Abundant Metal-Substrate Complexes: A Complementary Activation Strategy in Photoredox Catalysis.

[2] Hossain, A.; Bhattacharyya, A.; Reiser, O. *Science* **2019**, *364*, eaav9713: Copper's rapid ascent in visible-light photoredox catalysis.

Lecture of 3 September 2021, h 17.00-18.00

An Overview of Ferrocene Derivatives: Synthesis, Characterization, and Potential Applications

Ingrid Montes-González, Ambar Alsina-Sánchez, Alejandro Burgos-Suazo,
Delvin Caraballo-Rodríguez, Sara Delgado-Rivera, Daisy Díaz-Rohena,
Sebastián Henríquez-López, Giovanni Pérez-Ortiz

Department of Chemistry, University of Puerto Rico, Rio Piedras Campus, San Juan, PR.
E-mail: ingrid.montes2@upr.edu

Ferrocene, an organometallic compound from the metallocene family, has attracted the attention of scientists because of its stability and multiple applications (optical devices, redox mediators for enzyme sensors, and the synthesis of biological active compounds). Ferrocene has proven to be an excellent bioisostere that improves bioactivity, such as anticancer, antimalarial, antioxidant, antimicrobial, low cytotoxicity, and high lipophilicity. Chalcones, stilbenes, aromatic ethyne, adamantly, urea, thiourea scaffolds have shown multiple biological and medicinal properties, including anti-cancer potential. There is an increasing interest of many researchers to incorporate these cores as ferrocene derivatives that could provide a synergistic effect for the design and development of novel and more potent anti-cancer drugs. Our research group focuses on the synthesis and characterization of a series of ferrocenyl derivatives that include the above scaffolds, among others, and explore their potential biological applications (Figure 1). These derivatives have been synthesized employing synthetic methodologies such as Claisen-Schmidt, Sonogashira, Heck, and other well know reactions, with moderate to good yields and applying a greener approach when possible. Once the compounds are synthesized and characterized, their biological activity is studied against some cancer cell lines. Also, the radical scavenging properties of the compounds are explored by determining their potential as antioxidants using the DPPH assay. The synthesis, characterization, and biological assays results as well as the trends shown by these ferrocenyl derivatives will be elaborated.

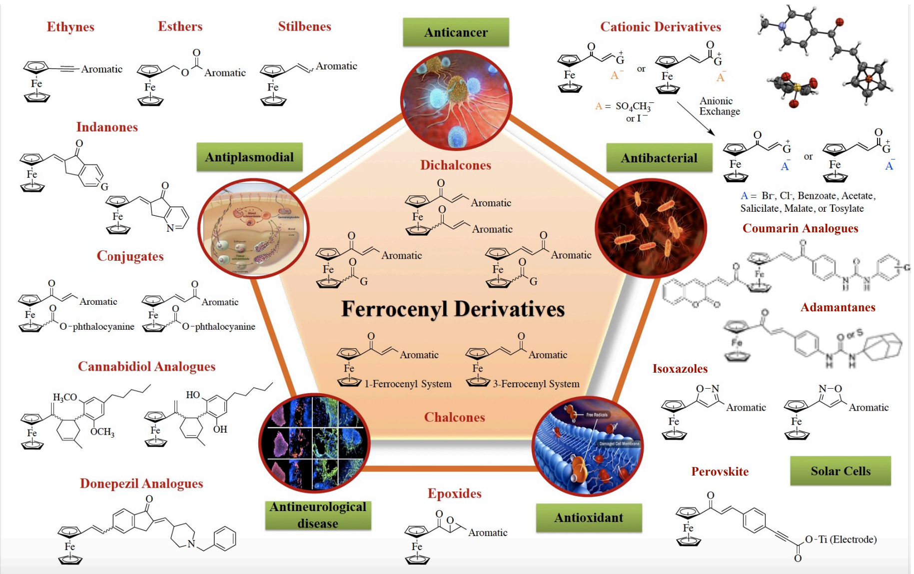


Figure 1

ABSTRACTS OF PARTICIPANTS

Abstract 1

Pd(II) Catalysts for the Synthesis of Functionalized Polyolefins: the Effect of a Fourth Monodentate Ligand.

Chiara Alberoni,[a]* Gabriele Balducci,[a] Maurizio Polentarutti,[b] Barbara Milani[a]

[a] Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Trieste, Via Licio Giorgieri 1, 34127 Trieste, Italy.
[b] Elettra – Sincrotrone Trieste, S.S. 14 Km 163.5 in Area Science Park, 34149 Basovizza, Trieste, Italy.
*E-mail = chiara.alberoni@phd.units.it

The introduction of polar functional groups into the polyolefin skeleton is one of the major unsolved problems in polymer synthesis, being recognized as the “polar monomer problem”.[1] The most sustainable approach to solve it is represented by the direct, controlled, homogeneously catalyzed copolymerization of ethylene with polar vinyl monomers. The main catalytic systems active for the copolymerization of ethylene with methyl acrylate are based on palladium(II) complexes of general formula [Pd(Me)(N-N)(NCMe)][X] or [Pd(Me)(P-O)(dmso/L)], with α-diiminic or phosphino-sulphonate ligands, respectively. They lead to copolymers with the polar monomer either at the end of the branches or into the main chain, respectively.[2]

As an alternative strategy to ligand design, we have now investigated the replacement of acetonitrile on [Pd(Me)(N-N)(NCMe)][PF_6] with a monodentate ligand, L, belonging to the family of pyridines. With this aim, we have synthesized and characterized, both in solution by NMR spectroscopy and in solid state by X-ray analysis (Figure 1), two series of Pd(II) complexes of general formula [Pd(Me)(N-N)(L)][PF_6].

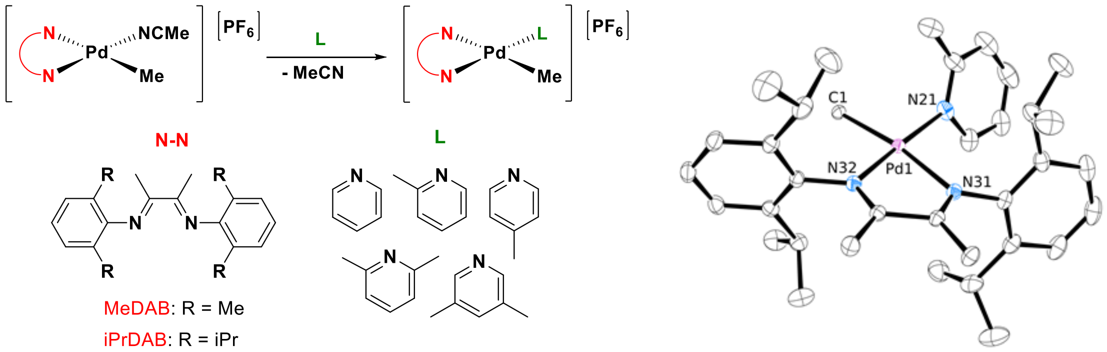


Figure 1 The Pd(II) complexes under investigation and ORTEP representation of one of them.

A detailed investigation of their catalytic behavior on the target reaction was performed pointing out that, despite the inhibiting effect of L on productivity with respect to acetonitrile, surprisingly enough L remarkably affects the microstructure of the produced macromolecules, thus suggesting that it remains close to the metal center during the catalytic process.

[1] Luckham, S. L. J.; Nozaki, K. *Acc. Chem. Rev.* **2021**, *54*, 344-355.
[2] (a) Tan, C.; Chen, C. *Angew. Chem. Int. Ed.* **2019**, *58*, 7192-7200; (b) Nakamura, A.; Anselment, T. M. J.; Claverie, J.; Goodall, B.; Jordan, R. F.; Mecking, S.; Rieger, B.; Sen, A.; van Leeuwen, P. W. N. M.; Nozaki, K. *Acc. Chem. Rev.* **2013**, *46*, 1438-1449.

Abstract 2

Ruthenium Diphosphine Carbonyl Complexes in Glioblastoma Cancer Treatment

Dario Alessi,[a]* Pierfrancesco del Mestre,[b] Denise Lovison,[a] Maurizio Ballico,[a] Irene G. Rolle,[b]
Daniela Cesselli,[b] Antonio P. Beltrami,[b] Walter Baratta[a]

[a] Dipartimento di Scienze Agroalimentari, Ambientali e Animali, Università di Udine, Via Cotonificio 108, I-33100 Udine, Italy.
[b] Dipartimento di Area Medica, Università di Udine, Via Colugna 50, I-33100 Udine, Italy.
* E-mail = dario.alessi90@libero.it

Our research group found that complexes of general formula [Ru(X)(dppb)(CO)(phen)]X are highly effective in the in vitro treatment of anaplastic thyroid cancer.[1] Herein we present the synthesis of related compounds using the chiral Binap and the dppe diphosphines. The toxicity of these compounds has been evaluated in vitro against glioblastoma cancer cells by the determination of the IC_{50} via MTT assay. The stability of these complexes in aerated water has also been investigated.

[1] Lovison, D.; Allegri, L.; Baldan, F.; Ballico, M.; Damante, G.; Jandlc, C.; Baratta, W. *Dalton Trans.* **2020**, *49,* 8375-8388.

Abstract 3

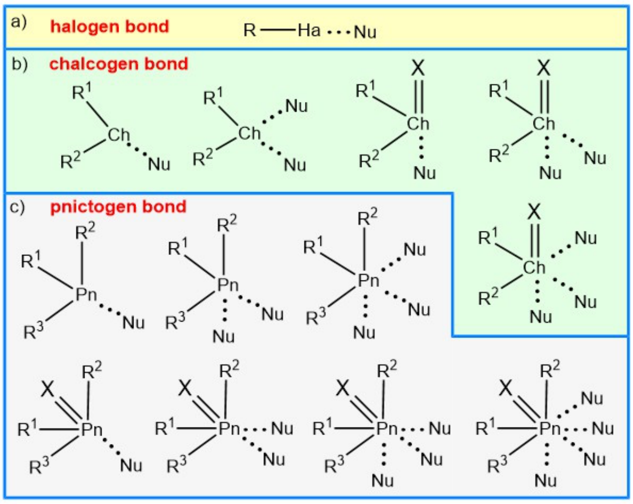
Chalcogen Bonding as a New Supramolecular Tool in Coordination Compounds

Vusala A. Aliyeva,[a]* M. Fátima C. Guedes da Silva,[a] Kamran T. Mahmudov,[a,b]
Armando J.L. Pombeiro[a]

[a] Centro de Química Estrutural, Instituto Superior Técnico, Universidade de Lisboa, Av. Rovisco Pais, 1049–001 Lisbon, Portugal.
[b] Department of Chemistry, Baku State University, Z. Xalilov Str. 23, Az 1148 Baku, Azerbaijan.
*E-mail = vusalaaliyeva1990@gmail.com

The chalcogen bond (ChB) is defined as a noncovalent interaction between the electron density deficient region (called as σ or π hole) of a covalently bonded chalcogen atom and a nucleophilic (Nu) site in the same (intramolecular) or another (intermolecular) molecular entity: R−Ch···Nu (Ch = O, S, Se or Te; R = C, Pn, Ch, metal, etc.; Nu = lone pair possessing Ha, Ch or Pn atom, π-system, anion, radical, etc.).[1] According to the σ-hole concept,[2] the number of possible positive surface electrostatic potential(s) on the extension of the corresponding σ covalent bond(s) on chalcogen atoms is usually higher than on halogen atoms[3] and comparable with those of pnictogens[4] (Scheme). ChB can assist synthesis, catalysis, molecular recognition, crystal engineering, drug design, protein-ligand interactions, etc.[1,5,6]

Like halogen and pnictogen bonds, the bond parameters (strength, tunability and high directionality) make ChB an unique supramolecular tool in the design of the secondary coordination sphere of metal complexes, which is an important synthetic strategy in the improvement of functional properties of materials. Herein we present a couple of examples, taken from the Cambridge Structural Database, in which ChB plays a crucial role in the decoration of secondary coordination sphere of coordination compounds, controlling their structure and formation of supramolecular 1D, 2D or 3D frameworks.



Scheme. Schematic illustration of halogen (a), chalcogen (b) and pnictogen (c) bonds (electron-withdrawing ability of substituents: $R^1 > R^2 > R^3$).

[1] Mahmudov, K.T.; Kopylovich, M.N.; Guedes da Silva, M.F.C.; Pombeiro, A.J.L. *Dalton Trans.* **2017**, *46*, 10121.
[2] Politzer, P.; Murray, J.S.; Clark, T.; Resnati, G. *Phys. Chem. Chem. Phys.* **2017**, *19*, 32166.
[3] Cavallo, G.; Metrangolo, P.; Milani, R.; Pilati, T.; Priimagi, A.; Resnati, G.; Terraneo, G. *Chem. Rev.* **2016**, *116*, 2478.
[4] Mahmudov, K.T.; Gurbanov, A.V.; Aliyeva, V.A.; Resnati, G.; Pombeiro, A.J.L. *Coord. Chem. Rev.* **2020**, *418*, 213381.
[5] Mahmudov, K.T.; Aliyeva, V.A.; Guedes da Silva, M.F.C.; Pombeiro, A.J.L. The Chalcogen Bond in Solution: Synthesis, Catalysis and Molecular Recognition (Chapter 11) in Halogen Bonding in Solution (Ed. S. Huber), Wiley-VCH, **2021**, pp. 363−382.
[6] Beno, B.R.; Yeung, K.-S.; Bartberger, M.D.; Pennington, L.D.; Meanwell, N.A. *J. Med. Chem.* **2015**, *58*, 4383.

Acknowledgments: This work was partially supported by the Fundação para a Ciência e Tecnologia (project UIDB/00100/2020 of Centro de Química Estrutural), Portugal. KTM acknowledges the FCT and Instituto Superior Técnico DL 57/2016 and L 57/2017 Program, Contract no: IST-ID/85/2018.

Abstract 4

Ru(II) Arene Complexes Bearing a Glucoconjugate *NHC* Ligand as Anticancer Agents: Synthesis, Characterization and Reactivity

Alfonso Annunziata,[a,b]* Maria Elena Cucciolito,[a,b] Antonello Merlino,[a] Paul J.Dyson,[c]
Francesco Ruffo[a,b]

[a] Dipartimento di Scienze Chimiche, Università degli Studi di Napoli Federico II, Complesso Universitario di Monte S. Angelo, via Cintia 21, 80126 Napoli, Italy. [b] Consorzio Interuniversitario di Reattività Chimica e Catalisi (CIRCC), via Celso Ulpiani 27, 70126 Bari, Italy. [c] Institut des Sciences et Ingenierie Chimiques, Ecole Polytechnique Federale de Lausanne (EPFL), Lausanne, Switzerland.
*E-mail = alfonso.annunziata@unina.it

Anticancer agents based on transition metals offer unlimited possibilities, due to the opportunity to choose the metal centre with its oxidation state, and ligands which consent to tune physical-chemical properties of the resulting complexes. Ruthenium compounds exhibit reduced toxicity compared to platinum complexes and excellent versatility in the mode of action. Hence, following the great success of the Ru(III) compounds NAMI-A and KP1019, Ru(II) arene complexes attracted great interest displaying notable anticancer and in some case antimetastatic activity.[1] Intense efforts have been carried out to fully disclose their in-solution chemistry, and their reactivity toward biological molecules. The rationale choice of the ligands, as well as the opportune functionalisation of the arene unit affect the lipophilicity, the rate of the ligands exchange, the cellular uptake, and their ability to target biomolecules.[2] Carbohydrate derived ligands represent an excellent example of functionalization for fine tuning biological properties of metal complexes, since a sugar residue can enhance biocompatibility, water solubility, and selectivity of the drug (Warburg Effect).[3] Within this frame, a library of novel Ru(II) arene complexes bearing a glucoconjugate NHC ligand (Figure 1), has been synthesized and fully characterized by several spectroscopic techniques.

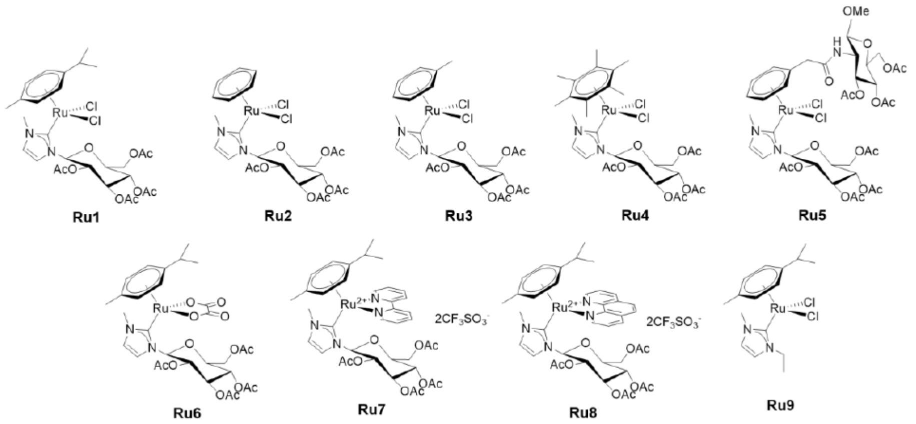


Figure 1

The influence of different arenes on the reactivity of the dichloro-complexes (**Ru1-Ru5** and **Ru9**) as well as the effect in replacing the chlorides with chelating ligands (**Ru6-Ru8**) in the *p*-cymene derivative (**Ru1**) was evaluated by studying their behaviour in aqueous media and their reactivity with relevant biological nucleophiles and model proteins.

[1] Steel, T. R.; Walsh, F.; Wieczorek-Błauż, A.; Hanif, M.; Hartinger, C. G. *Coord. Chem. Rev.* **2021**, *439*, 213890.
[2] Streciwilk, W.; Terenzi, A.; Misgeld, R.; Frias, C.; Jones, P. G.; Prokop, A.; Keppler, B. K.; Ott, I. *ChemMedChem* **2017**, *12*, 214–225.
[3] Pettenuzzo, A.; Pigot, R.; Ronconi, L. *Metallodrugs* **2016**, *1*, 36-61.

Abstract 5

Design, Synthesis and Reactivity of New Zwitterionic Imidazolium-based Species

Luca Bagnarelli,[a]* Riccardo Vallesi,[a]* Maura Pellei,[a] H. V. Rasika Dias,[b] Carlo Santini[a]

[a] University of Camerino, School of Science and Technology, via Sant'Agostino 1, 62032 Camerino (MC), Italy.
[b] Department of Chemistry and Biochemistry, The University of Texas at Arlington, Arlington, TX 76019-0065, USA.
*E-mail = luca.bagnarelli@unicam.it *E-mail = riccardo.vallesi@unicam.it

N-Heterocyclic Carbenes (NHCs) are an interesting family of ligands with donor properties comparable to phosphane ones. They can form complexes with transition elements and, among them, the coinage metals belonging to the 11th group of the periodic table. Metal-NHCs compounds have obtained a lot of interest in the last years because of their potential applications in catalysis, carbene transfer reactions and medicinal inorganic chemistry.[1] In this study, the rational design and synthesis of novel *N*-(alkyl/aryl)imidazolium-borates compounds and the corresponding reactions towards the deprotonation have been investigated. The imidazolium-trihydridoborate adducts have been obtained by the addition of BH_3·THF to the starting materials *N*-benzyl- or *N*-mesityl-imidazole. The related imidazolium-triphenylborate species have been prepared by the reaction of ammonium tetraphenylborate with benzylimidazole or mesitylimidazole with the loss of one of the phenyl groups. All these new species have been fully characterized, both analytically and spectroscopically, to confirm their structures by means of CHN elemental analysis, ^{1}H-NMR, ^{13}C-NMR, ^{11}B-NMR, FT-IR spectroscopy and electrospray ionization mass spectrometry (ESI-MS). Regarding the compounds (3-benzylimidazolium-1-yl)trihydridoborate, $(HIm^{Bn})BH_3$, and (3-mesitylimidazolium-1-yl)trihydridoborate, $(HIm^{Mes})BH_3$, single crystals suitable for the X-ray diffraction crystallography have been obtained by slow evaporation of $CHCl_3$ and $CHCl_3$/THF solutions, respectively. The reactivity of all novel compounds as carbene precursors has been evaluated with the aim to produce borate-NHC complexes and a new carbene-borate species has been synthesized via a microwaves-assisted method[2] (Figure 1).

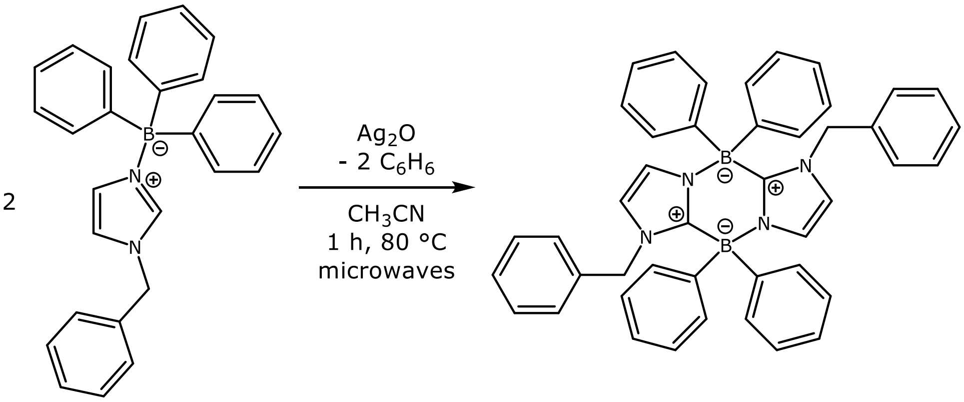


Figure 1 – Synthesis of the imidazabole species.

[1] Porchia, M.; Pellei, M.; Marinelli, M.; Tisato, F.; Del Bello, F.; Santini, C. *Eur. J. Med. Chem.* **2018**, *146*, 709-746.
[2] Pellei, M.; Vallesi, R.; Bagnarelli, L.; Rasika Dias, H. V.; Santini, C. *Molecules* **2020**, *25*, 3184.

Abstract 6

Cu(II) Pyrazolate-based Coordination Polymers: Synthesis, Characterization and Antibacterial Properties

Patrizio Campitelli,[a]* Corrado Di Nicola,[a] Alessia Tombesi,[a] Claudio Pettinari,[b] Fabio Marchetti,[a]
Riccardo Pettinari,[b] Simona Galli,[c] Stefania Scuri[b]

[a] University of Camerino, School of Science and Technology, Via S. Agostino 1, 62032 Camerino (MC), Italy.
[b] University of Camerino, School of Pharmacy, Via S. Agostino 1, 62032 Camerino (MC), Italy.
[c] Department of Science and High Technology, Via Valleggio 11, 22100 Como, Italy.
*E-mail = patrizio.campitelli@unicam.it

After the synthesis of $\{Cu^{I}[C(C_6H_4{\cdot}CN)_4]\}_n^{n+}$ as a first example of *"deliberately designed and constructed infinite framework"* by Robson and Hoskins in 1989,[1] an enormous variety of Coordination Polymers (CPs) extending in one, two or three dimensions and based on different metals and organic linkers, have been reported in literature. In this communication, eight Cu(II)-pyrazolate CPs have been yielded in different solvents adopting different synthetic strategies[2] and their solid-state characterization has been conducted by IR, XRPD, TGA/DTA, UV, E.A. and magnetic susceptibility. Moreover, the antibacterial activity the eight CPs against Gram-negative (*P. aeruginosa*, *E. coli*) and Gram-positive (*S. aureus*) bacteria has been investigated. Results of biological tests have highlighted the antibacterial properties of such CPs and the action mechanism through ROS production (Figure 1).

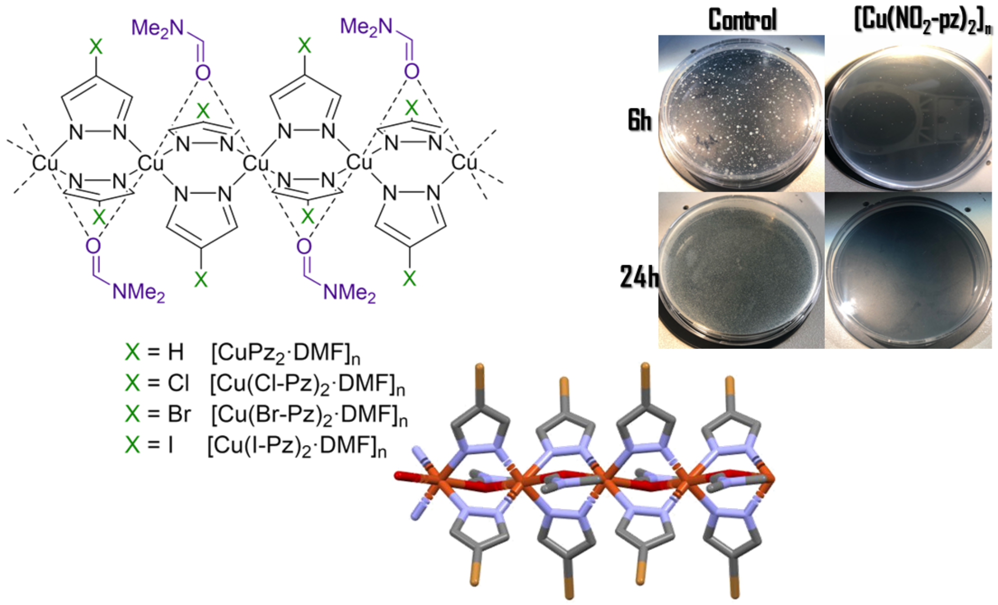


Figure 1 Schematic representation and XRPD Cu(II) Pyrazolate CPs structure and *E.coli* Growth Inhibition.

[1] Hoskins, B. F.; Robson, R. *J. Am. Chem. Soc.*, **1989**, *111*, 5962-5964.
[2] Di Nicola, C.; Tombesi, A.; Moroni, M.; Vismara, R.; Marchetti, F.; Pettinari, R.; Nardo, L.; Vesco, G.; Galli, S.; Casassa, S.; Pandolfo, L.; Pettinari, C. *CrystEngComm,* **2020**, *22*, 3294-3308.

Abstract 7

Functionalized 1,3,5-Triaza-7-phosphaadamantane Ligands and Their Cu^{I}/Cu^{II} and Zn^{II} Metal Complexes: Synthesis and Characterization

Nuno Reis Conceição,[a]* Abdallah G. Mahmoud,[b] M. Fátima C. Guedes da Silva,[a]
Armando J. L. Pombeiro[a,c]

[a] Centro de Química Estrutural, Instituto Superior Técnico, Universidade de Lisboa, Av. Rovisco Pais, 1049-001 Lisboa, Portugal.
[b] Dep. of Chemistry, Faculty of Science, Helwan University, Ain Helwan, 11795 Cairo, Egypt.
[c] Peoples' Friendship University of Russia (RUDN University), Research Institute of Chemistry, 6 Miklukho-Maklaya Street, Moscow, 117198, Russian Federation.
*E-mail = nunoconceicao@tecnico.ulisboa.pt

The cage-like phosphane 1,3,5-triaza-7-phosphaadamantane (PTA) exhibits the peculiar property of being soluble in water[1,2] therefore having potential for the development of a chemistry in aqueous medium. By avoiding (or reducing) the use of common yet pollutant organic solvents, an important step is taken for a "Green Chemistry" involving more sustainable and environmentally-friendly processes.

Functionalized PTA ligands (**HL^1Br** and **L^2Cl**, Figure 1) reacted with several Cu(I) metal salts to yield novel Cu(I) complexes, e.g., $[Cu(HL^1)_2Br_2]X$ (X= Br, I or BF_4), $[Cu(L^2)_2Cl_2]Br$. Moreover, the reaction of **HL^1Br** with copper(II) acetate yielded the novel Cu(II) complex $[Cu(L^1)_2]Br_2$, being the PTA derivative coordinated to the metal not through the P-atom (like in cuprous compounds) but via the carboxylate group of deprotonated L^1. Attempts to obtain heteronuclear complexes have been performed by reacting **HL^1Br** with both zinc acetate and copper(I) bromide.

The synthesized compounds were characterized through EA, NMR (^1H, ^{13}C, ^{31}P), ESI-MS, SCXRD (when applicable) and FTIR, and will be tested as catalysts in specific reactions.

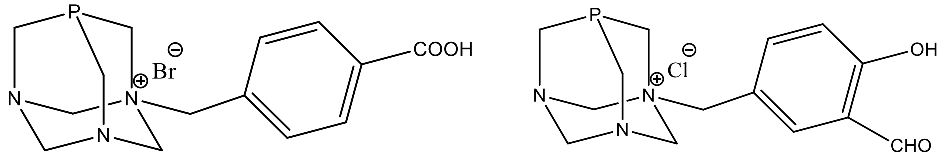


Figure 1 Functionalized PTA Ligands **HL^1Br** (left) and **L^2Cl** (right).

[1] Guerriero, A.; Peruzzini, M.; Gonsalvi, L. *Coord. Chem Rev*. **2018**, *355*, 328-361.
[2] Mahmoud, A. G.; Guedes da Silva, M. F. C.; Sokolnicki, J.; Smolénski, P.; Pombeiro, A. J. L. *Dalton Trans*. **2018**, *47*, 7290-7299.

Acknowledgements
The work is being supported by the Fundação para a Ciência e Tecnologia (FCT) (project UIDB/00100/2020 of Centro de Química Estrutural) and the RUDN University Strategic Academic Leadership Program. NRC acknowledges financial support from Research fellowship (for PhD student) BL2/2020_IST-ID of Centro de Química Estrutural (project 1801P.00974.1.01.01, UIDB/00100/2020) and *Programa Doutoral FCT* "Catalysis and Sustainability" CATSUS (PD/00248/2012).

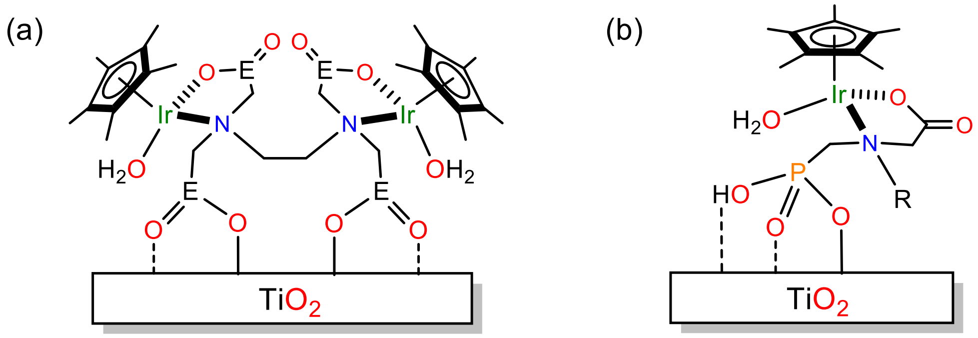
Abstract 8

Novel Di- and Mononuclear Homogeneous and Heterogenized Ir Water Oxidation Catalysts Bearing Cp* and Carboxylate/Phosphonate Ligands

Chiara Domestici,[a]* Leonardo Tensi,[a] Elisa Boccalon,[a,b] Fracensco Zaccaria,[a] Ferdinando Costantino,[a] Cristiano Zuccaccia,[a] Alceo Macchioni[a]

[a] Department of Chemistry, Biology and Biotechnology University of Perugia and CIRCC, Via Elce di Sotto, 8 – 06123 Perugia, Italy.
[b] Department of Industrial Engineering, University of Salerno, Via Giovanni Paolo II, 132 – 84084 Fisciano (SA), Italy.
*E-mail = chiara.domestici@unipg.it

The development of efficient water oxidation catalysts (WOCs) is crucial in the framework of constructing an artificial photo(electro)synthetic apparatus, where water can be used as source of electrons and protons for the generation of solar flues.[1,2] Among others, supported system appear particularly promising since they combine the best aspects of homogeneous and heterogeneous catalysis.[3] Recently, we have explored the possibility of combining the pentamethyl cyclopentadienyl ligand (Cp*), which usually imparts remarkable activity, with oxidation-resistant carboxylate and phosphonate anchoring groups. In this contribution, we will describe two novel classes of supported Cp*Ir-WOCs, based on cheap and readily available ligands: 1) EDTA and EDTMP, serving as anchoring and bridging tridentate ligands for two Cp*Ir fragments (Figure 1a)[4] and 2) glyphosate and glyphosine, acting as hybrid carboxylate/phosphonate ligands (Figure 1b).[5] The catalytic performance of these novel Cp*Ir heterogenized catalysts in WO driven by $NaIO_4$ as sacrificial oxidant will be presented and compared with that of their homogeneous counterparts.



1_TiO$_2$: E = C
2_TiO$_2$: E = P-OH

3_TiO$_2$: R = H
4_TiO$_2$: R = CH_2-P(O)(OH)$_2$

Figure 1 Sketches of the Cp*Ir heterogenized WOCs bearing phosphonate and carboxylate ligands.

[1] Armaroli, N.; Balzani, V. *Angew. Chemie - Int. Ed.* **2007**, *46*, 52–66.
[2] Armaroli, N.; Balzani, V. *Chem. - A Eur. J.* **2016**, *22*, 32–57.
[3] Macchioni A. *Eur. J. Inorg. Chem.* **2019**, *2019*, 7–17.
[4] Domestici, C.; Tensi, L.; Zaccaria, F.; Kissimina, N.; Valentini, M.; D'Amato, R.; Costantino, F.; Zuccaccia, C.; Macchioni, A. *Sci. Bull.* **2020**, *65*, 1614-1625.
[5] Domestici, C.; Tensi, L.; Boccalon, E.; Zaccaria, F.; Costantino, F.; Zuccaccia, C.; Macchioni, A. *Eur. J. Inorg. Chem.* **2021**, *2021*, 299–307.

Abstract 9

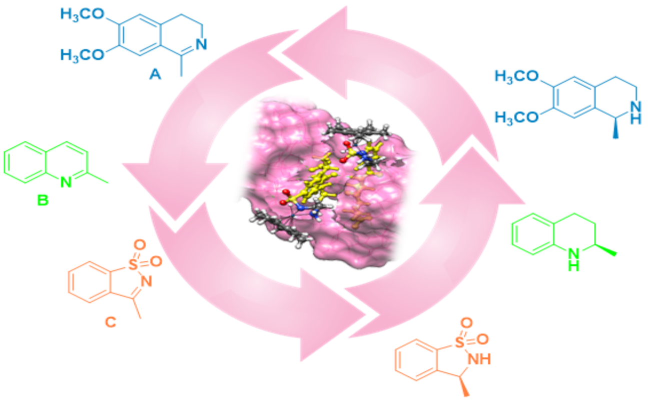
New Artificial Imine Reductases Based on an Iridium/Vancomycin System for the Asymmetric Reduction of Cyclic Imines

Giorgio Facchetti,[a]* Isabella Rimoldi[a]

[a] University of Milan, Department of Pharmaceutical Sciences, Via Golgi 19, 20133 Milano, Italy.
*E-mail = giorgio.facchetti@unimi.it

Artificial metalloenzymes, deriving from transition metal catalysts embedding within a biological environment, have recently risen up as a promising synthetic tool able to combine the reactivity of metal-based catalysis with the specificity of biocatalysis.[1] Dalbapeptides, such as vancomycin, teicoplanin and ristocetin are variously substituted heptapeptides whose antibiotic activity relies on their binding to the D-Ala-D-Ala dimer of peptidoglycan precursors thus leading to an irreversible inhibition of cell wall biosynthesis. This interaction is marked by such a low dissociation constant ($K_D = \sim 10^{-17}$M) that it makes vancomycin-based systems an innovative alternative to the classical biotin/(strept)avidin technology.[2,3]

In this context, a class of aminoethylbenzensulfonamide ligands functionalized with the D-Ala-D-Ala dimer were employed for the synthesis of hybrid catalysts in association with an iridium centre. In the presence of vancomycin, a new class of artificial reductases was obtained and applied to the Asymmetric Transfer Hydrogenation (ATH) of model imine substrates in different aqueous media. An encouraging 48% (*S*) *e.e.* was obtained in the asymmetric reduction of the salsolidine precursor in CH_3COONa 0.1 M buffer at pH 5 whereas in the case of quinolines, the *meta*-artificial metalloenzyme afforded the product in a significant 70% (*S*) *e.e.* when applied to quinaldine. Moreover, an unprecedented 35% (*R*) *e.e.* in the enantioselective reduction of chiral sultam precursor 3-methylbenzo[d]isothiazole-1,1-dioxide was realized under green reaction conditions.[4]



[1] Lewis, J. C. *ACS Catal.* **2013,** *3*, 2954-2975.
[2] Facchetti, G.; Rimoldi, I. *New J. Chem*. **2018**, *42*, 18773-18776.
[3] Facchetti, G.; Pellegrino, S.; Bucci, R.; Nava, D.; Gandolfi, R.; Christodoulou, M. S.; Rimoldi, I. *Molecules* **2019**, *24*, 2771-2779.
[4] Facchetti, G.; Bucci, R.; Fusè, M.; Erba, E.; Gandolfi, R.; Pellegrino, S.; Rimoldi, I. *Inorg. Chem.* **2021**, *60*, 2976-2982.

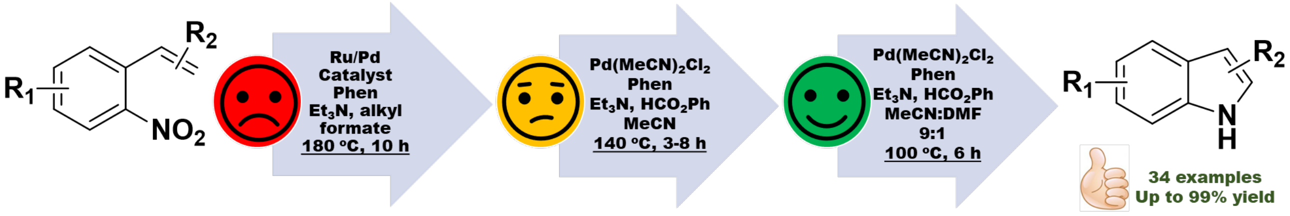
Abstract 10

Formate Esters as Efficient CO Surrogates in the Synthesis of Indoles by Reductive Cyclization of Nitro Styrenes

Manar Ahmed Fouad Abdellatif,[a,b]* Francesco Ferretti,[a] Fabio Ragaini[a]

[a] Dipartimento di Chimica, Università degli Studi di Milano, via Golgi 19, Milano, 20133, Italy.
[b] Chemistry Department, Faculty of Science, Alexandria University, P.O. Box 426, Alexandria, 21321, Egypt.
*E-mail = manar.abdellatif@unimi.it

More than thirty years ago, Cenini and co-workers reported the first reductive cyclization reaction of *o*-nitroarenes to indoles using carbon monoxide as the reductant, using different transition metals as catalysts under harsh conditions (220°C, 80 bar CO).[1] Despite of the high efficiency of this kind of reactions, they have not become of widespread use. This may be due to the need to use pressurized CO, requiring safety measures that are not accessible in most synthetic organic laboratories. Alkyl and aryl formate esters were employed by our group as effective, low-toxicicy and cheap *in-situ* CO sources in the Pd- and Pd/Ru-catalyzed reductive cyclization of *o*-nitroarenes to afford indoles. Since the cost of alkyl formates is minimal, the first investigations have been made by using them as CO sources. A bimetallic Ru/Pd catalytic system was required to achieve satisfactory yields for both the decomposition of formate and the reductive cyclization of *o*-nitrostyrenes. However, the results obtained were only achieved under forcing conditions (180 °C, up to 10 h). In contrast, when phenyl formate was used, complete conversion and good selectivity was achieved at a lower temperature (140 °C) and using a Pd/phenanthroline complex alone as a catalyst.[2] However, the moderately high temperature used leaded to a low selectivity in the cyclization of certain substrates. Here we report the results of further optimizations that can improve both the yield and selectivity. A lower reaction temperature and a mixed CH_3CN/DMF solvent system allowed to get improved yield for several substrates including some for which previous conditions failed to afford the indole. The same strategy was also applicable on a 2 gram-scale reaction, which verifies the reproducibility at a large scale. The reactions can be performed in a single cheap glass pressure tube, making this kind of reaction a "General Tool" for the synthetic chemist.[3]



[1] Crotti, C.; Cenini, S.; Rindone, B.; Tollari, S.; Demartin, F. *J. Chem. Soc. Chem. Commun.* **1986**, 784-786.
[2] Formenti, D.; Ferretti, F.; Ragaini, F. *ChemCatChem* **2018**, *10*, 148-152.
[3] Fouad, M. A.; Ferretti, F; Formenti; D.; Milani, F.; Ragaini, F. *Eur. J. Org. Chem*. in press. https://doi.org/10.1002/ejoc.202100789

Abstract 11

Synthesis of Diastereoisomerically Pure (Cyclopentadienone)Iron Complexes and their Application as Pre-Catalysts for the Asymmetric Hydrogenation of Ketones

Giovanni Maria Fusi,[a]* Tommaso Gandini,[b] Luca Pignataro,[b] Umberto Piarulli[a]

[a] Università degli Studi dell'Insubria, DiSAT, Via Valleggio 11, 22100, Como, Italy.
[b] Università degli Studi di Milano, Dipartimento di Chimica, via C. Golgi 19, 20133 Milano, Italy.
* E-mail = gmfusi@uninsubria.it

Iron-based catalysis has gathered growing attention in recent years as an alternative to noble metals, thanks to the low costs and low toxicity of iron, and to the wide applicability of new robust catalysts. Among these, (cyclopentadienone)iron complexes display catalytic activity in several chemical transformations, particularly those involving the heterolytic cleavage and transfer of H_2 (i.e. hydrogenation or transfer hydrogenation of polar double bonds).[1] During the last decade, the application of (cyclopentadienone)iron complexes has been extended also to enantioselective reductions of ketones and imines: several strategies for the preparation of stereoselective pre-catalysts were pursued,[2] but modest enantioselectivities were observed so far.

Here the synthesis of new chiral (cyclopentadienone)iron complexes (Figure 1 A) will be presented: the complexes possess a stereogenic plane generated by the two different substituents on the two sides of the carbonyl group of the cyclopentadienone. In this way better enantioselectivities could be achieved by modulating the difference in hindrance. The presence of the axially stereogenic (*R*)-1,1'-binaphthyl system allowed separation of the diastereomers formed upon complex formation, via simple chromatographic column on silica gel. Preliminary tests on the hydrogenation of acetophenone with complex **1a** (Figure 1 B) showed promising results in terms of enantioselectivity.

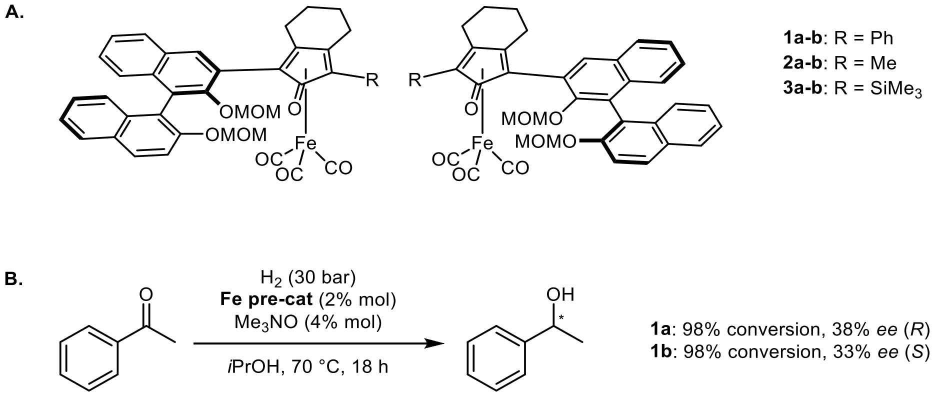


Figure 2 A. Structure of the complexes object of this study; B. Hydrogenation of acetophenone catalyzed by diastereomers 1a and 1b.

[1] (a) Quintard, A.; Rodriguez, J. *Angew. Chem. Int. Ed.* **2014**, *53*, 4044-4055; (b) Pignataro, L.; Gennari, C. *Eur. J. Org. Chem.* **2020**, *22*, 3192-3205.

[2] (a) Piarulli, U.; Vailati Facchini, S.; Pignataro, L. *Chimia* **2017**, *71*, 580-585; (b) Bai, X.; Cettolin, M.; Mazzoccanti, G.; Pierini, M.; Piarulli, U., Colombo, V.; Dal Corso, A.; Pignataro, L.; Gennari, C. *Tetrahedron* **2019**, *75*, 1415-1424.

Abstract 12

Metal-Organic Frameworks for One-pot Deacetalization−Knoevenagel Cascade Reactions

Anirban Karmakar,[a]* Armando J. L. Pombeiro[a]

[a] Centro de Química Estrutural, Instituto Superior Técnico, Universidade de Lisboa, Av. Rovisco Pais, 1049–001, Lisbon, Portugal.
* E-mail = anirbanchem@gmail.com

Metal–organic frameworks (MOFs) are crystalline coordination networks consisting of metal ions or clusters and multidentate organic ligands.[1] This area of research is currently undergoing a rapid growth due to their potential applications as functional materials in heterogeneous catalysts, magnetism, nonlinear optics, gas storage and separation, etc.[2] Moreover, MOFs constructed from amide based linkers have attracted considerable attention due to their interesting topologies as well as catalytic properties.[3] Thus, we have synthesized two different amide functionalized multifunctional carboxylate ligands and employed them for the construction of various MOFs using Zn(II) and Cd(II) metal ions. Solvothermal reactions of Zn(II) and Cd(II) nitrates with amide based ligands gives rise to four new metal organic compounds. We have characterized them by X-ray single crystal diffraction, elemental microanalysis, FT-IR, thermogravimetric analysis and powder X-ray diffraction analysis. These compounds heterogeneously catalysed the tandem deacetalization−Knoevenagel condensation reactions under conventional heating, microwave irradiation or ultrasonic irradiation (Figure 1) and can be recycled without losing activity.

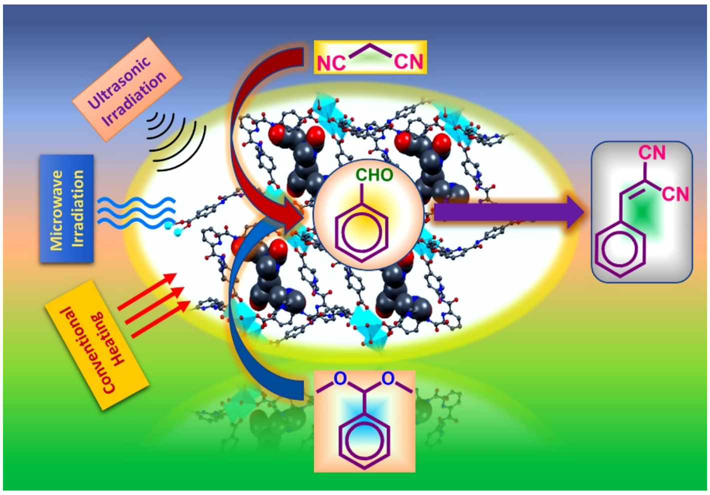


Figure 1 One-pot tandem deacetalization-Knoevenagel reactions catalyzed by MOFs using conventional heating, microwave and ultrasonic methods.

[1] Karmakar, A.; Titi, H. M.; Goldberg, I. *Cryst. Growth Des.* **2011**, *11*, 2621–2636.
[2] Karmakar, A.; Pombeiro, A. J. L. *Coord Chem Rev.* **2019**, *395*, 86-129.
[3] Karmakar, A.; Guedes da Silva, M. F. C; Pombeiro, A. J. L. *Dalton Trans.* **2014**, *43*, 7795–7810.

Acknowledgements This work has been supported by the Foundation for Science and Technology (FCT), Portugal (project UIDB/00100/2020). AK also thanks to Instituto Superior Técnico and FCT for Scientific Employment contract (Contrato No: IST-ID/107/2018) under Decree-Law no. 57/2016, of August 29.

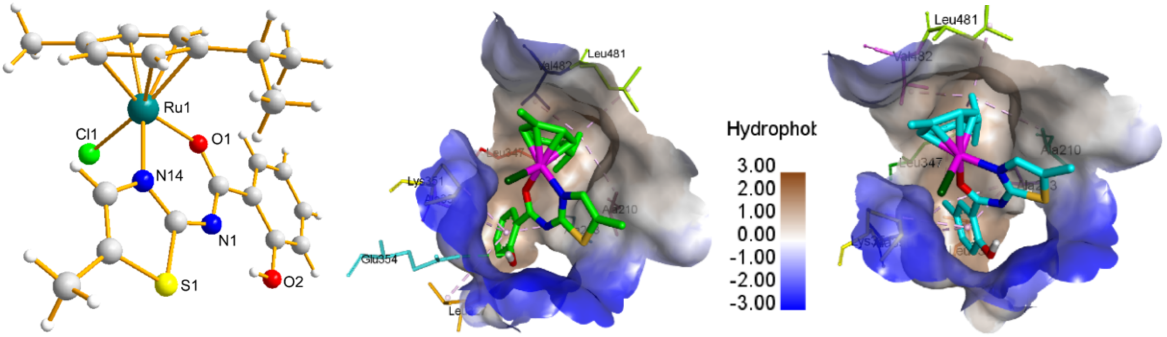
Abstract 13

Unveiling the Human Serum Albumin binding affinity of Thiazolyl appended (η^6-*p*-cymene)Ruthenium complexes

Rais Ahmad Khan,[a]* Ibtisam I. BinSharfan,[a] Ali Alsalme[a]

[a] Department of Chemistry, College of Sciences, King Saud University, P.O. Box 2455, Riyadh 11451, Kingdom of Saudi Arabia.
*Email: krais@ksu.edu.sa

Ruthenium(II) complexes is considered as a potential candidate alternative of the widely used platinum based drugs as an effective chemotherapeutics against cancer. In this context, we have designed, synthesized and characterized using various spectroscopic techniques the two new (η^6-cymene)ruthenium complexes **1** and **2** of thiazolyl motifs viz, (E)-2-(((5-methylthiazol-2-yl)imino) methyl)phenol (**L1**) and (E)-4-methyl-2-(((5-methylthiazol-2-yl)imino)methyl)phenol (**L2**), respectively. The molecular structure of ligand **L2** and complex **1** (Figure 1a) were obtained by the single crystal X-ray diffraction. HAS is an abundantly protein present in the human body and is useful for the transportation of drugs. These ruthenium compounds **1** and **2** were investigated for the interaction with human serum albumin (HAS) using *in-vitro* and computational studies (Figure 1b).



(a) (b)

Figure 1

[1] Usman, M.; Husain, F. M.; Khan, R. A.; Alharbi W.; Alsalme, A.; Al-Lohedan, H.; Tabassum, S. *New J. Chem.* **2021**, *45*, 2184-2199.
[2] Alharbi, W.; Hassan, I.; Khan, R. A.; Parveen, S.; Alharbi, K. H.; Bin Sharfan, I. I.; Alhazza, I. M.; Ebaid, H.; Alsalme, A. *Molecules* **2021**, *26*, 1606.
[3] Usman, M.; Khan, R. A.; Khan, M. R.; Farah, M. A.; Shaik, J. P.; Parine, N. R.; Khanjer, M. A.; Alsalme, A.; Tabassum, S. *Dalton Trans.* **2021**, *50*, 2253-2267.
[4] Khan, R. A.; Tabassum, S.; Farah, M. A.; Ali, M. S.; Alsalme, A.; Al-Lohedan, H.; Al-Anazi, K. M. *J. Biomol. Struct. Dyn.* **2019**, *37*, 3905-3913.
[5] Khan, R. A.; Asim, A.; Kakkar, R.; Gupta, D.; Bagchi, V.; Arjmand, F.; Tabassum, S. *Organometallics* **2013**, *32*, 2546-2551.

Abstract 14

The New Cage-Like Tetranuclear Silsesquioxanes of Tb^{3+}, Eu^{3+} and Eu^{3+} / Tb^{3+}: Synthesis, Structure and Luminescence Properties

Alena N. Kulakova,[a,b,c]* Alexey N. Bilyachenko,[a,b] Yannick Guari,[c] Joulia Larionova[c]

[a] Peoples' Friendship University of Russia (RUDN), Moscow, Russia.
[b] Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, Moscow, Russia.
[c] ICGM, Univ. Montpellier, CNRS, ENSCM, Montpellier, France.
*E-mail = alenkulakova@gmail.com

Polynuclear compounds based on lanthanide ions are attracting great attention of scientific groups due to their exceptional optical and magnetic properties. The photophysical properties of such compounds are promising for the development of new types of displays, sensors, etc.[1]

We report here the synthesis, structure, luminescence of new cage-like tetranuclear silsesquioxanes Tb^{3+}, Eu^{3+} and Eu^{3+}/Tb^{3+} (Figure 1). They present an unusual prism-like topology of cage architectures and lanthanide-characteristic emission, which makes them the first luminescent cage-like lanthanide silsesquioxanes. The mixed Eu^{3+}/Tb^{3+}-containing silsesquioxanes were studied as self-regulating temperature sensors based on LIR transitions Tb^{3+} and Eu^{3+} ($^5D_4 \rightarrow {}^7F_5$ and $^5D_0 \rightarrow {}^7F_2$). The sensor showed excellent linearity over a temperature range of 41-100°C and a maximum relative thermal sensitivity of 0.63% °C^{-1} at 68°C, indicating successful operation. This work opens up great prospects for the creation of a new class of temperature sensors based on cage-like lanthanide silsesquioxanes.

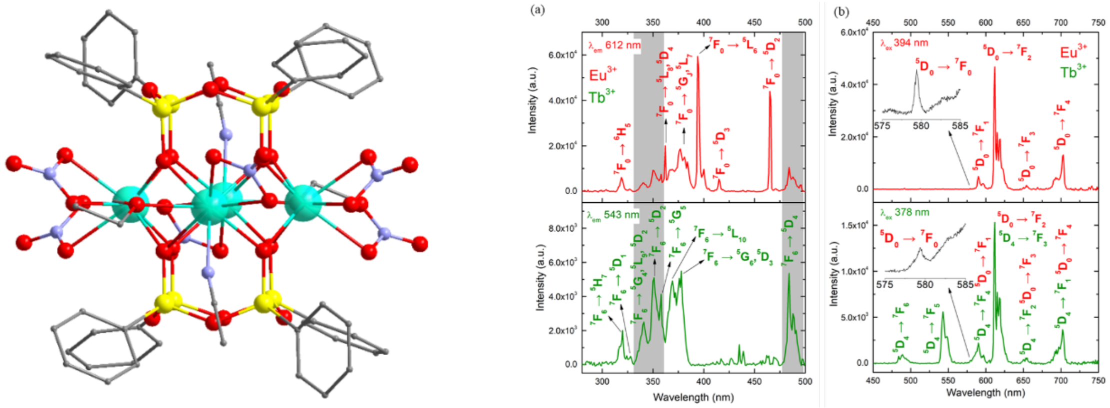


Figure 1 (left) Molecular structure Ln^{3+}-containing silsesquioxanes; Right **(**a) excitation spectra of Eu^{3+}/Tb^{3+} -containing silsesquioxanes monitored at λ_{em} = 612 (top) and λ_{em} =543 nm (bottom), and (b) emission spectra performed with λ_{ex} = 394 (top) and λ_{ex} = 398 nm (bottom). $Eu^{3+}$and Tb^{3+} transitions are written in red and green, respectively. Inserts: High-resolution emission spectra for the $^5D_0 \rightarrow {}^7F_0$ transition.

[1] Bünzli, J.-C.G.; Piguet C. *Chem. Soc. Rev.* **2005**, *34*, 1048–1077.

Acknowledgements This work was supported by the PRC2287 Premium 2019–2021 program and by the RUDN University Strategic Academic Leadership Program.

Abstract 15

Metal Phenolic Networks-decorated SPIONs for MRI Applications

Andrea Lazzarini,[a]* Angelo Galante,[b] Lorenzo Arrizza,[c] Marcello Crucianelli[a]

[a] DSFC, University of L'Aquila, via Vetoio (COPPITO 2), 67100, L'Aquila, Italy.
[b] MESVA, University of L'Aquila, via Vetoio (COPPITO 2), 67100, L'Aquila, Italy.
[c] Center for Microscopy, University of L'Aquila, via Vetoio (COPPITO 1), 67100, L'Aquila, Italy.
*E-mail = andrea.lazzarini@univaq.it

Iron oxide nanoparticles possessing superparamagnetic behavior (SPIONs) have found broad applications in Magnetic Resonance imaging,[1] especially for liver as target organ. For this specific application, they are usually derivatized by means of organic molecules or bio-compatible polymers,[2] such as PVP or PEG; however, the development of novel encapsulating materials is moving towards the employment of biological macromolecules, often recovered from wasted materials. In this sense, tannic acid (TA) has demonstrated to form Metal Phenolic Networks (MPNs) on various substrates by coordinating different metal ions in physiological environment.[3,4] The main issue with MPNs is their low stability in conditions different from the physiological ones, such as in the presence of cancer cells. In a preliminary study, in order to exploit the combination between SPIONs and Gd-coordinated MPNs, we reticulated tannic acid in the presence of Gd ions,[5] entrapped inside the formed network (see Figure 1a). By means of ATR-IR characterization, we observed the effective reticulation of TA, making the SPIONs dispersible and stable in physiological environment. However, longitudinal (r_1) and transverse (r_2) relaxivity values, typical for bare SPIONs systems, suggest that Gd ions might have undergo some aggregation process. Further studies will explore the effective coordination of Gd species once the reticulated network is formed.

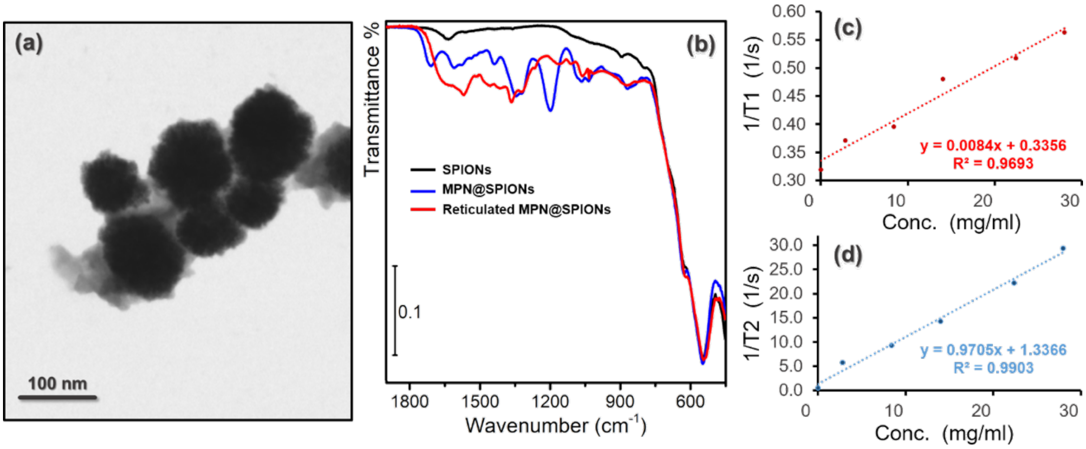


Figure 1 (a) STEM image of Reticulated MPNs@SPIONs; (b) ATR-IR of bare SPIONs, MPNs@SPIONs and Reticulated MPNs@SPIONs; (c) *r1* relaxivity curve; (d) *r2* relaxivity curve.

[1] Avasthi, A.; Caro, C.; Pozo-Torres, E.; Pernia Leal, M.; García-Martínet, M. L. *Top. Curr. Chem.* **2020**, *378*, 40.
[2] Liu, D.; Wu, W.; Ling, J.; Wen, S.; Gu, N.; Zhang, X. *Adv. Funct. Mater.* **2011**, *21*, 1498-1504.
[3] Ejima, H.; Richardson, J. J.; Liang, K.; Best, J. P.; van Koeverden, M. P.; Such, G. K.; Cui, J.; Caruso, F. *Science* **2013**, *341*, 154-156.
[4] Guo, J.; Ping, Y.; Ejima, H.; Alt, K.; Meissner, M.; Richardson, J. J.; Yan, Y.; Peter, K.; von Elverfeldt, D.; Hagemeyer, C. E.; Caruso, F. *Angew. Chem. Int. Ed.* **2014**, *53*, 5546-5551.
[5] Qin, J.; Liang, G.; Feng, B.; Wang, G.; Wu, N.; Deng, Y.; Elzatahry, A. A.; Alghamdi, A.; Zhao, Y.; Wei, J. *Chin. Chem. Lett.* **2021**, *32*, 842-848.

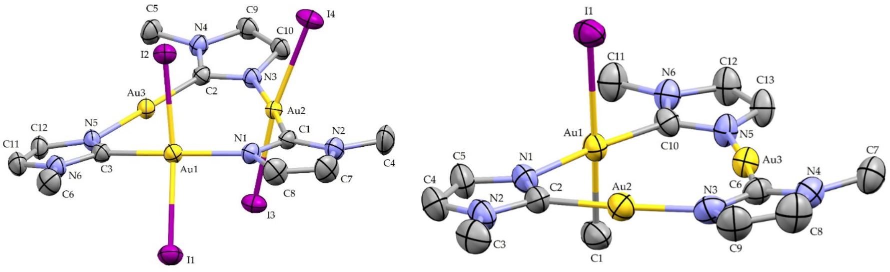
Abstract 16

New Perspective Views on the Gold Oxidation States in Imidazolate Au(I) Cyclic Trinuclear Compounds upon treatments with Classic Oxidants

Lorenzo Luciani,[a]* Claudia Graiff,[b] Gabriele Manca,[c] Rossana Galassi[a]

[a] University of Camerino, School of Science and Technology, Via S. Agostino 1, 62032 Camerino (MC), Italy.
[b] Department of Chemistry, Life Sciences and Environmental Sustainability, Product Development Università di Parma, Parco Area delle Scienze 17/A, 43124 Parma, Italy.
[c] Istituto di Chimica dei Composti Organo-Metallici, CNR-ICCOM, Sesto Fiorentino, Italy.
*E-mail = lorenzo.luciani@unicam.it

Cyclic trinuclear complexes (CTCs) are nine-membered ring metallacycles obtained by the reaction of C,N (imidazolate, pyridinate, carbeniate) or N,N (1,2,4-triazolate, pyrazolate) ligands with a proper 11th group M(I) metal precursor.[1] The CTCs exhibit outstanding emissive properties, metallaromaticity and π-acid/π-base features, making them suitable as materials for chemical sensing, molecular recognition, and optoelectronic applications.[2] In this work, we investigated the effect of different substituents on the pyrrolic N atoms toward the reactivity of Au(I) imidazolate CTCs, relatively to classic metal oxidation reactions with I_2 or CH_3I or addition of HCl. Despite the close similarity of these starting CTCs systems, we obtained different experimental outcomes. In the reaction with HCl we obtained mono-ligated or bis-ligated NHC gold(I) structures and with I_2 the formation of CTC units with square planar tetra-coordinated gold centers was observed. Remarkably, the addition of MeI draws the breakpoint between the behavior of methyl or benzyl imidazole CTCs: in methyl-imidazole CTCs a square planar Au center is present (Figure 1), while in benzyl imidazole CTCs mono- and bis NHC-Au(I) carbene structures were isolated. According to the same experimental conditions, only the presence of the two different substituents forks the outcomes. Theoretical studies provided essential support to discriminate two alternative mechanisms of addition: by the metal activation or by π-aromatic imidazole interaction, for the methyl-imidazole CTCs and the benzyl-imidazole CTCs respectively. Furthermore, Au-N and Au-C bond distances in the crystal structure of the compounds with square planar Au centers highlight very slight bond length differences from the starting CTCs. Computational calculations on these products attained electronic populations for the metal centers which are closer to d^{10} than to d^8 configurations. Both these evidences suggest that Au maintains unchanged its starting oxidation state of +1 and never attains the classically expected Au(III). Thus, a better description of the bonding in the case of the herein considered CTCs is obtained by evoking the ILFT (Inverted Ligand Field Theory).[3]



(a) (b)

Figure 1 ORTEP plot of the crystal structures of the CTCs obtained upon reaction with I_2 (a) and MeI (b). Hydrogen atoms are omitted for clarity.

[1] Galassi, R.; Rawashdeh-Omary, M. A.; Dias, H. V. R.; Omary, M. A. *Comments Inorg. Chem.* **2019**, *39*, 287–348.
[2] Zheng, J.; Lu, Z.; Wu, K.; Ning, G. H.; Li, D. *Chem. Rev.* **2020**, *120*, 9675-9742.
[3] Hoffmann, R.; Alvarez, S.; Mealli, C.; Falceto, A.; Cahill, T.; Zeng, T.; Manca, G. *Chem. Rev.* **2016**, *116*, 8173–8192.

Abstract 17

Solvent-Free Esterification of Acrylic Acid Promoted by Simple Zn(II) Catalyst

Massimo Melchiorre,[a]* Roberto Esposito,[b,c] Antonio Gallo,[b] Maria Elena Cucciolito,[b,c] Francesco Ruffo[b,c]

[a] ISusChem s.r.l., Piazza Carità, 32, 80134, Napoli, Italy.
[b] Dipartimento di Scienze Chimiche, Università degli Studi di Napoli Federico II, Complesso Universitario di Monte S. Angelo, via Cintia 21, 80126 Napoli, Italy.
[c] Consorzio Interuniversitario di Reattività Chimica e Catalisi (CIRCC), via Celso Ulpiani 27, 70126 Bari, Italy.
*E-mail = massimo.melc@gmail.com

The acrylic acid esters are bulk chemicals widely used in several products (polymers, UV-curing printing inks, adhesives, etc.) thanks to their ability to make radical cross-linking polymerization. However, this reactivity is a significant drawback to perform esterification reaction, and often it is necessary to use additives to increase the overall efficiency, such as solvents and inhibitors.[1,2]

We have recently investigated the esterification of fatty acids in solvent-free conditions promoted by zinc salts,[3] here we report preliminary results on the use of this reaction system for the synthesis of 2ethylhexyl acrylate (2-EHA) by direct esterification of the acrylic (AA) with 2-ethylhexyl alcohol (2-EH) (Figure 1). The effect of counter ion was investigated for a panel of zinc salts, and $Zn(ClO_4)_2$ revealed to be the most promising catalyst, affording high yield in such optimized conditions (0.1% mol of catalyst, AA to 2-EH molar ratio 1.2, 0.5% mol of polymerization inhibitor, 170°C).

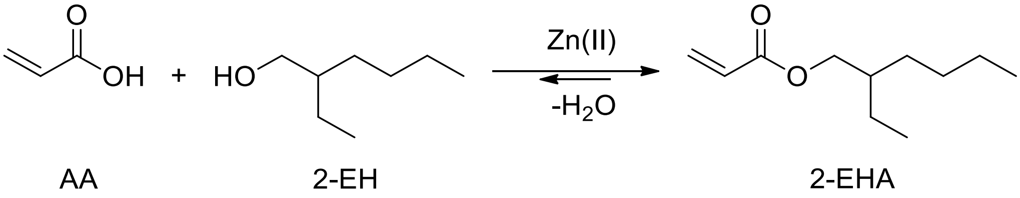


Figure 1

[1] Komoń T.; Niewiadomski P.; Oracz P.; Jamróz M. E. *App. Cat. A: Gen.* **2013**, 451, 127–136.
[2] Sert E.; Atalay F. S. *Ind. Eng. Chem. Res.* **2012**, 51, 6666−6671.
[3] Melchiorre, M.; Cucciolito M. E.; Di Serio, M.; Ruffo, F.; Tarallo, O.; Trifuoggi, M.; Esposito R. *ACS Sustain. Chem. Eng.* **2021**, 9, 6001−6011.

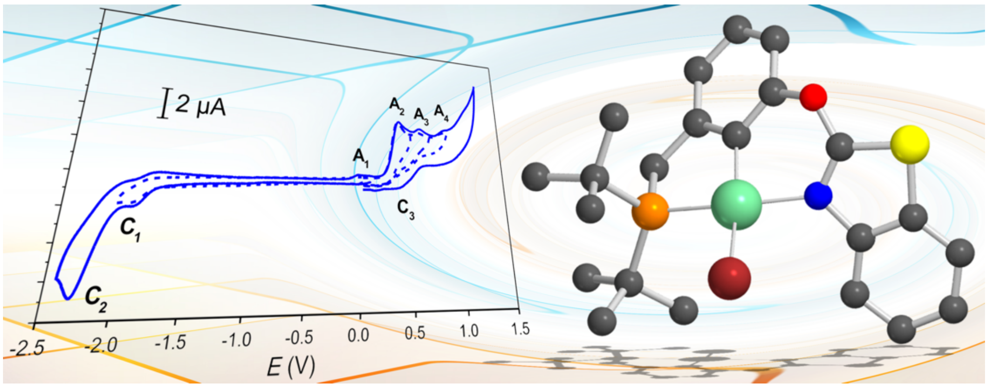
Abstract 18

Unsymmetrical Nickel (PCN) Pincer Complexes with a Benzothiazole Side Arm: Synthesis, Characterization and Electrochemical Properties

Giorgio Mercuri,[a,b]* Lapo Luconi,[b] Claudio Pettinari,[a] Giulia Tuci,[b] Zufar N. Gafurov,[c] Alexey A. Kagilev,[c] Vladimir I. Morozov,[c] Dmitry G. Yakhvarov,[c] Andrea Rossin,[b] Giuliano Giambastiani[b]

[a] University of Camerino, School of Pharmacy, Via S. Agostino 1, 62032 Camerino (MC), Italy.
[b] Consiglio Nazionale delle Ricerche - Istituto di Chimica dei Composti Organometallici (CNR-ICCOM), via Madonna del Piano 10, 50019, Sesto Fiorentino (Firenze), Italy.
[c] Arbuzov Institute of Organic and Physical Chemistry, FRC Kazan Scientific Center of RAS, Arbuzov Str. 8, 420088 Kazan, Russia.
*E-mail: giorgio.mercuri@unicam.it

The synthesis and exploitation of pincer ligands and of the related organometallic complexes is a popular research topic in modern organometallic chemistry.[1] The structural features, reactivity and stability of these complexes can be tuned for their application through a tailor-made design of their organic ligands with different donor-atoms.[2] On this regard, the use of ligands that bind metal centers in a tridentate fashion provides a huge stability for the central ion. In this work,[3] the synthesis of a new (PCN) pincer ligand with a benzothiazole side-arm: 2-(3-((di-tert-butylphosphino)methyl)phenoxy)benzo[d]thiazole ($^{\mathrm{BzTz}}$(H)PCN) is presented. The reactions of $^{\mathrm{BzTz}}$(H)PCN with suitable Ni(II) metal precursors led to the formation of the three new complexes ($^{\mathrm{BzTz}}$PCN)NiX [X = Br (**1**), F (**2**)] and [($^{\mathrm{BzTz}}$PCN)Ni(H_2O)]BF_4 (**3**) that were fully characterized both in solid state and in solution. Finally, comparative electrochemical measurements (CV and in situ EPR-spectroelectrochemistry) carried out on the halide complexes **1** and **2** revealed that the anodic oxidation process leads to the formation of stable Ni(III) species bearing a coordinated bromide ligand in case of **1** and a fluoride-free complex in case of **2**. The formation of halogen-free nickel species is of great interest since the presence of vacant coordination sites on the metal center is a prerequisite for active catalysts in various catalytic processes. In this context, electrochemical oxidation can be regarded as a new and greener tool for the activation of such type of complexes.



[1] Morales-Morales, D.; Pincer Compounds, in *Chemistry and Applications*, 1st ed., Elsevier, **2018**.
[2] van Koten, G. *Pure Appl. Chem.* **1989***, 61*, 1681-1694.
[3] Luconi, L.; Tuci, G.; Gafurov, Z.N.; Mercuri, G.; Kagilev, A.A.; Pettinari, C.; Morozov, V.I.; Yakhvarov, D.G.; Rossin, A.; Giambastiani, G. *Inorg. Chim. Acta* **2021**, *517*, 120182.

Abstract 19

The Strong Role of Imidazolium Salt on the Catalytic Performance of a Ruthenium Based Anionic Pre-catalyst for the Guerbet Reaction

Alessandro Messori,[a]* Nicola Monti,[a] Anna Gagliardi,[a] Cristiana Cesari,[a] Rita Mazzoni[a]

[a] Department of Industrial Chemistry “Toso Montanari”, viale Risorgimento, 4, 40136, Bologna, Italy.
*E-mail = alessandro.messori6@unibo.it

Biofuels represent a promising route to reduce our dependence on fossil fuels. Bio-ethanol is a bio-derived platform chemical that can be transformed into butanol and higher alcohols: species with higher energy density and better capability of being mixed with conventional fuel. Among the others, Guerbet reaction represents an appealing pathway for bio-ethanol refinery[1] especially when it is derived from waste or second generation (non-food) biomass.

Our group recently demonstrate **3a** (Figure 1) as an efficient pre-catalyst for the Guerbet reaction.[2] Here we report on the synthesis of a small library of similar complexes **3b-d** bearing imidazolium or ammonium cations (Figure 1) in order to rationalize the role of the countercation in Guerbet catalysts of type **3**.

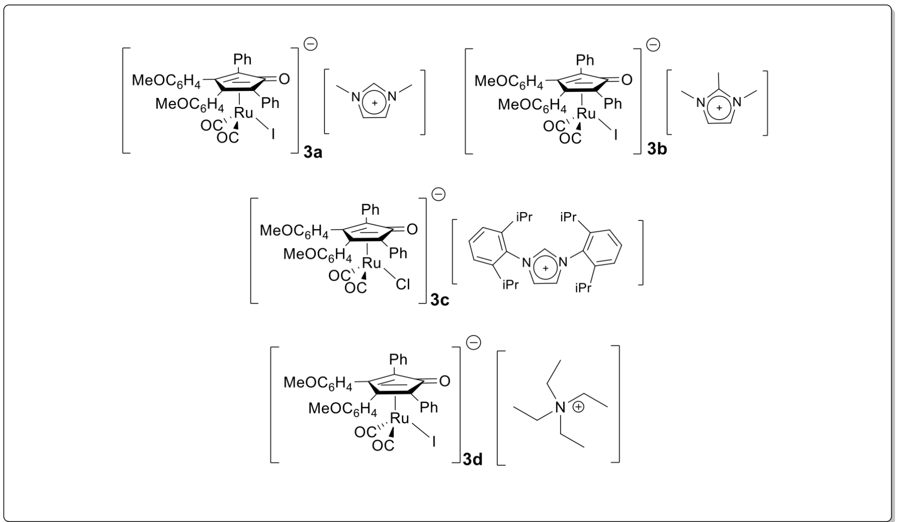


Figure 3 Pre-catalysts **3a-d** employed in this work.

The catalytic screening revealed that conversion, alcohols selectivity and carbon loss are highly dependent on the counterion, demonstrating a detrimental effect of NCN substituents for imidazolium salts in complexes **3b** and **3c**, negative effect is also pronounced while employing tetraethylammonium **3d** or Na^+ as the counterions. Results from the screening and designed reactivity will be discussed in correlation with steric encumbrance, acidity and hydrogen bonding which may affect the complex behavior in the mixture employed for the reaction: EtOH, EtO^-, high temperature (150 °C) and products from side reactions

[1] (a) Angelici, C.; Weckhuysen, B. M.; Bruijnincx, P. C. A. *ChemSusChem* **2013**, *6*, 1595–1614; (b) Posada, J. A.; Patel, A. D.; Roes, A.; Blok, K.; Faaij, A. P. C.; Patel, M. K. *Bioresour. Technol.* **2013**, *135*, 490–499; (c) Bruijnincx, P. C. A.; Weckhuysen, B. M. *Angew. Chem. Int. Ed.* **2013**, *52*, 11980–11987.

[2] Mazzoni, R; Cesari, C.; Zanotti, V.; Lucarelli, C.; Tabanelli, T.; Puzzo, F.; Passarini, F.; Neri, E.; Marani, G.; Prati, R.;Vigano, F; Conversano, A.; Cavani, F. *ACS Sustain. Chem. Eng.* **2019**, 7, 224–237.

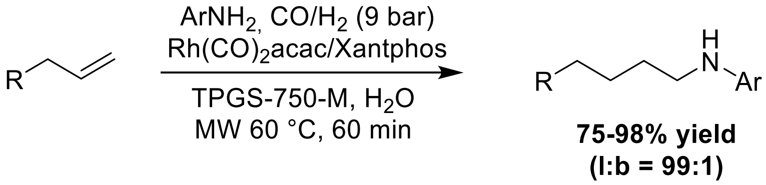
Abstract 20

Hydroaminomethylation of Terminal Alkenes in Water: Microwave and Micellar Catalysis Roles

Elisabetta Monciatti,[a]* Francesca Migliorini,[a] Elena Petricci[a]

[a]Dipartimento di Biotecnologie, Chimica e Farmacia, Università degli studi di Siena, Via Aldo Moro, 53100 Siena, Italy.
*E-mail = elisabetta.moncia@student.unisi.it

In the past years, we demonstrated that hydroformylation, hydroaminomethylation, and other similar tandem transformations can be carried out working in mild condition, by taking advantages from microwave irradiation.[1-3] We recently reported the possibility to improve the sustainability of hydroformylation reaction by coupling micellar and microwave catalysis.[4] Here are reported our last findings in the application of micellar catalysis on the microwave assisted hydroaminomethylation of terminal alkenes.



Scheme 1

This sustainable process (Scheme 1) is of general applicability to different alkenes and aniline and allows to obtain the linear aniline derivatives as the major regioisomers in good yields, in mild reaction conditions in term of temperature (60 °C), syngas pressure (9 bar), and time (60 min). Commercially available surfactant, catalyst, and ligand are used and the catalyst/ligand system can be recycled without impacting in both regioselectivity and yields.

[1] Petricci, E.; Mann, A.; Schoenfelder, A.; Rota, A.; Taddei, M. *Org. Lett.*, **2006**, *8*, 3725-3727.
[2] Petricci, E.; Mann, A.; Salvadori, J.; Taddei, M. *Tetrahedron Lett.*, **2007**, *48*, 8501-8504.
[3] Verheyen, T.; Santillo, N.; Marinelli, D.; Petricci, E.; De Borggraeve, W. M.; Vaccaro, L.; Smet, M. *ACS Appl. Polym. Mater.* **2019**, *1*, 1496-1504.
[4] Migliorini, F.; Dei, F.; Calamante, M.; Maramai, S.; Petricci, E. *ChemCatChem,* in press doi.org/10.1002/cctc.202100181

Abstract 21

Synthesis of Novel Ruthenium(II)- Arene Complexes with *N,O* or *N,N*-Pyrazolone-Based Hydrazones Ligands

Noemi Pagliaricci,[a]* Riccardo Pettinari,[a] Fabio Marchetti,[b] Claudio Pettinari,[a] Corrado Di Nicola[b]

[a] University of Camerino, School of Pharmacy, Via S. Agostino 1, 62032 Camerino (MC), Italy.
[b] University of Camerino, School of Science and Technology, Via S. Agostino 1, 62032 Camerino (MC), Italy.
*E-mail = noemi.pagliaricci@unicam.it

Arene ruthenium(II) complexes have been deeply studied in recent years, and their chemistry has been extensively studied for arenes such as benzene and p-cymene. They have found applications in catalysis, supramolecular assemblies, molecular devices. Additionally, they have recently shown antiviral, antibiotic, and anticancer activities.[1] We have previously reported the chemistry of several ligands, such as 4-acyl-5-pyrazolone ligands[2] and their hydrazone ligands, that after coordination to *p*-cymene ruthenium(II) framework display enhanced activities.[3] Here we extended our studies to the even more active pyrazolone-based hydrazones ligands in Figure 1 and to the (η^6-arene)Ru(II) complexes. The pyridine-containing HL4, HL6, and HL7 in the solid state were found in a zwitterionic form. The X-ray studies on the metal complexes display two different structural typologies for the chelating systems. While in the case of $(L1)^-$, $(L2)^-$, $(L3)^-$, and $(L5)^-$ the excepted N,O-chelation and formation of six-membered ring was found (Figure 2a), the pyridine containing $(L4)^-$, $(L6)^-$, and $(L7)^-$ ligands prefer to coordinate through the N atom of pyridine ring at the place of the oxygen of pyrazolone, affording a five-membered ring (Figure 2b).

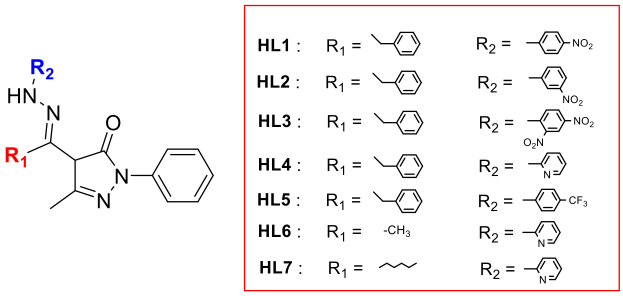


Figure 1 - Hydrazone ligands

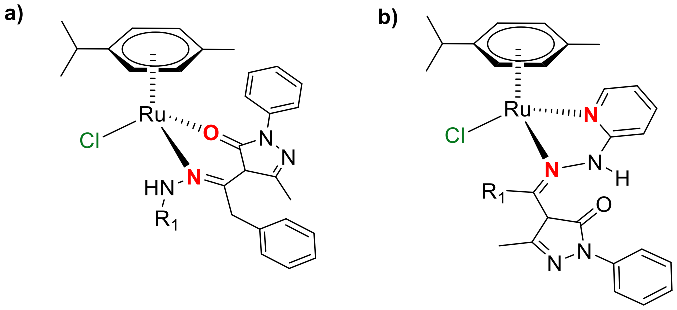


Figure 2 - N,O- (a) and N,N- (b) coordinating ligands

[1] Yan, Y. K.; Melchart, M.; Habtemariam, A.; Sadler, P. J. *Chem.Commun.* **2005**, 4764-4776.

[2] Caruso, F.; Monti, E.; Matthews, J.; Rossi, M.; Gariboldi, M.B.; Pettinari, C.; Pettinari, R.; Marchetti, F. *Inorg. Chem.* **2014**, 53, 3668-3677.

[3] Pettinari, R.; Marchetti, F.; Di Nicola, C.; Pettinari, C.; Galindo, A.; Petrelli, R.; Cappellacci, L.; Cuccioloni, M.; Bonfili, L.; Eleuteri, A.M.; Da Silva, M.F.C.G.; Pombeiro, A.J.K. *Inorg. Chem.* **2018**, 57, 14123-14133.

Abstract 22

Single-pot deacetalization-Knoevenagel tandem reactions in solvent-free conditions catalyzed by 1D Zn(II) coordination polymers

Anup Paul,[a]* Armando J. L. Pombeiro[a]

[a] Centro de Química Estructural, Instituto Superior Técnico, Universidade de Lisboa, Av. Rovisco Pais, 1049-001 Lisboa, Portugal.
*E-mail: anuppaul@tecnico.ulisboa.pt

Two new 1D CPs $[Zn(L^1)(H_2O)_4]_n.nH_2O$ (**1**) and $[Zn(L^2)(H_2O)_2]_n$ (**2**) were synthesised using flexible dicarboxylate pro-ligands [L^1 = 1,1'-(ethane-1,2-diyl)bis(6-oxo-1,6-dihydropyridine-3-carboxylic acid); L^2 = 1,1'-(propane-1,3-diyl)bis(6-oxo-1,6-dihydropyridine-3-carboxylic acid)], respectively. They were characterized by elemental, FT-IR thermogravimetric analysis and powder X-ray diffraction analysis. Furthermore, their structural characteristics were disclosed by single-crystal X-ray diffraction analysis. The topology of the CPs was illustrated by the topological analysis in which CP **1** was found to have a 3,4,6-connected trinodal net, whereas CP **2** demonstrates to have a 2,3,3,4,6,7-connected hexanodal net. Both the CPs were found to act as heterogeneous catalysts in one-pot tandem deacetalization–Knoevenagel condensation reactions under environmentally mild conditions (Figure 1). The yield for CP **1** in microwave-assisted solvent-free medium is 91%, while CP **2** recorded a slightly lower yield (87%) under the same experimental conditions. Additionally, catalyst **1** has been evaluated for its recyclability, which can be used number of times without compromising its catalytic efficiency.

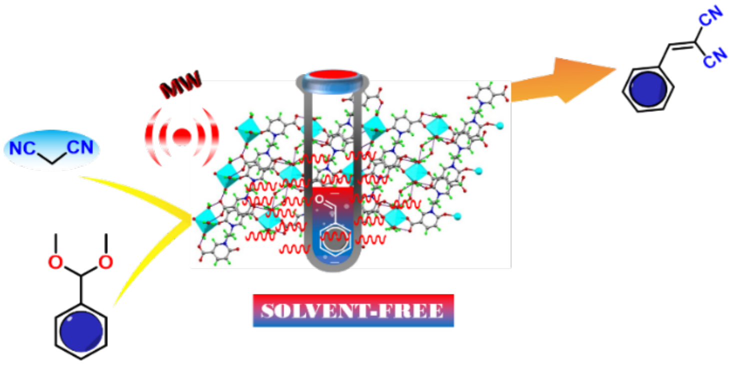


Figure 1 Catalytic activity of CPs **1** and **2**.

[1] Karmakar, A.; Paul, A.; Rúbio, G.M.D.M.; Soliman, M.; Guedes da Silva, M.F.C.; Pombeiro, A.J.L. *Front. Chem.* **2019**, *7*, 699.
[2] Paul, A.; Karmakar, A.; Guedes da Silva, M.F.C.; Pombeiro, A.J.L. *Catalysts* **2021**, *11*, 90.

Acknowledgements:
A. Paul acknowledges financial support from FCT and IST through "DL/57/2017" (Contract no. IST-ID/197/2019).

Abstract 23

Synthesis and Characterization of New Potential Anticancer (η^6-Arene)Ruthenium(II) Compounds

Lorenzo Pietracci,[a]* Riccardo Pettinari,[b] Fabio Marchetti,[a] Claudio Pettinari,[b] Corrado Di Nicola[a]

[a] University of Camerino, School of Science and Technology, Via S. Agostino 1, 62032 Camerino (MC), Italy.
[b] University of Camerino, School of Pharmacy, Via S. Agostino 1, 62032 Camerino (MC), Italy.
*E-mail = lorenzo.pietracci@unicam.it

Half-sandwich arene-Ru(II) complexes have been found as very interesting antiviral, antibiotic, and anticancer agents.[1] They represent potential alternatives to platinum-based drugs due to several attractive properties such as biocompatible ligand exchange rates, covalent binding with DNA and/or proteins, redox-accessible oxidation states, combined with a low toxicity.[2] In a recent work,[3] we have synthetized, characterized and investigated the biological activities of a series of neutral chlorinated arene-Ru(II) complexes, formed by coordination to the metal centre of the ligand 5-methyl-2-(pyridin-2-yl)-2,4-dihydro-3H-pyrazol-3-one (HL^{py}) and the corresponding acylpyrazolone with the 2,2,2-trifluoroacetyl fragment, i.e. 5-methyl-2-(pyridin-2-yl)-4-(2,2,2-trifluoroacetyl)-2,4-dihydro-3H-pyrazol-3-one ($HQ^{py,CF3}$) (Figure 1). As an expansion of this research line, we have now synthetized and characterized the corresponding charged arene-Ru(II) compounds, through the chlorine substitution with the PTA phosphine, using tetrafluoroborate as counterion (Figure 2).

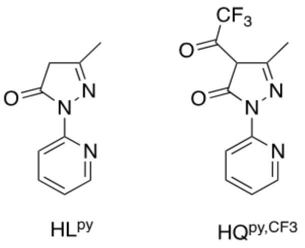


Figure 1

Arene: p-cymene; hexamethylbenzene

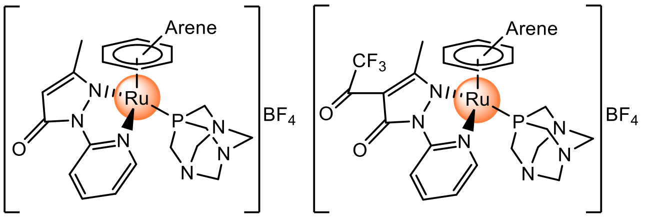


Figure 2

Then, a new phenyl containing analog ligand (HL^{ph}) has been synthetized and characterized also with X-Ray diffraction analysis (Figure 3), and the corresponding neutral and charged arene-Ru(II) complexes have been obtained and characterized. Biological activities are under investigation.

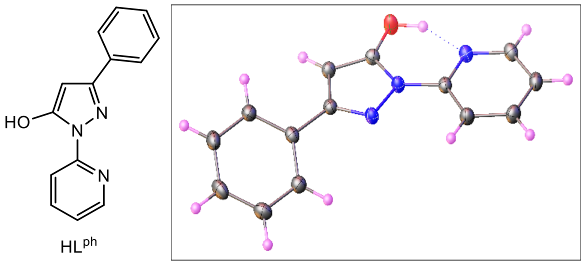


Figure 3

[1] Yan, Y. K.; Melchart, M.; Habtemariam, A.; Sadler, P. J. *Chem.Commun.* **2005**, 4764.
[2] Simović, A. R.; Masnikosa, R.; Bratsos, I.; Alessio, E. *Coord. Chem. Rev.* **2019**, *398*, 113011.
[3] Pettinari, R.; Marchetti, F.; Tombesi, A.; Di Nicola, C.; Pettinari, C.; Guo, C.; Zhang, Z.; Galindo, A.; Fadaei-Tirani, F.; Hadiji, M. H.; Dyson, P. *Inorg. Chim. Acta* submitted.

Abstract 24

Synthesis and Characterization of Novel Gallium (III) Complexes of 4-Acyl-pyrazolone Derivatives

Daphne Romani,[a]* Riccardo Pettinari,[b] Fabio Marchetti,[a] Corrado Di Nicola[a]

[a] University of Camerino, School of Science and Technology, Via S. Agostino 1, 62032 Camerino (MC), Italy.
[b] University of Camerino, School of Pharmacy, Via S. Agostino 1, 62032 Camerino (MC), Italy.
*E-mail = daphne.romani@unicam.it

The complexation of gallium with suitable chelators has raised great attention due to the potential pharmaceutical applications of the resulting compound,[1] which have been demonstrated to possess antibacterial and anticancer activity.[2] In this study we present recent achievements on the synthesis and characterization of novel coordination complexes obtained by the reaction between gallium(III) nitrate and different pyrazolone-based ligands (Figure 1), whose features have been deeply studied in the recent years and include antioxidant, antitumor and antimicrobial properties.[3] The potential of a combinational or even synergistic biological effect between Ga^{3+} and free ligand was investigated and the crystal structure obtained.

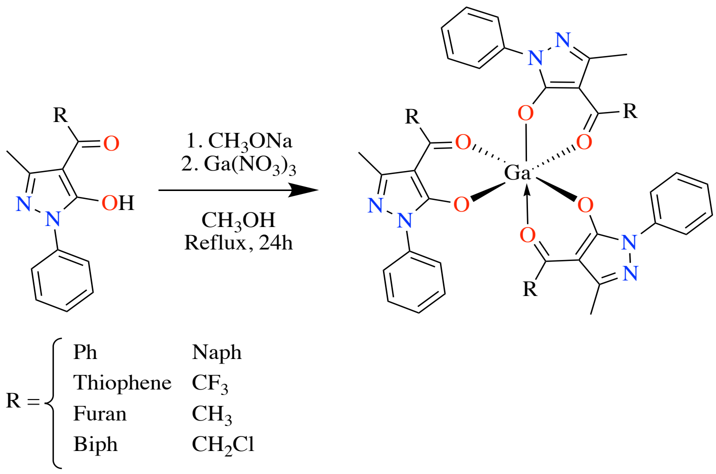


Figure 4

[1] Ellahioui, Y.; Prashar, S.; Gómez-Ruiz, S. *Inorganics* **2017**, *5*, 4.

[2] Aliabadi, A.; Hakimi, M.; Hosseinabadi, F.; Motieiyan, E.; Rodrigues, V.; Ghadermazi, M.; Marabello, D.; Abdolmaleki, S. *J. Mol. Struct.* **2021**, 1223, 129005.

[3] Marchetti, F.; Pettinari, C.; Di Nicola, C.; Tombesi, A.; Pettinari, R. *Coord. Chem. Rev.* **2019**, 401, 213069.

Abstract 25

NHC Complexes Silver and Gold Active in A^{3}coupling Reaction

Marco Sirignano,[a]* Annaluisa Mariconda,[b] Pasquale Longo[a]

[a] Department of Chemistry and Biology University of Salerno Via Giovanni Paolo II ,132-84084 Fisciano (SA), Italy.
[b] Department of Science, University of Basilicata, Viale dell'Ateneo Lucano 10, 85100 Potenza (PT), Italy.
*E-mail = msirignano@unisa.it

Propargylamines are an important class of scaffolds for the synthesis of organic compounds and have importance to produce drugs and agrochemicals.[1] Furthermore, Selegiline, Pargyline and Rasagyline are bioactive propargylamines used for the treatment of neurodegenerative diseases (e.g., Parkinson's and Alzheimer's diseases).[2] Originally, propargylamines are synthesized by nucleophilic addition of metal alkynyl compound to imine or enamine in harsh reaction conditions, producing amount of waste.

In the last decades, A^3 coupling reaction, catalyzed by transition metals have demonstrate to be an alternative methodology for the synthesis of propargylamines.[1] A^3 coupling reaction is a multicomponent reaction between an alkyne, amine, and aldehyde, giving water as only by-product.[3]

In this context, N-heterocyclic carbene (NHC) complexes of silver and gold have demonstrated to be able to promote A^3 coupling reaction to lead propargylamines.[4] Here, we report the synthesis, the characterization of two silver and two gold complexes bearing NHC, unsymmetrically N-substituted and having different group on backbone (hydrogen, chlorine). The gold complexes have shown a better catalytic active than silver analogs, and it was observed that the presence of chlorine atoms, on the backbone, have a positive effect in term of activity.

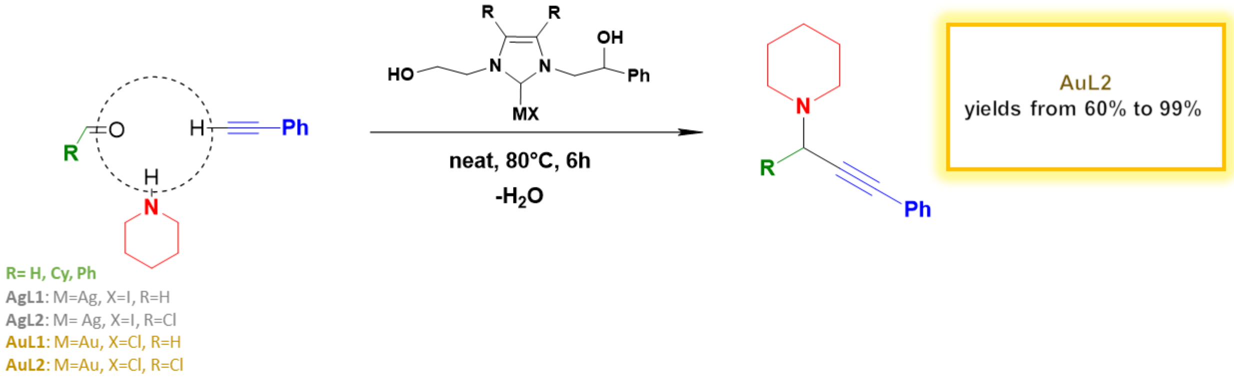


Figure 1 A^3 coupling reaction catalyzed by synthesized NHC silver and gold complexes.

[1] Lauder, K.; Toscani, A.; Scalacci, N.; Castagnolo, D. *Chem. Rev.* **2017**, *117*, 14091-14200.
[2] a) Langston, J. W.; Irwin, I.; Langston, E. B.; Forno, L. S. *Science* **1984**, *225*, 1480-1482; b) Chen, J. J.; Swope, D. *J. Clin. Pharmacol.*, **2005**, *45*, 878-894.
[3] a) Visbal, R.; Graus, S.; Herrera, R. P.; Gimeno, M. C. *Molecules* **2018**, *23*, 2255-2278; b) Wei, C.; Li, C. J. *J. Am. Chem. Soc*. **2003**, *125*, 9584-9585; c) Chen, W. W.; Bi, H. P.; Li, C. J. *Synlett* **2010**, 475-479.
[4] Mariconda, A.; Sirignano, M.; Costabile, C.; Longo, P. *Mol. Catal.* **2020**, *480*, 110570.

Abstract 26

Iridium-pyridine-2-sulfonamidate Complexes as Catalysts for the Chemical Regeneration of NADH with Phosphonic Acid

Leonardo Tensi,[a]* Gabriele Caricchi,[a] Cristiano Zuccaccia,[a] Filippo De Angelis,[a,b] Alceo Macchioni[a]

[a] Dipartimento di Chimica, Biologia e Biotecnologie and CIRCC, Università degli Studi di Perugia, Via Elce di Sotto 8-06123 Perugia, Italy.
[b] Computational Laboratory for Hybrid/Organic Photovoltaics(CLHYO), Istituto CNR di Scienze e Tecnologie Chimiche "Giulio Natta"(CNR-SCITEC), 06123 Perugia, Italy.
*E-mail = leonardo.tensi@studenti.unipg.it

The utilization of NAD(P)H (Nicotinammide Adenine Dinucleotide in its reduced form) in biochemical industrial processes is strictly related to its regeneration from cheap and affordable raw materials because of its high cost.[1] Organometallic complexes have been proposed as robust and versatile catalysts for NADH regeneration[2,3,4] but, unfortunately, their performances in term of efficiency and selectivity are much lower than those of enzymes so far. In this contribution, we report that the combination of the [Cp*Ir(R-pysa)NO_3] (pysa =κ^2-pyridine-2-sulfonamidate; R = H, 4-CF_3, and 6-NH_2) complexes with phosphonic acid $HP(O)(OH)_2$ as reducing agent constitutes a top-performing system for the chemical regeneration of NADH. The cooperative effect of the enhanced acidity at the metal, induced by the ancillary ligand, and the presence of the $-NH_2$ substituent in close proximity to the active center are the key factors for obtaining high performance for the chemical regeneration of NADH (TOF up to 3731 h^{-1},T= 313 K, pH = 6.58 by 0.4 M phosphite buffer).[5] In-depth kinetic and computational studies allow us to highlight the differences in terms of performance of the three catalysts and to understand the mechanism of the reaction of hydrogenation of the enzymatic cofactor.

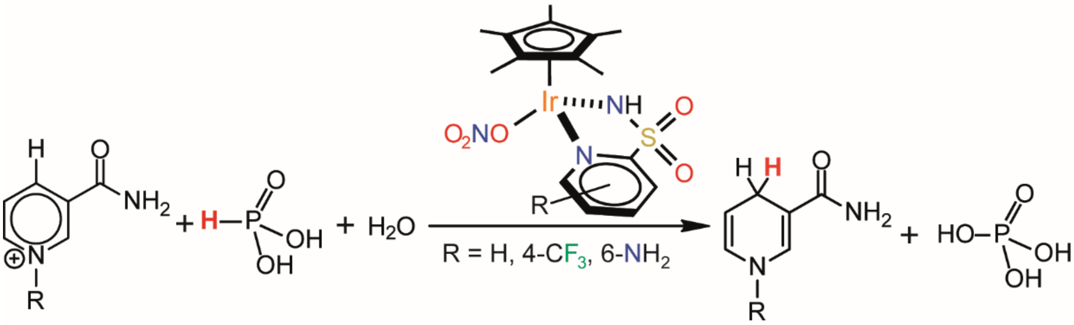


Figure 1

[1] Monti, D.; Ottolina, G.; Carrea, G.; Riva, S. *Chem. Rev.* **2011**, *111*, 4111-4140.
[2] Quinto, T.; Köhler, V.; Ward, T. R. *Top. Catal.* **2014**, *57*, 321-331.
[3] Fukuzumi, S.; Lee, Y.; Nam, W. *J. Inorg. Biochem.* **2019**, *199*, 110777.
[4] Bucci, A; Dunn, S.; Bellachioma, G.; Menendez Rodriguez, G.; Zuccaccia, C.; Nervi, C.; Macchioni, A. *ACS Catal.* **2017**, *7*, 7788–7796.
[5] Tensi, L.; Macchioni, A. *ACS Catal.* **2020**, *10*, 7945–7949.

Abstract 27

Functionalization of 3-Benzoyl-2-bromo-5-nitro-*N*-methoxyindole *via* Cross-Coupling Reactions

Federico Vavassori,[a]* Vincenzo Brancaccio,[a] Luca Gianoli,[a] Paolo Ballerio,[a] Andrea Penoni[a]

[a] Università degli Studi dell'Insubria, Dipartimento di Scienza e Alta Tecnologia (DiSAT), Via Valeggio 9, 22100 Como, Italy.
*f.vavassori1@uninsubria.it

2-Aryl-3-aroylindoles are small molecules reported in the literature as inhibitors of tubulin assembly: they were identified as vascular disrupting agents (VDAs), causing limitations to tumor cells blood flow. Among this class, Pinney and coworkers found that 2-(3′-hydroxy-4′-methoxyphenyl)-3-(3″,4″,5″-trimethoxybenzoyl)-6-methoxyindole, nicknamed Oxi8006, was the most powerful.[1] 2-Bromo-3-aroylindoles and similar *N*-methoxyindoles are interesting substrates that can be converted to these VDAs. In the past years in our laboratory a cyclization reaction between substituted nitrosoarenes and alkynes has been studied.[2] The reaction products are components of a class of indole derivatives, regioselectively substituted at C3 with the alkyne pendant. More recently prop-2-yn-1-ones with various aryl or heteroaryl groups at C1 were introduced:[3] this resulted in improved reaction yields and direct access to 3-aroylindole compounds. Functionalization of the alkynones at the terminal carbon with a halogen atom was done lately to obtain 2-Bromo-3-aroylindoles, which then can undergo cross-coupling reactions. 3-Benzoyl-2-bromo-5-nitro-*N*-methoxyindole is used as starting indole since it is easy to obtain and isolate. Here we report on the results we collected: Sonogashira reaction was tested but the outcome was not satisfying, while Suzuki reaction showed more promising results (Figure 1); at the moment we are conducting a substrate scope for Suzuki cross-coupling. Future developments of the project are the improvement of reaction conditions for alkyne cross-coupling and formation of C-N bonds via Buchwald – Hartwig reaction.

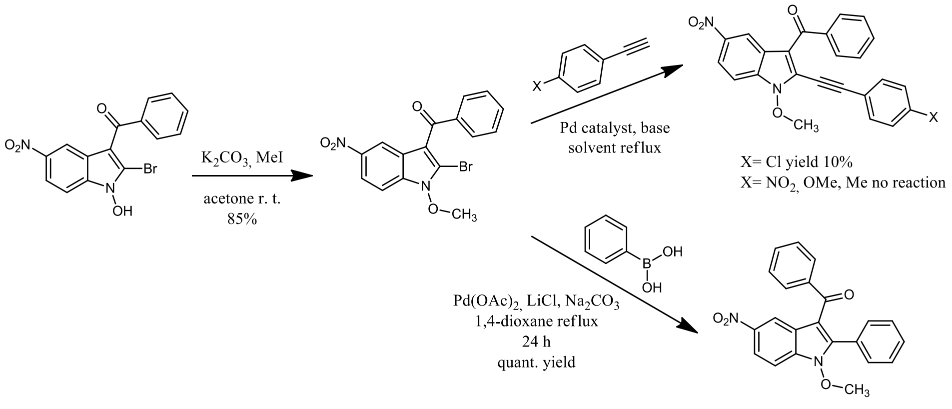


Figure 1

[1] (a) MacDonough, M. T.; Strecker, T. E.; Hamel, E.; Hall, J. J.; Chaplin, D. J.; Trawick, M. L.; Pinney, G. *Bioorg. Med. Chem.* **2013**, *21*, 6831–6843; (b) Hadimani, M. B.; MacDonough, M. T.; Ghatak, A.; Strecker, T. E.; Lopez, R.; Sriram, M.; Nguyen, B. L.; Hall, J. J.; Kessler, R. J.; Shirali, A. R.; Liu, L.; Garner, C. M.; Pettit, G. R.; Hamel, E.; Chaplin, D. J.; Mason, R. P.; Trawick, M. L.; Pinney, G. *J. Nat. Prod.* **2013**, *76*, 1668-1678.

[2] Penoni, A., Palmisano, G., Zhao, Y.-L., Houk, K. N., Volkman, J., Nicholas, K. M. *J Am Chem Soc.* **2009**, *131*, 653–661.

[3] Ieronimo, G., Palmisano, G., Maspero, A., Marzorati, A., Scapinello, L., Masciocchi, N., Cravotto, G., Barge, A., Simonetti, M., Ameta, K. L., Nicholas, K. M. Penoni, A. *Org. Biomol. Chem.* **2018**, *16*, 6853-6859.

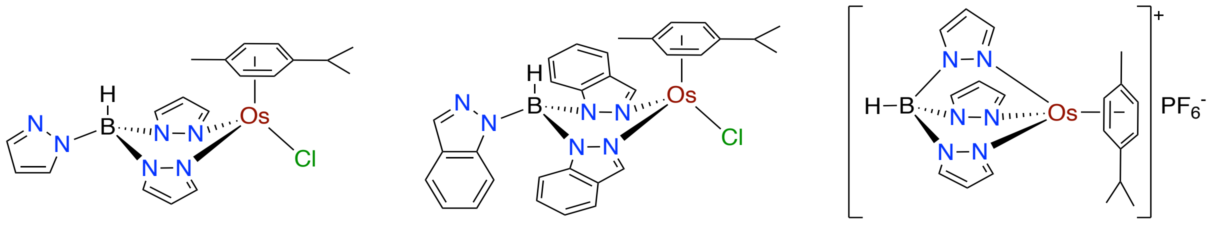
Abstract 28

Novel Scorpionate-type Osmium(II) Complexes

Federico Verdicchio, [a]* Riccardo Pettinari,[a] Claudio Pettinari,[a] Fabio Marchetti[b]

[a] University of Camerino, School of Pharmacy, Via S. Agostino 1, 62032 Camerino (MC), Italy.
[b] University of Camerino, School of Science and Technology, Via S. Agostino 1, 62032 Camerino (MC), Italy.
*E-mail = federico.verdicchio@unicam.it

Tris(pyrazolyl)borates, also known as *scorpionate* picturing their binding mode, are a highly successful class of supporting ligands and their complexes have found applications in fields such as catalysis, metal extraction and bioinorganic models. Their success stems largely from the flexibility they provide in tuning steric,[1] and to a lesser degree, electronic[2] properties. Up to now an enormous body of literature has appeared describing the syntheses and applications of polypyrazolylborate ligands and their metal complexes.[3,4] Since the first reported synthesis of the (arene)ruthenium(II) poly(pyrazolyl)borates,[5,6] many other different Ru(II) complexes have been synthesized with substituted ligands of the Tp^R family, standing out in applications like catalysis, antimicrobial and anticancer agents.[7] Despite the ever-growing interest in these (η^6-arene)Ru(II)Tp^R compounds, only few analogues with osmium have been prepared.[8] Here we report three new (η^6-cymene)Os(II) complexes with the ligands hydrotris(pyrazolyl)borate (Tp, complexes **1** and **3)** and hydrotris(indazolyl)borate (Tp^{4Bo}, complex **2**) (Figure 1). Complex **3** is similar to the compound synthesized by *Dickinson et al*. although with a different spectator ligand. Additionally, the κ^2 intermediate has been isolated and characterized (complex **1**). Whereas, complex **2** is the first report of the Tp^{4Bo} ligand with osmium.



[(η^6-cymene)Os(k^2-Tp)Cl] (**1**) [(η^6-cymene)Os(k^3-Tp^{4Bo})] (**2**) [(η^6-cymene)Os(k^3-Tp)][PF$_6$] (**3**)

Figure 1

[1] Trofimenko, S. *Scorpionates: the coordination chemistry of polypyrazolylborate ligands. World Scientific, 1999.*
[2] Dias, H. V. R.; Goh, T. K. H. H. *Polyhedron* **2004**, *23*, 273-282.
[3] Pettinari, C.; Trofimenko, S. *Scorpionates II: chelating borate ligands*. World Scientific, 2008.
[4] Paulo, A.; Correia, J. D. G.; Campello, M. P. C.; Santos, I. *Polyhedron* **2004**, *23*, 331-360.
[5] Restivo, R. J.; Ferguson, G. *J. Chem. Soc. Chem. Commun.* **1973**, 847-848.
[6] Restivo, R. J.; Ferguson, G.; O'Sullivan, D. J.; Lalor, F. J. *Inorg. Chem.* **1975**, *14*, 3046-3052.
[7] Pettinari, C.; Marchetti, F.; Cerquetella, A.; Pettinari, R.; Monari, M.; Mac Leod, T. C. O.; Martins, L. M. D. R. S.; Pombeiro, A. J. L. *Organometallics* **2011**, *30*, 1616-1626.
[8] Dickinson, P. W.; Girolami, G. S. *Inorg. Chem.* **2006**, *45*, 5215-5224.

Abstract 29

Synthesis of Novel Zinc Complexes of Schiff Bases with Antibacterial Activity

Sonila Xhafa,[a]* Alessia Tombesi,[a] Fabio Marchetti,[a] Claudio Pettinari,[b] Corrado Di Nicola,[a] Stefania Scuri[b]

[a] University of Camerino, School of Science and Technology, Via S. Agostino 1, 62032 Camerino (MC), Italy.
[b] University of Camerino, School of Pharmacy, Via S. Agostino 1, 62032 Camerino (MC), Italy.
*E-mail = sonila.xhafa@studenti.unicam.it

Schiff bases are a broad family of versatile ligands able to form chelating complexes with several metals in different oxidation states.[1] Many metal complexes with Schiff bases are known to possess biological properties such as antibacterial, antifungal, antitumor, antioxidant activities.[2]

These properties are probably related to the azomethine (-CH=N-) or imine (-C=N-) group, as the imino nitrogen provides a binding site in drug activity, that can be enhanced through complexation with various transition metals[3].

Here we report the synthesis and characterization of a series of new zinc(II) complexes with differently functionalized Schiff bases of pyrazolones (HL)[4] with general composition [Zn(L)$_2$(H$_2$O)$_2$] (Figure 1). The antibacterial activity of both ligands and complexes has been tested against Gram-positive bacteria, *Staphylococcus aureus* and Gram-negative bacteria, *Escherichia coli* using the agar diffusion method, displaying moderate to strong efficiency.

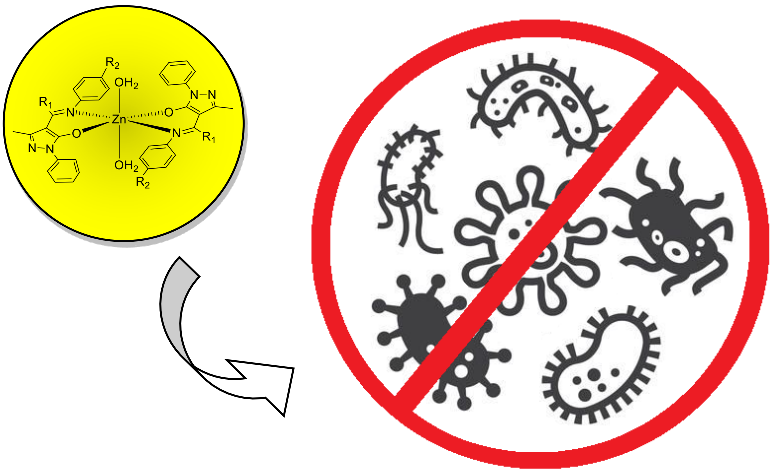


Figure 1

[1] Catalano, A.; Sinicropi, M. S.; Iacopetta, D.; Ceramella, J.; Mariconda, A.; Rosano, C.; Scali, E. Saturnino, C.; Longo, P. *Appl. Sci.* **2021**, *11*, 6027.
[2] Maher, K.; Mohammed, S. *Int. J. Curr. Res. Rev.* **2015**, 7, 6-16.
[3] Abayeh, O. J.; Achugasim, O.; Eruteya, O. C. *World Sci. News* **2021**, *160*, 16–36.
[4] Marchetti, F.; Pettinari, C.; Di Nicola, C.; Tombesi, A.; Pettinari, R. *Coord. Chem. Rev.* **2019**, *401*, 213069.

INDEX OF PARTICIPANTS

Title New Directions and Perspectives on Organometallic Chemistry
13th edition of the International School of Organometallic Chemistry, University of Camerino, Camerino, 1-3 September 2021
ISBN 9788867680528
Sponsored by University of Camerino