Role of Second Sphere Distal Residues in Oxygen Reduction Reaction Catalyzed by Iron Porphyrins

Arnab Ghatak, Abhishek Dey*

Senior Research Fellow, School of Chemical Sciences. IACS, India

Email: ghatak65arnab@gmail.com / icag2@iacs.res.in

Oxygen reduction reaction (**ORR**) is a complex multiproton/ multielectron process and factors that affect its rate and selectivity are of fundamental interest in order to design suitable catalyst. Iron porphyrins with covalently attached basic distal residues (**Fe-MARG and FeL3**) mimicking the active site of natural enzyme HRP, are shown to enhance the rate and $4H^+/4e^-$ selectivity of ORR compared to simple mono nuclear iron porphyrins under heterogeneous electrochemical condition.[1-2] In-situ surface enhanced resonance Raman spectroscopy coupled to rotating disc electrochemistry (**SERRS-RDE**) technique helps to identify two key intermediate species over self-assembled monolayer (SAM) modified electrode for these basic porphyrins depending on the nature of pedant residues. The spectroscopic investigation suggests "pull effect" from the distal structure for these porphyrins changes the distribution of intermediate species under steady state causing the enhancement in ORR rate as well as $4H^+/4e^-$ selectivity. [1] Density functional theory calculations indicate that not only the presence of hydrogen bonding from the pendant groups but also its relative spatial orientation with respect to the proximal and distal oxygen atom of a Fe^{III}–OOH intermediate species controls the selectivity of ORR.[1] In addition to this, involvement of the push effect from imidazole axial ligand and modification of guanidine moiety in the distal base further increases the selectivity.[2]

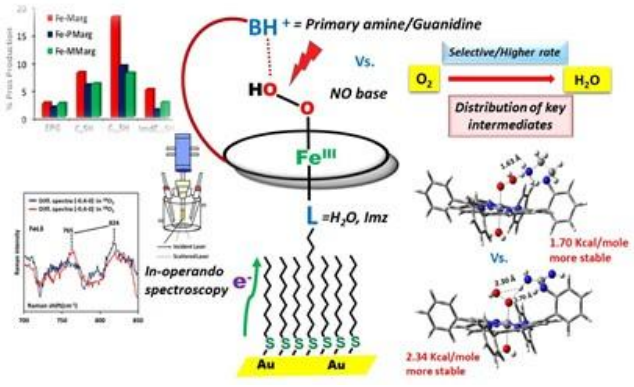


Figure 1: Schematic representation of the effect of distal basic residue over the iron porphyrin plane towards ORR along with the push effect by imidazole ligand.

1. A. Ghatak, S. Bhunia, A. Dey, *ACS Catal*. **2020**, *10*, 13136-13148.
2. A. Ghatak, S. Bhakta, S. Bhunia, A. Dey, *Chem. Sci*. **2019**, *10*, 9692-9698

Lanmodulin Peptides – Unravelling the Binding Properties of the EF-Hand Loop Sequences Stripped from the Structural Corset

S. G. Gutenthaler,[a] S. Tsushima,[b,c] R. Steudtner,[b] M. Gailer,[a] A. Hoffmann-Röder,[a] B. Drobot,[b*] L. J. Daumann[a*]

[a] Department of Chemistry, Ludwig-Maximilians-Universität, Munich, Germany

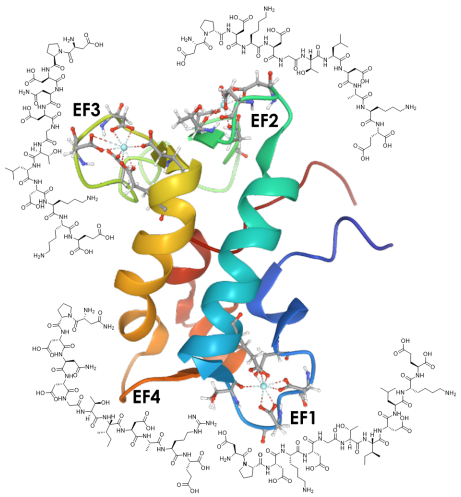
[b] Institute of Resource Ecology, Helmholtz-Zentrum Dresden-Rossendorf, Dresden, Germany

[c] World Research Hub Initiative, World Research Hub Initiative, Tokyo, Japan

Sophie.Gutenthaler@cup.uni-muenchen.de

The naturally lanthanide (Ln)-binding EF-Hand protein Lanmodulin (LanM) has a remarkable selectivity for Lns over Ca(II) and affinities in the pM/ µM range (depending on the binding site) which makes it an attractive target to address challenges in Ln separation.[1]

However, LanM's high selectivity and affinity for Lns and the differences between the four binding sites are not yet entirely understood. Both, cooperative effects and the amino acid (AA) sequences of the binding sites have been suggested.[1] Hence, we looked at it on the AA level by synthesising four 12-AA EF-Hand loop-based peptides and investigating the peptide-metal interactions with Eu(III), Tb(III), Cm(III) and Ca(II) using isothermal titration calorimetry, time-resolved laser induced fluorescence spectroscopy, circular dichroism spectroscopy and molecular dynamics simulations. We showed that all peptides have similar affinities for Lns in the µM range, a slightly higher affinity for Cm(III) and no binding to Ca(II), demonstrating that the differences in the Ln-binding sites and high Ln-affinities of LanM are largely an effect of pre-structuring (reduction of flexibility) in combination with cooperative effects. Our findings demonstrate that these peptides are a suitable starting point for the design of bio-inspired ligands for green Ln(/An) separation and recycling.[2]



[1] J. A. Jr. Cotruvo, E. R. Featherston, J. A. Mattocks, J. V. Ho, T.N. Laremore *J. Am. Chem. Soc.*, **2018**, *140*, 15056–15061.

[2] S. M. Gutenthaler, S. Tsushima, R. Steudtner, M. Gailer, A. Hoffmann-Röder, B. Drobot, L. J. Daumann, *chemrxiv,* **2021,** https://doi.org/10.26434/chemrxiv-2021-36s56.

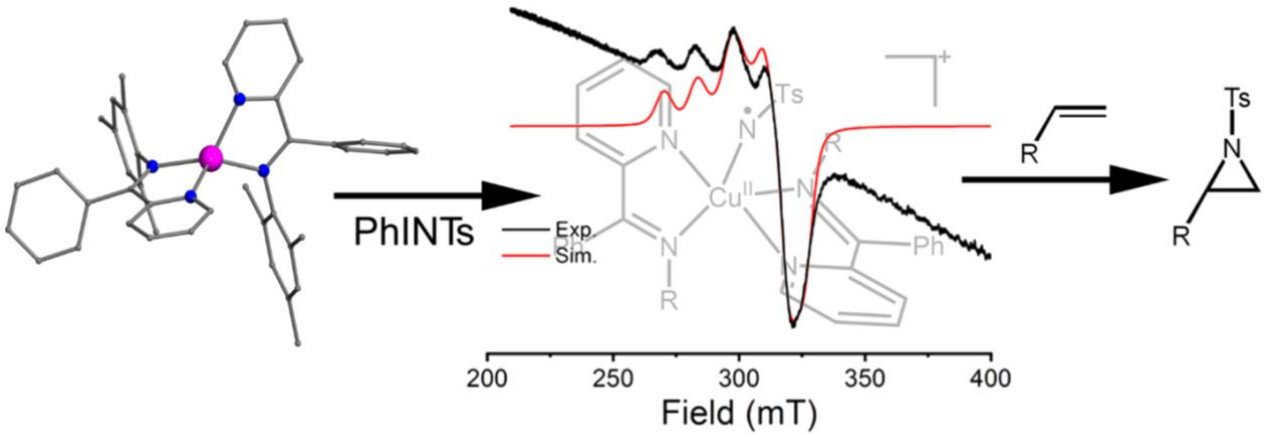
Aziridination of olefins mediated by a $[Cu(I)(L1)_2]^+$ complex via nitrene transfer reaction

Pardeep Kumar,[a] **Ashwani Chikara**,[a] Asmita Sen,[a] Maheswaran Shanmugam [a]*…

[a] Indian Institute of Technology Bombay, India

ashwanichikara815@gmail.com

Abstract: Copper-catalyzed aziridination of alkenes is dominated in the literature compared to any other metal catalysts. This catalytic reaction is believed to be mediated by the elusive Cu-nitrene intermediate. However, analytical characterization of this intermediate is extremely scarce in the literature. In this article, we intend to shed the light on the electronic structure of the Cu-nitrene intermediate. The reaction of Cu(I) salt in the presence of the redox-active bidentate Schiff base ligand ($C_{21}H_{20}N_2$; L1) led us to isolate a monomeric copper(I) complex with the molecular formula of $[Cu(L1)_2]ClO_4$. $2C_6H_6$ (**1**), which was structurally characterized. **1** behaves as an excellent catalyst that promotes the nitrene group transfer to the variety of alkenes in the presence of (N-(*p*-tolylsulfonyl)imino)phenyliodinane (PhINTs). The intermediate generated from **1** by the addition of PhINTs shows an *m*/*z* peak at 832.3079 g/mol which corresponds to an M^+ ion peak of the intermediate with the molecular formula of $[(L1)_2CuII\text{-}NTs]+$ (where Ts = Tosyl). Further, based on the detailed experimental studies (*in-situ* UV–Vis measurement and X-band EPR measurements) we propose that the active catalyst that possesses the copper ion in its +2 oxidation state under our experimental condition, whose electronic structure can be best described as $[(L1)_2CuII\text{-}NTs]^+$ nitrene radicals. The optimized structure of the Cu-nitrene intermediate suggests that the triplet state was found to be the ground state. Besides, we propose a mechanism for this catalytic reaction.



An Active Site Model for Lanthanide and Calcium Dependent Alcohol Dehydrogenases

V.A. Vetsova,[a] K.R. Fisher,[a] H. Lumpe,[a] A. Schäfer,[b] E.K. Schneider,[b] P. Weis,[b] L.J. Daumann[a]*

[a] Ludwig Maximilian University, Department of Chemistry, Butenandtstr. 5–13, 81377 Munich, Germany

[b] KIT, Institute of Physical Chemistry, Fritz-Haber-Weg 2, 76128 Karlsruhe, Germany

Email: vivech@cup.uni-muenchen.de

For a long time, it was assumed that most methylotrophic bacteria metabolize methanol solely by carrying the well-known Ca-dependent methanol dehydrogenase MxaF-MDH.[1] However, recent discoveries have shown that the methanotrophic bacterium *Methylacidiphilum fumariolicum* SolV is strictly Ln-dependent due to a XoxF-type MDH, which contains a Ln^{3+} ion in its active site.[2] Beside the metal ion, the enzyme's active site includes pyrroloquinoline quinone (PQQ) as a redox cofactor (Figure 1A), which gets reduced concurrent to methanol oxidation.

With the perspective to study the coordination chemistry of Ln in MDH and to compare it with the one of Ca, we reported a PQQ-based biomimetic complex system capable of oxidizing a benzylic alcohol to the respective aldehyde (Figure 1B).[3] Investigations using NMR as well as advanced mass spectrometry techniques allowed us to demonstrate the importance of charge and size of the complex cation (Figure 1C), as well as counterions and base. Furthermore, an EPR analysis of the obtained complexes and reaction mixtures show the presence of quinone-based radicals.

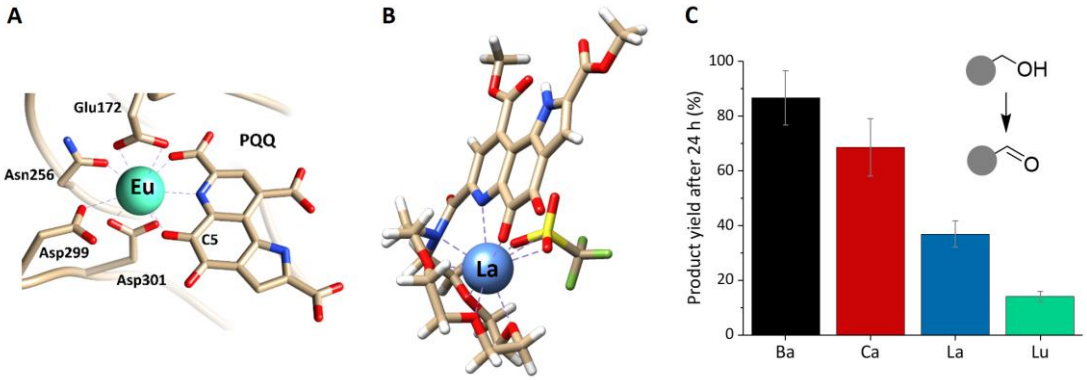


Figure 1. A: The active site of XoxF-MDH.[4] **B:** Calculated structure of the PQQMe_2-1-aza-15-crown-5-La-OTf complex. **C:** Obtained yields from the dehydrogenation reactions of 4-methylbenzyl alcohol by PQQMe_2-1-aza-15-crown-5 in the presence of different metal triflates and a base.

[1] C. Anthony, *Biochem. J.* **1996**, *320*, 697–711.

[2] A. Pol, T. R. M. Barends, A. Dietl, A. F. Khadem, J. Eygensteyn, M. S. M. Jetten, H. J. M. Op den Camp, *Environ. Microbiol.* **2014**, *16*, 255–264

[3] V. A. Vetsova, K. R. Fisher, H. Lumpe, A. Schäfer, E. K. Schneider, P. Weis, L. J. Daumann, *Chem. Eur. J.* **2021**, *27*, 10087-10098.

[4] B. Jahn, A. Pol, H. Lumpe, T. R. M. Barends, A. Dietl, C. Hogendoorn, H. J. M. Op den Camp, L. J. Daumann, *ChemBioChem* **2018**, *19*, 1147–1153.

Biomimetic oxygen activation with copper complexes of proton-responsive bis(oxazole) ligands

G. Duran-Solares,[a*] S. Dechert,[a] W. R. Browne,[b] F. Meyer[a]

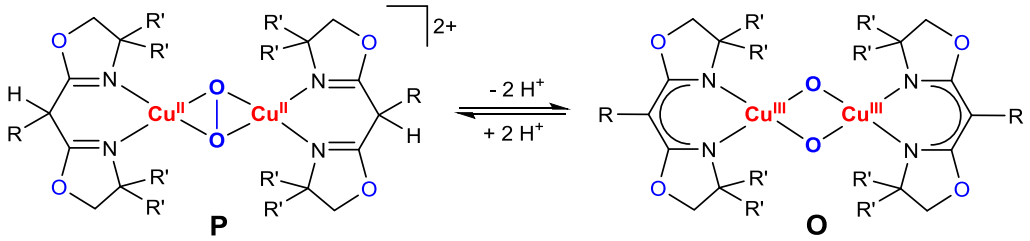
[a] University of Göttingen, Institute of Inorganic Chemistry, Tammannstr. 4, 37073 Göttingen, Germany

[b] Stratingh Institute for Chemistry, Faculty of Science and Engineering, University of Groningen, 747AG Groningen, The Netherlands

g.duransolares@stud.uni-goettingen.de

In nature there are several binuclear coupled copper proteins including the oxygen transporter Hemocyanin and related polyphenol oxidase enzymes such as Tyrosinase (Ty), which catalyses the hydroxylation of phenols to catechols with subsequent conversion to the corresponding quinones.[1] These so-called type III copper proteins contain two histidine-ligated copper ions that bind O_2 in μ–η^2:η^2-peroxo mode. Many synthetic complexes modelling the oxy form of the enzyme active site have been developed and have shown a preference for either the μ–η^2:η^2-peroxo dicopper(II) (**P**) or the bis(μ-oxido) dicopper(III) (**O**) core depending on the supporting ligand, the solvent and the nature of counterions.[2] In view of the potential of bioinspired copper complexes as catalysts for selective oxidations of organic substrates, elucidating the factors that govern the interconversion of these **P** and **O** intermediates and their distinct reactivity patterns is of great interest.

Recently we initiated the use of bis(oxazoline) (BOX) ligands in Cu/O_2 chemistry,[3] and we demonstrated that their **P** and **O** cores can be interconverted by peripheral (de)protonation events at the ligand backbone; this may be biologically relevant in view of the proton-responsive nature of histidine imidazoles.[4] We have now studied the reactive {Cu_2O_2} intermediates of a variety of different BOX ligands, their formation kinetics and acid/base induced **P**/**O** interconversion, as well as their reactivity towards substrates; the findings will be presented and discussed.



Acid/base triggered interconversion of P and O cores of {Cu_2O_2} intermediates.

[1] M. E. I. Solomon, D. E. Heppner, E. M. Johnston, J. W. Ginsbach, J. Cirera, M. Qayyum, M. Kieber-Emmons, C. H. Kjaergaard, R. G. Hadt, L. Tian, *Chem Rev.* **2014**, *114*, 3659-3853

[2] J. N. Hamann, B. Herzigkeit, R. Jurgeleit, F. Tuczek, *Coord. Chem. Rev.* **2017**, *334*, 54-66.

[3] A. Walli, S.Dechert, M. Bauer, S. Demeshko, F. Meyer, *Eur. J. Inorg. Chem.* **2014**, 4660-4676.

[4] V. E. Goswami, A. Walli, M. Förster, S. Dechert, S. Demeshko, M. C. Holthausen, F. Meyer, *Chem. Sci.* **2017**, *8*, 3031-3037.

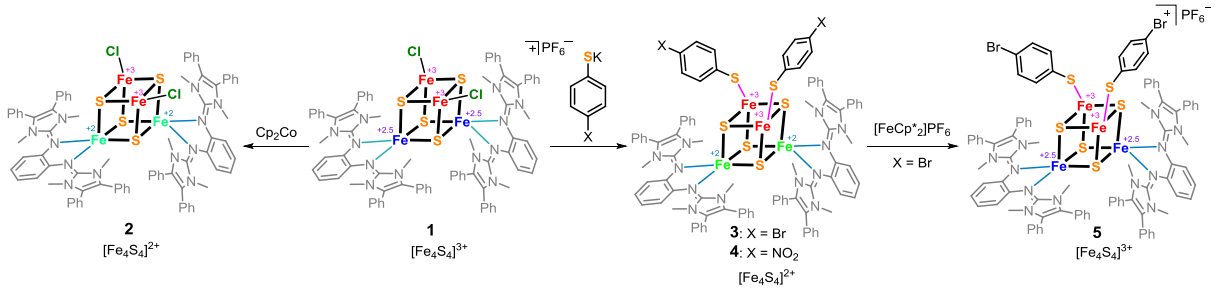
Synthesis of Well-Defined [2:2] Site-Differentiated [4Fe−4S] Clusters

Lanxia Hu, Sebastian Dechert, Sandeep Gupta, Serhiy Demeshko, Franc Meyer*

Institute of Inorganic Chemistry, Georg-August-Universität Göttingen Tammannstraße 4, 37077, Göttingen

lanxia.hu@stud.uni-goettingen.de

[4Fe−4S] clusters are essential components in organisms due to their functions in, e.g., electron transfer, catalytic molecular conversions, and transcriptional regulation.[1] Their broad utility in both biological and abiological contexts derives in part from the diversity of their geometric and electronic structures. Their role as models for plausible intermediates in biological process has motivated substantial effort toward generating synthetic [4Fe−4S] clusters.[2] Nevertheless, examples of the synthesis and characterization of [2:2] site-differentiated [4Fe−4S] clusters are extremely rare.[3] As such, we have begun investigating the chemistry of [4Fe−4S] clusters, and we herein report that a series of structurally characterized [2:2] site-differentiated [4Fe−4S] clusters can be stabilized by bidentate neutral imidazolin-2-imine ligands.[4] All of the investigated complexes were characterized by NMR and 57Fe Mössbauer spectroscopy as well as X-ray crystallography. Their electrochemical or chemical reductions and oxidations revealed rich redox chemistry. The geometric and electronic structures of the indicated [4Fe−4S] cores have all been elucidated.



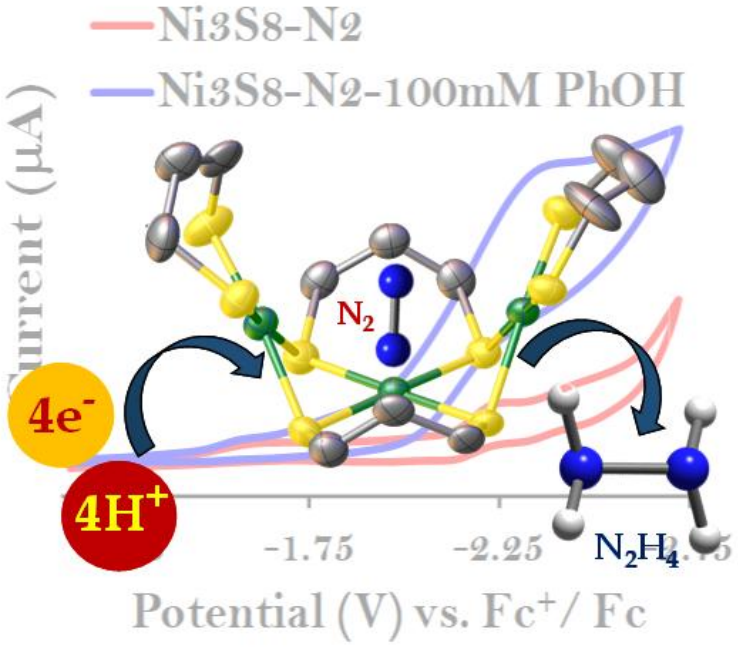
Reference:

[1] (a) Bertini, I.; Sigel, A.; Sigel, H. *Handbook on Metalloproteins*; Marcel Dekker: New York, **2001**; Chapter 10. (b) Messerchmidt, A.; Huber, R.; Poulos, T.; Wiehardt, K. *Handbook of Metalloproteins Vol. 1*; John Wiley & Sons: Chichester, U. K., **2001**; pp 543−552, 560−609.
[2] (a) Terada, T.; Hirabayashi, K.; Liu, D.; Nakamura, T.; Wakimoto, T.; Matsumoto, T.; Tatsumi, K. *Inorg. Chem.* **2013**, *52*, 11997. (b) Ye, M.; Thompson, N. B.; Brown, A. C.; Suess, D. L. M. *J. Am. Chem. Soc.* **2019**, *141*, 13330. (c) Brown, A. C.; Suess, D. L. M. *J. Am. Chem. Soc.* **2020**, *142*, 4 240. d c S imming, .; Sridharan, .; Thompson, N. .; ller, P.; Suess, D. L. M. *J. Am. Chem. Soc.* **2020**, *142*, 14314. (e) Sridharan, A.; Brown, A. C.; Suess, D. L. M. *Angew. Chem. Int. Ed.* **2021**, *60*, 12802.
[3] Han, J.; Coucouvanis, D. *Inorg. Chem.* **2002**, *41*, 2738.
[4] McSkimming, A.; Suess, D. L. M. *Inorg. Chem.* **2018**, *57*, 14904.

Electrocatalytic Reduction of Nitrogen to Hydrazine Using a Trinuclear Nickel Complex

P. Saha,[a] S. Amanullah,[b] A. Dey[a*]
[a] Indian Association for the Cultivation of Science, Kolkata, India
[b] CEA Paris-Saclay Gif-Sur-Yvette 91190, France
iparamitasaha@gmail.com, icps4@iacs.res.in

Activation and reduction of N_2 have been a major challenge to chemists and the focus since now has mostly been on the synthesis of NH3. Alternatively, reduction of N_2 to hydrazine is desirable because hydrazine is an excellent energy vector that can release the stored energy very conveniently without the need for catalysts. To date, only one molecular catalyst has been reported to be able to reduce N_2 to hydrazine chemically. A trinuclear T-shaped nickel thiolate molecular complex has been designed to activate dinitrogen. The electrochemically generated all Ni(I) state of this molecule can reduce N_2 in the presence of phenol as a proton donor. Hydrazine is detected as the only nitrogen-containing product of the reaction, along with gaseous H_2. The complex reported here is selective for the $4e^-/4H^+$ reduction of nitrogen to hydrazine with a minor overpotential of ~300 mV.[1]



[1] Saha P., Amanullah S., and Dey A. *J. Am. Chem. Soc.* **2020**, *142*, 17312−17317

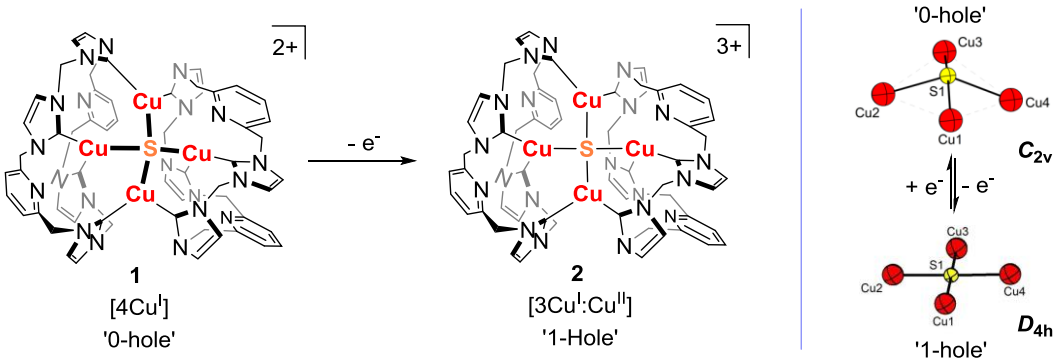
A Cu_4S Cluster in '0-Hole' and '1-Hole' States: Structural Model for the Active Cu_z^* site of N_2O Reductase

Y. Liu, S. Gupta, S. Dechert, F. Meyer*

Institute of Inorganic Chemistry, University of Göttingen, 37077 Göttingen, Germany

Yang.liu@chemie.uni-goettingen.de

Nitrous oxide (N_2O) is a harmful gas due to its dual roles as a potent greenhouse gas and ozone layer depletion agent.[1] In nature, the conversion of N_2O to N_2 and H_2O is catalyzed by the metalloenzyme nitrous oxide reductase (N_2OR) during the final step of the bacterial denitrification pathway.[2] The catalytic site of N_2OR, the so-called Cu_Z* or Cu_z site, features a μ_4-sulfur bridged tetranuclear copper core, which cycles between [$4Cu^I$] (0-hole) and [$3Cu^I$:Cu^{II}] (1-hole) states during the N_2O reduction.[1,3] To date, synthetic model complexes of Cu_Z*/Cu_z sites are extremely rare due to the difficulty in building the unique $Cu_4(\mu_4$-S) core structure.[4] Herein, we report the synthesis and characterization of [$Cu_4(\mu_4$-S)] clusters **1** and **2**, supported by a macrocyclic $(pyridine)_2(NHC)_4$ ligand, that were characterized in their '0-hole' (for **1**) and '1-hole' (for **2**) states, respectively, mimicking well the active states of the Cu_z* site during enzymatic N_2O reduction (Scheme 1). The significant geometry change of the $Cu_4(\mu_4$-S) core from **1** (τ_4(S) = 0.46, seesaw) to **2** (τ_4(S) = 0.03, square planar) upon oxidation was confirmed by their XRD structures (Scheme 1) and is unique among all known Cu_z* model complexes.[4] The electronic structures of **1** and **2** were further characterized by spectroscopic methods such as NMR, UV/Vis, and EPR as well as by SQUID magnetometry and DFT calculations. Furthermore, the reactivity of **1** towards N_2O and electrophilic reagents was investigated.



Scheme 1. $Cu_4(\mu_4$-S) clusters in '0-hole' and '1-hole' states, and their XRD core structures

[1] L. K. Schneider, A. Wust, A. Pomowski, L. Zhang, O. Einsle *Met. Ions Life Sci.* **2014**, *14*, 177.

[2] S. R. Pauleta, S. Dell'Acqua, I. Moura *Coord. Chem. Rev.* **2013**, 257, 332-349.

[3] E. M. Johnston, S. Dell'Acqua, S. Ramos, S. R. Pauleta, I. Moura, E. I. Solomon *J. Am. Chem. Soc.* **2014**, 136, 614.

[4] S. C. Rathnayaka, N. P. Mankad *Coord. Chem. Rev.* **2021**, *429*, 213718.

Mechanistic Insights into Superoxide Dismutation Driven by Dinuclear Manganese Complexes : The Role of the Mn_2-Core

Andrea Squarcina,[a*] Dominik Fehn,[b] Andreas Scheitler,[b] Laura Senft,[a] Philipp Maier,[a] Ralph Puchta[b] and Ivana Ivanović-Burmazović[a]

[a] Department of Chemistry, Ludwig-Maximilian-Universität München, 81375 München, Germany.

[b] Department of Chemistry and Pharmacy, FAU, 91058 Erlangen, Germany.

Email: andrea.squarcina@cup.uni-muenchen.de

In nature any failure in the mechanism of O_2 reduction turns out into the release of toxic reactive oxygen species (ROS). The ROS accumulation give rise to fast, barrier-less, short-range and non-selective oxidation steps, being responsible for the "oxidative stress" already linked to several pathologies like inflammation, neurodegenerative diseases and certain types of cancer.[1] The natural defense against ROS is provided by the combined action of superoxide dismutases (SOD), catalases (CAT) and glutathione peroxidase that with a cascade mechanism convert the superoxide radical anion ($O_2^{\bullet-}$) and H_2O_2 into O_2 and H_2O.

The dinuclear Mn_2L_2 core, has been recently reported to be a very active dual SOD/CAT functional analogue, enabling a cascade detoxification of $O_2^{\bullet-}$ to O_2.[2-4] Here, we discuss the SOD mechanism determining: (i) the catalytic activities with a direct method, (ii) the key intermediates involved in the dismutation process, (iii) discriminate between a single or di-Mn center catalysis in relation to the conformation of the Mn_2-core and (iv) introduce future applications.

Figure 1. Schematic representation of the key intermediates involved in the superoxide dismutation driven by the Mn_2-complexes.

References:

[1] T. Finkel, N. J. Holbrook, *Nature*, **2000**, *408*, 239.

[2] A. Squarcina, A. orar , F. Rigodanza, M. Carraro, G. Brancatelli, T. Carofiglio, S. Geremia, V. Larosa, T. Morosinotto, M. Bonchio, *ACS Catal.*, **2017**, 7, 1971.

[3] S. Signorella, C. Palopoli, G. Ledesma, *Coord. Chem. Rev.,* **2018**, 365, 75.

[4] I. Kenkel, A. Franke, M. rr , A. Zahl, C. k er-Benfer, J. Langer, M. R. i lipović, M. Yu, R. Puchta, S. R. Fiedler, M. P. Shores, C. R. oldsmith, Ivanović- I. Burmazović, *J. Am. Chem. Soc.*, **2017**, 139, 1472.

Electrocatalytic CO_2 reduction with transition metal complexes of the non-innocent Mabiq ligand

K. Rickmeyer[a], C. R. Hess[a]

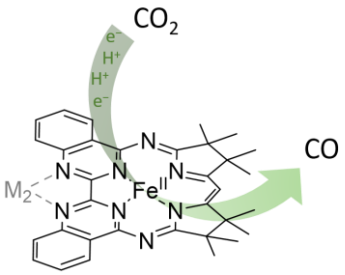
[a] Department of Chemistry and Catalysis Research Center, Technical University of Munich, Ernst-Otto-Fischer-Straße 1, 85748 Garching

e-mail: kerstin.rickmeyer@tum.de

Small molecule chemistry (e.g. CO_2 reduction, H_2 evolution…) plays a central role in efforts to store renewable energy in chemical bonds. In this regard, CO_2 represents an abundant and inexpensive source for C_1 building blocks. Molecular electro-catalysts play an integral role in these processes. The use of well-defined molecular catalysts provides unique access to detailed mechanistic and spectroscopic studies.[1] Hence, our understanding of the underlying processes can be increased, which consequently leads to the development of more stable and efficient catalysts.

Toward this end, we are developing small molecule activation catalysts based on the non-innocent macrocyclic biquinazoline ligand (Mabiq). Recently, we examined the ability of $[Co(Mabiq)(THF)]PF_6$ and $[Fe(Mabiq)(MeCN)_2]PF_6$ to act as electrocatalysts for CO_2 reduction. The role of the central metal on catalytic performance is noteworthy as the Fe-complex outperforms its Co-analogue both in terms of overpotential and faradaic efficiency. A combination of spectroscopic, electrochemical and computational methods were applied to study the CO_2 reduction mechanism by $[Fe(Mabiq)(MeCN)_2]PF_6$ in further detail. The investigations point toward a protonated intermediate, which highlights the ability of the Mabiq ligand to act as both an electron reservoir and proton storage site.[2]

The Mabiq ligand additionally provides a second metal binding site, which allows for further modification of the catalysts. We have already successfully synthesized various homo- and heterobimetallic Mabiq complexes. These complexes shed light on the influence of the neighboring metal site on the properties of the central metal-Mabiq unit.



[1] E. Boutin et al., *Chem. Soc. Rev.*, **2020**, *49*, 5772-5809.

[2] K. Rickmeyer et al., *ACS Catal.* **2022**, *12*, 3046-3057.

Chelators for Iron and Lanthanides

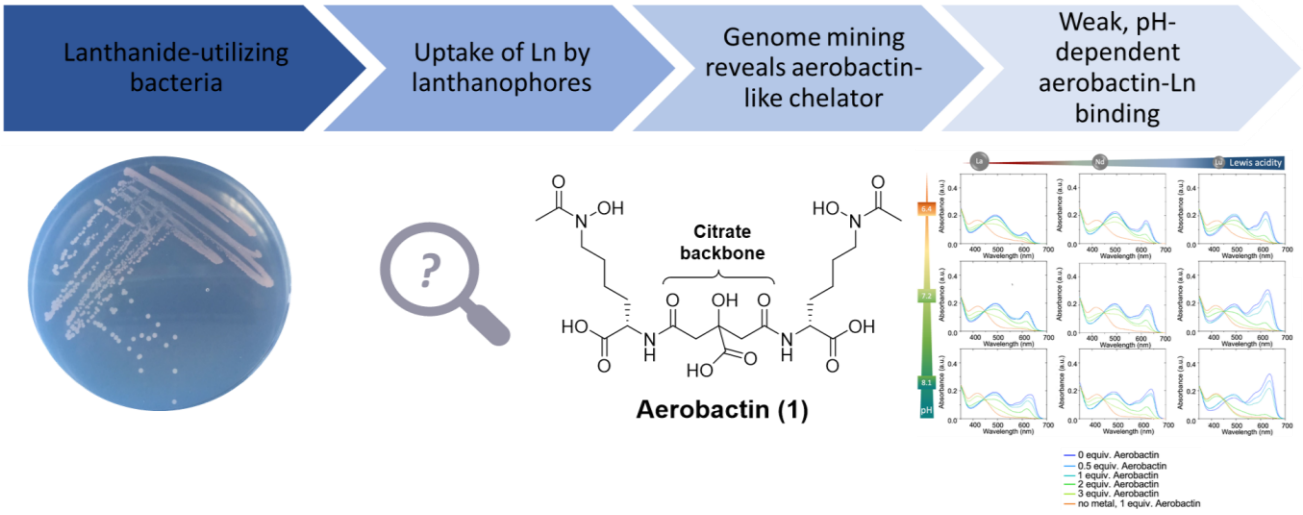
M. Tri Phi,[a] Sophie M. Gutenthaler,[a] Alexa M. Zytnick,[b] Nathan M. Good,[b] N. Cecilia Martinez-Gomez,[b] Lena J. Daumann[a]*

[a] Department of Chemistry, Ludwig-Maximilians-Universität München, Germany

[b] Department of Plant and Microbial Biology, UC Berkeley, USA

E-Mail: tri.phi@cup.uni-muenchen.de

Siderophores have been extensively studied for the past 70 years. Their remarkable affinity and selectivity towards Fe(III) is used in iron chelation therapy, imaging, heavy metal remediation and other research areas.[1-4] In the past years, lanthanides (Ln) have been firmly established as biological relevant due to their enzymatic role for the growth of methylotrophic bacteria.[5, 6] Similar to Fe(III), Ln are often poorly bioavailable. Bacteria produce siderophores to acquire iron from the environment. Contrary to Fe(III), the uptake system of Ln remains unclear. The methylotrophic bacterium *Methylorubrum extorquens* AM1 is able to thrive on Ln. The addition of an insoluble Ln_2O_3 to AM1 promotes the upregulation of a gene cluster encoding for the biosynthesis of metal chelator similar to siderophores. The gene cluster is termed Lanthanide Chelation Cluster and Phyre2 modeling suggests an aerobactin-like chelator (lanthanophore) to be involved.[7] Initial screening of aerobactin (1) with an indirect dye-based assay with various Ln revealed weak and pH-dependent aerobactin-Ln binding. Although complexation with Ln was observed, growth studies of the lanthanide-utilizing bacterial strain AM1 supplemented with (1) displayed no significant increase in growth rate.[7] Genome mining suggests a citrate-based siderophore, similar to (1), to be involved. Syntheses of alternative chelators and their coordination chemistry with Fe(III) and Ln(III) will be presented.



[1] R. C. Hider, X. Kong, *Nat. Prod. Rep.* **2010,** *27* (5), 637-657. [2] R. C. Hider, A. V. Hoffbrand, *NEJM* **2018,** *379* (22), 2140-2150. [3] E. Ahmed, S. J. M. Holmström, *Microb. Biotechnol.* **2014,** *7* (3), 196-208. [4] M. Petrik, C. Zhai, H. Haas, C. Decristoforo, *Clin. Transl. Imaging* **2017,** *5* (1), 15-27. [5] Y. Hibi, K. Asai, H. Arafuka, M. Hamajima, T. Iwama, K. Kawai, *J. Biosci. Bioeng.* **2011,** *111* (5), 547-549. [6] T. Nakagawa, R. Mitsui, A. Tani, K. Sasa, S. Tashiro, T. Iwama, T. Hayakawa, K. Kawai, *PLoS One* **2012,** *7* (11), e50480. [7] A. Zytnick, N. M. Good, C. C. Barber, M. T. Phi, S. M. Gutenthaler, W. Zhang, L. J. Daumann, N. C. Martinez-Gomez, *bioRxiv* **2022**, 2022.01.19.476857.

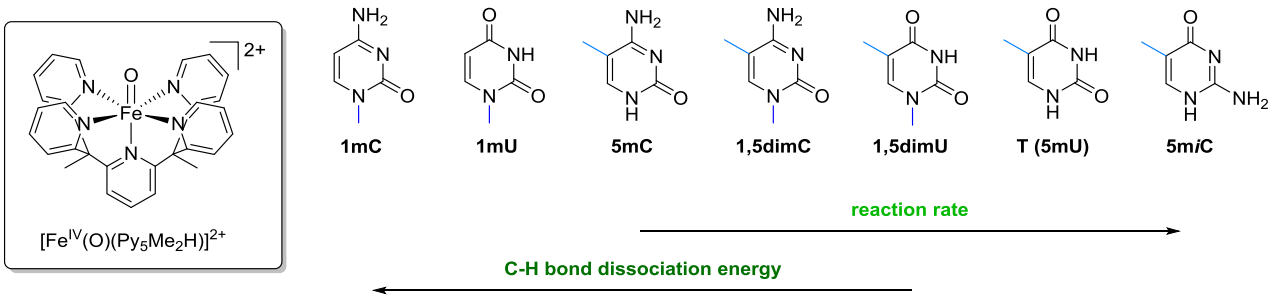
TET-Like Oxidation in 5-Methylcytosine and Derivatives: A Computational and Experimental Study

A. Menke,[a] N.S.W. Jonasson,[a] R. Janßen,[a] F.L. Zott,[a] H. Zipse,[a] L.J. Daumann[a]*

[a] Department of Chemistry, Ludwig-Maximilians-University Munich, Butenandtstr. 5-13, 81377 München, Germany

annika.menke@cup.lmu.de

The epigenetic marker 5-methylcytosine (5mC) is an important DNA modification expanding the 'DNA alphabet' as so-called fifth letter and creating a second layer of information in DNA. The usage of synthetic orthogonal nucleobase pairs in addition to the natural occurring nucleobases expands the DNA alphabet even further.[1] 5mC can be modified through a three-step oxidation performed by ten-eleven-translocation (TET) enzymes and as we have shown previously, the biomimetic iron(IV)-oxo complex $[Fe^{IV}(O)(Py_5Me_2H)]^{2+}$ can act as synthetic model for TET also oxidizing 5mC.[2] The reactivity of this iron(IV)-oxo complex towards a wider scope of methylated cytosine and uracil derivatives relevant for synthetic DNA applications was further investigated. Kinetic parameters were determined with UV-vis spectroscopy and oxidation products were identified using HPLC-MS and GC-MS.



The observations are corroborated by calculation of the C-H bond dissociation energies at the reactive sites which was found to be an efficient tool for reaction rate prediction of the iron(IV)-oxo complex towards methylated DNA bases.

[1] S. Hoshika, N.A. Leal, M.-J. Kim, M.-S. Kim, N.B. Karalkar, H.-J. Kim, A.M. Bates, N.E. Watkins, H.A. SantaLucia, A.J. Meyer, *Science* **2019**, *363*, 884–887.

[2] N.S.W. Jonasson, L.J. Daumann, *Chem -Eur.J.* **2019**, *25*, 12091-12097; D. Schmidl, N.S.W. Jonasson, E. Korytiakova, T. Carell, L.J. Daumann, *Angew. Chem. Int. Ed.* **2021**, *60*, 21457-21463.

New Trans-μ-Peroxido-Copper Complexes as Tyrosinase Model Systems

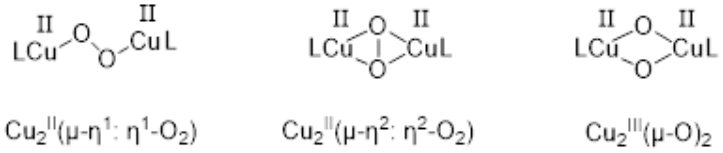
R. Dalhoff, [a] J. Heck, [a] C. Conrads, [a] A. Hoffmann [a] and S.Herres-Pawlis* [a]

[a] *Institute of Inorganic Chemistry, RWTH Aachen University, Landoltweg 1a, 52074 Aachen*

Rosalie.dalhoff@ac.rwth-aachen.de

The recent global goal to move towards more sustainable and environmentally friendly processes displays a great challenge for diverse chemical reactions. Regarding oxidation reactions, moving from the application of stoichiometric oxidants toward more atom efficient processes, biological systems present an interesting source of inspiration.[1] Activation of molecular dioxygen is a key step for many biological reactions. For instance, tyrosinase is a copper enzyme which enables the application of dioxygen for oxidation processes in melanin synthesis. Therefore, it activates dioxygen by binding it in a side-on bridging mode (μ-η^2: η^2) between two coordinated copper centers.[2]

To investigate the activity and the underlying mechanisms of the metalloprotein tyrosinase, several model systems have been developed so far.[3] Therefore, ligand systems which show structural similarities to the histidine residues coordinating the copper center in tyrosinase have been developed. The corresponding copper complexes were analyzed regarding their capability in mimicking tyrosinase activity.[3] Dioxygen activation has been observed not only by binding it in a side-on bridging mode (μ-η^2: η^2) but also in trans-μ-1,2-peroxido (Cu_2^{II}(μ-η^1: η^1-O_2)) bis-μ-oxido (Cu_2^{III}(μ-$O)_2$) bridging geometries.[4] This study focuses on the application of tetradentate ligand systems for tyrosinase model systems. The corresponding copper(I) complexes bind dioxygen in a trans-μ-1,2peroxido (Cu_2^{II}(μ-η^1: η^1-O_2)) geometry. These systems were investigated focusing on their spectroscopic and catalytic properties to obtain more information about the underlying mechanisms.



Cu_2^{II}(μ-η^1: η^1-O_2) Cu_2^{II}(μ-η^2: η^2-O_2) Cu_2^{III}(μ-$O)_2$

Figure 1: Different bridging modes of Cu_2-O_2-intermediates: a) trans-μ-1,2 peroxido (Cu_2II(μ-η^1: η^1-O_2)), b) peroxido (Cu_2^{II}(μ-η^2: η^2-O_2)) and c) bis-μ oxo (Cu_2^{III}(μ-$O)_2$) bridging geometries.[4]

[1] Claudia Wilfer, Patricia Liebhäuser, Hannes Erdmann, Alexander Hoffmann, Sonja Herres-Pawlis, *European Journal of Inorganic Chemistry* **2015**, *2015*, 494.

[2] C. Olivares, F. Solano, *Pigment cell & melanoma research* **2009**, *22*, 750.

[3] a) M. Paul, M. Teubner, B. Grimm-Lebsanft, C. Golchert, Y. Meiners, L. Senft, K. Keisers, P. Liebhäuser, T. Rösener, F. Biebl et al., *Chemistry – A European Journal* **2020**, *26*, 7556; b) P. Liebhäuser, K. Keisers, A. Hoffmann, T. Schnappinger, I. Sommer, A. Thoma, C. Wilfer, R. Schoch, K. Stührenberg, M. Bauer et al., *Chemistry* **2017**, *23*, 12171.

[4] P. Liebhäuser, A. Hoffmann, S. Herres-Pawlis in *Reference Module in Chemistry, Molecular Sciences and Chemical Engineering, Elsevier*, **2019**.

Electron transfer investigations with tyrosinase model complexes

Regina Schmidt,[a]* Rosalie Dalhoff,[a] Alexander Hoffmann[a] and Sonja Herres-Pawlis[a]

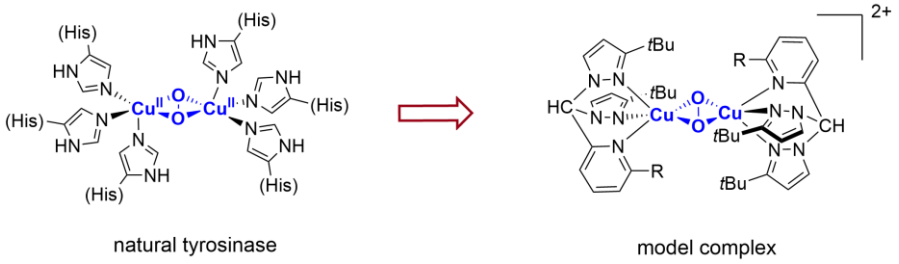
[a] Institute of Inorganic Chemistry, RWTH Aachen University, Landoltweg 1a, 52074 Aachen, Germany

regina.schmidt@ac.rwth-aachen.de

Modern bioinorganic chemistry uses natural concepts as examples for the development of new effective systems. Though, one aim is to mimic active centres of metalloenzymes to profit from the advantages of natural systems in an artificial context.

The enzyme tyrosinase is an ubiquitous enzyme which is capable to catalyse the *ortho* hydroxylation of tyrosine to L-Dopa as well as the following two-electron oxidation step to L-Dopaquinone.[1] The active form of tyrosinase consists of two copper centres which are each coordinated by three histidine residues and bridged by a μ-η^2:η^2 peroxido moiety.[2] In the presented model complex the histidine residues are mimicked by bis(pyrazolyl)methane ligands which feature excellent donor properties towards the copper centres.[3]
With the new ligand system the model complex is stable at room temperature for weeks which made it possible to obtain a crystal structure of the peroxido complex.

Beyond the catalytic features of the model complex towards artificial substrates also electron transfer reactions with different electron donors were investigated. Therein, the kinetics of the one-step two electron transfer reaction as well as thermodynamic parameters could be determined.[4,5]



natural tyrosinase — model complex

Figure 1: Active centre of tyrosinase (left) and the investigated model complex (right).

[1] Á. Sánchez-Ferrer, J. N. Rodríguez-López, F. García-Cánovas, F. García-Carmona, *Biochim. Biophys. Acta* **1995**, *1247*, 1.
[2] Y. Matoba, T. Kumagai, A. Yamamoto, H. Yoshitsu, M. Sugiyama, *J. Biol. Chem.* **2006**, *281*, 8981.
[3] a) A. Hoffmann, C. Citek, S. Binder, A. Goos, M. Rübhausen, O. Troeppner, I. Ivanović-Burmazović, E. C. Wasinger, T. D. P. Stack, S. Herres-Pawlis, *Angew. Chem. Int. Ed.* **2013,** *52*, 5398; *Angew. Chem.* **2013**, *125*, 5508. b) P. Liebhäuser, K. Keisers, A. Hoffmann, T. Schnappinger, I. Sommer, A. Thoma, C. Wilfer, R. Schoch, K. Stührenberg, M. Bauer, M. Dürr, I. Ivanović-Burmazović, S. Herres-Pawlis, *Chem. Eur. J.* **2017**, *23*, 12171.
[4] a) R. A. Marcus, *Angew. Chem. Int. Ed.* **1993**, *32*, 1111; *Angew. Chem.* **1993**, *105*, 1161. b) R. A. Marcus, N. Sutin, Biochim. Biophys. *Acta - Rev. Bioenerg.* **1985**, *811*, 265.
[5] a) H. Eyring, M. Polanyi. *Z. Phys. Chem. B.* **1931**, *12*, 279-311. b) H. Eyring, *J. Chem. Phys.* **1935**, *3*, 107.

Nitric Oxide Dioxygenation by Oxy-coboglobin Models Containing trans P-donor Ligand

Astghik Hovhannisyan[1], Garik Martirosyan[1], Lusine Harutyunyan[1], Alexei Iretskii[2]

[1]Molecule Structure Research Centre (MSRC) of the Scientific and Technological Centre of Organic and Pharmaceutical Chemistry National Academy of Sciences, 0014, Yerevan, Armenia, E-mail: ahovhan@gmail.com
[2]Department of Chemistry, Lake Superior State University, Sault Sainte Marie, MI 49783 USA

Nitric oxide (NO) is a well-known regulatory molecule in mammalian biology, the interactions of which with heme proteins play central roles in cardiovascular regulation and neurotransmission.[1] While sub-micromolar NO concentrations are sufficient to perform these functions, overproduction of NO can result in harmful consequences.[2]

This laboratory has previously described spectroscopic studies of the reaction of NO with the Co-porphyrins dioxygen complexes (L)Co(Por)(η^1-O_2) (Por = *meso*-tetraphenylporphyrinato (TPP^{2-}) and *meso*-tetra-p-tolylporphyrinato (TTP^{2-}), L = various N-donor ligands) assembled in low temperature sublimed layers. With the ammonia ligand the result was nitric oxide dioxygenation (NOD) leading to the formation of nitrate (NO_3^-) and oxidized Co^{III}-porphyrins.[3] In the case of pyridine, reactions proceeds in two pathways giving eventually nitrate and nitro species[4]. In this study the reaction of nitric oxide with specially constructed porous layered solids of the oxy–coboglobin models containing P-donor ligand - trimethylphosphine (TMP)Co(Por)(O_2) was monitored by FT-IR and UV-visible spectroscopy from 80 K to room temperature. The mechanism of the reaction, possible transient intermediates and final products are under further investigation. The intermediates will be characterized by FT-IR spectroscopy with the use of isotopically labeled $^{18}O_2$, ^{15}NO and $N^{18}O$ species.

1. Ford, P. C. Reactions of NO and Nitrite with Heme Models and Proteins. Inorg. Chem. 2010, 49, 6226.
2. Radi, R. Oxygen radicals, nitric oxide and peroxynitrite: Redox pathways in molecular medicine. Proc Natl Acad Sci USA. 2018, 115, 5839.
3. Kurtikyan, T. S.; Eksuzyan, S. R.; Hayrapetyan, V. A.; Martirosyan, G. G., Hovhannisyan, G. S.; Goodwin, J. A. Nitric oxide dioxygenation reaction by oxy-coboglobin models: In-situ low-temperature FTIR characterization of coordinated peroxynitrite. J. Amer. Chem. Soc. 2012, 134, 13861.
4. Kurtikyan T. S., Eksuzyan S. R., Goodwin J. A., Hovhannisyan G. S., Nitric Oxide Interaction with Oxy-coboglobin Models Containing trans Pyridine Ligand: Two Reaction pathways. Inorg. Chem. 2013, 52, 12046-12056.

Reductions of Nitrogen Oxyanions at a Copper(II) Cryptate: Role of Secondary Coordination Sphere

Aditesh Mondal, Kiran P Reddy and Subrata Kundu*

School of Chemistry, Indian Institute of Science Education and Research (IISER), Thiruvananthapuram 695551, India

aditeshmondal2318@iisertvm.ac.in, aditeshmondal20@gmail.com.

Transition-metal mediated transformations of nitrate (NO_3^-) and nitrite (NO_2^-) anions are of prime importance due to their implications in biogeochemical and physiological perspectives.[1] Importantly, insights into these transformations may enable the development of strategies for enhancing the bio-availability of 'N'-content in soil, thereby supporting higher crop productivity while suppressing NO_x pollution.[2] Enzymatically, the reduction of NO_3^- to NO_2^- ($NO_3^- + 2H^+ + 2e^- \rightarrow NO_2^- + H_2O$) and NO_2^- to NO ($NO_2^- + 2H^+ + e^- \rightarrow NO + H_2O$) are respectively mediated by Mo and Fe/ Cu containing metalloenzymes.[3,4] Notably, secondary coordination sphere around the metalloenzyme active sites assist substrate binding, proton/electron transfer, and stabilization of reactive intermediates.[5]

To understand the role of secondary coordination sphere interactions in the binding and reduction of nitrogen oxyanions, we utilize a heteroditopic macrobicyclic oxa-aza cryptand as the ligand scaffold to isolate nitrito/ nitrato-copper(II) cryptates.[6,7] A detailed kinetic study revealed that phenols are capable of reducing NO_2^- to NO through proton-coupled-electron-transfer (PCET) pathway in nitrito-copper(II) cryptate. Intriguingly, controlled protonation of the apical 3° amine in the secondary coordination sphere relative to the nitrito-copper(II) moiety leads to the isolation of a nitrito-copper(II) cryptate in a different protonation state. The presence of proton facilitates an unprecedented anaerobic nitration of phenol and NO liberation, which provides a new route for oxidative modification of phenol under hypoxia.[6]

In contrast to NO_2^- reduction, the transformation of NO_3^- to NO is more challenging due to its chemical inertness and weak coordination ability as a consequence of higher delocalized charge distribution. Herein we demonstrate the isolation and detailed characterization of nitrato-metal(II) cryptates (metal = Cu/ Zn).[7] X-ray crystal structures and other spectroscopic studies reveal that binding of NO_3^- at metal sites is facilitated through non-covalent interactions (NH···O, CH···O, and anion···π) between the cryptand and NO_3^-. Subsequently, reduction of NO_3^- to NO coupled to hydrazine (N_2H_4) oxidation to diazene (N_2H_2) has been demonstrated for the nitrato-copper(II) cryptate. A set of control experiments further suggest the importance of both the outer-coordination sphere interactions and the coordination of NO_3^- at a redox-active metal site for the reduction of NO_3^- to NO.[7]

[1] A. J. Timmons, M. D. Symes, *Chem. Soc. Rev.* **2015**, *44*, 6708–6722.
[2] N. Lehnert, B. W. Musselman, L. C. Seefeldt, *Chem. Soc. Rev.* **2021**, *50*, 3640–3646.
[3] C. Sparacino-Watkins, J. F. Stolz, P. Basu, *Chem. Soc. Rev.* **2014**, *43*, 676–706.
[4] L. B. Maia, J. J. G. Moura, *Chem. Rev.* **2014**, *114*, 5273–5357.
[5] M. W. Drover, *Chem. Soc. Rev.* **2022**, *51*, 1861–1880.
[6] A. Mondal, K. P. Reddy, J. A. Bertke, S. Kundu, *J. Am. Chem. Soc.* **2020**, *142*, 1726–1730.
[7] A. Mondal, K. P. Reddy, S. Som, D. Chopra, S. Kundu, *manuscript submitted.*

Time-Resolved Spectroscopic Investigations on Electro- and Photo-Catalytic CO_2 Reduction by a Fe-Porphyrin Catalyst

Amanullah SK,[a] Annamaria QUARANTA,[a] Zakaria HALIME,[b] Winfried LEIBL,[a] Ally AUKAULOO[b]

[a] Address: Institut de Biologie Intégrative de La Cellule (I2BC), CEA Paris Saclay, 91191 Gif-sur-Yvette, France

[b] Address: Institut de Chimie Moléculaire Et Des Matériaux d'Orsay (ICMMO), Université Paris Saclay, 91405 Orsay, France

amanullah.sk@cea.fr

Conversion of CO_2 into a valuable fuel using solar energy is one of the most attractive approaches to mitigate the global warming problem. However, for practical implementation of any of these carbon fixation strategies, the reduction should be selective. Mechanistic investigation of the CO_2 reduction process can unearth the factors responsible for imparting selectivity for different products. However, rarely have these intermediates been experimentally observed and characterized. As a result, there is a lack of insight into the electronic structure of these intermediates, which is key to understanding their reactivities. This work aims at investigating the catalytic cycle of a bioinspired iron porphyrin[1] in light-induced CO_2 reduction, and in particular to get insight into the structure-function relationship for these molecular architectures in order to proceed with a rational design of more efficient photocatalysts. To achieve our goal, we intend to combine electronic and vibrational spectroscopy to identify the key intermediate species formed during the catalytic cycle as well as the dynamics of the system. Fourier Transform Infrared difference spectroscopy is particularly sensitive to structure and bond changes occurring at the catalytic site during the different steps of the process, such as successive reduction steps, protons transfers, substrate binding, product formation, and release. This technique, associated with spectro-electrochemistry, transient absorption, EPR, and resonance Raman is being used to identify key intermediates as well as the limiting steps in the photoreaction.

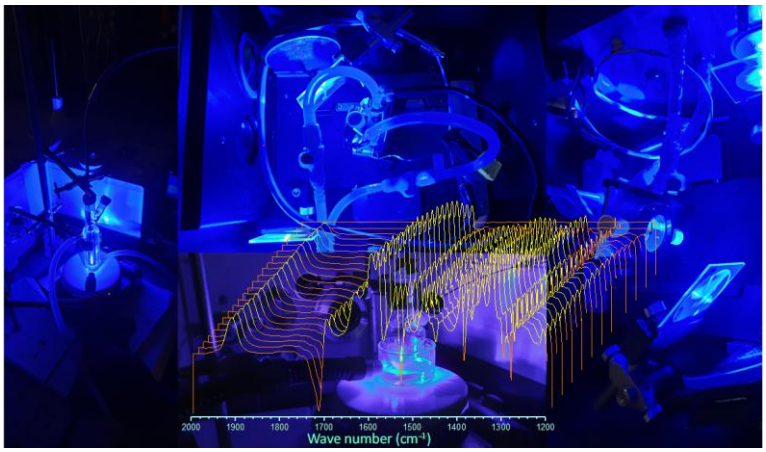


Figure 1. Schematic diagram of the spectroscopical investigation of the photocatalytic CO_2 reduction process

[1] P. Gotico, B. Boitrel, R. Guillot, M. Sircoglou, A. Quaranta, Z. Halime, W. Leibl, A. Aukauloo, *Angewandte Chemie International Edition*, **2019**, *58*, 4504-4509

[2] C. Zhang, D. Dragoe, F. Brisset, B. Boitrel, B. Lassalle-Kaiser, W. Leibl, Z. Halime A. Aukauloo *Green Chem.*, **2021**, *23*, 8979-8987

[3] E. Pugliese, P. Gotico, I. Wehrung, B. Boitrel, A. Quaranta, M. Ha-Thi, T. Pino, M. Sircoglou, W. Leibl, Z. Halime, A. Aukauloo *Angewandte Chemie International Edition*, **2022**, e202202924M.

Cooperative Chemobio-Catalysts for Hydrogenation Reactions

T. Sudmeier,[a]* S. Freakley,[b] K.A. Vincent[a]

[a] Inorganic Chemistry Laboratory, South Parks Rd, OX1 3QR, Oxford

[b] Department of Chemistry, University of Bath, Claverton Down, Bath, BA2 7AY

tim.sudmeier@chem.ox.ac.uk

Hydrogenation reactions account for 10-20% of all industrial chemical steps and will remain a key chemical technology in a circular economy dependent on renewable resources.[1] Classically used metal nanoparticle catalysts often require high hydrogen pressures, elevated temperature and organic solvents, and can suffer from poor selectivity and functional group tolerance. Biocatalysis provides the opportunity to perform highly selective hydrogenations in water and at milder conditions but oftentimes requires expensive cofactors.[1–3] Here, we explore a new concept in catalytic hydrogenation by combining bio- and heterogeneous chemo-catalysts containing cooperative active sites electronically connected via a conductive carbon support.

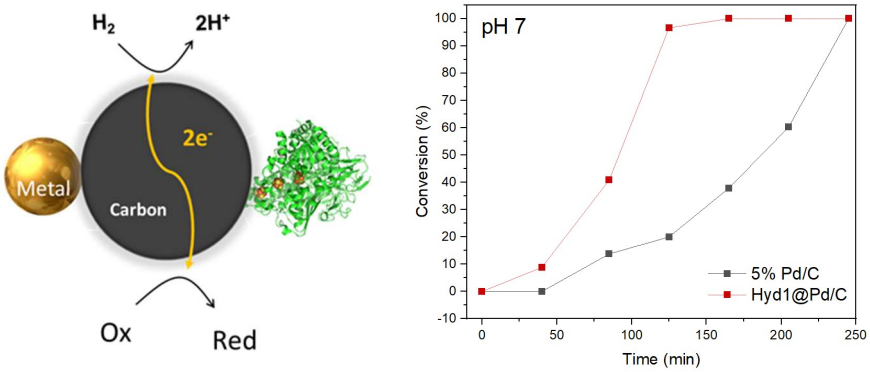


Figure 1. a) Schematic depiction of chemobio-catalyst consisting of a hydrogenase unit electronically coupled to palladium nanoparticles via a carbon support. **b)** Conversion vs time plot of the hydrogenation of 2-butynol under a partial H_2 pressure of 0.1bar using a commercial 5% Pd/C (black squares) and 5% Pd/C catalyst with a co-immobilised hydrogenase (red squares).

More specifically, we show how co-immobilising a hydrogenase enzyme with palladium nanoparticles on a carbon support leads to a significant rate enhancement in the hydrogenation of 2-butynol (Figure 1). The effect is observed in different pH regimes and buffer systems. On top of increasing the rate, the presence of a hydrogenase "booster" unit was shown to alleviate substrate poisoning of the palladium catalyst and lead to a different product distribution. In this work we demonstrate the benefits of electronically coupling enzymatic active sites to a heterogenous chemo-catalyst via a carbon support to facilitate hydrogenation reactions under low hydrogen pressures and mild temperatures.

[1] C. Zor, H.A. Reeve, J.H. Quinson, L.A. Thompson, T.H. Lonsdale, F. Dillon, N. Grobert, K. A. Vincent, Chem. Commun. **2017**, 53 (71), 9839–9841.

[2] X. Zhao, S.E. Cleary, C. Zor, N. Grobert, H.A. Reeve, K.A. Vincent, Chem. Sci. **2021**, 12 (23), 8105–8114.

[3] D. Wilbers, J. Brehm, R.J. Lewis, J. van Marwijk, T.E. Davies, D.J. Morgan, D.J. Opperman, M.S. Smit, M. Alcalde, A. Kotsiopoulos, S.T.L. Harrison, G.J. Hutchings, S.J. Freakley, Green Chem. **2021**, 23 (11), 4170–4180.

Design of water-soluble redox-active copper complex for biomolecule functionalization

Marie-Julie Tilly[a,b],Frederic Melin[c], Petra Hellwig[c], Sylvie Choua[d], Nolwenn Le Breton[d], Peter Faller[b], Laurent Raibaut[b], Marine Desage-El Murr[a]

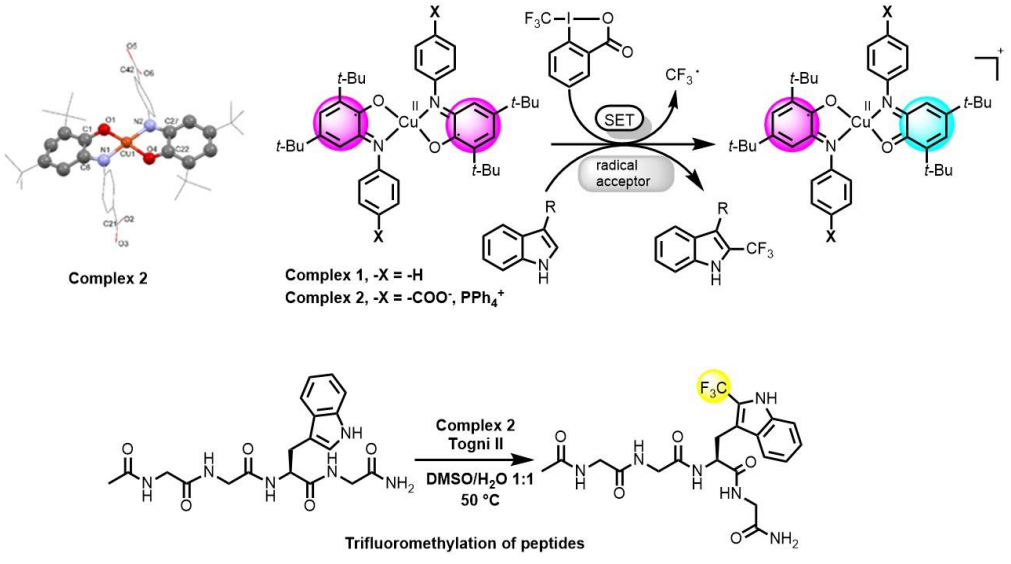
[a] OMECA, [b] BCB, [d] POMAM, Institut de Chimie, UMR 7177, Université de Strasbourg, 1 rue Blaise Pascal, 67000 Strasbourg, France

[c] LBS, Institut de Chimie, UMR 7140, Université de Strasbourg, 1 rue Blaise Pascal, 67000 Strasbourg, France

mj.tilly@unistra.fr

Incorporation of trifluoromethyl (CF_3) groups in biomolecules is an attractive and valuable goal due to the high sensitivity of the ^{19}F nucleus in NMR and allows to modulate properties of molecules. Common radical methods use strong oxidative conditions, leading to low selectivity, or expensive photoredox catalysts. The lack of mild conditions to create C-CF_3 bonds in complex biomolecules drove us to investigate the use of redox-active ligands, able to store and release electrons. The possible shuttling between the two redox states of the ligand enables controlled-radical generation. Our team has previously studied redox-active copper complex $Cu(SQ)_2$ **1**, bioinspired model of the enzyme Galactose Oxidase (GAO), and aims to expand its application scope in biological medium.[1,2]. Previous results have demonstrated its efficiency for selective radical trifluoromethylation of small indoles in organic solvents but complex **1** is insoluble in methanol or water.[3]

Within this context, water-soluble complex **2** was developed by incorporating an ionizable function (-X = -COO^-, PPh_4^+) on the ligand backbone. Full characterization of this new paramagnetic complex will be presented by spectroscopy, structural and analytical techniques. Our method was adapted in aqueous medium and applied to model peptides. Residue-specific selectivity studies were performed to assess the efficiency of our conditions. Complex **2** appears to promote selective trifluoromethylation under mild conditions and could act as a redox platform to catalyze transfer of other small groups (N_3, silyl groups) on Tryptophane (Trp).



1. D.L.J. Broere, R. Plessius, J.I. van der Vlugt, *Chem. Soc. Rev.*, **2015**, *44*, 6886-6915.
2. Chaudhuri, K. Wieghardt, T. Weyhermüller, T.K. Paine, S. Mukherjee, C. Mukherjee, *Biol. Chem.*, **2005**, *386*, 1023–1033.
3. J. Jacquet, S. Blanchard, E. Derat, M. Desage-El Murr, L. Fensterbank, *Chem. Sci*. **2016**, *7*, 2030-2036.

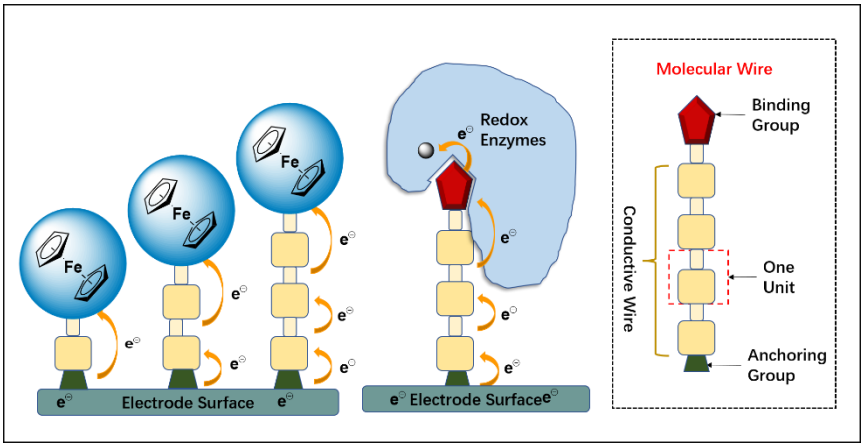
Novel 'molecular wires' for long-distance electron transfer between the hierarchical electrode surfaces and redox-active molecules

F. Fang[a]*, A. Sills[a], T. Bennett[a], N. Long[a], M. M. Roessler[a]

[a]Department of Chemistry, Imperial College London, Molecular Sciences Research Hub, White City Campus, W12 0BZ

f.fang20@imperial.ac.uk

Protein Film Electrochemistry (PFE) is a transformative technique that can enable detailed insights into the mechanisms of redox-active enzymes.[1] However, it relies on effective electron transfer between the electrode surface and the redox centre(s) within the protein.[2] This is especially important when coupling PFE with spectroscopic techniques such as electron paramagnetic resonance (EPR), which requires hierarchical electrode structures to achieve the required sensitivity.[3] New strategies are therefore needed to orient proteins onto hierarchical electrodes in an 'electroactive' configuration. Here, we propose a novel strategy, named 'molecular wire', to achieve both long distance and directed electron transfer between the electrode surface and the redox centre. A series of conductive molecular wires of different lengths were designed and synthetized, which are composed of three parts: an anchoring group, a conductive wire and a binding group. As proof of concept, we anchored ferrocene at the end of the conductive wire to



determine the electron transfer efficiency.

We demonstrate covalent attachment of the molecular wire onto indium-tin-oxide electrodes, investigate the length dependency of the molecular wire on conductivity,[4] and show that electron transfer is effective even over long distances in these hierarchical structures. This work will lie the

[1] P. A. Ash and K. A. Vincent, *Chem Commun (Camb)*, 2012, **48**, 1400-1409.
[2] N. D. J. Yates, M. A. Fascione and A. Parkin, *Chemistry*, 2018, **24**, 12164-12182.
[3] K. Abdiaziz, E. Salvadori, K. P. Sokol, E. Reisner and M. M. Roessler, *Chem Commun (Camb)*, 2019, **55**, 8840-8843.
[4] K. H. Khoo, Y. Chen, S. Li and S. Y. Quek, *Phys Chem Chem Phys*, 2015, **17**, 77-96

foundation for anchoring complex proteins with buried redox centres onto hierarchical electrodes effectively, to enable combined PFE and spectroscopic investigations.

Inertness of superoxide dismutase mimics Mn(II) complexes based on an open-chain ligand is a key feature for bioactivity and detection in intestinal epithelial cells

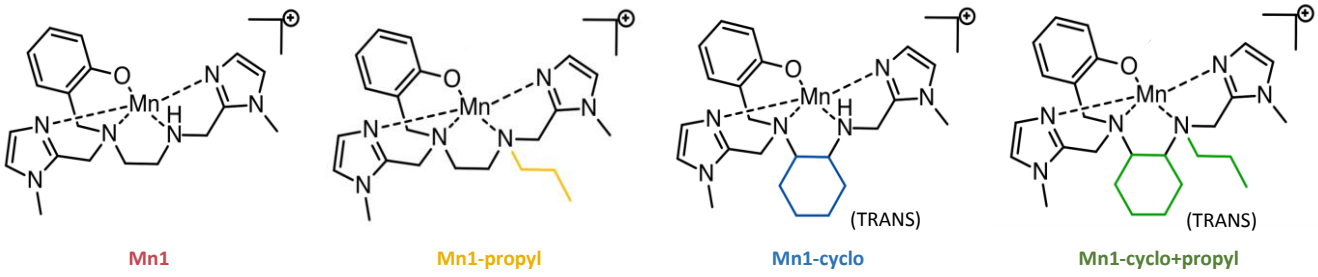
G. Schanne,[a,b]* M. Zoumpoulaki,[a] G. Gazzah,[a] S. Demignot,[b] P. Seksik,[b] N. Delsuc[a], C. Policar[a]

[a] Laboratory of Biomolecules, LBM, Department of chemistry, Ecole Normale Supérieure, PSL University, Sorbonne University, CNRS, 75005 Paris, France

[b] Saint Antoine Research Center, INSERM, UMRS 938, Metabolism-Inflammation Department, 184 rue du Faubourg Saint-Antoine, 75012 Paris, France

gabrielle.schanne@ens.psl.eu

Superoxide Dismutases (SODs) are metalloenzymes involved in the cellular antioxidant defenses. They regulate the concentration of the superoxide anion, a reactive oxygen species (ROS).[1] It has been shown that SOD defenses are weakened in intestinal epithelial cells of patients suffering from inflammatory bowel diseases (IBDs).[2] The resulting increase in ROS amount, leading to oxidative stress, may contribute to the pathogenesis in IBDs. Low-molecular weight complexes, mimicking SOD activity may be promising antioxidant metallodrugs for the treatment of IBDs. The research conducted in Policar's group has led to the development of the manganese complex Mn1, based on an open-chain ligand, that has shown anti-oxidant and anti-inflammatory activities in intestinal LPS-stressed epithelial cells, an inflammation model mediated by oxidative stress.[3] However, Mn1 is very flexible compared to the native SOD and is prone to metal-assisted dissociation in cells. Indeed, metal exchanges might occur between the manganese center and metal ions present in the biological environment. Aiming at improving the bioactivity of this SOD mimic, three new MnSOD mimics derived from Mn1 have been designed. Their structure include additional cyclohexyl and propyl groups. In one hand, by rigidifying the ligand structure, the cyclohexyl group may provide a compact and preorganized coordination cavity to encapsulate the manganese ion and may improve the inertness of the complexes. In the other hand, the propyl group may prevent any deprotonation issue during the subsequent speciation studies and



increases the lipophilicity of the complexes.

We have assessed the potential of new SOD mimics derived from Mn1 to demonstrate higher intrinsic SOD activity, higher lipophilicity and improved resistance to metal exchanges.[4] Very interestingly, the new Mn1 derivatives were shown to provide anti-inflammatory and antioxidant effects in intestinal LPS- stressed intestinal epithelial cells at lower doses than Mn1, which could be correlated to their higher stability in the cellular environment.[4] The anti-inflammatory activities of the four SOD mimics were also evaluated on a murine model of colitis chemically-induced by DNBS.The rationalization of the SOD mimics bioactivities can be boosted by the direct detection and quantification of the active species inside the cells. The detection of open-chain manganese complexes in biological environments is not straightforward due to their high lability and thus possible metal exchanges. Thanks to its higher kinetic inertness, Mn1-cyclopropyl was detected inside cell lysates by mass spectrometry and its intracellular concentration was estimated.[4]

1. Sheng, Y. *et al.*, *Chem. Rev.* **2014**, 114 (7), 3854–3918.
2. Kruidenier, L. *et al.*, *J. Pathol.* **2003**, 201 (1), 7–16.
3. Mathieu, E. *et al.*, *Inorg. Chem.* **2017**, 56 (5), 2545–2555
4. Schanne, G. *et al.*, *Oxidative Medicine and Cellular Longevity*. **2022**, https://doi.org/10.1155/2022/3858122

Self-base pairing of nucleotide monophosphates in Iron-polyamine-mononucleotide based ternary Coordination complex

Apurba Kumar Pal, Munirathinam Nethaji *

Department of Inorganic and Physical Chemistry, Indian Institute of Science, C.V. Raman Avenue, Bangalore 560012, India.

Email: apurbapal@iisc.ac.in, apurbakumar.pal2014@gmail.com

Hydrogen bonds formation between the complementary nucleobases is the essential process for the transfer of genetic information. Any mismatch in base pair formation sometime leads to the genetic diseases and DNA rearrangements. Along with B-form of DNA double helix, several alternative non-B form of DNA e.g, G-quadruplex(G4), intercalated motif (i-motif), Adenine-Adenine base pair mismatch (A-motif) etc are found in the fundamental biological process[1]. X-ray crystallography has been a useful tool to understand the structural details of these different form of DNA and base pair mismatches. But the main obstacle in this process is difficultness in crystallization of these genetic materials. Designing of small molecule model is an effective way to solve this issue. Keeping these things in mind, we have designed and synthesized four Iron-polyamine-nucleotide based ternary complexes (complex 1-4) where we used four different nucleotides namely adenine-5'-monophosphate (AMP), cytidine-5' monophosphate (CMP), 2'-deoxycytidine-5'-monophosphate (dCMP), cytidine-2' monophosphate(2'CMP). All the complexes have been characterised through single crystal X-ray diffraction. In complex 1 and complex 2 where we used adenine-5'-monophosphate (AMP), cytidine-5' monophosphate (CMP) as a nucleotide ligand, have base pairing between adenine-adenine (A-motif) and cytosine-cytosine (i-motif). It is worth to mention that mono- and dinucleotides are usually impotent to form stable hydrogen-bonded base pairs in water but in this case, in presence of metal ion and auxiliary ligand (polyamine), two mono nucleotides can form hydrogen bonds between them. To investigate the role of sugar ring in formation of i-motif structure we used 5'-dCMP in complex 3. Here we observed that changing in sugar ring conformation have a profound effect in stabilizing the i-motif structure in complex 2 and complex 3. In complex 4 we have used 2'CMP to check the specificity of formation of i-motif structure and effect of different binding mode with metal ion on the i-motif structure. Additionally, the chiralities of these coordination complexes were studied according to their crystal structures and solution-state circular dichroism spectroscopy.[2]

---

[1] Abou Assi, H.; Garavís, M.; González, C.; Damha, M J. Nucleic Acids Res. **2018**, *46*, 913–924.

[2] Pal, A K.; Nethaji, M. Manuscripts under preparation.

Design and Development of Boron based Proteasome Inhibitors

Surajit Sarker, Pandi Dhanalakshmi and Pakkirisamy Thilagar*

Department of Inorganic and Physical Chemistry, Indian Institute of Science, C.V. Raman Avenue, Bangalore 560012, India.

e-mail: surajits@iisc.ac.in, surajitsarker8@gmail.com

Proteasomes are large multi-catalytic protein complexes inside all eukaryotes, archaea, and in some bacteria. The primary function of the proteasome is to degrade the essential and damaged proteins by proteolysis, a chemical reaction that cleaves the peptide bonds. Enzymes that help such reactions are known as proteases. In eukaryotes, proteasomes are located in the nucleus and cytoplasm. They are part of a central mechanism by which the cells regulate the concentration of particular proteins and degrade the misfolded and disordered proteins. The proteasome-dependent cleavage of peptide bonds is an ATP-dependent process. The immune system also utilizes this protein degradation pathway to produce small peptides for presentation by MHC Class I molecules. Dysregulation of the proteasome leads to tumor progression and drug resistance.[1] The recent discovery of proteasome inhibitors is a novel strategy to overcome the aforementioned problems. However, the present proteasome inhibitors suffered heavily due to adverse effects like thrombopenia, fatigue, peripheral neuropathy, etc., which could be attributed to the non-selectivity of the drug towards normal proliferating cells in addition to cancerous cells. It is thus of high interest to find new molecules with higher selectivity and sensitivity, inhibit proliferation, and induce apoptosis in specific cancer cells.[2] In our venture, we have developed a library of boronopeptides based proteasome inhibitors. These new peptides showed improved cytotoxicity than the known anticancer drug Doxorubicin (~10-20 times higher cytotoxicity than Doxorubicin). Molecular Docking & Molecular Dynamics Simulation studies on these peptide-proteasome complexes show favorable binding of boronopeptides with the β1 and β5 active sites of the human constitutive proteasome with significant binding affinity, RMSD, RMSF & protein SSE values.[3] The intriguing findings obtained from these studies will be presented in this poster.

REFERENCES

(1) Andrew Paramore and Simon Frantz, *Nature Reviews, Drug Discovery,* Vol.2, **2003**, 611-12.

(2) Julian Adams, *Nature Reviews, Cancer,* Vol.4, **2004**, 349-60.

(3) S. Sarker et al. 2022 unpublished results.

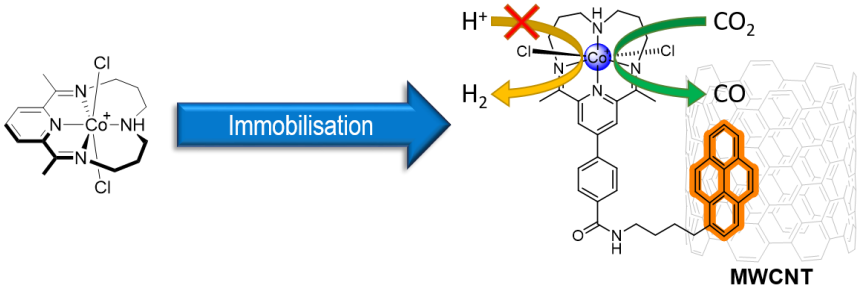
Cobalt-based Molecular Cathode for Selective Electrocatalytic CO2-to-CO Reduction in Aqueous Electrolyte

M. Haake,[a] T. Straistari,[a] M. Chavarot-Kerlidou,[a] B. Reuillard,[a]* V. Artero[a]*

[a] Univ. Grenoble Alpes, CNRS, CEA, IRIG, Laboratoire de Chimie et Biologie des Métaux, F-38054 Grenoble Cedex, France

Matthieu.Haake@cea.fr

Electrochemical conversion of CO_2 into hydrocarbons and/or useful chemicals using clean electricity from renewable energy sources is a promising strategy to close the carbon cycle.[1] The preparation of molecular heterogeneous catalysts stands as an attractive alternative. These hybrid catalysts combine the robustness of material-based heterogeneous catalysts with the ease of tuning molecular structures which usually showcase better selectivity at lower overpotentials.[2] Various hybrid molecular catalysts relying on earth-abundant metals have been developed. In particular, Co-based ones showed great promises for CO_2 conversion once incorporated to electrolysers devices.[3] Over the past decade, the cobalt complex based on a tetraaza macrocyclic ligand (Scheme 1) have shown promising activity for electrochemical CO_2 reduction under homogeneous organic conditions.[4,5] We modified the ligand scaffold of this complex in order to introduce a pyrene anchoring unit to allow its smooth immobilisation onto multi-walled carbon nanotube (MWCNT) based electrodes. The modified electrodes were fully characterised using standard electrochemical techniques. This new molecular cathode was then investigated for electrocatalytic CO_2 reduction in neutral aqueous media and showed currents up to 7 mA cm^{-2} and reasonable stability over time at a relatively low overpotential of 450 mV. From these electrolysis measurements a high CO selectivity and faradaic efficiency above 90% could be obtained, corresponding to TOF_{CO} values up to 3.29 s^{-1}. This hybrid catalyst matches the benchmark activities of other state-of-the-art cobalt catalysts.[3]



Scheme 1: The tetraaza macrocyclic Co-complex (left) and the modified tetraaza macrocyclic complex for immobilisation on MWCNT (right).

[1] O. S. Bushuyev, P. De Luna, C. T. Dinh, L. Tao, G. Saur, J. van de Lagemaat, S. O. Kelley, E. H. Sargent *Joule*, **2018**, *2*, 825–832.

[2] L. Sun, V. Reddu, A. C. Fisher, X. Wang *Energy Environ. Sci.* , **2020**, *13*, 374–403.

[3] K. Torbensen, B. Boudy, D. Joulié, N. von Wolff, M. Robert *Curr. Opin. Electrochem.*, **2020**, *24*, 49–55.

4 D. C. Lacy, C. C. L. McCrory, J. C. Peters *Inorg. Chem.*, **2014**, *53*, 4980–4988.

[5] W. Nie, D. E. Tarnopol, C. C. L. McCrory *J. Am. Chem. Soc.*, **2021**, *143*, 3764–3778.

02.

Synthesis of bio-inspired electrode materials for hydrogen evolution

A. Zamader,[a,b] B. Reuillard,[b] P. Marcasuzaa,[c] A. Bousquet,[c] L. Billon,[c] G.Berggren,[a] V. Artero[b]

[a]Department of Chemistry- Ångström Laboratory, Uppsala University, Box 523, SE-75120 Uppsala, Sweden.
[b]Univ. Grenoble Alpes, CNRS, CEA, IRIG, Laboratoire de Chimie et Biologie des Métaux, 17 rue des Martyrs, 38000 Grenoble, France.
[c]Universite de Pau et des Pays de l'Adour, E2S UPPA, CNRS, IPREM, 64053 Pau, France.
Email : afridi.zamader@gmail.com

[FeFe] hydrogenase enzymes have attracted tremendous attention for their reversible hydrogen production with remarkable catalytic rate (6000–9000 molecules H_2 Sec^{-1} per site) at marginal overpotential under physiological condition (pH 6-8) using only earth abundant metals.[1] Industrial usage of such enzymes is challenging due to their oxygen sensitivity and fragility.[2] However, they are also valuable blueprints in the development of synthetic catalysts for hydrogen production.[3] Hence, during the last few decades, structural and functional mimics of these enzymes have become of interest for large-scale hydrogen production as a promising alternative to carbon-based economy.[4]

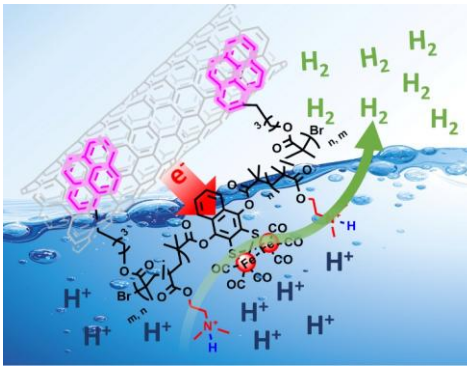


Figure 1. Schematic representation of metallopolymers immobilised on multi-walled carbon nanotubes (MWNTs) for H_2 production

Our recent work focuses on the preparation of oxygen stable hydrogen evolution catalyst (HEC) by embedding a $[FeS(CO)_3]_2$ core, a mimic of native enzyme, within functional polymeric scaffold, based on recently reported metallopolymers.[5] Specifically, we are developing a methodology to anchor these metallopolymers onto nanostructured electrode substrates such as multiwalled carbon nanotubes (MWNTs) in a stable manner. This has allowed thorough assessment of the catalytic performance of the cathode materials for hydrogen production at neutral pH using electrochemical methods coupled to gas chromatography and spectroscopic techniques.

References:

(1) Land, H.; Senger, M.; Berggren, G.; Stripp, S. T. *ACS Catal.* **2020**, *10* (13), 7069–7086.

(2) Stripp, S. T.; Goldet, G.; Brandmayr, C.; Sanganas, O.; Vincent, K. A.; Haumann, M.; Armstrong, F. A.; Happe, T. *Proc. Natl. Acad. Sci.* **2009**, *106* (41), 17331–17336.

(3) Esmieu, C.; Raleiras, P.; Berggren, G. *Sustain. Energy Fuels* **2018**, *2* (4), 724–750.

(4) Artero, V. Bioinspired Catalytic Materials for Energy-Relevant Conversions. *Nat. Energy* **2017**, *2* (9).

(5) Brezinski, W. P.; Karayilan, M.; Clary, K. E.; McCleary-Petersen, K. C.; Fu, L.; Matyjaszewski, K.; Evans, D. H.; Lichtenberger, D. L.; Glass, R. S.; Pyun, J. *ACS Macro Lett.* **2018**, *7* (11), 1383–1387.

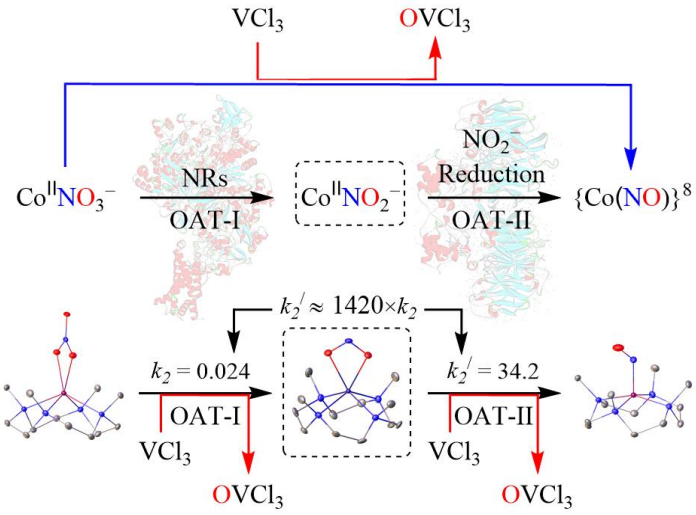
Oxygen atom transfer promoted nitrate to nitric oxide transformation: a step-wise reduction of nitrate / nitrite / nitric oxide†

Pankaj Kumar*†

†Department of Chemistry, Indian Institute of Science Education and Research (IISER), Tirupati 517507, India

pankaj@iisertirupati.ac.in

*Molybdo-Nitrate reductases (Mo-NRs),[1] a key biological enzyme, catalyzes the reduction of nitrate (NO_3^-) to nitrite (NO_2^-) in biological systems, which further reduces to nitric oxide (NO) either by Cu/Fe-nitrite reductase (Cu/Fe-NiRs)[2] enzymes or acid-induced NO_2^- reduction reactions. Mimicking the NRs chemistry followed by NiR chemistry in a single reaction sequence is always challenging. Hence, only very few approaches were made towards the direct conversion of NO_3^- to NO. In this present work, we have tried to mimic both NO_3^- reduction followed by the NO_2^- reduction chemistry in a single reaction sequence. Here, we demonstrate the reaction of a Co^{II}-nitrate complex (**2**) using the oxophilic complex VCl_3. We have verified the formation of a Co^{III}-nitrosyl complex ($\{Co^{III}\text{-}NO\}^8$, **4**) and V^V-Oxo (V^V=O) species in the reaction of **1** with VCl_3 via the proposed two consecutive oxygen atom transfer (OAT) reactions.[3] Mechanistic insights of the NO_3^- to NO transformation revealed that the reaction is proceeding via a Co^{II}-nitrite (**3**) intermediate. However, our efforts to isolate the intermediate from the reaction mixture are futile due to the slow conversion of nitrate to nitrite and the very fast conversion of nitrite to nitrosyl. However, further study of isolated complex **3** with VCl_3 generates NO and supports our mechanistic aspects. The present study is the first-ever report where a Co^{II}- NO_3^- generates $\{Co^{III}\text{-}NO\}^8$ via a Co^{II}- NO_2^- intermediate in two-step OAT reduction reactions.*.



Scheme 1.

References

[1] W. H. Campbell, Annu. Rev. Plant Physiol. Plant Mol. Biol., **1999**, *50*, 277–303.

[2] (a) B. A. Averill, Chem. Rev., **1996**, *96*, 2951–2964. (b) E. I. Tocheva, F. I. Rosell, A. G. Mauk and M. E. Murphy, *Science*, **2004**, *304*, 867–870.

[3] K. Kulbir,; S. Das,; T. Devi,; M. Goswami,; M. Yenuganti,; P. Bhardwaj,; S. Ghosh, S. C. Sahoo,; **P. Kumar,** *Chem. Sci.*, **2021**, *12*, 10605-10612.

Iron(II) bis-thiosemicarbazone complexes as catalysts for the oxidation of organic substrates – a combined experimental/computational study

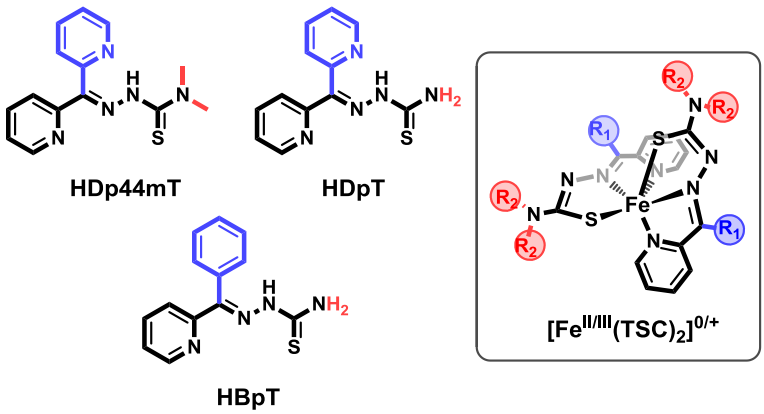
A.G. Algarra,[a]* M. J. Fernández-Trujillo,[a] C. E. Castillo,[a] M. G. Basallote,[a] M. Ferrer,[b] M. Martínez,[b]

[a] Departamento de Ciencia de los Materiales e Ingeniería Metalúrgica y Química Inorgánica, Universidad de Cádiz, Apartado 40, E-11510 Puerto Real, Cádiz, Spain

[b] Departament de Química Inorgànica i Orgànica, Secció de Química Inorgànica, Universitat de Barcelona, Martí i Franquès 1-11, E-08028 Barcelona, Spain

andres.algarra@uca.es

Recently, the kinetics of oxidation of different biologically-active Fe^{II} bis-thiosemicarbazone complexes (see figure below) with O_2 in water solution was studied by us.[1] DFT calculations suggested the formation under steady-state conditions of superoxo and hydroperoxo intermediates. Based on these results, we have now investigated whether they can be formed via the reaction of the complexes with H_2O_2 in acetonitrile solution. Interestingly, we found that the complexes can catalyze the oxidation of organic substrates. We have carried out a thorough kinetic study on the formation of the reaction intermediates, and also studied the catalytic processes using thioanisol and styrene as substrates by NMR. As no superoxo or hydroperoxo species are observed, DFT calculations have been used to propose possible structures for the intermediates detected. A summary of these results will be presented.



This work has been co-financed by the Ministry of Science, Innovation and Universities (PID2019-107006GB-C22) and the 2014-2020 ERDF Operational Programme and by the Department of Economy, Knowledge, Business and University of the Regional Government of Andalusia (FEDER-UCA18-106753).

[1] M. A. Gonzálvez, A. G. Algarra, M. G. Basallote, P.V. Bernhardt, M. J. Fernández-Trujillo and M. Martínez. *Dalton Trans.* **2019**, *48*, 16578-16587.

USE OF HAMMETT PLOT TO ELUCIDATE THE MECHANISM OF REACTIOS OF NON-HEME IRON COMPLEXES

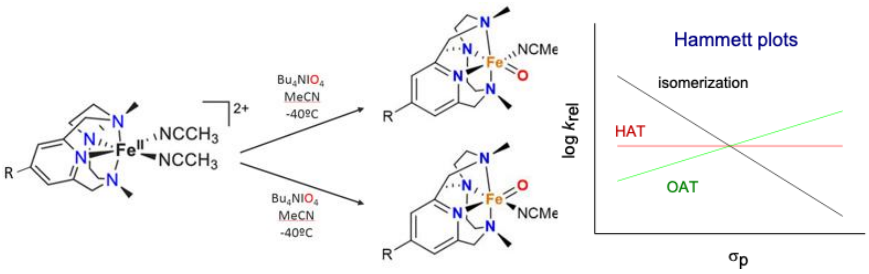
C.E. Castillo, [a]* M.C. Pérez-Segura, [a] V. Dantignana,[b] P.Besalú,[b] J.M. Luis,[b] A. Company,[b] M. Costas,[b] M.G. Basallote [a]

[a] Departamento de Ciencia de los Materiales e Ingeniería Metalúrgica y Química Inorgánica, Instituto de Biomoléculas (INBIO), Facultad de Ciencias, Universidad de Cádiz, Apdo. 40, 11510, Puerto Real, Cádiz.

[b] Institut de Química Computacional i Catàlisi (IQCC), Departament de Química, Universitat de Girona. C/ M. Aurèlia Capmany 69, 17003 Girona (Catalonia, Spain).

esther.castillo@gm.uca.es

Iron(IV) oxo intermediates are formed upon oxidation of biomimetic iron complexes of the oxygenase metalloenzymes. These intermediates are competent for oxidation of C-H and C=C bonds in substrates oxidation through hydrogen and oxygen atom transfer (HAT, OAT), and insight into the mechanism of the process is of paramount relevance to determine the parameters controlling the activity and selectivity of the catalyst. Previous studies with a non-heme iron complex supported by the neutral tetra-dentate N-based $PyNMe_3$ ligand reveal that, upon addition of periodate, this compound initially forms a mixture of two oxoiron(IV) isomers that evolve more slowly to form exclusively the thermodynamically favored one.[1] In this work we report kinetic studies on the isomerization process and the HAT and OAT reactions of both isomers. A family of $^{R}PyNMe_3$ complexes that differ in the nature of the R substituent at the pyridine ring are included in the study, and Hammett plots are used to explore the mechanistic details of the processes.



The Hammett plots reveal that the nature of the R substituent cause significant changes in the kinetics of isomerization and OAT processes but it does not have any effect on the kinetics of HAT processes. For the isomerization process, the negative slope indicates that some positive charge is built at the complex during the isomerization process. In contrast, the positive slope observed for OAT processes indicates that some negative charge is built at the $Fe^{IV}(O)$ intermediates, which suggests an electrophilic attack to the substrate.

Acknowledgements: This work has been co-financed by Ministry of Science, Innovation and Universities (PID2019-107006GB-C22) and 2014-2020 ERDF Operational Programme and the Department of Economy, Knowledge, Business and University of the Regional Government of Andalusia. (FEDER-UCA18-106753).

[1] Valeria Dantignana, Joan Serrano-Plana, et al., *J. Am. Chem. Soc.,* **2019**, 141, 15078–15091

Probing bis-Fe(IV) *MauG*: Isolation of Highly Reactive Radical Intermediates

S.Sarkar,[a] T. Guchhait[b] and S.P.Rath[a]*

[a]Department of Chemistry, Indian Institute of Technology Kanpur, Kanpur 208016, Uttar Pradesh, India

[b]Department of Chemistry, C. V. Raman Global University, Bhubaneswar 752054, Odisha, India

sabyasac@iitk.ac.in

A large number of diheme enzymes such as *MauG* and bacterial diheme cytochrome c peroxidases (bCcP) are known which catalyze various important chemical transformations in biology. The high valent bis-Fe(IV) intermediate of the *MauG* is stabilized by charge resonance facilitated by the tryptophan residue, which acts as a bridge between the two heme centers. Our group is presently engaged in exploring the various effects of heme-heme interaction, electronic communication, etc., in the model dihemes. Step-wise oxidations of a synthetic analog of *MauG* are performed in which two heme centers are bridged covalently *via* flexible linker containing a pyrrole moiety. One- and two-electron oxidations produce monocation radical and dication diradical intermediates, respectively, which, being highly reactive, undergo spontaneous intramolecular rearrangement involving the pyrrole bridge itself to form indolizinium-fused chlorin-porphyrin and spiro-porphyrinato heterodimers. Unlike in *MauG*, where the two oxidizing equivalents produce the bis-Fe(IV) redox state, the synthetic analog of the same, however, stabilizes two ferric hemes, each coupled with a porphyrin π-cation radical. The present study highlights the possible role played by the bridge in the electronic communication.

References

1 L.M. R Jensen, R. Sanishvili, V. L. Davidson, C. M. Wilmot, *Science* **2010**, *327*, 1392-1394.

2 Z. Ma, H. R. Williamson, V. L. Davidson, *Proc. Natl. Acad. Sci.* **2015**, *112*, 10896-10901.

3 J. Genga, K. Dornevila, V. L. Davidson, A. Liu, *Proc. Natl. Acad. Sci.* **2013**, *110*, 9639-9644.

4 A. K. Singh, M. Usman, S. Sarkar, G. Sciortino, D. Kumar, E. Garribba, S. P. Rath, *Inorg. Chem.* **2021**, *60*, 16492-16506.

5 A. Kumar, D. Sil, M. Usman, S. P. Rath, *Chem. Commun*. **2019**, *55*, 1588-1591.

6 A. K. Singh, M. Usman, G. Sciortino, E. Garriba, S. P. Rath, *Chem. Eur. J*. **2019**, *25*, 10098-10110.

7 T. Guchhait, S. Sarkar, Y. A. Pandit, S. P. Rath, *Chem. Eur. J*. **2017**, *23*, 10270-10275.

8 Y. A. Pandit, S. Sanfui, S. P. Rath, *Chem. Eur. J*. **2017**, *23***,** 13415-13422.

9 A. K. Singh, F. S. T. Khan, S. P. Rath, *Angew. Chem., Int. Ed.* **2017**, *56*, 8849-8854.

10 S. Dey, D. Sil; S. P. Rath, *Angew. Chem., Int. Ed.* **2016**, *55*, 996-1000.

11 D. Sil, S. Dey, A. Kumar, S. Bhowmik, S. P. Rath, *Chem. Sci.* **2016**, *7*, 1212-1223.

Investigation of bioinorganic reactions in wound healing supported by reactive chloroxo species

S. Genç[a], M. Dannhorn[a], Ph. Kurz[a]

[a] Institut für Anorganische und Analytische Chemie,
Albert-Ludwigs-Universität Freiburg, Albertstraße 21, 79104 Freiburg i. Br., Germany
semra.genc@ac.uni-freiburg.de

All over the world, people infected with cutaneous leishmaniasis suffer from open wounds that heal poorly or do not heal at all. Currently, two drugs are used to treat cutaneous leishmaniasis wounds: the first is an antimony(V) compound, which is inexpensive but has many side effects and is classified as toxic;[1] the second is an antibiotic consisting of aminoglycosides, that cannot be afforded by the majority of people in the most severely affected countries in the Americas, North Africa, the Middle East or Central Asia.[2,3] In cooperation with a local non-profit organization (*Waisenmedizin e.V.*) we are trying to provide people worldwide with a treatment for cutaneous leishmaniasis that is associated with fewer side effects and is nevertheless affordable - the chlorite containing LeiProtect® gel.

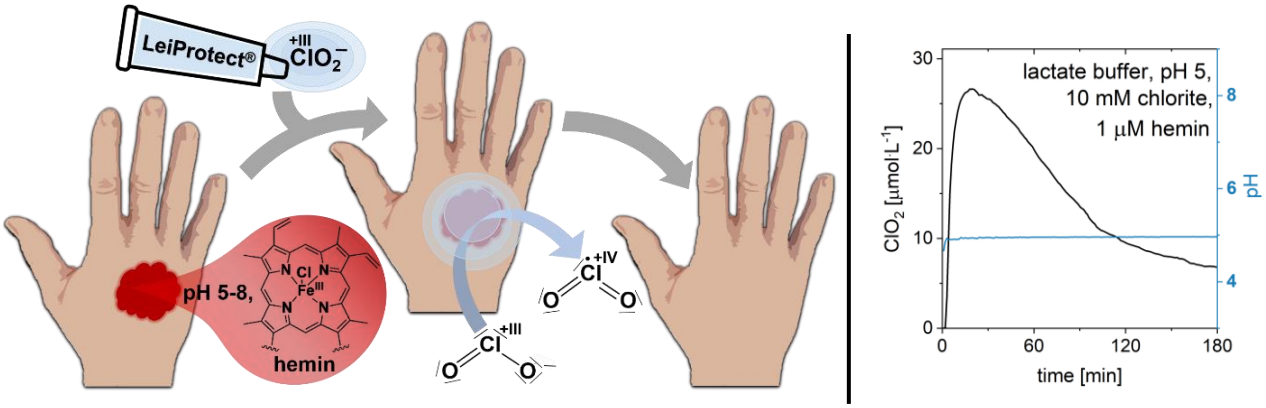


Figure 1: Left: scheme of LeiProtect® gel assisted healing of a cutaneous leishmaniasis wound; right: ClO_2 evolution trace detected with an amperometric ClO_2 sensor from a solution with [ClO_2^-] = 10 mM in lactate buffer (50 mM, pH 5.0) and 1 µM hemin.

Within this context, we will at first present an improved synthesis for pharmaceutical grade sodium chlorite solutions, but also experiments contributing to a better understanding of the bioinorganic processes involved in the disinfecting and wound healing effects of chloroxo species.

Early experiments concerning the mode of action of ClO_2^- as wound disinfactant were already performed by Elstner et al.[4,5] By using a very sensitive amperometric chlorine dioxide sensor system, we can detect the formation of µM concentrations of dissolved ClO_2 in chlorite solutions after lowering the pH and/or adding hemin. *In situ* formed chlorine dioxide could thus be an important active species to explain the well-documented enhancement in wound healing by sodium chlorite.[6,7]

[1] N. Salam, W. M. Al-Shaqha, A. Azzi, *PLoS Negl. Trop. Dis.* **2014**, *8*, e3208.
[2] B. Schlegel, R. E. Schmidt, J. H. Hengstmann, H. Hein (Hrsg.), *Enterale Resorption von Neomycin bei Infektionskrankheiten*, J.F. Bergmann-Verlag, München, **1979**.
[3] World Health Organization, WHO fact sheet about Leishmaniasis, **2022**, `www.who.int/news-room/fact-sheets/detail/leishmaniasis` (visited 01.04.2022).
[4] R. J. Youngman, G. R. Wagner, F. W. Kühne, E. F. Elstner, *Z. Naturforsch.* **1985**, *40*, 409.
[5] E. F. Elstner, *Z. Naturforsch.* **1988**, *43*, 893.
[6] S. Molkara, E. Poursoltani, K.-W. Stahl, M. Maleki, A. Khamesipour, C. Bogdan, M. Salehi, V. M. Goyonlo, *BMC Infect. Dis.* **2019**, 19, 1005.
[7] D. Debus, S. Genç, P. Kurz, M. Holzer, K. Bauer, R. Heimke-Brinck, M. Baier, A. Debus, C. Bogdan, K.-W. Stahl, *Am. J. Trop. Med. Hyg.* **2022**.

Tamoxifen-based compounds in the breast cancer therapy

A. Kazimir,[a]* B. Schwarze,[b] S. Jelača,[c] S. Mijatovic,[c] D. Maksimović-Ivanić,[c] E. Hey-Hawkins[a]

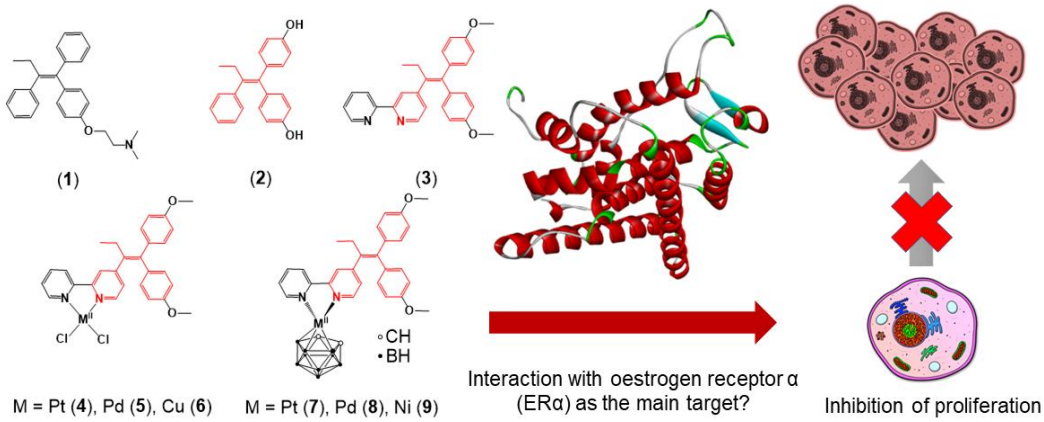
[a] *Institute of Inorganic Chemistry, Leipzig University, Germany*

[b] *Institute for Medical Physics and Biophysics, Leipzig University, Germany*

[c] *Department of Immunology, University of Belgrade, Serbia.*

alex.kazimir95@gmail.com

Tamoxifen (Scheme 1, **1**) is historically well known for its successful application in the therapy of the oestrogen receptor positive (ERα+) breast cancer.[1] In this study, we combine a tamoxifen-based ligand[2] (Scheme 1, **3**) with transition metal complex moieties of platinum(II), palladium(II), copper(II), and nickel(II)[3] containing chlorides (Scheme 1, **4-6**) or a bulky, hydrophobic and stable *nido*-dicarborate ligand (Scheme 1, **7-9**). We investigated the anticancer activity of the compounds **2-9** in *in vitro* cell assays.



Scheme 1: *In silico* docking studies suggest interaction of tamoxifen (**1**), dihydroxytamoxifen (**2**), tamoxifen-based ligand (**3**), chloride- (**4-6**) and carborane-containing complexes (**7-9**) *(tamoxifen-related unit is highlighted)* with oestrogen receptor α, which could be one way to inhibit cancer cell proliferation (depending on the ERα status of the cell lines).

The incorporation of a 2,2'-bipyridine unit into a tamoxifen-inspired structure **3** increases the cytotoxic activity compared to compound **2** against several cell lines including ERα+ human glioblastoma (U251), breast adenocarcinoma (MCF-7, MDA-MB-361) and triple negative (ERα−) MDA-MB-231. The formation of Pt^{II} and Pd^{II} chloride complexes (**4** and **5**) insignificantly improve the activity compared to ligand **3**. The ability of the Cu^{II} chloride moiety for ligand exchange in solution explains the significant rise of the cytotoxicity of **6** compared to **4** and **5**. However, the incorporation of a *nido*-carborate dianion into Pt and Ni complexes (**7** and **9**) neutralised on average their toxicity towards all studied cell lines, except compound **8** which was active against U251 and MDA-MB-231. The observed cytotoxicity data of compounds **3-6** and **8** against MDA-MB-231 (ERα−) suggest other off-target mechanisms rather than only ERα inhibition which is usual for metallodrugs.

[1] J. N. Mills, A. C. Rutkovsky, A. Giordano, *Curr. Opin. Pharmacol.* **2018**, *41*, 59–65.

[2] B. Schwarze, S. Jelača, L. Welcke, D. Maksimović- Ivanić, S. Mijatović, E. Hey- Hawkins, *ChemMedChem* **2019**, *14*, 2075-2083.

[3] M. Hanif, C. Hartinger, *Future Med. Chem.* **2018**, *10*, 615-617.

On the cytotoxicity of ruthenium/natural product or derivative complexes

A.A. Batista*[+], Analu Rocha*, J. Honorato# and Javier Ellena#
*Federal University of São Carlos, São Carlos, São Paulo, Brazil
University of São Paulo, São Carlos, São Paulo, Brazil
*[+] - e-mail:daab@ufscar.br

In the present work new ruthenium complexes containing monophosphine or diphosphine, and natural products as ligands, naphtoquinone derivatives, were synthesized and characterized, aiming to study their anticancer activities (Figure 1).

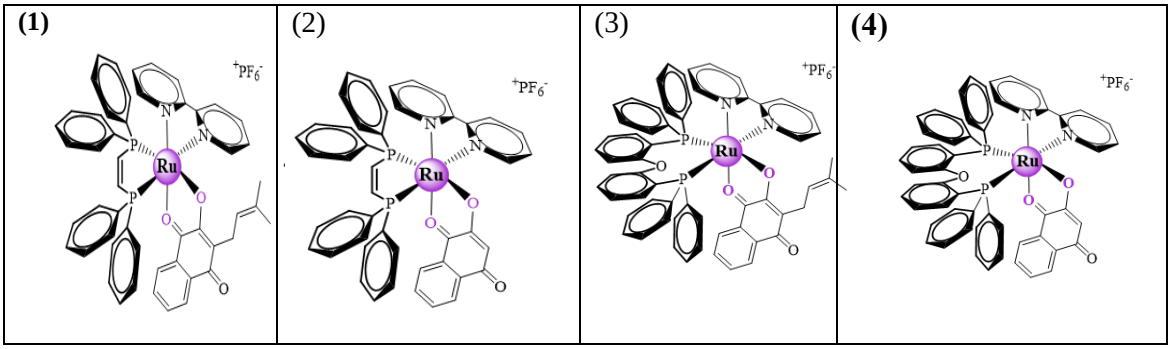


Figure 1. Structures of the ruthenium/phosphine complexes, with naphtoquinones.

The complexes showed to be more cytotoxic than the free ligands and than the widely used anticancer drug, cisplatin, under identical conditions. The cytotoxicity assays (IC50, µM), *in vitro*, of the complexes against breast human tumor cell lines, are below, and were carried out by the MTT method (48 h) (Table 1).

Table 1. IC50 (µM) for the ruthenium/phosphine/naphtoquinone complexes.

Complex	MDA-MB-231*	MCF-7**	MCF-10A	SI*	SI**	P
1	0.40 ± 0.01	0.91 ± 0.14	0.92 ± 0.17	2.3	1.0	0.24
2	0.21 ± 0.02	0.57 ± 0.02	2.18 ± 0.14	10.4	3.8	0.10
3	0.08 ± 0.02	0.10 ± 0.004	1.15 ± 0.10	14.4	11.5	0.37
4	0.10 ± 0.01	0.32 ± 0.04	2.55 ± 0.60	25.5	8.0	0.27
Cisplatin	2.33 ± 0.40	13.98 ± 2.02	29.45 ± 0.85	12.63	2.11	

SI = IC50 (non-tumor cells)/IC50 (tumor cells)

In addition, we have analyzed the effect of ruthenium complexes on the mechanism of cell death. The complexes have ability to interact with CT-DNA and HSA and whether they cause cytotoxic effects in different tumor cell lines. The authors acknowledge the financial support from CNPq, CAPES e FAPESP

Dioxygen activation with Co(II) complexes with nitro-substituted ligands

G. G. Morgan,[a]* D. Mc Laughlin,[a] V. Jakobsen,[a] C. Kelly,[a] H. Müller-Bunz[a]
[a] School of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland
grace.morgan@ucd.ie

Dioxygen activation in cobalt complexes has been well studied and uses for the phenomenon have been found in several different fields such as biomimetics,[1] transport and storage of oxygen and catalytic oxidation of organic substrates.[2] The mechanism of uptake of molecular oxygen by cobalt complexes has been extensively studied and it has been suggested that O_2 may undergo a one electron reduction to form a superoxide radical which quickly reacts with another cobalt site to form a peroxo dimer.[3] In this study we have investigated the oxidation of Co(II) to Co(III) *via* dioxygen activation. Our structural and spectroscopic studies suggest that in the binding process two Co(II) ions are oxidized to Co(III) and aerial O_2 is reduced to peroxide. It was possible to isolate and characterize a metastable peroxo Co(III) dimer intermediate which is stable at room temperature in the solid state when removed from the mother liquor, Figure 1. We have also studied the formation of the dimer using EPR spectroscopy which suggests the formation of a short-lived superoxide intermediate, Figure 2.

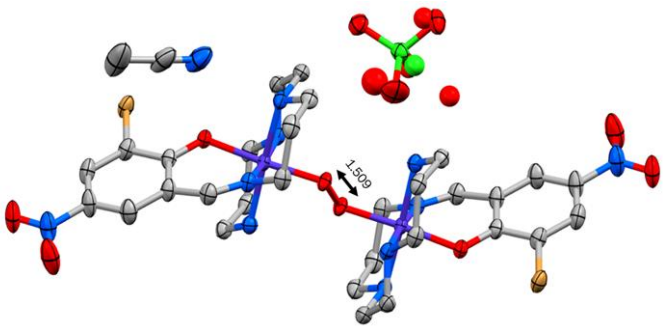


Figure 1: Crystal structure of Co(III) peroxo dimer

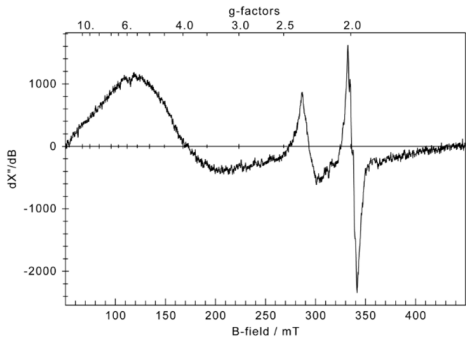


Figure 2: EPR spectrum of reaction mixture at 78K

1

[1] B. Hoffmann, D. Petering, *Proc. Natl. Acad. Sci. U.S.A.*, **1970**, *67*, 637-643.
[2] P. G. Cozzi, *Chem. Soc. Rev.*, **2004**, *33*, 410-421.
[3] A. T. Fiedler, A. A. Fischer, *J. Biol. Inorg. Chem.*, **2017**, *22*, 407-424.

Generation and Characterization of a Mononuclear non-Heme Fe(III)-Alkylperoxo Species from a Fe(IV)-Oxo Intermediate: Effect of Second-Sphere Interaction

T. Devi[a], K. Ray,[a]*

[a] Department of Chemistry, Humboldt-Universität zu Berlin, Germany

tarali.devi@hu-berlin.de

Iron–dioxygen adducts, such as iron(III)–hydroperoxo (Fe^{III}–OOH) and iron(III)–alkylperoxo (Fe^{III}–OOR) species have been postulated as key intermediates in the dioxygen activation and detoxification of reactive oxygen species by iron catalyzed heme and nonheme enzymatic systems.[1] The peroxide ligands of the iron(III)–hydroperoxo and –alkylperoxo species are cleaved either homolytically or heterolytically that results the generation of high-valent iron (IV or V)–oxo intermediates as active oxidants which are responsible for the oxidation of organic substrates.[2] The mechanism of the O–O bond cleavage of high spin or low-spin iron(III)–alkylperoxo species has been well established in nonheme iron models systems in presence of an external 'S'-donor ligand.[2] However, the regeneration of Fe(III)-alkylperoxo species from a Fe(IV)-oxo species has never been observed in the model system. In this work, the interconversion of a mononuclear Fe(IV)-oxo to a Fe(III)-alkylperoxo species has been studied using different spectroscopic techniques (UV-vis, Mössbauer, EPR, rRaman, XAS analysis). Also the effect of the secondary coordination sphere interaction on the generation and stability of the Fe(III)-alkylperoxo species is investigated.

References:

1. (a) S. Shaik, S. Cohen, Y. Wang, H. Chen, D. Kumar, W. Thiel *Chem. Rev.*, **2010**, *110*, 949–1017; (c) W. Nam *Acc. Chem. Res.*, **2007**, *40*, 465; (b) E. G. Kovaleva, J. D. Lipscomb *Nat. Chem. Biol.*, **2008**, *4*, 186–193.
2. (a) J. Kaizer, M. Costas, L. Que, Jr, *Angew. Chem., Int. Ed.*, **2003**, *42*, 3671–3673, (b) S. Hong, Y.-M. Lee, K.-B. Cho, M. S. Seo, D. Song, J. Yoon, R. Garcia-Serres, M. Clemancey, T. Ogura, W. Shin, J.-M. Latour, W. Nam *Chem. Sci.*, **2014**, *5*, 156–162.

Mimicking the Role of Distal Arginine Residue in the Mechanism of heme Nitrite Reductases

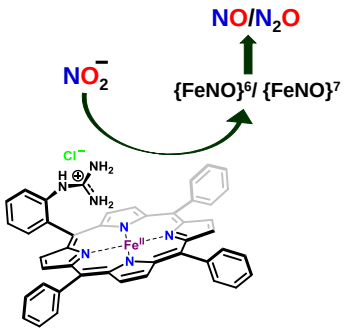
Ankita Sarkar,[a]* Abhushek Dey[b]

[a] Indian Association for the Cultivation of Science, Kolkata, India

[b] Indian Association for the Cultivation of Science, Kolkata, India

ankita16chem@gmail.com

Over the past two decades, bioinorganic chemistry and biomedical researchers have found nitric oxide (NO) as a biologically important nitrous molecule and the in vivo importance of NO in preoxic era on Earth. In the biochemical cycle of nitrogen and in signalling pathways, formation of NO from nitrite is a crucial step. Heme-depended nitrite reductases are very popular in biology as they play a dominant role in production, detection, transport and detoxification of NO. They are involved in both assimilatory and dissimilatory nitrite reduction and in bacterial denitrification pathway.[1-2] The active sites of these enzymes feature pendant 2nd sphere residues like arginine, lysine and histidine which are proposed to be the source of protons under the reaction conditions. Recently, our group has designed and developed a synthetic iron porphyrin with pendent protonated guanidine moiety (head group of arginine) to investigate the reduction of nitrite. A combination of kinetics and spectroscopic identification of species indicate that the protonated guanidine not only acts as the source of proton for nitrite reduction but also determines the selectivity of the product. The facile protonation of the guanidine moiety by an external proton source (proton recharge) enhances the rate of dissociation of NO from a $\{FeNO\}^6$ species making this step catalytically competent. Alternatively, under proton limited conditions, the reaction proceeds to generate N_2O via protonation of a $\{FeNO\}^7$ species albeit at a slower rate.



Iron-porphyrin complex with pendant guanidinium residue at its distal superstructure

1. Maia, L. B.; Moura, J. J. G., How Biology Handles Nitrite. *Chemical Reviews* **2014,** *114* (10), 5273-5357.

2. Hermann, B.; Kern, M.; La Pietra, L.; Simon, J.; Einsle, O., The octahaem MccA is a haem c–copper sulfite reductase. *Nature* **2015,** *520*, 706.

Expanding Our Understanding of Reactive Sulfur and Nitrogen Species Interaction with Metals

For bioinorganic chemists, sulfur is most commonly a chelating atom for ligand platforms, however many reactive sulfur species (RSS) have been shown to promote reactivity with increasingly consequential implications, for example, with the designation of hydrogen sulfide as the third gasotransmitter. We are interested in studying metal interactions with RSS, including hydrosulfide, polysulfides, and crosstalk species such as thionitrite (SNO-) and perthionitrite (SSNO-). This work describes the synthesis of complexes using RSS as reagents to further understand the utility of sulfur-based chemistry with biologically relevant metals. We have demonstrated polysulfide generation from molybdenum bound polysulfides ([TpMo(S)(S4)]-, Tp = hydrotris(3,5-dimethylpyrazol-1-yl)- borate) oxidizing hydrosulfide to form a tris(sulfido) Mo complex ([TpMo(S)3]-), the synthesis of nickel complexes baring RSS ligands, and studied the reactivity of SNO- and SSNO- with iron compounds relevant to the labile iron pool to generate MNIC and DNIC complexes that also have RSS based ligands. This work has impacted our understanding of how gasotransmitters and their derivatives may interact with metals endogenously and this work will have broad interest to the biological inorganic community.

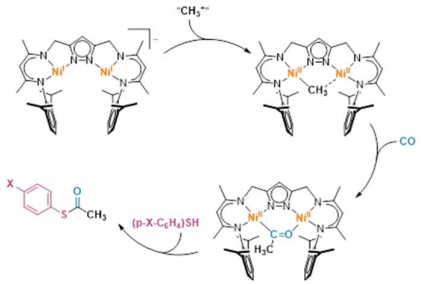
Capturing the key steps of Acetyl-CoA Synthase Reactivity with a Preorganized Dinickel Complex

V. Tagliavini,[a] T. Kothe, [a] S. Dechert,[a] F. Meyer [a]*

[a] University of Göttingen, Institute of Inorganic Chemistry, Tammannstr. 4, D-37077 Göttingen, Germany

valeria.tagliavini@uni-goettingen.de

Acetyl CoA Synthase (ACS) is part of the bifunctional enzyme CODH/ACS that performs the stepwise anaerobic CO_2 fixation into the essential metabolite acetylCoA for energy storage in the Wood-Ljungdahl pathway in bacteria and methanogenic archea. Two nickel ions bridged to a Fe/S cluster constitute the A cluster, the core structure of ACS[1]. Fundamental aspects of the ACS working mechanism remain a matter of debate, namely the sequence of methylation and CO binding events, the involvement of different redox states, and the synergistic action of both nickel centers in the reaction[2]. Few synthetic analogues have achieved the Ni-mediated conversion of CO, a CH_3^+ equivalent and a thiol into an acetyl thioester, which provided model reactions in support of selected steps of the enzymatic reaction[3,4]. CO binding prior to the transfer of the methyl group at a mononuclear β-diketiminato nickel complex according to a Ni^{II}/Ni^0 mechanism was reported by Limberg et al.[4] In the present work a preorganized dinickel site based on pyrazolato-bridged bis(β-diketiminato) ligand[5] reproduces a sequence where methylation precedes CO insertion, starting from a dinickel(I) state, and where all intermediates are stabilized via synergistic interaction with both metal ions. Characterization of the complexes and mechanistic investigations will be presented.



Dinickel site mediating bioinspired thioester formation from a thiol, CO and a CH_3^+ equivalent

[1] Y. Ilina, B. M. Martins, J.-H. Jeoung, H. Dobbek, *Met. Ions Life Sci.* **2020**, *20*, 381-413.

[2] M. Can, F. A. Armstrong, S. W. Ragsdale, *Chem. Rev.* **2014**, *114*, 4149-4174.

[3] (a) G. C. Tucci, R. H. Holm, *J. Am. Chem. Soc.* **1995**,117, 6489-6496; (b) T. C. Harrop, M. M. Olmstead, P. K. Mascharak, *J. Am. Chem. Soc.* **2004**, 126, 14714-14715; (c) W. G. Dougherty, K. Rangan, M. J. O'Hagan, G. P. A. Yap, C. G. Riordan, *J. Am. Chem. Soc.* **2008**, 130, 13510-13511 ; T. Matsumoto, M. Ito, M. Kotera, K. Tatsumi, *Dalton Trans*., **2010**, 39, 2995-2997.

[4] B. Horn, C. Limberg, C. Herwig, S. Mebs, *Angew. Chem. Int. Ed.* **2011**, 50, 12621-12625.

[5] D.-H. Manz, P. C. Duan, S. Dechert, S. Demeshko, R. Oswald, M. John, R. A. Mata, F. Meyer, *J. Am.Soc.* **2017**, *139*, 16720-16731.

Theoretical approaches for the study of biological and bio-inspired di-copper centers

Océane Mangel,[a*] Hélène Jamet,[a] Catherine Belle,[b] Aurore Thibon-Pourret[b]

[a] Université Grenoble Alpes, CNRS-UGA UMR 5250, Laboratoire DCM/Sith, CS 40700, 38058 Grenoble Cedex 9, France

[b] Université Grenoble Alpes, CNRS-UGA UMR 5250, Laboratoire DCM/Cire, CS 40700, 38058 Grenoble Cedex 9, France

oceane.mangel@univ-grenoble-alpes.fr

During the biosynthesis of melanin, the conversion of tyrosine into dopaquinone is catalyzed by tyrosinase, a di-copper enzyme, that contains a peroxide ion in the active form. As a dysfunction in the production of melanin can lead to health issues[1], tyrosinase reaction mechanism is actively studied, often by using the Streptomyces tyrosinase as a model[2]. To get a better understanding of this system, we used a QM/MM metadynamic approach, which lead us to model both the deprotonation of the tyrosine and the movement of one of the coppers, such as described by crystallographic studies[2]. We also witnessed an opening of the peroxide group. Our study will now focus on getting a better estimation of the energy barrier for those reaction steps.

Enzymes such as the tyrosinase, or the particulate methane monooxygenase (pMMO) are also a topic of interest for the design bio-inspired complexes. In the case of the pMMO, the key reaction is the activation of C-H bonds, otherwise hard to obtain in an environmentally benign and efficient way[3]. Several complexes have been synthesized to obtain a CuII-CuIII center, thought to be a key intermediate in the pMMO mechanism[4,5]. In our study, we modelled the previously obtained complexes with modified ligands, using a DFT approach to study the effect of the addition of functional groups on the complexes. Redox potentials were calculated using a previously developed method to check if the modification performed would be helpful in designing more efficient complexes. A mechanistic study using the intrinsic bond orbital method is now undertaken.

References:

1- M. Yaar, Journal of Investigative Dermatology, 2013, 133, 11–13

2- Y. Matoba, S. Kihara, N. Bando, H. Yoshitsu, M. Sakaguchi, K. Kayama, S. Yanagisawa, T.Ogura, M. Sugiyama, PLoS Biol, 2018, 16(12)

3- J. C. Lewis, P. S. Coelho and F. H. Arnold, Chem Soc Rev, 2011, 40(4), 2003-21

4- Y. Shiota and K. Yoshizaw, Inorg. Chem. 2009, 48, 838-845

5- J. A. Isaac, A. Thibon-Pourret, A. Durand, C. Philouze, N. Le Poul, and C. Belle, Chem. Commun., 2019, 55, 12711

Methyl viologen as mediator in semi-artificial photocatalytic hydrogen evolution.

M.T. Gamache,[a]* M. Lorenzi,[a] M. Senger,[b] G. Berggren[a]

[a] Department of Chemistry - Ångström, Molecular Biomimetics, Uppsala University, Lägerhyddsvägen 1, 75120 Uppsala, Sweden

[b] Department of Chemistry - Ångström, Physical Chemistry, Uppsala University, Lägerhyddsvägen 1, 75120 Uppsala, Sweden

mira.gamache@kemi.uu.se

Semi-artificial photosynthesis aims at combining highly efficient synthetic light-harvesters with the self-healing and outstanding catalytic properties of bio-catalysis. The photocatalytic reduction of water to form hydrogen gas is a promising approach to collect, convert, and store solar energy. Nature provides us with a highly efficient and specific bio-catalyst capable of driving this reaction: Hydrogenases. In semi-artificial photocatalytic systems that use an artificial photosensitizer coupled with a hydrogenase as the catalyst the restrictions of both synthetic catalysts and natural photosystems can be overcome. It also provides a suitable test system for examining semi-artificial photosynthetic assemblies for the identification of key parameters.

In this study, a whole-cell system consisting of *E.coli* bacteria, which heterologously expressed the *Cr*HydA1 [FeFe] hydrogenase enzyme, is combined with a sacrificial electron donor as well as an artificial photosensitizer. The addition of methyl viologen as an electron mediator and its impact on the whole-cell system are investigated. Photocatalytic assays show that the addition of methyl viologen increases the longevity as well as the activity of the hydrogen evolution. However, this increase comes at a cost of cell viability and cell integrity. Spectroscopic and catalytic studies are used to identify the mechanism behind electron transfer in the photocatalytic system as well as cell toxicity. The results are used to identify improved conditions for a more efficient semi-artificial whole-cell photocatalytic system.

Extraordinary Isostructural Crystals: Unexplored Morphologies of Chiral Crystals

Vivek Singh,[a] Lothar Houben,[b] Linda J. W. Shimon,[b] Sidney R. Cohen,[b] Yishay Feldman,[b] Ofra Golani,[c] Michal Lahav[a] and Milko E. van der Boom[a]

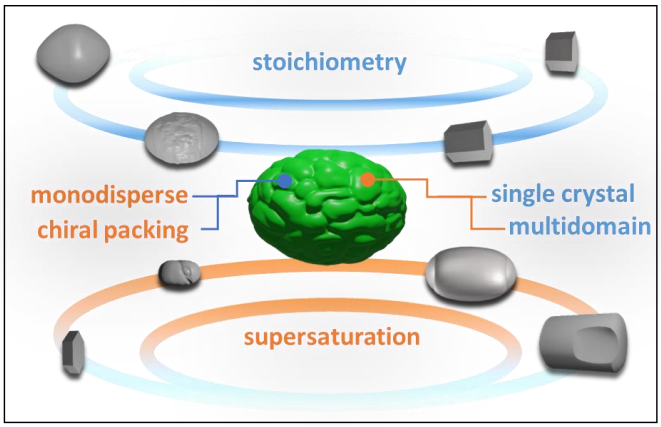
[a] Department of Molecular Chemistry and Materials Science, Weizmann Institute of Science, Israel

[b] Department of Chemical Research Support, Weizmann Institute of Science, Israel

[c] Department of Life Sciences Core Facilities, Weizmann Institute of Science, Israel

E-mail: vivek.singh@weizmann.ac.il

Understanding relation between crystal appearance and crystal structure is of fundamental interest in crystallography and material science. Typically, a crystal supposed to have a regular geometric form but very often nature challenges this preconception. The coordination bond between metal and ligands allows us to develop and design some extraordinary materials such as metal-organic frameworks (MOFs).[1] However, the factors that influence the growth of such crystals are not very well understood. Controlling dimensions and morphology is a challenge in these materials.[2] Moreover, morphological homogeneity, monodispersity and crystallographic phase purity are difficult to achieve and predict. In this work, we show a unique MOF where the multidomain appearance and the internal crystal structure contradict.[3] These monodispersed micron-sized crystals have a "*brain-like*" morphology. Remarkably, our X-ray diffraction and electron diffraction studies prove that these structures are single-crystals and homochiral. The porous framework has helical hexagonal and triangular channels. Interestingly, different reaction conditions generate a series of isostructural and monodispersed crystals. These results indicate that there are hidden rules to be discovered for fascinating single crystals expressing multidomain morphologies.



[1] Yaghi, O. *J. Am. Chem. Soc*. **2016**, *138*, 15507−15509.

[2] Malik, N.; Singh, V.; Houben, L.; Shimon, L.; Lahav, M.; van der Boom, M. E. *J. Am. Chem. Soc*. **2021**, *143*, 16913–16918.

[3] Singh, V.; Houben, L.; Shimon, L.; Cohen, S.; Golani, O.; Feldman, Y.; Lahav, M.; van der Boom, M. E. *Angew. Chem., Int. Ed*. **2021**, *60*, 18256–18264

Synthesis and anticancer activities orgnometallic conjugates with colchicine

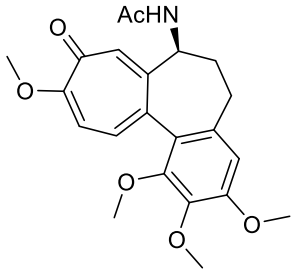
K. Kowalczyk,[a] A. Błauż, [b] B. Rychlik,[b] D. Plażuk,[a]

[a] Department of Organic Chemistry, Faculty of Chemistry, University of Lodz,91-403 Lodz, Poland

[b] Laboratory of Cytometry, Department of Molecular Biophysics, Faculty of Biology and Environmental Protection, University of Lodz, Pomorska 141/143, 90-236 Lodz, Poland

adres@email: karolina.kowalczyk@chemia.uni.lodz.pl

Colchicine **1** is a naturally occurring tubulin-binding poison due to its high systemic toxicity it is not used in cancer chemotherapy. Nonetheless, **1** is often chemically modified to reduce its systemic toxicity and to strengthen its activity toward cancer cells.[1] Schmalz and co-workers showed that replacing of N-acetyl moiety by 1,2,3-triazole moiety results in maintaining or even increasing the activity of such analogs.[2] Previous studies have shown that conjugation of metallocene moiety with colchicine not only increases cytotoxicity but also changed the mode of action in comparison **1**.[2,3] Continuing our study in the conjugation of **1** and organometallic moiety we will present a synthesis and biological activities a series bioconjugates of **1**.



1

Fig.1 Structures of tubulin-binding colchicine

Acknowledgement: The Authors thanks to National Science Centre Poland (NCN) for financial support of this work (contract No. UMO-2018/29/N/ST5/01976)

[1] S. Punganuru, H. Madala and K. Srivenugopal, Med Chem (Los Angeles), **2016**, 6, 165-17

[2] P. Thomopoulou, J. Sachs, N. Teusch, A. Mariappan, J.Gopalakrishnan and H.-G. Schmalz, ACS Med. Chem. Lett., **2016**, 7, 188-19

[3] K. Kowalczyk, A. Blauz, W. M. Ciszewski, A. Wieczorek, B. Rychlik and D. Plazuk, Dalton Trans., **2017**, 46, 17041-17052

ANTIFUNGAL, ANTIACETYLCHOLINESTERASE ACTIVITIES AND GC-MS DETERMINATION OF *MARRUBIUM VULGARE L*. LEAF EXTRACTS

Khaoula Menaiaia[1], *Fadila Khaldi*[1], *Amina Ouahab*[1]

1Laboratory of Sciences and Technology of Water and Environment,University of Mohamed Cherif Messaadia/PO Box 1553. 41000, Souk-Ahras, Algeria

Email: menaiaiakhaoula@gmail.com

The current work concerns a medicinal plant widely used by indigenous Algerians *Marrubium vulgare L*. of the lamiaceae family, this plant have extraordinary therapeutic properties. This research encompasses several aspects: a phytochemical study aimed to assess the CPG/MS analysis, as well as the antifungal and anti acetylcholinesterase activities of hexane, dichloromethane, acetone and methanol extracts from leaves of *Marrubium vulgare L*.

The chemical composition of the two extracts of *Marrubium vulgare L*. is determined by gas chromatography coupled with mass spectrometry (GC-MS). The results of the analysis showed that the hexane extract studied consists mainly of tetracontane followed by tetracosane, 7-Hexadecenal, (Z)-, Linolenic acid, 2-hydroxy-1-(hydroxymethyl) ethyl ester (Z,Z ,Z)-, Tetrapentacontane and n-Hexadecanoic acid while the dichloromethane extract is essentially composed of Naphtho[2,1-b]furan-2(1H)-one, decahydro-3a,6,6,9a-tetramethyl -, [3as-(3a.alpha.,5a.alpha.,9a.beta.,9b.alpha.)]- followed by Cyclopropaneacetic acid, 2-hexyl, Phenol, 2,2'-methylenebis[6-(1,1-dimethylethyl)-4-methyl, Ethyl iso-allocholate and 14-.beta.-H-pregna.

Indeed, for the antifungal activity evaluated, We have also tested the effect of the different extracts against two phytopathogenic fungi strains by the disc-diffusion method. The inhibitory effect were important for the two tested strains. The extracts of *M. vulgare* have important antifungal activity. Statistical analysis indicates no significant differences at $P > 0.05$. On the other hand, the results obtained following the study of anticholinesterase activity proved that hexane extract has significant antiacetylcholinesterase activity. Based on these results, it is right to conclude that *M. vulgare* is an important source of bioactive compounds with antifungal and anti-alzheimer properties.

Keywords: *Marrubium vulgare L*., antifungal activity, CPG/MS, antiacetylcholinesterase activity, phytochemical.

Mixed-valent dinuclear Mn complex from a tetradentate dipyrrin-based ligand: synthesis, structure & reactivity with O_2

J. Moutet,[a] F. Molton,[a] R. Guéret,[b] C. Philouze,[a] A. du Moulinet d'Hardemare,[a] F. Thomas,[a]* N. Leconte[a]*

[a] Department of Molecular Chemistry, Univ. Grenoble Alpes, France

[b] ICMG Nanobio Platform, Univ. Grenoble Alpes, France

nicolas.leconte@univ-grenoble-alpes.fr

The association of non-innocent ligands with earth-abundant metals has emerged as a promising bio-inspired strategy for the development of sustainable, efficient and reliable homogeneous catalysts, which meet the global economic and environmental concerns. In nature, the benefits of such a combination are well illustrated by metalloenzymes like Cytochrome P450 or Galactose Oxidase, where molecular O_2 plays also a prominent role. In addition, the synthesis of new redox-active ligands would not only allow the design of eco-compatible efficient catalysts, but also bring unsuspected reactivities.

In this area our research focuses on the design and the study of stable metal-radical species. We recently prepared and characterized a Mn^{III}-[bis(phenolato)dipyrrinato] complex from a N_2O_2 hybrid ligand, which features multiple ligand-centered redox events. On a reactivity aspect, changing the ligand oxidation state appeared as an easy mean to tune the reactivity of the complex and, consequently, the chemoselectivity of a reaction.[1]

Further developments in ligands design afforded a nitrogenated version with the bis(2-aminophenyl)dipyrrin analog. The related series of Ni complexes was prepared and deeply characterized, to attest the unique redox properties of the N_4 ligand.[2]

In the present work, our results related to the chemistry between the bis(2-aminophenyl)dipyrrin ligand and manganese will be presented.

[1] L. Lecarme, L. Chiang, J. Moutet, N. Leconte, D. Luneau, C. Philouze, O. Jarjayes, T. Storr, F. Thomas *Dalton Trans.* **2016**, *45*, 16325-16334.

[2] J. Moutet, C. Philouze, A. du Moulinet d'Hardemare, N. Leconte, F. Thomas *Inorg. Chem.* **2017**, *56*, 6380-6392.

Electrocatalytic Water Oxidation Activity of Molecular Copper Complexes: Effect of Redox-Active Ligands

Moumita Bera,[a] Kritika Keshari,[a] Akhil Bhardwaj,[b] Geetika Gupta,[a] Bhaskar Mondal[b] and Sayantan Paria[a*]*

[a] Moumita Bera, Department of Chemistry, Indian Institute of Technology Delhi, Hauz Khas, New Delhi 110016, India

[a] Kritika Keshari, Department of Chemistry, Indian Institute of Technology Delhi, Hauz Khas, New Delhi 110016, India

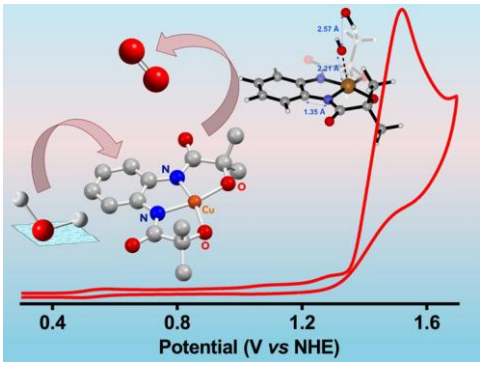
[a] Geetika Gupta, Department of Chemistry, Indian Institute of Technology Delhi, Hauz Khas, New Delhi 110016, India

[a] Sayantan Paria, Department of Chemistry, Indian Institute of Technology Delhi, Hauz Khas, New Delhi 110016, India

[b] Akhil Bhardwaj, School of Basic Sciences, Indian Institute of Technology Mandi, Kamand, Himachal Pradesh 175075, India

[b] Bhaskar Mondal, School of Basic Sciences, Indian Institute of Technology Mandi, Kamand, Himachal Pradesh 175075, India

Email: cyz178488@iitd.ac.in



Two molecular copper (II) complexes, $(NMe_4)_2[Cu^{II}(L_1)]$ (1) and $(NMe_4)_2[Cu^{II}(L_2)]$ (2), ligated by a N2O2 donor set of ligands [L_1 = N,N′-(1,2- phenylene)bis(2-hydroxy-2-methylpropanamide), and L_2 = N,N′-(4,5-dimethyl1,2-phenylene)bis(2-hydroxy-2-methylpropanamide)] have been synthesized and thoroughly characterized. An electrochemical study of 1 in a carbonate buffer at pH 9.2 revealed a reversible copper-centered redox couple at 0.51 V, followed by two ligand-based oxidation events at 1.02 and 1.25 V, and catalytic water oxidation at an onset potential of 1.28 V (overpotential of 580 mV). The electron-rich nature of the ligand likely supports access to high-valent copper species on the CV time scale. The results of the theoretical electronic structure investigation were quite consistent with the observed stepwise ligand-centered oxidation process. A constant potential electrolysis experiment with 1 reveals a catalytic current density of >2.4 mA cm^{-2} for 3 h. A one-electron-oxidized species of 1, $(NMe_4)[Cu^{III}(L_1)]$ (3), was isolated and characterized. Complex 2, on the contrary, revealed copper and ligand oxidation peaks at 0.505, 0.90, and 1.06 V, followed by an onset water oxidation (WO) at 1.26 V (overpotential of 560 mV). The findings show that the ligand-based oxidation reactions strongly depend upon the ligand's electronic substitution ; however, such effects on the copper-centered redox couple and catalytic WO are minimal. The energetically favorable mechanism has been established through the theoretical calculation of stepwise reaction energies, which nicely explains the experimentally observed electron transfer events. Furthermore, as revealed by the theoretical calculations, the O−O bond formation process occurs through a water nucleophilic attack mechanism with an easily accessible reaction barrier. This study demonstrates the importance of redox-active ligands in the development of molecular late-transition-metal electrocatalysts for WO reactions.

In vitro biological Water Gas Shift Reaction for Syngas cleanup

T. Pichon [a*], U. Contaldo[a,b], J. Perard[a], A. Le Goff [b], C. Cavazza[a*].

[a] LCBM, Bio-Energy and Environment team, CEA Grenoble, 17 Rue des Martyrs, 38054 Grenoble, France

[b] Université Grenoble Alpes, DCM UMR 5250, BEA, F-38000, Grenoble, France

thomas.pichon@cea.fr

Within the context of man-made climate change, the search for new means of powering our civilization in ways that impact atmospheric CO_2 levels positively is more important than ever. Liquid fuel is a significant part of our energy consumption, and is hardly replaceable when it comes to transportation, one of the largest CO_2 emitting sectors. Using biomass and biowaste as liquid fuel sources is an attractive solution to utilize recently fixed CO_2 and get a net zero emission energy carrier. An already used approach is biomass gasification to yield syngas, a gaseous mix mainly composed of H_2, CO and CO_2 as well as N_2 and various impurities (CH_4, H_2S, …). Turning syngas into liquid fuel requires a controlled H_2/CO ratio, which is regulated using the Water Gas Shift Reaction (WGSR): $CO + H_2O \rightleftharpoons CO_2 + H_2$. This reaction is carried out industrially at high temperatures and high-pressure using metal catalysts (Fe, Cr, Mg…). This process is sensitive to impurities, and results in poor yields. However, the WGSR is also carried out *in vivo* using two enzymes: Carbon Monoxide Dehydrogenase (CODH) and Hydrogenase (H_2ase), with CODH catalyzing the CO/CO_2 interconversion while H_2ase interconverts $2H^+/H_2$. Following a bio-inspired approach, we aim to design innovative enzymatic devices for efficient and sustainable *in vitro* bio-WGSR processes. In a first step, our team developed a protocol for the heterologous production in *E. Coli* of fully active recombinant [NiFe]CODH from *Rhodospirillum Rubrum* (RecRrCODH) that allows for large productions of pure enzyme in one day purification. Its immobilization on multi-walled carbon nanotubes (MWCNT) was also established and optimized to manage high catalytic currents both for CO oxidation and CO_2 reduction[1]. Our goal now is to immobilize both RecRrCODH and [NiFeSe]H_2ase on adamantane-modified MWCNT and carry out the water gas shift reaction. Crucial considerations include compatible pH for both enzymes, gas/liquid mass transfer and efficient electron transfers between both enzyme active sites. Preliminary experiments were carried out, with the successful immobilization of both [NiFeSe]H_2ase and [NiFe]CODH on adamantane-modified MWCNT, yielding high currents towards corresponding H_2 production and CO oxidation at low overpotential.

[1] U. Contaldo, B. Guigliarelli, J. Perard, C. Rinaldi, A. Le Goff, C. Cavazza, *ACS Catal.* **2021**, *11* (9), 5808–5817.

Characterization and reactivity study of non-heme high-valent iron–hydroxo complexes

Kritika Keshari,[a] Moumita Bera,[a] Lucía Velasco,[b] Sandip Munshi,[c] Geetika Gupta,[a] Dooshaye Moonshiram[b] and Sayantan Paria*[a]*

[a] Kritika Keshari, Department of Chemistry, Indian Institute of Technology Delhi, Hauz Khas, New Delhi 110016, India

[a] Moumita Bera, Department of Chemistry, Indian Institute of Technology Delhi, Hauz Khas, New Delhi 110016, India

[a] Geetika Gupta, Department of Chemistry, Indian Institute of Technology Delhi, Hauz Khas, New Delhi 110016, India

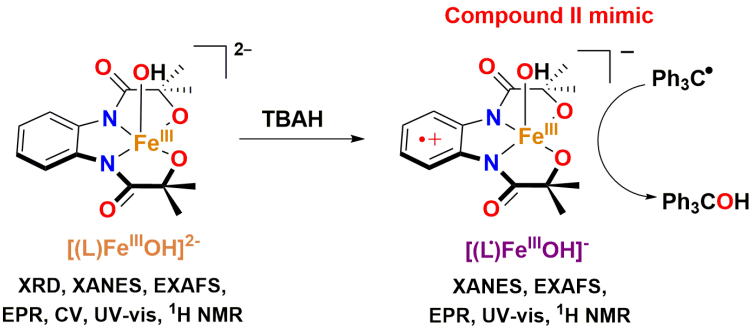
[a] Sayantan Paria, Department of Chemistry, Indian Institute of Technology Delhi, Hauz Khas, New Delhi 110016, India

[b] Lucía Velasco, Instituto Madrileño de Estudios Avanzados en Nanociencia (IMDEA Nanociencia, Calle Faraday, 9, 28049 Madrid, Spain)

[b] Dooshaye Moonshiram, Instituto Madrileño de Estudios Avanzados en Nanociencia (IMDEA Nanociencia, Calle Faraday, 9, 28049 Madrid, Spain)

[c] Sandip Munshi, School of Chemical Sciences, Indian Association for the Cultivation of Science, 2A & 2B Raja S. C. Mullick Road, Jadavpur, Kolkata 700032, India

Email: cyz188199@iitd.ac.in



A terminal $Fe^{III}OH$ complex, $[Fe^{III}(L)(OH)]^{2-}$ (**1**), has been synthesized and structurally characterized (H_4L= 1,2-bis(2-hydroxy-2-methylpropanamido) benzene). The oxidation reaction of **1** with one equiv. of *tris*(4-bromophenyl)ammoniumyl hexachloroantimonate (TBAH) or ceric ammonium nitrate (CAN) in acetonitrile at −45 °C results in the formation of a $Fe^{III}OH$ ligand radical complex, $[Fe^{III}(L^{\cdot})(OH)]^{-}$ (**2**), which is hereby characterized by UV-visible, ^{1}H nuclear magnetic resonance, electron paramagnetic resonance, and X-ray absorption spectroscopy techniques. The reaction of **2** with a triphenylcarbon radical further gives triphenylmethanol and mimics the so-called oxygen rebound step of Cpd II of cytochrome P450. Furthermore, the reaction of **2** was explored with different 4-substituted-2,6-di-*tert*-butylphenols. Based on kinetic analysis, a hydrogen atom transfer (HAT) mechanism has been established. A pK_a value of 19.3 and a BDFE value of 78.2 kcal/mol have been estimated for complex **2**.

Fighting oxidative stress thanks to Ni-SOD mimics

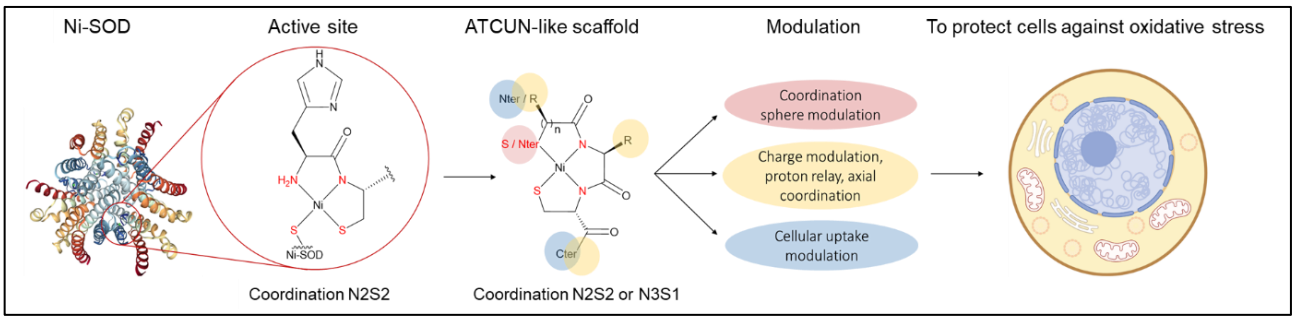
P. GUINARD,[a,b]* J. DOMERGUE,[a,b] J. PECAUT,[a] P. MALDIVI,[a] A. LE-GOFF,[b] O. PROUX, S. HOSTACHY,[a] C. DUBOC[b] and P. DELANGLE[a]

[a] CEA SyMMES - 17 avenue des Martyrs 38000 Grenoble
[b] DCM - 301 rue de la Chimie, 38610 Gières
[c] OSUG - 122 rue de la piscine, 38400 Saint Martin d'Hères
pawel.guinard@cea.fr

During the Great Oxidation event, 2.5 billion years ago, cyanobacteria started the production of huge amounts of dioxygen. Thus, living organisms of the time had to deal with the emergence of this species, at the origin of oxidative stress. Evolution endowed them with several strategies including protective enzymes in charge of the detoxification of Reactive Oxygen Species (ROS) from cells.[1] Among them, Ni-SOD is specialized in the capture and consumption of superoxide ($O_2^{\bullet-}$). Ni-SOD is a prokaryotic redox enzyme, which catalyses the dismutation of $O_2^{\bullet-}$ into H_2O_2 and O_2, thereby assisting cells to maintain optimal intracellular ROS concentrations.[2]

The remarkable catalytic activity of this enzyme prompted us to design small biomimetic Ni^{II} complexes with antioxidant properties as therapeutic agents for the numerous diseases causes by oxidative stress. These bio-inspired complexes also represent interesting tools to decipher the catalytic mechanism of this metalloenzyme.

The structure of Ni-SOD active site was mimicked by Ni^{II} complexes based on an ATCUN-like scaffold.[3] This motif enabled easy chemical modulation, formation of stable Ni^{II} complexes with square-planar geometry, and biocompatibility for future cellular assays. The complexes designed in this work show an intrinsic superoxide-dismutase activity, which can be tuned by modulating parameters such as coordination sphere, charge, presence of a proton relay, etc. The effects of these modulations on the catalytic activity will be discussed in the presentation.



1 C. Winterbourn *Nat. Chem. Biol.* **2008**, *4*, 278-286
2 H.D. Youn, E.J. Kim, J.H. Roe, Y.C. Hah, S.O. Kang *Biochem. J.* **1996**, *318 (Pt 3)*, 889-896
3 J. Domergue, P. Guinard, M. Douillard, J. Pécaut, O. Proux, C. Lebrun, A. Le Goff, P. Maldivi, P. Delangle, C. Duboc *Inorg. Chem.* **2021**, *60* (17), 12772-12780

CO_2 Reactivity of Biomimetic Organo-Diiron Complexes

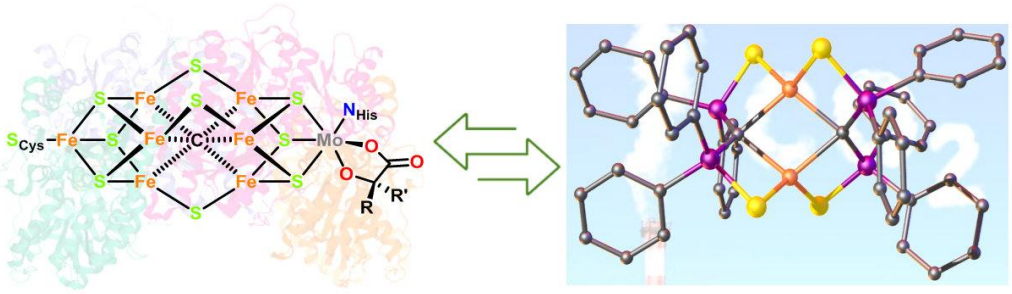
Sandip Munshi, Raphaël Ravel-Massol, Anthony Pujol, Nicolas Mézailles, Marie Fustier-Boutignon.

Laboratoire Hétérochimie Fondamentale et Appliquée (UMR 5069), Université de Toulouse (UPS), CNRS, 118 Route de Narbonne, F-31062 Toulouse, France

The conversion of CO_2 to value-added chemicals is a significant concern for bioinspired chemists. It is also a strike towards the growing anxiety about the increasing abundance of CO_2.[1] Nature's ability to reduce CO_2 into higher complex molecules (mainly via photosynthesis) inspired the bioinorganic community to come up with some model compounds with the selective conversion of CO_2.[2] Nevertheless, only a few multinuclear complexes (Mo/Cu[3], Ni/Fe[4]) inspired from enzymes specified in CO_2 fixation, are reported so far in the literature, which can catalyse the electroreduction of CO_2.

On another standpoint, nitrogenase cofactors are intensively studied for their ability to reduce N_2 to ammonia. During the past few years, it has been shown that its strong reducing capacity can be directed toward CO_2 reduction. Indeed, a slightly modified version of a Fe/Mo nitrogenase could reduce CO_2 to methane at room temperature.[5] This showed that such an iron/carbide and sulphur polymetallic structure is able to generate C-H bonds from C=O bonds.. Thus, the efficient activation of CO_2 toward total hydrogenation by a carbon and sulphur stabilized iron cluster should be a valuable route. The structural complexity of nitrogenase cofactor is however hampering the fine understanding of the reaction mechanism.

Taking inspiration from the nitrogenase, we propose to use bis-diphenylthiophosphinoylmethanediide as a versatile ligand for the preparation of a variety of closely related iron clusters. This gem-dianionic ligand $(SCS)^{2-}$ allowed us to prepare a set of bimetallic and tetrametallic structures, all of them featuring C^{2-}-Fe interactions reminiscent of the structural role of the carbide ligand in FeMo-co. Their reaction toward CO_2 has been studied in various redox states. Through this approach, we expect to be able to de-correlate important parameters such as the number and nature of metallic centres, the redox-states and spin states, the role the carbon-based coordination site. These systems indisputably enhance the arena of the CO_2 reactivity with bioinspired molecular catalysts.



Financial support by the ANR (ENigM, ANR-21-CE07-0007) as well as calculation facilities from CALMIP mesocenter are gratefully acknowledged.

References

[1] A. M. Appel, J. E. Bercaw, A. B. Bocarsly, H. Dobbek, D. L. DuBois, M. Dupuis, J. G. Ferry, E. Fujita, R. Hille, P. J. A. Kenis, C. A. Kerfeld, R. H. Morris, C. H. F. Peden, A. R. Portis, S. W. Ragsdale, T. B. Rauchfuss, J. N. H. Reek, L. C. Seefeldt, R. K. Thauer, G. L. Waldrop, *Chem. Rev.* **2013**, *113*, 6621−6658.

[2] Sk Amanullah, P. Saha, A. Nayek, Md E. Ahmed, A, Dey, *Chem. Soc. Rev.* **2021**, *50*, 3755−3823.

[3] A. Mouchfiq, T. K. Todorova, S. Dey, M. Fontecave, V. Mougel, *Chem. Sci.* **2020**, *11*, 5503–5510.

[4] Md E. Ahmed, S. Adam, D. Saha, J. Fize, V. Artero, A. Dey, C. Duboc, *ACS Energy Lett.* **2020**, *5*, 3837–3842.

[5] Z. Yang, V. R. Moure, D. R. Dean, L. C. Seefeldt, *Proc. Natl. Acad. Sci. U. S. A.*, **2012**, *109*, 19644.

Identical Spin Multi-State Reactivity Towards C-H Bond Activation in High-valent Fe/Mn-Oxo/Hydroxo Species

Asmita Sen, Gopalan Rajaraman*

Indian Institute of Technology Bombay, Powai, Mumbai-400076, India

Activation of C-H bonds using an earth-abundant metal catalyst is one of the top challenges of chemistry where high-valent Fe/Mn-O/OH biomimic species play an important role. There are several open questions related to the comparative oxidative abilities of these species, and a unifying concept that could accommodate various factors influencing the reactivity is lacking. To shed light on these open questions, here we have used a combination of the DFT (B3LYP-D3/def2-TZVP) and ab initio (DLPNO-CCSD(T); CASSCF/NEVPT2) calculations to study a series of high-valent metal-oxo/hydroxo species, [$M^{n+}H_3$buea(X)] (M = Fe and Mn, n = II to V, X = O/OH; H_3buea = tris[(N'-tert-butylureaylato)-N-ethylene)]aminato) towards the activation of dihydroanthracene (DHA). Detailed analysis unveils the following reactivity trend Fe^{V}=O > Mn^{III}=O > Mn^{IV}=O > Fe^{III}=O > Mn^{V}=O > Fe^{II}-OH > Mn^{II}-OH > Mn^{IV}-OH > Fe^{IV}-OH > Fe^{IV}=O > Fe^{III}-OH > Mn^{III}-OH and suggests that neither higher oxidation nor high-spin ground state yields superior reactivity. The secondary coordination sphere is found to play a vital role in controlling the reactivity wherein the H-bonding interactions reduce the crystal field strength, and this brings several excited states of the same spin multiplicity closer to the ground state resulting in the observation of identical spin multistate reactivity (ISMR) in $Mn^{III/IV}$=O and Fe^{II}-OH species. For Fe^{V}=O species, strong ligand spin polarization was detected, diminishing the crystal field leading to the exhibition of ISMR reactivity. The ISMR is found to control the basicity of the oxo/hydroxo group as well as the redox potentials. Further, when p*K*a > 15, a PT-ET mechanism for C-H bond activation is detected, and a higher $E_{1/2}$ value directs the reaction via the concerted HAT/PCET mechanism. On the other hand, for species that exhibit classical SSR/TSR reactivity, such as Mn^{II}-OH, Fe^{IV}=O, the secondary coordination sphere effect is found to be lethal. As the multireference character is absent in these species, they lack the electronic flexibility that ISMR species enjoy during the reaction, leading to sluggish/no reactivity for many species, including the popular Fe^{IV}=O species. As metalloenzymes' active sites have several H-bonding networks resembling the species studied here, this unlocks the possibility of having ISMR type reactivity for metalloenzymes to rationalize their superior catalytic abilities (Figure 1).

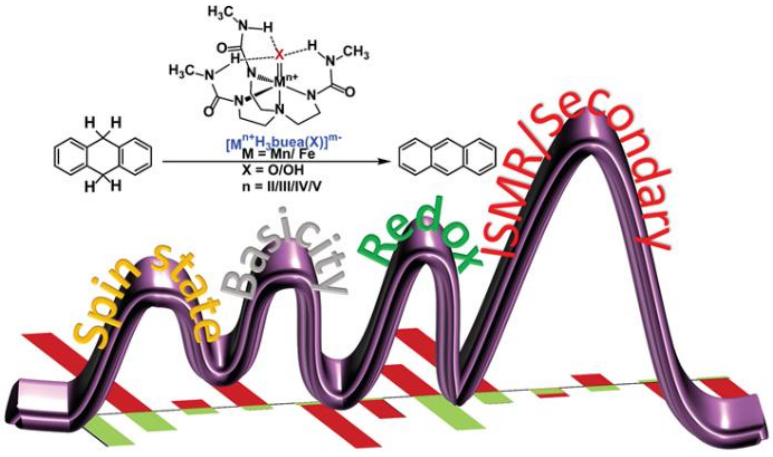


Figure 1: Various factors contributing to the reactivity of Fe/Mn-oxo/hydroxo species, and the role of ISMR.

Peroxide Activation and Substrate Oxidation by Cobalt(II) Complexes of Tris(pyrazolyl)methane Based Ligands: Evidence for a High-Valent Cobalt-Oxo Oxidant

A. Bera,[a]* Prof.T.K. Paine[a]

[a] School of Chemical Sciences, Indian Association for the Cultivation of Science, 2A & 2B Raja S. C. Mullick Road, Jadavpur-700032, India

E-mail: icab@iacs.res.in

Dioxygen activating metalloenzymes catalyze many biological oxidations such as hydroxylation of aliphatic C-H bonds, *cis*-dihydroxylation/epoxidation of alkenes, halogenations etc.[1] High-valent metal-oxo intermediates, capable of transferring oxygen atoms into the C–H and C=C bonds of substrates, have been implicated as the active oxidants in enzymatic reactions. Inspired by the diverse biological oxidations by nonheme enzymes, several synthetic models mimicking the structural and/or functional aspects of these metalloenzymes have been developed in the last decades.[2] The selective electron transfer for the reductive activation of dioxygen without quenching the active species remains a major issue in performing bio-inspired oxidation catalysis with dioxygen. Hence, most bio-inspired catalysts developed so far had to shunt this reduction process with peroxides or other oxidants.[2] However, many of these catalytic systems often exhibit non-selective oxidation of substrates due to the involvement of free radicals.

We have been exploring several bioinspired approaches to address these challenges. In case of peroxide activation, the generation of metal-based oxidant through heterolytic O-O bond cleavage of metal(III)-OOH(R) may be tuned using appropriate metal ions or Lewis/protic acid.[3],[4] As a part of this investigation, we have developed two cobalt(II) complexes $[Co^{II}(T_p^{Ph2}m)(CH_3CN)_3][ClO_4]_2$ (**1**) and $[Co^{II}(T_p^{PhMe}m)(CH_3CN)_3][ClO_4]_2$ (**2**) ($Tp^{Ph2}m$ = tris(3,5-diphenyl-1H-pyrazol-1-yl)methane) $T_p^{PhMe}m$ = tris(3-phenyl-5-methyl-1H-pyrazol-1-yl)methane) of the 2nd generation tris(pyrazolyl)methane ligands (T_pm) and investigated their efficiency in oxygenation of aliphatic C-H bonds using *m*-chloroperbenzoic acid (*m*-CPBA) as oxidant.[5] Both the complexes activate *m*-CPBA leading to the generation of a metal-based oxidant, which performs chemo-, regio- and stereoselective C-H bond hydroxylation. The stereo-electronic properties of the ligand on the reactivity of cobalt(II) complexes have been evaluated. The generation, electronic properties and reactivity of the *m*-CPBA-derived cobalt-oxygen oxidants will be presented.

References[1]

[1] M. Costas, M. P. Mehn, M. P. Jensen, L. Que Jr., *Chem. Rev*. **2004**, *104*, 939-986.
[2] K. Ray, F. F. Pfaff, B. Wang, W. Nam, *J. Am. Chem. Soc*. **2014**, *136*, 13942-13958.
[3] I. Ghosh, S. Banerjee, S. Paul, T. Corona, T. K. Paine, *Angew. Chem. Int. Ed*. **2019**, *58*, 12534-12539.
[4] R. D. Jana, A. Das, T. K. Paine, *Inorg. Chem*. **2021**, *60*, 5969-5979.
[5] A. Bera, I. Ghosh, T. K. Paine, **2022**, *manuscript under preparation*.

Photocatalytic system for olefin oxidation based on laccase, a renewable dioxygen dependent oxidoreductase

C. Righetti,[a]* M. Yemloul,[a] W. Leibl,[b] A.J. Simaan,[a] Y. Mekmouche,[a] T. Tron,[a]

[a] Aix Marseille Université, CNRS, BiosCiences, iSm2, Marseille, France

[b] Université Paris-Saclay, CEA, CNRS, (I2BC), Gif-sur-Yvette, France

claudio.righetti@etu.univ-amu.fr

Oxidation reactions are important chemical transformations but often require stoichiometric amounts of chemical oxidants that are often toxic. Conversely, nature uses molecular oxygen to perform oxidation of organic substrates via the use of cofactors such as metal ions in the active site of metalloenzymes. Developing robust photo-biocatalytic systems in which light absorption triggers electron-transfer events leading to oxidation of substrates, appears as an important approach to diminish our dependence on non-renewable energy sources, besides avoiding chemical activation by harsh oxidants or reductants. We choose to develop photo-biocatalytic systems relying on laccases, robust enzymes used in many industrial and biotechnological processes.[1] Laccases are multi-copper containing enzymes that naturally couple the 1-electron oxidation of organic substrates (such as phenol derivatives), to the 4-electron reduction of dioxygen to water. Recently, our group has shown that associating a photo-sensitizer (such as ruthenium or porphyrin-based) to a fungal laccase allows coupling the oxidation of molecules (not naturally oxidized by laccases) to the light-driven four-electron reduction of dioxygen to water.[2] This system allows to extend the biocatalytic repertoire accessible to laccases by using them as powerful and sustainable electron sink in the process of light-driven oxidation of organic substrates.[3] The system was however originally limited by a low efficiency of electron transfer between the sensitizer and the enzyme. With the goal to improve the system, we recently showed that an efficient photo-electron injection to the laccase can be achieved using methyl-viologen (MV^{2+}) as electron relay.[4] In this poster we present our last results using a photo-biocatalytic system associating a ruthenium sensitizer, an electron relay and laccase for an efficient oxidation of olefins using dioxygen as a renewable final electron acceptor. Different experiments were conducted in order to understand the role and effect of each of the constituents of the system. Evolution of the system to greener and metal-free sensitizers will be also discussed. Given the availability of various photosensitizers, the plasticity of laccases as well as the possibility to spatially organize the different components of the system (by grafting at controlled positions at the enzyme surface), it is likely that a great diversity of hybrid materials with applications in the fields of photo-catalysis can be created.

[1] Mate D. M. & Alcalde, M *Microb Biotechnol*, **2017**, *10*, 1457.
[2] Lazarides, T. et al *J. Am. Chem. Soc.*, **2013**, *135-8*, 3095-3103.
[3] Schneider L. et. al., *ChemSusChem*, **2015**, *8*, 3048-3051.
[4] Ferran R. et al, *iScience*, **2021**, *24*, 102378.

Using laccase/electrode interactions to understand electron transfer pathways

Q.J. Shen,[a] A. Ciaccafava,[a] M. Maffei,[a] A. J. Simaan,[a] Y. Mekmouche,[a] P. Rousselot-Pailley,[a] A. Le-Goff[b]*, and T, Tron[a]*

[a] Aix Marseille Université, CNRS, Centrale Marseille, iSm2 UMR 7313, 13397, Marseille, France

[b] University Grenoble Alpes and CNRS, DCM UMR 5250, F-38000 Grenoble, France

qiujuan.shen@etu.univ-amu.fr

Laccases are particularly robust copper-containing oxidases with distinctive spectroscopic features. In aerobic conditions, they couple the mono-electronic oxidation of phenolic substrates (at a T1 surface located Cu center) to the 4e- reduction of dioxygen into water (at an embedded tri-nuclear Cu center).[1] The search for efficient enzymatic fuel cells has facilitated the design of low potential/high current bioelectrodes for oxidizing or reducing substrates. Direct electron transfer (DET) between the electrode and the biocatalyst is influenced by protein orientation. Oriented immobilization of laccase onto an electroactive surface is a strategy to maximize the direct electron transfer between redox enzyme and electrodes. Our research group has previously shown synergistic combinations of laccase and muti-walled-carbon-nanotube (MWCNT) modified electrodes.[2] We also reported an efficient electrocatalytic reduction of molecular oxygen by a rationally-oriented fungal laccase covalently bound to MWCNTs as biocathode.[3]

In our work, we use several laccase variants to further characterize the DET between enzyme active sites and the electrode materials. We aim to get more insights into the structure of hybrid materials characterization, into different electron pathways and to better understand factors that influence the electrochemical behavior of the system.

[1] T. Tron, *Encyclopedia of Metalloproteins*, **2013**, 1066-1070.

[2] N. Lalaoui, P. Rousselot-Pailley, V. Robert, et al. *ACS Catalysis*, **2016**, *6*, 1894-1900.

[3] S. Gentil, P. Rousselot-Pailley, F. Sancho, et al. *Chemistry-A European Journal*, **2020**, *26*, 4798-4804.

Through-space electrostatic interactions in CO_2 reduction by metalloporphyrins

A. Smith,[a]* Z. Halime,[a] A. Aukauloo[a]

[a] Institut de Chimie Moléculaire et des Matériaux d'Orsay (ICMMO, UMR CNRS 8182), Université Paris-Saclay, Bat 420, Rue Doyen G. Poitou, Orsay, 91405, France

adrien.smith@universite-paris-saclay.fr

Transforming CO_2 into valuable reduced forms of carbon is a strategy that is currently attracting the interest of the scientific community. Converting and not only capturing CO_2 can be an efficient way to recycle this greenhouse gas by introducing non-fossil fuel based C1 building blocks back into the carbon cycle. The design of new molecular catalysts for the reduction of CO_2 is therefore essential to better understand how to activate and reduce efficiently this unreactive molecule. Metalloporphyrins have been shown to be good catalysts for CO_2 reduction[1]. When trying to optimize the performances of iron *tetra*-arylporphyrins, electron-withdrawing groups were introduced to lower the overpotential of CO_2 reduction, but at the expense of a lower turnover frequency. Looking at the structure of the Ni-Fe-S active site metal cluster of Carbon Monoxide Dehydrogenase (CODH), several positively charged groups appear to have an important role in the interconversion of CO_2 to CO. For this reason, our group and others introduced cationic functions in the second sphere of coordination of *tetra*-arylporphyrins with the objective to stabilize the Fe^{I}-$CO_2^{\bullet-}$ reactive intermediate that is formed during CO_2 reduction[2,3]. The benefits of these cationic groups were an important lowering of the overpotential and a higher catalytic rate. In this study, different iron porphyrins were synthetized with an imidazolium group at various distances from the metal center in order to better understand the effect of the positively charged moieties on the different steps of the reaction mechanism (see *Figure*). The goal of this study is to establish a Hammett's parameters like correlation for through space interactions that can guide the design of more efficient catalysts for CO_2 reduction.

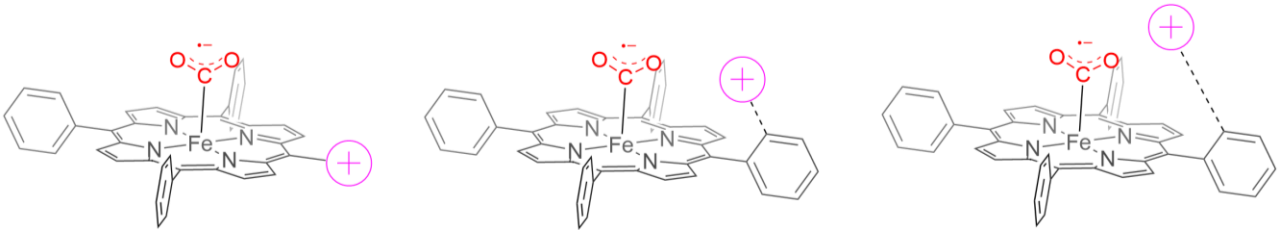


Figure: Simplified structures of targeted cationic derivatives of porphyrin catalysts with various distances of the cationic group to the Fe^{I}-$CO_2^{\bullet-}$ intermediate state

[1] M. Hammouche, D. Lexa, J.M. Savéant, M. Momenteau *J. Electroanal. Chem*, **1988**, *249*, 347-351.

[2] A. Khadhraoui, P. Gotico, B. Boitrel, W. Leibl, Z. Halime, A. Aukauloo *Chem. Commun.*, **2018**, *54*, 11630-11633.

[3] A. Khadhraoui, P. Gotico, W. Leibl, Z. Halime, A. Aukauloo *ChemSusChem*, **2021**, *14*, 1308-1315.

Well-defined iron sites on crystalline carbon nitrides: structure and N_2 reactivity

A. Genoux[a], M. Pauly[b], C. Choi[a], S. McGuigan[b], M. Fataftah[a], P. Maggard[b], H. Wang[a], and P. Holland[a]

[a]Department of Chemistry, Yale University, New Haven, Connecticut, USA

[b]Department of Chemistry, North Carolina State University, Raleigh, NC, 27695, USA

E-mail: alexandre.genoux@yale.edu

In recent years, crystalline carbon nitrides have gained significant interest for their photocatalytic activity and potential for solar energy conversion. Their structures are typically composed of stacked 2-dimensional layers, and form cavities that feature nitrogen donors that can act as ligands to bind metals. Herein, we accessed a new crystalline carbon nitrides containing Fe(II) sites (Figure 1). Structural insights were obtained by X-ray diffraction techniques. Mössbauer and SQUID magnetometry data indicate that the Fe(II) have a high-spin configuration. Overall, the ordered 3D-structure of crystalline carbon nitrides provides a well-defined coordination environment to the metal. The reduction of the Fe(II) sites were explored using organic reductants and the reactivity of this new material towards N2 was investigated.

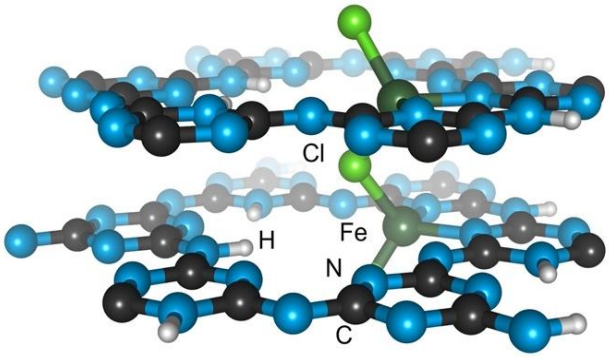


Figure 1. *Proposed structure for the local Fe-coordination site within the carbon nitride layers*

Bio-inspired polymer/metal oxides material for electrocatalytic water oxidation

M.-N. Collomb,[a*] B. Dautreppe,[a,b] S. Pouget,[c] D. Aldakov,[b] P. Reiss,[b] J. Fortage,[a]

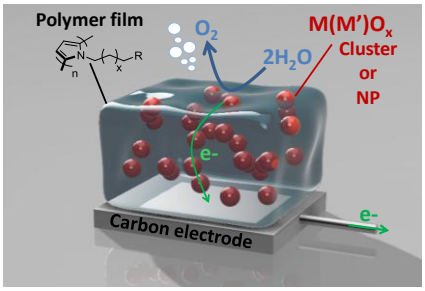
[a] Univ. Grenoble Alpes, CNRS, DCM/EMPRe 38000 Grenoble, France

[b] Univ. Grenoble Alpes, CEA, CNRS, IRIG/SyMMES/STEP, 38000 Grenoble, France

[c] Univ. Grenoble Alpes, CEA, CNRS, IRIG/MEM/SGX, 38000 Grenoble, France

marie-noelle.collomb@univ-grenoble-alpes.fr

Water oxidation into dioxygen (OER) remains a bottleneck in the scale-up of water-splitting and CO_2-reduction electrolyzers due to slow kinetics and large overpotential. A key challenge is the development of efficient, robust and cheap OER catalysts based on earth-abundant elements. Heterogeneous metal oxides or (oxy)hydroxides are the most promising catalysts in terms of activity and robustness**.** Since the pioneering work of Nocera in 2008[1] which reported the OER efficiency of electrodeposited Co oxides in phosphate buffer at pH 7 (called Co-Pi), coupled to their robustness and self-healing properties, intensive research efforts have focused on the development of OER-active oxides based on cheaper and more earth-abundant metals (Co, Ni, Mn, Fe, and Cu). A key factor in the performance of an electrocatalyst is its nanostructuration, the efficiency being significantly improved by increasing the active area/volume ratio while reducing the manufacturing cost. However, the reduction of the particles size for increasing the specific surface area of the catalyst leads to a decrease of their stability and can lead to aggregation. These limitations can be overcome by immobilizing the nanoparticles (NPs) in a polymeric or inorganic material.[2-4] In this context, we have recently designed bio-inspired nanocomposite electrode materials active and stable for water oxidation by a simple and versatile electrochemical method. These new materials consisting of sub-nanosized earth-abundant (mixed) metal oxides $M(M')O_x$ clusters (M, M' = Ni, Co, Fe…) dispersed into a polymer matrix substituted with anionic functions, mimicking the carboxylates rich environment of the natural Mn_4CaO_5 cluster of PSII and its sub-nanosized structure, two essential features for an outstanding catalytic efficiency. The method of elaboration of the nanocomposites, their characterization by several and complementary methods as well as their electrocatalytic performance for OER will be presented.



[1] M. W. Kanan, D. G. Nocera, *Science* **2008**, *321*, 1072-1075.

[2] Z. B. Shifrina, V. G. Matveeva, L. M. Bronstein, *Chem. Rev.* **2020**, *120*, 1350-1396.

[3] D. V. Morales, C. N. Astudillo, Y. Lattach, B. F. Urbano, E. Pereira, B. L. Rivas, J. Arnaud, J.-L. Putaux, S. Sirach, S. Cobo, J.-C. Moutet, M.-N. Collomb, J. Fortage, *Catal. Sci. Technol.* **2018**, *8*, 4030-4043

[4] D. V. Morales, C. N. Astudillo, V. Anastasoaie, B. Dautreppe, B. F. Urbano, B. L. Rivas, C. Gondran, D. Aldakov, B. Chovelon, D. André, J.-L. Putaux, C. Lancelon-Pin, S. Sirach, E.-M. Ungureanu, C. Costentin, M.-N. Collomb, J. Fortage, *Sustainable Energy & Fuels* **2021**, *5*, 4710-4723.

Design and Unmasking of Trivalent Copper for Catalysis

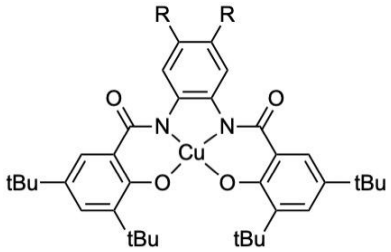
Guanqi Wang,[a] Yohann Moreau,[b] Olivier Jarjayes,[a]* and Fabrice Thomas[a]*

[a] Univ. Grenoble Alpes, CNRS, DCM, 38000 Grenoble, France.

[b] Univ. Grenoble Alpes, CEA, CNRS, IRIG-LCBM, 38000 Grenoble, France.

email address of the presenting author: guanqi.wang@univ-grenoble-alpes.fr

Due to the simplicity of this radical active site and its potentiality for highly selective catalytic oxidations, much efforts have developed small-molecule models of galactose oxidase (GOase) [1-5]. In this biomimetic approach number of Cu(II)-phenolate complexes system, one electron oxidized to be given the « active » form of the catalysts. A question then raised: Which parameters orientate the oxidation towards the ligand (affording the Cu(II)-phenoxyl radical) or the metal (affording the Cu(III)-phenolate form) ? The idea is to include chemical functions that can stabilize either valence tautomer (Cu(II)-phenoxyl radical and Cu(III)-phenolate) and quantify their effect. We developed main family of copper complexes illustrated in Figure to investigate the effect of substituent finely modulate the electronic structure. The complexes will be characterized by different way to realize their properties. According to the characterization of CV, UV-Vis-NIR, EPR and DFT calculation, these results suggest a fine modulation of the oxidation site by substituent effect: The more electron donating methoxy and NMe_2 groups favour a ligand-centered oxidation, whereas electron accepting favour a metal-centered process. The catalytic activity of the complexes were tested against the simple alcoholic substances like methanol. The DFT calculation well described the anion is a Cu(III) complex, its adduct with the substrate is a Cu(II) -radical system, which perfectly explains its reactivity towards alcohols. We can therefore propose that these Cu(III) complexes could be masked forms of Cu(II) -radical systems, and that this radical character manifests itself only in the presence of substrate. We can then ask the question of the relevance of independently developing series of compounds to mimic either active sites with metal with a high degree of oxidation or radical structures.



R = H, OMe, NO_2, NMe_2

[1] Chaudhuri, P.; Hess, M.; Florke, U., et al., *Angew. Chem. Int. Ed.*, **1998**, *37*, 2217-2220.
[2] Chaudhuri, P.; Hess, M.; Muller, J., et al., *J. Am. Chem. Soc.*, **1999**, *121*, 9599-9610.
[3] John, A.; Shaikh, M. M.; Ghosh, P., *Dalton Trans.*, **2008**, *21*, 2815-2824.
[4] Kochem, A.; Molloy, J. K.; Gellon, G., et al., *Chem. Eur. J.*, **2017**, *23*, 13929-13940.
[5] Lecarme, L.; Kochem, A.; Chiang, L., et al., *Inorg. Chem.*, **2018**, *57*, 9708-9719.

Modulation of the electrocatalytic activity for H2 production and CO2 reduction with bio-inspired complexes by ligand design

Lili SUN and Carole DUBOC
University Grenoble Alpes, UMR CNRS 5250, Département de Chimie Moléculaire, 38000 Grenoble, France
lili.sun@univ-grenoble-alpes.fr; carole.duboc@univ-grenoble-alpes.fr

In [FeFe]-hydrogenases, the amino moiety in the bridge serves as a proton relay, promoting the transfer a proton between the active site and the protein surface. Therefore, many biomimetic synthetic models bearing one pendant amine group have been previously described.[1] These works demonstrated that this potential proton relay is indeed used to mediate H_2 production in these electrochemical systems.[2]

In previous works of our group, the structural features and function of the active sites of the [NiFe]-, and [FeFe]- hydrogenases have been modeled with the electrocatalysts denoted as L^{N2S2}NiFeCp, L^{N2S2}NiFeCp* and L^{N2S2}FeFeCp (L^{N2S2} =2,2'-(2,2'-bipyridine-6,6'-diyl)bis(1,1'-diphenylethanethiolate) (Figure 2).[3-6] All these MFe (M=Ni or Fe) mimics with Cp or Cp* display good rates for hydrogen evolution reaction (HER) in acetonitrile in the presence of a mildly acid or in acidic aqueous solution after their heterogeneization on graphite electrodes. In addition, L^{N2S2}NiFeCp complex selectively and catalytically reduces CO_2 in acidic aqueous solution to produce a mixture of CH_4 and H_2 with faradaic yields of 12% and 66% for CH_4 and H_2, respectively (pH=4).[7]

In order to further improve the electrocatalytic activity of such systems, according to previous reports, we decide to develope a new bio-inspired NiFe electrocatalysts containing an amino-modified ligand to promote the hydrogen evolution reaction. We modify the L^{N2S2}NiFeCp complex at the Fe site with the introduction of a potential proton relay in the second coordination sphere, by replacing the Fe-bound cyclopentadienyl (Cp^-) by the ethyl diethylamine moity (N^*Cp^-), to investigate how this modification will affect the HER electrocatalytic performance of the resulting heterobinuclear NiFe complex. The $[NiFe(CO)CpN^*]^+$ complexe have been synthesized and characterized by IR and ESI-MS. Interestingly, the CVs of $[NiFe(CO)CpN^*]^+$ indicate that it can catalyze reduction of protons to H_2 and the reduction of CO_2 in CH_3CN at the lower catalytic potential value with respect to L^{N2S2}NiFeCp complex.

References[1]

[1] T. R. Simmons, T.R.Simmons, G. Berggren, M. Bacchi, M. Fontecave and V. Artero, *Coord. Chem. Rev.* **2014**, *270*, 127-150; [2] S. Roy, T. L. Groya and A. K. Jones, *Dalton Trans.* **2013**, *42*, 3843-3853; [3] D. Brazzolotto, M. Gennari, N. Queyriaux, T. R. Simmons, J. Pécaut, S. Demeshko,

F. Meyer, M. Orio, V. Artero, and C. Duboc, *Nat. Chem.* **2016**, *8*, 1054-1060; [4] M. E. Ahmed, S. Chattopadhyay, L. Wang, D. Brazzolotto, D. Pramanik, D. Aldakov, J. Fize, A. Morozan, M. Gennari, C. Duboc, A. Dey, and V. Artero, *Angew. Chem. Int. Ed.* **2018**, *57*, 16001–16004; [5] D. Brazzolotto, L. Wang, H. Tang, M. Gennari, N. Queyriaux, C. Philouze, S. Demeshko, F. Meyer, M. Orio, V. Artero, M. B. Hall, and C. Duboc, *ACS Catal.* **2018**, *8*, 10658-10667; [6] L. Wang, M. Gennari, A. Barrozo, J. Fize, C. Philouze, S. Demeshko, F. Meyer, M. Orio, V. Artero, and C. Duboc, *ACS Catal.* **2020**, *10*, 177-186; [7] M. E. Ahmed, S. Adam, D. Saha, J. Fize, V. Artero, A. Dey, and C. Duboc, *ACS Energy Lett.* **2020**, *5*, 3837-3842.

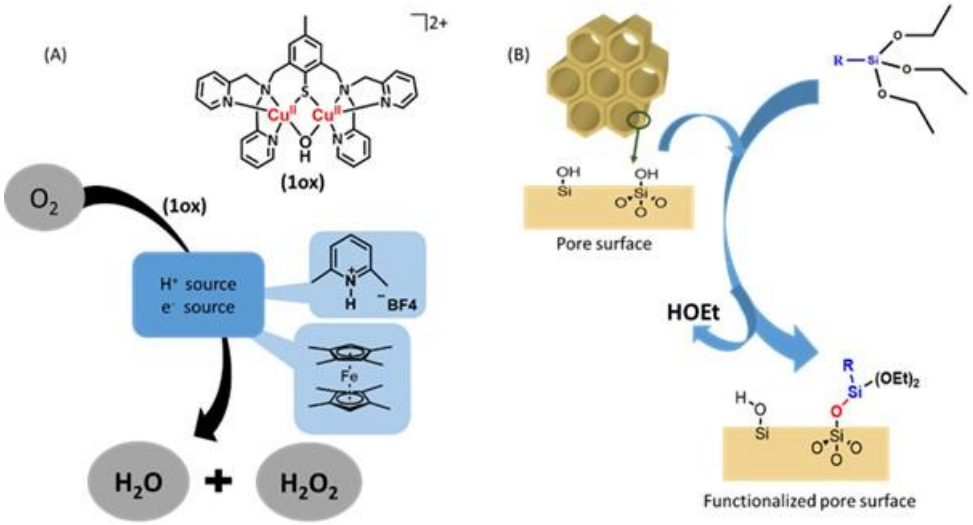
Bio-inspired and heterogeneous low water content hydrogen peroxide production in organic solvent.

Charlotte MAIA,[a*] Stéphane TORELLI,[b] Laurent BONNEVIOT,[c]
[a] DRF, IRIG, DIESE, LCBM, BioCE, CEA Grenoble
[b] DRF, IRIG, DIESE,LCBM, BioCE, CEA Grenoble
[c] Département de chimie, MFP, Ens-lyon
charlotte.maia@cea.fr

Hydrogen peroxide (H_2O_2) is a multipurpose green oxidant. Its most important industrial production comes from the anthraquinone process[1]. However, the latter presents a numerous of downfalls such as explosion risk, formation of pollutant waste and a product with a high water content.

In our team an alternative bio-inspired system was developed. This catalytic system exploits the reactivity of a dinuclear copper (II) complex with N/S coordination spheres for controlled O_2 reduction in the presence of electron and proton sources (octamethyferrocene and lutidinium salt, respectively, **Figure 1-(A)**). The overall catalytic system is effective with a selectivity of 90 % for H_2O_2 production[2]. Nevertheless, the produced H_2O_2 remains unusable due to side products accumulation derived from the reduced electron source, the deprotonated proton source and the catalyst. To overcome the uselessness of the formed product the whole catalytic system has to be supported for an easier removal from the medium. Thus, the goal of the project is to graft all the catalytic system onto a mesoporous silica, MCM-41[3].

The first focus was to synthetize a modified electron source compatible with the functionalization of MCM-41 (***Figure 1-(B)***). As a first step, we synthetized ferrocene derivatives with a silatrane moieties. As a second step, we are using these precursors to functionalize the MCM-41 and characterize the newly formed materials. To then test their catalytic properties against the properties of a model system in solution.



[1] Goor, G.; Glenneberg, J.; Jacobi, S., *Ullmann's Encyclopedia of Industrial Chemistry*; *Wiley*, 2**007**; p a13-443.
[2] Mangue, J.; Gondre, C.; Pécaut, J.; Duboc, C.; Ménage, S.; Torelli, S., *Chem Commun* **2020**, *56* (67), 9636–9639.
[3] Albela, B.; Bonneviot, L., *New J. Chem.* **2016**, *40* (5), 4115–4131.

Functional Structural Model Complexes for the Rabbit Lipoxygenase

E. Dobbelaar,[a] C. Rauber,[a] T. Bonck,[a] H. Kelm, [a] M. Schmitz, [a] M. E. de Waal Malefijt,[b] J. E. M. N. Klein,[b] H. J. Krüger[a,*]

[a] TU Kaiserslautern, Erwin-Schrödinger Str. 52-54, 67655 Kaiserslautern, Germany

[b] University of Groningen, Faculty of Science and Engineering, 9747 AG Groningen, The Netherlands

dobbelaar@chemie.uni-kl.de

Lipoxygenases are oxidoreductases that catalyse the hydroperoxidation of unsaturated fatty acids with oxygen via substrate activation by an overall H-atom abstraction. The two mechanistically relevant states for the rabbit Lipoxygenase (rLOX) are a pseudo-octahedral cis-hydroxo(carboxylato)iron(III) complex with four histidine residues and its reduced aqua iron(II) counterpart.[1] The synthesis and stabilization especially of mononuclear hydroxo iron(III) model complexes is challenging because of their tendency to form μ-oxo bridged dinuclear species.[2,3] Previous efforts have described either structural model complexes for lipoxygenases, however at the expense of functionality, or functional model complexes with only limited resemblance to the structural and electronic properties of the enzymatic active site.[2,4] We report the first examples of model complexes for the iron site of the rabbit lipoxygenase in both oxidation states that mimic both structural and functional properties of the enzyme. This was achieved by employing the tetradentate macrocyclic ligand *N,N'*-di-*tert*-butyl-2,11-diaza[3.3](2,6)-pyridinophane (L-N4^{t}Bu$_2$), a carboxylate unit, and a hydroxide/aqua ligand.[5] Experimental and theoretical studies support a concerted proton-coupled electron-transfer (cPCET) reactivity analogous to the enzyme (Figure 1). We experimentally determined the bond dissociation free energy (BDFE) for the iron(III) complex to be 72.4 kcalmol^{-1} and reveal the importance of the intramolecular hydrogen bond interaction between the carboxylate and the hydroxo/aqua ligands for the C-H and O-H abstraction reactivity.

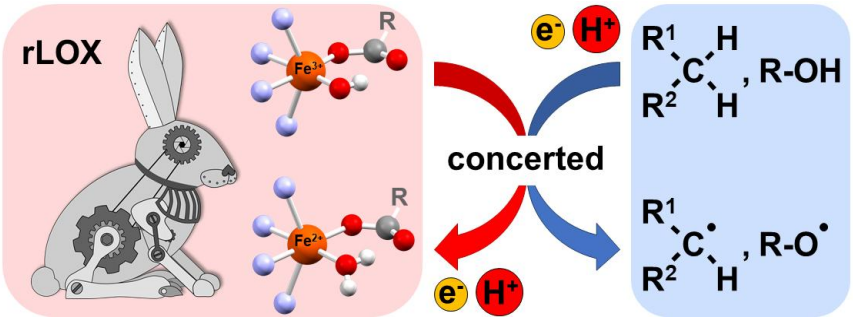


Figure 1. Synthetic analogue complexes (simplified) for the active site in rLOX display structural, functional (and mechanistic) analogy to enzyme.

[1] A. Andreou *et al.*, *Phytochemistry*, **2009**, *70*, 1504-1510. [2] S. Ogo *et al.*, *Angew. Chem.*, **1998**, *110*, 2198-2200. [3] L. Bénisvy *et al.*, *Inorg. Chem.*, **2006**, *45*, 2403-2405. [4] C. R. Goldsmith *et al.*, *J. Am. Chem. Soc.*, **2002**, *124*, 83-96. [5] E. Dobbelaar *et al.*, *J. Am. Chem. Soc.*, **2021**, *143*, 13145-13155.

Uranyl-binding peptides to shed light on uranium toxicity at the molecular level

Fanny Laporte,[a] Yves Chenavier,[a] Alexandra Botz,[a] Christelle Gateau,[a] Colette Lebrun,[a] Sarah Hostachy,[a]* Claude Vidaud,[b] Pascale Delangle[a]*

[a] IRIG, SyMMES, Université Grenoble Alpes, CEA, CNRS, Grenoble INP, Grenoble, France

[b] CEA, Biosciences and Biotechnologies Institute of Aix-Marseille, Bagnols sur Céze, France

sarah.hostachy@cea.fr, pascale.delangle@cea.fr

Uranium is a natural element widely found in the environment, due to both natural occurrence and industrial applications. Despite its ubiquitous distribution, uranium has no essential role in living organisms and presents radiological and chemical toxicities. Despite significant recent advances in the field, there is still a serious lack of knowledge about the molecular interactions responsible for uranium toxicity. The underlying mechanisms need to be unraveled to predict the effect of uranium on living organisms and to help in designing efficient detoxification agents.

A biomimetic strategy exploiting constrained peptides was applied in our laboratory to shed light on uranium binding to biomolecules.[1] Short peptide sequences are simple models of metal-binding sites in proteins that provide structural and thermodynamic data, which are not accessible directly with large biological molecules. This metal most stable form in vivo is the uranyl cation, UO_2^{2+}, which prefers four to six oxygen donors in its equatorial plane, perpendicular to O-U-O bonds. We designed a series of cyclic decapeptides binding uranyl through the oxygen donors from aspartates or glutamates and phosphoserines, in a predictive way. A phosphate-rich peptide demonstrated a very large affinity for uranyl, which is reminiscent of uranium binding by one of the most affine native uranium target, namely osteopontin.[2] This prompted us to propose a tetraphosphorylated coordination environment for the binding of UO_2^{2+} by this protein.

We also deigned an original uranyl-binding fluorescent probe, based on a peptidic rigid turn structure that pre-orients two unnatural amino acid side chains to efficiently coordinate uranyl in the equatorial plane. This probe shows an affinity for UO_2^{2+} in the range of those of native proteins, and fluorescent properties that enable the detection of uranyl binding in biological media.[3] It was validated thanks to the well-characterized cyclic peptides developed in our group and allowed us to evaluate the uranyl-binding affinity of four native proteins.

The biomimetic strategies presented here show how peptide design is powerful to decipher interactions of metal ions with biomolecules, interactions which are highly related to their toxicity.

[1] A. Garai, P. Delangle, *J. Inorg. Biochem.*, **2020**, *203*, 110936.

[2] F.A. Laporte, C. Lebrun, C. Vidaud, and P. Delangle, *Chem. Eur. J.*, **2019**, *25*, 8570-8578.

[3] F.A. Laporte, Y. Chenavier, A. Botz, C. Gateau, C. Lebrun, S. Hostachy, C. Vidaud, and P. Delangle, *Angew. Chem. Int. Ed.*, **2022**, e202203198.

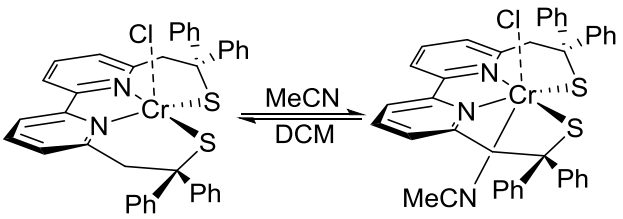
Spin-state and oxygen reactivity of Cr(III) complexes with a tetradentate bipyridine bis-thiolate ligand

Kaiji Shen,[a]* Marcello Gennari,[a] Carole Duboc[a]

[a] Univ Grenoble Alpes, CNRS, UMR 5250 DCM, F-38000 Grenoble, France

kaiji.shen@univ-grenoble-alpes.fr

In order to explore new homogeneous catalysts for the oxygen reduction reaction (ORR) domain, we investigated a unique Cr(III) dithiolate complex, [Cr^{III}LCl] (L = 2,2′-(2,2′-bipyridine-6,6′-diyl)bis(1,1-diphenylethanethiolate)). Its reactivity towards dioxygen is spin-state dependent depending on the presence of a coordinating solvent molecule in a sixth position. The high spin penta-coordinating complex reacts with dioxygen and oxidizes ferrocene stoichiometrically in CH_2Cl_2, while its hexa-coordinating counterpart, shows no reactivity with dioxygen in acetonitrile.



Stable M(II)-Radicals and Nickel(III) Complexes of a Bis(phenol) N-Heterocyclic Carbene Chelated to Group 10 Metal Ions

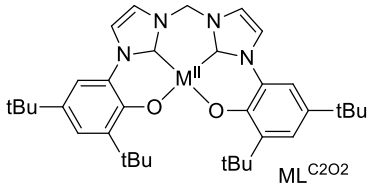
R. Kunert, C. Philouze, O. Jarjayes, and F. Thomas

Université Grenoble Alpes, UMR CNRS-5250, Département de Chimie Moléculaire, Grenoble F-38000, France

Olivier.Jarjayes@univ-grenoble-alpes.fr

The interplay between high-valent metal centers and radical ligands is essential in biocatalysis for metalloenzymes such as cytochrome P450, galactose oxidase, and glyoxal oxidase. This original reactivity has stimulated the design of biomimetic radical complexes. For example, electron-rich di-tert-butylphenolate is a precursor of persistent phenoxyl radical species that has been used for designing model compounds for galactose oxidase[1]. This hard donor is also capable in some instances of stabilizing metal ions under unusual high-valent oxidation states, such as Cu(III) while it does not easily accommodate low-valent copper. In order to overcome this latter limitation and to design robust and multi-redox-stable systems, we recently focused our attention on redox-active ligands incorporating N-heterocyclic carbenes (NHCs). While examples of redox-active NHCs are yet rather rare[2], these moieties are well-known to easily accommodate electron-rich metals. But, more recently, NHCs have also shown to be able to bind high-valent metal centers, including Cu(III), or Co(IV) for example[3,4]. This propensity to form stable complexes over a wide range of redox states has prompted us to incorporate NHCs alongside phenolates in our design of redox-active ligands.

We recently developped an innovative tetradentate ligand $H_4L^{C2O2}Br_2$ (see figure) and the study of its coordination to group 10 transition metals (M= Ni, Pd, Pt). We thoroughly assessed the electronic structure of the neutral precatalysts and the oxidised species and presented the first reported Ni(III) complex featuring NHC donors in a coordinating media of pyridine.



M = Ni: NiL^{C2O2}
Pd:PdL^{C2O2}
Pt: PtL^{C2O2}

[1] F. Thomas, *Eur. J. Inorg. Chem.* **2007**, *2007*, 2379-2404.
[2] A. A . Danopoulos, T. Simler, P. Braunstein *Chem. Rev.* **2019**, *119*, 3730−3961.
[3] Z. S. Ghavami, M. R. Anneser, F. Kaiser, P. J. Altmann, B. J. Hofmann, J. F. Schlagintweit, G. Grivani, F. E. Kühn, *Chem. Sci*. **2018**, *9*, 8307–8314.
[4] J. A. Bellow, S. A. Stoian, J. van Tol, A. Ozarowski, R. L. Lord, S. Groysman, *J. Am. Chem. Soc.* **2016**, *138*, 5531–5534.