SABIC

7 - 11 JANUARY 2024 . KOLKATA

6TH SYMPOSIUM ON ADVANCED BIOLOGICAL INORGANIC CHEMISTRY

Venue: Altair Boutique Hotel, Saltlake, Kolkata

BOOK OF ABSTRACTS


SERB
DIA


ROYAL SOCIETY
OF CHEMISTRY


JEOL


ACS
Chemistry for Life®

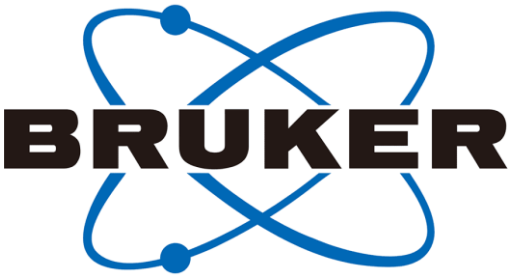

LASER
SCIENCE
Bringing Tomorrow's Technology Today

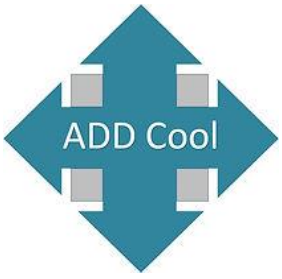

SBIC
The Society of
Biological Inorganic Chemistry
Bringing inorganic chemistry to life


tifr


INDIAN ASSOCIATION FOR THE CULTIVATION OF SCIENCE
FOUNDED BY MAHENDRALAL SIRCAR 1876


Merck


BRUKER


ADD Cool


JBIC
2023
Journal of
Biological
Inorganic
Chemistry


CH Instruments, Inc.
Electrochemical Instrumentation


WILEY

About the Conference…

Indian Association for the Cultivation of Science (IACS), Kolkata and Tata Institute of Fundamental Research (TIFR), Mumbai are jointly organizing the **6th Symposium on Advanced Biological Inorganic Chemistry (SABIC 2024)** Conference in Kolkata between Jan 7-11, 2024.

The 1st SABIC was organized by TIFR during October 7-11, 1996 and subsequently the 2nd symposium was held during November 20-24, 2000 at TIFR. The 3rd SABIC was organized in conjunction with the second Asian Biological Inorganic Chemistry Conference (AsBiC-II) at Goa during December 6-10, 2004. The 4th SABIC was held at TIFR in 2009. The 5th SABIC was held in Kolkata in 2017 and was attended by a large number of very distinguished scientists all over the world.

The present conference will be on the recent developments in Bio-inorganic Chemistry. Different areas of this broad discipline including metals in medicine, metals in diseases, metalloenzymes and their models, artificial metalloenzymes, sensing, approaches to cancer therapy, spectroscopy and dynamics, bio-inspired catalysis, metal clusters, metals in environment and their regulation will be covered. Experts from all over the world have graciously agreed to present their findings and participate in the conference. This conference will provide an excellent opportunity for all especially the students to be updated with the most recent exciting developments in the area.

SABIC 2024- National Advisory Committee

Prof. A. R. Chakravarty
IISc, Bangalore

Prof. V. Chandrasekhar
TIFR, Hyderabad

Prof. J. K. Bera
IIT, Kanpur

Prof. G. Mugesh
IISc, Bangalore

Prof. S. Sengupta
IISER, Kolkata

Prof. T. K. Paine
IACS, Kolkata

Prof. D. Maity
IIT, Mumbai

Prof. A. Mukherjee
IISER, Kolkata

Prof. J. Dasgupta
TIFR, Mumbai

Prof. S. Bhattacharya
Jadavpur University

Prof. G. K. Lahiri
IIT, Mumbai

Prof. S. Mandal
IISER, Mohali

Prof. R. Gupta
University of Delhi

Prof. A. Dutta
IIT, Mumbai

Prof. C. V. Sastri
IIT, Guwahati

Prof. ASR Koti
TIFR, Mumbai

Prof. A. Hazra
IISER, Pune

Convenors

Prof. Abhishek Dey,
IACS, Kolkata

Prof. Somdatta Ghosh Dey,
IACS, Kolkata

Prof. Ankona Dutta,
TIFR, Mumbai

Prof. Shyamalava Mazumdar,
TIFR, Mumbai

Volunteers

Soumya Samanta

Chinmay Dey

Rabin Kumar Poria

Srijan Sengupta

Kumarjit Banerjee

Rimi Ghosh

Somnath Das

Arkaprabha Das

Sudip Barman

Souvik Dinda

Puja Pal

Kushal Sengupta

Ankita Sarkar

Asmita Singha

Abhijit Nayek

Madhuparna Roy

Soumili Ghosh

Arnab Roy

Triparna Roy

Suman Patra

Contents

Program schedule 09-13

Lecture Abstracts

- **Day-1 07.01.24 (Sunday)** 14-40
- **Day-2 08.01.24 (Monday)** 41-88
- **Day-3 09.01.24 (Tuesday)** 89-138
- **Day-4 10.01.24 (Wednesday)** 139-184
- **Day-5 11.01.24 (Thursday)** 185-207

Poster Abstracts 208-480

Program			
	7th January, 2024		
8:00 – 11:00	**Registration**		
11:00 – 11:15	**Opening Session** Prof. Somdatta Ghosh Dey, IACS and Prof. Samaresh Mitra, TIFR (retired)		
11:15-12:00	**Plenary Lecture**: Metal complexes in biological environments: a new frontier in inorganic chemistry **Clotilde Policar**, PSL University, France (Phoenix I and II)		**Session chair**: Prof. A.R Chakravarty, IISc
12:00-12:45	**Plenary Lecture**: Illuminating the cell biology of zinc **Amy Palmer**, University of Colorado, Boulder (Phoenix I and II)		
12:45 – 13:45	Lunch		
13:45 – 16:15	**Sensing (Phoenix I)**	**Session in Honour of Kenneth Raymond (Phoenix II)**	**Approaches for Cancer Therapy (Galaxy)**
	Chair: Gautam Lahiri	**Chair**: Andrew Borovik	**Chair**: Arindam Mukherjee
	Pradip Mascharak (KL) Emily L. Que (KL) Jaeheung Cho (IL) Chandan Mukherjee (IL) R. Mayilmurugan (IL) Krishna Bhabak (IL) Alivia Mukherjee (OL)	Paul Walton (KL) Ankona Dutta (KL) P.S. Mukherjee (KL) Lena Daumann (KL) Vincent Pecoraro (KL)	Christian Hartinger (KL) Arumugam Kuppuswamy (IL) Asish Patra (IL) Sanjay Mandal (IL) Pijus Sasmal (IL) Rupam Dinda (IL) Subhendu Karmakar (OL) Parna Gupta (OL)
16:15 – 16:45	Tea break		
16:45 – 17:30	**Plenary Lecture**: Using Theoretical Spectroscopy in (Bio)Inorganic Chemistry **Frank Neese**, MPI, Mulheim, Germany (Phoenix I and II)		**Session Chair**: Prof. S. Bhattacharya
17:30 – 18:15	**Plenary lecture**: Metalloenzyme megacomplexes involved in the hydrogenotrophic methanogenic pathway **Seigo Sima**, MPI, Marburg, Germany (Phoenix I and II)		
18:30 – 20:00	**Poster Session I**		
20:00 -	**Opening dinner**		

8th January, 2024			
9:00 – 9:45	**Plenary Lecture**: Metal-Oxygen Intermediates in Dioxygen Activation and Formation Reactions **Wonwoo Nam**, Ewha Womans University, South Korea (Phoenix I and II)		**Session chair**: Prof. Shyamalava Mazumdar, TIFR
9:45 – 10:30	**Plenary Lecture**: Chemical Functions of Oxidation Active Species on Metal Complexes **Shinobu Itoh**, Osaka University, Japan (Phoenix I and II)		
10:30-11:00	Tea break		
11:00 – 13:30	**Artificial metalloenzymes and Bio-inspired mimics (Phoenix I)**	**Spectroscopy and Dynamics (Phoenix II)**	**Approaches for Cancer Therapy (Galaxy)**
	Chair: Seigo Sima	**Chair**: Carole Duboc	**Chair**: Christian Hartinger
	Takashi Hayashi (KL) Anabella Ivancich (KL) Kara Bren (KL) Osami Soji (IL) Alexandria Deliz Liang (IL) Patricia Rodriguez-Macia (IL)	Nick Cox (KL) James K McCusker (KL) Lisa Olshansky (IL) Sean Eliot (IL) Soumya Ghosh (OL) Thomas Lohmiller (OL)	Arindam Mukherjee (KL) Nils Metzler-Nolte (KL) Justin Wilson (IL) Malay Patra (IL) Guangyu Zhu (IL) Priyankar Paira (OL) Samya Banerjee (OL) Dulal Musib (OL) Riya Ghanti (OL)
13:30 – 14:30	Lunch		
14:30 – 16:50	**Metalloproteins (Phoenix I)**	**Electronic structure (Phoenix II)**	**Chemical Science Symposium (Galaxy)**
	Chair: Kara Bren	**Chair**: Nick Cox	**Chair**: Serena DeBeer
	Michael T. Green (KL) Jason Shearer (KL) Joshua Telser (IL) P Carver (IL) Ankur Gupta (IL) Dabasis Das (IL) Chandradeep Ghosh (OL)	Gautam Lahiri (KL) Prashanta Ghosh (IL) Gopalan Rajaraman (IL) Wesley Browne (IL) Apparao Draksharapu (IL) Siddhant Dhingra (OL) Sanjib Ganguly (OL) Ravi Kumar (OL)	Jitendra K. Bera (KL) Dibyendu Das (KL) Debabrata Maiti (KL) Pradyut Ghosh (KL)
16:50 – 17:15	Tea break		
17:15 – 18:00	**Plenary Lecture**: Inspired by Nitrogenase: Dihydride Complexes for the H_2 -Releasing Reductive Activation of Challenging Substrates **Franc Meyer**, University of Gottingen, Germany (Phoenix I and II)		**Session chair**: V. Chandrasekhar, IIT Kanpur
18:00 – 18:45	**Plenary Lecture**: Bio-inspired catalyst design for small molecule activation in multi-electron reduction processes **Carole Duboc**, University of Grenoble-Alpes, France (Phoenix I and II)		
19:00 – 20:30	**Poster session II**		

9th January, 2024			
9:00 – 9:45	**Plenary Lecture**: Rational design of the active site in bacterial Cytochrome P450 **Shyamalava Mazumdar**, TIFR Mumbai (Phoenix I and II)		**Session chair**: M. Palaniandavar
9:45-10:00	Tea break		
10:00 – 12:00	**Bio-inspired catalysis (Phoenix I)**	**CO_2 Reduction (Phoenix II)**	**Chemical Science Symposium (Galaxy)**
	Chair: Pradyut Ghosh	**Chair**: Jennifer Yang	**Chair**: Vincent Artero
	Sankar Rath (KL) C.V. Sastri (KL) Way-Zen Lee (IL) Christian Goldsmith (IL) Christian Limberg (IL) Evelina Venckute (OL)	Marc Robert (KL) Ulf-Peter Apfel (IL) Charles McRory (IL) Idan Hod (IL) Ayan Datta (IL) Subal Dey (OL)	Sayam Sengupta (KL) Mi Hee Lim (KL) Liviu Mirica (KL) Timothy Storr (KL)
12:00-13:00	**Group photo session (open air space in Capella, 20th floor)**		
13:00 – 14:00	Lunch		
14:00 – 16:30	**Bio-inspired catalysis (Phoenix I)**	**Bio-inspired Catalysis (CO_2/NO_2) (Phoenix II)**	**Bio-inorganic chemistry of Cu (Galaxy)**
	Chair: Takahiko Kojima	**Chair**: Marc Robert	**Chair**: Liviu Mirica
	David Goldberg (KL) Bas de Bruin (IL) Shiyu Zhang (IL) Joyanta Choudhury (IL) Soumyajit Roy (IL) Nanda Paul (OL) Sudha Yadav (OL) Debashis Adhikari (OL) Nipa Chongdar (OL)	Ally Aukauloo (KL) Smaranda Marinescu (IL) Takehiro Ohsoumyajitta (IL) Regina Trevino (IL) Pankaj Kumar (IL) Pokhraj Ghosh (OL) Uttam Ghorai (OL)	Peter Faller (KL) Isabel Moura (IL) George E Cutsail III (IL) Jalila Simaan (IL) Kaushik Ghosh (IL) Anuj K Sharma (OL) M. Murali (OL) V. Rajendiran (OL) Tanmoy Saha (OL)
16:30 – 17:00	Tea break		
17:00 – 17:45	**Plenary Lecture**: Geometric and Electronic Structural Contributions to Fe/O_2 Reactivity: Correlations between metalloenzyme and heterogeneous catalysis **Edward Solomon**, Stanford University, USA (Phoenix I and II)		**Session chair**: Prof. R.N. Mukherjee, IIT Kanpur
17:45 – 18:30	**Plenary Lecture**: Twists and Turns in Exploring the Reactivity of Nonheme Fe^{IV}=O Complexes: How Critical Is the Iron Spin State? **Lawrence Que Jr.**, University of Minnesota, USA (Phoenix I and II)		
18:30 onwards	**Banquet Dinner** **Chief Guest:** Vinod K Singh, IIT Kanpur Musical performance by "Beat Blasters" Surprising guest-performances By ……you'll have to wait and see 😊		

10th January, 2024			
9:00 – 9:45	**Plenary Lecture:** Bioinspired Fe(IV)-oxido complexes: controlling proton/electron transfer and spin states within mono- and binuclear systems **Andrew Borovik**, UC Irvine, USA (Phoenix I and II)		**Session chair**: Prof. R. Gupta, University of Delhi
9:45 – 10:30	**Plenary Lecture**: 3D Domain Swapping of Metalloproteins: Basics and Recent Development **Shun Hirota**, NAIST, Japan (Phoenix I and II)		
10:30-11:00	Tea break		
11:00 – 13:00	**2nd sphere in bio-inspired catalysis (Phoenix I)**	**Nitrogen and its oxides (Phoenix II)**	**Bio-Inspired Catalysis (O_2) (Galaxy)**
	Chair: Jalila Siman	**Chair**: Jose Moura	**Chair**: Frank Meyer
	Vincent Artero (KL) Arnab Dutta (IL) Raja Angamuthu (IL) James A. Birrell (IL) Gustav Berggren (IL) Suman K Barman (OL)	Kyle M Lancaster (KL) Timothy Warren (KL) Cyrille Costentin (IL) Tsai-Te Lu (IL) Subrata Kundu (IL) Michael O. Lengel (OL)	Tapan K Paine (KL) Kallol Ray (KL) Thierry Tron (IL) Ankan Paul (IL) Karuppasamy Sundaravel (OL) Bittu Chandra (OL) M. Sankarlingam (OL)
13:00 – 14:00	Lunch		
14:00 – 16:00	**Bio-inspired catalysis (Phoenix I)**	**CO/CO_2 (Phoenix II)**	**O_2 (making and breaking) (Galaxy)**
	Chair: RN Mukherjee	**Chair**: Kallol Ray	**Chair**: Gary Brudvig
	Julie Kovacs (KL) Amit Majumdar (IL) Ebbe Norlander (IL) Takahiko Kojima (IL) Gayan Wijeratne (IL) Sagnik Chakrabarti (OL)	Stephen W. Ragsdale (KL) Jose J. Moura (IL) Maria Romao (IL) Sven T. Stripp (IL) Kushal Sengupta (IL) Ayan Bera (OL)	Antoni Llobet (KL) Sukanta Mandal (IL) Galia Mayan (IL) Charles W Machan (IL) Biswajit Mondal (IL)
16:00 – 16:30	Tea break		
16:30 – 17:15	**Plenary Lecture**: Advanced spectroscopic studies of C-H bond activating enzymes and molecular Catalysts **Serena DeBeer,** MPI-CEC, Germany (Phoenix I and II)		**Session chair**: Prof. S. Das, Jadavpur University
17:15 – 18:00	**Plenary Lecture**: Coordination Design of Protein Assemblies from Cage to Crystal **Takafumi Ueno**, Tokyo Institute of Technology, Japan (Phoenix I and II)		
18:30 – 20:00	**Poster session III**		

11th January, 2024			
9:00 – 9:45	**Plenary Lecture**: Nitrogenase: Redox Catalysis out of Bounds **Oliver Einsle**, University of Freiburg, Germany (Phoenix I and II)		**Session chair**: Prof. P. K. Bharadwaj
9:45 – 10:30	**Plenary Lecture**: Structure-Function Studies of the O_2 - Evolving Complex in Photosystem II from Synechocystis sp. PCC 6803 **Gary Brudvig**, Yale University, USA (Phoenix I and II)		
10:30-11:00	Tea break		
11:00 – 13:00	**Metal-Clusters (Phoenix I)**	**Metals in Environment (Phoenix II)**	**Metal Regulation (Galaxy)**
	Chair: Chandan Mukherjee	**Chair**: A. Majumdar	**Chair**: Shinobu Itoh
	Theodore Agapie (KL) Victor Mougel (IL) Bènèdicte Burlat (IL) Rabindra K Behera (IL) Aniket Vartak (IL) Manas Panda (OL)	Eva Freisinger (KL) Pabitra Chatterjee (IL) Gouriprasanna Roy (IL) Sayantan Paria (IL) Soumen K Manna (IL)	Pascale Delangle (KL) Roland K. O. Sigel (IL) Ritika Gautam (IL) Avisek Das (IL) Nikhil Malvankar (IL) Arnab K Nath (OL)
13:00 – 14:00	**Closing session with poster awards** (Phoenix I and II)		
14:00	Lunch and departure		

Lecture Abstracts

07.01.2024

SABIC 2024

DAY-1: 07.01.2024 (Sunday)

07.01.2024

Metal complexes in biological environments: a new frontier in inorganic chemistry

Prof. Clotilde POLICAR

Department of chemistry, Ecole Normale Supérieure (ENS-PSL), PSL-university 24rue Lhomond, 75005 Paris.

Laboratoire des BioMolécules, LBM, Département de chimie, École normale supérieure, PSL University, ENS-PSL, Sorbonne Université, CNRS, 75005 Paris,France

E-Mail : clotilde.policar@ens.psl.eu

Metal complexes are increasingly used for biological applications. Cell penetration, cell distribution and speciation of the metal complexes in biological environment are important to their bio-activity. It is therefore key to study metal complexes meant for therapeutic purposesdirectly in cells or biological environment and correlate bioactivity with information on intracellular distribution and speciation. Microfluorescence X is a rapidely developing technique able to image heavy elements, including metal ions.[1]

The talk will describe our approach for the design of Mn-based catalytic antioxidants mimickingantioxidant enzymes getting inspiration from Mn-superoxide dismutase.[2–4] We will present how we study in cells, including evaluation of the bioactivity, imaging[5,6] and analyses of their speciation.[6,7]

References

1. J. H. Lovett and H. H. Harris, *Curr. Opin. Chem. Biol.*, 2021, **61**, 135–142.
2. C. Policar, in *Redox Active Therapeutics*, eds. I. Batinić-Haberle, J. S. Rebouças and I. Spasojević, Humana Press, published by Springer Nature, 2016, pp. 125–164.
3. E. Mathieu, A.-S. Bernard, E. Quévrain, M. Zoumpoulaki, S. Iriart, C. Lung-Soong, B. Lai, K. Medjoubi, L. Henry, S. Nagarajan, F. Poyer, A. Scheitler, I. Ivanović-Burmazović, S. Marco, A. Somogyi, P. Seksik, N. Delsuc and C. Policar, *Chem. Commun.*, 2020, **56**, 7885–7888.
4. C. Policar, J. Bouvet, H. C. Bertrand and N. Delsuc, *Current Opinion in Chemical Biology*, 2022, **67**, 102109.
5. E. Mathieu, A.-S. Bernard, N. Delsuc, E. Quévrain, G. Gazzah, B. Lai, F. Chain, P. Langella, M. Bachelet, J. Masliah, P. Seksik and C. Policar, *Inorg. Chem.*, 2017, **56**, 2545–2555.
6. G. Schanne, M. Zoumpoulaki, G. Gazzah, A. Vincent, H. Preud'homme, R. Lobinski, S. Demignot, P. Seksik, N. Delsuc and C. Policar, *Oxidative Medicine and Cellular Longevity*, 2022, **2022**, Article ID 3858122.
7. M. Zoumpoulaki, G. Schanne, N. Delsuc, H. Preud'homme, E. Quévrain, N. Eskenazi, G. Gazzah, R. Guillot, P. Seksik, J. Vinh, R. Lobinski and C. Policar, *Angewandte Chemie*, 2022, e202203066.

Illuminating the cell biology of zinc

Amy E Palmer

Department of Biochemistry and BioFrontiers Institute, University of Colorado Boulder, 3415 Colorado Ave, Boulder CO 80303 USA

07.01.2024

There are over two thousand proteins encoded by the human genome that bind zinc, where zinc binding is predicted to be essential for function. At the cellular level zinc is important for DNA synthesis, cell proliferation, differentiation, and apoptosis. Given the importance of Zn^{2+} in cell biology and human health, it is astounding that we still don't understand the mechanisms of how Zn^{2+} levels and dynamics impact basic cellular functions and give rise to disease. Our lab has developed a suite of genetically encoded fluorescent sensors for Zn^{2+} and has used these sensors to quantify Zn^{2+} in different organelles in mammalian cells. Our results reveal that the labile Zn^{2+} pool is very low (hundreds of pM in the cytosol) but that cells experience Zn^{2+} dynamics and fluxes in response to cellular processes and environmental perturbations. Although the conventional view of Zn^{2+} in biology is that it is constitutively and stably bound to the proteins that comprise the zinc proteome, there is growing evidence that the proteome may sense and respond to Zn^{2+} dynamics in cells. This talk will focus on our discoveries that Zn^{2+} dynamics profoundly influence fundamental cellular processes such as gene expression, interactions between transcription factors and chromatin, and the mammalian cell cycle.

07.01.2024

Taming of the Shrew: Controlled Carbon Monoxide Delivery to Combat Malignancies

Pradip K. Mascharak

Department of Chemistry and Biochemistry

University of California, Santa Cruz

The recent surprising discovery of the salutary effects of low doses (50-200 ppm) of carbon monoxide (CO) in diseases like pulmonary arterial hypertension, COPD, and arterial wall lesions from balloon angioplasty has initiated intense research effort toward exploration of the therapeutic benefits of this so-called toxic gas. Results of such studies have also indicated that moderate doses (>250 ppm) of CO causes rapid reduction of cancer cells (but not normal cell) through cell apoptosis via disruption of mitochondrial function. In addition, CO dramatically sensitizes cancer cells to chemotherapy and imparts antiproliferative effect toward colon, breast, ovary, pancreas, and other cancers. Because of its toxic nature, it is however difficult to employ gaseous CO in hospital settings. We have recently shown that photoactive and biocompatible metal carbonyl complexes with designed ligands can deliver suitable doses of CO to cellular targets under the total control of light. In addition, we have shown that these photosensitive CO-releasing molecules (photoCORMs) can be conveniently used to kill human breast and colon cancer cells in a dose-dependent manner through light-induced CO release. Recently we have been successful in incorporating several fluorescent photoCORMs within the pores of silica nanoparticles (SNPs) and have demonstrated (a) their accumulation within cancer cells, (b) fluorescence tracking of the process of CO delivery within the cancer cells, and (c) their eradication by a dose-dependent CO photo delivery. Results from these experiments as well their promise in translation to animal models will be discussed.

Selected References:

1. CO release from Mn(I)-based photoCORMs with Single Photons in the Phototherapeutic Region. *Chem. Commun*. **2021**, *57*, 1101-1105.
2. Light-Assisted and Remote Delivery of Carbon Monoxide to Malignant Cells and Tissues: Photochemotherapy in the Spotlight. *J. Photochem. Photobiol. C: Photochem. Rev.* **2020**, *42*, 10034.
3. Diminished Viability of Human Ovarian Cancer Cells by Antigen-specific Delivery of Carbon Monoxide with a family of Photoactivatable Antibody-photoCORM Conjugates. *Chem. Sci.* **2019**, *11*, 467-473.
4. Therapeutic Potential of Two Visible Light Responsive Luminescent photoCORMs: Enhanced Cellular Internalization Driven by Lipophilicity. *Inorg. Chem*. **2019**, *58*, 14522-14531.
5. A Luminescent Manganese PhotoCORM for CO Delivery to Cellular Targets under the Control of Visible Light. *Inorg. Chem*. **2018**, *57*, 1766-1773.
6. CO-induced Eradication of Colorectal Adenocarcinoma cells by a Luminescent photoCORM grafted on Biocompatible Carboxymethyl Chitosan. *Chem. Commun*. **2017**, *53*, 5519-5522.
7. Synthesis, Structures and CO Release Capacity of a Family of Water-Soluble photoCORMs: Accessment of Biocompatibilty and their Phototoxicity Towards Human Breast Cancer Cells. *Inorg. Chem*. **2017**, 56, 1534-1545.
8. A Theranostic Two-tone Luminescent photoCORM Derived from Rhenium and (2-pyridyl) benzothiazole: Trackable CO Delivery to Malignant Cells. *Inorg. Chem*. **2016**, *55*, 7852-7858.
9. Rapid Eradication of Human Breast Cancer Cells through Trackable Light-triggered CO Delivery by Mesoporous Silica Nanoparticles Packed with a Designed photoCORM. *ACS Chem. Mater*. **2015**, 27, 8387-8397.

Fluorescent probes for monitoring expression and metalation of metallo- beta-lactamase antibiotic resistance enzymes

07.01.2024

Emily L. Que,[a] Sky Price [a], Radhika Mehta[a], Dorothea Hudson[a], Walter Fast[b]

[a] *Department of Chemistry, The University of Texas at Austin, Texas, USA* [a] *Division of Chemical Biology and Medicinal Chemistry, The University of Texas at Austin, Texas, USA*

E-mail: emilyque@cm.utexas.edu

Metallo-β-lactamases (MBLs) grant resistance to a broad spectrum of β-lactam antibiotics including last-resort carbapenems and is emerging as a global antibiotic resistance threat. Limited zinc availability adversely impacts the ability of MBLs to provide resistance, but many clinical variants have emerged that are more resistant to zinc scarcity. To provide novel tools to study metal ion sequestration in host-pathogen interactions and the dynamic metalation state of MBLs in these contexts, we are developing fluorescent probes that bind to the dizinc of active site of The development of reversible turn-on fluorescent probes for the metalation state of MBLs provides a means to monitor the impact of metal ion sequestration by host defense mechanisms and to detect inhibitor target engagement during the development of therapeutics to counter this resistance determinant. Recent developments in our lab along this research theme will be discussed.

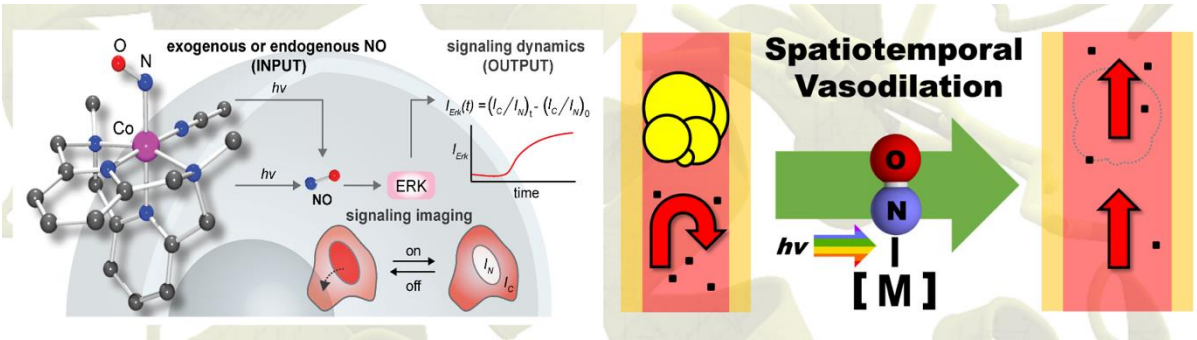
07.01.2024

A Photo-Responsive Iron Nitrosyl Complex for Vasodilation

Jaeheung Cho

Department of Chemistry, UNIST, Ulsan 44919, Korea

The development of metallodrugs, a class of therapeutic agents containing metal ions, has emerged as a crucial avenue in modern medicinal chemistry. Their unique properties and interactions offer distinct advantages, revolutionizing the landscape of drug design, and opening new possibilities for targeted treatments and enhanced therapeutic efficacy. Retinal vascular occlusion is a prevalent cause of visual impairment. While various approaches, including vasodilators, have been investigated for the treatment, there is currently no effective method available. Herein, we present a novel strategy for treating vascular occlusions by using a photo-responsive iron-nitrosyl complex, $[Fe(TBDAP)(NO)(H_2O)]^{2+}$ (**1**), which acts as a spatiotemporally controllable nitric oxide transporter. Complex **1** was synthesized and characterized using various chemicophysical techniques including X-ray crystallography. Its ability to selectively dilate normal retinal blood vessels and reperfuse the occluded vessels was demonstrated in animal disease models.



References

"Artificial control of cell signaling using a photocleavable cobalt(III)-nitrosyl complex" *Angew. Chem. Int. Ed.* 58, 10126, **2019**.

"Photodynamic treatment of acute vascular occlusion by using an iron-nitrosyl complex" *Chem*, 9, 1309, **2023**.

Development of 'Smart' MRI Contrast Agents for Diagnosis of Diabetes and Early-Stage Detection of Cancer

07.01.2024

Chandan Mukherjee[1]

[1]Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati 781039, Assam, India.

Email: cmukherjee@iitg.ac.in

Magnetic resonance imaging in the presence of a contrast agent has emerged as an indispensable non-invasive imaging modality for the early-stage diagnosis of many diseases. [1] Nevertheless, the primary challenge remained to develop biogenic, thermodynamically stable and kinetically inert contrast agents with a high relaxivity value. In this endeavor, mononuclear, mono(aquated), and thermodynamically stable Mn(II) complexes of hexadentate chelating ligands have been explored. The complexes-impregnated porous silica nanoparticles with surface functionalization have been investigated to achieve “Zn(II) ion-responsive” and “folate-receptor- selective” smart contrast agents for diagnosis of diabetes (beta-cells) and early-stage detection of cancer, respectively. The concentration-dependent changes in the image intensities in T1- and T2-weighted phantom images put forward the biocompatible nanoparticles as a potential dual-mode MRI contrast agent. Furthermore, organ- specific *in vivo* studies have reinforced the applicability of the newly established systems. The synthesis and contrast ability of the newly developed bare and porous silica nanosphere-entrapped systems will be discussed in detail.

References:

[1] Wahsner, J.; Gale, E. M.; Rodríguez-Rodríguez, A.; Caravan, P. Chemistry of MRI Contrast Agents: Current Challenges and New Frontiers. Chem. Rev. 2019, 119, 957-1057.

07.01.2024

Smart Fe(II/III)-Based MRI Contrast Agents

Ramasamy Mayilmurugan*

Department of Chemistry, Indian Institute of Technology Bhilai, Durg, Bhilai, India

Email: murugan@iitbhilai.ac.in

Our inorganic chemical biology projects focus on MRI and optical imaging of intracellular nitric oxide (NO), L-cysteine, and pH environment of cancer cells. We have successfully designed and synthesized several Fe(II) macrocyclic ligand complexes demonstrated as pH-responsive PARACEST MRI contrast agents (CAs). Our group recently showed that the rhodamine appended high spin Fe(III)-O6 complexes as dual-modal T1 MRI/optical imaging agents for imaging tumor cells' NO and acidic pH environments. The MRI unit has functioned through second-sphere water interactions. The functionalization of this MRI core Fe(III)-O6 with C_{12}-alkyl chain conjugates and interaction with external marker IR780 dye forms an aggregated matrix. It functioned as a smart "MRI-ON-Fluorescence ON" imaging agent for imaging acidic pH environments of tumor cells. Further, the biotin group is conjugated to the MRI core Fe(III)-O6 for delivering larger amounts of Fe(III) CA. The biotin attachment increased the 'payload' of CA in the tumor environment by targeting biotin metabolism and providing better visualization of cancer cells. In addition, several other Fe(III) and Mn(II/III) complexes are synthesized as redox-responsive T1-CAs. Specifically, a series of Mn(III) complexes of 1,4-diazepane-based bisphenolate ligands are reported as redox-active CA. They are found to be sensitive towards the biological redox buffer molecule L-cysteine (Cys).

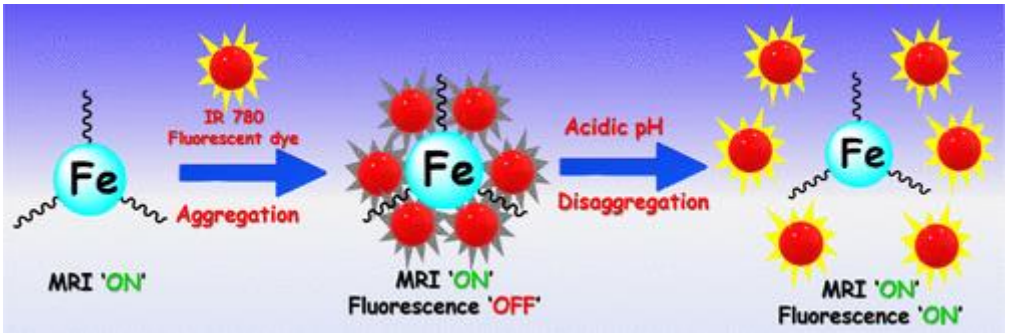


Figure 1. Smart Fe(III)-based MRI probing mechanism for tumor cell imaging..

References:

(1) Maheshwaran, D.; Senthil Kumaran, S.; Mayilmurugan, R. *ACS Biomater. Sci. Eng.* **2023**, *9*, 3570-3580. Maheshwaran, D.; Nagendraraj, T.; Balaji, S.; Kumaresan, G.; Senthil Kumaran, S.; Mayilmurugan, R. *Dalton Trans.* **2020**, *49*, 14680; Bond, C. J.; Sokolow, G. E.; Crawley, M. R.; Burns, P. J.; Cox, J. M.; Mayilmurugan, R.; Morrow, J. R. *Inorg. Chem.* **2019**, *58*, 8710.; Priyanga, S.; Khamrang, T.; Velusamy, M.; Karthi, S.; Ashokkumar, B.; Mayilmurugan, R. Dalton Trans. **2019**, *48*, 1489.; Maheshwaran, D.; Priyanga, S.; Mayilmurugan, R. *Dalton Trans.* **2017**, *46*, 11408.; Maheshwaran, D.; Nagendiraj, T.; Mayilmurugan, R. *Eur. J. Inorg. Chem.* **2017**, 1007.

Stimuli-Responsive Turn-On Fluorogenic Processes toward theDelivery of Hydrogen Sulfide and Drugs

07.01.2024

Krishna P. Bhabak

Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati-781039

E-mail id: kbhabak@iitg.ac.in

Owing to the enormous side-effects of many drugs during their direct administration, the specific stimuli-responsive drug delivery from the suitable prodrugs has attracted wide research attention. However, the proper and consistent monitoring of the drug delivery process from the non-fluorogenic prodrugs is the major inconvenience. The development of specific stimuli-activatable turn-on fluorogenic probes/prodrugs is advantageous for the convenient and real-time monitoring of the drug delivery processwith high level of sensitivity. Moreover, the drug-induced toxicities could be reduced further by the adjuvant delivery of gasotransmitters such as hydrogen sulfide (H2S). The present talk will primarily highlight our recent strategies in developing the bio- analyte-responsive turn-on fluorogenic donors of H2S (gasotransmitter)[1,2] and the anti-cancer/ anti-inflammatory drugs along with H2S[3-5] (Figure 1).

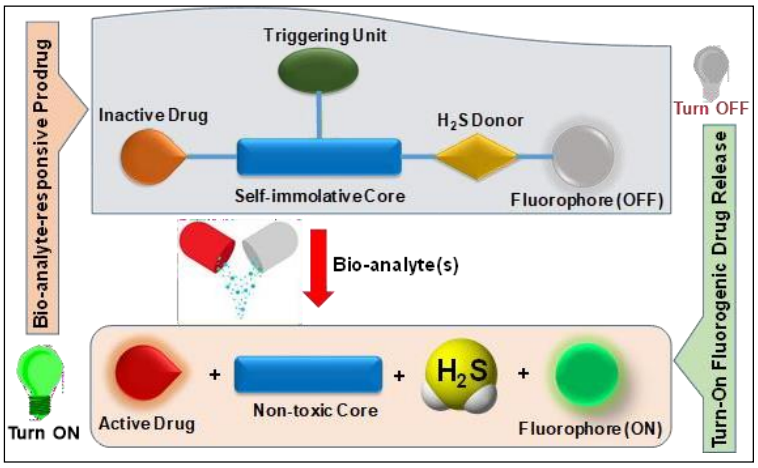


Figure 1. Schematic representation of the turn-on fluorogenic drug delivery strategies.

References:

1. Mahato, S. K.; Bhattacherjee, D.; Bhabak, K. P.; *Chem Commun*, **2020**, *56,* 7769-7772.
2. Mahato, S. K.; Bhattacherjee, D.; Barman, P.; Bhabak, K. P.; *J Mater Chem B*, **2022**, *10*, 2183-2193.
3. Sufian, A.; Bhattacherjee, D.; Barman, P.; Srivastava, A.; Thummer, R. P.; Bhabak, K. P. *Chem. Commun.* **2022**, *58*, 7833-7836.
4. Mahato, S. K.; Barman, P.; Badirujjaman, Md.; Bhabak, K. P. *Chem. Commun*., **2023**, *59*,4802-4805.
5. Sufian, A.; Badirujjaman, Md.; Barman, P.; Bhabak, K. P. *Chem. Eur. J.* **2023** (*in press*)

07.01.2024

Photolysis of cobalamins produces olefin products: in-situ monitoring of photochemistry and product formation

Alivia Mukherjee, Roseanne Sension, Nicolai Lehnert*, James Penner-Hahn*

Department of Chemistry and Department of Biophysics, The University of Michigan, Ann Arbor, Michigan 48109-1055, United States

The role of sunlight in Nature is frequently misconstrued as being exclusively linked to photosynthesis, despite the existence of numerous other photochemical processes occurring in plants and microorganisms. The recent discovery of the importance of photosensitivity in CarH and its involvement in regulating carotenoid production in response to light, has piqued interest among researchers. When Adenosylcobalamin (AdoCbl or coenzyme B_{12}) in CarH is photoexcited, it causes the tetrameric CarH to dissociate into monomers, which then release the bound DNA, upregulating carotenoid production and protecting the organism from photooxidative damage. There is mechanistic uncertainty underlying CarH's ability to safeguard DNA from damage. It accomplishes this by transforming 5'-deoxyadenosyl radicals into the non-reactive compound 4',5'-anhydroadenosine, which is a departure from the cyclic product typically observed after AdoCbl illumination. Our work employs time-resolved and steady-state photolysis experiments to investigate the unusual reactivity of the adenosyl radical. In contrast to earlier photolytic studies, in an anaerobic environment, we form a stable Cob(II)alamin photoproduct, which does not require the presence of a radical trap for its generation. Our data demonstrate a possible alternative pathway, diverging from the proposed mechanism that Co-hydride formation is pivotal in the formation of the alkene product in the transcriptional regulator CarH. Time-resolved absorption spectroscopy experiments on AdoCbl instead indicate that alkene photoproduct(s) are formed under single-turnover conditions without formation of Co-hydride. These results further our understanding of the photochemical behavior of cobalamins, which can help in elucidating mechanistic details of CarH and other cobalamin-dependent photoresponsive proteins.

References:

1. Takano, H.; Mise, K.; Hagiwara, K.; Hirata, N.; Watanabe, S.; Toriyabe, M.; Shiratori-Takano, H.; Ueda, K.; DiRita, V. J. Role and Function of LitR, an Adenosyl B12-Bound Light-Sensitive Regulator of Bacillus megaterium QM B1551, in Regulation of Carotenoid Production. *J. Bacteriol.* **2015**, *197*, 2301-2315.
2. Jost, M.; Fernández-Zapata, J.; Polanco, M. C.; Ortiz-Guerrero, J. M.; Chen, P. Y.-T.; Kang, G.; Padmanabhan, S.; Elías-Arnanz, M.; Drennan, C. L. Structural basis for gene regulation by a B12-dependent photoreceptor. *Nature* **2015**, *526*, 536-541.
3. Ortiz-Guerrero Juan, M.; Polanco María, C.; Murillo Francisco, J.; Padmanabhan, S.; Elías-Arnanz, M. Light-dependent gene regulation by a coenzyme B12-based photoreceptor. *Proc. Natl. Acad. Sci. U.S.A.* **2011**, *108*, 7565-7570.
4. Bam, R.; Pollatos, A. S.; Moser, A. J.; West, J. G. Mild olefin formation via bio-inspired vitamin B12 photocatalysis. *Chem. Sci.* **2021**, *12*, 1736-1744.
5. Toda, M. J.; Mamun, A. A.; Lodowski, P.; Kozlowski, P. M. Why is CarH photolytically active in comparison to other B12-dependent enzymes? *J. Photochem. Photobiol. B: Biol.* **2020**, *209*, 111919.

The active sites of copper oxygenases and their reactivity with H_2O_2

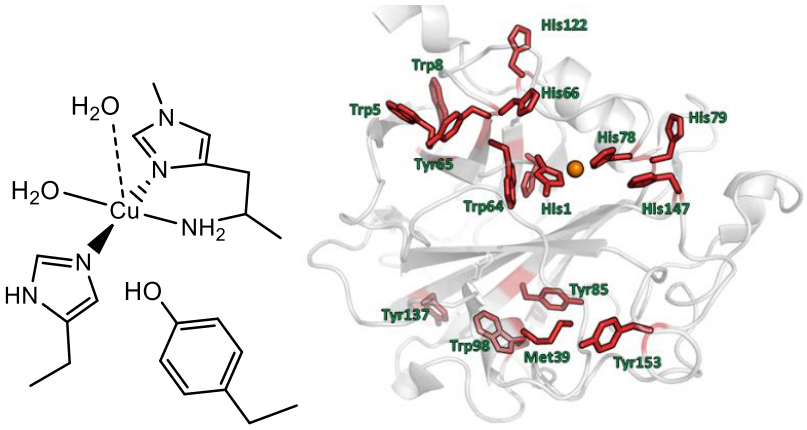
Paul H. Walton

Department of Chemistry, University of York, Heslington, York, UK, YO10 5DD

paul.walton@york.ac.uk

07.01.2024

Lytic polysaccharide monooxygenases (LPMOs) are relatively recently discovered enzymes that catalyse the oxidation of polysaccharides, leading to chain cleavage. LPMOs has transformed our understanding of biomass degradation, and—moreover—are now critical components in the enzymatic breakdown of biomass in the second generation bioethanol industry.[1] We and others have also recently shown that LPMOs are key virulence factors in major plant diseases.[2]



Active site structure of an LPMO and oxidized amino acids (red) following treatment with H_2O_2.

We have also examined the action of oxidizing agents on the enzyme which has been shown to enhance the activity of the enzymes on saccharidic substrates, but also lead to rapid inactivation of the enzyme, presumably through protein oxidation.[3] In this talk, in addition to a description of the structure and reactivity of LPMOs, I will show that the use of UV/vis, CD, XAS, EPR, MCD, MS and resonance Raman spectroscopies augmented with DFT calculations, reveals the way in which copper oxygenases deal with oxidizing species generated from uncoupled turnover of peroxide in the absence of substrate.[4]

[1] K. E. H. Frandsen, P. H. Walton *et al*, *Nature Chem. Biol*. 298—303 (2016).
[2] F. Sabbadin, P. H. Walton *et al*, *Science*, **373**, 774-779 (2021).
[3] A. Paradisi, P. H. Walton *et al, J. Am. Chem. Soc*. 18585—18599 (2019).
[4] J. Zhao, P. H. Walton *et al*, *J. Am. Chem. Soc*. 20672–20682 (2023).

07.01.2024

Pre-Designing Fluorescent Chemical Sensors for Imaging Metal Ions in Living Systems

Ankona Datta

Department of Chemical Sciences, Tata Institute of Fundamental Research, 1 Homi Bhabha Road, Mumbai, India; ankona@tifr.res.in

Redox-active metal ions like Cu, Fe, and Mn are essential co-factors required for enzyme function. Labile or weakly bound pools of these metal ions have been implicated in neural function, signaling, immunity against pathogens, and importantly as anti-oxidants. Impaired regulation of these metal ions, is however, linked to severe pathological conditions including multiple neurological disorders and cancers. Tracking the localization and distribution changes of metal ions within living systems using fluorescent metal ion sensors can afford insights into metal ion homeostasis and also guide therapeutic routes for metal-induced and related disorders. Looking into the future, metal ion sensor design and development requires a rational workflow along with most importantly the ability to design and synthesize multiple variants of a working sensor, based on the biological context. Thus far our research group at TIFR has utilized insights from coordination chemistry to design, synthesize, and develop novel fluorescent sensors for detecting biologically-relevant metal ions,[1] with a focus on Mn(II) sensing and recently Cu(II/I) sensing.[2-4] In our molecular sensing journey, we realized on multiple occasions the necessity for developing strategies where sensors could be pre-designed with precisely predictable outcomes. In this talk, I will briefly describe our metal ion sensing journey, challenges that we faced, and elaborate our maiden attempt in the computationally-guided design of metal ion sensors that we have recently experimentally realized.[5]

References:

1. Das, S.; Khatua, K.; Rakshit, A.; Carmona, A.; Sarkar, A.; Bakthavatsalam, S.; Ortega, R.; Datta, A., Emerging chemical tools and techniques for tracking biological manganese. *Dalton Transactions* **2019,** *48* (48), 7047-7061.

2. Gupta, K.; Datta, A., An activity-based fluorescent sensor with a penta-coordinate N-donor binding site detects Cu ions in living systems. *Chemical Communications* **2023,** *59* (53), 8282-8285.

3. Das, S.; Carmona, A.; Khatua, K.; Porcaro, F.; Somogyi, A.; Ortega, R.; Datta, A., Manganese Mapping Using a Fluorescent Mn^{2+} Sensor and Nanosynchrotron X-ray Fluorescence Reveals the Role of the Golgi Apparatus as a Manganese Storage Site. *Inorganic Chemistry* **2019**.

4. Bakthavatsalam, S.; Sarkar, A.; Rakshit, A.; Jain, S.; Kumar, A.; Datta, A., Tuning macrocycles to design 'turn-on' fluorescence probes for manganese(II) sensing in live cells. *Chemical Communications* **2015,** (51), 2605-2608.

5. Kahali, S.; Das, S.; Kundu, R.; Gupta, K.; Bhattacharya, B.; Nath, A.; Datta, A., A Water-soluble, Cell-permeable Mn(II) Sensor Enables Visualization of Manganese Dynamics in Live Mammalian Cells. *ChemRxiv, 10.26434/chemrxiv-2023-d4fp9* **2023**.

Chemistry in Confined Nanospace

Partha Sarathi Mukherjee

Department of Inorganic and Physical Chemistry, Indian Institute of Science, Bangalore- 560012, India. E-mail: psm@iisc.ac.in

The chemical and physical properties of chemical entities in confined nanospace are often different from their usual bulk behavior due to the restricted rotational and translational motions. Design of discrete coordination architectures and light-promoted chemical reactions in their confined space will be presented. My lecture will also focus on our recent observation on the role of the shape of reaction vessels on the fate of chemical reaction (Figure 1). Aqueous molecular architecture for the separation of isomeric polyaromatic hydrocarbons by simple aqueous extraction will be focused.

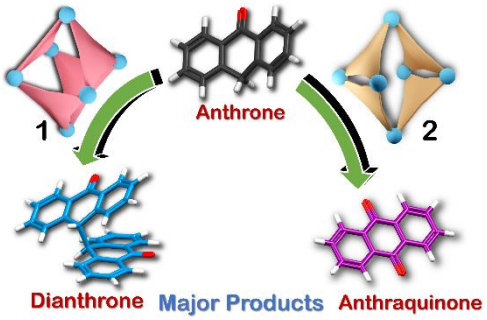


Figure 1 Cavity-shape dependent divergent synthesis.

References:

1. Howladar, P.; Mondal, B.; Chowdhury, P.; Zangrando, E.; Mukherjee, P. S. *J. Am. Chem. Soc.* **2018**, *140*, 7952.

2. Arppitha, B. S.; Venkataswarulu, M.; Bhandari, P.; Clegg, J.; Mukherjee, P. S. *J. Am. Chem. Soc.* **2022**, *144,* 7504.

3. Howlader, P.; Zangrando, E.; Mukherjee, P. S. *J. Am. Chem. Soc.* **2020**, *142,* 9070.

4. Banerjee, R.; Chakraborty, D.; Chan, Y. T.; Mukherjee, P. S. *Angew Chem. Int. Ed.* **2023**, *62,* e202305338.

5. Saha, R.; Mondal, B.; Mukherjee, *Chem. Rev.* **2022**, *122*, 12244.

6. Banerjee, R.; Chakraborty, D.; Mukherjee, P. S. *J. Am. Chem. Soc.* **2023**, *145,* 7692.

7. Chakraborty, D.; Ali, S.; Chowdhury, P.; Neil, H.; Mukherjee, P. S. *J. Am. Chem. Soc.* **2023**, *145,* in press.

07.01.2024

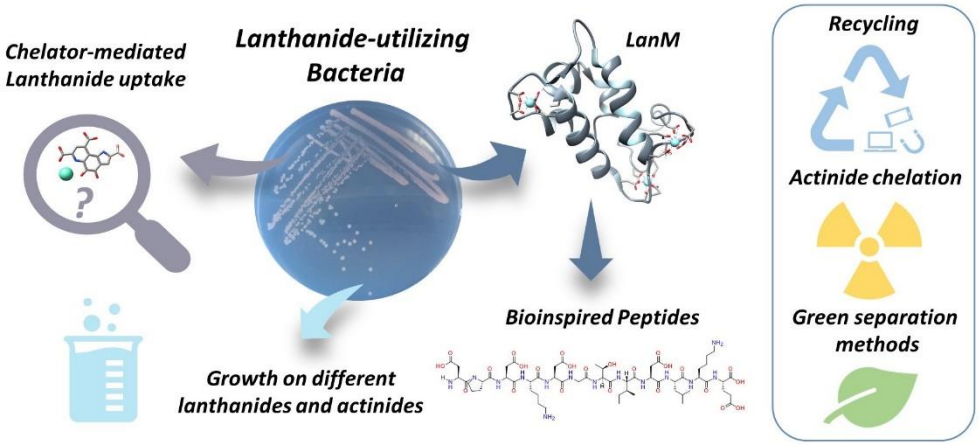
A decade of surprises: Biological relevance of lanthanides (and actinides) for bacteria - a perspective

Lena Daumann

Heinrich-Heine-Universität Düsseldorf, Chair of Bioinorganic Chemistry, Universitätsstr. 1, 40225 Düsseldorf

Lanthanides (Ln) are essential ingredients sprinkled in a multitude of applications in our daily life, especially important for sustainable and clean energy applications and for medicinal applications. However, owing to their chemical similarity, separation of Ln is tedious. In the past decade, the role of Ln for many bacteria has been firmly established, and bacterial strains that take up Ln and use them in the active sites of quinone-dependent methanol dehydrogenases (MDH) have been extensively studied.[1] Our studies with the strictly lanthanide-dependent extremophile *Methylacidiphilum fumariolicum* SolV and demonstrate, that the trivalent actinides americium and curium can also support growth in the absence of the essential lanthanides. In fact, the bacteria seem make no distinction between lanthanide and actinide ions if they have the correct size and oxidation state.[2] From Ln-using bacteria, proteins and small chelators with remarkable selectivity and affinity for lanthanides have been identified that have the potential to be used in ln separation and recycling.[3-7] This lecture aims to give a glimpse on the developments in this new field of lanthanide-dependent bacterial metabolism and will present the structure and metal binding investigation of the first lanthanophore (small molecule chelator similar to siderophores).

Figure 1 Bacteria that use Ln have evolved several biomolecules capable of binding Ln and actinides.



References:

[1]L.J. Daumann *Angew. Chem. Int. Ed.* **2019**, *58*, 12795.

[2]H. Lumpe et al. *Chem. Eur. J.* **2020**, *26*, 10133.

[3]H. Singer *et al. Angew. Chem. Int. Ed.* **2023**, *62*, e202303669

[4]J. Cotruvo *et al. J. Am. Chem. Soc.* **2018**, *140*, 15056

[5]S. Gutenthaler *et al. Inorg. Chem. Front.* **2022**, 9, 4009.

[6]H. Singer *et al. Chem. Sci.* **2021**,*12*, 15581.

Siderophores to Supramolecules: The Road to Luminescent Metallacrowns

07.01.2024

Vincent L. Pecoraro[a], Elvin Salerno[a], Tim Lathion[a,b], Alex Falco[a,c], Soroush Naseri[a], Sahil Kapila[a], Svetlana Eliseeva[b], Stephane Petoud[b], Mateo Tegoni[c]

[a]Department of Chemistry, University of Michigan, Ann Arbor; [b]Centre Biophysiques Moleculaire, CNRS, Orleans; [c]Department of Inorganic Chemistry, University of Parma

Ken Raymond has been a major contributor to both the fields of siderophore chemistry and metallosupramolecular assembly. He also has founded a company that developed the most efficient emissive Tb coordination complex. This contribution will show how hydroxamic acid ligands (from siderophores) can be used to assemble metallosupramolecular structures (metallacrowns) that have exceptional properties for stimulating Near Infrared emission from lanthanides such as Yb(III) and Er(III).

07.01.2024

From Protein-targeted Anticancer Agents to Understanding Metal Complex–Protein Interactions

Christian G. Hartinger

University of Auckland, School of Chemical Science, Auckland 1010, New Zealand

c.hartinger@auckland.ac.nz

Bioactive metal complexes are often considered promiscuous in their binding to proteins, in that they interact with a variety of proteins and a multitude of amino acids on a protein surface can be metallated. This confuscates the identification of specific interactions of relevance and bioactivity, as not all metalation events will contribute equally or may even be detrimental. The exception to this observation is the organometallic anticancer agent plecstatin-1, which was found to bind to plectin.[1]

In this contribution, I will discuss concepts we use in anticancer metallodrug design (Figure 1) and metallomics strategies to interrogate their modes of action. I will focus on the impact of ligand structures on the binding of their organometallic complexes to proteins,[2] which will be complemented by observations of unexpected reactions and surprising behavior in the presence of these biomolecules.[3] These studies lead us to develop an improved understanding of the driving forces for protein surface metalation and selectivity for some sites over others. Overall, it appears as a combination of parameters contributes to the selectivity of binding including primary and secondary protein structures, steric demand of metal complex co-ligands and the presence of surface grooves with complementary features to those of the binding metal moieties that facilitate hydrophobic and/or electrostatic interactions.

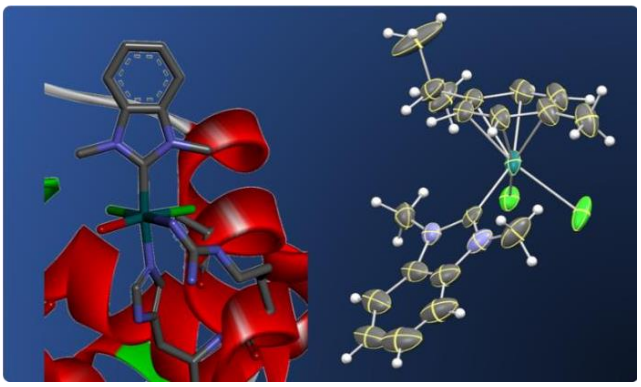


Figure 1. Unconventional adducts formed between anticancer organometallics and proteins.

References

[1] a) T. R. Steel, F. Walsh, A. Wieczorek-Błauż, M. Hanif, C. G. Hartinger, *Coord. Chem. Rev.* **2021**, *439*, 213890; b) W. D. J. Tremlett, D. M. Goodman, T. R. Steel, S. Kumar, A. Wieczorek-Błauż, F. P. Walsh, M. P. Sullivan, M. Hanif, C. G. Hartinger, *Coord. Chem. Rev.* **2021**, *445*, 213950.

[2] a) D. Truong, M. P. Sullivan, K. K. H. Tong, T. R. Steel, A. Prause, J. H. Lovett, J. W. Andersen, S. M. F. Jamieson, H. H. Harris, I. Ott, C. M. Weekley, K. Hummitzsch, T. Söhnel, M. Hanif, N. Metzler- Nolte, D. C. Goldstone, C. G. Hartinger, *Inorg. Chem.* **2020**, *59*, 3281-3289; b) M. Hanif, J. Arshad,

J. W. Astin, Z. Rana, A. Zafar, S. Movassaghi, E. Leung, K. Patel, T. Söhnel, J. Reynisson, V. Sarojini, R. J. Rosengren, S. M. F. Jamieson, C. G. Hartinger, *Angew. Chem., Int. Ed. Engl.* **2020**, *59*, 14609-14614.

[3] M. P. Sullivan, M. Cziferszky, I. Tolbatov, D. Truong, D. Mercadante, N. Re, R. Gust, D. C. Goldstone, C. G. Hartinger, *Angew. Chem., Int. Ed. Engl.* **2021**, *60*, 19928-19932.

07.01.2024

Gold-based Next Generation Cancer Therapeutics

Meredith Miles, Kevin Sidoran, Selvakumar Jayaraman, Dilsha SamanaliWickramasinghe and Kuppuswamy Arumugam

Department of Chemistry, Wright State University, 3640 Colonel Glenn Hwy, Dayton,USA

Gold(I) complexes containing N-heterocyclic carbenes have shown great promise as cancer treatment drugs because of their ability to target thiol-functional groups found in the Thioredoxin Reductase (TrxR) system.[1] The inhibition of TrxR coupled with thegeneration of reactive oxygen species (ROS) by exogenous agents has proven to beeffective in inducing apoptosis in cancer cell lines.[2] The results presented in here illustrate that the dual targeting approach of reducing ROS tolerance while increasingROS production leads to antioxidant homeostasis. This perturbs the system from bothends thus overwhelming the network and promoting cell death.[2] To achieve such a systems-based approach to targeting the antioxidant pathway, ferrocene[2] and quinone[3] functionalized N-heterocyclic carbene Au(I) complexes were designed, synthesized, and biologically tested in a series of human cancer cells. This presentation will detail our recent findings in dual targeting cancer drug design.

References:

[1] S. J. Berners-Price and A. Filipovska, *Metallomics*, **2011**, *3*, 863-873.
[2] McCall, R., Sidoran, K., Magda, D., Mitchell, N., Bielawski, C., Lynch, V., Sessler, J. andArumugam, K., *Chem. Sci*., **2016**, *7*, 1245-1256.
[3] McCall, R., Miles, M., Kocerha, J., Sittaramane, V., Burney, B., Patel, Z., Sideman, J. K., Grossi, A.D., Sessler, L. J., Arumugam, K., and Arambulaa, F. J., *Chem. Sci*., **2017**, *8*, 5918-5929.

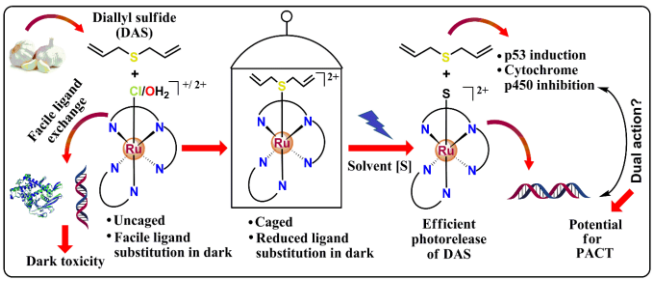
07.01.2024

Modulation of Electronic Structures & Photochemistry of Ruthenium Complexes for Therapeutic Applications

Ashis K. Patra
Department of Chemistry, Indian Institute of Technology Kanpur, Kanpur 208016, U.P., India, E-mail: akpatra@iitk.ac.in

Ruthenium coordination chemistry offers diverse structural flexibility and stereochemistries, accessible and tunable redox and electronic properties, ligand substitution kinetics for reactions with biotargets or metabolites, etc.[1] Moreover, Ru(II) complexes offer exciting and tunable photophysical properties involving the deactivation of photo-excited states via photo-substitution reactions. Therefore, with a rational design approach and understanding of the electronic nature of ligands at the molecular level, we can have spatiotemporal control on the selective release of bioactive ligands to precisely target certain biological processes that optimize their therapeutic potential.[2] We are engaged in studying and optimizing new-generation cytotoxic Ru-complexes compounds aiming for improved therapeutic efficacy with multi-targeted synergistic effects.[3-6] Studying the photophysics and photochemistry of Ru(II)-based photocages for developing cytotoxic photochemotherapeutic compounds offers unique advantages in photochemotherapies (PDT/PACT).

In this presentation, I will highlight a few rational design principles with strategic conjugation of bioactive ligands and varying polypyridyl ligands to alter their excited electronic states, lipophilicity, and ROS generation efficiencies.[3-5] Recently, we reported thorough photochemistry studies of a series of Ru(II) polypyridyl-based photocages for anticancer phytochemical diallyl sufide (DAS).[6] Ru(II)-DAS caged molecules show reasonable dark stability, while undergoing facile ligand-photo substitution in visible light, satisfying an important criteria for spatiotemporal control for selective obliteration of cancer with photoactivated chemotherapy (PACT).



References:

1. R. G. Kenny, C. J. Marmion, *Chem. Soc. Rev.* **2019**, *119*, 1058-1137.
2. S. Bonnet, *J. Am. Chem. Soc*. **2023**, *145*, 23397-23414.
3. P. Srivastava, M. Shukla, G. Kaul, S. Chopra, A. K. Patra, *Dalton Trans.*, **2019**, *43*, 15139-15152.
4. P. Kumar, I. Mondal, R. Kulshreshtha, A. K. Patra, *Dalton Trans.*, **2020**, *49*, 13294-13310.
5. P. Srivastava, M. Verma, A. Kumar, P. Srivastava, R. Mishra, S. Sivakumar and A. K. Patra, *Dalton Trans.*, **2021**, *50*, 3629-3640.
6. R. Mishra, A. Saha, P. Chatterjee, A. Bhattacharyya, A. K. Patra, *Inorg. Chem.* **2023**, 10.1021/acs.inorgchem.3c02038.

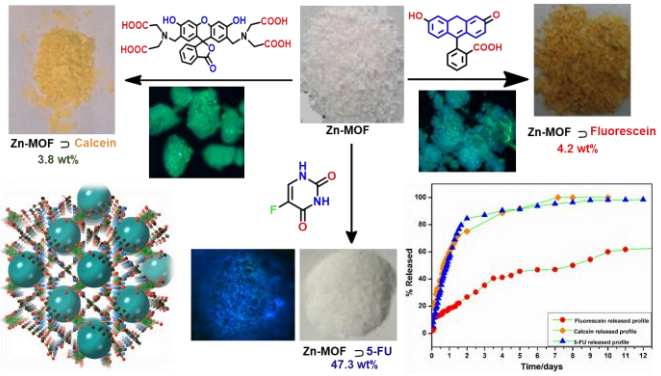
07.01.2024

Nanoscale Anti-Cancer Drug Delivery by a Smart and Biocompatible Metal-Organic Framework Carrier

Sanjay Mandal

Department of Chemical Sciences, IISER Mohali, Sector 81, SAS Nagar, Mohali, PB 140306, INDIA

Porous functional metal-organic frameworks (MOFs) have been targeted for theirs potential in biomedical applications, specifically in drug delivery systems, due to high surface areas, tailorable pore sizes, tunable functionalities, etc. In order to contribute to this emerging field, we designed a Zn-MOF of a bioactive triazine-based tetracarboxylate displaying good biocompatibility and efficient nano carrier property in the presence of 5-fluorouracil (5-FU), calcein, and fluorescein. We employed different spectroscopic techniques and simulation to follow its drug loading capacity. The Zn-MOF effectively demonstrated the selective encapsulation of electron-rich 5-FU molecules through electrostatic attraction, achieving a relatively high loading capacity of up to 47.3 wt%. The release of all drugs was performed in PBS buffer at pH 7.4 (simulated blood environment). The strong host-guest interactions provided 82% and 97% release of 5-FU after 2 and 12 days, respectively, which is a medically reasonable rate. Additionally, cytotoxicity of the 5-FU loaded Zn-MOF was performed in presence of breast cancer cells and showed good biocompatibility.



References:

(1) Keskin, S.; Kızılel, S. *Ind. Eng. Chem. Res.* **2011**, *50*, 1799–1812.
(2) Bernini, M. C.; Fairen-Jimenez, D.; Pasinetti, M.; Ramirez-Pastor, A. J.; Snurr, R. Q. *J. Mater. Chem. B* **2014**, *2*, 766-774.
(3) Parsaei, M.; Akhbari, K. *Inorg. Chem.* **2022**, *61*, 5912−5925.
(4) Hu, Z.; Qiao, C.; Xia, Z.; Li, F.; Han, J.; Wei, Q.; Yang, Q.; Xie, G.; Chen, S.; Gao, S. *ACS Appl. Mater. Interfaces* **2020**, *12*, 14914−14923.
(5) Dong, Z.; Sun, Y.; Jun Chu, J.; Zhang, X.; Deng, H. *J. Am. Chem. Soc.* **2017**, *139*, 14209−14216.

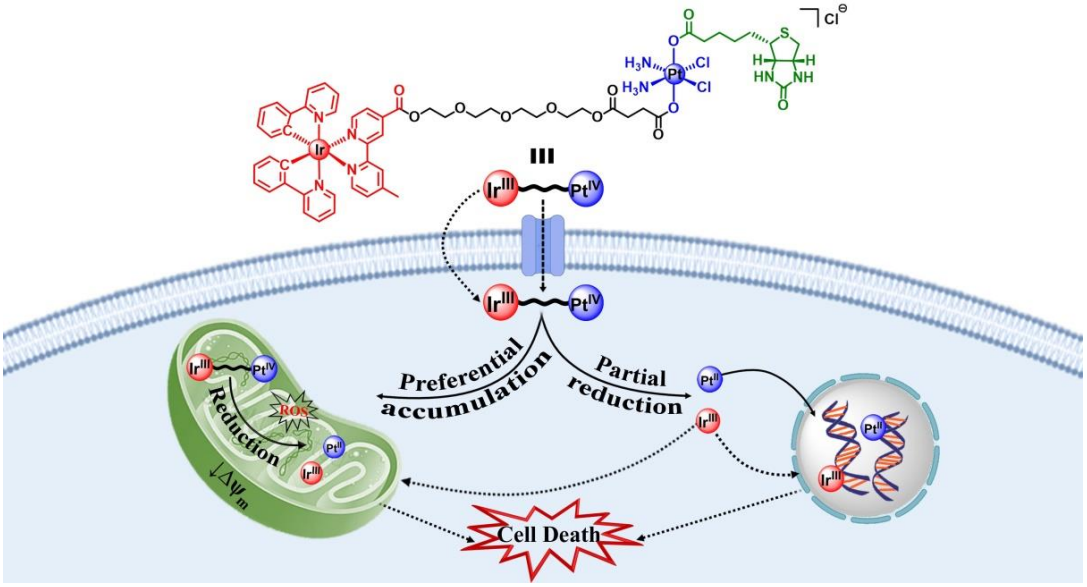
Mitochondria-Targeted Heterobimetallic Iridium(III)-Platinum(IV) Conjugates as Potent Anticancer Theranostic Agents

07.01.2024

Pijus K. Sasmal

School of Physical Sciences, Jawaharlal Nehru University, New Delhi 110067, India

Abstract: Pt(IV) prodrugs have emerged as a promising alternative to circumvent the drawbacks of Pt(II)-based anticancer drugs, namely cisplatin, carboplatin and oxaliplatin.[1] The Pt(IV) prodrugs can be activated by intracellular reducing agents (*e.g.,* glutathione, ascorbate) to generate cytotoxic Pt(II) congeners which are well-known to accumulate in the nucleus. Recently, researchers have demonstrated that mitochondrial dysfunction causes several diseases, including cancer.[2] Therefore, we have developed a new class of heterobimetallic Ir(III)-Pt(IV) (**IriPlatin**) conjugates as mitochondria-targeted potent anticancer theranostic agents.[3] The conjugates preferentially accumulate within the mitochondria of cancer cells due to the attachment of mitochondria targeting cyclometalated Ir(III) complexes with Pt(IV) prodrug and demonstrate potent anticancer activity in various 2D monolayer cancer cells, including the cisplatin-resistant cells in the low nanomolar concentrations and 3D multicellular tumor spheroids. The mechanistic investigation of conjugates suggests that the loss of MMP, generation of ROS, and caspase-3 mediated apoptosis are responsible for cell death. The design, anticancer activity, and in-depth mechanistic investigation of **IriPlatin** conjugates will be discussed in the presentation.



References:

1. Johnstone, T. C.; Suntharalingam, K.; Lippard, S. J. *Chem. Rev.* **2016**, *116*, 3436–3486.
2. Vyas, S.; Zaganjor, E.; Haigis, M. C. *Cell* **2016**, *166*, 555–566.
3. Gupta, A.; Pandey, A. K.; Mondal, T.; Bhattacharya, J.; Sasmal, P. K. *J. Med. Chem.* **2023**, *66*, 8687–8704.

07.01.2024

Recent advances in the use of luminescent organotin(IV) complexes for cytotoxicity and cellular imaging

Rupam Dinda* and Sushree A. Patra
Department of Chemistry, National Institute of Technology, Rourkela, Odisha- 769008, India

Over recent decades, among the main group compounds, heavier group 14 complexes are currently receiving enormous attention due to their exclusive cytotoxic and imaging properties *in vitro* and *in vivo*. Precisely, tin(IV) complexes have emerged as desirable candidates in the field of molecular imaging due to their unique structural and photophysical properties.[1] Nowadays, compounds with luminescent properties are essential in diagnosis and therapeutic uses. A fluorescent compound with low cytotoxicity, high photostability, and organelle specificity would help in the diagnosis of physiological disorders related to that specific organelle. In short, it can act as a real-time tracking bioimaging agent. Similarly, fluorescent compounds with high cytotoxic properties help in evaluating the cell death mechanism more accurately. Till now many organotin(IV) compounds have been studied as cytotoxic agents. However, their mechanistic pathways of cell death are still less explored. In the field of bioimaging, to date hardly any tin(IV) compounds are reported as organelle-specific markers. In light of this trend, our group has recently started working in organotin(IV) chemistry integrating different types of O- and/or N- and/or S- donor ligands.[2,3] Few of the studied compounds exhibited very promising results. Therefore, the encouraging findings from the biological investigations of organotin(IV) complexes will offer a fresh avenue for investigating the potential applications of these organotin complexes in "biomedical molecular imaging," or the diagnosis and therapeutic uses. Here in this presentation, I will basically focus on some of the recent interesting results of my group obtained from this luminescent tin(IV) chemistry and their applications.

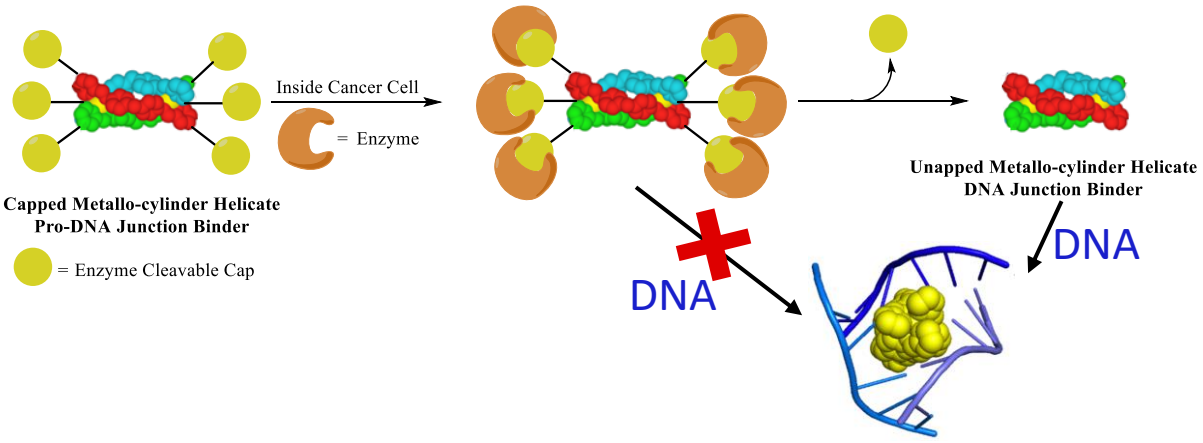
References:
1) G. Sahu, S. A. Patra, P. D. Pattanayak and R. Dinda*, *Chem. Commun.*, 2023, 59, 10188
2) S. A. Patra, G. Sahu, D. Mohapatra, P. D. Pattanayak, and R. Dinda*, *Organometallics*, 2023, 42, 1934.
3) S. A. Patra, G. Sahu, P. D. Pattanayak, T. Sasamori and R. Dinda*, *Inorg. Chem.*, 2022, 61, 16914.

Turning On DNA Junction Binding in Cancer Specific Condition

Subhendu Karmakar and Michael J. Hannon

School of Chemistry, University of Birmingham, Birmingham, B15 2TT, UK,

Email: s.karmakar@bham.ac.uk; m.j.hannon@bham.ac.uk



Metal-based cancer therapeutics (platin drugs) serve crucial roles in clinics.[1] DNA is the prime target of these drugs which are effective against various types of cancer but come with side-effects and toxicities.[2, 3] They were not designed to act selectively on cancer cells and the best (cisplatin) was discovered serendipitously. Supramolecular chemistry allows us to design various molecular architectures that can interact with nucleic acids, selectively by non-covalent interactions.[4] Our research group have pioneered tetra-cationic triple-stranded metallo-cylinder helicates that recognise Y-shaped DNA three-way junction (3WJ) structures resembling DNA replication forks. The result is powerful agents that target the specific structure responsible for cancerous cell DNA replication.[5-7] We are now seeking designs that are targeted to a specific location and so will be selective just for cancer cells. We have derivatized a metallo-cylinder helicate with groups that prevents DNA binding but can be cleaved by the enzyme (NAD(P)H:quinone oxidoreductase 1, NQO1) overexpressed in many cancers[8,9] so that the DNA recognition by the metallo-cylinder will only be possible in the cancer cell. We show that the pro-DNA junction binder itself does not bind DNA 3WJs in gel electrophoresis, but in the presence of the NQO1 the groups are cleaved and the DNA 3WJ binding is switched on. In presence of an NQO1 inhibitor the binding remains switched off. The pro-DNA junction binder does not show binding to broader genomic DNA structures by circular and linear dichroism studies.

References:

1. Apps M. G. and Wheate N. J. *et al. Endrocr-Relat. Cancer.* **2015**, *22*, R219; **2**. Oun R. and Wheate N. J. *et al. Dalton Trans.* **2018**, *47*, 6645; **3**. Galluzzi L. and Kroemer G. *et al. Oncogene.* **2012**, *31*, 1869; **4**. Hannon M. J. *Chem. Soc. Rev.*, **2007**, *36*, 280; **5**. Hooper C. A. J. and Hannon M. J. *et al. J. Am. Chem.* Soc. **2020**, *142*, 20651; **6**. Hotze A. C. G. and Hannon M. J. *et al. Chem. Biol*. **2008**, *15*, 1258; **7**. Cardo L. and Hannon M. J. *et al. Sci. Rep.* **2018**, 13342; **8**. Danson S. *et al. Cancer. Treat. Rev.* **2004**, *30*, 437; **9**. Zhang K. and Jiang S. *et al. J Med. Chem*. **2018**, *61*, 6983.

07.01.2024

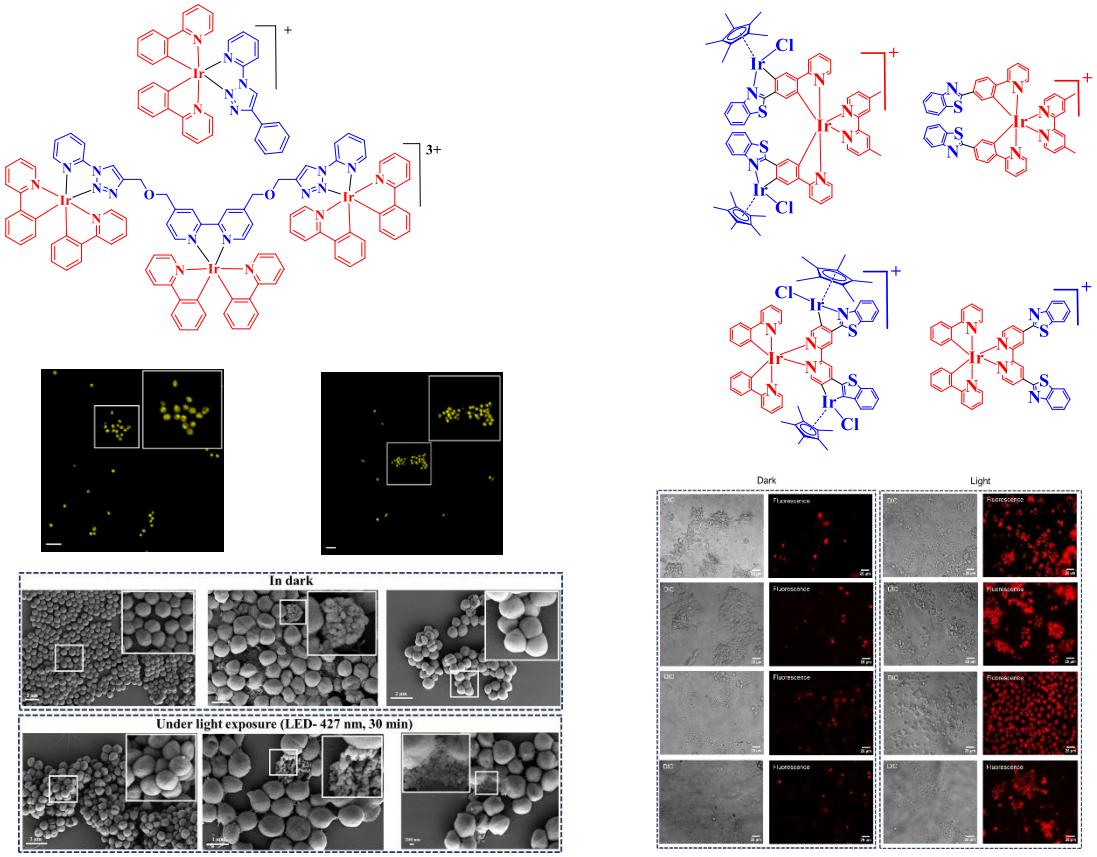
Mono and Trinuclear Cyclometalated Iridium(III) Complexes: Cellular and bacterial imaging, Anticancer/Antimicrobial Photodynamic therapy

Bishnu Das,[1] Subhadeep Gupta,[2] Anushka Mandal,[2] Amirul I Mallick[2] and Parna Gupta[1]

[1]Department of Chemical Sciences, [2]Department of Biological Sciences,

IISER Kolkata, Mohanpur, Nadia, West Bengal - 741246

Luminescent cyclometalated iridium(III) complexes have emerged as potential cellular imaging agents and can drive apoptotic or necrotic cell death through photodynamic processes. We present here the organelle-specific localization, Differential bacterial imaging, photodynamic therapeutic potential of mono and trinuclear organometallic iridium(III) complexes in human MCF7 breast carcinoma cells and Methicillin-resistant *Staphylococcus aureus* (MRSA) with mono and trinuclear iridium(III) complexes.



References:

1. B. Das, S. Gupta, A. Mondal, K. J. Kalita, A. I. Mallick* and Parna Gupta*, *J. Med. Chem.* 2023, ASAP, https://doi.org/10.1021/acs.jmedchem.3c01875
2. B. Das, P. Biswas, A. I. Mallick* and Parna Gupta*, **Under Review.**

Using Theoretical Spectroscopy in (Bio)Inorganic Chemistry

Frank Neese[1]

[1]Max Planck Institute für Kohlenforschung, Kaiser-Wilhelm Platz 1, 45470 Mülheim an der Ruhr, Germany

Bioinorganic Chemistry has a great tradition of using advanced spectroscopy to get insight into the structure and mechanism of metalloenzymes. Since the active sites in such enzymes often feature unique geometric structures with complex and unprecedented electronic structures, deductions based on fingerprinting alone often have limited validity. Hence, successful data interpretation is frequently only possible by combining experiment and quantum chemistry. Over the course of the last three decades, we have developed the ORCA program suite that is specifically designed to aid in this endeavor. While ORCA has grown into a widely used, powerful general purpose quantum chemistry tool, it has unique capabilities for treating metalloenzyme active sites. In the talk, I will provide an outline of the general approach we are following upon treating actual problems in (bio)inorganic catalysis and will also comment on the increased capabilities of ORCA 6.0 which will be released in early 2024.

07.01.2024

Metalloenzyme megacomplexes involved in the hydrogenotrophic methanogenic pathway

Seigo Shima[1], Shunsuke Nomura[1], Pablo San Segundo[2] & Bonnie Murphy[2]

[1]Max Planck Institute for Terrestrial Microbiology, Karl-von-Frisch Straße 10, 35043 Marburg, Germany and 2Max Planck Institute of Biophysics, Max-von-Laue-Str. 3, 60438 Frankfurt am Main, Germany

Most methanogenic archaea produce methane, a potent greenhouse gas, by reducing CO_2 through the hydrogenotrophic methanogenic pathway as an energy metabolism [1]. Formylmethanofuran dehydrogenase (Fmd) catalyses the reduction of CO_2 to form formylmethanofuran. Fmd contains molybdopterin or tungstopterin as a prosthetic group at the CO_2 reducing active site [2]. The low potential electrons required for the reduction of CO_2 are derived from the flavin-based electron bifurcation reaction catalysed by the heterodisulfide reductase (Hdr) complex [3], in which Hdr is complexed with an electron donor module; hydrogenase (Mvh) or formate dehydrogenase (Fdh). In some methanogens, Fmd and the Hdr complex are known to form a megacomplex in which low-potential electrons are directly transferred to Fmd via polyferredoxin [4]. In this talk, we will present survival strategies of methanogens under nickel-limited conditions, where [Fe]-hydrogenase becomes the main H_2-activating enzyme instead of [NiFe]-hydrogenases and a novel electron-donating module complexes with Hdr. We will also discuss the electron transfer mechanism in the Mvh/Fdh-Hdr-Fmd megacomplexes.

References:

1. Shima, S., Huang, G., Wagner, T. & Ermler, U. (2020) Structural basis of hydrogenotrophic methanogenesis. *Annu Rev Microbiol* **74**, 713-733.
2. Wagner, T., Ermler, U. & Shima, S. (2016) The methanogenic CO_2 reducing-and-fixing enzyme is bifunctional and contains 46 [4Fe-4S] clusters. *Science* **354**.
3. Wagner, T., Koch, J., Ermler, U. & Shima, S. (2017) Methanogenic heterodisulfide reductase (HdrABC-MvhAGD) uses two noncubane [4Fe-4S] clusters for reduction. *Science* **357**, 699-702.
4. Watanabe, T., Pfeil-Gardiner, O., Kahnt, J., Koch, J., Shima, S. & Murphy, B. J. (2021) Three-megadalton complex of methanogenic electron-bifurcating and CO_2-fixing enzymes. *Science* **373**, 1151-1155.

08.01.2024

SABIC 2024

DAY-2: 08.01.2024 (Monday)

08.01.2024

Metal-Oxygen Intermediates in Dioxygen Activation and Formation Reactions

Wonwoo Nam

Department of Chemistry and Nano Science, Ewha Womans University, Seoul 120-750, Korea

Dioxygen is essential in life processes, and enzymes activate dioxygen to carry out a variety of biological reactions. One primary goal in biomimetic research is to elucidate structures of reactive intermediates and mechanistic details of dioxygen activation and oxygenation reactions occurring at the active sites of enzymes, by utilizing synthetic metal-oxygen complexes. A growing class of metal-oxygen complexes, such as metal–superoxo, –peroxo, –hydroperoxo, and –oxo species, have been isolated, characterized spectroscopically, and investigated in various oxygenation reactions. During the past decade, we have been studying the chemical and physical properties of various reactive intermediates in oxygenation reactions, such as high-valent iron(IV)- and manganes(V)-oxo complexes of heme and non-heme ligands in oxo-transfer and C-H activation reactions, non-heme metal-peroxo complexes in nucleophilic reactions, and non-heme metal-superoxo complexes in electrophilic reactions. The effects of supporting and axial ligands on structural and spectroscopic properties and reactivities of metal-oxygen adducts have been extensively investigated as well. In this presentation, I will present our recent results on the synthesis and structural and spectroscopic characterization of mononuclear nonheme metal-dioxygen intermediates as well as their reactivities in electrophilic and nucleophilic oxidation reactions.

08.01.2024

Chemical Functions of Oxidation Active Species on Metal Complexes

Shinobu Itoh

Department of Molecular Chemistry, Division of Applied Chemistry,
Graduate School of Engineering, Osaka University

Oxidation reactions utilizing reactive species generated on metal ions are important processes in biological reactions and various catalytic reactions. A typical example is dioxygen (O_2) activation on iron and copper metal ions in the enzyme active sites. Although it appears to be a simple reaction, the diversity in structure, physicochemical properties, and reactivity of the generated reactive oxygen species makes it difficult to control them. In metalloenzyme active centers, this is accomplished by skillfully exploiting the coordination geometry of the metal centers, electronic interactions with the coordinating atoms, and weak interactions in the secondary coordination sphere. Metalloenzymes are also known to cooperate with redox-active amino acid side chains (phenol group of tyrosine, thiol group of cysteine, indole group of tryptophan, *etc*.), coenzymes, or organic cofactors in the enzyme active site to perform the various enzymatic functions. Inspired by the essence of such metalloenzyme functions, we have been trying to create various metal-oxidizing active species and exploring their functions and catalytic applications. These studies are important not only for the elucidation of enzyme functions but also for the development of new catalysts.

In this lecture, our studies on the following subjects are introduced: [1] Model studies on newly found amino acid derived redox active organic cofactors. [2] Dioxygen activation by copper and nickel complexes. [3] Molecular mechanism of type-3 copper proteins and application.

Shinobu Itoh, *et al.* Active Site Models for Galactose Oxidase and Related Enzymes, *Coord. Chem. Rev*. **198**, 3-20 (2000).

Shinobu Itoh, *et al.* Monooxygenase Activity of Type-3 Copper Proteins, *Acc. Chem. Res.* **40** (7), 592–600 (2007).

Shinobu Itoh, Developing Mononuclear Copper–Active-Oxygen Complexes Relevant to Reactive Intermediates of Biological Oxidation Reactions, *Acc. Chem. Res.* **48** (7), 2066-2074 (2015).

Shinobu Itoh, *et al.* Controlling Dicopper Protein Functions, *Bull. Chem. Soc. Jpn.* **2016***, 89 (7),* 733–742 (2016).

Shinobu Itoh, Generation and Functions of Oxidation Active Metal Species, *Bull. Jpn. Soc. Cord. Chem*. **81**, 3-19 (2023).

08.01.2024

Artificial Metalloenzymes with Myoglobin Heme Pocket Scaffolds

Takashi Hayashi

Department of Applied Chemistry, Graduate School of Engineering, Osaka University, 2-1 Yamadaoka, Suita 565-0871, Japan

Myoglobin is a well-known hemoprotein responsible for the binding and storage of dioxygen. The heme cofactor binds to the protein matrix via non-covalent and coordination interactions, whereas native myoglobin exhibits little or no enzymatic activity as seen in hemoenzymes such as cytochrome P450 and peroxidase. Therefore, it is quite challenging to convert myoglobin to an artificial metalloenzyme. Our group has focused on the myoglobin modification over two decades, particularly the replacement of heme with artificial metalloporphyrinoids as a cofactor. The removal of the heme cofactor from myoglobin can easily provide an apoprotein as a useful reaction scaffold where an artificial cofactor can be inserted into the vacant heme pocket. The obtained proteins have been found to exhibit enzymatic activities toward peroxidation, hydroxylation, nitrile synthesis or cyclopropanation.[1] In this talk, recent results on hydroxylation of inert alkane C–H bonds and cyclopropanation of olefins via metal-oxo and metal-carbene species, respectively, will be presented.

Porphycene, a constitutional isomer of porphyrin, is very attractive as a ligand for artificial metallocofactors, and myoglobins reconstituted with iron, manganege and cobalt porphycenes are available. Particularly, it is found that the axial histidine in myoglobin strongly coordinates to iron porphycene compared to native heme.

Hydroxylation of inert C(sp^3)–H bond is one of the challenging reactions in organic synthesis. Although myoglobin has same heme cofactor as seen in cytochrome P450s, the hydroxylation activity cannot be detected. In contrast, myoglobin reconstituted with manganese porphycene is found to catalyze the C–H bond hydroxylation of alkanes.[2] Enantioselectivity is observed by mutanted protein matrices.

Cyclopropanation of styrene with ethyl diazoacetate, an abiological reaction, is accelerated by myoglobin reconstituted with iron porphycene. Furthermore, the reaction intermediate was successfully detected by transient UV-vis spectra using a stopped-flow apparatus. Theoretical study supports the fact that iron porphycene is an appropriate cofactor for the formation of the carbene species.[3]

References:

1. K. Oohora, A. Onoda, T. Hayashi, *Acc. Chem. Res. 52*, 945 (2019).
2. K. Oohora, H. Meichin, Y. Kihira, H. Sugimoto, Y. Shiro, T. Hayashi, *J. Am. Chem. Soc. 139*, 18460 (2017).
3. K. Oohora, H. Meichin, L. Zhao, M. W. Wolf, A. Nakamura, J. Hasegawa, N. Lehnert, T. Hayashi, *J. Am. Chem. Soc. 139*, 17265 (2017).

De novo heme catalysts: synthetic α-helical coiled-coils with unprecedented heme&Trp redox cofactors for bioinspired catalysis

Anabella Ivancich

CNRS, Research Unit UMR 7281, CNRS & Aix-Marseille University. Marseille,France.

Heme (Fe^{III} protoporphyrin IX) is an essential cofactor in metalloproteins being involved in fundamental biological processes such as oxidative metabolism, oxygen storage and transport, signal transduction and drug metabolism. The heme site of heme-containing proteins is rather versatile, thus catalyzing a variety of biologically- relevant chemical reactions ranging from the disproportionation of H_2O_2 (catalases[1]),oxidation and haloperoxidation of organic substrates (monofunctional heme peroxidases [2], bi-functional catalase-peroxidases[1]) to oxygenation reactions (cyt P450 monooxygenases and nitric oxide synthases[2]). Such a functional versatility mainly relies on differences in the heme coordination (*i.e*. Tyr, His, or Cys as axial ligands) and on the 2nd sphere coordination to the heme iron. The heme active site forms the (Fe^{IV}=O $Por^{\ddot{Y}+}$) intermediate as highly-oxidizing species for catalysis, the latter being enhanced by the concerted reactions with specific Trp/Tyr being the oxidation sites in the catalytic cycle with the (Fe^{IV}=O $Trp^{\ddot{Y}}$) or (Fe^{IV}=O $Tyr^{\ddot{Y}}$) intermediates allowing heme enzymes to accomplish reactions unattained by the heme-only, such as anti-tuberculosis prodrug activation by KatG bi-funcional peroxidases [3a] or biomass bioconversion by lignin peroxidases [3b]. Exploiting *de novo* metalloprotein design [4], we are developing novel artificial catalysts with heme&Trp redox cofactors, mimicking the strategies used by the natural catalysts/heme enzymes. We have obtained an unprecedented artificial protein with aheme cofactor, using the self-assembling GRAND peptides (three stranded colied- coils in the apo form), in which heme can coordinate to either His or Cys as a functionof pH [5], thus mimicking peroxidases or cyt P450 monooxygenases, respectively, allin one single artificial metalloprotein. Modified peptide sequences that are expected tomodify the distal side of the Cys-coordinated heme or the pKa of the Cys16 ligand to the heme, as well as introducing a site to stabilize a Trp radical formed subsequently to the (Fe^{IV}=O $Por^{\ddot{Y}+}$) intermediate, will be discussed.

[1] Ivancich, A., Loewen, P.C. Electron Transfer in Catalases and Catalase-Peroxidases, *Encyclopediaof Biophysics,* **2018**, Ed. Roberts, G. and Watts A., Springer. DOI: 10.1007/978-3-642-35943-9_51-1. [2] Poulos, T. L. *Chem. Rev.* **2014**, *114*, 3919-3962.

[3] (a) Singh, R., Switala, J., Loewen, P.C., **Ivancich, A**. *J. Am. Chem. Soc.* **2007**, 129, 15954-15963. (b) Smith, A.T., Doyle, W.A., Dorlet, P., **Ivancich, A**. *Proc. Natl. Acad. Sci. USA* **2009**, 106, 16084-16089.

[4] Koebke, K.J., Pinter, T.B.J., Pitts, W.C., Pecoraro, V.L. *Chem. Rev.* **2022**, *122*, 12046-12109.
[5] Koebke, K., Kuhl, T., Schopp-Cothenet, B., Lojou, E., Demler, B., Iranzo, O., Pecoraro, V.L., Ivancich,A. *Angew. Chem. Int. Ed.***, 2021**, *60*, 3974-3978.

08.01.2024

Cobalt Cytochrome Catalysts for CO_2 Conversion

Alison A. Salamatian[a], Jose L. Alvarez-Hernandez[a], Linda Leone[b], Angela Lombardi[b], Kara L. Bren*[a]

[a]Department of Chemistry, University of Rochester, Rochester, NY 14627-0216, USA

[b]Department of Chemical Sciences, University of Naples Federico II, Complesso Universitario Monte S. Angelo, via Cintia 45, 80126 Naples, Italy

Developing CO_2 as a building block for a range of products is of high interest. A primary challenge in the activation and conversion of CO_2 to useful products is suppressing the competing hydrogen evolution reaction. For catalysts functioning in water, a desired solvent and proton source, selectively reducing CO_2 is particularly challenging. Here, we report the use of cobalt-substituted cytochrome *c* derivatives as well as a synthetic cytochrome *c* mimic ("mimochrome") for the electrochemical and photochemical reduction of CO_2 to CO, achieving selectivity for CO production exceeding 90%. In electrocatalytic systems, we demonstrate that selectivity depends on applied potential and the pK_a of the proton source (in water, protonated buffer), and propose that avoiding formation of a formal Co(I) species and the use of relatively basic proton donors favors CO over H_2 production. Advances toward applying these concepts to photochemical systems for CO_2 reduction will be reported.

08.01.2024

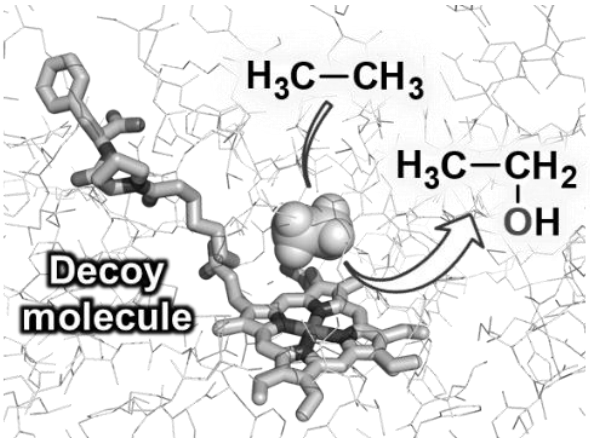
Use of Decoy Molecules to Manipulate P450BM3 Biotransformations

Osami Shoji

Department of Chemistry, Graduate School of Science, Nagoya University,

Furo-cho, Chikusa-ku, Nagoya, 464-8602, Japan

Cytochrome P450BM3 (P450BM3) is one of the most promising P450s as potential biocatalysts for applications in green synthetic chemistry, as they possess high activity for the hydroxylation of inert substrate C–H bonds. Because the substrate-binding is crucial for the generation of active species of P450BM3 (Compound I), substrates whose structures are primarily different from that of their native substrates (long-alkyl-chain fatty acids) cannot be hydroxylated by P450BM3. To enable oxidation of non-native substrates by P450BM3 without any mutagenesis, we have developed a series of "decoy molecules," inert dummy substrates, with structures resembling native substrates. Decoy molecules fool P450BM3 into generating Compound I, enabling the catalytic oxidation of non-native substrates other than fatty acids. The catalytic activity for non-native substrate hydroxylation was significantly enhanced by employing perfluorinated carboxylic acids modified with amino acids (PFC-Amino acids). Recently, we have demonstrated that various amino acids (N-acyl amino acids), as well as amino acid dimers having a completely different structure from fatty acids, can serve as decoy molecules. Benzene was more efficiently hydroxylated in the presence of these decoy molecules. We also have confirmed that wild-type P450BM3 expressed in *E.coli* can be activated by adding amino acid derivatives as decoy molecules to the culture medium, and benzene was hydroxylated without supplementing with NADPH. Activities of the whole-cell biocatalyst drastically varied depending on the structure of decoy molecules added to the cell suspension, suggesting that the difference in permeability between decoy molecules may affect the activation of intracellular P450BM3. The phenol yield reached 59 % when N-heptyl-L-prolyl-L-phenylalanine (C7-Pro-Phe) was employed as the decoy molecule. More recently, we have succeeded in further enhancing the catalytic activity for benzene and gaseous alkane hydroxylation by systematic screening of decoy molecules. Furthermore, we have found that one of the decoy molecules can accelerate the crystallization of P450BM3 and reported crystal structures of the various flavours of P450BM3.



References: *Angew. Chem. Int. Ed.* **2020,** *59* (19), 7611-7618. *ChemCatChem* **2019,** *11* (19), 4709-4714. *Angew. Chem. Int. Ed.* **2018,** *57* (38), 12264-12269. *Angew. Chem. Int. Ed.* **2022**, 61, e202111612.

08.01.2024

Metalloenzyme engineering with non-canonical amino acid incorporation

Sandro Fischer, Anton Natter, Benjamin Manser, Alexandria Deliz Liang

University of Zurich, Winterthurerstrasse 190, Zurich, CH, 8057

Metalloenzymes are rich targets for protein engineering. The scope of directed evolution with the 20 proteinogenic amino acids is, however, limited for direct mutation of the primary coordination sphere. The incorporation of non-canonical amino acids into proteins can help address this limitation. In this work, we look at expanding the scope and efficiency of non-canonical amino acid incorporation to create and apply new tools for engineering metalloenzymes. Addressing efficiency of incorporation of non-canonical amino acids is focused on high-throughput engineering of aminoacyl-tRNA synthetase/tRNA pairs. For our application of non-canonical amino acid engineering of metalloenzymes, we specifically target copper- and zinc-binding enzymes, which have flexible coordination chemistry. Herein, we describe the design of new non-canonical amino acids to test hypotheses for structure-function relationships based on fundamental inorganic coordination chemistry principles. From these studies, we find that changes in enzymatic activity can often be predicted from such principles, but additional factors should be considered with semi-rational selection of non-canonical amino acid incorporation.

Expanding the Biocatalytic Toolbox for Sustainable Chemistry: Semi-synthetic and Artificial Metalloenzymes for Energy Conversion

Patricia Rodriguez-Macia

School of Chemistry and Leicester Institute for Structural and Chemical Biology, University of Leicester, University Road, Leicester, LE1 7RH, UK

Reactions such as H_2 production or sequestration and fixation of atmospheric CO_2 are central for limiting global warming and renewable energy storage. Yet, they still represent challenges for industry.[1] Studying natural metalloenzymes is important to answer fundamental questions in chemistry and biology as well as to develop design criteria for producing new efficient catalysts for sustainable energy conversion and storage.

Hydrogenase are key metalloenzymes for H_2 metabolism, operating at very high rates under ambient conditions using only Earth-abundant metals. [FeFe] hydrogenases display the highest activity and reversibility among all hydrogenases. Their unique organometallic active site, the H-cluster, consists of two subsites linked via S-Cys: a catalytic binuclear iron subsite coordinated by the biologically unusual CN^- and CO strong-field ligands, and a canonical [4Fe-4S] cluster. In addition to the H-cluster, many [FeFe] hydrogenases also contain accessory iron-sulfur clusters serving as electron relays between the buried active site and the protein surface.[2] [FeFe] hydrogenases can now be produced in high yield and purity by using a semi-synthetic approach where the apo-enzyme (i.e. the enzyme lacking the active site) is recombinantly produced in *E. coli* and subsequently reconstituted *in vitro* with chemically synthesised active-site cofactors.[3]

In this talk, I will show how the semi-synthetic approach can be applied to study mechanistic aspects of these fascinating enzymes, as well as to produce semi-synthetic and artificial metalloenzymes with modified active sites to explore novel reactivities. We have independently modified both the protein scaffold and the active-site cofactor to screen different combinations and produce a set of new semi-synthetic and artificial metalloenzymes to seek for novel properties. Various hydrogenase families as well as *de novo* designed peptides are being explored as protein scaffolds, together with synthetic active-site cofactors with different combinations and substitutions of the strong-field ligands and bridgehead groups. The structure and reactivity of the semi-synthetic and artificial systems have been investigated in detail by a combination of spectroscopic techniques alongside electrochemistry and X-ray crystallography. This has helped to elucidate the role of the biologically-unique coordination environment of the active-site H-cluster in hydrogenases, toward the generation of artificial metalloenzymes to introduce new-to-nature reactions into the bioinorganic toolbox.

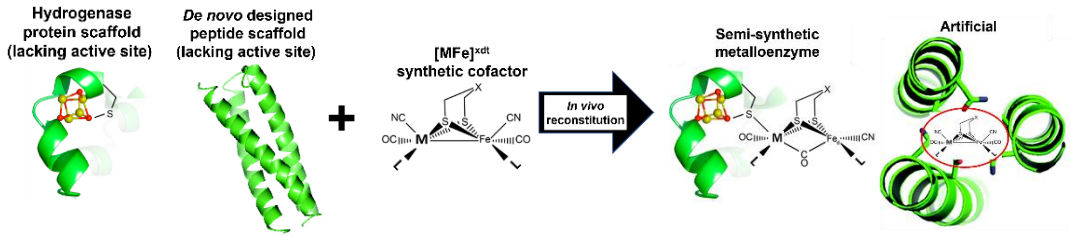


Figure 1: Scheme showing *in vitro* reconstitution of natural and artificial protein scaffolds with synthetic cofactors.

References: [1]Yue *et al., Renewable Sustainable Energy Rev.* **2021**, *146*, 111180; [2]Birrell *et al., Coord. Chem. Rev.* **2021**, *449*, 214191**;** [3]Berggren et al., *Nature* **2013**, *499*, 66–69

Activation of the Mn_4CaO_5 cofactor of Photosystem II as studied by High Field EPR and MCD spectroscopy

J. Langley[a]*, J. Morton[a], R. Purchase[a], J-R. Shen[b], E. Krausz[a], N. Cox[a]

[a]Research School of Chemistry, Australian National University, Canberra, Australia;

[b]Research Institute for Interdisciplinary Science and Graduate School of Natural Science and Technology, Okayama University, Okayama, Japan

*nick.cox@anu.edu.au

The structure of the S_3 state of the Mn_4CaO_5 of Photosystem II (PSII) was recently reported using high field EPR spectroscopy [1] and XFEL crystallography [2-3]. It is this 'final' meta-stable S_3 state that proceeds to O_2 formation step following a further photo-oxidation event. These data are consistent with an all octahedral Mn^{IV} complex, requiring an additional water molecule to bind to cofactor to during the S_2 to S_3 transition, but the precise mechanism of water molecule insertion remains unclear. Historically, two approaches have been used to investigate intermediates of the S-state cycle that cannot be readily trapped and characterized: i) chemical modification of the cofactor; and ii) low temperature photochemistry. Here we describe new high field EPR and MCD data targeting intermediates of the S_2 to S_3 transition.

i) High Field EPR data of chemical modified forms of the S_3 state are consistent with the cofactor adopting two, structural distinct forms. These data include Ca^{2+}/Sr^{2+} ion exchange, the binding of substrate analogs and the pH dependence of the S_2 to S_3 transition [4].

ii) MCD identifies the chromophore(s) responsible for the low temperature photochemistry of the cofactor - a series of sharp bands assigned to Mn^{IV} ($^4A_2 \rightarrow {}^2E$) spin-flip transitions [5]. It is shown that these data are fully consistent with spin coupling models developed from earlier EPR/ENDOR studies and with the redox isomerism model, which explains the two S_2 state forms of the cofactor.

Together, these data suggest that the S_2 to S_3 state transition proceeds in a step-wise fashion, with cofactor deprotonation and oxidation occurring before water molecule insertion [6]. Furthermore, they support substrate water insertion being coupled to spin state conversion of the cofactor [7]. The possible extension of these same methods towards the study of the O-O bond formation step is briefly discussed.

[1] Cox N, *et al.* (2014) Electronic structure of the oxygen-evolving complex in photosystem II prior to O-O bond formation. *Science* 345:804-808.
[2] Suga M, *et al.* (2015) Native structure of photosystem II at 1.95 A resolution viewed by femtosecond X-ray pulses. *Nature* 517:99-103.
[3] Kern J, *et al.* (2018) Structures of the intermediates of Kok's photosynthetic water oxidation clock *Nature* 563:412-425.
[4] Chrysina *et al.* (2019) New intermediate in the activation of nature's water splitting cofactor. *Proc. Natl. Acad. Sci. U.S.A* 116 (34), 16841-16846
[5] Morton J *et al. Biochim. Biophys. Acta* 1859:88-98 (2018)
[6] Retegan M, *et al.* (2016) A five-coordinate Mn(IV) intermediate in biological water oxidation: spectroscopic signature and a pivot mechanism for water binding. *Chemical Science* 7(1):72-84.
[7] Krewald V *et al.* (2016) Spin state as a marker for the structural evolution of nature's water-splitting catalyst. *Inorg. Chem. 55*:488–501

08.01.2024

The Photophysics and Photochemistry of First-row Transition Metal Complexes: Quantum Coherence, the Marcus Inverted Region, and Applications in Excited-state Chemistry

James K. McCusker

Department of Chemistry, Michigan State University, 578 South Shaw Lane, East Lansing, Michigan USA 48824

There has been considerable renewed interest in the photophysical properties of first-row transition metal complexes, driven in part by a long-standing desire to shift to earth-abundant materials for a variety of photolytic applications.[1] A significant challenge to achieving this goal is the fundamental difference in the excited-state properties of first-row metal complexes as compared to their second- and third-row congeners subsequent to light absorption.[2] Our group has been working on understanding the origins of this difference in an effort to develop design principals that will assist in overcoming these intrinsic challenges and develop new paradigms for the creation of photo-active first-row chromophores for applications in solar energy conversion strategies as well as photoredox catalysis.

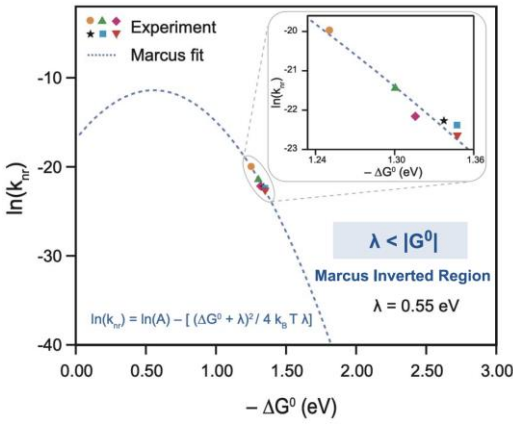


Figure 1. Photophysical data on a series of Co(III) polypyridyl complexes. The data reveal that the excited-state relaxation dynamics of this class of compounds occur in the Marcus inverted region, which allowed for their application in photoredox C-N bond formation chemistry. From ref. 5.

This presentation will provide a brief survey of the work we have been engaged in over the past several years employing a combination of synthetic chemistry and ultrafast spectroscopy. Our primary focus have been on compounds involving metals having a d^6 valence electronic configuration.[2] In the case of Fe(II), the use of vibronic coherence was found to provide what amounts to a roadmap for effective synthetic design to lengthen the lifetime of MLCT excited states,[3] whereas the excited-state redox activity of Co(III) ligand-field excited states[4] coupled with dynamics occurring in the Marcus inverted region (Figure 1) enabled previously unknown applications in photoredox catalysis.[5] Future directions envisioned for this line of research will also be discussed.

References

1. McCusker, J.K. *Science* **2019**, *363*, 484-488.
2. For a recent review with regard to d^6 metals in particular, see: Sinha, N.; Wenger, O. *J. Am. Chem. Soc.* **2023**, *145*, 4503-4520.
3. Paulus, B.C.; Adelman, S.L.; Jamula, L.L.; McCusker, J.K. *Nature* **2020**, *582*, 214-218.
4. Alowakennu, M.M.; Ghosh, A.; McCusker, J.K. *J. Am. Chem. Soc.* **2023**, *145*, 20786-20791.
5. Chan, A.Y.; Ghosh, A.; Yarranton, J.T.; Twilton, J.; Jin, J.; Arias-Rotondo, D.M.; Sakai, H.A.; McCusker, J.K.; MacMillan, D.W.C. *Science* **2023**, *382*, 191-197.

08.01.2024

Organic Reactions in Water: C-H bond photoactivation using enzyme-like nanocavities

Jyotishman Dasgupta*

Department of Chemical Sciences, Tata Institute of Fundamental Research (TIFR), Mumbai, India. *E-mail: dasgupta@tifr.res.in

Enzymes are proteins that catalyze non-spontaneous organic reactions in physiological conditions. Remarkably the water-insoluble organic substrates are usually encapsulated in hydrophobic protein cavities, which constitute reaction hotspots in enzymes. We have devised a new catalytic photoredox paradigm using water-soluble cationic nanocages [1] that mimic the enzyme cavity while providing a modular host-guest photoactivation strategy. [2, 3, 4] Through the potent combination of light activation and substrate pre-organization in water, we demonstrate facile yet selective aerobic oxidation of hydrocarbon C-H bonds under ambient conditions using proton-coupled electron transfer (PCET).[2, 4, 5, 6. 7] In fact we have recently shown that we can translate this concept to all-organic cationic nanocages. [8] The success of our designed artificial photoenzyme hints at the crucial role of electric fields in driving reactions within nanospaces. At the end, I will discuss alternate schemes for metal-based O_2 activation based C-H bond fuctionalization which also emerges to be special in aqueous confinement.

References:

[1] M. Fujita; *Nature* **1995**, 378, 469–471.

[2] R. Gera, A. Das, A. Jha and J. Dasgupta*; *J. Am. Chem. Soc.* **2014**, 136, 15909.

[3] A. Das, A. Jha, R. Gera and J. Dasgupta*; *J. Phys. Chem. C* **2015**, 119, 21234–21242.

[4] R. Gera and J. Dasgupta*; *PCCP* **2021**, 23, 9280-9284.

[4] A. Das, I. Mandal, R. Venkatramani, J. Dasgupta*; *Science Adv.* **2019**, 5, 2, eaav4806.

[5] S. Paul, A. Das and J. Dasgupta*; submitted

[6] S. Ghoshal, A. Das, D. Roy, and J. Dasgupta*; under revision

[7] D. Roy, S. Paul, and J. Dasgupta*; *AngewChem* **2023**; https://doi.org/10.1002/anie.202312500

[8] D. Roy, S. Paul, and J. Dasgupta*; *ChemComm* **2023;** https://doi.org/10.1039/D3CC03987K

08.01.2024

Emergent Properties from Dynamicity in Biomimetic Coordination Complexes

Lisa Olshansky

University of Illinois, Urbana-Champaign

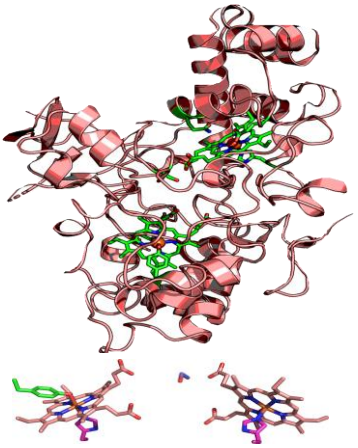
Biological systems often rely on triggered structural rearrangements to exert control over metallocofactor reactivity. Whether triggered by protein-protein interactions, electron injection, or proton transfer events, the conformational dynamicity of embedded coordination complexes is often intrinsically linked to catalytic activity. However, examining this interplay in natural systems is often extremely challenging if not impossible. Accordingly, model complexes that encapsulate key active site features, and which can accommodate inner sphere structural rearrangements have a role to play in understanding the relevance of dynamicity in biocatalysis. To these ends, we report the preparation and examination of three conformationally dynamic coordination complexes in which the incorporation of dynamicity directly results in emergent properties not previously observed in rigid homologs. These properties include rapid electron transfer rates, access to unusual magnetic states, and controlled substrate binding modes. All of these works aim to define and quantify the impacts of conformational dynamicity, and then to leverage those impacts in applications ranging from solar energy conversion, to biomedical imaging, and the development of novel (bio)catalytic systems.

Spectroscopy, enzymology and electrochemistry of the bacterial cytochrome c peroxidase superfamily

Sean J. Elliott, Boston University, Boston, MA 02215

elliott@bu.edu

The bacterial cytochrome *c* peroxidase (bCCP) superfamily encompasses well described family members that are responsible for the periplasmic reduction of hydrogen peroxide, but also members such as MauG, which uses the same oxidant to achieve long-range oxidation of tryptophan side-chains to generate the tryptophan tryptophanyl quinone (TTQ) cofactor of methylamine dehydrogenase. All bCCP family members are thought to couple the redox reactivity of a peroxidatic heme center (nominally five-coordinate) to the electron-transfer capacity of a second *c*-type heme. Recently, greater diversity of this family has been demonstrated by us and others, who have found bCCP family members widely distributed in the genera *Burkholderia*, and a tryptophan oxidizing bCCP has been reported in methanobactin biosynthesis. The representative chemistry of bCCPs at large is poorly understood, and few mechanistic studies have been possible for any of the family members to date. Here, we will present recent advances in the elucidation of bCCP structure- function relationships, including efforts to understand how the heme coordination impacts potential reactivity, the direct observation of high valent catalytic intermediates, and an unforeseen variation of the heme environments, through bioinformatic and biophysical studies.



08.01.2024

Can a Substrate Bound to a Remote Site Impact Electron Transfer Rate in Cytochrome P450cam?

Ananya Nayak, Mohammad Sahil, Jagannath Mondal*, Soumya Ghosh*

Tata Institute of Fundamental Research Hyderabad, Hyderabad, Telangana 500046, India

Recent studies have shown that the resting state of P450cam in solution, in the presence of substrate (camphor), is best described as a 3-site state where 3 substrates are bound at the same time (*J. Am. Chem. Soc.* 2023, 145, 43, 23488). It has been previously reported that electron transfer from [2Fe-2S] cluster to the active site in P450TT can occur via multiple pathways when the distance between the two sites is ~ 17 Å (*J. Am. Chem. Soc.* 2021, 143, 2, 1005). These findings beg the question whether the rate constant for the long range electron transfer from the reduced form of the iron-sulphur cluster to the heme active site (oxidized form) in P450cam, where the distance between the donor and acceptor sites is ~ 15-17 Å, is affected by the simultaneous binding of the three susbtrates.

Small Molecule Activation at Bioinspired Transition Metal Centers Studied by Advanced EPR Techniques

Dustin Kass,[a] Amanda Opis Basilio,[a] Nikolai Kochetov,[b] Beatrice Battistella,[a] Shengfa Ye,[c] Alexander Schnegg,[b,d] Kallol Ray,[a] Thomas Lohmiller[a,d]

[a]Institute of Chemistry, Humboldt-Universität zu Berlin, Berlin, Germany
[b]Max Planck Institute for Chemical Energy Conversion, Mülheim a. d. Ruhr, Germany
[c]State Key Laboratory of Catalysis, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, China
[d]Helmholtz Zentrum Berlin für Materialien und Energie GmbH, Berlin, Germany

Small molecules are key substrates in processes that are central for sustainable energy scenarios, such as the reductive conversions of N_2 into ammonia, of CO_2 into chemical fuels or the reduction of O_2 in fuel cells. A major challenge due to their relative stability is their binding and activation by efficient, stable catalysts, ideally based on cheap materials, such as the abundant transition metals used in biocatalysis by metalloenzymes. Rational design of improved homogeneous catalysts requires understanding of the structural and electronic aspects that facilitate these steps.

EPR spectroscopy provides a versatile toolbox for obtaining essential information on paramagnetic states of metal catalysts and reactive intermediates. Hyperfine spectroscopies, which most often comprise pulse EPR experiments such as ENDOR, ESEEM or HYSCORE, allow for the detection and characterization of electron-nuclear interactions. Hence, they can provide invaluable structural information about the metal center itself as well as the atomic environment of the reactive spin centers, e.g. on ligand conformations and substrate binding. Furthermore, by determining the interaction strength, they represent a direct probe for the spin density distribution. For high-spin states ($S > 0$), high-frequency EPR is particularly well suited for profound investigation of the electronic structure. Especially frequency-domain THz-EPR is a powerful tool to elucidate interaction parameters such as the zero-field splitting and even exchange interactions of electron spins.

The usefulness of EPR spectroscopy, often in combination with theoretical computations and other experimental techniques, for studying small molecule activation will be demonstrated by means of several intriguing examples, such as low-coordinate Fe centers, as well as oxygen activation by dicopper [1], iron-copper [2] and dimanganese [3] complexes.

[1] Lohmiller, T.; Spyra, C.-J.; Dechert, S.; Demeshko, S.; Bill, E.; Schnegg, A.; Meyer, F. *JACS Au* **2022**, *2*, 1134-11443.

[2] Kass, D.; Lohmiller, T.; Katz, S.; Mebs, S.; Haumann, M.; Dau, H.; Hildebrandt, P.; Ray, K. *in preparation*

[3] Battistella, B.; Lohmiller, T.; Cula, B.; Hildebrandt, P.; Kuhlmann, U.; Dau, H.; Mebs, S.; Ray, K. *Angew. Chem. Int. Ed.* **2023**, *62*, e202217076.

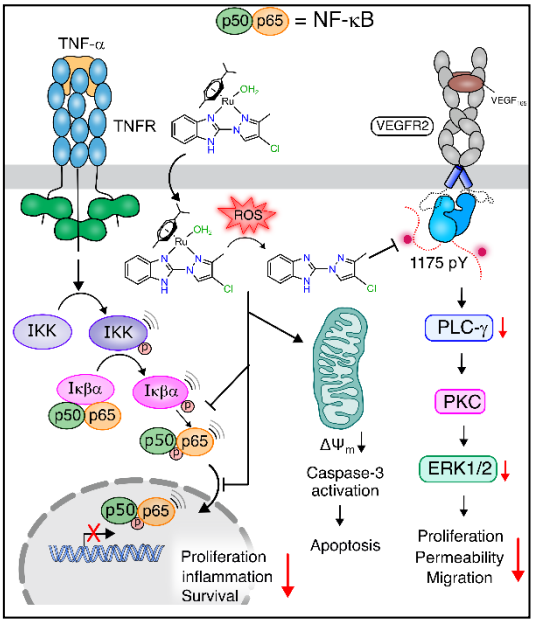
08.01.2024

Inhibition of NF-κB mediated proinflammatory transcription by Ru(II) complexes in triple negative breast cancer

Arindam Mukherjee

Department of Chemical Sciences and Centre for Advanced Functional Materials (CAFM), Indian Institute of Science Education and Research Kolkata, Mohanpur campus, Mohanpur-741246, India.

The development of metal complexes with potential applications as chemotherapeutic agents against cancer or other diseases is a process guided by a diverse set of intriguing principles. We are inspired to design ligands encompassing small molecules as integral part of our physiology including metabolites (e.g. orotic acid), compounds in clinical trials or FDA approved drugs.[1] The ligands are carefully selected for their ability to target a protein or pathway of interest and impede the proliferation, metastasis, or angiogenesis of cancer cells when acting independently. However, as part of the metal complex, the unified entity, targets a distinctly different protein, influenced by variations in both structural and electronic factors. This approach ensures to exploit the challenging conditions in the environment of cancer cell (e.g. ROS abundance) where upon dissociation of the metal complex instead of being ineffective it unleashes the organic warhead on a specific protein target. In this backdrop we used Ru(II) complexes to target nuclear factor kappa beta (NF-κB) which is active in triple-negative breast cancers (TNBCs) in promoting inflammation, proliferation, epithelial-mesenchymal transition (EMT), metastasis, and drug resistance.[2] Additionally, NF-κB contributes to the expression of vascular endothelial growth factor (VEGF), thereby supporting VEGFR2-dependent angiogenesis. During my lecture attention would be drawn to a family of Ru(II) complexes with ability to inhibit the phosphorylation and translocation of the NF-κB heterodimer (p50/p65) to the nucleus, thereby disabling its transcriptional capacity to upregulate the inflammatory signalling pathway. The complexes bear ligands that inhibit angiogenesis as standalone component generated through the ROS rich environment of cancer cells.



References: [1] a) M. Maji, I. Bhattacharya, S. Acharya, M. P. Chakraborty, A. Gupta and A. Mukherjee, *Inorganic Chemistry* **2021**, *60*, 4342-4346; b) P. Kumari, S. Ghosh, S. Acharya, P. Mitra, S. Roy, S. Ghosh, M. Maji, S. Singh and A. Mukherjee, *Journal of Medicinal Chemistry* **2023**, *66*, 14061-14079; c) S. Roy, P. Mitra, S. Acharya, S. S. Roy, S. Ghosh, M. Maji, N. Modak, N. Ghosh, M. Acharya, S. Singh and A. Mukherjee, *Inorganic Chemistry Frontiers* **2022**, *9*, 5840-5852. [2] Y. He, M. M. Sun, G. G. Zhang, J. Yang, K. S. Chen, W. W. Xu and B. Li, Signal Transduction Targeted Ther., 2021, 6, 425.

Exploring Approaches for Targeting of Cancer Cells and Intracellular Delivery of Metal-Based Drug Candidates

Nils Metzler-Nolte*

Inorganic Chemistry I – Bioinorganic Chemistry, Ruhr University Bochum, Germany

Email: nils.metzler-nolte@rub.de

Our group uses the unique spectroscopic and chemical properties of organometallic complexes in metal-peptide conjugates for biomedical applications. The experimental challenge is to identify air- and water stable organometallic compounds with the desired properties, and to devise methods for the mild, biocompatible synthesis of bioconjugates with these metal complexes. In particular, Au compounds have received increasing attention as promising anti-tumor agents recently.[1, 2] The proposed mode of action involves anti-mitochondrial activity, leading to redox stress and finally apoptosis. There are, however, severe side-effects associated with existing Au compounds. We aim to make Au compounds tumor-specific by either conjugating them to targeting peptides or by encapsulating them in liposomes.

This lecture presents the solid phase synthesis of metal-peptide conjugates for cellular targeting.[3, 4] The peptides were derived from sequences known for enhanced and / or cell-type specific uptake (e.g. TAT peptides), or for intra-cellular delivery (such as nuclear or mitochondrial localization). Gold compounds include phosphine derivatives as well as Au complexes of N-heterocyclic carbenes (NHCs). Using the well-established Cu-catalyzed azide-alkyne cycloaddition reaction (CuAAC) or an uncatalyzed, chemoselective “iClick” cycloaddition reation for bioconjugation we could link the Au complexes to the desired peptides with high yield and purity. Biochemical and cell biology results are presented that support enzyme inhibition as the mode of action.[5] Interestingly, these Au-peptide bioconjugates show no cross-resistance to the well-established Pt antitumor drugs. In more recent work, new concepts for enzyme-activated Au-peptide bioconjugates, Au-based theranostics, or encapsulation in liposomes are explored to make such conjugates specific for cancer tissues.[6]

References:

1. C. G. Hartinger, N. Metzler-Nolte, P. J. Dyson, *Organometallics* **31** (2012) 5677 - 5685.
2. G. Gasser, N. Metzler-Nolte, *Curr. Opinion Chem. Biol.* **16** (2012) 84 - 91.
3. D. Siegmund, N. Metzler-Nolte, “Medicinal Organometallic Chemistry“, Ch. 8 in *Bioorganometallic Chemistry* (W. Weigand, U.-P. Apfel, Eds.) De Gruyter (2020) 319 - 350.
4. H. B. Albada, N. Metzler-Nolte, *Chem. Rev.* **2016**, *116*, 11797.
5. S. D. Köster, H. Alborzinia, S. Can, I. Kitanovic, S. Wölfl, R. Rubbiani, I. Ott, P. Riesterer, A. Prokop, K. Merz, N. Metzler-Nolte, *Chem. Sci.* **3** (2012) 2062.
6. A. Luengo, I. Marzo, M. Reback, I. M. Daubit, V. Fernández-Moreira, N. Metzler-Nolte, M. Concepción Gimeno*, *Chem. Eur. J.* **26** (2020) 12158 – 12167.

08.01.2024

Radiometal Chelation Strategies for Both Therapy and Diagnosis

Justin J. Wilson*, Kevin Lee, Thines Kanagasundaram, Aohan Hu

Department of Chemistry and Chemical Biology, Cornell University, Ithaca, NY 14853, United States of America

The use of radioactive metal ions, or radiometals, within nuclear medicine has led to significant advances in the treatment and diagnosis of human disease.[1] In recent years, there has been significant efforts to apply radiometals that emit alpha particles for therapy.[2] If directed properly to tumour sites, these alpha particles can eradicate malignant cells. A key requirement for bringing alpha-emitters to tumours specifically is that they be conjugated to a biological targeting vector via a bifunctional chelating agent, a chelator that can rapidly complex and stably retain the radiometal in vivo.[3] In our lab, we have developed a number of successful bifunctional chelators for alpha-emitting radiometals with large ionic radii, like $[^{225}Ac]Ac^{3+}$, $[^{213}Bi]Bi^{3+}$, and $[^{212}Pb]Pb^{2+}$.[4,5] A limitation of these chelators, however, is that they are ineffective for smaller radiometal ions with diagnostic properties, like $[^{111}In]In^{3+}$, $[^{44}Sc]Sc^{3+}$, and $[^{89}Zr]Zr^{4+}$. Therefore, applying the same chelator for both the large therapeutic alpha-emitters, as well as the smaller diagnostic radiometals with equally high efficacy is currently not possible, thereby preventing the development of theranostic agents with these radionuclides. In this talk, we discuss our recent efforts to design chelators with equal efficacy for both alpha-emitting therapeutic radiometals, as well as diagnostic radiometals. New ligand design approaches that enable conformational flexibility to accommodate ions of different sizes are discussed,[6,7] in addition to their use for theranostic nuclear medicine applications.

1. Ramogida, C. F.; Orvig, C. *Chem. Commun.* **2013**, *49*, 4720.
2. Kim, Y.-S.; Brechbiel, M. W. *Tumor Biol.* **2012**, *33*, 573
3. Price, E. W.; Orvig, C. *Chem. Soc. Rev.* **2014**, *43*, 260.
4. Thiele, N. A.; Brown, V.; Kelly, J.; Amor-Coarasa, A.; Jermilova, U.; MacMillan, S. N.; Nikolopoulou, A.; Ponnala, S.; Ramogida, C. F; Robertson, A. K. H.; Rodríguez-Rodríguez, C.; Schaffer, P.; Williams, C., Jr.; Babich, J. W.; Radchenko, V.; Wilson, J. J. *Angew. Chem., Int. Ed.* **2017**, *56*, 14712.
5. Hu, A.; Wilson, J. J. *Acc. Chem. Res.* **2022**, *55*, 904.
6. Hu, A.; MacMillan, S. N.; Wilson, J. J. *J. Am. Chem. Soc.* **2020**, *142*, 13500.
7. Hu, A.; Aluicio-Sarduy, E.; Brown, V.; MacMillan, S. N.; Becker, K. V.; Barnhart, T. E.; Radchenko, V.; Ramogida, C. F.; Engle, J. W.; Wilson, J. J. *J. Am. Chem. Soc.* **2021**, *143*, 10429.

08.01.2024

Multitarget Antitumor Agents: Influence of Kinetic Lability on Pharmacokinetics and Pharmacodynamics

Malay Patra, * Manikandan M., Shubhankar Gadre, Tushar R. Panda

Department of Chemical Sciences, TIFR, Mumbai, India

Email: malay.patra@tifr.res.in

Even in the modern era of precision medicine and immunotherapy, chemotherapy with platinum (Pt) drugs, cisplatin, carboplatin and oxaliplatin, remain among the most commonly prescribed medications against a variety of cancers.[1] Despite spectacular clinical success, inherent and/or acquired chemoresistance increasingly reduces the effectiveness of Pt-based therapy. In addition to this, dose-limiting toxic side effects such as nephrotoxicity, neurotoxicity and myelosuppression, limits the wider applicability. Our lab is actively involved in the search for novel Pt antitumor agents superior to clinically used drugs and understanding the structure-function relationship.[2-3] Since, kinetic lability or reactivity is the key determinant of anticancer efficacy, resistance and side effects, we embarked on an effort to rationally design next generation of Pt drugs by tuning the reactivity. Using a combination of *in vitro* and *in vivo* assay, we identified a few lead candidates with remarkable *in vivo* efficacy, low Pt-cross resistance and reduced systemic toxicity.[4] The design, in-depth *in vitro* mechanistic investigation, *in vivo* data and the impact of kinetic lability on pharmacokinetic and pharmacodynamic processes of these agents will be discussed.

References.

(1) Rottenberg, S.; Disler, C.; Perego, P. The rediscovery of platinum-based cancer therapy. *Nat. Rev. Cancer* **2021**, *21*, 37-50.

(2) Gadre, S.; Manikandan, M.; Duari, P.; Chhatar, S.; Sharma, A.; Khatri, S.; Kode, J.; Barkume, M.; Kasinathan, N. K.; Nagare, M.; Patkar, M.; Ingle, A.; Kumar, M.; Kolthur-Seetharam, U.; Patra, M. A rationally designed bimetallic platinum (II)-ferrocene antitumor agent induces non-apoptotic cell death and exerts in vivo efficacy. *Chem. Eur. J.* **2022**, e202201259.

(3) M, M.; Gadre, S.; Chhatar, S.; Chakraborty, G.; Ahmed, N.; Patra, C.; Patra, M. Potent Ruthenium–Ferrocene Bimetallic Antitumor Antiangiogenic Agent That Circumvents Platinum Resistance: From Synthesis and Mechanistic Studies to In Vivo Evaluation in Zebrafish. *J. Med. Chem.* **2022**, *65*, 16353-16371.

(4) Panda, T. R.; Manikandan, M.; Vaidya, S. P.; Sinha, S.; Chhatar, S.; Mehrotra, M.; Chakraborty, S.; Gadre, S.; Duari, P.; Ray, P.; Patra, M. The Power of Kinetic Inertness in Improving Platinum Anticancer Therapy by Circumventing Resistance and Ameliorating Nephrotoxicity. *Angew. Chem. Int. Ed.* **2023**, *62*, e2023039.

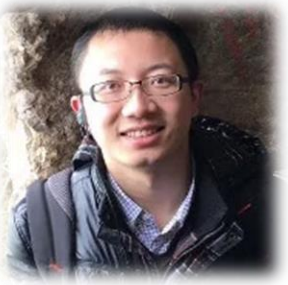
08.01.2024

Controllable activation of platinum anticancer drugs in vivo

Guangyu Zhu [a,b*]

a) Department of Chemistry, City University of Hong Kong, Hong Kong SAR, P. R. China, b) City University of Hong Kong Shenzhen Research Institute, Shenzhen, P. R. China

guangzhu@cityu.edu.hk



Despite the broad clinical applications of platinum-based anticancer drugs including cisplatin, their side effects and resistance issues have encouraged researchers to look for novel metal-based anticancer complexes. Non-traditional platinum compounds especially Pt(IV) complexes have been extensively studied and they hold great promise to be further developed as the next-generation platinum drugs.[1,2] Selective activation of prodrugs within a tumor is particularly attractive because of their low damage to normal tissue. In this presentation, I will introduce the design, activation mechanism, and antitumor activity of photo- and sono-activatable Pt(IV) prodrugs.[3-6] These small-molecule prodrugs have controllable activation properties: they are shown to be inert in the dark but under short-period irradiation with low intensity of visible light or ultrasound, and without the need for any external catalyst, the prodrugs are efficiently reduced. The prodrugs display superior antitumor activity both in vitro and in vivo in human carcinoma models. I will also introduce our recent progress in photooxidation therapy by utilizing our Pt(IV) photooxidants.[7] The controllable activation property and superior antitumor activity of these prodrugs may suggest a novel strategy for the design of next-generation platinum prodrugs to reduce the adverse effects and conquer the drug resistance associated with traditional platinum chemotherapy

References:

[1] Wang Z, Deng Z, and Zhu G. *Dalton Trans.,* 2019, *48*, 2536-2544 [Invited Review and Cover Article]
[2] Xu Z, Deng Z, Wang Z, and Zhu G. *Coord. Chem. Rev.,* 2021, *442*, 213991
[3] Wang Z, Zhu G, *et al. Chem,* 2019, *5*, 3151-3165
[4] Deng Z, Zhu G, *et al. J. Am. Chem. Soc.,* 2020, *142*, 7803-7812 [Supplementary Cover]
[5] Deng Z, Zhu G, *et al. Chem. Sci.,* 2021, *12*, 6536 [Outside Back Cover]
[6] Liu G., Zhu G, et al. *Sci. Adv.,* 2023, *9*, eadg5964
[7] Deng, Z., Zhu, G., *et al. Nat. Chem., 2023, 15*, 930

08.01.2024

Tuning the Design of Mitochondria Specific Half-Sandwich and Cyclometallated Ru(II)/Ir(III)/Re(I)-Complexes to Unveil the Dynamic Therapy Against Cancer

Dr. Priyankar Paira

Department of Chemistry, School of Advanced Sciences (SAS),
Vellore Institute of Technology (VIT), Tamilnadu,Vellore-632014,
India, 8110020748, **E-mail**: priyankar.paira@vit.ac.in

To abate the world-wide rampant prevalence of cancer, recently we have developed mitochondria targeted DNA intercalating Ru(II)/Ir(III)/Re based half-sandwich and cyclometallated complexes for ROS mediated selective dynamic therapy in absence or presence of light (CDT or PDT) enhancing the therapeutic potential against the distinct tumour microenvironment (TME) and elevated GSH level. It has been visualised that these scaffolds are very dexterous to damage DNA, deplete GSH level and increase the oxidative stress through ROS generation. The significant cell cycle arrest, stimulation of p53 genes, upregulation of Bax family proteins and down regulation of Bcl-2 upon administration of these scaffolds against various cancer cell lines, triggers the mitochondrial intrinsic pathway for apoptosis through activation of
a cascade of different caspases.[1, 2]

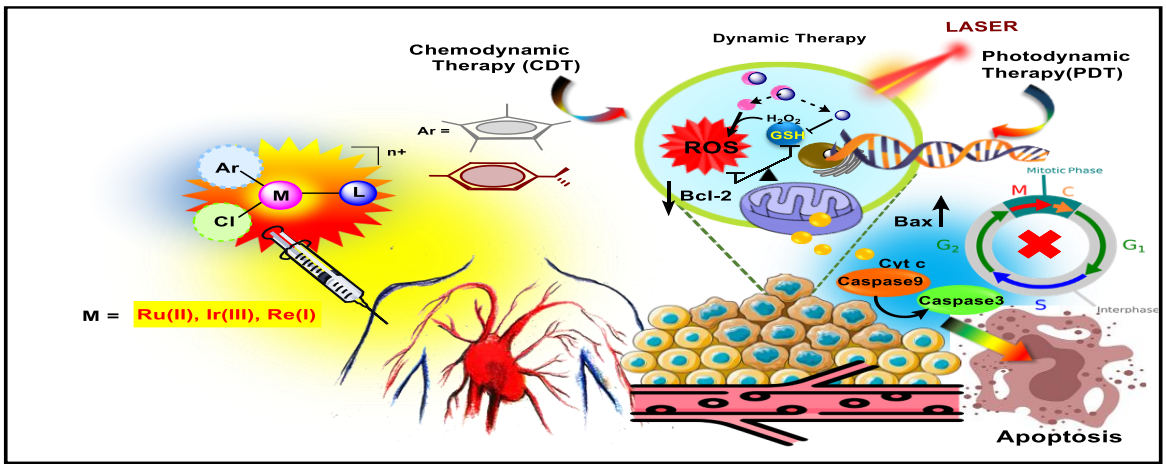


Figure 1: Strategies for destruction of cancer cells

References:

1. *Roy, N.; Sen, U.; Madaan, Y.; Muthukumar, V.; Vardhan, S.; Sahoo, S. K.; Panda, D.; Bose, B.; Paira, P. Mitochondria-Targeting Click-Derived Pyridinyltriazolylmethylquinoxaline-Based Y-Shaped Binuclear Luminescent Ruthenium(II) and Iridium(III) Complexes as Cancer Theranostic Agents.* Inorg. Chem. ***2020***, 59, *17689-17711.*

2. *Kar, B.; Paira, P. One pot three component synthesis of DNA targeting phototoxic Ru(II)-p-cymene dipyrido[3,2-a:2',3'-c]phenazine analogues.* Dalton Trans. ***2022***, 51, *15686-15695.*

08.01.2024

Development of Metal-based Photocatalytic Anticancer Agents

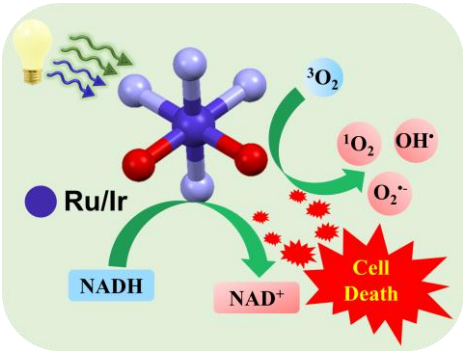
Dr. Samya Banerjee

Department of Chemistry, Indian Institute of Technology (BHU), Varanasi,

Uttar Pradesh 221005, India (Email: samya.chy@itbhu.ac.in)

Currently, the market available cancer chemotherapeutics are facing major problems like severe side effects, and various types of cancer-producing resistances.[1] These problems have limited the clinical application of chemotherapy.[1,2] The worldwide burden of cancer could rise by 47% in 2040 with respect to 2020.[2] Thus, a new generation of cancer drugs that can overcome the drawbacks of chemotherapy with a novel mechanism of action is urgently needed to save the cancer-affected population of the globe. Importantly, metal complexes possess the largely unexplored potential to enhance the immunomodulatory effects of chemotherapeutic agents.[3] The design concepts for metallodrugs are in their infancy and need to be more widely explored.

The talk highlights the metal-based photocatalytic anticancer drug development which is the core focus of our lab.[4-11] Of late, the concept of photocatalytic cancer therapy as an alternative to chemotherapy with a novel mechanism of action and target site is being pursued by our group.[4-11] This therapy provides spatiotemporal control over the activation of catalytic amounts of drugs at the target cancer site.[4-11] This new concept of "photocatalytic cancer therapy" can overcome cis-platin resistance with no harmful effects on normal cells *in vivo* and *in vitro*.[4-11] Ir(III) and Ru(II)-based photocatalysts[4-11] induced intracellular NADH or NAD(P)H photo-oxidation in cancer cells at catalytic concentrations to create in-cell redox imbalance and metabolic disorder, which leads to cell death.[4-11] Moreover, these Ir(III) and Ru(II)-based photocatalysts were also able to overcome the hypoxia-related cancer drug resistance problems.[4-11] Overall, these Ir(III) and Ru(II)-based photocatalysts have the potential to emerge as next-generation clinical cancer therapeutics.



References:

[1] D. Wang *et al.*, Nat. Rev. **2005**, *4*, 307-320. [2] H. Sung *et al.*, *Ca-Cancer J. Clin.* **2021**, *71*, 209-249. [3] A. Terenzi *et al.*, *J. Inorg. Biochem.* **2016**, *165*, 71-79. [4] S. Banerjee, P. J. Sadler *et al.*, *Nat. Chem.* **2019**, *11*, 1041-1048. [5] S. Banerjee, H. Huang *et al.*, *Angew. Chem. Int. Ed.* **2021**, *60*, 9474-9479. [6] S. Banerjee, H. Huang *et al.*, *Dalton Trans.* **2022**, *51*, 10875-10879. [7] S. Banerjee, *et al.*, *Chem. Eur. J.* **2022**, *28*, e202103346. [8] R. Kushwaha, S. Banerjee *et al.*, *Angew. Chem. Int. Ed.* **2022**, *61*, e202202098. [9] R. Kushwaha, S. Banerjee *et al.*, *Chem. Commun.* **2023**, *59*, 3083-3086. [10] A. K. Yadav, S. Banerjee *et al.*, *ChemBioChem*, **2023**, e202300033. [11] R. Kushwaha, S. Banerjee *et al.*, *Chem. Asian J.* **2023**, *18*, e202300047.

Cyclopentadienyl- and tetraphenylborate-based Ru(II) drug candidates for triple-negative breast cancer (TNBC) therapy

Dulal Musib,[a] and Annie Castonguay*[a]

[a] INRS-Centre Armand-Frappier Santé Biotechnologie, Université du Québec, Laval, QC, Canada, H7V 1B7

Organoruthenium complexes are known to exhibit a wide range of biological activities. Some of them have shown great promise in cancer therapy and have successfully entered clinical trials.[1] Notably, cyclopentadienyl ruthenium (CpRu) complexes have shown to be particularly active against triple negative breast cancer, an aggressive type of breast cancer that is difficult to treat.

We and others have recently shown that BPh_4 displays a synergistic anticancer activity with cationic organoruthenium complexes when used as counterions.[2] In order to further investigate the role of the BPh_4 in these complexes, we have designed two families of cyclopentadienyl ruthenium (CpRu) complexes in which BPh_4 is either a counterion or is covalently linked to the ligand, resulting in a zwitterion. For both families, the Ru zwitterion-functionalized cyclopentadienyl complexes demonstrated enhanced anticancer activity against the triple-negative breast cancer cell line compared to their ruthenium cation counterparts. Moreover, preliminary results indicate that both types of boron-containing complexes preferentially accumulate in different organelles, providing insights into their mechanism(s) of action. Further studies are warranted to elucidate the exact pathways through which these complexes exert their cytotoxic effects and to explore their potential as anticancer drug candidates.

This presentation will discuss our latest results regarding the synthesis, characterization and the biological properties of these boron-based organoruthenium complexes.

References:

[1] a) Thota, S.; Rodrigues, D. A.; Crans, D. C.; Barreiro, E. J. J. Med. Chem., 2018, 61, 5805–5821. b) Lee, S. Y.; Kim, C. Y.; Nam, T. Drug. Des. Devel. Ther., 2020, 14, 5375–5392.

[2] a) Haghdoost, M. M.; Golbaghi, G.; Guard, J.; Sielanczyk, S.; Patten, S. A.; Castonguay, A. Dalton Trans., 2019, 48, 13396-13405. b) Martínez-Alonso, M.; Sanz, P.; Ortega, P.; Espino, G.; Jalón,F. A.; Martín, M.; Rodríguez, A. M.; López, J. A.; Tejel, C.; Manzano, B. R. Inorg. Chem. 2020, 59, 19, 14171– 14183. c) Loughrey, B. T.; Healy, P. C.; Parsons, P. G.; Williams, M. L. Inorg. Chem., 2008, 47, 8589– 8591. d) G. Golbaghi, M. M. Haghdoost, D. Yancu, Y. López de los Santos, N. Doucet, S. A. Patten, J. T. Sanderson and A. Castonguay, Organometallics, 2019, 38, 702–711.

08.01.2024

Rhenium Complexes of Some Aromatic Thiohydrazides and Their Anticancer Properties

Riya Ghanti,[1] Dolan Sengupta,[2] Snigdha Gangopadhyay,[1] Pijush Kanti Gangopadhyay,[1] Sanchita Goswami,[1] Jayanta Bag,[1] Kuntal Pal,[1] Chandan Das,[3] Arnab Dutta,[3] Arnab Chakrabarty,[4] Siddik Sarkar[4]

[1]Department of Chemistry, University of Calcutta, 92, A. P. C. Road, Kolkata – 700009
[2]Department of Chemistry, Dum Dum Motijheel College, 1 Motijheel Avenue, Kolkata – 700074
[3]Department of Chemistry, IIT Bombay, Powai, Maharastra – 400076
[4]Department of Cancer Biology & Inflammatory Disorder, CSIR-IICB, Translational Research Unit of Excellence, Salt Lake Sector V, Kolkata - 700091

Standard rhenium(VII) compound (perrhenic acid or ammonium perrhenate) reduced with hydrazine hydrochloride in acid medium, reacts with aromatic thiohydrazide ligands (H_3**L**), for example, thiobenzhydrazide (H_3**L**$_1$), 2-hydroxythiobenzhydrazide (H_3**L**$_2$), furan-2-thiohydrazide (H_3**L**$_3$) and thiophene-2-thiohydrazide (H_3**L**$_4$) to form compounds with general formula $Re(HL)_3$. The compounds have been characterized by ESI-MS, UV-visible, infrared, NMR, EPR spectroscopy, cyclic voltammetry, and studies of magnetic properties. The unusual trigonal prismatic structure of the compounds has been solved by X-ray diffraction. The compounds inhibit growth of human ovarian cancer cell lines SKOV3 (adenocarcinoma) and PA1 (teratocarcinoma) at μM level of concentration. Of the compounds, $Re(H$**L**$_2)_3$ is the most effective one. The mode of action of the compound, studied by DNA binding property and CFDA-SE/PI dual staining method, reveals selective cancer cell killing without affecting normal cell. The compounds in solution should be stored at -90°C. In solution, at room temperature, rhenium catalyses oxidation of the ligands; some oxidation products have been isolated and its structure is determined.

Electronic Relaxation Data and the Importance of Excited State Mixing in Determining the Properties of Compound I

Michael Green

University of California, Irvine

Recently, a selenolate-ligated P450 compound I (SeP450-I) intermediate was shown to be more reactive towards C-H bonds than its thiolate-ligated counterpart. To gain insight into how the selenolate axial ligand influences the reactivity of compound I, we have investigated the electronic structure of the SeP450-I intermediate using variable temperature Mossbauer (VTM) spectroscopy. Analysis of the VTM data indicate that electronic spin relaxation rates are significantly slower in SeP450-I than in P450-I. Efforts to analyze these and other data in terms of a standard ligand field model indicate that excited state mixing within the ferryl moiety plays an important role in determining electronic properties of compound I species. For SeP450-I, P450-I, and chloroperoxidase compound I, we find that electronic relaxation times correlate with the magnitude of the exchange coupling and track with reactivity towards C-H bonds.

08.01.2024

One Structural Elements Multiple Applications: Repurposing The Metal-Binding Hook of Nickel Superoxide Dismutase

Jason Shearer

Department of Chemistry, Trinity University, San Antonio, TX 78212 U.S.A.

Nickel containing superoxide dismutase (NiSOD) is a microbial metalloenzyme that catalyzes the disproportionation of superoxide into hydrogen peroxide and dioxygen. In solution, the metalloenzyme is found as a homohexemer with each monomer containing one mononuclear nickel-site. The nickel-site is found at the protein *N*-terminus–the nickel cofactor (Ni^{2+}/Ni^{3+}) is coordinated within a nickel-binding loop structure defined by the first six residues from the *N*-terminus with the consensus sequence HCXXPC. Some time ago, we demonstrated that small peptides based on the NiSOD *N*-terminal sequence are capable of coordinating nickel in a coordination environment reminiscent of NiSOD. These NiSOD metallopeptide based mimics are capable of reproducing the key structural, reactive and spectroscopic properties of the metalloenzyme. In this talk it will be shown that the peptide-loop is highly modular and allows access to a variety of metal-sites with different properties. For example, cobalt coordination to a modified NiSOD binding hook will reproduce the structure and function of cobalt-containing nitrile hydratase while iron coordination will reproduce the function of non-heme mononuclear iron dioxygenases.

Spectroscopic Studies of Heme Proteins/Enzymes Involved in Small Molecule Sensing/Activation

Joshua Telser,[1] Richard J. Jodts,[2] Brian R. Weaver,[3] Judith N. Burstyn,[3] Christopher P. Martin,[4] Jonathan D. Caranto[4]

[1] Department of Biological, Physical and Health Sciences, Roosevelt University, Chicago, IL 60605 USA
[2] Department of Chemistry, Northwestern University, Evanston, IL 60208 USA
[3] Department of Chemistry, University of Wisconsin, Madison, WI 53706 USA
[4] Department of Chemistry, University of Central Florida, Orlando, FL 32816 USA

Hemes are among the most widespread and important cofactors in biochemistry. Best known among the heme proteins are the oxygen transport and storage proteins, respectively hemoglobin and myoglobin. The best known among the heme enzymes is the heme oxidase cytochrome P450 (CYP), found throughout living systems including a vital role in human metabolism of xenobiotics.[1] There are, however, many other heme enzymes/proteins of interest besides these “paradigm” examples, in particular other hemes with proximal thiolate coordination.[2] These include the carbon monoxide (CO) sensing protein CooA[3] and the nitric oxide (NO)-dependent nitrating enzyme TxtE, which is a cytochrome P450 homologue.[4] Ferric heme, i.e., porphyrin with Fe(III) $3d^5$, can be in the high-spin (S = 5/2) or low-spin (S = 1/2) ground state. In either spin state, electron paramagnetic resonance (EPR) spectroscopy can provide valuable information on electronic structure and substrate/product/inhibitor binding. Specialized forms of EPR, such as electron nuclear double resonance (ENDOR) and electron spin echo envelope modulation (ESEEM) spectroscopies can provide even more information, specifically about nuclei that comprise the active site environment.[5] We describe EPR and ENDOR studies on both CooA and TxtE, including parallel comparative studies on a P450 (CYP119) enzyme. All three of these systems contain heme with proximal cysteine thiolate coordination, yet the electronic effect of this ligand differs in each case. In the case of CooA, in collaboration with the Burstyn group, a series of single point mutants probes the effects of H-bonding on structure. In the case of TxtE, in collaboration with the Caranto group, only wild type has been investigated thus far, but the effect of substrate (L-tryptophan) and analogs is explored.

References

1. Ortiz de Montellano, P. R., Hydrocarbon Hydroxylation by Cytochrome P450 Enzymes. *Chem. Rev.* **2010**, *110*, 932-948.
2. Smith, A. T.; Pazicni, S.; Marvin, K. A.; Stevens, D. J.; Paulsen, K. M.; Burstyn, J. N., Functional Divergence of Heme-Thiolate Proteins: A Classification Based on Spectroscopic Attributes. *Chem. Rev.* **2015**, *115*, 2532-2558.
3. Clark, R. W.; Youn, H.; Parks, R. B.; Cherney, M. M.; Roberts, G. P.; Burstyn, J. N., Investigation of the Role of the N-Terminal Proline, the Distal Heme Ligand in the CO Sensor CooA. *Biochemistry* **2004**, *43*, 14149-14160.
4. Martin, C. P.; Chen, M.; Martinez, M. F.; Ding, Y.; Caranto, J. D., The Ferric-Superoxo Intermediate of the TxtE Nitration Pathway Resists Reduction, Facilitating Its Reaction with Nitric Oxide. *Biochemistry* **2021**, *60*, 2436-2446.
5. Hoffman, B. M., ENDOR (and ESEEM) in Bioinorganic Chemistry. *Proc. Natl. Acad. Sci. U. S. A.* **2003**, *100*, 3575-3578.

08.01.2024

Iron therapy in patients with inflammatory bowel disease: the role of Fe deficiency and iron supplementation.

Carver PL

Department of Clinical Pharmacy, University of Michigan College of Pharmacy, 428 Church Street

Ann Arbor, MI USA 48109-1065.

Michigan Medicine, University of Michigan Health System, Ann Arbor, MI USA 48109E-mail: E-mail: peg@umich.edu

Patients with inflammatory bowel disease (IBD) experience disrupted iron homeostasis and cellular Fe accumulation, often accompanied by anemia and non-anemic Fe deficiencywhich negatively impacts the quality of life in this patient population, and significantly burdens the healthcare system. The pathogenesis of iron deficiency in IBD patients is multifactorial, including intestinal bleeding, malabsorption, and inadequate oral intake. While oral iron is safe, affordable, and easy to administer, patients often suffer from intolerable gastrointestinal side effects, and particularly in IBD patients, oral iron may increase inflammation and contribute to flares. Intravenous (IV) iron is considered first-line treatment for patients with active disease, severe anemia, oral iron intolerance, and erythropoietin requirements. [1,2]
We examined the hospital records of all patients admitted for a non-infectious event, who had an underlying diagnosis of IBD. IBD patients treated with intravenous iron (IV Fe) and/or transfusions of red blood cells (RBC) for iron deficiency anemia (IDA) were compared to a control group of untreated IBD patients. We compared severity of IBD, duration of hospital stay, number and types of infections during hospitalization, and pathogens causing infections. Data collection included demographic information, Fe indices (iron, transferrin, ferritin, iron saturation (TSAT), hemoglobin (Hgb), and hematocrit (Hct), hepcidin, Fe products / formulations, and dosages, RBC timing and amount, and administration of Fe chelators. Risk factors for infection were assessed by multivariate logistic regression.
IDA was common in hospitalized patients with IBD. Hgb and Hct increased significantly with IV Fe or RBC (or both) treatment. Correction of the Fe deficiency in IBD patients with IV Fe can improve IDA but may result in an increased risk of infection and an increased hospital stay.[1]

References:

1. L. A. Maas, M. Krishna and A. M. Parian. Dig Dis Sci 2023 Vol. 68 Issue 2: 357-369.

2. J. Stein, A. Aksan, K. Farrag, A. Dignass and H. H. Radeke. Expert Opinion on Pharmacotherapy 2017 Vol. 18 Issue 16:1721-1737

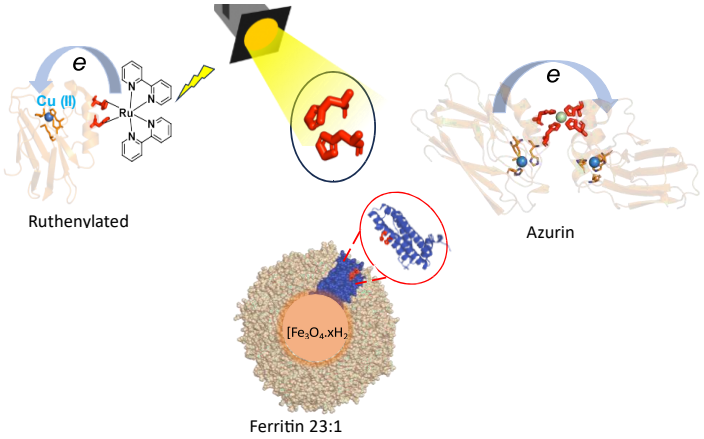
08.01.2024

Employing Protein-Protein Interactions to Build Pathways for Electron-Transfer

Ankur Gupta

IISER Bhopal, Department of Chemistry, Bhopal, India

Metabolic processes are dependent on an electron-transport chain (ETC) and a terminal electron acceptor (usually O2) for efficient generation of food/energy.[1] Functioning of such an ETC involves a harmonic exchange of electrons among an array of electron-transfer (ET) proteins and redox cofactors ultimately leading to the reduction of the terminal acceptor.[2] ET processes involve diffusion, collisions, and occasionally conformational changes among the redox partners exchanging electrons.[3] The research in our group derives motivation from such ET processes where we try to modulate intermolecular ET among proteins of interest by modification of surface exposed residues. I will present how a surface engineered bis-his tag on an electron-transfer protein – azurin – was used to purify, induce dimerization, and modulate ET across the azurin dimers.[4] The tag was further utilized to site-selectively label the protein surface with [Ru(bpy)2Xn] complexes which, upon light irradiation, show efficient communication with the redox active size of the protein.[5] Finally, a bis- his tag installed on a Ferritin monomer is exploited to generate heterooligomeric (23:1) ferritin for potential applications related to ET and catalysis.[6] Such protein assemblies, including the ones involving covalent crosslinkers, help to understand and modulate ET for biotechnological applications.



Scheme depicting the spotlight on the engineered bis-his tag and its applications to study intermolecular interactions and electron-transfer

References:

1. Nicholls, D. G. and Ferguson, S. J., *Bioenergetics 2,* Academic Press, New York, **1992**.
2. Winkler, R. J.; Gray, H. B. *Chem Phys Lett.* **2009,** *483*, 1-9.
3. Tripathi, S.; Li, H.; Polous, T. L. *Science.* **2013,** *340*, 1227-1230.
4. Negi, A.; John, A.; Gupta, A. *Manuscript under submission.*
5. Negi, A.; Murugan, S; Gupta, A. *Manuscript under preparation.*
6. Negi, A.; Gupta, A. *Manuscript under preparation.*

08.01.2024

Deciphering a Membrane-Bound Hydrocarbon-Producing Metalloenzyme

Debasis Das

Department of Inorganic and Physical Chemistry,

Indian Institute of Science, Bangalore, India

Abstract: Biosynthetically produced 1-alkenes hold immense value as sustainable alternatives to fossil fuels and find widespread applications in polymer, lubricant, and detergent industries. UndB is the only known membrane enzyme capable of converting naturally abundant fatty acids to 1-alkenes. However, despite diverse applications, UndB remains poorly understood since its discovery nearly a decade ago. We present here insights into the molecular basis of UndB catalysis and the mechanism of UndB reaction at the membrane interface. We unravel UndB as a diiron-enzyme that utilizes a conserved histidine cluster at the active site. We decipher the dependency of UndB activity on molecular oxygen and electrons and identify the most efficient redox partners of UndB. We elucidate the catalytic intricacies of UndB and establish it as the most efficient decarboxylase in producing industrially valuable medium-chain 1-alkenes. Further, we engineer UndB, substantially improve the enzyme's activity, and develop a novel whole-cell biocatalyst utilizing the engineering UndB for highly efficient conversion of naturally abundant free fatty acids to 1-alkenes.

References:

1. Iqbal, T.; Murugan, S.; Rajendran, K.; Sidhu, J. S. and **Das, D.* 2023**, https://chemrxiv.org/engage/chemrxiv/article-details/64379e3d08c86922ffe2f5ac

3. Iqbal, T. and **Das, D.*** ***Biochemistry***, **2022**, 61, 10, 909–921 [Featured on the **Front Cover** of the journal]

4. Iqbal, T.; Chakraborty, S.; Murugan S. and **Das, D.*** ***Chemistry - An Asian Journal***, **2022**, 17, e2022001 [Featured on the **Front Cover** of the journal]

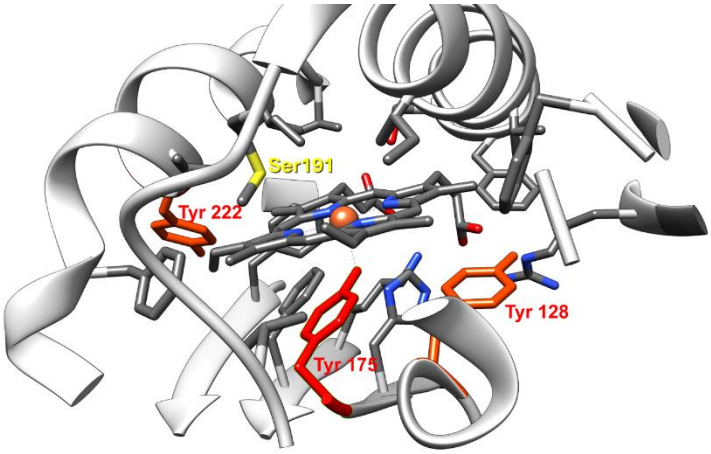
08.01.2024

One Tyrosine and No Histidine (in distal pocket) makes Sfh5 a Weak Catalase

Chandradeep Ghosh, Vytas Bankaitis

Sec14 protein renowned for their lipid transfer functions within the cell signaling pathway, along with its protein homologs, possesses a lipid binding cavity at its core. Interestingly, Sfh5 (Sec-14-homologue 5) exhibits significant structural and sequential homology with Sec14; however, it fails to demonstrate any lipid transfer activity. Instead, Sfh5 expresses with a heme center in its active site. The crystal structure reveals that the heme is tethered to the protein backbone through a tyrosine residue (Tyr175). Despite displaying considerable catalase activity, the heme center in Sfh5 functions as a relatively weak catalase compared to natural catalases.

Analysis of the protein's second-sphere structure indicates that the absence of a histidine residue at the distal pocket contributes to its low catalytic property. Introducing a properly oriented histidine at the distal pocket by replacing the Ser191, significantly enhances the catalytic activity. In addition to the absence of histidine, coupled with the presence of a tyrosine near the distal pocket, acts as a radical shunt, diverting oxidizing equivalents from the heme-Fe center and slowing down its H_2O_2 dissociation rate. Notably, replacing this tyrosine (Tyr222) with a phenylalanine group leads to a manifold increase in catalytic activity. This study focuses on the engineering of the unconventional heme binding protein Sfh5, aiming to enhance its catalase activity systematically. The objective is to investigate the potential evolution of a class of heme-bound proteins (catalases) from lipid transfer proteins, such as Sec14.



Active site structure of Sfh5

Reference

Khan, D.; Lee, D.; Gulten, G.; Aggarwal, A.; Wofford, J.; Krieger, I.; Tripathi, A.; Patrick, J. W.; Eckert, D. M.; Laganowsky, A.; Sacchettini, J.; Lindahl, P.; Bankaitis, V. A. *eLife* **2020**, *9*, e57081.

Bankaitis V. A., Mousley C.J., Schaaf G. *Trends in Biochemical Sciences* 2010, 35:150–160.

08.01.2024

Metal-Ligand Synergy in Defining Delicate Electronic Form and Its Implication

G. K. Lahiri

Department of Chemistry, IIT Bombay, Powai, Mumbai-400076

lahiri@chem.iitb.ac.in

Reversible electron reservoir feature of redox non-innocent ligand extends metal- ligand synergy in suitably designed molecular frameworks primarily due to the closeness in energy of their frontier molecular orbitals, which in turn facilitates molecular bistability as well as catalytic events. In this context, the present deliberation would be focused in the direction of highlighting inner sphere electron transfer at the metal-ligand interface (M^nL^p«$M^{n+1}L^{p-1}$) and its implication in terms of resonating and dynamic valence tautomeric forms from the broader perspective of sensitive electronic structural issue as well as its impact on chemical noninnocence of the coordinated substrate moiety.

Representative articles:

Lahiri *et al.* *Inorg. Chem.* **2023**, *62*, 14507; *Inorg. Chem.* **2022**, *61*, 6347; *Inorg. Chem.* **2021**, *60*, 18260; *Angew. Chem. Int. Ed.* **2021**, *60*, 11206; *Chem. Eur. J.* **2021**, *27*, 5461; *Inorg. Chem.* **2020**, *59*, 1355; *Inorg. Chem.* **2019**, *58*, 11458; *Chem. Commun.* **2017**, *53*, 4006.

CPET and HAT Reactions Based on 1,4-Naphthoquinone Derivatives

Souvik Mukherjee and Prasanta Ghosh*

Department of Chemistry, Ramakrishna Mission Residential College (Autonomous),Narendrapur, Kolkata 700 103, India, E-mail: ghosh@pghosh.in

In a current search, a spontaneous methoxylation of 2-(quinolin-8-ylamino)naphthalene- 1,4-dione coordinated to a high spin cobalt(II) ion, promoted concerted proton electron transfer (CPET) reaction oxidizing cobalt(II) to cobalt(III) in air and subsequent demethoxylation induced reduction of cobalt(III) to cobalt(II) producing H_2O_2 are authenticated. The cobalt(III)/cobalt(II) electron transfer (ET) potential of the designed complex in CH_2Cl_2 is -0.27 V vs Fc^+/Fc redox couple. However, in presence of MeOH the reduction potential decreases to -1.02 V due to CPET involving MeOH proton. In certain solvents, spontaneous demethoxylation giving back the original complex and reactive methoxyl radical producing H_2O_2 in air are substantiated. Overall one molecule of MeOH produces one molecule of H_2O_2.[1]

It is further established that (1,4-naphthoquinone)-NH-N=C(OH)Ph (H_3L) coordinated to octahedral ruthenium(II) activates $^3O_2$ molecule spontaneously by a hydrogen atom transfer (HAT). HAT from the -NH- function of H_3L to $^3O_2$ and subsequent ($2e+2H^+$) oxidation forming (1,3,4-trioxonaphthalen)=N-N=C(OH)Ph (HL^{OX}) has been confirmed. The same was reproduced with the osmium analogue. The $H_3L \rightarrow HL^{OX}$ transformation occurs via (3- hydroperoxy-1,4-naphthoquinone)=N-N=C(O^-)Ph (HL^{OOH-}) as an intermediate. The primary step is the generation of $H_2L^{\bullet-}$ and hydroperoxide ($OOH^\bullet$) radicals. $H_2L^{\bullet-}$ is delocalized over the aromatic ring and incites coupling reactions via ortho carbon and produces coordinated HL^{OOH-}. In solution, the homolytic cleavage of the peroxo bond leads to the aromatic ring oxidation affording L^{OX-}. The kinetics of the reaction has been analyzed.[2]

References

1. Mukherjee, S.; Maji, K.; Saha, P.; Ghosh, P. *Chem. Eur. J. 2023, e202302291*. DOI: 10.1002/chem.202302291

2. Mukherjee, S.; Mandal, S.; Ghosh, P. *unpublished results*

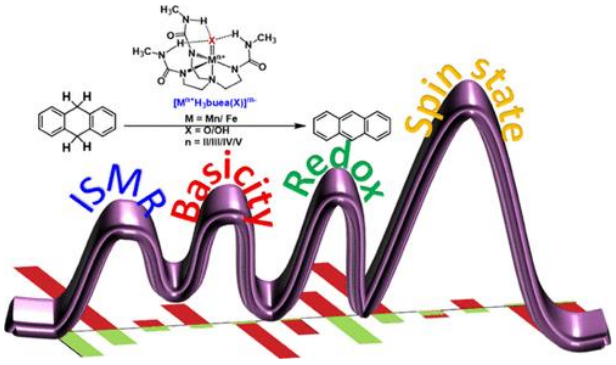
08.01.2024

Identical Spin Multi-State Reactivity (ISMR) Towards C-H Bond Activation in Metal-Oxo/Hydroxo Species

Gopalan Rajaraman

[a] Department of Chemistry, Indian Institute of Technology Bombay, IIT Bombay, Powai − 400076, Mumbai, Maharashtra, India *E-mail: gopalan.rajaraman@gmail.com

The challenge of activating C−H bonds using widely available metal catalysts on Earth is one within the field of chemistry. In particular, high-valent Mn/Fe oxo(hydroxo) biomimic species play a crucial role in this area. However, questions persist about how these species compare in their ability to oxidize compounds, and the field lacks a unified concept that can explain the various factors influencing reactivity. To shed light on these mysteries, our study takes an approach using both density functional theory (DFT) (B3LYP-D3/def2-TZVP) and ab initio (CASSCF/NEVPT2) calculations. We specifically focus on a series of high-valent metal-oxo species [$M^{n+}H_3$buea(O/OH)] (M = Mn and Fe, n = II to V; H_3buea = tris[(N′-tert-butylureaylato)-N-ethylene)]-aminato) and explore their interactions with dihydroanthracene (DHA). In addition to these considerations, our investigation delves into the hydrogen bonding network within the ligand structure. This network has an impact on the energy difference between the ground state and excited states, bringing excited states with the same spin multiplicity close together in energy. This unique arrangement leads to reactivity through one of these states, effectively reducing the barriers for activating C−H bonds. In our analysis, we have gained insights not only into the oxidative capabilities of high-valent Mn/Fe oxo(hydroxo) species but also developed a logical framework that explains previously perplexing trends in reactivity observed in different systems. This multidimensional approach enhances our comprehension of C−H bond activation and provides valuable guidance for future progress in the field of catalysis and metal-mediated reactions. (1)



References:

(1) Rajaraman and coworkers, *Inorg. Chem.* 2023, 62, 37, 14931–14941.

Organic oxidations with iron and manganese catalysts – a total analysis approach to elucidating mechanisms and origins of H_2O_2 decomposition

C. Maurits de Roo, Andy S. Sardjan, Johann B. Kasper, Ronald Hage, Wesley R. Browne

Stratingh institute for Chemistry, Faculty of Science and Engineering, University of Groningen, Nijenborgh 4, 9747AG Groningen The Netherlands, brownegroup.eu

The oxidation of organic compounds and especially alkene oxidation is central to fine chemical production. H_2O_2 is the oxidation of choice for atom efficiency and minimizing environmental impact. Its activation by 1st transition metals is especially attractive but presents the challenge to suppress the wasteful and potentially hazardous decomposition of H_2O_2 to water and O_2. The species responsible for substrate oxidation and H_2O_2 decomposition can be expected to respond differently to changes in reaction conditions. Common approaches are the use of additives, and in particular carboxylic acids,[1] as well as maintaining a low steady state concentrations of oxidant.[2] Catalyst discovery and optimization for overall efficiency benefits from in line reaction monitoring and in this lecture we will discuss the use of combined spectroscopies in reaction monitoring with two examples to illustrate how a total analysis mechanistic approach can be used to understand why various approaches to reaction optimization work or not. [3]

References:

1) J. Chen, A. Draksharapu, D. Angelone, D. Unjaroen, S. K. Padamati, R. Hage, M. Swart, C. Duboc, W R. Browne, *ACS Catal.* **2018**, *10*, 9665
2) P. Saisaha, J. Dong, T. Meinds, J. W. de Boer, R. Hage, F. Mecozzi, J. B. Kasper, W. R. Browne, ACS Catalysis **2016**, *6*, 3486
3) J.B. Kasper, P. Saisaha, C. M. de Roo, M. J.Groen, L. Vicens, M. Borrell, J. W. de Boer, R. Hage, M.C. Costas, W. R. Browne, ChemCatChem **2023**, *doi.org/10.1002/cctc.202201072*

08.01.2024

High Valent Mn species:

A structural mimic of photosystem II

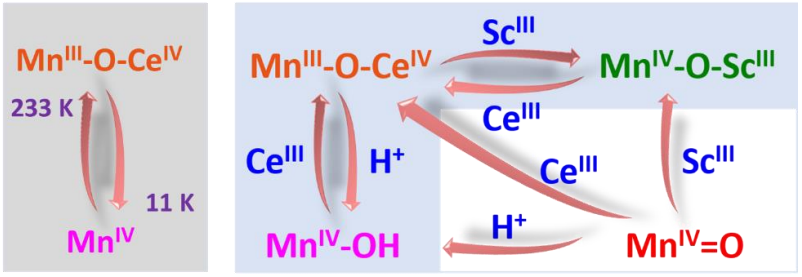
Apparao Draksharapu*

Assistant Professor, Southern Laboratories-208A, Department of Chemistry, Indian Institute of Technology Kanpur, Kanpur-208016, India.

appud@iitk.ac.in

Lewis acid-bound high valent Mn-oxo species are of great importance due to their relevance to photosystem II. Here we report the synthesis of a unique $[(BnTPEN)Mn(III)–O–Ce(IV)(NO_3)_4]^+$ adduct (**2**), by the reaction of (BnTPEN)Mn(II) (**1**) with 4 eq. ceric ammonium nitrate. **2** has been characterized using UV/Vis, NMR, resonance Raman spectroscopy, as well as by mass spectrometry. Treatment of **2** with $Sc(III)(OTf)_3$ results in the formation of (BnTPEN)Mn(IV)–O–Sc(III) (**3**), while $HClO_4$ addition to **2** forms (BnTPEN)Mn(IV)–OH (**4**), reverting to **2** upon $Ce(III)(NO_3)_3$ addition (Scheme 1). **2** can also be prepared by the oxidation of 1 eq. $Ce(III)(NO_3)_3$ with $[(BnTPEN)Mn(IV)=O]^{2+}$ (**5**). In addition, the EPR spectroscopy revealed an elegant temperature-dependent equilibria between **2** and Mn(IV) species. The binding of redox-active Ce(IV) boosts electron transfer efficiency of **2** towards ferrocenes. Despite having a component only in the Mn(III) oxidation state, **2** can nevertheless carry out O-atom and H-atom transfer reactions more typical of Mn(IV).

While with the support of a tetradentate ligand framework namely BPMEN, we were able to characterize a high valent $[Mn(V)=O(salicylate)]^+$ complex with remarkable reactivity. The unprecedented study starting from a non-heme neutral polypyridine ligand framework paves a path for mimicking the natural active site of photosystem II under ambient conditions. I will talk about our little journey to mimic the closest photosystem II structural model.



Scheme 1. Schematic diagram illustrating (left) the temperature dependent equilibrium between Mn(III)–O–Ce(IV) and Mn(IV) species and (right) the equilibria of Mn(III)–O–Ce(IV) with other high valent Mn(IV) species in solution.

References:

(1) Y. Umena, K. Kawakami, J. R. Shen, N. Kamiya, Nature **2011**, *473*, 55–60.
(2) S. Gupta, P. Arora, R. Kumar, A. Awasthi, B. Chandra, R. Eerlapally, J. Xiong, Y. Guo, L. Que, Jr., A. Draksharapu, **2023**, *submitted*.
(3) P. Arora, S. Gupta, S. K. Vechalapu, R. Kumar, A. Awasthi, S. Senthil, S. Khanna, D. Allimuthu, A. Draksharapu, *Chem. Eur. J.* **2023**, 29, e20230150.

08.01.2024

^{1}H NMR-based assay for studying the substrate scope of a 2-OG and Fe (II) dependent Pseudomonal Ethylene-forming enzyme

Siddhant Dhingra, Luke Harrington, Lennart Brewitz, Zhihong Zhang, and Christopher J. Schofield*.

Chemistry research laboratory, Department of Chemistry, University of Oxford, Oxford.

Ethylene is a phytohormone with functions in. leaf senescence and fruit-ripening. Several plant-infecting microorganisms have been reported to produce ethylene to alter plant metabolism, including e.g. *Pseudomonas* which uses the L-arginine, Fe (II), and 2-oxoglutarate (2-OG) dependent ethylene-forming enzyme (PsEFE) to catalyze the formation of ethylene from 2-OG (Fig.1a) [1]. 2-OG is converted to ethylene via a Grob-type oxidative fragmentation reaction (Fig.1b) [2]. Concomitantly, PsEFE also catalyses the hydroxylation of L-arginine and the oxidative decarboxylation of 2-OG to succinic acid[1]. A ^{1}H NMR assay was optimised by sequential acquisitions of the reaction mixtures under varied pH conditions and/or the absence of different components to understand their significance in enzymatic catalysis. It was aimed to employ this assay to explore the formation of substituted olefins while using various 2-OG derivatives. The optimized NMR PsEFE assay was employed to investigate the potential of C-3 or C-4 substituted 2-OG derivatives as alternative co-substrates. Even though formation of the corresponding substituted olefin products (**2**, Fig. 2) was not detected, the corresponding ω-hydroxy acids (**1**, Fig 2) and diacid (**3**, Fig. 2) were observed as the only reaction products. These alcohols and diacids are of biological and industrial importance, broadening the scope of PsEFE for large- scale production of relevant compounds. For example, γ-hydroxybutyricacid (GHB), which is formed from 2-oxoadipate is a neuroactive natural product known to induce euphoria. These results have opened avenues for more mechanistic explorations in PsEFE catalysis. They also highlight the scope of PsEFE in enzymatic synthesis of not only ethylene but also various diacids and ω-hydroxy acids. The findings highlight the scope of NMR in understanding products of enzymatic catalysis, quantifying turnover, and providing insights into reaction mechanisms.

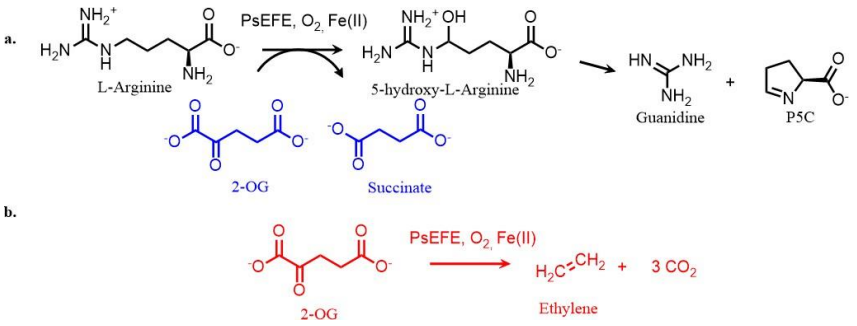


Figure 1: Different reaction pathways in PsEFE catalysis

References:

1. Martinez, S. & Hausinger, R. P. Biochemical and Spectroscopic Characterization of the Non-Heme Fe(II)- and 2-Oxoglutarate-Dependent Ethylene-Forming Enzyme from Pseudomonas syringae pv. phaseolicola PK2. Biochem., **2016**, *55,* 5989-5999.

2. Zhang, Z. *et al.* Structural and stereoelectronic insights into oxygenase-catalyzed formation of ethylene from 2-oxoglutarate. Proc. Natl. Acad. Sci. U S A., **2017,***114*, 4667–4672.

08.01.2024

Role of redox non-innocent azo-oximes in metal mediated bioinspired redox transformation and in redox catalysis

Sanjib Ganguly

Department of Chemistry, St. Xavier's College (Autonomous), Kolkata-700016, India

Email: icsgxav@gmail.com icsg@sxccal.edu

Ligands containing azo functions in conjunction with oxime group have been found to have the aptitude to accept electron(s) upon coordination with suitable metal centres to form azo-anion radical complexes,[1] thereby revealing their redox non-innocent behaviour. The ability of electron acceptance may be adjusted by suitable choice of ancillary ligands and this property has been exploited to bring about bioinspired redox transformations like transformation of metal carbonyl to metallocarboxylic acid via nucleophilic attack of water.[2] Also, the metal oximes may be converted to corresponding imines by reduction with ascorbic acid/ sodium borohydride.[3] The reactions have been found to proceed *via* PCET[4] pathway. Furthermore, the ability of such ligands of trapping electron upon coordination is currently being employed in our laboratory in redox catalysis for hassle-free and economical synthesis of utility organic chemicals.

References

1. Sanjib Panda, Suman Dhara, Aditi Singh, Sanchaita Dey, Goutam Kumar Lahiri, *Coord. Chem. Rev*. **2023,** *475*, 214895.
2. Shuvam Pramanik, Sima Roy, Tapas Ghorui, Sanjib Ganguly, Kausikisankar Pramanik, *Inorg. Chem.*, **2016**, *55, 4*, 1461.
3. Soumitra Dinda, Shuvam Pramanik, Jaydeep Basu, Sarat Chandra Patra, Kausikisankar Pramanik, Sanjib Ganguly, *Dalton Trans*., **2022**, *51*, 10121.
4. Christopher J. Gagliardi, Brittany C. Westlake, Caleb A. Kent, Jared J. Paul, John M. Papanikolas, Thomas J. Meyer, *Coord. Chem. Rev*. **2010**, *254*, *21-22*, 2459.

08.01.2024

Unveiling the Oxidized State of Glutamate Coordinated O_2-Tolerant [NiFe]-Hydrogenase

Ravi Kumar[a], Matthias Stein[a,*]

[a]Max Planck Institute for Dynamics of Complex Technical Systems, Molecular Simulations and Design Group, Sandtorstrasse 1, 39106 Magdeburg, Germany

Hydrogenases are metalloenzymes that catalyze the conversion of molecular hydrogen to protons and electrons and *vice versa*. Based on active site compositions, they are classified into three categories, [FeFe]-, [NiFe]- and [Fe]-hydrogenases. Oxidation of molecular hydrogen is mainly performed by [NiFe]-hydrogenases, while the [FeFe]-and [Fe]-hydrogenases are biased towards the production of molecular hydrogen.[1-2] Shomura et al. reported the structure of the oxygen-tolerant [NiFe]-hydrogenase from *H. thermoluteolus* and suggested an unusual coordination of the active site nickel atom.[3] In the active site nickel in the oxidized state a terminal cysteine residue is displaced to a μ-cysteine bridging position by a bidentate coordination of a nearby Glu32. Recently, Kulka-Peschke et al. suggested an uncommon closed-shell Ni(IV)Fe(II) through the spectral features to this state.[4] In biological systems, such a high oxidation state of nickel with soft ligands was unprecedented and prompted further investigation. Here, we provide some arguments for why we consider the assignment of the Ni(IV) oxidation state in the soluble hydrogenase (SH) as ambiguous and not fully plausible.[5] An energetically low-lying broken-symmetry Ni(III)Fe(III) state of the active site appears more probable. It also reproduces well the spectral properties and the coordination sphere of the oxidized state of the [NiFe]-hydrogenase.[5] Then Ni(III)Fe(III) open-shell singlet (S = 0) is produced via antiferromagnetic spin-coupling of Ni-d^7 and Fe-d^5 with evenly distributed spin densities over both metal atoms. Finally, some suggestions are provided for experimental chemists to clarify the final assignment of redox states.[5]

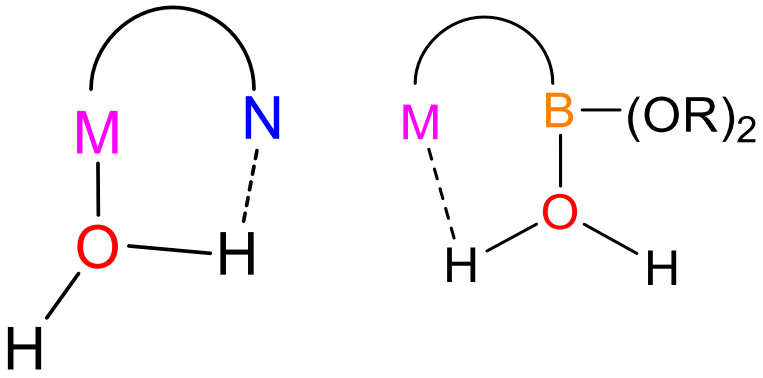
References:

1. Albracht, S. P. J.; Cammack, R.; Frey, M.; Robson, R., Hydrogen as a Fuel. Learning from Nature. 2001; p 110.
2. Vignais, P. M.; Billoud, B., Occurrence, Classification, and Biological Function of Hydrogenases: An Overview. Chem. Rev. 2007, 107, 4206.
3. Shomura, Y.; Tai, H.; Nakagawa, H.; Ikeda, Y.; Ishii, M.; Igarashi, Y.; Nishihara, H.; Ogo, S.; Hirota, S.; Higuchi, Y., Structural Basis of the Redox Switches in the NAD+-Reducing Soluble [NiFe]-Hydrogenase. Science 2017, 357, 928.
4. Kulka-Peschke, C. J.; Schulz, A.-C.; Lorent, C.; Rippers, Y.; Wahlefeld, S.; Preissler, J.; Schulz, C.; Wiemann, C.; Bernitzky, C. C. M.; Karafoulidi-Retsou, C.; Wrathall, S. L. D.; Procacci, B.; Matsuura, H.; Greetham, G. M.; Teutloff, C.; Lauterbach, L.; Higuchi, Y.; Ishii, M.; Hunt, N. T.; Lenz, O.; Zebger, I.; Horch, M., Reversible Glutamate Coordination to High-Valent Nickel Protects the Active Site of a [NiFe] Hydrogenase from Oxygen. J. Am. Chem. Soc. 2022, 144 (37), 17022-17032.
5. Kumar, R.; Stein, M., The Fully Oxidized State of the Glutamate Coordinated O_2-Tolerant [NiFe]-Hydrogenase Shows a Ni(III)/Fe(III) Open-Shell Singlet Ground State. J. Am. Chem. Soc., 2023, 145, 10954 - 10959

Water as a Reactant in Organometallic Catalysis

Jitendra K Bera
Department of Chemistry, Indian Institute of Technology Kanpur, Kanpur 208016 India, E-mail: jbera@iitk.ac.in

High O-H bond dissociation energy and unfavourable thermodynamics render water a difficult reagent to be exploited in chemical reactions. Bringing a catalytically relevant water molecule from the bulk water to the vicinity of the metal center is one of the most critical steps. A cooperating ligand compensates for the thermodynamic loss by H-bond interaction with the water molecule. Carefully designed ligand scaffolds, which hold the metal center and simultaneously offer a H-bond acceptor, have been devised for water activation and subsequent utilization in organic transformations. In this talk, hydration of nitriles and alkynes, olefin oxygenation, alcohol oxidation to acid and oxidative deamination of primary amines by using water will be discussed.



References
[1] Pal, N. K; Singh, K.; Patra, M; Yadav, S.; Pandey, P. P.; Bera, J. K. *Green Chemistry*, **2023**, *25*, 6212.
[2] Daw, P.; Sinha, A.; Rahaman, S. M. W.; Dinda, S.; Bera, J. K. *Organometallics* **2012,** *31*, 3790−3797.
[3] Ghatak, T.; Sarkar, M.; Dinda, S.; Dutta, I.; Rahaman, S. M. W.; Bera, J. K. *J. Am. Chem. Soc.* **2015,** *137*, 6168−6171.
[4] Sarbajna, A.; Dutta, I.; Daw, P.; Dinda, S.; Rahaman, S. M. W.; Sarkar, A.; Bera, J. K. *ACS Catal.* **2017,** *7*, 2786−2790.
[5] Singh, K.; Sarbajna, A.; Dutta, I.; Pandey, P.; Bera, J. K. *Chem.−Eur. J.* **2017,** 23, 7761.

08.01.2024

Adaptive Life Inspired Nanomaterials via Systems Chemistry

* Dibyendu Das

*dasd@iiserkol.ac.in, Dept of Chemical Sciences and
CAFM,IISER Kolkata, India

ABSTRACT

There remain critical gaps in our understanding of the emergence of functional biopolymers in the origins of Earth's biosphere. Extant proteins, evolved over millions of years, carry out an impressive array of responsibilities, from catalysis and molecular recognition to motility and compartmentalization. One of the major goals of our lab is to investigate the possible origins of advanced enzymatic functions from folds of short peptide based paracrystalline phases.[1-2] Further, we are excited about understanding the non-equilibrium structures of living systems. I will show our recent discoveries of simple chemical systems that can be substrate-driven to access higher energy self-assembled states, just as seen in natural microtubules. Further, I will attempt to sketch our aims of developing self-assembled autonomous materials that can show temporal control of functions [3-7]

Keywords: short peptide; non-equilibrium; self-assembly; autonomous materials; microtubules.

References

1. B. Sarkhel, A. Chatterjee and D. Das*. J. Am. Chem. Soc. 2020 142 4098-4103.
2. S.P. Afrose, C. Mahato, P. Sharma, L. Roy, and D. Das*. J. Am. Chem. Soc. 2022, 144, 673-678.
3. S. Pal, A. Reja, S. Bal, B. Tikader and D. Das* Angew. Chem. Int. Ed. 2022, e202111857.
4. S. Bal, C. Ghosh, P. Parvin and D.Das* Nano Lett. 2023(ASAP:10.1021/acs.nanolett.3c03135).
5. S. Goswami, A. Reja, S. Pal, A. Singh, and D. Das *. J. Am. Chem. Soc. 2022 144, 42, 19248–19252
6. A. Reja, S. Pal, K. Mahato, B. Saha, M. D. Piane, G.M. Pavan, and D. Das* J. Am. Chem. Soc. 2023, 145, 38, 21114–21121
7. C. Ghosh, S. Ghosh, A. Chatterjee, P. Bera, D. Mampallil, P. Ghosh and D. Das Nat. Commun. 2023 14, 5903

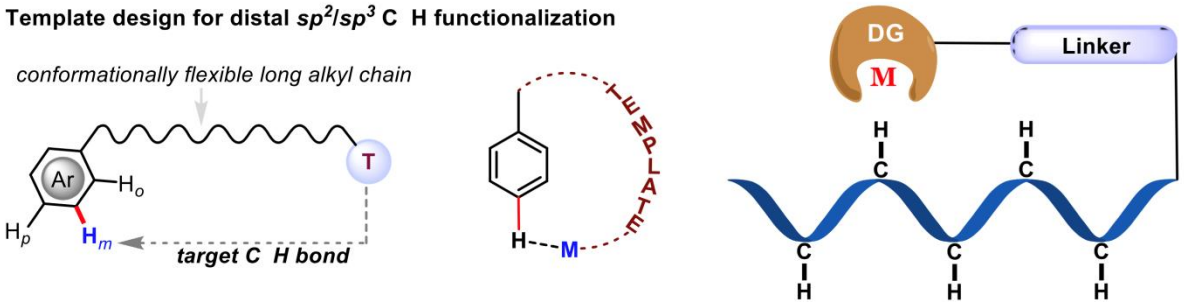
08.01.2024

En-Lightening C-H functionalization

Debabrata Maiti
IIT Bombay
dmaiti@iitb.ac.in

The scientific community has long sought to emulate nature's mechanisms, particularly in understanding how enzymes achieve chemical transformations with precision. Through extensive research, we have gained a thorough understanding of how enzymes catalyze the functionalization of inert C–H bonds in a regio- and stereoselective manner, utilizing metal-active sites. Taking inspiration from these natural processes, we have successfully developed catalytic methods for the functionalization of carbon–hydrogen (C–H) bonds. The Fujiwara–Moritani reaction is one of such reaction which made significant impact on the development of modern C–H activation methodologies. Despite the traditional approach's widespread applicability in various fields, issues related to reactivity and regioselectivity have limited its effectiveness. To revive this remarkable reaction, it is necessary to establish a mechanistic framework that allows simultaneous control over both reactivity and regioselectivity. The conventional high-temperature conditions required for olefination often lead to undesired multiple functionalizations at different sites.

In our work, we have successfully established a photoredox catalytic system by merging a palladium catalyst with an organo-photocatalyst (PC). This innovative system enables selective oxidative olefination of diverse arenes and heteroarenes in a highly regioselective manner. The utilization of visible light plays a crucial role in driving these "regioresolved" Fujiwara–Moritani reactions, eliminating the need for silver salts and high thermal energy. Our catalytic system also exhibits compatibility with both proximal and distal olefination, facilitated by the appropriate directing groups (DGs). This versatility allows us to engage the entire spectrum of C(sp^2)–H olefination. The broad scope of this protocol allows for the synthesis of diverse compounds, including natural products, chiral molecules, and drugs. The established mechanistic insights further enhance our understanding of this reaction, enabling future advancements in this field. Importantly, this method offer significant advantages over traditional synthetic approaches, both in terms of economic feasibility and environmental impact.



Recent Refernces:

J. Am. Chem. Soc. **2022**, 144, 4; *Science*, **2021**, *372*, 701; *Nat. Commun.* **2021**, *12*, 1393; *Angew. Chem. Int. Ed.* **2021**, *60*, 14030; *J. Am. Chem. Soc.*, **2020**, 142, 12453; *J. Am. Chem. Soc*., **2020**, *142*, 3762

08.01.2024

Imidazolium and Triazole Functionalities in Anion Chemistry

Pradyut Ghosh

School of Chemical Sciences, Indian Association for the Cultivation of Science, 2A & 2B, Raja S. C. Mallick Road, Kolkata - 700 032, INDIA

Email: icpg@iacs.res.in

Anions are indispensable in nature because of the significant role played by them in some of the biological processes e.g., signal transduction, energy storage to living organisms, and environmental issues, such as, eutrophication of water body etc. Recognition of anions has mostly been controlled through hydrogen bonding (HB) interactions. However, halogen bonding (XB) is evolving as a new type of interaction in Supramolecular Chemistry in general and also in the designing of selective anion receptors. The focus of this talk is based on our experimental findings regarding halogen bonding based halide and perrhenate recognition and extraction in imidazolium based tripodal and tetrapodal receptors,[1-3] monomeric vs. polymeric hexapodal imidazolium receptors for efficient extraction of perrhenate from aqueous medium,[4-5] and selective sensing and extraction of phosphates by utilizing some bis-heteroleptic Ru(II) and Ir(III) complexes of pyridyl triazole (selected recent works) as selective and sensitive probes for sensing and extraction of phosphates via halogen as well as hydrogen bonding inraction.[6-10]

References:

1. Chakraborty, S.; Dutta, R.; Ghosh, P. *Chem. Commun.* **2015**, *51*, 14793-14796.

2. Chakraborty, S.; Maji, S.; Ghosh, R.; Jana, R.; Datta, A.; Ghosh, P. *Chem. Commun.* **2019**, *55*, 1506 - 1509.

3. Ghosh, R.; Ghosh, T. K.; Pramanik, S.; Islam, A. S. M.; Ghosh, P. *ACS Appl. Mater. Interfaces* **2023**, *15*, 21, 25184–25192.

4. Ghosh, R.; Ghosh, T. K.; Ghosh, P. *Dalton Trans.* **2020**, *49*, 3093-3097.

5. Ghosh, R.; Ghosh, T. K.; Ghosh, P. *Chem. Commun.* **2021**, *57*, 5578-5581.

6. Mondal, S.; Sarkar, K.; Ghosh, P. *Inorg. Chem.* **2021**, *60*, 9084-9096.

7. S. Mondal, T. K. Ghosh, B. Chowdhury, P. Ghosh; *Inorg. Chem.*, **2019**, 58, 15993–16003.

8. Ghosh, T. K.; Chakraborty, S.; Chowdhury, B.; Ghosh, P. *Inorg. Chem.* **2017**, *57*, 5371-5382.

9. Ghosh, T. K.; Mondal, S.; Bej, S.; Nandi, M.; Ghosh; P. *Dalton Trans.* **2019**, *48*, 4538-4546.

10. Rashid, A.; Mondal, S.; Mondal, S.; Ghosh, P. *Chem, Asian J.*, **2022**, *17*, e2022003.

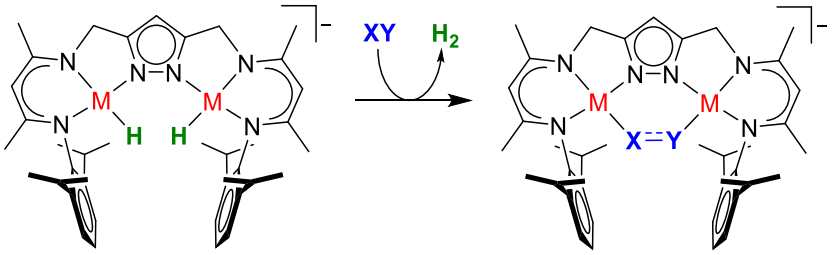
Inspired by Nitrogenase: Dihydride Complexes for the H_2-Releasing Reductive Activation of Challenging Substrates

Franc Meyer

University of Göttingen, Institute of Inorganic Chemistry, Tammannstr. 4,
D-37077 Göttingen, Germany; Email: franc.meyer@chemie.uni-goettingen.de

Metalloenzyme active sites provide great inspiration for the design of new types of catalysts for the activation of small inert molecules, and for substrate transformations relevant to sustainable energy schemes. Work in our group has exploited the use of compartmental pyrazolate-based ligand scaffolds for preorganizing two metal ions at tunable distances to enable metal-metal cooperativity, to enforce constrained substrate binding modes, and to emulate bioinorganic reactivity and isolate key intermediates [1].

The focus of this lecture will be on systems that use H_2 release from dinuclear metal hydride complexes to provide the required reducing equivalents for the binding and subsequent transformation of ubiquitous molecules such as O_2, H_2O, NO, or N_2 [2], also enabling key reactivity steps observed for multimetallic enzymes such as Acetyl-CoA Synthase (ACS). Spectroscopic and kinetic investigations as well as DFT calculations for these systems are revealing electronic structure contributions to reactivity, and are providing important mechanistic insight.



References:

[1] K. E. Dalle, F. Meyer, *Eur. J. Inorg. Chem.* **2015**, 3391-3405.

[2] (a) D.-H. Manz, P.-C. Duan, S. Dechert, S. Demeshko, R. Oswald, M. John, R. A. Mata, F. Meyer, *J. Am. Chem. Soc.* **2017**, *139*, 16720-16731; (b) P.-C. Duan, D.-H. Manz, S. Dechert, S. Demeshko, F. Meyer, *J. Am. Chem. Soc.* **2018**, *140*, 4929-4939; (c) E. Ferretti, S. Dechert, S. Demeshko, M. C. Holthausen, F. Meyer, *Angew. Chem. Int. Ed.* **2019**, *58*, 1705–1709; (d) E. Ferretti, S. Dechert, F. Meyer, *Inorg. Chem.* **2019**, *58*, 5154−5162; (e) H. Stevens, P.-C. Duan, S. Dechert, F. Meyer, *J. Am. Chem. Soc.* **2020**, *142*, 6717−6728; (f) P.-C. Duan, R. S. Schulz, A. Römer, B. E. Van Kuiken, S. Dechert, S. Demeshko, G. E. Cutsail III. S. DeBeer, R. A. Mata, F. Meyer, *Angew. Chem. Int. Ed.* **2021**, *60*, 1891-1896.

08.01.2024

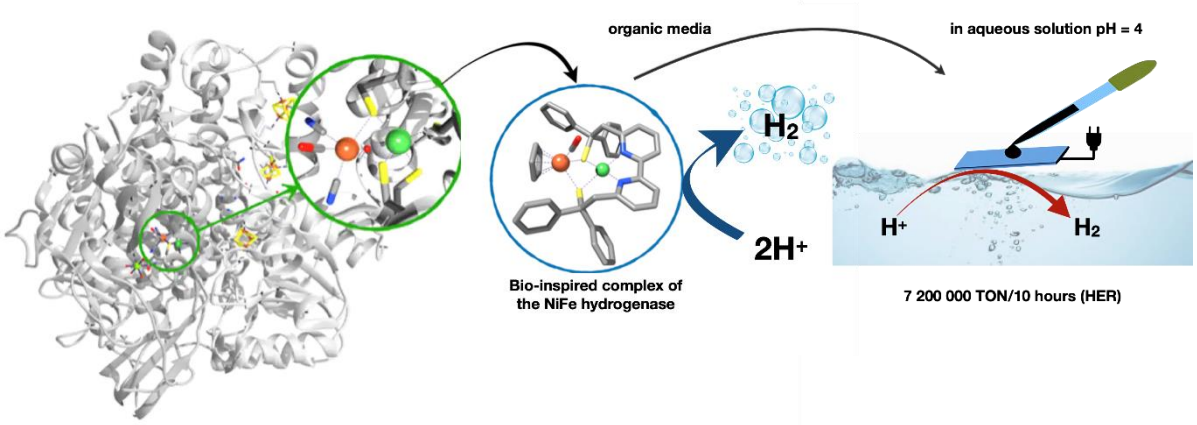
Bio-inspired catalyst design for small molecule activation in multi-electron reduction processes

M. Gennari, N. Laloui, C. Duboc
University Grenoble-Alpes-CNRS, Grenoble, France

carole.duboc@univ-grenoble-alpes.fr

The activation of small molecules in multi-electron reduction catalysis has become an important area of research due to the challenges associated with the energy and environmental problems facing our society. These redox processes are generally promoted by metal ions. In our aim to develop efficient complexes for such catalytic processes, we focused on thiolate-based scaffolds, as thiolate-metal complexes are widely present in the active site of enzymes catalyzing the reactions of interest. Examples include the hydrogenases, which reversibly reduce protons to generate H_2 (see Figure). Our aim is to design innovative catalysts (for H_2 production and O_2 reduction) that are robust and active in water, based on the use of thiolate-based ligands and noble-free metal ions.

In particular, we will describe how we have designed our most efficient catalytic systems. This involved a systematic exploration of series of complexes to assess the impact of the metal, the first coordination sphere, particularly with regard to the pivotal role of the thiolate during catalysis, and the second coordination sphere, where a potential proton relay can be introduced. We will also present mechanism studies, including the generation and characterization of intermediate species, to unveil the key factors for enhanced activity. Finally, we will also discuss how we can modify the catalytic conditions to optimize the catalytic process (homogeneous or heterogeneous conditions, how to supply electrons, i.e., chemically, via electro-assisted or photo-assisted processes).



SABIC 2024

DAY-3: 09.01.2024 (Tuesday)

09.01.2024

Rational design of the active site in bacterial Cytochrome P450:

Shyamalava Mazumdar

Tata Institute of Fundamental Research,

Homi Bhabha Road, Colaba, Mumbai 400005, India

Email: shyamal@tifr.res.in

Cytochrome P450 is a large superfamily of heme containing mono-oxygenase enzymeinvolved in activation of C-H bond to form mono oxygenated products. The overall catalytic reaction involves following steps:

$$R\text{-}H + O_2 + 2e^- + 2H^+ = R\text{-}OH + H_2O$$

Mono-oxygenation

(i) binding of the substrate at the active site of the enzyme located near the heme so that the target site of the substrate lies close to the iron centre of the heme for rapid transfer of active oxygen. (ii) first electron transfer to the heme producing five coordinated ferrous heme. (iii) binding of molecular oxygen to the iron centre of the heme and subsequent second electron and proton transfer accompanied by electronicrearrangement leading to formation of the putative compound I intermediate containingoxo-Ferryl heme radical. (iv) transfer of oxygen atom to the target site of the substrateforming the product, and release of water along with the product from the active site of the enzyme at the final step. Detailed molecular structure analyses of all these steps in a cytochrome P450 enzyme, and appropriate modification of the amino acids in thevicinity of the heme centre have been used to optimize each of these steps for a givenunnatural substrate. This approach can provide a rational design of the active site of the enzyme for efficient enzymatic activity. Our group has designed a large number ofmodifications in and around the active site of a thermostable cytochrome P450 to achieve tunability in substrate recognition with enhancement in the catalytic activity ofthe enzyme. The present talk would discuss the current status of the development of efficient biocatalysts by rationally designed cytochrome P450 and outline our efforts inthis area.

09.01.2024

Diheme Enzyme *MauG*: Our Understanding Towards Nature's Design

S P Rath

Department of Chemistry, IIT Kanpur, Kanpur-208016, India. Email: sprath@iitk.ac.in

MauG is a terminal enzyme involved in the biosynthesis of the catalytic tryptophan tryptophenylquinone (TTQ) cofactor of methylamine dehydrogenase (MADH). Although two heme units are physically separated in the enzyme, they share electronefficiently behaving as a single diheme unit. A tryptophan residue, positioned midwaybetween the heme centers, has been postulated to act as a bridge for electronic communications. *MauG*-catalyzed TTQ biosynthesis is accomplished through radicalchemistry and initiated using H2O2 as the oxidant which produces stable bis-Fe(IV) redox state (Figure 1). These attractive features have prompted us to investigate on such diheme enzyme and the results will be highlighted in the talk.[1-5]

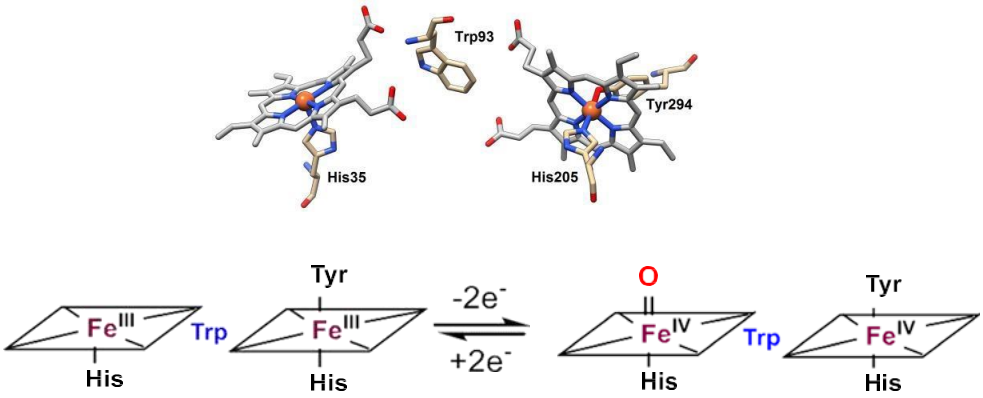


Figure 1. Relative orientation of hemes and the intervening tryptophan residue in *MauG* (PDB ID code 3L4M), *top*, and formation of bis-Fe(IV) state of MauG, *bottom*.

References:

(1) a) Dhamija, A.; Chandel, D.; Rath, S. P. *Chem. Sci.*, **2023**, *14*, 6032. b) Singh, A.; Khan, F.S.T.; Rath, S. P. *Angew. Chem. Int. Ed.* **2017**, *56*, 8849. c) Dey, S.; Sil, D.; Rath, S. P. *Angew. Chem. Int. Ed.* **2016**,*55*, 996. d) Sil, D.; Rath, S. P. *Chem. Sci.*, **2016**, *7*, 1212. e) Sahoo, D.; Rath, S. P. *Angew. Chem. Int.Ed.* **2015**, *54*, 4796.

(2) a) Sarkar, S.; Sarkar, P.; Pati, S. K.; Rath, S. P. *ACS Catal.* **2022**, *12*, 9589. b) A. K. Pandey, S. P.Rath, *Chem. Commun.* **2019**, *55*, 7926. c) A. Kumar, S. P. Rath, *Chem. Commun.* **2019**, *55*, 1588.

(3) a) Shah, S. J.; Pandit, Y. A.; Garribba, E.; Rath, S. P. *Chem. Eur. J.* **2023**, *29*, 0000. b) Saha, B.; Rath, S. P. *Inorg. Chem.* **2022**, *61*, 2154. c) Pandit, Y. A.; Rath, S. P. *Inorg. Chem.* **2022**, *61*, 5270. d)Singh, A. K.; Rath, S. P. *Inorg. Chem.* **2021**, *60*, 16492. e) Kumar, A.; Rath, S. P. *Chem. Eur. J.* **2021**,*27*, 11428. f) Singh, A. K.; Rath, S. P. *Chem. Eur. J.* **2020**, *26*, 14405. g) Kumar, A.; Rath, S. P. *Chem.Eur. J.* **2020**, *26*, 7869. h) Singh, A. K.; Rath, S. P. *Chem. Eur. J.* **2019**, *25*, 10098.

(4) a) Sanfui, S.; Rath, S. P. *Inorg. Chem.* **2023**, *62*, 0000. b) Sanfui, S.; Rath, S. P. *J. Inorg. Biochem.***2023**, *240*, 112109. c) Sanfui, S.; Rath, S. P. *Inorg. Chem.* **2022**, *61*, 8419. d) Khan, F. S. T.; Rath, S. P.*Inorg. Chem.* **2021**, *60*, 12870. e) Pandey, A. K.; Rath, S. P. *Inorg. Chem.* **2020**, *59*, 12988.

(5) a) Sil, D.; Khan, F.S.T.; Rath, S. P. *Adv. Inorg. Chem.* **2023**, *81*, 95. b) Sarkar, S.; Khan, F.S.T.; Guchhait, T.; Rath, S. P. *Coord. Chem. Rev.* **2023**, *479*, 215003. c) Mondal, P.; Rath, S. P. *Coord. Chem.Rev.* **2020**, *405*, 213117.

09.01.2024

Modulating the reactivity of nonheme Iron(IV)-oxo through equatorial ligand field perturbation

Chivukula V. Sastri*

Department of Chemistry, IIT Guwahati, Assam, 781039, India.
Email: sastricv@iitg.ac.in

Equatorial Ligand Field Perturbation refers to the modification of the ligand environment around a metal center, particularly in transition metal complexes, by changing the equatorial ligands. By altering the nature of equatorial ligands (for example, by changing their size, charge, or electronic properties), chemists can effectively tune the electronic structure and reactivity of the metal center. This perturbation can have a significant impact on the redox potentials, bonding interactions, and reaction mechanisms of the metal complex. Steric and electronic effects are two vital tuning probes at the equatorial ligand filed that manifests the reactivity profiles for these systems. Our group have studied the role of these equatorial ligand field perturbations around nonheme Iron(IV)-oxo core with the help of engineered N4Py ligand framework. Where, the ortho-substitution of bulky quinoline moiety in the N4Py ligand shows a dramatic rate enhancement in sulfoxidation and C-H bond activation reactions.[1] Similarly, alkyl/aryl substitution at the 6th position in the pyridine ring of methylene carbon of N4Py ligand framework resulted in a rate enhancement in sulfoxidation and C-H bond activation reactions, but no change in reaction mechanism and selectivity was observed.[2] Which led us to dig deep into the equatorial ligand field perturbation around the Iron(IV)-oxo core by the introduction of weak σ-donor like sulfur/oxygen in the primary coordination sphere. So, we have reported the synthesis, characterization and reactivity of a novel biomimetic N4S ligated iron(IV)-oxo complex and compared the results with its analogous N5-ligated iron(IV)-oxo complex. Through a detailed experimental and computational approach, we found a dramatic change in the reaction mechanism and rate enhancement in oxygen atom transfer reactions and hydrogen atom transfer reactions. But, the mehanistic switch can not only be attributed due to the sulfur. Additional experiments are undergoing in our lab to further prove our point. These findings provide insight into the reactivity of sulphur ligated iron(IV)-oxo centers and their role in various metalloenzymes.
This research not only expands our fundamental understanding of nonheme iron(IV)-oxo reactivity but also paves the way for the rational design of novel catalysts with tailored reactivity profiles. The insights gained from this study have broad implications in the field of inorganic chemistry, offering new avenues for the development of efficient and selective catalytic systems.

Keywords: Nonheme Iron(IV)-Oxo, Equatorial Ligand Field, Reactivity Modulation, Oxygen Atom Transfer, Catalysis, Spectroscopy, Computational Chemistry.

References

1. Mukherjee, G.; Lee, C. W. Z.; Nag, S. S.; Alili, A.; Cantú Reinhard, F. G.; Kumar, D.; Sastri, C. V.; de Visser, S. P. *Dalton. Trans.* **2018**, *47*, 14945-14957.
2. Mukherjee, G.; Alili, A.; Barman, P.; Kumar, D.; Sastri, C. V.; de Visser, S. P. *Chem. Eur. J.* **2019**, *25*, 5086-5098.

09.01.2024

Diverse Pathways of a Manganese(III) Superoxo Complex Reacting with Various Phenols

Yao-Cheng Tian,[a] Peng Zhang,[b,c] Kuan-Ting Lin,[a] Chung-Wei Fu,[a] Shengfa Ye,*[,b] and Way-Zen Lee*[,a]

[a] Department of Chemistry, National Taiwan Normal University, Taipei 11677 (Taiwan)
[b] State Key Laboratory of Catalysis, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023 (China)
[c] University of Chinese Academy of Sciences, Beijing 100049 (China)

In our long-term investigation on O_2 activation facilitated by enzymatic mimics, we have prepared homogeneous Fe^{III}-, Co^{III}-, and Mn^{III}-superoxo complexes via addition of O_2 to their divalent precursors at low temperatures.[1-3] The Mn^{III}-superoxo complex, $Mn(BDP^{Br}P)(O_2^{\bullet})$ (**1**, $H_2BDP^{Br}P$ = 2,6-bis((2-(S)-di(4-bromo)phenylhydroxylmethyl-1-pyrrolidinyl)methyl)pyridine), was found to react with TEMPOH yielding a corresponding Mn^{III}-hydroperoxo complex, $Mn(BDP^{Br}P)(OOH)$ (**2**).[3] Furthermore, treatment of **1** with trifluoroacetic acid (TFA) led to formation of a Mn^{IV}-hydroperoxo complex, $[Mn(BDP^{Br}P)(OOH)]^+$ (**3**).[4] In addition, we have recently reported the bond dissociation free energy (BDFE) of the OO-H bond of **2** to be 81.5 kcal/mol from the Bordwell relationship.[5] Reaction of **1** with 4-dimethylaminophenol at −80 °C produces a 4-dimethylaminophenoxy radical, suggesting a concerted proton electron transfer reaction occurs, whereas high valent Mn^{IV}-hydroperoxo **3** is remarkably afforded as complex **1** reacting with 4-nitrophenol in the same reaction conditions, indicating a proton transfer reaction proceeds. Further inspections on the other two phenols, 4-chlorophenol (^{Cl}PhOH) and 4-methoxyphenol (^{MeO}PhOH), show the reactions of **1** with ^{Cl}PhOH and ^{MeO}PhOH via a proton transfer followed by an electron transfer. UV-vis and EPR spectroscopic studies along with DFT calculations were carried out to confirm these three different reaction pathways are proceeded for O-H bond activation of various phenols by the same Mn(III)-superoxo **1**.

References

1. Chiang, C. W.; Kleespies, S. T.; Stout, H. D.; Meier, K. K.; Li, P. Y.; Bominaar, E. L.;* Que, L., Jr.;* Munck, E.;* Lee, W. Z.* *J. Am. Chem. Soc.* **2014**, *136*, 10846−10849.
2. Wang, C. C.; Chang, H. C.; Lai, Y. C.; Fang, H.; Li, C. C.; Hsu, H. K.; Li, Z. Y.; Lin, T. S.; Kuo, T. S.; Neese, F.; Ye, S.;* Chiang, Y. W.;* Tsai, M. L.;* Liaw, W. F.;* Lee, W. Z.* *J. Am. Chem. Soc.* **2016**, *138*, 14186−14189.
3. Lin, Y. H.; Cramer, H. H.; van Gastel, M.; Tsai, Y. H.; Chu, C. Y.; Kuo, T. S.; Lee, I. R.;* Ye, S.;* Bill, E.;* Lee, W. Z.* *Inorg. Chem.* **2019**, *58*, 9756−9765.
4. Y.-H. Lin, Y. Kutin, M. van Gastel, E. Bill, A. Schnegg,* S. Ye,* W.-Z. Lee,* *J. Am. Chem. Soc.,* **2020**, *142*, 10255−10260.
5. Tian, Y.-C.; Jiang, Y.; Lin, Y.-H.; Wang, C.-C.; Ye, S.;* Lee, W.-Z.* *JACS Au* **2022**, *2*, 1899–1909.

09.01.2024

Highly Active Catalysts for Hydrogen Peroxide Dismutation Illustrate a New Way to Functionally Mimic Catalase

Karbalaei, Sana; Goldsmith, Christian R.

Department of Chemistry and Biochemistry, Auburn University, Auburn, AL 36849, United States

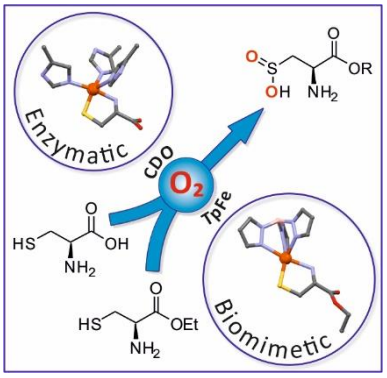
Previously reported functional mimics for catalase tend to closely approximate the binuclear manganese and heme active sites of known catalase enzymes. Despite their structural fidelity, these mimics are not effective catalysts for H_2O_2 dismutation, with activities that are many orders of magnitude below those of the enzymes. We have found that manganese, iron, and even zinc complexes with the quinol-containing ligand H_4qp4 are active catalysts for H_2O_2 degradation, with turnover numbers that greatly exceed those of the manganese-porphyrin complexes that represent the standard in this field. The redox activity of the organic portion of the catalyst can enable even redox-inactive Zn(II) to accelerate H_2O_2 dismutation. The H_4qp4 complexes are not competent superoxide dismutase mimics, suggesting that O_2^- and H_2O_2 dismutation by coordination complexes with quinol-containing ligands proceed through fundamentally different pathways.

Faithful Structural and Functional Models for the Cysteine/Cysteamine dioxygenases

Christian Limberg*, Kilian Weißer, Lars Müller, Madleen Sallmann

Humboldt-Universität zu Berlin, Brook-Taylor-Straße 2, 12489 Berlin, Germany

Mononuclear non-heme iron enzymes, which activate dioxygen for the subsequent oxygenation of substrates, are a fascinating class of metalloproteins. The cysteine dioxygenase (CDO) is a representative of the $(His)_3Fe$-enzyme family and catalyzes the reaction between cysteine and dioxygen to yield cysteine sulfinic acid, which lies at the branching point of cysteine catabolism.



Sulfinic acids are of significant interest in pharmaceutical chemistry and highly useful synthons for further valuable compounds (like sulfones) or for further (coupling)reactions. However, their synthesis often involves costly reagents and harsh conditions and a route via catalytic O_2 oxidation of thiols would be a significant advancement. Understanding of the CDO may guide the way to suitable catalysts and hence the development of synthetic model complexes that mimic the active sites of these enzymes is a valuable but also challenging target: iron oxidation instead of S-oxygenation as well as overoxidation at the S atom has to be avoided.

Here we report our progress in the development of low-molecular weight analogues, were the $(His)_3Fe$ moiety is simulated by a tris(pyrazolyl)borate-iron complex metal fragment.[1-5] Recent findings concerning the replacement of thiolates by selenium-based substrates are also presented.[1]

References:

1. K. Weißer, E. T. K. Weber, B. Cula, S. Wolff, C. Limberg, Promiscuity in molecular mimics of the Cysteine Dioxygenase – The effects of selenium in the substrate and cobalt as the central metal ion, **2023**, manuscript in preparation.
2. L. Müller, S. Hoof, M. Keck, C. Herwig, C. Limberg, Enhancing tris(pyrazolyl)borate-based models of cysteine/cysteamine dioxygenases via the sterics – increased reactivities, full product characterization and hints to initial superoxide formation *Chem. Eur. J.* **2020**, *26*, 11851-11861.
3. M. Sallmann, B. Braun, C. Limberg, Dioxygenation of cysteamine to hypotaurine at a tris(pyrazolyl)borate iron(II) unit - cysteamine dioxygenase mimicking? *Chem. Commun.* **2015**, *51*, 6785-6787.
4. M. Sallmann, S. Kumar, P. Chernev, J. Nehrkorn, A. Schnegg, D. Kumar, H. Dau, C. Limberg, S. P. de Visser, Structure and mechanism leading to formation of the cysteine *Chem. Eur. J.* **2015**, *21*, 7470–7479.
5. M. Sallmann, I. Siewert, L. Fohlmeister, C. Limberg, C. Knispel, A Trispyrazolylborato Iron Cysteinato Complex as a Functional Model for the Cysteine Dioxygenase, *Angew. Chem. Int. Ed.* **2012**, *51*, 2234-2237

09.01.2024

Expanding the Biocatalytic Toolbox with Rationally Designed Salophen-bound Artificial Metalloproteins

E. Venckute[1], P. Rodríguez Maciá[2] and A. G. Jarvis[1]

[1] School of Chemistry, Joseph Black Building, University of Edinburgh, David Brewster Rd, Edinburgh EH9 3FJ, United Kingdom

[2] School of Chemistry, George Porter Building, University of Leicester, University Rd, Leicester LE1 7RH, United Kingdom

First-row transition metal salen and salophen complexes demonstrate catalytic activity in a wide range of synthetic reactions, including C-H bond functionalisation and small molecule activation.[1,2] Such versatile activity stems from the first coordination sphere and the electronic properties of the bound metal species that can tune access to the reactive high-valent metal states, such as ferryl-oxo [Fe(IV)=O].[1] Due to structural similarity to porphyrin cofactors, synthetic salen and salophen complexes can act as cofactor mimics in heme proteins, such as myoglobin (Mb), and, thus, are attractive building blocks for designing new artificial metalloproteins (ArMs). When bound within a chiral protein scaffold, such synthetic cofactors can equip the active metal centre with enhanced reactivity and also high enantio- and/or regio-selectivity. To date, ArMs comprising a salophen-Mb duo have only been employed in sulfoxidation reactions and, thus, the full scope of such systems as biohybrid catalysts remains underexplored.[3] Herein we present that a Mb variant (MbQ) acts as an efficient scaffold for supramolecular binding of Co, Fe and Mn salophen derivatives. Using spectroscopic methods (UV-vis, CD) and native MS, stability of the corresponding ArM systems was investigated, whereas direct electrochemistry methods (protein-film voltammetry) allowed to probe differences in their redox behaviour. Second coordination sphere variants were produced and reconstituted with both porphyrin and salophen cofactors to compare their electrochemical properties and explore further applications of the corresponding ArM systems in (electro)catalysis.

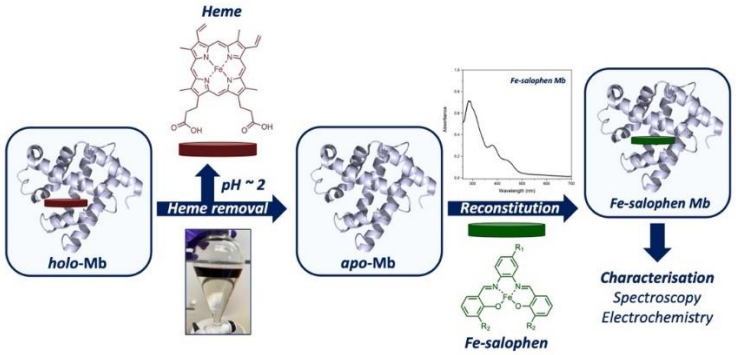


Figure 1. Reconstitution of *apo* myoglobin (Mb) with synthetic salophen cofactor.

1. W. Liu, J. T. Groves, *Angew. Chem. Int. Ed.*, **2013**, *52*, 6024-6027.
2. E. Pizzolato, M. Natali, B. Posocco, A. M. Lopez, I. Bazzan, M. Di Valentin, P. Galloni, V. Conte, M. Bonchio, F. Scandola, A. Sartorel, *Chem. Commun.*, **2013**, *49*, 9941-9943.
3. T. Ueno, T. Koshiyama, M. Ohashi, K. Kondo, M. Kono, A. Suzuki, T. Yamane, Y. Watanabe, *J. Am. Chem. Soc.*, **2005**, *127*, 6556-6562.

Molecular catalytic reduction of CO_2 beyond 2 electrons

Marc Robert

1. Université Paris Cité, Laboratoire d'Electrochimie Moléculaire, CNRS, F-75006, Paris, France
2. Institut Universitaire de France, F-75005, Paris, France

Reduction of carbon dioxide has as main objective the production of useful organic compounds and fuels - *renewable fuels* - in which solar energy would be stored. Molecular catalysts can be employed to reach this goal, either in photochemical or electrochemical (or combined) contexts. They may in particular provide excellent selectivity thanks to easy tuning of the electronic properties at the metal and of the ligand second and third coordination sphere. Recently it has been shown that such molecular catalysts may also be tuned for generating highly reduced products such as formaldehyde, methanol and methane, leading to new exciting advancements. Obtaining C-C coupling products is an additional intriguing possibility. Our recent results will be discussed, using earth abundant metal (Fe, Co) porphyrins and phthalocyanines as well as related complexes as catalysts.

References

1. M. Robert, W. A. Goddard III, R. Ye et al. *Nat. Catal.* **2023**, 6, 818.

2. M. Robert, B. Liu et al. *Nat. Commun.* **2023**, 14, 3401.

3. M. Robert et al. *Chem. Eur. J.* **2022**, e202200697.

4. T. F. Jaramillo, M. Robert et al. *Angew. Chem. Int. Ed.* **2019**, 58, 16172.

5. J. Bonin, M. Robert et al. *Nature* **2017**, 548, 74.

09.01.2024

Crossing the Valley of Death: From Lab-scale to Pilot-scale CO_2 Reduction Chemistry (…and more)"

Ulf-Peter Apfel

Ruhr University Bochum, Universitätsstraße 150, 44801 Bochum &
Fraunhofer UMSICHT, Osterfelderstraße 3, 46047 Oberhausen

The growing societal and political emphasis on environmentally friendly technologies has sparked significant interest in electrolysis technologies within the scientific community. This development is reflected in the multitude of potential catalysts for hydrogen and oxygen production, as well as CO_2 reduction. However, only a few of these candidates have thus far achieved the status of widespread application. Nevertheless, process engineering reports have received scant attention when it comes to the utilization of new catalysts, electrode, and cell concepts that could be suitable for the market. In both, catalyst development as well as reaction engineering much can be learnt from nature providing sophisticated enzymatic machineries.

Here, it becomes evident that a comprehensive approach involving optimized electrode designs made from novel materials in appropriate cells is crucial for future applications. In this context, we present examples of how electrodes with new catalysts can be shaped and integrated into zero-gap cells for hydrogen production, CO_2 reduction, and organic reactions, shedding light on the major challenges on the path to practical implementation.

References: J. T. Kleinhaus, J. Wolf, K. Pellumbi, L. Wickert, S. C. Viswanathan, K. junge Puring, D. Siegmund, U.-P. Apfel, Chem. Soc. Rev. 2023, https://doi.org/10.1039/D3CS00419H; D. Tetzlaff, T. Rensch, L. Messing, P. Schäfer, S. Grätz, D. Siegmund, L. Borchardt, U.-P. Apfel, Chem. Sci. 2023, https://doi.org/10.1039/D3SC04542K; R. Rad, T. Gehring, K. Pellumbi, D. Siegmund, E. Nettmann, M. Wichern, U.-P. Apfel, Cell Reports Physical Science 2023, https://doi.org/10.1016/j.xcrp.2023.101526; L. Hoof, N. Thissen, K. Pellumbi, K. junge Puring, D. Siegmund, A. Mechler, U.-P. Apfel, Cell Reports Physical Science 2022, 3, 100825.

09.01.2024

Electrochemical CO_2 Reduction with Polymer-Catalyst Composites: Modulating Activity and Selectivity by Controlling the Catalyst's Microenvironment

Charles C. L. McCrory

University of Michigan, Department of Chemistry,
Ann Arbor, MI, 48109, USA

The selective electrochemical reduction of CO_2 in the CO_2 reduction reaction (CO_2RR) is a crucial strategy for storing energy from intermittent sources in the form of chemical bonds (e.g. solar fuels) and as a pathway to converting CO_2 in industrial waste streams to value-added products. State-of-the-art solid-state catalysts produce useful products, but typically do so non-selectively with H_2 production from competitive water reduction. Alternatively, molecular catalysts show promise for the selective reduction of CO_2 to single products, but usually perform with lower activity compared to their solid-state analogues. My research group is focused on the development of new catalytic systems for the CO_2RR that operate with the selectivity of molecular catalysts but the activity of solid-state catalysts. In this talk, I will present some of our work using polymer encapsulation to increase the catalytic activity and selectivity of molecular catalysts for the CO_2RR. In particular, we show that encapsulating cobalt phthalocyanine within a coordinating polyvinylpyridine polymer leads to a dramatic enhancement in its activity and selectivity for the CO_2RR in aqueous phosphate solution. Using a combination of electroanalytical studies and *in situ* electrochemical X-ray absorbance measurements, we demonstrate that the encapsulating polymer modulates all coordination spheres surrounding the catalyst active site, and that this has a profound impact on the catalytic performance and mechanism.

09.01.2024

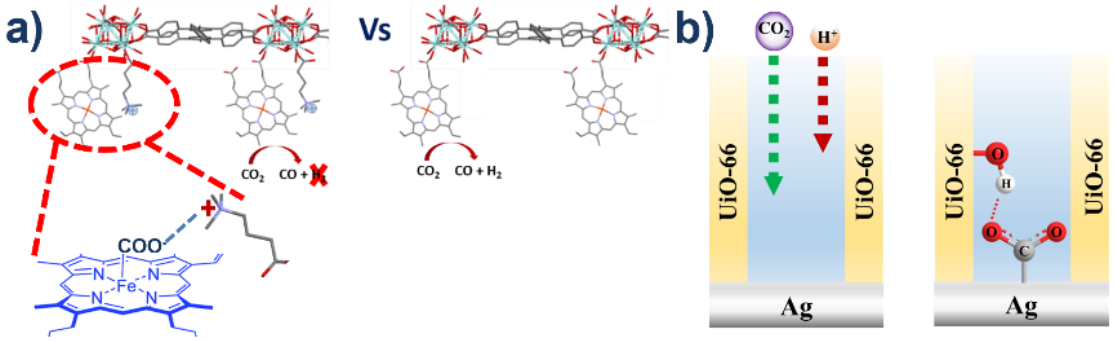
Molecular Manipulation of Heterogeneous Electrocatalysis Using Metal-Organic Frameworks

R. Shimoni,[1] A. Ghatak, [1] S. Shankar Golla, [1] S. Mukhopadhyay,[1] I. Liberman,[1] I. Hod*[1]

[1] *Department of Chemistry at Ben-Gurion University of the Negev (BGU), Beer-Sheva, Israel*

Electrocatalytically driven reactions that produce alternative fuels and chemicals are considered as a useful means to store renewable energy in the form of chemical bonds. in recent years there has been a significant increase in research efforts aiming to develop highly efficient electrocatalysts that are able to drive those reactions. Yet, despite having made significant progress in this field, there is still a need for developing new materials that could function both as active and selective electrocatalysts.

In that respect, Metal–Organic Frameworks (MOFs), are an emerging class of hybrid materials with immense potential in electrochemical catalysis. Yet, to reach a further leap in our understanding of electrocatalytic MOF-based systems, one also needs to consider the well-defined structure and chemical modularity of MOFs as another important virtue for efficient electrocatalysis, as it can be used to fine-tune the immediate chemical environment of the active site, and thus affect its overall catalytic performance. Our group utilizes Metal-Organic Frameworks (MOFs) based materials as a platform for imposing molecular approaches to control and manipulate heterogenous electrocatalytic systems. In this talk, I will present our recent study on electrocatalytic schemes involving MOFs, acting as: a) electroactive unit that incorporates molecular electrocatalysts, or b) non-electroactive MOF-based membranes coated on solid heterogenous catalysts.



References:

[1] Shimoni, R.; Zhuocheng Shi, Z.; Binyamin, S.; Yang, Y.; Liberman, I.; Ifraemov, R.; Mukhopadhyay, S.; Zhang, L.; Hod, I., Angewandte Chemie Int.Ed., 2022, 10.1002/anie.202206085.

[2] Mukhopadhyay, S.; Shimoni, R.; Liberman, I.; Ifraemov, R.; Rozenberg, I.; Hod, I., Angewandte Chemie Int.Ed., 2021, 60, 13423–13429.

[3] Liberman, I.S; Shimoni, R.S; Singh, C.P.PD; Hod, I., Journal of the American Chemical Society, 2020, 142 (4), 1933-1940.

[4] Shimoni, R.; He, W.; Liberman, I.; Hod, I., Journal of Physical Chemistry C, 2019, 123, 9, 5531-5539.

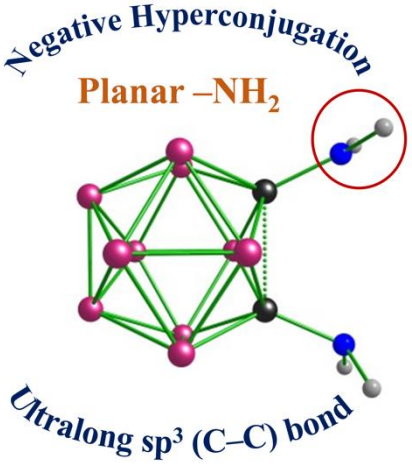
09.01.2024

Harnessing Quantum Mechanical Tunneling for Catalysis

Ayan Datta

School of Chemical Sciences, Indian Association for the Cultivation of Sciences
Kolkata, India-700032
Email: spad@iacs.res.in

Abstract: Classical interpretation for the kinetics of chemical reactions involves the rate of crossing of barriers by the molecules. Hence, most of the mechanistic studies across chemistry have been to reduce the barrier height by stabilizing the transition state (TS). Nevertheless, many molecules undergo chemical transformations through direct quantum tunneling rather than climbing the barrier. This leads to counterintuitive products for many reactions particularly at low temperatures. The talk will focus on few computational studies on such reactions where tunneling plays a very important role even at not so low temperatures. Examples from our research group and our collaborations with experimentalists will be discussed.



References

1. N. Mandal, A. K. Pal, P. Gain, A. Zohaib, Ayan Datta, *J. Am. Chem. Soc.* **2020**, 142, 5331-5337.
2. N. Mandal, Ayan Datta, *Chem. Commun.* **2020**, 56, 15377 – 15386.
3. S. Karmakar, Ayan Datta, *J. Org. Chem.* **2017**, 82, 1558-1567.
4. S. Karmakar, Ayan Datta, *J. Phys. Chem. B*, **2016**, 120, 945-952.
5. S. Karmakar and Ayan Datta, *J. Phys. Chem. B,* **2015***, 119*, 11540.
6. S. Karmakar, Ayan Datta, *Angew. Chem. Int. Ed.* **2014**, *53*, 9587.
7. A. Nijamudheen, S. Karmakar, Ayan Datta, *Chemistry - A European Journal*, **2014**, 20, 14650.
8. S. Karmakar and Ayan Datta, *J. Phys. Chem. B*, **2014**, 118, 2553.
9. D. Jose, Ayan Datta, *Angew. Chem. Int. Ed.* **2012**, 51, 9389.
10. K. Bhattacharyya, S. Karmakar, Ayan Datta, PCCP, **2017**, 19, 22482.

09.01.2024

Electrocatalytic CO_2 Reduction by Bioinspired Cobalt-Thiolate Complexes

Subal Dey

Department of Chemical Science, IISER Berhampur, Odisha, India: Email: skdey85@gmail.com

Abstract: Electrocatalytic CO2 reduction to value added carbon products using intermittent energy source herald potential to store and convert energy in chemical bonds.[1] Natural enzymes e.g. – CO dehydrogenases or N2ases are known to catalyseCO2 reduction to energy dense products at the expense of natural reducing equivalents at minimum energy cost.[2] Interestingly, all such enzymes bear bi to polynuclear metal-thiolato cofactors at their active sites. On the other hand, transitionmetal thiolate complexes are very lesser known to execute similar jobs. A series of cobalt complexes with 2-pyridine thiolate ligands have been synthesized and characterized with apparently innocent NÇN or PÇP supporting ligand.[3,4] The electrochemical CO2RR of these complexes are performed under nonaqueous homogeneous medium in presence of proton sources. These complexes show highly selective generation of formic acid and CO depending on the choice of ligand. Observed product selectivity has been correlated with the thermochemical properties (hydricity) of the putative Cobalt-hydride intermediates or the electronic nature of the cobalt centre and the choice of proton donors. Additional electrochemical investigations supported by theoretical calculations have indicated that one of the pyridine arms is de-coordinated on reduction to provide open site for exogeneous ligand binding. Such masked basic sites either shuttles the proton for form cobalt- hydride species or provides the H-bond to cobalt carboxylate species dictating the product selectivity. The competitive pathways i.e. metal-carboxylate pathway *vs* metal-hydride pathway are also governed by the choice of ligand. An optimized ligand framework leads to the most efficient CO2 to formic acid generation catalyst from overpotential point of view. Moreover, cobalt complex with pyridine-bis-methylthiolateligand inherites substrate binding site that has been found to be most efficient as no additional energy is compensated for pyridine de-coordination.[5] The study depicts an overview of electronic, thermochemical and choice of substrate in product directed catalyst designing.

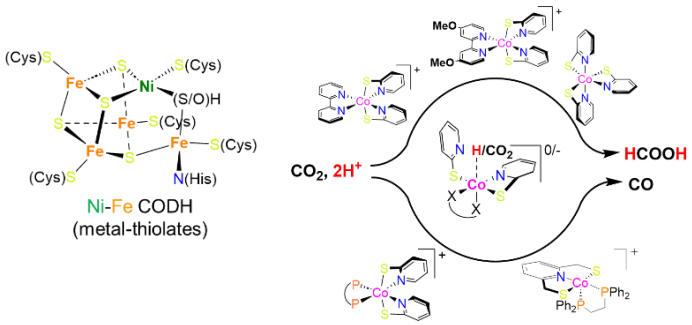


Fig 1: Metal-thiolate active site at Ni-Fe CO dehydrogenase (*left*). The cobalt pyridinethiolate complexes for electrocatalytic CO_2RR.

References:

(1) R. Francke, B. Schille, M. Roemelt; Homogeneously Catalyzed Electroreduction of Carbon Dioxide: Methods, Mechanisms, and Catalysts. Chem. Rev. 2018, 118 (9), 4631−4701

(2) M. Can, F. A. Armstrong, S. W. Ragsdale; Structure, Function, and Mechanism of the Nickel Metalloenzymes, CO Dehydrogenase, and Acetyl-CoA Synthase. Chem. Rev. 2014, 114 (8), 4149−4174

(3) S. Dey, T. K. Todorova, M. Fontecave* V. Mougel*; Electroreduction of CO_2 to Formate with low overpotential using Cobalt Pyridine Thiolate Complexes. Angew. Chem. Int. Ed. 2020,59, 15726- 15733

(4) Md. E. Ahmed, A. Rana, R. Saha, S. Dey*, A. Dey*; Homogeneous Electrochemical Reduction of CO_2 to CO by a Cobalt Pyridine Thiolate Complex. Inorg. Chem. 2020, 59, 5292−5302

(5) S. Dey , Md. E. Ahmed, A. Dey*; Activation of Co(I) state in a Cobalt Dithiolato Catalyst for Selectiveand Efficient CO_2 Reduction to CO. Inorg. Chem. 2018, 57, 5939–5947

09.01.2024

Bioinorganic Strategies to Study Multiple Facets in Alzheimer's Disease

Mi Hee Lim

Korea Advanced Institute of Science and Technology (KAIST), Department of Chemistry, Daejeon, South Korea

Alzheimer's disease (AD), associated with degeneration of neurons and synapses in the brain, leads to motor impairment and eventual fatality. Neurodegeneration could be related to various interconnected features, including (i) plaque formation from amyloid-β (Aβ) peptide fragments, (ii) metal ion dyshomeostasis and miscompartmentalization, as well as (iii) inflammation and increased oxidative stress due to overproduction of reactive oxygen species (ROS). The inter-relations between some of these pathological factors have been investigated. Metals are found entangled in the Aβ plaque and likely contribute to Aβ neurotoxicity and oxidative stress. ROS have been shown to increase the rate of Aβ plaque formation. Our understanding of the correlation between these elements and AD neuropathogenesis has been very limited, however. There is currently no cure for AD; therapies are focused on symptomatic relief targeting the decrease in the levels of acetylcholine, only one of the multiple factors causing the disease.[1-3] To find a cure for AD, we require a better understanding of the relationship between various causative factors of this devastating disease. Towards this goal, we have been developing suitable chemical tools capable of targeting and regulating multiple underlying factors or identifying the pathogenic networks composed of their direct interactions and reactivities.[4-11]

References:
[1] *Chem. Soc. Rev.* **2012**, *41*, 608.

[2] *Acc. Chem. Res.* **2014**, *47*, 2475; *Acc. Chem. Res.* **2021**, *54*, 3930.
[3] *Chem. Rev.* **2019**, *119*, 1221.

[4] *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 21990.

[5] *Chem. Sci.* **2015**, *6*, 1879.

[6] *J. Am. Chem. Soc.* **2014**, *136*, 299.

[7] *J. Am. Chem. Soc.* **2015**, *137*, 14785.

[8] *Nat. Commun.* **2016**, *7*, 13115.

[9] *Proc. Natl. Acad. Sci. USA* **2020**, *117*, 5160.

[10] *J. Am. Chem. Soc.* **2020**, *142*, 8183.

[11] *Nat. Chem.* **2022**, *14*, 1021-1030.

09.01.2024

Coordination Chemistry on the Brain: Applications to Neuroimaging in Alzheimer's Disease

Liviu M. Mirica

Department of Chemistry, Beckman Institute for Advanced Science and Technology,and the Neuroscience Program, University of Illinois at Urbana−Champaign, 600 S.Mathews Avenue, Urbana, Illinois 61801, USA

E-mail: *mirica@illinois.edu*

This presentation will report on the development of multifunctional compounds with high affinity for β-amyloid peptide aggregates and metal ions as potential positron emission tomography (PET) imaging agents for early diagnosis of Alzheimer's disease. We have successfully synthesized a series of benzothiazole, stilbene, and benzofuran-furfuryl bifunctional compounds with nanomolar affinity for β-amyloid aggregates.[1-4] Radiolabeling with Cu-64 generates PET imaging agents that show appreciable in vivo *brain uptake, leading to the successful PET imaging of β-amyloidaggregates in the brains of 5xFAD mice versus those of WT mice.[5-9] In addition, the recent development of novel lipophilic metal chelators that can cross the blood-brain barrier (BBB) will also be presented.*

References

[1] Cho, H.-J.; Sharma, A. K.; Zhang, Y.; Gross, M. L.; Mirica, L. M., "A Multifunctional Chemical Agent asan Attenuator of Amyloid and Tau Burden and Neuroinflammation in Alzheimer's Disease", *ACS Chem. Neurosci.* **2020**, *11*, 1471–1481, https://doi.org/10.1021/acschemneuro.0c00114

[2] Sun, L.; Cho, H.-J.; Sen, S.; Arango, A. S.; Bandara, N.; Huang, Y.; Huynh, T. T.; Rogers, B. E.; Tajkhorshid, E.; Mirica, L. M., Amphiphilic Distyrylbenzene Derivatives as Potential Therapeutic and Imaging Agents for the Soluble Amyloid-β Oligomers in Alzheimer's Disease. *J. Am. Chem. Soc.* **2021**, *143*, 10462-10476, https://doi.org/10.1021/jacs.1c05470

[3] Yu, Z.; Guo, W.; Patel, S.; Cho, H.-J.; Sun, L.; Mirica, L. M., Amphiphilic Stilbene Derivatives Attenuatethe Neurotoxicity of Soluble Aβ42 Oligomers by Controlling Their Interactions with Cell Membranes. *Chem. Sci*, **2022**, *13*, 12818-12830, https://doi.org/10.1039/D2SC02654F

[4] Yu, Z.; Moshood, Y.; Wozniak, M. K.; Patel, S.; Terpstra, K.; Llano, D. A.; Dobrucki, L. W.; Mirica, L. M.;* Amphiphilic Molecules Exhibiting Zwitterionic Excited-State Intramolecular Proton Transfer and Near-Infrared Emission for the Detection of Amyloid β Aggregates in Alzheimer's Disease, *Chem. Eur.J.*, **2023**, e202302408, http://dx.doi.org/10.1002/chem.202302408

[5] Cho, H.-J.; Huynh, S.; Rogers, B. E.; Mirica, L. M., "Successful Design of a Multivalent Bifunctional Chelator for Diagnostic ^{64}Cu PET Imaging in Alzheimer's Disease", *Proc. Natl. Acad. Sci. U.S.A.,* **2020**,*117*, 30928-30933, http://doi.org/10.1073/pnas.2014058117

[6] Huang, Y.; Cho, H.-J.; Bandara, N.; Sun, L.; Tran, D.; Rogers, B. E.; Mirica, L. M., "Metal-Chelating Benzothiazole Multifunctional Compounds for the Modulation and ^{64}Cu PET Imaging of Aβ Aggregation", *Chem. Sci.* **2020,** *11*, 7789-7799, https://doi.org/10.1039/d0sc02641g

[7] Wang, Y.; Huynh, T. T.; Cho, H.-J.; Wang, Y.-C.; Rogers, B. E.; Mirica, L. M., Amyloid β-Binding Bifunctional Chelators with Favorable Lipophilicity for ^{64}Cu Positron Emission Tomography Imaging in Alzheimer's Disease. *Inorg. Chem.* **2021**, *60*, 12610–12620, https://doi.org/10.1021/acs.inorgchem.1c02079

[8] Huang, Y.; Huynh, T. T.; Sun, L.; Hu, C.-H.; Wang, Y.-C.; Rogers, B. E.; Mirica, L. M., Neutral Ligandsas Potential ^{64}Cu Chelators for Positron Emission Tomography Imaging Applications in Alzheimer's Disease. *Inorg. Chem.,* **2022**, *61*, 4778−4787, https://doi.org/10.1021/acs.inorgchem.2c00621

[9] Terpstra, K.; Wang, Y.; Huynh, T. T.; Bandara, N.; Cho, H.-J.; Rogers, B. E.;* Mirica, L. M.* Divalent 2-(4-Hydroxyphenyl)benzothiazole Bifunctional Chelators for ^{64}Cu PET Imaging in Alzheimer's Disease, *Inorg. Chem.*, **2022**, *61*, 20326–20336, https://doi.org/10.1021/acs.inorgchem.2c02740

09.01.2024

Designing Multifunctional Molecules to Control Protein Misfolding

Tim Storr[a]

[a]Simon Fraser University, Department of Chemistry, 8888 University Drive, Burnaby, BC, V5A 1S6, Canada. E-mail: tim_storr@sfu.ca

The interaction between metal ions, ligands, and biomolecules play a fundamental role in bioinorganic chemistry, from metalloenzymes to medicine. In addition to balancing charge, small molecules can tune stability and associated reactivity via diverse interaction pathways and redox activation. This talk will focus on the development of multifunctional molecules that target similar protein misfolding and aggregation pathways in neurodegenerative disease and cancer. We are targeting the amyloid-beta (Aβ) peptide in Alzheimer's disease by designing molecules to inhibit Aβ aggregation and formation of toxic reactive oxygen species (ROS) associated with dysregulated metal ions.[1] We are also investigating the tumour suppressor protein p53. In over 50% of cancers, mutations render this protein inactive leading to loss or alteration of Zn-binding at the core site and aggregation.[2] We are developing multifunctional molecules that act as Zn metallochaperones, modulate mutant p53 aggregation, and rescue protein function.[3]

References:

1. Bataglioli, J., Gomes, L., Maunoir, C., Smith, J., Cole, H., McCain, S., Sainuddin, T., Cameron, C., McFarland, S., Storr, T. *Chem. Sci.* **2021**, *12*, 7510; Gomes, L. M. F., Mahammed, A., Prosser, K. E., Smith, J. R., Silverman, M. A., Walsby, C. J., Gross, Z., Storr, T. A Catalytic Antioxidant for Limiting Amyloid-Beta Peptide Aggregation and Reactive Oxygen Species Generation, *Chem. Sci.* **2019**, *10*, 1634
2. Miller, J. J., Gaiddon, C., Storr, T. *Chem. Soc. Rev.* **2020**, *49*, 6995; *J. Biol. Inorg. Chem.* **2022**, *27*, 393; *Curr. Opin. Chem. Biol.* **2023**, *72*, 102230.
3. Miller, J. J., Blanchet, A., Orvain, C., Nouchikian, L., Reviriot, Y., Clarke, R. M., Martelino, D., Wilson, D., Gaiddon, C., Storr, T. *Chem. Sci.*, **2019**. *10*, 10802; *Chem. Eur. J.* **2018**, *24,* 17734; *J. Inorg. Biochem*. **2023**, *242*, 112164.

09.01.2024

Radical Rebound at Nonheme Iron: $Fe^{III}(X)(Y)$ Complexes and Their Metal-Ligand Radical Transfer Reactivity

David P. Goldberg, Vishal, Yadav, and Lyupeng Wen

Johns Hopkins University, Department of Chemistry, Baltimore, MD 21218, USA

Abstract: Nonheme iron metalloenzymes and analogous synthetic catalysts that carry out C-H functionalization, including hydroxylation and halogenation reactions, are proposed to rely on a radical transfer step from an iron(III)(hydroxide) intermediate to a carbon radical (R•). The terminal ferric hydroxide species forms via hydrogen atom transfer (HAT) from C-H bonds to an $Fe^{IV}(O)$ (ferryl) intermediate, the active oxidant in the system. The product-determining step occurs when the incipient carbon radical (R•) must recombine with either the OH group (rebound) or a second metal ligand X in the coordination sphere. When X = halide, the radical transfer step leads to halogenation instead of hydroxylation. Determining the factors that control the selectivity of metal-ligand radical transfer (rebound) is of fundamental importance for understanding both the metalloenzymes and related synthetic catalysts. A series of nonheme iron complexes that include *cis*-ligated ($Fe^{III}(OH)(X)$ (X = halide, thiolate) complexes will be described, and their preferential radical transfer reactivity toward carbon radicals (R•) will be discussed. A new set of non-hydroxo $Fe^{III}(X)(Y)$ complexes and their comparable reactivity with R• substrates provides further insight into the factors that lead to radical transfer selectivity. Characterization of these complexes includes X-ray crystallography, Mössbauer and EPR spectroscopies. Density functional theory calculations help to rationalize the observed radical transfer selectivity.

References:

1) Yadav, V.; Wen, L.; Yadav, S.; Siegler, M. A.; Goldberg, D. P. “Selective Radical Transfer in a Series of Nonheme Iron(III) Complexes,” *Inorg. Chem.* **2023**, *62*, 17830 – 17842.
2) Yadav, V.; Wen, L.; Rodriguez, R. J.; Siegler, M. A.; Goldberg, D. P. “Nonheme Iron(III) Azide and Iron(III) Isothiocyanate Complexes: Radical Rebound Reactivity, Selectivity, and Catalysis,” *J. Am. Chem. Soc.*, **2022**, *144*, 20641 – 20652.
3) Gerard, E. F.; Yadav, V.; Goldberg, D. P.; de Visser, S. P. “What Drives Radical Halogenation versus Hydroxylation in Mononuclear Nonheme Iron Complexes? A Combined Experimental and Computational Study,” *J. Am. Chem. Soc.,* **2022,** *144*, 10752 – 10767.
4) Yadav, V., Siegler M. A., Goldberg, D. P., “Temperature-Dependent Reactivity of a Non-heme $Fe^{III}(OH)(SR)$ Complex: Relevance to Isopenicillin N Synthase”, *J. Am. Chem. Soc*., **2021**, *143*, 46 – 52.
5) Yadav, V.; Rodriguez, R. J.; Siegler, M. A.; Goldberg, D. “Determining the Inherent Selectivity for Carbon Radical Hydroxylation Versus Halogenation with $Fe^{III}(OH)(X)$ Complexes: Relevance to the Rebound Step in Nonheme Iron Halogenases,” *J. Am. Chem. Soc.*, **2020**, *142*, 7259 – 7264.

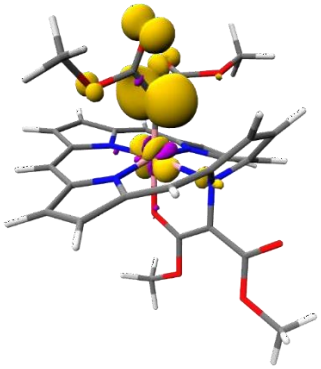
09.01.2024

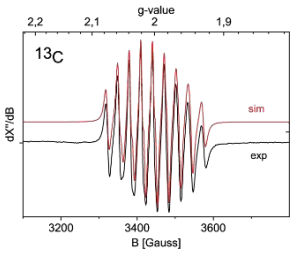
Bio-Inspired Synthesis of Ring Compounds using MetalloradicalCatalysis

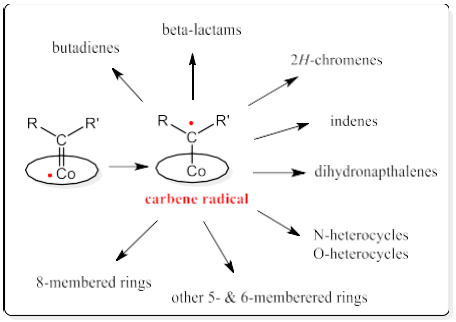
Bas de Bruin

Homogeneous Catalysis Group, van 't Hoff Institute for Molecular Sciences,University of Amsterdam, Science Park 904, 1098 XH Amsterdam. E-mail: b.debruin@uva.nl

Radicals are intrinsically reactive, and were long believed to be too reactive to be selective. However, in the coordination sphere of transition metals highly selective radical-type processes are certainly possible. In fact, radical-type reactions are tremendously important in several bio-synthetic pathways mediated by metallo- enzymes. Inspired by such intriguing catalytic radical-type transformations mediated by metallo-enzymes, we are currently investigating new catalytic transformations mediated by synthetic (open-shell) organometallic catalysts. Special interest in such open-shell organometallic species comes from their expected higher and different reactivity compared to their closed-shell counterparts, and these 'metallo-radicalcomplexes' may well allow us to steer and control radical-type reactions.[1]







In this contribution the available bio-inspired tools to steer and control the reactivity of cobalt(II) metalloradicals are discussed. In several cases, this metal triggers the formation of 'substrate radicals' in the coordination sphere of the metal, which are keyintermediates in a variety of new catalytic radical-type transformations.[1,2] This presentation is focused on the application of cobalt(II) in catalytic reactions involving 'carbene radicals'[2] Reactivity studies, EPR spectroscopy and complementary DFT calculations are used to unravel the open-shell pathways of the paramagnetic Co^{II} species.[3]

[1] a) V. Lyaskovskyy, V., B. de Bruin, *ACS Catalysis*, **2012**, *2*, 270. b) A. I. Olivos Suarez, V. Lyaskovskyy, B. de Bruin, et al. *Angew. Chem. Int. Ed.* **2013**, *52*, 12510.

[2] a) N.P. van Leest, B. de Bruin, et al., ACS Catalysis 2020, 10, 7449-7463. b) N.P. van Leest, B. deBruin, et al., *J. Am. Chem. Soc.* **2020**, *142*, 552-563.

[3] Epping, R.F.J; de Bruin, B. et al. *Nat. Chem.* **2022**, *14*, 550-557 DOI: 10.1038/s41557-022-00905-4.

09.01.2024

C-H functionalization inspired by copper enzymes

Shiyu Zhang

151 West Woodruff Ave. Columbus OH USA 43221

High-valent Cu(III) complexes have long been proposed as important intermediates in biological redox processes and organic transformations involving the activation of C-H bonds. However, the proposed high-valent Cu(III) intermediates often elude detection due to their fleeting lifetimes. In the first part of my talk, I will present a series of dicopper (II,III) coordination complexes as models to understand the reactivity of NO and NO_2^- at dicopper enzymes. We discovered that dicopper complex could activate NO or NO_2^- to generate a unique dicopper (II,III) oxo nitrosyl species $[Cu_2(\mu\text{-}O)(\mu\text{-}NO)]^{2+}$. Inspired by the oxidative reactivity of dicopper (II,III) oxo nitrosyl species, we developed a catalytic C-H hydroxylation strategy using NO as terminal oxidant. In the second part of my talk, I will discuss how synthetic models of monocopper oxygenases can be applied in the synthesis of pharmaceutically relevant organic molecules. Inspired by lytic polysaccharide monooxygenases, we develop a general Cu^{II}/Cu^{III} platform to activate simple nucleophiles (Nu) toward C-H functionalization. Oxidation of Cu^{II}-Nu to Cu^{III}-Nu endows the Nu moiety with hydrogen atom transfer and radical capture reactivity. Building on this platform, we have established a catalytic C-H fluorination method that selectively produces monofluorinated products in an undivided electrochemical cell at room temperature.

References:

1. *J. Am. Chem. Soc.* **2023**, 145, 17779–17785.
2. *Chem. Catalysis,* **2023**, 3, 100491.
3. *Chem. Sci.* **2023**, 14, 1301-1307.
4. *J. Am. Chem. Soc.,* **2020**, *142*, 8514–8521.
5. *J. Am. Chem. Soc.* **2019**, *141*, 10159-10164.

09.01.2024

'*Catalytic*' NADP+/NADPH Cofactor Analogues

Joyanta Choudhury

Organometallics & Smart Materials Laboratory, Department of Chemistry

IISER Bhopal, Bhopal 462066, India, (Email: joyanta@iiserb.ac.in)

In the Calvin cycle, the atmospheric CO_2 is "fixed" (reduced) into sugars. Here, the reduced nicotinamide adenine dinucleotide phosphate (NADPH) acts as the hydride transfer (HT) cofactor to reduce the "captured" CO_2 molecule (in the form of 1,3-bisphosphoglycerate) into glyceraldehyde-3-phosphate, which is further utilized for biosynthesis of sugars and biomass. In the presence of sunlight, the ferredoxin-$NADP^+$ reductase (FNR) enzyme catalyzes the regeneration of NADPH from the oxidized $NADP^+$ cofactor (produced in the Calvin cycle) by the transfer of electrons and protons from photosystem I (PS I), where water acts as the terminal source of proton and electron. Thus, in a sense, the cofactor NADPH acts like a "catalyst" for CO_2 reduction with the help of a suitable electron/proton supply chain. Chemists target to mimic this CO_2-reduction process by developing synthetic analogues of the natural NADPH cofactor.

Unfortunately, despite extensive investigation over decades, all synthetic NADPH model compounds/analogues (AH) developed so far, only act as "*stoichiometric*" reductant for the reduction of CO_2. The main bottleneck for the "*catalytic*" use of these compounds has been their inefficient regeneration from the corresponding oxidized forms ($NADP^+$ versions) through $2e^-/1H^+$ (or effectively H^-) transfer chemistry employing a suitable, mild, terminal hydride source. This is due to several fundamental challenges such as (i) facile irreversible dimerization of the one-electron reduced radical species ($A^\bullet$) prior to the desired reaction, (ii) difficult protonation of the one-electron-reduced radical species ($A^\bullet$) for its ($AH^{\bullet+}$) further one-electron reduction to form the hydride (AH), and (iii) instability of the anionic species (A^-) generated through high-potential injection of the second electron ($A \rightarrow A^\bullet \rightarrow A^-$) to the radical species ($A^\bullet$). Optimum hydricity (ΔG_{H-}) and self-exchange reorganization energy (λ_{AH}) values of the hydrides (AH) are the other key issues for effective HT reactions.

Recently, by employing our in-house well-developed Rh-catalyzed '*rollover annulation*' protocol,[1] we synthesized a unique class of dicationic heterohelicenes empowered with redox-active imidazolium-fused central pyridine motif. Capitalizing their unique structural and electronic attributes, we exploited the $NADP^+$/NADPH-like hydride-transfer redox cycle with these bis-imidazolium-embedded heterohelicenes for CO_2 reduction and similar reduction reactions in a "*catalytic*" manner.[2-3] The chemistry involved in this discovery will be discussed in the presentation.

[1] (a) Ghorai, D.; Dutta, C.; Choudhury, J. *ACS Catal.* **2016**, *6*, 709–713. (b) Karak, P.; Dutta, C.; Dutta, T.; Koner, A. L.; Choudhury, J. *Chem. Commun.* **2019**, *55*, 6791–6794. (c) Karak, P.; Rana, S. S.; Choudhury, J. *Chem. Commun.* **2022**, *58*, 133–154. (d) Karak, P.; Choudhury, J. *Chem. Sci.* **2022**, *13*, 11163–11173.

[2] Karak, P.; Mandal, S. K.; Choudhury, J. *J. Am. Chem. Soc.* **2023**, *145*, 7230–7241.

[3] Karak, P.; Mandal, S. K.; Choudhury, J. *J. Am. Chem. Soc.* **2023**, *145*, 17321–17328.

09.01.2024

Metal-Ligand Cooperative Approaches in Homogeneous Catalysis Using Well-Defined Transition Metal Complexes of Redox-Noninnocent Ligands

Dr. Nanda D. Paul
Associate Professor
Department of Chemistry
Indian Institute of Engineering Science and Technology, Shibpur
Botanic Garden, Howrah 711103, India
Email: ndpaul@gmail.com; ndpaul2014@chem.iiests.ac.in

Abstract: The chemistry of transition metal complexes of redox noninnocent ligands has gained immense attention over the years because of its interesting electronic structures. The primary research in this area was focused on understanding the ambiguous electronic structure and bonding of such complexes. Only in the last decade it has shifted more to catalysis and, very recently, towards more physical applications upon realizing the fact that redox-noninnocent ligands, other than coordinating metal ions and offering steric control, can participate synergistically with the metal ions during electron transfer events and influence a chemical transformation in many ways.

This lecture will be focused on the plausible application of a few well-defined transition metal complexes of some chosen redox-noninnocent ligands in homogeneous catalysis. A few examples will be discussed, how taking advantage of ligand-centered redox events, multi-electron chemical transformations and radical-type reactions can be achieved using 3d-metal-catalysts, avoiding thermodynamically unfavorable metal-centered redox events.

References:

(1) Sikari, R.; Sinha, S.; Chakraborty, G.; Das, S.; van Leest, N. P.; Paul, N. D.* *Adv. Synth. Catal.* **2019**, *361*, 4342–4353.
(2) Das, S.; Mondal, R.; Chakraborty, G.; Guin, A. K.; Das, A.; Paul, N. D.* *ACS Catal.* **2021**, *11*, 7498−7512.
(3) Mondal, R.; Guin, A. K.; Pal, S.; Mondal, S.; Paul, N. D.* *Org. Chem. Front.* **2022**, *https://doi.org/10.1039/D2QO01196D*.
(4) Sinha, S.; Sahad E, M.; Mondal, R.; Das, S.; Manamel, L. T.; Brandão, P.; Bruin, B. de.; Das, B. C.; Paul, N. D.* *J. Am. Chem. Soc.* **2022**, *DOI: https://doi.org/10.1021/jacs.2c08941*.

09.01.2024

Sulfur oxygenation via a thiolate ligated nonheme iron superoxide intermediate: Relevance to thiol dioxygenases

Sudha Yadav, David P. Goldberg

Johns Hopkins University, Baltimore, MD, USA, 21218

Mononuclear nonheme iron enzymes represent one major class of O_2 activating enzymes and are known to perform diverse reactivity, including C-H hydroxylation, halogenation, monooxygenation, and dioxygenation. One of the subclass is thiol dioxygenases (TDOs) that convert thiols to their corresponding sulfinic acids using dioxygen as an oxidant. The mechanism of TDOs, however, is poorly understood and represents a major gap in knowledge of nonheme iron oxygenases. None of the proposed Fe-oxygen intermediates have been experimentally characterized. A proposed mechanism involves the initial formation of a cis thiolate-ligated iron superoxide intermediate followed by attack on the bound sulfur ligand. Homolytic O-O bond cleavage is then proposed, leading to the formation of an iron (IV)-oxo intermediate that supplies the second O atom to sulfur. This presentation will focus on recent results involving the synthesis of a new nonheme iron(II) complex which reacts with O_2 to give a thiolate-ligated iron(III) superoxide species at low temperature, characterized by UV-vis, Mössbauer, EPR, CSIMS, and ATR-FTIR. This species then converts to an S-oxygenated iron(II)(sulfinate) product. A new tetradentate ligand, with three neutral nitrogen donors and one anionic thiolate donor and with H-bonding groups in secondary coordination sphere ($BNPA^{Me_2}SH$) was synthesized to carry out this work. The implicated mechanism of O_2 activation and S-oxygenation for this new nonheme iron(II) complex is directly analogous to the proposed mechanism for the TDOs.

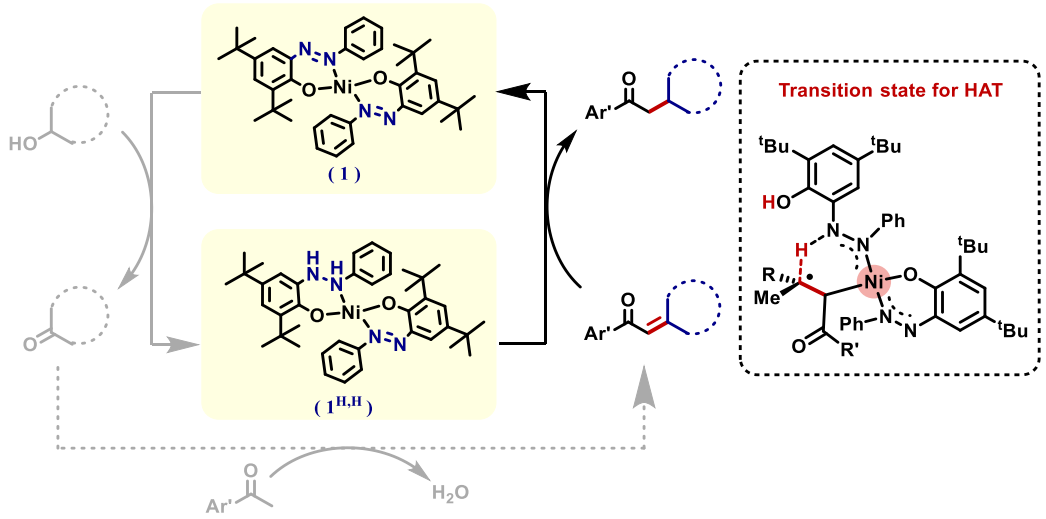
09.01.2024

A ligand redox-promoted olefin and imine hydrogenation following radical pathway

Debashis Adhikari

Department of Chemical Sciences, Indian Institute of Science Education and Research Mohali, SAS Nagar-140306, India

Hydrogenation of olefins and imines is an important process and that becomes further appealing when the source of the hydrogen is an alcohol. We have developed a nickel catalyst where the ligand backbone contains an azo motif. With the help of the azo/hydrazo, $2e^-/2H^+$ redox couple the catalyst can easily dehydrogenate alcohols and redelivers the stripped hydrogen on an in situ generated enone.[1-3] In this lecture, the details of hydrogenation following a radical pathway will be described. The substrate olefin likely binds to nickel, which helps in the electron transfer from the mono-reduced azo ligand. This even showcases the covalency in the metal-ligand bond which promotes the redox process in co-operative fashion. The generality of the mechanistic sketch was further proved by studying an imine hydrogenation, which also proceeds through one electron reduction of the imine. This radical-promoted mechanistic scheme is in strong contrast to the metal-ligand bifunctionality-driven hydrogenation reactions where the intermediacy of the metal-hydride is ubiquitous. Furthermore, the traditional Noyori-type hydrogenation involving metal-hydride follows a two-electron pathway. Our investigated pathway offers a complementary hydrogenation path to this two-electron chemistry.



References:

1) A. K. Bains, A. Kundu, S. Yadav and D. Adhikari *ACS Catal.*, 2019, **9**, 9051-9059.
2) A. K. Bains, A. Kundu, D. Maiti and D. Adhikari, *Chem. Sci.*, 2021, **12**, 14217-14223.
3) A. K. Bains, A. Biswas and D. Adhikari *Adv. Synth. Catal.*, 2022, **364**, 47-52

09.01.2024

Unique features of a Sensory [FeFe] hydrogenase

Nipa Chongdar, * James A Birrell, Edward J. Reijerse, Patricia Rodriguez-Macia, Krzysztof Pawlak, Constanze Sommer, Olaf Rudiger, Wolfgang Lubitz, Hideaki Ogata

INSPIRE Faculty Fellow
Indian Institute of Technology Goa

[FeFe] hydrogenases catalyze the interconversion of molecular hydrogen to protons and electrons at exceptionally high rates. Their active site, the H-cluster, comprises a [4Fe–4S] cluster covalently linked to a unique [2Fe] subcluster. Based on amino acid sequence phylogeny, [FeFe] hydrogenases are categorized into prototypical and electron bifurcating, ancestral, and sensory types. The sensory type [FeFe] hydrogenases (HydS) are predicted to play a role in transcriptional regulation by detecting the H_2 level of the cellular environment. HydS contains the hydrogenase domain with distinct modifications in the active site pocket, three additional [4Fe-4S] clusters (F-clusters), and a Per-Arnt-Sim (PAS) domain (Figure 1A). Notably, the PAS domain is absent in some sensory [FeFe] hydrogenases, classified as the "group-D" [FeFe] hydrogenases. This work presents the biochemical and spectroscopic characterization of a heterologously expressed, artificially maturated HydS from the hyperthermophilic bacterium *Thermotoga maritima* (*Tm*HydS) (1). *Tm*HydS shows lower H_2 conversion activities than the prototypical catalytic hydrogenases, in line with its sensory function. Using Infrared (IR) spectroelectrochemistry, three redox states of the *Tm*HydS H-cluster were identified. Though the IR signatures of all three redox states closely resemble those from the prototypical [FeFe] hydrogenases, the [2Fe] subcluster of HydS displays a very positive redox potential compared to the highly active prototypical enzymes (1). The *Tm*HydS contains altered amino acids surrounding the H-cluster (Figure 1B). Using site-directed mutagenesis, the influence of amino acids in the second coordination sphere of *Tm*HydS on its functional spectroscopic and redox properties is investigated (2). It was observed that the mutation of serine 267 to methionine in *Tm*HydS led to a drastic decrease in activity. Spectroelectrochemical titration revealed a 50 mV lower redox potential for the [4Fe–4S] subcluster in the S267M variant, supporting the notion that redox tuning of both halves of the H-cluster is crucial for activity.

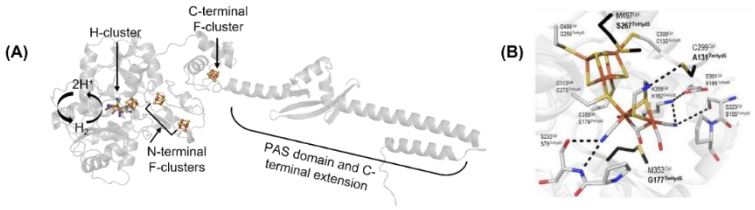


Figure 2. (A) Alphafold model of *Thermotoga maritima* HydS with cofactors docked into it. (B) Close-up view of the H-cluster, including the surrounding second coordination sphere amino acids in the *Clostridium pasteurianum* (*Cp*I) (prototypical catalytic hydrogenase) crystal structure. Amino acid positions are labeled with *Cp*I (top) and *T. maritima* HydS (bottom) identities. Amino acids colored in black (bold) were mutated in this study.

Reference:

(1) Unique Spectroscopic Properties of the H-Cluster in a Putative Sensory [FeFe] Hydrogenase. Chongdar N, Birrell J.A., Pawlak K., Sommer C., Reijerse E.J., Rüdiger O., Lubitz W.*, Ogata H.* *Journal of the American Chemical Society*, 2018, **140**, 1057–1068.

(2) Redox tuning of the H-cluster by second coordination sphere amino acids in the sensory [FeFe] hydrogenase from *Thermotoga maritima*. Chongdar N*, Rodríguez-Maciá P., Reijerse E.J., Lubitz W., Ogata H.*, Birrell J.A.*. *Chemical Science*, 2023, **14**, 3682–3692

On Sustainable Catalysis by Soft-oxometalates (SOMs)

Soumyajit Roy

EFAML, Materials Science Center, Department of Chemical Sciences,
Indian Institute of Science Education & Research Kolkata, 741246, WB, India.
E-mail: s.roy@iiserkol.ac.in
Website: soumyajit-roy.com

Sustainable catalytic systems based on charged metal oxides are studied by us over the last years and are known as soft-oxometalates (SOMs). Such studies have helped us to see the effect of time on SOMs and enabled fabrication of catalytic micro-chips to plastic conductors. The understanding of time related information of such systems are useful. Such insights can help us to achieve catalytic applications of CO_2 reduction to C_1, C_2 products like formic acid, formaldehyde, methanol, ethanol, ethanoic acid etc. We will demonstrate the workings of a chalcogenide system based on MoS_2 and demonstrate how Sulphur vacancies can be crucial in CO_2 conversion. We will show the effect of vacancies in giving rise to CO_2 reduction products like Formic Acid and Methanol and how dynamical effects are involved in product distribution in the context of CO_2RR. The presentation will conclude highlighting the future direction our lab focuses to take.

References:

1. S. Roy, "Soft-oxometalates beyond crystalline polyoxometalates: formation, structure and properties", CrystEngComm 16 (2014) 4667. Selected as Cover page for the India Issue of CrystEngComm to celebrate year of crystallographhy.
2. C. I.Ezugwu, S. Liu, C.Li, S. Zhuiykov, S. Roy*, F. Verpoort*, Coord. Chem. Rev. 450 (2022) 214245
3. S. Ghosh, A. Dev Ranjan, S. Das, R. Sen, B. Roy, S. Roy* and A. Banerjee,* Nanoletters, 21 (2021) 10.
4. S.Paul, S.Gonglach, M. Haas, F.Pillwein, S. S. Sreejith, S. Barman, R. De, S.Müllegger, P.Gerschel, U-P.Apfel, H. Coskun, A. Aljabour, P. Stadler, W.Schöfberger*, S. Roy*, Nature Commun. 10, Article number: 3864 (2019).
5. R. De, S.Gonglach, S.Paul, M.Haas , S. S. Sreejith , P. Gerschel , U-P. Apfel, H. Vuong , J. Rabeah , S. Roy* and W. Schöfberger*, Angew. Chem. Int. Ed. 59 (2020) 10527.

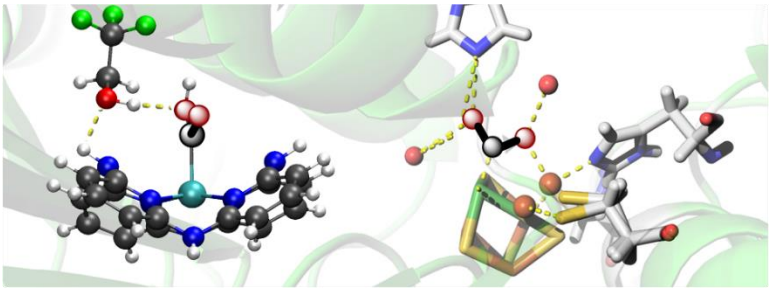
09.01.2024

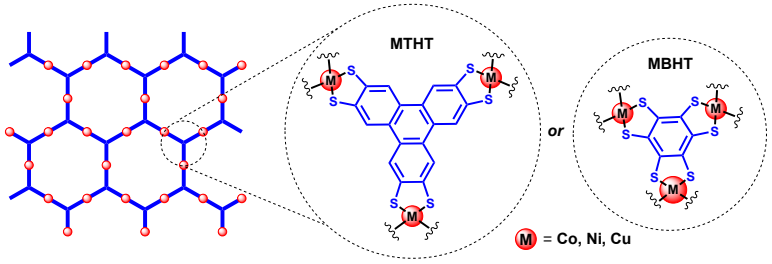
Biologically Inspired Catalytic Systems for Solar-to-Fuel Technologies

Smaranda C. Marinescu, *University of Southern California*

Research in the Marinescu group focuses on the development of novel catalytic systems for efficient *solar-to-fuel* technologies. Inspired by biological systems, we design molecular catalysts that involve hydrogen bonding networks capable of small molecule activation through multiple proton and electron transfers. Given the scale of potential applications, we focus our studies on species that contain abundant elements, require benign (aqueous) solvents, and display high activity, selectivity, and stability during the catalytic process. We are also interested in the heterogenization of complexes via coordination polymers or covalent attachment to surfaces, which is important for large-scale applications. To these ends we developed coordination complexes and polymers that display unique activity towards the activation of small molecules, such as H_2O and CO_2.

We have shown that cobalt complexes with pendant secondary amine (NH) moieties act as highly efficient electrocatalysts for the reduction of CO_2 to CO, and the proposed mechanism involves the formation of a hydrogen-bonding network intermediate that enables direct proton transfer from acid to the activated CO_2 substrate. In addition to CO_2 reduction, we also developed catalytic systems for the conversion of water into H_2, such as the dithiolene-based coordination complexes and polymers that display remarkable electrocatalytic activity for the hydrogen evolution reaction (HER). We have also shown that cobalt phosphinothiolate complexes catalyze the electrochemical reduction of CO_2 to formate with excellent selectivity. We have also explored the immobilization of well-known CO_2-reduction catalysts, such as metal porphyrins or rhenium bipyridine tricarbonyl moieties, via incorporation into covalent-organic frameworks or via covalent attachment through robust diazonium reductive coupling. We expect the design principles discovered in these studies to have a profound impact towards the development of advanced materials and sustainable technologies.





Electrocatalytic CO_2 Reduction with Cofacial PorphyrinDimers

Takehiro Ohta[1], Mami Mitori[1], Tomoyuki Takeyama[1], Masayuki Wakioka[2],Tatsuya Higaki[2], Roger E. Cramer[3], Yasuhiro Ohki[2]

[1]*Department of Applied Chemistry, Sanyo-Onoda City University, Yamaguchi756-0884, Japan*

[2]*Institute for Chemical Research, Kyoto University, Kyoto 611-0011, Japan*

[3]*Department of Chemistry, University of Hawaii, Hawaii 96822-2275, United States*

09.01.2024

Reduction of CO2 into useful carbon resources such as CO is an important reaction to overcome the limited supply of fossil fuels and the greenhouse effect of CO2. This reaction requires a large negative potential due to reorganization energy in formation of an anion radical intermediate at the initial stage of the reaction. Previously, Naruta and coworkers reported highly efficient and selective conversion of CO2 to CO catalyzed by cofacial iron porphyrin dimers,1 and more research is needed to understand the molecular mechanism of pacman effect on CO2 reduction. Thus, we carried out x-ray crystal structural analysis of an iron porphyrin dimer, and the structure and reactivity of other metal porphyrin dimers were also studied. The structure of iron porphyrin dimer shown in Fig. 1(a) indicates that the dinuclear iron(III) centers are bridged by □-oxo ligand with the Fe•••Fe distance of 3.5 Å, implying the ability of the binding pocket to accommodate reaction intermediates during catalysis. The structure of zinc porphyrin dimer (Fig. 1(b)) shows that the dinuclear zinc(II) centers are separated by 5.8 Å and an oxygen ligand assignable to water binds to each zinc(II) center.2 The zinc porphyrin dimer exhibits higher electrochemical CO2 reduction reactivity compared to the monomer in DMF/H2O solution. Details of structure and electrochemical CO2 reduction of porphyrin dimers will be discussed.

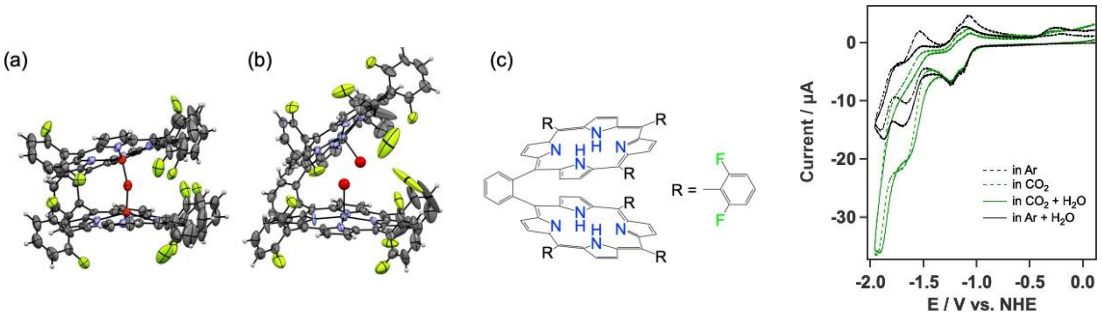


Fig. 1. ORTEP of porphyrin dimers with dinuclear iron centers(a), with dinuclear zinc centers (b), and schematic drawing of free base porphyrin dimer (c) Fig. 2. Cyclic voltammogramof zinc porphyrin dimer.

References

1. Zaki, Z. N.; Mohamed, E. A.; Naruta, Y. *Sci. Rep.* **2016**, *6*, 24533.
2. Mitori, M.; Wakioka, M.; Ohki, Y.; Cramer, R. E.; Ohta, T. Electrocatalytic CO_2 Reduction with a Cofacial Zinc Porphyrin Dimer, In *10th Asian Biological Inorganic Chemistry Conference*, Hyogo, Japan, Nov28–Dec3, 2022, P-119.

09.01.2024

Electro and photo catalytic CO_2 reduction with metalloporphyrins holding second coordination sphere functionalities.

Authors: P. Gotico,[a] M. Sircoglou,[b] W. Leibl,[a] Z. Halime,[b] A. Aukauloo [a,b]

a: ICMMO, Université Paris-Saclay, UMR 8182 CNRS, Institut de Chimie Moléculaire et des Matériaux d'Orsay, 91400, Orsay, France,
b: CEA, CNRS, Institute for Integrative Biology of the Cell (I2BC), 91198, Gif-sur-Yvette, France.

Among the many catalytic materials currently being investigated to tackle the reduction of CO_2, molecular catalysts containing a series of first-row transition metal catalysts, including N-based macrocyclic and polypyridyl complexes of Mn, Fe, Co and Cu have shown very appealing activity toward CO_2 reduction.[1-3] The ongoing challenges reside in the discovery of highly active cost-efficient performing catalysts. The unique assets of molecular catalysts hinge on the versatile design of ligands sets that can control the electrochemical properties and chemical selectivity of the corresponding metal complexes. In this process, chemists often seek for inspiration from the unmatched reactivity pattern of active sites of metalloenzymes. We are developing functionalized metalloporphyrins with multipoint hydrogen-bonding donors, cationic groups and bimetallic systems for the activation and reduction of CO_2.[5-10]

References:

1. S. Amanullah, P. Saha, A. Nayek, M. E. Ahmed, A. Dey, *Chem. Soc. Rev.* **2021**, *50*, 3755-3823.

2. E. Boutin, L. Merakeb, B. Ma, B. Boudy, M. Wang, J. Bonin, E. Anxolabehere-Mallart, M. Robert, *Chem. Soc. Rev.* **2020**, *49*, 5772-5809.

3. P. T. Smith, E. M. Nichols, Z. Cao, C. J. Chang, *Acc. Chem. Res.* **2020**, *53*, 575-587.

4. E. M. Nichols, J. S. Derrick, S. K. Nistanaki, P. T. Smith and C. J. Chang, *Chem. Sci.*, 2018, **9**, 2952–2960.

5. P. Gotico, Z. Halime, A. Aukauloo, *Dalton Trans* **2020**, *49*, 2381-2396.

6. P. Gotico et al, *Angew Chem Int Ed* **2019**, *58*, 4504-4509.

7. P. Gotico et al, *Angew. Chem. Int. Ed. Engl.* **2020**, *59*, 22451-22455.

8. E. Pugliese et al, *Angew. Chem. Int. Ed. Engl.* **2022**, *61*, e202117530.

9. C. Zhang et al. *Angew. Chem. Int. Ed. Engl.* **2022**, e202214665

10. P. Gotico et al, *ChemSusChem*, **2021**, *14*, 1308-1315

09.01.2024

Investigating the Role of Secondary Sphere Charge Effects on CO_2 Reduction Through the Study of an Artificial Enzyme

Regina E. Treviño[1], Joseph A. Laureanti, Wendy J. Shaw[1]

[1] Pacific Northwest National Laboratory, 902 Battelle Blvd, Richland, WA 99354

Nature's enzymes have championed clean energy conversion reactions with high selectivity and activity, often utilizing various complex elements expanding far beyond the active site. Often many of these elements contribute synergistically, deeming their individual contributions difficult to study or assign. Development and rational design of artificial enzymes has served as tools for the detailed study and understanding of these complex enzymes ranging from active site mimics to rational design of secondary and coordination spheres. We have approached the construction of an artificial enzyme by employing a robust protein scaffold, lactococcal multidrug resistance regulator, LmrR, providing a secondary sphere around a molecular rhodium complex, $[Rh^{I}(PN^{gly}P)_2]^{-}$. While each individual component demonstrates incompetence towards catalysis, covalent attachment of the rhodium complex to LmrR (Rh-LmrR) has demonstrated catalytic activity towards CO_2 hydrogenation to formate in solution. Further, site-directed mutagenesis to introduce positive charges in the outer coordination sphere demonstrated a 2-3-fold increase in activity for one Rh-LmrR construct, in which the positive charge is positioned close to the rhodium center while also having a high residence time, compared to other constructs demonstrating similar activity to the wild-type. We have begun the expansion of this work by studying the role of charge as a whole within this artificial enzyme through the introduction of both local and global negative charges through site-directed mutagenesis in order to understand its contribution to catalysis. Understanding outer coordination sphere effects on catalytic activity will provide an additional building block in facilitating the construction of rationally design robust catalysts.

09.01.2024

Nitric Oxide and its Derivatives: A Catalytic Cycle

Pankaj Kumar*

Department of Chemistry, IISER Tirupati, Tirupati-517507, Andhra Pradesh

pankaj@iisertirupati.ac.in; pankajatiisert@gmail.com

Nitric oxide (NO) plays a significant role in various physiological processes such as neurotransmission, vascular regulation, platelet disaggregation, and immune response to multiple infections.[1] Therefore, to maintain an optimal concentration of NO, nitrate reductase (NR), nitrite reductase (NiR)[2]. While NO synthase (NOS)[3] enzymes are available for NO biosynthesis, if overproduced, NO Dioxygenase (NOD) enzymes convert NO to biologically benign NO_3^-. NR catalytically transforms the NO_3^- to NO_2^- via the O-atom transfer (OAT) reaction via Mo/W-based enzymes. While NiR enzymes catalyze the conversion of NO_2^- to NO in the presence of acid (H^+).[2] Biological dysfunction may lead to NO overproduction, which is usually converted to NO_3^- in the presence of NOD enzymes. This regular interconversion helps in maintaining the biological NO homeostasis. This report will also explain the reduction of NO_2^- to NO via acid-induced reaction[4] and OAT chemistry at Co[5]/Fe/Cu centers. In addition, we will also be presenting the NO oxidation reaction of $\{CoNO\}^8$ to understand the mechanistic aspects of these reactions.[6] A new pathway for NiR enzyme activity was observed with one equivalent proton (H^+) generating M-NOs (or NO generation) with H_2O_2 (which further decomposes to H_2O). In addition, VCl_3-induced NO_3^-/NO_2^- reduction was also confirmed on Co-center. Further, to complete the NO-biological cycle, we reacted the M-NO with OH^-/O^{2-}, showing the formation of the M^{n+}-NO_2^-, in contrast to one of our previous reports of $\{CoNO\}^8$ with O_2, leading the generation of Co^{II}-NO_3^- (NOD product).[7]

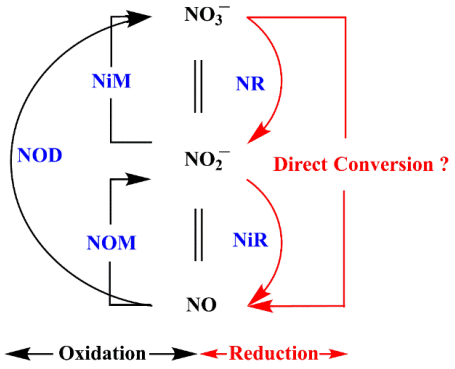


Figure 1. Interconversion of nitrate → nitrite → nitric oxide and vice versa

References

1. (a) R. F. Furchgott, *Angew. Chem., Int. Ed.*, 1999, **38**, 1870-1880. (b) L. J. Ignarro, *Angew. Chem., Int. Ed.*, 1999, **38**, 1882-1892.
2. E. I. Tocheva, F. I. Rosell, A. G. Mauk, M. E. Murphy, *Science*, 2004, **304**, 867-870.
3. R. G. Knowles, S. Moncada, *Biochem. J.*, 1994, **298**, 249-258.
4. P. Y. M. Ajmal, S. Ghosh, Y. Narayan, Y. Yadav, C. S. Sahoo, P. Kumar, *Dalton Trans.*, **2019**, 48, 13916.
5. K. Kulbir, S. Das, T. Devi, M. Goswami, M. Yenuganti, P. Bhardwaj, S. Ghosh, S. C. Sahoo, P. Kumar, *Chem. Sci.*, **2021**, *12*, 10605.
6. S. Das, K. Kulbir, S. Ghosh, C. S. Sahoo, P. Kumar, *Chem. Sci.*, **2020**, *11*, 5037.
7. P. Kumar, Y.M. Lee, Y.J. Park, M.A. Siegler, K. D. Karlin, W. Nam, *J. Am. Chem. Soc.*, **2015**, 137, 4284.

09.01.2024

Sequence of NO Binding and Electron Transfer at a Single Cu Site Contrasts the Signaling Outputs

Pokhraj Ghosh, Timothy H. Warren

Department of Chemistry, Michigan State University, East Lansing, MI, USA

The reductive coupling of nitric oxide to physiologically benign nitrous oxide represents a pivotal step in the denitrifying pathway of the global nitrogen cycle. Within the mononuclear type II site of copper nitrite reductase (CuNiR), which has evolved for the reduction of NO_2^- to NO, there is a further reduction of NO to N_2O under high NO flux. This process involves electron transfer from the adjacent type I site. Theoretical studies on the nitric oxide reductases (NORs), having binuclear Fe/Cu active sites, suggest that dianionic hyponitrite $[ON=NO]^{2-}$ may form from 2 equiv. NO via the transfer of 1-electron from each metal center.

To comprehend the reduction of NO at a single Cu site, we investigate the sequential assembly of NO molecules and electron transfer process at a $[Cu^I]$ center supported by a β-diketiminate ligand. Initially, one NO molecule binds at a single $[Cu^I]$, forming a $\{CuNO\}^{11}$ complex. However, this complex is unstable to a second NO, resulting in the formation of a reactive hyponitrite complex $[Cu](\kappa^2\text{-}O_2N_2)$. This species can be stabilized by 1-electron reduction to give a *cis*-hyponitrite $\{[Cu^{II}](\kappa^2\text{-}O_2N_2)[Cu^I]\}^-$ intermediate that forms upon addition of NO and Cp*2Fe to $[Cu^I]$. Importantly, this takes place by outer-sphere reductants similar to the type I and Cu_A electron-transfer sites (~0.26 V vs NHE). Furthermore, the $\{[Cu^{II}](\kappa^2\text{-}O_2N_2)\}^-$ intermediate is isolated by removing the bound $[Cu^I]$. Interestingly, the $\{CuNO\}^{11}$ complex can also be stabilized by 1-electron reduction to give a $\{CuNO\}^{12}$ intermediate, $\{[Cu^I](\eta^2\text{-}NO)\}^-$, which forms by the addition of potassium naphthalenide. These two intermediates, $\{[Cu^{II}](\kappa^2\text{-}O_2N_2)\}^-$ and $\{[Cu^I](\eta^2\text{-}NO)\}^-$, isolated during NO reduction pathway at a [Cu] site, yield different signaling products upon protonation. While, adding a proton to $\{[Cu^{II}](\kappa^2\text{-}O_2N_2)\}^-$ forms N_2O and copper(II) hydroxide, the $\{[Cu^I](\eta^2\text{-}NO)\}^-$ intermediate generates HNO upon protonation. The HNO produced is trapped by 2 equiv. of PPh_3 as $O=PPh_3$ and $HN=PPh_3$. Consequently, the overall sequence of NO binding and electron-transfer at a [Cu] site contrasts the signaling outputs.

Oxidation of $\{[Cu^{II}](\kappa^2\text{-}O_2N_2)\}^-$, at potentials greater than 0.73 V vs NHE, generates the reactive *cis*-hyponitrite complex $[Cu](\kappa^2\text{-}O_2N_2)$. This reactive complex exhibits facile hydrogen atom transfer (HAT) reactivity with substrates of modest C−H bond strength, such as 9,10- dihydroanthracene, xanthene, and cumene (BDE's = 76–85 kcal/mol). The HAT reaction by the reactive $[Cu](\kappa^2\text{-}O_2N_2)$, conceived as a synchronous electron and proton addition, indicates that reduction and protonation processes work in concert to leverage the anaerobic oxidizing potential of NO.

09.01.2024

Electrocatalytic oxidation of dinitrogen to nitric acid via direct Ten–electron transfer using manganese phthalocyanine

Ashadul Adalder and Uttam Kumar Ghorai

Department of Industrial Chemistry & Applied Chemistry, Swami Vivekananda Research Centre, Ramakrishna Mission Vidyamandira, Belur Math, Howrah, 711202, India

Abstract: Ammonia produced through the energy intensive Haber–Bosch process, undergoes catalytic oxidation for the manufacture of commercial nitric acid in the age–old Ostwald process. This two–step energetically non–viable industrial process demands the quest of an alternative single step electrocatalysis from the last century[1]. The quest ends up in optimism when we unravel a ten–electron pathway associated with electrochemical dinitrogen oxidation reaction (N_2OR) to nitric acid by manganese phthalocyanine (MnPc) hierarchical nano–structures (HNs) at STP. The catalyst delivers nitric acid yield of 513.2 μmol h^{-1} g^{-1}_{cat} and faradaic efficiency (F.E.) of 33.9% @ 2.1 V vs. RHE in 0.05 N H_2SO_4. The excellent N_2OR abilities are attributable to specific selectivity, the presence of a greater number of exposed active sites, recyclability, and long-term stability. Mn atoms are connected to pyrrolic and pyridinic nitrogen via Mn-N_4 coordination, according to the XAFS. Theoretical simulations based on DFT confirm that the Mn-N_4 site of MnPc is the primary active centre for N_2OR, which suppresses OER. This work opens up a new field for the development of a carbon-neutral sustainable society by demonstrating the successful example of single step nitric acid production using Mn-N_4 active site-based metal phthalocyanine electrocatalyst via dinitrogen oxidation[2].

References:

1. A. Adalder and U. K. Ghorai* et. al, "*Progress of electrochemical synthesis of nitric acid: catalyst design, mechanistic insights, protocol and challenges*" **J. Mater. Chem. A, 2023**,11, 10125-10148

2. A. Adalder and U. K. Ghorai* et. al, "*Selective Electrocatalytic Oxidation of Nitrogen to Nitric Acid Using Manganese Phthalocyanine*", **ACS Appl. Mater. Interfaces 2023**, 15, 34642–34650

09.01.2024

Biological and Medicinal Chemistry of Copper

Peter Faller

Institut de Chimie (CNRS UMR 7177), University of Strasbourg, CNRS, 4 rue B. Pascal, 67081 Strasbourg Cedex (France)

pfaller@unistra.fr

Copper ions are essential for almost all living organisms and a tight control of copperbinding and coordination is important as copper is potentially dangerous, often *via* itshigh capacity to activate dioxygen and hence catalyze the production of reactive oxygen species. Several diseases are linked more or less to a dyshomeostasis of copper such as Wilson's and Menkes genetic disorders, Alzheimer's disease, canceretc... Thus, interfering in copper metabolism *via* small ligands is of interest astherapeutic approach.

Inorganic copper-complexes can be applied or formed *in situ* via chelation of endogenous Cu. Biological activity can consist of supplying, sequestering or transporting Cu, or by catalysing targeted chemical reactions often via dioxygen activation. Later is thought to be of high importance in development of anti-cancer drugs or for antimicrobials.

During the last years we worked on the Cu chemistry of several endogenous or exogenous ligands. This includes the aim to understand the role of Cu bound to the amyloid peptides related to neurodegenerative disease, the reactivity of several classical ligand types (thiosemicarbazones, phenanthroline, dithiocarbamate, bleomycin, etc.) used in anticancer and antimicrobial activity, the development of sensors to detect Cu(II) in biological fluids and others. In this context, recentadvancements are reported which were made around mechanistic insights in the anticancer activity of Cu-complexes with α-pyridyl thiosemicarbazones [1, 2], the redox-cycling of Cu-amyloid-beta [3] or the development of a Cu-shuttle to prevent Cu-amyloid-beta toxicity [4].

References

[1] Falcone E, Ritacca AG, Hager S, Schueffl H, Vileno B, El Khoury Y, Hellwig P, Kowol CR, HeffeterP, Sicilia E, Faller P. *J Am Chem Soc.* 144, 14758-14768 (2022)

[2] Ritacca AG, Falcone E, Doumi I, Vileno B, Faller P, Sicilia E. *Inorg Chem.*, 62, 3957-3964 (2023).

[3] Falcone E, Nobili G, Okafor M, Proux O, Rossi G, Morante S, Faller P, Stellato F. *Angew Chem IntEd Engl.* 62, :e202217791.(2023)

[4] Okafor M, Gonzalez P, Ronot P, El Masoudi I, Boos A, Ory S, Chasserot-Golaz S, Gasman S, Raibaut L, Hureau C, Vitale N, Faller P. *Chem Sci.,*13, 11829-11840. (2022)

09.01.2024

Unique Cu cluster in the mitigation of N_2O

(N_2O a green house gas)

Isabel Moura

LAQV, NOVA School of Science and Technology | FCT NOVA, Portugal

isabelmoura@fct.unl.pt

Nitrous oxide (N_2O) is a powerful greenhouse gas that contributes to global warming. One way to mitigate its impact is to use of nitrous oxide reductase (N_2OR), an enzyme that converts N_2O into nitrogen gas. N_2OR is found in certain bacteria and is composed of a copper cluster, which plays a critical role in its catalytic activity. In this study, we investigate the potential of utilizing N_2OR and copper clusters as a means of reducing N_2O emissions. We explore different methods for producing N_2OR and copper clusters, as well as their effectiveness in converting N_2O to nitrogen gas.

The microbial denitrification. pathway accounts for the dissimilatory transformation of nitrate and nitrite, in four reactions catalyzed by different metalloenzymes, that sequentially convert nitrate into dinitrogen (with nitrite, nitric oxide and N_2O as intermediates). In this talk we will address the structure/function relationship of the N_2Or that reduces N_2O, using a toolbox of spectroscopic, kinetic, electrochemical and structural techniques aiming to better understand the enzyme to enhance its N2O mitigation potential. *Marinobacter hydrocarbonoclasticus* N_2OR has two copper centers, CuA, the electron transfer center, and "CuZ", the catalytic center. "CuZ" is a unique center in biological systems, since it has a sulfide bridging a distorted tetrahedron of copper ions , and the copper ions are also coordinated by seven histidine side chains.

Aknowledgements : We thank Esther Pierce, E.Solomon, S.R.Pauleta, S.Dell'Acqua,Cíntia Carreira and José Moura for many contributions. Project supported by FCT MCTES (PTDC/QUI-BIQ/116481/2010, PTDC/BBB-BIQ/0129/2014 and PTDC/2022.01152).

09.01.2024

Elucidating the Copper Active Site of Lytic Polysaccharide Monooxygenases with Advanced EPR Spectroscopies

George E. Cutsail III[1,2*], Julia Haak[1,2] Ole Golten[3], Morten Sørle[3], Vincent Eijsink[3]

[1]Max Planck Institute for Chemical Energy Conversion, D-45470, Germany; [2]Unviersity of Duisburg-Essen, D-45141, Germany; [3]Norwegian University of Life Sciences, N-1432, Norway; *email: george.cutsail [at] cec.mpg.de

Lytic polysaccharide monooxygenases (LPMOs)[1] form a wide class of monocopper enzymes that break down lignocellulose material via oxidative cleavage at the glycosidic bond. All LPMOs have a distinct and well-recognizable monocopper active site, composed of only two histidine amino acids, forming what is commonly referred to as the 'His-brace.'

The resting-state Cu(II) LPMO structure is often characterized by EPR spectroscopy due to the technique's high sensitivity to the copper's electronic structure. However, despite the common active-site among all LPMOs, diverse EPR signals are observed due to influences of other coordinating ligands (i.e. waters). Flexibility in this His-brace has been previously observed, and the role of the unique N-terminus amine ligand in catalysis are unknown.[2]

In my talk, I will discuss our work on deciphering the various copper EPR responses one may observe and their electronic and structural origins. Advanced pulsed hyperfine techniques, such as electron nuclear double resonance spectroscopy, yield more insight into the various ligands. Through a combination of advanced EPR spectroscopies, isotopic labelling, and DFT computations, we are building a complete picture of the LPMO copper active-site.

[1] K. K. Meier, S. M. Jones, T. Kaper, H. Hansson, M. J. Koetsier, S. Karkehabadi, E. I. Solomon, M. Sandgren, B. Kelemen, *Chemical Reviews*. **2018**, *118*, 2593–2635.

[2] 1. L. Ciano, G. J. Davies, W. B. Tolman, P. H. Walton, Bracing copper for the catalytic oxidation of C–H bonds. *Nat Catal*. **2018**, *1*, 571–577.

09.01.2024

Bio-inspired models for copper-containing Lytic PolysaccharideMonoOxygenase

Rébecca Leblay, Yongxing Wang, Bruno Faure, Maylis Orio, Marius Réglier, A. Jalila Simaan

CNRS, Aix Marseille University ; iSm2, Saint Jérôme campus, Marseille, FranceE-mail: jalila.simaan@univ-amu.fr

LPMOs are copper-containing enzymes produced by some bacteria and fungi, amonga consortium of enzymes that collectively act to degrade recalcitrant polysaccharidessuch as cellulose or chitin.[1] LPMO catalyze the hydroxylation of a strong C-H bond at the glycosidic linkage of polysaccharides leading to glycosidic bond cleavage. The active center is composed of a mononuclear copper ion ligated by two histidines in anunusual histidine brace motif (Fig. 1A).[2] It is not clear whether the natural oxidant employed by LPMO is O2 or H2O2. In both cases, it is proposed that the reduced Cu(I)state would react with either of the co-oxidant to produce a Cu(I)-(H2O2) intermediate that would undergo O-O bond homolysis in a controlled Fenton-type reactivity.

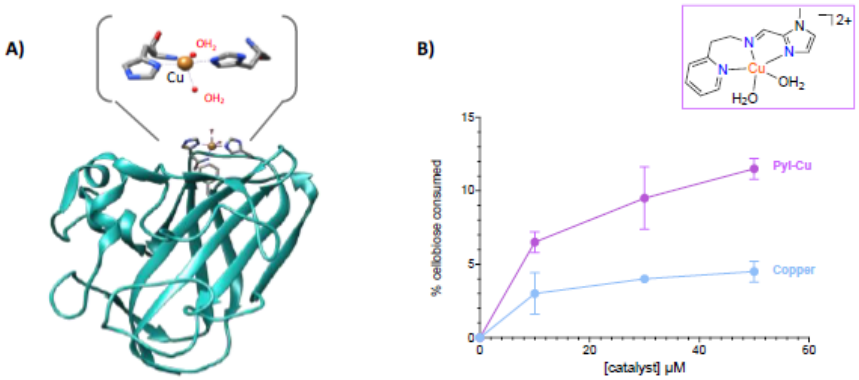


Figure 1. A) Structure of a bacterial LPMO and view of the copper coordinating ligands B) cellobiose (dimer of glucose) degradation after 2 hours by a LPMO bioinspired model (phosphate buffer pH 7.5; 2 mM H_2O_2).

Our group combines studies on enzymatic systems[3] and on bioinspired metal-containing complexes.[4] A few years ago, we have reported two LPMO-bioinspired models promoting the oxidative cleavage of a model substrate, *para*-nitrophenyl-β-D-glucopyranoside (*p*-NPG), in presence of hydrogen peroxide in aqueous solutions (Fig. 1B).[4a] These complexes were recently shown to display activity on substrates ofincreasing complexity.[4c] Our recent results directed towards the design and reactivityof model complexes inspired by the active site of LPMO will be presented.

Acknowledgement: The authors acknowledge the financial support of ECOS-NORD (projectM17P01), Region-Sud PACA (EJD) and ANR (ANR-22-CE07-0032-03, COSACH)

References:

[1]. Z. Forsberg, *et al*., *Curr. Opin. Struct. Biol.* **2019**, *59*, 54–64[2].
P. H. Walton, *et al*., *FEBS Lett* **2023**, *597*, 485–494

[3]. a) A. Munzone, *et al*., *FEBS J.* **2020**, *287*, 3298–3314 b) R.J. Gómez-Piñeiro, *et al*., *Inorg. Chem*.

2022, 61(20), 8022-8035

[4]. a) A. L. Concia, *et al*. *Inorg. Chem.* **2017**, *56*, 1023–1026 b) S. Gamboa-Ramirez, *et al*., *Chem. Eur. J.*

2022, 28 (66), e202202206 c) R. Leblay, *et al*., *ChemCatChem,* DOI:10.1002/cctc.202300933

09.01.2024

Modulation and detection of amyloid aggregation by transition metal complexes

Kaushik Ghosh[a,b*]

[a]Department of Chemistry, Indian Institute of Technology, Roorkee-247667, Uttarakhand

[b]Department of Biosciences and Bioengineering, Indian Institute of Technology, Roorkee- 247667, Uttarakhand

Email: Kaushik.ghosh@cy.iitr.ac.in

Protein misfolding and aggregation have been associated with several human neurodegenerative disorders, such as Alzheimer's, prions, and Parkinson's diseases *etc*. Recently, transition metal complexes have received considerable attention in protein aggregation studies due to their interesting photophysical and photochemical properties. The interaction of various metal complexes based on Ru(II), Ru(III), Pd(II), V(II), Co(II), and Pt(II) was explored for the modulation, and sensing of protein aggregation in Alzheimer's Aβ(1-42, 1-40, 25-35), prion's PrP^C(106-126) and Parkinson's α-synuclein proteins. Our group mainly focused on the design and synthesis of various coordination complexes for the interactions, modulation and detection of protein aggregation in Aβ(1-42, 25-35) and PrP^C (106-126) peptides. Amyloid aggregation was studied using thioflavin-T (ThT) fluorescence assay, and the secondary structure of peptides was analysed by CD and TEM spectroscopy. Interaction and binding were examined by MALDI-TOF mass spectrometry and molecular docking studies. Metal complexes based on Ru(II) and Pd(II) significantly inhibited protein aggregation and amyloid fibril formation due to the strong binding of complexes to His residues, scavenging of ROS generated and loss of ordered β-sheet formation. Ni(II)-based metal complexes showed detection of amyloid aggregation in PrP(106-126) peptides. Hence, we propose that transition metal complexes could be presented as therapeutic molecules and potential probes for amyloid detection in metallo-pharmaceutical research against neurodegenerative diseases.

References:

(1) Singh, S.; Navale, G. R.; Agrawal, S.; Sarkar, D.; Sarma, M.; Choudhury, A. R.; Ghosh, K. Design and Synthesis of Piano-Stool ruthenium(II) Complexes and Their Studies on the Inhibition of Amyloid β (1–42) Peptide Aggregation. *Int. J. Biol. Macromol.* **2023**, *239*, 124197.

(2) Saini, R.; Navale, G. R.; Singh, S.; Kisan, H.; Chauhan, R.; Agrawal, S.; Sarkar, D.; Sarma, M.; Ghosh, K. Inhibition of Amyloid β 1 – 42 Peptide Aggregation by Newly Designed Cyclometallated Palladium Complexes. *Int. J. Biol. Macromol.* **2023**, *248*, 125847.

(3) Navale, G. R.; Chauhan, R.; Saini, S.; Roy, P.; Ghosh, K. Effect of Cycloastragenol and Punicalagin on Prp(106–126) and Aβ(25–35) Oligomerization and Fibrillizaton. *Biophys. Chem.* **2023**, *302*, 107108.

(4) Navale, G. R.; Rana, A.; Saini, S.; Singh, S.; Saini, R.; Chaudhary, V. K.; Roy, P.; Ghosh, K. An Efficient Fluorescence Chemosensor for Sensing Zn(II) Ions and Applications in Cell Imaging and Detection of Zn(II) Induced Aggregation of PrP(106–126) Peptide. *J. Photochem. Photobiol. A Chem.* **2023**, *441*, 114703.

09.01.2024

Azo-Stilbene and Pyridine-Amine Hybrid Multifunctional Molecules to Target Metal Mediated Neurotoxicity and Amyloid-β Aggregation in Alzheimer's disease

Anuj K. Sharma*[a], Monika Rana[a], Liviu M. Mirica[b]

[a]Department of Chemistry, Central University of Rajasthan, NH-8, Bandarsindri,

Kishangarh, Ajmer, RJ, 305817

Department of Chemistry, University of Illinois at Urbana-Champaign, Urbana, Illinois 61801, United States

Email: anuj.sharma@curaj.ac.in; aks.iitk@gmail.com

Neurodegenerative diseases such as Alzheimer's diseases (AD) are associated with progressive neuronal cell death and a common correlation is aberrant protein misfolding and aggregation of the Aβ peptide. Transition metal ions (Cu, Fe and Zn) have been shown to promote aggregation and oxidative stress through formation of Aβ-metal complexes. In this context, integrating molecular scaffolds rationally is used here to generate multifunctional molecules as modulators for metal-induced abnormalities. This work encompasses few azo-stilbene (AS) derived compounds, the rationale behind the design, their synthesis, characterization and metal chelation ability [Cu(II) and Zn(II)]. The molecular frameworks of the designed compounds consist of stilbene as an Aβ interacting moiety; whereas N,N,O and N,N,N,O donor atoms are linked to generate the metal chelation moiety. Further, we went on exploring their multifunctionality w.r.t. to (i) their metal chelating capacities (ii) their utility to modulate the aggregation pathways of both metal-free and metal-bound amyloid-β, (iii) scavenge free radicals, (iv) inhibit the activity of acetylcholinesterase and (v) cytotoxicity. Moreover, the compounds were able to sequester Cu2+ from the Aβ-Cu complex as studied by UV-visible spectroscopic assay. Molecular docking studies were also performed with Aβ and acetylcholinesterase enzyme. Overall, the studies presented here qualify these molecules as promising candidates for further investigation in quest for finding Alzheimer's treatment.

References:

[1] Rana, M.; Cho, H.J.; Arya, H.; Bhatt, T. K.; Bhar, K.; Mirica, L. M.; Sharma, A. K.* Inorg. Chem. 2022, 61, 10294.
[2] Sharma, A. K.; Pavlova, S. T.; Kim, J.; Kim, J.; Mirica, L. M. Metallomics 2013, 5, 1529.
[3] Crichton, R. R.; Dexter, D. T.; Ward, R. J. Coord. Chem. Rev. 2008, 252, 1189.
[4] Rodríguez-Rodríguez, C.; Telpoukhovskaia, M.; Orvig, C. Coord. Chem. Rev. 2012, 256, 2308.
[5] Sharma, A. K.; Pavlova, S. T.; Kim, J.; Finkelstein, D.; Hawco, N. J.; Rath, N. P.; Kim, J.; Mirica, L. M. J. Am. Chem. Soc. 2012, 134, 6625.
[6] Braymer, J. J.; DeToma, A. S.; Choi, J.-S.; Ko, K. S.; Lim, M. H. Int. J. Alzheimer's Dis. 2011, ID 623051.
[7] Choi, J.-S.; Braymer, J. J.; Nanga, R. P. R.; Ramamoorthy, A.; Lim, M. H. Proc. Natl. Acad. Sci. U.S.A. 2010, 107, 21990.
[8] Rana, M.; Roy, T. K.; Sharma, A. K.* Inorg. Chim. Acta, 2018, 471, 419.

09.01.2024

Monocopper(II) Complexes as Functional Mimics for type-3 Copper Oxidase

Mariappan Murali
Coordination and Bioinorganic Chemistry Research Laboratory
Department of Chemistry, National College (Autonomous), Tiruchirappalli 620 001
Tamil Nadu, India murali@nct.ac.in

Metalloenzymes containing transition metals are still being studied in terms of their structural or functional models. From an environmental and biological perspective, catechol metabolism is crucial. *In vivo* metabolism of catechol to o-quinone is caused by a type-3 copper oxidase such as catechol oxidase. The active site of the *met*-form of the catechol oxidase consists of a hydroxo-bridged dicopper(II) center, each of which is coordinated to three histidine nitrogens and assumes a trigonal pyramidal geometry with nitrogen in the apical position. So far, dicopper(II) (Cu···Cu < 5 Å) systems have been identified as the most functional models of catechol oxidase, whereas monocopper(II) systems are relatively uncommon. However, the catalytic efficiency of these model complexes is significantly less than that of the native biological enzymes. Therefore, improvement of the catalytic efficiencies of these complexes is a great challenge and with this aim, several modifications were made in the coordination environment of the closely-knit copper ions. We found that there are three important factors, that enhance the catalytic efficiency of the monocopper(II) complex as a catalyst: (i) the complex provides distorted square pyramidal (4+1) coordination geometry around copper(II) with the labile binding site(s); (ii) the crystal packing of the complex reveals the presence of self-assembled molecular association to form dimer due to non-covalent interactions such as (a) intermolecular hydrogen bonding, (b) inter-pair π-π stacking and (c) C-H···π interactions; and (iii) the complex shows the reversible change of oxidation state at high positive redox potential. Thus, we have synthesized a monocopper(II) complexes of the type [Cu(L1-L4)(bpy/phen/Hdpa/pybzim)](ClO_4) [H(L1), (2-(dimethylamino)ethyl)imino)-methyl)phenol; H(L2), 2-(diethylamino)-ethyl)imino)methyl)phenol; H(L3), 2-(dimethyl-amino)ethyl)imino)methyl) naphthalen-2-ol; H(L4), 2-(diethylamino)ethyl)imino)methyl)-naphthalen-2-ol; bpy, 2,2'-bipyridine; phen, 1,10-phenanthroline; Hdpa, 2,2'-dipyridylamine; pybzim, 2-(2-pyridyl)benzimidazole]. The structural characterization in both solid and solution state and the promising catalytic activity of monocopper(II) complexes as functional mimics for catechol enzyme will be discussed.

References:

1. Geremann, C.; Eicken, C.; Krebs, B. The crystal structure of catechol oxidase: new insight into the function of type-3 copper proteins. *Acc. Chem. Res.*, **2002**, *35*, 183-191.
2. Koval, A. I.; Gamez, P.; Belle, C.; Selmeczi, K.; Reedijk, J. Synthetic models of the active site of catechol oxidase: mechanistic studies. *Chem. Soc. Rev.*, **2006**, *35*, 814-840.
3. Murali, M.; Sathya, V.; Selvakumaran, B. Fate of model complexes with monocopper center towards the functional properties of type 2 and type 3 copper oxidases. *J. Biol. Inorg. Chem.*, **2021**, *26*, 67-79.

09.01.2024

Ferrocene conjugated thiosemicarbazone and its Cu(II) heteroleptic complexes for evaluating their DNA/Protein binding efficiency, nuclease activity, and cytotoxicity

R. Kartikeyan[1], M. Anjaneyulu[1], S. Abhay Kumar[2], V. Prabha[1], S. Veeresh Kumar [3], V. Yellamandayya[4], D. Siva Sundara Kumar[2], **V. Rajendiran** [1,*]

[1]Department of Chemistry, School of Basic and Applied Sciences, Central University of Tamil Nadu, Thiruvarur, India – 610 005

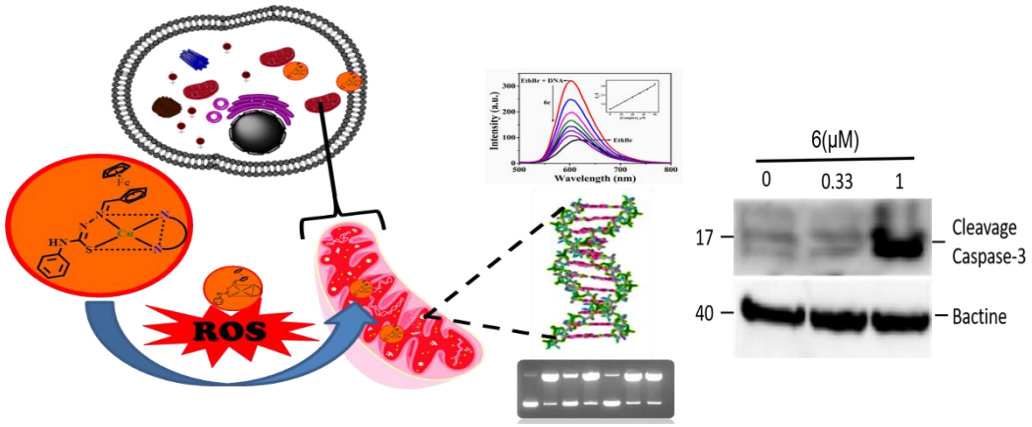
[2]Department of Microbiology, School of Life Sciences, Central University of Tamil Nadu, Thiruvarur, India – 610 005

[3]Department of Internal Medicine, Carver College of Medicine, The University of IOWA, IOWA, IA 52242, USA

[4]Department of Biotechnology, Daegu University, South Korea

*rajendiran@cutn.ac.in

Ferrocene conjugated compounds have aroused the interest of researchers in recent years due to their multiple therapeutical applications. Following the discovery of ferrocifen as an anticancer agent in 1996, which is in the preclinical evaluation, a significant breakthrough in the medicinal chemistry of ferrocene derivatives occurred. In recent days, more attention has been focussed on designing of mixed-ligand Cu(II) complexes for alternative to Pt-based drug.[1] Thus, in the present investigation, a series of mixed-ligand ferrocene conjugated simple and heteroleptic copper(II) complexes of the types ferrocene-2-aldehyde-4(N) phenyl thiosemicarbazone, (**1**), [Cu(L)(H_2O)(NO_3)] (**2**) and [Cu(L)(diimine)](NO_3) (**3**-**6**), respectively, where L (4-phenyl-1-(ferrocene-2-ylmethylene)thiosemicarbazone) is a primary ligand and diimine viz., 2,2'-bipyridine (bpy; **3**), 1,10-phenanthroline (phen; **4**), 5,6-dimethyl-1,10-phenanathroline (5,6-dmp; **5**) and 3,4,7,8-tetramethyl-1,10-phenanthroline (3,4,7,8-tmp; **6**) as co-ligands have been synthesized and characterized and evaluated their DNA/protein binding, DNA cleavage, and cytotoxicity. The DNA and HSA binding studies infer that the 5,6-dmp and 3,4,7,8-tmp containing complexes **5** and **6**, respectively, involve stronger DNA and protein binding interactions as compared to other complexes in the series. The redox-active complexes **5** and **6** display significant DNA cleavage in the presence of reducing agent ascorbic acid whereas in the presence of H_2O_2 complexes **4** and **5** display higher DNA cleavage. The mechanistic study reveals that complexes can able to create oxidative stress by generating freely diffusible hydroxyl radicals even under hypoxic conditions. Remarkably, the complex **6** which exhibits a higher oxidative DNA cleavage causes more cytotoxicity in the HCT116 and HCT15 colon cancer cells, following **6**, a higher DNA and protein binding complex **5** exhibits higher cytotoxicity. Importantly, both the complexes display higher cytotoxicity compared to cisplatin and low cytotoxicity with the normal colon CCD841CoN cells. Further, ROS study reveals that the complexes **5** and **6** demonstrate production of ROS and these results were consistent with the Western blot analysis, which also revealed increased levels of cleaved caspase-3 after treatment of **6.** We believe that if we do more research on these bioorganometallic complexes containing biocompatible metal ions like Fe(II) and Cu(II), they will be able to emerge as new types of anticancer agents.



References:

1. Kartikeyan, R.; Murugan, D.; Ajaykamal, T.; Varadhan, M.; Rangasamy, L.; Velusamy, M.; Palaniandavar, M.; Rajendiran, V. Mixed Ligand Copper(II)-Diimine Complexes of 2-Formylpyridine-N^4-Phenylthiosemicarbazone: Diimine Co-Ligands Tune the in Vitro Nanomolar Cytotoxicity. *Dalt. Trans.* **2023**, *52* (26), 9148–9169. https://doi.org/10.1039/D3DT00213F.

09.01.2024

Investigation and comparison of *in vitro* and *in silico* methods shed light on antimicrobial properties exhibited by curcumin and its transition metal complexes.

[1]Tanmoy Saha and [2]Saurabh Das

[1]PhD research Scholar, Department of Chemistry, (Inorganic Section), Jadavpur University, Kolkata-700032, India

[2]Professor, Department of Chemistry, (Inorganic Section), Jadavpur University, Kolkata-700032, India

Curcumin possesses an intriguing molecular structure that exhibits a diverse range of therapeutic potentials. However, therapeutic implications of this substance are significantly impeded due to its suboptimal bio-availability that may be attributed to its inherent instability and limited solubility in aqueous environment. In a valiant endeavour to surmount this intrinsic constraint and cultivate curcumin-derived antibacterial agents, we have successfully synthesized and thoroughly investigated metal complexes comprising copper (II) and zinc (II) in conjunction with curcumin. The structural framework was established through utilisation of Density Functional Theory (DFT) calculation. In the present investigation, we undertook a comprehensive examination of the complexes, namely Cu(Cur) and Zn(Cur), with a particular focus on their stability and antibacterial efficacy. Furthermore, we endeavoured to elucidate the potential mechanism of action of these complexes, drawing insightful comparisons to the parent compound, Curcumin. The phenomenon of complex formation yielded enhanced stability across a range of diverse physiological conditions. The enhanced stability was corroborated through the utilisation of UV–Vis spectroscopy and HPLC techniques. By achieving an enhanced stability under biological conditions, it was observed both Cu(Cur) and Zn(Cur) demonstrated remarkable and significantly amplified efficacy in comparison to curcumin when combating both *E. coli* and *S. aureus*. An *in vitro* Calcein leakage assay provided evidence indicating that the complex in question induced prompt membrane permeabilization in bacterium *Staphylococcus aureus*. The veracity of this mode of action that disrupts the membrane was further substantiated through utilisation of microscopic visualisation techniques. Through an *in silico* investigation, it was identified that Curcumin, along with metal complexes possess the ability to effectively engage with FtsZ Proteins, consequently impeding the process of FtsZ protofilament assembly. Consequently, suppression of Z-ring formation ensues, resulting in the inhibition of cytokinesis and impeding bacterial proliferation. The remarkable efficacy of the complexes, enhanced over that of Curcumin, by their favourable toxicological profile, characterised by their lack of hemolytic and cytotoxic effects on mammalian cells is worthy of further pursuation, rendering them a highly promising contender for *in vivo* studies. In its entirety, this study represents a discerning evaluation that champions the antimicrobial capacity of this enduring, membrane-focused and innocuous compounds, introducing novel viewpoints for a therapeutic utilisation in combating bacterial infections.

References

1. ***T.Saha**, S.Sappati, S.Das, An insight into the mixed quantum mechanical-molecular dynamic simulation of a Zn^{II}-Curcumin complex with a chosen DNA sequence that supports experimental DNA binding investigations*, **International Journal of Biological Macromolecules**, ***2023**, 245 125305*

2. P.Kumar, **T.Saha**, S,Behara, S.Gupta,S.Das, K.Mukhopadhyay, Enhanced efficacy of a Cu2+ complex of curcumin against gram-positive and gram-negative bacteria: attributes of complex formation, ***Journal of Inorganic Biochemistry,* 2021**,222,111494

3. **T. Saha,** S. Singha, S, Kumar, S. Das, Spectroscopy driven DFT computation for a structure of the monomeric Cu^{2+}-Curcumin complex and thermodynamics driven evaluation of its binding to DNA: Pseudo-binding of Curcumin to DNA. ***Jour. Mol. Struc***., **2020**, **1221**, 128732.
4. **T.Saha,** P.Kumar, N.Sepay, D.Ganguly, K.Tiwari, K.Mukhopadhyay, S.Das, Multitargeting antibacterial activity of a synthesized Mn^{2+} complex of curcumin on gram-positive and gram-negative bacterial strains, ***ACS omega***., **2020**, 5, 27, 16342-16357

09.01.2024

Geometric and Electronic Structural Contributions to Fe/O_2 Reactivity: Correlations between metalloenzyme and heterogeneous catalysis

Edward I. Solomon
Department of Chemistry, Stanford University, Stanford, *CA USA*

Most of the major classes of non-heme iron metalloenzymes use high spin Fe(II) sites to activate O2. These had been refractory to spectroscopic definition. Thus we developed a variable- temperature, variable-field magnetic circular dichroism (VTVH MCD) spectroscopic methodology that defined a general mechanistic strategy used by these non-heme Fe(II) enzyme classes to control O2 activation. This leads to Fe/O2 intermediates that go on to perform a wide range of selective catalysis. This talk will then focus on using Nuclear Resonance Vibrational Spectroscopy (NRVS) to define the geometric structures and VTVH MCD the electronic structuresof Fe(IV)=O intermediates in these metalloenzymes and, coupled to electronic structure calculations, define how their Frontier Molecular Orbitals (FMOs) control reactivity. These methods will then be extended with site selectivity to define the Fe active sites in metallozeolites that take CH4 to CH3OH at room temperature and their relation to the metalloenzymes.

09.01.2024

Twists and Turns in Exploring the Reactivity of Nonheme FeIV=O Complexes: How Critical Is the Iron Spin State?

Lawrence Que, Jr., Bittu Chandra, Nabhendu Pal, Abhishek Das, and Srikanth Dasari
University of Minnesota, Minneapolis, MN, USA

Nature has evolved nonheme iron enzymes for the selective functionalization of target substrates utilizing high- valent iron-oxo intermediates to carry out the hydroxylation and halogenation of C–H bonds as well as C=C bond epoxidation [*JBIC* **2017,** *22*, 339] Such oxidations are typically carried out by *S* = 2 Fe(IV)=O oxidants as described by Krebs and Bollinger in the their seminal efforts in characterizing such enzymes with a 2-His-1-carboxylate active site [*Acc. Chem. Res.* **2007,** *40*, 284]. However, Guo et al. [*ACIE **2023**, 62, e202309362*] have recently reported the first example of an *S* = 1 oxoiron(IV) species in biology that is found in an active site consisting of four His ligands plus a weaker-field sulfenate anion. This latest discovery broadens the scope of high-valent Fe=O chemistry that has been found in nature.

Efforts to synthesize small molecules that mimic such nonheme Fe=O oxidants have been reported by a number of laboratories, thus far resulting in the characterization of about a hundred synthetic complexes. 90% of these have been found to have *S* = 1 ground states, with the remainder having *S* = 2 centers [*Chem. Rev.* **2018**, *118*, 2554]. However most of the complexes have been found to have relatively low oxidative reactivity, including most of *S* = 2 complexes described thus far, which have trigonal bipyramidal geometry. The one striking exception among the *S* = 2 Fe=O complexes is $[Fe^{IV}(O)(TQA)(MeCN)]^{2+}$ (TQA = tris(quinolylmethyl)amine), which differs from the other *S* = 2 complexes in having an octahedral geometry and is to date the most reactive of the synthetic complexes characterized thus far (*JACS* **2015***, 137*, 2428). Its HAT reactivity at 233 K is comparable to that found in iron enzymes at 5 ^{o}C (after adjusting for the temperature difference). However there is an *S* = 1 complex that is just slightly less reactive than the TQA complex, namely the *S* = 1 $[Fe^{IV}(O)(Me_3NTB)(MeCN)]^{2+}$ (Me_3NTB = tris((N-methylbenzimidazol- 2-yl)-methyl)amine), first described by Nam and coworkers in 2011 (*Chem. Sci.* **2011***, 2, 1039*). These observations suggest that an *S* = 2 spin state is not essential to elicit the high HAT reactivity found for the nonheme iron oxygenases.

This plenary lecture will build on this background and present recent developments from my laboratory. The first story describes our current efforts on the chemistry of the $[Fe^{IV}(O)(TMC)]$ complex, the first nonheme $Fe^{IV}(O)$ complex to be crystallized in my lab in 2003 (*Science*, **2003**, *299*, 1037), with a focus on our recent efforts in the epoxidation of olefins. In comparing the oxidative reactivity of the two topological isomers of $[Fe^{IV}(O)(TMC)(CH_3CN)]^{2+}$, we have found TMC-*syn* (*Inorg. Chem*., **2015**, *54*, 11055)to show HAT reactivity 2-3-fold higher than found for the *anti* isomer. Surprisingly, significantly larger differences in OAT reactivity of 2-3 orders of magnitude are observed for the *syn* isomer, simply by a simple flip of the Fe=O unit orientation (*PNAS*, under review) .

The second story originates from the observation that the *S* = 1

$[Fe^{IV}(O)(Me_3NTB)(MeCN)]^{2+}$ complex first reported by Nam (*Chem. Sci.* **2011**, *2*, *1039*) exhibits HAT rates just 30% slower than those of the *S* = 2 $[Fe^{IV}(O)(TQA)(MeCN)]^{2+}$ complex we described in 2015 (*J. Am. Chem. Soc.* **2015**, *137*, 2428). This similarity in oxidation rates strongly suggests that the $Fe^{IV}(O)$ spin state cannot be the sole factor that determines oxidative reactivity. In support of this hypothesis, we have just found a new *S* = 1 complex with an HAT reactivity that is 2-fold higher than that found for the *S* = 2 TQA complex and 3-fold higher than that found for the *S* = 1 Me_3NTB complex. These studies reveal a marvelous complexity in the factors that control the reactivity of nonheme iron oxidants. Spectroscopic comparisons will also be discussed.

09.01.2024

Catalyst development for sustainable oxidation reactions

Sayam Sen Gupta

Department of Chemical Sciences, IISER Kolkata, Mohanpur 741246

sayam.sengupta@iiserkol.ac.in

Catalysts that selectively oxidize C-H bonds and mimic natural Fe-containing enzymes have the power to re-orient organic synthesis. Although iron complexes are known to activate H_2O_2 to perform selective oxidation of unactivated C-H bonds, all of them only operate in organic solvents. It is extremely challenging to design synthetic iron complexes that perform selective C-H oxidation in nature's solvent "water" (mimicking the metalloenzyme cytochrome P450). In this talk, I will discuss designing iron complexes that even in the absence of a protein scaffold can activate H2O2 and perform very selective, fast, and scalable C-H oxidation in complex organic molecules including natural products in 100% water. This iron complex, a modified "picket-fence" Fe-bTAML complex, can oxidize C-H and C=C bonds in several organic substrates with low catalyst loadings (1-4 mol%) and a small excess of H_2O_2 (2-3 equiv) in water. Subsequently, I will discuss strategies for the exclusion of solvent from these C-H oxidation reactions under mechanochemical conditions. Applications of such solvent-free reactions in the upcycling of commercial hydrocarbon polymers will be discussed.

References:

Sandipan Jana *et. al. Chemical Science*, **2023**, DOI: 10.1039/D3SC03495J

SABIC 2024

DAY-4: 10.01.2024 (Wednesday)

10.01.2024

Bioinspired Fe(IV)-oxido complexes: controlling proton/electron transfer and spin states within mono- and binuclear systems

A. S. Borovik
Department of Chemistry, University of California, Irvine CA 92698
USA

Metalloproteins perform functions not yet achieved in abiotic systems. One reason for this lack of function is the inability of control of the microenvironments about the metal centers. Microenvironments are defined as the volume of space proximal to the metal centers that encompass the secondary coordinate spheres. Results from structural biology point to non-covalent interactions within microenvironments as instrumental in regulating function. Therefore, the function and dysfunction of metalloproteins can be understood within the context of changes within their microenvironments. We are developing systems that allows for the confinement of metal center within hosts to regulate the properties of the immobilized metal centers. One of our approaches revolves around the development of new ligand frameworks that are multi-functional in that they can bind a variety of different metal ions and simultaneously control both the primary and secondary coordination spheres. An example is the phosphinic amido ligand $[poat]^{3-}$ (*N,N′,N″*-[nitrilotris(ethane-2,1-diyl)]tris(*P,P*-diphenylphosphinic amido) that can form $[Fe(II)poat]^{-}$ complex which can be converted into a high spin Fe(IV)-oxido complex. In addition, it can be used as a synthon to assemble discrete bimetallic complexes. This presentation will describe how local environments around Fe(IV)-oxido unit have a major impact on the electronic structure. Also discussed will be our efforts to assembled discrete FeFe bimetallic complexes with oxido and hydroxido bridged cores and we demonstrate that these systems can control proton and electron transfer processes over four oxidation states from $Fe^{II}Fe^{II}$ to $Fe^{IV}Fe^{III}$.

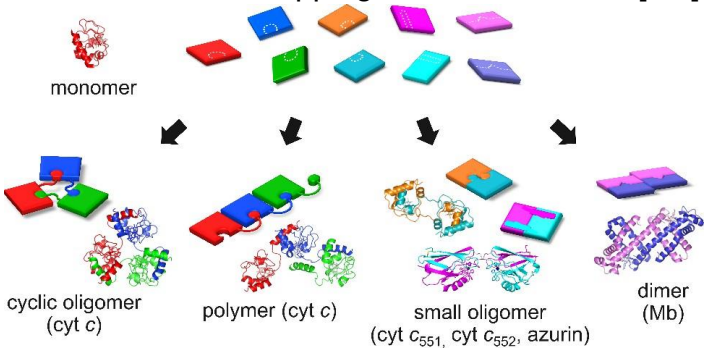
3D Domain Swapping of Metalloproteins:Basics and Recent Development

Shun Hirota

Graduate School of Science and Technology, Nara Institute of Science andTechnology, Japan

Metalloproteins are responsible for many biological reactions; thus, construction of protein assemblies will increase the use of metalloproteins. Three-dimensional (3D) domain swapping is a protein oligomerization phenomenon that exchanges the same domain or secondary structural element between molecules of the same protein. Domain swapping was first reported in 1994 for diphtheria toxin. Since then, domain swapping has been observed in a variety of proteins.

Our research group has shown that various metalloproteins, including heme proteins and a copper protein, can undergo domain swapping [1]. For example, it has been known for half a century that cytochrome *c* (cyt *c*) forms polymers, but the polymerization mechanism remained unknown. We found by X-ray crystallographic and spectroscopic analyses that cyt *c* forms polymers by successive domain swapping, where the C-terminal helix is displaced from its original position in the monomer and cyt *c* loses its electron transfer function [2]. We have also utilized domain swapping to construct various heme protein assemblies, including nanoring, nanocage, tetrahedron, heterodimer with different active sites, and amyloid fibril [3]. In this lecture, basics and our recent developments on domain swapping will be introduced [1,4].



References:

1. Hirota, S.; Mashima, T.; Kobayashi, N. *Chem. Commun*. **2021**, *57*, 12074-12086 (review).
2. a) Hirota, S.; Hattori, Y.; Nagao, S.; Taketa, M.; Komori, H.; Kamikubo, H.; Wang, Z.; Takahashi, I.; Negi, S.; Sugiura, Y.; Kataoka, M.; Higuchi, Y. *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 12854-12859; b) Parui, P. P.; Sarakar, Y.; Majumder, R.; Das, S.; Yang, H.; Yasuhara, K.; Hirota, S. *Chem. Sci.* **2019**, *10*, 9140-9051.
3. a) Lin, Y.-W.; Nagao, S.; Zhang, M.; Shomura, Y.; Higuchi, Y.; Hirota, S. *Angew. Chem. Int. Ed.* **2015**, *54*, 511-515; b) Miyamoto, T.; Kuribayashi, M.; Nagao, S.; Shomura, Y.; Higuchi, Y.; Hirota, S. *Chem. Sci.* **2015**, *6*, 7336-7342; c) Yuyama, K.; Ueda, M.; Nagao, S.; Hirota, S.; Sugiyama, T.; Masuhara, H. *Angew. Chem. Int. Ed.* **2017**, *56*, 6739-6743.

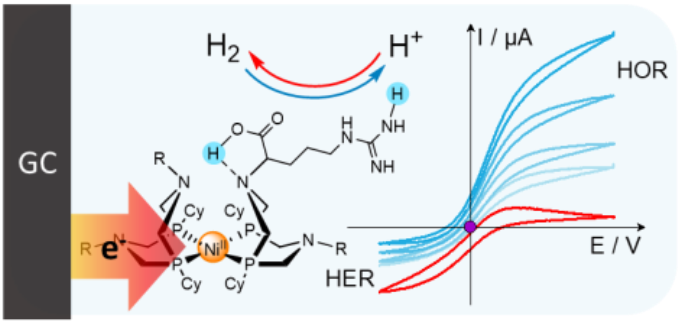
4. a) Xie, C.; Shimoyama, H.; Yamanaka, M.; Nagao, S.; Komori, H.; Shibata, N.; Higuchi, Y.; Shigeta, Y.; Hirota, S. *RSC Advances* **2021**, 11, 37604-37611; b) Hirota, S.; Chiu, C.-L.; Chang, C.-J.; Lo, P.-H.; Chen, T.; Yang, H.; Yamanaka, M.; Mashima, T.; Xie, C.; Masuhara, H.; Sugiyama, T. *Chem. Commun.* **2022**, *58*, 12839-1284; c) Sakai, T.; Mashima, T.; Kobayashi, N.; Ogata, H.; Duan, L.; Fujiki, R.; Hengphasatporn, K.; Uda, T.; Shigeta, Y.; Hifumi, E.; Hirota, S. *Nat. Commun.*, accepted.

Proton relays in molecular electrocatalysis: how do they allow for bidirectional/reversible behavior?

Vincent Artero

Laboratoire de Chimie et Biologie des Métaux, Université Grenoble Alpes, CNRS, CEA, Grenoble, France; e-mail: vincent.artero@cea.fr

Catalysis in hydrogenases and other metallenzymes involved in CO_2 transformation only requires Earth-abundant metal centers, the reactivity of which is enhanced thanks to the presence of basic sites acting as proton relays [1] at their vicinity. Such active sites have been used as an inspiration to design new synthetic catalysts for H_2 evolution [2-4] and oxidation [5,6]. Specification, catalytic platforms with installed proton relays display bidirectional [7] and, in rare cases, reversible catalysis [5]. In this presentation we will show how a detailed molecular electrochemistry study can help understanding and quantifying the role of the protons relays related to these remarkable behaviors [8].



References

1. Saveant, J. M. *Angew. Chem. Int. Ed.* **2019**, *58*, 2125-2128.
2. Sun, D.; Harshan, A. K.; Pecaut, J.; Hammes-Schiffer, S.; Costentin, C.; Artero, V. *Chemelectrochem* **2021**, *8*, 2671-2679.
3. Queyriaux, N.; Sun, D.; Fize, J.; Pecaut, J.; Field, M. J.; Chavarot-Kerlidou, M.; Artero, V. *J. Am. Chem. Soc.* **2019**.
4. Li, C.-B.; Bagnall, A. J.; Sun, D.; Rendon, J.; Koepf, M.; Gambarelli, S.; Mouesca, J.-M.; Chavarot-Kerlidou, M.; Artero, V. *Sustainable Energy & Fuels* **2022**, *6*, 143-149.
5. Wiedner, E. S.; Appel, A. M.; Raugei, S.; Shaw, W. J.; Bullock, R. M. *Chem. Rev.* **2022**, *122*, 12427–12474.
6. Schild, J.; Reuillard, B.; Morozan, A.; Chenevier, P.; Gravel, E.; Doris, E.; Artero, V. *J. Am. Chem. Soc.* **2021**, *143*, 18150-18158.
7. Ahmed, M. E.; Nayek, A.; Krizan, A.; Coutard, N.; Morozan, A.; Dey, S. G.; Lomoth, R.; Hammarstrom, L.; Artero, V.; Dey, A. *J. Am. Chem. Soc.* **2022**, *144*, 3614-3625.
8. Reuillard, B.; Costentin, C.; Artero, V. *Angew. Chem. Int. Ed.* **2023**, *62*, e202302779.

Bio-inspired catalyst design strategy for sustainable H_2 production in water

Arnab Dutta

Department of Chemistry
Interdisciplinary Programme for Climate Studies
Indian Institute of Technology Bombay
(Email: arnab.dutta@iitb.ac.in)

The current global energy requirement is primarily dependent on conventional fossil fuels (coal, oil, natural gas), which invariably emit a copious amount of CO_2, leading to adverse climate change effects. Renewable energy resources (solar, wind, tidal, etc.) have emerged as apt alternatives to resolve this conundrum; however, they require a stable energy vector due to their intrinsic intermittence. Hydrogen molecule fits the bill as it can be directly used in a fuel cell for energy production following a greener pathway. Therefore, hydrogen production has become a bustling research area via sustainable methods. Since water is an abundant resource of protons and covers over 71% of the planet, hydrogen evolution from water becomes useful. Our group has developed a strategy for designing synthetic catalysts based on the architectural framework of enzyme active sites.[1,2] The inclusion of proton exchanging outer coordination sphere feature is found to be a key component for enhancing the catalytic performance for an otherwise weak catalyst core. This outer coordination sphere feature can be incorporated in the form of amino acids, vitamins, neurotransmitters, drug molecules, and even nucleic bases.[3–7] The evolution of this unique genre of bio-inspired catalysts and its optimized application for electrochemical and photochemical H_2 evolution will be discussed in this presentation.

References:

(1) Dolui, D.; Khandelwal, S.; Majumder, P.; Dutta, A. The Odyssey of Cobaloximes for Catalytic H2 Production and Their Recent Revival with Enzyme-Inspired Design. *Chem. Commun.* **2020**, *56* (59), 8166–8181. https://doi.org/10.1039/D0CC03103H.

(2) Dolui, D.; Ghorai, S.; Dutta, A. Tuning the Reactivity of Cobalt-Based H2 Production Electrocatalysts via the Incorporation of the Peripheral Basic Functionalities. *Coord. Chem. Rev.* **2020**, *416*, 213335. https://doi.org/10.1016/j.ccr.2020.213335.

(3) Dolui, D.; Khandelwal, S.; Shaik, A.; Gaat, D.; Thiruvenkatam, V.; Dutta, A. Enzyme-Inspired Synthetic Proton Relays Generate Fast and Acid-Stable Cobalt-Based H2 Production Electrocatalysts. *ACS Catal.* **2019**, *9* (11), 10115–10125. https://doi.org/10.1021/acscatal.9b02953.

(4) Mir, A. Q.; Saha, S.; Mitra, S.; Guria, S.; Majumder, P.; Dolui, D.; Dutta, A. The Rational Inclusion of Vitamin B6 Boosts Artificial Cobalt Complex Catalyzed Green H2 Production. *Sustain. Energy Fuels* **2022**, *6*, 4160–4168. https://doi.org/10.1039/D2SE00734G.

(5) Afshan, G.; Ghorai, S.; Rai, S.; Pandey, A.; Majumder, P.; Patwari, G. N.; Dutta, A. Expanding the Horizon of Bio-Inspired Catalyst Design with Tactical Incorporation of Drug Molecules. *Chem. – Eur. J.* **2023**, *29* (21), e202203730. https://doi.org/10.1002/chem.202203730.

(6) Ghorai, S.; Khandelwal, S.; Das, S.; Rai, S.; Guria, S.; Majumder, P.; Dutta, A. Improving the Synthetic H2 Production Catalyst Design Strategy with the Neurotransmitter Dopamine. *Dalton Trans.* **2023**, *52* (6), 1518–1523. https://doi.org/10.1039/D2DT03509J.

(7) Mir, A. Q.; Das, S.; Rai, S.; Shah, N. A.; Majumder, P.; Dutta, A. Crafting Fast and Efficient H2 Evolution Electrocatalysts with Tactical Inclusion of Nucleobases. *ACS Catal.* **2023**, *13* (12), 8238–8246. https://doi.org/10.1021/acscatal.3c01384.

10.01.2024

Sequestration and Activation of Environmentally Detrimental Molecules Utilizing Bioinspired Systems and Interactions

Raja Angamuthu

Department of Chemistry and Department of Sustainable Energy Engineering, IIT Kanpur, Kanpur 208016, India

In order to achieve a cleaner atmosphere, we need to simultaneously develop cleaner, sustainable and affordable energy sources that would help in avoiding the usage of fossil fuels and we need to clean the environment as at present the amount of CO_2, SO_2 and CFCs is alarming. Our laboratory at IIT Kanpur try to contribute to address both the aforementioned issues. On one hand we develop metal hydrides and organic hydrides that are synthesised in solvent-free sustainable reactions, which can activate detrimental molecules such as CO_2 and SO_2 into value added products. For example, stoichiometric SO_2 activation was achieved using organic hydride donors such benzimidazolines and benzothiazolines forming benzimidazolium bisulphate and banzothiazolium bisulphate under ambient conditions utilizing aerial oxygen. In recent days, we were able to employ metal complexes of koneramines as catalysts to activate SO_2. On the other hand, we have developed materials that efficiently absorb CO_2, SO_2 and CFCs at ambient conditions which can then be concentrated and/or activated into value added products. Our laboratory chose to sequester the gases utilizing bioinspired weak interactions such as lone pair$\cdots\pi$ (aryl) interactions where 2,4,6-trisubstituted-1,3,5-trazines were employed as host molecules possessing electron-deficient valleys that attracts the lone-pair(s) of SO_2. These interactions are strong enough to capture SO_2 and retain in the lattice till 110 ºC. Aforementioned ongoing efforts will be portrayed in short.

References:

[1] S. Mehrotra, S. Raje, A. K. Jain, R. J. Butcher, R. Angamuthu, Triazine based eccentric Piedfort units towards a single source hydrogen bonded network, *Chem. Commun.* **2022**, *58*, 11815-11818.

[2] M. Chahal, S. Raje, G. Kotana, R. Angamuthu, Binding Enabled Catalytic Activation of SO_2 by Copper Koneramine Complexes Under Ambient Conditions, *Green Chem.* **2019**, *21*, 6372-6380.

[3] S. Mehrotra, S. Raje, A. K. Jain, R. Angamuthu, Benzimidazolines Convert Sulfur Dioxide to Bisulfate at Room Temperature and Atmospheric Pressure Utilizing Aerial Oxygen, *ACS Sus. Chem. Eng.* **2017**, *5*, 6322-6328.

[4] S. Mehrotra, R. J. Butcher, R. Angamuthu, Benzothiazoline Converts SO_2 to Sulfuric Acid en Route to Benzothiazole, *ACS Sus. Chem. Eng.* **2016**, *4*, 6517−6523.

Exquisite fine-tuning of the active-site electronic structure in [FeFe] hydrogenases

James A. Birrell

School of Life Sciences, University of Essex, Wivenhoe Park, Colchester, CO4 3SQ, UK

Abstract body: [FeFe] hydrogenases are the most active natural catalyst for the interconversion of protons and electrons with molecular hydrogen. Their active-site cofactor (the H-cluster) is composed a canonical [4Fe-4S] cluster ($[4Fe\text{-}4S]_H$) linked covalently to a unique di-iron subcluster ($[2Fe]_H$) by a cysteine amino acid residue. In $[2Fe]_H$, the two Fe ions are further coordinated by a bridging 2-azapropane-1,3-dithiolate (ADT) ligand, three CO ligands (two terminal, one bridging) and two CN^- ligands, leaving an open coordination site on one of the Fe ions where H_2 activation or formation occurs. The strong-field CO and CN^- ligands stabilize the low-valent, low-spin Fe(II) and Fe(I) oxidation states in $[2Fe]_H$ (e.g. Fe(II)Fe(I) in the active oxidized H_{ox} state) and the Fe ions cycle through Fe(I) and Fe(II) during catalysis. The H-cluster is buried in a protein matrix, which provides gas channels for H_2 (and inhibitors such as CO, O_2 and SH_2) diffusion to and from the H-cluster, as well as a proton transfer pathway (PTP) and an electron transfer chain formed of iron-sulfur cluster cofactors. Overall, the protein matrix provides the perfect balance of polar and non-polar interactions (Figure 1) that exquisitely tune the electronic structure of the H-cluster so that it accepts electrons on $[4Fe\text{-}4S]_H$ at redox potentials close to the thermodynamic potential of the $2H^+/H_2$ couple, and that electron transfer is strictly coupled to protonation of the ADT ligand in $[2Fe]_H$. Furthermore, a cysteine that forms part of the proton transfer pathway and whose thiol group is adjacent to the ADT ligand, not only functions as a gate-keeper for protons but also influences the electronic structure of the H-cluster via interactions with the ADT ligand. I will present recent findings that paint a detailed picture of the electronic structure of the H-cluster in [FeFe] hydrogenases and how it can be exquisitely tuned by the protein environment. I will discuss how the protein environment plays a crucial role in ensuring strict proton-coupled electron transfer and optimal thermodynamic stability of catalytic intermediates, in particular the crucial iron-hydride intermediate. These findings are based on studies of [FeFe] hydrogenases from a range of organisms, as well as site-directed mutants, and chemically modified active-site cofactors. All of this has been made possible by the revolutionary discovery that the H-cluster in [FeFe] hydrogenases can be reconstituted with synthetic cofactors, allowing chemically altered cofactors to be inserted as well as production, purification and mutagenesis of [FeFe] hydrogenases from diverse organisms in the versatile host *Escherichia coli*. Thus, I will also discuss how this technology has been used to date and how it might be used in the future.

Utilizing the diversity of [FeFe] hydrogenase to probe the effect(s) of the active site pocket and proton transfer pathways on catalytic performance

Gustav Berggren

Molecular Biomimetics, Department of Chemistry - Ångström, Uppsala University, Uppsala, Box-523, SE-751 20, Sweden

[FeFe] hydrogenase is a highly diverse enzyme family, that can be divided into at least four phylogenetic groups denoted Group A–D.[1-3] The so-called "prototypical" Group A [FeFe] hydrogenases have been extensively studied and found to generally catalyze the interconversion of H^+ and H_2 with high rates and remarkable energy efficiencies. Despite featuring the same organometallic cofactor (the H-cluster), recently characterized examples from Group C and D display modest catalytic rates.[4, 5] In the case of the Group D enzymes, this is also combined with a substantial over-potential requirement.[5, 6]

Here I will summarize our recent efforts at identifying the structural features that give rise to these diverging catalytic properties. Using the Group D [FeFe] hydrogenase from *Thermoanaerobacter mathranii* (*Tam*HydS) as a model, and combining loss- and gain-of-function studies, we have probed both substrate transport pathways and the active-site canopy.

In short, we report on our initial findings identifying a set of highly conserved amino acid residues that constitute a possible alternative proton transfer pathway, unique to the Group D enzymes.[7] Furthermore, three variants of *Tam*HydS have been prepared, introducing key amino acid residues that are conserved in Group A: a sulfur-rich active-site canopy around the H-cluster (**AS**), the proton-transfer-pathway (**PTP**), and a "combined" variant (**CM**=AS+PTP). Neither **AS** nor **PTP** showed improved catalytic performance. However, the **CM** variant increased the H_2 production rate of wild-type *Tam*HydS up to 165-fold, underscoring the synergistic interplay between the active-site and the substrate transport pathway(s) in enabling efficient catalysis. Arguably, these findings highlight the importance of exploring a broader range of [FeFe] hydrogenases to fully unravel the influence of the polypeptide framework on the performance of the H-cluster.

1. S. L. Benoit, R. J. Maier, R. G. Sawers and C. Greening, *Microbiol. Mol. Biol. Rev.*, 2020, **84**, e00092-00019.
2. S. Poudel *et al*, *Biochimica et Biophysica Acta (BBA) - General Subjects*, 2016, **1860**, 1910-1921.
3. H. Land, M. Senger, G. Berggren and S. T. Stripp, *ACS Catalysis*, 2020, **10**, 7069-7086.
4. N. Chongdar, J. A. Birrell, K. Pawlak, C. Sommer, E. J. Reijerse, O. Rüdiger, W. Lubitz and H. Ogata, *J. Am. Chem. Soc.*, 2018, **140**, 1057-1068.
5. H. Land *et al*, *Chem. Sci.*, 2020, **11**, 12789-12801.
6. A. Fasano, H. Land, V. Fourmond, G. Berggren and C. Léger, *J. Am. Chem. Soc.*, 2021, **143**, 20320-20325.
7. P. R. Cabotaje, K. Walter, A. Zamader, P. Huang, F. Ho, H. Land, M. Senger and G. Berggren, *ACS Catalysis*, 2023, **13**, 10435-10446.

Electrocatalytic Hydrogen Evolution by Nickel Complexes: Mechanistic Aspects and Role of Ligand Framework

Suman K. Barman

Department of Chemical Sciences, Indian Institute of Science Education and Research Mohali, Sector 81, Punjab-140306, India

In the context of carbon-neutral energy, H_2 can act as an energy carrier and can be an encouraging alternate option to traditional fossil fuels. Electrocatalytic Hydrogen evolution reaction (HER) can reserve energy in the form of H_2 and when needed the stored energy can be released via hydrogen oxidation reaction. Pt is the most efficient electrocatalyst for HER. However, the scarcity and high cost of Pt have inspired continuous search for efficient catalyst with low cost and high abundance. Commonly for HER, metal-hydride intermediate is found to be catalytically responsible species where metal center is involved in both electron and proton transfer processes. In recent times, there have been continuously growing interest on the ligand participation for HER either via synergetic electron transfer provided by redox active ligand along with metal center and/or promoting proton transfer process. Increasing local proton concentration by basic moiety of the ligand can facilitate the proton transfer to the reaction center. Sufficient local proton concentration may lower the entropic factor required for the protonation of catalytic intermediate. Keeping in mind the possibility of ligand assisted HER, we have developed Ni(II) based electrocatalyst for homogenous HER. Role of ligand framework in the context of electron and proton transfer processes have been explored. Mechanistic aspects of HER by those Ni(II) based complexes have been explored via electrochemical and computational studies.

References:

1) Tong, L.; Duan, L.; Zhau, A.; Thummel, R. P. *Coord. Chem. Rev.* **2020**, *402*, 213079.

2) Ahmed, M. E.; Nayek, A.; Križan, A. Coutard, N.; Morozan, A.; Dey, S. G.; Lomoth R.; Hammarström, L.; Artero, V.; Dey, A. *J. Am. Chem. Soc.* **2022**, *144*, 3614−3625.

3) He, S.; Huang, F.; Wu, Q.; Zhang, P.; Xiong, Y.; Yang, J.; Zhang, R.; Wang, F.; Chen, L.; Liu, T. L.; Li, F.; *Angew. Chem. Int. Ed.* **2021**, 60, 25839–25845.

4) Lin, S.; Banerjee, S.; Fortunato, M. T.; Xue, C. Huang, J.; Sokolov, A. Y.; Turro, C. *J. Am. Chem. Soc.* **2022**, *144*, 20267−20277.

10.01.2024

Living on Nitrogen

Kyle M. Lancaster

Department of Chemistry and Chemical Biology, Baker Laboratory, Cornell University, Ithaca NY 14850 USA

Ammonia oxidizing bacteria (AOB) and archaea (AOA) are microorganisms that subsist solely off of inorganic nitrogen as cellular fuel. Their primary metabolisms are initiated by ammonia monooxygenase, which is an integral membrane Cu protein that hydroxylates NH_3 using an O_2. The AOB and AOA pathways share NH_2OH as a common metabolite, but their pathways for its oxidation differ. AOB use a multi-heme protein, hydroxylamine oxidoreductase, to convert NH_2OH to NO. The enzyme used by AOA is unknown. This lecture will discuss possible mechanisms whereby NO is oxidized enzymatically by AOB to the known, stoichiometric oxidation product of AOB metabolism: NO_2^-. This lecture will also discuss AOA enzymes that are putatively involved in NH_2OH oxidation.

Nitric Oxide Signaling Chemistry at Copper and Lewis Acid Sites

Timothy H. Warren

Michigan State University, Department of Chemistry, East Lansing, MI USA

Nitric oxide (NO) plays numerous, disparate biological roles which range from signaling in the respiratory system to vasodilation in the cardiovascular system to host defense against microbial pathogens. Nonetheless, discrete molecular mechanisms involved are not well understood: molecular relatives such as nitrite (NO_2^-) can also serve as reservoirs of NO-like behavior. Thus, understanding the discrete mechanistic pathways by which NO and NO_2^- form, interconvert, and react with molecular targets of biological relevance is critical to understand the molecular basis for physiological effects ascribed to NO and its relatives.

Employing a family of biologically relevant copper model complexes, we examine the reactivity and interconversion of NO, RSNOs, NO_2^-, and NO_3^-. These studies offer mechanistic insight into the copper-catalyzed release (and uptake) of NO via RSNOs as well as conversion of NO_2^- and NO_3^- to NO that generate S-based signaling molecules. We also describe the reductive coupling of NO at copper(I) centers that involves novel reduced NO and *cis*-hyponitrite intermediates such as $\{[Cu](ONNO)[Cu]\}^-$ complexes and examine chemical triggers for N_2O release. These *cis*-hyponitrite complexes also reveal how copper sites can help release the tremendous oxidizing capability of NO, a more powerful oxidant than O_2. Additionally, we illustrate how Lewis acid sites may regulate important redox interconversions in nitric oxide signaling chemistry. Redox innocent Lewis acids greatly facilitate the reduction of RSNOs and NO_2^- and can change their signaling output upon reduction.

10.01.2024

Electrochemical Reduction of N_2O: Redox vs. Chemical Catalysis

Cyrille Costentin

Univ Grenoble Alpes, CNRS, DCM, 38000 Grenoble, France

Homogeneous electrochemical catalysis of N_2O reduction to N_2 is investigated with a series of organic catalysts and transition metal complexes (rhenium and manganese bipyridyl carbonyl complexes as well as iron porphyrins). An activation-driving force correlation is revealed with the organic species characteristic of a redox catalysis involving an outersphere electron transfer from the radical anions or dianions of the reduced catalyst to N_2O. By contrast, we will show that catalysis involving transition metal complexes requires getting a free metal coordination site to bind N_2O. It implies that the generation of a strong coordinating ligand as product or co-product of the reaction might be detrimental for an efficient catalysis because it can bind the metal center and block or slow down the catalytic process. This self-modulation phenomenon is revealed and illustrated via a thorough spectro-electrochemical investigation of the mechanism of the electrochemical reduction of nitrous oxide with rhenium bipyridyl triscarbonyl complexes $[Re(bpy)(CO)_3X]^{n+}$ (X = CH_3CN, Cl^-, n = 0 or 1) as catalyst. The mechanism of N_2O reduction with iron porphyrin as catalyst will also be presented and the peculiar role of proton donors described and discussed.

References:

1. Deeba, R; Molton, F; Chardon-Noblat, S; Costentin, C. *ACS Catal,* **2021**, *11*, 6099.
2. Deeba, R; Chardon-Noblat, S; Costentin, C. *Chem. Sci.* **2021**, *12*, 12726.
3. Deeba, R; Chardon-Noblat, S; Costentin, C. *ChemElectroChem,* **2021**, *8,* 3740.
4. Deeba, R; Chardon-Noblat, S; Costentin, C. *ACS Catal,* **2023**, *13*, 8262.
5. Deeba, R; Collard, A.; Rollin, C.; Molton, F.; Chardon-Noblat, S; Costentin, C. *ChemElectroChem,* **2023**, *10,* e202300350.

Metal-Ligand Cooperation in Dinitrosyl Iron Complexes for Small Molecule Activation and Biomedical Application

Tsai-Te Lu

Institute of Biomedical Engineering and Department of Chemistry, National Tsing Hua University, Hsinchu 300044, Taiwan.

Biomimetic study of synthetic dinitrosyl iron complexes (DNICs) unravels that the (1) redox-active nature of DNIU, (2) metal-ligand cooperation in DNICs, and (3) facile interconversion between mononuclear and dinuclear DNICs facilitate their reactivity toward small molecule activation, catalysis, and biomedical application.[1-4] In particular, nucleophilic activation of CO_2 by dinuclear DNIC $[(NO)_2Fe(m\text{-}^{Me}Pyr)_2Fe(NO)_2]^{2-}$ (**2**, ^{Me}Pyr = 3-methylpyrazolate) results in the formation of CO_2-captured complex $[(NO)_2Fe(^{Me}PyrCO_2)]^-$ (**2-CO₂**, $^{Me}PyrCO_2$ = 3-methyl-pyrazole-1-carboxylate). Single-crystal structure, spectroscopic, reactivity, and computational study unravels **2-CO₂** as a unique intermediate for reductive transformation of CO_2 promoted by Ca^{2+}. Moreover, sequential reaction of **2** with CO_2, $Ca(OTf)_2$, and KC_8 established a synthetic cycle, **2** → **2-CO₂** → $[(NO)_2Fe(m\text{-}^{Me}Pyr)_2Fe(NO)_2]$ (**1**) → **2**, for selective conversion of CO_2 into oxalate.[4] In the second part, substrate-gated transformation of a pre-catalyst into an iron-hydride intermediate for catalytic dehydrogenation of dimethylamine borane (DMAB) will be discussed. Dinuclear DNIC [K-18-crown-6-ether][$(NO)_2Fe(m\text{-}^{Me}Pyr)(m\text{-}CO)Fe(NO)_2$] (**3**, ^{Me}Pyr = 3-methylpyrazolate) was explored as a pre-catalyst for the dehydrogenation of dimethylamine borane (DMAB) with a turnover number of 6.0±0.2. Upon evolution of $H_{2(g)}$ from DMAB triggered by **3**, parallel conversion of **3** into $[(NO)_2Fe(N,N'\text{-}^{Me}PyrBH_2NMe_2)]^-$ and an iron-hydride intermediate $[(NO)_2(CO)Fe(m\text{-}H)Fe(CO)(NO)_2]^-$ (**A**) was evidenced by XRD/NMR/IR/NRVS experiments and supported by DFT calculations. Through reaction of complex $[(NO)_2Fe(h^2\text{-}BH_4)]^-$ (**4**) with $CO_{(g)}$ as an alternative synthetic route, moreover, isolated intermediate A featuring catalytic reactivity toward dehydrogenation of DMAB supports a substrate-gated transformation of pre-catalyst **3** into iron-hydride intermediate **A** as the active species for generation of $H_{2(g)}$.[2] Recent investigation on the ligand control over selective superoxide-mediated NO monooxygenation and superoxide-dioxygen interconversion will be discussed in the last part.[1] During the superoxide-induced conversion of DNIC **1** into DNIC [(K-18-crown-6-ether)$_2(NO_2)$][$Fe(m\text{-}^{Me}Pyr)_4(m\text{-}O)_2(Fe(NO)_2)_4$] (**5-K-crown**) and an $[Fe^{3+}(^{Me}Pyr)_x(NO_2)_y(O)_z]_n$ adduct, stoichiometric NO monooxygenation yielding NO_2^- occurs without the transient formation of peroxynitrite-derived •OH/•NO_2 species. To study the isoelectronic reaction of $O_{2(g)}$ and the one-electron reduced DNIC **1**, a DNIC featuring an electronically localized $\{Fe(NO)_2\}^9$-$\{Fe(NO)_2\}^{10}$ electronic structure, [K-18-crown-6-ether][$(NO)_2Fe(m\text{-}^{Me}Pyr)_2Fe(NO)_2$] (**1-red**), was successfully synthesized and characterized. Oxygenation of DNIC **1-red** leads to the similar assembly of DNIC **5-K-crown**, of which the electronic structure is best described as paramagnetic with weak anti-ferromagnetic coupling among the four S = 1/2 $\{Fe^{III}(NO^-)_2\}^9$ units and S = 5/2 Fe^{3+} center. In contrast to DNICs **1** and **1-red**, DNICs $[(NO)_2Fe(m\text{-}SEt)_2Fe(NO)_2]$ (**6**) and [K-18-crown-6-ether][$(NO)_2Fe(m\text{-}SEt)_2Fe(NO)_2$] (**3-red**) display a reversible equilibrium of "**3** + O_2^- ⇋ **3-red** + $O_{2(g)}$", which is ascribed to the covalent [Fe(m-SEt)2Fe] core and redox-active $[Fe(NO)_2]$ unit.

References:

1. Cheng-Jhe Liao, Yu-Ting Tseng, Yu-An Cheng, Loise Ann Dayao, Linda Iffland-Mühlhaus, Leland B. Gee, Ryan D. Ribson, Ting-Shan Chan, Ulf-Peter Apfel*, Tsai-Te Lu* "Ligand Control of Dinitrosyl Iron Complexes for Selective Superoxide-Mediated Nitric Oxide Monooxygenation and Superoxide–Dioxygen Interconversion" *J. Am. Chem. Soc.* **2023**, *145*, ASAP.
2. Yu-Ting Tseng, Vladimir Pelmenschikov,* Linda Iffland-Mühlhaus, Donato Calabrese, Yu-Che Chang, Konstantin Laun, Chih-Wen Pao, Ilya Sergueev, Yoshitaka Yoda, Wen-Feng Liaw, Chien-Hong Chen,* I-Jui Hsu,* Ulf-Peter Apfel,* Giorgio Caserta,* Lars Lauterbach,* and Tsai-Te Lu* "Substrate-Gated Transformation of a Pre-Catalyst into an Iron-Hydride Intermediate $[(NO)_2(CO)Fe(m\text{-}H)Fe(CO)(NO)_2]^-$ for Catalytic Dehydrogenation of Dimethylamine Borane" *Inorg. Chem.* **2023**, *62*, 769-781.
3. Cheng-Ru Wu, Yi-Da Huang, Yong-Huei Hong, Ya-Hsin Liu, Manmath Narwane, Yu-Hsiang Chang, Trinh Kieu Dinh, Hsin-Tzu Hsieh, Yi-Jen Hseuh, Ping-Ching Wu, Chih-Wen Pao, Ting-Shan Chan, I-Jui Hsu, Yunching Chen, Hung-Chi Chen,* Ting-Yu Chin,* Tsai-Te Lu* "Endogenous Conjugation of Biomimetic Dinitrosyl Iron Complex with Protein Vehicles for Oral Delivery of Nitric Oxide to Brain and Activation of Hippocampal Neurogenesis" *JACS Au* **2021**, *1*, 998-1013.
4. Yu-Ting Tseng, Wei-Min Ching, Wen-Feng Liaw,* Tsai-Te Lu* "Dinitrosyl Iron Complex [K-18-crown-6-ether][(NO)2Fe(MePyrCO2)]: Intermediate for Capture and Reduction of Carbon Dioxide." *Angew. Chem.* **2020**, *59*, 11819-11823.

10.01.2024

Modelling Nitrite to Nitric Oxide Conversion at Mononuclear Copper(II) and Zinc(II) Sites

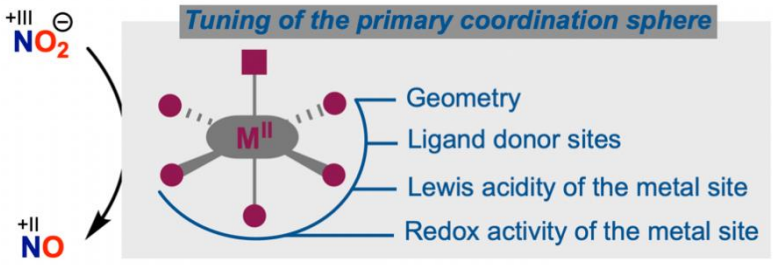
Subrata Kundu,* and coworkers

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

***email**: skundu@iisertvm.ac.in

Transformations of nitrogen oxides (NO_x) are relevant to mammalian physiology, biogeochemical N-cycle, and environmental chemistry. For instance, while serving as an important gasotransmitter, the potent toxic nature of NO requires tightly controlled generation and utilization of NO through a set of redox transformations involving various transition metals (*e.g.* Fe, Cu). Interestingly, both nitrite reductase (**NIR**: nitrite-to-NO) and NO oxidase (**NOO**: NO-to-nitrite) activities are known to be mediated by the reduced and oxidized forms of dinuclear [FeCu] assembly of cytochrome *c* oxidase (C*c*O), respectively. In contrast, *type-I Cu* sites (e.g. ceruloplasmin in blood plasma) typically mediate **NOO** activity, whilst *type-II Cu* site catalyze the **NIR** process. Notably, the reactivity profile of the red Cu protein (e.g. nitrosocyanin) featuring an unusual *type-I Cu* site is poorly understood. On the other hand, insights into the factors influencing the transformation of nitrite-to-NO at the redox-inactive mononuclear zinc(II) site of carbonic anhydrase remain in its infancy.

This talk aims to show the reactivity of various structurally characterized mononuclear $[Cu^{II}(nitrite)]^+$ complexes towards substituted phenols (as the tyrosine models) or *N*-benzyl-1,4-dihydronicotinamide (as the NAD(P)H model). This study highlights the tuning of the primary coordination sphere for modulating the NO_x-reactivity at the copper(II/I) redox couple. Furthermore, nitrite-to-NO transformation at the systematically tuned Lewis acidic zinc(II) site in the presence of external reductants (such as thiol and catechol) sheds light on the factors controlling the reactivity of the mononuclear $[Zn^{II}(nitrite)]^+$ motifs.



References:

1. Mondal, A.; Reddy, K. P.; Bertke, J. A.; Kundu, S. *J. Am. Chem. Soc.* **2020**, *142*, 1726
2. Gupta, S.; Arora, S.; Mondal, A.; Stieber, S. C. E.; Gupta, P.; Kundu, S. *Eur. J. Inorg. Chem.* **2022**, e202200105.
3. Anju, B. S.; Nair, N. R.; Kundu, S. *Angew. Chem. Int. Ed.* **2023**, e202311523.
4. Anju, B. S.; Nair, N. R.; Kundu, S. *unpublished results*.

Synthesis and characterization of non-heme iron hyponitrite complexes

Michael O. Lengel, Hai T. Dong, Debangsu Sil, Carsten Krebs*, Nicolai Lehnert*

Department of Chemistry and Department of Biophysics The University of Michigan, Ann Arbor, Michigan 48109-1055, United States

Flavodiiron NO reductases (FNORs) are enzymes implicated in microbial pathogenesis. Pathogens possessing these enzymes exhibit resistance towards nitric oxide (NO), a crucial component of the human immune defense. These FNOR enzymes afford microbial proliferation by reducing NO to nitrous oxide (N_2O) using a non-heme diiron active site. Despite extensive efforts, intermediates involved in the pathway for NO to N_2O reduction at the non-heme diiron active sites of FNORs have not been observed. The key proposed species by computational studies involved in the N-N coupling of the two NO units to form N_2O are iron-hyponitrite species. The exact coordination chemistry of non-heme iron centers with hyponitrite, however, remains largely unknown and underexplored. In synthetic complexes, hyponitrite binding has been primarily observed at copper, nickel, platinum, and ruthenium metal centers. Thus far, only two structurally characterized iron-hyponitrite species have been reported in the literature, one heme complex and the other being a dinitrosyl iron complex (DNIC) Herein, we describe the structural and electronic characterization of non-heme iron complexes with pre-formed hyponitrite. Using tris(2-pyridylmethyl)amine (TPA) ligand derivatives, we were able to prepare and study the coordination chemistry of hyponitrite with non-heme iron centers. Our work provides us with the opportunity to obtain structures of non-heme iron-hyponitrite complexes, for the first time, and investigate their chemical reactivity.

Dioxygen Activating Nonheme Iron(II) Complexes with Biomimetic Functions

Tapan Kanti Paine

School of Chemical Sciences, Indian Association for the Cultivation of Science,
2A & 2B Raja S. C. Mullick Road, Jadavpur, Kolkata 700 032.
Email: ictkp@iacs.res.in

Aerobic organisms involve dioxygen-activating iron enzymes to perform various metabolically relevant chemical transformations. Among these enzymes, mononuclear nonheme iron enzymes reductively activate dioxygen to catalyze diverse biological oxidations, including oxygenation of C-H and C=C bonds and C-C bond cleavage with amazing selectivity.[1] Several nonheme enzymes utilize organic cofactors as electron sources for dioxygen reduction, leading to the generation of iron-oxygen intermediate that act as active oxidants in the catalytic cycle.[2] These unique enzymatic reactions influence the design of small molecule synthetic compounds to emulate enzyme functions and to develop bioinspired catalysts for performing selective oxidation of organic substrates with dioxygen.[3] Selective electron transfer during dioxygen reduction on iron centers of synthetic models by sacrificial reductant requires appropriate design strategies. Taking lessons from the role of enzyme-cofactor complexes in the selective electron transfer process, our group utilized ternary iron(II) complexes supported by polydentate ligands for dioxygen reduction and bioinspired oxidations.[3c,4] In addition, appropriately designed iron complexes activate dioxygen in the presence of suitable model substrates as co-ligands display reactivity mimicking the functions of nonheme iron oxygenases. The nature of coordinated sacrificial reductants/substrates directs the selective electron transfer for dioxygen reduction and dioxygen-dependent oxidation/oxygenation reactions by iron complexes. The role of sacrificial reductants/substrates on the mechanism of dioxygen reduction on iron centers and the biomimetic functions of nonheme iron(II) complexes will be presented in the talk.

References

[1] (a) Costas, M.; Mehn, M. P.; Jensen, M. P.; Que, L., Jr. *Chem. Rev.* **2004**, *104*, 939; (b) Kovaleva, E. G.; Lipscomb, J. D. *Nat. Chem. Biol.* **2008**, *4*, 186; (c) Poulos, T. L. *Chem. Rev*. **2014**, *114*, 3919;

[2] (a) Hausinger, R. P. *Crit. Rev. Biochem. Mol. Biol.* **2004,** *39*, 21; (b) Richter, M. *Nat. Prod. Rep.* **2013,** *30*, 1324.

[3] (a) Ray, K.; Pfaff, F. F.; Wang, B.; Nam, W. *J. Am. Chem. Soc.* **2014**, *136*, 13942. (b) Sahu, S.; Goldberg, D. P., *J. Am. Chem. Soc.* **2016,** *138*, 11410; (c) Ghosh I., Paine. T. K. *Comprehensive Coordination Chemistry-III* (Third Edition), **2021**, *8*, 378.

[4] (a) Chatterjee, S.; Paine, T. K. *Acc. Chem. Res.* **2023**, *56*, 3175. (b) Sheet, D.; Bhattacharya, S.; Paine, T. K. *Chem. Commun.* **2015**, *51*, 7681; (c) Sheet, D.; Paine, T. K. *Chem. Sci.* **2016**, *7*, 5322. (d) Sutradhar, S., Rahaman, S.; Bhattacharya, S.; Paine, T. K. **2023**, *manuscript submitted*.

10.01.2024

Small molecule activation at transition metal centers: structure-function correlations

Kallol Ray

Department of Chemistry, Humboldt-Universität zu Berlin, Berlin (Germany).

Small molecule activation constitutes one of the main frontiers of inorganic and organometallic chemistry, with much effort directed towards the development of new processes for the selective and sustainable transformation of abundant small molecules such as dioxygen (O_2), water (H_2O), hydrogen peroxide (H_2O_2) or protons (H^+) into high-value chemical feedstocks and energy resources. Because nature mostly uses metal ions to activate these relatively inert molecules and modulate their reactivity, much inspiration for the field has come from bioinorganic chemistry. This talk will focus on some of the recent highlights from our group on homogenously catalyzed bioinspired activation of small molecules, as well as stoichiometric reactions that further our understanding towards such ends. It will cover many aspects of small molecule activation including: organometallic chemistry, spectroscopy, synthesis, and detailed mechanistic studies involving trapping of reactive intermediates. The demonstrated examples will help to emphasize the continuous effort of our group in uncovering the structure- reactivity relationships of biomimetic model complexes, which may allow vital insights into the prerequisites necessary for the design of efficient catalysts for the selective functionalization of unactivated C–H bonds, O_2/H_2O/H_2O_2 activations, or H^+ reductions by using cheap and readily available first-row transition metals under ambient conditions.

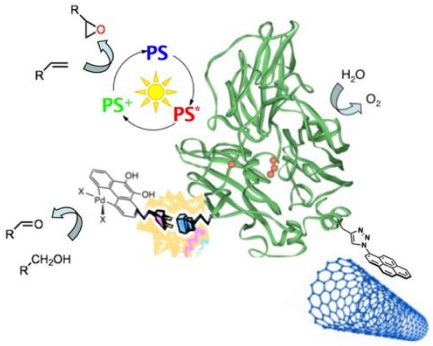
Multi-Copper Oxidases in Hybrid Catalysis

Thierry Tron

Aix Marseille University, CNRS, Centrale Méditérannée, Marseille, France

E-mail: thierry.tron@univ-amu.fr

Hybrid catalysis exploit synergies that can appear between different catalysts, e.g. chemo- and bio-catalysts. Combining catalysts makes it possible both to carry out several stages of transformations and to offer new opportunities in terms of selectivity, efficiency and type of transformations. Understanding the contribution of each partner when associating a synthetic catalyst, an enzyme and a material is necessary to benefit from the best synergy.



Laccases are biocatalysts with great robustness, high oxidation power and substrate versatility.[1] Their unique set of copper centres - a near-surface located mononuclear type 1 and an embedded tri-nuclear cluster (TNC) made of a type 2 and a binuclear type 3 - couple the oxidation of substrates (organic or metal ions) to dioxygen reduction.[2] We shape new catalysts based in particular on oriented functionalization of a laccase surface with different "plug-ins". From our initial demonstrations on bi-molecular systems - *a sensitizer/laccase system coupling the light driven four-electron reduction of dioxygen to water*[3] *to the photo-oxidation of styrene*[4] *or a Pd(II)/ laccase system competent for the aerobic oxidation of alcohol in mild conditions*[5] - we will present architectures based on the oriented grafting of the enzyme surface.[6] Our most recent results on improved hybrid photocatalysts and functionalized laccase will be discussed.[7]

[1] T. Tron, in Encyclopedia of Metalloproteins, Springer, New York, 2013, 1066
[2] E. Solomon, U. Sundaram, T. Machonkin, *Chem. Rev.*, 1996, 96, 2563
[3] T. Lazarides et al., *J. Am. Chem. Soc*. 2013, 135, 3095
[4] L. Schneider et al., *Chem. Sus. Chem*., 2015, 8, 3048)
[5] Y. Mekmouche et al., *Chem. Sci*., 2015, 6,1247
[6] a) N. Lalaoui et al., ACS Catalysis, 2016, 6, 1894; b) V. Robert et al., Chem. Plus Chem., 2017, 82, 607; c) S. Gentil et al., Chem. Eur. J., 2020, 26, 4798.
[7] a) R. Farran et al., *iScience*, 2021, 24, 102378 ; b) U. Contaldo et al., *J. Mater. Chem. A*, 2023,11, 10850 ; c) F. Yang et al. *Chem Plus Chem*, 2023, 88, e202300156

10.01.2024

The Not so Innocent Water Molecule/s in the Enzyme Pocket of Non-Heme Iron Dioxygenases

Rounak Nath, Rabindra Nath Manna, Biman Jana, Tanmay Malakar, Sneha Panja, **Ankan Paul**

Indian Association for the Cultivation of Science Kolkata

2A & 2B Raja SC Mullick Road

Non-heme Iron dioxygenase enzymes facilitate a host of diverse oxidation reactions. This talk will primarily focus on the mechanistic intricacies of Non-heme iron dioxygenases which catalyse C-C bond cleavage as revealed through Long Range Molecular Dynamics Simulations and hybrid Quantum Mechanical/Molecular Mechanics (QM/MM) investigations. Our theoretical endeavour indicates that the presence of even a single water molecule can have a telling effect on the crucial relay proton transfers for facilitating Catalysis. Furthermore, water molecule/s within the enzyme pocket stabilize the metal bound O_2 molecule and O-O and C-C cleavage.[1-2]

References:

[1] "*Unravelling the Crucial Role of Single Active Water Molecule in the Oxidative Cleavage of Aliphatic C–C Bond of 2,4'-Dihydroxyacetophenone Catalyzed by 2,4'-Dihydroxyacetophenone Dioxygenase Enzyme: A Quantum Mechanics/Molecular Mechanics Investigation,*" R. N. Manna, T. Malakar, B. Jana, A. Paul *ACS Catal.* **2018**, *8*, 10043.

[2] "*Decoding regioselective reaction mechanism of gentisic acid catalyzed by the gentisate 1, 2-dioxygenase enzyme,*" R. Nath, R. N. Manna, A. Paul, *Catal Sci. Tech.* **2022**, *12*, 5742.

Nonheme Iron(III) complexes of 3N and N_3S Donor ligands as functional models for C-C bond Cleaving Dioxygenases

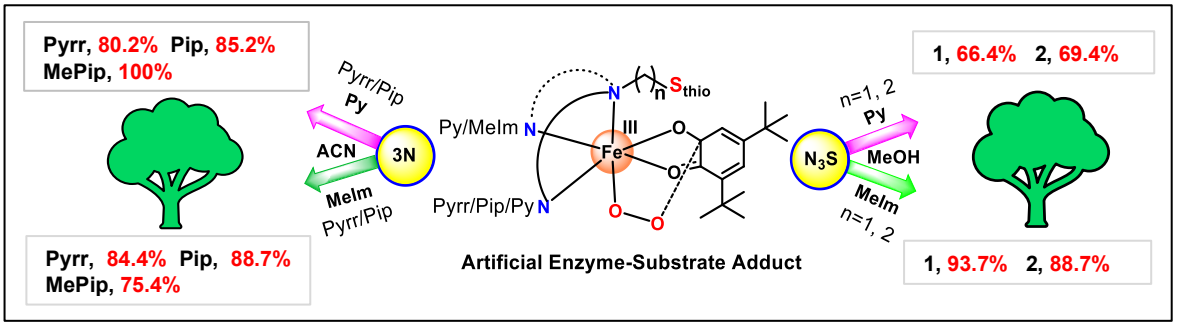
Karuppasamy Sundaravel*[1]

[1]Department of Chemistry, Bharathiar University, Coimbatore 641 046,

Tamil Nadu, India.

[1]E-mail: sundaravel.k@gmail.com;sundaravel.k@buc.edu.in

Dioxygen activating enzymes with mononuclear nonheme iron active site perform a variety of important biological functions such C-H bond activation, epoxidation, alcohol oxidation, sulfoxidation, desaturation and regiospecific C-C cleavage of aromatic pollutants.[1,2] However, the reactivity and mechanism of C-C bond cleavage of catechols afford by biomimetic iron(II/III) are remain elusive and governed by several factors. Herein, we report the synthesis of a series of mononuclear iron(III) complexes [Fe(L1)Cl_3]-[Fe(L10)Cl_3] of systematically tailored tri- and tetradentate 3N and N_3S donor ligands and characterized them by various analytical techniques[2,3]. The 3,5-di-*tert*-butylcatecholate adduct of the complexes **1 - 10** show two intense bands in visible region (540 - 900 nm) as the result of DBC^{2-}–to–iron(III) ligand-to-metal charge-transfer transitions in CH_3CN (**1 - 6**) and CH_3OH (**7 - 10**). During electrochemical analysis, all the complexes display $Fe^{III} \rightarrow Fe^{II}$ redox couple in the potential range –0.260 to +0.617 V. The dioxygenase activity of present complexes produces major amount of extradiol cleavage products (**75 - 100%**) over the intradiol cleavage products (4 - 14%) even in the presence of coordinating solvent and coordinating anion. Indeed, the present investigation clearly reveals that meticulous design of ligand architectures dictate the cleavage mechanism selectively towards nature's more common extradiol pathway.



Reference:

1. K. Sundaravel, T. Dhanalakshmi, E. Suresh, M. Palaniandavar, Dalton Trans. 48 (2008) 7012–7025.
2. T. Shapterhasmi, N. Palani, M. Velusam, N. S. P. Bhuvanesh, K. Sundaravel, S. Easwaramoorthi, Inorg Chimica Acta. 537 (2022) 120924.
3. N. Palani, K. Sundaravel. Unpublished Work.

10.01.2024

A New Twist in the Reactivity of the Topological Isomers of $[Fe^{IV}(O)(Me_4cyclam)]^{2+}$: Enhanced Reactivity for the *syn*-isomer over *anti* in H-Atom/O-Atom Transfer Reactions

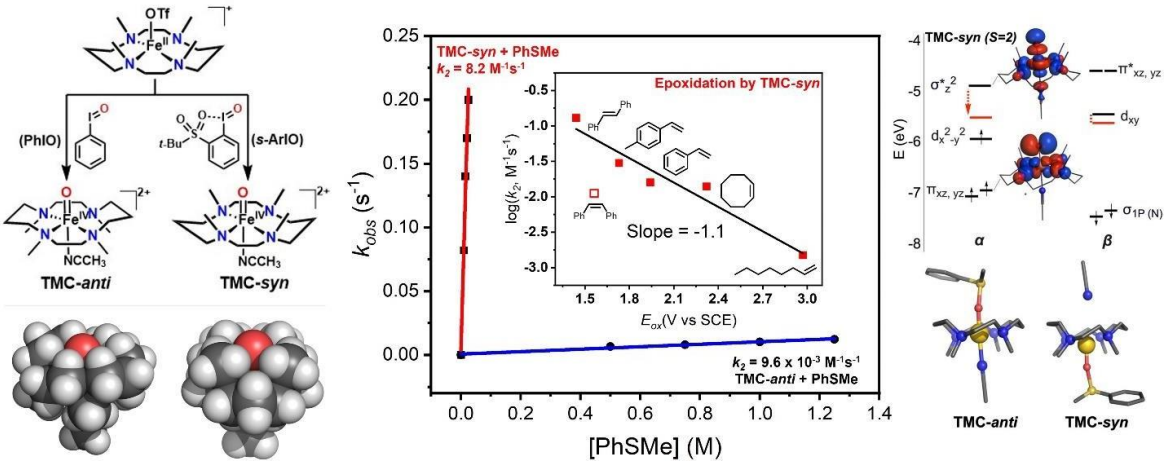
Bittu Chandra[1], Faiza Ahsan[2], Marcel Swart,[2]* and Lawrence Que, Jr.[1]*

[1]Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455, USA

[2]IQCC and Department of Chemistry, University of Girona, 17003 Girona,

Spain Email: bittu001@umn.edu and larryque@umn.edu

Oxoiron(IV) species are key intermediates in biological and abiological oxidations like C-H hydroxylation and halogenation as well as olefin epoxidation. Over a hundred such synthetic nonheme oxoiron(IV) complexes have been documented since the report of *anti*-$[Fe^{IV}(O)(TMC)(CH_3CN)]^{2+}$ (TMC = 1,4,8,11- tetramethyl-1,4,8,11-tetraazacyclotetradecane, or Me_4cyclam) 20 years ago, the first crystallographically characterized example of a synthetic oxoiron(IV) complex in a nonheme ligand environment. Here we present TMC-*anti* and TMC-*syn,* the two topological isomers of $[Fe^{IV}(O)(TMC)(CH_3CN)]^{2+}$, which differ in the orientation of their Fe^{IV}=O units relative to the four methyl groups of the TMC ligand framework. The *anti*-isomer is obtained from the reaction of its $[Fe^{II}(TMC)]$ precursor with PhIO, while the *syn* isomer can be generated simply by switching the PhIO oxidant to the sterically bulkier 2-^{t}BuSO$_2$-C$_6$H$_4$IO (*s*-ArIO). The Fe^{IV}=O unit of TMC-*anti* points away from the four methyl groups, while that of TMC-*syn* is surrounded by the methyl groups. TMC-*syn* reacts with HAT substrates at 1.5 to 3-fold faster rates than TMC-*anti*, but the reactivity difference increases dramatically in oxygen-atom transfer (OAT) reactions. R_2S substrates are oxidized into R_2S=O products at rates 2-3 orders of magnitude faster by TMC-*syn*. Even more remarkably, TMC-*syn* epoxidizes all the olefin substrates in this study, while TMC-*anti* reacts only with *cis*-cyclooctene but at a 100-fold slower rate. Comprehensive quantum chemical calculations have uncovered the key factors governing such reactivity differences found between these two topological isomers.



One-Step Aromatic Hydroxylations Catalysed by Nickel(II) Complexes of Pentadentate Ligands

Anjana Rajeev K and Muniyandi Sankaralingam*

Bioinspired & Biomimetic Inorganic Chemistry Lab, Department of Chemistry, National Institute of Technology Calicut, Kozhikode, Kerala-673601, India
*Email: msankaralingam@nitc.ac.in

Targeting selective one-step oxidation of arenes under mild conditions has become a challenging and exciting scientific area that has drawn larger attention in recent years; because naturally available oxygenase enzymes efficiently and selectively perform such transformations under normal atmospheric conditions.[1] Inspired by naturally occurring oxygenase enzymes, numerous attempts to catalyze the oxidation of arenes using first-row transition metal catalysts have been made.[1,2] Thus, we have designed, synthesized and characterized the series of pentadentate ligands, and isolated their nickel(II) complexes to investigate the catalytic ability toward aromatic substrates. The complexes show better catalytic activity with a good selectivity in arene oxidations and the results will be discussed during the presentation.

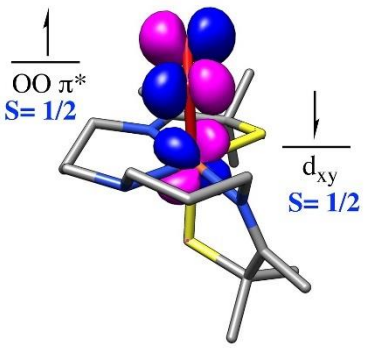
References

1. (a) Rajeev, A.; Balamurugan, M.; Sankaralingam, M. *ACS Catal.,* **2022**, *12*, 9953-9982; (b) Sankaralingam, M.; Balamurugan, M.; Palaniandavar, M. *Coord. Chem. Rev.,* **2020**, *403*, 213085.
2. (a) Kimura, E.; Machida, R. J. *Chem. Soc.,Chem.Commun.***1984**,499-500. (b) Morimoto, Y.; Bunno, S.; Fujieda, N.; Sugimoto, H.; Itoh, S, *J. Am. Chem. Soc.,* **2015**, *137*, 5867 – 5870. (c) Muthuramalingam, S.; Anandababu, K.; Velusamy, M.; Mayilmurugan, R. *Catal. Sci. Technol.,* **2019**, *9*, 5991 - 6001. (d) Masferrer-Rius, E.; Borrell, M.; Lutz, M.; Costas, M.; Gebbink, R. J. M. K.; *Adv. Synth. Catal.* **2021**, *363*, 3783–3795.

Cleavage of Strong C-H Bonds by a Thiolate-Ligated Fe^{III}-Superoxo Complex

Julie A. Kovacs, Maike N. Lundahl, and Shilpa Bhatia
Department of Chemistry, University of Washington, Campus Box 351700, Seattle, WA 98195, USA

Thiolate (RS^-) ligands have been shown to lower the activation barrier to O_2 binding and facilitate peroxo O-O bond cleavage and the cleavage of strong C-H bonds. We will describe an aliphatic thiolate-ligated Fe(II) complex that reacts with dioxygen (O_2) to form an unprecedented example of a reactive iron superoxo (RS-Fe(III)-O_2) intermediate that is capable of cleaving strong C-H bonds. A thiolate-ligated iron superoxo is proposed to play a key role in the biosynthesis of β-lactam antibiotics, as well as the prevention of cancerous tumor metastases. Isopenicillin N-synthase (IPNS) catalyzes the former, and cysteine dioxygenase (CDO) the latter. Very few iron superoxo compounds have been reported, and none are capable of cleaving strong C-H bonds. Spectroscopic characterization, and calibrated DFT and TD-DFT calculations, show that the frontier orbitals of our RS-Fe(III)-O_2 consist of two strongly coupled unpaired electrons of opposite spin, one in a superoxo π^*(O-O) orbital, and the other in an Fe(d_{xy}) orbital.[1] Both the calculated and experimental electronic absorption spectrum are similar to that of the putative IPNS superoxo intermediate, as well as an intermediate involved in the catalytic cycle of CDO. The rate at which our superoxo converts to a putative iron hydroperoxo (Fe(III)-OOH) is shown to depend on the C-H bond strength of the solvent or sacrificial H-atom donor, and a deuterium isotope effect (k_H/k_D= 4.8), comparable to that of IPNS (k_H/k_D= 5.6), is observed.[1] The bond dissociation energy (BDE) of the C-H bonds cleaved by our RS-Fe-O_2 superoxo compound (92 kcal/mol) are comparable to those cleaved by the IPNS enzyme (93 kcal/mol). The mechanism of formation of our RS-Fe-O_2 superoxo, and the effect of beta-deuterium incorporation into ligand backbone on C-H its bond cleaving properties, will be described.



the

[1]Blakely, M. N.; Dedushko, M.A.; Poon, P. C. Y.; Villar-Acevedo, G.; Kovacs, J. A., *J. Am. Chem. Soc.* **2019**, *141*, 1867-1870.

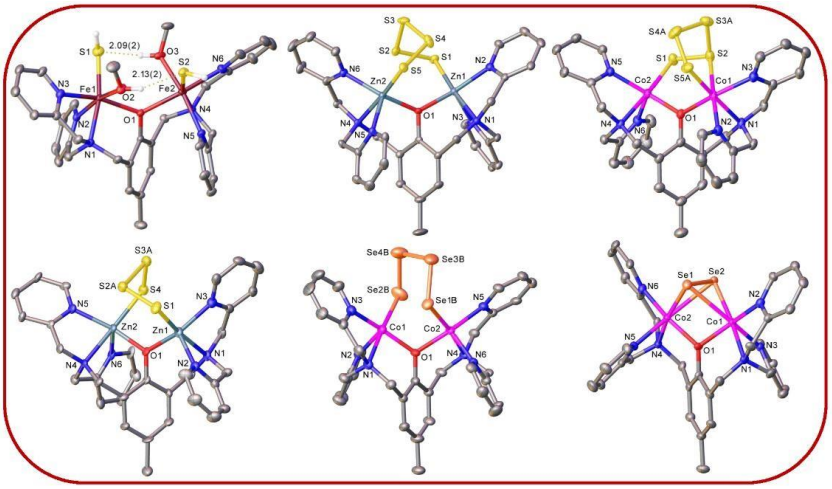
10.01.2024

Generation of Hydrosulfide, Polysulfide and Polyselenide from Transition Metal-Thiolate Complexes

Amit Majumdar

School of Chemical Sciences, Indian Association for the Cultivation of Science,Kolkata-700032, India, Email: icam@iacs.res.in

Transition metal complexes featuring coordinated thiolate ligands have been utilized for the generation of hydrosulfide, polysulfide and polyselenide. While the transition metal mediated hydrolysis of C-S bonds of thiolates allowed the isolation of transitionmetal-hydrosulfide complexes,[1-8] the two-electron redox reaction of coordinated thiolates with externally added elemental sulfur/selenium produced transition metal-polysulfide/polyselenide complexes.[9-11] Synthesis and reactivity of these new types of transition metal complexes toward nitric oxide, elemental chalcogen, phosphines, and selected organic substrates will be presented.



References:

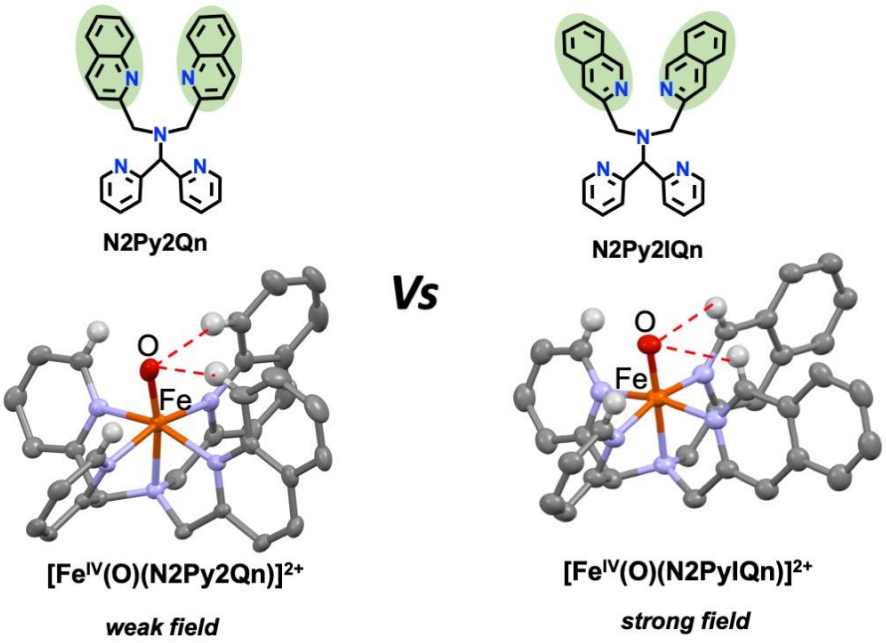
1. Chakraborty, A.; Ganguly, T.; Majumdar, A. *Inorg. Chem.* **2023**, *62*, 11095-11111
2. Das, A.; Ganguly, T.; Majumdar, A. *Inorg. Chem.* **2021**, *60*, 944-958
3. Pal, N,; White, C.J.; Demeshko, S.; Meyer, F.; Lehnert, N.; Majumdar, A. *Inorg. Chem.* **2021**, *60*, 15890-15900
4. Ganguly, T.; Majumdar, A. *Inorg. Chem.* **2020**, *59*, 4037-4048
5. Ganguly, T.; Das, A.; Majumdar, A. *Inorg. Chem.* **2019**, *58*, 9998-10011
6. Pal, N.; Majumdar, A. *Dalton Trans.* **2019**, *48*, 5903-5908
7. Ganguly, T.; Das, A.; Jana, M.; Majumdar, A. *Inorg. Chem.*, **2018**, *57*, 11306-11309
8. Jana, M.; Majumdar, A. *Inorg. Chem.* **2018**, *57*, 617-632
9. Atta, S; Majumdar, A. *Chem. Eur. J.* **2023,** *29*, e202203579
10. Hossain, K.; Majumdar, A. *Inorg. Chem.* **2022**, *61*, 6295-6310
11. Hossain, K.; Majumdar, A. **2024,** *Work Under Progress*

Influence of stereoelectronic effects on hydrogen atom and oxygen atom transfer reactions involving high-valent iron-oxo complexes

Yong Li, Justin Nilsson, Ebbe Nordlander

Chemical Physics, Department of Chemistry, Lund University, Box 124, SE-221 00 Lund, Sweden

The roles of high-valent iron-oxo intermediates in a number of heme[1] and non-heme[2] oygenases are well-established. Several Fe(IV)=O complexes have been synthesized as biomimetic models for such intermediates.[3] This lecture will discuss the steric and electronic effects of various equatorial substituents on the hydrogen atom and oxygen atom transfer reactivities of $[Fe(IV)=O(L)]^{2+}$ complexes, where L is a pentadentate ligand based on the N4Py framework.



References:

1. J.D. Finnigan, C. Young, D.J. Cook, S.J. Charnock, G.W. Black, *Adv. Protein Chem. Struct. Biol.*, **122**, 289 (2020)

2. C. Krebs, D. Galonic Fujimori, C.T. Walsh, J. Martin Bollinger, Jr., *Acc. Chem. Res.*, **40**, 484 (2007)

3. (a) S. Kal, S. Xu, L. Que, Jr., Angew. Chem. Int. Ed., 59, 7332 (2020) (b) W. Nam., *Acc. Chem. Res.*, **48**, 2415 (2015)

Catch-and-Release strategy for selective oxidation of methane to methanol Fe complexes in aqueous medium

Takahiko Kojima

Department of Chemistry, University of Tsukuba, Tsukuba, Ibaraki 305-8571, Japan

Abstract body: Please keep the abstract limited to 500 words

Toward utilization of natural gas as carbon resources, efficient and selective oxidation of gaseous alkanes such as methane should be developed to produce useful materials. Although numerous attempts have been made to provide catalysts for methane oxidation using transition metal complexes, satisfactory results have yet to be obtained in terms of selectivity in methanol formation and catalytic performance represented by high turnover numbers.[1] Herein, molecular Fe(II) complexes having *N*-heterocyclic carbene (NHC) as a part of pentadentate ligands, which allow us to form hydrophobic second coordination spheres (SCSs) made of four aromatic rings, have been prepared to tackle one of "holy-grail" reactions in aqueous medium. One methane molecule can be captured in the SCS in the vicinity of the Fe centre due to CH/π interaction. The Fe(II)-aqua complex was oxidized by NaS_2O_8 to be a low-spin Fe(IV)-oxo complex, which was spectroscopically characterized, through proton-coupled electron transfer. At 323 K, methane (0.98 Pa) was oxidized to be methanol in the conversion of 4.1% and selectivity of 83% with a turnover number of 500.[2]

References:

1. H. Fujisaki, T. Kojima, *Catal. Sci. Technol.* **2023**, *13*, 4270-4284.
2. H. Fujisaki, T. Ishizuka, H. Kotani, Y. Shiota, K. Yoshizawa, T. Kojima, *Nature* **2023**, *616*, 476-481.

10.01.2024

Investigating Heme Superoxo and Peroxo Mediated Pathways of Heme Enzymes Using Functional SyntheticMimics

Gayan B. Wijeratne*[1], Pritam Mondal[2], Shanuk Rajapakse[1], Izumi Ishigami[3], Garrett B. Tolbert[1], Syun-Ru Yeh[3]

[1]Department of Chemistry and Biochemistry, The University of Alabama, Tuscaloosa, AL 35287USA, [2]Department of Chemical Sciences, IISER Mohali, Punjab 140306, India, [3]Department ofBiochemistry, Albert Einstein College of Medicine, The Bronx, NY 10461 USA

Heme enzymes mediate a plethora of paramount reaction pathways in a wide varietyof organisms, including humans, wherein dioxygen activating heme enzymes are prevalent. [1, 2] Interestingly, a number of pivotal geometric and electronic parameters in concert fine-tune such heme centers for their specialized reactivities, which strongly modulate the reactivity properties of their relevant reaction intermediates. Dioxygen activating heme enzymes shuttle through a distinct panel of heme-dioxygen intermediates, wherein the exact active oxidant can vary according to the specific heme enzyme in question. [2] Mid-valent (i.e., heme Fe(III) containing) heme-oxygen adducts are the first members of this series of intermediates, which are followed by the formation of high-valent (i.e., heme Fe(IV) containing) heme-oxygen species afterthe cleavage of the dioxygen derived O–O bond. These high-valent heme intermediates typically are strong oxidants, which competently facilitate the selective,high-yielding cleavage of strong substrate bonds. [3] Accordingly, the chemistries of high-valent intermediates have been rigorously evaluated over the past severaldecades, and a majority of their principal reactivity properties are well documented in the contemporary literature. Attributes of mid-valent heme-oxygen intermediates, on the other hand, are only faintly understood, and in-depth studies into their reactivity properties are severely lacking. [4, 5] Nonetheless, heme enzymes where mid-valent intermediates are active oxidants/key species are rapidly emerging as potent drug targets (e.g., tryptophan/indoleamine 2,3-dioxygenases, aromatase, heme oxygenase, nitric oxide synthase, etc.),[6] warranting a clear comprehension into theirprecise chemical properties. Moreover, unlike their high-valent counterparts, mid- valent heme-oxygen adducts exhibit significantly versatile chemical properties, making the unequivocal description of their bio-relevant chemistries quite challenging. Synthetic model systems can be powerful probes in this endeavor, where important geometric and electronic properties of the heme center can be modified more feasibly and straightforwardly, and readily investigated in detail by various spectroscopic and computational methods. [7, 8] This work utilizes small molecule synthetic analogs of mid- valent heme-oxygen intermediates in evaluating their key bio-relevant reaction properties, and factors that govern the mechanistic subtleties of corresponding reaction landscapes. Characterization of important reaction intermediates, and salientstructure-function relationships will also be discussed in detail.

References:

[1] T. L. Poulos, *Chem. Rev.* **2014**, *114*, 3919-3962; X. Huang, J. T. Groves, *Chem. Rev.* **2018**, *118*, 2491-2553.

[2] S. M. Adam, G. B. Wijeratne, P. J. Rogler, D. E. Diaz, D. A. Quist, J. J. Liu, K. D. Karlin, *Chem.Rev.* **2018**, *118*, 10840-11022.

[3] H. Fujii, in *Heme Peroxidases* (Ed.: E. Raven, Dunford, B.), The Royal Society of Chemistry, **2016**, pp. 181-217; K. Ray, F. Heims, M. Schwalbe, W. Nam, *Curr. Opin. Chem. Biol.* **2015**, *25*,159-171.

[4] P. Mondal, G. B. Wijeratne, *J. Am. Chem. Soc.* **2020**, *142*, 1846-1856.

[5] P. Mondal, I. Ishigami, E. F. Gérard, C. Lim, S.-R. Yeh, S. P. de Visser, G. B. Wijeratne, *Chem.Sci.* **2021**, *12*, 8872-8883.

[6] P. Mondal, G. B. Tolbert, G. B. Wijeratne, *J. Inorg. Biochem.* **2022**, *226*, 111633-111645.

[7] P. Mondal, S. Rajapakse, G. B. Wijeratne, *J. Am. Chem. Soc.* **2022**, *144*, 3843-3854.

[8] P. Mondal, I. Ishigami, S.-R. Yeh, G. B. Wijeratne, *Angew. Chem. Int. Ed.* **2022**, *61*,e202211521.

10.01.2024

Characterization of Paramagnetic States in a Nickel Hydrogen Evolution Electrocatalyst

Sagnik Chakrabarti, Soumalya Sinha, Giang Tran, Hanah Na, Liviu M. Mirica*

Significant progress has been made in the bioinorganic modeling of the paramagnetic states (Ni-L - a formal Ni(I)-Fe(II) state, and Ni-C - formally a Ni(III)-Fe(II) state) which are believed to be involved in the hydrogen redox chemistry catalyzed by [NiFe] hydrogenases. However, the characterization and isolation of intermediates involved in mononuclear Ni electrocatalysts which are reported to operate through a Ni(I/III) cycle have largely remained elusive. Most reported compounds which invoke paramagnetic Ni intermediates are either catalytically inactive or feature ligand-centered radicals.

In this study[1], we report a Ni(II) complex (NCHS2)Ni(OTf)2, where NCHS2 is 3,7-dithia-1(2,6)-pyridina-5(1,3)-benzenacyclooctaphane, that is an efficient electrocatalyst for the hydrogen evolution reaction (HER) with turnover frequencies of ~3,000 s^{-1} and an overpotential of 670 mV with trifluoroacetic acid as the proton source. This electrocatalyst follows a hitherto unobserved HER mechanism involving C-H activation, which manifests as an inverse kinetic isotope effect for the overall hydrogen evolution reaction, and Ni(I)/Ni(III) intermediates, which have been characterized by EPR spectroscopy. We further validate the possibility of the involvement of Ni(III) intermediates by the independent synthesis and characterization of organometallic Ni(III) complexes bearing the $NC^{-}S2$ ligand, which features a carbanion donor.

References:

1. Chakrabarti, S.; Sinha, S.; Tran, G.N.; Na, H.; Mirica, L. M. Characterization of paramagnetic states in an organometallic nickel hydrogen evolution electrocatalyst. *Nat Commun* **14**, 905 (2023).

Organometallic Chemistry, Gas Tunnels, and An Active Site Alcove Are Required for Anaerobic Carbon Dioxide Fixation

Seth Wiley[1,2], Claire Griffith[1], Peter Eckert[3], Alexander P. Mueller[4], Robert Nogle[4], Séan D. Simpson[4], Michael Köpke[4], Mehmet Can[1,5], Ritimukta Sarangi[6], Catherine Drennan[7], Kevin Kubarych[3], Stephen W. Ragsdale[1]*

[1]Dept. of Biological Chemistry, Univ. of Michigan Medical School, Ann Arbor, MI 48109-0606;[2]Current Address: Biosciences Center, National Renewable Energy Laboratory, Golden, CO 80401; [3]Dept. of Chemistry, Univ. of Michigan, Ann Arbor, MI 48109; [4]LanzaTech Inc., 8045 Lamon Ave, Skokie, IL, USA 60077; [5]Current Address: Dept. of Biochemistry, Faculty of Pharmacy, Ankara Medipol University, Ankara, Turkey 06050; [6]Stanford Synchrotron Radiation Lightsource, SLAC National Accelerator Laboratory, Menlo Park, CA 94025; [7]Catherine A. Drennan, Dept of Chemistry & Dep of Biology, Massachusetts Institute of Technology, Cambridge, MA 02139

Abstract body: One of the largest threats facing humanity is the increasing global concentration of greenhouse gases, carbon dioxide and methane, in the atmosphere, affecting wide-reaching aspects such as rising sea levels, ocean acidification, and severe climate conditions. There is an urgent need to better understand carbon fixation and apply the understanding thus gained to enhance CO_2 uptake from the atmosphere and efficiently convert it into fuels and valuable chemicals. There are six known CO_2 fixation pathways and among these, the Wood- Ljungdahl (or reductive acetyl-CoA) Pathway (WLP) (summarized in Fig. 1) is the only one that both generates and utilizes carbon monoxide as an intermediate. The WLP also it is the only autotrophic pathway that generates net ATP. Found in strictly anaerobic microbes, this ancient pathway allows microbes to grow on H_2 and CO_2 as their sole energy and carbon sources and is important to the evolution of life, as it was present in the last universal common ancestor.

At the heart of the WLP is CO dehydrogenase/acetyl-CoA synthase (CODH/ACS). Rich in Ni and FeS clusters, CODH catalyzes CO_2 reduction to CO, which then travels through an interprotein tunnel to the ACS active site. Then, the CO is fixed into acetyl-CoA via a series of nickel-based organometallic intermediates (Ni- CH_3, Ni-CO, Ni-acetyl), which have been recently elucidated. The lecture will describe our recent elucidation of each of these organometallic intermediates, elucidation of the CO gas tunnel, and the discovery of a molecular alcove required for ACS to productively bind CO, form a key nickel-carbonyl intermediate in the ACS mechanism, and for autotrophic growth of microbes by the WLP.

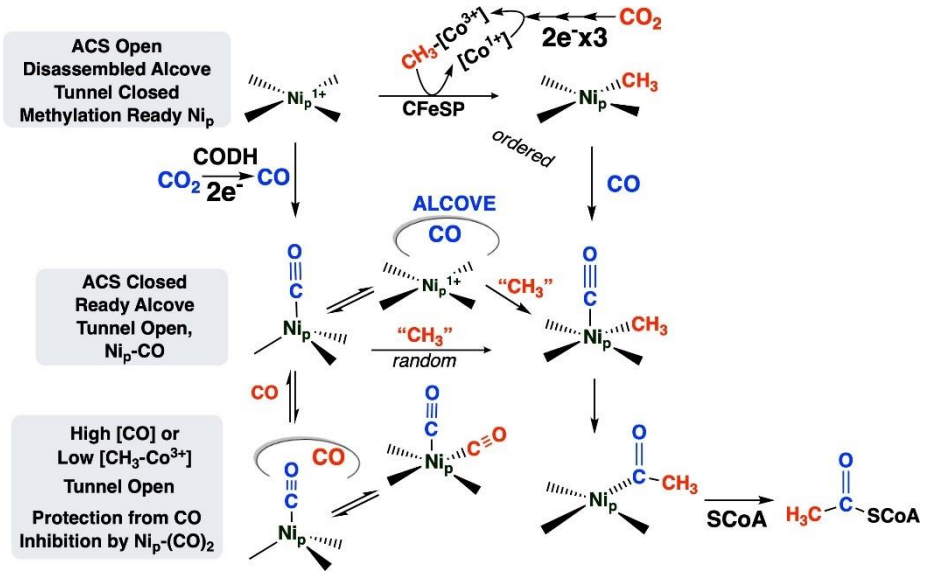
References:

1. Cohen, S.E., et al. (2020) Crystallographic characterization of the carbonylated A-cluster in carbon monoxide dehydrogenase/acetyl-CoA synthase, ACS Catalysis, *10*: 9741-9746.

2. James, C.D., et al. (2020) ^{13}C electron nuclear double resonance spectroscopy shows acetyl-CoA synthase binds two substrate CO in multiple binding modes and reveals the importance of a CO- binding 'alcove', *J. Am. Chem. Soc.*, 142, 15362-15370.

3. Can M, et al. (2023) Characterization of Methyl- and Acetyl-Ni Intermediates in Acetyl CoA Synthase Formed during Anaerobic CO_2 and CO Fixation. *J. Am. Chem. Soc.*. 145:13696-708.

Figure:



Metal-dependent formate dehydrogenases:how do they catalyse the reduction of CO_2?

José J.G. Moura, Agnese Bertinelli, André Amador, Luis Pereira, Navendu Paul,Luisa B. Maia

LAQV, REQUIMTE, NOVA School of Science and Technology | NOVA FCT, Portugal

Biocatalysis is attracting the attention of scientists and engineers eager to develop greener, more sustainable, processes to maintain our modern lifestyle without further destroying the Planet. Enzymes operate under truly green conditions, at ambient temperature and pressure, in water, close to neutral pH; they offer exceptional substrate and product selectivities and specificities, coupled with high specific activity (only a very low percentage of catalyst/enzyme is needed) and an excellent kinetic performance. Hence, enzymes can teach us important chemical lessons to design improved artificial, hybrid or bio-catalysts and catalytic processes for CO_2 activation and conversion into added-value compounds.
In this communication, the reaction mechanism of metal-dependent formate dehydrogenase will be reviewed, highlighting the different lines of evidence that support the metal-sulfido-dependent, hydride transfer mechanism of CO_2 and formate interconversion.

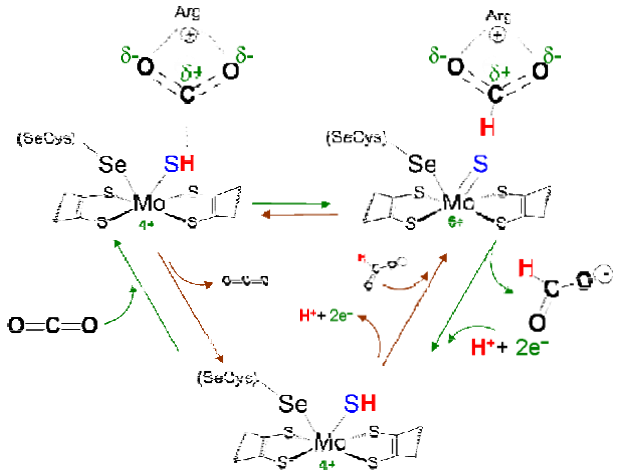


Figure 1. Proposed formate dehydrogenase reaction mechanism.

References

Maia L, et al., Carbon Dioxide Utilisation -The Formate Route, 2021, 29-81 (Open Access)Maia L, et al., Inorg. Chim. Acta, 2017, 455, 350
Maia L, et al., J. Am. Chem. Soc., 2016, 138, 8834.
Maia L, et al., Molybdenum and tungsten-containing enzymes: an overview, Royal Society ofChemistry, 2017, pag 1-80 (Open Access)
Niks D, et al., J. Biol. Chem., 2016, 291 1162-1174

Acknowledgements

This work was supported by the PTDC/BTA-BTA/0935/2020 project and also by the Associate Laboratory for Green Chemistry - LAQV (UIDB/50006/2020 and UIDP/50006/2020), which are financed by national funds from Fundacão para a Ciência e a Tecnologia, MCTES (FCT/MCTES). LBM also thanks to FCT/MCTES, for the CEEC-Individual Program Contract.

One step forward in understanding the biological reduction of CO_2 to formate by a W formate dehydrogenase

C. Mota[1], G. Vilela-Alves[1], A.R. Oliveira[2], R.R. Manuel[2], V. Fourmond[3], C. Léger[3], B. Guigliarelli[3], I.A. Cardoso Pereira[2], Maria João Romão[1]

[1]Associate Laboratory i4HB and UCIBIO, Applied Molecular Biosciences Unit, NOVA-FCT, Universidade NOVA de Lisboa, Caparica, Portugal; [2] ITQB-NOVA, Universidade NOVA de Lisboa, Av. da República, Oeiras, Portugal; [3]Laboratory of Bioenergetics and Protein Engineering, Aix Marseille University, CNRS, BIP, Marseille, France.
Email: mjr@fct.unl.pt

The reversible interconversion of CO2 into formate by Mo/W-Formate dehydrogenases (Fdhs) placed these enzymes on the spotlight, probing a promising route not only for green gas sequestration but also a sustainable way to produce fuel.

FdhAB is a periplasmic heterodimer and the main responsible for CO2 reduction in *Desulfovibrio vulgaris* (*Dv*) [1]. It comprises a pyranopterin cofactor in the active site (W-bisMGD, selenocysteine and a sulfido ligand) and four [4Fe4S] clusters responsible for electron transfer. Contrary to most other Fdhs, this enzyme is oxygen-tolerant and can be purified aerobically [2]. Due to its robustness and high catalytic activity, *Dv*FdhAB is a suitable model for biocatalytic applications for CO2 reduction.

Biochemical and structural studies on *Dv*FdhAB unveiled oxidized and reduced forms of the enzyme and unique features related to its robustness [2,3].

The requirement for its pre-activation with reducing agents led us to consider a disulfide bridge 25 Å away from the active site.

A C872A variant prevents the formation of this disulfide and was shown to be catalytically like the pre-activated wild-type enzyme in the absence of reducing agents. Structural studies of the C872A, of other mechanistic relevant variants and of protein-ligand complexes were combined with biochemical and spectroscopic studies. We could show that DvFdhAB activity is controlled by a redox switch based on an allosteric disulfide bond that is reversible in vivo [4].

Published and on-going studies will be presented with focus on the enzymatic mechanism for CO2 reduction.

References:
[1] Silva, S. M. et al (2013) *Microbiology,* 159, 1760–1769.
[2] Oliveira, A. R. et al (2020) *ACS Catalysis*, 10, 3844–3856.
[3] Oliveira, A. R. et al (2022) *ACS Chemical Biology*, 17, 1901–1909,
[4] Oliveira, A. R. et al (2023) *Nature Chemical Biology*, *in press*

This work is financed by national funds from FCT - Fundação para a Ciência e a Tecnologia, I.P., project UIDP/04378/2020 and UIDB/04378/2020 and the project LA/P/0140/2020.

Infrared Spectroscopy Reveals Metal-independent Carbonic Anhydrase Activity in Crotonyl-CoA Carboxylase/Reductase

Aharon Gomez[1], Matthias Tinzl[2], Gabriele Stoffel[2], Hendrik Westedt[2], Helmut Grubmüller[3],Tobias J. Erb[2,4], Esteban Vöhringer-Martinez[1], Sven T. Stripp[5,6]

[1]Departamento de Físico Química, Facultad de Ciencias Químicas, Universidad de Concepción, Concepción [2]Department of Biochemistry and Synthetic Metabolism, Max-Planck-Institute for Terrestrial Microbiology, Karl-von-Frisch-Str. 10, D-35043 Marburg, Germany

[3]Department of Theoretical and Computational Biophysics, Max-Planck-Institute for Multidisciplinary Sciences,Am Fassberg 11, 37077 Göttingen, Germany

[4]Center for Synthetic Microbiology (SYNMIKRO), Karl-von-Frisch-Str. 14, 35032 Marburg, Germany

[5]Freie Universität Berlin, Experimental Molecular Biophysics, Arnimallee 14, 14195 Berlin, Germany

[6]Technische Universität Berlin, Division of Physical Chemistry, Strasse des 17. Juni 124, 10623 Berlin, Germany

Abstract

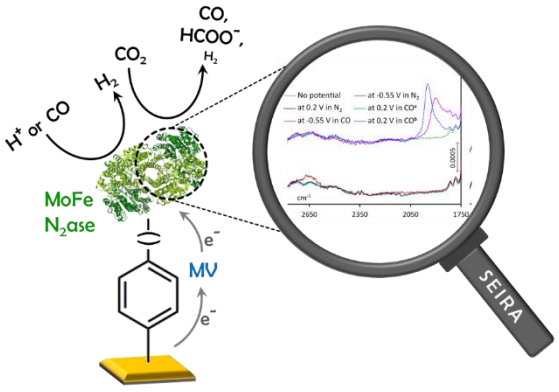
The conversion of CO_2 by enzymes such as carbonic anhydrase or carboxylases plays a crucial role in many biological processes. However, in situ methods following CO_2 hydration or carboxylation reactions at the active site are limited. Here, we used infrared spectroscopy to study the interaction of CO_2, water, bicarbonate, and other reactants with β-carbonic anhydrase from Escherichia coli (EcCA) and crotonyl-CoA carboxylase/reductase from Kitasaospora setae (KsCcr), two of the fastest CO_2-converting enzymes in nature. Our data reveal that KsCcr possesses a so far unknown metal-independent CA-like activity. Site-directed mutagenesis of conserved active site residues combined with molecular dynamics simulations tracing CO_2 distributions in the active siteof KsCCr identify an 'activated' water molecule, forming the hydroxyl anion that attacks CO_2 and yields bicarbonate (HCO_3^-). Computer simulations also explain why substrate binding inhibits the anhydrase activity. Altogether, we demonstrate how in situ infrared spectroscopy combined with molecular dynamics simulations provides a simple, yet powerful new approach to investigate the atomistic reaction mechanisms of different enzymes with CO_2.

Spectroelectrochemistry with Nitrogenase

Kushal Sengupta

Nitrogen (N), an essential element for life, makes up 78% of Earth's atmosphere as chemically inert dinitrogen (N_2). N_2 reduction into ammonia (NH_3), a bioavailable form of N, is a critical step in the biogeochemical nitrogen cycle and has an essential agronomic and economic impact. Compared to industrial Haber-Bosch process, biological N_2 fixation (BNF) occurs at ambient temperature and pressure. The catalyst for BNF is Nitrogenase. Although initially Mo-dependent nitrogenase (Mo-N_2ase) was discovered, over the years' other kinds of nitrogenase (V-dependent and Fe-dependent) have caught attention too. The field has gained even wider importance with the knowledge that it can reduce not just N_2 but a family of other substrates like CO, CO_2, hydrazine, etc. All these discoveries have cultivated a great interest in nitrogenase bioelectrocatalysis over the last several years for a wide range of applications. In this work the catalytic protein (MoFe protein) of Mo-N_2ase has been assembled on Au electrodes via covalent attachment without the use of any polymer or Nafion layers which facilitates unperturbed diffusion of e^-/H^+ and substrates to the active site. The assemble N_2ase biohybrid is catalytically active towards its native substrate and alternate substrate (like CO_2) under physiological conditions. MoFe has been.

Surface enhanced infra-red absorption spectroscopy (SEIRA) coupled to electrochemical studies on these bioelectrode under steady state catalytic condition or under inhibited conditions (like CO) led to the detection of intermediates. Under catalytic conditions a vibrational stretching corresponding to S-H was observed. The belt sulfurs of the active site have long been thought to be site of protonation in the N_2ase mechanistic cycle. In presence of CO at the same redox potential this particular vibration is absent/very weak, but instead gives rise to mixture of vibrations which correspond to different CO bound redox states of the active site.



Tailoring Cobalt Complexes with Redox Non-Innocent Ligands for enhanced Electrocatalytic CO_2 Reduction: Introspection from Geometry, electronic Structure, and Spin State

Ayan Bera[a], Sarah Bimmerman[b], Dr. Thomas Lohmiller[a][c], Dibya Jyoti Barman[a], Ulf-Peter Apfel*[b],[d], and Kallol Ray*[a]

[a] Institut für Chemie, Humboldt-Universität zu Berlin, Berlin, Germany
[b] Faculty of Chemistry and Biochemistry, Ruhr-Universität Bochum, Germany
[c] Helmholtz Zentrum Berlin für Materialien und Energie GmbH, Berlin, Germany
[d] Fraunhofer UMSICHT, Osterfelder Straße 3, 46047 Oberhausen (Germany)

The reductive conversion of CO2 into various valuable C-based fuels renders a uniqueway of solving global energy problems and mitigating greenhouse gas in a sustainable manner[1]. Catalysts based on transition metals play a pivotal role in electrochemicaland photochemical CO2 reduction [2-3]. As the reduction of CO2 possesses unique challenges in terms of selectivity and overpotential under the electrocatalytic CO2 reduction reaction conditions, understanding the electronic structures, and spin statesof a complex and its corresponding reduced intermediates is the state of the art for the discernment of better molecular electrocatalysts. Employing redox non-innocent ligands to promote the mixing of metal-ligand orbitals and achieve substantial electron delocalization has arisen as a promising approach[4-5]. This strategy, frequently harnessed by both biological and heterogeneous catalysts, aims to reduce overpotential and enhance selectivity in comparison to the hydrogen evolution reaction(HER) [6].

Herein, we report a series of cobalt complexes as potential electrocatalysts based ona redox non-innocent ligand system. This ligand served as a flexible foundation for making synthetic modifications, distinguishing it from the initial ligand. We explored the impact of both geometry and electronic structures on the electrocatalytic CO2 reduction reaction by systematically modifying the ligands.

The starting complexes, as well as the one-electron and two-electron-reduced species, have been isolated and characterized by electrochemistry, X-ray crystallography, UV-Vis, and EPR spectroscopy. Various spectroscopic techniques and DFT calculations have unveiled the influence of ligand modifications on the electronic structure of the reduced intermediates. A remarkable structure-activity relationship is revealed from this series for the reactivity and selectivity of the CO2 reduction reaction. The role of the proton sources has also been evaluated by employing different proton sources during catalysis.

References:

[1] Senftle, T. P.; Carter, E. A., *Acc Chem Res* **2017,** *50* (3), 472-475.
[2] Francke, R.; Schille, B.; Roemelt, M., *Chem Rev* **2018,** *118* (9), 4631-4701.
[3] Kinzel, N. W.; Werle, C.; Leitner, W., *Angew Chem Int Ed Engl* **2021,** *60* (21), 11628-11686.[4] Queyriaux, N., *ACS Catalysis* **2021,** *11* (7), 4024-4035.
[5] Queyriaux, N.; Abel, K.; Fize, J.; Pécaut, J.; Orio, M.; Hammarström, L., *Sustainable Energy & Fuels* **2020,** *4* (7), 3668-3676.

[6] Derrick, J. S.; Loipersberger, M.; Chatterjee, R.; Iovan, D. A.; Smith, P. T.; Chakarawet, K.; Yano, J.;Long, J. R.; Head-Gordon, M.; Chang, C. J., *J Am Chem Soc* **2020,** *142* (48), 20489-20501.

10.01.2024

Biologically Inspired Hybrid Molecular Materials for Energy Applications

Antoni Llobet

Institute of Chemical Research of Catalonia (ICIQ), Barcelona Institute of Science and Technology (BIST), Av. Països Catalans 16, E-43007 Tarragona, Spain.

E-mail: allobet@iciq.cat

The replacement of fossil fuels by a clean and renewable energy source is one of the most urgent and challenging issues our society is facing today, which is why intense research is devoted to this topic.[1] Nature has been using sunlight as the primary energy input to oxidize water and reduce CO_2 to generate carbohydrates (a solar fuel) for over a billion years. Inspired but not constrained by nature, artificial systems can be designed to capture light and oxidize water and reduce protons or other compounds such as CO_2 to generate useful chemical fuels. One of the key aspects for the efficient design of useful devices for the making solar fuels is the understanding and mastering of the catalysts involved in both the anodic and cathodic reactions. The talk will describe the initial developments up to the state of the art, of molecular catalysts and their anchoring on conductive and semiconductive surfaces. The latter is crucial for the generation of powerful hybrid molecular anodes and cathodes for the production of solar fuels.[2]

[1] (a) Matheu, R.; Llobet, A. et al. *Nat. Rev. Chem.* **2019,** *3,* 331–341. (b) Vereshchuk, N.; Llobet, A. et al. *Chem. Soc. Rev.* **2023**, *52,* 196-211.

[2] (a) Hoque, Md. A.; Gil-Sepulcre, M.; Llobet, A. et al. *Nat. Chem*. **2020**, *12*, 1060–1066. (b) Schindler, D.; Gil-Sepulcre, M.; Llobet, A.; Würthner, F. et al. *Adv. Energy Mater*. **2020**, 2002329. (c) Gil-Sepulcre, M.; Llobet, A. et al. *J. Am. Chem. Soc.* **2021**, *143*, 11651–11661. (d) Gil-Sepulcre, M.; Llobet, A. *Nat. Catal.* **2022**, 5, 79-82, (e) Beiler, A. M.; Llobet, A. et al. *ACS Energy Lett*. **2023**, 8, 1, 172–178.

Molecular Water Oxidation Catalysis with Tailor-Made Ruthenium Complexes

Sukanta Mandal

Department of Chemistry, Indian Institute of Technology Kharagpur, Kharagpur-721302, India.

Email: sukanta.mandal@chem.iitkgp.ac.in

The conversion and storage of solar energy through high-energy chemicals, such as hydrogen, by splitting water hold great promise for addressing the world's growing energy demands and environmental concerns. Among the various steps involved in water splitting, water oxidation is considered the most challenging, requiring efficient Water Oxidation Catalysts (WOCs) to facilitate the process. In recent years, developing highly efficient WOCs has become a focal point in renewable energy research. Ruthenium-based WOCs have emerged as significant contenders in this field due to their unique combination of enriched redox properties, robust nature, and superior catalytic performance compared to other transition metal-based molecular catalysts. This presentation will delve into the chemistry of water oxidation reactions catalyzed by newly developed ruthenium complexes.[1-4] It will explore the critical role of ligand framework design, with a particular emphasis on incorporating redox-non-innocent character within the supporting ligands and fine-tuning the secondary coordination sphere. These strategies might show immense promise in developing highly efficient water oxidation catalysts.

$$2H_2O \xrightarrow{\text{Ru-WOCs}} O_2 + 4H^+ + 4e^-$$

References:

1. Kundu, A.; Barman, S. K.; Mandal, S. *Inorg. Chem.* **2022**, *61*, 1426-1437.
2. Ghosh, A.; Dasgupta, S.; Kundu, A.; Mandal, S. *Dalton Trans.* **2022**, *51*, 10320-10337.
3. Kundu A.; Dey, S. K.; Dey, S.; Anoop, A.; Mandal, S. *Inorg. Chem.* **2020**, *59*, 1461−1470.
4. Kundu, A; Khan, S.; Dey, S.; Dutta, C; Anoop, A.; Mandal, S. *Eur. J. Inorg. Chem.* **2019**, 164–177.

Bio-inspired Electrocatalysts for Water Oxidation

Galia Maayan
Schulich Faculty of Chemistry, Technion – Israel Institute of Technology, Haifa, Israel

The production of “green” hydrogen from water via electrolysis is a promising avenue for the development of renewable energy technologies. The first step in water electrolysis is water oxidation (WO), which is thermodynamically challenging both in natural and artificial systems (ΔE° = 1.23 V, ΔG = 113 kcal mol^{-1}), and is consideredthe bottleneck of the process, as it involves the transfer of four electrons, and requiresmultiple bond rearrangement. In nature, this transformation is catalyzed by the oxygen-evolving complex in photosystem II, which is a CaMn4O5 cluster. In this process, a non-catalytic tyrosine residue assists in transferring protons and electrons between the catalytic center and the oxidant and serves as a hydrogen-bonding site to provide H2O and H^+ shuttle pathways to and from the catalytic Mn site. A formidabletask is therefore to develop electrocatalysts for WO that can mimic such cooperativity between active metal centers and organic moieties from the second coordination sphere. Ideally, such catalysts should be based on earth abundant transition metals, and be fast, stable, and highly efficient, while operating with low overpotential. Inspiredby this biological concept, we use two different approaches for the design of WO electrocatalysts. Our first approach is to incorporate several functional side chains within peptidomimetic oligomers, for mimicking a second coordination sphere about embedded metal centers, such as Cu and Co.[1-4] Our second approach is to mimic thestructure of the OEC together with its organic second coordination sphere by developing water-soluble Mn12O12(O2R)16(H2O)4 (Mn12) clusters.[5-7] In my talk I will present several Mn12 clusters and demonstrate the role of the organic ligands,surrounding the catalytic Mn core, in achieving stable Mn-oxo center (in one case alsore-usable), and efficient homogeneous electrocatalytic WO activity near natural pH 6,with very low overpotential[5,7] (in one case with a record of only 74 mV!).[6] I will also show for the first time a proposed mechanism for WO catalyzed by Mn12 cluster.

References:

1. T. Ghosh, P. Ghosh & G. Maayan “A Copper-Peptoid as a Highly Stable, Efficient and Reusable Homogeneous Water Oxidation Electrocatalyst”, *ACS Catal.* **2018**, *8* (11) 10631-10640.

2. G. Ruan, L. Engelberg, P. Ghosh & G. Maayan “A Co(III)-Peptoid Complex as a Fast Electrocatalystfor Homogeneous Water Oxidation with Low Overpotential”, *Chem. Commun.*, **2021**, *57*, 939-942.

3. G. Ruan, P. Ghosh, N. Fridman & G. Maayan “A Di-Copper-Peptoid in a Non-Innocent Borate Bufferas a Very Fast Electrocatalyst for Homogeneous Water Oxidation with Low Overpotential”, *J. Am. Chem. Soc.*, **2021**, *143* (28) 10614–10623.

4. G. Ruan, N. Fridman & G. Maayan “Borate Buffer as a Key Player in Cu-Based Homogeneous Electrocatalytic Water Oxidation”, *Chem. – A Eur. J.*, *28* (66) **2022**, e202202407.

5. G. Maayan*, N. Gluz & G. Christou “A Bioinspired Soluble Manganese Cluster as a WO Electrocatalyst with Low Overpotential”, *Nat. Cat.* **2018**, *1*, 48-54. **Highlighted in *Nat. Catal.*, 1, 2018**.

6. T. Ghosh & G. Maayan “Efficient Homogeneous Electrocatalytic Water Oxidation by a Manganese Cluster with Overpotential of Only 74 mV”, *Angew. Chem.* **2019**, *58*, 2785–2790.

7. N. Gluz & G. Maayan “The Role of the –OH Groups within Mn_{12} Clusters in Electrocatalytic Water Oxidation”, *Chem – A Eur. J* **2021**, *27*(19), 6034-6043.

Bioinspired Electrochemical Dioxygen Reduction

Charles W. Machan*, Emma N. Cook, Mary Jo McCormick

Department of Chemistry, University of Virginia,
P.O. Box 400319, Charlottesville, VA, 22904-4319

The utilization of dioxygen (O_2) in synthetic and catalytic processes is continuously inspired by examples from nature, where it is essential for converting chemical energy, the degradation of harmful substances, metabolism, and the generation of important biomolecules. Due to its natural abundance, researchers have been working on harnessing the oxidizing power of O_2 in capital and energy-intensive processes to lower costs and the possibility of adverse environmental impact. Besides these applications, the oxygen reduction reaction (ORR) is also of interest for fuel cell applications, where fuel oxidation and oxygen reduction are decoupled into discrete electrochemical reactions.

One challenge in the activation and reduction of O_2 is its triplet ground state, which inhibits reactivity with singlet organic substrates with limited spin polarization. Nature has overcome this challenge by employing open-shell transition metal centers that favorably react with O_2. Iron (Fe), copper (Cu), and manganese (Mn) are most commonly found in enzymatic active sites that activate O_2 due to their redox flexibility and their natural abundance. Some notable examples of these include hemoglobin, dioxygenases, lipoxygenases, monooxygenases, and superoxide dismutase, among many others. The prevalence of earth-abundant first-row transition metals for O_2 reduction in nature has led to of the development of homogeneous ORR catalysts based on Mn, Fe, cobalt (Co), and Cu active sites. However, despite the prevalence of Mn-centered enzymatic active sites for O_2 activation and reduction, there is a lack of synthetic Mn-based electrocatalysts for the ORR in comparison to Fe and Co.

Our group has been motivated by the sparse number of Mn-based electrocatalysts for the ORR and has focused on developing porphyrinic and non-porphyrinic Mn-centered catalysts that reduce O_2, comparing them to Co- and Fe-based complexes. Using mechanistic understanding of the catalytic cycles involved, we have been able to direct selectivity to either H_2O or H_2O_2 as the primary product, using ligand modification and co-catalytic additives. In some cases, mimicking the active sites of known enzymes has also produced competent catalysts under synthetic conditions, informing new design strategies for the ORR.

References:

Pegis, M. L.; Wise, C. F.; Martin, D. J.; Mayer, J. M. Oxygen Reduction by Homogeneous Molecular Catalysts and Electrocatalysts. *Chem. Rev.* **2018,** *118*, 2340–2391.

Cook, E.N.; Machan, C.W. “Homogeneous Catalysis of Dioxygen Reduction by Molecular Mn Complexes” *Chem. Commun.* **2022**, *58*, 11746–11761.

Nichols, A.W.; Cook, E.N.; Gan, Y.J.; Miedaner, P.R.; Dressel, J.M.; Dickie, D.A.; Shafaat, H.S.; Machan, C.W. “Pendent Relay Enhances H_2O_2 Selectivity During Dioxygen Reduction Mediated by bpy-based Co-N_2O_2 Complexes” *J. Am. Chem. Soc.* **2021**, *143*, 13605–12073.

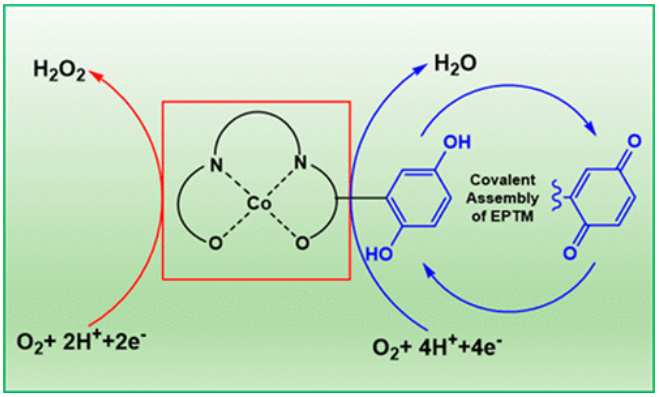
Cook, E.N.; Dickie, D.A.; Machan, C.W. “Catalytic Reduction of Dioxygen to Water by a Bioinspired Non-Heme Iron Complex via a 2+2 Mechanism” *J. Am. Chem. Soc.* **2021**, *143*, 16411–16418.

10.01.2024

Demystifying the Role of Covalently Attached Electron–Proton Transfer Mediator in Oxygen Reduction Reaction Catalyst

Biswajit Mondal, Department of Chemistry, IIT Gandhinagar, Gujarat-382355

The role of covalent attachment of benzoquinone/hydroquinone as electron–proton transfer mediators in ORR is investigated, and it is found that the catalysis is much more efficient as compared to Co(Sal) (Sal = salophen) alone or Co(Sal) and quinoneused separately in terms of selectivity toward H2O formation. While Co(Sal) has only a 3% Faradaic yield for H2O formation, under the same conditions, the Faradaic yieldfor H2O formation is 80% with Co(Sal-H2Q).



Ref: *ACS Catal.* **2023,** *13,* 12643–12647

Advanced spectroscopic studies of C-H bond activating enzymes and molecular catalysts

Serena DeBeer[1]

[1]Max Planck Institute for Chemical Energy Conversion, Stiftstr. 34-36, 45470 Mülheim an der Ruhr, Germany

The ability to activate and functionalize C-H bonds in controlled and sustainable fashion remains one of the holy grails of chemistry. It is here that nature provides much inspiration, with enzymes such as methane monooxygenases enabling the direct and selective oxidation of methane to methanol - utilizing either a copper active site in the particulate form or a dinuclear iron site in the soluble form of the enzyme. Our understanding of the nature of these active sites and their mechanisms has greatly benefited from spectroscopic developments. In the present talk, I will present our groups recent spectroscopic studies on methane monooxygenases, as well as recent work on lytic polysaccharide monooxygenases. Finally, 2p3d resonant inelastic X-ray scattering (RIXS) spectroscopic development efforts focused on high-valent iron oxo model complexes will be presented. These RIXS studies provide a unique experimental probe of two-state reactivity, enabling the previously elusive spin forbidden triplet to quintet transitions to be experimentally observed and correlated directly to reactivity.

Coordination Design of Protein Assemblies from Cage to Crystal

Takafumi Ueno

School of Life Science and Technology, Living Systems Materialogy (LiSM) Research Group, International Research Frontiers Initiative (IRFI), Tokyo Institute of Technology, B55, 4259 Nagatsuta-cho, Midori-ku, Yokohama 226-8501, Japan

Protein assemblies have recently become known as potential molecular scaffolds for applications in coordination and bioinorganic chemistry. Efforts to design protein assemblies to construct protein-based hybrid materials with metal ions, metal complexes, and nanoparticles now represent a growing field with a common goal of providing novel and mimicking natural functions. We have systematically investigated the essential roles of protein assemblies for coordination and biosupramolecular functionalization. Here, we focus on our recent progress in the rational design of protein assemblies using bioinorganic chemistry for (1) exploration of catalytic reactions, (2) construction of functional protein architectures, and (3) in vivo applications.

References: (1) T. T. Pham, S. Abe, K. Date, K. Hirata, T. Suzuki, and T. Ueno, Displaying a protein cage on a protein crystal by in-cell crystal engineering, ***Nano Lett.***, doi/10.1021/acs.nanolett.3c02117. (2) C. Lu, X. Peng, B. Maity, X. Sheng, Y. Zhou, T. Ueno, Z. Liu, D. Lu, Novel Au(I)-based artificial metallo-cycloisomerase for catalyzing the cycloisomerization of γ-alkynoic acids, ***ACS Catal.***, 13, 9918–9924 (2023). (3) M. Taher, B. Maity, T. Nakane, S. Abe, T. Ueno, and S. Mazumdar, Controlled Uptake of an Iridium Complex inside Engineered apo-Ferritin Nanocages: Study of Structure and Catalysis, ***Angew. Chem. Int. Ed.***, 61, e2021116623 (2022). (4) B. Maity, M. Taher, S. Mazumdar*, and T. Ueno* Artificial metalloenzymes based on protein assembly, ***Coord. Chem. Rev.,*** 469, 214593 (2022). (5) T. K. Nguyen, S. Abe, M. Kasamatsu, B. Maity, K. Yamashita, K. Hirata, M. Kojima and T. Ueno, In-Cell Engineering of Protein Crystals with Nanoporous Structures for Promoting Cascade Reactions, ***ACS Appl. Nano. Mater.,*** 4, 1672-1681 (2021). (6) H. Tabe, H. Takahashi, T. Shimoi, S. Abe, T. Ueno, Y. Yamada, Photocatalytic hydrogen evolution systems constructed in cross-linked porous protein crystals ***Appl. Catal., B,*** 237, 1124-1129 (2018). (7) B. Maity, S. Abe, and T. Ueno, Observation of gold sub-nanocluster nucleation within a crystalline protein cage, ***Nat. Commun.,*** *8*,14820 (2017).

SABIC 2024

DAY-5: 11.01.2024 (Thursday)

Nitrogenase: Redox Catalysis out of Bounds

Oliver Einsle

Institute of Biochemistry, University of Freiburg, 79104 Freiburg, Germany

The reaction of biological nitrogen fixation catalysed by the enzyme nitrogenase involves breaking the most stable substrate, the N_2 molecule. This reduction requires an overpotential around –1.6 V and should simply not be feasible at ambient conditions in an aqueous milieu. Nitrogenases nevertheless excel at their task, but this requires a series of optimizations and highly unusual tweaks that we slowly start to unravel.

To break the N_2 triple bond, highly reducing electrons must be generated *in situ*, ideally in the presence of substrate N_2 and shielded from solvent water that they would immediately react with. Nature achieves this by starting with electrons at unusually low potential and transferring them to the nitrogenase system, where ATP hydrolysis is used to convey further reducing power. In the enzyme, they are used to supercharge the complex active site cofactor. All this, however, is not sufficient to react with N_2, and a final, unique catalytic trick must be pulled to provide another boost to overcome the stability of this unique substrate.

In recent years, biochemical, spectroscopic, and structural studies on nitrogenases have provided insights into the catalytic mechanism for the reduction of N_2 and the alternative substrate CO that outline comprehensive, functional principles. Both reactions – the biological versions of the Haber-Bosch and Fischer-Tropsch processes – hold essential clues and reveal common themes. Following an electron from central metabolism through the various activation steps to the nitrogenase cofactor an onto the substrate, I will summarize our current state of understanding of this unique and essential enzyme system.

References:

Einsle O (2023) Catalysis and Structure of Nitrogenases. ***Curr Opin Struct Biol***, 83, 102719.

Trncik C, Detemple F & Einsle O (2023) Iron-based Biological Nitrogen Fixation: Fe-Nitrogenase underscores common principles of Nitrogenase Catalysis. ***Nature Catal,*** 6, 415-424.

Rohde M, Laun K, Zebger I, Stripp ST & Einsle O (2021) Two ligand-binding sites in CO-reducing V nitrogenase reveal a general mechanistic principle. ***Sci Adv***, 7, eabg4474.

Rohde M, Grunau K & Einsle O (2020) CO binding to the FeV Cofactor of CO-reducing Vanadium Nitrogenase at Atomic Resolution. ***Angew Chem Intl Ed***, 59, 23626-23630.

Einsle O & Rees DC (2020) Structural Enzymology of Nitrogenase Enzymes. ***Chem Rev*** 120, 4969-5004.

Harris DF, Lukoyanov DA, Kallas H, Trncik C, Yang ZY, Compton P, Kelleher N, Einsle O, Dean DR, Hoffman BM & Seefeldt LC (2019) Mo-, V-, and Fe-Nitrogenases Use a Universal Eight-Electron Reductive-Elimination Mechanism To Achieve N_2 Reduction. ***Biochemistry***, 58, 3293-3301.

Sippel D, Rohde M, Netzer J, Trncik C, Gies J, Grunau K, Djurdjevic I, Decamps L, Andrade SLA & Einsle O (2018) A bound reaction intermediate sheds light on the mechanism of nitrogenase. ***Science***, 359, 1484-1489.

Sippel D, Einsle O (2017) The structure of vanadium nitrogenase reveals an unusual bridging ligand. ***Nature Chem Biol***, 13, 956-960.

Structure-Function Studies of the O_2-Evolving Complex in Photosystem II from *Synechocystis* sp. PCC 6803

Gary W. Brudvig[1,2], David A. Flesher[2], Christopher J. Gisriel[1], Jimin Wang[2] and Richard J. Debus[3]

[1]Department of Chemistry, Yale University, New Haven, CT 06520, USA.
[2]Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, CT 06520, USA.
[3]Department of Biochemistry, University of California, Riverside, CA 92521, USA.

Photosystem II (PSII) uses light energy to split water into protons, electrons and oxygen. In this reaction, Nature has solved the difficult chemical problem of efficient four-electron oxidation of water to yield O_2 without significant side reactions. In order to use Nature's solution for the design of materials that split water for solar fuel production, it is important to understand the structure of the catalytic site and the mechanism of the reaction. Mechanistic studies have made use of site-directed mutagenesis to probe the function of amino-acid residues in and around the O_2-evolving complex (OEC), a Mn_4CaO_5 cluster in PSII. A majority of the site-directed mutagenesis studies of have utilized the cyanobacterium *Synechocystis* sp. PCC 6803. However, without a high-resolution structure of PSII from *Synechocystis* 6803, interpretations of biophysical studies of mutated PSII complexes have relied on the structures of PSII from thermophilic cyanobacteria. Recently, we solved the cryo-electron microscopy structure of wild-type *Synechocystis* 6803 PSII to 1.93-Å resolution (1). This structure, which reveals significant differences around the OEC between thermophilic and mesophilic PSII, provides a platform for determination of structures of mutated *Synechocystis* 6803 PSII complexes. Our progress on the structures of three mutated *Synechocystis* 6803 PSII complexes (D1-D170E, D2-317A and D1-D61A) will be described.

1. Gisriel, C. J., Wang, J., Liu, J., Flesher, D. A., Reiss, K. M., Huang, H.-L., Yang, K. R., Armstrong, W. H., Gunner, M. R., Batista, V. S., Debus, R. J., and Brudvig, G. W. (2022) *Proc. Natl. Acad. Sci. U.S.A. 119*, e2116765118, https://doi.org/10.1073/pnas.2116765118.

11.01.2024

Synthetic Cluster Models of Inorganic and Organometallic Active Sites in Proteins

Theodor Agapie

Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 91106, USA

Complex inorganic active sites perform challenging catalytic transformations in biological systems, such as water oxidation by photosystem II and nitrogen reduction in nitrogenase. The effect of cluster structure on the physical and chemical properties of these active sites is not well understood. We have developed methodologies for the rational synthesis of homo- and hetero-metallic cluster models of protein active sites, which allow for systematic structure-property studies. Distal redox and ligand changes have been demonstrated to have a substantial effect on the reactivity and binding of ligands relevant to small molecule conversions. Carbon-based bridging ligands have been incorporated to probe potential effects of the interstitial carbide in nitrogenase, and were found to have a profound effect on electronic structure. Spectroscopic studies of models with structures or redox states relevant to the protein active site provide benchmarking for the biological systems. Implications for function and spectroscopy will be discussed.

From On-Demand Redox Potential Modulation To Catalytic Applications: New Avenues For Synthetic Iron-Sulfur Clusters

Victor Mougel, Subal Dey, Liam Grunwald, Fabio Masero, Mariko Inoue

Department of Chemistry and Applied Biosciences, ETH Zürich, Vladimir-Prelog-Weg 2, 8093 Zürich, Switzerland

Cubane-type iron-sulfur clusters are some of nature's most ancient and versatile cofactors. However, seemingly simple, their main function is electron transfer, that can be coupled to proton transfers. While being ubiquitous in enzymatic systems, a few significant functions remained to be modeled using synthetic molecular mimics.

In this talk, we will introduce the use of synthetic Fe_4S_4 clusters acting as concerted proton electron transfer (CPET) mediators for electrocatalytic metal hydride generation, exploited in the context of CO_2 reduction.[1] Further exploring bio-inspired strategies for electron transfers and storage, we will report here the preparation of the first complete redox series of Fe_4S_4 complexes that covers all oxidation states accessible by one-electron transformations of the individual Fe-atoms ($[Fe_4S_4]^{4+}$-$[Fe_4S_4]^{0}$).[2] The redox potential of Fe_4S_4 cubanes is often conceived as a static parameter, which fails to explain some of Nature's more elaborate electron transfer mechanisms, particularly conformationally gated ones.[3] Further replicating the modulation of electric fields in enzymatic systems with our synthetic models, we will present here the case of a synthetic $Fe_4S_4(SR)_4$ model complex exhibiting dynamic redox potentials on-demand. This can be used to control the occurrence of formerly "uphill" electron transfers similar to these observed in Fe_4S_4-containing ATPases, archerases.

[1] S. Dey, F. Masero, E. Brack, M. Fontecave, V. Mougel, *Nature*, **2022**, *607* (7919), *499-506*

[2] L. Grunwald, M. Clémancey, D. Klose, L. Dubois, S. Gambarelli, G. Jeschke, M. Wörle, G. Blondin, V. Mougel, *PNAS*, **2022**, *119* (31), *e2122677119*

[3] L. Grunwald, M. Inoue, P. Cendoya, M. Wörle, V. Mougel, *Chem,* **2023**, *DOI:10.1016/j.chempr.2023.09.023*

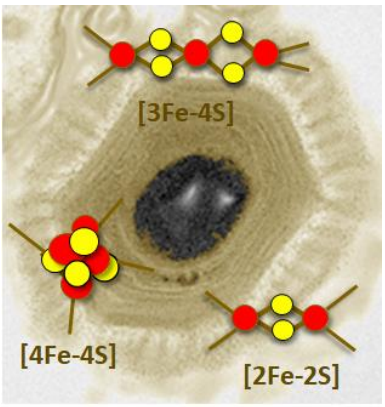
11.01.2024

High iron-sulfur cluster plasticity in giant virus proteins: At the crossroad between synthetic and biological worlds

Srour Batoul[1], Alejandro Villalta[2], Gaspard Toulis[1], Audrey Lartigue[2], Martin Clémancey[3], Bruno Guigliarelli[1], Geneviève Blondin[3], Chantal Abergel[2], Bénédicte Burlat[1]

[1] Laboratoire de Bioénergétique et Ingénierie des Protéines, CNRS/AMU, Marseille, France
[2] Laboratoire Information Génomique et Structurale, CNRS/AMU, Marseille, France
[3] Laboratoire de Chimie et Biologie des Métaux, CEA/CNRS/UGA, Grenoble, France

Iron-sulfur (Fe-S) clusters are essential to all forms of life. They have been proposed to emerge very early in a prebiotic world, the "iron-sulfur world", from which early forms of life have built a powerful chemistry used for catalysis and energy production that is still presently used to fuel life on Earth.[1] Fe-S clusters are major players in electron transfer reactions, catalysis, signal sensing, or protein structure. Fe-S proteins are then pivotal in many essential multicellular processes.



In ***Mimiviridae* giant viruses**, we recently identified a **new family of Fe-S cluster-binding proteins,** named GciS for Glycine/Cysteine-rich Iron-sulfur proteins.[2] Giant viruses are nucleocytoplasmic large DNA viruses with up to 2.8 Mb genomes encoding 1,500 proteins, most of them without resemblance with other cellular or viral proteins.[3] Their discovery, 20 years ago, revolutionized Virology and Biology by reviving the questions of the origin of viruses in general, the role they might have played in the emergence and evolution of life on Earth, and the possible persistence of ancestral processes.

The GciS proteins have no predicted function, they all share low-complexity sequences enriched in glycine and cysteine. Combining biochemical, structural, and spectroscopic approaches, we established the unique structural ability of all GciS proteins to spontaneously stabilize a linear [3Fe-4S] cluster, a geometry that was first evidenced in synthetic Fe-S models in early 80's and never associated to any physiological function in native proteins.[4] The Gcis proteins can also stabilize classical [2Fe-2S] and cubane [4Fe-4S] clusters, and perform clusters interconversions. These properties appear to be related to the large redox-driven conformational flexibility of the GciS protein, that could oligomerize *in vitro* into 20 nm-diameter spheroidal structures that may further assemble into Fe-S cluster-containing fibrils. Our hypothesis is that GciS proteins may be critical for virus adaptation and supports a role of GciS in Fe-S cluster assembly, scavenging and/or recycling during viral infection.

References

1. Beinert, H., Iron-sulfur proteins: ancient structures, still full of surprises. ***J. Biol. Inorg. Chem.* 2000,** *5* (1), 2-15. **2.** Villalta, A.; Srour, B.; Lartigue, A.; Clémancey, M.; Byrne, D.; Chaspoul, F.; Loquet, A.; Guigliarelli, B.; Blondin, G.; Abergel, C.; Burlat, B., Evidence for $[2Fe\text{-}2S]^{2+}$ and Linear $[3Fe\text{-}4S]^{1+}$ Clusters in a Unique Family of Glycine/Cysteine-Rich Fe-S Proteins from Megavirinae Giant Viruses. ***J. Am. Chem. Soc.* 2023,** *145* (5), 2733-2738. **3.** Abergel, C.; Legendre, M.; Claverie, J. M., The rapidly expanding universe of giant viruses: Mimivirus, Pandoravirus, Pithovirus and Mollivirus. ***FEMS Microbiol. Rev.* 2015,** *39* (6), 779-96. **4.** Holm, R. H.; Lo, W., Structural Conversions of Synthetic and Protein-Bound Iron-Sulfur Clusters. ***Chem. Rev.* 2016,** *116* (22), 13685-13713.

Self-assembled Ferritin Protein Nanocage: More than Just an Iron Reservoir

Rabindra Kumar Behera*, Abhinav Mohanty, Akankshika Parida

Department of Chemistry, National Institute of Technology, Rourkela, India

Iron, the fourth most abundant element in the Earth's crust, is central to both chemistry and biology. While the cellular requirement of iron ranges from 10^{-6} M to 10^{-3} M, the Fe(III) solubility under physiological conditions is only ~ 10^{-18} M. Ferritins decrease this gap inside the living cells by synthesizing protein-coated hydrated ferric oxy/hydroxide mineral ($Fe_2O_3.xH_2O$), achieving iron concentration equivalent to ~ 0.2 M. In this talk, I will present the bio-mineralization reaction that occurs inside the confined ferritin protein nanocage and how the protein cage (self-assembly) and phosphate impacts the process. In addition, this talk will discuss two new functions, catalase (H_2O_2 disproportionation) and Dps-like DNA protection activities of heme binding ferritin (bacterioferritin) from *Mycobacterium*, along with its usual ferroxidase/mineralization activity. This unique ferritin, executes multiple functions in order to possibly cope up with the host generated oxidative stress and to promote pathogenesis.

References:

1. Parida A., Mohanty A., Raut R. K., Padhy I., Behera, R.K.; *Inorganic Chemistry*, **2023**, 62(1), 178–191.
2. Mohanty A., Parida A., Subhadarshanee B., Behera, N., Subudhi, T., Koochana P. K., Behera, R.K.; *Inorganic Chemistry,* **2021**, 60(22), 16937-16952.
3. Parida, A; Mohanty, A; Kansara, B; Behera, R.K.; *Inorganic Chemistry*, **2020**, 59(1), 629-641.
4. Mohanty, A; Subhadarshanee, B; Barman, P; Mahapatra, C; Aishwarya, B.; Behera, R.K.; *Inorganic Chemistry*, **2019**, 58(8), 4741-4752.

11.01.2024

Exploration of an Fe-S cluster containing Domain of Unknown Function (DUF2284) in the anaerobic biosynthesis of vitamin B12

Aniket Vartak*, Yamini Mathur and Amrita Hazra*$

Department of Biology, Chemistry, Indian Institute of Science Education and Research (IISER) Pune, Pashan, Pune-411008

Abstract:

Vitamin B12 is an important member of the larger cobamide family of cofactors owing to its role in key human metabolic functions such as DNA synthesis and regulation, amino acid metabolism, and fatty acid degradation[1]. The mechanism of the enzymes involved in anaerobic B12 biosynthesis is yet to be fully explored, especially those that produce the lower ligand moiety of vitamin B12, namely 5,6-dimethylbenzimidazole (DMB). The biosynthesis of DMB in anaerobes is orchestrated by the *bza* operon[2], consisting of enzymes BzaA-E and a Domain of Unknown Function (DUF2284). The DUF2284, found exclusively in bacteria and archaea, is one among > 1000 orphan protein domains whose biochemical action and significance remain unknown. The DUF2284 has been observed in different gene neighbourhoods of prokaryotic genomes existing as a separate entity or fused with other enzymes such as the methyltransferase BzaC in case of the *bza* operon[3]. To glean preliminary insights into DUF2284, we carefully inspected the sequences of 71 DUF 2284 that lie within the *bza* operon as well as 300 that lie outside the operon. The presence of characteristic cysteine repeats and subsequent experimental validation through the purification and UV-Vis characterization of the *Eubacterium limosum* BzaC homolog with the DUF domain supports the presence of a Fe-S cluster. This opens up different possibilities as small Fe-S cluster proteins are reported to be involved in a wide range of functions
- substrate binding in radical-SAM enzymes, dehydratases, DNA binding, scaffold, and Fe-S cluster carriers[4].

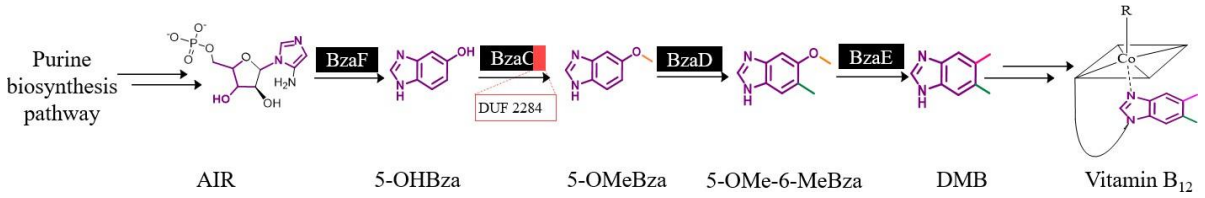


Figure 1: Anaerobic biosynthesis of lower ligand of vitamin B12 by the *bza* operon enzymes through various benzimidazole intermediates. Amino imidazole ribotide (AIR) coming from purine biosynthesis pathway undergoes a rearrangement to form 5-hydroxybenzimidazole which undergoes subsequent methylations to give 5-methoxybenzimidazole, (5-OMeBza), 5-methoxy-6-methylbenzimidazole (5- Ome-6-MeBza) and 5,6-dimethylbenzimidazole (DMB); which gets incorporated into corrinoid structure as a lower ligand of vitamin B12.

Further, we phylogenetically mapped the DUF2284 sequences, and then cloned DUF 2284

homologs from distinct origins and are in the process of purifying them to conduct biochemical characterization. Our studies on DUF 2284 will shed new light on its activity, especially for ones in different genetic contexts. In the context of DMB biosynthesis in vitamin B12, the presence of DUF fused to BzaC is strongly correlated with the presence of BzaD and BzaE, the next two mechanistically unexplored methyltransferase enzymes in the pathway. This opens up the hypothesis that the DUF2284 helps in the activity of BzaD and BzaE by perhaps providing an appropriate scaffold for the methyl transfer reactions or as a carrier of the Fe-S cluster. Overall, our efforts to understand the role of DUF2284 will not only uncover the role of an unknown domain, but will also aid in understanding the complex mechanistic enzymology of anaerobic vitamin B12 biosynthesis.

References:

1. Roth, J. R., Lawrence, J. G. & Bobik, T. A. Cobalamin (Coenzyme B12): Synthesis and Biological Significance. Annu. Rev. Microbiol. 50, 137–181 (1996).
2. Hazra, A. B. et al. Anaerobic biosynthesis of the lower ligand of vitamin B12. Proc. Natl. Acad. Sci. U. S. A. 112, 10792–7 (2015)
3. Mathur, Y., Sreyas, S., Datar, P.M., Sathian, M.B., and Hazra, A.B. CobT and BzaC catalyze the regiospecific activation and methylation of the 5-hydroxybenzimidazole lower ligand in anaerobic cobamide biosynthesis. Journal of Biological Chemistry 295(31): 10522–10534 (2020)
4. Johnson, D., Dean D., Smith A., Johnson M., Structure, Function and Formation of Biological Iron-sulfur clusters., Annu. Rev. Biochem., 74, 247-281, 2005.

Bioinspired Smart and Responsive Molecular Materials

Prasenjit Giri, Dibyendu Dey, Diotima Bhattacharjee, Prasita Mazumder, Manas K Panda*

Department of Chemistry, Jadavpur University, Kolkata-700032

Email: mannup25@gmail.com

Nature provides numerous examples of smart systems that are smart and responsive to external stimuli or environmental cues. To mention a few examples, movement of sunflower plant under sunlight direction, pressure induced movements of mimosa pudica or venus flytrap, humidity and temperature induced flower blooming, self-healing of plant stem or human bone etc. These systems continue to inspire scientists to develop artificial materials that mimic such processes. For example, light-powered plants can autonomously change their shape, size or display static/ dynamic motion in presence of natural light/sunlight. Mimicking such functions in the laboratory, i.e developing light powered autonomous micro/macro-machines using soft organic/metal organic molecular material represents one of the most difficult challenges in today's research and demands huge imagination, skills, and tedious efforts from the involved researchers. Smart organic crystalline materials that can display macroscopic responses such as shape deformation, size alteration or motion under light illumination have emerged as potential candidates for this purpose. The design of such molecules is accomplished by incorporating a photo-active unit that can absorb photons to initiate photo-response and a suitable supramolecular synthon for non-covalent interactions for the propagation. On the simplest mechanistic view, the molecular motion triggered by light is cooperatively amplified to supramolecular to macroscopic scale with the help of intermolecular cooperative mechanism involving reconfigurable non-covalent interactions. While few such molecular crystals have been reported to exhibit fascinating macroscopic mechanical responses, the quest for developing new molecular systems having superior or novel mechanical responses is a never-ending process in material chemistry research. In this talk, we shall discuss some of the novel light responsive and self-healing materials that have recently been developed in our laboratory.

The multifaceted nature of metallothioneins across organisms: Insights beyond metalation and structural states

Eva Freisinger

Department of Chemistry, University of Zurich, Zurich, Switzerland
freisinger@chem.uzh.ch

Metallothioneins (MTs) constitute a widespread family of small, cysteine-rich proteins ubiquitous in various life forms. *In vitro*, MTs exhibit the capability to coordinate an array of soft metal ions; however, *in vivo* the range of target ions is narrowed down to Zn^{II} and Cu^{I}, fulfilling essential homeostatic roles. Another physiological function associated with metal ions is the detoxification of, mainly, Cd^{II} and Hg^{II} resulting in thermodynamically highly stable complexes.

The protein ligands, known as thioneins, typically lack secondary structural elements, granting their backbones substantial flexibility. This structural feature enables efficient formation of metal-thiolate clusters, significantly enhancing the metal ion binding capacity of the respective MT. Yet, this high flexibility presents challenges in determining their structure, thus limiting the availability of 3D structures, which predominantly encompass fully-metalated species.

However, metal-free or sub-metalated species are likely functionally more relevant, particularly concerning their physiological role as metal ion binders. Our research aims to explore both metalation pathways[1] and fully structured MT species[2] by integrating spectroscopic measurements with biochemical methodologies. This includes the determination of protonation constants of potential ligands,[3] specific residue mutations, and the evaluation of MT domains or truncated versions. Our investigation primarily focuses on MTs sourced from three families: plants, fungi, and bacteria.

We gratefully acknowledge the financial support for this project provided by the Swiss National Science Foundation (SNSF) and the University of Zurich.

References:
1. A. Salim, S. Chesnov, E. Freisinger J. Inorg. Biochem., 2020, 210, 111157.
2. J. Habjanič, O. Zerbe, E. Freisinger Metallomics, 2018, 10, 1415-1429.
3. M. Perinelli, M. Tegoni, E. Freisinger Inorg. Chem., 2020, 59, 16988-16997.

11.01.2024

Opto-electrochemical Probes for Measuring Small Molecular Biothiols: Clinical Testing of Cardiac Samples

Pabitra B. Chatterjee

Analytical & Environmental Science Division and Centralized Instrument Facility,

CSIR-Central Salt & Marine Chemicals Research Institute, Bhavnagar, Gujarat, India

Email: pbchatterjee@csmcri.res.in

Small molecular biothiols viz., cysteine, homocysteine, and glutathione, play key roles in human health and diseases. Aberrant levels of these species in human blood indicate several chronic and degenerative illnesses. As a result, alterations in biothiol concentrations have been identified as markers for various lifestyle-related diseases. Therefore, early stage quantification of these markers is unavoidable for the initial diagnosis of various pathological disorders and assessing the recovery of patients undergoing different pivotal treatments. Literature has witnessed a paramount interest in developing probes for biomarkers ranging from small biomolecules to large glycans, proteins, etc. This presentation describes the chemistry of water-soluble inorganic/organic compounds, particularly metal complexes with small molecular biological thiols at physiological pH. The remarkable affinity of the compounds toward a specific biothiol, even in the presence of other congeners, has offered us to test the clinical potential of the promising candidate. This presentation also describes results from clinical investigation of cardiac patients' blood samples for selective homocysteine quantification. Results from the clinical validation studies have established the feasibility of further development of point-of-care-testing (POCT) assay to measure disease-linked biomarkers present in human body fluids.

[1] Yin, C. X.; Xiong, K. M.; Huo, F. J.; Salamanca, J. C.; Strongin, R. M. *Angew. Chem. Int. Ed.,* **2017**, *56*, 13188.

[2] Xu, Z.; Huang, X.; Han, X.; Wu, D.; Zhang, B.; Tan, Y.; Cao, M.; Liu, S. H.; Yin. J.; Yoon, J. *Chem* **2018**, *4*, 1.

[3] Debnath, S.; Nair, R. R.; Ghosh, R.; Kiranmai, G.; Radhakishan, N.; Nagesh, N.; Chatterjee, P. B. *Chem. Commun*, **2022**, *58*, 9210.

Biomimetic Studies for the Detoxification of Environmental Pollutants

Gouriprasanna Roy*, Rudra Shankar Pati, Amirul Islam, Rakesh Kumar Rai

Department of Chemistry,

Indian Institute of Technology Tirupati (IITT), Yerpedu, Tirupati, AP - 517619

Email: gproy@iittp.ac.in

Methylmercury (Me–Hg^+) is a ubiquitous environmental pollutant and a potent neurotoxin. It accumulates at high levels in food chains, mainly in fish and seafood, and therefore, consumption of contaminated foods poses a significant risk to human health.[1] Exposure to ethylmercury (Et–Hg^+) is another serious concern in the developing countries where Et–Hg^+-containing antimicrobial agent "*Thimerosal*" is commonly used as a preservative in multiuse vials of vaccines and other medicines.[2] Likewise, arsenic is another ubiquitous environmental toxin and human carcinogen that also poses a serious threat to human health. Arsenic contamination is most prevalent in areas of West Bengal, Jharkhand, Bihar and Uttar Pradesh, in the flood plain of Ganga River.[3]

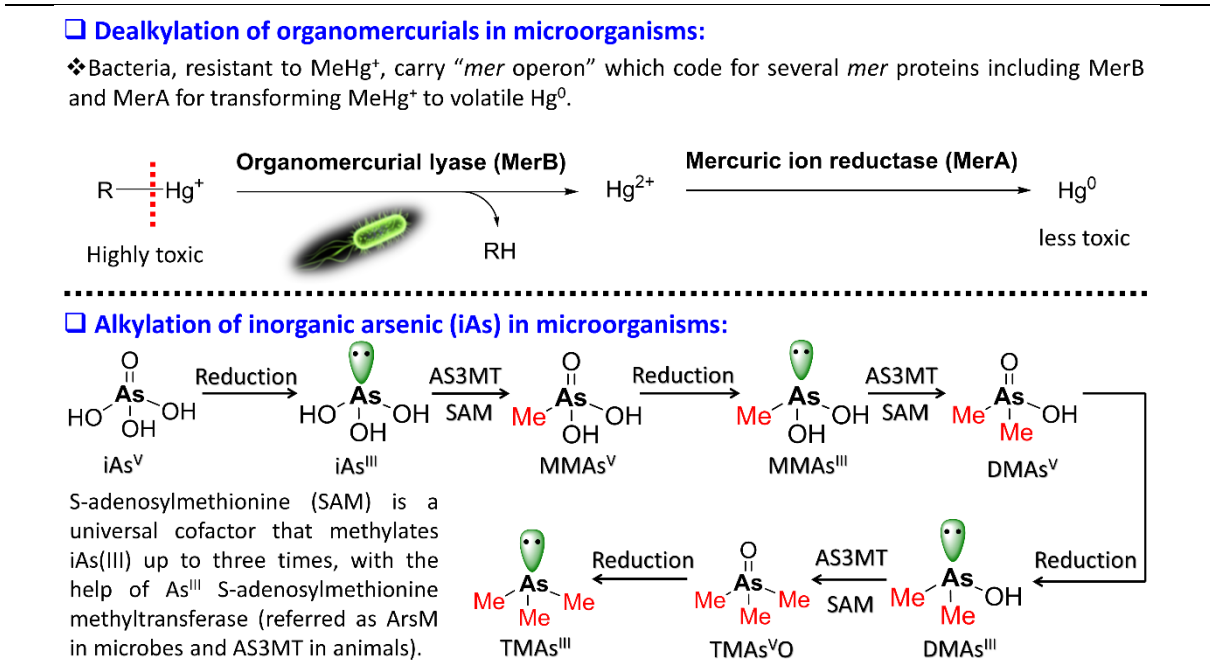


Figure 1. Mercury and arsenic detoxification in microorganisms. Dealkylation of organomercurials and alkylation of inorganic arsenic compounds in microorganisms.

In nature, however, several microorganisms have been reported to detoxify organomercurials including Me–Hg^+ by converting them to less toxic biologically inert species. For instance, bacterial organomercurial lyase (MerB) catalyzes the protolytic cleavage of the otherwise inert Hg–CH_3 bond of Me–Hg^+ and produces methane (CH_4) gas and ionic mercury Hg^{2+},

while a second enzyme mercuric ion reductase (MerA) subsequently reduces the product Hg^{2+} to volatile Hg^0.[4]

On the other hand, methylation of inorganic arsenic (iAs) is widespread in nature, observed in bacteria, fungi, algae, plants, and animals. It is recognized as an established detoxification process in many organisms including humans. S-adenosylmethionine (SAM) is a universal cofactor that methylates iAs(III) up to three times, with the help of As^{3+} S-adenosylmethionine methyltransferase (referred as ArsM in microbes and AS3MT in animals), producing the trivalent methylated arsenic species such as methylarsenite ($MMAs^{3+}$), dimethylarsenite ($DMAs^{3+}$), and volatile less toxic trimethylarsine ($TMAs^{3+}$).[5,6] Several enzymes, mostly present in microorganisms, efficiently detoxify organomercurials ($R–Hg^+$) and iAs through demethylation and methylation pathways, respectively. In this presentation, I will mostly focus on the development of synthetic smart molecules in our laboratory, inspired by the mother nature, for the detoxification of various toxic mercury and arsenic compounds.

References:

(1) Clarkson, T. W.; L Magos *Crit. Rev. Toxicol.* **2006**, *36*, 609−662.
(2) Geier, D. A.; King, P. G.; Hooker, B. S.; Dórea, J. G.; Kern, J. K.; Sykes, L. K.; Geier, M. R. *Clinica Chimica Acta* **2015**, *444*, 212−220.
(3) a) Acharyya, S. K., Chakraborty, P., Lahiri, S., Raymahashat, B. C., Guha, S., Bhowmik, A. *Nature,* **1999**, *401*, 545−546. b) Nickson, R., McArthur, J., Burgess, W., Ahmed, K.M., Ravenscroft, P. and Rahmanñ, M. *Nature*, 1998, *395*, 338.
(4) Omichinski, J. G. *et al. J. Biol. Chem.* **2009**, *284*, 938–944.
(5) Mukhopadhyay, R.; Rosen, B.P.; Phung, L. T.; Silver, S. *FEMS Microbiol. Rev.*, **2002**, *26*, 311−325.
(6) a) Cullen, W. R. *Chem. Res. Toxicol.* **2014**, *27*, 457 – 461. b) Mandal, B.K., Ogra, Y.; Suzuki, K.T. *Chem. Res. Toxicol.,* **2001**, *14*, 371−378. c) Mandal, B.K., Ogra, Y., Anzai, K.; Suzuki, K.T. *Toxicol. Appl. Pharmacol.*, **2004**, *198*, 307−318. d) Dheeman, D. S.; Packianathan, C.; Pillai, J. K.; Rosen, B. P. *Chem. Res. Toxicol.* **2014**, *27*, 1979 – 1989.

Selective Catalytic Conversion of Nitrite to Ammonium by an Oxygen-Tolerant Molecular Cobalt Complex

Sayantan Paria

Department of Chemistry, Indian Institute of Technology Delhi

In the biological system, the reduction of NO_2^- to NH_4^+ is catalyzed by cytochrome *c* nitrite reductase and the siroheme-containing nitrite reductases.[1-3] The development of electrocatalysts for reducing NO_2^- to NH_4^+ and an understanding of the reaction mechanism have attracted considerable attention among synthetic chemists in recent years.

In this study, a molecular hexacoordinate Co^{III} complex of a bis-pyridine-monooxime donor set of ligands, $[Co^{III}(L^{N3O})_2]^+$ (**1**, Figure 1), has been synthesized and thoroughly characterized. Electrocatalytic NO_2^- reduction catalyzed by **1** was investigated in a 0.1 M sodium phosphate buffer solution (PBS) at pH 7, which revealed the selective conversion of NO_2^- to NH_4^+ with 96 % Faradaic efficiency. Experimental investigations revealed the initiation of catalytic reaction begins through the coordination of NO_2^- to Co^I via the dissociation of one of the pyridine arms of the ligands, which makes the catalyst highly selective for the NO_2^- reduction reaction (NO_2^-RR). Additionally, **1** showed catalytic activity in the presence of NH_2OH and NO, assisted in the reduction of these substrates to NH_4^+ in 0.1 M PBS. Kinetic studies showed that the NH_2OH reduction reaction (NH_2OHRR) occurred at a much faster rate compared to the reduction of NO_2^-. However, the reduction of NO by **1** occurred at a slower rate than NH_2OHRR, implying that the rate-limiting step in the $6e^-/8H^+$ reduction process is the formation of NO.

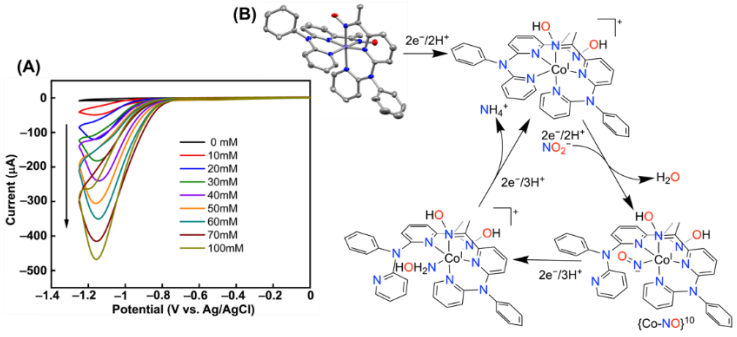


Figure 1. (A) Cyclic voltammogram of **1** (0.025 mM) in 0.1 M phosphate buffer solution in the presence of varying amounts of $NaNO_2$, at a scan rate of 100 mV/s. (B) X-ray structure of **1** with 50 % ellipsoid probability and the reaction pathway involved in the NO_2^- reduction reaction.

Further, **1** was found inactive for the oxygen reduction reaction in PBS at pH 7, thus functioning efficiently NO_2^-RR under an oxygen atmosphere. We suggest that the ligand oxime scaffold works as a proton relay site during NO_2^-RR.

References:

1. S. Besson, M. G. Almeida and C. M. Silveira, *Coord. Chem. Rev.*, **2022**, *464*, 214560.
2. D. Bykov and F. Neese, *Inorg. Chem.*, **2015**, *54*, 9303-9316.
3. O. Einsle, A. Messerschmidt, R. Huber, P. M. H. Kroneck and F. Neese, *J. Am. Chem. Soc.*, **2002**, *124*, 11737-11745.

11.01.2024

Metabolic reprogramming associated with Arsenic and salt stress response in plants: cues for climate resilience

Soumen Kanti Manna

Biophysics & Structural Genomics Division, Saha Institute of Nuclear Physics, 1/AF Bidhannagar, Kolkata, West Bengal 700 064

Homi Bhabha National Institute, BARC Training School Complex, Anushaktinagar, Mumbai, Maharashtra 400 094, India

Abstract: The weather pattern is getting increasingly erratic with climate change. Alongside, the indiscriminate use of ground water is increasing the risk of Arsenic contamination in crops like paddy, which is the staple food for around half of the world population. While the lack of rainfall is increasing salinity in some areas, flooding in the low-lying coastal areas is also causing increase in soil salinity. These are threats to the food security of the world. In order to find solutions to these problems, it would be essential to understand how plants respond to these stresses. Since metabolism is the outcome of the upstream signalling and biochemical cascade following gene environment interactions, untargeted metabolic profiling was used to characterize the rearrangement of the biochemical landscape in response to these stresses. In paddy, we identified a novel role of tryptophan and phenylpropanoid in response to Arsenic stress. On the other hand, in soybean, a differential temporal pattern of accumulation of osmoprotective metabolites was found to be associated with the ability to withstand salt stress. These studies revealed important roles of metabolic reprogramming in response to these abiotic stresses. These may help to develop more resilient agricultural strategies by manipulating the associated signalling and metabolic pathways to mitigate the challenge of climate change.

Bioinspired Cu chelators or how bioinorganic chemistry may help treating the Wilson's disease

Pascale DELANGLE

SyMMES (University Grenoble Alpes, CEA, CNRS, GRE-INP), CEA Grenoble, 17 rue des martyrs, 38054 Grenoble, France

Among metals, copper (Cu) is an essential element, which is used as a cofactor in many redox proteins involved in vital processes. However, free Cu is very toxic even at low concentrations since it can promote Fenton-like reactions and oxidative stress. Therefore, the intracellular Cu concentration is rigorously controlled to ensure that it is provided only to the essential enzymes and does not accumulate to toxic levels in cells. Cu regulation involves the +I oxidation state, i.e. Cu^+, classified as a soft metal ion in the Pearson's theory. Therefore, Nature developed sulfur-rich proteins, involving thiolates of cysteine residues to coordinate Cu^+ and control Cu intracellular concentration.[1]

Efficient Cu^+ chelators were designed by mimicking high affinity copper-binding sites in copper chaperones[2] or metallothioneins,[3] which involve the thiolate functions of cysteines in their Cu binding sites. Some of these chelators were derived to obtain prochelators targeted to the asialoglycoprotein receptors (ASGP-R) to induce their endocytosis in hepatic cells and to propose efficient intracellular Cu^+ chelation.

In this keynote lecture, the design, the affinity and selectivity of Cu^+ bioinspired chelators will be presented, as well as their potential interest for sequestering other toxic metals.[4] Then, their targeting to the liver cells will be explored to propose a localized copper treatment of Wilson's disease, a major genetic disorder of copper metabolism in humans.[5] The mechanism of action of the corresponding prochelator demonstrates that this molecule is able to relocate Cu in cellular models and promote Cu excretion in a murine model of Wilson's disease.[6]

References:

[1] P. Delangle, E. Mintz, *Dalton Trans.* **2012**, *41*, 6359-6370.
[2] A. M. Pujol, M. Cuillel, O. Renaudet, C. Lebrun, P. Charbonnier, D. Cassio, C. Gateau, P. Dumy, E. Mintz, P. Delangle, *J. Am. Chem. Soc.* **2011**, *133*, 286-296.
[3] A. M. Pujol, C. Gateau, C. Lebrun, P. Delangle, *J. Am. Chem. Soc.* **2009**, *131*, 6928-6929
E. Mesterházy, C. Lebrun, A. Jancsó, P. Delangle, *Inorg. Chem.* **2018**, *57*, 5723-5731.
[4] L. I. Szekeres, P. Maldivi, C. Lebrun, C. Gateau, E. Mesterházy, P. Delangle, A. Jancsó, *Inorg. Chem.* **2023**, *62*, 6817-6824
R. Das, M. Claron, C. Lebrun, J. Pecaut, S. Ambala, C. Gateau, G. Roy, P. Delangle, *J. Inorg. Biochem.* **2021**, *222*, 111518.
[5] A. M. Pujol, M. Cuillel, A.-S. Jullien, C. Lebrun, D. Cassio, E. Mintz, C. Gateau, P. Delangle, *Angew. Chem. Int. Ed.* **2012**, *51*, 7445-7448.
[6] M. Monestier, A. M. Pujol, A. Lamboux, M. Cuillel, I. Pignot-Paintrand, D. Cassio, P. Charbonnier, K. Um, A. Harel, S. Bohic, C. Gateau, V. Balter, V. Brun, P. Delangle, E. Mintz, *Metallomics* **2020**, *12*, 1000-1008.

tRNA processing and recoding of gut phages; *theta* ribozymes,discovery and function of a novel subgroup of HDV-like ribozymes

Roland K. O. Sigel

Department of Chemistry, University of Zurich
Winterthurestrasse 190, 8057 Zurich, Switzerland

Trillions of microorganisms inhabit the human body, constituting the microbiome. The gut microbiome is mainly composed of bacteriophages and is increasingly linked to human health and disease.[1] Bacteriophages, which are the dominant gut virome constituents, can utilize suppressor tRNAs to switch to alternative genetic codes (e.g.,the UAG stop-codon is reassigned to glutamine) while infecting hosts with the standard bacterial code.[2] We recently discovered a novel subgroup of minimal hepatitis delta virus (HDV)-like ribozymes[3] – theta (q) ribozymes – potentially involved in the code switch leading to the expression of recoded lysis and structural phage genes.[4] These q ribozymes are predominantly found at the 3'-end of freshly transcribed bacteriophage-encoded tRNAs, indicating a role in viral tRNA maturation and/or regulation. While all amino acids are encoded to various amounts by the associated tRNAs, every fifth associated tRNA is a suppressor tRNA, indicating a crucial role of this novel ribozyme. We tested numerous q ribozymes of the >1'750 unique examplesand demonstrate their HDV-like self-scission behaviour *in vitro*. They show a remarkable difference in self-cleavage activity, a distinct dependence on Mg^{2+} concentration, as well as pH dependence. Together with mutational analysis, these findings corroborate their fold into a classical pseudo-knot structure with a strictly conserved cytosine as the catalytic centre crucial for acid-base catalysis. This novel subgroup of HDV-like minimal ribozymes is the first example of small ribozymes usedas an alternative to large enzymes that usually process tRNA 3'-ends. Hence, the short list of biological functions of small HDV-like ribozymes is expanded and a potential new player involved in the code switch of certain recoded gut bacteriophages is introduced.

Financial support by the Swiss National Science Foundation and the University of Zurich is gratefully acknowledged.

[1] Duan, Y., Young, R. & Schnabl, B. *Nature Rev. Gastroenterol. Hepatol.* **2022**, 19, 135–144.

[2] Peters, S. L. et al. *Nature Commun.* **2022**, 13, 5710.

[3] Webb, C.-H. T. & Lupták, A. *RNA Biol.* **2011**, 8, 719–727; Riccitelli, N. J., Delwart, E. & Lupták, A. *Biochemistry* **2014**, 53, 1616–1626.

[4] Kienbeck, K., Malfertheiner, L., Zelger-Paulus, S., Johannsen, S., von Mering, C. & Sigel, R. K. O. *under revision* **2023**.

Molecular mechanisms of biological copper trafficking: Insights from multiscale simulations of model systems

Avisek Das
School of Chemical Sciences, Indian Association for the Cultivation of Science, Kolkata, India

Copper is an essential trace metal present in cellular environments of all kingdoms of life. Due to its redox activity, excess copper can cause irreparable damage to cells, giving rise to serious detrimental outcomes for the whole organism, for example, Wilson and Menken diseases in humans. Nature has evolved delicate molecular machineries to handle copper inside the cell, as a result, concentration of free copper in the cytosol is vanishingly small. A major pathway in biological copper trafficking, which has been on the forefront of bioinorganic chemistry research over the last two decades, involves transfer of Cu(I) between the chaperone proteins and the metal binding domains of the copper ATPases situated on the membranes of certain intracellular organelles. The copper binding sites in both types of trafficking proteins are identical and are composed of a pair of cysteine residues. The thiols are deprotonated in the holoprotein. Despite the availability of detailed structural information about the main molecular actors, crucial mechanistic details of the transport process remain poorly understood. Two questions of particular interest are the coupled motion of protons and the copper ion, and the influence of non-covalent protein-protein interactions on the chemical reaction steps. Computational modeling of these molecular events is challenging due to the presence of strong solvent effects and significant molecular disorders in the binding loops. We recently developed a novel multiscale method to deal with the solvent effect and validated our approach in a model system consisting of known copper chelators. Our analysis suggested the presence of energy barrier in the deprotonation step upon initial binding of a thiol to the Cu(I) center bound to two thiolates and indicated that this step could be the rate determining step of the entire multi-step chemical reaction. This observation has important implications in the biological context. We extend our approach, at the QM/MM level of theory, to models of protein-protein complexes composed of peptide segments. Preliminary data provide important insights into the molecular dynamics in the key steps of the copper transfer reaction. The atomically detailed information furnished by our studies is difficult to obtain by direct experimental techniques because of the spectroscopically silent nature of the Cu(I) ion.

How do microbes breathe without oxygen or soluble electron acceptors?

Protein nanowires: structures, functions, and ultrafast electron transfer mechanisms

Nikhil S. Malvankar

Dept. of Molecular Biophysics. & Biochemistry, Microbial Sciences Institute, Yale

Deep in the ocean or underground, where there is no oxygen, *Geobacter* "breathe" by projecting tiny hair-like protein filaments called "nanowires" into the soil, to dispose of excess electrons resulting from the conversion of nutrients to energy, cleaning up radioactive sites. Although it is long known that *Geobacter* use filaments for electron transfer (*Nature* 2002, 2005), it was not clear what they are actually made of and why they are conductive.

Our studies have revealed a surprise: the nanowires have a core of hemes lining up to create a continuous path along which electrons travel (*Cell*'19, *Nature Chem.Bio.*'20, *Nature Micro.-*'23) and and can be engineered with atomic precision using recombinant DNA technology, making for remarkably versatile electronic components.

We have further found that *Geobacter* pili remain hidden inside the cell and serve as a piston to secrete nanowire-forming cytochromes (*Nature* 2021) rather than functioning as a nanowire themselves as previously thought (*Current Opinion* 2020).

These studies solve a longstanding mystery to explain our previous findings that these bacteria transport electrons via nanowires (*Nature Nano.* 2014) over 100-times their size to electron acceptors (*Nature Nano.* 2011) and partner cells (*Science* 2010) and store electrons when acceptors are absent akin to how humans use their lungs (*ChemPhysChem* 2012) .

Our contact-free measurements of intrinsic electron conductivity in individual protein nanowires reveals how energetics and proximity of proton acceptors modulate conductivity by 100-fold (*PNAS* 2021, *Biochem. Journal* 2021). We have also developed synthetic protein nanowires with tunable conductivity and programmable self-assembly using non-natural click chemistry functionality (*Nature Comm.* 2022).

In this talk I will present our efforts to identify the physical and molecular mechanism of high conductivity of microbial cytochrome nanowires. Our conducting-probe AFM measurements show one of the highest electronic conductivity ever reported in proteins (> 100 S/cm) (*Nature Chem.Bio.*'20). Femtosecond transient absorption spectroscopy and quantum dynamics simulations reveal ultrafast (<200 fs) electron transfer between nanowire hemes upon photoexcitation, enhancing carrier density and mobility. Photoconductive atomic force microscopy shows up to 100-fold increase in photocurrent in purified individual nanowires. Photocurrents respond rapidly (<100 ms) to the excitation and persist reversibly for hours (*Nature Comm.*'22). Furthermore, nanowires and biofilms show non-classical temperature dependence of conductivity with cooling accelerating electron transport by 300-fold.

Our efforts to computationally model the heme redox potential and conductivity of nanowires yielded up to a billion-fold lower conductivity than

experiments (JPCB'21, JPCB'22), illustrating that the existing computational models based on electron hopping assumption fail to capture electron transfer in biological nanowires. This raises the possibility that biological nanowires employ a fundamentally different, currently unknown mechanism. Thus, existing models predict the same conductivity for all nanowires with computed timescales for heme-to-heme electron transfers (100 ns), million-fold lower than that measured using transient absorption in excited-state (*Nature Comm.*) and conductivity in ground-state for fully hydrated (*Nature* & *Cell*) or air-dried nanowires (*Science Adv.*).

Notably, multiple computational studies have predicted that invoking quantum effects could account for the high conductivity of these nanowires (*Nanotechology*'20, *IEEE*'21, *ACS Nano*'23). I will present our efforts to experimentally assess these computational predictions using multiple probes such as light, temperature, electric and magnetic fields. I will also discuss how our studies are helping to understand, predict and control extracellular electron transfer by nanowires used by diverse environmental microbes to capture, convert and store energy.

11.01.2024

REDOX MODULATION OF HEALTH AND DISEASE: From Inorganic Chemistry to Translational Medicine

Ritika Gautam

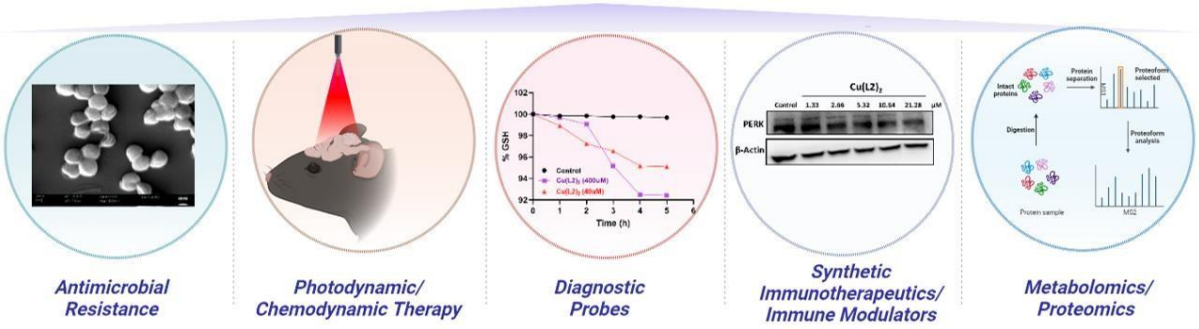
Department of Chemistry

Indian Institute of Technology Kanpur
Email: rgautam@iitk.ac.in

Abstract:

Biological Inorganic Chemistry is a burgeoning field in science. Our research group focuses on developing molecules and materials that positively impact human health. Our key strategyis to utilize modern inorganic, organometallic, and supramolecular chemistry to design and develop novel metal-based drugs that has capability to alter cellular metal trafficking and homeostasis to combat emerging pathogens and infection. We target metal – ligand interaction dynamics for site-selective drug discovery. The rapid emerging investigation in thefield of metalloenzymes and coordination chemistry is establishing a new platform for utilization of metal-biologically relevant ligand interactions for development of new drugs withtherapeutic application for illnesses, such as, neurodegenerative disorders, cancer, metabolicor autoimmune syndromes, and microbial infections. Specifically, the project includes, a). Design and synthesis of pharmaceutically relevant drugs by employing metal – ligand interactions dynamics, b). Synthesis of transition metal complexes with a potential to undergobiological processes like, electron transfer, small molecule catalytic activation and redox sensing, c). explore new avenues for these ligands and metal complexes in the field of therapeutics, diagnostics, immune modulators, anion recognition, and metal ion sensors, andd). utilize proteomics and metabolomics profile to establish the mechanism of action and determine the target site.

Metallodrugs



References and Notes:

1. Mjos, K. D.; Orvig, C. Metallodrugs in Medicinal Inorganic Chemistry. *Chem.Rev.* **2014**, *114*, 4540– 4563
2. Albada, B.; Metzler-Nolte, N. Organometallic–Peptide Bioconjugates: Synthetic Strategies and Medicinal Applications. *Chem. Rev.* **2016**, *116*, 11797– 11839

Anaerobic heme metabolism by a Microbiome Species produces protoporphyrin IX

Arnab Kumar Nath[1], Ronivaldo Rodrigues da Silva[1], Margaux M. Meslé[1], , Mensur Dlakić[2], Jennifer L. DuBois[1]

[1]Department of Chemistry and Biochemistry, Montana State University, Bozeman, MT 59717, USA

[2]Department of Microbiology and Cell Biology, Montana State University, Bozeman, MT 59717, USA

Bacteroides thetaiotaomicron (*B. theta*) is a member of the phylum Bacteroidetes and representative of species that are abundant in healthy gastrointestinal (GI) tract flora.[1,2,3,4] Heme metabolism by species like these is notable since the Bacteroidetes are obligate anaerobes and heme auxotrophs. We have shown that Bacteroidetes are sensitive to host dietary iron restriction but proliferate in heme-rich environments. are associated with colon cancer and typical of infected surgical wounds. Our work has focused on understanding heme metabolism by *B. theta* at both the system-wide and individual molecular levels. In *Bacteroides*, heme metabolism has previously been associated with the 6-gene heme metabolism uptake (*hmu)* operon, *hmuYRSTUV*.[1,2] The proteins encoded by these genes are predicted to be responsible for the uptake, trafficking, and removal of iron from heme[3], though many of these roles remain speculative. Among these *hmu* encoded proteins, the HmuS, an inner membrane bound protein and a member of the CobN/CbiX family of metal/porphyrin chelatases, is hypothesized to be necessary for catalyzing the removal of ferrous iron from heme in Gram-negative bacteria.[1,3,5] To verify this hypothesis and to reveal the unique anaerobic Fe removal pathway in *B. theta,* HmuS has been overexpressed using a recombinant bacterial plasmid carrying the corresponding gene. We present here initial spectroscopic and analytical results based on both the purified protein and *B. theta* cellular lysates.

References:

1. Lewis JP, Plata K, Yu F, Rosato A, Anaya C. 2006. Transcriptional organization, regulation and role of the Porphyromonas gingivalis W83 hmu haemin-uptake locus. Microbiology (Reading) 152:3367–3382.

2. Richard KL, Kelley BR, Johnson JG. 2019. Heme uptake and utilization by Gram-negative bacterial pathogens. Front Cell Infect Microbiol 9:81.

3. Rocha ER, Bergonia HA, Gerdes S, Smith CJ. 2019. Bacteroides fragilis requires the ferrous-iron transporter FeoAB and the CobN-like proteins BtuS1 and BtuS2 for assimilation of iron released from heme. MicrobiologyOpen 8:e00669.

4. Gruss A, Borezee-Durant E, Lechardeur D. 2012. Environmental heme utilization by heme-auxotrophic bacteria. Adv Microb Physiol 61:69–124.

5. Olczak T, Simpson W, Liu XY, Genco CA. 2005. Iron and heme utilization in Porphyromonas gingivalis. FEMS Microbiol Rev 29:119–144.

Poster Abstracts

Electro-catalytic CO_2 Reduction to Syngas and HCOOH by Homogeneous Fc-NAP_2

Sk Samim Akhter[a] and Sumanta Kumar Padhi*[a]

[a] Artificial Photosynthesis Laboratory, Department of Chemistry and Chemical Biology, Indian Institute of Technology (Indian School of Mines), Dhanbad, 826004.

Abstract

The burgeoning field of catalytic carbon dioxide (CO_2) reduction represents a pivotal domain within sustainable energy research. The utilization of polypyridyl ligands to effectuate the conversion of CO_2 into value-added products is notably infrequent. This investigation focuses on the employment of Fc-NAP_2 (Fc-NAP_2 = 1,1-bis[1,8-naphthyrid-2-yl]ferrocene) as a catalyst for CO_2 reduction in a CH_3CN/H_2O (90:10, v/v) solvent system under homogeneous electrochemical conditions at -1.6 V vs. saturated calomel electrode (SCE). The Fc-NAP_2 catalyst demonstrates notable efficacy in the generation of carbon monoxide (CO), formic acid (HCOOH), and hydrogen gas (H_2) from CO_2 through a proton-coupled two-electron reduction mechanism, exhibiting an overpotential of 735 mV vs. SCE. The observed turnover frequencies (TOF) and faradaic efficiencies for CO, H_2, and HCOOH are determined to be 8.5 h^{-1}, 14 h^{-1}, 4.61 h^{-1}, and 11.9±0.09%, 19.4±0.08%, 10.8±0.02%, respectively, at -1.6 V vs. SCE following 3 hours of electrolysis.

Formate Dehydrogenase on a Cu(II)-based Molecular Catalyst and Deciphering the Mechanism by DFT studies

Aman Mishra; [a] Dr. Sumanta Kumar Padhi [a]*

[a] Artificial Photosynthesis Laboratory, Department of Chemistry and Chemical Biology, Indian Institute of Technology (Indian School of Mines), Dhanbad, 826004.

Abstract

Formic acid (FA) is one of the most likely liquid organic hydrogen carriers (LOHC) and has drawn much interest because of the need to develop sustainable energy sources. Effective and ecologically friendly catalytic formic acid dehydrogenation remains a difficulty. This work has synthesized and characterized the $N3Q_3$ ligand and $[Cu(N3Q_3)Cl]Cl$ complex using a variety of techniques, including X-ray diffraction, mass spectrometry, NMR spectroscopy, EPR spectroscopy, cyclic voltammetry, and DFT calculation. In the presence of HCOONa, the dehydrogenation of formic acid using a molecular and homogenous catalyst $[Cu(N3Q_3)Cl]Cl$ is examined in this study. As a 1:1 CO_2 and H_2 mixture evolves, the mononuclear copper complex demonstrates catalytic activity towards the dehydrogenation of formic acid in H_2O. Based on the studies conducted at different temperatures, the activation energy of formic acid dehydrogenation was determined to be Ea = 86 kJ/mol. It was discovered that the breakdown of HCOOH requires 82 kJ of Gibbs free energy at 298 K. According to the DFT analyses, the $[Cu(N3Q3)(HCOO^-)]^+$ is generated via an uphill rearrangement process that is followed by decarboxylation. The rate-determining step is the first step in forming a transition state. In the presence of H_3O^+, the $[Cu(N3Q3)(H^-)]^+$ enters an active state that releases H_2 and produces the $[Cu(N3Q3)(OH_2)]^{2+}$.

Photosensitizer Free Novel K[Cu(NDPA)] Catalyzed Solar-Driven CO2 Reduction in Water

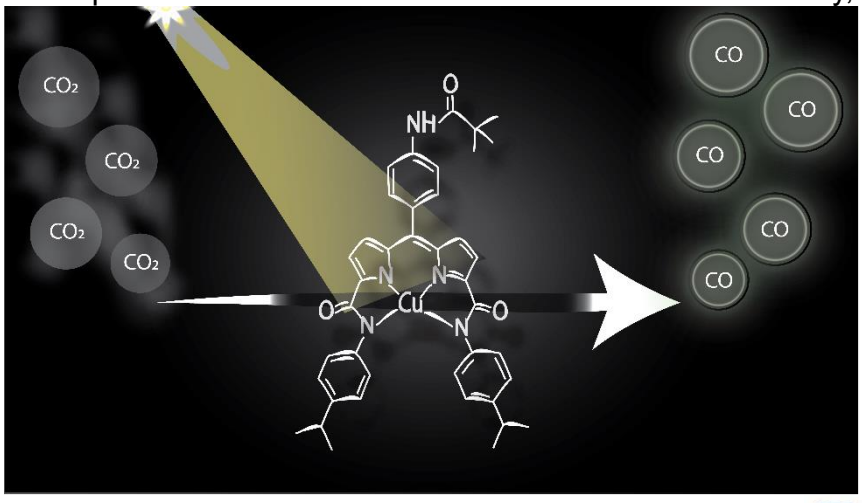
Soumadip Das[a], Navonil Chakrabarti[a], Aritra Roy[a], Aniruddha Sarkar[a], Biswajit Maiti[b], Sayam Sen Gupta[a]*

[a]Department of Chemical Sciences, Indian Institute of Science Education and Research Kolkata, India

[b]Department of Chemistry, Institute of Science, Banaras Hindu University, Varanasi, India

*Corresponding author's E-mail: sayam.sengupta@iiserkol.ac.in

In a world threatened by rising levels of CO_2, its reduction to value-added chemicals seems to be the only beacon of light to counter the danger of climate change. This chemical transformation of CO_2 will not only solve the intractable challenge of cleaning up the environment but also widen the prospect of securing clean energy.[1] As such, designing molecules that can effectively channel solar energy, the most used and most accessible source of renewable energy, is imperative. Since the external photosensitizer was not in direct contact with the catalyst, the majority of previously documented photocatalysts frequently depended on the photosensitizer's intramolecular electron transfer efficiency to the catalyst.[2] Efforts to remedy this include the introduction of a photosensitizing arm to the catalyst, but such attempts yielded an inferior TOF of 92.3h^{-1} with a binuclear Ru(II) complex [3] and a TOF of 50.83 h^{-1} with a FeTPP [4] complex. To that effect, a non-photosensitized catalyst is much more efficient. Therefore, putting together such robust systems, capable of both light harvesting and electron transfer, with earth-abundant elements is the need of the day.[2] Addressing this, here, a new Cu complex (K[CuNDPA]) bearing a dipyrrin amide-based trianionic tetradentate ligand has been presented, which is capable of harnessing solar energy without any external photosensitizer and photocatalytically reducing CO_2 to CO in water with a TON as high as 1132, a TOF of 560 h^{-1} and a selectivity of 99.37%. This complex also shows hemilability in water, which plays a role in the proton relay mechanism. The catalytic efficiency of this novel complex is significantly higher than the solely reported non-sensitized catalyst using the first-row transition metal-based Cu purpurin[5] complex, having a TON of 4.4 in the presence of BIH as a sacrificial donor. In this study, the photophysical



properties of K[CuNDPA] were explored. Triethyl amine served as a sacrificial donor, and water served as a proton source in the reductive cycle, which has been mechanistically and theoretically studied as well. This work opens up a new domain of earth-abundant robust molecular catalysts that can perform photocatalysis without the aid of any external photosensitizers.

References:

1. Dalle, K. E.; Warnan, J.; Leung, J. J.; Reuillard, B.; Karmel, I. S.; Reisner, E., Electro- and Solar-Driven Fuel Synthesis with First Row Transition Metal Complexes. *Chemical Reviews* **2019,** *119* (4), 2752-2875.
2. Lee, S. K.; Kondo, M.; Okamura, M.; Enomoto, T.; Nakamura, G.; Masaoka, S., Function-Integrated Ru Catalyst for Photochemical CO_2 Reduction. *Journal of the American Chemical Society* **2018,** *140* (49), 16899-16903.
3. Ishizuka, T.; Hosokawa, A.; Kawanishi, T.; Kotani, H.; Zhi, Y.; Kojima, T., Self-Photosensitizing Dinuclear Ruthenium Catalyst for CO_2 Reduction to CO. *Journal of the American Chemical Society* **2023,** *145* (42), 23196-23204.
4. Kosugi, K.; Akatsuka, C.; Iwami, H.; Kondo, M.; Masaoka, S., Iron-Complex-Based Supramolecular Framework Catalyst for Visible-Light-Driven CO_2 Reduction. *Journal of the American Chemical Society* **2023,** *145* (19), 10451-10457.
5. Yuan, H.; Cheng, B.; Lei, J.; Jiang, L.; Han, Z., Promoting photocatalytic CO_2 reduction with a molecular copper purpurin chromophore. *Nature Communications* **2021,** *12* (1), 1835.

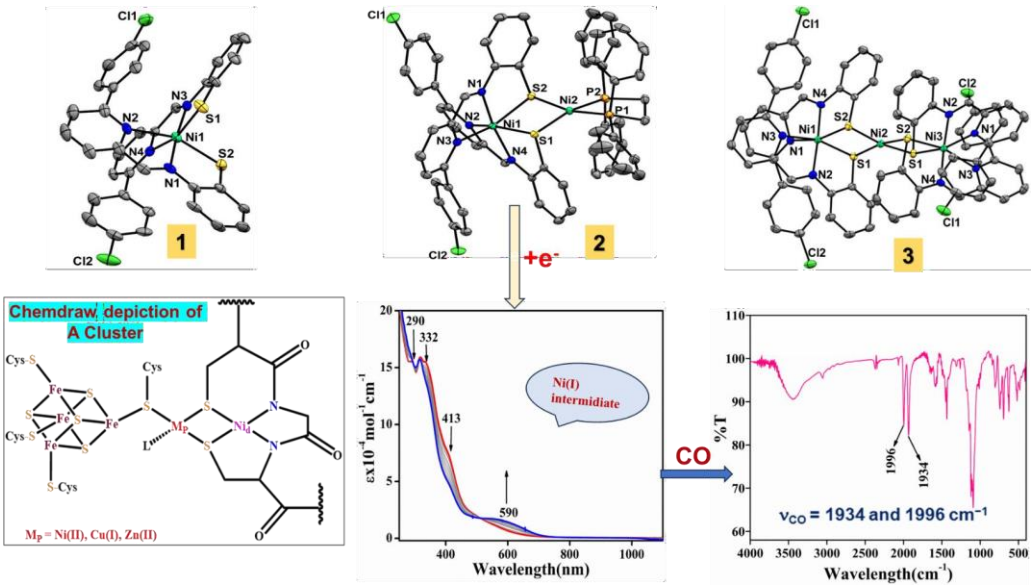
Structure, Electrochemical properties and CO reactivity of Nickel Complexes: Synthetic Analogues for Ni_p sites of the A-Cluster of Acetyl Coenzyme A Synthase/CO Dehydrogenase

Aniruddha Das,[a] Anirban Bhandari,[a] Shibaditya Kumar,[a] Apurba Kumar Patra*[a]

[a] Department of Chemistry, National Institute of Technology Durgapur, MahatmaGandhi Avenue, Durgapur 713 209, India

Abstract:

Primordial life processes stand on carbon-carbon bond formation from prebiotic precursors like carbon dioxide and carbon monoxide.1 Nickel-containing bifunctional metalloenzyme, carbon monoxide dehydrogenase (CODH)/acetyl coenzyme A synthase (ACS) plays two vital roles namely the reduction of CO2 to CO (CODH activity) that occurs at the C-cluster of the enzyme and the other is the synthesis of the biological metabolite, acetyl-CoA (ACS activity) that occurs at the A-cluster of the enzyme, utilizing the CO generated from C-cluster, a –CH3 group and the Coenzyme- A thiol. 2,3 The biochemical reactivity of the native enzyme reveals that the acetyl-CoA synthesis takes place at the labile Mp site of the A cluster (represented as Mp site in Scheme-1; M = Ni(II) or Cu(I) or Zn(II)) which has three Cys-S and an unknown ligand (L) coordination to Ni(II). The synthetic models for the Nip site are limited, though relatively more examples of Nid models are reported. In this poster, we present the synthesis, spectroscopic characterization including X-ray structure of few Ni(II)- thiolate complexes (mono-, bi- and tri-nuclear NiII complexes such as 1-3 and the hetero bi- and tri-nuclear complexes as 4 and 5 containing the Ni-Cu and Ni-Zn-Ni core respectively) as the model for Nip site. The X-ray crystal structure of 2 & 3 reveal a nearly square planar Ni(II)P2S2 and Ni(II)S4 moiety respectively those may mimic the reactivity of the Nip site of ACS. The lability of these NiS4 /NiP2S2 moieties have been checked by treating with phenanthroline that support the lability of Mp site of A cluster. The spectroelectrochemical studies and CO reactivity have been presented in details that may help to understand the mechanism of ACS activity of the enzyme. Generation of Ni(I) species following electrochemical or chemical reduction and subsequent Ni(I)- carbonyl species formation are spectroscopically evident (EPR spectrum of NiI species: g1 = 2.12, g2 = 2.02, g3 = 2.00; FTIR of NiI-(CO)2 adduct: □CO = 1934 and 1996 cm−1). Noteworthy, the □CO of model are comparable to that of the CO-bonded reduced A-cluster that displays the □CO at 1996 cm-1.



References:

(1) Manesis, A. C.; Yerbulekova, A.; Shearer, J.; Shafaat, H. S.; by Marcetta Darensbourg, E. Thioester Synthesis by a Designed Nickel Enzyme Models Prebiotic Energy Conversion. **2022**.https://doi.org/10.1073/pnas.

(2) Manesis, A. C.; O'Connor, M. J.; Schneider, C. R.; Shafaat, H. S. Multielectron Chemistry within a Model Nickel Metalloprotein: Mechanistic Implications for Acetyl-CoA Synthase. *J Am Chem Soc* **2017**, *139* (30), 10328–10338. https://doi.org/10.1021/jacs.7b03892.

(3) Bhandari, A.; Chandra Maji, R.; Mishra, S.; Kumar, A.; Barman, S. K.; Das, P. P.; Ghiassi, K. B.;Olmstead, M. M.; Patra, A. K. Model Complexes for the Nip Site of Acetyl Coenzyme A Synthase/Carbon Monoxide (CO) Dehydrogenase: Structure, Electrochemistry, and CO Reactivity..*Inorg Chem* **2018**, *57* (21), 13713–13727. https://doi.org/10.1021/acs.inorgchem.8b02276.

CO_2 Valorization: Electrochemical and Photoelectrochemical Conversion to Diverse Feedstocks

Anwesha Banerjee, Tannu Kaushik, Vaibhav Trivedi, Diya Bose, Suhana Karim*, Yashwant Pratap Kharwar*, and Arnab Dutta*

Department of Chemistry, Indian Institute of Technology Bombay, Powai-400076, Mumbai, Maharashtra, India.

The sustainability of the modern world is contingent upon devising strategies to lessen CO_2 emissions. Consequently, the industrial sectors that rely on fossil fuels face substantial difficulties; nonetheless, this energy paradigm shift presents chances for ingenuity and a re-evaluation of the techno-economic future. Understanding that carbon dioxide is both a resource and a culprit adds pragmatism to our efforts and turns the trip into a convoluted quest for balance and sustainability.

The synthesis of catalysts necessitates the role of an expert weaver in the alchemical furnace of CO_2 reduction, producing essential and commercially viable chemicals. Witness the biomimicry embodied in the biomass-derived carbon catalyst—a monument to our capacity to draw inspiration from nature's own carbonaceous reserves, meticulously built to shepherd the trip from greenhouse gas to valuable commodities. Here, we have modelled the basic architecture of carbon monoxide dehydrogenase (CODH) enzyme and moulded self-assembled copper oxide quantum dots anchored on an N-doped carbon motif (Cu_xO/NC) for generating an active CO_2 reducing electrocatalyst. This catalyst demonstrated a proclivity towards CO_2 reduction with a maximum Faradaic efficiency of ~95% towards CO_2RR to different products, mainly methanol (51%), formate (35%), and CO (9%) at an applied potential of -0.55V vs. RHE. The intricacies of reaction pathways, intermediates, and surface interactions vitally regulate the product selectivity during this CO_2 electroreduction. The detailed analysis indicated that the copper-based quantum dots play a crucial role in converting CO_2 into formate and ethanol with an appreciable catalytic efficiency. Next, this material is incorporated into an electrolyzer as we explore the possibilities of practical application of CO_2 electroreduction. This convergence of accuracy and possibility signals a concrete transition toward a cleaner and sustainable future originating from the fundamental knowledge of bio-inspired catalyst design and electrochemistry.

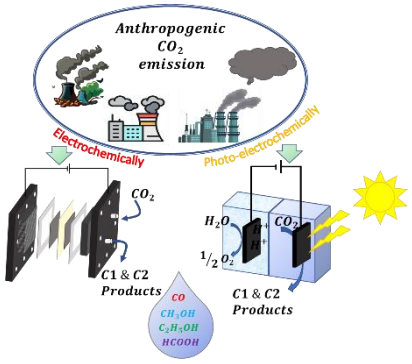


Figure. 1. Schematic representation of converting CO_2 to C1 and C2 products via electro and photo- electrochemical processes.

Plasmonic nanomaterials are regarded as leading photocatalysts due to their adjustable absorbance profile and enhanced selectivity, allowing for controlled molecular transformations. The strong plasmonic confinement of light energy enhances the electric field intensity at the metal nanoparticle surface, resulting in exceptional optical extinction

properties and thermal effects. A hybrid catalyst was designed by combining plasmonic gold nanoparticles' light absorption properties with copper-based molecular catalysts, mimicking the CODH enzyme to create an "antenna-reactor" complex. This nature-inspired plasmonic gold nanoparticle and molecular complex dyad expedites solar energy-driven CO_2 reduction into C1 and C2 reduction products with high efficiency.

This molecular opera addresses environmental concerns and transforms a once-dangerous gas into a variety of rare and beneficial commodities. This sleek science story blends conventional processes with inventiveness, delivering an elegant and potent story.

References:

1. Matsagar, B. M.; Yang, R. X.; Dutta, S.; Ok Y. S.; Kevin C. W. W. Recent progress in the development of biomass-derived nitrogen-doped porous carbon. *J. Mater. Chem. A,* **2021**, *9*, 3703-3728

2. Sargent, E. H. *et al.* Quantum-Dot-Derived Catalysts for CO2 Reduction Reaction. *Joule*. **2019**, *3*, 1703–1718.

3. Maity, T.; Jain S.; Solra M.; Barman S.; Rana S. Robust and Reusable Laccase Mimetic Copper Oxide Nanozyme for Phenolic Oxidation and Biosensing. *ACS Sustainable Chem. Eng.* **2022**, *10*, 1398-1407

Direct Capturing & Electrochemical Conversion of CO_2 using Bio-inspired Molecular Complexes

Chandan Das*[a], Somnath Guria*[a], B. Rajeshswaree*[a], Rathindranath Biswas*[a], Nilarun Koley[a], Thinles Dolkar[a], Ajay Kumar[a], Arnab Dutta[a]*

[a] Department of Chemistry, IIT Bombay, Mumbai, India-400076.
*Contacts: daschandancu16@gmail.com arnab.dutta@iitb.ac.in,

Abstract

Exponential increase of anthropogenic CO_2 emissions has caused disastrous environmental outcomes in the form of climate change effects. Carbon capture and conversion (CCUS) technologies are regarded as a major strategy to tackle the CO_2 problem. Currently, expensive and hazardous amine-based solvents are utilized for CO_2 removal from industrial flue gases. However, the overall cost and requirement of significant area for establishing the CO_2 capture units have posed serious questions about the long-term use of the amine solutions. Taking inspiration from the architecture of carbonic anhydrase enzyme[1], we have designed a synthetic zinc-based molecular complex that converts the CO_2 molecule into carbonate and bicarbonate in an aqueous medium under ambient conditions of temperature, pressure and pH. This aqua-based CO_2 capture technique works with industrial graywater and can sustain the presence of SO_x and NO_x in the flue gas. To further convert this captured CO_2 into industrially relevant feedstock materials, we have replicated the essential features of carbon monoxide dehydrogenase (CODH) enzyme in the form of peripheral protic functionalities around a molecular copper complex[2]. This copper complex[3] displays reversible interconversion[4] between CO_2 and CO in both organic and aqueous media under electrocatalytic conditions. This catalyst operates with minimal energy penalty (overpotential) on either side of the CO_2/CO equilibrium potential without the generation of any other side products. These efforts highlight the potential of biomimetic catalyst design strategy towards alleviating a global challenge and ushering us into a carbon-neutral future harbouring a circular economy.

Key words: CCUS, Bio-inspired catalyst design, Reversible electrocatalysis, CO_2 capture, CO_2 Conversion.

References:

1. Verma, M.; Bhaduri, G.A..; Phani Kumar, V.S.; Deshpande, P.A. 2021. *Ind. Eng. Chem. Res.* **2021,** *60*, 4777-4793.
2. Parkin, A.; Seravalli, J.; Vincent, K. A.; Ragsdale, S. W.; Armstrong, F. A.*; J. Am. Chem. Soc.* **2007**, 129, 10328–10329.
3. Guria, S.; Dolui, D.; Das, C.; Ghorai, S.; Vishal, V.; Maiti, D.; Lahiri, G. K.; Dutta, A. *Nat Commun* **2023**, *14*, 6859.
4. Dutta, A.; Appel, A.M.; Shaw, W.J.; *Nat. Rev. Chem.* **2018,** *2*, 244-252.

Effect of electrostatic and hydrogen-bonding interactions of a meso-substituted porphyrin on CO_2 reduction

Soumili Ghosh‡, Suman Patra‡, Abhishek Dey*

School of Chemical Science, Indian Association for the Cultivation of Science, 2A Raja SC Mullick Road, Kolkata, WB, India 700032

Reduction of CO_2 to value added chemicals is now of global interest to achieve sustainable and clean energy. This work focuses on synthesis, characterization and reactivity studies of a meso-substituted porphyrin having both electrostatic and hydrogen-bonding interactions. Characterization of this porphyrin has been done using NMR spectroscopy, mass spectrometry, UV-Visible spectroscopy and single crystal XRD. Both electrostatic and hydrogen-bonding effects cumulatively decreases the overpotential and determines the product selectivity upon CO_2 reduction. Electrochemical studies followed by GC-TCD and Ion-exchange chromatography reveals that CO_2 can be reduced to C1 and C2 products at a lower overpotential using H_2O as the proton source. Also, the ratio of the products changes with variation of the amount of H_2O used during the electrochemical studies.

Outer-Coordination Sphere Interaction in a Molecular Iron Catalyst Allows Selective Methane Production from Carbon Monoxide and Carbon Dioxide

Suman Patra ‡, Sarmistha Bhunia ‡, Dibyajyoti Saha, Soumili Ghosh, Abhishek Dey*

School of Chemical Science, Indian Association for the Cultivation of Science, 2A Raja SC Mullick Road, Kolkata, WB, India 700032

Reduction of oxides of carbon (CO and CO_2) into fixed forms of carbon is desirable to achieve sustainable and clean energy. Carbon monoxide (CO), an intermediate product in CO_2 reduction, is challenging to reduce which, in turn, jeopardizes the direct reduction (both electrochemical and photochemical) of CO_2 by $8e^-/8H^+$ to CH_4. Iron porphyrins can efficiently reduce CO_2 to CO by $2e^-/2H^+$ but further reduction is halted by rapid dissociation of CO from the reduced iron centre. This work show that CO can indeed be reduced upon inclusion of a pendent pyridine in the second coordination sphere of an iron porphyrin complex efficiently and selectively to CH_4 using water as the proton source. In-situ spectro-electrochemistry and theoretical modelling indicate that the pendent pyridine moiety imposes a hydrogen bonding interaction between the bound CO and adjacent water molecule which stabilizes two low-valent CO adducts i.e., Fe(I)-CO and Fe(0)-CO porphyrins, allowing its complete reduction, via a Fe(II)-CHO species, to CH_4. The ability to activate and reduce CO by ne^-/nH^+ via second sphere hydrogen bonding interaction in a mononuclear iron porphyrin opens newer pathways to valorise both CO and CO_2 to valuable C_1 products.

References:

Dey A, Bhunia S, Patra S, Saha D, Ghosh S. Second Sphere Interaction Allows Selective Reduction of CO and CO2 to CH4. ChemRxiv. Cambridge: Cambridge Open Engage; 2022.

Cobalt-NHC-based Molecular Electrocatalysts for the Electrochemical Hydrogen Evolution Reaction (eHER) and CO_2 Reduction Reactions (eCO_2RR)

Sanajit Kumar Mandal and Joyanta Choudhury*

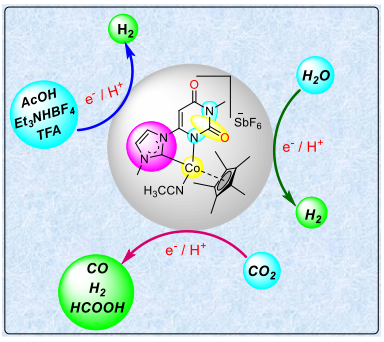
Organometallics & Smart Materials Laboratory (OSML)

Department of Chemistry, IISER Bhopal, Bhopal-462066

Email: sanajit17@iiserb.ac.in; joyanta@iiserb.ac.in

Abstract

H_2 is regarded as a potential sustainable energy carrier and as a promising replacement for non-renewable fossil fuels, and hence H_2 production via proton (ideally from H_2O) reduction reaction has become a central focus of research.[1] In parallel, CO_2 is also considered to be used for the generation of energy-dense carbon-based liquid and gaseous fuels,[2] and therefore, a variety of catalytic platforms have been investigated for CO_2 reduction to alternative fuels.[3] From the sustainability point of view, earth-abundant elements-based organic electrocatalysts show promise in the field of electrochemical proton (H^+) and CO_2 reduction reactions.[4,5] However, low activity and durability under electrochemical conditions pose a great challenge for future research toward the drastic improvement of these catalysts. Alternatively, the earth-abundant 1st-row transition metal-based electrocatalysts gained immense interest due to their high catalytic efficiency and enhanced durability operating under low overpotential. Interestingly, the structure and function of the primary and secondary active sites of the natural hydrogenases along with the mechanistic understanding of H_2 production via proton reduction, have had a tremendous influence on the recent developments toward designing efficient artificial molecular eHER and eCO_2RR electrocatalysts.[6] The existing challenges associated with the design of these catalysts include their long-term operational durability, efficient proton-transfer through secondary-sphere, and product selectivity (CO *vs* HCOOH *vs* H_2 for eCO_2RR). The current ongoing approaches to address the above issues rely on modulating the hydricity of the metal-hydride intermediates, pK_a of the proton source, the effect of the secondary coordination sphere, and the employment of suitable additives.



In the present work, initially detailed mechanistic investigation on amino-pyridine-anchored strongly sigma-donating N-heterocyclic carbene (NHC) ligand-based molecular Co catalysts (**Co-^{NHC}AP**) was conducted to understand the intramolecular proton-transfer ability of the pendant amino groups.[7] Based on the knowledge gained, later proton-responsive nucleobases such as uracil- and caffeine motifs were utilized as ligand-pendant on the NHC backbone to derive water-soluble cobalt-based electrocatalysts **Co-^{NHC}U** and **Co-^{NHC}Caf** in order to enable efficient intramolecular-proton transfer during the catalytic cycle. Eventually, the **Co-^{NHC}U** catalyst was found to provide the maximum turnover frequency (TOF_{max}) in the range of 10000-14000/s for the H_2 production reaction from the acid sources like Et_3NHBF_4 and CF_3COOH with Faradaic efficiencies of 93–98% at the overpotential range of

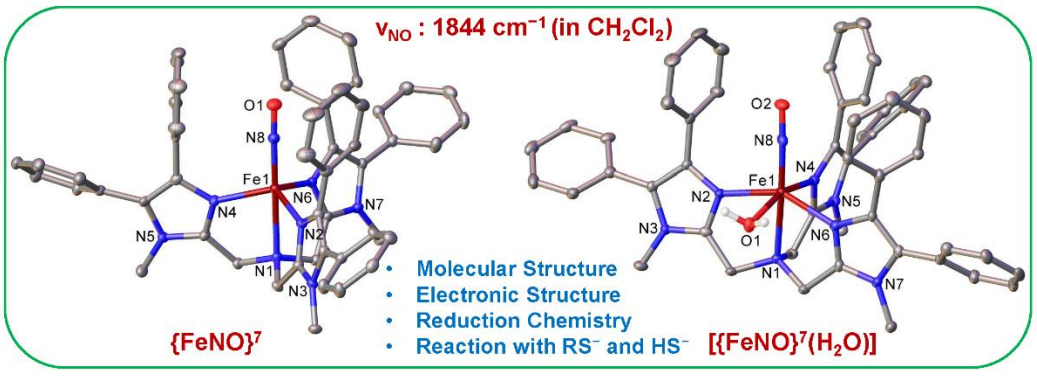
0.50–0.78 V.[8] Later on, the **Co-^{NHC}U** and **Co-^{NHC}Caf** catalysts were successfully utilized for the H_2 production from neutral H_2O with a very high catalytic rate (TOF_{max}) in the range of 15000-30000/s.[9] For the eCO_2RR reaction, interestingly, the **Co-^{NHC}U** catalyst provided around 75% CO selectivity, 80% H_2 selectivity, and 60% HCOOH selectivity as a function of different operating conditions.[10] These results will be illustrated and elaborated in the present poster.

References: (1) E. S. Wiedner, A. M. Appel, S. Raugei, W. J. Shaw, and R. M. Bullock, *Chem. Rev.* **2022**, *122*, 12427−12474. (2) S. Dey, T. K. Todorova, M. Fontecave, and V. Mougel, *Angew. Chem. Int. Ed*. **2020**, *59*, 15726 – 15733. (3) A. Kumar, R. Bhardwaj, **S. K. Mandal**, and J. Choudhury, *ACS Catal*. **2022**, *12*, 8886−8903. (4) P. Karak, **S. K. Mandal**, J. Choudhury, *J. Am. Chem. Soc*. **2023**, *145*, 7230−7241. (5) P. Karak, **S. K. Mandal**, J. Choudhury, *J. Am. Chem. Soc.* **2023***, 145,* 17321−17328. (6) L. Sun, C. Duboc, and K. Shen, *ACS Catal*. **2022**, *12*, 9159−9170. (7) **S. K. Mandal**, A. Gupta, J. Choudhury, *Manuscript submitted.* (8) **S. K. Mandal**, C. Sunil, J. Choudhury, *Manuscript under review.* (9) **S. K. Mandal**, J. Choudhury, *Manuscript submitted.* (10) **S. K. Mandal**, J. Choudhury, *Manuscript under preparation.*

Reactivity Of Thiolate and Hydrosulfide with a Mononuclear $\{FeNO\}^7$ Complex Featuring very High N-O Stretching Frequency

Soumik Karmakar and Amit Majumdar*
Email: cssk2340@iacs.res.in
School of Chemical Sciences, Indian Association for the Cultivation of Science, Kolkata-700032, India

Synthesis, characterization, electronic structure,and redox reactionsof a mononuclear $\{FeNO\}^7$ complex with a very high N-O stretching frequency in solution are presented. Nitrosylation of $[(L_{KP})Fe(DMF)]^{2+}$ (**1**) (L_{KP} = tris((1-methyl-4,5-diphenyl-1H-imidazol-2-yl)methyl)amine)produced a five-coordinate$\{FeNO\}^7$complex,$[(L_{KP})Fe(NO)]^{2+}$ (**2**). While complex **2** could accommodate an additional water molecule to generate a six-coordinate $\{FeNO\}^7$complex,$[(L_{KP})Fe(NO)(H_2O)]^{2+}$ (**3**), the coordinated H_2O in **3** dissociates to generate **2** in solution.Molecular structure of **2** features a nearly linear Fe-N-O unit with a Fe-N distance of 1.744(4) Å, N-O distance of 1.162(5) Å and <Fe-N-O angle of 178.3° while that of **3** features a slightly bent Fe-N-O unit with Fe-N distance of 1.750(5) Å, N-O distance of 1.157(6) Å and <Fe-N-O angle of 173.3°.Complexes, **2** and **3**,display a very high N-O stretching frequency of 1844 cm^{-1}in solution.Investigation of the reduction of **2** by FTIR-SEC and EPR spectroscopy shows the generation of a$\{Fe(NO)_2\}^9$ species and the results have been corroborated by electronic structure calculations. Furthermore, the reaction of **2** with bezenethiolate (PhS^-) and hydrosulfide (HS^-)allowed the unambiguous characterization of a DNIC, $[Fe(SPh)_2(NO)_2]^{1-}$,and an unprecedented complex, $[\{(L_{KP})Fe(DMF)\}_2\{Fe_6S_6(NO)_6\}]^{2+}$, featuring aniron-sulfurprismane dianion.

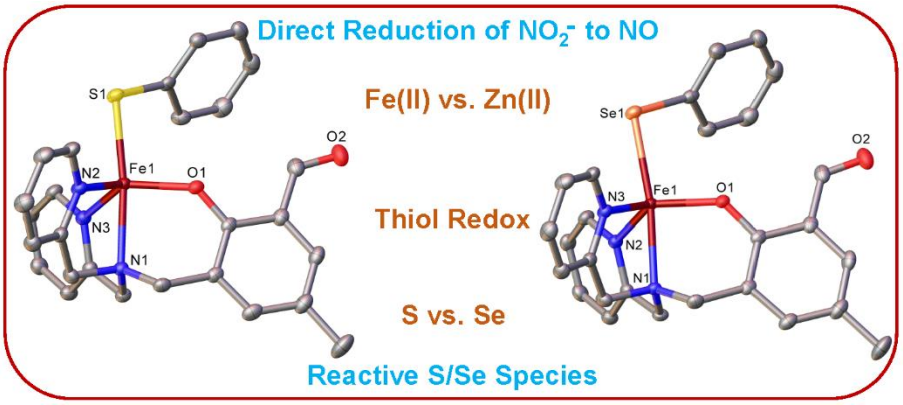


1. Moncada, S.; Palmer, R. M.; Higgs, E. A. *Pharmacol. Rev.***1991**, *43*, 109-142.
2. Moncada, S.; Higgs, E. A. *Brit. J. Pharmacol.***2006**, *147*, S193-S201.
3. Culotta, E.; Koshland, D. E. *Science* **1992**, *258*, 1862-1865.
4. Ignarro, L. *Nitric Oxide: Biology and Pathobiology*. Academic Press: San Diego, 2000.
5. Karmakar,S.; Patra,S.; Pramanik, K.; Dey, A.*;Majumdar, A.* *Work Under Progress*.

Reduction of Nitrite to Nitric Oxide and Generation of Reactive Chalcogen Species by Mononuclear Fe(II) and Zn(II) Complexes of Thiolate and Selenolate

Sayan Atta and Amit Majumdar*
Email: cssa2224@iacs.res.in
Indian Association for the Cultivation of Science, Kolkata-700032, India

Comparative reactivity of a series of new Zn(II) and Fe(II) compounds, [(Py2ald)M(ER)] (M = Zn / Fe, E = S / Se, R = Ph), and $[(Py2ald)M]_2^{2+}$ (M = Zn / Fe) is presented. Compound [(Py2ald)Zn(SPh)] could react with nitrite (NO_2^-) to produce [(Py2ald)Zn(ONO)], which, upon treatment with thiols and PhSeH (proton source), could regenerate [(Py2ald)Zn(SPh)] and [(Py2ald)Zn(SePh)] respectively, along with the production of nitric oxide (NO) where the yield of NO increases in the order ^{t}BuSH<<$PhCH_2SH$<PhSH<PhSeH. In contrast to this, $[\{(Py2ald)Fe\}_2](BPh_4)_2$, [(Py2ald)Fe(SPh)] and [(Py2ald)Fe(SePh)] could affect direct reduction of NO_2^- in the absence of proton to generate NO and $[\{(Py2ald)(ONO)Fe\}_2$-μ_2-O] with the latter regenerating its percussor upon treatment with 4 and 6 equiv of PhEH (E = S/Se), respectively, along with the generation of NO. Finally, a comparative study of the mononuclear Zn(II) and Fe(II) compounds for the transfer of the coordinated thiolate/selenolate and generation and transfer of reactive sulfur/selenium species (RES^-, E = Se, S) to a series of organic substrates has been provided.



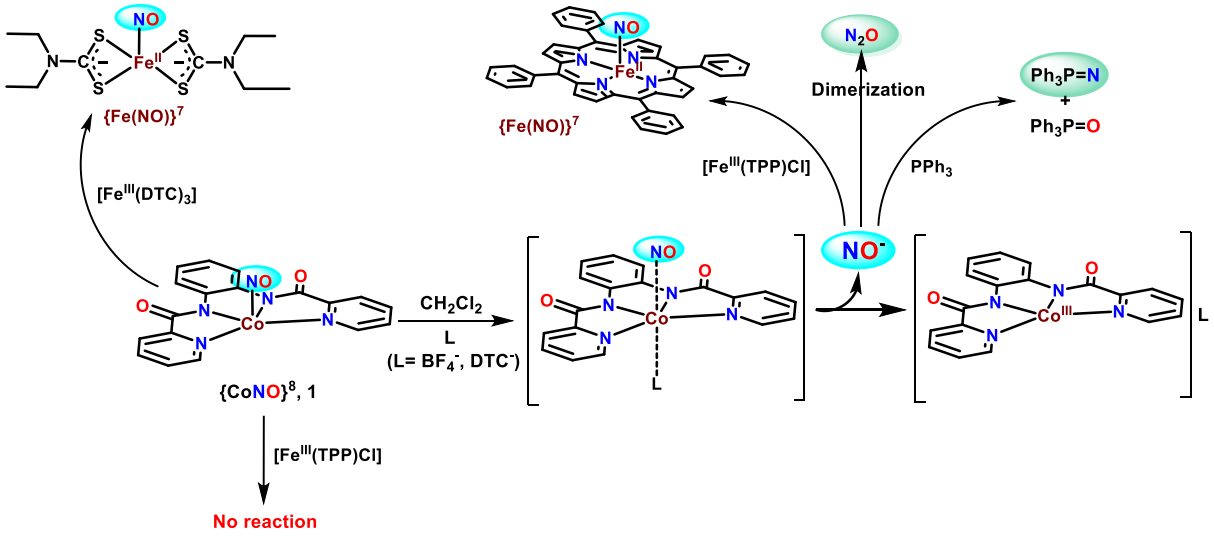
1. Atta, S.; Majumdar, A. *Chemistry – A European Journal* **2023**, 29, e202203579.
2. Atta, S.; Mandal, A.; Saha, R.; Majumdar, A.* *Work Under Progress*.

Sixth Ligand Induced HNO/NO^- Release by a Five-Coordinated Cobalt(II)-Nitrosyl Complex Having $\{CoNO\}^8$ Configuration

Shankhadeep Saha, Biplab Mondal*

Indian Institute of Technology Guwahati, Assam, India

The one electron reduced form of well-known biological signalling molecule Nitric Oxide (NO), Nitroxyl (NO^- or HNO) has some unique characteristics and can act as a therapeutic agent. But Nitroxyl is a short-lived species. Hence a donor molecule is required for its utilization. Metal nitrosyls (MNO) of suitable electronic configuration can be considered as potential HNO donor. Herein we report a cobalt-nitrosyl complex having $\{CoNO\}^8$ configuration along with its synthesis and spectral/structural characterization. The penta-coordinated $\{CoNO\}^8$ complex, **1** $[Co^{II}(BPB)(NO)]$ (BPB = 1,2-bis(pyridine-2-carboxamido)benzenate^{2-}) acts as an HNO/NO^- donor in presence of a sixth coordinating ligand such as imidazole, BF_4^-, DTC^- (DTC = diethyldithiocarbamate) etc which is confirmed by the presence of well-known NO^- acceptor like $[Fe^{III}(TPP)Cl]$ (TPP = tetraphenylporphyrin) and $[Fe^{III}(DTC)_3]$. Complex, **1** reacts with PPh_3 in presence of $HBF_4.Et_2O$ to give $Ph_3P{=}NH$ and $Ph_3P{=}O$ which confirms the HNO release. The release of HNO is further confirmed by the presence of N_2O in the head-space gas of the reaction vessel.



Scheme 1: Overall reactions

Reference:

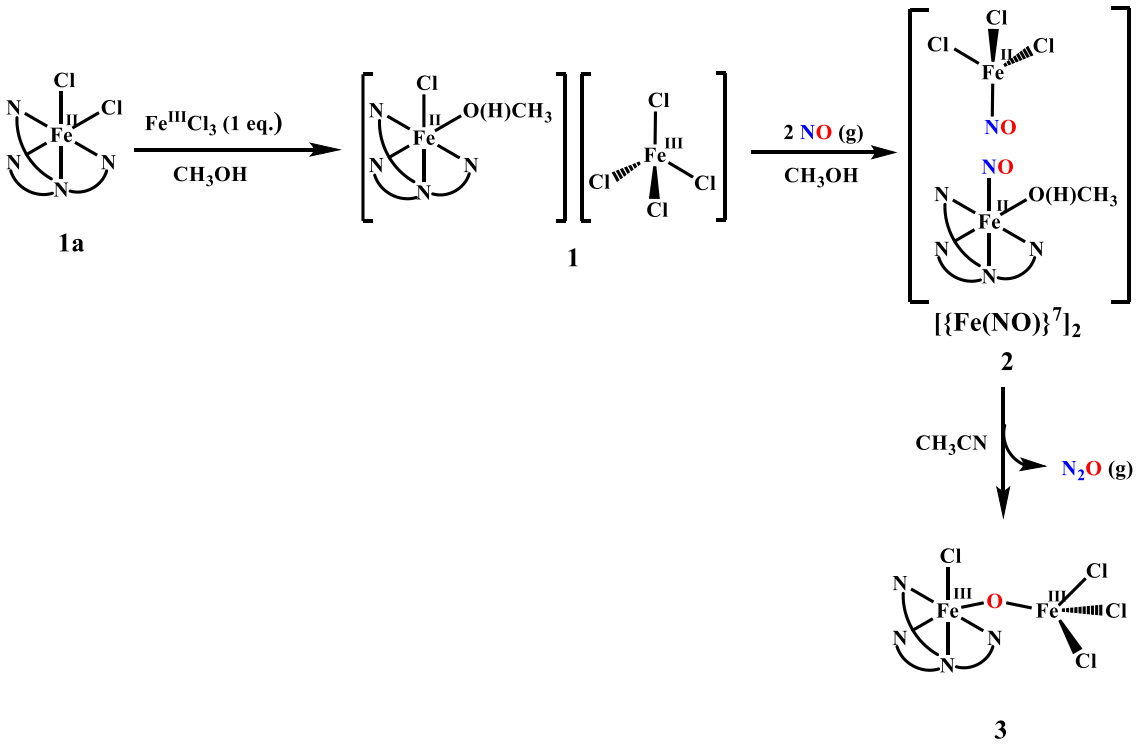
Saha, S.; Maity, S.; Mazumdar, R.; Samanta, B.; Ghosh, R.; Guha, A.; Mondal, B. *Inorg. Chem.*, **2023**, *62*, 17074–17082.

Small molecule model for nitric oxide reductase

Riya Ghosh[1], and Biplab Mondal[1*]

Indian Institute of Technology Guwahati, Assam, India

Flavodiiron nitric oxide reductase (FNOR) is an iron containing membrane bound bacterial enzyme that catalyzes the reduction of nitric oxide (NO) to less toxic nitrous oxide (N_2O). Active site form of bacterial nitric oxide reductase contains non-heme dinuclear ferric centers. Complex **1**, $[Fe^{II}L(Cl)(CH_3OH)][Fe^{III}Cl_4]$ (L = bis[(di(3,5-dimethyl-1H-pyrazolyl)methyl)]-(2-pyridylmethyl)amine) having a dinuclear iron core with two different coordination environment was synthesized and characterized structurally. The mixed valent diiron complex **1** upon reductive nitrosylation in methanol medium results in di-iron dinitrosyl complex **2** $[Fe^{II}L(NO)Cl][Fe^{II}Cl_3(NO)]$. Complex **2** in acetonitrile solution releases nitrous oxide (N_2O) with concomitant formation of μ-oxo di-ferric complex **3**. It is proposed that the reaction proceeds through a direct mechanism to form the N–N bond to generate ferric hyponitrite intermediate which decomposes to give N_2O and μ-oxo di-ferric complex. N_2O produced during the reaction was monitored *via* GC-MS. Thus, this complex **1** has been identified as catalytically relevant model for enzymatic di-iron active sites of NO reducing enzymes.



Scheme 1. Mechanistic stepss for N_2O formation from the [hs-{FeNO}^{7}]$_2$ complex.

References:

1. Hino, T.; Nagano, S.; Sugimoto, H.; Tosha, T.; Shiro, Y. *Biochim. Biophys. Acta,* **2012,** *1817*, 680-687**.**
2. Berto, T. C.; Speelman, A. L.; Zheng, S.; Lehnert, N. *Coord. Chem. Rev.* **2011,** *255,* 2764.

Acid-induced conversion of nitrite to nitric oxideat the copper(II) center: a new catalytic pathway

Prabhakar Bhardwaj and Pankaj Kumar*
Department of Chemistry, Indian Institute of Science Education and Research (IISER),Tirupati 517507, India

Email: pankaj@iisertirupati.ac.in

Acid-induced nitrite ($NO2^{-}$) reduction to nitric oxide (NO) on the Cu/Fe center is one of the key steps of the nitrogen cycle and serves as an essential path of NO generation. Here, we present a comparative study of catalytic acid-induced $NO2^{-}$ reduction chemistry of Cu^{II}-nitritocomplexes, $[(Me2BPMEN)Cu^{II}(NO2^{-})]^{+}$ (**1**) & $[(H2BPMEN)Cu^{II}(NO2^{-})]^{+}$ (**2**). Both the Cu^{II}-$NO2^{-}$
complexes showed the formation of NO(g) with H2O2 when reacted with one equiv acid (H^{+}) via the formation of a presumed Cu^{II}-nitrous acid ($[Cu\text{-}ONOH]^{2+}$) intermediate. However, the H2O2 amount decreases with time or an increase in H^{+} equiv and completely disappearswhen H^{+} is more than ~ two equiv and shows the generation of H2O. We detected the released NO(g) using headspace gas mass spectrometry. Mechanistic investigations using ^{15}N-labeled-$^{15}NO2^{-}$ & ^{18}O-labeled-$^{14}N^{18}O2^{-}$ revealed that the N-atom in the NO is derivedfrom $^{18}ONO^{-}$ ligand, which was further confirmed by observing ^{15}NO & $N^{18}O$ gas in the headspace gas mass spectrometry, respectively. We have also followed and characterizedthe formation of H2O2 (one-fold H^{+}) and H2O (two-fold H^{+}) and described why biological $NO2^{-}$reduction reactions generate NO with H2O. We have observed over 90 % recovery of **1** afterten catalytic cycles of NO(g) generation.

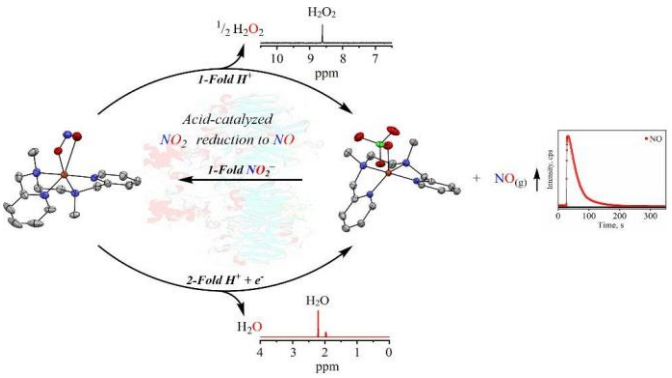


Figure 1 Catalytic cycle of copper-based nitrite reduction.

References:

1. Bhardwaj P.; Kulbir; Das, S.; Devi, T.; Kumar, P.; *Inorg. Chem. Front.* **2023.** DOI: 10.1039/d3qi01637d.

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

Ankita Sarkar,[1] Abhishek Dey,[2]

[1] *Address: 2A and 2B Raja S. C. Mullick Road, Kolkata 700032, India, ankita16chem@gmail.com*

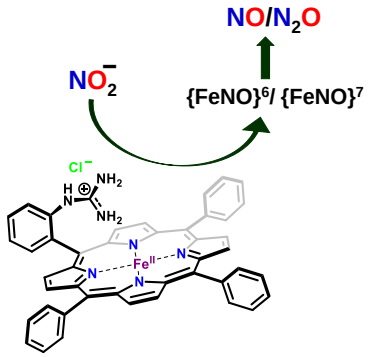
[2] *Address: 2A and 2B Raja S. C. Mullick Road, Kolkata 700032, India,*

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.

References:

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.



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

Reduction of Nitrite to Nitric Oxide and Nitroxyl at Cobalt(II)

Adarsh C. K., Anju B. S., and Subrata Kundu*

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

Thiruvananthapuram 695551, India adarshck20@iisertvm.ac.in,

skundu@iisertvm.ac.in

The reduction of nitrite (NO_2^-) is an important biochemical process due to its significance in biogeochemistry and physiology.[1] For example, nitrite anion serves assource of nitric oxide (NO) under hypoxia in the mammalian physiology. Copper and iron sites of various metalloenzymes are well known to catalyse nitrite reductase (NiR)activity for one-electron reduction of nitrite to NO.[2] Several examples of various transition metal mediated $1e^-$ reduction of nitrite to NO have been illustrated in the literature, whilst the demonstration of $2e^-$ reduction of nitrite to nitroxyl (NO^-/HNO) remains rare.[3] It is noteworthy that nitroxyl (NO^-/HNO) is proposed to be involved in distinct signalling activities along with its proposed intermediacy in the six-electron reduction of nitrite to ammonia mediated by cytochrome *c* nitrite reductase (*Cc*NiR).[4]

We herein employ a set of mononuclear cobalt(II)-nitrite complexes, which reacts with aliphatic thiol and provide NO and $\{Co(NO)2\}^{10}$ complex. Interestingly, the reactions ofthe same cobalt(II)-nitrite complex with relatively more acidic thiophenol results in HNO as assessed by the trapping experiments utilizing triphenylphosphine. A detailedstudy provide insights into the underlying mechanism and the factor controlling the NOversus NO^-/HNO generation from nitrite at the cobalt(II) site.

Reference

[1] J. O. Lundberg, E. Weitzberg, M. T. Gladwin, *Nat Rev Drug Discov* **2008**, *7*, 156–167.[2] L. B. Maia, J. J. G. Moura, *Chem Rev* **2014**, *114*, 5273–5357.

[3] F. Doctorovich, D. E. Bikiel, J. Pellegrino, S. A. Suárez, M. A. Martí, *Acc Chem Res* **2014**, *47*,2907–2916.

[4] D. Bykov, F. Neese, *Inorg Chem* **2015**, *54*, 9303–9316.

Selenium Dioxide Mediated Disproportionation of Nitrite

Tuhin Sahana, Adwaith K V, and Subrata Kundu*

adwaith19@iisertvm.ac.in, kvadwaithkv@gmail.com
School of Chemistry, Indian Institute of Science Education and Research (IISER)
Thiruvananthapuram 695551, India

Disproportionation of nitrite anion ($3NO_2^- + 2H^+ + 2NO + NO_3^- + H_2O$) is an importantstep in various physiological and pathological conditions and thus transforms nitrite tonitrate ($NO3^-$) and nitric oxide (NO). Nitrous acid (HNO2), generated from the protonation of nitrite anion at the low pH conditions of the stomach and ischemic tissues, is known to undergo disproportionation *via* N2O3.[1,2] Interestingly, ferric heme*b* protein in nitrophorin catalyses nitrite dismutase activity at neutral pH. The proposed catalytic cycle for the heme-Fe mediated disproportionation reaction involves oxygenatom transfer (OAT), where nitrite anion acts as both an O-atom donor as well as acceptor.[3] Considering the emerging reactivity of nitrite anion towards various electrophilic chalcogen compounds,[4,5] we are curious to investigate the reactions of selenium dioxide (SeO2) with nitrite. This work illustrates that nitrite anion reacts with SeO2 in anhydrous solvents, leading to nitrate and NO. Multinuclear NMR (^{77}Se and ^{1}H) studies have been utilised to identify the intermediates (such as nitroso-selenite, $O2SeONO^-$) en route to the final products. The nitroso-selenite intermediate is capable of *N*-nitrosating a secondary amine (Ar2NH), thereby acting as a NO^+ equivalent. Moreover, the proposed nitroso-selenite intermediate could also be generated independently from the reaction of nitrosonium ion (NO^+) and selenite (Na2SeO3). As a future scope, the present findings imply that various biologically relevant electrophilicchalcogen compounds may be suitable for nitrite dismutase reactivity in different physiological contexts.

References:

[1] J. L. Zweier, A. Samouilov, P. Kuppusamy, *Biochim. et Biophys. Acta* **1999**, *1411,* 250-262.
[2] M. R. Dent, A. W. Demartino, J. Tejero, M. T. Gladwin, *Inorg. Chem.* **2021**, *60*, 15918–15940.
[3] C. He, B. D. Howes, G. Smulevich, S. Rumpel, E. J. Reijerse, W. Lubitz, N. Cox, M. Knipp, *J.Am. Chem. Soc.* **2015**, *137*, 4141–4150.
[4] T. Sahana, A. K. Valappil, A. S. P. R. Amma, S. Kundu, *ACS Org. and Inorg. Au* **2023**, *3*, 246-253.
[5] G. Kolliyedath, T. Sahana, S. M. Johnson, S. Kundu, *Angew. Chem. Int.l Ed.* **2023**, e202313187.

Modelling of NO_x Reactivity at the Mononuclear Copper Sites

Balakrishnan S Anju, Neeraja R. Nair, Subrata Kundu*

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

The conversion of nitrogen oxides (NO_x), particularly nitrite (NO_2^-) and nitric oxide (NO), at copper sites are of great interest from the physiological as well as biogeochemical contexts.[1] For instance, *T1Cu* sites, commonly referred to as blue copper sites, involve a $(His)_2(Met)(Cys)Cu$ core for the transformation of NO-to-nitrite, thereby modulating NO homeostasis in blood plasma.[2] Although the one-electron reduction of nitrite-to-NO ($NO_2^- + e^- + 2H^+ \rightarrow NO + H_2O$) in mammals is primarily mediated by the iron/molybdenum sites of deoxyhemoglobin, cytochrome *c* oxidase (C*c*O), and xanthine oxidase,[2] the nitrite reductase (NIR) activity in prokaryotes utilizes *T2Cu* sites with a $(His)_3Cu–OH_2$ motif.[2] Interestingly, recent reports unveil the structural details of a unusual *T1Cu* protein, often referred to as a red copper protein, such as Nitrsoscyanin (**NC**).[3] Notably, the structural features and the spectroscopic signatures of **NC** in the oxidized and reduced states are hybrid of both *T1Cu* and *T2Cu* sites. Although the precise function of **NC** remains unclear till date, its unique structural aspects and presence in the nitrite-rich environments suggest a possible involvement in denitrification processes. This work herein employs a set of copper(II/I) complexes modelling the geometric features of the copper sites in **NC** to demonstrate the nitrite-to-NO transformation in the presence of various biologically relevant reductants such as phenols and 1-benzyl-1,4-dihydronicotinamide.[4] Furthermore, the same copper site has been demonstrated to interact with NO leading to the generation of a metastable $\{CuNO\}^{10}$ species, which transforms to nitrite in the presence of water and base.

References:

(1) (a) Gladwin, M. T. *Nat. Chem. Biol.* **2005**, *1*, 245. (b) Lundberg, J. O.; Weitzberg, E.; Gladwin, M. T. *Nat. Rev. Drug Discov.* **2008**, *7*, 156.

(2) Maia, L. B.; Moura, J. J. G. *Chem. Rev.* **2014**, *114*, 5273.

(3) Basumallick, L.; Sarangi, R.; George, S. D.; Elmore, B.; Hooper, A. B.; Hedman, B.; Hodgson, K. O.; Solomon, E. I. *J. Am. Chem. Soc.* **2005**, *127*, 3531.

(4) Anju, B. S.; Nair, N. R.; Kundu, S. *Angew. Chem. Int. Ed.* **2023**, *e202311523.*

Nitrite Reduction Coupled to the Transformation of Thiocarbonyls to Sulfane Sulfur via (Per)thionitrite

Gayathri Kolliyedath, Tuhin Sahana, Silpa Mary Johnson, and Subrata Kundu*

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

gayathri.k19@iisertvm.ac.in, gayathrikolliyedath96@gmail.com

Hydrogen sulfide (H_2S) and nitric oxide (NO) are now recognized as small molecule bioregulators (SMB) in mammalian biology, although they were historically consideredas toxic gases.[1] Cross-talks between H_2S and NO leads to the possible generation ofdifferent reactive sulfur, oxygen, and, nitrogen species (RSONs).[2] For instance, thionitrite (SNO^-) and perthionitrite ($SSNO^-$) serve as vital intermediates, which playsignificant roles in both H_2S and NO biochemistry.[3] This work demonstrates the reaction of nitrite anion with CS_2 to provide (per)thionitrite (SNO^-/$SSNO^-$) species under ambient conditions.[4] A detailed spectroscopic investigation including multinuclear NMR, UV-vis, and HRMS confirms the formation of (per)thionitrite as theintermediates, which subsequently transform to NO and other reactive sulfur species. Moreover, the reaction of nitrite with various other stable biorelevant thiocarbonyl compounds such as thiocarbamate, thioacetic acid have also been illustrated in generating (per)thionitrite. Employment of thiol or triphenylphosphine in the reaction of nitrite and thiocarbonyls illustrates the conversion of thiocarbonyl moiety to sulfane sulfur. Hence, this work reveals a new biologically relevent pathway for the simultaneous generation of sulfane sulfur and NO under metal-free conditions via cross-talk intermediates such as (per)thionitrite.

References

[1] G. K. Kolluru, X. Shen, S. Yuan, C. G. Kevil, *Antioxid. Redox Signaling* **2017**, *26*, 936–960.
[2] J. P. Marcolongo, M. F. Venâncio, W. R. Rocha, F. Doctorovich, J. A. Olabe, *Inorg. Chem.* **2019**, *58*, 14981–14997.
[3] I. Ivanovic-Burmazovic, M. R. Filipovic, *Inorg. Chem.* **2019**, *58*, 4039–4051.
[4] G. Kolliyedath, T. Sahana, S. M. Johnson, S. Kundu, *Angew. Chem. Int. Ed.* **2023**, e202313187.

Chalcogen Bonding Interactions Activate Nitrite Anion TowardsNitroxyl (HNO/NO⁻) Generation

Tuhin Sahana, Adwaith K. V., and Subrata Kundu*

sahana.tuhin17@iisertvm.ac.in,

tschem99@gmail.com
School of Chemistry, Indian Institute of Science Education and Research (IISER)
Thiruvananthapuram 695551, India

Chalcogen bonding (ChB) plays a crucial role in molecular recognition, thereby modulating different biochemical transformations and bioactivities.[1] For example, the unique binding ability of Ebselen (**Ebs**) to various protein domains is often attributed to the presenceof a selenium site, which renders it a potential drug under clinical trial against different pathogens, including hepatitis C virus (HCV), human immunodeficiency virus (HIV), SARS- CoV-2, etc.[2] Consistent with the previously reported interactions of **Ebs** with various small molecular species such as peroxide, superoxide, and hydroxyl radical,[3] we herein hypothesize that the presence of two σ-holes corresponding to the Se-N and Se-C bonds in**Ebs** may interact with nitrite anion and impact subsequent reactivity profile.

This work illustrates the interaction of nitrite anion with the σ-holes of **Ebs,** leading to the association complex **[Ebs□NO2□]**. The activated nitrite moiety in **[Ebs□NO2□]** serves as a potent nitrosating intermediate and is capable of catalyzing the transformation of amine to *N*-nitrosamine. Intriguingly, **[Ebs□NO2□]** also mediates 2e□ reductive transformations of nitrite to nitroxyl (HNO/NO□) in the presence of reductants such as 1-Benzyl-1,4-dihydronicotinamide (BNAH, a NADPH model) as well as triphenylphosphine (Ph3P). Of broader significance, thepresent work shows that a drug candidate like **Ebs** may significantly influence the biochemicalsignaling processes involving nitrite/nitric oxide/nitroxyl species.

References:

[1] Scilabra, P.; Terraneo, G.; Resnati, G.; *Acc. Chem. Res.* **2019**, *52*, 1313−1324.

[2] M. de Munnik, C. T. Lohans, P. A. Lang, G. W. Langley, T. R. Malla, A. Tumber, C. J. Schofield and J.Brem, *Chem. Commun.,* **2019**, *55*, 10214–10217.

[3] Thomas, S. P.; Satheeshkumar, K.; Mugesh, G.; Row, T. N. G.; *Chem. Eur. J.*, **2015**, *21*, 6793–6800.

Tuning the Reactivity of Nitrite at Copper(II) Towards the Generation of Nitric Oxide

Dhanusree C. Kakkarakkal, Rejith R Radhamani, and Subrata Kundu* School of Chemistry, Indian Institute of Science Education and Research (IISER), Thiruvananthapuram 695551, India
dhanusreeck20@iisertvm.ac.in, skundu@iisertvm.ac.in

Transformation of nitrite to nitric oxide mediated by transition metal sites is animportant process both in physiology and biogeochemistry. In mammals, reduction ofnitrite to NO is crucial under hypoxic conditions and are being catalyzed by iron- containing nitrite reductases such as hemoglobin and binuclear iron/copper-containingcytochrome c oxidase (CcO). Moreover, the biogeochemical denitrification pathway involves copper-containing nitrite reductase enzymes (CuNIR) present in many denitrifier organisms.[1] To gain insights into the enzymatic mechanism relevant to thesemetalloenzyme active sites, many first-row transition metal-containing nitrite model complexes have been previously synthesized and characterized. The possible mechanistic pathways include: (a) acid-mediated NO release; (b) proton-transfer assisted nucleophilic attack of the substrates like phenols, thiols, and amine; (c) oxygen atom transfer (OAT) pathway from metal nitrite complex in the presence of oxophilic species like phosphine, thioethers, CO;[2-3] (d) proton-coupled electron transfer (PCET) from substrates like phenols.[4-5] The first three pathways have been relatively well demonstrated with wide ranges of Fe/Cu-nitrite complexes, but the example of PCET-mediated nitrite reduction is rare. Herein, we employ a set of closelyrelated copper(II)-nitrite complexes supported by systematically tuned ligands for investigating the role of ligands on nitrite reduction reactivity. A detailed kinetic analysis along with electrochemical studies reveal the factors influencing the reduction of nitriteto nitric oxide at copper(II) through OAT and PCET pathways.[6]

References:

[1] Z. Sakhaei, S. Kundu, J. M. Donnelly, J. A. Bertke, W. Y. Kim, T. H. Warren, *Chem. Commun.* **2017**, *53,* 549–552.

[2] S. Maria, S, T. Chattopadhyay, S. Ananya, S. Kundu, *Inorganica Chim. Acta* **2020**, *506,* 119515-119516.

[3] M. Stauffer, Z. Sakhaei, C. Greene, P. Ghosh, J. A. Bertke, T. H. Warren, *Inorg. Chem.* **2021***, 60,* 15968-15974.

[4] A. Mondal, K. P. Reddy, J. A. Bertke, S. Kundu, *J. Am. Chem. Soc.* **2020,** *142*, 1726-1730.

[5] B. S. Anju, N.R. Nair, S. Kundu, *Angew. Chem.Int. Ed*. ***2023*** *e202311523.*

[6] D.C. Kakkarakkal, R. R. Radhamani; S. Kundu, *Manuscript in preparation*.

Inept N_2 Activation of Tri-Nuclear Nickel Complex with Labile Sulfur Ligands Facilitates Selective N_2H_4 Formation in Electrocatalytic Conversion of N_2

Anuj Kumar Ray[a], Ankan Paul[a*]

[a]School of Chemical Science, Indian Association for the Cultivation of Science,

Jadavpur, Kolkata- 700032.

The conversion of N_2 to N_2H_4 under benign conditions is highly desirable as it can serve as energy storage vector [1]. It has been recently reported that N_2 to N_2H_4 conversion can be achieved electrochemically by using a tri-nuclear $[Ni_3S_8]^{2-}$ complex [2]. There are hardly any precedents of Nitrogen Reduction Reaction (NRR) by molecular catalysts having Ni and the highly unusual selectivity for N_2H_4 over NH_3 makes this electrochemical reduction unique. We have conducted a systematic theoretical study employing calibrated Density Functional Theory [3] to unearth the mechanisms of NRR ($4e^-/4H^+$) and Hydrogen Evolution Reaction ($2e^-/2H^+$). This work presents a guided methodology for predicting reaction pathway taking into account the working electrochemical potential. Our findings unravel a curious case of ligand lability working in tandem with metal centers in facilitating this unprecedented electrocatalytic activity. Furthermore, it is shown that the poor N-N bond activation property of Ni is responsible for this unusual selectivity.

1. J. A. Carvalho, C. Bressan, J. L. G. Ferreira; Analysis of hydrazine as an alternate source of energy, *Energy,* **13** (1988), 149-152.

2. P. Saha, S. Amanullah, A. Dey; Electrocatalytic Reduction of Nitrogen to Hydrazine Using a Trinuclear Nickel Complex, *J. Am. Chem. Soc.,* **142** (2020), 17312-17317.

3. J. J. Moreno, S. L. Hooe, C. W. Machan; DFT Study on the Electrocatalytic Reduction of CO_2 to CO by a Molecular Chromium Complex, *Inorg. Chem.,* **60** (2021), 3635-3650.

Nitrite Reactivity of Copper(II) Complexes Supported by N_2S^{thiol} Donor Ligands

Shibaditya Kumar,[a] Saikat Mishra,[a] Aniruddha Das,[a] Milan Maji,[a] Apurba Kumar Patra*[a]

[a)]Department of Chemistry, National Institute of Technology Durgapur, Mahatma Gandhi Avenue, Durgapur 713 209, India

Abstract:

Nitrite (NO_2^-) can act as bioactive reservoir of nitric oxide (NO); the latter is an important molecule in living system that can regulate several key physiological processes including vasodilation, neurotransmission, immune stimulation and cell death.[1,2] Nitrite reactivity of copper complex supported by N,S^{thiol} donor ligand is lacking. Again, NO binding to the type 1 copper (His_2Cu-SCys) site is ambiguous whether occurs at Cu or Cys-S. A structurally characterized model complex shows NO binding at thiolato-S (i.e. S-nitrosylation) instead of copper(I/II).[3] In this poster we present the nitrite reactivity with two copper(II) complexes, [(L1)CuCl] (**1**) and [(L2)CuCl] (**2**), supported by N,S^{thiol} donor ligands, 2-((pyridin-2-ylmethylene)amino)- 4-(trifluoromethyl)benzenethiol (**HL1**) and 2-((pyridin-2-ylmethylene)amino)benzenethiol (**HL2**) respectively. The complexes, **1** and **2** displays quasireversible cyclic voltammogram at $E_{1/2}$ = +0.023 V and -0.056 V vs NHE respectively. Complex **2** shows NO_2^- binding upon reaction with $NaNO_2$ in presence of dioxygen(O_2) and generates a copper(II) bound nitrite complex [(L2)Cu^{II}(ONO)] (**4**), whereas following similar synthesis procedure complex **1** exhibits formation of Na[($L1^{COSO3}$)Cu^{II}(ONO)] (**3**), where $L1^{COSO3}$ is the di-anionic form of the modified ligand, 2-(picolinamido)-4-(trifluoromethyl)benzenesulfonic acid, generated *in situ* from L1 (Figure 1). The mechanism of **1** to **3** conversion has been studied by several spectroscopic methods (UV-Vis, EPR, FT-IR etc.) considering the reaction of **1** with $Na^{14/15}NO_2$ in presence or absence of O_2. Reaction in absence of O_2 leads to the

formation of a $\{CuNO\}^{11}$ intermediate, $[(L1^{SO})Cu(^{14/15}NO)]$(**3**$^{\#}$) following intramolecular oxo atom transfer (OAT) from Copper(II) bound nitrite to the thiolato-S of L1. The $\nu_{^{14/15}NO}$ observed in the FTIR spectra are 1712 and 1680 cm^{-1} respectively. The electronic absorption and EPR spectral results support the formation of **3**$^{\#}$. The **3**$^{\#}$ activates another molecule of O_2 and subsequently forms $[(L1^{SO2})Cu(^{14/15}NO_2)]$ (**3**$^{\#\#}$), evident from FTIR spectra; the latter eventually transform to **3** in presence of excess O_2 following mechanism as shown in the Scheme 1 below.

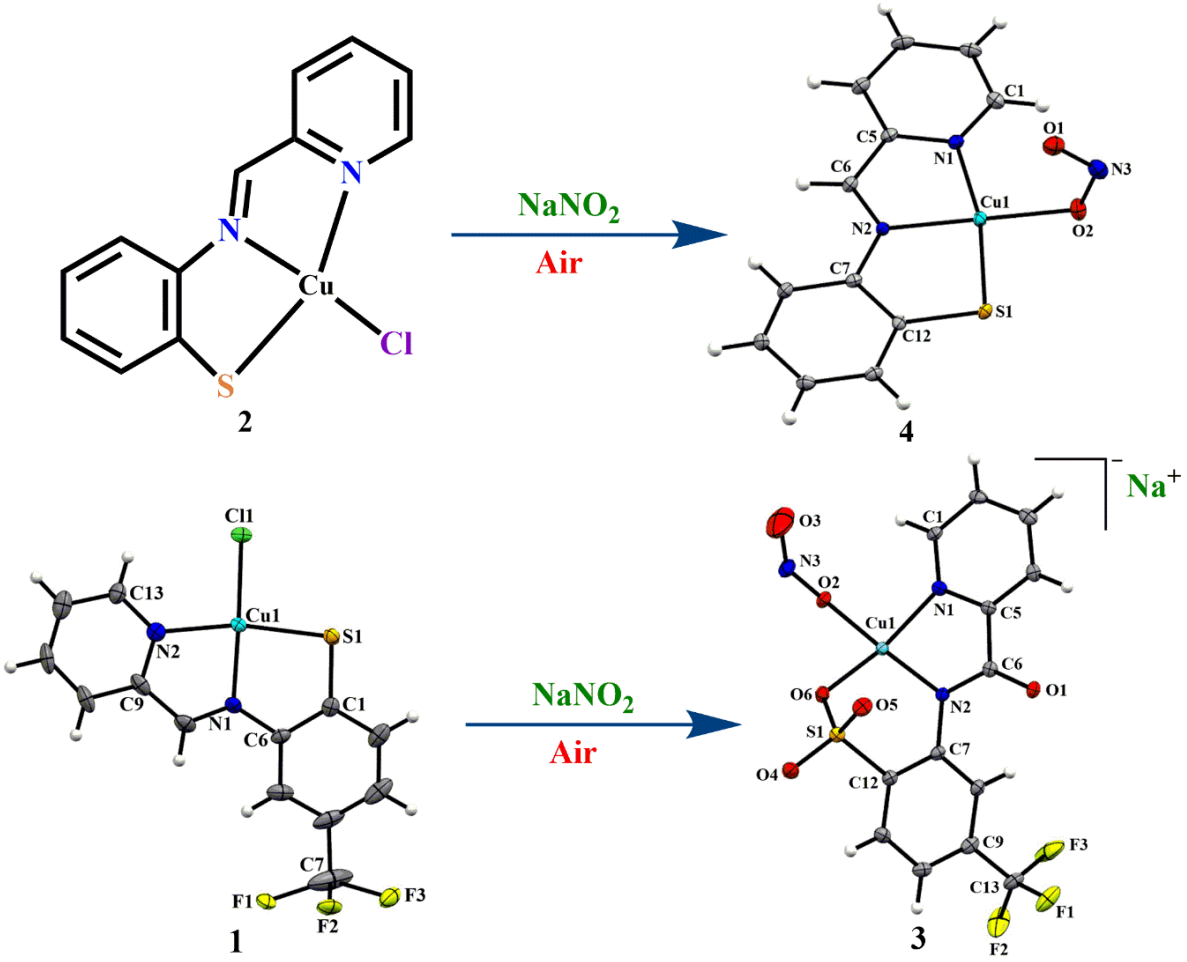
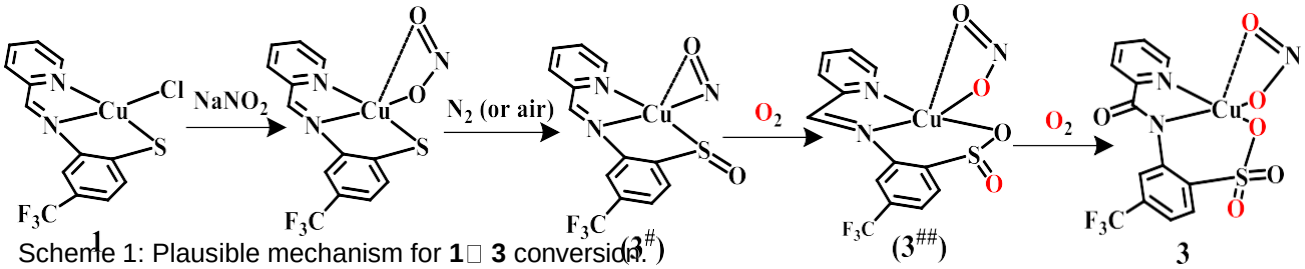


Figure 1: Chemdraw structure of **2** and ORTEP diagrams of **1**, **3** and **4**.



Scheme 1: Plausible mechanism for **1** → **3** conversion.

References:

1) Lundberg, J.; Weitzberg, E.; Gladwin, M. The nitrate–nitrite–nitric oxide pathway in physiology and therapeutics. *Nat. Rev. Drug Discov.* **2008**, *7*, 156–167.
2) Shiva, S.; Wang, X.; Ringwood, L.; Xu, X.; Yuditskaya, S.; Annavajjhala, V.; Miyajima, H.; Hogg, N.; Harris, Z. L.; Gladwin, M. T. Ceruloplasmin is a NO oxidase and nitrite synthase that determines endocrine NO homeostasis. *Nat. Chem. Biol.* **2006,** *2*, 486–493.
3) Zhang, S.; Melzer, M. M.; Sen, S. N.; Ölçüm, N. C.; Warren, T. H. A motif for reversible nitric oxide interactions in metalloenzymes. *Nature Chem.* **2016**, *8*, 663–669.

Electrocatalytic Ammonia Oxidation Mediated by Copper Complexes and Development of Ammonia Fuel Cells

Suchismita Ghosh*, Chandan Das*, Gulafshan, Suman Maity, and Arnab Dutta*

Department of Chemistry, Indian Institute of Technology, Bombay, Powai, Mumbai

Hydrogen molecule has been earmarked as the key component for the futuristic renewable energy-driven infrastructure. Nonetheless, the primary challenges to using hydrogen as a fuel are related to the logistics of safely handling and transporting massive amounts of liquid hydrogen. Ammonia can be utilized as a feasible mediator to address those lingering issues. Ammonia has one of the lowest source-to-tank costs due to its high hydrogen content in the molecular structure. Hydrogen to ammonia is already an established industrial process; however, the release of hydrogen from ammonia is still performed via energetically inefficient thermal processes. Room temperature direct ammonia fuel cells (DAFCs) have recently received increased attention, particularly for low-energy and rapid ammonia-to-hydrogen conversion. Ammonia oxidation reaction (AOR), which is the key step in establishing a DAFC, is thermodynamically challenging due to the strong N-H bond ($BDFE_{N-H}$ = 99.4 kcal/mol)[1], but transition metal-based molecular catalysts offer an energetically feasible pathway for AOR. Taking inspiration from the architecture of natural enzyme ammonia oxidation monooxygenase (AMO), we have developed a series of molecular copper complexes[2] coordinated by redox active ligands that mediate electrochemical ammonia oxidation in solution phase, even in the presence of air. Cyclic voltammetry (CV) and UV-vis spectroelectrochemistry (UV-SEC) studies were conducted to investigate the electrochemical and electrocatalytic properties of the molecular catalysts to gain insights into the mechanistic pathway. The catalytic data exhibit first-order rate dependency on both the molecular catalyst and the substrate ammonia. A battery of complementary spectroscopic techniques (EPR, in-situ UV-SEC, and FTIR) and electrochemical experiments were performed next, which unravel the formation of a vital copper-hydrazine intermediate. The electrocatalytic data illustrated a moderately fast catalytic reaction is (TOF ~188 s^{-1}), which is substantially higher than any previously reported copper catalysts.[3] Controlled potential electrolysis (CPE) and gas chromatography (GC) techniques highlighted an energy efficient ammonia oxidation to N_2 conversion with a Faradaic efficiency of 83%. The GC analysis further displayed a clean ~1:3 splitting of NH_3 into N_2 and H_2. This catalyst was able to catalyze both gaseous and solvent dissolved ammonia efficiently. Finally, this catalyst was assembled in a direct ammonia fuel cells (DAFCs), which operated room temperature with a high peak power density of 350 $mWcm^{-2}$, while displaying excellent stability under strong alkaline conditions. Hence, this catalyst can be a stepping stone in our journey towards an ammonia/H2-based energy transduction strategy.

Key Words: Ammonia oxidation reaction (AOR), Electrocatalysis, Homogeneous catalysis, Bio-inspired catalyst design, Direct ammonia fuel cell (DAFC).

References:

1. Warren, J. J.; Tronic, T. A.; Mayer, J. M. Thermochemistry of Proton-Coupled Electron Transfer Reagents and its Implications. *Chem. Rev.* **2010**, 110, 6961−7001.

2. Das.C†.; Ghosh, S†.; Maity. S.; YP Kharwar.; Dutta. A. (Manuscript under preparation,†: contribute equally)

3. Ahmed, M. E.; Raghibi Boroujeni, M.; Ghosh, P.; Greene, C.; Kundu, S.; Bertke, J. A.; Warren, T. H. Electrocatalytic Ammonia Oxidation by a Low-Coordinate Copper Complex. *J. Am. Chem. Soc.* **2022**, 144 (46), 21136–21145.

Homogeneous Electrocatalytic Nitrite Reduction to Ammonia by Iron Porphyrins containing Second Sphere Proton Transfer Residues

Sudip Barman, Paramita Saha, Abhishek Dey*

School of Chemical Sciences,

Indian Association for the Cultivation of Science

Jadavpur, Kolkata- 700032

Abstract:

Nitrite plays an important role in biogeochemical nitrogen cycles. In nature, metalloenzymes Cytochrome *c* Nitrite Reductase (CcNiR) and Siroheme containing Nitrite Reductase (CSNiR) both catalyze conversion of nitrite (NO_2^-) to ammonium (NH_4^+) using six electrons and eight protons ($NO_2^- + 8H^+ + 6e^- = NH_4^+ + 2H_2O$) and whereas heme d_1 containing nitrite reductase (Cd_1NiR) catalyzes NO_2^- to NO using one electron and two protons ($NO_2^- + 2H^+ + e^- = NO + H_2O$). Ammonia is intrigued as a potential carbon free energy carrier and a main feedstock for fertilizers, chemicals and pharmaceutical products.NH_3 is industrially produced by Haber-Bosch process using very harsh conditions which releases a very large amount of CO_2 into the atmosphere. Therefore, there is an urgent need for an alternative and sustainable route for ammonia production. Recently, electrocatalytic ammonia production from nitrite has been an attractive area of research, but achieving high Faradaic efficiency and avoiding competitive HER are still challenging. To best of our knowledge, nitrite reduction to ammonia reported so far were observed with water soluble iron-porphyrin complexes in buffer solution. Electrochemical generation of ammonia (NH_3) from nitrite (NO_2^-) catalyzed by Iron 1,3-Di-amido-pyridyl-tetraphenylporphyrin [FeIII(DA-Py)(Cl)] has been developed in this study. Controlled potential electrolysis of [FeIII(DA-Py)(Cl)] solution with nitrite (NO_2^-) in presence of 30 equivalent xylidinium chloride as a proton source (pK_a 10.98 in acetonitrile) at -0.77 V (vs $Fc^{+/0}$) generates nitric oxide with >90% Faradaic efficiency and at -1.4V (vs $Fc^{+/0}$) generates 78% ammonia and almost 12.9% nitric oxide. The mechanism and the optimum conditions for electrochemical conversion of NH_3 from NO_2^- catalyzed by [FeIII(DAPy)(Cl)] were studied in details by electrochemical and spectroelectrochemical methods.

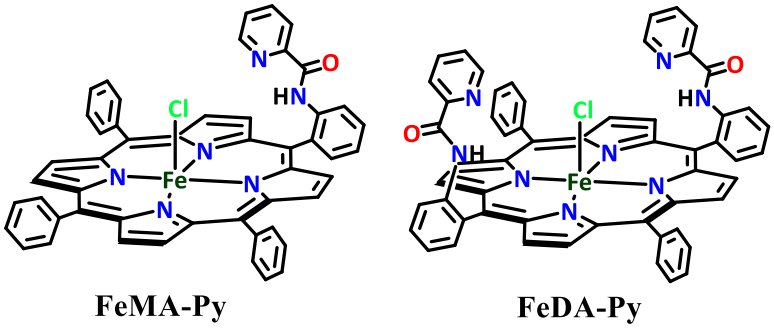


Figure: Structures of Synthesized Electrocatalyst for Nitrite Reduction

References:

(1) Shu-Hua Cheng, Y. Oliver Su; *Inorg. Chem*.,**1994**, *33*, 5847—5854

(2) Yuwu Chi*, Jingyuan Chen, and Koichi Aoki; *Inorg. Chem.,* **2004**, *43*, 8437−8446

(3) Mark H. Barley, Matthew R. Rhodes, and Thomas J. Meyer*; *Inorg. Chem.,* **1987**, *26*, 1746-1750

(4) Mark H. Barley, Thomas J. Meyer; *J. Am. Chem. Soc.*,**1986**, 108, *19,* 5876–5885

An Attempt to Use Peroxynitrite as NO Trigger from Ruthenium Nitrosyl Metal Complexes by Nitration of Tyrosine-based Axial Ligand

Shubham Sahu, Sagar Kumar, Govindasamy Mugesh**Department of Inorganic & Physical Chemistry Indian Institute of Science, Bangalore-560012*

Email: mugesh@iisc.ac.in

Nitric Oxide (NO) is an important gaseous signalling molecule in mammalians. Mainly, it helpsin maintaining rate of blood flow in vessels and hence maintains blood pressure and homeostatic supply of oxygen and nutrients to various body-parts. It also acts as a messengerin nerve cells of brain and as defender against pathogens (bacteria, fungi, virus etc.) in immune cells.

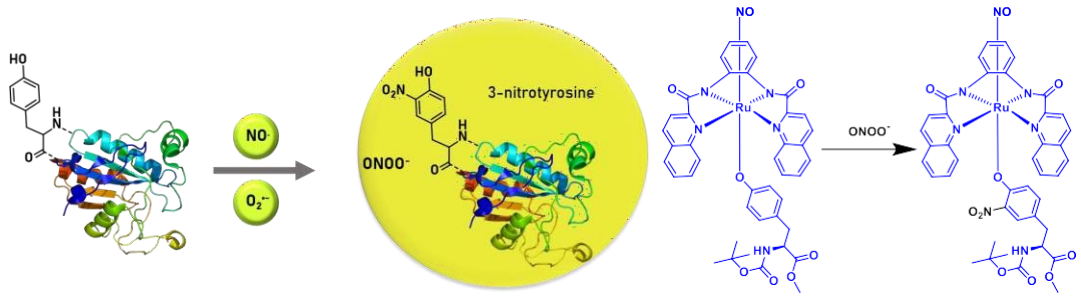


Figure: Protein tyrosine nitration as observed in biological systems (left) Nitration of synthesized Ru-nitrosyl tyrosine-derivative by peroxynitrite (right).

Various strategies/stimuli (light, enzyme, pH induced etc.) have been applied to release nitricoxide in biological systems. Ruthenium nitrosyl complexes have shown a great potential as anticancer agents. NO is a double-edge sword that means it can have both beneficial as wellas toxic roles depending upon its concentration. Here, we are trying to explore the positive aspect of NO in the context of cardiovascular complications. Oxidative stress (specifically peroxynitrite) has been found to be a severe concern in various cardiovascular diseases. Therefore, our aim is to utilize this highly toxic species for the good cause i.e. trigger NO release without light or increase the sensitivity of Ru-nitrosyl tyrosine derivatives towards light.

References:

(1) Loscalzo, J. and Welch G.; *Prog. Cardiovasc. Dis.* **1995,** *38,* 87-104.(2) Cosby, K., et al.; *Nat. Med.* **2003,** *9,* 1498-1505.

(3) Mocellin, S. et al.; *Med. Res. Rev.,* **2007,** *27,* 317-352.

(4) Rose, J. M. et al.; *J. Am. Chem. Soc.* **2008,** *130,* 8834–8846.

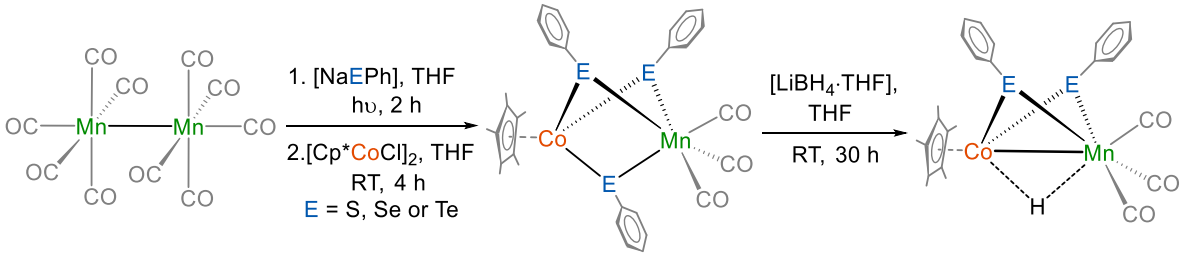
Bioinspired Chalcogenate Bridged Co/Mn Heterodinuclear Complexes for Electrocatalytic Hydrogen Production

Shivankan Mishra, Thinles Dolkar, Anvay Pareek, B. Rajeshwaree, Dillip Maity*, Arnab Dutta*, Sundargopal Ghosh*

Department of Chemistry

Indian Institute of Technology Madras, Chennai-600036, Tamil Nadu, India

To address the global energy crisis and have a source that is carbon neutral, there is an indispensable need to develop catalysts for hydrogen evolution. Nature has produced efficient enzymes called hydrogenases(H_2ases), i.e., [NiFe], [FeFe], and [Fe]H_2ases, each with a different metal content at the active site.[1] [NiFeSe]-H_2ases are a subclass of [NiFe]-H_2ases with a selenocysteine residue instead of cysteine, providing high catalytic activity and O_2 tolerance, making them ideal catalysts for H_2 evolution.[2] Many bioinspired heteronuclear transition metal (TM) complexes with thiolate ligands have been designed and synthesized; however, heterodinuclear transition metal complexes comprising heavier chalcogen atoms (Se or Te) are rare. In this context, we have synthesized half-sandwiched trichalcogenate-bridged MnCo heterobimetallic complexes $[(CO)_3Mn(EPh)_3(Cp^*Co)]$ (E = S, Se, Te), which further reacted with $[LiBH_4{\cdot}THF]$ yielding corresponding dichalcogenate hydride-bridged complexes $[(CO)_3Mn(EPh)_2(\mu\text{-}H)(Cp^*Co)]$ (E = S, Se, Te).[3] Electrocatalytic activity of these complexes in hydrogen production using acids as proton sources were investigated. The dichalcogenate hydride-bridged complex $[(CO)_3Mn(TePh)_2(\mu\text{-}H)(Cp^*Co)]$ shows excellent electrocatalytic H_2 production in the presence of fluoroboric acid. The key results of this work will be presented.



Scheme: Syntheses of di- or trichalcogenate-bridged heterobimetallic complexes.

References:

(1) (a) Lubitz, W.; Ogata, H.; Rudiger, O.; Reijerse, E; *Chem. Rev.*, **2014**, *114*, 4081-4148. (b) Schilter, D.; Camara, J. M.; Huynh, M. T.; Hammes-Schiffer, S.; Rauchfuss, T. B., *Chem. Rev.*, **2016**, *116*, 8693-8749.

(2) Wombwell, C.; Caputo, C.A.; Reisner, E.; *Acc. Chem. Res.*, **2015**, *48*, 2858-2865.

(3) Pathak, K.; Mishra, S.; Bairagi, S.; Rajeshwaree, B.; Dutta, A.; Ghosh, S.; *Organometallics*, **2023**, *42*, 133-145.

Bio-inspired catalyst design strategy for green hydrogen production

Santanu Ghorai, Srewashi Das, Naseer Ahmad Shah, Thinles Dolkar, Arnab Dutta*

Department of Chemistry, Indian Institute of Technology Bombay, Mumbai, India.
E-mail: 204036004@iitb.ac.in, arnab.dutta@iitb.ac.in

Production of green hydrogen from water electrolysis using renewable energy sources will be a key enabler in the global transition towards a carbon-neutral energy framework.[1] In nature, hydrogenase enzymes reduce protons from water at a very low overpotential values while operating at high turnover rates. An array of synthetic catalysts have been design by following the footsteps of hydrogenase architecture.[2] In this regard, an axial N-heterocycle-ligated cobaloxime core ($Co\text{-}N_5$) provides an excellent platform for the development of a model catalyst for HER. The poor solubility and instability of such cobaloxime derivatives in acidic aqueous medium limit its industrial application. Later on, these limitations were overcome with the rational incorporation of peripheral protic functionalities surrounding the cobaloxime core that imitates the enzymatic outer coordination sphere. In this work, we have strategically incorporated small amines, amino acids, vitamins, neurotransmitters (dopamine), drug molecules (isoniazide), and even nucleic bases to generate a pool of artificial outer coordinating sphere mimics surrounding the cobaloxime core. This has led to the generation of new genres of active H_2 production catalysts with boosted photo- and electrocatalytic H_2 evolution properties with an improved aqueous and air-stability.[3]Among them, the nucleic base appended complexes are found to be the leading H_2 production catalyst with turnover frequencies of ~12700 s^{-1} and overpotential around ~400 mV.[4] Nonetheless, these catalysts cease their H_2 evolution activity to minimum below pH 4.0. To overcome this, we synthesized a new complex containing a tripodal $Cu\text{-}N_6$ core, which produces H_2 at a rate of ~42500 s^{-1} with moderate overpotential even at very acidic media (~pH 1.0). Hence, this demonstrates the importance of bio-inspired catalyst design strategy for effective HER in aqueous conditions. Moreover, this unique enzyme-inspired catalyst design strategy can be heterogenized in electrolyzers for industrial green hydrogen production.

Reference:

(1) *Science*.176.4041.1323

(2) *ACS Catal.* **2019**, *9* (11), 10115–10125.

(3) *Chem. Commun.* **2020**, *56* (59), 8166–8181.

(4) *ACS Catalysis*, 2023, 13, 8238–8246.

(5) *Dalton Transactions*, 2023, 52, 1518-1523

Sustainable electrodes for green H_2 production from the alkaline water

Gulafshan*, Sukanta Saha*, Manodip Pal, Tarik Aziz, Arnab Dutta*

Chemistry Department

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

*Corresponding author, arnab.dutta@iitb.ac.in

Green hydrogen is regarded as the leading alternative for sustainable fuel, as we are trying to reduce fossil fuel utilization in an attempt to mitigate the carbon footprint. Categorizing competitive substitutes to fossil-fuel-based energy constitutes one of the prime research goals of this decade. Hydrogenase enzyme architecture is one of the major sources of inspiration as the scientific community is trying to emulate the efficient H_2 evolution reaction (HER) activity of the benchmark Pt/C. This unique hallmark of the enzyme is its protein scaffold-based outer coordination sphere (OCS), which has been artificially mimicked during synthetic catalyst design. This tactical inclusion promised to showcase improved hydrogen production at a rapid rate and exceptional efficiency in the solution phase. However, these homogeneous models fail to meet the practical features, such as durability, operational recyclability, and cost. Hence, a proper heterogenization of these bio-inspired catalysts is required to fulfill their potential as a technologically and economically viable solution for H_2 production on an industrial scale. Herein, we have introduced a tactically designed OCS feature on a silica-based template and anchored it to a synthetic molecular cobalt complex through an amine linker. It enables a highly robust and stable silica-supported molecular catalyst for promising large-scale green H2 production from alkaline water. In alkaline seawater, the catalyst illustrated superior catalytic performance in electrocatalytic conditions (TOF 3635 s^{-1}, overpotential 320 mV at 60 °C). These advances can potentially bridge the gap between molecular and materials catalysis by incorporating active site principles from bioinorganic chemistry, specifically in the form of an outer coordination sphere.

Seawater splitting is reckoned as the best way for HER, considering the shortage of potable water all over the world. Recent scientific endeavors have spotlighted the pivotal roles played by sulfide and double-layer hydroxide catalysts in revolutionizing this transformative technology. Transition metal phosphides (TMPs) offer another unique platform for developing electroactive materials, owing to their superior metalloid characteristics, redox-active oxidation properties, and decent electrical conductivity. TMPs have demonstrated remarkable electrocatalytic performance, including high activity and extensive durability towards hydrogen evolution reaction (HER) in acidic and alkaline as well as neutral electrolytes. We have now engineered a high electrochemical surface area (ECSA) of transition metal-based phosphide (Ni_2P) by assembling an interface with layered double hydroxides (LDH) and mild-oxidized carbon nanotubes (O-

CNT). This multi-functional Ni_2P@LDH_O-CNT exhibited not only an enhanced cathodic HER activity in a robust alkaline medium but also maintained an impressive durability for a full water-splitting by driving oxygen evolution reaction (OER). This HER and OER active dual catalyst can replace both state-of-the-art Pt and Ir-based electrocatalysts. This multi-functional Ni_2P@LDH_O-CNT exhibited not only an enhanced cathodic HER activity in robust alkaline medium but also maintained an impressive durability for a full water-splitting by driving oxygen evolution reaction (OER). This HER and OER active dual catalyst can replace both state-of-art Pt and Ir-based electro-catalysts. The Ni_2P@LDH_O-CNT exhibited a low overpotential for HER (107 mV @10 mA cm^{-2} and OER (482 mV @300 mA cm^{-2}), which competes with 20 wt% Pt/C, indicating the excellent potential of this new material for hydrogen evolution reaction in an alkaline medium. Additionally, we have prepared transition metal sulfide (TMS)-based catalysts that illustrated exceptional electron transfer properties. This material is strategically incorporated with LDH to utilize its tremendous potential in stable catalytic activities. Here, we have employed a monolithic cobalt sulfide CoS_2 with an interfacial FeCo $(OH)_2$ layered double hydroxide heterostructures (FeCo $(OH)_2$-CoS_2) to probe it as an active and stable alkaline electrocatalyst for seawater splitting. This hetero-interface electrode (FeCo $(OH)_2$-CoS_2/NF) offers practically high current density in the cathodic direction with low overpotential (207mV @ 100mAcm^{-2}) in regular water (pH 14.0). Interestingly, this catalyst maintained its superior reactivity in an alkaline seawater media (pH 13.0, 207mV @ 100mAcm^{-2}), which matched the state-of-the-art synthetic catalysts. This innovative strategy for generating multi-functional catalysts leads us to a new avenue in exploring new electrode materials relevant to energy conversion and storage technologies.

Electrocatalytic Hydrogen Generation by Ni-PN³P Pincer Complexes: Role of Anchoring Phosphorus Substituents in Tuningthe Reactivity

Neha Gupta,[a] Kuo-Wei Huang,[b] Sudipta Chatterjee[a,b]

[a]Department of Chemistry, Birla Institute of Technology and Science (BITS) – Pilani, K KBirla Goa Campus, Goa 403726, India

[b]KAUST Catalysis Centre and Division of Physical Science and Engineering, King Abdullah University of Science and Technology, Thuwal 23955-6900, Saudi Arabia

Abstract body: Hydrogen, an alternative energy source with a very high gravimetric energy density, produces carbon free water as the sole combustion product and therefore, can boost the energy sector by reducing the carbon footprint.[1] As a result, efforts have been made for several decades to catalyze electrocatalytic hydrogen evolution reaction (eHER) in an efficient and sustainable way.[2] In nature, hydrogenase enzyme is known to drive reversible hydrogen production with a high catalytic rate.[3] The detailed mechanistic understanding of hydrogenase guides the design of synthetic catalysts for direct application in electrocatalysis toward HER.[4] Deciphering the role of nickel (Ni) center in the active site of Ni-Fe hydrogenases, extensive research has been done to explore the reactivity of Ni site in molecular complexes. Recently, the use of Pincer ligand architecture has been evolved dramatically in electrocatalysis due to their versatility, flexibility, and stability.[5] Various Ni-pincer-based molecular complexes have been reported in the literature and tested for HER where the alteration in ligand backbone, particularly the donor atoms, found to play a vital role in eHER activity as well as stability.[6] However, the electronic effect on the catalytic activity due to the alteration in substituents on donor atoms has not been investigated yet. In this work, air-stable Ni(II)PN³P complexes have been synthesized which differ only in P-substituents. Interestingly, the redox potentials ($E_{1/2}$) are shifted by ~100 mV for $Ni^{II/I}$ and $Ni^{I/0}$ couples toward positive potential when bulky *tert*-butyl groups were gradually replaced by phenyl rings on each P-atom. Based on these observations, electrocatalytic HER activity for these complexes have been investigated in the presence of acids of different strength. The catalytic rate was found to be ~100 s^{-1} for all three complexes with 100 mM acetic acid. Electrochemical data under catalytic conditions show some unprecedented results for the metal-complex containing asymmetric ligand. Interestingly, the overpotentials required for eHER (ηHER) have been found to be reversed to the trend of $E_{1/2}$ values which can be attributed to the electronic effects of P-substituents. Mechanistic pathways for catalytic cycles have been proposed based on the experimental findings that are further supported by theoretical calculations.

References:

1. *Renew. Sust. Energ. Rev.,* **2019,** *120*, 109620.

2. *Appl. Sci.,* **2020**, *10*, 7708.
3. *Bioresour. Technol.,* **2011,** *102***,** *8423*.
4. *Chem. Rev.,* **2016**, *116*, 8693; *Int. J. Mol. Sci.,* **2023**, *24*, 8605; *Organometallics.,* **2023**, *42,* 1607.
5. *Catalysts.,* **2020**, *10*, 773.
6. *Inorg. Chem.,* **2012**, *51*, 8704; *Catal. Sci. Technol.*, **2022**, *12*, 7494; *Eur. J. Chem.,* **2021**, *27,* 13518.

Facile Electrocatalytic Proton Reduction by a [Fe-Fe]-Hydrogenase Bio-Inspired Synthetic Model Bearing a Terminal CN^- Ligand

Abhijit Nayek[†a], Subal Dey[†a], Suman Patra[a], Atanu Rana[a], Pauline N. Serrano[b], Simon J. George[b], Stephen P. Cramer[b,c], Somdatta Ghosh Dey[a] and Abhishek Dey[a*]*

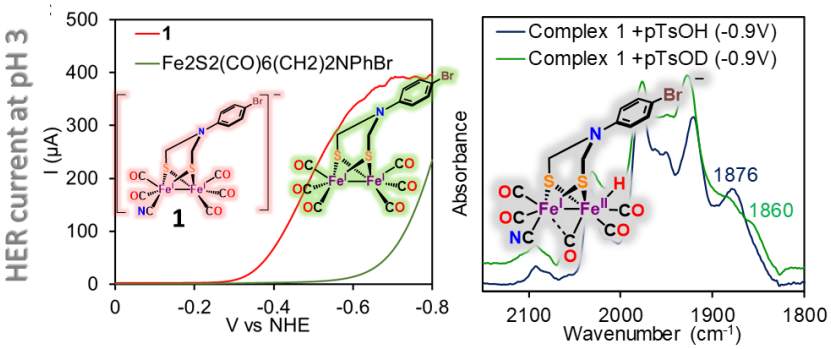
[a] School of Chemical Science, Indian Association for the Cultivation of Science, Kolkata, India-700032.

[b] Department of Chemistry, University of California, Davis CA 94616, USA.

[c] Physical Biosciences Division, Lawrence Berkeley National Laboratory, Berkeley CA 94720, USA

Email ID: icsgd@iacs.res.in , icad@iacs.res.in

An azadithiolate bridged CN^- bound pentacarbonyl bis-iron complex, mimicking the active site of [Fe-Fe] H_2ase is synthesized. The geometric and electronic structure of this complex is elucidated using a combination of EXAFS analysis, infrared and Mössbauer spectroscopy and DFT calculations. The electrochemical investigations show that complex **1** effectively reduces H^+ to H_2 between pH 0-3 at diffusion-controlled rates (10^{11} $M^{-1}s^{-1}$) i.e., 108 s^{-1} at pH 3 with an overpotential of 140 mV. Electrochemical analysis and DFT calculations suggest that a CN^- ligand increases the pKa of the cluster enabling hydrogen production from its Fe(I)-Fe(0) state at pHs much higher and overpotential much lower than its precursor bis-iron hexacarbonyl model which is active in its Fe(0)-Fe(0) state. The formation of a terminal Fe-H species, evidenced by spectroelectrochemistry in organic solvent, via a rate determining proton coupled electron transfer step and protonation of the adjacent azadithiolate, lowers the kinetic barrier leading to diffusion-controlled rates of H_2 evolution. The stereo-electronic factors enhance its catalytic rate by 3 order of magnitude relative to a bis-iron hexacarbonyl precursor at the same pH and potential.



References:

1. S. Dey, A. Rana, S. G. Dey and A. Dey, *ACS Catal.*, 2013, **3**, 429–436.
2. C. Esmieu and G. Berggren, *Dalt. Trans.*, 2016, **45**, 19242–19248
3. M. Winkler, M. Senger, J. Duan, J. Esselborn, F. Wittkamp, E. Hofmann, U.-P. Apfel, S. T. Stripp and T.Happe, *Nat. Commun.*, 2017, **8**, 16115.

Electrocatalytic Hydrogen Evolution Reaction by Bio-Inspired μ-Oxo Iron Complex with a Redox-Active Ligand having Proton Shuttle

Pankaj Kumar[#a], *Bharath M*[#a], *Anjumun Rasool*[b], *Serhiy Demeshko*[c], *Suresh Bommakanti*[d], *Rajeev Gupta**[e], *Manzoor Dar**[b], *Munmun Ghosh**[a]

a- Department of Chemistry, Ashoka University, Delhi NCR, Haryana, India.
b- Department of Chemistry, Islamic University of Science and Technology, Awantipora 192122 Pulwama, Kashmir, India.
c- Institute of Inorganic Chemistry, University of Göttingen, Germany
d- National Institute of science education and research, Bhubaneshwar, India
e- Department of Chemistry, Delhi University. Delhi. India

The role of proton relay near an open site of iron in [Fe-Fe]-hydrogenase (H2ase) proved to be crucial for hydrogen evolution reaction (HER) with remarkable rate and lower overpotential. Installation of proton relay in secondary coordination sphere as well as redox-active ligand was determined to be critical for tuning the catalytic activity.[1,2] In the present work we have shown electrocatalytic hydrogen evolution reaction (HER) by a μ-oxo dinuclear iron complex **[(Cl-Fe^{III}-L)$_2$-O]** (**Fe^{III}L**), featuring pyridine 2,6-dicarboxamide based thiazoline derived redox-active center. The crystal structure includes uncoordinated thiazolinium group and a μ-oxo group which act as proton channel in the catalytic cycle. The electrochemical responses in dimethylformamide (DMF) revealed that neutral **Fe^{III}L** complex exhibited a metal-centered reduction followed by a ligand-based reduction. In the presence of exogenous acids of varying strengths, **Fe^{III}L** displays electro-assisted catalytic response at distinct applied potential. Further investigation, utilizing both experimental data and density functional theory (DFT) calculations, reveal that fast-irreversible protonation of μ-oxo group in **Fe^{III}L** occurs upon reduction from Fe^{III} to the Fe^{II} in the presence of acid. Stepwise electron transfer and protonation reactions on the metal center and the ligand were studied through DFT to understand the thermodynamically favorable pathways. An operational ECEC or EECC (E stands for electron transfer and C stands for proton transfer step) mechanisms are proposed depending on the acidic strength and applied potential.

References

1. Schilter, D.; Camara, J. M.; Huynh, M. T.; Hammes-Schiffer, S.; Rauchfuss, T. B. Hydrogenase Enzymes and Their Synthetic Models: The Role of Metal Hydrides. *Chem. Rev.* **2016**, *116* (15), 8693-8749.

2. DuBois, M. R.; DuBois, D. L. The roles of the first and second coordination spheres in the design of molecular catalysts for H_2 production and oxidation. *Chem. Soc. Rev.* **2009**, *38* (1), 62.

Proton source-controlled mechanism of electrocatalytic hydrogen evolution reaction by pyridine-2,6-dicarboxamide based iron complex's

Bharath M[a], Meenakshi Rana[a], Vyom Prakash Tyagi[a], Suresh Bommakanti[b], Rajeev Gupta*[c] Aryya Ghosh*[a] and Munmun Ghosh*[a]

ABSTRACT

In the present study, we report the synthesis and electrocatalytic activity of a hexa-coordinated Fe(III)complex $Fe[L^1]_2$ towards hydrogen evolution reaction (HER). $Fe[L^1]_2$ displayed disparate pathways for HER in presence of acids with varying pK_a values in DMF. In presence of strong acid CF_3COOH (TFA), the hexa-coordinate complex undergo rupture, and the degraded species absorbed to the electrode surface as a Fe-containing film. Whereas in presence of weaker acids like $HNEt_3^+$ (TEA) and CH_3COOH (AcOH), complex displayed a metal-assisted ligand-centered pathway with better acid stability even at high substrate concentration. A maximum faradaic efficiency of 86% was observed for $Fe[L^1]_2$ when titrated with TEA. Geometry optimization of intermediates by DFT studies helped in understanding the mechanism for HER. Probable sites for protonation and reduction were evaluated by calculating the equilibrium constants and reduction potentials. A plausible metal-assisted ligand centered pathway is proposed for HER after gathering several insights from experimental and theoretical results. We also showed heterogeneous activity of the catalysts for HER under harsh conditions. Further we are exploring the activity of similar pyridine-2,6-dicarboxamide based iron complex's as heterogeneous catalyst towards small molecule activation.

PET Plastic Waste Valorisation by Metal-free Electrocatalyst with Co-generation of H_2

Bhavana R, Biswajit Mondal*
Department of Chemistry, Indian Institute of Technology Gandhinagar, Palaj-382355
rbhavana@iitgn.ac.in

Abstract

Plastic waste raises a multitude of concerns due to its disruptive influence on the environment and ecosystems.[1] The electrochemical conversion of polyethylene terephthalate (PET) waste into commodity chemicals has the potential to contribute to the establishment of a circular plastic economy, offering a sustainable approach. However, one major challenge in converting PET waste into useful C_2 products is the lack of an economically feasible and selective electrocatalyst to direct the oxidation process.[2,3] In the current research, metal-free (2,2,6,6- tetramethyl-1-piperidin-1-yl)oxyl (TEMPO) has been explored which can operate at low onset potential of 1.19 V *vs*. RHE in promoting electrochemical conversion of PET hydrolysate into glycolate with remarkable faradaic efficiency across a range of pH and applied potentials, combined with the production of hydrogen at the cathode. Chronoamperometry at a constant potential of 1.53 V *vs.* RHE yielded glycolate of 42.50% and 42.88% from Ethylene glycol and PET hydrolysate oxidation respectively with TEMPO at pH 10. Mechanistic insight has been elucidated by extending the oxidation of TEMPO to glycolate, oxalate, and formate which are the intermediate products being formed in Ethylene glycol oxidation. This work may provide a paradigm for developing PET upcycling technologies that have strong selectivity towards glycolate.

Keywords: *PET Plastic Waste, Metal-free Catalyst, Glycolate, Hydrogen production*

References:

(1) Yan, Y.; Zhou, H.; Xu, S.-M.; Yang, J.; Hao, P.; Cai, X.; Ren, Y.; Xu, M.; Kong, X.; Shao, M.; Li, Z.; Duan, H. Electrocatalytic Upcycling of Biomass and Plastic Wastes to Biodegradable Polymer Monomers and Hydrogen Fuel at High Current Densities. *J Am Chem Soc* **2023**, *145* (11), 6144–6155. https://doi.org/10.1021/jacs.2c11861.

(2) Du, M.; Zhang, Y.; Kang, S.; Xu, C.; Ma, Y.; Cai, L.; Zhu, Y.; Chai, Y.; Qiu, B. Electrochemical Production of Glycolate Fuelled By Polyethylene Terephthalate Plastics with Improved Techno-Economics. *Small* **2023**, *19* (39). https://doi.org/10.1002/smll.202303693.

(3) Zou, Y.; von Wolff, N.; Rauch, M.; Feller, M.; Zhou, Q.; Anaby, A.; Diskin-Posner, Y.; Shimon, L. J. W.; Avram, L.; Ben-David, Y.; Milstein, D. Homogeneous Reforming of Aqueous Ethylene Glycol to Glycolic Acid and Pure Hydrogen Catalyzed by Pincer-Ruthenium Complexes Capable of Metal–Ligand Cooperation. *Chemistry – A European Journal* **2021**, *27* (14), 4715–4722. https://doi.org/10.1002/chem.202005450.

Electrocatalytic Oxidation of Hydrogen by a series of bioinspired [Fe-Fe]-H_2ase Complexes

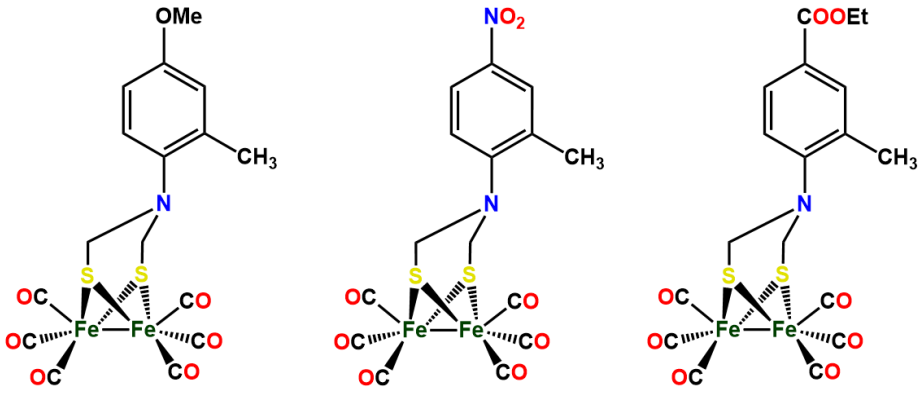
Rabin Kumar Poria, Abhijit Nayek, Somdatta Ghosh Dey* and Abhishek Dey*

School of Chemical Science, Indian Association for the Cultivation of Science,

Kolkata, India-700032

Email ID: icad@iacs.res.in, icsgd@iacs.res.in

Development of inexpensive and non-toxic electrocatalysts is the major concern for conversion of chemical energy to electrical energy efficiently which can be better replacement of costly Pt electrode in fuel cells. Naturally found hydrogenases are the metalloenzymes which are most efficient for Hydrogen production as well as hydrogen oxidation. We have already reported a series of oxygen tolerant hydrogenases model complexes mimicking the azadithiolato (ADT) bridged 2Fe subsite with synthetic procedures and crystallographic characterisations. The substituted arenes having the substitution in ortho and para position are attached with the bridgehead N atom in the S to S linker, $(\mu\text{-}S_2(CH_2)_2NAr)[Fe(CO)_3]_2$. The substituent at the ortho position on the arene offers steric control of the orientation of bridgehead N atoms, affecting their proton uptake and translocation ability. Here we have reported the effect on electrocatalytic homogeneous heterolytic cleavage of hydrogen on introducing electron withdrawing and donating group at the para position of the arene at various hydrogen concentration and varying external base (Et_3N) concentration.



References:

1. Md E. Ahmed, S. Dey, M.Y. Darensbourg, and A. Dey, J. Am. Chem. Soc. 2018, 140, 12457−12468.
2. Md E. Ahmed, A. Nayek, A. Križan, N. Coutard, A. Morozan, S. G. Dey, R. Lomoth, L. Hammarström, V. Artero, and A. Dey, J. Am. Chem. Soc. 2022, 144, 3614−3625.

Srijit Sen

Ashoka University

Abstract:

Amino acids play important role during the enzymatic catalysis of metalloenzymes. Here we have designed an amino acid based outer coordination sphere in form of protic functionalities, such as neutral amino acids, acidic amino acids and phenolic -OH group containing amino acids at the periphery of the iron-salen like complexes. Inclusion of such groups activate electrocatalytic H_2 evolution for an otherwise inactive iron-salen like core. The complexes having carboxylic acid groups exhibited unique pH-switchable catalytic H_2 production. The complexes show their activity below pH 6. Even though acidic amino acids have one more carboxylic acid group they are showing poor catalytic reactivity than neutral amino acids. Most probably due to acidic hydrogen exchange between two carboxylate groups rather than taking part in proton shuttling for H_2 production. These results highlight that an inactive metal complex can be activated for specific small molecule activation via rational inclusion of outer coordination sphere functionalities.

C-H bond activation facilitated by nickel(II) complexes having mighty claws

Anjana Rajeev and Muniyandi Sankaralingam*

Bioinspired & Biomimetic Inorganic Chemistry Lab, Department of Chemistry, National Institute of Technology Calicut, Kozhikode-673601, Kerala, India

*Email: msankaralingam@nitc.ac.in

Efficient oxidation of readily available hydrocarbons remains an ambitious objective in synthetic chemistry due to the widespread application of oxidised products.[1,2] Moreover, conventional methods employed for the commercial preparation of these oxidised products are associated with several drawbacks, such as high energy consumption, safety concerns, and adverse environmental impacts. In this regard, several attempts to develop simpler and more potent oxidation techniques were reported using a variety of metal complexes in the presence of suitable oxidants such as molecular oxygen, hydrogen peroxide, *t*-butyl hydroperoxide, and *m*-chloroperbenzoic acid (*m*-CPBA). However, the higher bond dissociation energy of C-H bonds poses challenges in obtaining the desired oxidised products with good yield and selectivity, and the process requires powerful catalysts to achieve beneficial results. Notably, owing to their excellent catalytic activity and adaptability in a range of chemical transformations, pincer ligands attracted a lot of study interest. In the present study, we synthesized a series of *NNN*-type tridentate pincer ligands (L1(H)-L4(H)) and isolated their corresponding nickel(II) complexes (**1-4**). The characterizations of complexes were done using a suite of modern techniques such as ^{1}H NMR, ATR-IR, ESI-MS, and single crystal XRD. Further, the catalytic activity of these complexes was investigated for the oxidation of a benchmark substrate cyclohexane in the presence of different oxidants. All the complexes showed appreciable activity in the presence of *m*-CPBA as the oxidant in DCM-CH_3CN (v/v =3:1) solvent mixture at 60 ^{o}C to yield cyclohexanol as the major product and chlorocyclohexane, cyclohexanone and caprolactone as the minor products. Under the optimised reaction conditions, complexes showed activity in the order **1** > **2** > **3** > **4**, which can be rationalized by the steric-electronic properties of the respective ligands. Also, the formation of a metal-based oxidant [(L)Ni^{II}-*m*-CPBA] was identified during the reaction of the catalyst with *m*-CPBA using UV-vis spectroscopy and ESI-MS.[3] The results will be discussed in detail during the presentation.

References:

(1) Sankaralingam, M.; Balamurugan, M.; Palaniandavar, M.; *Coord. Chem. Rev.* **2020**, *403*, 213085.
(2) Rajeev, A.; Balamurugan, M.; Sankaralingam, M.; *ACS Catal*. **2022**, *12*, 9953-9982.
(3) Rajeev, A.; Sankaralingam, M. Oxygen Atom Transfer Reactions, **2023**, *1*, 62-90.

Activation of inert C-H bonds of aliphatic alkanes using molecular dioxygen as the oxidant

Srijan Sengupta, Soumya Samanta, Manjistha Mukherjee, Sarmistha Bhunia and Abhishek Dey*

School of Chemical Sciences, Indian Association for the Cultivation of Science, 2A & 2B Raja S.C. Mullick road, Kolkata-700032

Email: srijansengupta381@gmail.com, icad@iacs.res.in

Catalytic oxidation of inert sp^3 C-H bonds of aliphatic alkanes using an environment friendly oxidant like dioxygen has been a goal of the scientific community for a long time. This oxidation reaction is performed in nature by a heme-based oxygenase enzyme called Cytochrome P450. It generates highly oxidizing intermediates (compound 0, compound 1, compound 2) in the process of dioxygen activation leading to O-atom incorporation in organic substrates, unlike oxidase enzymes where the intermediates are reduced by the reductase component of the enzyme. The same process has been mimicked by iron-porphyrin model complexes attached to self-assembled monolayer (SAM) covered electrodes, which generate the same intermediates while reacting with O_2. The SAM covered electrodes slow down the electron transfer rate from the electrode to the porphyrin complex thus showing more selectivity towards oxygenase activity rather than oxidase activity. Dioxygenase and monooxygenase activity using these synthetic iron porphyrins in this system has already been shown on substrates like toluene, styrene, cinnamaldehyde, adamantane by our group previously. We have recently shown the accumulation of Fe(III)-superoxo intermediate at steady state using SERRS-RDE technique and also shown the dioxygenation reaction on 2,3-dimethylindole, catalyzed by this intermediate. Our next goal was to oxidize inert C-H bonds of aliphatic alkanes using model iron-porphyrin complexes. Catalytic hydroxylation of inert 1° C-H bonds of n-pentane and 2° C-H bond of cyclopentane has been shown in aqueous buffer solutions by using heterogeneous electrochemical technique. The reactivity of the model iron-porphyrin complexes towards these substrates shows high dependance on the size and nature of the distal pocket which permits or does not permit the entry of the substrates. The hydroxylated products have been characterized by GC-MS and GC-FID techniques.

References:

(1) Mukherjee, M.; Dey, A. Electron Transfer Control of Reductase versus Monooxygenase: Catalytic C–H Bond Hydroxylation and Alkene Epoxidation by Molecular Oxygen. *ACS Cent Sci* **2019**, *5* (4), 671–682.
(2) Mukherjee, M.; Dey, A. Catalytic C–H Bond Oxidation Using Dioxygen by Analogues of Heme Superoxide. *Inorg Chem* **2020**, *59* (11), 7415–7425.
(3) Samanta, S.; Sengupta, S.; Biswas, S.; Ghosh, S.; Barman, S.; Dey, A. Iron Dioxygen Adduct formed during Electrochemical Oxygen Reduction by Iron Porphyrins show Catalytic Heme Dioxygenase Reactivity. *J. Am. Chem. Soc.* 2023, 145, 48, 26477–26486

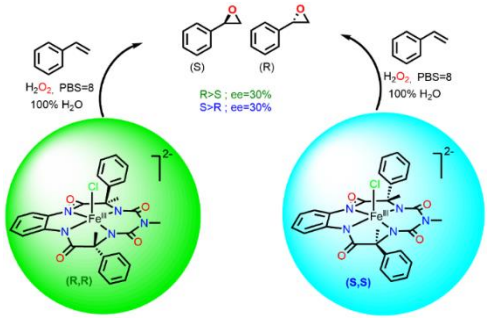
Enantioselective C-H Bond Activation By Non-Heme Oxoiron(V) Chiral Catalyst

Doyel Dey Biswas, Sayam Sen Gupta*

Department of Chemical Sciences, Indian Institute of Science Education and Research Kolkata, India

*Corresponding author's E-mail: sayam.sengupta@iiserkol.ac.in

The development of new chiral catalysts and asymmetric catalytic methods have been an active area of research in recent years, allowing chemists to access complex chiral molecules with high selectivity and efficiency. Asymmetric catalysis of C-H bonds inspired from cytochrome P450 has drawn special attentions because of high selectivity, well characterised mechanistic cycle and ambient reaction conditions. There are many reports on homogeneous chiral catalysts which gives stereoselective hydroxylated product and epoxides upon oxidation of C-H bonds and olefins respectively with green terminal oxidant like H_2O_2. Most of the reactions are performed at lower temperature and the active intermediate till not characterised. Here we reported a new generation of TAML catalyst, $[Et_4N]_2[((Ph,Me)bTAML)Fe^{III}(Cl)]$ which upon oxidation with H_2O_2 in water gives high yield of hydroxylated and epoxides products. The mechanistic cycle of this catalyst during the oxidation of C-H bond is through well-known active intermediate $Fe^{V}(O)$. Our strategy was to prepare chiral catalyst from the reported racemic $[Et_4N]_2[((Ph,Me)bTAML)Fe^{III}(Cl)]$ catalyst. Here in this work, we have resolved racemic starting material with Evan's oxazolidinone to separate the two diastereomers which consequently gives rise to two different catalysts which are enantiomers to each other. The catalysts were separately treated with H_2O_2 in water and the oxidations of styrene were performed with high ee.



References:

1. M. Milan, M. Bietti and M. Costas, Chem. Commun., 2018, 54, 9559

2. S. Jana, P. De, C. Dey S. G. Dey, A. Dey and S. S. Gupta **Chem. Sci.**, 2023,**14**, 10515-10523

Proximity Enabled Photochemical C–H Functionalization using a Covalent Organic Framework Confined Fe_2^{IV}–*μ*–oxo Species in Water

Poulami Majumder[1,2], Sayam Sen Gupta*[1] and Rahul Banerjee*[1,2].

[1]Department of Chemical Sciences, Indian Institute of Science Education and Research, Kolkata, Mohanpur 741246, India.

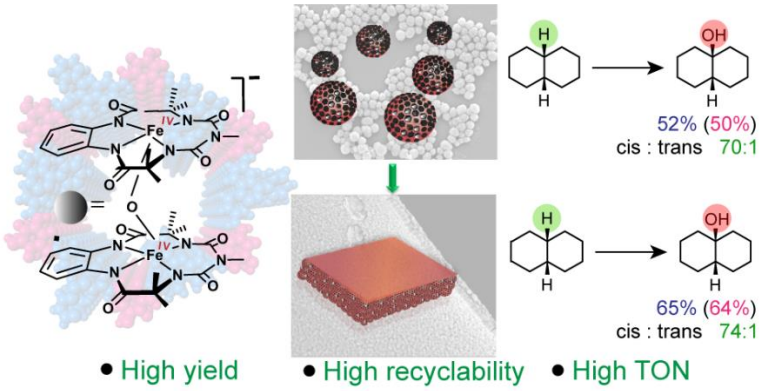
[2]Centre for Advanced Functional Materials, Indian Institute of Science Education and Research, Kolkata, Mohanpur 741246, India.

Email: pm17ip005@iiserkol.ac.in

Email: sayam.sengupta@iiserkol.ac.in

Email: r.banerjee@iiserkol.ac.in

Abstract: Water has been recognized as an excellent solvent for maneuvering both the catalytic activity and selectivity, especially in the case of heterogeneous catalysis. However, maintaining the active catalytic species in their higher oxidation states (IV/V) while retaining the catalytic activity and recyclability in water is an enormous challenge. Herein, we have developed a solution to this problem using covalent organic frameworks (COF) to immobilize the $(Et_4N)_2[Fe^{III}(Cl)$bTAML] molecules, taking advantage of the COF's morphology and surface charge**.** By using the visible light and $[Co^{III}(NH_3)_5Cl]Cl_2$ as sacrificial electron acceptor within the COF, we have successfully generated and stabilized the $[(bTAML)Fe^{IV}–O–Fe^{IV}(bTAML)]^-$ species in water. The COF backbone simultaneously acts as a porous host and as a photosensitizer. This is the first time that the photochemically generated Fe_2^{IV}–μ–oxo radical cation species has demonstrated high catalytic activity with moderate to high yield for the selective oxidation of the unactivated C–H bonds, even in water. To enhance the catalytic activity and achieve good recyclability, we have developed a TpDPP COF film by transforming the TpDPP COF nanospheres. We have achieved the regio and stereoselective functionalization of unactivated C–H bonds of alkanes and alkenes (3°:2° = 102:1 for adamantane with COF film) which is improbable in homogeneous conditions. The film exhibits C–H bond oxidation with higher catalytic yield (32-98%) and a higher degree of selectivity (*cis*:*trans* = 74:1; 3°:2° = 100:1 for *cis*-decalin).



References:

1. Sasmal, H. S.; Bag, S.; Chandra, B.; Majumder, P.; Kuiry, H.; Karak, S.; Sen Gupta, S.; Banerjee, R. Heterogeneous C−H Functionalization in Water via Porous Covalent Organic Framework Nanofilms: A Case of Catalytic Sphere Transmutation. *J. Am. Chem. Soc*. **2021**, *143*, 8426−8436.

2. Sen Gupta, S.; Stadler, M.; Noser, C, A.; Ghosh, A.; Steinhoff, B.; Lenoir, D.; Horwitz, C, P.; Schraman, K, W.; Collins, T. J. Rapid Total Destruction of Chlorophenols by Activated Hydrogen Peroxide. *Science* **2002**, *296*, 326–328.

3. Sasmal, H. S.; Halder, A.; Kunjattu H, S.; Dey, K.; Nadol, A.; Ajithkumar, A. T.; Bedadur, P. R.; Banerjee, R. Covalent Self-Assembly in Two Dimensions: Connecting Covalent Organic Framework Nanospheres into Crystalline and Porous Thin Films. *J. Am. Chem. Soc*. **2019**, *141*, 20371−20379.

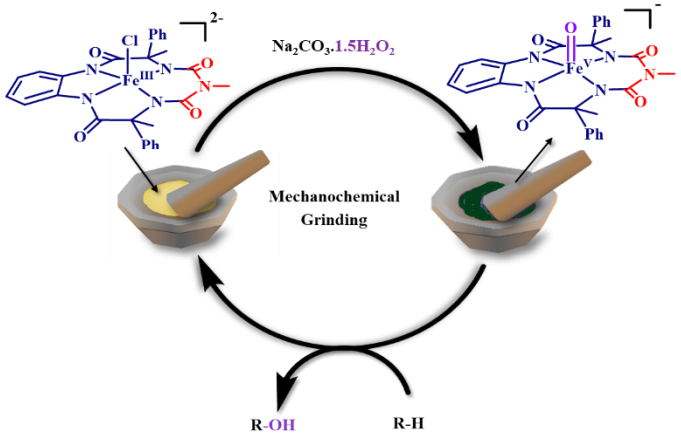
Solvent-free Hydroxylation of C-H bonds by Fe-complex: A Green Approach for Activation of Small Molecules and Polymers

Debasmita Chatterjee[a], Samir H. Chikkali[b], Swaminathan Sivaram[c*], and Sayam Sen Gupta[a*]

[a] Department of Chemical Sciences, Indian Institute of Science Education and Research, Kolkata, India
[b] Polymer Science and Engineering Division, CSIR-National Chemical Laboratory, Dr. Homi Bhabha Road, Pune 411008, India
[c] Department of Chemistry, Indian Institute of Science Education and Research Pune Dr. Homi Bhabha Road, Pune 411008, India
Email (dc18rs094@iiserkol.ac.in and sayam.sengupta@iiserkol.ac.in)

In the past few decades, there have been significant advances made in "solventless" solid-solid reactions. Such mechanochemically promoted processes often provide advantages over standard solvent-based methods, including higher yields, shorter reaction times, lower catalyst loadings, and mostly the avoidance of organic solvents and elevated reaction temperatures.

Herein this report, we have successfully eliminated solvent from the reaction system and come up with a green mechanochemical approach for oxidizing a wide array of substrates, including hydrophobic molecules, to natural products and medicinal drugs by a biomimetic Fe-bTAML catalyst. This methodology was successfully implemented for functionalizing the polyolefins, a major contributor to the landfill. We employed sodium percarbonate as an oxidant, which is a green and cheap source of solid H_2O_2. This is a truly green process since both the catalyst and oxidant are known to be non-toxic, and the only purification required would be to wash the excess oxidant and inactivated catalyst in water, thus addressing the hazardousness of an organic solvent in the reaction. We were able to characterize the reactive intermediate by solid-state UV, solid-state EPR, and mass spectrometry. All these measurements predict our reactive intermediate as oxoiron(V).



References

(1) Chen, M.S.; White, M.C.; *Science*, 2007, **318**, 783-787

(2) Ghosh, M.; Singh, K.K.; Panda, C.; Sen Gupta, S.; *J. Am. Chem. Soc.*, 2014, **136**, 9524–9527

How do Single Point Mutations Tame the Stereoselectivity in a Chemoenzymatic C(sp^3)−H Insertion

Ritwika Chatterjee and Garima Jindal*

Department of Organic Chemistry, Indian Institute of Science, Bangalore, Karnataka, India-560012

Abstract

New-to-nature enzymes have emerged as powerful catalysts in recent years for streamlining various stereoselective organic transformations. While synthetic strategies employing engineered enzymes have witnessed proliferating success, there is limited clarity on the mechanistic front and more so when considering molecular-level insights on the role of selected mutations, dramatically escalating catalytic competency and selectivity. We have investigated the mechanism and correlation between mutations and exquisite stereoselectivity of a lactone carbene insertion into the C(sp^3)−H bond of substituted aniline, catalyzed by two mutants of a cytochrome P450 variant, “P411” (engineered through directed evolution) in which the axial cysteine has been mutated to serine, utilizing various computational tools.[8] The pivotal role of S264 and L/R328 mutations in the active site has been delineated computationally using two cluster models, thus rationalizing the enantiodivergence. We have attempted to provide the much-needed insights into the origin of enantiodivergence, furnishing a mechanistic framework for understanding the anchoring effects of H-bond donor residues with the lactone ring. This study is expected to have important implications in the rational design of stereodivergent enzymes and toward successful *in silico* enzyme designing.[9]

([8]) Zhou, A.Z.; Kai Chen, K.; Arnold, F.H. *ACS Catal.* **2020**, *10*, 5393–5398.
([9]) Chatterjee, R.; Jindal, G. ***Chem. Sci.***, **2023**,***14***, 8810-8822.

Exploring C-H bond activation by monomeric Fe(III)-OH complexes: a biomimetic model of lipoxygenase-like activity

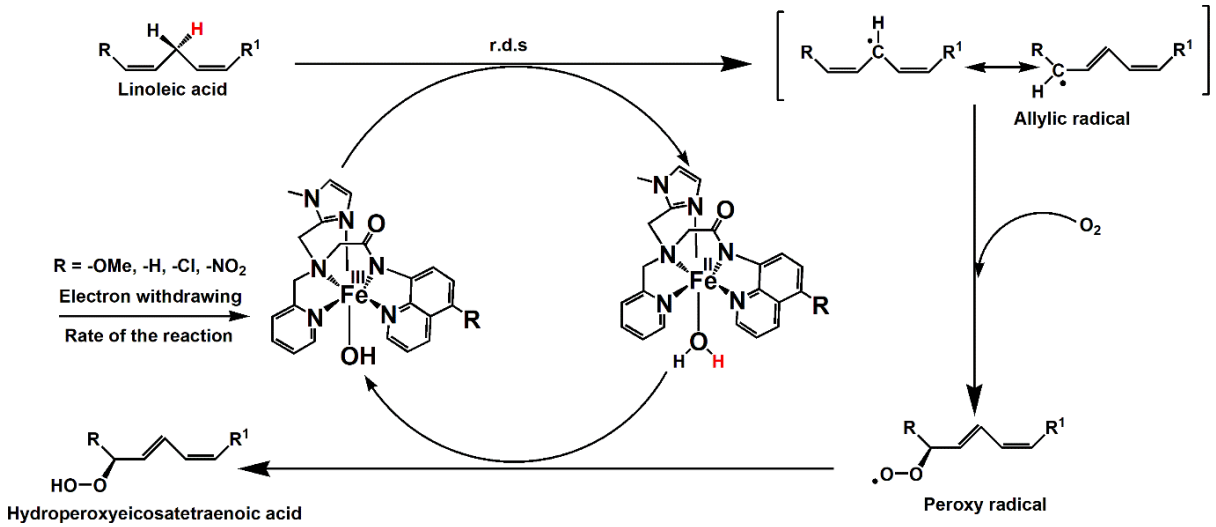
Mofijul Molla [a] and Sukanta Mandal*[a]

[a] Department of Chemistry, Indian Institute of Technology Kharagpur, Kharagpur-721302, India.

Email: sukanta.mandal@chem.iitkgp.ac.in;

mofijul.molla2013@gmail.com

The synthesis and characterization of four new monomeric $[Fe^{III}(OH_2)(L^R)]^{2+}$ complexes supported by L^R [{L^R (L = 2-(((1-methyl-1*H*-imidazol-2-yl)methyl)(pyridin-2-ylmethyl)amino)-N-(quinolin-8 yl)acetamide) (R= *p*-OMe, *p*-H, *p*-Cl, *p*-NO_2)}] ligand that undergoes PCET in H_2O to afford a rare example of monomeric $[Fe^{III}(OH)(L^R)]^{+}$ complexes as a biomimetic model of the lipoxygenase active site. Among the complexes, the redox potential of $Fe^{III/II}$ couple follows an order $[Fe^{III}(OH_2)(L^{OMe})]^{2+}$<$[Fe^{III}(OH_2)(L^{H})]^{2+}$<$[Fe^{III}(OH_2)(L^{Cl})]^{2+}$<$[Fe^{III}(OH_2)(L^{NO2})]^{2+}$, implying that the para-substitutions on the quinolinyl moiety fine-tune the electronic properties of the $[Fe^{III}(OH_2)(L^R)]^{2+}$ complexes. The bond dissociation free energies (BDFE) for the Fe^{II}-(HOH) were calculated by using the experimentally determined values for the p*K*a and $E_{1/2}$ of the $[Fe^{III}(OH_2)(L^R)]^{2+}$ complexes measured in an aqueous solution. These thermodynamic parameters affect the reactivity with substrates like linoleic acid. The reactivity exhibits a substituent group-dependent order of -NO_2 > -Cl > -H > -OMe.



Porphyrin-based photoredox catalysis: An easy and efficient method for C-H activation of organic substrates

Anu and Dr. Iti Gupta*

Department of Chemistry, Indian Institute of Technology Gandhinagar,

Village Palaj, Gandhinagar-382355, Gujarat. E-mail: iti@iitgn.ac.in*

Porphyrins are the tetrapyrrolic heterocyclic compounds present in the heme group, cytochromes, chlorophyll, enzymes, etc., and play a significant role in photosynthesis and oxygen transport.[1] Photocatalysis is a sustainable and green approach in organic synthesis as light is an inexpensive, non-hazardous renewable energy source. Porphyrins can be used as photocatalysts because they harvest light energy and convert this into chemical energy, similar to photosynthesis. Metalloporphyrins (Mg, Fe, Co, Ni, Zn, Rh, Pd, Sn, Pt, etc.) showed good photocatalytic activity for organic transformations such as oxidations, reductions, epoxidation, carbon−carbon, and carbon-heteroatom bond formations in recent years.[2] Along with the excellent absorption in the visible range, porphyrins undergo oxidation and reduction processes, making them suitable candidates as photoredox catalysts.

Our group at IIT Gandhinagar is involved in the chemistry of donor-acceptor (D-A) porphyrins and we have synthesized A_3B and A_2B_2 type porphyrins and their Pd(II) complexes.[3,4] These complexes have been used for the photo-oxidation of aldehydes to carboxylic acids with 80-98% yield. In this poster, we present the synthesis and characterization of a series of zinc porphyrins and 21-thiaporphyrins having heterocyclic moieties at *meso*-positions.[5] The synthesized porphyrins were tested for the C-H arylation of heteroarenes with different *ortho*, *meta,* and *para*-substituted anilines (up to 73%). Frontier molecular orbitals and the excited state redox potentials of porphyrins were calculated by using TD-DFT. An efficient and sustainable approach has been demonstrated for the C-H activation, borylation, thiolation, and selenylation of arenes and heteroarenes.

References:

1. Senge, M. O.; MacGown, S. A.; O'Brein, J. M. *Chem. Commun*. **2015**, *51*, 17031.

2. Majek, M.; Filace, F.; von Wangelin, A. J. *Beilstein J. Org. Chem*. **2014**, *10*, 981-989.

3. (a) Manav, N.; Lone, M.; Raza. M. K.; Chavda J.; Mori, S.; Gupta, I. *Dalton Trans*. **2022**, *51*, 3849. **(b) Kesavan, P.E.; Gupta I. Front. Chem. 2019. (c) Vedamalai, M.; Kedariya, D.; Vasita, R.;** Gupta, I. ***Sens. Actuators B Chem*. 2018, *263*, 137. (d) Pandey**, V.; **Raza, M. K.;** Joshi, P.; Gupta, I. ***J.Org. Chem.* 2020,** *85*, 6309**. (e) Das,** S.; Bhat, H. R.; **Balsukuri, N.;** Jha, P. C.; Hisamune, Y.; Ishida, M.; Furuta, H.; Mori, S; Gupta, I. ***Inorg. Chem. Front.* 2017,** *4*, 618-638. (f) Das, S.; Balsukuri, N.; Praseetha E. K.; Gupta, I. *Aust. J. Chem.* **2015**, *68*, 896. (g) Das, S.; Gupta, I. *J. Porphyr. Phthalocyanines* **2019**, *23*, 367.

4. (a) **Gupta, I.; Pandey**, V.; Jain, D.; Pareek, N. ***Inorg. Chimica Acta* 2020**, *502*, 119339. **(b)** Janaagal, A.; Pandey, V.; Sabharwal, S.; Gupta, I. *J. Porphyr. Phthalocyanines* **2021**, *25*, 571.

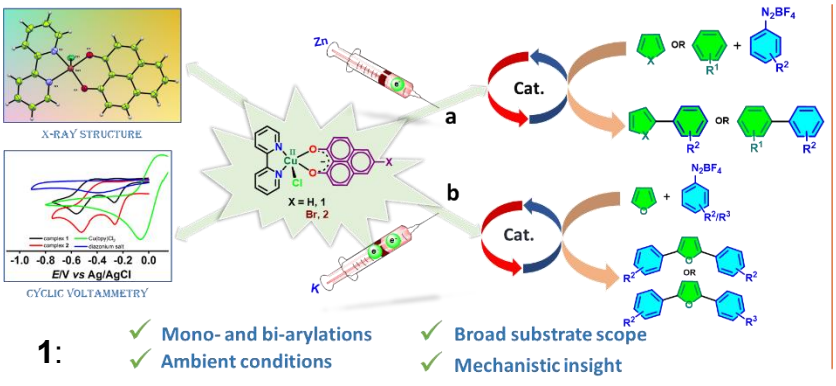
5. Janaagal, A.; Sanyam; Mondal, A.; Gupta, I. *J. Org. Chem.* **2023**, *88*, 9424-9431.

A newfangled torch for economically attractive arylation of arene and heteroarene C–H bonds with a designer's copper(II) catalyst

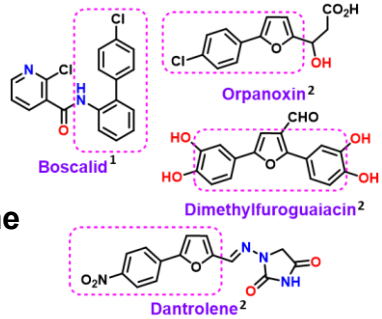
Krishnendu Paramanik[a], Hari Sankar Das[a]*

[a] Department of Chemistry, University of North Bengal,
Darjeeling-734013, West Bengal, India

Direct C–H arylation of arenes and heteroarenes emerges as a powerful and efficient synthetic method for the construction of thought-provoking C–C bonds in organic chemistry. It allows the preparation of ubiquitous structural motifs found in many organic materials, pharmaceuticals, agrochemicals, liquid crystals, etc. [1,2] Here in, we introduce a newly designed phenalenyl (PLY)-based copper-bipyridine (BPY) heterolaptic complex of the form [(BPY)Cu^{II}(PLY)Cl], **1** as a cheap and efficient catalytic system for the direct arylation of arene and heteroarene C–H bonds with aryldiazonium salts (Scheme 1). A wide range of arenes and heteroarenes were mono-arylated without any source of light or heat at ambient conditions (Scheme 1a). Just a catalytic amount of mild reducing agent, such as zinc is required to activate the catalyst. With a slight modification of the reaction conditions, two successive arylations (bi-arylation) of furan were also achieved successfully using the same catalyst for the first time when a strong reducing agent, potassium, was used (Scheme 1b). It may be noted that the mono-arylated furans and bi-arylated furans are the core part of some highly important drug molecules. Along with **1**-catalysed C–H arylation, the crucial role of each unit of **1** in this catalytic reaction was established by combining structural, electrochemical, spectroscopic, theoretical and mechanistic results. The copper and PLY units are mainly playing key roles such as dissociation of the aryldiazonium salt to the aryl radical, activation of the arene part, etc. in the present radical-based C–H arylation reaction. The BPY unit in **1**, stabilizes the reactive intermediates through delocalization of charge density. A substitution at the PLY ligand has also been carried out to tune the electronic nature of the catalytic system.



Scheme



Phenalenyl ligand-based Cu-complex catalyzed mono- (a), and bi-arylation (b) of arenes and heteroarenes

References: **1**. H. Mayer, D. Golsch, H. Isak, J. Schröder, US 7241896B2, 2007.
2. X. Wang, A. Lerchen, C. G. Daniliuc and F. Glorius, *Angew. Chem. Int. Ed.*, 2018, **57**, 1712.

Role of Covalency, Cooperativity, and Coupling Strength Dictating the C–H Bond Activation Reactivity in Ni_2E_2 (E = O, S, Se, and Te) Complexes

Sunita Sharma,[a] Bhawana Pandey,[a] Gopalan Rajaraman*[a]

[a] Department of Chemistry, Indian Institute of Technology Bombay, IIT Bombay, Powai − 400076, Mumbai, Maharashtra, India *E-mail: gopalan.rajaraman@gmail.com

Dinickel dichalcogenide complexes hold vital multifaceted significance across catalysis, electron transfer, magnetism, materials science, and energy conversion. Understanding their structure, bonding, and reactivity is crucial for all aforementioned applications. These complexes are classified as dichalcogenide, subchalcogenide, or chalcogenide based on metal oxidation and coordinated chalcogen, and due to the associated complex electronic structure, ambiguity often lingers about their classification. [1, 2] In this work, using DFT, CASSCF, and DLPNO-CCSD(T) methods, we have studied in detail $[(NiL)_2(E_2)]^{[3]}$ (L= 1,4,7,10- Tetramethyl 1,4,7,10 tetraazacyclododecane; E = O, S, Se and Te) complexes and explored their reactivity towards C–H bond activation for the first time. Our study suggests the reactivity order of $\{Ni_2O_2\}$ > $\{Ni_2S_2\}$ > $\{Ni_2Se_2\}$ > $\{Ni_2Te_2\}$ for C–H bond activation, and the origin of the difference in reactivity was attributed to the difference in the Ni–E bond covalency, and electronic cooperativity between two Ni centers that switch among the classification during the reaction. Notably, the reactivity trend is found to be correlated to the strength of the antiferromagnetic exchange coupling constant J – offering a hitherto unknown route to fine-tune the reactivity of this important class of compounds.

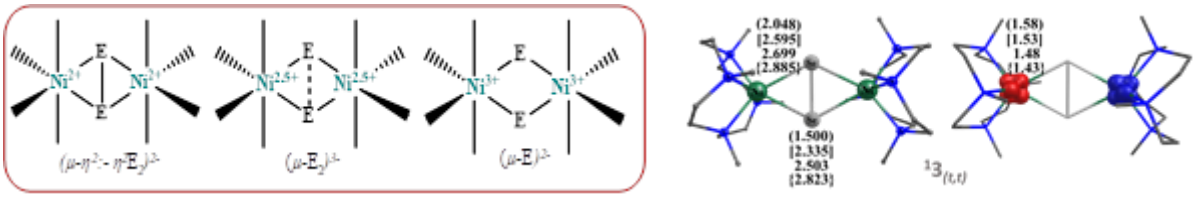


Figure 1. a) Schematic representation of all the three possible bonding modes preferred by dichalcogenides (E_2) to the dinuclear metal complexes b) DFT optimised geometries and spin density plots of complexes $^{1}3_{(t,t)}$. The curve, square and curly brackets are for 1, 2, and 4, respectively.

References

(1) S. A. Yao, V. Martin-Diaconescu, I. Infante, K. M. Lancaster, A. W. Götz, S. DeBeer, J. F. Berry, J. Am. Chem. Soc., 137 (2015), 4993-5011.

(2) S. A. Yao, K. M. Lancaster, A. W. Götz, S. DeBeer, J. F. Berry, Chem. Eur. J., 18 (2012), 9179-9183.

(3) J. Wallick, C. G. Riordan, G. P. Yap, J. Am. Chem. Soc., 135 (2013), 14972-14974.

O_2 Activation by a Coordinated -NH- Function: HAT andAromatic Ring Oxidation[1]

Souvik Mukherjee, Subhadip Sett, Sandip Mondal and Prasanta Ghosh*

Department of Chemistry

Ramakrishna Mission Residential College (Autonomous), Narendrapur

Narendrapur, Kolkata 700 103

Herein we disclose a unique method of oxidation of the 1,4-naphthoquinone ring in air. We report that (1,4-naphthoquinone)-NH-N=C(OH)Ph (H_3L) coordinated to octahedral ruthenium(II) and osmium(II) ions activates $^3O_2$ molecule spontaneously. Hydrogen atom transfer (HAT) from the -NH- function of H_3L to $^3O_2$ and subsequent ($2e+2H^+$) oxidation forming (1,3,4-trioxonaphthalen)=N-N=C(OH)Ph (HL^{OX}) has been authenticated. The $H_3L \rightarrow HL^{OX}$ transformation occurs via (3-hydroperoxy-1,4- naphthoquinone)=N-N=C(O^-)Ph (HL^{OOH-}) as an intermediate. The primary step is the HAT generating $H_2L^{\bullet-}$ and hydroperoxide ($OOH^{\bullet}$) radicals. $H_2L^{\bullet-}$ is delocalized over the aromatic ring and incites coupling reactions via ortho carbon and producescoordinated HL^{OOH-}. In solution, the homolytic cleavage of the peroxo bond leads the aromatic ring oxidation affording L^{OX-}. Ruthenium(II) and osmium(II) complexes of types, $[M^{II}(H_2L^-)(PPh_3)_2X]$, $[M^{II}(HL^{OOH-})(PPh_3)_2X]$ and *trans*-$[M^{II}(L^{OX-})(PPh_3)_2X]$ were
successfully isolated in good yields. Notably, the cyclic voltammograms of all the complexes exhibit reversible anodic waves due to M^{III}/M^{II} redox couples. The rate constants of the $[M^{II}(H_2L^-)(PPh_3)_2X] \rightarrow [M^{II}(HL^{OOH-})(PPh_3)_2X]$ conversions determined by the time drive UV-Vis spectroscopy in dry CH_2Cl_2, wet CH_2Cl_2 and D_2O wet CH_2Cl_2 in air at 298 K follow the order, $k_{CH2Cl2\text{-}H2O} > k_{CH2Cl2\text{-}D2O} > k_{CH2Cl2}$. It is establishedthat the rate constants are dependent on the $^3O_2$ content of the solution but not on the concentration of the complex.

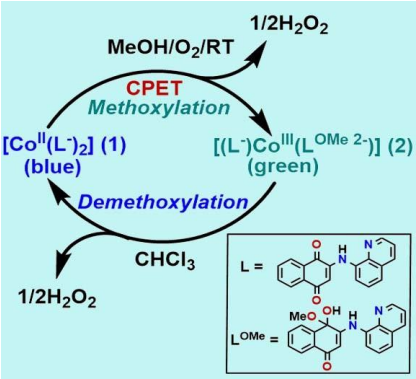
References:

1. Mukherjee, S.; Sett, S.; Mondal, S.; Ghosh, P. *unpublished results*

A Methoxylation Promoted CPET Reaction[1]

Souvik Mukherjee, Kuntal Maji, Pinaki Saha and Prasanta Ghosh* Department of Chemistry
Ramakrishna Mission Residential College (Autonomous), Narendrapur Narendrapur, Kolkata 700 103

The manuscript discloses a methoxylation reaction to an aromatic carbonyl function that carries out a CPET reaction oxidizing a transition metal ion. Spontaneous methoxylation of a redox non-innocent fragment coordinated to a high spin cobalt(II) ion, promoted concerted proton electron transfer (CPET) reaction oxidizing cobalt(II) to cobalt(III) in air and subsequent demethoxylation induced reduction of cobalt(III) to cobalt(II) producing H_2O_2 are authenticated. The cobalt(III)/cobalt(II) electron transfer (ET) potential of the designed complex in CH_2Cl_2 is -0.27 V vs Fc^+/Fc redox couple. However, in presence of MeOH the reduction potential decreases to -1.02 V due to CPET involving MeOH proton. In $CH_2Cl_2/CHCl_3$ spontaneous demethoxylation occurs giving back the original complex and reactive methoxyl radical that reacts with O_2 producing H_2O_2. Overall one molecule of MeOH produces one molecule of H_2O_2. To analyze the involvement of the proton, the rate constants of the CPET reactions in CH_2Cl_2-MeOH (2:1) and CH_2Cl_2-CD_3OD (2:1) and the demethoxylation reaction in $CHCl_3$ at 330 K were determined by time drive UV-Vis spectroscopy.



References:

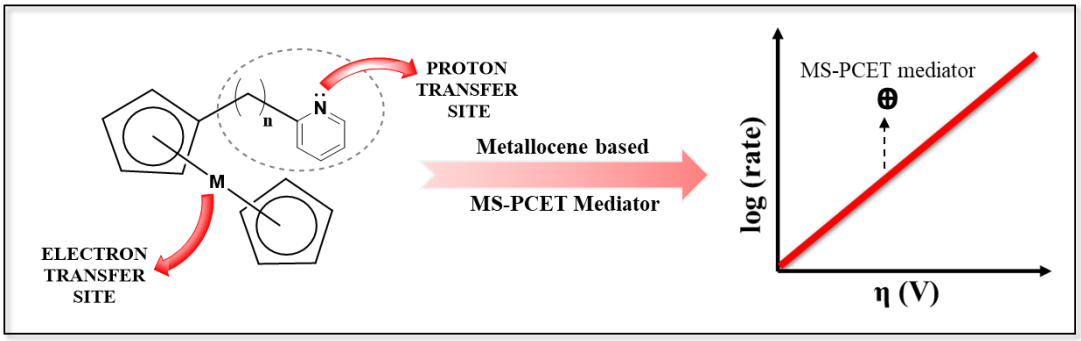
1. Mukherjee, S.; Maji, K.; Saha, P.; Ghosh, P. *Chem. Eur. J. 2023, e202302291*. DOI: 10.1002/chem.202302291

Development of MS-PCET Mediator for Electrochemical Oxidation of Small Organic Molecules

Tarisha Gupta and Biswajit Mondal*

Department of Chemistry, IIT Gandhinagar, Palaj-382055

Proton-coupled electron transfer (PCET) plays a crucial role in biological and chemical processes by coupling electron transfer (ET) and proton transfer (PT) in a single concerted step [1]. PCET reactions often exhibit kinetic advantages, resulting in faster rates than that of individual rates of their stepwise ET or PT components. Hence, these are energetically favourable [2]. However, to enhance the reactivity, either the abstracting species need to be a more potent electron oxidant or the resulting reduced state need to be a stronger Brønsted base. Unfortunately, these two properties are inversely correlated and interdependent within a single molecule. Multisite PCET (MS-PCET) allows independent modulation of proton and electron transfer abilities. It involves separate Brønsted bases and single electron oxidants, where the proton and electron sites are decoupled at the individual sites [3]. In order to develop an efficient mediator, MS-PCET brings the possibility of breaking the linear scaling relationship between log (*rate*) and driving force (overpotential). In this work, we demonstrate the possibility of benzylic C-*H* (BDFE = 75-85 kcal mol^{-1}) activation using ferrocene-based mediators. Our goal is to develop Brønsted base-appended ferrocene derivative as an MS-PCET mediator, with independent ET and PT sites intramolecularly. This newly developed MS-PCET mediator aims to help in achieving the enhanced rate and reduced onset potential for the electrochemical organic oxidation.



References:

[1] Morris, W. D., & Mayer, J. M. (2017). Separating proton and electron transfer effects in three-component concerted proton-coupled electron transfer reactions. *Journal of the American Chemical Society*, *139*(30), 10312-10319.

[2] Yayla, H. G., & Knowles, R. R. (2014). Proton-coupled electron transfer in organic synthesis: novel homolytic bond activations and catalytic asymmetric reactions with free radicals. *Synlett*, *25*(20), 2819-2826.

[3] Nguyen, L. Q., & Knowles, R. R. (2016). Catalytic C–N bond-forming reactions enabled by proton-coupled electron transfer activation of amide N–H bonds. *ACS Catalysis*, *6*(5), 2894-2903.

Hydrogen Atom Transfer by a High-Valent Iron−Fluoride complex

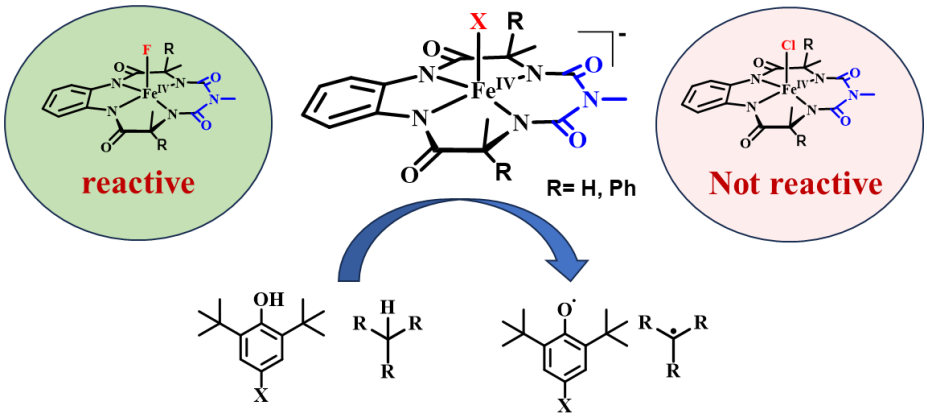
Himangshu Kuiry [a], Sayam Sen Gupta [a*]

[a] Department of Chemical Sciences, Indian Institute of Science Education and Research, Kolkata, India

Email: sayam.sengupta@iiserkol.ac.in

In nature, many Fe and Cu-containing metalloenzymes perform saturated hydrocarbon oxidation reactions through oxidative C-H activation, forming hydroxylated, halogenated, and desaturated products. Hydrogen atom transfer (HAT) activation of the inert C−H bond is postulated to occur via a high-valent metal–oxo or bridging oxo species. More recent efforts have focused on the capability of M-OX (OX = OH, OR, O_2C−R, ONO_2) and metal-imido entities in oxidative C-H bond activation, demonstrating that a terminal M=O is not a prerequisite for hydrocarbon oxidation.

In search of hydrogen atom transfer reaction by a high valent metal complex, we found that a high valent iron−fluoride complex $Fe^{IV}F$-(PhMe-bTAML) (**2**) can easily abstract hydrogen atom from O-H and C-H bonds of phenol and hydrocarbon, respectively. The high valent Fe-F complex was prepared from $Fe^{III}F$-(PhMe-bTAML) (**1**) by oxidizing it with selectfluor-PF_6 or magic blue-PF_6 in DCM at room temperature. Both the complexes **1** and **2** were characterized by UV-vis, EPR spectroscopy, mass spectrometry, and X-ray single-crystal spectroscopy. Kinetic data and product analysis demonstrate a hydrogen atom transfer mechanism for phenol and hydrocarbon oxidation. We observed that the analogous $Fe^{IV}Cl$-(PhMe-bTAML) was utterly unreactive for the hydrogen atom transfer reaction of the O-H and C-H bond. At the same time, the pKa and potential of Complex **2** and HF formation (BDE-137 kcal/mol) as the product drive the reaction in the case of Complex **2.**



✓ First spectroscopic evidence of Fe^{IV}-F complex mediated HAT

References:

1. Panda, C.; Doyle, L. M.; Gericke, R.; McDonald, A. R. *Angew. Chem., Int. Ed*. **2021**, 60, 26281−26286
2. Bower, J. K.; Cypcar, A. D.; Henriquez, B.; Stieber, S. C. E.; Zhang, S. *J. Am. Chem. Soc*. **2020**, 142, 8514–8521
3. Mondal, P.; Lovisari, M.; Twamley, B.; McDonald, A. R. *Angew. Chem., Int. Ed*. **2020**, 59, 13044−13050

Ligand-radical promoted hydrogen atom transfer to expedite (de)hydrogenation relevant to borrowing hydrogen catalysis

Abhishek Kundu, Amreen K. Bains, Rahul Singh, Debashis Adhikari*

Department of Chemical Sciences, Indian Institute of Science Education and Research Mohali, SAS Nagar-140306, India

Redox-active ligands pervade their role far beyond being a supporting ancillary. Here in we describe the prowess of redox-active azophenolate ligand backbone and its preponderant role in the electron transfer and hydrogen atom transfer (HAT) steps to drive the dehydrogenation and hydrogenation steps relevant to borrowing hydrogen catalysis. To describe the process, we showcase how redox-active azophenolate ligand in an earth-abundant nickel catalyst has been utilised to pave the alcohol dehydrogenation and hydrogenation of an in situ generated imine or olefin via radical pathway. A series of control reactions, detection of critical reaction intermediates, radical probe experiments, a set of kinetic experiments, further aided by DFT calculations altogether suggest the precise one-electron path and also indicate the nonparticipation of metal-hydride during this process. Notably, the redox noninnocence of the azophenolate backbone, as well as imposed noninnocence of the substrate olefin, when bound to the catalyst allows such mechanism to happen. This dehydrogenation mechanistic profile closely resembles the galactose oxidase-based copper phenoxide chemistry. Beyond N-alkylation and C-alkylation reactions, this methodology also has been extended to (de)hydrogenation cascade and successfully employed for stereoselective synthesis of (n+1)-membered cycloalkanes from 1,n-diols with methyl ketones. Specifically, the radical-induced (de)hydrogenations differ significantly from the traditional metal hydride-based methods and are complementary to the widely used two-electron-driven dehydrogenation / dehydrogenation reactions.

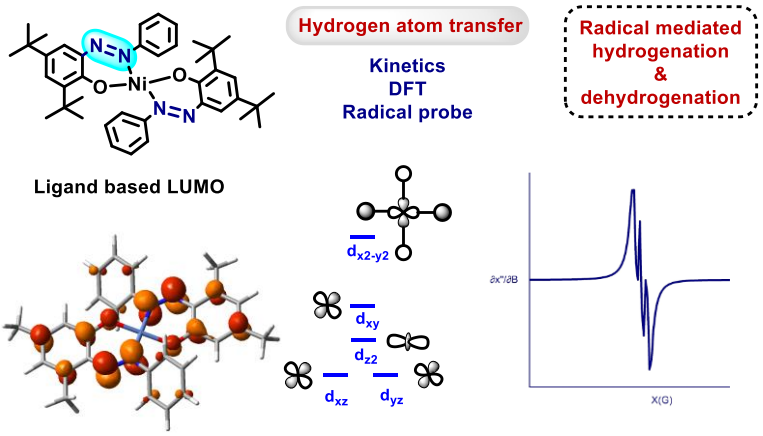


Figure xx. Ligand radical promoted HAT for dehydrogenation and hydrogenation.

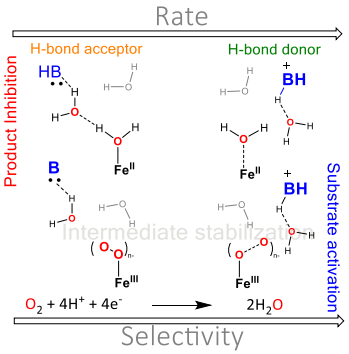
References: (1) *ACS Catal.* **2019**, *9*, 9051. (2) *Chem. Sci.*, **2021**, *12*, 14217. (3) *ACS Catal.* **2022**, *12*, 13075. (4) *Organometallics*, **2023**, *42*, 1759.

2nd Sphere Hydrogen Bond Donors and Acceptors Affect the Rate and Selectivity of Electrochemical Oxygen Reduction by Iron Porphyrins Differently

Soumya Samanta[a], Arnab Ghatak[a], Abhijit Nayek[a], Somdatta Ghosh Dey*[a], Abhishek Dey*[a]

[a] School of Chemical Sciences, Indian Association for the Cultivation of Science, Kolkata

The factors that control the rate and selectivity of 4e-/4H+ O_2 reduction is important for efficient energy transformation as well as for understanding the terminal step of respiration in aerobic organisms. Inspired by the design of naturally occurring enzymes which are efficient catalysts for O_2 and H_2O_2 reduction, several artificial systems have been generated where different 2nd sphere residues have been installed to enhance the rate and efficiency of the $4e^-/4H^+$ O_2 reduction. These include hydrogen bonding residues like amines, carboxylates, ether, amides, phenols etc. In some cases, improvements in the catalysis where recorded whereas in some cases improvements were marginal or non-existent. In this work we use an iron porphyrin complex with pendant 1,10-phenanthroline residues which show a pH dependent variation of rate of electrochemical O_2 reduction reaction (ORR) over two orders of magnitude. In situ surface enhanced resonance Raman spectroscopy reveal the presence of different intermediates at different pH's reflecting different rate determining steps at different pH's. These data in conjunction with density functional theory calculations reveal that, when the distal 1,10-phenanthroline is neutral it acts as a hydrogen bond acceptor which stabilizes H_2O (product) binding to the active Fe^{II} state and retards the reaction. However, when the 1,10-phenanthroline is protonated, it acts as a hydrogen bonding donor which enhances O_2 reduction by stabilizing Fe^{III}-O^{2-} and Fe^{III}-OOH intermediates and activating the O-O bond for cleavage. Based on these data general guidelines for controlling the different possible rate determining steps in the complex multi-step $4e^-/4H^+$ ORR is developed and bio-inspired principle-based design of efficient electrochemical ORR is presented.



1. K. Sengupta, S. Chatterjee, S. Samanta and A. Dey, Proc. Natl. Acad. Sci. U. S. A., 2013, 110, 8431.

2. S. Chatterjee, K. Sengupta, B. Mondal, S. Dey and A. Dey, Acc Chem Res, 2017, 50, 1744–1753.

3. S. Mukherjee, A. Nayek, S. Bhunia, S. G. Dey and A. Dey, Inorg. Chem., 2020, 59, 14564-14576.

4. A. Ghatak, S. Samanta, A. Nayek, S. Mukherjee, S. G. Dey and A. Dey, Inorg Chem, 2022, 61, 12931–12947.

Developing bidirectional oxygen reduction and oxygen evolution electrocatalyst for practical applications

Aritra Guha*, Abhishek Saini*, Chandan Das, Subho Ghosh, Tarik Aziz*, Yashwant P. Kharwar*, Arnab Dutta*

Department Of Chemistry, IIT Bombay, Powai, Maharastra-400076, India

The oxygen reduction reaction (ORR) is vital for the operation of multiple direct energy transduction applications, including fuel cell and metal-air battery devices. The development of efficient catalysts for oxygen reduction reaction (ORR) and oxygen evolution reaction (OER) is essential to drive the interconversion between O_2 and water molecules during this energy exchange process. We have imitated this enzymatic architecture in a relatively smaller Co(L-histidine)$_2$ complex.[1] This *in situ*-generated complex catalyzes O_2 through two distinct pathways: a two-electron O_2/H_2O_2 reduction (TOF = 250 s^{-1}) and a four-electron O_2 to H_2O production (TOF = 66 s^{-1}), expedited by the formation of the key trans-μ-1,2-Co(III)-peroxo intermediate. Moreover, this complex exhibits remarkable efficiency in the OER direction while producing O_2 at a rapid rate (TOF = 15606 s^{-1}) at anodic potentials, utilizing a Co(IV)-oxo species. Furthermore, This complex establishes its versatility by executing both ORR and OER under photocatalytic conditions in neutral water, with the aid of an appropriate photosensitizer (Eosin-Y) and redox mediators (triethanolamine for ORR and $Na_2S_2O_8$ for OER), achieving notable turnover numbers. These results mark a significant milestone in the development of dual-purpose electro and photoactive bidirectional ORR/OER catalysts operating effectively in neutral water. The intricate cohesion between the transition metal active site, electron mediator, and proton exchange groups is key for enabling bidirectional electrocatalysis. Next, the same tactics were implied in the form of a Ce-doped Ni-Co-layered double hydroxide (LDH) surrounded by active N-doped graphitic carbon (N@C) to develop a unique N@C_LDH-CeO_2 material. All components in this material operate synergistically to display bidirectional ORR/OER activity in alkaline aqueous conditions. N@C_LDH-CeO_2 displayed exceptional energy efficiency, which was measured by the relatively low potential difference (ΔE) of 0.74 V between the half-wave potential of ORR ($E_{1/2}$) and the OER potential at the current density of 10 mA cm^{-2} (Ej_{10}). The presence of N and Ce-doping modulated the ORR and OER activity, respectively, as N@C_LDH-CeO_2 displayed an ample number of active sites during electrocatalysis on either side. N@C_LDH-CeO_2 was next assembled in a rechargeable zinc-air battery (ZAB) to utilize its bidirectional OER/ORR activity. This ZAB achieves one of the highest reported energy densities (894.3 Wh kg^{-1}), appreciable power density (243 mW cm^{-2}), and excellent specific capacity (698 mA h g^{-1} @ 10 mA cm^{-2}), along with a remarkable durability of 270.0 hours for more than 1600 continuous cycles. This material was active in a ZAB

assembly as This material remains active even in a solid-state ZAB assembly, where it successfully transduces energy to an electronic device. The significance of a rational combination of multifunctional materials to create a synergistic catalyst with improved activity, stability, and selectivity towards practically applicable bidirectional OER/ORR activity.

References:

(1) Saini, A.; Das, C.; Rai, S.; Guha, A.; Dolui, D.; Majumder, P.; Dutta, A. *iScience,* **2023**, *26* (11), 108189.

Oxygen Reduction by Iron Porphyrins with Covalently Attached Pendent Thiol Group

Souvik Dinda,[1] Soumya Samanta,[2] Triparna Roy,[3] Abhishek Dey*

[1]School of Chemical Sciences

[2]School of Chemical Sciences

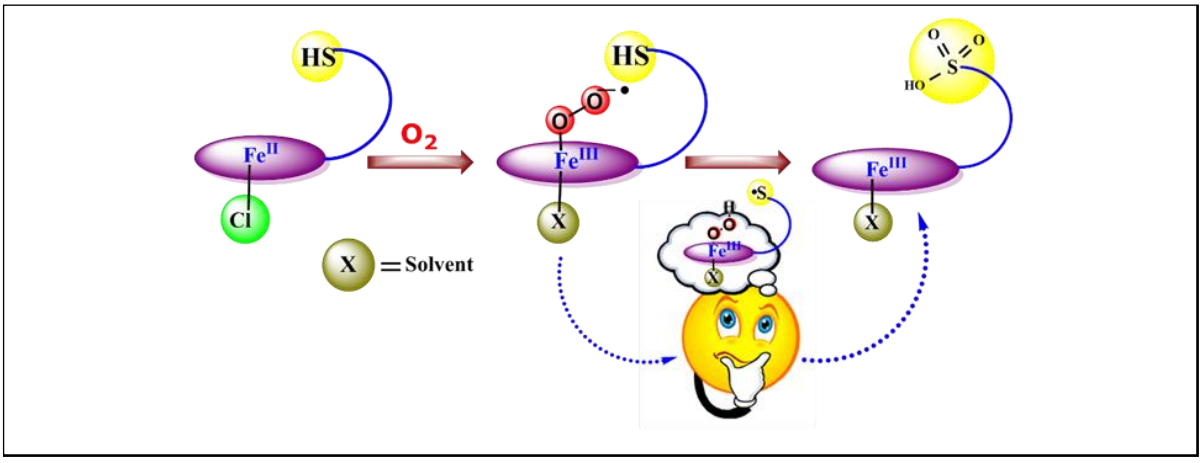
[3]School of Chemical Sciences

Indian Association for the Cultivation of Science, 2A Raja SC Mullick Road, Kolkata 700032, India

Email: icad@iacs.res.in

Thiols participate in both proton transfer and electron transfer processes in nature either in distinct elementary steps or in a concerted fashion[1]. Our investigations using synthetic iron porphyrin system have shown that thiols can react with ferric superoxide intermediate formed during O_2 reduction reaction through a proton coupled electron transfer (PCET) process. Mechanism of the reaction investigated by trapping the intermediates in organic solution suggests that Fe^{III}-$O_2^{\cdot -}$ species to Fe^{III}-OOH species proceeds via PCET when thiol group is present[2]. The data show that Fe^{III}-OOH intermediate species proceeds to a ferryl intermediate Compound II species and following a PCET the pendent thiol group undergoes oxidation via plausible radical formation.

.



References

1. B. Cardey, S. Foley, M. Enescu, *J. Phys. Chem. A*, **2007**, *111*, 50, 13046–13052

2. A. Singha, A. Mondal, A. Nayek, S. G. Dey, Dey, A. Dey, *J. Am. Chem. Soc,* **2020,** *142,* 52, 21810-21828

Catalytic Four-Electron Reduction of Oxygen to Water by Molecular Cobalt Complexes Consisting of a Proton Exchanging Site at the Secondary Coordination Sphere

Avijit Das, Aakash Santra, Priya Jain, Pravin P. Ingole, Sayantan Paria*

Ph.D. research Scholar, Indian Institute of Technology Delhi, Hauz Khas, New Delhi, 110016, India

In this study, we designed and synthesized a series of mononuclear Co^{III} complexes of a bis-pyridine-bis-oxime ligand where the oxime site can participate in reversible proton exchange reactions. Electrocatalytic ORR of 1 was investigated in aqueous buffer solutions and acetonitrile containing trifluoroacetic acid as the proton source. We observed that in a 0.1 M phosphate buffer solution (PBS), 1 is selective for $4e^-/4H^+$ reduction of O2 at pH 4, and the selectivity decreases with increasing the buffer medium's pH. However, in a 0.1 M acetate buffer solution (ABS), 1 remained highly selective for the cleavage of the O−O bond to produce H2O at pH 4 and pH 7. The overpotential (η) of H2O formation (ca. 0.8−0.65V) decreased proportionally with increasing pH in PBS and ABS. In acetonitrile, 1 remained highly selective for $4e^-/4H^+$ reduction for electrocatalytic and chemical ORR. An overpotential of 760 mV was estimated for H2O production in acetonitrile. Kinetic analysis suggests the first-order dependence of catalyst concentration on the reaction rate at 25°C. However, the formation of a peroxo-bridged dinuclear cobalt(III) complex was noted as a reaction intermediate in the ORR pathway in acetonitrile at −40°C. We conjecture that the oxime scaffold of the ligand works as a proton-exchanging site and assists in the proton-coupled electron transfer (PCET) reactivity to cleave the O−O bond in the acidic buffer solutions and acetonitrile, further corroborated by theoretical studies. Density functional theory (DFT) calculation suggests that the acetate ion works as a mediator at pH 7.0 for transferring a proton from the oxime scaffold to the distal oxygen of the Co^{III}(OOH) intermediate, responsible for high selectivity toward $4e^-/4H^+$ reduction of O2.

After establishing the role of oxime moiety, an extra proton exchanging site in the ligand backbone will be incorporated. This will further help us to develop a linear scaling relationship between all the substituents by checking the reactivity and selectivity of ORR.

Catalytic Reduction of Oxygen by Non-Heme Iron Complexes: Exploring the Effect of Secondary Coordination Sphere Proton Exchanging Site

Aakash Santra, Avijit Das, Simarjeet Kaur and Sayantan Paria

Department of Chemistry, Indian Institute of Technology Delhi

The development of efficient earth-abundant catalysts for oxygen reduction reaction (ORR) is crucial, considering its importance in fuel cell technology.[1] Major efforts were made to develop molecular catalysts of different macrocyclic ligands.[2-3] However, a limited number of non-heme Fe complexes are known as ORR catalysts.[4-7]

In this study, we prepared non-heme Fe^{III} complexes (**1** and **2**) of monoanionic N_4 donor set of ligands (Figure 1). **1** is supported by L^H, consisting of two pyridine and two oxime donor nitrogen atoms around Fe. In **2**, the primary coordination sphere of Fe remained similar to **1**, except the oxime protons of the ligand were replaced with a bridging $-BPh_2$ moiety. X-ray structures of the Fe^{II} complexes (**1a** and **2a**) revealed similar Fe−N distances. However, Fe^{III}/Fe^{II} potential of **1** appeared at −0.3 V vs. Fc^+/Fc, which is shifted to 0.07 V vs. Fc^+/Fc in **2**, implying L^{BPh2} is more electron deficient than L^H. **1** showed electrocatalytic oxygen reduction reaction (ORR) in acetonitrile in the presence of trifluoroacetic acid (TFAH) as the proton source at $E_{cat/2}$ = −0.53 V and revealed selective $4e^-/4H^+$ reduction of O_2 to H_2O. **1** showed effective overpotential (η_{eff}) of 1.06 V and turnover frequency (TOF) of 6.5 s^{-1}. Strikingly, **2** remained inactive for electrocatalytic ORR.

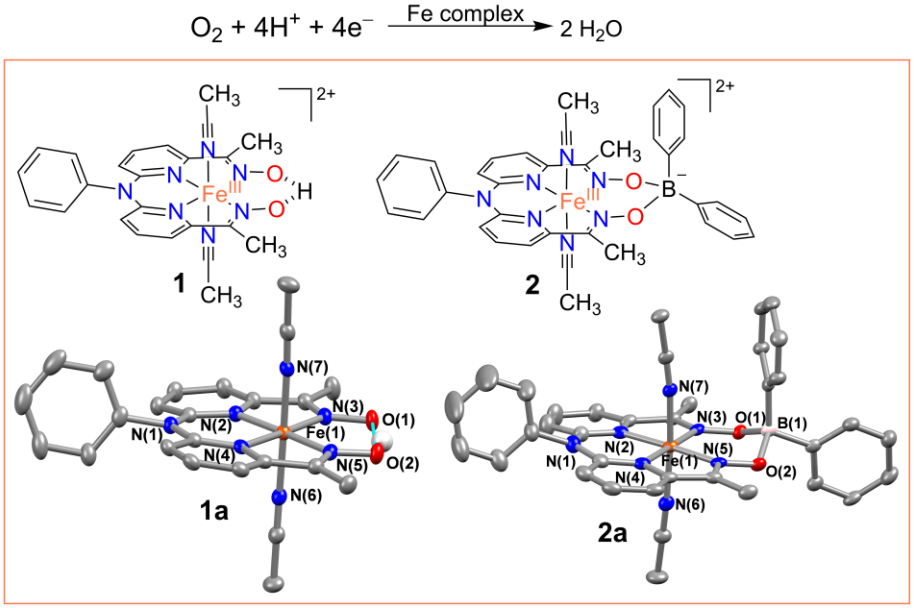


Figure 1. Catalytic $4e^-/4H^+$ reduction of O_2 by non-heme Fe complexes (**1** and **2**). X-ray structure of the Fe^{II} complexes with 50% ellipsoid probability.

Chemical ORR of **1** has been investigated using decamethylferrocene as the electron source, and a similar rate equation was noted to that of the electrocatalytic pathway. A k_{cat} of 6.7×10^4

M^{-2} s^{-1} was found chemically. Complex **2**, however, chemically enhances the $4e^-/4H^+$ reduction of O_2 and exhibits a TOF of 0.24 s^{-1} and a k_{cat} value of 4.5×10^2 M^{-1} s^{-1}. Based on the experimental observations, we demonstrate that the oxime backbone of the ligand in **1** works as a proton exchanging site in the $4e^-/4H^+$ reduction of O_2.

References:

1. H. A. Gasteiger and N. M. Markovic, *Science*, 2009, **324**, 48-49.
2. S. Dey, B. Mondal, S. Chatterjee, A. Rana, S. Amanullah and A. Dey, *Nat. Rev. Chem.*, 2017, **1**, 0098.
3. M. L. Pegis, C. F. Wise, D. J. Martin and J. M. Mayer, *Chem. Rev.*, 2018, **118**, 2340-2391.
4. L. Wang, M. Gennari, F. G. Cantu Reinhard, J. Gutierrez, A. Morozan, C. Philouze, S. Demeshko, V. Artero, F. Meyer, S. P. de Visser and C. Duboc, *J. Am. Chem. Soc.*, 2019, **141**, 8244-8253.
5. X. Lu, Y.-M. Lee, M. Sankaralingam, S. Fukuzumi and W. Nam, *Inorg. Chem.*, 2020, **59**, 18010-18017.
6. E. N. Cook, D. A. Dickie and C. W. Machan, *J. Am. Chem. Soc.*, 2021, **143**, 16411–16418.
7. E. N. Cook, S. L. Hooe, D. A. Dickie and C. W. Machan, *Inorg. Chem.*, 2022, **61**, 8387-8392.

Demystifying The Role of Covalently Attached Electron-Proton Transfer Mediator in Oxygen Reduction Reaction Catalyst

*Anjila Siddiqui, and Biswajit Mondal**

Department of Chemistry, IIT Gandhinagar, Palaj, 382355

Oxygen reduction reaction (ORR) forms an important part of fuel cell where it occurs at the cathode, while the other half is constituted by fuel oxidation at the anode. This process forms a promising way to derive electrical energy from chemical energy required to cope up with the soaring energy demand (1). The reaction can proceed via two electron-proton pathway to give hydrogen peroxide or by four electron-proton pathway producing water. Molecular complexes of transition metals have been found active towards reduction of dioxygen. Multi-proton and multi-electron nature of ORR makes it kinetically challenging. Activation of oxygen molecule by metal involves formation of metal-oxygen intermediate that can be stabilized with H-bonding, H-atom etc. Electron-proton transfer mediator (EPTM) possesses faster kinetics and can help in mediating electrons and protons. In one of the studies, Benzoquinone-Hydroquinone (BQ/ H_2Q) redox mediator was used in combination with Co-Salophen for ORR and the synergy between them directed the reaction towards water formation selectively along with the enhanced rate (2). Redox mediator can be anchored in the ligand assembly to study the intramolecular effect rather than adding externally. Therefore, we have covalently attached H_2Q along with salophen ligand. This assembly was found to be effective with Co-H_2Q, where catalyst was more selective towards water formation compared to EPTM unattached analogue (Co-Sal) (3). In future, we aim to study the effect of other transition metals such as Fe, Mn, Cu, etc. with the same ligand system.

References:

(1) Pegis, M. L.; Wise, C. F.; Martin, D. J.; Mayer, J. M. Oxygen Reduction by Homogeneous Molecular Catalysts and Electrocatalysts. *Chem. Rev.* **2018**, *118* (5), 2340–2391.

(2) Anson, C. W.; Stahl, S. S. Cooperative Electrocatalytic O2 Reduction Involving Co(Salophen) with p-Hydroquinone as an Electron-Proton Transfer Mediator. *J. Am. Chem. Soc.* **2017**, *139* (51), 18472–18475.

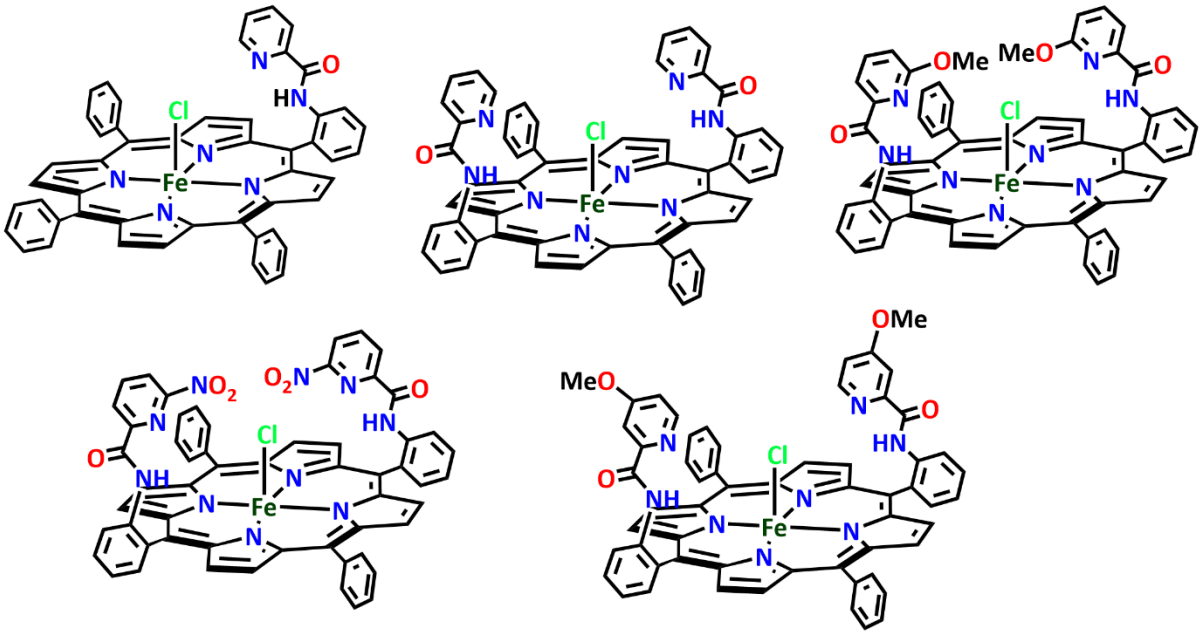
(3) Dinda, S.; Siddiqui, A. I.; Behera, S.; Mondal, B. Demystifying the Role of Covalently Attached Electron–Proton Transfer Mediator in Oxygen Reduction Reaction Catalyst. *ACS Catal.* **2023**, 12643–12647.

Effect of pka on O_2-reduction reactions

Arnab Roy, Sudip Barman, Paramita Saha and Abhishek Dey

Indian Association for the Cultivation of science, 2A &2B Raja S.C Mullick Road ,Jadavpur, Kolkata-32

The reduction of molecular oxygen (O_2) to water is a fundamental process in nature and is key to a sustainable fuel cell technology. A set of Iron porphyrins bearing second-sphere residues with various substituted pyridine moieties have been synthesized in order to investigate the pka dependencies on the rates of O_2 reduction reaction as well as on the percentage of PROS generated. The substituted moieties includes both ortho and para substituted electron donating -OMe group as well as ortho substituted electron withdrawing -NO_2 group. The structures of the porphyrins are shown below:



References:

1. J. Am. Chem. Soc. 2018, 140, 9444−9457
2. Faraday Discuss., 2022, 234, 143–158
3. ACS Cent. Sci. 2016, 2, 850−856

The synergy between electrochemical substrate oxidation and the oxygen reduction reaction to enable aerobic oxidation

Snehanjali Behera, Biswajit Mondal*

Department of Chemistry, IIT Gandhinagar, Palaj, 382355
Email id: behera_snehanjali@iitgn.ac.in

Aerobic oxidation reactions catalysed by heterogeneous metal catalysts occurs through redox cycling at the metal centre by substrate oxidation and consecutive oxygen reduction reaction (ORR) to either H_2O or H_2O_2, where the oxygen reduction gives the initial driving force to the catalyst for substrate oxidation and the electrons and protons released during the process are utilised for ORR[1]. This type of mechanism generally found in Cyt-P450 where the high-valent Fe =O intermediate is formed during the ORR cycle and is the key intermediate for C–H hydroxylation[2]. The same aerobic oxidation transformation can also be considered as two decoupled half-cell reactions, *viz.* anodic substrate oxidation reaction and oxygen reduction reaction which proceeds *via* mixed potential[3]. This suggests that an efficient ORR catalyst can be a suitable candidate for an aerobic oxidation catalyst provided the same redox couple is involved in both the half-cell reactions, wherein the redox potential predicts the mixed potential for the overall process. In this work, Fe PANI/C a well-known M-N-C ORR catalyst has been chosen to test the above mentioned hypothesis. Wherein hydrazine oxidation is the anodic oxidation reaction. Fe PANI/C shows an excellent activity in both alkaline aqueous and non-aqueous medium for electrochemical ORR and hydrazine, hydrazine like small molecule oxidation with near quantitative Faradaic yield and taken together correlated with hydrazine like small molecule aerobic oxidation reaction to valuable azo dye product. The mechanistic study reveals that the catalyst shares a common redox couple $Fe^{II/III}$ for both the half-cell reactions, ORR and hydrazine oxidation reaction, which helps in generating a mixed potential region by making Fe PANI/C as an efficient aerobic oxidation catalyst.

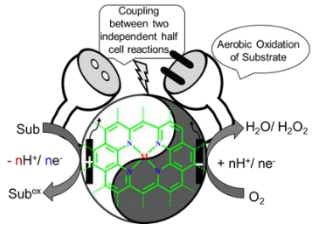


Fig 1. Scheme showing synergy between two independent half-cell reaction, substrate oxidation and ORR to enable aerobic substrate oxidation by Fe PANI/C catalyst.

References:
1. J. S. Bates, M. R. Johnson, F. Khamespanah, T. W. Root and S. S. Stahl, *Chem. Rev.,* 2022, **9,** 6233–6256
2. S. Chatterjee, K. Sengupta, S. Samanta, P. K. Das and A. Dey, *Inorg. Chem.,* 2013, **52,** 9897–9907
3. J. Ryu, D. T. Bregante, W. C. Howland, R. P. Bisbey, C. J. Kaminsky and Y. Surendranath, *Nat. Catal.,* 2021, **4,** 742–752

Rerouting a multi-copper oxidase to catalyze water oxidation

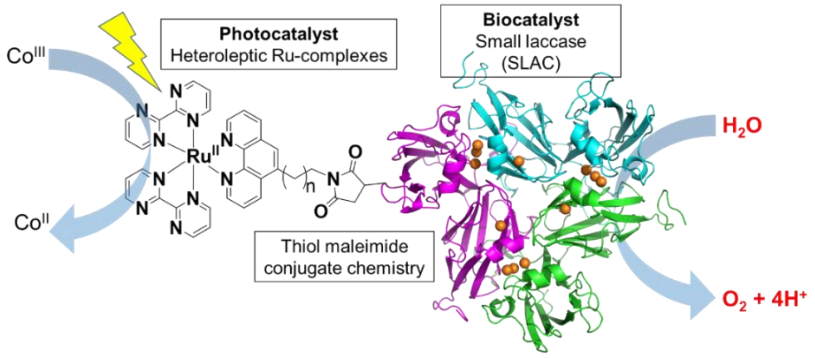
Bharti Paliwal, Indhu M. Nair, Ankur Gupta*

Department of Chemistry, IISER Bhopal

(Email: bharti18@iiserb.ac.in)

Abstract: Escalating consumption of energy and fuel demand technologies and methodologies to exploit abundantly available renewable energy sources. At the same time, nature stores energy in the form of chemical bonds (carbohydrates) by converting solar energy to chemical energy through photosynthesis[1]. During the process, PS-II uses photon (sunlight) energy to oxidize water at the OEC (oxygen evolution center), and the electrons produced are eventually used in the Calvin cycle to reduce CO_2. Inspired by nature, researchers have tried to mimic the natural photosystem and achieve water oxidation. The latter is a thermodynamically and kinetically demanding process, and many potential (inorganic) photocatalytic systems have been developed[1b] to achieve the same. Light-driven water oxidation, having a particular focus, has also resulted in various biomimetic photocatalytic systems[1c].

In our work, we want to design a photo-biocatalytic system consisting of a light-harvesting antenna (photocatalyst), which tethers covalently at an anchoring site of a (bio-)catalyst. The designed system is proposed to catalyze water oxidation via artificial photosynthesis. Photo-induced water oxidation via transition-metal-based catalysts (e.g., ruthenium complexes) is known in the literature, accompanied either by an external bias (electrochemically)[2] or visible light (photochemically)[3]. Using an enzyme, laccase- a multi-copper oxidase, Pita and coworkers achieved electrooxidation of water in the absence[4a] and presence[4b] of visible light at low over-potentials. Providing an external bias to the bio-electrochemical system, they could reverse the natural laccase cycle, i.e., oxygen reduction and scavenge the electrons from water. Inspired by the work, we chose small laccase (SLAC) as the biocatalyst, which conjugates to the photocatalyst via thiol-maleimide covalent linkage. We have chosen ruthenium-complexes having 2,2'-bipyrimidyl and 2,2'-bipyrazyl ligand systems as the photocatalysts due to their broad range of the visible spectrum, long-lived excited states and high positive redox potentials. We hypothesize exploiting the excited state redox properties of the complexes to back-pedal the biological activity of SLAC, which in turn will catalyze water oxidation.



Scheme: A photo-biocatalytic design proposed to catalyse water oxidation.

References:

1. (a) Moore, G.F.; Brudvig, G. W. *Annu. Rev. Condens. Matter Phys.* **2011**, *2 (1),* 303–327. (b) Blakemore, J.D. et al. *Chem. Rev.* **2015**, 115(23), 12974–13005. (c) Reisner, E. et al. *Chem. Soc. Rev.*, **2020**, 49, 4926-4952.
2. Nocera, D. G. *Acc. Chem. Res.* **2012**, *45* (5), 767–776
3. Concepcion, J. J. et al. *Proc. Natl. Acad. Sci. U. S. A.* **2008**, *105* (46), 17632–17635
4. (a) Pita, M. et al. *J. Am. Chem. Soc.* **2014**, *136,* 5892–5895. (b) Tapia, C. et al. *ACS Catal.* **2017**, *7* (7), 4881–4889

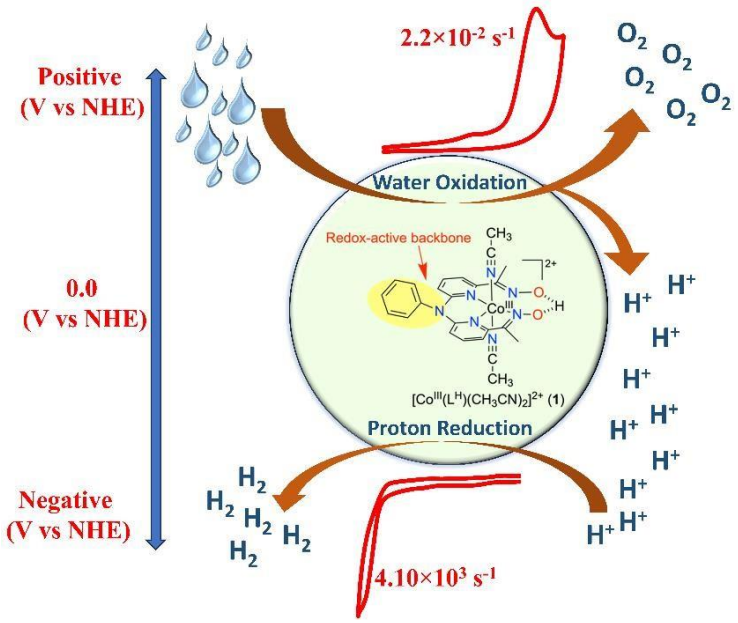
Electrocatalytic water oxidation and proton reduction by a molecular cobalt complex of a N_4 donor ligand consisting of a redox active scaffold at the secondary coordination sphere

Afsar Ali[a], Rajneesh Varma, Avijit Das, Aakash Santra, Sayantan Paria*

[a]National Post Doctoral Fellow

IIT Delhi, Houz Khas, New Delhi (110016) India.

Over the last few decades, economic development and climate change have been rising environmental issues caused by using non-renewable energy sources. Hence, renewable energy resources have emerged as a potential alternative for the widely utilized fossil fuels for the generating of environment-friendly energy infrastructure in recent years.[1,2] On the other hand, carbon-neutral renewable energy resources like solar, wind, hydropower, and geothermal do not emit any hazardous side products. Solar energy is reckoned as the best option to fit the role due to its global abundance and availability. However, Natural photosynthesis converted sunlight into chemical energy (carbohydrates) via reduction of CO_2 and water oxidation.[3,4]



Molecular catalysts play a crucial role in understanding the mechanism of water oxidation reaction/proton reduction reaction, characterization of the reaction intermediates, and fine-tuning the catalytic efficiencies.[5] In this study, we have explored The electrocatalytic water oxidation (WO) and proton reduction activity by molecular complexes **1-2** and **3** respectively. **1** works as a homogeneous electrocatalyst for the WO reaction in a 0.1 M phosphate buffer solution over a broadpH range (4 to 11). However, complex **2** is inactive for water oxidation rection. A ligand-centred oxidation process was observed before the catalytic peak, which supports the WO

reaction through the generation of the oxidative hole. Interestingly, we have installed dimethylamine group at secondary coordination sphere in complex **3**, which

assist for proton relay formation toward active site. Herein, complex **1** and **3** are activefor proton reduction reaction in 0.1 M PBS (pH range from 4 to 7). All synthesized complexes (**1, 2** and **3**) have shown homogeneous nature of catalysis which was confirmed by SEM, EDX techniques and electrochemical investigation.

References:

(1) Le, J. M.; Bren, K. L. Engineered Enzymes and Bioinspired Catalysts for Energy Conversion. *ACS Energy Lett.* **2019**, *4* (9), 2168–2180. https://doi.org/10.1021/acsenergylett.9b01308.

(2) Salamatian, A. A.; Bren, K. L. Bioinspired and Biomolecular Catalysts for Energy Conversion andStorage. *FEBS Letters* **2023**, *597* (1), 174–190. https://doi.org/10.1002/1873-3468.14533.

(3) Bren, K. L. Multidisciplinary Approaches to Solar Hydrogen. *Interface Focus* **2015**, *5* (3), 20140091. https://doi.org/10.1098/rsfs.2014.0091.

(4) Dey, A.; A. Houle, F.; E. Lubner, C.; Sevilla, M.; J. Shaw, W. Introduction to (Photo)Electrocatalysis for Renewable Energy. *Chemical Communications* **2021**, *57* (13), 1540–1542. https://doi.org/10.1039/D0CC90530E.

(5) Bera, M.; Kaur, S.; Keshari, K.; Moonshiram, D.; Paria, S. Characterization of Reaction Intermediates Involved in the Water Oxidation Reaction of a Molecular Cobalt Complex. *Inorg.Chem.* **2022**, *61* (51), 21035–21046. https://doi.org/10.1021/acs.inorgchem.2c03559.

Molecular Ruthenium(III) Complexes for Water Oxidation Catalysis: Impact of Redox-Non-Innocent Ligand

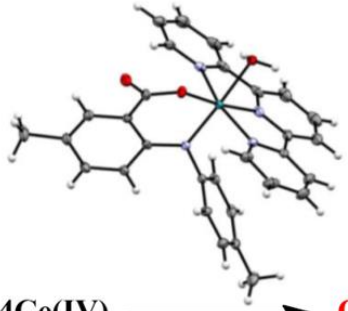
Sreeja Dasgupta,[a] Ayyan Ghosh,[a] Sukanta Mandal*[a]

[a] Department of Chemistry, Indian Institute of Technology Kharagpur, Kharagpur-721302, India.

Email: sukanta.mandal@chem.iitkgp.ac.in;

ajeers96@kgpian.iitkgp.ac.in

The enormous growth of the world population and consequently increasing energy consumption led to an urgent need to find a sustainable and environmentally friendly energy resource (mainly carbon free). Visible-light-driven water splitting presents a promising and sustainable approach to converting solar energy into high-energy chemicals like hydrogen (H_2). However, the water oxidation step ($2H_2O \rightarrow O_2 + 4H^+ + 4e^-$) presents a significant challenge due to its formidable kinetic and thermodynamic barrier ($\Delta G° = +113.38$ kcal/mol), which acts as a primary bottleneck impeding the overall water splitting reaction. Overcoming these challenges requires a molecular-level understanding of the water oxidation process and the development of efficient catalysts.[1-3] Molecular ruthenium complexes supported by anionic, redox-non-innocent ligands have been synthesised in this context. These complexes demonstrate remarkable catalytic activity in water oxidation, facilitated by forming formal high-valent Ru(VII) species through a series of proton-coupled electron transfer steps. The redox-non-innocent behaviour of the anionic ligand framework helps the accumulation of oxidative equivalents in cooperation with the metal centre, thereby enabling multi-electron transfer reactions, such as water oxidation. The poster will highlight the benefit of using redox-non-innocent ligands in a designed catalyst, which may pave the way for developing advanced water oxidation catalysts.



$$2H_2O + 4Ce(IV) \longrightarrow O_2 + 4H^+ + 4Ce(III)$$

References:

1. Ghosh, A.; Dasgupta, S.; Kundu, A.; Mandal, S. Dalton Trans. 2022, 51, 10320-10337.
2. Kundu, A.; Barman, S. K.; Mandal, S. Inorg. Chem. 2022, 61, 1426-1437.
3. Kundu A.; Dey, S. K.; Dey, S.; Anoop, A.; Mandal, S. Inorg. Chem. 2020, 59, 1461−1470.

Dangling Carboxylic Group Participates in O-O Bond Formation Reaction to Promote Water Oxidation Catalyzed by a Ru Complex: An Oxide Relay Pathway

Animesh Kundu[1,2], and Sukanta Mandal*[2]

[1]Department of Basic Science & Humanities, Institute of Engineering & Management (IEM) Kolkata, Salt Lake - 700091, W.B., India
[2]Department of Chemistry, Indian Institute of Technology (IIT) Kharagpur Kharagpur - 721302, W.B., India

Email : sukanta.mandal@chem.iitkgp.ac.in
Animesh.Kundu@iem.edu.in

Abstract: Two mononuclear ruthenium(II) complexes of types $[Ru(trpy)(HL^1)(OH_2)]^{2+}$ (**1^{Aq}**) and $[Ru(trpy)(L^2\text{-}\kappa\text{-}N^2\text{-}O)]$ (**2**) [where trpy = 2,2':6',2"-terpyridine, HL^1 = 2-(2- pyridyl)benzimidazole, H_2L^2 = 2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-4-carboxylic acid] have been synthesized and thoroughly characterized by analytical, and spectroscopic (UV-vis, NMR, HRMS, IR) techniques. Complex **1^{Aq}** has been further characterized by X-ray crystallography. In acidic aqueous medium (pH 1), complex **2** undergoes carboxylate/water exchange readily to form an aqua-ligated complex $[Ru(trpy)(H_2L^2\text{-}\kappa\text{-}N^2)(OH_2)]^{2+}$ (**2^{Aq}**) having a dangling carboxylic group. This exchange phenomenon has been followed by IR, ^{1}H NMR and UV-vis spectroscopic techniques. Electrochemical analyses of **1^{Aq}** and **2^{Aq}** (Pourbaix diagram) suggest the generation of a formal Ru^V=O species that can potentially promote the oxidation of water. A comparative study of water oxidation activity catalyzed by **1^{Aq}** and **2^{Aq}** is reported here to see the effect of dangling carboxylic group in catalytic performance. Complex **2^{Aq}** shows enormously higher rate of reaction than **1^{Aq}**. The pendant carboxylic group in **2^{Aq}** participates in an intramolecular O-O bond formation reaction with reactive formal Ru^V=O unit to form percarboxylate intermediate, and provides an electron deficient carbon center where water nucleophilic attack takes place. The isotope labelling experiment using ^{18}O-labelled water verifies the attack of water at the carbon center of carboxylic group, rather than direct attack at the oxo of formal Ru^V=O unit. The present work provides an experimental evidence of uncommon functionality of carboxylic group, the oxide relay, in molecular water oxidation chemistry.

Keywords : Ruthenium Complex, Water Oxidation, Catalysis, Oxide Relay Mechanism.

Reference : Kundu, A.; Barman, S. K.; Mandal, S. *Inog. Chem.***2022**, *61*, 1426 – 1437.

Efficiency Conceptualization Model in the light of Bio-Inspired Molecular Water Oxidation Catalysts

Himangshu Pratim Bhattacharyya and Manabendra Sarma*

Indian Institute of Technology Guwahati, Assam, India 781039

*Email: msarma@iitg.ac.in

To compute the catalytic efficiency in terms of turnover numbers (TONs) is a demanding task. With the commencement of the DFT era, it is possible to outline the efficiencies quantitatively. Developing novel methods to recognize the efficiency of this state-of-the-art approach is an urgent necessity. In the present work, we developed a model, the efficiency conceptualization model (ECM), that uses reliable DFT computations to predict the turnover number (TON) of catalysts. For the suitability of comparison, the method was implemented under the experimental conditions of temperature, pressure (1 atm), and p^H. To execute the model, twenty-six experimentally synthesized bio-inspired transition metal-based molecular catalysts for water oxidation reaction were considered. The results from our calculation replicate the experimental trend with the highest TON, $\tau^0_{computed\ TON}$ = 4429 (in M06-L) for MWOC-24 against the experimental TON, $\tau^0_{experimental\ TON}$ = 2000.

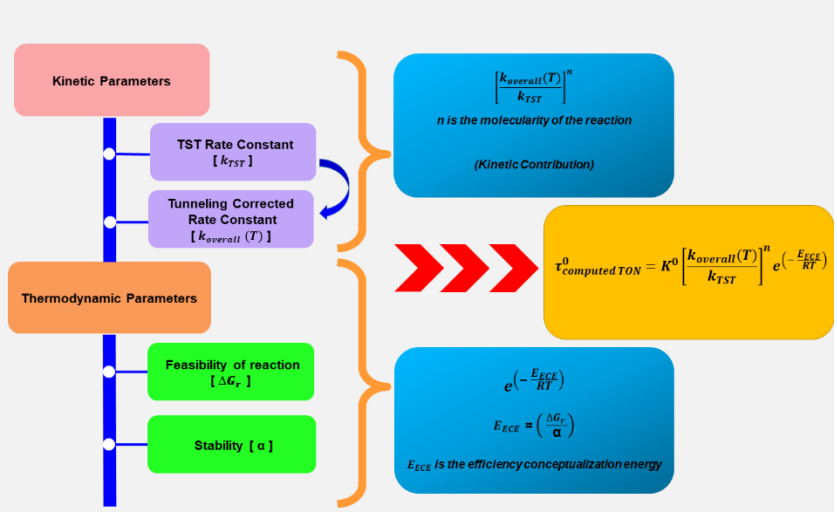


Figure 1. The efficiency conceptualization model (ECM) to evaluate TON of bio-inspired transition metal-based molecular catalysts.

References:

1) Kozuch, S.; Shaik, S. How to conceptualize catalytic cycles? The energetic span model. *Acc. Chem. Res.* **2011**, *44*, 101– 110.
2) Bhattacharyya, H.P.; Sarma, M. (Under Review)

Redox-active Sn(II) to lead to $SnFe_2O_4$ spinel as a bi-functional water splitting catalyst

Anubha Rajput [1], Biswarup Chakraborty* [1]

[1]Department of chemistry, Indian Institute of Technology Delhi, Hauz Khas, New Delhi 110016,
Email: Anubha.Rajput@chemistry.iitd.ac.in

Despite several reports on metal ferrites for water splitting studies, p-block metal containing ferrite, $SnFe_2O_4$, is a less explored spinel oxide for electrocatalytic study. In our recent work, solvothermally prepared ca. 5 nm $SnFe_2O_4$ nanoparticles deposited on nickel foam (NF) has been shown as a bi-functional electrocatalyst to split water into O_2 and H_2.[1] In alkaline pH, the $SnFe_2O_4$/NF electrode exhibits oxygen evolution reaction (OER) and hydrogen evolution reaction (HER) activity at moderate overpotentials while the fabricated water electrolyzer $SnFe_2O_4$/NF(-)/(+)$SnFe_2O_4$/NF operates at a cell potential of 1.69 V along with a fair chronoamperometric stability (Figure 1). Cyclic voltammetry (CV) study with $SnFe_2O_4$ identified the prominent redox features for the Fe^{III}/Fe^{II} and $Sn^{II/0}$. Detailed studies have found that Sn^{II} sites are active for the HER and Sn^0 species is formed to accelerate the HER, whereas Fe^{III} sites play the lead role in the OER. Under the electrocatalytic water splitting condition, $SnFe_2O_4$ showed notable long-term stability whereas hydrolytic dissolution is common for other transition metal based catalyst. Herein, the active participation of redox-active Sn metal in water splitting is observed, which remarkably differs from the reported metal ferrites where the s-block and p-block metal counterparts remain redox inactive.

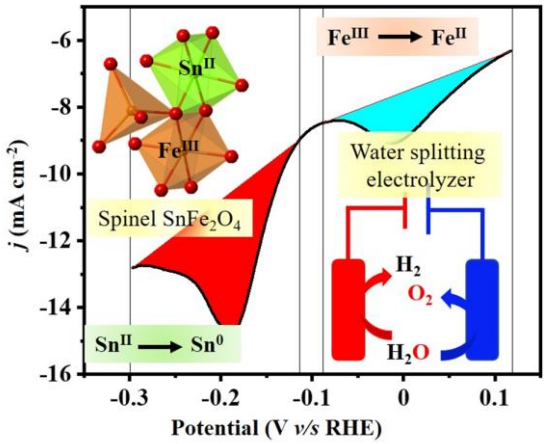


Figure 1. $SnFe_2O_4$ as bi-functional water-splitting catalyst with active redox-participation of Sn and Fe.

References:

1. A. Rajput, A. A. Pandey, A. Kundu and B. Chakraborty, *Chem. Commun.*, **2023**, *59*, 4943 4946.

An Intramolecular Cobalt-Peptoid Complex as an Efficient Electrocatalyst for Water Oxidation in Low Overpotential

Suraj Pahar, Prof. Galia Maayan*
Schulich Faculty of Chemistry
Technion-Israel Institute of Technology

Abstract: Water electrolysis is one of the simplest ways to produce hydrogen by artificial photosynthesis, which can be an alternate clean energy source and an effective strategy to cope with future energy crisis. Oxidation of water to dioxygen requires multi-proton/electron transfer as well as several bond rearrangements, therefore it is considered a bottleneck towards the development of catalytic system. Moreover, the high overpotential and slow kinetics are the crucial factors that limit its applicability. Thus, designing a highly efficient, cheap, and stable molecular catalyst for water oxidation based on non-precious metals is still a great challenge. Inspired by enzymatic catalysis, which is based on cooperativity between a metal center and the functional organic molecules located in the scaffold around the metal center, our group is developing catalytic systems that are based on peptide mimics called peptoids (N-substituted glycine oligomers), bearing various metal-binding side chains. Our group previously showed that peptoids represent an excellent scaffold for embedding metal centers. Thus, copper-peptoid complexes, bearing one metal-binding side chain, were developed as water oxidation electrocatalysts in pH > 9. It was demonstrated that the peptoid scaffold plays a unique role in stabilizing the high oxidation state of the metal center, resulting in the overall stability and high activity of the catalyst. A similar cobalt-peptoid complex was also developed in our group as an electrocatalyst and as a photocatalyst for water oxidation but high stability was not achieved. Based on the previous findings, I will present how I have tried to overcome the stability problem by synthesizing a peptoid trimer bearing two metal-binding side chains that can coordinate the cobalt ion stronger by forming an intramolecular cobalt complex. I demonstrated that this complex is much more stable than the previous one and acts as an efficient homogeneous catalyst for electrocatalytic water oxidation in aqueous phosphate buffer solution at pH 7 with catalytic turnover number (TON) 17.1 and a high Faradaic efficiency of up to 92% in 10 hours at an overpotential of 433 mV.

References

1. T. Ghosh, P. Ghosh, and G. Maayan, “A Copper-Peptoid as a Highly Stable, Efficient, and Reusable Homogeneous Water Oxidation Electrocatalyst”, ACS Catal. 2018, 8, 10631−10640.
2. G. Ruan, L. Engelberg, P. Ghosh and G. Maayan, “A unique Co(III)-peptoid as a fast electrocatalyst for homogeneous water oxidation with low overpotential.” *Chem. Commun.,* 2021, **57**, 939 —942.
3. G. Ruan, P. Ghosh, N. Fridman, G. Maayan, “A Di-Copper-Peptoid in a Noninnocent Borate Buffer as a Fast Electrocatalyst for Homogeneous Water Oxidation with Low Overpotential.” J. Am. Chem. Soc. 2021,143, 10614–10623.
4. **S. Pahar**#, K. Majee# and Galia Maayan, “A Cobalt-based Peptoid as an Efficient Catalyst for Visible Light Driven Water Oxidation” – Submitted.
5. **S. Pahar** and G. Maayan “An Intramolecular Cobalt-Peptoid Complex as an Efficient Electrocatalyst for Water Oxidation in Low Overpotential” – In preparation.

Enhancing Secondary Iron Overload Treatment: Design, Synthesis and Evaluation of Zwitterionic Carbon Nanodots-Deferoxamine Conjugated

Pradnya Pachpatil[a,c], Avik Chakaraborty[b], Jitesh Rathee[a], Somnath Ghosh[b,c], Dibakar Goswami[a,c]

[a] Bioorganic Division,Bhabha atomic research center, Trombay 400085

[b] Radiation Medicine Center Parel , Mumbai 400012

[c]Homi Bhabha National institute, Anushaktinagar ,Mumbai-400094

Secondary iron overload affects millions of people, necessitating iron chelators as the primary treatment. However, the FDA-approved iron chelator, Deferoxamine, exhibits numerous side effects, including infection, gastrointestinal bleeding, and liver fibrosis. These undesirable effects are attributed to its unwanted biodistribution, alongwith chelator excretion via feces, leading to infections and gastric complications. Iron overload patients have increased liver iron which leads to liver dysfunction as well as reduced billary excreation. Interestingly, iron overload rarely affects renal compliance, making renal clearability advantageous. Therefore, there is an need for novel chelation agents which offer improved pharmacokinetics and biodistribution, as well as efficacy and safety. To address these challenges, we utilized carbon nanodots (CND) as vectors due to their biocompatibility, bioavailability, low toxicity, ease of synthesis, and functionalization capabilities. It is known that zwitterionic nanoparticles with smaller hydrodynamic diameter (HD) are preferred for renal clearance. Herein, we have designed a novel nanochelator by conjugating Deferoxamine with zwitterionic CND[1] and have aimed to enhance its biodistribution and half-life. Zwitterionic CND was prepared using a combination of natural sugar and amino acid via hydrothermal method, and was conjugated to desferrioxamine to get a nanochelator with 5-7 nm size range, ensuring renal clearability. Using the ^{68}Ga conjugate of the chelator, we compared the biodistribution of DFO and CND-DFO in C57BL/6 mice through a cut-and-count method at various time points. Remarkably, CND-DFO demonstrated reduced deposition in muscle, brain, heart, lungs, liver, spleen, stomach, and intestine, with predominant distribution in the kidney. This can be beneficial to circumvent the toxic side effects of desferroxamine . In the in-vivo experiments using iron-overloaded C57BL/6 mice CND-DFO conjugate was able to mitigate the iron levels to a higher extent than the parent DFO, which signifies its avantage over DFO.

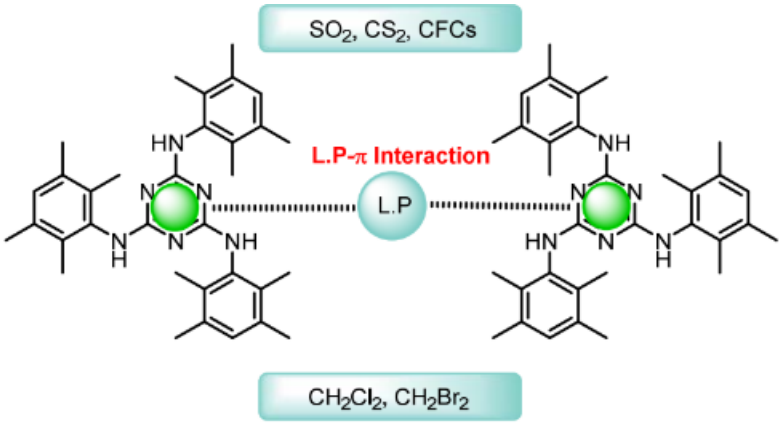
References

1. Kang H, Han M, Xue J, et al. Renal clearable nanochelators for iron overload therapy. *Nat Commun*. 2019;10(1). doi:10.1038/s41467-019-13143-z

Employing bio-inspired lone pair-π interactions in sequestration and activation of environmentally detrimental molecules

Neha Kumari and Raja Angamuthu*
Laboratory of Inorganic Synthesis and Bioinspired Catalysis (LISBIC)Department of Chemistry
Indian Institute of Technology KanpurEmail:
nehak21@iitk.ac.in

Noncovalent interactions (NCIs) are ubiquitous in nature. These interactions play a key role in stabilizing biomolecules, host-guest chemistry, and in formation of supramolecular assembliesincluding hydrogen bonding, π-π stacking, cation-π, anion-π, and lone pair-π interactions.[1,2] In comparison to covalent bonds, intra and inter molecular interactions are weak and exhibit much lower energy and directionality. While hydrogen bonding, π-π stacking, cation-π, and anion-π interactions have been extensively studied and employed by chemists, lone pair-π interactions are yet to be seen at work, especially in sequestration chemistry. Herein, we synthesised a symmetrical-trisubstituted 1,3,5-triazine molecules as a stable host that can form piedfort dimer with sufficient area (inter-disc distance ~ 9 Å) in between two C_3N_3 ring to park environmentally detrimental molecules such as sulphur dioxide, carbon disulfide, and halocarbons. Substituted triazines with hydrophobic periphery allows the tuning of inter-disc distance between adjacent C_3N_3 rings and interaction between neighboring molecules.[3,4] The investigation of the solid-state structures using single crystal X-ray diffraction (SCXRD)revealed the presence of inter molecular interactions (lone pair-π interaction) involving the centroid of triazine and electronegative atom of its surroundings molecules.



References:

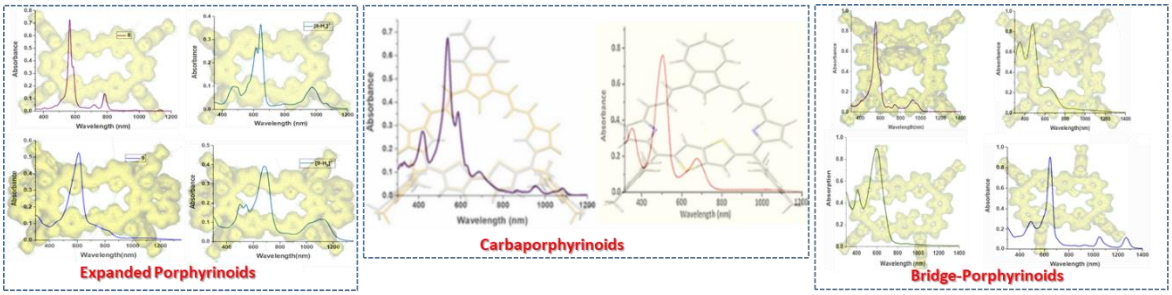
1. M. Giese, M. Albrecht, and K. Rissanen, *Chem. Commun*., **2016**, *52*, 1778.
2. E. Nagy, E. St Germain, P. Cosme, P. Maity, A. C. Terentis, and S. D. Lepore, *Chem. Commun*., **2016**, *52*, 2311.
3. S. Mehrotra, S. Raje, A. K. Jain, A. Jain, P. Kandasamy, R. J. Butcher, and R. Angamuthu, *Chemistry Select*, **2018***, 3,* 4844-4850.
4. S. Mehrotra, S. Raje, A. K. Jain, R.J Butcher, and R. Angamuthu, *Chem. Commun.,* **2022**, *58*, 11815-11818.

Adoptive Aromaticity with NIR Absorption of Carba Porphyrinoids and Expanded CarbaPorphyrinoids

Sumit Sahoo, Harapriya Rath

School of Chemical Sciences, IACS, Jadavpur, Kolkata,700032

Aromaticity is considered as one of the most important concepts in modern organic chemistry that determines structure, stability, and reactivity of the molecules.[1] Aromatic compounds having absorptions and emissions in the red or near-infrared (NIR) region are capable materials for a broad range of applications such as photodynamic therapy dyes, semiconductors in light-emitting diodes, photo-sensitizers in solar cells and microscopic imaging agents.[1, 2] In the never-ending challenges to synthetically arrive at new generation heteroannulenes exhibiting aromaticity, unique reactivity and unusual spectroscopic characteristics, one the most challenging task is the macrocyclic cavity size alteration and perturbing electronic structure of the macrocycles by replacement of carbon(s) in place of pyrrole nitrogen(s), the so called Carbaporphyrins.[3] Thus the scientific content of my poster highlights syntheses and structural isolation of NIR absorbing carbaporphyrinoids and expanded (carba)porphyrinoids with sustained aromaticity either via tropylium character of a dipolar aromatic hydrocarbon or lack of dual macrocyclic π-conjugation or via N-confusion.[4]



References

1. Schleyer, P. v. R. Introduction: Aromaticity. *Chem. Rev.* **2001**, *101*,1115−1118.

2. Lash, T. D. *Carbaporphyrinoid Systems. Chem. Rev. 2017, 117, 2313–2446.*

3. *Sahoo, S.; Jana, M.; Rath; H. Tailor-made aromatic porphyrinoids with NIR absorption.* ***Chem. Commun.*** *2022,* ***58****, 1834-1859.*

4 (a) Sahoo, S.; Velmurugan, G.; Comba, P.; ,Rath, H.; *meso-meso* 1,3-bis(*E*-vinyl) azulene bridged tetrathiaoctaphyrins: Synthesis, Spectroscopic and Theoretical Characterization. *Org. Chem. Front.* **2023,** *10*, 5601-5609. (b) Sahoo, S.; Mahadavaiah, M. H.; Usharani, D.; Rath, H. NIR Absorbing Aromatic *E*-Ethylene Bridged Hexaphyrins (2.1.1.2.1.1): Synthesis, Characterization, and Protonation Studies. *Org. Lett.* **2023**, *25*, 9, 1491–1496; (c) Sahoo, S.; Gunasekaran, V.; Chakraborty, B.; Comba, P.; Rath, H. NIR Absorbing Aromatic (Antiaromatic) Vinylogous Carbasapphyrins (3.3.1.0.1) with built-in Fused Dipolar Aromatic Hydrocarbon: Synthesis and Characterization. *Org. Chem. Front.* **2021**, *8*, 6909-6915. (d) Sahoo, S.; Sangeetha, M.; Bera, S.; Usharanin, D.; Rath, H. Targeted Synthesis of meso-Aryl Substituted Aromatic *trans*-Doubly N-confused Dithia/Diselena [18] porphyrins (1.1.1.1) with NIR Absorption: Spectroscopic, and Theoretical Characterization. *Org.Biomol. Chem.* **2020,** *18***,** 6058-6062.

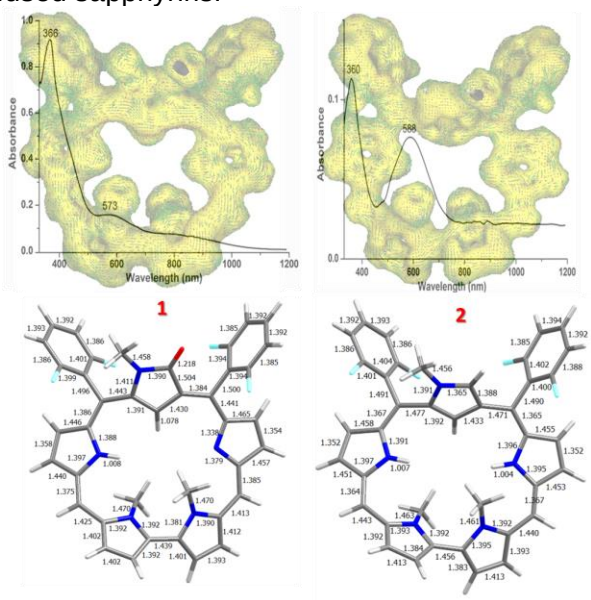
Fully conjugated and cross-conjugated doubly *meso*-free N-confused Sapphyrins

Sumit Sahoo,[a] Nilesh Ranjan Ghosh, [a] Peter Comba [b*] and Harapriya Rath [a*]

[a] School of Chemical Sciences, IACS, Jadavpur, Kolkata,700032

[b] Heidelberg University, Institute of Inorganic Chemistry and Interdisciplinary Center for Scientific Computing, Im Neuenheimer Feld 270, 69120 Heidelberg, GERMANY.

NIR absorption dyes based on fused coplanar porphyrin oligomers represented by *meso*–*meso*, β–β, β–β triply linked porphyrin arrays (porphyrin tapes), with spectacular bathochromic shift up to 2800 nm in specific case have been pioneered by Osuka et al. and Kim et al.[1] These properties in long and rigid molecular shapes suggest their potential use as molecular wires. The N-confusion-fusion dichotomy conglomerated with the bathochromic effects brought about by expanded N-confused porphyrinoids has surged scientific demands for unravelling more and more such structural analogues.[2] The scientific content of my poster highlights retrosynthetic design, structural isolation and in depth DFT level theoretical studies of doubly *meso*-free N-confused sapphyrins and their chemical functionalization to arrive at *meso*-*meso* and/or *meso*-b dimeric N-confused sapphyrins.[3]



References

1. Kim, D.; Osuka, A.; *Acc. Chem. Res*. **2004**, *37*, 735-745.
2. (a) Sessler, J. L..; Cho, D.-G.; Stepien, M.; Lynch, V.; J. Yoon, Z. S.; Kim, D. *J. Am. Chem. Soc.* 2006, *128*, 12640–12641. (b) Pushpan, S. K.; Srinivasan, A.; Anand, V. G.; Venkatraman, S.; Chandrashekar, T. K.; Joshi, B. S.; Roy, R.; Furuta, H. *J. Am. Chem. Soc.* **2001**, *123,* 5138–5139. (c) Gupta, I,; Srinivasan, A.; Morimoto, T.; Toganoh, M.; Furuta, H. Angew. Chem. Int. Ed. **2008**, *47*, 4563–4567.
3. Sahoo, S.; Ghosh, N.; Comba, P.; Rath, H. (manuscript submitted)

Organometallic Copper complexes of core modified N-methyl N-confused porphyrinoid vs doubly N-confused porphyrin

Anirban Panua,[a] Peter Comba*[b] and Harapriya Rath*[a]

a: School of Chemical Sciences, Indian Association for the Cultivation of Science,2A/2B Raja SC Mallick Road, Jadavpur, Kolkata 700032, India.
b: Heidelberg University, Institute of Inorganic Chemistry and Interdisciplinary Center for Scientific Computing, Im Neuenheimer Feld 270, 69120 Heidelberg, Germany.

Abstract:
Among the N-Confused porphyrin analogues, doubly N-Confused porphyrins having two inner core carbon and two nitrogen atoms efficiently stabilize the unusual metal oxidation state.[1] Restricting NH tautomerism of N-confused pyrrole ring(s) via N-alkylation has led to stabilization of smallest ever [16] anti-aromatic doubly N-confused porphyrin in very specific instance,[2a] whereas incorporation metallocene such as ferrocene unit in such macrocyclic conjugation pathway led to peripherally coordinated diasteromeric Rh(I).[2b] While, swaping pyrrole N with chalcogen (s) such as S/O results core modified N-confused porphyrin with altered electronic structure.[3] Thus, this poster highlights *meso*-aryl substituted highly stable Hückel type core-modified aromatic N-confused thia [18] porphyrin that has been utilized towards the formation of organometallic copper complex via inner CH bond activation.[4] Contrarily, symbiotic generation of doubly N-confused porphyrin via N-methyl N-confused pyrrole and N-confused pyrrole moieties as synthons led to organometallic copper complex via double inner CH activation. The sustained dia(para)magnetic ring current effect of all the macrocycles via in depth spectroscopic characterisation, electrochemical studies and DFT level theoretical studies will be highlighted in the poster.[4]

References:

1. Furuta, H.; Asano, T.; and Ogawa, T. *J. Am. Chem. Soc.,* **1994**, 116, 767.

2. **a.** Halder, N.; Sangeetha, M,; Usharani, D.; and Harapriya Rath. *J. Org. Chem*., **2020**, 85, 2059−2067.
b. Halder, N.; Sahoo, K. C.; Gourav, K.; Usharani, D.; and Harapriya Rath. *J. Org. Chem*., **2021**, 86, 8015−8026.

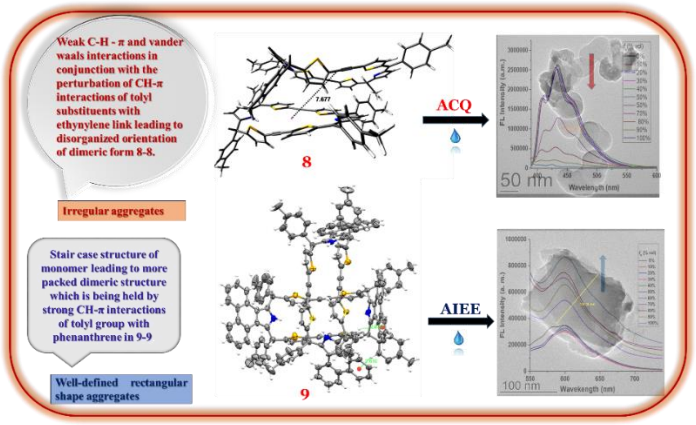
3. Sprutta, N.; and Latos-Grażyński, L, *Org. Lett*., **2001**, 3, 1933.

4. Panua, A.; Comba,P ,; and Rath, H. (Manuscript under review).

Core-modified Expanded phlorinoid and Calix[6]phyrinoid with Tunable Properties: Synthesis and Characterization

Sumit Sahoo,[†] Pallab Chaterjee,[†] Dandamudi Usharani,[§*] and Harapriya Rath[†*]

Fluorescent materials have gained much attention in diverse fields, such as fluorescent biological labels, sensors, and light-emitting diodes. [1] Porphyrins have been widely used in image-guided surgery [2] and the fluorescence detection of malignancies. [3] However, the aggregation caused quenching (ACQ) effect [4a], which reduces the maximum fluorescence imaging capability of porphyrins, is brought on by their propensity to form □-□ stacking aggregates through driving forces like hydrogen bonding, van der Waals interactions, electrostatic interactions, and hydrophobic effects. [4] In this context, recent years have witnessed the unique phenomenon widely researched as aggregation-induced emission [5] and aggregation-induced enhanced emission [6] as a potential solution to ACQ in some organic molecules. The scientific content of my poster highlights structural revelation via x-ray crystal structure and spectroscopic analyses of two hitherto unknown highly stable single conformer of ACQ type fluorophore based on core-modified ethynylene-cumulene linked expanded phlorinoid and AIEE type fluorophore based on ethynylene linked Calix [6]phyrin.[7]



References

1. a) Jenekhe, S. A; Osaheni, J. A. Excimers and Exciplexes of Conjugated Polymers. Science. 1994; 265.765–768. (b) Friend, R.H; Gymer R. W; Holmes, A. B; Burroughes J. H; Marks, R. N; Taliani, C; Bradley, D. D. C; Dos Santos, D. A.; Br das, J. L; Lçgdlund, M; Salaneck, W. R. Electroluminescence in conjugated polymers. Nature. 1999, 397,121–128. (c) Deans, R; Kim, J; Machacek, M. R; Swager, T. M. A Poly(p-phenyleneethynylene) with a Highly Emissive Aggregated Phase. J. Am. Chem. Soc. 2000,122, 8565–8566.

2. (a) Ethirajan, M; Chen, Y; Joshi, P; Pandey, R. K. The role of porphyrin chemistry in tumor imaging and photodynamic therapy. Chem. Soc. Rev. 2011, 40,340–362. (b) Ng KK, Lovell JF and Zheng G. Lipoprotein-Inspired Nanoparticles for Cancer Theranostics. Acc. Chem. Res. 2011, 44, 1105–1113.

3. Lovell, J. F.; Roxin, A.; Ng, K. K.; Qi, Q.; McMullen, J. D.; DaCosta, R.S.; Zheng, G. Porphyrin-cross-linked hydrogel for fluorescence-guided monitoring and surgical resection.Biomacromolecules. 2011, 12, 3115–3118.

4. Birks, J. B. Photophysics of Aromatic Molecules, Wiley: New York, 1970.

5. Xie, Z.; Yang, B.; Xie, W.; Liu, L.; Shen, F.; Wang, H.; Yang, X.; Wang, Z.; Li, Y.; Hanif ,M.; Yang, G.; Ye, L.; Ma ,Y. A Class of Nonplanar Conjugated Compounds with Aggregation-Induced Emission: Structural and Optical Properties of 2,5-Diphenyl-1,4-distyrylbenzene Derivatives with All Cis Double Bonds. J. Phys. Chem. B. 2006; 110: 20993–21000.

6. An, B. K.; Kwon, S. K.; Jung, S. D.; Park, S. Y. Enhanced Emission and Its Switching in Fluorescent Organic Nanoparticles. J. Am. Chem. Soc. 2002; 124: 14410 –14415.

7. Sahoo S, Chatterjee P, Sangeetha S, Dandamudi U, Rath, H. J. Org. Chem. (manuscript under revision)

Organometallic Cu complexes of *meso-meso* bridged monocyclic Doubly N-confused Hexaphyrin and bicyclic Doubly N-confused Hexaphyrin

Manik Jana[a], Dage Sundholm,[b]* and Harapriya Rath[a]*

[a] School of Chemical Sciences, IACS, KOLKATA-700032

[b] Department of Chemistry, University of Helsinki, Finland, FIN-00014

N-confused porphyrins (NCPs) and their higher analogues via stabilization of unusual metal oxidation states exhibit extraordinary photophysical/chemical properties.[1] Bicycloaromaticity refers two (or more) potentially aromatic circuits containing within the same non-planar molecular framework and share the same π electrons, which is more prominent in topologically nonplanar expanded porphyrinoids through *meso-meso* bridging linkages.[2] The competitive □ conjugation pathways (monocyclic/bicyclic) in specific expanded porphyrinoids has led dual macrocyclic aromaticity, thus paving ways for possibility of new generation molecular switches. Thus, the scientific content of this poster reveals an attempt to us switching of *meso-meso* bridged monocyclic □ conjugated doubly N-confused hexaporhyrinoid to the corresponding bicyclic doubly N-confused hexaporphyrinoid. This monocyclic □ conjugation to bicyclic □ conjugated doubly N-confused hexaporphyroid has been achieved merely via chemical oxidation and Cu metallation, the details of spectroscopic studies and DFT level theoretical investigations conclusively support such notion.[3]

References:

[1] a) H. Furuta, T. Asano, T. Ogawa, *J. Am. Chem. Soc.* **1994**, *116*, 767; b) G. R. Geiser III, D. M. Haynes, J. S. Lindsey, *Org. Lett.* **1999**, *1*, 1455.

[2] W. Y. Cha, T. Kim, A. Ghosh, Z. Zhang, X. S. Ke, R. Ali, V. M. Lynch, J. Jung, W. Kim, S. Lee, S. Fukuzumi, J. S. Park, J. L. Sessler, T. K. Chandrashekar, D. Kim, *Nat. Chem.*, **2017**, *9*, 1243.

[3] M. Jana, D. Sundholm, H. Rath (Manuscript under review).

A Singlet-Diradical Co(III)-Dimer as Non-volatile Resistive Switching Device. Synthesis, Redox-Induced Interconversion and Current-Voltage Characteristics

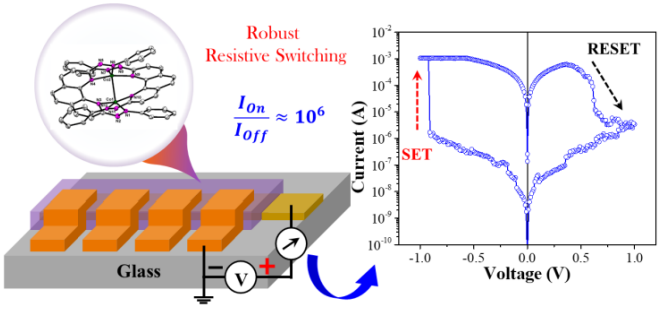
Subhankar Khanra,[a] Suman Sinha,[a] Muhammed Sahad E,[b] Nanda D. Paul*

[a]*Department of Chemistry, IIEST, Shibpur, Botanic Garden, Howrah 711103, India*

[b]*School of Physics,IISER TVM,Maruthamala PO, Vithura, Thiruvananthapuram 695551, India*

Email: ndpaul2014@chem.iiests.ac.in, ndpaul@gmail.com, ksubhankar585@gmail.com.

Abstract: A ligand-centered redox controlled strategy for the synthesis of an unusual binuclear di-radical cobalt(III)-complex $[Co_2^{III}(L^{\bullet 3-})_2]$ (**1**) featuring two three-electron reduced trianionic-mono-radical 2,9-bis(phenyldiazo)-1,10-phenanthrolineligands ($\mathbf{L}^{\bullet 3-}$) and two intermediate-spin cobalt(III) centers having a Co-Co bond. Controlled ligand-centered oxidationof **1** afforded two mononuclear complexes $[Co^{II}(L^{\bullet -})(L^0)]^+$ ($[\mathbf{3}]^+$)and $[Co^{II}(L^0)_2]^{2+}$ ($[\mathbf{2}]^{2+}$) which upon further ligand-centered reduction yielded a di-azo-anion diradical complex $[Co^{II}(L^{\bullet -})_2]$ (**4**). In complex **1**, two three-electron reduced di-azo-anion mono-radical ligands ($\mathbf{L}^{\bullet 3-}$) bridge two intermediate Co(III)-centers at a distance of 2.387(2)Å while upon oxidation, one of the coordinating azo-arms of **L** becomes pendant and in complexes $[\mathbf{2}]^{2+}$, $[\mathbf{3}]^+$, and **4**, two tetradentate ligands coordinate a single Co(II)-center in a tridentate meridional fashion with one uncoordinated azo-arm from each of the ligands. Spectroscopic analysis, DFT studies, and control experiments were performed to understand the electronic structures and ligand-centered redox-controlled interconversion. The application of complex **1** as molecular memory device (memristor) was also explored and it showed encouraging results as a memristor with a current ON/OFF ratio (> 10^4) and is highly promising for resistive RAM/ROM applications.



References:(1) Suman, S.; Muhammed, S. E.; Rakesh, M.; Siuli, D.; Litty, T. M.; Paula, B.; Bas, de B.; Bikas, C. D.; Nanda, D. P. *J. Am. Chem. Soc.* **2022**, *144*, 20442−20451.

(2) Siuli, D.; Suman, S.; Upasona, J.; Rina, S.; Ananya, S.; Suman, B.; Paula, B.; Nanda, D. P. *Inorg. Chem.* **2018**, *57*, 5830–5841.

Metal-Organic Cage Receptors for selective recognition and sensing of Bile acids

Bhaswati Paul[#,‡], Ramalingam Natarajan[#,‡*]

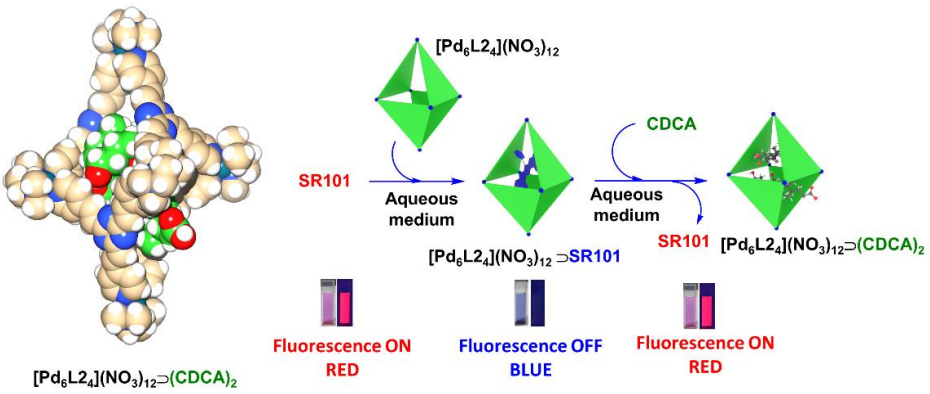
[#]Organic & Medicinal Chemistry Division, CSIR-Indian Institute of Chemical Biology, 4 Raja SC Mullick Road, Kolkata 700032, India

[‡]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad, 201002, India.

Email: mntibp2016@gmail.com

Abstract:

Developing synthetic supramolecular receptors for encapsulation-mediated recognition and selective sensing of steroids is challenging. Despite a limited number of receptors having affinity with steroids, none exists to bind steroidal bile acids with stronger affinity selectively. Herein, we report a novel C_2-symmetric metal-organic cage $[Pd_6\mathbf{L2}_4](NO_3)_{12}$, built by coordination-driven self-assembly of conformationally flexible ligand **L2**. The receptor encompasses a partly open hydrophobic pocket of roughly 1103 Å^3 volume in water. The receptor represents a slightly expanded version of the well-known Fujita's $[Pd_6\mathbf{L1}_4](NO_3)_{12}$ cage (462 Å^3). We examined both cages for steroid recognition in water. ^{1}H NMR titrations established a few similar and various unlike characteristics. $[Pd_6\mathbf{L1}_4](NO_3)_{12}$ forms 1:1 host-guest complexes with bile acids and other hydrophobic steroids mainly by hydrophobic interactions. In contrast, the expanded $[Pd_6\mathbf{L2}_4](NO_3)_{12}$ cage accommodates two steroid entities (1:2) in its spacious cavity. The latter exhibits a stronger affinity for amphiphilic bile acids to encapsulate them as dimers, promoted by cooperative inter-guest hydrogen bonding. $[Pd_6\mathbf{L2}_4](NO_3)_{12}$ has a five times stronger solubility enhancement ability for cholic acid (CA), with almost no affinity for the hydrophobic lithocholic acid (LCA). Notably, $[Pd_6\mathbf{L1}_4](NO_3)_{12}$ cage shows a strong affinity for LCA. Further, we demonstrate an indicator displacement assay to selectively sense chenodeoxycholic acid (CDCA), deoxycholic acid (DCA), and ursodeoxycholic acid (UDCA) with the $[Pd_6\mathbf{L2}_4](NO_3)_{12}$ cage-sulforhodamine101 dye complex. The sensing strategy demonstrates nanomolar detection limits through colourimetric (blue to red) and turn-on fluorescence response in aqueous media.



Water-soluble coordination polymers of Li^+, Na^+, K^+, and Ba^{2+} with an anionic Iron(III) complex acting as a binder ligand

Chanreingam Long and Manabendra Ray*

Department of Chemistry, IIT Guwahati, Guwahati, Assam, India 781039
email: manabray@iitg.ac.in

Binding of sodium, potassium and calcium ions play essential roles in ion pumps, muscle contraction or siderophores.[1-3] Binding is essentially ionic and kinetically labile, with little preference for ligands other than oxygen donors such as carboxylates or phenolates. The size and charge of the ions are the primary distinguishing factor. Most of our understanding of their binding preferences, coordination geometry and bond parameters comes from crown ethers, cryptands and metallacrown complexes.[4-7] Earlier, we observed the binding of Na^+ and K^+ with metal complexes of L-amino acid derivatives through the carboxylates of the complex, forming cryptand-like cages.[8,9] Due to architectural limitations, comparing the binding of ions with different sizes and charges within a similar environment could not be done. Here, we have structurally characterized and compared the Li^+, Na^+, K^+, and Ba^{2+} salts of the same coordinatively saturated anionic Fe(III) complex. All are water-soluble and recrystallizable coordination polymers. The present system is far away from biology, but it provides a tool to compare and understand the 'coordination chemistry' of alkali metal and alkaline earth metal ions, their structures and properties in solids and solutions.

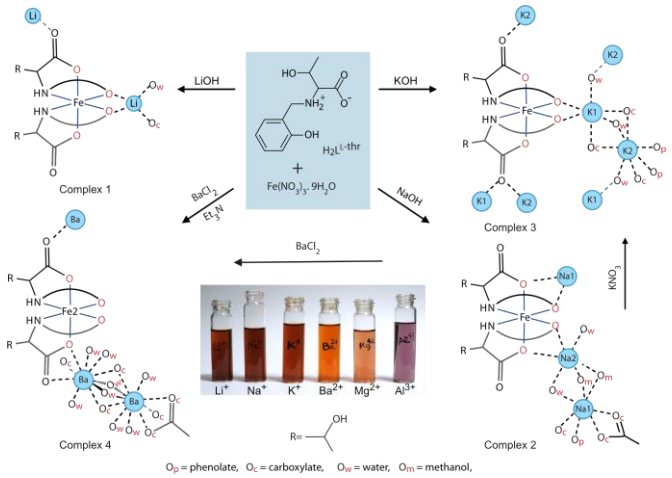


Figure 1. Synthesis and transformation of the structurally characterized complexes.

1. Michael V. Clausen, Florian Hilbers, and Hanne Poulsen, *Frontiers in physiology*, **2017**, *8*, 371.
2. Ivana Y. Kuo and Barbara E. Ehrlich, *Cold Spring Harb Perspect Biol* **2015**, *7*, a006023
3. Jos Kramer, Özhan Özkaya & Rolf Kümmerli, *Nat Rev Microbiol* **2020**, *18*, 152.
4. C. J. Pedersen, *Angew. Chem. Int. Ed.*, **1988**, *27*, 1021.
5. J. L. Lehn, *Angew. Chem. Int. Ed.,* **1988**, *27*, 89.
6. G. Mezei, C.M. Zaleski andV. L. Pecoraro, *Chem. Rev.*, **2007**, *107*, 4933.
7. E. R. Trivedi, S. V. Eliseeva, J. Jankolovits, M. M. Olmstead, S. Petoud and V. L. Pecoraro, *J. Am. Chem. Soc.*, **2014**, *136*, 1526.
8. Mrigendra Dubey, Rik Rani Koner, and Manabendra Ray, *Inorg. Chem.* **2009**, *48*, 9294
9. Mrigendra Dubey and Manabendra Ray *Cryst. Eng. Comm.* **2013**, *15*, 9648

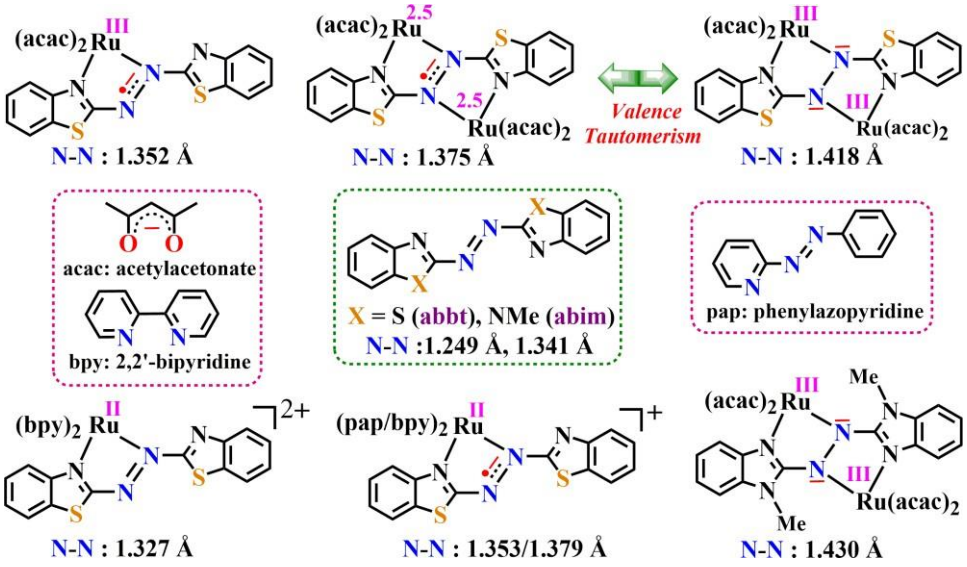
Inner-Sphere Electron Transfer Induced Diverse Electronic Forms at Ruthenium-Azoheteroarene Interface

Aditi Singh and Goutam Kumar Lahiri*
Department of Chemistry, Indian Institute of Technology Bombay, Powai, Mumbai,400076

Email: singhaditi203@gmail.com, lahiri@chem.iitb.ac.in

Transition metal complexes incorporating redox active ligands extended utility in catalytic, biological and industrial processes due to their multielectron storage capacity and facile electron transfer processes. In this regard, inner-sphere electron transfer at the ruthenium-azo interface (N=N, azoheteroarenes, $[\text{-N-N-}]^{0/\bullet-/2-}$) offers a unique opportunity to achieve electron reservoirs and bistability in molecular systems. Electronically rich {Ru(acac)$_2$} (acac: acetylacetonato) fragment on coordination to 2,2-azobis(benzothiazole) (abbt) led to metal-to-ligand charge transfer (MLCT) induced isolation of valence tautomers involving $[\{(acac)_2Ru^{2.5}\}_2(\mu\text{-abbt}^{\bullet-})]/[\{(acac)_2Ru^{III}\}_2(\mu\text{-abbt}^{2-})]$.[1] Contrary to that, electronically deficient $\{Ru^{II}(bpy)_2\}$ (bpy: 2,2′-bipyridine) and $\{Ru^{II}(pap)_2\}$ (pap: phenylazopyridine) metalfragments with abbt directed the formation of bistable electronic forms $[Ru^{II}(bpy)_2(abbt^0)]^{2+}/[Ru^{II}(bpy)_2(abbt^{\bullet-})]^+$ and $[Ru^{II}(pap)_2(abbt^{\bullet-})]^+$, respectively, via the effective role of polar protic solvent as a redox equivalent (alcohol to aldehyde).[2] Moreover, relatively electron rich azobis(1-methylbenzimidazole) (abim) with {Ru(acac)$_2$} facilitated the exclusive formation of the two-step intramolecular electrontransfer (IET) product $[\{(acac)_2Ru^{III}\}_2(\mu\text{-abim}^{2-})]$ (Scheme).[3] Besides structural authentication and electronic forms along the redox chain of the complexes were scrutinized by spectroelectrochemistry (UV-vis-NIR/EPR) in combination with theoretical (DFT/TD-DFT)calculations.

Scheme: Electronic form of Ruthenium-azoheteroarenes



References:

1. Singh, A.; Dey, S.; Panda, S.; Lahiri, G. K. *Angew. Chem. Int. Ed.* **2021**, *60*, 11206-11210.2. Singh, A.; Dey, S.; Panda, S.; Lahiri, G. K. *Inorg.Chem.* **2021**, *60*, 18260-18269.

3. (a) Panda, S.; Singh, A.; Dey, S.; Huang, K. W.; Lahiri, G. K. *Dalton Trans.* **2022**, *51*, 2547-2559.

(b) Singh, A.; Singh, B.; Dey, S.; Indra, A.; Lahiri, G. K. *Inorg. Chem.* **2023**, *62*, 2769-2783.

Towards a Naphthalimide-Based Mn(II) SelectiveFluorescence Sensor

*Chiranjit Pradhan, Ankona Datta**

Department of Chemical Sciences, Tata Institute of Fundamental Research, Mumbai,India

Email: chiranjit.pradhan@tifr.res.in; ankona@tifr.res.in

Manganese, an indispensable trace metal crucial for all living organisms, plays a pivotal role in the catalytic function of multiple metalloenzymes, sustains brain function, acts as an antioxidant, and engages in various metabolic processes.[1] Excessive accumulation of Mn can lead to a neurological disorder resembling Parkinson's disease, known as Manganism.[1] Therefore, studying Mn ion homeostasis under physiological and pathophysiological conditions is both intriguing and imperative. Detecting Mn^{2+} ions within living cells requires a non-invasive technique with precise spatial (µm) and temporal (ms) resolution. Fluorescence confocal microscopy fulfils these criteria. However, designing a selective Mn^{2+} binding ligand is challenging due to the low affinities of Mn^{2+} ions for most ligands with N-, O-, and S-donor atoms. Additionally, the paramagnetic nature of Mn^{2+} ions can quench sensor fluorescence. Our group has successfully addressed these challenges by developing Mn^{2+} ion sensors, utilizing BODIPY as a responsive unit and a PeT-based sensing modality.[2,3] Due to challenges associated with BODIPY, such as synthetic complexity and limitedphotostability, we are exploring the use of Naphthalimide dye as an alternative.[4] Naphthalimide offers advantages like chemical stability, easy synthesis, higher photo-stability, tunable emission wavelength, and increased fluorescence quantum yields.[5] In this context, we have designed a Mn^{2+} responsive fluorescence sensor using Naphthalimide dye as the reporter unit. In my poster, I will present the design, synthesis, and characterization of the novel sensor.

References:

1. Das, S.; Khatua, K.; Rakshit, A.; Carmona, A.; Sarkar, A.; Bakthavatsalam, S.; Ortega, R.;Datta, A. *Dalton Transactions* **2019**, *48* (21), 7047–7061
2. Bakthavatsalam, S.; Sarkar, A.; Rakshit, A.; Jain, S.; Kumar, A.; Datta, A. *ChemicalCommunications* **2015**, *51* (13), 2605–2608.
3. Kahali S, Das S, Datta A, et al. ChemRxiv. Cambridge: Cambridge Open Engage; 2023; 10.26434/chemrxiv-2023-d4fp9
4. Wüstner, D; Christensen, T; Sage, D *Molecules* **2014**, *19*, 11096-11130
5. Kagatikar, S., Sunil, D. A. *J Mater Sci* **2022**, *57, 105–139*

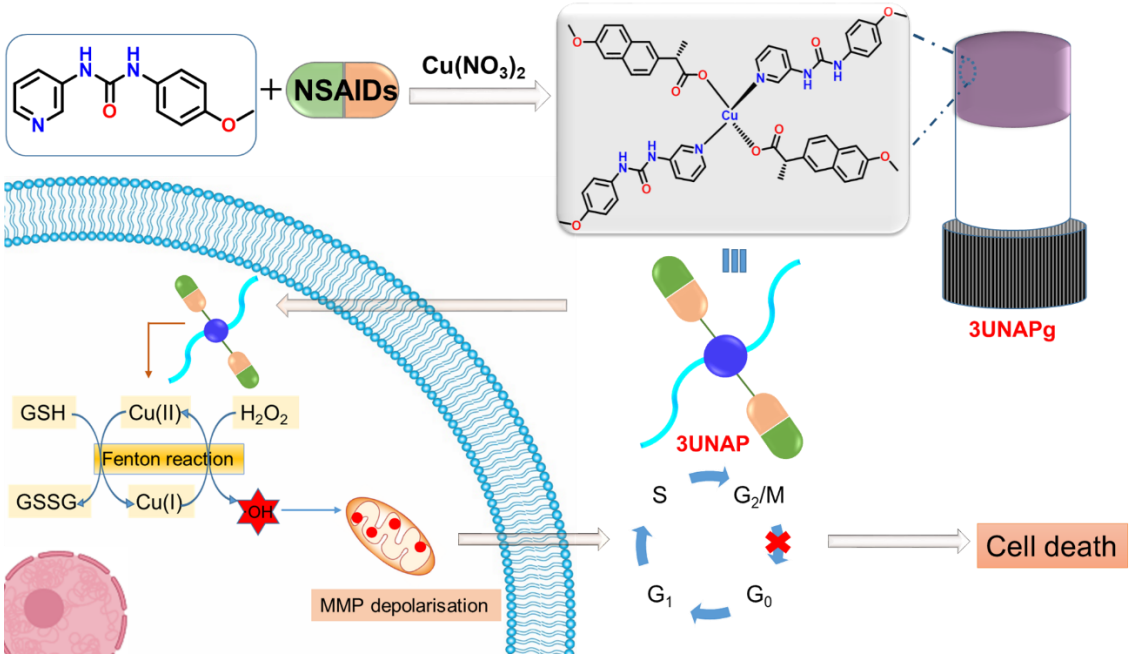
Developing supramolecular metallogel based drug delivery system involving Fenton reaction triggered cell death

Abhishek Dutta, Sourabh Bera*, Parthasarathi Dastidar**

**School of chemical sciences, Indian Association for the Cultivation of Science, Kolkata-700032, and India*

Email Id: csad2317@iacs.res.in., ocpdastidar@gmail.com.

A series of non-steroidal anti-inflammatory drug (NSAID) coordinated Cu (II) complexes was synthesized. The design of coordination complex is such that it could produce metallogel in specific solvent system including water. All the coordination complexes were characterized by FT-IR, X-ray crystallography and metallogels were characterized by powder X-ray crystallography, transmission electron microscopy. The Cu (II) complex namely 3UNAP can generate hydroxyl radical in presence of peroxide produced in cancer cell which in turn inhibit the reduction of oxidized glutathione[1]. The cell cycle study revealed the arrest of in G2/M phase of cell cycle resulted in cancer cell death.



References:

1) S. Kateryna, B. Petr, Selective induction of programmed cell death using synthetic biology tools, *Seminars in Cell and Developmental Biology,* **2004**, *156*, 74 – 92.

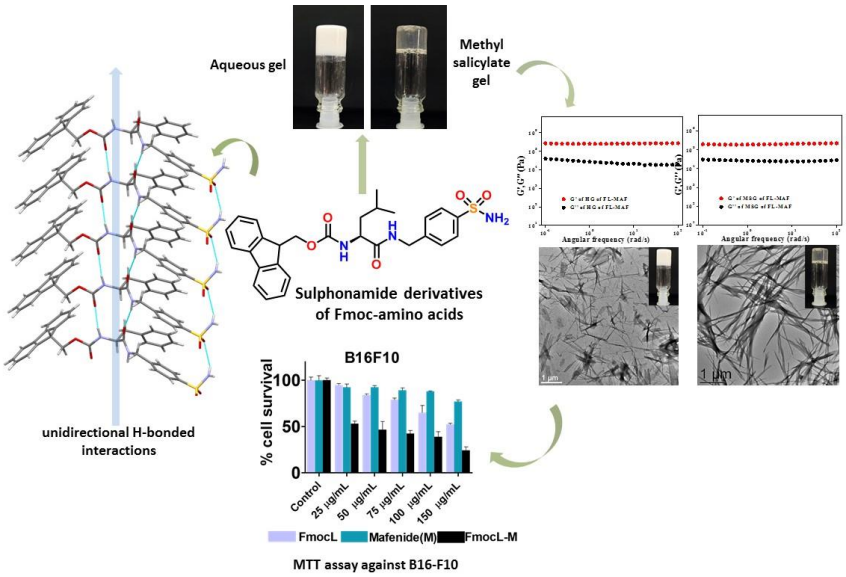
Sulphonamide derivatized Fmoc-amino acids based supramolecular gel showing anti-cancer activity against B16-F10 melanoma cells.

Nabanita Roy[a], Parthasarathi Dastidar[a*]

[a] School of Chemical Science, Indian Association for the Cultivation of Science, Kolkata, India-700032.

Email ID: csnr2318@iacs.res.in, ocpdastidar@gmail.com

Sulphonamides are recently studied as well-known scaffolds for anti-cancer activities[1]. Various sulphonamide derivatives are known to exhibit excellent anticancer properties in both *in vitro* and *in vivo* against diverse cancer cell lines[2]. But little efforts have been made for the development of supramolecular gels containing sulphonamide derivatized small molecules and their actions against any skin cancer cell line. In this project, we have synthesized a series of Fmoc- amino acid-sulphonamide derivatives and their biological properties were studied. 3 out of 4 compounds gave aqueous gels. Gels were characterized by rheology and TEM. Single crystal XRD and Powder XRD analysis proved the presence uni-directional H-bonded interactions present within the gelator molecules. One derivative **FmocL-Mf** showed anticancer property against B16-F10 mouse melanoma cell line supporting the utility of such sulphonamide derived molecules against skin-cancer.



References:

1. A. E. Mekabaty, H.M. Awad, *J. Heterocyclic Chem.*, 2020. **57**, 1123-1132
2. R. M. M. E. Hazek, N. H. Zaher, H. E. S. Emam, M. G. E. Gazzar, A. Khalil, *Sci. Rep.*, 2023, **13**, 5782

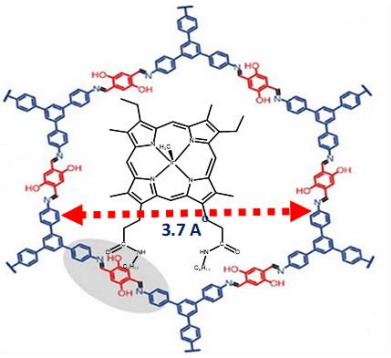
Heterogenous catalysis using COF encapsulated Ir-porphyrin

Sai H. Rekapalli[a], Prof. *Shyamalava Mazumdar*[a]

[a] Department of Chemical Sciences, TIFR Colaba Campus, Mumbai, India

Abstract:

Cyclopropanation reactions play are important in the synthesis of complex organic molecules such as drugs etc. Engineered heme proteins incorporating porphyrin scaffolds with non-native metals [1] such as Iridium and Rhodium have demonstrated catalytic prowess, particularly in reactions involving carbene insertion into un-activated olefins. Several studies have been reported to achieve enhanced product yield, and efficient enantioselectivity of the cyclopropanation reaction using diverse types of catalysts ranging from engineered enzymes [2] to organometallic compounds. However, there has been no report on use of heterogeneous catalytic system for this reaction using a heme and it's analogue.



The present study delves into the realm of heterogeneous catalysis, exploring a variety of materials, including supported metal catalysts, Metal-Organic Frameworks (MOFs), and Covalent Organic Frameworks (COFs). COFs, a unique class of compounds in reticular chemistry, are recognized for their catalytic activities, driven by their exceptional structural attributes such as stability, porosity, designability, and tunability [3].

We are interested in heterogenous catalysis by a least explored region of biomimetic structural material synthesized by encapsulating and anchoring the functionalized Iridium-Mesoporphyrin IX complex inside a mesoporous COF. The structurally functionalized metal complex center can alter the stereoselectivity of the cyclopropanation reaction may be due to the presence of sterically hindering alkyl substituents that restrict the substrate entry channel. Synthesis, characterization, and evaluation of this innovative catalyst, providing insights into the fascinating realm of heterogenous catalysis would be presented in the poster.

References:

[1] Abiological catalysis by artificial haem proteins containing noble metals in place of iron Key, H., Dydio, P., Clark, D. *et al., Nature* 534, 534–537 (2016)

[2] Enantioselective Enzyme-Catalyzed Aziridination Enabled by Active-Site Evolution of a Cytochrome P450, Frances H. Arnold, *ACS Central Science* 2015 *1* (2), 89-93

[3] Covalent Organic Frameworks for Heterogeneous Catalysis: Principle, Current Status, and Challenges, Jia Guo and Donglin Jiang, ACS Central Science *2020* 6 *(6), 869-879*

Generation and Characterization of A High Spin Fe(III)-Alkylperoxo Species Stabilized by Anionic *cis*-Ligand: An Implication to SOR Enzyme Reactivity

Tarali Devi,[a,c] Stefan Mebs,[b] Kallol Ray[c]*

[a]*Department of Inorganic and Physical Chemistry, IISc Bangalore, India*

[b]*Department of Physics, Freie University of Berlin, Germany*

[c] *Department of Chemistry, Humboldt University of Berlin, Germany*

E-mail Id: kallol.ray@chemie.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] In the biomimetic system, the mechanism of the O–O bond cleavage of iron(III)–alkylperoxo species has been investigated in both high-spin or low-spin sates of nonheme iron models that generate a high-valent iron(IV)oxo species by homolytic O-O bond cleavage mechanism.[3] The rate of such O-O bond cleavage reactions were found to be dramatically accelerated by the addition of Lewis bases occupying the 6th coordination of the iron(III)–alkylperoxo species in both -*cis* and -*trans* fashion.[3] However, the generation of iron(III)–alkylperoxo species stabilized by anionic *cis*-ligand and its role on O-O bond cleavage has never been documented. In this work, the generation and stability of a mononuclear a Fe(III)-alkylperoxo species has been studied using different spectroscopic techniques (UV-vis, Mössbauer, EPR, rRaman, XAS analysis). Also, the control of anionic *cis*-ligand in the O-O bond cleavage reactions has been investigated with combined experimental and theoretical studies.

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) W. Nam, H. J. Han, S.-Y. Oh, Y. J. Lee, M.-H.. Choi, S.-Y. Han, C. Kim, S. K. Woo, W. Shin *J. Am. Chem. Soc.* 2000, 122, 36, 8677–8684; (b) S. Yokota, H. Fujii, J. *Am. Chem. Soc.* **2018**, *140*, 5127–5137.

3. (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.

Peripheral non-covalent interactions change the geometry of the host Fe(III) complex during recognition of chiral amino alcohol, depending on the location of the chiral centre

Somnath Paik and Manabendra Ray*

Department of Chemistry, IIT Guwahati, Guwahati, Assam, India 781039
email: somnathpaik@iitg.ac.in

Non-covalent interactions are essential in the chiral recognition of adrenaline or triggering structural changes in the choline receptor.[1,2] Getting structural information or bond parameters on these interactions is difficult as many biological systems are not amenable to structural characterization. We use small metal complexes as chiral hosts and study the interactions with chiral amino alcohols.[3-5] The role of metal ions is to rigidify the host, avoiding the synthesis of large organic hosts, which are less amenable to structural characterization. In this work, a coordinatively saturated iron(III) complex of l-tryptophan-derived ligand, $(NEt_4)[FeL_2]$, binds the (*R*)-isomer of either 2-amino-1-propanol or meta octopamine from a racemic mixture through metathesis. The coordination geometry of the iron(III) complex in the resulting two host-guest salts is very different (Figure 1). If $(NEt_4)[CoL_2]$, isostructural with $(NEt_4)[FeL_2]$, is used, then the final host-guest salt does not show significant structural change unless heated at 60˚C for several hours. We conclude that the non-covalent interactions here are strong enough to modify the structure of a kinetically labile Fe(III) complex but insufficient to do the same on an inert Co(III) complex without extra energy.

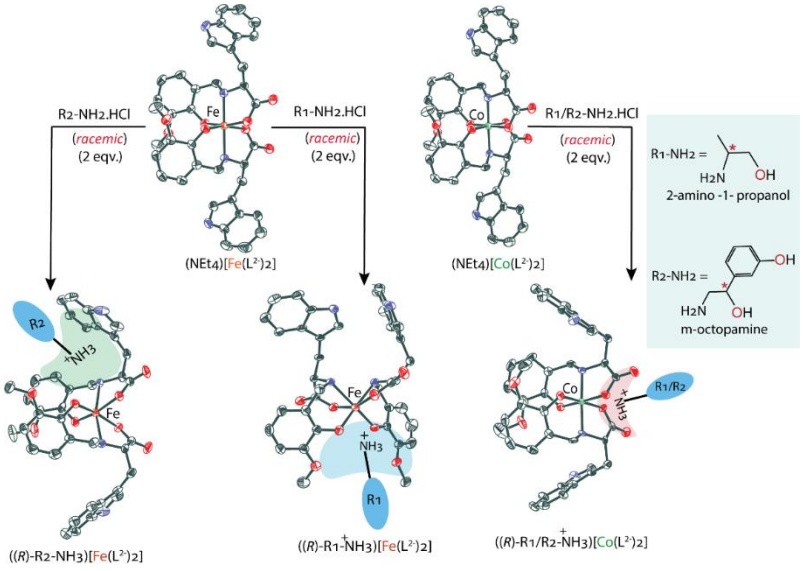


Figure 1. Different structures of the host-guest complexes recognizing different chiral amino alcohols.

References:

1. Thomas Schrader, Angew. Chem. **1996**, *108*, 2816
2. Nigel Unwin, Q Rev Biophys., **2013**, *46*, 283.
3. Subash C. Sahoo, Manabendra Ray, Chemistry A European Journal, **2010**, *16*, 5004.
4. Chandani Rani Das, Subash K. Sahoo, and Manabendra Ray, Crystal Growth & Design, **2014**, *14*, 3958.
5. Chandani rani Das, Tanmay Dutta and Manabendra Ray, Inorganica Chimica Acta, **2019**, *486*, 367

Redox Induced Diverse Reactivity of Bis(aldimine) Ligandson Selective Ru-Platform

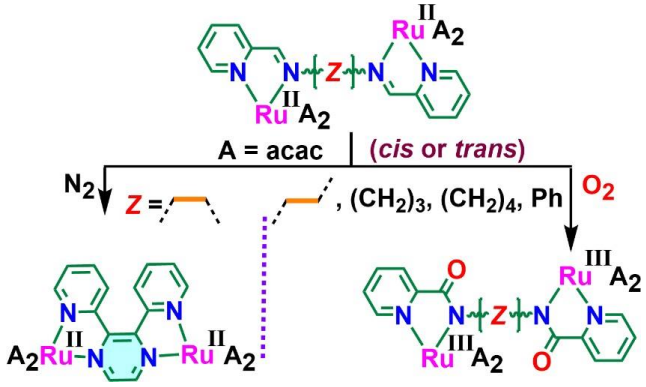
Mitrali Biswas and Goutam Kumar Lahiri*

Department of Chemistry, Indian Institute of Technology Bombay, Powai, Mumbai,400076

Email: mitralibiswas@gmail.com, lahiri@chem.iitb.ac.in

Electron shuttling on the metal-ligand interface facilitated multifarious structure- reactivity corelation of redox non-innocent bis(aldimine) derivatives in presence of electron rich ruthenium [Ru(acac)$_2$(CH$_3$CN)$_2$]. The reactivity profile principally varied as a function of ligand backbone and conformation of the linker (Z) (*syn*/*anti*). In this context, *syn*-configured ethylene linked bis-aldimine unit (Z= (CH$_2$)$_2$) derived *cis*- diruthenium complex underwent redox mediated cyclisation *via* intramolecular C-C coupling[1] whereas, corresponding *anti*-form (ethylene linker) of the metal bound ligandexperienced simultaneous two-fold oxygenation at the ligand backbone via dioxygen activation to generate Ru^{III}Ru^{III} complex. Subsequently, propylene (Z= (CH$_2$)$_3$) and butylene (Z= (CH$_2$)$_4$) spacer derived ligands encountered identical oxygenation process to yield diruthenium(III,III) complexes (*cis*/*trans*).[2] Alternatively, on moving from aliphatic to aromatic spacer i.e. *p*-phenylene (Z = Ph), the similar ligand bound *trans*-diruthenium complex encountered stepwise activation of molecular dioxygen toresult in modified ligand derived isovalent Ru^{III}Ru^{III} complex via the intermediacy of mixed valent Ru^{II}Ru^{III} species.[3] Intricate mechanistic outline for the genesis of all the functionalised metal complexes have been authenticated by experimental (crystallography, UV-vis. kinetics, hydrogen evoluation, isotope labelling) and theoretical (transition state) aspects.

Scheme. Representation of the complexes



References

1. Biswas, M.; Dey, S.; Panda, S.; Dutta, A.; Lahiri, G. K.; *Inorg. Chem.*, **2022**, *61*, 6347-6352.
2. Biswas, M.; Dey, S.; Dhara, S.; Panda, S.; Lahiri, G. K.; *Dalton Transations,* (under revision)
3. Biswas, M.; Dey, S.; Das, A.; Paine, T. K.; Panda, S.; Lahiri, G. K.; *Chem. Eur. J.*, **2022**, *28*, e202202088.

Synthesis, characterization and reactivity of non-heme manganese compound

Jeffrey L. Viegas, [a,b] Dattaprasad D. Narulkar,[a] Sunder N. Dhuri [a,*]

[a] School of Chemical Sciences, Goa University, Taleigao, Goa, 403 206, India.
[b] Carmel College of Arts, Science & Commerce for Women, Nuvem, Goa, India.
Email: sndhuri@unigoa.ac.in

Metal-oxygen species are common reactive intermediates that are found in the O–O bond formation and activation reactions. In recent years efforts are made to design novel ligands and transition metal compounds to understand the correlation of their geometric and electronic structure with its reactivity. Such materials are known to provide a good insight into the mechanistic pathway of metalloenzymes. Herein, we present the characterization and reactivity of a mononuclear compound [Mn(N3Py2)(H_2O)]($ClO4)_2$ 1 synthesised by the reaction of a pentadentate non-heme ligand *N,N′*-dimethyl-*N*-(2-(methyl(pyridin-2-ylmethyl)amino)ethyl)-*N′*-(pyridin-2-ylmethyl)ethane-1,2-diamine) (N3Py2) and Mn(II)($ClO_4)_2$.6H_2O. The ligand N3Py2 has been prepared and characterized by ^{1}H-NMR spectroscopy, Compound 1 has been characterized by CHNS, IR, U.V-Vis, EPR, SCXRD and ESI-MS techniques. A mononuclear manganese peroxo(III)- complex [Mn^{III}(N3Py2)(O_2)]$^+$ 1a was generated in-situ by the reaction of [Mn(N3Py2)(H_2O)]($ClO_4)_2$ 1 with H_2O_2 in presence of triethylamine at 25°C in CH_3CN as evident from spectroscopic techniques and ESI-MS. The reactivity of 1a in aldehyde deformylation using 2-phenylpropionaldehyde(2PPA) was studied and the reaction kinetics was monitored by UV-visible spectroscopy. A kinetic isotope effect (KIE)=1.7 was obtained in the reaction of 1a with 2-PPA and α-[D_1]-PPA, suggesting nucleophilic character of 1a. The activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for the aldehyde deformylation reaction were obtained from Erying plot by performing the reactions at different temperature ranging from 288 to 303 K. The reactivity of **1a** with *para*-substituted benzaldehyde yields positive hammet ρ value of 3.0 which suggests the nucleophilic character of **1a** in aldehyde deformylation reaction. The catalytic activity of **1** was investigated in alkene epoxidation reactions in presence of PhIO as oxidant. The GC analysis shows the formation of epoxides in good yields.

References

1) Nam, W.; Lee, Y. M.; Fukuzumi, S. Acc. Chem. Res. **2018**, 51(9), 2014-2022.
2) Narulkar, D. D.; Ansari, A.; Vardhaman, A. K.; Harmalkar, S. S.; Lingamallu, G.; Dhavale, V.M.; Sankaralingam, M.; Das, S.; Kumar, P.; Dhuri, S. N. Dalton Trans., **2021**, 50, 2824.
3) Narulkar, D.D.; Srivastava, A. K.; Butcher, R. J.; Ansy, K. M.; Dhuri, S. N. *Inorganica Chim. Acta.* **2017**, 467, 405–414.

Synthesis of Porphyrin with Covalently Attached Four Pendant Thiol Groups

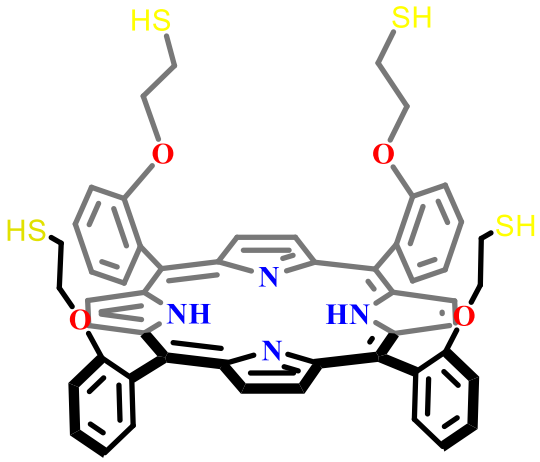
Kumarjit Banerjee, Souvik Dinda, Abhishek Dey*

School of Chemical Sciences

Indian Association for the Cultivation of Science, 2A Raja SC Mullick Road, Kolkata 700032, India

Email: icad@iacs.res.in

Thiols participate in both proton transfer and electron transfer processes in nature either in distinct elementary steps or in a concerted fashion[1]. Toward this goal, we have developed routes for the preparation of thiol-derivatized porphyrin. A tetraphenylporphyrin derivative with four thiol moieties, 5,10,15,20-tetrakis [o-(2- mercaptoethoxy)-phenyl] porphyrin, H_2(o-TMEPP), has been synthesized[2]. Now, we have synthesized 2Fe-2S cluster[3], $(Et_4N)_2$ $[Fe_2S_2Cl_4]$ and tried to attach it with this thiol-derivatized porphyrin.



5,10,15,20-tetrakis [o-(2- mercaptoethoxy)-phenyl] porphyrin

References

1. B. Cardey, S. Foley, M. Enescu, *J. Phys. Chem. A*, **2007**, *111*, 50, 13046–13052.
2. Daniel T. Gryko, Christian Clausen, and Jonathan S. Lindsey*, *J. Org. Chem.* **1999**, *64,* 8635-8647.
3. Wong, G. B.; Bobrik, M. A.; Holm, R. H. *Inorg. Chem.* **1978**, 17, 3, 578–584.

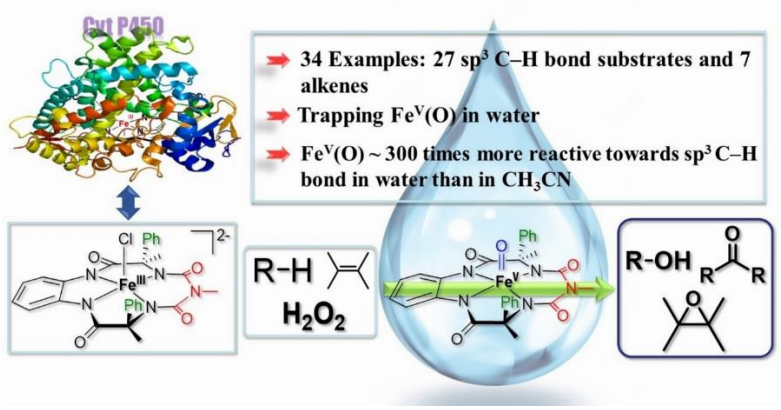
Highly Regioselective Oxidation of C–H Bonds in Water using Hydrogen Peroxide by a Cytochrome P450 mimicking Iron Complex

Puja De, [a] Sandipan Jana, [a] Chinmay Dey, [b] Somdatta Ghosh Dey, *[b] Abhishek Dey, *[b] and Sayam Sen Gupta*[a]

[a]Department of Chemical Sciences, Indian Institute of Science Education and Research, Kolkata; Mohanpur, 741246, India, Email: sayam.sengupta@iiserkol.ac.in, pd19rs052@iiserkol.ac.in

[b]School of Chemical Sciences, Indian Association for the Cultivation of Science, Kolkata, West Bengal 700032

Cytochrome P450, one of nature's oxidative workhorse, catalyze oxidations of C–H bonds in complex biological settings. Extensive research has been conducted over the past five decades to develop a fully functional mimic that activates O_2 or H_2O_2 in water to oxidize strong C–H bonds. We report the first example of a synthetic iron complex that functionally mimics cytochrome P450 in 100% water using H_2O_2 as the oxidant. This iron complex, in which one methyl group is replaced with a phenyl group in either wing of the macrocycle, oxidized unactivated C–H bonds in small organic molecules with very high selectivity in water (pH 8.5). Several substrates (34 examples) that contained arenes, heteroaromatics, and polar functional groups were oxidized with predictable selectivity and stereoretention with moderate to high yields (50-90%), low catalyst loadings (1-4 mol%) and a small excess of H_2O_2 (2-3 equiv) in water. Mechanistic studies indicated the oxoiron(V) to be the active intermediate in water and displayed unprecedented selectivity towards 3° C–H bonds. Under single-turnover conditions, the reactivity of this oxoiron(V) intermediate in water was found to be around 300 folds higher than that in CH_3CN, thus implying the role water plays in enzymatic systems.



References:

1. *Chem. Sci.*, 2023,**14**, 10515-10523
2. *J. Am. Chem. Soc.* 2013, **135**, 14052-14055
3. *Org. Lett.* 2017, **19**, 746-749
4. *Inorg. Chem.* 2017, **56**, 10852-10860.
5. *J. Am. Chem. Soc.* 2015, **137**, 9704-9715

Computationally guided bioengineering of active site, substrate access pathway, and water channels of thermostable cytochrome P450, CYP175A1 for catalyzing alkane hydroxylation reaction

Mohd Taher[a*], Kshatresh Dutta Dubey[b]*, Shyamalava Mazumdar[a]*

[a]Department of Chemical Sciences, Tata Institute of Fundamental Research, Homi Bhabha Road, Colaba, Mumbai 400005, India

[b]Department of Chemistry, School of Natural Science, Shiv Nadar Institution of Eminence Delhi-NCR, 201314, India

MT: chiraltaher@gmail.com, SM: shyamal@tifr.res.in

Abstract: Cytochrome P450 forms one of the largest super-families of enzymes and are distributed throughout almost in all the biological lifeforms. The active site of the P450s invariably contain a heme as the prosthetic group bound to a cysteine through thiolate linkage to the Fe metal centre. Laboratory evolved variants of cytochrome P450 BM3 are known to hydroxylate alkanes[1] but have certain limitations such as low thermal stability and use of expensive electron donor NADPH. Due to these challenges it is tough to expect them as industrially viable catalysts. We have rationally evolved a thermostable variant of cytochrome P450 i.e. CYP175A1[2] into an alkane hydroxylating enzyme (Figure 1). Rationally designed variants of CYP175A1 were shown to be catalytically active towards the long chain alkanes such as hexadecane.[3] A series of mutants have been made and evaluation of the catalytic activity have been performed. Characterization of the evolved enzymes showed that the evolved variants were fairly thermally stable. This study paves a way towards the development of thermally stable biocatalyst for alkane hydroxylation.

Figure1: Schematic representation of rational design of CYP175A1 for alkane hydroxylation.

1. Peters, M. W.; Meinhold, P.; Glieder, A.; Arnold, F. H., Journal of the American Chemical Society 2003, 125 (44), 13442-13450.
2. Yano, J. K.; Blasco, F.; Li, H.; Schmid, R. D.; Henne, A.; Poulos, T. L.,. Journal of Biological Chemistry 2003, 278 (1), 608-616.
3. Taher, M.; Dubey, K. D.; Mazumdar, S.; Chemical Science (in press).

Bio-Nano-Electrocatalysis of Substrate by Wild Type CYP175A1 and Mutated CYP175A1

Dineshkumar Yadav [a, b], Shivram S. Garje [b] & Shyamalava Mazumdar[a]*

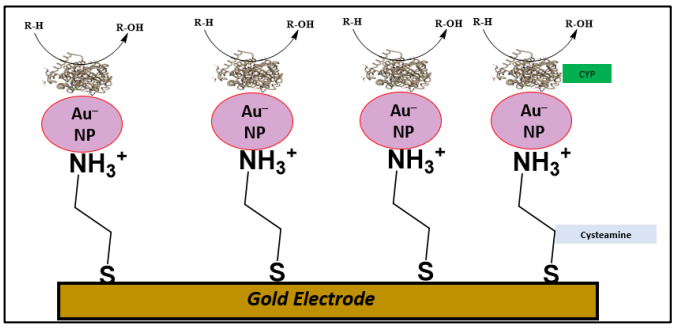
[a] Department of Chemical sciences, TIFR, Mumbai, India

[b] Department of Chemistry, University of Mumbai, Mumbai, India

shyamal@tifr.res.in

Abstract:

CYP175A1 is one of the known thermostable Cytochrome P450, which is capable of catalysing stereo and regiospecific Monooxygenation reaction of the wide range of substrate. Direct Electrochemistry between Gold electrode and CYP175A1 does not exhibit a Proper Redox peak in Cyclic voltammetry around –325mV vs Ag/AgCl. For efficient electron transfer between Electrode and Catalytic active Heme centre requires modification of Electrode. In this scheme, Gold Electrode is modified cysteamine and Gold Nanoparticle, which can efficiently bind with CYP175A1. The average size of Gold Nanoparticle is 14nm. This modification able to catalyse the monooxygenation of substrate. The Wild type and its surface mutated CYP175A1 Q333C, where additional cysteine can enhance electron transfer. As mutation site is much closer to Heme centre, cysteine bind with gold nanoparticle which leads to enhancement of electron transfer. The Surface mutation is performed by PCR and plasmids are amplified on His- tag PRSF DUET vector. The Electro catalytic activity of WT CYP175A1 and Mutated CYP175A1 Q333C and F329H/Q333C can be studied in the details.



References:

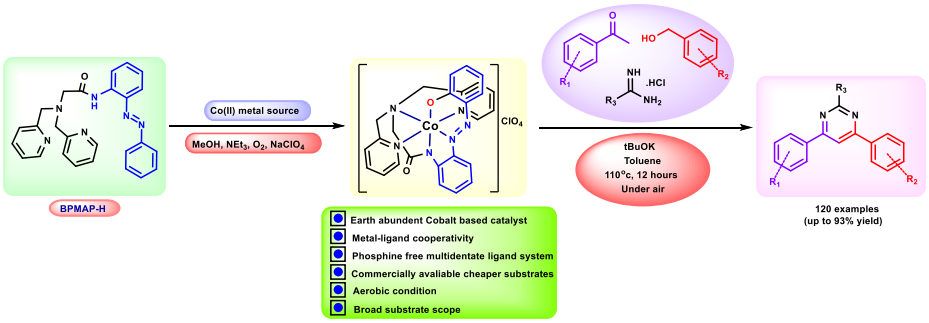
- Frens G 1973 Controlled nucleation for the regulation of the particle size in monodisperse gold suspensions. Nature physical science 241 20.
- Mhaske SD, Ray M & Mazumdar S 2021 Covalent conjugation of Single walled CNT with CYP101 mutant for direct electrocatalysis. Analytical biochemistry 626

Bio-inspired synthesis of a versatile cobalt(III) catalyst via activation of molecular oxygen and its application in multicomponent synthesis of pyrimidines

Prashant[a] and Kaushik Ghosh*[a]

[a]Department of chemistry, Indian Institute of Technology, Roorkee 247667, India. Email: Kaushik.ghosh@cy.iitr.ac.in

Bio-inspired synthesis is the development or findings of novel molecules such as transition metal complexes, having aim to better understand and study nature's critical structural features. In this study we have synthesized a novel pentadentate ligand (E)-2-(bis(pyridin-2-ylmethyl)amino)-N-(2-(phenyldiazenyl)phenyl)acetamide (BPMAP-H) having carboxamide with azo donor group. Design and synthesis of pentadentate ligand having amide moieties is inspired from various metalloproteins having metal center bounded with carboxamido nitrogen at active sites such as nitrile hydratase, acetyl Co-A synthase/CO dehydrogenase and Ni-containing super oxide dismutase. Metal center in higher oxidation states is stabilised by this kind of interaction, and the active sites of these enzymes exhibit impressive reactivity. For example, unlike other non-heme iron enzymes, the Fe(III) centre of the Fe-containing nitrile hydratase does not participate in any redox reactions; rather, it serves as a Lewis acid and catalyses the hydrolysis of organic nitriles. Inspiring from active sites of such enzymes BPMAP-H ligand is utilized for synthesis of a low spin Co(III) complex [Co(III)BPMAP-O]ClO_4 in presence of atmospheric oxygen via oxygen activation. Eventually the pentadentate ligand becomes a hexadentate ligand (BPMAP-O) in final complex and provide a hexacoordinated Co(III) complex having phenolate group trans to carboxamide moiety. Both ligand and complex are well characterized by different spectroscopic techniques like UV-visible, IR, ^{1}H NMR, ^{13}C NMR, ^{13}C DEPT 135, HRMS and Single crystal XRD. This Co(III) complex is then utilized as a catalyst for sustainable, eco-friendly, practical, and less expensive multicomponent synthesis of pyrimidine derivatives via dehydrogenative coupling of aromatic ketones and benzyl alcohol with various amidines. A total 120 derivatives of 2,4,6-trisubstituted pyrimidine were synthesised and characterised having isolated yields of up to 93% in presence of air at 110 °C.



References:

(1) Fukuzumi, S.; Mandal, S.; Mase, K.; Ohkubo, K.; Park, H.; Benet-Buchholz, J.; Nam, W.; Llobet, A. Catalytic Four-Electron Reduction of O 2 via Rate-Determining Proton-Coupled Electron Transfer to a Dinuclear Cobalt-μ-1,2-Peroxo Complex. *J. Am. Chem. Soc.* **2012**, *134* (24), 9906–9909.

(2) Corona, T.; Padamati, S. K.; Acuña-Parés, F.; Duboc, C.; Browne, W. R.; Company, A. Trapping of Superoxido Cobalt and Peroxido Dicobalt Species Formed Reversibly from CoII and O2. *Chem. Commun.* **2017**, *53* (86), 11782–11785.

(3) Nurdin, L.; Spasyuk, D. M.; Fairburn, L.; Piers, W. E.; Maron, L. Oxygen-Oxygen Bond Cleavage and Formation in Co(II)-Mediated Stoichiometric O2 Reduction via the Potential Intermediacy of a Co(IV) Oxyl Radical. *J. Am. Chem. Soc.* **2018**, *140* (47), 16094–16105.

(4) Schlagintweit J.F.; Altmann P.J.; Bçth A.D.; Hofmann B.J.; Jandl C.; Kaußler C.; Nguyen L.; Reich R.M.; Pçthig A. and Kehn F.E. Activation of Molecular Oxygen by a Cobalt II Tetra-NHC Complex *Chem. Eur. J.* **2021**, 27, 1311 – 1315.

(5) Deibl, N.; Ament, K.; Kempe, R. A Sustainable Multicomponent Pyrimidine Synthesis. *J. Am. Chem. Soc.* **2015**, *137* (40), 12804–12807.

(6) Mastalir, M.; Glatz, M.; Pittenauer, E.; Allmaier, G.; Kirchner, K. Sustainable Synthesis of Quinolines and Pyrimidines Catalyzed by Manganese PNP Pincer Complexes. *J. Am. Chem. Soc.* **2016**, *138* (48), 15543–15546.

(7) Sultana Poly, S.; Siddiki, S. M. A. H.; Touchy, A. S.; Ting, K. W.; Toyao, T.; Maeno, Z.; Kanda, Y.; Shimizu, K. I. Acceptorless Dehydrogenative Synthesis of Pyrimidines from Alcohols and Amidines Catalyzed by Supported Platinum Nanoparticles. *ACS Catal.* **2018**, *8* (12), 11330–11341.

(8) Prashant, Ghosh k.*(Manuscript communicated).

Exploring the Role of Sulphur Ligation in Modulating the Oxidative Reactivity of High-Valent Nonheme Iron (IV)-Oxo Intermediates

Jagnyesh Kumar Satpathy,[a] Payal Panwar,[a] Chivukula V. Sastri*[a]

[a]Department of Chemistry

IIT Guwahati

Email: sastricv@iitg.ac.in

Sulfur-ligated oxoiron (IV) centers are supposed to be the crucial oxidants in the catalytic cycles of various oxygen-activating iron enzymes, such as cytochrome P450 (P450), NO synthase (NOS), and isopenicillin N synthase, etc.[1,2] Mainly, Cis-thiolate ligated oxoiron (IV) moieties are thought to be the reactive intermediates for a variety of chemical reactions, such as sulfur-oxygenation, Hydrogen-atom transfer reactions, and C-S bond formation reactions in non-heme iron enzymes. How sulphur ligation affects the structure and catalytic properties of catalytic reaction centres remains an unresolved question and is the focus of this work. Herein, we report the synthesis, characterization and reactivity of a novel biomimetic N4S ligated iron(IV)-oxo complex and compare the results with its analogous N5-ligated iron(IV)-oxo complex. Through a detailed experimental and computational approach, we demonstrate a dramatic change in the reaction mechanism and rate enhancement in oxygen atom transfer reactions and hydrogen atom transfer reactions. Additionally, the introduction of the sulphur-ligand leads to a reduction in the deuterium kinetic isotope effect in hydrogen atom transfer reactions. These findings provide insight into the reactivity of sulphur ligated iron(IV)-oxo centers and their role in various metalloenzymes.

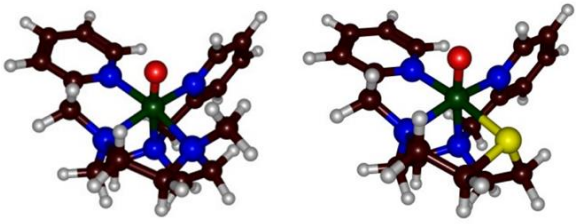


Figure 1. Oxidants used in this study.

References:

(1) Meunier, B.; de Visser, S. P.; Shaik, S.; *Chem. Rev*, **2004**, *104*, 3947-3980.

(2) Denisov, I. G.; Makris, T. M.; Sligar, S. G.; Schlichting, I.; *Chem. Rev*, **2005**, *105*, 2253-2278.

Equatorial Perturbation Driven Reaction Bifurcation in Non-Heme Iron Complexes for Chlorite Oxidation

Limashree Sahoo,[a] Jagnyesh Kumar Satpathy,[a] Chivukula V. Sastri*[a]

[a]Department of Chemistry

IIT Guwahati

Email: sastricv@iitg.ac.in

Chlorine oxyanions have various applications, such as bleaching and oxidizers in rocket fuels. However, their high solubility in water and long environmental lifetimes have led to ecological concerns, especially regarding drinking water quality. This study focuses on the conversion of chlorite to chlorine dioxide, which is of significant interest as it exhibits superior antimicrobial activity and generates less harmful byproducts for water treatment. Two nonheme iron (II) complexes capable of producing chlorine dioxide from chlorite at room temperature and pH 5.0 are presented. These complexes oxidize chlorite through high-valent iron (IV)-oxo intermediates formed in-situ. The study establishes second-order rate constants for chlorite oxidation and investigates the effects and mechanisms involved by substituting a methyl group on the secondary coordination sphere of the FeIV(O)(N4Py) system. By employing kinetic analysis and spectroscopic investigations, the crucial elements for the reaction mechanism in chlorite oxidation are identified. These findings pave the way for future advancements in this field.

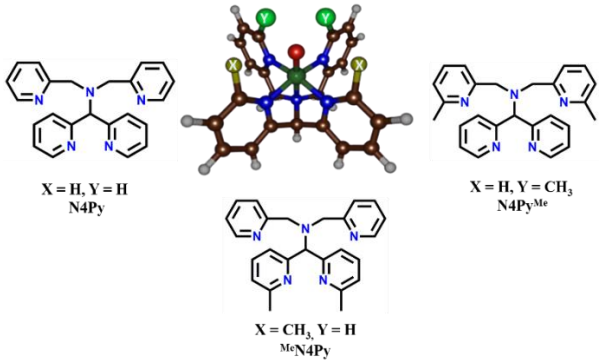


Figure 1. Ligands and Oxidants used in this study.

References:

(1) P. Barman, A. S. Faponle, A. K. Vardhaman, D. Angelone, A.M Löhr, W. R. Browne, P. Comba,C. V. Sastri, S. P. de Visser, Inorg. Chem. 2016, 55, 10170−10181.

(2) D. S. Hicks, D. Kim, S. Xiong, G. A. Medvedev. J.Caruthers, S. Hong, W. Nam, M. M. Abu-Omar, J.Am. Chem. Soc. 2014, 136, 9, 3680–3686.

(3) M. J. Zdilla Dr. A. Q. Lee, M. M. Abu-Omar, Angew. Chem. Int. Ed. 2008, 47, 7697 –7700.

(4) T. P. Umile, J. T. Groves, Angew. Chem. Int. Ed. 2011, 50, 695−698.

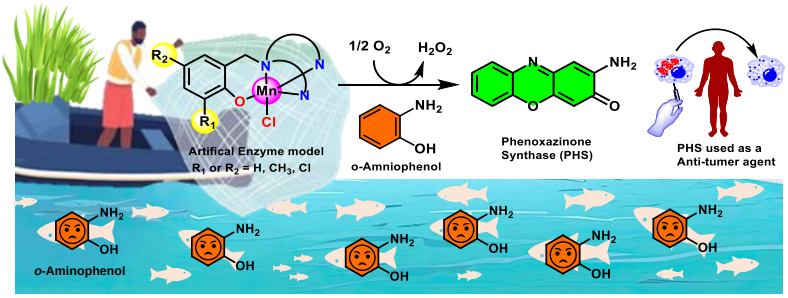
Mononuclear Manganese(II) Complexes of N_3O Donor Ligands as Biomimetic Model for Phenoxazinone Synthase

Narasimman Palani,[1] Karuppasamy Sundaravel[1*]

[1*]Bioinorganic Research Laboratory, Department of Chemistry, *Bharathiar University, Coimbatore, Tamil Nadu – 641046, India*

E-mail: sundaravel.k@buc.edu.in

Synthesis of biomimetic models for metalloenzymes continues to increase its interest towards the small molecule activation such as O_2, N_2 and CO_2. The phenoxazinone synthase (PHS) enzyme involved in oxidative bioprocess, such as the synthesis of powerful antineoplastic agent actinomycin D. Although earlier reports and synthesized complexes help us to understand the mechanisms of the PHS processes, but their turnover numbers are far less compared to the native enzymes. In addition, only a few synthetic manganese(II) models reported to mimic the PHS activity[1,2]. We have been successfully synthesized a series of mononuclear manganese(II) complexes $[Mn(L1)Cl_2]$ - $[Mn(L3)Cl_2]$ (**1** - **3**) containing tetradentate N_3O donor ligands and thoroughly characterized them by different analytical techniques such as FT-IR, ^1H NMR, UV-vis, EPR and ESI-MS spectroscopy[3]. All the complexes **1 – 3** exhibit phenoxazinone synthase like activity with the impressive turnover numbers (K_{cat}: **1,** 2.54×10^6, **2,** 8.93×10^6, **3,** 3.81×10^6 h^{-1}). Among the complexes **1 – 3**, **2** showing highest PHS activity, these catalytic efficiencies difference clearly attributed to the variations in structures of the complexes and formation of active Mn^{III} species in solution during catalysis. The present report clearly indicates that better performance of our Mn(II) molecular systems than the earlier reports. The plausible mechanism has been reiterated based on the experimental data via ESI-MS spectral data. The formation of H_2O_2 as an intermediate substrate is honestly indicating the molecular oxygen involved in the catalytic cycle.



References:

1. D. K. Bhattacharya.; L. K. Das.; S. Giriad.; A. Ghosh. *Dalton. Trans*. **2018**. *48*, 9385–9399.
2. A. Mendieta.; J. R. Alvarez-Idaboya.; V. M. Ugalde-Saldívara.; M. Flores-Alamoa.; A. Armentaa.; G. Ferrer-Suetab.; L. Gasquea. I*norg. Chem.* **2023**, *62*, 41, 16677–16690.
3. N. Palani, K. Sundaravel. Unpublished Work.

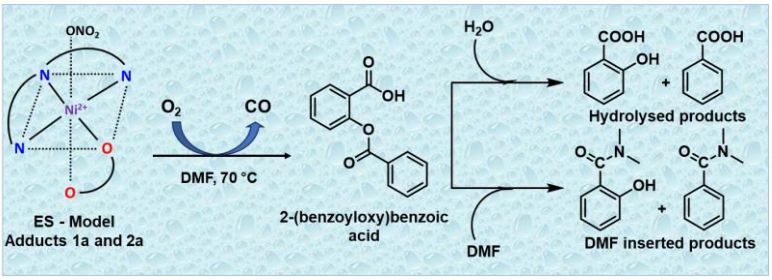
Probing the Chelate ring Size effect on the Dioxygenation of Flavanols Using Nickel(II) Complexes

Karthickram Devaraj[1] and Karuppasamy Sundaravel[1*]

[1]Bioinorganic Research Laboratory, Department of Chemistry, Bharathiar University, Coimbatore – 641046, Tamil Nadu, India.

e-mail-sundaravel.k@buc.edu.in

Nickel metal centre(s) is commonly found in the active sites of the metalloproteins and catalyse various oxidation reactions by activating dioxygen. Nickel–dioxygen adduct has been crystallographically characterised for quercetin dioxygenase (2,4-QDO), which obtained during the oxygenolysis of the flavonol. 2,4-QDO performs the degradation of quercetin by inserting dioxygen molecule and furnish 2-(3,4-dihydroxybenzoyloxy)-4,6-dihydroxybenzoate and CO. Herein, we report two nickel(II) containing 3-hydroxyflavone bounded adducts which are differing in chelate ring size of the 3N donor ligand architecture. The proposed enzyme-substrate (ES) adducts of the type [Ni(L)(fla)(NO_3)] (**1a** - **2a**) (Where L1 = N^1-benzyl-N^2-(2-(benzylamino)ethyl)ethane-1,2-diamine, L2 = N^1-benzyl-N^3-(3-(benzylamino)propyl)propane-1,3-diamine were characterised using various spectroscopic techniques and electrochemical methods. Kinetic experiments were done at 70 ºC in presence of O_2 in order to achieve the enzyme-like reactivity of the nickel(II) adducts. In this present study, the influence of chelate ring size effect on the rate of dioxygenation and product formation have been demonstrated.



Scheme. Schematic representation of oxygenative degradation pathway of ES-model adducts **1a** and **2a**.

References:

1. D. Jeong, S. Sun, D. Moon, J. Cho, *J. Inorg. Biochem.,* 2022, **226**, 111632.

2. Y. J. Sun, Q. Q. Huang, J. J. Zhang. *Dalton Trans.,* 2014, **43**, 6480.

3. N. Podder, S. Dey, A. Anoop, S. Mandal, *Dalton Trans.,* 2022, **51**, 4338.

4. D. Karthickram, K. Sundaravel, unpublished work.

Increased Robustness and Selectivity of a Nonheme Iron Complex Anchored on Merrifield Resin in Bioinspired Catalytic Oxidation

Abhijit Bera, Madhubonti Pal[#], Poulami Pal[$], and Tapan Kanti Paine*

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

Email: [#]scsmp2866@iacs.res.in ; [$]scspp2835@iacs.res.in

Abstract

High-valent iron-oxo species are often implicated as the key oxidants in the catalytic cycles of dioxygen-activating mononuclear nonheme iron enzymes.[1-2] The enzymatic reactions have inspired the synthesis and reactivity studies of non-heme iron(IV)–oxo complexes of polydentate ligands.[3-4] Considerable progress has been made in developing catalytic systems employing non-heme iron complexes and various oxo transfer regents.[5-6] However, bimolecular decay and ligand oxidations often result in poor selectivity and low catalytic activity, as well as non-recyclability of the catalyst.[7-8] Covalent anchoring or non-covalent immobilizations of homogeneous catalysts on solid support can be considered one of the options to overcome these challenges. These solid supports are expected to bring sustainability to selective catalytic oxidations.[9] To explore that possibility, we have investigated the effect of immobilization of the mononuclear nonheme iron(II)-HTPEN complex [H-TPEN: *(N¹, N¹, N²*-tris(pyridin-2-ylmethyl)ethane-1,2-diamine] on its catalytic activity and selectivity in bioinspired oxidation reactions. The complex has been covalently anchored to Merrifield resin (MPR), and the supported complex effectively performs catalytic oxygen-atom transfer reactions (OAT) and C-H bond hydroxylation with excellent regioselectivity and stereoretention in the presence of a terminal oxidant. The robustness, efficiency, and recyclability of the anchored catalyst will be presented in this poster.

References

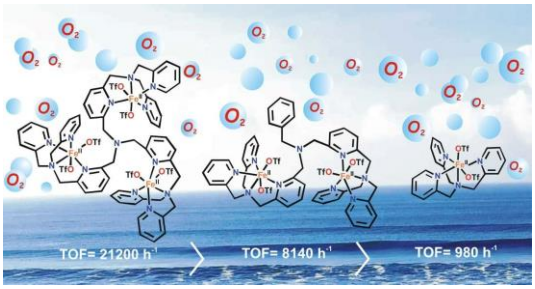
[1] C. Krebs, D. G. Fujimori, C. T. Walsh, J. M. Bollinger, Jr., *Acc. Chem. Res.* **2007**, *40*, 484-492.
[2] S. Kal, L. Que, Jr., *J. Biol. Inorg. Chem.* **2017**, *22*, 339-365.
[3] K. Ray, F. F. Pfaff, B. Wang, W. Nam, *J. Am. Chem. Soc.* **2014**, *136*, 13942-13958.
[4] A. R. McDonald, L. Que, Jr., *Coord. Chem. Rev.* **2013**, *257*, 414-428.
[5] X. Engelmann, I. M.-Pérez, K. Ray, *Angew. Chem. Int. Ed.* **2016**, *55*, 7632-7649.
[6] W. Nam, Y.-M. Lee, S. Fukuzumi, *Acc. Chem. Res.* **2014**, *47*, 1146-1154.
[7] D. Sheet, T. K. Paine, *Chem. Sci.* **2016**, *7*, 5322-5331.
[8] M. Grau, A. Kyriacou, F. C. Martinez, I. M. de Wispelaere, A. J. P. White, G. J. P. Britovsek, *Dalton Trans.* **2014**, *43*, 17108-17119.
[9] A. Fingerhut, O. V. Serdyuk, S. B. Tsogoeva, *Green Chem.* **2015**, *17*, 2042-2058.

Highly Active Homogeneous Nonheme Iron Catalysts in Chemical Water Oxidation: Effect of Nuclearity on Catalytic Efficiency

Subhankar Sutradhar,[a] Sachidulal Biswas,[a] Sabyasachi Mahapatra,[a] Achintesh N. Biswas,[b] and Tapan Kanti Paine*[a]

[a]School of Chemical Sciences, Indian Association for the Cultivation of Science, 2A & 2B Raja S. C. Mullick Road, Jadavpur, Kolkata-700032, India.
[b]Department of Chemistry, National Institute of Technology Sikkim, Ravangla, South Sikkim-737139, India.

ABSTRACT: The development of efficient catalysts based on abundant, inexpensive, and environmentally benign metals capable of mimicking the activity of the oxygen-evolving complex (OEC) in Photosystem II is one of the most challenging goals in bioinspired catalysis. Despite good progress in this area, a proper understanding of the factors that govern the O-O bond formation by the high-valent metal-oxo intermediates is yet to be obtained. Although multinuclear systems are often implicated to store redox equivalents needed for water oxidation more efficiently than their mononuclear congeners, a systematic study using mono- and multinuclear complexes with a common ligand platform toward water oxidation reactions is sparsely reported. These shortcomings have inspired the present work, wherein we have explored the efficiency of different iron complexes of varying nuclearity in water oxidation catalysis.



Here we present a comparative study of the water oxidation activity of three iron(II) complexes, $[(L1)Fe_3(OTf)_6]$ (**1**), $[(L2)Fe_2(OTf)_4]$ (**2**), and $[(TPA)Fe(OTf)_2]$ (**3**) supported by trinucleating (L1), dinucleating (L2) and mononucleating tris(2-pyridylmethyl)amine (TPA) nitrogen donor ligand framework, respectively. All the complexes efficiently catalyze the water oxidation reaction at near-neutral pH using Oxone® as the oxidant. Among the three, complex 1 is found to be the most efficient catalyst exhibiting a turnover frequency (TOF) of 21200 h^{-1} emphasizing the role of nuclearity in the water oxidation reaction. Complex **1** represents the most active homogeneous iron-based chemical oxidation catalyst reported to date. [1], [2] An iron(V)-oxo intermediate [3], [4], formed via iron(IV)-oxo resting state, is implicated in the O-O bond formation step. Oxone® mediates the iron-oxo generation and the subsequent nucleophilic attack of water at the iron-oxo unit leads to the formation of dioxygen. The iron-based water oxidation catalysis presented here not only shows the impact of nuclearity and appropriate ligand geometry in the development of artificial photosynthetic models but also provides useful information about the self-decay pathway of iron-oxo species in the presence of water.

REFERENCES

1. Fillol, J. L.; Codolà, Z.; Garcia-Bosch, I.; Gómez, L.; Pla, J. J.; Costas, M., Efficient water oxidation catalysts based on readily available iron coordination complexes. *Nat. Chem.* **2011,** *3*, 807-813
2. D'Agostini, S.; Kottrup, K. G.; Casadevall, C.; Gamba, I.; Dantignana, V.; Bucci, A.; Costas, M.; Lloret-Fillol, J.; Hetterscheid, D. G. H., Electrocatalytic Water Oxidation with α-$[Fe(mcp)(OTf)_2]$ and Analogues. *ACS Catal.* **2021,** *11*, 2583-2595.
3. Wei, X.-Z.; Ding, T.-Y.; Wang, Y.; Yang, B.; Yang, Q.-Q.; Ye, S.; Tung, C.-H.; Wu, L.-Z., Tracking an $Fe^{V}(O)$ Intermediate for Water Oxidation in Water. *Angew. Chem. Int. Ed.* **2023**, e202308192.
4. Kal, S.; Xu, S.; Que, L., Jr., Bio-inspired Nonheme Iron Oxidation Catalysis: Involvement of Oxoiron(V) Oxidants in Cleaving Strong C−H Bonds. *Angew. Chem. Int. Ed.* **2020,** *59*, 7332-7349.

Lewis Acid Promoted Selective Epoxidation of Alkenes with H_2O_2 Catalyzed by Iron Salts: "Masked" Fenton or Metal-Oxo Catalyst?

Sabyasachi Mahapatra,[a] Rahul Dev Jana,[a] Satadal Paul,[b] and Tapan Kanti Paine[a]*

[a] School of Chemical Sciences, Indian Association for the Cultivation of Science, 2A and 2B Raja S.C. Mullick Road, Jadavpur, Kolkata 700032, India. Email:ictkp@iacs.res.in

[b] Department of Chemistry, Bangabasi Morning College, Kolkata 700009, India.

The development of sustainable catalytic methods for selective epoxidation of alkenes continues to be a challenging objective in oxidation chemistry.[1] In that pursuit, a large number of iron-based catalysts that affect the epoxidation of C=C bonds with peroxides have been reported.[2] However, most of the catalytic systems rely on supporting ligands and often display non-selective oxidation of substrates via free radical pathways. While exploring the ability of iron-based molecular complexes in affecting catalytic oxygenation, we have developed a catalytic method for selective epoxidation of alkenes with hydrogen peroxide by iron salts in the presence of a Lewis acid in acetonitrile. The catalytic activity of the iron salt/H_2O_2/$Sc(OTf)_3$ system is observed in nitrile solvents only. The oxidizing power of iron salt and peroxide in acetonitrile is promoted by the Lewis acid, scandium(III) triflate leading to the selective catalytic epoxidation of a series of alkenes without the requirement of any supporting ligand framework. An electrophilic oxidant, which does not exchange its oxygen atom with water, is involved in the epoxidation reactions. Theoretical studies indicate that simultaneous and intramolecular existence of the Fe(III)-OH and OH• en route Fe(II) – peroxo to Fe(IV) – Oxo / Fe(III) – Oxyl conversion hints towards a "masked" Fenton system involved midway in the reaction pathway.[3] The efficacy of the catalytic system and mechanistic pathways involving metal-based oxidant leading to selective epoxidation reactions will be presented.

References:

[1] C. Bolm, M. Beller, Transition metals for organic synthesis, Vol. 1, Wiley-VCH, Weinheim, ***2004****.*
[2] W. N. Oloo, L. Que, Jr., Acc. Chem. Res. ***2015****, 48, 2612-2621.*
[3] S. Mahapatra, R. D. Jana, S. Paul, T. K. Paine, 2023, manuscript submitted

Wacker-type Aerobic Oxidation of Olefins Catalysed by an Iron(II) Complex: Intermediacy of an Oxo-Bridged Diiron(III) Species in the Catalytic Cycle

Sourav Pal[a], Tapan K. Paine[b] and Jitendra K. Bera*[a]

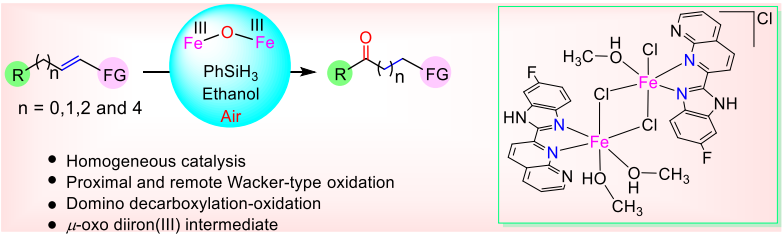
[a] S. Pal and Prof. J.K. Bera

Department of Chemistry
Indian Institute of Technology Kanpur, Kanpur, Uttar Pradesh, 208016
E-mail: souravp@iitk.ac.in, jbera@iitk.ac.in

[b] Prof. T.K. Paine

Department of Chemistry
Indian Association of Cultivation of Science
2A&2B Raja S. C. Mullick Road, Jadavpur, Kolkata-700032(India)
E-mail: ictkp@iacs.res.in

A naphthyridine-benzimidazole-based Fe(II) catalyst has been designed for the selective Wacker-type oxidation of olefins into corresponding ketones using aerial oxygen as the oxidant and phenylsilane as hydrogen source under ambient conditions. Dioxygen activation at the non-heme iron centre resulted in the formation of μ-oxo di-Fe^{III} intermediate, which was characterized by x-ray crystallography and other spectroscopic techniques. The presence of electron-withdrawing substituent such as fluorine on the ligand backbone accelerated the efficiency of the catalyst. The catalytic method was applied for a wide range of substrates such as aromatic, long-chain aliphatic, and biologically relevant olefins and the reaction shows high functional group tolerance, selectivity, and excellent conversion. Moreover, this system is also effective for domino decarboxylation-oxidation of α,β-unsaturated carboxylic acids to methyl ketones, remote Wacker-type oxidation of olefins and oxidation of phenylallenes to cinnamaldehyde derivatives. Kinetic isotope experiments show that the cleavage of the Si–H bond of phenylsilane affects the reaction rate. The prearranged methanol ligated to iron centre exerts a secondary coordination sphere hydrogen bonding with an oxygen atom of the Fe(III)-alkylperoxo species to facilitate the heterolytic O−O bond cleavage. Labeling experiments demonstrated that phenylsilane and air act as additional hydrogen and oxygen atom sources, respectively in the ketone product Several mechanistic experiments were conducted to corroborate the reaction pathway.



References:

1. J. Trouvé, K. Youssef, S. Kasemthaveechok, R. Gramage-Doria, *ACS Catal* **2023**, 4421–4432
2. F. Puls, P. Linke, O. Kataeva, H. J. Knölker, *Angew. Chem. Int. Ed.* **2021**, *60*, 14083–14090
3. F. Puls, H. J. Knölker, *Angew.Chem.Int.Ed.,* **2018**,57,1222–1226

Substrate Oxidation vs. Water Oxidation by Nonheme Complexes: Influence of Urea Groups on Supporting Ligands in Directing the Reaction Pathways

Rajib Samanta,[a] Ivy Ghosh,[a] Tapan Kanti Paine*

School of Chemical Sciences, Indian Association for the Cultivation of Science, 2A & 2B Raja S. C. Mullick Road, Jadavpur, Kolkata, 700032. E-mail: csrs2319@iacs.res.in

Many dioxygen-activating nonheme iron enzymes involve iron-hydro/alkylperoxo (Fe-OOH(R)) and high-valent iron-oxo species as active oxidants to perform important biological oxidations.[1] High valent iron-oxo species also display a remarkable competence towards water oxidation to form dioxygen.[2] These enzymatic reactions inspired synthetic chemists to develop small molecule models with the objective to gain insights into the reaction pathways that govern their diverse reactivities.[3] In the peroxide activation paradigm, (Fe-OOH(R)) or iron(IV)-oxo species have been detected, whereas iron(V)-oxo-hydroxo intermediates have been implicated as the active oxidants in catalytic oxygenation of substrates.[1] High-valent iron-oxo species have potential in selective oxygenations, but unproductive decay pathways often compromise the efficiency and selectivity of catalytic reactions. Understanding the mechanism of self-decay of iron-oxygen intermediates in the absence of substrates and the influence of water (in solvent) on the decay process via the proton-coupled electron transfer (PCET) process would provide solutions for directing them to substrate oxidation. In that direction, we have explored the peroxide-dependent reactivity of a series of nonheme iron(II) complexes supported by tetradentate ligands containing one, two, and three urea groups. The iron(II) complexes of ligands with one or two urea groups react with cumyl hydroperoxide (CmOOH) to generate the corresponding iron(III)-alkylperoxo intermediate. While the complex with two urea groups efficiently oxygenates the C-H and C=C bonds of hydrocarbons with chemo- and stereo-selectivity,[4] the complex with one urea group performs chemical oxidation of water. The role of urea groups in directing the reactivity for substrate oxidation vs water oxidation will be presented in this poster.

References:

(1) A. Company, J. Lloret-Fillol, M. Costas, in *Comprehensive Inorganic Chemistry II (Second Edition)* (Eds.: J. Reedijk, K. Poeppelmeier), Elsevier, Amsterdam, **2013**, pp. 487.

(2) C. Krebs, D. G. Fujimori, C. T. Walsh, J. M. Bollinger, *Jr., Acc. Chem. Res*., **2007**, *40*, 484.

(3) I. Ghosh, T. K. Paine, in *Comprehensive Coordination Chemistry III* (Eds.: E. C. Constable, G. Parkin, L. Que Jr), Elsevier, Oxford, **2021**, pp. 378.

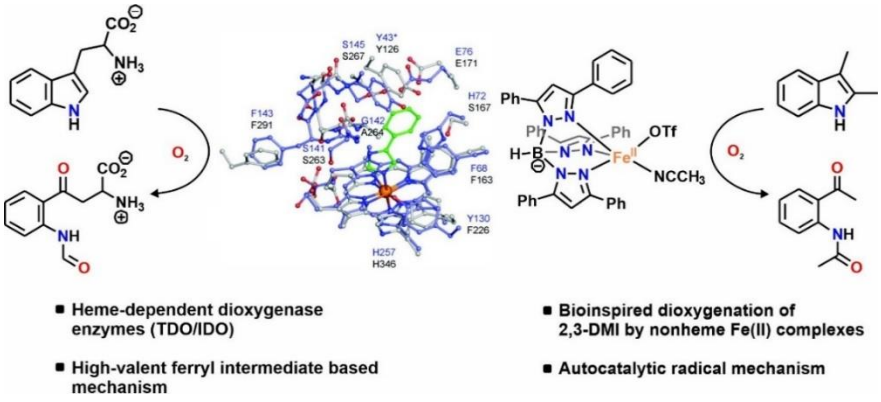
(4) I. Ghosh, S. Banerjee, S. Paul, T. Corona, T. K. Paine, *Angew. Chem. Int. Ed.*, **2019**, *58*, 12534.

Autocatalytic Dioxygenation of 2,3-Dimethylindole (2,3-DMI) with O_2 by a Bioinspired Nonheme Iron(II) Complex

Eliza Ghosh[1], Tapan Kanti Paine*

[1]E-mail address: cseg2218@iacs.res.in. School of Chemical Sciences, Indian Association for the Cultivation of Science, 2A & 2B Raja S. C. Mullick Road, Jadavpur, Kolkata – 700032.

Tryptophan 2,3-dioxygenase (TDO) and indoleamine 2,3-dioxygenase (IDO) are the heme enzymes that catalyze the rudimentary and foremost steps of tryptophan (Trp) catabolism in the kynurenine pathway.[1] These enzymes cleave the indole ring of tryptophan at 2,3 position and incorporate dioxygen without any additional cofactor or cosubstrate generating *N*-formyl kynurenine (NFK). The incorporation of dioxygen in L-Trp has been reported to involve a high-valent iron-oxo intermediate. For the last several decades, numerous efforts to delineate the mechanism of dioxygenation by these enzymes. However, the oxygenation pathway has not been unambiguously established yet. Along with enzymatic studies, attempts have been made to develop functional models[2], and a few synthetic TDO/IDO models based on metalloporphyrins have been reported to display catalytic oxidation of indole derivatives.[3] In recent years, synthetic heme superoxide models that cleave the 2,3-double bond of a series of indole substrates mimicking the tryptophan oxidation chemistry of TDO/IDO enzymes have been developed.[4] This model systems elucidate the involvement of iron-oxo intermediates in the reaction pathway.[4]



With an objective to gain insights into the mechanism of TDO/IDO, we have explored the dioxygen-dependent reactivity of a series of nonheme iron(II) complexes of polydentate nitrogen-donor ligands toward substituted indoles. During the course of our investigation, we found a different reaction mechanism for the catalytic C2-C3 bond cleavage of 2,3-dimethylindole (2,3-DMI) with dioxygen by the iron(II) complexes supported by the Tp^{Ph2} (hydrotris(3,5-dimphenylpyrazolyl)borate), TPA (tris(2-pyridylmethyl)amine) and 6-Me_3TPA (tris(6-methyl-2-pyridylmethyl)amine) ligands. In the presence of excess 2,3-DMI, the complexes activate dioxygen to yield N-(2-acetylphenyl)acetamide (NAPA) in catalytic turnover. Spectroscopic and mechanistic studies unravel the involvement of an autocatalytic radical mechanism in the reaction pathway. The catalytic activity of the complexes, the autocatalytic reaction mechanism, and the effect of supporting ligand on the C-C bond cleavage reactivity will be presented.

References:

[1] I. Shin, Y. Wang, A. Liu, *Proc. Natl. Acad. Sci. U.S.A.* **2021**, *118*, e2106561118.

[2] J. Tsuji, H. Kezuka, H. Takayanagi, K. Yamamoto, *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2369-2373.

[3] K. Ohkubo, T. Sagawa, H. Ishida, *Inorg. Chem.* **1992**, *31*, 2682-2688.

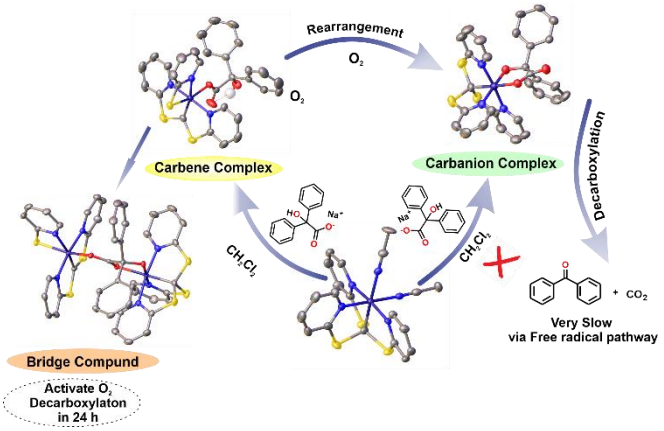
[4] P. Mondal, G. B. Wijeratne, *J. Am. Chem. Soc.* **2020**, *142*, 1846-1856.

Iron(II)-Benzilate Complexes of Mixed N,C-Donor Ligands: Dioxygen-Dependent Carbene to Carbanion Ligand Rearrangement and Oxidative Decarboxylation of Benzilate

Arghyadip Bhowmik, Sridhar Banerjee, Partha Halder, Satadal Paul and Tapan Kanti Paine*

School of Chemical Sciences, Indian Association for the Cultivation of Science, 2A & 2B Raja S. C. Mullick Road, Jadavpur, Kolkata, 700032. E-mail: intab@iacs.res.in

Bioinspired iron(II)-benzilate complexes of polydentate ligands have been shown to activate dioxygen to perform oxidative decarboxylation of benzilate to benzophenone. In the reaction pathways, different iron-oxygen species, depending upon reaction conditions, are generated in situ *via* selective electron transfer from benzilate to metal-coordinated oxygen. Mechanistic studies revealed that the dioxygen activation by iron(II)-benzilate complexes largely depends on the nature of the supporting ligands and additives (Lewis acid/protic acid)[1]. Most of the reported complexes are high-spin, and depending upon ligand denticity, the reactivity of active iron-oxygen species varies[1b, 2]. To expand our understanding in this direction, a mononuclear iron(II)-benzilate complex $[(L^2)Fe^{II}(PyS)(benzilate)]$ (**2**) (L^1 = tris(2-pyriylthio)methanido, L^2 = bis(2-pyridylthio)carbene and PyS = pyridine-2-thiolate) was synthesized from an iron(II) acetonitrile complex $[(L^1)Fe^{II}(CH_3CN)_2](ClO_4)$ (**1**)[3]. Reactivity studies with dioxygen and theoretical investigations indicate that **2** initially undergoes a dioxygen-dependent rearrangement of the carbene ligand (L^2) to generate the carbanionic ligand (L^1) and finally produces $[(L^1)Fe^{III}(benzilate)]^+$ (**3**). In contrast, the diiron-bridged-benzilate complex $[(L^1)Fe^{III}(benzilate)(L^2)Fe^{II}(PyS)](ClO_4)$ (**4**) affords quantitative decarboxylation in the reaction with dioxygen. The influence of iron-carbon bonding interactions on the dioxygen reductivity of the complexes and the dioxygen-dependent rearrangement of the ligand on the iron center will be presented.



References:

[1] a) S. Chatterjee, T. K. Paine, *Angew. Chem. Int. Ed.* **2016**, *55*, 7717-7722; b) S. Chatterjee, T. K. Paine, *Accounts of Chemical Research* **2023**.
[2] B. Chakraborty, R. D. Jana, R. Singh, S. Paria, T. K. Paine, *Inorg. Chem.* **2017**, *56*, 359-371.
[3] a) N. Kuwamura, R. Kato, K. i. Kitano, M. Hirotsu, T. Nishioka, H. Hashimoto, I. Kinoshita, *Dalton Trans.* **2010**, *39*, 9988-9993; b) P. Halder, T. K. Paine, *Inorg. Chem.* **2011**, *50*, 708-710.

Synthesis, Characterisation and Phenoxazinone Synthase Activity of Cobalt(II) Complexes of N_2O Donor Ligands

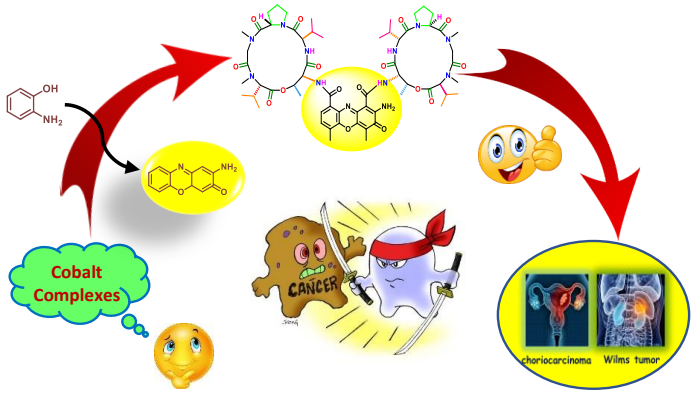
Kannan Sree Vidya[1] and Karuppasamy Sundaravel[1*]

Bioinorganic Research Laboratory, Department of Chemistry

Bharathiar University, Coimbatore – 641046, Tamil Nadu, India

E-mail: sundaravel.k@buc.edu.in

The impetus to modelling of enzyme active sites comes from their potential to provide insight to the mechanistic pathways of the native enzymes, establish the role of that particular metal in the active site and to design better catalysts inspired by nature. Among the various metalloenzymes, phenoxazinone synthase enzyme mimicking has been a growing interest in catalytic oxidation of organic compounds mediated by first-row transition metal complexes. This biological oxidation reactions involves oxidative condensation of 2-aminophenol to phenoxazinone chromophore, which functions in the final step of biosynthesis of natural antibiotic, antineoplastic agent actinomycin D under mild conditions in presence of molecular oxygen. Actinomycin D acts by inhibiting DNA directed RNA synthesis and is used clinically for the treatment of wilm's tumor and also certain types of cancer. To better mimic the PHS enzyme-like activity, we synthesised two new cobalt(II) complexes (**Co1** - **Co2**) of N_2O donor ligands [(2-((pyridin-2-ylmethyl)amino)ethan-1-ol) **(L1)** and (1-((pyridin-2-ylmethyl)amino)-propan-2-ol) **(L2)**] and characterized by UV-vis, AT-IR, ^{1}H & ^{13}C NMR, TG-DTA and electrochemical techniques. From reaction kinetic experiments, cobalt(II) systems showed the desired enzymatic activity by activating O_2 and observed that they are efficient catalyst for the formation of phenoxazinone chromophore in aqueous medium.



References:

1. Anangamohan, P.; Narayana, C. J.; Paula, B. *New J. Chem.*, 2017, 41, 9784-9795.

2. Alan, M.; Juan, R.; Victor, M.; Marcos, F.; Alfonso, A.; Gerardo, F.; Laura, G. *Inorg. Chem.* **2023**, 62, 41, 16677-16690.

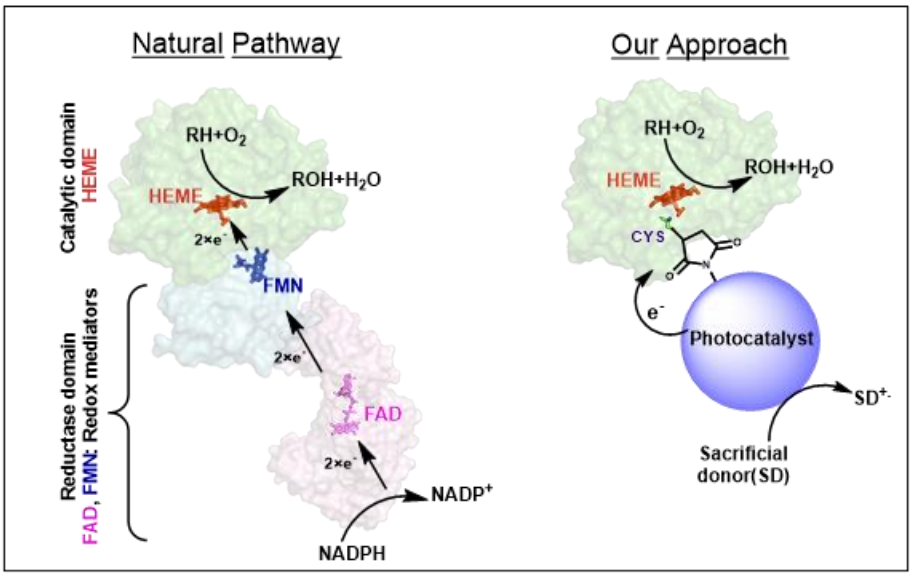
3. Sree Vidya, K.; Sundaravel, K. – Unpublished work.

Light-Induced Electron Transfer in Cytochrome P450

Ashima Negi, Ankur Gupta*

ashima16@iiserb.ac.in, IISER Bhopal, Department of Chemistry, India

Sunlight, a renewable and readily available source of energy, has excited chemists about the environmentally friendly synthesis of valuable chemicals through photocatalysis.[1] The inspiration is derived from nature where green algae and plants have evolved to convert sunlight into chemical energy. Following nature's example, researchers have developed artificial photosynthetic systems with inorganic catalysts[2] or biocatalysts.[3] The latter surpasses the former in terms of high chemo-, regio- and stereoselectivity. Among the myriad of biocatalysts, cytochrome P450 is a versatile candidate as it can perform hydroxylation, epoxidation, drug metabolism, etc., and has a broad substrate spectrum.[4] Here, we have combined the power of photocatalysis with biocatalysis by constructing an artificial photosynthetic system of Cyt P450 in covalent conjunction with a metal-based Ru polypyridyl or metal-free eosin Y photocatalyst. The hybrid design enhances the versatility of Cyt P450 by providing an alternative approach for supplying the necessary electrons and carrying out its native reactions upon visible light excitation, bypassing the need for redox partners and NADPH. The work demonstrates the strategic positioning of the photocatalyst on Cyt P450 and provides insight into the correlation between the bioconjugation strategy and electron transfer rate from photocatalyst to heme active site. The investigation involves tracking rates through the observation of oxygen consumption kinetics under light irradiation, allowing for correlation with subsequent product formation.



Schematic representation of the hybrid enzyme: Cytochrome P450 as Photobiocatalyst

References:

1. Liu, C.; Colón, B. C.; Ziesack, M.; Silver, P. A.; Nocera, D. G. *Science.* **2016,** *352*, 1210.
2. Skubi, L. K.; Blum, R.T.; Yoon, P. T. *Chem. Rev.* **2016**, *116*, 10035.
3. Eidenschenk, K.C.; Cheruzel, L. *Journal of Inorganic Biochemistry*. **2020**, *213*, 111253.
4. Jung, S. T.; Lauchli, R.; Arnold, F. H. *Current Opinion in Biotechnology.* **2011**, *6*, 809.
5. Negi, A.; Gupta, A. *Manuscript under preparation.*

Increased Robustness and Selectivity of a Nonheme Iron Complex Anchored on Merrifield Resin in Bioinspired Catalytic Oxidation

Abhijit Bera, Madhubonti Pal[#], Poulami Pal[$], and Tapan Kanti Paine*

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

Email: [#]scsmp2866@iacs.res.in ; [$]scspp2835@iacs.res.in

Abstract

High-valent iron-oxo species are often implicated as the key oxidants in the catalytic cycles of dioxygen-activating mononuclear nonheme iron enzymes.[1-2] The enzymatic reactions have inspired the synthesis and reactivity studies of non-heme iron(IV)–oxo complexes of polydentate ligands.[3-4] Considerable progress has been made in developing catalytic systems employing non-heme iron complexes and various oxo transfer regents.[5-6] However, bimolecular decay and ligand oxidations often result in poor selectivity and low catalytic activity, as well as non-recyclability of the catalyst.[7-8] Covalent anchoring or non-covalent immobilizations of homogeneous catalysts on solid support can be considered one of the options to overcome these challenges. These solid supports are expected to bring sustainability to selective catalytic oxidations.[9] To explore that possibility, we have investigated the effect of immobilization of the mononuclear nonheme iron(II)-HTPEN complex [H-TPEN: *(N¹, N¹, N²*-tris(pyridin-2-ylmethyl)ethane-1,2-diamine] on its catalytic activity and selectivity in bioinspired oxidation reactions. The complex has been covalently anchored to Merrifield resin (MPR), and the supported complex effectively performs catalytic oxygen-atom transfer reactions (OAT) and C-H bond hydroxylation with excellent regioselectivity and stereoretention in the presence of a terminal oxidant. The robustness, efficiency, and recyclability of the anchored catalyst will be presented in this poster.

References

[1] C. Krebs, D. G. Fujimori, C. T. Walsh, J. M. Bollinger, Jr., *Acc. Chem. Res.* **2007**, *40*, 484-492.
[2] S. Kal, L. Que, Jr., *J. Biol. Inorg. Chem.* **2017**, *22*, 339-365.
[3] K. Ray, F. F. Pfaff, B. Wang, W. Nam, *J. Am. Chem. Soc.* **2014**, *136*, 13942-13958.
[4] A. R. McDonald, L. Que, Jr., *Coord. Chem. Rev.* **2013**, *257*, 414-428.
[5] X. Engelmann, I. M.-Pérez, K. Ray, *Angew. Chem. Int. Ed.* **2016**, *55*, 7632-7649.
[6] W. Nam, Y.-M. Lee, S. Fukuzumi, *Acc. Chem. Res.* **2014**, *47*, 1146-1154.
[7] D. Sheet, T. K. Paine, *Chem. Sci.* **2016**, *7*, 5322-5331.
[8] M. Grau, A. Kyriacou, F. C. Martinez, I. M. de Wispelaere, A. J. P. White, G. J. P. Britovsek, *Dalton Trans.* **2014**, *43*, 17108-17119.
[9] A. Fingerhut, O. V. Serdyuk, S. B. Tsogoeva, *Green Chem.* **2015**, *17*, 2042-2058.

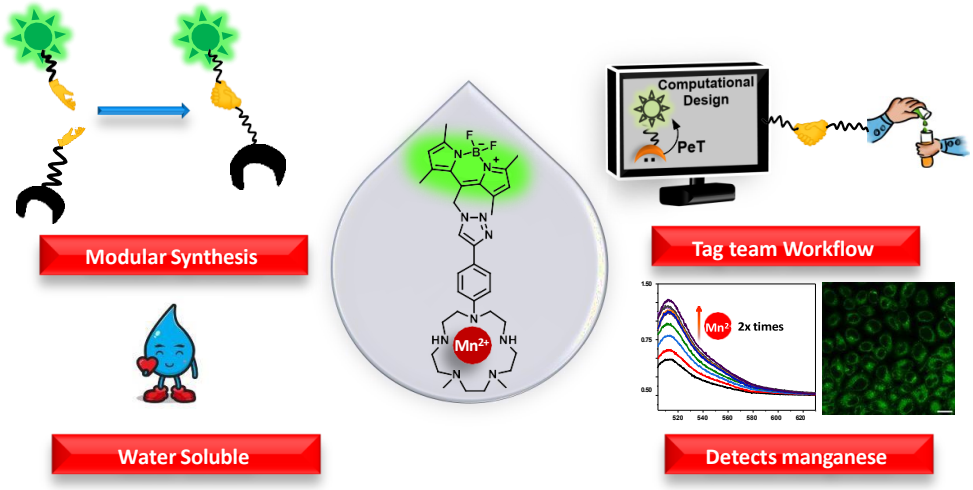
A Reversible, Water-soluble, 'Clicked' Fluorescent Sensor Detects Manganese Ions

Sujit Kumar Das,[a] Smitaroopa Kahali, Ankona Datta[a]*

[a] *Department of Chemical Sciences, Tata Institute of Fundamental Research, Mumbai, Maharashtra, India.*

E-mail: sujit.das@tifr.res.in, ankona@tifr.res.in

Manganese (Mn) ions are essential for all forms of life in both protein bound and labile forms.[1] Recent studies have indicated the role of this metal ion in host- immunity against pathogens[2] and its mis-regulation in cancers.[3] A direct consequence of Mn^{2+} ion dysregulation is a neurological disorder with symptoms similar to Parkinson's disease.[4] A chemical sensor that can permeate living cells and report on Mn^{2+} ion localization in a fluorescence confocal microscopy platform can provide key mechanistic information on both physiological and pathophysiological roles of Mn^{2+} ions. Hence, we have developed a reversible, water-soluble, cell- permeable fluorescent probe for Mn^{2+} ion detection. The molecule was designed based on a computational work-flow for pre-designing photo-induced electron transfer (PeT) based sensors, developed recently in our group.[5] The designed molecule was synthesized in 13 steps via a 'Click' reaction-based scheme for attaching a dye unit to a water-soluble Mn^{2+} ion binding scaffold. With this molecule we could address the challenge of selectively detecting Mn^{2+} ions which are difficult to track due to low binding affinities of Mn^{2+} ions based on the Irving-Williams series.[1] The sensor selectively detected Mn^{2+} ions over other physiologically relevant metal ions in water. I will present the details of the synthesis and characterization of our novel water-soluble, small-molecule-based, 'turn-on' fluorescent Mn^{2+} sensor.



References

1 Das S, Datta A, et al. Dalton Trans., 2019, 48, 7047-7061.
2 Brophy MB, Nolan EM, ACS Chem. Biol., 2015, 10, 641-651.
3 Rozenberg JM, Borisov N, et al. Biomedicines., 2022, 10, 1072-1090.
4 Tuschl K, Valdivia L, et al. Nat Commun., 2016, 7, 11601-116017.
5 Kahali S, Das S, Datta A, et al. ChemRxiv. Cambridge: Cambridge Open Engage; 2023, 10.26434/chemrxiv-2023-d4fp9.

Synthesis, Characterisation and Photophysical Studies of bis-indole pyridine based Ni^{II} and Fe^{III} Complexes

Aniruddha Sarkar, Arun Pal, Noufal Kandoth, Ayan Dutta, Sayam Sen Gupta*

Department of Chemical Sciences
Indian Institute of Science Education and Research, Kolkata, 741246, India
(e-Mail: as18rs004@iiserkol.ac.in, sayam.sengupta@iiserkol.ac.in)

Abstract:

Recently photoactive first-row metal-based photosensitisers are found to be more appealing over conventional, least-Earth abundant and more expensive, 4d/5d based metal complexes acting as photosensitisers or photoredox catalysts. This current scenario has drawn our attention to develop a futuristic sustainable photochemistry application based on photosensitizing metal complexes made of first-row based transition metal elements such as $Fe^{II/III}$, Co^{III}, Ni^{II}, Cu^{I}, Cr^{III} *etc*. However, it's a challenging pursuit owing to the presence of low-lying d-d states (MC), which makes it troublesome to counter the very fast excited state deactivation and further use these metal complexes for various photochemical applications. This hurdle has some part resolved by modelling and engineering strong field ligands (either strong σ donor or π^* acceptor), which can push those MC states either so high in energy or stabilize the CT states. In this context, we present here a photoactive complexes of square planner Ni^{II} and octahedral Fe^{III} based on bis-idnole pyridine (BIP) ligand which can be promoted as photosensitizers to make a sustainable photochemistry applications.

The Ni^{II} complexes are very well known in dual photoredox catalysis (Ir/Ni) and it has been found that Ni center has a photoactive state by which it can form an excited state (^{3}MLCT) state upon photoexcitation which directly takes part in the photoredox catalysis without even external photocatalyst (Ir^{III}). However, due to lack of reports to identify the photoactive state of Ni^{II}, there is a growing scientific interest in probing this ^{3}MLCT state[1-4]. For the first time, we have isolated [LNi^{II}-Py/Lut] complex which was characterised by Uv-Vis, ^{1}H NMR, HR-MS, Cyclic Voltammetry, SC-XRD and DFT studies; has a ^{3}MLCT excited state has been probed by Transient absorption spectroscopy (TA) and akin to CT states has been probed by steady-state measurements (Spectroelectrochemistry and UV-vis study). Our study shows that due to the high planarity induced by rigid tridented BIP ligand helps to hold the less distorted structure in an excited state (^{3}MLCT) ~39 ps lifetime.

The [L_2Fe^{III}] [NBu_4] has been synthesized and characterised by UV-vis, HR-MS, Cyclic Voltammetry, EPR and SC-XRD measurement which showed NIR luminescence at 820 nm upon excitation at 756 nm in dichloromethane. The excited state has been probed by Transient Absorption spectroscopy (TAS) having a long ESA component around $\geq$ 2ns which is also corroborated by TCSPC measurement getting quenched in the presence of a reductive quencher; akin to a ^{2}CT state [5-7].

References:

1. Liu, Q.; Thorne, L.; Kozin, I.; Song, D.; Seward, C.; D'Iorio, M.; Tao, Y.; Wang, S., New red–orange phosphorescent/electroluminescent cycloplatinated complexes of 2,6-bis(2′-indolyl)pyridine. *Journal of the Chemical Society, Dalton Transactions* **2002,** (16), 3234-3240.
2. Ogawa, T.; Sinha, N.; Pfund, B.; Prescimone, A.; Wenger, O. S., Molecular Design Principles to Elongate the Metal-to-Ligand Charge Transfer Excited-State Lifetimes of Square-Planar Nickel(II) Complexes. *J. Am. Chem. Soc.* **2022,** *144* (48), 21948-21960.
3. Ting, S. I.; Garakyaraghi, S.; Taliaferro, C. M.; Shields, B. J.; Scholes, G. D.; Castellano, F. N.; Doyle, A. G., 3d-d Excited States of Ni(II) Complexes Relevant to Photoredox Catalysis: Spectroscopic Identification and Mechanistic Implications. *J. Am. Chem. Soc.* **2020,** *142* (12), 5800-5810.
4. Ogawa, T.; Wenger, O. S., Nickel(II) Analogues of Phosphorescent Platinum(II) Complexes with Picosecond Excited-State Decay. *Angew. Chem. Int. Ed.* **2023,** *n/a* (n/a), e202312851.
5. McCusker, J. K., Electronic structure in the transition metal block and its implications for light harvesting. *Science* **2019,** *363* (6426), 484-488.
6. Kjær, K. S.; Kaul, N.; Prakash, O.; Chábera, P.; Rosemann, N. W.; Honarfar, A.; Gordivska, O.; Fredin, L. A.; Bergquist, K.-E.; Häggström, L.; Ericsson, T.; Lindh, L.; Yartsev, A.; Styring, S.; Huang, P.; Uhlig, J.; Bendix, J.; Strand, D.; Sundström, V.; Persson, P.; Lomoth, R.; Wärnmark, K., Luminescence and reactivity of a charge-transfer excited iron complex with nanosecond lifetime. *Science* **2019,** *363* (6424), 249-253.
7. Steube, J.; Kruse, A.; Bokareva, O. S.; Reuter, T.; Demeshko, S.; Schoch, R.; Argüello Cordero, M. A.; Krishna, A.; Hohloch, S.; Meyer, F.; Heinze, K.; Kühn, O.; Lochbrunner, S.; Bauer, M., Janus-type emission from a cyclometalated iron(iii) complex. *Nat. Chem.* **2023**.

Oxidative Desaturation of Aliphatic C-C Bonds with Dioxygen by a Biomimetic Iron(II)-α-Ketoacid Complex Anchored to Poly(Vinylbenzyl Chloride)

Abhijit Bera, Pradip Bhunia, and Tapan Kanti Paine*

School of Chemical Sciences, Indian Association for the Cultivation of Science, 2A & 2B Raja S. C. Mullick Road, Jadavpur, 700032. E-mail: scspb2880@iacs.res.in

α-Ketoglutarate-dependent mononuclear nonheme iron enzymes involveiron(IV)-oxo intermediates as the active oxidant to catalyze a diverse range of metabolically relevant biochemical reactions, including hydroxylation, ring fragmentation, C–C bond cleavage, epimerization, desaturation, endoperoxidation and heterocycle formation.[1]However, the reaction pathways for different functions share common initial steps of hydrogen atom transfer (HAT) from the substrate. The resultant Fe(III)-OH species and substrate radical combination then diverges to the different outcomes. While the OH-rebound step for C-H bond hydroxylation shows a low activation barrier, the factors suppressing rebound in the reactions other than hydroxylation is poorly understood.[2] The aliphatic C-C bond desaturation is one such reaction that requires second HAT step.

Although a number of bioinspired functional models of α-ketoglutarate-dependent mononuclear nonheme iron enzymes have been reported,[3] but none has been reported to display the aliphatic C-C bond desaturation. In that direction,we have developed a mononucleariron(II)-benzoylformate (BF)complex supported by the {6-(hydroxymethyl)-2-pyridylmethyl}bis(2-pyridylmethyl) amine (TPAOH) ligand covalently anchored topoly(vinylbenzyl chloride) (PVBC). The model complex performs selective desaturation activity of aliphatic C-C bond rather than C-H hydroxylation.[4] The role of polymer backbone in directing the reactivity of the anchored complex for selectivedesaturation will be presented.

References

[1] J. M. Bollinger, Jr.; W.-c. Chang, M. L. Matthews, R. J. Martinie, A. K. Boal, C. Krebs, C. *In 2-Oxoglutarate-Dependent Oxygenases*; R. P. Hausinger, C. J. Schofield, Eds.; The Royal Society of Chemistry: London, 2015; p 95.

[2] (a) S. Ye, C. Riplinger, C.; A. Hansen, C. Krebs, J. M. Bollinger, F. Neese, *Chem. - Eur. J.***2012**, *18*, 6555. (b) N. P. Dunham,W.-c. Chang,A. J. Mitchell,R. J. Martinie,B. Zhang,J. A. Bergman,L. J. Rajakovich,B. Wang,A.Silakov,C.Krebs,A. K. Boal,J. M. Bollinger, Jr., *J. Am. Chem. Soc.* **2018**, *140*, 7116.

[3] I. Ghosh, T. K. Paine, Comprehensive Coordination Chemistry III, Vol 8, Elsevier, 2021, 378–411.

[4] A. Bera, P. Bhunia, T. K. Paine, **2023**, *unpublished.*

Intrinsic Electric Field Effects in Redox Active Systems

Prateek Saini*, Piyali Mahapatra*, Ayan Santra*

*Department of Chemistry, Indian Institute of Technology Bombay

Powai, Mumbai, Maharashtra, 400076

Converting abundant feedstock such as CO_2 and N_2 to value-added products such as CH_3OH and NH_3, respectively, is a promising strategy to store electrical energy in chemical bonds. These electrochemical reduction processes are, however, multi-electron and multi-proton in nature, which require facile catalysts to mediate the myriad electron transfer, proton transfer, and substrate activation steps at low driving forces or mild overpotentials. For such multi-electron processes, minimizing the overall overpotential translates to achieving closely spaced redox potentials for sequential electrochemical reductions of the metal complex mediator/catalyst. Standard approaches for tuning the reduction potential of metal complexes involve changing the electronic structure at the metal center and/or the ligand environment around the metal ion. The present work quantifies the electric field effects in the primary as well as in the secondary coordination sphere of first-row transition metal complexes [Cu(II) and Fe(II)] as a function of distance, nature of the ligands as well as the dielectric environment around the metal complex. Using a combination of density functional theory-based calculations, experimental syntheses, spectroscopic, analytical and electrochemical validations of the *in-silico* predictions, the effect of these electric fields in modulating the reduction potential of metal complexes as well as their electrocatalytic activity towards CO_2 activation is quantitatively shown.

References:

(1) Reath, A. H., Ziller, J. W., Tsay, C., Ryan, A. J., & Yang, J. Y. (2017). Redox Potential and Electronic Structure Effects of Proximal Nonredox Active Cations in Cobalt Schiff Base Complexes. *Inorg. Chem*, *56*, 3713–3718. https://doi.org/10.1021/acs.inorgchem.6b03098

(2) Chantarojsiri, T.; Ziller, J. W.; Yang, J. Y. Incorporation of Redox-Inactive Cations Promotes Iron Catalyzed Aerobic C-H Oxidation at Mild Potentials. *Chem Sci* **2018**, *9* (9), 2567–2574. https://doi.org/10.1039/c7sc04486k.

(3) Boutin, E., Wang, M., ohn Lin, J. C., Mesnage, M., Mendoza, D., Lassalle-Kaiser, B., Hahn, C., Jaramillo, T. F., Marc Robert, and, Boutin, E., Wang, M., Mesnage, M., Mendoza, D., Robert, M., Lin, J. C., Hahn, C., Jaramillo, T. F., & Lassalle-Kaiser, B. (2019). Aqueous Electrochemical Reduction of Carbon Dioxide and Carbon Monoxide into Methanol with Cobalt Phthalocyanine. *Angewandte Chemie International Edition*, *58*(45), 16172–16176. https://doi.org/10.1002/ANIE.201909257

(4) Tse, E. C. M.; Schilter, D.; Gray, D. L.; Rauchfuss, T. B.; Gewirth, A. A. Multicopper Models for the Laccase Active Site: Effect of Nuclearity on Electrocatalytic Oxygen Reduction. *Inorg Chem* **2014**, *53* (16), 8505–8516. https://doi.org/10.1021/ic501080c.

Design and Fabrication of Electrochemical Cell to Solve the Various Problems in Electrochemistry

Yashwant Pratap Kharwar, Suhana Karim, Vaibhav Trivedi, and Prof. Arnab Dutta*

Department of Chemistry, Indian Institute of Technology Bombay, Powai-400076,Mumbai, Maharashtra, India.

Corresponding author e-mail: arnab.dutta@iitb.ac.in, arnabdutta.iitb@gmail.com

Abstract

The electrochemical cells generate electrical energy from chemical reactions (i.e. Galvanic cells) or use electricity to conduct chemical reactions (i.e. Electrolytic cells).Fuel cell is an electrochemical Galvanic cell in which chemicals (such as hydrogen and oxygen in form of gas) are provided externally to the device. It produces electricitywith water and heat as only byproducts. Metal-air batteries are another type of Galvanic cell in which oxygen from air is used at cathode and a solid metal is used asthe anode to generated electricity. Many electrochemical cells have been designed tostudy the various types of electrochemical reactions in various conditions such as temperature, pressure and concentration and for the various applications (Examples;H-Cell, Hull cell, Jacketed cell, etc.).

Problems 1:

Though various electrochemical cells are capable of study of electrode chemical reaction by variation in temperature of electrolytes but if we want to study thetemperature variation in only working electrodes (i.e. electrode materials), in three electrode modes, there is no such cell is available.

Problem 2:

The first limitation of H-cell is the distance between the two compartments (i.e. distance, l). By decreasing this distance (l) we can solve the following issues.

(a) Time travel in migration of ions from one electrode to other through electrolyticsolution.
(b) Cross-over of electrolyte/solution from one compartment to others.
(c) Ions selectivity like anions or cations.

References:

1. Alkire, R.C.; Kolb, D.M.; Lipkowsky & J. Ross, P.N. (Eds.). (2009). *Advances in Electrochemical Science and Engineering, Volume 11, Chemically modified electrodes,* WILEY-VCH Verlag GmbH & Co. KGaA, ISBN 978-3-527-31420-1, Weinheim Germany.
2. Aoki, K. & Osteryoung, J. (1981) Diffusion-Controlled Current at the Stationary Finite Disk Electrode. *J. Electroanal. Chem.* Vol.122, No.1, (May 1981), pp. 19-35, ISSN 1572-6657.
3. Aoki, K. (1991) Nernst Equation Complicated by Electric Random Percolation at Conducting Polymer- Coated Electrodes. *J. Electroanal. Chem.* Vol.310, No.1-2, (July 1991), pp. 1–12, ISSN 1572-6657
4. Lingane JJ, Gardner Swain C, Fields M (1943) J Am Chem Soc. 65:1348.
5. Lund H (2001) Practical problems in electrolysis. In: Lund H, Hammerich O (eds) Organicelectrochemistry, 4th edn. Marcel Dekker, New York, pp 223-292.
6. Smith WH, Bard AJ (1975) J Am Chem Soc 97:5203.
7. Farber E (1961) Great chemists. Interscience Publishers, New York.

Zinc Stabilized Azo-anion Radical in Multielectron Chemical Transformations: An Exclusively Ligand Centered Redox Controlled Approach

Sucheta Mondal[a,c], Nanda D. Paul*[b,c]
[a]Research Scholar, [b]Associate Professor
[c]Department of Chemistry, IIEST Shibpur, Howrah, 711103, India

Abstract: Two well-defined Zn(II)-complexes [Zn(L^a)Cl_2] (**1a**) and [Zn(L^b)Cl_2] (**1b**) of redox noninnocent azo-aromatic ligands 2-((4-chlorophenyl)diazenyl)-1,10-phenanthroline (**L^a**) and 2-(phenyldiazenyl)-1,10-phenanthroline) (**L^b**), respectively, were used as catalysts in this work. The catalysts **1a** and **1b** are two five-coordinate Zn(II)-complexes where one tridentate 2-arylazo-1,10-phenanthroline ligand (**$L^{a/b}$**) and two chlorido ligands are bound in a distorted square-pyramidal geometry (τ=0.24). In the presence of zinc-dust or ^{t}BuOK, the catalyst undergoes ligand-centered reduction to form the catalytically active azo-anion radical species [**1a/b**]$^-$ which is highly efficient for dehydrogenation of saturated heterocycles as well as cascade synthesis of diverse N-heterocycles, including quinolines, quinazolines, pyrimidines, and pyridines via dehydrogenative functionalization of alcohols. The catalyst is also compatible with the *N*-alkylation of amines with alcohols. Mechanistic investigation reveals that the dehydrogenation reactions proceed via a one-electron hydrogen atom transfer (HAT) pathway. Further, control reactions and DFT studies indicate that electron transfer events occur at the azo-chromophore throughout the catalytic process, which shuttles between neutral azo, one-electron reduced azo-anion radical, and two-electron reduced hydrazo forms acting both as electron and hydrogen reservoir keeping the Zn(II)-center as a template (Figure 1).

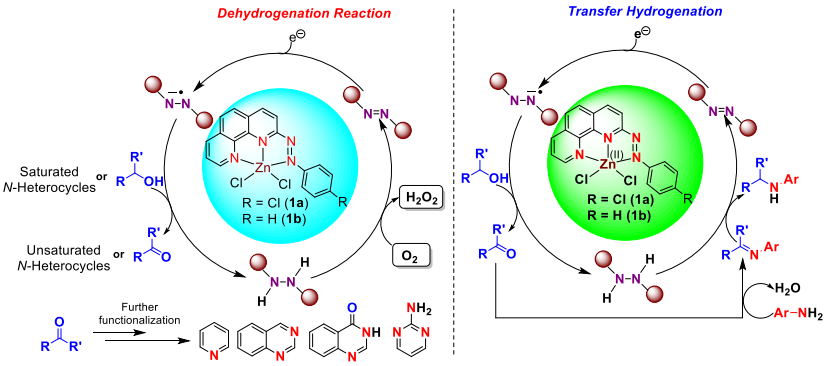


Figure 1 Schematic Representation of Dehydrogenation and Transfer Hydrogenation Reaction.

References

(1) Das, S.; Mondal, R.; Chakraborty, G.; Guin, A. K.; Das, A.; Paul, N. D.; *ACS Catal.,* **2021**, *11*, 7498-7512.

(2) Paul, N. D.; *J. Org. Chem.,* **2023**, *88,* 3650−3665.

(3) Chakraborty, S.; Mondal, R.; Pal, S.; Guin, A. K.; Roy, L.; Paul, N. D.; *J. Org. Chem.,* **2023**, *88,* 771−787.

(4) Das, S.; Mondal, R.; Guin, A. K.; Paul, N. D.; *Org. Biomol. Chem.,* **2022**, *20,* 3105–3117.

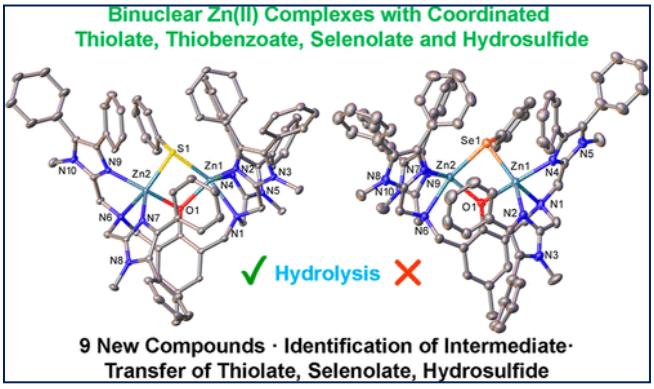
Hydrolysis and Transfer Reactivity of the Coordinated Thiolate, Thiocarboxylate, and Selenolate in Binuclear Zinc(II) Complexes

Anuj Baran Chakraborty, and Amit Majumdar*

Email: csabc2339@iacs.res.in

Indian Association for the Cultivation of Science, Kolkata-700032, India

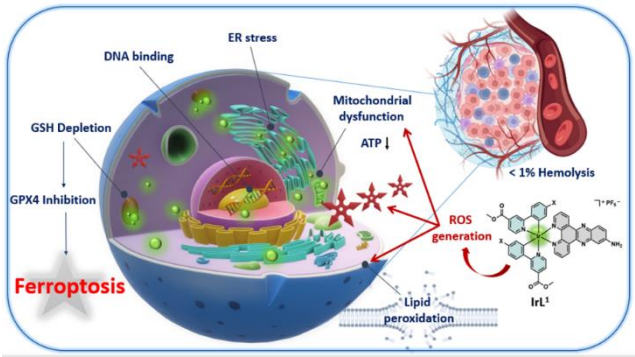
Desulfurization of organosulfur compounds is a highly important reaction due to its relevance to the hydrodesulfurization process of fossil fuels, which removes sulfur from crude oil as H_2S with the aid of a molybdenum sulfide-cobalt catalyst at high pressure and temperature. In contast to this, a very recent discovery of hydrolytic desulfurization involving transition metals like Co(II), Fe(II), Ni(II) proceeded through ambient condition. However there was no evidence found for Zn(II) mediated hydrolytic desulfurization in literature. The hydrolytic C-S bond cleavage of several aliphatic and aromatic thiolates to yield the corresponding alcohols/phenols has been demonstrated for the first time to be mediated by a new binuclear Zn(II) complex, $[Zn_2(PhBIMP)(DMF)_2]^{3+}$ (where PhBIMP is the anion of 2,6-bis[bis[(N-1-methyl-4,5-diphenylimidazoylmethyl)amino]methyl]-4-methylphenol). Additionally, the formation of a hydrosulfde-bridged complex, $[Zn_2(PhBIMP)(\mu\text{-}SH)(DMF)]^{2+}$, has been thoroughly characterized as the end product. The binuclear Zn(II)-thiolate complexes $[Zn_2(PhBIMP)(\mu\text{-}SR)]^{2+}$ (R = Ph, 3-Br-C_6H_4) have also been synthesized by avoiding the C−S bond cleavage reaction. Based on the findings of the experiments conducted on the impacts of H_2O and Et_3N on the precursur complexes, the complex $[Zn_2(PhBIMP)(\mu\text{-}SR)(OH)]^{1+}$ has been suggested as the active intermediate that comes before the cleavage of C–S bonds. The hydrolysis of the coordinated thiobenzoate to yield $[Zn_2(PhBIMP)(\mu\text{-}O_2CPh)(MeCN)]^{2+}$ is also demonstrated by the complex $[Zn_2(PhBIMP)(\mu\text{-}SCOPh)(DMF)]^{2+}$. However, unlike thiolato and thiobenzoate complexes the benzeneselenolate-bridged complex, $[Zn_2(PhBIMP)(\mu\text{-}SePh)]^{2+}$, does not generate the species, $[Zn_2(PhBIMP)(\mu\text{-}SePh)(OH)]^{1+}$, in solution, and in line with that, the coordinated benzeneselenolate does not undergo hydrolysis to generate hydroselenide and phenol. Finally, a comparison analysis of the transfer reactivity of the bridging −SH, −SPh, −SC(O)Ph, and −SePh ligands in the binuclear Zn(II) complexes to particular organic substrates has been carried out to highlight the distinctive variations in the reactivity of these bridging ligands.



Cellular Accumulation and Endoplasmic Reticulum Localized Iridium (III) Complexes as Efficient Ferroptosis Inducers

Ayushi Chaudhary, and Dr. Ritika Gautam
Department of Chemistry
Indian Institute of Technology Kanpur
Email: ayushic21@iitk.ac.in, rgautam@iitk.ac.in

Recent research underscores the urgent need to address cancer and its recurrence on a global scale. Ferroptosis, an emerging non-apoptotic form of programmed cell death, has emerged as a promising target for anticancer therapy since its initial proposal in 2012. This iron-dependent regulated cell death is triggered by uncontrolled lipid peroxidation (LPO) and heightened reactive oxygen species (ROS).[1-2] While reported ferroptosis inducers are primarily small organic molecules, their off-target toxicity and limited half-life hinder their clinical application. Developing ferroptosis inducers with both highly selective tumor targeting and low cytotoxicity to normal cells remains a challenging goal. Metal-based anticancer drugs offer significant versatility compared to small molecules in tuning a given molecule's properties. In this context, we synthesized a series of organometallic iridium (III) complexes as potent anticancer candidates, operating through a mechanism distinct from cisplatin-based chemotherapy regimens. Thorough characterization through various techniques, including ^{1}H, ^{13}C NMR, ESI-MS, UV-vis, and FT-IR, revealed that the lead compound IrL^{1} localized in the endoplasmic reticulum, displaying significantly higher cytotoxicity (IC_{50} value of 0.33 μM) against the triple-negative breast cancer cell line MDA-MB-231 compared to cisplatin. IrL^{1} effectively generated ROS, induced LPO, and depleted glutathione, suggesting the ferroptosis-mediated pathway for cancer cell death. It also caused the loss of mitochondrial membrane potential, impaired adenosine triphosphate (ATP) generation, exhibited DNA intercalation, induced endoplasmic reticulum (ER) stress, and caused less than 1% hemolysis of human RBCs. Furthermore, IrL^{1} displayed high cytotoxicity against 3D multicellular tumor spheroids and demonstrated antibacterial properties with an MIC value of 0.94 μM against gram-positive bacteria Staphylococcus aureus. This suggests the drug's potential for eliminating bacterial infections at malignant sites. Overall, our work introduces an effective strategy for developing multifaceted organometallic Ir(III) complexes providing protection against microorganisms and the tumor microenvironment.



References:

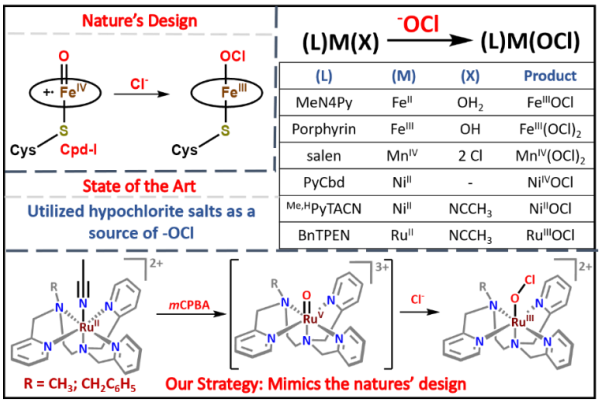
(1) Jiang, X.; Stockwell, B. R.; Conrad, M.; Nat. Rev. Mol. Cell Biol., **2021**, 22, 266–282.
(2) Stockwell, B.R.; Friedmann Angeli. J.P.; et.al.; Cell, **2012**, 149, 1060–1072.

Generation of Ru(III)-hypochlorite with resemblance to heme dependent haloperoxidase enzyme

Rakesh Kumar,[a] Faiza Ahsan,[b] Ayushi Awasthi,[a] Marcel Swart,[b,c*] and Apparao Draksharapu,[a,*]

[a] *Southern Laboratories - 208A, Department of Chemistry, Indian Institute of Technology Kanpur, Kanpur-208016 (India).* appud@iitk.ac.in
[b] *IQCC & Departament de Química, Universitat de Girona, 17003 Girona, Spain*
[c] *ICREA, 08010, Barcelona, Spain.* marcel.swart@gmail.com

Haloperoxidase enzymes utilize metal hypohalite species to halogenate aliphatic and aromatic C–H bonds to C–X (X = Cl, Br, I) in nature.[1] A very few metals' hypochlorite adducts (2 with Fe, 1 with Mn, 2 with Ni, 1 with Ru) were spectroscopically characterized in the literature. Importantly, in all the cases hypochlorite is used as a source of ClO^- to form M^{n+}-OCl adducts.[2] None of the reported systems employed the strategy of natures' design, *i.e.*, nucleophilic attack of chloride on high valent metal oxo species. The present study is the first of its kind that mimics the synthesis of a metal hypochlorite in the same way the nature employed in heme dependent chloroperoxidases where high valent Cpd-I reacts with chloride ion (Cl^-) to form Fe^{III}-OCl species. The reaction of $[(L)Ru^{II}(NCCH_3)]^{2+}$ (L is a pentaddentate ligand) with *m*CPBA in the presence of chloride ions in $CH_3CN:H_2O$ generated a novel $(L)Ru^{III}$-OCl species at room temperature. This hypochlorite adduct could also be obtained by the direct reaction of NaOCl and $HClO_4$ with $(L)Ru^{II}$ complexes as well.[3] Computational studies suggests the involvement of Ru^V=O as an active intermediate, which upon reacts with Cl^- to form $(L)Ru^{III}$-OCl. $(L)Ru^{III}$-OCl is capable of conducting oxygen atom transfer and hydrogen atom abstraction reactions of various organic substrates.[4]



References:

1) (a) A. Timmins and S. P. de Visser, in Advances in Protein Chemistry and Structural Biology, ed. T. Karabencheva-Christova, Elsevier Inc, 1st edn, 2015, 100, vol. 5, pp. 113–151; (b) K. H. van Pée, in Methods in Enzymology, ed. D. A. Hopwood, Elsevier Inc, 2012, 516, vol. 12, pp. 237–257.
2) (a) Z. Cong, S. Yanagisawa, T. Kurahashi, T. Ogura, S. Nakashima and H. Fujii, J. Am. Chem. Soc., 2012, 134, 20617–20620. (b) A. Draksharapu, D. Angelone, M. G. Quesne, S. K. Padamati, L. Gómez, R. Hage, M. Costas, W. R. Browne and S. P. de Visser, Angew. Chem., Int. Ed., 2015, 54, 4357–4361. (c) A. Draksharapu, Z. Codolá, L. Gómez, J. Lloret-Fillol, W. R. Browne and M. Costas, Inorg. Chem., 2015, 54, 10656–10666; (d) T. Corona, A. Draksharapu, S. K. Padamati, I. Gamba, V. Martin-Diaconescu, F. Acuna- Pareś, W. R. Browne and A. Company, J. Am. Chem. Soc., 2016, 138, 12987–12996. (e) I. Araki, K. Fukui and H. Fujii, Inorg. Chem., 2018, 57, 1685–1688.
3) R. Kumar, A. Awasthi, S. Gupta, R. Eerlapally and A. Draksharapu, *Dalt. Trans.*, 2022, **51**, 12848–12854.
4) R. Kumar, F. Ahsan, A. Awasthi, M. Swart and A. Draksharapu, *Dalt. Trans.*, 2023, **52**, 12552-12559.

Artificial metalloenzyme catalyzed enantiodivergent synthesis of isoindolones

Prasun Mukherjee †[1], Anjali Sairaman†[2], Hirak Jyoti Deka,[1] Shubhanshu Jain[1], Sandip Kumar Mishra[1], Sayan Roy[1], Prasenjit Bhaumik*[2], Debabrata Maiti*[1]

[1]Department of Chemistry, Indian Institute of Technology Bombay, Powai, Mumbai 400076, Maharashtra, India.

[2]Department of Biosciences and Bioengineering, Indian Institute of Technology Bombay, Powai, Mumbai 400076, Maharashtra, India.

Abstract:

Combining enzyme and transition metal catalysis within artificial metalloenzymes has broadened the scope of new to nature reactions and efficiently solved several problems in asymmetric organometallic catalysis. Streptavidin, a homotetrameric protein, along with a biotinylated metal complex is one of the promising artificial metalloenzymes for its application in diverse non-natural reactions. Biocatalysis has shown tremendous potential in bringing together greener reagents and methods delivering products with excellent chemo, stereo and regioselectivities. Thus, rightfully has been in the spotlight for the past decade. However, the use of such biocatalysts is limited by protein stability, substrate solubilities and scope of the reactions. The application of an artificial metalloenzyme is one way to complement biocatalysis in substrate scope and protein stability albeit at the cost of transition metals usage. Our quest to efficiently synthesize chiral isoindolones, preferably in an enantiodivergent and a sustainable way, led to utilizing artificial metalloenzymes (ArMs) as our platform.

Here, we report a streptavidin-biotin-Rh(III) system to synthesize chiral isoindolones with up to 94:6 e.r. involving a directed inner-sphere C-H activation followed by diazo insertion. A high-resolution crystal structure of streptavidin with the biotinylated Rh(III) cofactor inclined us to rationally engineer mutants at the position of N49 for enantiodivergence. This is the first report of enzyme catalyzed enantiodivergent route for the synthesis of complex isoindolone derivatives.

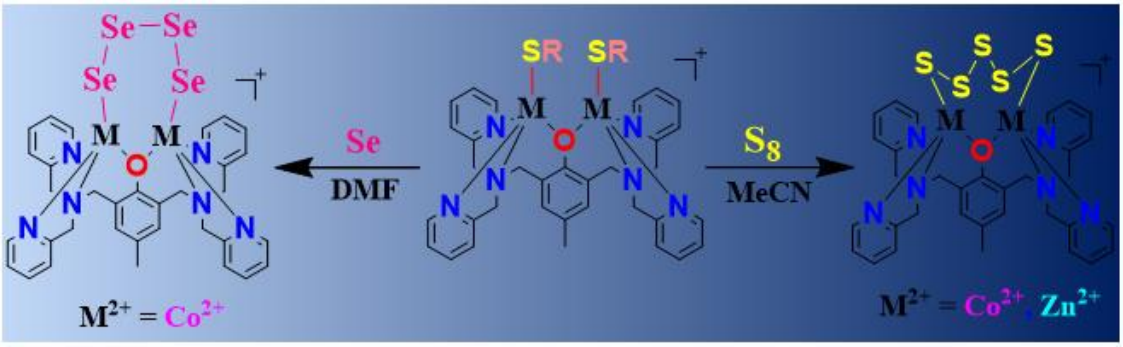
Generation and Comparative Reactivity of Polychalcogenide Chains in Binuclear Transition Metal Complexes

Kamal Hossain and Amit Majumdar*

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

Email: cskh2263@iacs.res.in

The polychalcogenides are important because of their structural diversity and relevance to many important processes such as hydrodesulfurization of crude oil, hydrogenation of unsaturated and aromatic hydrocarbons, biosynthesis of metalloproteins etc.[1] The general synthetic procedures of transition metal polychalcogenide complexes include either (i) the oxidation of low-valent transition metal salts or zero-valent metal by the treatment of elemental chalcogens, or (ii) the treatment of Na_2S_x or Na_2Se_x with metal complexes. Here we present a new synthetic strategy for the synthesis of unprecedented binuclear transition metal-polychalcogenide complexes. The strategy involves the two-electron oxidation of binuclear transition metal-thiolate bis(thiolate) complexes with elemental chalcogens. Synthesis, molecular structures, and detailed reactivity of these new type of transition metal polychalcogenide complexes with phosphines, cyanide, elemental chalcogen, and electrophilic alkynes are presented.[2, 3]



- Synthesis of binuclear Co(II) and Zn(II) polychalcogenide complexes
- Reactions of polychalcogenide complexes with desulfurizing agents
- Treatment of proton source to polysulfides complexes
- Interconversion of polychalcogenides complxes and transfer of polysulfides

1. M.G. Kanatzidis; S-P. Huang, *Coord Chem. Rev.* **1994**, *130,* 509-621.
2. Hossain, K.; **Majumdar, A.*** ***Inorg. Chem.*** **2022**, *61*, 6295-6310.
3. Hossain, K.; **Majumdar, A.*** *Work Under Progress*

Copper(II) Complexes containing N_2O Donor Ligands as Models for Phenoxazinone Synthase

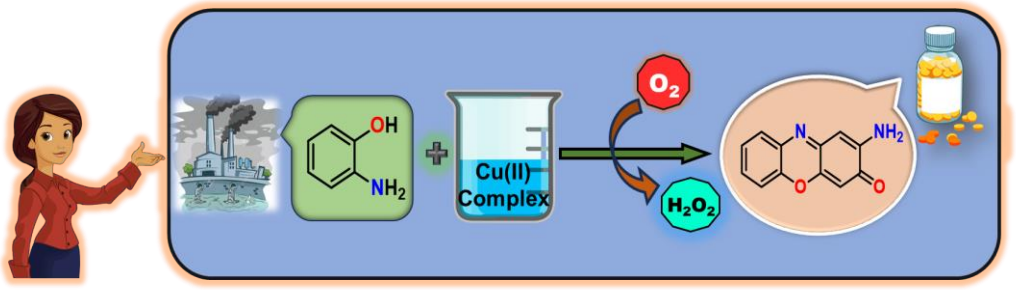
Ganesh Yamuna[1], Karuppasamy Sundaravel[1*]

[1]*Bioinorganic Research Laboratory, Department of Chemistry*\

Bharathiar University, Coimbatore - 641046, Tamil Nadu, India

**E-mail: sundaravel.k@buc.edu.in*

Copper is considered as one of the most significant bioactive transition metals found in active site of various metalloenzymes. Copper containing enzymes like catechol oxidase, amine oxidase, galactose oxidase, phenoxazinone synthase (PHS), superoxide dismutase and blue copper proteins were found to perform important redox process and useful organic transformations in living organisms, due to their ability to easily shuttle between Cu(I)-to-Cu(II) oxidation states. PHS is a multicopper sites containing enzyme which catalyzes the penultimate step in biosynthesis of actinomycin D[1] (Act-D). Act-D is a potential anti-cancer drug used in treatment of different kind of tumours like Wilm's tumour, Kaposi's sarcoma, rhabdomyosarcoma etc. In this present work, we have synthesized two new copper(II) complexes containing N_2O donor ligand scaffolds (where, *L1 = 1-((pyridin-2-ylmethyl)amino)propan-2-ol; L2 = 2-((pyridin-2-ylmethyl)amino)ethanol*) as potential small molecular models for PHS[2]. The ligands L1, L2 and their copper(II) complexes **1, 2** were characterised by various physical methods. PHS enzyme-like kinetics of the present copper(II) complexes were evaluated using 2-aminophenol as a model substrate. The present molecular machines exhibit excellent PHS-like activity with impressive turn-over number in water at RT even at micromolar concentration.



References:

1. Nirmala, P.; Sukantha, M. *New J. Chem.* **2020**, 44, 12793-12805.
2. Alan, M.; Juan, R. A.; Victor, M. U.; Marcos, F.; Alfonso, A.; Gerardo, F.; Laura, G. ***Inorg. Chem.*** **2023**,**62**, 16677-16690.
3. Yamuna, G.: Sundaravel, K.-Unpublished work.

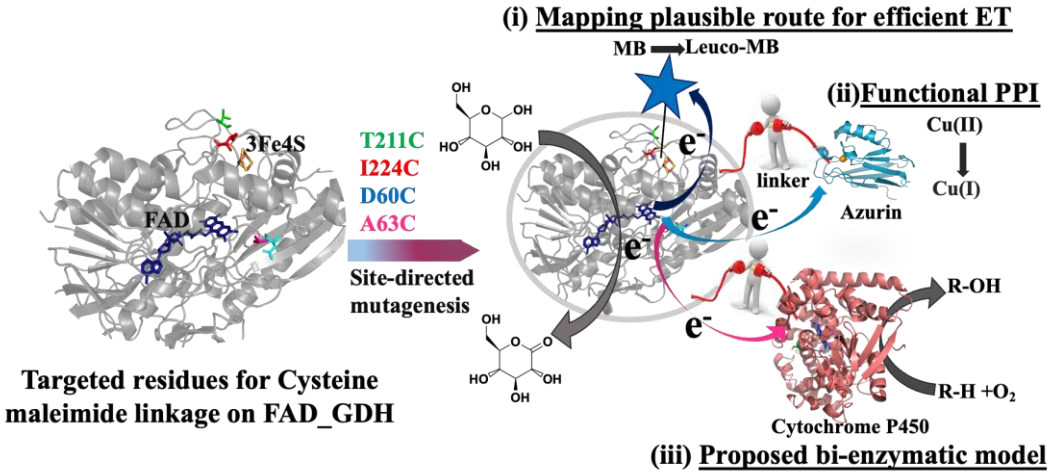
Electron Ballet: Choreographing Self-Sufficient Redox System

Rachna Sharma, Akshaya Ann John, Ankur Gupta*

Department of Chemistry, IISER Bhopal

Electron-transfer (ET) reactions are fundamental in biochemical processes, requiring precise organisation of redox components to prevent charge recombination.[1] Nevertheless, emulating nature's adeptness in the laboratory is challenged by exclusive protein functions, insulating glycoprotein shells, and complexities of cofactor regeneration. Previously reported attempts at *in situ* redox cofactor regeneration, like mediator immobilisation and enzyme genetic fusion, encountered problems including stability, mediator diffusion, and ET regulation.[2-4]

We aim to exploit natural ET pathways and establish a favourable route towards developing a new-to-nature, bi-enzymatic and bifunctional system. The key lies in the strategic alignment of redox enzymes along their efficient ET pathway. We have employed Flavin-containing glucose dehydrogenase (FAD-GDH) as our model enzyme to harness electrons from glucose, a ubiquitous and abundant fuel source. Mapping plausible positions for electron extraction from the catalytic site is achieved by monitoring reduction rates of a redox dye methylene blue (MB), anchored at rationally introduced cysteine residues on FAD-GDH. To shed light on protein-protein interaction (PPI) and functional ET without mediators, we have successfully tethered the non-catalytic ET protein Azurin at these specific sites using bifunctional linkers of varying lengths. Ongoing work involves the integration of a catalytic partner, like cytochrome P450 monooxygenase, to obtain a bi-functional hetero protein dimer with complementary functions, offering versatile applications from biotechnology to pharmaceuticals.



References:

(1) Beratan, D. N.; Onuchic, J. N.; Winkler, J. R.; Gray, H. B. *Science*. **1992**, 11 (12), 1740–1741.
(2) Holland, J. T.; Lau, C.; Brozik, S.; Banta, S. *J Am Chem Soc* **2011**, *133* (48), 19262–19265.
(3) Lee, Y. S.; Baek, S.; Lee, H.; Reginald, S. S.; Kim, Y.; Kang, H.; Choi, I. G.; Chang, I. S. *ACS Appl Mater Interfaces* **2018**, *10* (34), 28615–28626.
(4) Kokorin, A.; Parshin, P. D.; Bakkes, P. J.; Pometun, A. A.; Tishkov, V. I.; Urlacher, V. B. *Sci Rep* **2021**, *11* (1), 1–13.

De novo Pyridine-2,6-dicarboxamide Ligands and their corresponding Cu(II) and Zn(II) complexes mitigating oralcavity colonization: Inhibitor of MRSA/VRSA by targetingMurB enzyme

Kajal Chaudhary[1], Bhumika Agrahari[1], Ritika Gautam[1]*

[1]Department of Chemistry, IIT Kanpur, Kanpur 208016, Uttar Pradesh, India E-mail: kajalc20@iitk.ac.in

Antibiotic resistance-induced infectious diseases are the leading cause of death worldwide. [1,2] The increasing morbidity and mortality resulting from the resistance of bacteria to antibiotics, accompanied by high medical costs, has become a severe ultimatum to global public health. [3,4] Therefore, there is an immediate need to developnovel antibacterial agents. In this perspective, the work illustrates the synthesis and characterization of a new series of Pyridine-2,6-dicarboxamide ligands and their Cu(II)and Zn(II) complexes in high yield (85–87%). All ligands were characterized by ^{1}H, $^{13}C\{1H\}$ NMR, and ESI-MS, and the structure of the ligands and complexes was established by single crystal X-ray studies. The synthesized compounds were screened against five bacterial strains, *A. baumannii*, *E. coli*, *S. aureus*, *P. aeruginosa*, and *K. pneumoniae*. The ligands and their Cu(II) and Zn(II) complexes showed potent activity against *S. aureus* with MICs in the range 2-16 μg/mL and 4-64 μg/mL, respectively, with low hemolytic and cytotoxic activities. SEM and AFM imaging studies were performed to understand the mechanism of cell death, and the results revealed that cell wall disruption is the main reason for bacterial cell death. The resultswere supported by the PI/DAPI staining, DISC3(5) depolarization, PI-uptake, and K- efflux assays. Also, the docking results were in agreement with the biological study, where the antimicrobial property of L^{11} can be attributed to the interaction with the S.*aureus* MurB present in the cell wall. In addition, it also showed good antibacterial activity against Vancomycin-resistant Enterococcus (VRE) and Vancomycin-sensitive Enterococcus (VSE) with MICs in the range of 2-8 μg/mL. The lead compound displayed high activity against clinical isolates of MRSA (methicillin-resistant S. aureus) and VRSA (Vancomycin-resistant S. aureus) with MIC values of 2-4 μg/mL. Finally, the efficiency of L^{11} ligand and CuL^{11} complexes was evaluated in rodent models of dental biofilm. Topical administration of the compounds was successfully able to improve oral hygiene by inhibiting the formation of biofilm. Taken together, thestudy shed light on the class of potent antibacterial and antibiofilm agents for combating *S. aureus* infections.

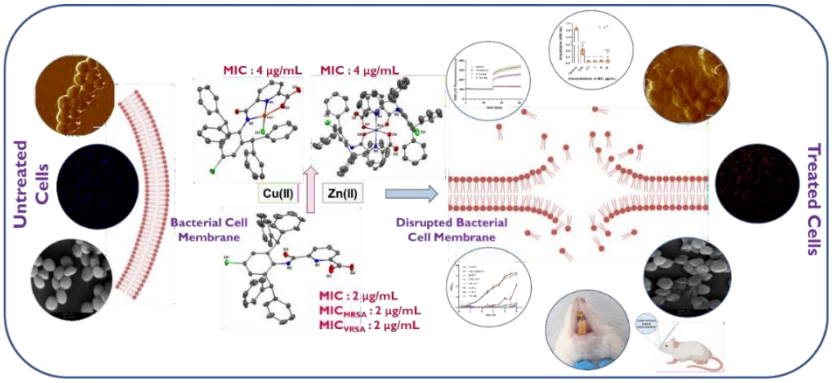


Figure 1 Abstract illustration: IIIuminating the battle against bacteria: A comprehensive study on de novo pyridine-2,6-dicarboxamide ligands as antibacterialagent and mechanism of action.

References:

(1) Brown, E. D.; Wright, G. D. Antibacterial drug discovery in the resistance era. *Nature.* **2016**, 529, 336-343
(2) Goff, D. A.; Kullar, R.; Goldstein, E. J. C.; Gilchrist, M.; Nathwani, D.; Cheng, A. C.; Cairns, K. A.; Escandón-Vargas, K.; Villegas, M. V.; Brink, A.; van den Bergh, D.; Mendelson, M. A global call from five countries to collaborate in antibiotic stewardship: united we succeed, divided we might fail. *LancetInfect. Dis.* **2017**, *17*, 56-63
(3) Willyard, C.; The drug-resistant bacteria that pose the greatest health threats. *Nature*. **2017**, *543*, 15
(4) Privalsky, T. M.; Soohoo, A. M.; Wang, J.; Walsh, C. T.; Wright, G. D.; Gordon, E. M.; Gray, N. S.; Khosla, C. Prospects for Antibacterial Discovery and Development. *J. Am. Chem. Soc.* **2021**, *143*, 21127-21142

Novel Cu(II) Complexes of Sirtinol Analogues for Enhanced Chemodynamic Therapy: Targeting Glutathione Depletion and Lipid Peroxidation

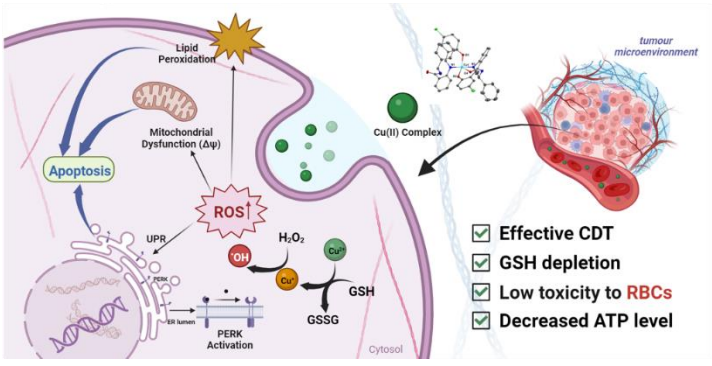
Ashwini Kumar and Dr. Ritika Gautam*

Department of Chemistry, IIT Kanpur-208016, India

Email: kmrash@iitk.ac.in

Chemodynamic therapy (CDT) is an innovative method of treating cancer that combines medicine and chemistry. By catalyzing the excess H_2O_2 in cancer cells, it targets and damages them by generating the extremely lethal hydroxyl radical (·OH), which contributes to oxidative stress and causes cell death. The high H_2O_2 levels in the tumor microenvironment limit the generation of hydroxyl radicals to the tumor location. Despite this, glutathione (GSH), a robust reactive oxygen species (ROS) scavenger, is frequently overproduced by cancer cells as a means of adaptation. Reducing GSH levels to promote oxidative stress is a reasonable strategy to improve CDT and create potent anticancer medicines. Research suggests that specific redox-active metal compounds could be effective CDT agents.

Herein, we have synthesized a series of Cu(II) complexes of Sirtinol analogue molecules (histone deacetylase inhibitors) known as HL1-8. Ligands were characterized using spectroscopic techniques like ^{1}H and ^{13}C NMR, UV-vis, and ESI-MS mass spectrometry. Additionally, the metal complexes were characterized by the SC-XRD, UV-Vis, EPR, and ESI-MS mass techniques. The biological activity of the synthesized compounds was evaluated on various cancer cell lines, such as MDA-MB-231, MCF-7, HCT-116, and A549. Of these, **$Cu(L2)_2$** showed the most excellent cytotoxicity against MCF-7 breast cancer cells (IC_{50} = 5.32 μM at 72 hours) and exceptional antiproliferative activity across all cell lines. Upon in vitro investigations, **$Cu(L2)_2$** have been observed to generate ROS (·OH), depleting GSH level, mitochondrial dysfunction, decreased ATP level, lipid peroxidation and PERK protein level reduction which triggers endoplasmic reticulum stress. These findings suggest that $Cu(L2)_2$ has a promising potential as an CDT agent, particularly in breast cancer treatment.



References:

1. Z. Chen et. al, *J. Med. Chem*. **2022**, 65, 6, 5134–5148.
2. A. Mai et. al, *J. Med. Chem*. **2005**, 48, 24, 7789–7795.
3. E. Tomat et. al, *Chem. Commun*. **2015**, 51, 5104-5107.
4. X Tai et. al, *Dalton Trans*. **2020**, 49, 11851-11858.

Functional Models for Dioxygen-activating Quercetin 2,4-Dioxygenase Enzymes: Copper(II)-Flavonolate Complexes with Diimine Co-ligands

Abdul Salam Shajahan,[a] Andivelu Ilangovan,[a]* and Mallayan Palaniandavar[a]*

[a]*School of Chemistry, Bharathidasan University, Tiruchirappalli 620 024, Tamil Nadu, India*

Abstract

Flavonoids are polyphenolic pigments found in higher plants and some fungi. Numerous flavonoids such as quercetin (3,5,7,3,4-pentahydroxyflavone) are well known for their antioxidant and antimicrobial properties. Being present in many fruits and vegetables, they provide an important source of antioxidant and antibacterial dietary supplement for humans. Microbicidal flavonoids get into the soil, and get exposed to bacteria and fungi. In response, soil microorganisms develop effective catabolic systems utilizing flavonoids as a carbon source with the help of flavonol 2,4-dioxygenase metallo (FDO) enzymes. The FDO enzymes can transform flavonoids into the corresponding depsides (phenolic carboxylic acid esters) under aerobic conditions. They catalyze the oxygenation of flavonol derivatives, which involves the cleavage of two carbon–carbon bonds in the organic substrate molecule, incorporation of both atoms of molecular oxygen and the concomitant production of carbon monoxide. Not surprisingly, these metalloenzymes dependent on copper and nickel have drawn the attention of bioinorganic chemist in the last decades.[1] The X-ray crystal structure of natural fungal copper(II) 2,4-QueDs enzyme from *Aspergillus japonicas* contain a type II copper bound to histidine imidazoles in the active site. In search of efficient and sustainable regio- and stereoselective catalytic systems for oxidation reactions, we have isolated and investigated many mixed ligand Cu(II)-flavonolate complexes as functional models for the enzyme [2]. These complexes display interesting EPR spectral properties, like low $A_{//}$ values, which are typical of type-II copper enzymes. The strong π-delocalization of electron density from Cu(II) into flavonolate (fla^-) accounts for the novel EPR properties. Also, we have synthesized mixed ligand Ni(II)-flavonolate complexes to demonstrate the importance of π-backbonding from Ni(II) to coordinated flavonolate [3]. In the present study, we have isolated new mixed ligand complexes of the type $[Cu(diimine)(fla)]^+$, where H(fla) is 3-hydroxyflavonone, and diimines are 2,2-bypyridine, 1,10-phenanthroline etc., and studied them as functional models for Cu(II) 2,4-QueD enzymes. The X-ray crystal structure of $[Cu(diimine)(fla)]^+$, where diimine is 5,6-dimethyl-1,10-phenanthroline, has been determined. The complex shows a dimeric coordination structure with Cu(II) having a CuN_2O_2O' chromophore. Upon exposure to dioxygen at 70-80 ºC, all the Cu(II)-flavonolate complexes undergo catalytic oxygenative degradation in DMF solution, as seen from the disappearance of the LMCT band at 430 nm. The rate of dioxygenation has been correlated with the Cu^{II}/Cu^{I} reduction potentials and the novel EPR properties of the complexes.

References

1. J. Pap, J. Kaizer and G. Speier, *Coord. Chem. Rev.* **2010**, 254, 781–793.
2. T. Ajaykamal, Martin Köckerling, and M. Palaniandavar, *Inorg. Chim. Acta*, **2023**, 556,121673.
3. T. Ajaykamal and M. Palaniandavar, *RSC Adv*. **2023**, **13**, 24674-24690.

Deciphering the mechanism of MRSA targeting copper(II) complexes of *NN*$_2$ pincer-type ligands

[a]Athulya Das, [b]Shanmugaraj Gowrishankar, [a]Muniyandi Sankaralingam*
[a]Bioinspired & Biomimetic Inorganic Chemistry Lab, Department of Chemistry, National Institute of Technology Calicut, Kozhikode-673601, Kerala, India.
[b]Department of Biotechnology, Science Campus, Alagappa University, Karaikudi-630003, India.
*Email: msankaralingam@nitc.ac.in

As per the world health organization (WHO), antimicrobial resistance (AMR) stands as a significant peril to the global health and development right now.[1] Therefore, continuous efforts should be made to develop medications with greater efficacy against microbes. As a result, transition metal complexes have emerged as an effective treatment for this aliment over the last decades.[2] In this regard, aminoquinoline-based copper(II) pincer complexes **1**−**3** were synthesized, characterized, and subjected to antimicrobial activity.[3] It is remarkable to mention that the hemolysis by these complexes at a maximum concentration of 1024 µg/mL was only <15%, suggesting their less toxicity. Moreover, the complexes effectively inhibited the proliferation of Gram positive bacterium MRSA and the fungus *Candida albicans*. Among these, complex **2** exhibited a promising MIC value of 16 µg/mL against MRSA. This result was found to be surpassing the activity of the standard antibacterial drug kanamycin which has an MIC of 64 µg/mL under identical conditions. It is also important to mention that the corresponding ligands were not active against the present pathogens, suggesting the importance of copper metal in the antimicrobial action. The results of the Alamar blue cell viability test and the spot assay for MBC/MFC were consistent with the MIC values. Furthermore, the most plausible mechanism of action was elucidated through *insilico* techniques and found to be inhibition of cell wall biosynthesis and dysfunction of antibiotic sensing proteins in MRSA. Likewise, the potential antifungal action could be attributed to the dysfunction of cell surface adhesion proteins.

References

1. WHO, Cancer and AMR. https://www.who.int/health-topics/, accessed 11.11.2023.
2. Masternak, J.; Zienkiewicz-Machnik, M.; Kowalik, M.; Wawrzycka-Jabłonska, A.; Rogala, P.; Adach, A.; Barszcz, B. *Coord. Chem. Rev.* **2016**, *327-328*, 242-270.
3. Das, A.; Sangavi, R.; Gowrishankar, S.; Kumar, R.; Sankaralingam, M. *Inorg. Chem*. **2023**, https://doi.org/10.1021/acs.inorgchem.3c02480.

Copper(II) Complexes of Pentadentate Ligands as Biomimetic Model of LPMO Enzyme

Akhila George, Muniyandi Sankaralingam*

Bioinspired and Biomimetic Inorganic Chemistry Lab, Department of Chemistry, National Institute of Technology Calicut, Kozhikode-673601, Kerala, India

*Email: msankaralingam@nitc.ac.in

Lytic Polysaccharide Monooxygenases (LPMO), are mononuclear copper-containing enzymes identified in 2010. They have garnered significant attention due to their ability to initiate the degeneration of recalcitrant polysaccharides such as cellulose or chitin using oxidative mechanisms. LPMOs are expected to have significant industrial relevance due to their intricate oxidation mechanism and widespread presence in the natural environment. The hydroxylation of the glycosidic linkages in polysaccharides by LPMO necessitates the presence of an oxygenated co-substrate like O_2 or H_2O_2. Studies have demonstrated the coexistence of both routes, with the possibility of a shared common intermediate, Cu(I)-O_2H_2. The advancement of LPMO-like catalytic systems would have a technological impact on the utilization of recalcitrant biomass as a source of sustainable feedstock. Moreover, there are still unresolved inquiries pertaining to the oxidizing co-substrate, active copper oxygen species, and the precise mechanism underlying C-H activation. With all of the above considerations, we have designed and synthesized copper(II) complexes with pentadentate ligand architectures to investigate the LPMO mimicking activity. Furthermore, the complexes were characterized using a range of spectroscopic techniques. The complexes underwent LPMO-like activity by employing the model substrate, *p*-nitrophenyl-β-D-glucopyranoside, with H_2O_2 as the oxidant in an aqueous environment. The oxidative cleavage products were identified using UV-visible, GC/ GC-MS analysis. The detailed results will be presented during the presentation.

References:

(1) Meier, K.K.; Jones, S.M.; Kaper, T.; Hansson, H.; Koetsier, M.J.; Karkehabadi, S.; Solomon, E.I.; Sandgren, M. and Kelemen, B. *Chem. Rev.* **2018**, 118(5), 2593-2635.

(2) Concia, A.L.; Beccia, M.R.; Orio, M.; Ferre, F.T.; Scarpellini, M.; Biaso, F.; Guigliarelli, B.; Réglier, M. and Simaan, A.J. *Inorg. Chem.* **2017**, 56(3), 1023-1026.

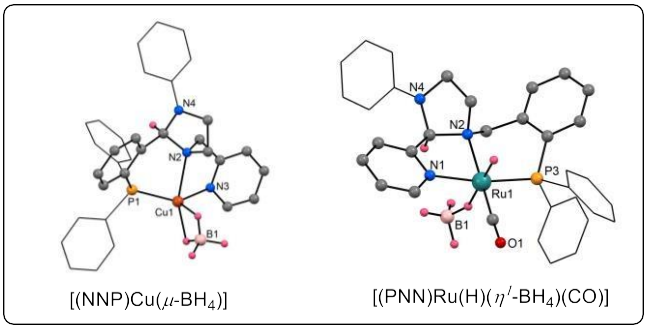
(3) Fukatsu, A.; Morimoto, Y.; Sugimoto, H.; and Itoh, S. *Chem. Commun.* **2020**, 56(38), 5123-5126.

Copper(I) and Ruthenium(II) complexes of Bioinspired Ligands of soft and Hard Donors: Xanthates and Dithioformates from Metal-Borohydrides

Archana Yadav and Raja Angamuthu*

Laboratory of Inorganic Synthesis and Bioinspired Catalysis (LISBIC) Department of Chemistry, Indian Institute of Technology Kanpur Email: archanay20@iitk.ac.in, raja@iitk.ac.in

Metal borohydrides are industrialized as hydride transfer reagents in organic transformation, catalysis, energy storage, activating small molecules and precursors for synthesizing metal hydrides.[1,2] The insertion of environmentally detrimental molecules such as CO_2, CS_2, and COS into metal hydride and their subsequent functionalization is interesting due to their potential as sources of C1 molecules for generating useful organic compounds. Herein, we report highly flexible variants of koneramine [3,4] (NNP and PNN) comprising hard and soft donors. Copper(I) and Ru(II) borohydride complexes were synthesized, isolated, and fully characterized by $^{1}H/^{31}P$ NMR, ESI-MS and SC-XRD. Metal borohydride reactivity with CS_2 to form xanthate and thioformate was investigated.



References:

1. S. Raje and R. Angamuthu, *Green Chem.*, **2019**, *21*, 2752-2758.
2. M. Chahal, S. Raje, G. Kotana and R. Angamuthu, *Green Chem.*, **2019**, *21*, 6372–6380.
3. S. Raje, S. Gurusamy, A. Koner, S. Mehrotra, S. J. Jennifer, P. G. Vasudev, R. J. Butcher and R. Angamuthu, *Chem. Asian J.*, **2016**, *11*, 128–135.
4. S. Raje, N. Mondivagu, M. Chahal, R. J. Butcher and R. Angamuthu, *Chem. Asian J.*, **2018**, *13*, 1458–1466.

Optochemical control of Cu(I) homeostasis in mammalian cells

Pritam Kumar Pain, Dipanwita Palit, Meenakshi Shegane, Rajnish Pratap Singh, Dr. Debasish Manna*

Department of Chemistry

IISER Bhopal

Email: dmanna@iiserb.ac.in

Abstract: The redox active copper atom is a crucial co-factor for the essential cellular processes in all forms of life. Electron exchange by cuproenzymes help in metabolism, synthesize hormones, and act as neurotransmitters. Cellular homeostasis is often required and in the case of copper it is inevitable. The increase in copper levels evidently enhances the chances of cancer, Wilson's disease, even lead to neurodegenerative diseases like Alzheimer's.[1] Since copper is an essential element, the complete depletion of copper by the chelators could have adverse effect in many cellular functions. To overcome this issue, an additional layer of control/stimuli over the chelator would be beneficial.[2] In the last several years, light has been used as an external stimulus to control various biological functions due to its non-invasive nature. In this regard, we have designed a photocaged copper chelator which can be activated by light on demand. The efficiency of the copper chelation was confirmed by absorption and fluorescence studies. We have further investigated the copper chelation in HeLa cells in the presence of a turn-on copper specific fluorophore.[3] The copper dependent trafficking of ATPases was studied by immunostaining after incubation with PKP1 for both in presence and absence of light.

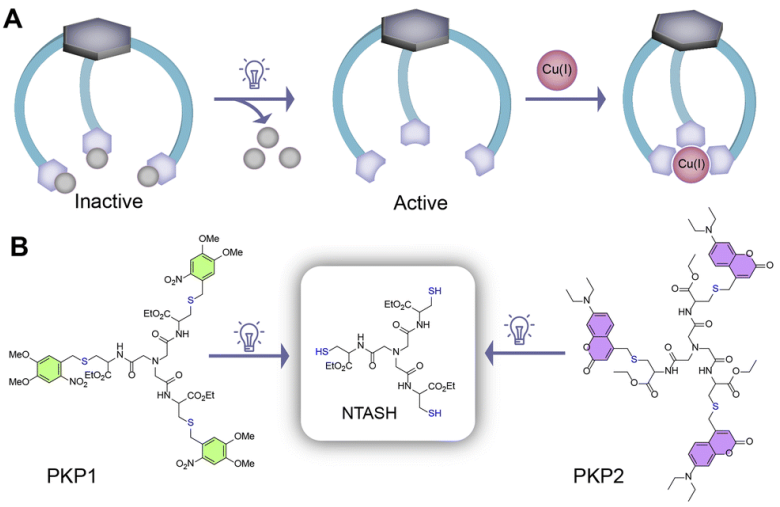


Figure 1 (A) Schematic representation of the photocaged Cu(I) chelator. (B) Cu(I) chelators PKP1 and PKP2 photocaged with NVOC and the coumarin group.

References:

(1) Lutsenko, S.; Curr. Opin. Chem. Biol. **2010**, *14*, 211-217.

(2) Pujol, A. M.; Cuillel, M.; Jullien, A. S.; Lebrun, C.; Cassio, D.; Mintz, E.; Gateau, C.; Delangle, P.; Angew. Chemie. Int. Ed. **2012**, *51*, 7445-7448.

(3) Pain, P. K.; Palit, D.; Shegane, M.; Singh, R. P.; Manna, D.; Chem. Commun. **2023**, *59*, 2315-2318.

Deciphering the Effect of Tridentate (N_2O) Amine *versus* Imine Ligands of Copper(II) Complexes in Phenoxazinone Synthase Activity

Thasnim P Mohammed, Muniyandi Sankaralingam*

Bioinspired & Biomimetic Inorganic Chemistry Lab, Department of Chemistry, National Institute of Technology Calicut, Kozhikode, Kerala 673601 India.
Email: msankaralingam@nitc.ac.in

A sequence of amine (**1**–**6**) and imine (**1'**–**6'**) based copper(II) complexes with N2O ligand donors have been synthesized and well-characterised using distinct spectroscopic techniques and elemental analysis.[1-2] Functional analogy was observed between the structural features of the copper(II) complexes and catalytic activity for an oxidase enzyme, namely phenoxazinone synthase (PHS). Effectively, all the complexes exhibited PHS-mimicking activity by converting 2-aminophenol (OAP) into 2-aminophenoxazin-3-one (APX), a C-C bond coupled product. Elaborately, investigated the effect of oxygen, electronic and auxiliary ligands on the catalytic rate. A critical comparison of the reactivity using the present amine complexes with their respective imine counterparts have been achieved in terms of both experimental as well as theoretical analysis. For instance, the kinetic measurement reveals that the amine based copper(II) complexes showed turnover numbers in the range of $6.3 \times 10^4 – 3.9 \times 10^5$ h^{-1} and the imine complexes exhibited a range of $2.4 \times 10^5 – 6.2 \times 10^6$ h^{-1}. Observably, the imine-based copper(II) complexes showed relatively better activity than the amine-based complexes. In this context, the coupling of the OAP moiety using imine-based complexes (ΔG = -5.8 kcal/mol) is found to be thermodynamically more favorable than the complexes with amine moieties (ΔG = +3.3 kcal/mol). Moreover, the implications of the mechanism have been experimentally made by obtaining mass data of mono-adduct and substantiated the radical-centred transient species coming after the mono-adduct using computational analysis.[1-2] Overall, the work presents that the complexes exhibit excellent activity in mimicking PHS and the detailed results will be presented during the presentation.

References:

1. T. P. Mohammed, A. George, M. P. Sivaramakrishnan, P. Vadivelu, S. Balasubramanian, M. Sankaralingam, *J. Inorg. Biochem.* **2023**, *247*, 112309.
2. A. S. Thennarasu, T. P. Mohammed, M. Sankaralingam, *New J. Chem.*, **2022**, ***46***, 21684–21694.

Biotransformation of Inorganic Arsenic by Functional Models of methyltransferase AS3MT enzyme

Rudra Shankar Pati, Rakesh Kumar Rai, Amirul Islam, Gouriprasanna Roy*

Department of Chemistry, Indian Institute of Technology Tirupati, Tirupati - 517619, India

PhD Scholar

Email: gproy@iittp.ac.in; cy20d002@iittp.ac.in

Arsenic is one of the most ubiquitous toxic environmental contaminants that poses a serious threat to human health because of the occurrence, persistence, and toxicity of various arsenic compounds.[1] It consistently ranks first on the Agency for Toxic Substances and Disease Registry's (ATSDR 2022) substance priority list (http://www.atsdr.cdc.gov/spl/). According to the World Health Organization (WHO), an estimated more than 200 million people worldwide are at risk of exposure to elevated arsenic concentrations (WHO's permissible limit of As is 10 µg/L), mostly in form of inorganic arsenic (iAs), including arsenite (iAs^{III}) and arsenate (iAs^{V}), in ground water and food.[2-5] Chronic exposure of arsenic can cause skin lesions, neurological defects, atherosclerosis, cancer, and other adverse health effects. Member of every kingdom, from bacteria to humans, with the help of an enzyme called methyltransferase, As^{III} S-adenosylmethionine methyltransferase (referred as ArsM in microbes and AS3MT in animals) transfer methyl group from S-adenosylmethionine (SAM) to arsenite, producing the trivalent species methylarsenite (MAs^{III}), dimethylarsenite ($DMAs^{III}$), and to a limited degree, volatile trimethylarsine ($TMAs^{III}$).[6] Biotransformation of inorganic arsenic to the less toxic $DMAs^{III}$ and $TMAs^{III}$ are considered to be the detoxification pathway in many organisms. In this poster we will discuss the development of several functional models of AS3MT which facilitate the biotransformation of more toxic iAs to less toxic $DMAs^{III}$ and $TMAs^{III}$ organoarsenic compounds under physiologically relevant conditions.

References:

(1) Sankpal, U. T.; Pius, H.; Khan, M.; Shukoor, M. I.; Maliakal, P.; Lee, C. M.; Abdelrahim, M.; Connelly, S. F.; and Basha, R.; *Tumor Biol.*, **2012**, *33*, 1265–1274.
(2) Huang, L.; Wu, H.; and Van Der Kuijp, T. J.; *Int. J. Environ. Health Res.*, **2015**, *25*, 432–452.
(3) Naujokas, M. F.; Anderson, V.; Ahsan, V.; Vasken Aposhian, H.; Graziano, J. H.; Thompson, C.; and Suk, W. A.; *Environ. Health Perspect.*, **2013**, *121*, 295–302.
(4) Bhattacharjee, P.; Chatterjee, D.; Singh, K. K.; and Giri, A. K.; *Int. J. Hyg. Environ. Health*, **2013**, *216*, 574–586.
(5) Hubaux, R.; Becker-Santos, D. D.; Enfield, K. S.; Rowbotham, D.; Lam, S.; Lam, W. L.; and Martinez, V. D.; *Mol. Cancer*, **2013**, *12*, 20.
(6) Dheeman, D. S.; Packianathan, C.; Pillai, J. K.; and Rosen, B. P.; *Chem. Res. Toxicol.*, **2014**, *27*, 1979–1989.

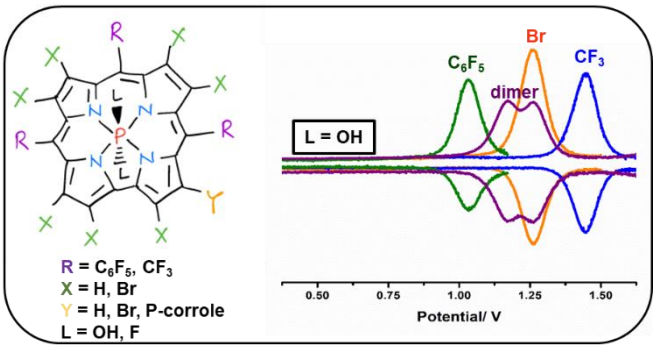
Modulation of Photophysical Properties and Redox Potentials by Axial Ligation and Macrocycle Modification in Phosphorous Corroles

Woormileela Sinha[1] and Zeev Gross[2]

[1]Department of Chemistry, BITS Pilani K K Birla Goa Campus, Zuarinagar, NH17B, Goa 403726, INDIA; [2] Schulich Faculty of Chemistry, Technion-Israel Institute of Chemistry, Haifa 32000 (Israel)

Email: woormis@goa.bits-pilani.ac.in

Phosphorous corroles have gained popularity in the recent years by virtue of their stability and outstanding photophysical properties.[1] Given their utilization in a wide range of applications starting from photodynamic therapy and inactivation to photocatalytic transformations,[2] we have demonstrated the interplay between their photophysical variables and redox potentials.[3] This was studied by design of a series of derivatives that differ in terms of the macrocyclic skeleton significantly, with substitutions at either *-β* or *-meso* positions resulting in different monomeric or dimeric complexes (Scheme 1). The effect of changing the axial ligation at the phosphorous centers on the photophysical and redox behavior in the complexes was also deciphered.



Scheme 1: Square-wave voltammograms of dihydroxyphosphorus complexes of corroles indicating the role of substitutions (*-meso*, *-β* or axial ligation) on the redox potentials. Potentials are versus Ag/AgCl and in the presence of 0.1 M TBAP in acetonitrile.

References:
1. Liang, X.; Mack, J.; Zheng, L.-M.; Shen, Z.; Kobayashi, N. *Inorg. Chem.* **2014**, *53*, 2797-2802.
2. Lee, W.; Zhan, X.; Palma, J.; Vestfrid, J.; Gross, Z.; Churchill, D. G. *Chem. Commun.* **2021**, *57*, 4605-4641.
3. Sinha, W.; Fridman, N.; Mahammed, A.; Gross, Z. *Isr. J. Chem.* **2023**, *63*, e202300036.

Exploring the Role of Sulphur Ligation in Modulating the Oxidative Reactivity of High-Valent Nonheme Iron (IV)-Oxo Intermediates

Jagnyesh Kumar Satpathy,[a] Payal Panwar,[a] Chivukula V. Sastri*[a]

[a]Department of Chemistry

IIT Guwahati

Email: sastricv@iitg.ac.in

Sulfur-ligated oxoiron (IV) centers are supposed to be the crucial oxidants in the catalytic cycles of various oxygen-activating iron enzymes, such as cytochrome P450 (P450), NO synthase (NOS), and isopenicillin N synthase, etc.[1,2] Mainly, Cis-thiolate ligated oxoiron (IV) moieties are thought to be the reactive intermediates for a variety of chemical reactions, such as sulfur-oxygenation, Hydrogen-atom transfer reactions, and C-S bond formation reactions in non-heme iron enzymes. How sulphur ligation affects the structure and catalytic properties of catalytic reaction centres remains an unresolved question and is the focus of this work. Herein, we report the synthesis, characterization and reactivity of a novel biomimetic N4S ligated iron(IV)-oxo complex and compare the results with its analogous N5-ligated iron(IV)-oxo complex. Through a detailed experimental and computational approach, we demonstrate a dramatic change in the reaction mechanism and rate enhancement in oxygen atom transfer reactions and hydrogen atom transfer reactions. Additionally, the introduction of the sulphur-ligand leads to a reduction in the deuterium kinetic isotope effect in hydrogen atom transfer reactions. These findings provide insight into the reactivity of sulphur ligated iron(IV)-oxo centers and their role in various metalloenzymes.

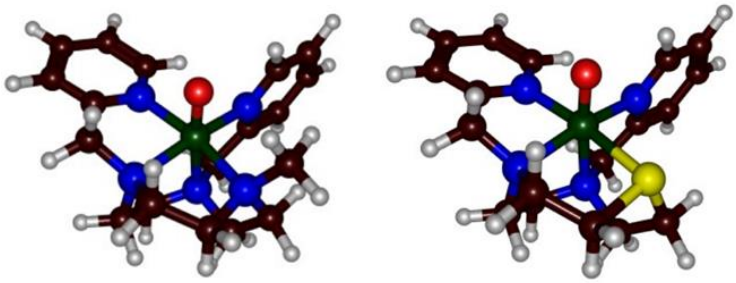


Figure 1. Oxidants used in this study.

References:

(1) Meunier, B.; de Visser, S. P.; Shaik, S.; *Chem. Rev*, **2004**, *104*, 3947-3980.

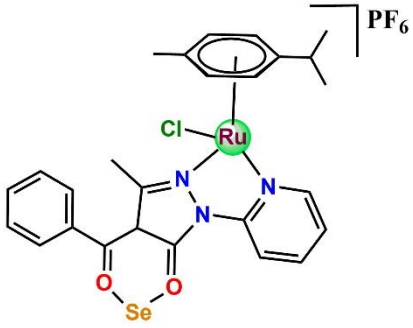
(2) Denisov, I. G.; Makris, T. M.; Sligar, S. G.; Schlichting, I.; *Chem. Rev*, **2005**, *105*, 2253-2278.

A selenium-containing Ru(II)-arene Complexes for ROS-mediated DNA Cleavage and Anticancer activity

K. Sugantharam[a], C. Sumithaa[a] and M. Ganeshpandian[a]*

[a]*Department of Chemistry, SRM Institute of Science & Technology, Kattankulathur – 603203, Chennai, Tamil Nadu.*

Organoruthenium anticancer complexes are receiving wider attention in the context of developing non-platinum based anticancer drugs.[1] The "piano-stool" geometry of such complexes provides a wide scope to modulate their anticancer properties. The antitumor activity of many Ru(II)-arene complexes has been related to their enhanced DNA binding affinity, which involves covalent and/or noncovalent modes of DNA interaction.[2] It is noteworthy that the combination of organoruthenium moiety and clinical drug in a single molecule has been shown, in some instances, to enhance pharmacological activity and reduce toxicity in comparison to the parent drug.[3] In this work, two half-sandwich Ru(II)-arene complexes of the type [Ru(η^6-arene)(Se-apmp)Cl](PF$_6$) **1** & **2**, where arene is *p*-cymene (**1**) or benzene (**2**) and Se-apmp is Seleno-acyl-1-(2-pyridyl)3-methyl pyrazolone have been isolated. The complexes have been characterized well by using various analytical and spectroscopic techniques. The selenium present in the complexes is found to influence the ROS-mediated DNA cleavage activity of the complexes. The cytotoxicity of complexes against MCF-7 breast and A549 lung cancer cell lines has been investigated using MTT assay. The mode of cell death has been established using AO/EB staining method. The results of our systematic investigations will be presented and discussed.



|Ru(*p*-cym)(Se-apmp)Cl|PF$_6$

References

1. Medicinal Organometallic Chemistry, ed. G. Jaouen and N. Metzler-Nolte, Springer-Verlag, Heidelberg, 2010, vol. 32, p. 21

2. G. Gasser, I. Ott and N. Metzler-Nolte, J. Med. Chem., 2011, 54, 3

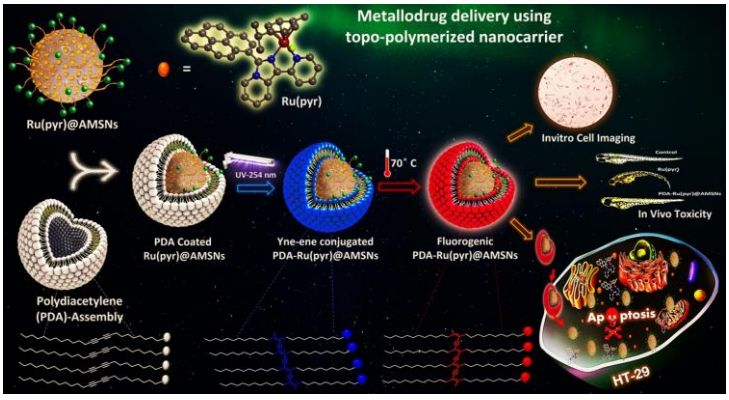
3. C. Sumithaa and M. Ganeshpandian, Molecular Pharmaceutics, 2023, 20, 3, 1453 – 1479.

Theragnostic applications of Ru(arene) nanomedicine against colorectal cancer

C. Sumithaa,[a] P. Gajda-morszewski,[b] M. Velusamy,[c] M. Brindell,[b] O. Mazuryk[b]* and M. Ganeshpandian[a]*

[a]Department of Chemistry, SRM Institute of Science and Technology, Kattankulathur 603 203, Tamil Nadu, India.
[b]Jagiellonian University, Faculty of Chemistry, Department of Inorganic Chemistry, Gronostajowa 2, 30-387, Cracow, Poland.
[c]Department of Chemistry, North Eastern Hill University, Shillong 793022, India.

The precise strategies that aim to optimize the design of both metallodrug and metallodrug carriers jointly in a concerted effort are important for developing cancer nanomedicine.[1,2] In this work, three half-sandwich ruthenium(II) complexes with pyridylimidazo[1,5-a]pyridine ligand functionalized with polycyclic aromatic moiety (**Ru(nap)**, **Ru(ant)**, **Ru(pyr)**) are evaluated as possible anticancer candidates and polydiacetylene (PDA)-coated amino-functionalized mesoporous silica nanoparticles (**AMSNs**) are designed as a functional nanocarrier for drug delivery.[3] In order to modulate the anticancer potency of **Ru(pyr)**, AMSNs are used to encapsulate the complex and then diacetylene self-assembly is allowed to deposit on the surface of the nanoparticles. Owing to the ene-yne polymeric skeleton in the backbone, a non-fluorescent AMSNs turn into red-emissive particles, which are exploited for cell imaging applications. The release profile analysis reveals that a π-conjugated polymer enables pH-responsive and sustained release of complex from nanocarrier. The PDA gatekeepers have also been proven to enhance cellular internalization and reduce the Zebrafish embryo toxicity of organoruthenium complex.



References

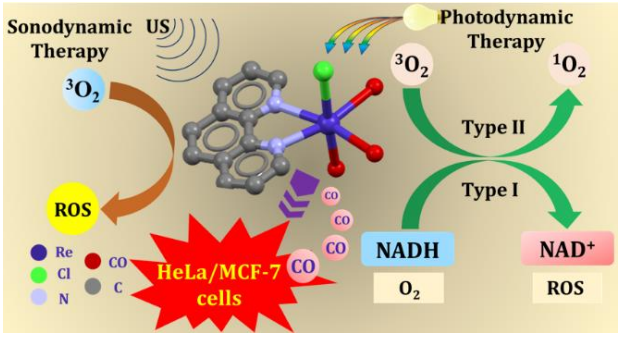
1. C. Sumithaa and M. Ganeshpandian, Molecular Pharmaceutics, 2023, 20, 3, 1453 – 1479.
2. C. Sumithaa, T. Manjunathan, O. Mazuryk, S. Peters, R. S. Pillai, M. Brindell, P. Gopinath and M. Ganeshpandian ACS Applied Biomaterials, 2022, 5, 7, 3241–3256.
3. C. Sumithaa, P. Gajda-morszewski, W. Ishaniya, T. Khamrang, M. Velusamy, NSP. Bhuvanesh, M. Brindell, O. Mazuryk, and M. Ganeshpandian, Dalton Trans., 2023, Communicated.

A Comparative Study of Sonodynamic and Photoactivated Cancer Therapies with Re(I)-Tricarbonyl Complexes

Rajesh Kushwaha,[a] Virendra Singh,[b] Dr. Biplop Koch,[b] Dr. Samya Banerjee[a*]

[a]Department of Chemistry, Indian Institute of Technology (BHU), Varanasi, Uttar Pradesh 221005. [b]Department of Zoology, Banaras Hindu University, Varanasi, Uttar Pradesh 221005. (Email: rajeshkushwaha.rs.chy21@itbhu.ac.in samya.chy@itbhu.ac.in)

Light-based photoactivated chemotherapy (PACT) and ultrasound-based sonodynamic therapy (SDT) have emerged as new non-invasive cancer treatments to overcome drug resistance problems with minimal side effects.[1,2] Both therapies have presented promising results with metal complexes, but no comparative study has been reported yet.[1,2] Herein, we have performed a comparative study of PACT and SDT with Re(I)-tricarbonyl complexes against cancer cells. In this regard, Re(I)-tricarbonyl complexes viz., $[Re(phen)(CO)_3Cl]$ (**Re1**), $[Re(phen\text{-}NO_2)(CO)_3Cl]$ (**Re2**), $[Re(phen\text{-}NH_2)(CO)_3Cl]$ (**Re3**), where phen = 1, 10-phenanthroline; phen-NO_2 = 5-nitro-1, 10-phenanthroline; phen-NH_2 = 5-amino-1, 10-phenanthroline, were synthesized and fully characterized. The crystal structure of **Re2** depicted a distorted octahedral geometry around Re(I) with facial carbonyls and axial chloride. **Re1**-**Re3** were stable under dark conditions, but release CO upon light/ultrasound exposure. The observed photo-physical data and TD-DFT calculations indicated the potential of **Re1**-**Re3** to act as a good photo/sono-sensitizer. **Re1** did not display any dark or light/ultrasound-triggered anticancer activity, **Re2** and **Re3** displayed concentration-dependent anticancer activity upon light/ultrasound exposure against HeLa and MCF-7 cells. Interestingly, **Re3** produced $^1O_2$ and OH• on light exposure. Thus, it can act as both type-I and type-II photosensitizer.[3,4] **Re3** induced photocatalytic NADH oxidation in PBS.[5] To the best of our knowledge, this is the first time NADH photo-oxidation has been achieved with Re(I) complex. The light/sono-activated cell death mechanism revealed that **Re3** produced ROS-mediated apoptotic cell death. Interestingly, **Re3** showed slightly better anticancer activity under light exposure as compared to ultrasound exposure.



References:

(1) P. J. Sadler *et al. Angew. Chem. Int. Ed.* **2020**, *59*, 61-73. (2) R. Kushwaha, S. Banerjee *et al. ChemBioChem* **2023**, *24*, e202200597. (3) H. Huang, S. Banerjee *et al. Angew. Chem. Int. Ed.* ***2022****, 61, e202202098.* (4) K. K. Lo *et al. J. Am. Chem. Soc.* **2022***, 144,* 14420–14440. (5) R. Kushwaha, S. Banerjee et al. *Inorg. Chem.* **2023**, (submitted).

Neurotransmitter coordinated Ru (II)-p-cymene complexes cytotoxic to CSC enriched 3D spheroids of pancreatic and oral carcinoma.

Banshi Roy[a], Souryadip Roy[a], Rimpa Nandi[b], Shilpendu Ghosh[a], Arpan Mukherjee[a], Sujato Mukherjee[a], Sandeep Singh[b]*, Arindam Mukherjee[a]*

aDepartment of Chemical Sciences and Centre for Advanced Functional Materials (CAFM), Indian Institute of Science Education and Research Kolkata, Mohanpur campus, Mohanpur-741246, India.

[b]National Institute of Biomedical Genomics, Kalyani, Nadia, West Bengal 741251.

Cancer is a global hazard to human health, and pancreatic cancer progresses quietly, making early identification difficult. Among various cancers, Pancreatic adenocarcinoma (PAC) is an aggressive, fast-growing cancer that is difficult to cure because it stays unnoticed until it has reached an advanced stage (5-year survival rate less than 8%)[1]. Moreover, the Transient Receptor Potential Melastatin type 8, TRPM8 ion channel is aberrantly expressed in pancreatic adenocarcinoma. Neurotransmitters have emerged as key small molecules in the pancreatic adenocarcinoma microenvironment (TME)[2]. Certain neurotransmitters and their derivatives have been identified to be TRPM8 agonists/antagonists[3]. Platinum drugs are of almost no benefit to pancreatic cancer patients due to development of resistance and the incapacity of Pt(II) drugs to destroy cancer stem cells (CSCs). Currently, several Ru complexes are under human clinical trials due to their unique mechanism of action compared to the Pt(II) drugs[4]. We present here neurotransmitter ligand based Ru(II) complexes which show excellent cytotoxicity against CSCs of pancreatic adenocarcinoma and oral squamous carcinoma (a major health burden in India). The complexes demonstrate excellent solution stability in physiological pH of 7.4. The in vitro cytotoxicity against pancreatic cancer cells showcases IC_{50} as low as ca. 1 μM with IC_{50} of 5-10 μM against CSC enriched 3D Spheroids of Pancreatic adenocarcinoma and oral squamous carcinoma.

References

1. McGuigan A, Kelly P, Turkington RC, Jones C, Coleman HG, McCain RS. Pancreatic cancer: A review of clinical diagnosis, epidemiology, treatment, and outcomes. *World J Gastroenterol* **2018**, 24(43), 4846-4861.

2. Tan, X.; Sivakumar, S.; Bednarsch, J.; Wiltberger, G.; Kather, J. N.; Niehues, J.; de Vos-Geelen, J.; Valkenburg-van Iersel, L.; Kintsler, S.; Roeth, A.; Hao, G.; Lang, S.; Coolsen, M. E.; den Dulk, M.; Aberle, M. R.; Koolen, J.; Gaisa, N. T.; Olde Damink, S. W. M.; Neumann, U. P.; Heij, L. R., Nerve fibers in the

tumor microenvironment in neurotropic cancer—pancreatic cancer and cholangiocarcinoma. *Oncogene* **2021,** *40* (5), 899-908.

3. Jeff DeFalco, Daniel Steiger, Michelle Dourado, Daniel Emerling, Matthew A.J. Duncton, 5-Benzyloxytryptamine as an antagonist of TRPM8, *Bioorganic & Medicinal Chemistry Letters*, 2010; 20 (23): 7076-7079.

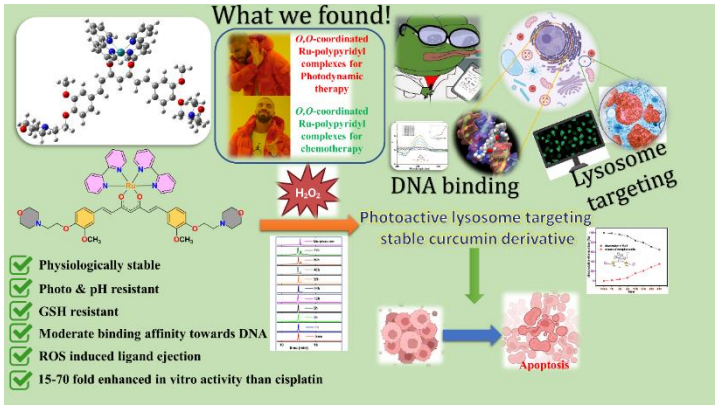
4. Monro, S.; Colón, K. L.; Yin, H.; Roque, J., III; Konda, P.; Gujar, S.; Thummel, R. P.; Lilge, L.; Cameron, C. G.; McFarland, S. A., Transition Metal Complexes and Photodynamic Therapy from a Human-Centred Approach: Challenges, Opportunities, and Highlights from the Development of TLD1433. *Chemical Reviews* **2019,** *119* (2), 797-828.

Sweet delivery for photoactive lysosome targeting Ru^{II} complex selectively to cancer: alteration in activity from arene to bipyridyl

Souryadip Roy, Sujato Mukherjee and Arindam Mukherjee*:

IISER Kolkata, Mohanpur, India

Half-sandwich Ru-arene complexes with curcuminoids exhibit excellent chemotherapeutic potentials but their photoactivity is still unravelling many features. We designed a photoactive Ru (II) complex of morpholine functionalized curcumin scaffold accumulating mostly in the lysosome and inhibiting the proliferation of cancer stem cell (CSC) enriched 3D-spheroids of Notch1 overexpressing variant of oral squamous carcinoma SCC070. The complex, remarkably, is the first photoactive Ru (II) complex to demonstrate the capability to kill CSCs while downregulating cMYC, an essential gene for the Warburg effect in cancer cells.[1] The work is further extended by replacing the arene motif with bis-bipyridyl core to exploit the photo reactivity of Ru-bipyridyls. The two new complexes, Ru bis-bipyridyl complexes of curcumin and morphocumin, provided important information on O, O-coordinating Ru bipyridyls in PDT. The studies revealed the effect of responsive stimuli other than light upon the complexes in terms of ligand ejection suggesting a scope for Photo-activated Chemotherapy. Studies on the $[Ru^{II}(bpy)_2(curcumin)]$ and $[Ru^{II}(bpy)_2(morphocumin)]$ helps differentiate chemotherapeutic vs. photodynamic behaviour and disadvantages of the O, O-coordination in such complex structures while designing PDT agents. However, the commendable stability of the $[Ru^{II}(bpy)_2(morphocumin)]$ (**Ru2**) at physiological pH and the release of the stable lysosome targeting morphocumin in the presence of excess H_2O_2, presents a viable therapeutic target for enhanced toxicity in ROS rich cancer microenvironment. The selectivity is further enhanced by using, water soluble, glucose functionalized polymeric nanoparticles (GBPNs) to deliver **Ru2** exploiting the overexpression of glucose transporters in cancer cells due to 'Warburg effect'.



References:

1. S. Roy, P. Mitra, S. Acharya, S. S. Roy, S. Ghosh, M. Maji, N. Modak, N. Ghosh, M. Acharya and S. Singh, A photoactive lysosome targeting Ru II complex downregulates stemness genes in oral squamous cell carcinoma, *Inorganic Chemistry Frontiers*, 2022, **9**, 5840-5852.

Isatin-Hydrazone based Cyclometallated Iridium(III) Complexes for Triggering ROS-Induced Non-Apoptotic Cell Death in Triple-Negative Breast Cancer Cells

Sujato Mukherjee[a]‡, Shilpendu Ghosh[a]‡, Arindam Mukherjee[a]*

‡ These authors equally contributed to the work

[a]Department of Chemical Sciences and Centre for Advanced Functional Materials (CAFM), Indian Institute of Science Education and Research Kolkata, Mohanpur campus, Mohanpur-741246, India.

Breast cancer occurrences has surpassed lung cancer in 2020 making it a cancer of highest occurrence. In India, nearly 60% of breast cancer cases are diagnosed at advanced stages (III or IV).[1] Triple Negative Breast Cancer (TNBC), a particularly concerning form of breast cancer has limited treatment options due to lack of molecular targets and poor prognosis. We present cyclometallated Ir(III) complexes of isatin-hydrazones, showcasing remarkable cytotoxicity against Triple-Negative Breast Cancer (TNBC) cells (MDA-MB-231). The detailed characterization of these molecules was achieved through X-ray crystallography, elucidating the unambiguous structures of three ligands and one metal complex. The complexes exist as a dynamic mixture of geometric isomers, swiftly interconverting in the presence of a 10mM Phosphate Buffer with 4mM NaCl at pH 7.4. Intriguingly, they exhibit a non-apoptotic pathway of cell death, suggesting a potential way to treat tumors resistant to traditional apoptotic pathways.[2] The complexes display lipophilicity (using RP-HPLC), in the range of 2.5 - 3, aligning with Lipinski's rule of five. The flow-cytometric DCFHDA assay shows generation of Reactive Oxygen Species (ROS) in cells on treatment by the complexes which may be the reason for activation of the non-apoptotic cell death pathway.

References

1. Sung, H.; Ferlay, J.; Siegel, R. L.; Laversanne, M.; Soerjomataram, I.; Jemal, A.; Bray, F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J. Clin. 2021, 71 (3), 209-249.
2. Woo, Y.; Lee, H.-J.; Jung, Y. M.; Jung, Y.-J., Regulated necrotic cell death in alternative tumor therapeutic strategies. *Cells* **2020**, 9 (12), 2709.

Oxidation catalysis in cancer cell mediated by a Re (VII)-oxo complex: A new strategy for designing catalytic anticancer agents

Shubhangi Das,[a] Gourab Chakroborty,[b] Chinmoy Patra[b] and Malay Patra[*,a]

a. Medicinal Chemistry and Cell Biology Laboratory, Department of Chemical Sciences, Tata Institute of Fundamental Research, Homi Bhabha Road, Mumbai, Maharashtra 400005, India
b. Agharkar Research Institite, Gopal Ganesh Agarkar Road, Pune, Maharashtra 411004, India

Cancer, a leading cause of death with 10 million fatalities in 2020, is commonly treated with platinum (II) drugs, including cisplatin, carboplatin, and oxaliplatin.[1] These drugs, while successful, have limitations, such as toxic side effects and platinum resistance in cancer cells.[1] In the past decade, researchers have sought new anticancer agents known as 'catalytic metallo-drugs' to address these issues.[2-4] These agents, based on metals like Ir (III), Rh (III), Ru(II), and Os (II), disrupt vital processes in cancer cells through catalytic reactions.

One example is Ir (III) complexes, which catalyze transfer hydrogenation reactions in cancer cells by imbalancing the NADH/NAD^+ equilibrium, generating H_2O_2.[3] These metallo-drugs offer advantages like lower toxicity and a novel mechanism of action, combating chemotherapy resistance. Rhenium (Re) complexes have also shown potent anticancer properties. Re(I) complexes with a [$Re(CO)_3$] core and photo-activatable Re(I) complexes trigger cell death. Re(III) clusters, particularly paddle-wheel dirhenate(III) complexes, exhibit promising anticancer activity with low toxicity.

Methyltrioxorhenium (VII) ($MeReO_3$, MTO) and related derivatives are known for catalyzing oxidative transformations, such as olefin epoxidation and thiol oxidation.[5-6] Cystine and glutathione are abundant intracellular thiols, making them targets for catalytic oxidation. Re(VII)-oxo complexes have potential in this regard.

Hence, we have synthesised a novel Re(VII)-oxo catalyst, [Me_4Phen)Re(O)$_3$Cl], efficiently enters cancer cells and catalyzes thiol oxidation using intracellular H_2O_2. This process increases oxidative stress in cancer cells, which are more susceptible to redox imbalance. This catalyst exhibits higher antiproliferative effects in cancer cells compared to normal cells and overcomes platinum resistance. Mechanistically, thiol oxidation leads to the depletion of mitochondrial membrane potential and induces ER-stress, ultimately triggering apoptosis in cancer cells. The compound apart from showing excellent in vitro antiproliferative activity also showed antiangiogenic properties in zebra fish larvae model.

References:

1. Johnstone, T.C., Suntharalingam, K., Lippard, SJ., *Chem Rev.*, **2016 Mar 9**; 116(5):3436-86.
2. Dougan, S.J., Habtemariam, A., McHale, S.E., Sadler, P.J., *PNAS*, **2008**; 105 (33) 11628-11633
3. Soldevila-Barreda, J., Romero-Canelón, I., Habtemariam, A. Sadler, P.J., *Nat Commun,* **2015**, 6,6582
4. Zhang, X., Ponte, F., Borfecchia, E., Martini, A., Sanchez-Cano, C., Sicilia, E., Sadler, P.J., *Chem. Commun.*, **2019**, **55**, 14602-14605
5. Kühn, F.E., Scherbaum, A., Herrmann, W.A., *J. Organomet. Chem.*, Volume 689, Issue 24, **2004**, Pages 4149-4164.
6. Adam, W, Herrmann, W.A., Lin, J., and Saha-Móller, C.R., *J. Org. Chem.* **1994**, 59, 8281-8283

Synthesis of Mitochondria-targeting, Luminescent Various N^N Heterocyclic Ligand-based Ru(II)/Ir(III)/Re(I) Metal Complexes as A Potential Photochemotherapeutics Against Cancer Stem Cells‡

Binoy Kar, and Priyankar Paira*

PhD Research Scholar, Department of Chemistry, School of Advanced Sciences, Vellore Institute of Technology, Vellore-632014, Tamil Nadu, India.
E-mail: 2016binoychem@gmail.com

The antiproliferative potential of metal complexes with various N^N heterocyclic ligands like arylimidazophenanthroline, and dipyridophenazine (dppz) are very endearing for a long since in order to hold back the proliferation of many cancers. A series of novel Ru(II)/Ir(III)/ Re(I) based organometallic complexes have, therefore, been synthesized toassess their anticancer aptitude against HeLa (human epitheloid cervix carcinoma), MCF-7 (breast cancer), Caco-2 (colon adenocarcinoma), A549 (lung adenocarcinoma) and HCT-116 (human colorectal cancer), HEK-293 (normal human embryonic kidney cell), and HCT-116 cancer stem cell lines (CSCs) by attacking the mitochondria, "The Power House of Cell" of the respective cancer cells through DNA damage and reducing the mitochondrial membrane potential (MMP). The cytotoxic screening of the synthesized complexes against cancer cells has revealed that these complexes are more proficient compared to cisplatin. On average, the cytotoxicity of all the complexes is indeed doubledupon light irradiation and also exhibited significant photo and dark selectivity against cancer cells concerning normal cells. The anticancer potential has been seen to be prominent due to the production of a profuse amount of reactive oxygen species (ROS) from damaged mitochondria and then G1 or G2/M phase cell cycle arrest by complexes. The screening of protein expression has unveiled that pro-apoptotic Bax protein is beingoverexpressed upon treatment of ruthenium complexes whereas iridium complexes are triggering the expression of anti-apoptotic Bcl-2 protein**.** Moreover, all the complexes arevery ardent to interact with DNA and serum albumin having significant binding constant values. Again, these complexes also exhibited good stability in 10% DMSO-buffer and under 1 mM GSH conditions. The decent lipophilic nature helps them to penetrate the cancer cell membrane and the considerable quantum yield (ϕ_f) values have attested to their luminescent property attributing bioimaging potential.

References:

1. Novohradsky, V.; Zamora, A.; Gandioso, A.; Brabec, V.; Ruiz, J.; and Marcha, V. *Chem. Commun.* **2017***, 53,* 5523-5526.
2. Hanif, Md.; Hartinger, C. G. *Future Med. Chem*. **2018**, *10*, 615-617.
3. Suntharalingam, K.; Lin, W.; Johnstone, T. C.; Bruno, P. M.; Zheng, Y. R.; Hemann, M. T.; Lippard,S. J. *J. Am. Chem. Soc*. **2014**, *136*, 14413–14416.
4. Satheesh, N. J.; Samuel, S. M.; Büsselberg, D. *Biomolecules.* **2020**, *10*, 79.
5. Zhou, Y.; Xia, L.; Wang, H.; Oyang, L.; Su, M.; Liu, Q.; Lin, J.; Tan, Y.; Liao, Q.; Cao, D. *Oncotarget*. **2018***, 9,* 33403-33415.

Rising of a photo-responsive Imidazophenanthroline based Ir (III) Cyclometalated Complex Towards Effective Cancer Therapy

Sreejani Ghosh[a], Priyankar Paira*

[a] Department of Chemistry, School of Advanced Sciences, Vellore Institute of Technology (VIT), Kapadi, Tamil Nadu, India- 632014

8110020748,8910097130

E-mail: sreejanighosh0506@gmail.com

The worldwide prevalence of malicious cancer is a great threat to mankind. As the microenvironment keeps on changing based on different types of cancer, it reveals challenges to treat this perilous disease. The multidrug resistance, tumor-associated hypoxic circumstances, and elevated intracellular GSH levels are the major obstructions for chemotherapeutics to eradicate the cancer. For this very cause, photodynamic therapy (PDT) offers an effective non-invasive approach for selectively abating cancer under the irradiation of light. Therefore, we have developed an imidazo-phenanthroline-based photo-active cyclometalated Iridium (III) complex that has the capability of generating a copious amount of ROS, which significantly damaged the DNA and triggered the release of p53 proteins. Moreover, it created a nuisance for the mitochondria by reducing the mitochondrial membrane potential (MMP), which stimulated the release of cytochrome c to the cytosol initiating the intrinsic caspase pathway for apoptosis. This complex was also able to bind with the human serum albumin (HSA) showing good transportation aptitude through the bloodstream. In a nutshell, this photoactive complex can be successfully employed to heal cancer and it may bring prosperity to modern cancer therapy in the imminent future.[1, 2]

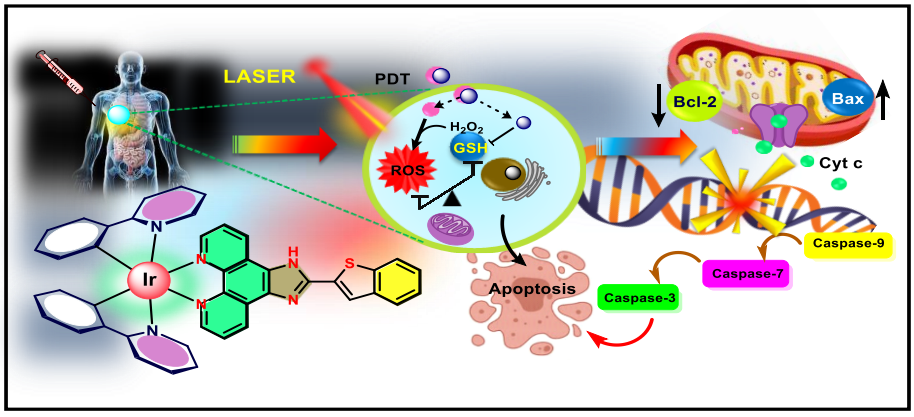


Figure: - A Mechanistic Approach of the Complex for Destruction of Cancer Cells

References:-

1. Zafon, E.; Echevarría, I.; Barrabés, S.; Manzano, B. R.; Jalón, F. A.; Rodríguez, A. M.;Espino, G. Photodynamic therapy with mitochondria-targeted biscyclometallated Ir (III) complexes. Multi-action mechanism and strong influence of the cyclometallating ligand. *Dalton Transactions* **2022,** *51*, 111-128.
2. Das, U.; Paira, P. Synthesis, characterization, photophysical, electrochemical properties and biomolecular interaction of 2, 2′-biquinoline based phototoxic Ru (II)/Ir (II) complexes. *Dalton Transac*.**2023, 52**, 12608-12617

Construction of Antimetastatic and Antiproliferative Re(I) Tricarbonyl Complexes under the Light of Experimental and Theoretical Approach to Combat TNBC

Nilmadhab Roy[a], Priyankar Paira*

[a]Department of Chemistry, School of Advanced Sciences (SAS), Vellore Institute of Technology (VIT), Tamil Nadu, Vellore-632014, India, 8110020748, 7719342439

E-mail: nmr.chem1@gmail.com

The worst prognosis, lack of ER, PR, and HER-2 biomarkers, strong invasive and metastatic competency, harsh tumour microenvironment (TME), and presence of glutathione (GSH) to maintain redox homeostasis makes the triple-negative breast cancer (TNBC) very difficult to treat. In the current scenario, no specific therapeutic approach has been developed so far. Therefore, in view to annihilate the TNBC and resist its keen metastatic competency, we have developed highly potent Re(I)-tricarbonyl complexes. These complexes have been boosted with the efficiency to deactivate the vimentin protein, glutathione depletion, and DNA damage, triggering the p53 gene expression along with the downregulation of Bcl-2 and upregulation of BAX, fueling up the caspases activity leading the TNBC cells to apoptosis.[1]

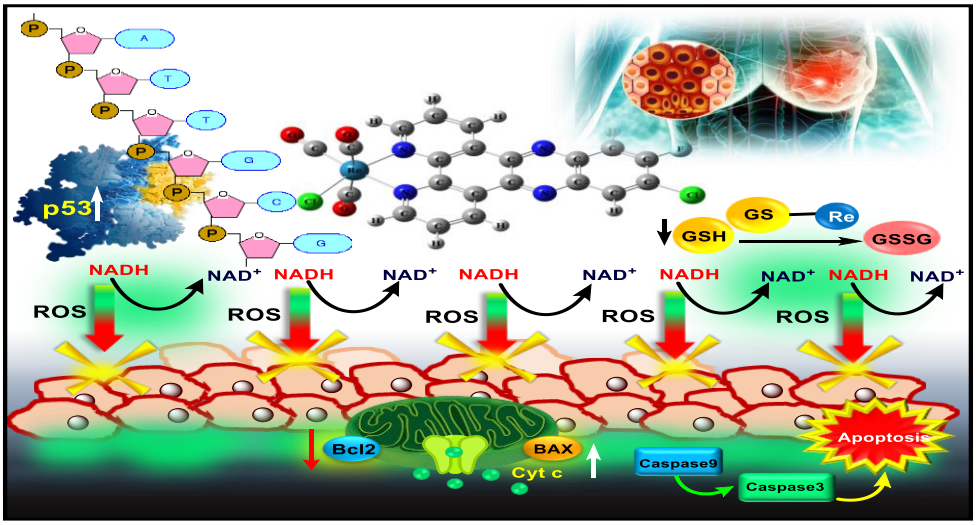


Figure 1: Mechanistic Approach of Re (I)-tricarbonyl complexes against TNBC

References:

1. Roy, N.; Shanavas, S.; Kar, B.; Babu, L. T.; Das, U.; Vardhan, S.; Sahoo, S. K.; Bose, B.; Vijayaraghavan, R.; Paira, P. G2/M-Phase-Inhibitory Mitochondrial-Depolarizing Re(I)/Ru(II)/Ir(III)- 2,2′-Bipyrimidine-Based Heterobimetallic Luminescent Complexes: An Assessment of In Vitro Antiproliferative Activity and Bioimaging for Targeted Therapy toward Human TNBC Cells. *ACS OMEGA* **2023**, *8*,12283-12297.

Pyrene Based Ru (II)/Ir(III)/Re(I)-Imidazophenanthroline Complexes For Enhanced Photoactivated Chemotherapy (PACT) in Curing Triple Negative Breast Cancer

Rishav Das, Priyankar Paira*

Department of Chemistry, School of Advanced Sciences (SAS), Vellore Institute of Technology (VIT), Tamilnadu, Vellore-632014, India, 8110020748

E-mail: rishav.das2021@vitstudent.ac.in

In current context, photoactivated chemotherapy (PACT) has been seemed to be very effective to vanquish the vehemence of triple-negative breast cancer (TNBC), which is associated with poor prognosis, lack of specific target, high chance of relapse and strong metastatic ability.[1] Therefore, we have aspired to design GSH resistant phototoxic Ru(II)/ Ir(III)/ Re (I) based pyrene imidazophenathroline complexes to selectively avert the triple-negative breast cancer. All the complexes have shown remarkable phototoxicity against MDA-MB-231 TNBC cell line releasing profuse amount of singlet oxygen ($^1O_2$) as reactive oxygen species (ROS) under the irradiation of visible light. In connection with this, complexes are capable of interacting to DNA with highest binding constant along with higher protein binding affinity.[2] Succinctly, it can be said that these complexes may bring the light of hope in treatment of TNBC.

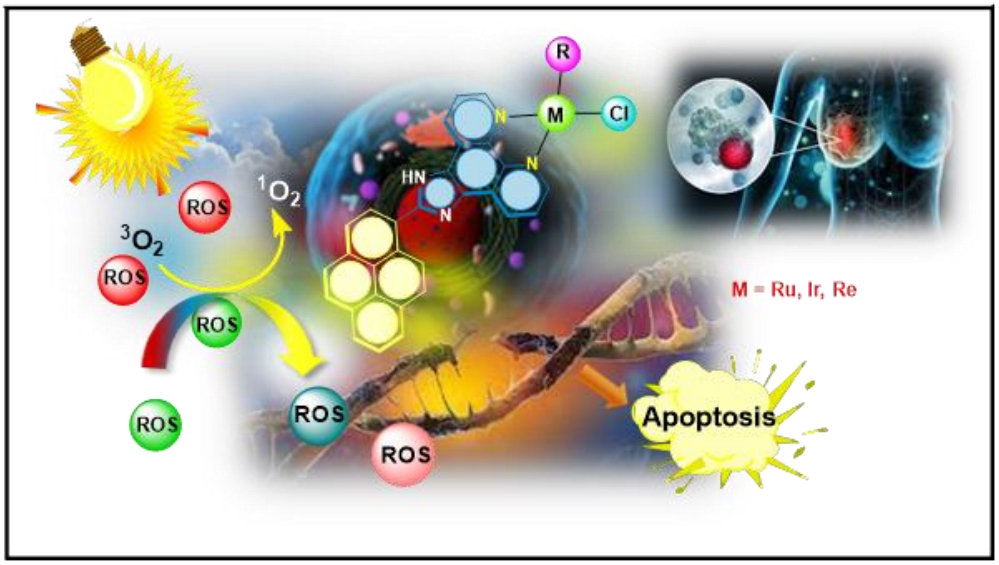


Figure 1: Mechanistic Approach of Re (I)-tricarbonyl complexes against TNBC

References:

1. Roy. N.; Shanavas S.; Kar. B.; Babu. L. T.; Das U.; Vardhan S.; Sahoo S. K., Bose B.; Rajagopalan V.; Paira P.; *ACS Omega* **2023**, *8*, 12283–12297
2. Das. R.; Paira. P.; *Dalton Trans.* **2023**, *52*, 15365-15376

Mitochondria-targeted luminescent 11-{naphthalen-1-yl} dipyrido [3,2-a:2',3'-c] phenazine based Ru(II)/Ir(III)/Re(I) complexes for HCT-116 colorectal cancer stem cells therapy

Utpal Das, Priyankar Paira*

Department of Chemistry, School of advanced sciences, Vellore Institute of Technology Vellore-632014, Tamil nadu, India.

E-mail: ud9263150@gmail.com
Priyankar.paira@vit.ac.in

To develop a class of theranostic metal complexes that exhibited target specific in nature, water-soluble property, cancer cell permeability, cytoselectivity and luminescence, with the goal of discovering suitable medications capable of diagnosing as well as suppressing the proliferation of cancer cells. In this aspect mitochondria-targeted luminescent 11-{naphthalen-1-yl} dipyrido [3,2-a:2',3'- c] phenazine based Ru(II)/Ir(III)/Re(I) complexes has been prepared for HCT-116 colorectal cancer stem cells therapy. Our study findings successfully established the dose-dependent cytotoxic potential of IrL complex on HCT-116 colorectal cancer stem cells (CRCSCs). IrL complex revealed the subcellular localization of the compound in cytoplasm thereby directing to a possible mitochondrial localization and resultant mitochondrial dysfunction. The level of BAX and Bcl-2 was further quantified by qRT PCR. The expression of proapoptotic BAX showed increased expression in IrL treated cell compared to the control indicating the potential of IrL complex for apoptotic induction.

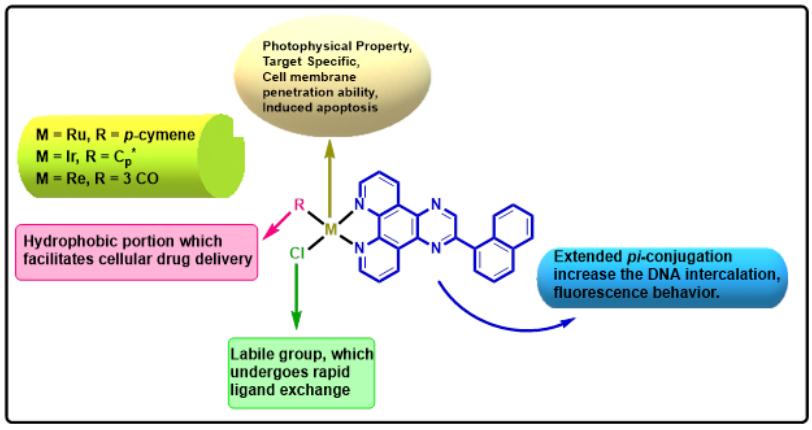


Fig. 1 Structural design of 11-{naphthalen-1-yl} dipyrido [3,2-a:2',3'-c] phenazine-based Ru(II), Ir(III), and Re(I) complexes.

References:

1. Das, U.; Shanavas, S.; Nagendra, A. H.; Kar, B.; Roy, N.; Vardhan, S.; Sahoo, S. K.; Panda, D.; Bose, B.; Paira, P. *ACS Appl. Bio Mater.* **2023**, *6* (2), 410–424.

Versatile Ruthenium Complexes investigated for their Anti-cancer Potential and for Catalyzing Alkylation Reactions of Amine and Alcohol

Surabhi Bhatt, Hemant Joshi, Anuj K. Sharma*

Department of Chemistry, Central University of Rajasthan, NH-8, Bandarsindri, Kishangarh, Ajmer, RJ, 305817

E-mail: *2018phdch005@curaj.ac.in, hemant.joshi@curaj.ac.in, anuj.sharma@curaj.ac.in*

Ruthenium (Ru) complexes are becoming increasingly popular for their promising anticancer activities because of their variable oxidation states, optimum ligand exchange rates, low in general toxicity and high selective cytotoxicity towards proliferative cells, water solubility and octahedral geometry for tuning electronic and steric properties of complexes.[1,2] NAMI-A, KP1019, NKP1339 and TLD1443 are Ru based complexes, have previously been used in clinical trials.[3,4] From our group, different series of Ru(II) arene chlorido organometallic complexes are developed and fully characterized. In addition, their anticancer potential and detailed mechanism of action is also attempted.

For selected Ru complexes, other very important reactions which are also bio-inspired are being tried. Alkylation of amines and alcohol, functional groups is currently a vibrant field of investigation due to their high bioactivity and importance in nature.[5] These Ru complexes were also found to be efficient catalyst for the synthesis of *N*-alkylation reactions and thus explored for both biological and catalytic applications.[6] Overall, a series of versatile Ru systems with good biological and catalytic potential will be discussed in this presentation.

References:

1. Khan, T. A.; Bhar, K.; Thirumoorthi, R.; Roy, T. K.; Sharma, A. K. *New J. Chem.* **2020**, 44, 239-257.
2. Peacock, A.F.A.; Sadler, P.J. *Chem. Asian J.* **2008**, 3(11), 1890-1899.
3. Lee, S.Y.; Kim, C.Y.; Nam, T.G. *Drug Des Devel Ther.* **2020**, 14, 5375-5392.
4. Kumar, S.; Riisom, M.; Jamieson, S.M.F.; Kavianinia, I.; Harris, P.W.R.; Nolte N.; Brimble, M.A.; Hartinger, C.G. *Inorg. Chem..* **2023**, 62, 35, 14310-14317.
5. Bhatt, S.; Rana, M.; Sharma, A. K.; Joshi, H. *Asian J. Org. Chem.* **2023**, 12(6), e202300158.
6. Bhatt, S.; Meena, N.; Kumar, M.; Bhuvanesh, N.; Kumar, A.; Sharma, A. K.; Joshi, H. *Chem. Asian J.* **2022**, 17(21), e202200736.

Tuning the Mechanism of Cancer Cell Death with Variation of Ancillary Ligands and Coordination Mode of Metal

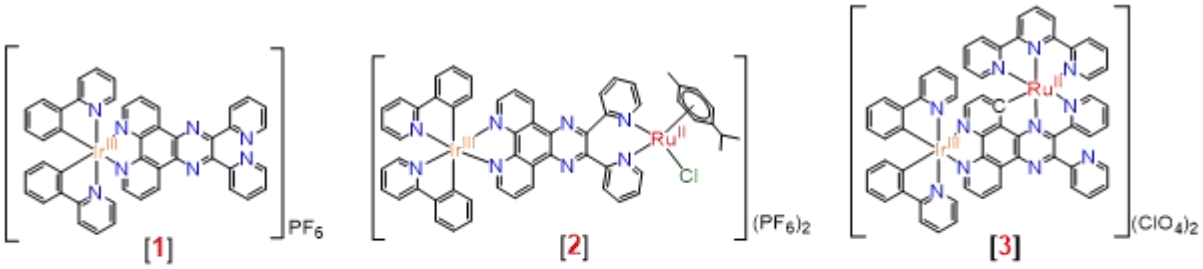
Saumyaranjan Mishra and Srikanta Patra*

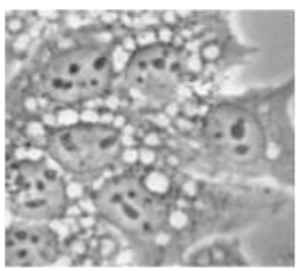
School of Basic Sciences, Indian Institute of Technology Bhubaneswar, Jatni 752050 Odisha

Email: srikanta@iitbbs.ac.in

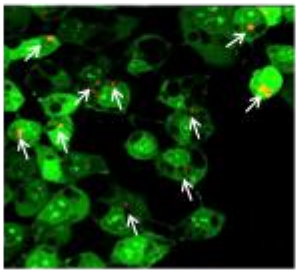
Abstract:

Herein, we present a mononuclear cyclometalated iridium [**1**] complex and its heterodinuclear iridium-ruthenium analogues [**2**] and [**3**] using a semi-flexible phenanthroline-pyrazine-based (phpy) ligand with different binding modes. The formations and different binding modes (N^N ∩ N^N for [2] and N^N ∩ N^N^C- [**3**]) of the complexes are confirmed through x-ray crystallography studies. The complexes display moderately good anticancer activity against human breast cancer cell lines MCF-7. The mechanistic investigation reveals that [**1**] induces natural product like paraptotic mode of cell death, whereas by introducing a second metal centre, the mode of action is changed to autophagy for [**2**] (using [Ru(p-cym)Cl] framework) and combined apoptosis and autophagy for [**3**] while using [Ru(tpy)] framework.

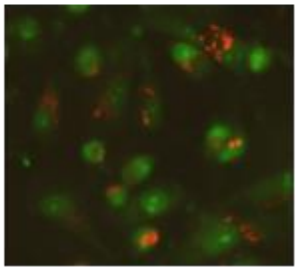




Paraptosis



Autophagy



Apoptosis and Autophagy

References:

1. S Mishra, SK Tripathy, D Paul, P Laha, MK Santra, S Patra; Inorg. Chem., 2023, 62 (18), 7003–7013.

2. SK Tripathy, U De, N Dehury, S Pal, HS Kim, S Patra; Dalton Trans., 2014, 43 (39), 14546-14549.

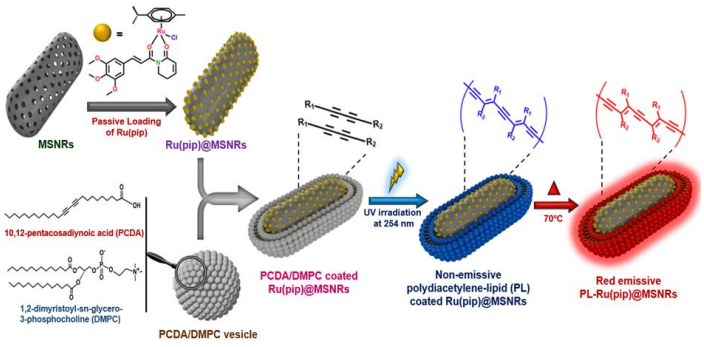
3. SK Tripathy, U De, N Dehury, P Laha, MK Panda, HS Kim, S Patra; Dalton Trans., 2016, 45 (38), 15122-15136.

Polydiacetylene/lipid-coated silica nanorods for sustainable release and anticancer efficacy of Ru(arene) complex bearing piperlongumine natural product

W. Ishaniya,[a] M. Subramani,[b] S.Rajendran,[b] and M.Ganeshpandian[a*]

[a]*Department of Chemistry, SRM Institute of Science & Technology, Kattankulathur – 603203, Chennai, Tamil Nadu.*
[b]*Chemistry division, School of Advanced Sciences, Vellore Institute of Technology, Chennai-600127, Tamilnadu, India*

A suitable drug delivery strategy for metallodrug is as significant as the strategies adopted for efficient metallodrug design.[1] In this study, piperlongumine, which is isolated from long pepper, is coordinated with Ru(II)-*p*-cymene moiety to obtain the organoruthenated complex containing the natural product (**Ru(pip)**). Next, with an aim to modulate the antiproliferative activity of Ru(pip) using a drug delivery strategy, the complex is loaded into mesoporous silica nanorods (**MSNRs**) followed by providing gatekeeper effect using polydiacetylene-lipid (**PL**) hybrid bilayer.[2] Given the unique optical properties of polydiacetylene,[3] the PL coating modifies non-fluorescent MSNRs into red-emissive particles (**PL-Ru(pip)@MSNRs**). The release profile studies reveal that the ene-yne conjugation in PL coating ensures the slow release of the complex from nanoparticles irrespective of the pH. On the other hand, Ru(pip) release from MSNRs in a simulated cancer cell medium is slightly higher than in a physiological medium after PL coating. While Ru(pip) exhibits both necrotic and apoptotic mode of cell death, PL-Ru(pip)@MSNRs preferably induces apoptotic mode of cell death in MCF-7 and THP-1 cancer cells. Also, the nanoformulation exhibits a higher percentage of cell cycle arrest in G0/G1 phase than Ru(pip).



References

1. C. Sumithaa and M. Ganeshpandian, Molecular Pharmaceutics, 2023, 20, 3, 1453 – 1479.
2. W. Ishaniya, C. Sumithaa, M. Subramani, K. Aswathy, MR. Ganesh, A. MadanKumar, R. Saravanakumar, and M. Ganeshpandian, Dalton Trans., 2023, Under revision
3. W. Ishaniya, C. Sumithaa, S. Saravanan, S. Vimalraj, and M. Ganeshpandian, Journal of Drug Delivery Science and Technology, 2022, 72,103415

Combating Vasculogenesis and Cancer Stem Cell Resilience by a Single Molecule Anticancer Chemotherapy Agent

Shilpendu Ghosh[a], Sayar Ghosh[b], Banshi Roy[a], Manas pratim Chakraborty[b], Santanu saha Roy[c], Sujato Mukherjee[a], Moulinath Acharya[c], Rahul Das[b]*, Arindam Mukherjee[a]*

[a]Department of Chemical Sciences, Indian Institute of Science Education and Research Kolkata, Mohanpur campus-741246, West Bengal, India

[b]Department of Biological Sciences, Indian Institute of Science Education and Research Kolkata, Mohanpur campus-741246, West Bengal, India

[c]National Institute of Biomedical Genomics, Kalyani 741251, India.

Cure for cancer often requires a combination of drugs targeting different aspects. Administering two compounds independently and expecting them to be both present at the required site at desired concentrations can be challenging, but a novel approach involves creating a single molecule that would inhibit two important targets simultaneously. Here in we present a series of molecules inhibiting both VEGFR2 and ALDH1A1 with one molecule to disrupt angiogenesis and target cancer stem cells, potentially improving cancer treatment efficacy. Combining these actions may offer a comprehensive approach, inhibiting both vascular support and cancer stem cell resilience, potentially enhancing the efficacy of cancer treatment. VEGFR-2 inhibitor (Vascular Endothelial Growth factor receptor 2)[1] and ALDH1A1 inhibitor[2,3] (Aldehyde dehydrogenase) has not yet been combined into one molecule although the site targeting motif can be efficient for both proteins due to similarity in the molecular design that has been overlooked. Initial results from our approach show promising mechanism of action with three times better in-cell target affinity for VEGFR2 inhibition compared to existing drugs. The compounds remain stable in physiological conditions and exhibit superior affinity selectivity, as demonstrated in cell and Fli1:GFP transgenic zebrafish studies.

References

1. McTigue, Michele, et al. Proceedings of the National Academy of Sciences 109,45 (2012): 18281-18291.

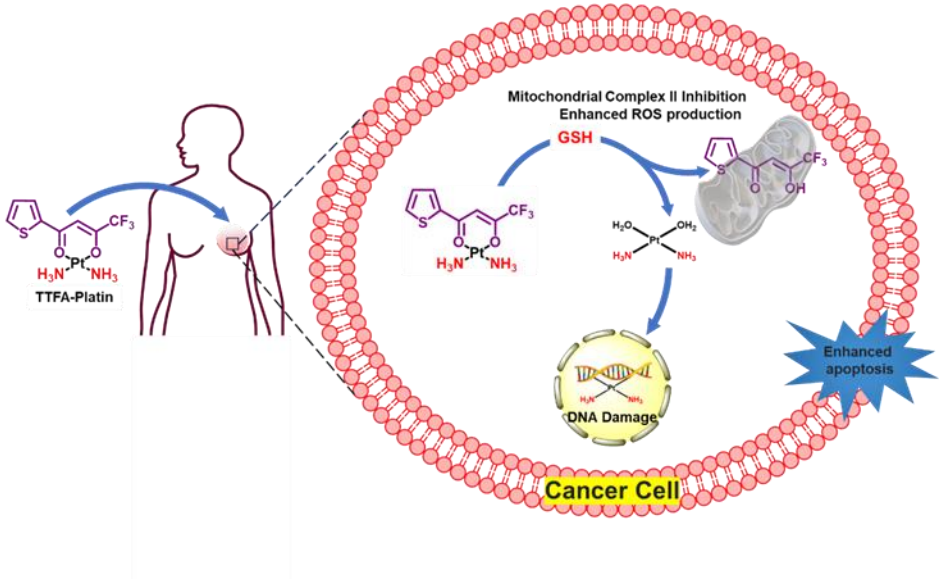
2. Kimble-Hill, Ann C., et al. Journal of medicinal chemistry 57,3 (2014): 714-722.

3. Dinavahi, Saketh S., et al. European Journal of Medicinal Chemistry 187 (2020): 111962.

Synergistic Enhancement of Therapeutic Efficacy through Mitochondrial Destabilization by Platinum-Based Combination Prodrug: for Improved Cancer Treatment

Megha Biswas[1], Kanishka Chaudhary[1], Swati Shree Padhy[2], R Selvi Bharathavikru[2] and Rakesh Kumar Pathak[1*]
[1]Department of Chemical Sciences, [2]Department of Biological Sciences
Indian Institute of Science Education and Research Berhampur (IISER BPR)
Engineering School Road, Berhampur - 760010, Odisha
Email id: meghab@iiserbpr.ac.in

In order to improve the treatment of cancer, this research investigates the development of a novel combination prodrug that targets mitochondrial destabilization by combining platinum-based therapeutics with an inhibitor of the succinate dehydrogenase (SDH)-ubiquinone binding site 2-Thenoyltrifluoroacetone (TTFA). In both normal and altered cells, the mitochondrion is essential for many different cellular functions, such as synthesis, metabolism, energy production, signaling, and cellular homeostasis maintenance[1]. It comprises proteins that are essential for cellular growth, development, and the regulation of apoptosis. By targeting mitochondrial respiratory complexes, inhibitors can specifically destabilize mitochondria, leading to electron leakage and the generation of reactive oxygen species (ROS), which contribute to mitochondrial membrane permeabilization (MMP)[2]. Thus, it assumes a pivotal function in determining cellular destiny. Hence targeting mitochondria can be a promising strategy for the treatment of cancer. Chemotherapeutic drugs based on platinum, such as carboplatin and cisplatin, have been widely used to treat cancer Nevertheless, the development of resistance in cancerous cells may jeopardize the effectiveness of these platinum-based treatments[3]. To overcome this limitation, the present work aims to examine the potential of augmenting the cytotoxic effectiveness of platinum-based drugs like cisplatin by co-administering them with a mitochondrial targeting agent, such as TTFA. The precise mechanism underlying the synergistic effect of TTFA and platinum drugs is also investigated in this work.



Keywords: Platinum-based Therapeutics; Mitochondrial membrane permeabilization (MMP); Combination Therapy; Reactive Oxygen Species (ROS).

References:

1. Y. Qin, X. Jiang, Q. Yang, J. Zhao, Q. Zhou, Y. Zhou, *Frontiers in Oncology* **2021**, 11, 672781.

2 B. Kruspig, K. Valter, B. Skender, B. Zhivotovsky, V. Gogvadze, *Biochim Biophys Acta* **2016,** 1863, 2065-71.

3 R. Oun, Y. E. Moussa, N. J. Wheate, *Dalton Trans* **2018**, **47**, 6645-6653.

A Substitutionally Inert Platinum Anti-Cancer Agent Designed to Tackle Chemo-resistance and Nephrotoxicity Issues of Platinum Chemotherapy

Tushar Ranjan Panda and Malay Patra

Department of Chemical Sciences, Tata Institute of Fundamental Research (TIFR), Mumbai

E-mail: tushar.panda@tifr.res.in , malay.patra@tifr.res.in .

Even in the modern era of precision medicine and immunotherapy, chemotherapy with platinum (Pt) drugs remains among the most commonly prescribed medications against a variety of cancers. Unfortunately, the broad applicability of these blockbuster Pt drugs is severely limited by intrinsic and/oracquired resistance, and high systemic toxicity. Considering the strong interconnection between kineticlability and undesired shortcomings of clinical Pt drugs, a series of kinetically inert organometallic Pt based anticancer agents with a novel mechanism of action were rationally designed. Using a combination of *in vitro* and *in vivo* assays, it was demonstrated that the development of a remarkably efficacious but kinetically inert Pt anticancer agent is feasible.[1] Along with exerting promising antitumorefficacy in Pt-sensitive as well as Pt-resistant tumors *in vivo*, our best candidate has the ability to mitigate the nephrotoxicity issue associated with cisplatin. In addition to demonstrating, for the first time,the power of kinetic inertness in improving the therapeutic benefits of Pt based anticancer therapy, wehave described the detailed mechanism of action of our best kinetically inert antitumor agent.

The design, *in vitro* mechanistic investigation and *in vivo* data will be discussed in the presentation.

Reference:

1. T. R. Panda, M. Manikandan, S. P. Vaidya, S. Chhatar, S. Sinha, M. Mehrotra, S. Chakraborty, S. Gadre, P. Duari, P. Ray, M. Patra, *Angew. Chem. Int. Ed*. **2023**, 62, e2023039.

Next Generation Bimetallic Anticancer Agents

Manikandan M, Malay Patra*,

Research scholar, Medicinal Chemistry and Cell Biology Lab,

DCS, Tata Institute of Fundamental Research Mumbai

manikandan.m@tifr.res.in, malay.piu@gmail.com

Platinum drugs cisplatin, carboplatin and oxaliplatin are the frontline treatment options for a variety of localized as well as metastatic cancers.[1] However, their efficacy is often comprised due to inherent and acquired resistance in cancers. To circumvent this issue, we recently designed dual-targeting platinum-ferrocene (**Pt-Fc**) bimetallic hybrids with potent anticancer activity. The **Pt-Fc** derivative has much lower platinum cross-resistance compared to cisplatin, but was unable to circumvent the resistance completely.[2,4] Encouraged by the lack of cross-platinum resistance of Pt-Fc compounds, we synthesized a Ru-Fc derivative (**1**) and evaluated its anticancer potential *in vitro*. Moreover, we performed a structure activity relationship on this class of compound (**1 - 6**) to understand the role of various functionalities. We confirmed by comparing IC_{50} values in platinum sensitive and resistance cancer cells that **1** has the ability to circumvent Pt resistance. Our in vivo experiments using zebrafish conclusively established the potent antiangiogenetic activity of **1**.[3] To the best of our knowledge, this is the first report on evaluation of toxicity and antiangiogenetic activity of a Ru-Fc bimetallic conjugate. Now, even though the compound is excellent in overcoming platinum resistance and has excellent anti-angiogenicity, the plasma stability is relatively poor because of the labile Ru-Cl bond. So now we synthesized a bimetallic compound, where the ferrocene β-diketonate ligand is incorporated into a Ru-bipyridyl system. This innovative molecule shows nanomolar toxicity in cancer cell lines, effectively overcoming platinum resistance, and displays excellent in-vivo toxicity (manuscript submitted).

1. Johnstone, T. C.et al., The Next Generation of Platinum Drugs: Targeted Pt(II) Agents, Nanoparticle Delivery, and Pt(IV) Prodrugs. *Chem. Rev*. **2016**, 116 (5), 3436-3486.

2. Shubhankar Gadre, **Manikandan M**, Malay Patra* et al., A rationally designed bimetallic platinum (II)-ferrocene antitumor agent induces non-apoptotic cell death and exerts in vivo efficacy. *Chem.A Eur. J*. **2022**, 28, No. e202201259

3. **Manikandan M**, Malay Patra* et al., Potent Ruthenium−Ferrocene Bimetallic Antitumor Antiangiogenic Agent That Circumvents Platinum Resistance: From Synthesis and Mechanistic Studies to In Vivo Evaluation in Zebrafish. *J. Med. Chem*. **2022**, 65, 24, 16353–16371.

4. **Manikandan M**, Malay Patra* et al., Improving In Vivo Tumor Accumulation and Efficacy of Platinum Antitumor Agents by Electronic Tuning of the Kinetic Lability. *Chem. Eur. J*. **2023**, e202302720.

Mn(II)-Complex Confined Porous Silica Nanomaterial as Zn(II)-Responsive "Smart" MRI Contrast Agent to Examine Pathological Condition of Pancreas

Riya Mallik,[a] and Chandan Mukherjee[a]*

[a]*Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati-781039, Assam, India.*

Email: mallik@iitg.ac.in

Clinically approved MRI contrast agents are mostly Gd(III)-based and primarily nonspecific. Hence, developing non-gadolinium-based organ-specific and bio-responsive contrast agents through pH, enzyme action, and secondary metal ion gradient has drawn paramount attention for superior diagnosis of pathological abnormalities. Type-1 and Type-2 diabetes mellitus are metabolic disorders governed by the functional efficiency of pancreatic β-cells and are largely affected by blood glucose levels. The activities of the cells toward insulin production, storage, and secretion are accompanied by Zn(II) ions. Thus, developing Zn(II) ions-responsive MRI-contrast agents has earned considerable interest in the non-invasive pathology of the cell. In this context, we have synthesized a seven-coordinate, mono(aquated) Mn(II) complex (**1**), which is confined within the porous silica nanosphere of size 13.2 nm to engender Mn(II)-based MRI contrast agent, Complex **1**@SiO_2NP. The surface functionalization of the nanosphere by Py_2Pic organic moiety for the selective binding of Zn(II)-ions renders Complex **1**@SiO_2–Py_2PicNP that exhibits longitudinal relaxivity, r_1 = 13.19 $mM^{-1}s^{-1}$. Eventually, r_1 of the functionalized nanomaterial increases linearly with the increment of Zn(II) ions concentration and reaches 39.01 $mM^{-1}s^{-1}$ in the presence of 40 fold excess of the ions, at physiological condition (0.6 mM serum albumin protein at pH 7.4). Thus, Zn(II)-responsive contrast enhancement *in vivo* is envisaged employing the nanoparticle. Indeed, a 138 % contrast enhancement in the pancreas is visualized by administering 10 μmol/kg (w.r.t [MnII]) dosage of Complex **1**@SiO_2–Py_2PicNP along with the glucose stimulus in 12 h fasted healthy C57BL/6 mice at 7 T. The pharmacokinetics and further biodistribution analysis on Mn(II) ions after the tissue digestion suggested that the nanoparticle excreted from the body in both hepatobiliary and renal pathways within 24 h, without having any adverse effect on the body.

A novel cobalt (III)-based bio-reductive prodrugs for hypoxia selective doxorubicin assisted anticancer activity

Sharmila Wahengbam,[a] Neha Masarkar ,[c] Himanshi Sharma, [b] Mithun Roy[a]*

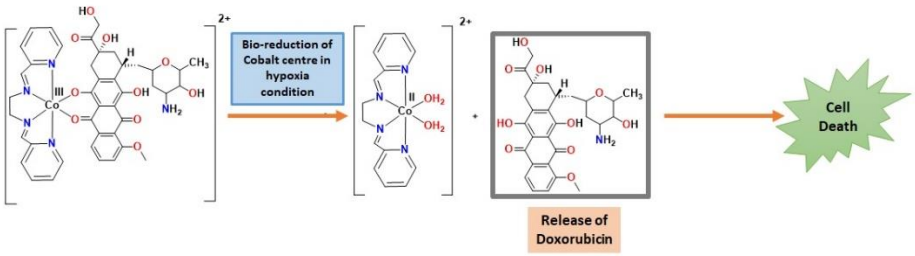
[a]*Department of Chemistry, NIT Manipur, Manipur, India*

[b]*All India Institute of Medical Sciences, Bhopal*

[c]*Kusuma school of biological sciences, IIT Delhi*

Email: mithunroy@nitmanipur.ac.in

Solid tumours are characterized with hypoxia that played a critical role in cell proliferation, metabolism, tumour invasion and metastasis. Tumour hypoxia has developed resistance to conventional chemotherapy, radiotherapy and also oxygen dependent photodynamic therapy. To improve the prognosis of the treatment, a bio-reductive activated prodrug concept has been developed to significantly target the hypoxia reductive microenvironment. Herein we developed a cobalt based bio-reductive prodrug for releasing doxorubicin in hypoxia condition. Doxorubicin is an anthracycline class of chemotherapeutic drugs which are commonly used for breast cancer chemotherapy. The spectroscopic and electrochemical properties of the complex was evaluated and the interaction of the complex with cellular reductase Glutathione (GSH) were monitored through florescence spectroscopy for 72h at different phosphate buffer saline solutions pH ranging from 3-8 pH and different GSH concentration ranging from 2-10mM. There is an increase in the intensity of doxorubicin upon addition of GSH due to the reduction of Co(III)/Co(II). The amount of drug release is calculated using Korsmeyer Peppas Equation and found that the rate of release was highest in 10mM of GSH which is equivalent to the concentration of GSH found in tumor cellular micro-environment. The complex also shows high binding affinity of 43963.271 M^{-1} with BSA indicating that the drug has potential to interact with the serum protein. Cytotoxicity assays of complex in A549, HaCaT, HT-29 is reported and the complex also exhibits a remarkable cytotoxicity in MDA-MB 231 with an average IC_{50} value of 14.08 µM.



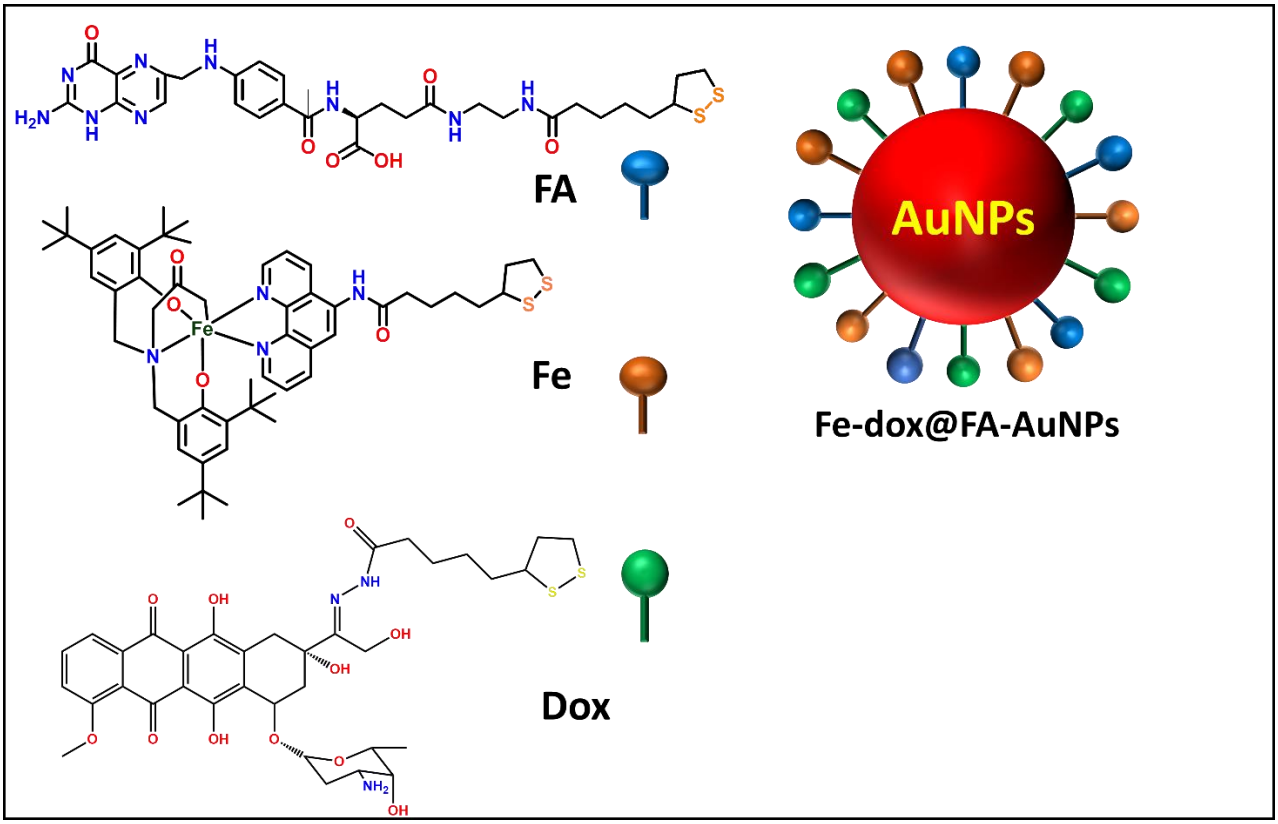
References:

1. T.W. Failes, W.H. Trevor, *Dalton Trans.*15, **2006**,1895-1901.
2. I.C.A de Souza, S. de Souza Santana, J.G. Gómez, G.P. Guedes, J. Madureira, S.M. de Ornelas Quintal, M. Lanznaster, *Dalton Trans*, *49*, **2020**,16425-16439.
3. S.S. Santana, M. Lanznaster,, *Inorg. Chem. Com*. **2023,** *153*, 110810.

Iron(III)-phenolate complex-functionalized gold nanocomposites as the strategic tools for targeted photo-cytotoxicity in red light and cancer-selective drug release

Maynak Pal,[a] Aarti Upadhyay[b] and Mithun Roy[a]*
[a]Department of Chemistry, National Institute of Technology Manipur, Langol-795004, Imphal (Manipur),
[b]Indian Institute of Science, Department of Inorganic and Physical Chemistry.
E-mail: maynakpal1234@gmail.com, mithunroy.iisc@gmail.com

The LMCT transitions and associated photo-redox chemistry of photo-activable iron(III)-phenolate complexes are of potential importance in light-assisted cytotoxicity for cancer therapy. The light gives temporal control over the cytotoxicity of the complex and minimizes the side effects arising from unwanted systemic side effects. Although the typical LMCT transitions in iron(III)-phenolate complexes are observed in the range 450-600 nm, which could be the limiting factor in clinical consideration of such iron(III) complexes. However, surface functionalization of iron(III)-complexes into the gold nanoparticles (AuNPs) resulted in the remarkable shift in the SPR bands at 660 nm making the nanoconjugate (**Fe@AuNPs**) suitable for photocytotoxic applications in the clinical arena of cancer therapy.[1] The **Fe@AuNPs** exhibited remarkable red light-induced photocytotoxicity in cancer cells (A549) with IC_{50} (μg mL^{-1}): 56.1 (red light), >500 (dark) leaving the normal cells (WI-38) unaffected. Later folic acid was co-functionalized into **Fe@AuNPs** (Loading: 1.63 μg of folic acid per mg of nanoconjugate) to achieve targeted photocytotoxicity, and the nanoconjugate (**Fe@FA-AuNPs**) resulted in significant folate-assisted uptake in folate(+) cancer cells. The nanoconjugate, **Fe@FA-AuNPs** exhibited enhanced photocytotoxicity in folate(+) cancer cells (HeLa) with IC_{50} (μg mL^{-1}): 27.8 (red light), >200 (dark), while **Fe@FA-AuNPs** was significantly less toxic in folate(-) cancer cells (A549) or normal cells (HPL1D), and the overall studies were the example of targeted photocytotoxicity.[2] Further functionalization of anthracycline anticancer drug, doxorubicin (dox) in Fe@FA-AuNPs resulted in new nanocomposite (**Fe-dox@FA-AuNPs**) (Loading: 1.67 μg of folic acid, 2.58 μg of dox per 1 mg of **Fe-dox@FA-AuNPs**) which has emerged as the strategic tools for targeted chemo-phototherapeutic applications through a single platform. We observed a folate-assisted uptake of the Fe-dox@FA-AuNPs, selective release of doxorubicin (dox) under the reduced pH of the cancer cells and doxorubicin-related cytotoxicity (IC_{50}: 105.5 μg mL^{-1} in HeLa in dark), remarkable enhancement in cytotoxicity of **Fe-dox@FA-AuNPs** in red light (IC_{50}: 1.55 μg mL^{-1} in HeLa in red light).[3]



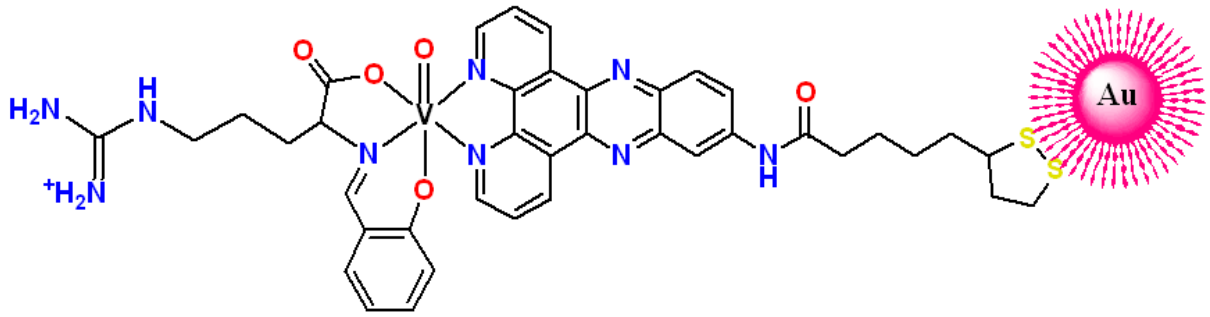
References:
1. M. Pal, V. Ramu, D. Musib, A. Kunwar, A. Biswas, M Roy, *Inorg. Chem.*, **2021**, *60*, 6283–6297.
2. M. Pal, A. Upadhyay, N. Masarkar, A. Bera, S. Mukherjee, M. Roy, Submitted to *Dalton Trans.*, **2023.**
3. Manuscript under preparation

Red-light activable oxovanadium(IV) complex functionalized gold nanoparticles as a potential tool for photochemotheraputic applications

Gobinda Bag,[a] Romabai Chanu,[a] Maynak Pal,[a] Mithun Roy* [a]

[a] Department of Chemistry, National Institute of Technology Manipur, Langol, Imphal, Manipur, India, Pin 795004

Photodynamic therapy has emerged as a non-invasive alternative treatment strategy in the past few decades for its tumoral control of the activity of the drug by application of light irradiation. To minimize the hepatotoxic side effects of the first-generation photosensitizers, transition metal complexes were developed for photo-chemotherapeutic applications. Among the transition metals, oxovanadium complexes are a suitable choice for low metal toxicity in the human body. However these complexes lack in terms of solubility and targeting. Thus we developed red-light activable oxovanadium(IV) complexes that ensure enhanced therapeutic activity on photo-activation through the singlet oxygen generation making the prodrug system remarkably cytotoxic against cancer cells.Oxovanadium(IV) complex [VO(L^1)(L^2)](acac) functionalized with gold nanoparticles where L^1 = L-salicylidenearginine and L^2 = N-(dipyrido[3,2-a:2',3'-c]phenazin-11-yl)-5-(1,2-dithiolan-3-yl)pentanamide synthesized, characterized and photocytotoxicity study was performed in HeLa cells in dark and red light. The complex shows a d-d band in the 780 nm to 860 nm region. Photophysical studies of the complex generally involve the generation of singlet oxygen generation ($^1O_2$) along with the presence of a triplet excited state of the complex was probed through perylene assay in detail. In addition, oxovanadium complex functionalized gold nanoparticle (AuNP) can enhance the anticancer activity by generating ROS ($^1O_2$, •OH) when activated with red to near-IR light.



References:

1. P. K. Sasmal, A. K. Patra, M. Nethaji, A. R. Chakravarty, Inorg. Chem., 2007, 46, 11112-11121.
2. S. Banerjee, P. Prasad, A. Hussain, I. Khan, P. Kondaiah, A. R. Chakravarty, 2012, 48, 7702-7704.
3. P. Prasad, I. Khan, P. Kondaiah, A. R. Chakravarty, Chem. Eur. J. 2013, 19, 17445 – 17455.

Mn(II) Polypyridyl Complexes: Precursors to High Valent Mn(V)=O Species and Inhibitors of Cancer Cell Proliferation

Pragya Arora, Sikha Gupta, Sai Kumari Vechalapu, Rakesh Kumar, Ayushi Awasthi, Sathyapriya Senthil, Shweta Khanna, Dharmaraja Allimuthu* and Apparao Draksharapu*

Department of Chemistry, Indian Institute of Technology Kanpur, Kanpur-208016 (India)

Email: pragya20@iitk.ac.in

Abstract: Mn(V)-oxo species has been proposed as the key intermediate for catalyzing the thermodynamically unfavourable water oxidation reaction in plants.[1] Numerous reports highlight the potential of such high-valent Mn-oxo species in catalysing various crucial chemical transformations.[2] Herein, the $[(L)Mn^{II}]^{2+}$ (L = neutral polypyridine ligand framework) has been employed in generating a putative Mn^{V}=O species in the presence of *m*CPBA (*m*CPBA = *m*-Chloroperoxybenzoic acid) at room temperature. The proposed Mn^{V}=O species is capable of performing the aromatic hydroxylation of Cl-benzoic acid derived from *m*CPBA to give $[(L)Mn^{III}$(*m*-Cl-salicylate)$]^{+}$ which in the presence of excess *m*CPBA generates a metastable $[(L)Mn^{V}(O)$(*m*-Cl-salicylate)$]^{+}$, characterized by UV/Vis absorption, EPR, resonance Raman spectroscopy, and ESI-MS studies. Further, a plausible mechanism has been proposed for the formation of $[(L)Mn^{V}(O)$-*m*-Cl-salicylate)$]^{+}$ from $[(L)Mn^{III}$(*m*-Cl-salicylate)$]^{+}$. The characterized transient $[(L)Mn^{V}(O)$-*m*-Cl-salicylate)$]^{+}$ exhibits high reactivity for oxygen atom transfer reactions, supported by the electrophilic character depicted from Hammett studies using a series of para-substituted thioanisoles. Finally, evaluation for the intracellular effect of synthesized Mn(II) complexes revealed an enhanced intracellular ROS and mitochondrial dysfunction to prevent the proliferation of hepatocellular carcinoma and breast cancer cells.[3]

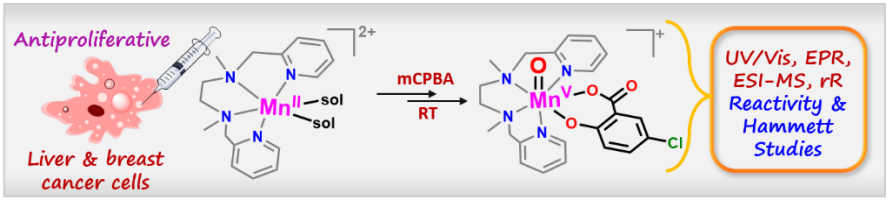


Figure 1 Formation of proposed Mn(V)=O by the action of *m*CPBA on Mn(II)-polypyridyl complexes at room temperature.

References:

(1) J. S. Kanady, E. Y. Tsui, M. W. Day and T. Agapie, *Science*, **2011**, *333*, 733–737.

(2) X. Engelmann, I. Monte-Pérez and K. Ray, *Angew. Chemie - Int. Ed.*, **2016**, *55*, 7632–7649.

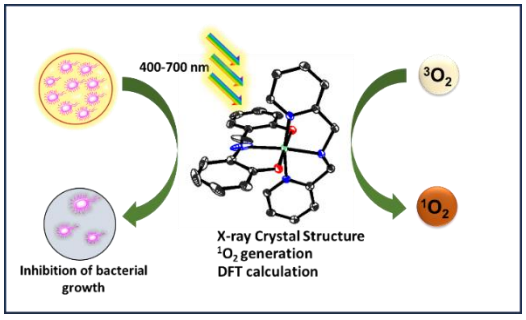
(3) P. Arora, S. Gupta, S. K. Vechalapu, R. Kumar, A. Awasthi, S. Senthil, S. Khanna, D. Allimuthu and A. Draksharapu, *Chem. Eur. J.*, **2023**, doi.org/10.1002/chem.202301506.

Polypyridyl-based Co(III) Complexes of Vitamin B_6 Schiff base for Photoactivated Antibacterial Therapy

Apurba Mandal,[a] Rohit Rai,[b] Sukanta Saha,[c] Arif Ali Mandal,[a] Ashish Kumar Yadav,[a] Arnab Dutta,[c] Prodyut Dhar,*[b] Samya Banerjee*[a]

[a]Department of Chemistry, [b]Biochemical Engineering, Indian Institute of Technology (BHU), Varanasi-221005, India, [c]Department of Chemistry, IIT Bombay, Mumbai-400076, India. (Email: apurbamandal.rs.chy22@itbhu.ac.in; samya.chy@itbhu.ac.in)

The uncontrolled increase in antibacterial resistance is a growing global threat to humankind.[1] Therefore, new antibacterial drugs with novel mechanisms of action are required to overcome this challenge. Recently, metal-based photoactivated-antibacterial therapy has attracted significant interest in this aspect.[2] Although $Co^{2+/3+}$ complexes have shown promising therapeutic applications due to their biocompatible and bio-essential nature,[3] but, the efficacy of Co complexes as photo-activated antibacterial agents is rarely explored.[4] In this regard, five novel polypyridyl-Co(III) complexes of various biocompatible Schiff bases *viz*., [Co(dpa)(L_1)]Cl (**1**), [Co(dpa)(L_2)]Cl (**2**), [Co(L_3)(L_2)]Cl (**3**), [Co(L_3)(L_1)]Cl (**4**), and [Co(L_4)(L_1)]Cl (**5**), where dpa = bis(2-pyridylmethyl)amine ; H_2L_1 = (E)-2-((2-hydroxybenzylidene)amino)phenol; H_2L_2 = (E)-5-(hydroxymethyl)-4-(((2-hydroxyphenyl)imino)methyl)-2-methylpyridin-3-ol; L_3 = 4'-phenyl-2,2':6',2''-terpyridine (ph-tpy); L_4 = 4′-ferrocenyl-2,2′:6′,2″-terpyridine (Fc-tpy) were synthesized and characterized.[5] X-ray structures of **1**, **3**, and **4** revealed a distorted octahedral $Co^{III}N_4O_2$ coordination core.[5] The absorption bands of these complexes were observed in the visible range with a λ_{max} at ~ 430-485 nm. Complex **5** displayed an extra absorption band near 545 nm because of the ferrocene moiety. These absorptions in the visible region reflected the potential of the complexes to act as photo-activated antibacterial agents. All these complexes showed reactive oxygen species (ROS)-mediated antibacterial effects against *S. aureus* and *E. coli* upon exposure to low-energy visible light (0.5 J/cm^2, 400-700 nm) with MIC values in the range of 0.5 to 2 μg/mL.[5] Additionally, **1**-**5** did not show any toxicity toward A549 (Human Lung adenocarcinoma) cells, reflecting their selective bacteria-killing abilities.[5]



References:

[1] J. O'Neil, *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations*, 2016. [2] C. Weng *et al*. *JACS Au*, 2021, **1**, 1348-1354. [3] N. S. Bryce *et al*. *Chem. Sci*., 2011, **2**, 2135. [4] S. Banerjee *et al. ChemBioChem,* 2023, **24**, e202300033. [5] A. Mandal, S. Banerjee *et al*. *Dalton Trans*., 2023 (Submitted).

Selective Cytotoxicity to Cancerous Cells, Production of ROS, and Induction of Apoptosis in Copper(II) Complexes of CuN_4S Core

Balasubramaniam Selvakumaran[a] and Mariappan Murali[a,*]

[a]*Coordination and Bioinorganic Chemistry Research Laboratory,*

Department of Chemistry, National College (Autonomous), Tiruchirappalli 620 001

Tamil Nadu, India murali@nct.ac.in

Many transition metal complexes have been developed as possible anticancer chemotherapeutic drugs in the fight against cancer. To address the outstanding clinical concerns with cisplatin, new metal-based anticancer compounds with enhanced biological activity, increased selectivity, decreased toxicity, and distinct modes of action are being designed and synthesized. One of the metal ions are the focus of significant investigation is copper, which has recently come to be recognized as a crucial component of several cancer treatment drugs. Numerous in vitro tests and a few in vivo studies using a wide range of copper-based complexes as cytotoxic agents have shown their antitumor activity while maintaining lower toxicity than cisplatin. Through several approaches, including DNA interaction, mitochondrial dysfunction, proteasome inhibition, production of reactive oxygen species (ROS), and DNA damage, copper-based complexes cause the death of cancer cells. Through a variety of distinct modes of action, Cu complexes can cause apoptosis via higher generation of ROS in tumor cells, which are promising in cancer therapy and have emerged as new hotspots in cancer treatment research. So, we have synthesized eight novel mixed-ligand copper(II) complexes of the type $[Cu(L)(phen)](ClO_4)$ from S-methyldithiocarbazate Schiff bases [H(L1)-H(L8)] and 1,10-phenanthroline (phen) ligands. The coordination geometry around the Cu(II) ion is distorted square pyramidal (τ, 0.24-0.49) with CuN_4S chromophore. The electronic and EPR spectra disclose that the geometry of the Cu(II) complexes in the solid state is preserved in solution, and they display quasi-reversible electrochemistry. They exhibit excellent in vitro cytotoxicity to A549 cancer cells without affecting the normal L132 cells, and are superior to cisplatin. The DCHF-DA experiment indicated that cancer cells produce more ROS than normal cells. Further, they cause cell death mainly through apoptotic mode, as revealed by the observation of a higher percentage of apoptotic cells in AO/EB or DAPI-stained cancer cells. Thus, ROS generation in tumor cells is implicated in cytotoxicity, demonstrating the versatile nature of presently accessible mixed-ligand copper(II) complexes for cancer therapy using ROS-induced apoptotic cell death.

References:

1. Masuri, S.; Vanhara, P.; Cabiddu, M. G.; Moráň, L.; Havel, J.; Cadoni, E.; Pivetta, T. Copper(II) phenanthroline-based complexes as potential anticancer drugs: A walkthrough on the mechanisms of action. *Molecules* **2022**, *27*, 49.
2. Nunes, P.; Yildizhan, Y.; Adiguzel, Z.; Marques, F.; Pessoa, J. C.; Acilan, C.; Correia, I. Copper(II) and oxidovanadium(IV) complexes of chromone Schiff bases as potential anticancer agents. *J. Biol. Inorg. Chem.* **2022**, *27*, 89-109.
3. Sangeetha, S.; Ajaykamal, T.; Murali, M. Copper(II) complexes of 2-methyl-8-hydroxyquinoline and tri/diimine co-ligand: DFT calculations, DNA and BSA binding, DNA cleavage, cytotoxicity and induction of apoptosis. *New J. Chem.*, **2021**, *45*, 7578-7593.

Hetero-metallic [Fe(III)-Mn(I)] bimetallic complexes for photoactivated chemotherapeutic applications

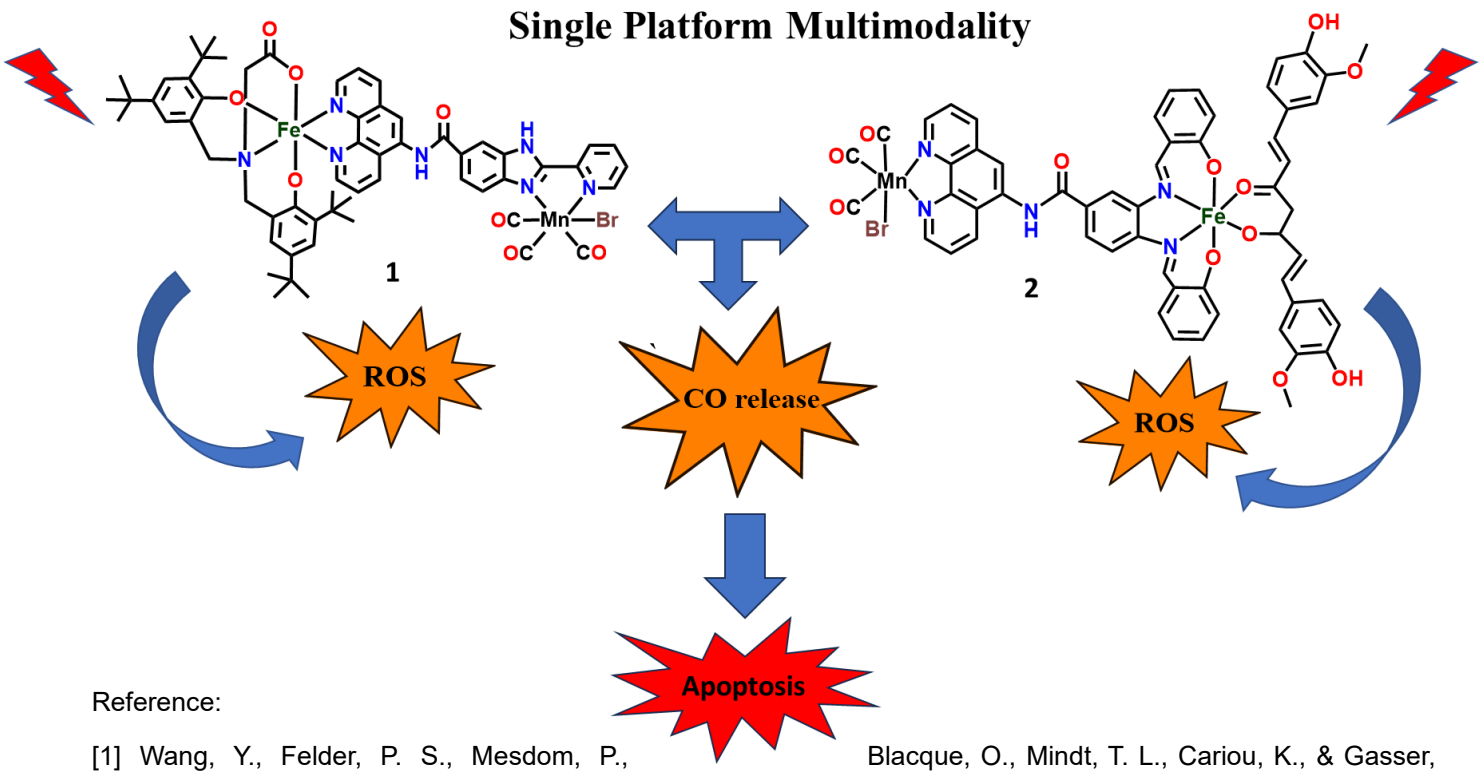
Abhishek Panwar,[a] Nidhi Aggarwal,[b] Mithun Roy[a*]

[a]Department of Chemistry, NIT Manipur, Manipur, India

[b]Department of Chemical Biology Unit, Institute of Nano Science and Technology, Phase-10, Sector 64, Mohali, Punjab, 160062, India

Email: mithunroy@nitmanipur.ac.in

The use of bimetallic system in photodynamic therapy has emerged as a promising strategy against cancer [1]. Bimetallic complexes, in the presence of light, shows dual activation of metal via different transition like LMCT or MLCT which results in the generation or release of toxic species that causes apoptosis in cancer cells. Bimetallic complexes like (Ru-Pt) have been known for showing promising photochemotherapeutic applications, however, their use is limited due to heavy metal toxicity as well as non-tumour specificity. Hence, more research is going on regarding this mixed metal strategy that can be used for newer treatment modalities in PDT i.e. photoactivated chemotherapeutics (PACT). Here, we have designed two hetero bi-metallic Fe(III)-Mn(I) complexes having general formula for complex **1** i.e [Fe(L1)(phen)- (L2)Mn(CO)$_3$Br], where L1 can be classified as Bis(3,5-di-tert-butyl-2-hydroxybenzyl)glycine , L2 can be classified as 2-(pyridin-2-yl)-1H-benzo[d]imidazole-5-carboxylic acid, and another for complex **2** i.e [(Curcumin)Fe(L1)-(aminophen)Mn(CO)$_3$Br], where L1 is a 3,4-bis[(2-hydroxyphenyl)methylene)amino] benzoic acid. In these two mixed metal complexes, complex **1** having Fe (III)-phenanthroline moiety is responsible for the generation of hydroxyl radicals via LMCT transition that induces oxidative stress in cancer cells, while complex **2** having curcumin appended Fe(III) moiety act as a singlet oxygen generator which is toxic to cancer cells leading to cellular apoptosis while Mn(I)-imidazole moiety or Mn(I)-phen moeity is responsible for CO release through visible light via MLCT transition that triggers caspase-dependent apoptosis in cancer cells. Both these apoptosis pathways can be achieved in a single platform through this bimetallic system. Moreover, it can be considered as a next-generation photoactivated chemotherapeutic agent for cancer treatment modality. Here in, all the synthetic procedure, all the characterization, photochemical as well as photophysical studies and remarkable photocytotoxicity in a human cervical cancer cell line (HeLa) are reported to explore its photoactivated chemotherapeutic applications.



Reference:

[1] Wang, Y., Felder, P. S., Mesdom, P., Blacque, O., Mindt, T. L., Cariou, K., & Gasser, G. (2023), ChemBioChem, e202300467, https://doi.org/10.1002/cbic.202300467.

Facile synthesis of biocompatible di-peptide decorated silver nanoparticles and evaluation of its anticancer and antimicrobial efficacy

Totan Ghosh

Assistant Professor, Maulana Abul Kalam Azad University of Technology West Bengal; Simhat, Haringhata, Nadia -741249

The nano-based delivery system become a responsive and potential therapeutic approach against various types of cancer and multidrug resistance bacterial infections with a convenient synthesis process, customization, and site-specific targeting. In this study, self-assembled di-peptide (Met-Leu) functionalized silver nanoparticle (SAP@AgNPs) was fabricated *via* bottom-up approach using $NaBH_4$ as a reducing agent. The physiochemical properties of synthesized SAP@AgNPs were observed by various standard characterisation techniques like, UV-Vis, FTIR, SEM which reveals the self-assemblies nanoparticles like structure having dipeptide on its surface. The synthesized SAP@AgNPs further evaluated for its anticancer potency against the human chronic leukemia cell line (K562) via the cell viability assay (MTT) where the IC_{50} was found at 0.03017nM. Furthermore, it showed dose dependent antibacterial efficacy against clinically isolated multidrug resistant bacteria both Gram-positive (*Staphylococcus aureus*) and Gram-negative (*Escherichia coli).* Notably, SAP@AgNPs exhibited higher antibacterial effect against the *Escherichia coli* (MIC: 0.03nM; MBC: 0.04nM) as compare to *Staphylococcus aureus* (MIC: 0.04nM; MBC: 0.05nM). As evident from fluorescent imaging, the ROS generation, mitochondrial membrane damage and DNA damage were found to be the key factors for leukemic and bacterial cell death. In vitro cytotoxicity evaluation revelled that, synthesized SAP@AgNPs has no significant toxicity up to the concentration of 0.05nM against the human healthy RBCs. Additionally, from the *in-silico* studies, it was confirmed that synthesized nanoparticles showed promising interaction with various marker proteins of bacterial and leukemic cells which predicted the cause of cell death at molecular level.

Keywords: di-peptide, self-assembled, silver nanoparticle, antibacterial, anticancer

A Co^{III} complex of 1-amino-4-hydroxy-9,10-anthraquinone mimics actions of anthracycline anti-cancer drugs: An experimental approach

[a,b]Somenath Banerjee, [c]Dhanasekaran Dharumadurai, [a]Partha Sarathi Guin, [b]Saurabh Das*

[a]Department of Chemistry, Shibpur Dinobundhoo Institution (College), Howrah 711 102, India

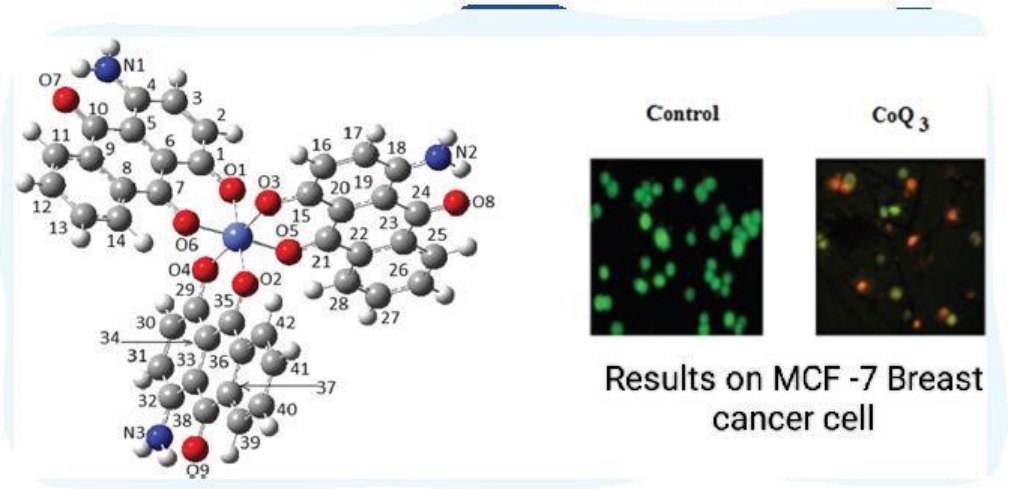
[b]Department of Chemistry (Inorganic Chemistry Section),

Jadavpur University, Raja S. C. Mullick Road, Kolkata 700 032, India [c]Department of Microbiology, School of Life Sciences, Bharathidasan University, Tiruchirappalli 620 024, India

E-mail: me_somenath_05@yahoo.com

Abstract

A Co^{III} complex of 1-amino-4-hydroxy-9,10-anthraquinone (QH) having molecular formula CoQ_3 was prepared and characterized by elemental analysis, FTIR, UV-Vis, fluorescence spectroscopy and mass spectrometry. In the absence of a single crystal, structure could not be obtained from single crystal X-ray diffraction. Powder X ray diffraction data was obtained for CoQ_3. Computational methods were used to obtain an optimized structure based on spectroscopic information and mass spectrometry. Electrochemical properties of the prepared complex were analyzed using cyclic voltammetry to evaluate several electrochemical parameters crucial for drug action. These indicate considerable changes from that of QH. MCF-7 human breast cancer cells were treated with the complex and QH. IC_{50} obtained after 24 hour incubation of the complex was 95 ± 0.05µg/mL. The study showed MCF-7 human breast cancer cells underwent early and late apoptosis following interaction with CoQ_3.



Theoretical Investigation of Heteroatom Substitution Effects on Iron (IV)-Oxo Complex Reactivity

Rolly Yadav, Chivukula Vasudeva Sastri

Department of Chemistry,

Indian Institute of Technology, Guwahati, Assam,781039

Abstract:

High-valent oxoiron (IV) i.e. (Fe^{IV}=O) species serve as crucial reactive intermediates in the activation of dioxygen and the oxygenation of organic substrates within mononuclear nonheme iron enzymes. Numerous ligand frameworks, designed to emulate enzyme reactivity, have been documented. These frameworks showcase how alterations in ligand architecture, both in axial and equatorial positions, can lead to heightened selectivity and reactivity[1-2]. The incorporation of weak field ligand donor atoms has proven to be a potent strategy, significantly augmenting and influencing the reactivity of the system[3-4]. In this context, our research employs Density Functional Theory (DFT)-based theoretical investigations to comprehend the impact of heteroatom substitution in lieu of one of the nitrogen in the equatorial plane of the ligand. Our studies delve into the intricate factors influencing changes in reaction mechanisms and rate enhancements observed in oxygen atom transfer and hydrogen atom transfer reactions following the introduction of equatorial heteroatom substitution.

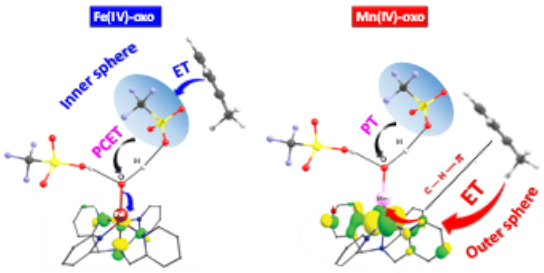
Refrences:

1. H. Park, D. Lee, *Chem. Eur. J.* 2020, *26*, 5916−5926.
2. R. Kumar, B. Pandey, A. Sen, M. Ansari, S. Sharma, G. Rajaraman, *Coord. Chem. Rev.* 2020, *419*, 213397.
3. I. Monte-Pérez, X. Engelmann, Y.-M. Lee, M. Yoo, E. Kumaran, E. R. Farquhar, E. Bill, J. England, W. Nam, M. Swart, K. Ray, *Angew. Chem. Int. Ed*. **2017**, *56*, 14384–14388.
4. J. Deutscher, P. Gerschel, K. Warm, U. Kuhlmann, S. Mebs, M. Haumann, H. Dau, P. Hildebrandt, U. P. Apfel, K. Ray, *Chem. Commun*. **2021**, *57*, 2947–2950.

Decoding the Electronic Origins of Outer-Sphere & Inner-Sphere Electron Transfer in High-Valent Non-Heme Metal-oxo Species

Neethinathan Johnee Britto, Asmita Sen, Gopalan Rajaraman*
Department of Chemistry, Indian Institute of Technology Bombay,
Powai, Mumbai 400 076, India
E-mail: rajaraman@chem.iitb.ac.in

The electron transfer (ET) step is one of the crucial processes in biochemical redox reactions that occur in nature. Although metalloenzymes possessing metal-oxo units at their active site are typically associated with outer-sphere electron transfer (OSET) processes, biomimetic models, in contrast, have been found to manifest either an inner-sphere electron transfer (ISET) or OSET mechanism. This distinction is clearly illustrated through the behaviour of $[(N4Py)Mn^{IV}(O)]^{2+}$ (**1**) and $[(N4Py)Fe^{IV}(O)]^{2+}$ (**2**) complexes, where complex **1** showcases an OSET mechanism, while complex **2** exhibits an ISET mechanism, in their reactions involving C-H bond activation and oxygen atom transfer reactions in the presence of a Lewis acid.[1] However, the precise reason for this puzzling difference remains elusive. Our calculations indicate that when the substrate (toluene) approaches both **1** and **2** that is hydrogen bonded with two HOTf molecules (denoted as **1-HOTf** and **2-HOTf**, respectively), proton transfer from one of the HOTf molecules to the metal-oxo unit is triggered and a simultaneous electron transfer occurs from toluene to the metal centre.[2] Interestingly, the preference for OSET by 1-HOTf is found to originate from the choice of MnIV=O centre to abstract spin-down (β) electron from toluene to its $\delta(d_{xy})$ orbital. On the other hand, in **2-HOTf**, a spin state inversion from triplet to quintet state takes place during the proton (from HOTf) coupled electron transfer (from toluene) preferring a spin-up (α) electron abstraction to its $\sigma^*(d_{z2})$ orbital mediated by HOTf giving rise to ISET. In addition, **2-HOTf** was calculated to possess a larger reorganisation energy, which facilitates the ISET process via the acid. The absence of spin-inversion and smaller reorganisation energy switch the mechanism to OSET for **1-HOTf**. Therefore, for the first time, the significance of spin-state and spin-inversion in the electron transfer process has been identified and demonstrated within the realm of high-valent metal-oxo chemistry.



References:
[1] N. Sharma, Y.-M. Lee, X.-X. Li, W. Nam, S. Fukuzumi, *Inorg. Chem.* **2019**, *58*, 13761–13765.
[2] N. Johnee Britto, A. Sen, G. Rajaraman, *Chem. Asian J.* **2023**, e202300773.

Effect of Protein Environment on reactivity of Aldehyde Deformylating Oxygenase (ADO): A QM/MM Approach

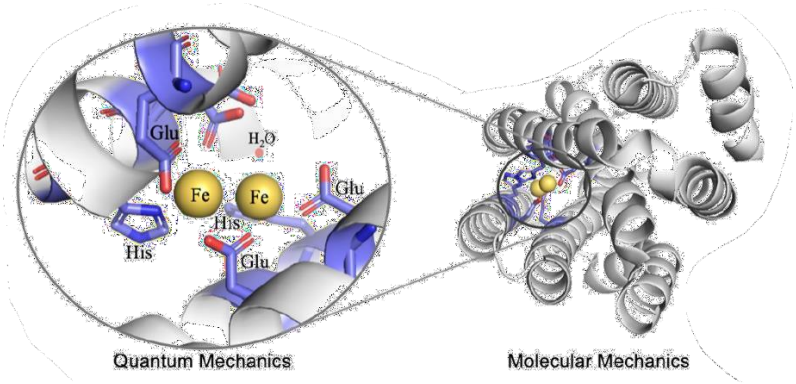
Thakur Rochak kumar Rana[a], R. Nath[b], S. A. Siddiqui[c], K. D. Dubey[c*], A. Paul[b*],

Gopalan Rajaraman[a,*]

[a]Indian Institute Of Technology Bombay, Mumbai

E-mail: rochakrana@gmail.com, rajaraman@gmail.com

Enzymes play a vital role in nature, but deciphering their mechanisms is a scientific challenge. Today, we can manipulate enzymes by mutating key residues through directed evolution. This approach is effective but random. A deeper understanding of how enzymes work can enhance design protocols and guide smarter mutation and screening methods. Unlike drug-protein interactions, where the lock-and-key concept suffices, comprehending enzyme catalysis is more complex. The protein environment can play a crucial role in the selective generation of hydrocarbons with high efficiency and high turnover numbers in the enzymatic catalytic reaction.As the bio-mimic small model system does not have the protein environment, the selective production of hydrocarbons will be lost and may end up with no reaction. The negative result withthe small bio mimic model will actually help us to understand if we try to produce fuels at a high rate or efficiency so that we are able to judge whether we are able to produce hydrocarbon or not.We will also check whether the barrier height is suitable for the biomimetic catalyst or not. In theQM/MM study with the entire protein environment, we will see whether the extent of the substrate trigger channel actually helps to form a product or not. Therefore, the protein environment will play a very important in making society with the availability of biofuels. Illuminating the electronicand structural properties, as well as the mechanism of ADO at the molecular level, is helpful in gaining insight into these biologically important systems and the knowledge that can be utilized inthe design of new biomimetic hydrocarbon Production models or these systems in the laboratory



1. Bollinger Jr & Co-worker, JACS, 2013, 135 (42), 15801-15812

2. Helen M. Berman, Nucleic Acids Research, Volume 28, 2000, 235–242,

Mechanism of CO_2 cycloaddition reaction using 3d-4f catalyst: A DFT and ab-initio exploration

Purva Dua, Asmita Sen, Gopalan Rajaraman*

Department of Chemistry, IIT Bombay, Powai, Mumbai 400076, India

**E-mail: rajaraman@chem.iitb.ac.in*

Mechanistic cycle for already synthesized 3d-4f heterometallic helicates formulated Zn_3LnL_4 (H_2L=N-(2-hydroxybenzylidene) amino) ethyl)-2-hydroxybenzamide, Ln = Gd(III) (**1**), Dy(III) (**2**), Er(III) (**3**)), is proposed for the cycloaddition reaction of CO_2 with epoxides using DFT and ab-initio CASSCF/RASSI-SO method. The catalyst is proven to be highly effective in the formation of cyclic carbonates with the TOF as high as 38000 h^{-1} reported with a very low -catalyst loading (0.001 mol %). While there are several mechanistic studies that explore the activation of CO_2 using transition metal catalyst, exploring such mechanism for {3d-4f} catalyst is challenging due to (i) paramagnetic Ln(III) ions have orbitally degenerate ground state and large spin-orbit coupling (except Gd(III)). Therefore, an approach beyond DFT methods is required to address the problem (ii) computing the potential energy surface of such catalytic transformations in multimetallic clusters pose various mechanistic challenges as there are several sites available for the reactivity. Our work discloses i) site selectivity and effect of lanthanide on CO_2 activation and ii) the role of spin-orbital coupling on CO_2 activation.

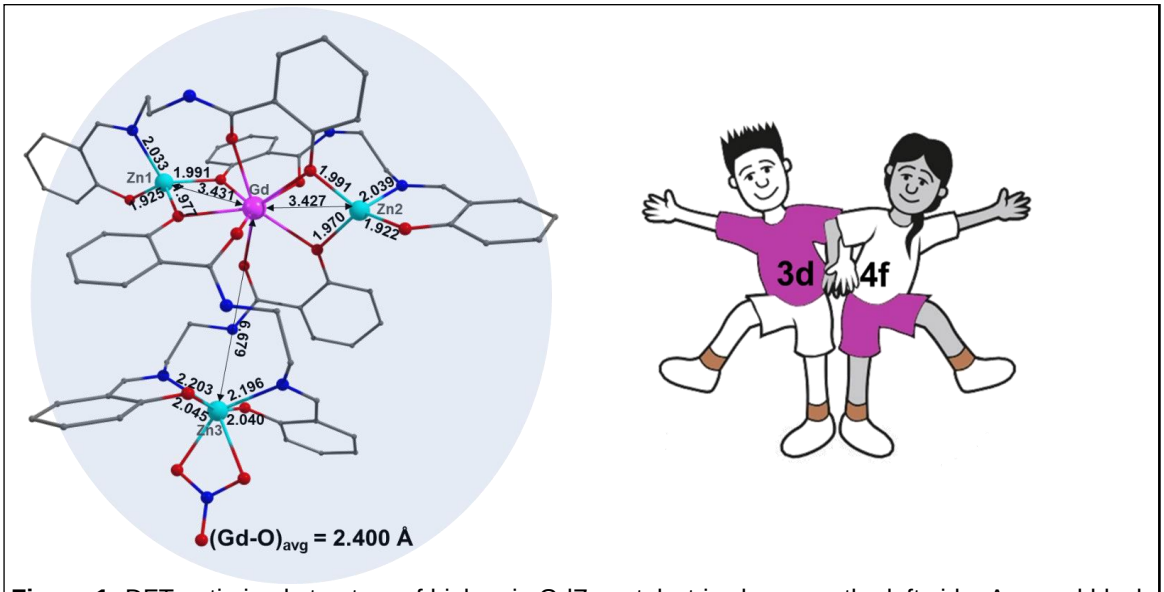


Figure 1: DFT optimized structure of high spin GdZn catalyst is shown on the left side. Arrowed black lines show the Gd-Zn distances. Color code: Gd ^{III} - purple, Zn ^{II} - cyan, C- grey, N – blue, and O - red (Hydrogens are not shown for clarity). Catalyst showing 3d-4f cooperativity on the right

References:

1) H. Yang, G. Gao, W. Chen, L. Wang and A. W. Liu, *Dalton Trans.* **49**, pp. 10270-10277 (2020).

Unraveling the Regioselective Reaction Mechanism of Gentisic Acid Catalyzed by Wild-Type Gentisate 1,2-Dioxygenase Enzyme and Assessing Substrate Specificity in Light of the G106A Mutation

Rounak Nath[a], Rabindranath Manna[b], Sneha Panja[c], Ankan Paul*[a]

[a]School of Chemical Sciences
Indian Association for the Cultivation of Science
Jadavpur, Kolkata 700 032, West Bengal

[b]S.N.Bose National Centre for Basic Science
Salt Lake, Kolkata 700 106, West Bengal

[c]Indian Institute of Science Education and Research
Berhampur 760 010, Odisha

Gentisate 1,2-dioxygenase (GDO), a ring-fission non-heme dioxygenase enzyme, displays a unique regioselective reaction with gentisic acid (GTQ) in the presence of molecular oxygen. Classical molecular dynamics simulations were carried out for both the wild-type GDO and its mutated variants, Asp174Glu and Asp174Ala, revealing the presence of three active water molecules at the enzyme's active site, pivotal in facilitating the oxidative cleavage of an aromatic C–C bond in the GTQ substrate [1]. Additionally, employing quantum mechanics/molecular mechanics (QM/MM) calculations, we unveiled three distinct reaction mechanisms explaining the regioselective oxidation of GTQ by the GDO enzyme. The formation of the main product, maleylpyruvate, via pathway A emerged as the most favorable mechanism, with a rate-determining barrier of 21.4 kcal mol^{-1}. Our study underscores the essential role of active water molecules in stabilizing the O_2 molecule and aiding in O–O and C–C bond cleavage, while also highlighting the crucial anchoring function of Asp174 in the enzymatic cycle. Moreover, upon introducing the G106A mutation to the wild-type enzyme, a significant change in catalytic activity was observed with two different substrates, salicylate and GTQ, attributable to the presence of a hydrogen bond network with water and the 5'-OH group of GTQ, which is absent in salicylate [2]. Long-range classical molecular dynamics simulations of both the wild-type GDO and its G106A mutant variant, each complexed with two different substrates, confirmed the existence of an inter molecular hydrogen bond network which is aligned with previous findings.

References:

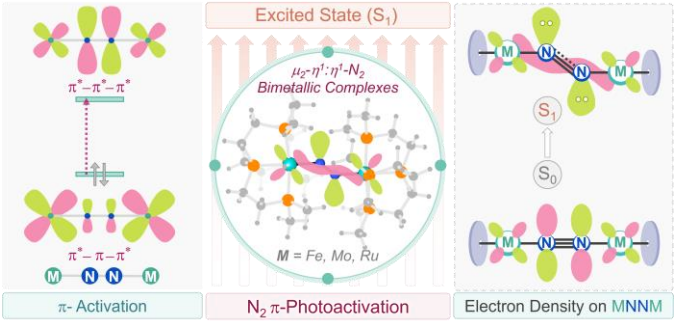
1. R., Nath, R.N, Manna, A., Paul, *Catal. Sci. Technol.* **12** (2022) 5742-5751.
2. E., Eppinger, M., Ferraroni, S., Burger, L., Steimer, G., Peng, F., Briganti, A., Stolz, *Biochim. Biophys. Acta* **1854** (2015) 1425-1437.

μ_2-η^1:η^1-N_2 Bridged Bimetallic Dinitrogen Complexes: Geometry of the First Excited State in Connection to N_2 π-Photoactivation

Akhil Bhardwaj[1], Bhaskar Mondal[1]*

[1]School of Chemical Sciences, Indian Institute of Technology Mandi, Himachal Pradesh 175075, India

Multi-metallic clusters play key catalytic roles in biological systems, such as the FeMo cofactor in the nitrogenase enzyme that binds to molecular dinitrogen. In synthetic chemistry, bimetallic end-on μ_2-η^1:η^1-N_2 bridging dinitrogen complexes is a biomimetic catalyst that can achieve N_2 activation. Such catalysts have also served as the platform for photochemical N_2 activation, largely for the N−N cleavage. However, the alternate N−N π-photoactivation route has remained largely unexplored. In the current study, we have strengthened the notion of weakening the N−N bond through the population of π* orbital upon electronic excitation from the ground to the first excited state using four prototypical complexes based on Fe, Mo, and Ru. The complexes possess characteristic N−N π* based LUMO (π*-π*-π*) centered on their M−N−N−M core, which was earlier postulated by Reiher et. al. [1] to play a central role in the N_2 photoactivation. Vertical electronic excitation of the highest oscillator strength involves transitions to the N−N π*-based acceptor orbital (π*-π*-π*) in the representative complexes. This induces geometry relaxation of the first excited metal-to-nitrogen (π*) charge transfer (^{1}MNCT) [2] state leading to a “zigzag” M−N−N−M core in the equilibrium structure. Obtaining the equilibrium geometry in the first excited state with the full-sized complexes widens the scope of N−N π-photoactivation with μ_2-η^1:η^1-N_2 bridging dinitrogen complexes. Promisingly, the elongated N−N bond and bent ∠MNN angle in the photoexcited S_1 state resemble their radical- and di-anion forms, which lead toward thermodynamically feasible N−N protonation in the S_1 excited state.



References:

1. Reiher, M.; et. al. *Chem. Eur. J.* **2004**, *10*, 4443–4453.
2. Bhardwaj, A.; Mondal, B. *Chem. Eur. J.* **2023**, e202301984. (In Press)

Deciphering the Role of Proline 4-hydroxylation at *Yaa* in *Gly-Xaa-Yaa* Triplet in Collagen Stability

Ashutosh Joshi[1], Bhaskar Mondal[2], Trayambak Basak[1]
[1]School of Biosciences and Bioengineering, IIT Mandi, Himachal Pradesh, India
[2]School of Chemical Sciences, IIT Mandi, Himachal Pradesh, India

Collagen is a triple helical structure made up of a tripeptide motif (*Gly-Xaa-Yaa)*. Proline (Pro) and 4-hydroxyproline (4-HyP) prevalently occupy *Xaa* and *Yaa* positions, respectively.[1,2] The gauche conformation due to the hydroxyl (−OH) group of (R)-stereoisomer of 4-HyP favoring *exo* ring pucker and the n → π* charge-transfer interaction between carbonyl moieties favoring the *trans*-conformation of the peptide bond help in the triple helix formation and stabilization.[1] In this work, the role of steric and electronic effects in collagen structure has been investigated using the density functional theory (DFT), benchmarked against ab initio MP2 (second-order Møller-Plesset perturbation theory) method. A set of 24 density functionals was used for the benchmarking. Realistic tripeptide models of collagen single strands have been used for the first time to obtain the electronic-level details that can decipher the role of 4-Hyp.[3] The selected density functionals were used to explore the electronics of 4-HyP in Gly-Pro-4-HyP (GPO^4) tripeptide and compared with Gly-Pro-Pro (GPP) tripeptide. From the benchmarking, we found that M062X and M052X are methods of choice to study the structure of collagen and the n → π* charge-transfer interactions. The GPO^4 with 4(R)-HyP-exo is electronically more stable than GPP tripeptides. The reason for the stability is the cumulative effect of forward and reverse n → π* charge-transfer interactions, stabilizing GPO^4 over GPP tripeptide. Moreover, we studied tripeptide models containing all 4 conformers of 4-HyP, 4(R)-HyP-exo, 4(R)-HyP-endo, 4(S)-HyP-exo, and 4(S)-HyP-endo. Based on the previous literature, the gauche conformation favoring exo ring pucker with R-stereoisomer should preferably stabilize the tripeptide model. This, we indeed found in our tripeptide model, as evidenced through the electronic energy of the tripeptide model bearing 4(R)-HyP-exo. Therefore, we can conclude that the underlying reason for collagen stability is mainly due to the ring pucker of 4-HyP rather than R- and S-stereoisomerism of 4-HyP. The same effect will be reflected in the binding energy in the collagen triple helical structure. In summary, we have benchmarked the optimal DFT method and established the model to study the sequence-structure relationship in collagen biochemistry. Moreover, we present the first study describing collagen stability using all conformers of 4-HyP at Yaa in the Gly-Xaa-Yaa tripeptide model and in a triple helix.

References

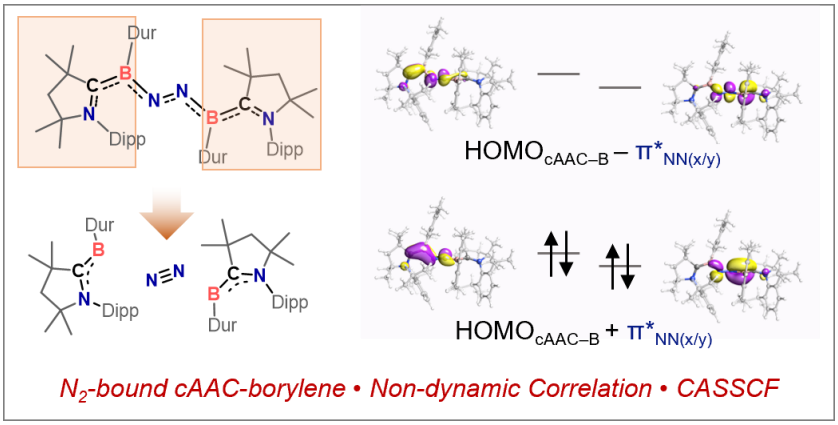
(1) Shoulders, M. D.; Raines, R. T. *Ann. Rev. Biochem*. **2009**, pp 929–958.
(2) Bella, J. *Biochem. J*. **2016**, pp 1001–1025.
(3) Jakobsche, C. E.; Choudhary, A.; Miller, S. J.; Raines, R. T. *J. Am. Chem. Soc.* **2010**, *132.*

Decoding the Electronic Structure of N_2-bound cAAC-borylene at the CASSCF level

Susovon Ghosh and Bhaskar Mondal*

School of Chemical Sciences, Indian Institute of Technology Mandi, Himachal Pradesh 175005, India.

Activation of inert N_2 molecule has been unique to the bio-inspired transition metal catalysts till recently. Ability of transition metals to form σ-donation and π-back-donation interaction with N_2 is the key to this success [1]. Recent progress in main-group chemistry towards the activation and conversion of N_2 have led to the revelation that base-trapped borylene complexes can accomplish this challenging activation process [2]. Our work presents a multiconfigurational complete active space self-consistent field (CASSCF)-based electronic structure investigation on the N_2-bound cAAC-borylene species isolated by Braunschweig et. al [3]. The synergistic bonding between the borylene units and N_2 involving the donation from the N–N σ to the unoccupied orbital of borylene and back-donation from the occupied orbital of borylene to the N–N π* has been unequivocally established using CASSCF-derived natural orbitals and electronic configuration. The unique bonding of the B–N–N–B core in N_2 bound cAAC-borylene and the resulting geometry have also been compared with the M–N–N–M core of a prototypical transition metal(M)–N_2 complex. Finally, the change in the electronic structure and geometry of the N_2-bound borylene species on two-electron reduction was also investigated in the context of N_2 activation. This detailed electronic structure and bonding interaction enrich the understanding of the intricate bonding between base-trapped borylene and dinitrogen.



References

[1] L. S. Yamout , M. Ataya , F. Hasanayn , P. L. Holland , A. J. M. Miller and A. S. Goldman , *J. Am. Chem. Soc.*, **2021**, **143**, 9744–9757

[2] M.-A. Légaré , G. Bélanger-Chabot , R. D. Dewhurst , E. Welz , I. Krummenacher , B. Engels and H. Braunschweig , *Science*, **2018**, **359** , 896–900

[3] Ghosh, S.; Bhardwaj, A.; Mondal, B. *Dalt. Trans.* **2023**, *52*, 12517–12525.

Role of explicit solvation in computational modeling of chemical reactions: Mechanism of Cu(I) transfer between thiolate-based chelators in water

Soumak Ghosh †, Sk Hasibo Hassan †, and Avisek Das *

School of Chemical Sciences, Indian Association for the Cultivation of Science, Kolkata, India

Solvation plays important roles in controlling thermodynamic and kinetic aspects of chemical reactions. The conventional approaches to treat solvation in electronic structure methods are likely to become inadequate when the reacting solutes have strong electrostatic and hydrogen bonding interactions with the solvent and undergo significant structural changes during the course of the reaction. In this article, we present evidence of such solvent and structural effects in the computational study of Cu(I) transfer reaction between thiolate-based chelators dithiobutylamine (DTBA) and dithiotheritol (DTT) in water, inspired from biological copper trafficking phenomena. We propose a general solution to the problem by combining classical molecular dynamics (MD) simulation of the bulk system and static quantum chemistry calculations. The fluctuating solvation shell was estimated from MD and energetics was assessed by averaging QM energies of a series of suitably chosen molecular clusters constructed from the MD snapshots. Applying this approach, we propose a reaction pathway with estimates of relative intermediate stabilities and barriers, which suggest the overall reaction to be reversible in nature and likely to go through three coordinated intermediates, confirming previous studies on similar protein analogues. An interesting fact emerged from our study was the strong indication that the rate determining step could be the deprotonation of initial thiol bound Cu(I) complex, without involving any Cu-S bonds. The proposed method will lead to better treatment of solvations, and these mechanistic insights will aid our understanding of biological copper(I) trafficking.

†Equal contributions

References:

(1) Basdogan, Y.; Keith, J. A. A paramedic treatment for modeling explicitly solvated chemical reaction mechanisms. Chemical Science 2018, 9, 5341–5346, DOI: 10.1039/c8sc01424h

(2) Skyner, R. E.; McDonagh, J. L.; Groom, C. R.; Mourik, T. V.; Mitchell, J. B. A review of methods for the calculation of solution free energies and the modelling of systems in solution. Physical Chemistry Chemical Physics 2015, 17, 6174–6191, DOI: 10.1039/C5CP00288E

Electronic Structure and Nitrene Transfer Reactivity of Co- and Fe-Porphyrin-Nitrene

Mayank Mahajan and Bhaskar Mondal*

School of Chemical Sciences, Indian Institute of Technology Mandi, Himachal Pradesh 175075, India

Metal-bound nitrene species are the crucial intermediate in catalytic nitrene transfer reactions exhibited by engineered enzymes and molecular catalysts. The electronic structure of such species and its correlation with nitrene transfer reactivity has not been fully understood yet. In this work, we have performed an in-depth electronic structure analysis and nitrene transfer reactivity of two prototypical metal-nitrene species derived from Co^{II}(TPP) and Fe^{II}(TPP) (TPP = meso-tetraphenylporphyrin) complexes and tosyl azide nitrene precursor in aziridination reaction[1,2]. Parallel to the well-known "cobalt(III)-imidyl" electronic structure of the Co-porphyrin-nitrene species[2], the underlying formation mechanism and electronic structure of the elusive Fe-porphyrin-nitrene has been established using density functional theory (DFT) and multiconfigurational complete active space self-consistent field (CASSCF) calculations. Electronic structure evolution analysis for the metal-nitrene formation step and CASSCF-derived natural orbitals advocates that the electronic nature of the metal-nitrene (M–N) core of Fe-porphyrin-nitrene possess "imido-like" [(TPP)Fe^{IV}⋯NTos] (Tos = tosyl), which is in stark contrast to "imidyl" nature of the Co-porphyrin-nitrene [(TPP)Co^{III}–•NTos]. This difference between Co- and Fe-nitrene has been attributed to the additional interactions between Fe-d_π and N-p_π orbitals in Fe-nitrene, which is further complemented by the shortened Fe–N bond length of 1.71 Å. This stronger M–N bond in Fe-nitrene as compared to the Co-nitrene is also reflected in the higher exothermicity ($\Delta\Delta H$ = 16 kcal/mol) of the Fe-nitrene formation step. The "imido-like" character renders a relatively lower spin population on the nitrene nitrogen (+0.42) in the Fe-nitrene complex, which undergoes the nitrene transfer to the C=C bond of styrene with a considerably higher enthalpy barrier ($\Delta H^‡$ = 10.0 kcal/mol) as compared to the Co congener ($\Delta H^‡$ = 5.6 kcal/mol) possessing higher nitrogen spin population (+0.88) and relatively weaker M–N bond (Co–N = 1.80 Å)[3]. The current findings on the distinct electronic structure between Co- and Fe-porphyrin-nitrene can be used as a guide to developing strategies for tuning the electronic characteristics of the M−N core in metal-bound nitrenes aiming at targeted reactivities.

References

(1) Liu, Y.; Che, C. M. *Chem. Eur. J.* **2010**, *16*, 10494–10501.

(2) Goswami, M.; Lyaskovskyy, V.; Domingos, S. R.; Buma, W. J.; Woutersen, S.; Troeppner, O.; Ivanović-Burmazović, I.; Lu, H.; Cui, X.; Zhang, X. P.; Reijerse, E. J.; DeBeer, S.; van Schooneveld, M. M.; Pfaff, F. F.; Ray, K.; de Bruin, B. *J. Am. Chem. Soc.* **2015**, *137*, 5468–5479.

(3) Mahajan, M.; Mondal, B. *Inorg. Chem.* **2023**, *62*, 5810–5821.

Crossover of Exchange Coupling from Antiferro- to Ferromagnetism in a New Family of Phenoxo-bridged Dicopper(II) complexes involving Cu_2O_2-bridging unit: A Comprehensive Structure-Magnetism Correlation Study

Dhrubajyoti Mondal

Assistant Professor, Department of Chemistry, Visva-Bharati (A Central University), Santiniketan 731235, West Bengal, India

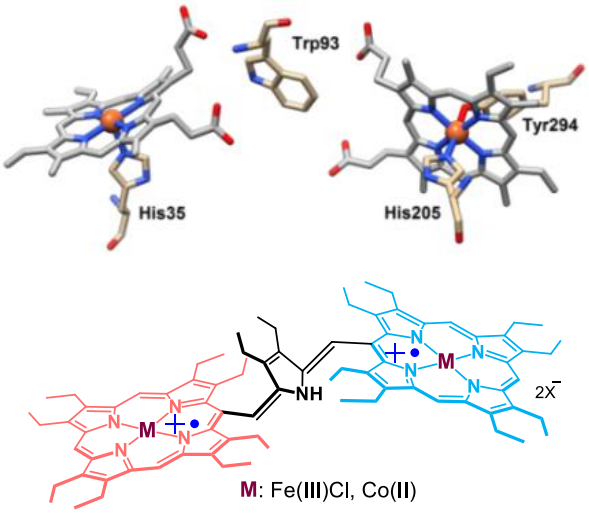
Abstract: There are several examples of hydroxo-, alkoxo-, and phenoxo-bridged dicopper(II) complexes in the literature that involve a Cu_2O_2-bridging moiety, mainly due to its significance for molecular magnetism and copper enzymes. Five neutral bis(*μ*-phenoxido)dicopper(II) complexes, $[Cu_2(L^{Me,Me,Me})_2]$ (**1**), $[Cu_2(L^{Me,Me,Et})_2]\cdot CH_2Cl_2$ (**2**), $[Cu_2(L^{i\text{-}Pr,i\text{-}Pr,i\text{-}Pr})_2]\cdot 2H_2O$ (**3**), $[Cu_2(L^{t\text{-}Bu,Me,i\text{-}Pr})_2]$ (**4**), and $[Cu_2(L^{t\text{-}Bu,t\text{-}Bu,i\text{-}Pr})_2]\cdot H_2O$ (**5**) have been synthesized and characterized by single crystal X-ray diffraction analyses, magnetic studies, and density functional theory (DFT) calculations, in which the ligands [$H_2L^{Me,Me,Me}$ = *N,N*-bis(2-hydroxy-3,5-dimethylbenzyl)-*N′,N′*-dimethyl-ethylene-1,2-diamine, $H_2L^{Me,Me,Et}$ = *N*,*N*-bis(2-hydroxy-3,5-dimethylbenzyl)-*N′*,*N′*-diethyl-ethylene-1,2-diamine, $H_2L^{i\text{-}Pr,i\text{-}Pr,i\text{-}Pr}$ = *N*,*N*-bis(2-hydroxy-3,5-diisopropylbenzyl)-*N′*,*N′*-diisopropylethylene-1,2-diamine, $H_2L^{t\text{-}Bu,Me,i\text{-}Pr}$ = *N*,*N*-bis(2-hydroxy-3-*tert*-butyl-5-methyl-benzyl)-*N′*,*N′*-diisopropylethylene-1,2-diamine, and $H_2L^{t\text{-}Bu,t\text{-}Bu,i\text{-}Pr}$ = *N*,*N*-bis(2-hydroxy-3,5-di-*tert*-butylbenzyl)-*N′*,*N′*-diisopropylethylene-1,2-diamine] contain the same [O,N,N,O]-donor atoms combination but differ in substituents at phenol rings and at an amino nitrogen atom. The effect of these remote substituents on the nature of exchange coupling interactions (ferromagnetic *vs* antiferromagnetic) between the copper(II) ions has been investigated. The average Cu-O-Cu angle, Cu-O-Cu-O torsion angle, and Cu···Cu separation in **1** – **5** are varied systematically by these remote ligand substituents in the range 98.6 – 83.3°, 26.0 – 46.5°, and 2.982 – 2.633 Å, respectively. As a result, the intramolecular spin-spin coupling in these complexes are changing gradually from strong antiferromagnetic (J = –395 cm^{-1}, where $\hat{\mathbf{H}} = -J\hat{\mathbf{S}}_1\hat{\mathbf{S}}_2$) to moderate ferromagnetic (+53.2 cm^{-1}) regime. The crossover angle at which the magnetic interaction changes from antiferromagnetic to ferromagnetic (J = 0) is determined to be at *ca*. 87° for this series of dicopper(II) complexes. DFT calculations support the experimentally determined crossover angle and disclose various magneto-structural correlations in the series **1** – **5**.

Cooperativity in Dication Diradical Porphyrin Dimer Catalyzed Oxa-Diels-Alder Reactions: Spectroscopic and Mechanistic Insights

D. Samanta, S. Sarkar, and S. P. Rath*

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

Hetero-Diels-Alder reaction, a prominent synthetic procedure for the construction of six-membered heterocyclic compounds, useful in the syntheses of natural products. Especially, cycloaddition of aldehydes to dienes, used to fabricate pyran scaffolds, is arguably the most efficient and atom economical approach; hence, has been widely exploited in the syntheses of natural products and physiologically active substances. The present investigation delineates a maiden example of employing earth-abundant metals like iron and cobalt in a novel pyrrole-bridged dication diradical porphyrin dimer as competent catalyst for the oxa-Diels–Alder (ODA) reaction of unactivated aldehydes and simple dienes under relatively mild conditions with lower catalyst loading, which previously had limited opportunities in the presence of the unsaturated bonds, and with high functional-group tolerance. Various spectroscopies, like UV-vis-NIR, ^{19}F and ^{1}H NMR, EPR, ESI-MS, and IR corroborated well with the DFT results; enabling us to delve deeper into the reaction mechanism intricately, formerly unrevealed. The efficacy of such dimeric catalyst over its monomeric analogue is manifested in the cooperative effect, which gave excellent yields even with very low catalyst loading. Moreover, counteranions are decisive in dictating the outcome of the reaction, and their influence is being thoroughly investigated.[2-6]



Scheme 1. Relative Orientation of Hemes and the Intervening Tryptophan Residue in MauG,[1] *top*, and the Dication Diradical Catalyst Used, *bottom*.

Keywords: cooperativity; dication diradical complex; Diels-Alder reaction; DFT study; porphyrin π-cation radical

References:

1. Jensen, L. M. R.; Sanishvili, R.; Davidson, V. L.; Wilmot, C. M. *Science* **2010**, *327*, 1392.
2. Sarkar, S.; Sarkar, P.; Samanta, D.; Pati, S. K.; Rath, S. P. *ACS Catal.* **2022**, *12*, 9589.
3. Singh, A. K.; Khan, F. S. T.; Rath, S. P. *Angew. Chem. Int. Ed.* **2017**, *56*, 8849.
4. Dey, S.; Sil, D.; Rath, S. P. *Angew. Chem. Int. Ed.* **2016**, *55*, 996.
5. Sil, D.; Dey, S.; Kumar, A.; Bhowmik, S.; Rath, S. P. *Chem. Sci.* **2016**, *7*, 1212.
6. Guchhait, T.; Sarkar, S.; Pandit, Y. A.; Rath, S. P. *Chem. Eur. J.* **2017**, *23*, 10270.

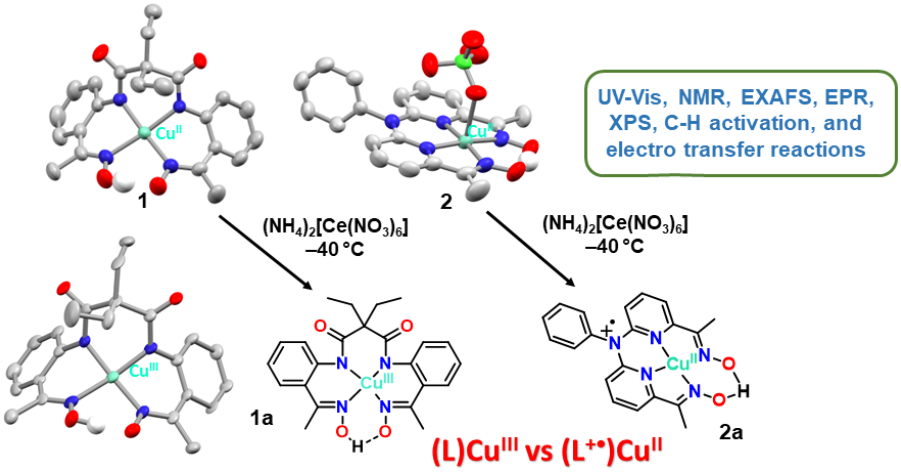
Spectroscopic Characterization of Oxidized Cu^{II} Complexes: Comparing the Bond Dissociation Free Energy and Reorganization Energy of Cu^{III} vs Ligand Oxidized Cu^{II} Complexes

Simarjeet Kaur,[a] Avijit Das,[a] Lucía Velasco,[b] Dooshaye Moonshiram, [b] and Sayantan Paria [a]

[a]Department of Chemistry, Indian Institute of Technology Delhi, New Delhi, India

[b]Instituto de Ciencia de Materiales de Madrid, Madrid, spain

Copper is a frequently found metal ion at the active site of different metalloenzymes, involved in versatile redox reactions such as activation of dioxygen, reduction of NO_2^- and NO, electron transfer reactions, etc.[1] Cu-catalyzed synthetic small molecule transformation reactions are also very well known. Nevertheless, the isolation and characterization of high-valent Cu species are very challenging, and the existence of Cu^{III} has been debated in recent literature.[2, 3]



In this study, two molecular Cu^{II} complexes (**1** and **2**) of the N_4 donor set of ligands have been prepared and thoroughly characterized (Figure 1). Electrochemical measurements revealed that the first oxidation event occurred at 0.03 and 0.49 V vs. Fc^+/Fc in methanol for **1** and **2**, respectively. One electron oxidation of the Cu complexes by ceric ammonium nitrate resulted in the generation of the oxidized Cu species (**1a** and **2a**), which were thoroughly investigated by various spectroscopic techniques, including X-ray absorption spectroscopy, and X-ray structure determination for **1a**. A comparison of the Cu–N bond distances of **1** and **1a** showed a drastic shortening of $Cu–N_{amide}$ and $Cu–N_{oxime}$ bond lengths, typically observed in the Cu-derived oxidation process.[4] X-ray absorption near edge structure (XANES) of **1** showed pre-edge transition at 8980.98 eV, which is 1.6 eV shifted to 8982.58 eV in **1a**. However, there was no shift of the pre-edge transition, which was observed at 8980.98 eV for **2** and **2a**. The 1s→4p main transition, along with a 1s→(4p+shakedown) transition, showed a larger energy shift of 1.25 eV from 8989.70 to 8990.95 eV upon oxidation of **1** to **1a**. In contrast, only a 0.54 eV shift of 1s→4p transition was noted between **2** (8990.17 eV) and **2a** (8990.71 eV). Thus, the XANES data imply the existence of +III and +II oxidation states in **1a** and **2a**, respectively. Additionally, the reactivity of the oxidized Cu complexes has been investigated towards electron transfer and C–H/O–H activation reactions. The bond dissociation free energy (BDFE) and reorganization energy of the Cu^{II} complexes have been estimated and compared.

References:

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

2 I. M. DiMucci, J. T. Lukens, S. Chatterjee, K. M. Carsch, C. J. Titus, S. J. Lee, D. Nordlund, T. A. Betley, S. N. MacMillan and K. M. Lancaster, *J. Am. Chem. Soc.*, **2019**, *141*, 18508-18520.

3 B. L. Geoghegan, Y. Liu, S. Peredkov, S. Dechert, F. Meyer, S. DeBeer and G. E. Cutsail, *J. Am. Chem. Soc.*, 2022, **144**, 2520-2534.

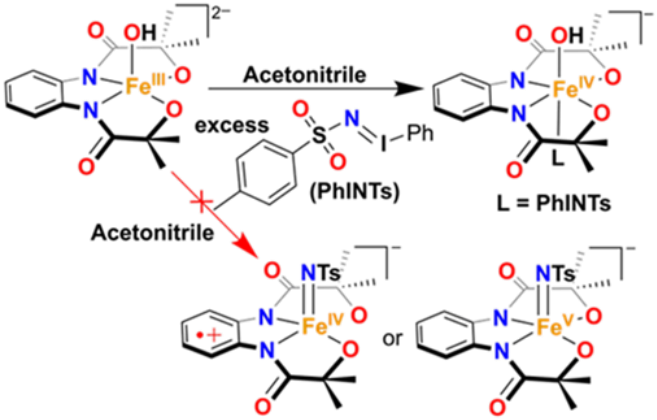
4 M. Bera, S. Kaur, K. Keshari, A. Santra, D. Moonshiram and S. Paria, *Inorg. Chem.*, **2023**, *62*, 5387-5399.

A Functional Model of Compound II of Cytochrome P450: Spectroscopic Characterization and Reactivity Studies of a Fe^{IV}-OH Complex

Kritika Keshari,[a] Aakash Santra,[a] Lucía Velasco,[b] Maxime Sauvan,[b] Simarjeet Kaur,[a] Dooshaye Moonshiram,[b]* Sayantan Pariaa*

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

[b]Instituto de Ciencia de Materiales de Madrid, Consejo Superior de Investigaciones Científicas, Sor Juana Inés de la Cruz, 3, 28049, Madrid, Spain



The reaction of a mononuclear Fe^{III}(OH) complex (**1**) with N-tosyliminobenzyliodinane (PhINTs) results in the formation of a Fe^{IV}(OH) species with a coordinated PhINTs trans to the Fe-OH bond (**3**), instead of the formation of high-valent Fe=NTs compound. Species **3** has been characterized by an array of spectroscopic techniques and represents a rare example of a synthetic Fe^{IV}(OH) complex. The reaction of **1** with the one-electron oxidizing agent was reported to form a ligand-oxidized Fe^{III}(OH) complex (**2**). **3** revealed a one-electron reduction potential of –0.22 V *vs* Fc^+/Fc at –15 °C, which is 150 mV anodically shifted than **2** (E_{red} = -0.37 V vs. Fc^+/Fc at –15 °C), inferring **3** to be more oxidizing than **2**. **3** reacted spontaneously with (4-OMe-C_6H_4)$_3$C$^\bullet$ to form (4-OMe-C_6H_4)$_3$C(OH) through the rebound of the OH group and displayed significantly faster reactivity than **2**. Further, the activation of the C–H hydrocarbon and phenolic O–H bond by **2** and **3** were compared and showed that **3** is a stronger oxidant than **2**. A detailed kinetic study has established the occurrence of CPET/HAT transfer reaction of **3**. Studying one-electron reduction of **2** and **3** using decamethylferrocene (Fc*) revealed a higher k_{et} of **3** than **2**. We suggest the enhanced reactivity of **3** compared to **2** occurred due to the presence of a coordinated ligand trans to the Fe-OH bond in **3**, which enhances the reactivity through the push effect. The study established that the primary coordination sphere around Fe and the redox state of the metal center is very crucial in controlling the reactivity of high-valent Fe-OH complexes.

Insight into the mechanism of Sulfite Reductase using model system Fe (II)TPP

Triparna Roy and Abhishek Dey*

Indian Association for the Cultivation of Science, 2A & 2B, Raja Subodh Chandra Mallick Rd, Jadavpur, Kolkata, West Bengal 700032.

Reduction of sulfite to sulfide is a crucial step of geochemical sulfur cycle which controls both biochemical sulfur assimilation and respiration of sulfate reducing bacteria. Sulfite and SO_2 both having sulphur in the same oxidation state and SO_2 being a very detrimental environmental pollutant it seems important to track the mechaism of its reduction to more benign forms.In this study of SO_2 reduction two key intermediates are trapped and characterized; an initial Fe(III)-SO_2^{2-} species which undergoes proton assisted S-O bond cleavage to form an Fe(III)-SO [(1)]. Previous study of dissimilatory sulphate reduction emphasised on the importance of two conserved cysteines residues [(2)], our preliminary study in Fe (II)TPP model system also reinforces on this result.

1. A. Bhattacharya, A. Kumar Nath, A. Ghatak, A. Nayek, S. Dinda, R. Saha, S. Ghosh Dey, A. Dey, *Angew. Chemie Int. Ed.* **2023**, *62*, e202215235.

2. A. A. Santos, S. S. Venceslau, F. Grein, W. D. Leavitt, C. Dahl, D. T. Johnston, I. A. C. Pereira, *Science (80-.).* **2015**, *350*, 1541–1545.

Structural And Spectroscopic Characterization of High Valent Cobalt Diamond Core

Parkhi sharma,[a] Rakesh Kumar,[b] Sikha Gupta,[c] and Apparao Draksharapu*[a]

Department of Chemistry, Indian Institute of Technology Kanpur, Kanpur-208016

Email: appu@iitk.ac.in

High valent metal-oxygen species have been studied as models for biological systems as they are the key intermediates in the activation of strong sp^3 C-H bonds. In nature, soluble methane monooxygenase, an iron-dependent enzyme, is known for hydroxylating methane to methanol via "diamond core" diiron(IV) intermediate **Q**.[1] Various synthetic models have been characterized that incorporate diiron complexes, with limited oxidizing ability. As a result, researchers are focused on obtaining other high-valent diamond core species like cobalt to study such transformations.[2] In this work, we have structurally characterized a $Co^{III}_2(\mu\text{-}O)_2$ diamond core species (**1**) supported by electronically-rich tetradentate tris(2-pyridyl methyl)amine (TPA*) ligand and designed a new route to synthesize such dicobalt complexes. The intermediate was further characterized by UV-vis absorption, ^{1}H NMR, and resonance Raman spectroscopy. Such high-valent diamond core complexes can be oxidized to form $Co^{III,\,IV}_2(\mu\text{-}O)_2$ (**2**) via one-electron oxidation of **1**. **2** is an EPR active species and is a potent oxidant for various substrates. To the best of our knowledge, we present the crystal structure of a $Co^{III}_2(\mu\text{-}O)_2$ diamond core for the first time.

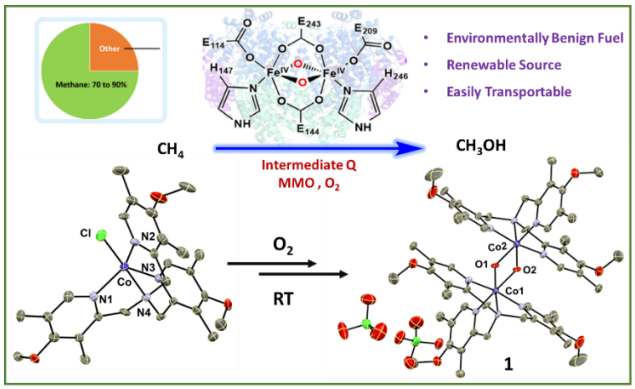


Figure 1. Formation of $Co^{III}_2(\mu\text{-}O)_2$ diamond core species via dioxygen at room temperature.

References:

(1) Matthew O. R.; Amy C, R.; *J. Biol. Inorg. Chem*, **2017**, *22*, 307.
(2) Hong-Yan, W.; Edgar, M.; Sascha, O.; Anders, T.; *Angew. Chem., Int. Ed.*, **2014**, *53*, 14499−14502.

Synthesis and characterization of $Mn^{IV}(O)(\mu\text{-}O)Ce^{IV}$ species: A closest mimic of PS II

Sikha Gupta, Pragya Arora and Apparao Draksharapu*

Department of Chemistry

Indian Institute of Technology, Kanpur

The most essential element for life on earth is oxygen, which plants produce through the oxygen evolving complex (OEC) of Photosystem II (PS II).[10] OEC contains Mn_4CaO_5 cluster, where a Mn_3CaO_4 cubane core with a pendant manganese atom attached to Ca^{2+} via bridged oxygen.[11] Surprisingly, the enzyme is inactive in the absence of Ca^{2+} ions. However, the exact function of Ca^{2+} has been elusive.[12] This observation has precipitated a surge of interest in understanding how Lewis acid (LA), activate manganese-oxo species. It has been reported that the binding of LA to the manganese−oxo complexes remarkably enhances their oxidizing power by increasing the redox potential.[13,14] Cerium(IV) ammonium nitrate (CAN) is a chemical oxidant and acts as redox active Lewis acid has been frequently used in artificial water oxidation reactions.[15, 16] To

[10] Y. Umena, K. Kawakami, J. R. Shen, N. Kamiya, *Nature* **2011**, *473*, 55–60.
[11] M. Suga, F. Akita, K. Hirata, G. Ueno, H. Murakami, Y. Nakajima, T. Shimizu, K. Yamashita, M. Yamamoto, H. Ago, J. R. Shen, *Nature* **2015**, *517*, 99–103.
[12] E. Y. Tsui, R. Tran, J. Yano, T. Agapie, *Nat. Chem.* **2013**, *5*, 293–299.
[13] J. Chen, Y. Lee, K. M. Davis, X. Wu, M. S. Seo, K. Cho, H. Yoon, Y. J. Park, S. Fukuzumi, Y. N. Pushkar, W. Nam, *J. Am. Chem. Soc.* **2013**, *135* (24), 6388−6391.
[14] H. Yoon, Y. M. Lee, X. Wu, K. Bin Cho, R. Sarangi, W. Nam, S. Fukuzumi, *J. Am. Chem. Soc.* **2013**, *135*, 9186–9194
[15] D. Hong, S. Mandal, Y. Yamada, Y. M. Lee, W. Nam, A. Llobet, S. Fukuzumi, *Inorg. Chem.* **2013**, *52*, 9522–9531
[16] Z. Codolà, L. Gómez, S. T. Kleespies, L. Que, M. Costas, J. Lloret-Fillol, *Nat. Commun.* **2015**, *6*, 5865.

understand the catalytic mechanism and function of the metal ions present in OEC, synthesis of the closest structural and functional model systems are essential. In this line, we have synthesized a $[LMn^{IV}(O)(\mu\text{-}O)Ce^{IV}(NO_3)_3]^+$, (L = tetradentate ligand). The newly formed species was characterized by UV-Vis, electron paramagnetic resonance (EPR), resonance Raman spectroscopy along with ESI-MS spectrometry. This complex paves a new path to achieve the goals as it is the closest mimic of active site fragment of PS II.

References:

[1] Y. Umena, K. Kawakami, J. R. Shen, N. Kamiya, *Nature* **2011**, *473*, 55–60.
[1] M. Suga, F. Akita, K. Hirata, G. Ueno, H. Murakami, Y. Nakajima, T. Shimizu, K. Yamashita, M. Yamamoto, H. Ago, J. R. Shen, *Nature* **2015**, *517*, 99–103.
[1] E. Y. Tsui, R. Tran, J. Yano, T. Agapie, *Nat. Chem.* **2013**, *5*, 293–299.
[1] J. Chen, Y. Lee, K. M. Davis, X. Wu, M. S. Seo, K. Cho, H. Yoon, Y. J. Park, S. Fukuzumi, Y. N. Pushkar, W. Nam, *J. Am. Chem. Soc.* **2013**, *135* (24), 6388−6391.
[1] H. Yoon, Y. M. Lee, X. Wu, K. Bin Cho, R. Sarangi, W. Nam, S. Fukuzumi, *J. Am. Chem. Soc.* **2013**, *135*, 9186–9194
[1] D. Hong, S. Mandal, Y. Yamada, Y. M. Lee, W. Nam, A. Llobet, S. Fukuzumi, *Inorg. Chem.* **2013**, *52*, 9522–9531
[1] Z. Codolà, L. Gómez, S. T. Kleespies, L. Que, M. Costas, J. Lloret-Fillol, *Nat. Commun.* **2015**, *6*, 5865.

Spectroscopically discerning the formation and characterization of a *formal* Ni(V) species

Ayushi Awasthi, Rakesh Kumar, Raju Eerlapally and Apparao Draksharapu*
Department of Chemistry, Indian Institute of Technology, Kanpur-208016, India.
Email: appud@iitk.ac.in

Nature's extremely vital metalloenzymes, *i.e.*, Cytochrome P450s and Galactose Oxidases exploit non-innocent ligands to form reactive high valent intermediates for oxidation reactions.[1] This strategy works well for the late 3d metals where accessing high valent states is rather challenging.[2] In this regard, Ni^{II}(salen) complexes have been one of the most promising avenues for those aiming to generate high valent Ni species.[3, 4] This talk is based on one such inquisitiveness where a Ni^{II}(salen) (Figure 1) was treated with *m*CPBA to form a novel Ni(III) bisphenoxyl diradical species, formally analogous to a high valent Ni(V) species. Electrochemical and spectroscopic analyses using UV-Vis and EPR further revealed oxidation events on the ligand as well as on the metal centre to yield a Ni(III) bisphenoxyl diradical species, $Ni^{III}(L^{\bullet\bullet})$.[5] Further, we studied the conditions (*i.e.*, addition of exogenous ligands like pyridine and quinoline) that alter this equilibrium and decides where an effective unpaired electron would localize in Ni(III) bisphenoxyl diradical species.[6] However, the use of *m*CPBA limits the disclosure of the processes involved in the production of a *formal* Ni(V) species. Therefore, by varying the potential and concentration of an electron transfer oxidant, CAN with acid along with the temperature, we also observed that the formation of intermediate species such as Ni(III) and a *formal* Ni(IV) prior to the generation of a *formal* Ni(V) species in CH_3CN. This study benefits the pioneers in understanding the mechanisms of the crucial systems, where now a presence of high valent species like a *formal* Ni(V) could also be plausible. The intermediates discussed here have also been explored as a potential candidate for vital OAT, HAT or ET reactivities making them one of the likely intermediate in the Ni-salen catalyzed oxidation reactions.

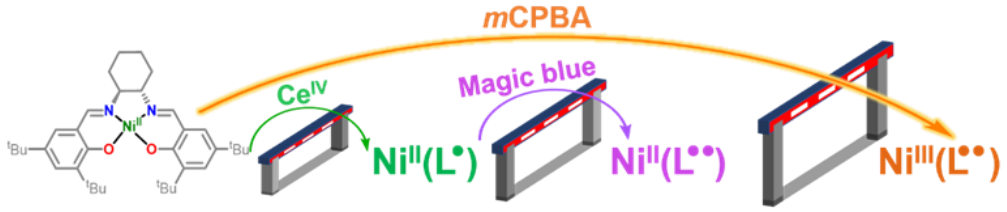


Figure 1. Scheme depicting the strategies to form various oxidizing species with **1** to date.

References

(1) Itoh, S.; Taki, M.; Fukuzumi, S.; *Coord. Chem. Rev.* **2000**, *198*, 3–20. (2) Shimazaki, Y.; Tani, F.; Fukui, K.; Naruta, Y.; Yamauchi, O.; *J. Am. Chem. Soc.* **2003**, *125*, 10512–10513.
(3) Storr, T.; Wasinger, E. C.; Pratt, R. C.; Stack, T. D. P.; *Angew. Chemie. Int. Ed.* **2007**, *46*, 5198–5201. (4) Dunn, T. J.; Webb, M. I.; Hazin, K.; Verma, P.; Wasinger, E. C.; Shimazaki, Y.; Storr, T.; *Dalt. Trans.* **2013**, *42*, 3950–3956.
(5) Awasthi, A.; Leach, I. F.; Engbers, S.; Kumar, R.; Eerlapally, R.; Gupta, S.; Klein, J. E. M. N.; Draksharapu, A.; *Angew. Chemie Int. Ed.* **2022**, *61*, 202211345.
(6) A. Awasthi, S. C. Mallojjala, R. Kumar, R. Eerlapally, J. S. Hirschi, and A. Draksharapu, *Chem. Eur. J.* ***2023***, e202302824, https://doi.org/10.1002/chem.202302824.

Spectroscopic characterization, reactivity of a Cu(III) species supported by a proline-based pseudo peptide and effect of Lewis acid

Raju Eerlapally, and Apparao Draksharapu*

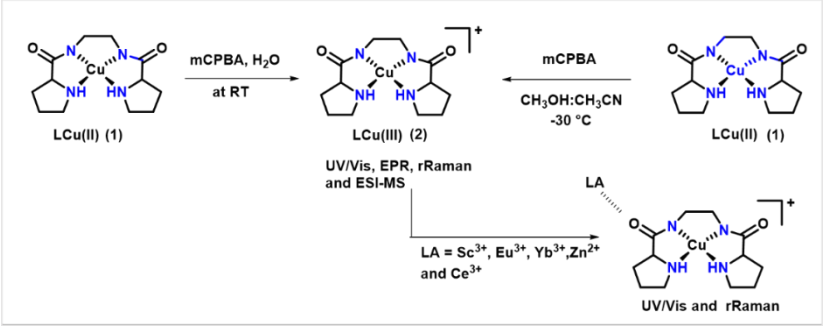
SL-208A, Department of Chemistry, Indian Institute of Technology Kanpur, Kanpur-208016, India.

Email: eerlapallyraju83@gmail.com *and* appud@iitk.ac.in

Inspired by the copper-based metalloenzymes, we intend to incorporate amino acids into our ligand system that enable us to have active copper intermediates, that serve as a structural and functional model for the enzymes. Herein, we discuss the synthesis of a C_2 symmetric proline-based pseudo peptide LH_2 (N,N'-(ethane-1,2-diyl)bis(pyrrolidine-2-carboxamide)) that supports the formation of LCu(III) *via* a (L)Cu(III)-OH intermediate in MeOH:CH_3CN (1:20) at -30 ˚C. From the comparative studies with the pyridine analog Cu(II) complex, it was manifested that incorporation of amino acid in the ligand framework reduces the Cu(III)/Cu(II) redox potential significantly, to react readily with *m*CPBA (Scheme 1). The generated LCu(III) is characterized by various spectroscopic techniques like UV/Vis, EPR, NMR and ESI-MS.[1] Since most of the functional activity of these metalloenzymes in nature takes place in water, we tried to generate the species in water and succeeded in these effort. The generated LCu(III) can perform hydrogen atom transfer and electron transfer reactions. We further explored the effect of redox inactive Lewis acids like Sc^{3+}, Eu^{3+}, Yb^{3+} and Zn^{2+} on the stability and the reactivity of LCu(III) species. In the presence of LA the redox potential of Cu(III)/Cu(II) increased by 0.4 V. Remarkably, addition of redox active Ce^{3+} causes the decay of Cu(III), to form a distinctive dimeric Cu(II) species. The binding of LA to the amide oxygen of pseudo peptide was confirmed by the UV/Vis and resonance Raman spectroscopy where the band of C=O vibration shifted upon LA addition. It is noteworthy to mention that the species discussed here is one of the active intermediates proposed in catalytic cycles of the Dopamine β monooxygenase (DβM) and Peptidylglycine alpha-hydroxylating monooxygenase (PHM) enzymatic.[3,4]

Scheme 1: Strategies to form LCu(III) intermediate in various solvents.

References:



1. R. Eerlapally, S. Gupta, A. Awasthi, R. Kumar and A. Draksharapu, *Dalton Trans.*, **2023**, *52*, 8645.
2. S. Hong, Y. M. Lee, M. Sankaralingam, A.K. Vardhaman, Y. J. Park, K. B. Cho, T. Ogura, R. Sarangi, S. Fukuzumi and W. Nam, *J. Am. Chem. Soc*., **2016**, *138*, 8523−8532
3. J. P. Kilman, *J. Biol. Chem.,* **2006**, *281*, 3013–3016.
4. T. Kamachi, N. Kihara, Y. Shiota and K. Yoshizawa, *Inorg. Chem,* **2005**, *44,* 4226–4236

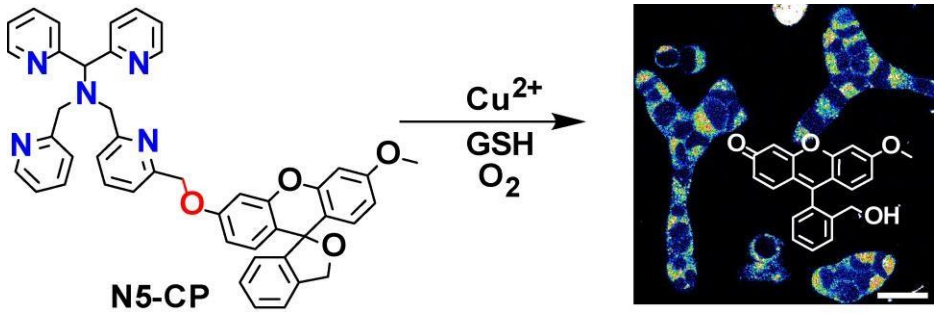
Activity-Based Sensing via a Cu^{II}-Hydroperoxo Species? Detecting Cu Ions In Vivo

Kunika Gupta[a], *Ankona Datta*[a]*

[a] *Department of Chemical Sciences, Tata Institute of Fundamental Research, Mumbai, Maharashtra, India.*

E-mail: kunika.gupta@tifr.res.in, ankona@tifr.res.in

Activity-based fluorescent metal ion sensors consist of a fluorophore conjugated to a metal-binding scaffold.[1] Binding of a specific metal ion to the scaffold results in a metal-catalysed reaction that leads to the release of the fluorophore that was initially quenched in the apo sensor.[1] Fluorophore release leads to increased fluorescence which reports on the metal ion binding event and is equivalent to sensing the presence of the metal ion. This strategy has gained importance over other metal ion sensing methods as it avoids fluorophore quenching due to unpaired electrons on metal ions as the fluorophore detaches from the sensing unit upon metal ion binding. Further, the detection of metal ions like Mn^{2+} and Fe^{2+} that are inherently weak binders to known ligands,[2] might be feasible via this strategy as an activity-based sensing response does not solely rely on metal-binding to the scaffold. Importantly, activity-based sensors can be synthesized through a modular synthetic strategy where the dye and the scaffold can be synthesized separately and then conjugated. Thus far most activity based sensors were based on bi-, tri-, and tetra-N donor ligands with a prevalence of ligands with pyridine-N donors.[1] These sensors mostly had preferential selectivity toward metal ions that are stronger binders based on the Irving-Williams Series.[1] To access sensors for the weak binding metal ions, we explored the effect of increasing the number of N-donor atoms to five in the metal binding scaffold of an activity-based sensor. We developed a novel activity-based sensor with 5-N donor sites. The sensor was highly selective toward Cu ions and afforded a 63 times fluorescence enhancement in the presence of Cu ions. The sensor could detect Cu ions in both living cells and in a live zebrafish larval model.[3] Interestingly, the sensor functioned only in the presence of glutathione and ambient oxygen.[3] To elucidate the sensing mechanism, intermediates and products were characterised. The results indicated the involvement of a Cu^{II}-hydroperoxo species in the catalytic sensing mechanism.[3] Majority of the reported activity-based sensors for metal ions function in the presence of glutathione and ambient oxygen. Hence, we expect that our proposed mechanism, supported by both prior literature evidence and our experiments, will be applicable to the class of activity-based sensors which act via metal-mediated oxidative cleavage. Finally, our results indicated the need for further fine-tuning of scaffold design to access sensors for metal ions that lie lower in the Irving-Williams series. The sensor design, sensing mechanism, and biological studies will be presented.



Scheme depicting Cu ion sensing via the novel 5-N donor containing activity-based sensor.

References

1 D. A. Jovan, S. Jia and C. J. Chang, Inorg. Chem., 2019, 58, 13546–13560.

2 S. Das, K. Khatua, A. Rakshit, A. Carmona, A. Sarkar, S. Bakthavatsalam, R. Ortega and A. Datta, Dalt. Trans., 2019, 48, 7047–7061.

3 K. Gupta and A. Datta, Chem. Commun., 2023, 59, 8282–8285.

An integrated sequence-structure-function approach to understand sulfur transfer and metabolism in bacteria

Rajdip Chakraborty and Amrita Hazra

Department of Chemistry,

Indian Institute of Science Education and Research (IISER) Pune,

Dr. Homi Bhabha Road, Pashan, Pune - 411008

Abstract:

H_2S and its downstream metabolic reactive sulfur species (RSS) are implicated in the regulation of oxidative stress and other crucial signalling processes in bacteria and mammals. The signalling mechanism by sulfur includes post-translationally modifying protein cysteine thiols (-SH) to persulfides (-S-SH), which subsequently result in the structural and functional modification of target proteins. In mammalian cells such post-translational modifications are implicated in the regulation of several severe diseases (Alzheimer's disease, Parkinson's disease etc.). In bacterial cells, exogenously supplied sulfides or overexpression of the H_2S biogenesis enzymes have been observed to impart protection against antibiotic-induced oxidative stress. The pathway through which such protection is imparted is still poorly known.

The class of enzyme that transfers a sulfur atom from one molecule to another and contributes to the biogenesis of RSS and H_2S are the two closely related sulfurtransferases - Thiosulfate sulfurtransferase (TST) and 3-mercpatopyruvate sulfurtransferase (3-MST). TST uses thiosulfate ($S_2O_3^{2-}$) and 3-MST uses 3-mercpatopyruvate (derived from cysteine catabolism) as the source of sulfur for catalysing sulfur-transfer reactions.

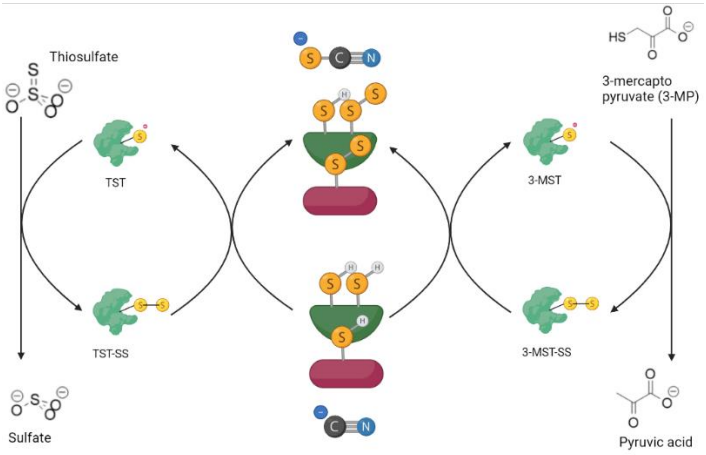


Figure 3: The sulfur transfer reaction catalysed by Sulfurtransferases

To better understand the physiological and mechanistic differences between 3-MST and TSTs in the cellular context, we explore the structure-sequence-function relationship between a host of

their bacterial homologues. Both TST and 3-MST contain the Rhodanese domain, a structural fold associated with the function of sulfur transfer. A functionally active Rhodanese domain contains at its active site a conserved and catalytically active cysteine residue which launches a nucleophilic attack on the S of the substrate (either 3-MP or $S_2O_3^{2-}$). We found that the structural organization of 3-MST and TSTs are quite divergent across homologues while the fold remains highly conserved. The prokaryotic TSTs are mostly single domain Rhodanese while all the prokaryotic and eukaryotic 3-MSTs have tandem repeat of the Rhodanese domain. Interestingly, the tandem repeat-Rhodaneses have only one domain active while the structurally similar second domain is likely inactive. In this regard, we examined the phylogenetic relationship between the two enzymes and tried to under the relationship between the single domain of TST and the two domains of 3-MST in the model organism *Escherichia coli*. Further, we conducted preliminary investigations of the physiological and structural differences between the single domain TSTs (*glpE*, *pspE*) and 3-MST (*sseA*) along with *in vitro* characterization of a select 3-MST and TST homologues. Finally, we have examined the physiological role of these enzymes in *Escherichia coli* in the presence of a variable range of sulfur sources. Such a study will allow us to present an integrated molecular understanding of cellular sulfur metabolism and subsequently design activators and inhibitors that control sulfur homeostasis in bacteria.

Reference:

1. Filipovic, M. R., Zivanovic, J., Alvarez, B., & Banerjee, R. (2018). Chemical Biology of H2S Signaling through Persulfidation. In *Chemical Reviews* (Vol. 118, Issue 3, pp. 1253–1337). American Chemical Society. https://doi.org/10.1021/acs.chemrev.7b00205
2. Cipollone, R., Ascenzi, P., & Visca, P. (2007). Common themes and variations in the rhodanese superfamily. In *IUBMB Life* (Vol. 59, Issue 2, pp. 51–59). https://doi.org/10.1080/15216540701206859
3. Shukla, P., Khodade, V. S., Sharathchandra, M., Chauhan, P., Mishra, S., Siddaramappa, S., Pradeep, B. E., Singh, A., & Chakrapani, H. (2017). “on demand” redox buffering by H2S contributes to antibiotic resistance revealed by a bacteria-specific H2S donor. *Chemical Science*, *8*(7), 4967–4972. https://doi.org/10.1039/c7sc00873b
4. Bora, P., Manna, S., Nair, M. A., Sathe, R. R. M., Singh, S., Sreyas Adury, V. S., Gupta, K., Mukherjee, A., Saini, D. K., Kamat, S. S., Hazra, A. B., & Chakrapani, H. (2021). Leveraging an enzyme/artificial substrate system to enhance cellular persulfides and mitigate neuroinflammation. *Chemical Science*, *12*(39), 12939–12949. https://doi.org/10.1039/d1sc03828a

An enzyme engineering approach to the biosynthesis and utilization of FAD nucleobase analogues

Ateek Shah and Amrita B. Hazra*

Indian Institute of Science Education and Research (IISER) Pune, Dr. HomiBhabha Road, Pashan, Pune - 411008, India

Email: ateek.shah@students.iiserpune.ac.in

Coenzymes such as flavin adenine dinucleotide (FAD), S-adenosyl methionine(SAM), and nicotinamide adenine dinucleotide (NAD) conduct very different cellular functions, yet they contain in common the nucleoside adenosine in their structure. Thesource of adenosine for the biosynthesis of these coenzymes is adenosine triphosphate (ATP). Even though nucleotide triphosphates (NTPs) such as ATP, GTP,CTP, and UTP differ from one another only on the basis of the nucleobase, high selectivity exists for the choice of nucleotide in various enzymatic reactions. In this work, we specifically probe the molecular, mechanistic, and physiological basis of thechoice of NTP in the FAD biosynthesis pathway.

The biosynthesis of FAD typically utilizes two molecules of ATP - the first one activates riboflavin (vitamin B2) to form flavin mononucleotide (FMN), and the secondone couples with FMN to form FAD. Both these steps require a divalent metal ion specifically magnesium ion (Mg^{2+}) for the reaction to succeed; however, other metal ions such as Fe^{2+} and Co^{2+} can also be tolerated. We interrogated the choice of NTP for the second step in FAD biosynthesis using *E. coli* FAD synthetase, a bifunctional enzyme that converts riboflavin to FMN using the riboflavin kinase domain followed byadenylation resulting FAD in the FMN adenylyl transferase (FMNAT) domain. We haveengineered the FMNAT domain to produce mutants with altered NTP specificity whichsynthesize FAD nucleobase analogues under *in vitro* conditions. Heterologous expression of these mutants in *E. coli* demonstrates the synthesis of the FADnucleobase analogue within cells. Finally, on replacing the native FAD synthetase onthe bacterial genome with the mutant, we observe the biosynthesis of FAD nucleobaseanalogues. This mutant strain survives better under antibiotic stress of aminoglycosides and β-lactam such as streptomycin and ampicillin showing antibioticresistance. Conventional methods for creating antibacterial agents rely on blocking crucial mechanisms associated with antibiotic resistance, which makes it important tounderstand how unnatural molecules, such as FAD nucleobase analogues, aid antibiotic resistance, which can help increase antibiotics' efficacy. Besides this, the biosynthesis of FAD nucleobase analogues lays the foundation for their use instudying the molecular role of FAD in cellular metabolism and as bio-orthogonal reagents in biotechnology and synthetic biology.

Design, Synthesis and Mechanistic Insights of Manganese (I) Based Photoactivable Carbon Monoxide (CO) Releasing Complexes

Pranali Dhotre and Govindasamy Mugesh*

Department of Inorganic & Physical Chemistry, Indian Institute of Science Bangalore.

pranalid@iisc.ac.in, mugesh@iisc.ac.in

Carbon monoxide (CO) is a known gasotransmitters like nitric oxide (NO), hydrogen sulphide (H_2S). It is produced endogenously in mammals as a result of haem catabolism via the breakdown of haem by using haem oxygenase enzyme (HO-1, HO-2, HO-3). It has been reported that CO has remarkable effect in biological processes like vasodilation, redox signalling, inhibition of platelet aggregation etc. in lower (nM range) concentration, and for anti-cancer application in slightly higher concentration (μM range). Due to lack of target specificity in direct inhalation of CO gas, researchers have focussed on synthesizing CO releasing molecules. Among those, organometallic CO releasing complexes have been widely synthesized which release CO by various stimuli like enzyme, solvent, pH, light etc. As biologically CO is sensitive to its concentration, controlled release of CO is very important for practical applications. Metal complexes provide handle to control their CO release behaviour by tuning the ligands as required.

Various CO donors have been used as anti-cancer agents. Here, we plan to explore vasodilatory response of CO donor metal complexes in endothelial cells. For this purpose, we have synthesised a series of manganese (I) based photo CO releasing complexes by varying bidentate ligand with single element change in ligand moiety, symmetric ligand and ligand with increasing conjugation for red shift in MLCT absorbance. Their CO releasing ability has been determined by irradiating visible light (Blue light 420-480 nm). Quantification of CO released is done by myoglobin (Mb) assay. Further, to evaluate the rate of CO released we studied the factors affecting CO releasing rate like solvent, temperature, pH of solution and light (white light 400-800 nm). For mechanistic study we examined real time change in IR, NMR with irradiation.

In my poster, I will be discussing how a single atom change in the ligand can alter the electron density on the metal centre which eventually affect MLCT and rate of release of CO. This data is also supported by theoretical studies (DFT and TDDFT).

References:

1. U Schatzschneider *Br. J. Pharmacol.* **2015**,*172*, 1638.
2. M. N. Pinto, P. K. Mascharak, *J. Photochem. Photobio. C: Photochem. Rev.* **2020**, *42* ,100341.
3. S. J. Carrington, I. Chakraborty, J. M. L. Bernard, P. K. Mascharak *ACS Med. Chem. Lett.* **2014**, *5*, 1324.
4. M. Hu, Y. Yan, B. Zhu, F. Chang, S. Yu, G. Alatan, *RSC Adv.* **2019**, *9*, 20505.

A "synthetic" approach to understanding vitamin B_1 biosynthesis and the effect of nutrient availability on patterning microbial communities that rely on vitamin B_1 exchange

Shweta Nikhar and Amrita Hazra

Department of Chemistry, Indian Institute of Science Education and Research (IISER) Pune, Dr. Homi Bhabha Road, Pashan, Pune - 411008

Microbial cocultures or consortia are a group of interacting microbial populations found in diverse environmental niches. Microbial community members routinely exchange nutrients among themselves. Such co-operation and division of labor is widespread in nature, leading to positive and negative interactions between consortia members. The exchange of biomolecules such as sugar, amino acids, vitamins, and fermentation by-products occurs commonly between natural and synthetic microbial consortia members. In our lab, we aim to understand the various modes and mechanisms by which vitamin B1 (thiamin) and its intermediates are exchanged within members of microbial co-cultures. Vitamin B_1 is composed of two rings - 4-amino-5-hydroxymethyl-2-methyl pyrimidine (HMP) and 4-methyl-5-(2-hydroxyethyl) thiazole (THZ) - which are then enzymatically coupled together to produce B_1. While HMP is synthesized *de novo* using mainly one enzyme, THZ biosynthesis employs six different enzymes. Besides these, various transporters and kinases salvage the two intermediates and produce thiamin.

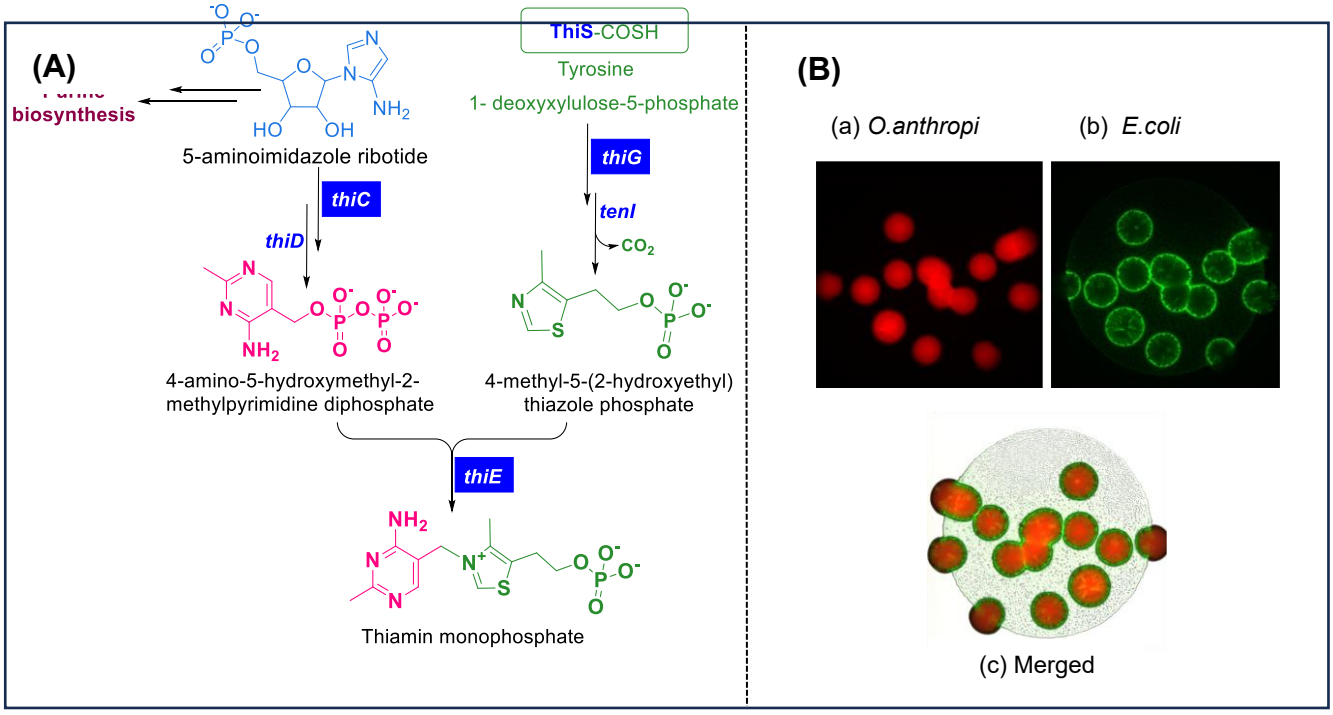


Figure:(A) Thiamin biosynthesis pathways in *E. coli* K-12 MG1655 (B) Visualizing the coculture pattern of *E.coli* (GFP) and *O.anthropi* (mCherry)

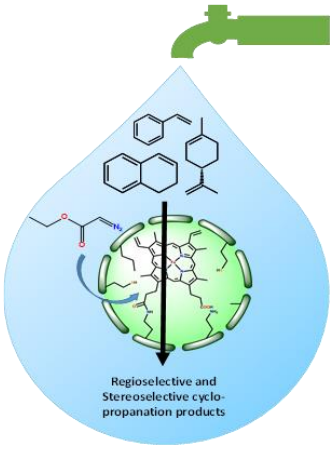
To understand the routes and mechanisms by which thiamin and its intermediates are exchanged, we established a defined series of thiamin-dependent synthetic cocultures using *Escherichia coli* thiamin biosynthesis pathway mutants. Growth assays and fluorescence studies with these co-cultures allowed us to establish that thiamin and HMP are easily exchanged, while THZ exchange is restricted within microbial communities. In this study, I present some quantitative studies to understand how microbial co-cultures evolve when thiamin is available versus not provided in the growth medium. *Ochrobactrum anthropi* lacks a *thiC* gene and hence is a natural HMP auxotroph. We have studied the coculture pattern between *Escherichia coli* mutants and *Ochrobactrum anthropi* with different nutrient availability. Such an analysis of vitamin B_1 biosynthesis in synthetic co-cultures will allow for understanding the general rules of nutrient cross-feeding among members in a community while facilitating the design of synthetic communities for various biotechnological applications.

Heterogeneous Stereoselective catalytic cyclopropanation of structurally diverse alkenes in aqueous medium

Atish Bhattacharyya[a], *Shyamalava Mazumdar*[a]*

[a] Department of Chemical Sciences, Tata Institute of Fundamental Research, Homi Bhabha Road, Colaba, Mumbai 400005, India

atish.bhattacharyya@tifr.res.in, **shyamal@tifr.res.in*



In recent years, sustainable approaches to chemical synthesis using bio-catalysts have gained interest. Metal porphyrins in biological catalysts have shown high catalytic efficiency, regioselectivity, and stereoselectivity in suitable environments, making them highly valuable for cyclopropanation. However, the availability of stable enzymes that can catalyze multiple useful reactions is limited [1]. Enzyme mimics have been used in green chemistry to achieve stereoselective reactions, but they face challenges such as lower catalytic activity and limited long-term stability [2].

Our goal is to develop a heterogeneous catalyst for cyclopropanation in an aqueous medium by utilizing metal-porphyrins within confined spaces, such as silica core-shell structures, to achieve high stereoselectivity [2].

In this study, we specifically investigated -NH2 and -CH3 functionalized silica, which are highly water-stable and capable of creating a hydrophobic asymmetric environment around the immobilize metal-porphyrins. We utilize the readily available metal-porphyrin, Hemin, as the catalytic center. We have observed an increase in the longevity, recyclability of the catalyst due to its easy recovery and regeneration from the reaction mixture with high trans selectivity.

References:

[1] Coelho PS, Brustad EM, Kannan A, Arnold FH, Science, 2013 Jan 18; 339 (6117): 307-10

[2] Chen, X., Zhao, T. & Zou, J., *Microchim Acta* **164**, 93–99 (2009)

Tuning the Electronics of Bis(tridentate)ruthenium(II) Complexes with high ROS ($^1O_2$) generation: Modification tothe Ligand Skeleton with varying the Aromaticity beyond Classical Extended π–Conjugation Group Decoration

Abhijit Saha and Ashis K. Patra*

Department of Chemistry, Indian Institute of Technology Kanpur – 208016.

Email: asaha@iitk.ac.in

Ruthenium(II)-polypyridine complexes with extended π-conjugation are known to exhibit high $^1O_2$ generation quantum yield (Φ_Δ) by visible light absorption, which is making them useful as potential PDT agents.[1-3] Herein, we have designed and synthesized 8-hydroxyquinoline (8-HQ) based monoanionic N,N,O- chelating tridentate ligands [8HQbzX = **1-H**(8HQbzthiazole), **2- H**(8HQbzimidazole), **3-H**(8HQbzoxazole)] with varying the aromaticity in the heterocyclic azolering. These new classes of chromophores are promising regarding their tunable redox properties and intense visible absorption. Preparation of three new bis(heteroleptic)Ru(II)-complexes namedas **Ru1**, **Ru2**, and **Ru3** have been shown here, which exhibited strong Ru(dπ) → 8HQbzX(π*) metal-to-ligand-charge transfer (MLCT) absorption with maxima at 546 nm, 530 nm, and 535 nmin acetonitrile for **Ru1**, **Ru2**, and **Ru3** respectively, red-shifted from the Ru(dπ) → ttpy(π*) absorption at 490 nm observed for $[Ru(ttpy)_2]^{2+}$ in the same solvent, where; ttpy = *p*-tolyl- terpyridine. The electrochemical behavior of the Ru-complexes of 8-HQ derivatives is highly dependent on the charge of the central metal atom that will strongly influence its ground state oxidation potential. We observe a steady decrease in Ru^{II}/Ru^{III} oxidation potential from +1.25 V for $[Ru^{II}(ttpy)_2]^{2+}$ to +0.72 V for $[Ru^{II}(ttpy)(\mathbf{1})]^+$, to +0.63 V for $[Ru^{II}(ttpy)(\mathbf{2})]^+$, to +0.75 V for $[Ru^{II}(ttpy)(\mathbf{3})]^+$ respectively as the monoanionic 8-HQ analogue are introduced around the ruthenium centre. Generation of singlet oxygen ($^1O_2$) by the complexes in presence of the green LED light (λ_{irr} = 530nm) has been determined by a chemical trapping method using DPBF (1,3- diphenylisobenzofuran) as a probe by UV-vis spectrophotometer. For the determination of $^1O_2$ - generation quantum yield (Φ_Δ) of the complexes, $[Ru(bpy)_3]^{2+}$ (Φ_Δ = 0.57 in CH_3CN) used as a reference.[4-5]

References:

1. Maria C. DeRosa, and Robert J. Crutchley, *Coord. Chem. Rev.* **2002**, *233-234*, 351-371.
2. Yao Liu, Richard Hammit, Daniel A. Lutterman, Lauren E. Joyce, Randolph P. Thummel, andClaudia

Turro, *Inorg. Chem.* **2009**, *48*, 375-385.
3. Thomas N. Rohrabaugh, Jr., Kelsey A. Collins, Congcong Xue, Jessica K. White, Jeremy J. Kodanko, and Claudia Turro, *Dalton Trans.* **2018**, *47,* 11851-11858.
4. Priyaranjan Kumar, Prerana Singh, Sanjoy Saren, Sandip Pakira, Sri Sivakumar, and Ashis K.Patra, *Dalton Trans.* **2021**, *50*, 8196-8217.
5. Robin Vinck, Albert Gandioso, Pierre Burckel, Bruno Saubamea, Kevin Cariou, and Gilles Gasser, *Inorg. Chem.* **2022**, *61*, 13576-13585.

Deciphering the catalytic function of a versatile Redox Enzyme: Fungal CytochromeP450 Reductase

Kalpana Rajendran,[a] Dr. Debasis Das*

[a]Department of inorganic and physical chemistry,

Indian Institute of Science, Bangalore, India.

Abstract:

Cytochrome P450 reductase (CPR) are flavin containing redox enzymes that play predominant role in propagating the electron transfer from NADPH to many partner proteins, such as Cytochrome P450 monooxygenase (CYP450) and heme oxygenase. CPR enzymes are composed of four distinct domains, the N-terminal transmembrane segment, followed by the FMN, FAD and NADPH binding domains. These enzymes are reported to reduce other proteins that are present inside the cell, like Cytochrome b5, cytochrome C and few more involved in fatty acid elongation system. Recent studies have shown that CPRs could also metabolize nitro compounds, anti-cancer drugs, and aromatic azo compounds, demonstrating the versatility of CPR enzymes[1]. Although these enzymes were represented as typical electron transfer proteins, their practical applicability was hampered by its dependency on the expensive co-factor NADPH and importantly their self-catalytic ability are relatively obscure. Hence, we aimed to explore the catalytic activity of a potential CPR enzyme from fungal origin, which is reported to be involved in microbial drug biotransformation. We also aimed to overcome the requirement of expensive NADPH, which always remained a huge hurdle on the applicability of these CPR enzymes. Hence, in order to get insight into the catalytic function and to unveil the true potential, we purified the fungal NADPH-dependent CPR enzyme by over expressing it in simple *E.coli* host. We evaluated the enzyme activity with different substrates, including the non-physiological and physiological model substrates such as ferric cyanide, MTT, PMS, DCIP and Cytochrome C, respectively. We found that the purified CPR enzyme was able to catalyze the divalent reduction of nitro compounds, anti-cancer drugs, dyes with tetrazolium rings and azo compounds by utilizing NADPH as co-factor. Next, we then evaluated the auxiliary activity of purified CPR with CYP450 decarboxylase enzyme. Further, to overcome the requirement of NADPH for catalysis, we planned to fuel the enzyme activity by light, by developing a Photobiocatalytic system[2,3]. To our surprise the enzyme also exhibited significant photo-biocatalytic activity, that was not previously observed in CPR class of enzymes, thereby highlighting the importance and versatility and promiscuity of our

purified CPR enzyme. Though CPR is from fungal origin, it excellently supported the photo-biocatalytic auxiliary activity of bacterial heme-containing and diiron containing decarboxylases enzymes. Next, by utilizing the enzyme's innate ability of nitro reduction, we tried to enlarge its synthetic scope to catalyze some pharmaceutically important nitro-compounds through photo-biocatalysis. Further we have also carried out the mechanistic studies and protein engineering studies for better understanding of the electron transfer pathway and the intermediates involved in accomplishing the light-mediated activity. Overall, our findings would provide new insights into the diverse function of purified CPR enzyme, representing the first example of a photo-induced CPR system.

References:

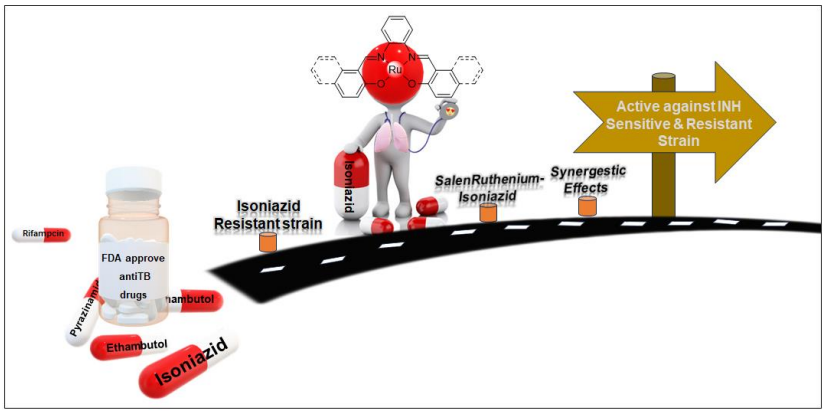
(1) Roth, S., Niese, R., Müller, M. and Hall, M., Redox Out of the Box: Catalytic Versatility Across NAD (P) H-Dependent Oxidoreductases. ***Angewandte Chemie***, **2023.**
(2) Harrison, W., Huang, X. and Zhao, H., Photobiocatalysis for abiological transformations. ***Accounts of chemical research***, **2022.**
(3) Lujan, A.P., Bhat, M.F., Tsaturyan, S., van Merkerk, R., Fu, H. and Poelarends, G.J., Tailored photoenzymatic systems for selective reduction of aliphatic and aromatic nitro compounds fueled by light. ***Nature Communications***, **2023.**

Synergistic effects of Ruthenium salen isoniazid complexes against Isoniazid sensitive and isoniazid-resistant strain

Juhi Sayala[a], Nitin Shukla[a], A. K. Patra[a*]
Email: akpatra@iitk.ac.in, juhi@iitk.ac.in
[a]Department of Chemistry, India
Institute of Technology Kanpur, Kanpur-208016, India

Ruthenium's pharmacologically favorable oxidation states (II–IV) under physiological conditions, with low interconversion energy barriers, enable rapid cellular state changes.[1, 2, 3] Ruthenium(III) complexes offer diverse drug design opportunities due to variable oxidation states, tunable electronic structures, and favorable physicochemical properties. Novel anti-TB drugs are crucial for overcoming tuberculosis challenges, including patient nonadherence, treatment side effects, MDR and XDR strains, drug interactions, and latent bacteria. Coordinating INH with metal complexes is a potential strategy to address issues related to INH therapy.[4]

Herein, we present a series of tetradentate Ru(II)-salen complexes: $[Ru(N_2O_2)(INH)]PF_6$ constructed salen; tetradentate ligands as cage for the Ruthenium isoniazid complxes and an N-donor isoniazid (INH) ligand (FDA approved antiTB drug). The complexes were thoroughly characterized and their physicochemical and photophysical properties were extensively studied. These salen ligands stabilize the Ruthenium complexes in higher oxidation state. Ruthenium complexes exhibiting activity against INH resistant strains. Mechanistic study of ruthenium complexes against Tuberculosis studied thoroughly via different techniques.



Keywords: Synergistic effects, Antituberculosis activity, Isoniazid.

References:

1 A. Bergamo, G. Sava, *Dalton Trans.,* 2011, **40**, 7817-7823.

2 P. Kumar, P. Singh, S. Saren, S. Pakira, S. Sivakumar, A. K. Patra, *Dalton Trans.,* 2021, **50**, 8196-8217.

3 P. Kumar, P. Singh, S. Saren, J. Sayala, S. Sivakumar, A. K. Patra, *Dalton Trans.*, 2022, **51,** 18416–18437.

4 A. Tavares, W. Franco, *J. Biol. Inorg. Chem.,* 2014, **140**, 236-244.

A comparative Study on Photo-triggered Release of Different Types of Symmetrical Bidentate Ligands from Heteroleptic Ru(II) Terpyridyl Systems

Pritha Chatterjee, Ramranjan Mishra, Ashis K. Patra*

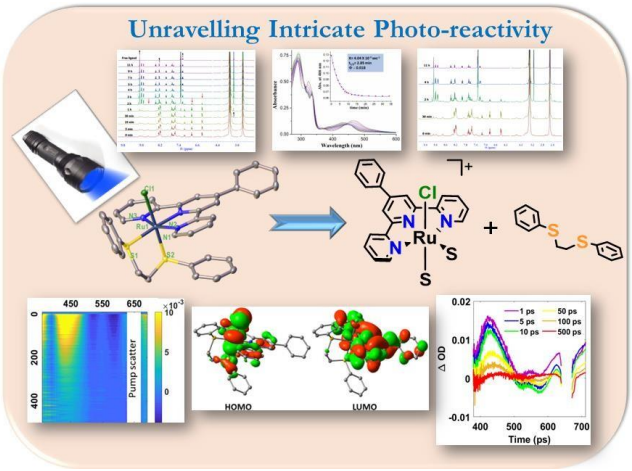
Department of Chemistry, Indian Institute of Technology Kanpur, Kanpur-208016, UttarPradesh, India

E-mail: prithac20@iitk.ac.in

Photochemistry of ruthenium(II) polypyridyl complexes has widespread and versatile applications in energy storage, solar energy conversion, photocatalysis, photochromic switching, etc.[1] From thelast few decades light has been used extensively as a trigger to activate metal-based anticancer agents.[2] Ru(II)-polypyridyl complexes have been extensively used in the field of photoactivated chemotherapy due to their unique and tunable excited state properties.

Photosubstitution of the bidentate ligand is more challenging than the monodentate ones due to thechelate effect. Several groups reported the photorelease of bidentate ligands from [Ru(L2)3] type complexes where Ru(II) is coordinated to three bidentate ligands.[3,4,5] The introduction of a tridentate ligand like N3-donor terpyridine serves to attribute steric strain around the metal centredue to it's smaller bite angle compared to ideal [Ru(L2)3] octahedral geometry, which increases therate of such photoreactivity.[6] The photorelease of bidentate ligands by incorporating such steric strain using tridentate N3-donors is yet to be explored in literature.

Herein, we have strategically synthesized and well-characterized four complexes having general formula [Ru(ptpy)(L-L)Cl]PF6 (ptpy = phenyl terpyridine), with four electronically different bidentate ligands: L-L =1,2-Bis(phenylthio)ethane, L-L = *N,N,N',N'*-Tetramethylethylenediamine,L-L = Bis[2-(diphenylphosphino)phenyl] Ether and L-L = N^1,N^2-Diphenylethane-1,2-diimine. Here we have used both amine and imine type of *N,N*-donor ligands. We have only observed thephoto-release of S^S and N^N (amine) bidentate ligands. I will present the synthesis, characterization, molecular structures, and comparative photochemical reactivity in different typesof coordinating solvents like DMSO, acetonitrile and pyridine by time-dependent UV-Vis and NMR spectroscopy. DFT calculations were also used to rationalize the photophysical and electrochemical properties. We observed that the photoreactivity of thioether (S^S)-based Ru(II) complex is faster than diamine-based (N^N) Ru(II) complex in all the solvents as well as the lifetime of the ^{3}MLCT state of $[Ru(ptpy)(S^S)Cl]^+$ is lower than diamine based complex as predicted by transient absorption spectroscopy.



References:

1. Bonnet et al., *Dalton Trans.*, **2017**, *46*, 9969–9980.
2. Gasser et al., *Chem. Sci.*, **2015**, *6*, 2660–2686.
3. Glazer et al., *J. Am. Chem. Soc.*, **2012**, *134*, 8324–8327.
4. Bonnet et al., *Chem. Commun.*, **2017**, *53*, 6768–6771.
5. Turro et al., *Inorg. Chem.*, **2011**, *50*, 4384–4391.
6. McMillin et al., *Inorg. Chem.*, **1991**, *30*, 659–666.

Investigation and comparison of *in vitro* and *in silico* methods shed light on antimicrobial properties exhibited by curcumin and its transition metal complexes.

[1]Tanmoy Saha and [2]Saurabh Das

[1]PhD research Scholar, Department of Chemistry, (Inorganic Section), Jadavpur University, Kolkata-700032, India

[2]Professor, Department of Chemistry, (Inorganic Section), Jadavpur University, Kolkata-700032, India

Abstract

Curcumin possesses an intriguing molecular structure that exhibits a diverse range of therapeutic potentials. However, therapeutic implications of this substance are significantly impeded due to its suboptimal bio-availability that may be attributed to its inherent instability and limited solubility in aqueous environment. In a valiant endeavour to surmount this intrinsic constraint and cultivate curcumin-derived antibacterial agents, we have successfully synthesized and thoroughly investigated metal complexes comprising copper (II) and zinc (II) in conjunction with curcumin. The structural framework was established through utilisation of Density Functional Theory (DFT) calculation. In the present investigation, we undertook a comprehensive examination of the complexes, namely Cu(Cur) and Zn(Cur), with a particular focus on their stability and antibacterial efficacy. Furthermore, we endeavoured to elucidate the potential mechanism of action of these complexes, drawing insightful comparisons to the parent compound, Curcumin. The phenomenon of complex formation yielded enhanced stability across a range of diverse physiological conditions. The enhanced stability was corroborated through the utilisation of UV–Vis spectroscopy and HPLC techniques. By achieving an enhanced stability under biological conditions, it was observed both Cu(Cur) and Zn(Cur) demonstrated remarkable and significantly amplified efficacy in comparison to curcumin when combating both *E. coli* and *S. aureus*. An *in vitro* Calcein leakage assay provided evidence indicating that the complex in question induced prompt membrane permeabilization in bacterium *Staphylococcus aureus*. The veracity of this mode of action that disrupts the membrane was further substantiated through utilisation of microscopic visualisation techniques. Through an *in silico* investigation, it was identified that Curcumin, along with metal complexes possess the ability to effectively engage with FtsZ Proteins, consequently impeding the process of FtsZ protofilament assembly. Consequently, suppression of Z-ring formation ensues, resulting in the inhibition of cytokinesis and impeding bacterial proliferation. The remarkable efficacy of the complexes, enhanced over that of Curcumin, by their favourable toxicological profile, characterised by their lack of hemolytic and cytotoxic effects on mammalian cells is worthy of further pursuation, rendering them a highly promising contender for *in vivo* studies. In its entirety, this study represents a discerning evaluation that champions the antimicrobial capacity of this enduring, membrane-focused and

innocuous compounds, introducing novel viewpoints for a therapeutic utilisation in combating bacterial infections.

References

5. ***T.Saha****, S.Sappati, S.Das, An insight into the mixed quantum mechanical-molecular dynamic simulation of a Zn^{II}-Curcumin complex with a chosen DNA sequence that supports experimental DNA binding investigations,* ***International Journal of Biological Macromolecules****, **2023**, 245 125305*

6. P.Kumar, **T.Saha**, S,Behara, S.Gupta,S.Das, K.Mukhopadhyay, Enhanced efficacy of a Cu2+ complex of curcumin against gram-positive and gram-negative bacteria: attributes of complex formation, ***Journal of Inorganic Biochemistry,*** **2021**,222,111494

7. **T. Saha,** S. Singha, S, Kumar, S. Das, Spectroscopy driven DFT computation for a structure of the monomeric Cu^{2+}-Curcumin complex and thermodynamics driven evaluation of its binding to DNA: Pseudo-binding of Curcumin to DNA. **Jour. Mol. Struc**., **2020**, **1221**, 128732.
8. **T.Saha,** P.Kumar, N.Sepay, D.Ganguly, K.Tiwari, K.Mukhopadhyay, S.Das, Multitargeting antibacterial activity of a synthesized Mn^{2+} complex of curcumin on gram-positive and gram-negative bacterial strains, ***ACS omega***., **2020**, 5, 27, 16342-16357

Determining the Redox Potential of Heme, Embedded in Bacterioferritin Protein Shell, by Spectrophotometry: An Alternative Approach to Electrochemistry

Swagatika Mallik, Rabindra Kumar Behera*

National Institute of Technology Rourkela -769008, Odisha, India

Iron homeostasis is critical to both host and pathogen, where ferritins play a vital role. These protein nanocages sequester excess toxic, free iron and store them as iron biominerals. While higher organisms synthesize only non-heme ferritin, bacteria such as *Mycobacterium tuberculosis*, the causative agent of tuberculosis, expresses both heme and non-heme binding ferritins. However, the exact role of heme remains an enigma despite our recent finding i.e. increasing heme content increases reductive iron release, suggesting its possible role as an electron mediator [1]. Therefore, determining the reduction potential ($E_{1/2}$) of heme in bacterioferritin becomes crucial. However, the electrode based analytical methods were found to be unsuccessful, as protein cage prevented heme-electrode contact. Here, we report a spectrophotometric method (dye + enzyme based), which not only maintains anaerobic conditions but also facilitates heme reduction to determine the $E_{1/2}$ value. Further, the impact of co-axial ligands (Met/Met) and caged iron mineral on heme reduction potential were also investigated. Interestingly, the $E_{1/2}$ values of heme in wild-type, its coaxial variant and iron loaded bacterioferritin is found to be negative, which are further rationalized based on structural and spectroscopic analysis. These findings may not only help to understand the role of heme but also will guide to choose suitable reducing agent, manipulate the heme environment for controlling microbial growth and developing bacterioferritin cage towards, new, non-natural functions [2-3].

References

1. Behera *et al*. Alteration of Coaxial Heme Ligands Reveals the Role of Heme in Bacterioferritin from Mycobacterium tuberculosis. *Inorganic Chemistry* **2020**, 59, 1, 629-641.
2. Lu *et al*. Metalloproteins Containing Cytochrome, Iron−Sulfur, or Copper Redox Centers. *Chem. Rev.* **2014**, 114, 8, 4366–4469.
3. Dey *et al*. Introduction: Catalysis beyond the First Coordination Sphere. *Chem. Rev*. **2022**, 122, 14, 11897–11899.

Iron Mobilization from Intact Ferritin: Effect of Differential Redox Activity of Quinone Derivatives

Narmada Behera, Rabindra Kumar Behera*

National Institute of Technology Rourkela-769008, Odisha, India

Ferritins are nanocage proteins that sequester and concentrate excess free iron as ferric oxy-hydroxide biomineral in its central nanocavity and functions as cellular storehouse [1]. Although ferritin releases iron in a controlled fashion for various cellular metabolic activities, the mechanism of its release, *in vivo*, remains unclear and debatable. Reductive iron mobilization from the intact ferritin cage can be a reasonable pathway/possibility *in vivo*, due to the reducing nature of the cytosol. However, NADH, a physiological reducing agent was not sufficient to mobilize significant amount of ferritin iron, when used alone [2]. Therefore, the current work utilizes a series of quinone (as electron mediator), in conjugation with NADH, that differ in size, substituents and reduction potential, to facilitate the reductive iron mobilization, *in vitro*. Quinones are versatile electron mediators that facilitate important biological processes by undergoing both 1 and 2 electron transfer steps. Our result on structure-reactivity of quinone mediators highlight at-least two important findings: 1. Electron relay depends on midpoint potential ($E_{1/2}$) value i.e. quinones with $E_{1/2}$ values lying at a favorable range (not too close not too far) with respect to NADH exhibited better electron relay, 2. Iron release is dictated by molecular structure i.e. quinones with chelation sites releases higher amounts of iron, by reductive pathway. Further, the impact of in situ generated ROS viz. superoxide ($O_2^{\bullet-}$), peroxide (H_2O_2) and intermediates (semiquinone) were analyzed and correlated with the kinetics of iron release. This quinone mediated iron mobilization can not only be exploited for iron removal during biological iron overload conditions but also provides insight towards plant/microbial iron acquisition processes to control their growth.

References

1. Theil, E. C.; Tosha, T.; Behera, R. K., Solving Biology's Iron Chemistry Problem with Ferritin Protein Nanocages. *Acc Chem Res* **2016,** *49* (5), 784-91.

2. Koochana, P. K.; Mohanty, A.; Parida, A.; Behera, N.; Behera, P. M.; Dixit, A.; Behera, R. K., Flavin-mediated reductive iron mobilization from frog M and Mycobacterial ferritins: impact of their size, charge and reactivities with NADH/O(2). *J Biol Inorg Chem* **2021,** *26* (2-3), 265-281.

Rapid Ferroxidase Activity and Iron Mineralization in Ferritin: Impact of Intrinsic Electron Relay Stations

Gargee Bhattacharyya, Biswamaitree Subhadarshanee, Rabindra Kumar Behera*

National Institute of Technology, Rourkela-769008, Odisha, India

Despite being an indispensable co-factor for myriad essential life functions, excess iron is toxic. To maintain the balance between its essentiality and toxicity, nature has devised a spherical nanocaged protein - 'ferritin' - that can store up to ~4500 iron atoms, reversibly, in the form of hydrated ferric oxyhydroxide mineral and facilitate controlled iron release to support physiological processes [1,2]. The ferroxidase/mineralization activity of ferritin and its mineral dissolution involves a complex interplay of redox reactions, possibly through long range electron transfer (ET), in multiple steps, *via* various electron relay stations (i.e., heme and intrinsic redox active amino acids of protein cage) [1,3]. Till date the mechanism and ET pathways in ferritin are not well-defined. Therefore, to better understand these ET pathways, we attempt to reveal the critical amino acids associated with its rapid ferroxidase and iron-mineralization activity by site directed mutagenesis (SDM) and stopped flow kinetics. Ferritin mutants with rational substitutions of its conserved/semi-conserved redox active amino acids have been successfully designed to study their impact on the iron oxidation/mineralization ability. All the synthesized ferritin variants were seen to retain their self-assembled form and iron-loading ability, but a drastic difference was seen in the rapid iron oxidation kinetic profiles of certain variants which indicates the possible role of these specific redox active amino acid residues in ET pathways. These findings not only helped to reveal critical amino acids residues and to understand the underlying mechanisms of ferritin iron mineralization but may also help in understanding the ET pathways associated with several other biological processes [4].

References:

1. Behera, R. K., Theil, E. C., *Proc Natl Acad Sci U S A*. **2014,** 111(22) 7925-7930.
2. Taher, M., Maity, B., Nakane, T., Abe, S., Ueno, T., Mazumdar, S., *Angew Chem Int Ed.* **2022**, 61(13) e202116623.
3. Bradley, J. M., Svistunenko, D. A., Lawson, T. L., Hemmings, A. M., Moore, G. R., Le Brun, N. E. *Angew. Chem. Int. Ed.* **2015***,* 54, 14763 –14767.
4. Gray, H. B., Winkler, J. R., *Proc Natl Acad Sci U S A*.**, 2015,** 112(35) 10920-10925.

Impact of Oxoanion on Formation and Dissolution of Iron Mineral: Implication in Understanding the Ferritin Core

Tanaya Subudhi, Rabindra Kumar Behera*

National Institute of Technology, Rourkela

Iron, a crucial element, is inextricably intertwined in various stages of living and non-living systems. Its existence in two different oxidation states (Fe^{2+}/Fe^{3+}) is not only a virtue but also troublesome (low solubility of Fe^{3+} at neutral pH and Fenton's reaction by Fe^{2+}). As a solution to this essentiality and toxicity dilemma, nature devised a globular multimeric protein nanocage: ferritin, to detoxify and store iron in soluble ferrihydrite bio-mineral form. Bio-minerals of native ferritins are associated with variable amounts of phosphate depending upon their source (Pi : Fe ~0.1 in animals, and Pi : Fe ~0.5 -1.0 in plant/bacteria). Whether the occurrence of a low Pi : Fe ratio in animal ferritins is just a coincidence or a consequence of ferritin electrostatics at the pore/cage is not well understood. Moreover, the natural selectivity of phosphate over other oxoanion is intriguing. Similar to phosphate other oxoanions may stabilize Fe^{3+} to modulate the redox and optoelectronic properties of bare and ferritin-encapsulated ferrihydrite minerals. Therefore, a comparison of bare and protein-encapsulated oxoanion-doped iron minerals may give insights into the impact of oxoanion on the structure, stability, and reactivity of iron bio-mineral. So a detailed investigation was performed on a series of oxoanion-doped ferrihydrite which closely resembles, the iron mineral found in nature. The physicochemical properties of oxoanion doped iron mineral were compared to justify their percentage incorporation by natural selection.

References:

1. Parida, A.; Mohanty, A.; Kansara, B.; Behera, R.K. *Inorganic Chemistry,* ***2020***, *59*, 629-641.

2. Hilton, R.J.,Zhang, B., Watt, G.D.; Watt, R.K. *Journal of inorganic biochemistry,* ***2012****, 108*, 8-14.

Gastric Stability of Bare and Biopolymer Fabricated Ferritin: Implication Towards Potential Dietary Iron Supplement

Rohit Kumar Raut, Rabindra Kumar Behera*

National Institute of Technology Rourkela-769008, Odisha, India

Anemia is a serious global public health problem affecting around 2 billion people worldwide. About 50% of anemic cases are related to iron deficiency anaemia (IDA), making it the most prevalent nutritional disorder [1]. The currently available oral iron supplements (mainly inorganic iron salts or complexes such as ferrous sulphate, ferrous ascorbate etc.) are taken in the form of a "Fe^{2+} burst," and are associated with oxidative stress, infections and gastrointestinal upsets. In this work, we investigated the gastric stability of "ferritins", for using them as potential dietary iron supplement to address these limitations. Ferritins - the cellular iron repositories - self-assembled protein nanocage architectures; are naturally bestowed with iron-scavenging (up to 4500 Fe atoms) and anti-oxidative properties [3, 4]. The *in vitro* data shows that though unmodified ferritins are quite resistant to conformational changes induced by acidic pH (in stomach environment), their cage integrity and mineral retention is compromised on longer incubation and higher concentrations of pepsin. To further retain its structural and functional aspects under gastric conditions, we fabricated the ferritins with an enteric coating biopolymer. The modified ferritins exhibited better cage integrity and slow iron release profile, implying that the biopolymer can potentially help ferritin proteins to stabilize and retain its iron bio-mineral content throughout the digestive tract, preventing any unwanted leakage till the intact ferritins are internalized/absorbed by intestinal receptors.

References:

1. WHO. *Accelerating anaemia reduction: a comprehensive framework for action.*; World Health Organization, Geneva, Switzerland, **2023**.

2. Crichton, R. The Essential Role of Iron in Biology. In *Iron Metabolism: From Molecular Mechanisms to Clinical Consequences*, Wiley, **2016**; p 22.

3. Theil, E. C.; Tosha, T.; Behera, R. K. Solving Biology's Iron Chemistry Problem with Ferritin Protein Nanocages. *Accounts of chemical research* **2016**, *49* (5), 784-791.

4. Parida, A.; Behera, R. K. Iron Accumulation in Ferritin. Methods in molecular biology **2023**, 2671, 121-134.

Monitoring Kinetics of Enzyme-catalyzed Reactions by Amperometry

Satyabrat Behera, Jonak Mahanta, Rabindra Kumar Behera*

National Institute of Technology, Rourkela-769008, Odisha, India

The Clark-type electrodes are regularly used to measure oxygen concentration in real time, both in liquid (dissolved O_2) and gaseous (pO_2) samples, based on the amperometric principle (i.e., the current measured at a constant voltage, is directly proportional to the concentration of the analyte). There are important metabolic/antioxidative enzymes, which either consume or generate O_2 during its catalytic cycle. For example, glucose oxidase (GOx) catalyses the oxidation of *β*-D-glucose to gluconic acid, by utilizing molecular O_2 (one of the substrates) as an electron acceptor. GOx as an enzyme has a wide range of industrial usage such as in food processing, glucose sensing, and fuel cells. This work investigates the enzymatic activity of GOx by using Clark-type electrode and determines various enzymatic parameters by implementing Michaelis-Menten kinetics to the dissolved O_2 consumption data. The kinetic parameters (K_M and k_{cat}) obtained from our amperometry based dissolved O_2 consumption correlates well with the reported values, obtained by other spectrophotometric and electroanalytical techniques.

Reference:

(1) Sierks M. R.; Bock, K.; Refn, S.; Svensson, B., Biochemistry **1992**, 31 (37), 8972-7.

A chemical model of TET enzyme for selective oxidation of hydroxymethyl cytosine to formyl cytosine

Dipanwita Palit, Shubhankar Kundu, Pritam Kumar Pain, Rajdeep Sarma,
Dr. Debasish Manna*
Department of Chemistry
Indian Institute of Science Education and Research Bhopal, Bhopal, MP-462066
Email: dmanna@iiserb.ac.in

Methylcytosine, an epigenetic modification of the genomic DNA, plays a crucial role in the modulation of DNA transcription and other genetic functions.[1] Methylation of the cytosine residue at 5th positions by DNA-methyl transferases (DNMTs) is extensively studied and well understood. But the TET-mediated (Ten Eleven Translocation enzyme) DNA-demethylation pathway, which upregulates gene expression, still holds questions to be answered. Although TET enzymes were discovered more than a decade ago, the mechanism of selective C-H activation by TET enzyme has remained a mystery. The large bond dissociation energy (BDE) of C-H bonds particularly makes it difficult to selectively cleave these bonds and study their mechanism.[2] Here, we have reported a Fe complex of tetra amido macrocyclic ligand (TAML), Fe^{III}TAML, which shows TET-like activity through selective oxidation of 5-hmC (hydroxymethylcytosine) to its oxidative derivatives by forming a high valent Fe-oxo intermediate in the presence of H_2O_2 under physiologically relevant conditions.[3] Detailed HPLC analysis provides us a wide reaction condition for the 5-hmC→5-fC (formylcytosine) oxidation which supports the Fe^{III}TAML as a chemical model of the TET enzyme.[4] This study shines the light for future efforts on better understanding of the roles of 5-hmC and the TET enzyme mechanism.

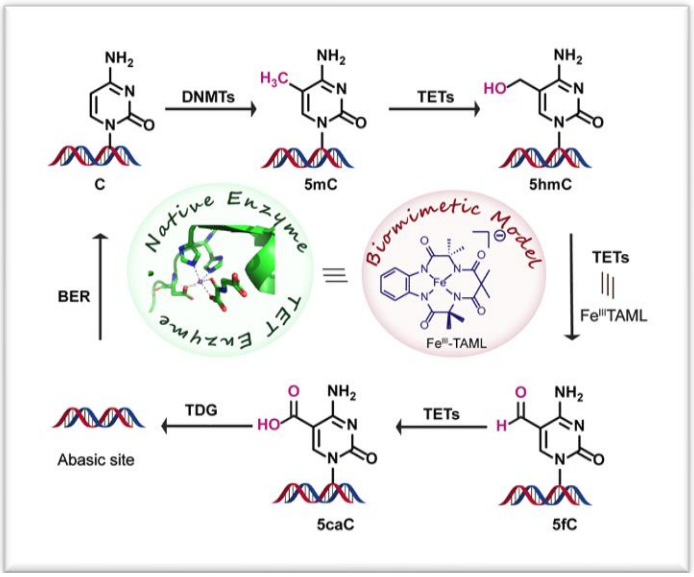


Figure 1 Cyclic representation of DNA methylation-TET mediated DNA demethylation and the structure of the chemical model of TET enzyme.

References:

(1) Smith, Z. D.; Meissner, A.; *Nat. Rev. Genet.* **2013**, *14*, 204-220.

(2) Sappa, S.; Dey, D.; Sudhamalla, B.; Islam, K.; *J. Am. Chem. Soc.* **2021**, *143*, 11891-11896.

(3) DeNardo, M. A.; Mills, M. R.; Ryabov, A. D.; and Collins, T. J.; *J. Am. Chem. Soc.* **2016**, *138*, 2933–2936.

(4) Palit, D.; Kundu, S.; Pain, P. K.; Sharma, R.; Manna, D.; *Inorg. Chem.* **2023**, *62*, 10039–10043.

Mechanistic Investigation and Engineering of a Membrane-Bound Hydrocarbon Producing Metalloenzyme

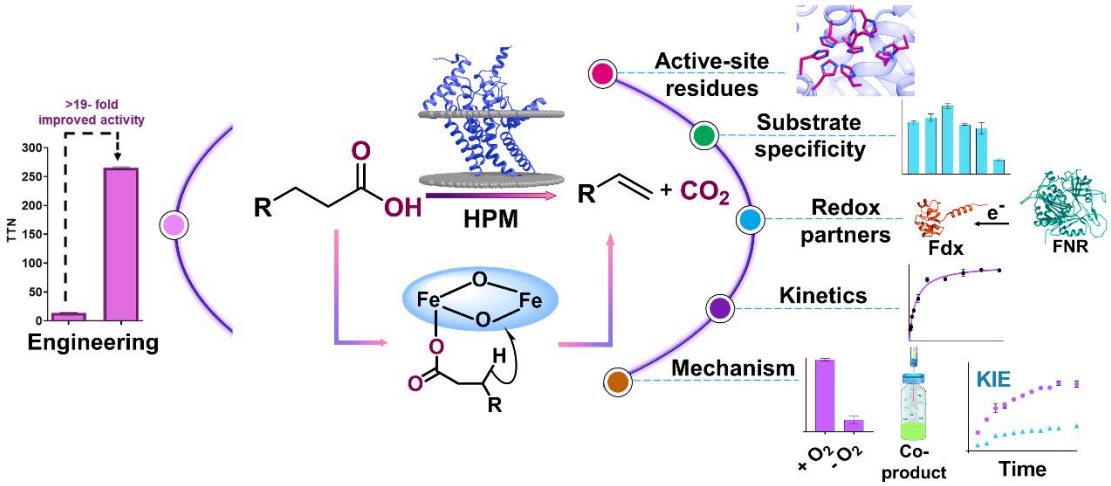
Tabish Iqbal

Indian Institute of Science (IISc), Bangalore-560012, India

The increasing concerns about global warming due to the use of fossil fuels have triggered enormous interest in developing renewable and eco-friendly biofuels. Since hydrocarbons such as alkanes/alkenes are the major components of fossil fuels, their biosynthesis in a sustainable fashion has gained tremendous attention in the past few decades.[1-3] In this regard, a membrane-bound hydrocarbon producing metalloenzyme (HPM) has gathered significant interest for the production of 1-alkenes. However, despite its importance, this enzyme has remained enigmatic due to its recalcitrant membrane-bound nature.[4, 5]

Recently, we have deciphered this enzyme's long-standing mystery.[6] In our studies, we have performed thorough biochemical investigation and deciphered the mechanistic plot of this enzyme. We have established the metal-identity of this enzyme and identified the key residues essential for the activity of HPM. Further, we established that HPM is an oxygen and redox-dependent enzyme and have identified the optimal redox partner proteins to support its *in vitro* activity. We also determined the substrate specificity and Michaelis-Menten kinetics of the enzyme. Moreover, we have also provided the first mechanistic insight of HPM, by providing the basis of a C-H and a C-C bond cleavage performed by HPM.[6]

Further, we have engineered the HPM for the highest titer production of 1-alkenes, to date.[7] Our approach of investigating HPM, a challenging integral membrane enzyme, will not only open new avenues in membrane-protein biochemistry but will also direct the science towards utilizing such enzymes for the production of next generation of biofuels.



References:

1. Liao, J. C.; Mi, L.; Pontrelli, S.; Luo, S., Fuelling the future: microbial engineering for the production of sustainable biofuels. *Nature Reviews Microbiology* **2016,** *14* (5), 288-304
2. Peralta-Yahya, P. P.; Zhang, F.; Del Cardayre, S. B.; Keasling, J. D., Microbial engineering for the production of advanced biofuels. *Nature* **2012,** *488* (7411), 320-328
3. Zhou, Y. J.; Kerkhoven, E. J.; Nielsen, J., Barriers and opportunities in bio-based production of hydrocarbons. *Nat Energy* **2018,** *3* (11), 925-935.10.1038/s41560-018-0197-x
4. Intasian, P.; Prakinee, K.; Phintha, A.; Trisrivirat, D.; Weeranoppanant, N.; Wongnate, T.; Chaiyen, P., Enzymes, In Vivo Biocatalysis, and Metabolic Engineering for Enabling a Circular Economy and Sustainability. *Chem Rev* **2021,** *121* (17), 10367-10451.10.1021/acs.chemrev.1c00121
5. Iqbal, T.; Chakraborty, S.; Murugan, S.; Das, D., Metalloenzymes for Fatty Acid-Derived Hydrocarbon Biosynthesis: Nature's Cryptic Catalysts. *Chem Asian J* **2022,** *17* (10), e202200105.10.1002/asia.202200105
6. Iqbal, T.; Murugan, S.; Rajendran, K.; Sidhu, J. S.; Das, D., Oxidative decarboxylation of fatty acids to terminal alkenes by a membrane-bound metalloenzyme, UndB. *ACS Catalysis (Aceepted)* **2023**.
7. Iqbal, T., An Engineered Membrane-Bound Enzyme for Efficient Hydrocarbon Production. *Science Advances (Under review)* **2023**.

Novel synthesis of substituted 3-(phenylcarbamoyl)benzoic acid: Evaluation as potential antimicrobial agents

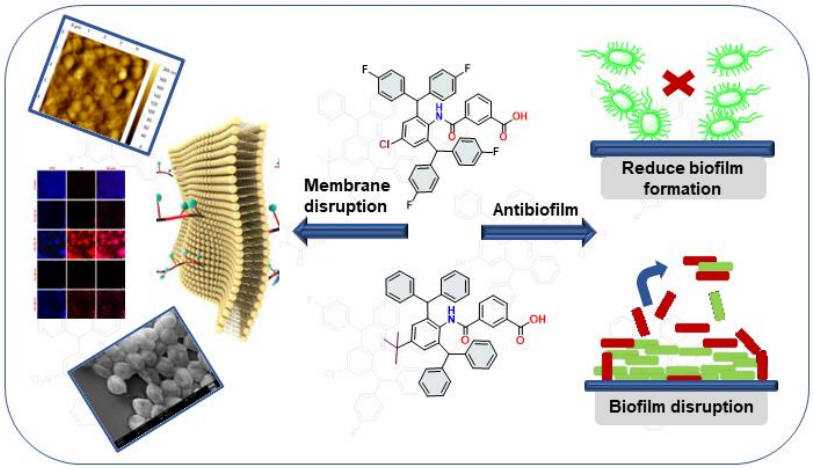
Himanshu Sonker and Dr. Ritika Gautam

Department of Chemistry, Indian Institute of Technology, Kanpur 208016, India

Email: himansk@iitk.ac.in

One of the top 10 global public health threats, antimicrobial resistance is predicted to outnumber deaths due to cancer by the year 2050. Also, the development and global spread of resistant strains of bacteria, called superbugs, have become a major area of concern. Additionally, *S. aureus* is one of the most widespread pathogens, capable of causing skin infections, as well as other severe infections worldwide. The development of resistance to methicillin and vancomycin, which are the last resort to treat several serious bacterial infections, together with the high cost of medical treatment and, decrease in invention of novel antibiotic scaffolds have posed a great threat to mankind. Therefore, there is an immediate need to develop novel antibacterial agents.

In our continuous effort to develop new antimicrobials, a series of substituted derivatives of 3-(phenylcarbamoyl)benzoic acid were prepared that are novel to bacteria. All compounds were characterized by the ^{1}H, $^{13}C\{^{1}H\}$ NMR, and Mass spectroscopy and structure of the analogues were further confirmed by single crystal X-ray studies. The synthesized compounds were tested for their anti-bacterial property against five bacterial strains, namely *A.baumannii*, *E.coli*, *S.aureus*, *P.aeruginosa*, and *K.pneumoniae*. The overall susceptibility is higher in *S.aureus*. The Minimum inhibitory concentration(MIC) of the molecules ranged from 1 to 16 µg/mL. The mechanism of inhibition of bacteria, morphologies and membrane integrities were studied by Scanning electron microscopy and Atomic force microscopy. Furthermore, fluorescence microscopy was performed using 4′,6-diamidino-2-phenylindole (DAPI) and propidium iodide (PI) dyes to support the antibacterial mechanism of compound H_2L13 on the cell membrane of *S. aureus*. This molucules also showed good antibacterial activity against vancomycin-resistant *Enterococcus (VRE) and* vancomycin-sensitive *Enterococcus* (VSE) with MIC of 4 µg/mL. The toxicity of compound H_2L13 toward HEK-293 cells was investigated by live/dead assay. More significantly, The said molecule showed strong inhibition on biofilm formation of *S. aureus* on their MIC also.



Reference-

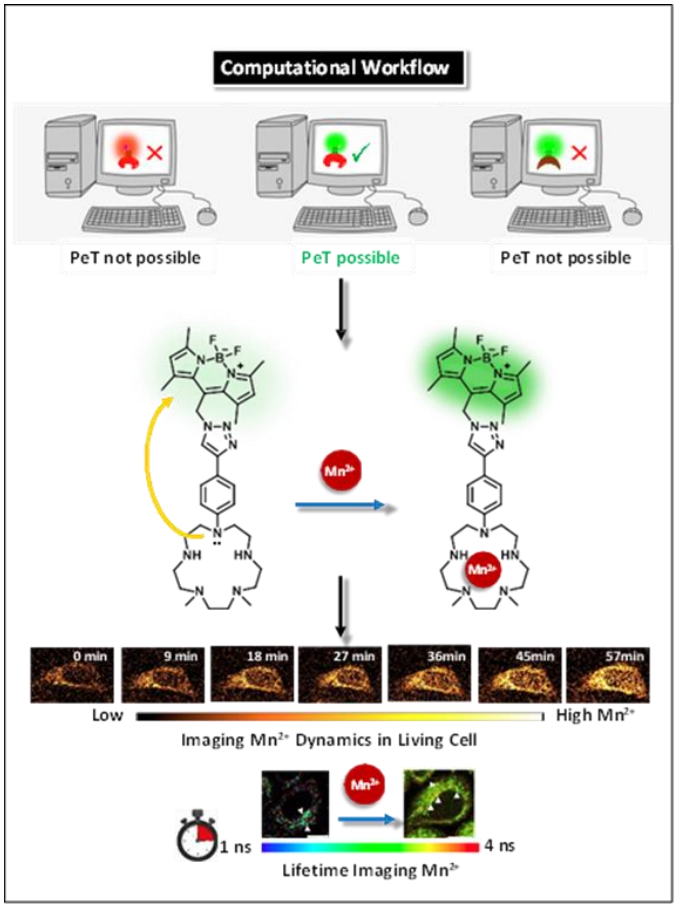
- Yong Guo et. al., *J. Med. Chem*. **2021**, *64*, 12903−12916.
- Svetlana G. Churusova et. al., *Inorg. Chem*. **2021**, *60*, 9880−9898.
- John P. Clare et. al., *J. Am. Chem. Soc***. 2005**, *127*, 10739-10746.
- Ehab Ghazy et. al., *European Journal of Medicinal Chemistry*, **2021,** *225,* 113745.
- Young-Hwan Jung et. al., *J. Med. Chem*. **2020**, *63*, 9563−9589.
- Andrea Unzue et.al., *J. Med. Chem*. **2016**, *59,* 1350−1356.
- Koen Vandyck et. al., *J. Med. Chem*. **2018**, *61*, 6247−6260.

Evaluating Design Criteria for PeT-based 'Turn-on' Fluorescent Metal Ion Sensors

Smitaroopa Kahali,[a] Sujit Kumar Das,[a] Kunika Gupta,[a] Ravindra Venkatramani,[a] Ankona Datta[a]*

[a] *Department of Chemical Sciences, Tata Institute of Fundamental Research, Mumbai, Maharashtra, India.*

E-mail: smitaroopa.kahali@tifr.res.in, ankona@tifr.res.in



Spatio-temporal fluctuations in distributions of bio-metals are functionally related to key cellular processes and disruptions are linked to severe pathophysiological conditions. For obtaining insights into metal ion dynamics in living cells, photo-induced electron- transfer (PeT)-based 'turn-on' fluorescent sensors are proven successful chemical- tools. A method to predict whether PeT will occur in a designed fluorescent metal ion sensor a priori, can afford a path to pre-design effective 'turn-on' sensors. Hence, we have designed a density functional theory (DFT) and time-dependent DFT (TD- DFT)-based workflow for screening molecules based on the ability to exhibit an efficient PeT quenched metal-unbound state. To experimentally test the workflow, we decided to develop PeT- based 'turn-on' fluorescent sensors for detecting Mn^{2+} ions within living systems. Mn^{2+} ions are necessary both in labile and protein-bound forms for all life forms ranging from bacteria, to plants and animals.[1] Designing Mn^{2+} selective binding ligands is, however, challenging owing to low binding affinities of Mn^{2+} ions toward most N-, O-, and S-donor atom containing ligands.[1]

Designing Mn2+ selective binding ligands is, however, challenging owing to low binding affinities of Mn2+ ions toward most N-, O-, and S-donor atom containing ligands.1 By scrutinizing the biological binders of Mn2+ ions, we opted for a planar pentacoordinate arrangement of N- atoms as an Mn2+ ion binding scaffold.2 A library of sensors was designed by linking

the binding scaffolds with dye units in silico and two molecules for which PeT was feasible based on computations, were synthesized. PeT was observed for both molecules. One of the sensors was selective toward Mn2+ ions, water-soluble and cell-permeable, and was used to image Mn2+ ions in living cells.3 I will detail our computational work-flow, and applications of the novel Mn2+ ion sensor for Mn2+ ion detection in vitro and in living cells.3

References

1 Das S, Datta A, et al. Dalton Trans., 2019, 48 (21), 7047-7061;

2 Bakthavatsalam S, Datta A, et al. ChemComm, 2015, 51 (13), 2605-2608.

3 Kahali S, Das S, Datta A, et al. ChemRxiv. Cambridge: Cambridge Open Engage; 2023;

10.26434/chemrxiv-2023-d4fp9

Modulation of aggregation of Human Prion Protein PrP(106-126) by indole based cyclometallated palladium complex

Rahul Chauhan,[a] Saakshi Saini,[b] Partha Roy,[b] Kaushik Ghosh,[a,b]*

[a]Department of Chemistry, Indian Institute of Technology, Roorkee- 247667, Uttarakhand

[b]Department of Biosciences and Bioengineering, Indian Institute of Technology, Roorkee-247667, Uttarakhand

Email: Kaushik.ghosh@cy.iitr.ac.in

Abstract:

The spontaneous aggregation of misfolded or infectious forms of prion protein has been shown to cause neurotoxicity in brain cells, leading to the progression of prion disorders. Bovine spongiform encephalopathy in animals and Creutzfeldt-Jakob disease (CJD) in humans are examples of these disorders. Square planar complexes containing labile ligands and indole-derived compounds were discovered to be excellent at inhibiting protein aggregation. In the present study we have synthesized indole based schiff base ligand and its cyclometallated palladium complex. We have conducted studies to understand how complex effected and interacted with PrP(106-126) during the aggregation, fibrillation and amyloid formation. The complex is characterized by different spectroscopic techniques like NMR, UV-Visible, IR, HRMS. Molecular structure is determined by single crystal X-ray crystallography. The complex showed strong binding affinity to PrP106-126 and affected the conformation and aggregation of this active peptide in a different binding mode. The interactions of the compound with the peptide were investigated by UV-Vis absorption spectroscopy, MALDI-TOF mass spectrometry, CD spectroscopy, TEM images and molecular docking studies while the kinetic study of aggregation was assessed using thioflavin-T binding assays. The viability of the complex on neuronal HT-22 cells was assessed using MTT assay. The findings suggest that different mechanisms are used by the compound to modulate the peptide's aggregation, and that the anti-aggregation properties are primarily determined by the metal's physicochemical properties and reactivity, rather than by the ligand itself. Therefore, we suggest that complex may be offered as a possible therapeutic molecule in metallo-pharmaceutical studies aimed at treating Prions disease (PD).

References:

(1) Prusiner, S. B. Prions. *Proc. Natl. Acad. Sci.* **1998**, *95* (23), 13363–13383. https://doi.org/10.1073/pnas.95.23.13363.

(2) Frontzek, K.; Bardelli, M.; Senatore, A.; Henzi, A.; Reimann, R. R.; Bedir, S.; Marino, M.; Hussain, R.; Jurt, S.; Meisl, G.; Pedotti, M.; Mazzola, F.; Siligardi, G.; Zerbe, O.; Losa, M.; Knowles, T.; Lakkaraju, A.; Zhu, C.; Schwarz, P.; Hornemann, S.; Holt, M. G.; Simonelli, L.; Varani, L.; Aguzzi, A. A Conformational Switch Controlling the Toxicity of the Prion Protein. *Nat. Struct. Mol. Biol.* **2022**, *29* (8), 831–840. https://doi.org/10.1038/s41594-022-00814-7.

(3) Collinge, J. Mammalian Prions and Their Wider Relevance in Neurodegenerative Diseases. *Nature*. **2016**, pp 217–226. https://doi.org/10.1038/nature20415.

(4) Walsh, P.; Simonetti, K.; Sharpe, S. Core Structure of Amyloid Fibrils Formed by Residues 106-126 of the Human Prion Protein. *Structure* **2009**, *17* (3), 417–426. https://doi.org/10.1016/j.str.2008.12.018.

(5) Suh, J. M.; Kim, G.; Kang, J.; Lim, M. H. Strategies Employing Transition Metal Complexes to Modulate [illegible] **9**, pp 8–17. https://doi.org/10.1021/acs.inorgchem.8b02813.

(6) Wang, Y.; Feng, L.; Zhang, B.; Wang, X.; Huang, C.; Li, Y.; Du, W. Palladium Complexes Affect the Aggregation of Human Prion Protein PrP106-126. *Inorg. Chem.* **2011**, *50* (10), 4340–4348. https://doi.org/10.1021/ic102331x.

(7) Li, B.; Xu, C.; Lv, Y.; Liu, G.; Sun, X.; Sun, Z.; Xu, X.; Chen, W.; He, L.; Song, Y. F. Vanadium-Substituted Polyoxometalates Regulate Prion Protein Fragment 106-126 Misfolding by an Oxidation Strategy. *ACS Appl. Mater. Interfaces* **2023**, *15* (29), 34497–34504. https://doi.org/10.1021/acsami.3c04969.

Redox Modulation of Lipophilic Quinoline-Imidazolium Derivatives in Health and Disease

Sayari Dewan,[a] Ritika Gautam*

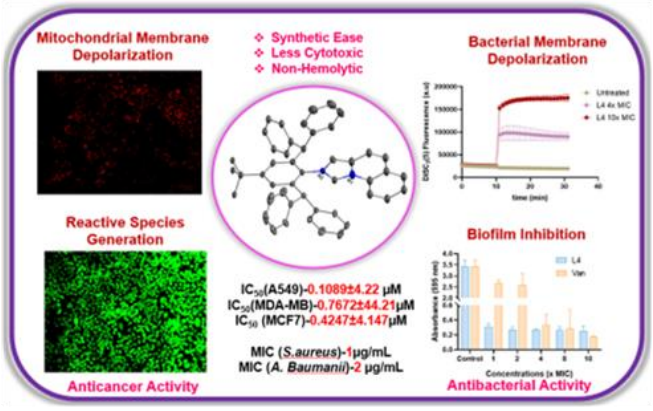
[a]*Department of Chemistry*

Indian Institute of Technology Kanpur, Kanpur 208016, Uttar Pradesh, India

Email: sayarid21@iitk.ac.in

Despite innumerous efforts to combat cancer including immunotherapy, radiotherapy, surgery, chemodynamic therapy, humans have failed to find an effective solution to the deadly disease, as conventional drugs like cisplatin are limited by the problem of low bioavailability or inherent cytotoxicity. To address this issue, in this work a series of novel fluorescent quinoline-imidazolium derivatives having superior lipophilicity and excellent cytotoxicity are synthesized and characterized by ^{1}H NMR, ^{13}C NMR, ESI-MS, UV-Vis, as well SC-XRD techniques. The molecules when screened against breast adenocarcinoma cell lines MDA-MB-231 and MCF-7, human lung adenocarcinoma cell line A549, and normal human embryonic kidney cell line HEK-293 using MTT assay revealed their outstanding cytotoxicity. All the synthesized derivatives were observed to be stable in physiologically relevant conditions for a period of up to 2 hours. Upon further investigation, the most active molecule, L4, was observed to have a multimodal path of action against A549 cells. Not only it could generate reactive oxygen species as observed by intense green fluorescence by DCFH-DA assay, but also being cationic in nature it could depolarize mitochondrial membrane potential, eventually leading to cancer cell apoptosis.

Recent literature has divulged that patients suffering from cancer are highly prone to bacterial infections, and for that purpose, the synthesized derivatives were screened for their minimum inhibitory concentration (μg/mL) against five bacterial strains, *A.baumannii*, *E.coli*, *S.aureus*, *P.aeruginosa*, and *K.pneumoniae.* The derivatives were found to target gram-positive *S. aureus* and gram-negative *A. baumanii*. selectively. The corresponding MIC values for the most active molecule L4 was 1 μg/mL and 2 μg/mL respectively, which were comparable to a very common antibiotic levofloxacin. The MIC only changed two folds in presence of physiological salts like NaCl, $ZnCl_2$, KCl, $FeCl_3$, $MgCl_2$, thus confirming the effectiveness of the molecule in physiological conditions. Scanning Electron Microscope images showed the morphological changes in the treated group of bacteria, with irregular shape fractured cells and cellular debris**.** The cationic nature of the molecule aided in depolarization of bacterial membrane as revealed by $DISC_3(5)$ assay. This was further confirmed by the leakage of DNA in the treated *S. Aureus* cells**.** The molecule could also inhibit bacterial biofilm, even at 1X concentration also. Lastly, the molecules were also observed to have very low toxicity to human erythrocytes, L4 having only about 8 % haemolysis at 32X concentrations. In conclusion, L4 has potential to act as a multifaceted drug not only in treatment of cancer, but also in bacterial infections too.



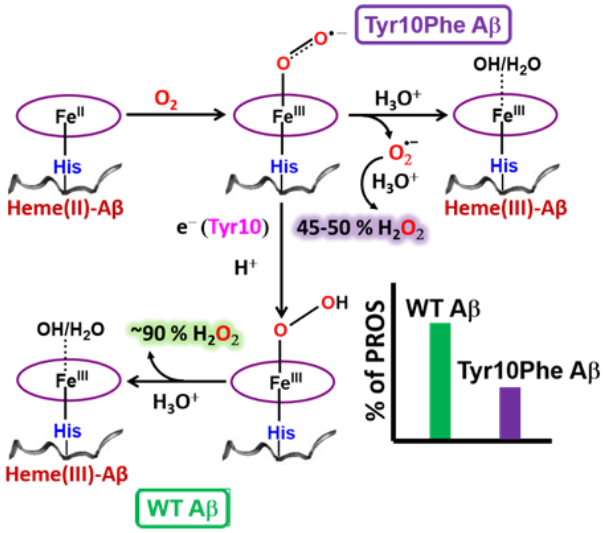
Rapid autoxidation of ferrous heme-Aβ complexes relevant to Alzheimer's Disease: Mechanism and insight into the role of the Tyr10 residue

Madhuparna Roy and Somdatta Ghosh Dey

Indian Association for the Cultivation of Science

2A & 2B, Raja S. C. Mullick Road, Jadavpur, Kolkata 700 032

Heme bound Aβ peptides have been reported to reduce O_2 by $2e^-$ to H_2O_2 which may result in oxidative stress commonly encountered in Alzheimer's disease. While previous reports could show formation of an Fe-O_2 species using heme-Aβ and synthetic iron porphyrin bound Aβ complexes in dry DMF medium, the challenge lies in isolating and characterizing such an intermediate under physiological conditions due to the hydrolysis prone and hence transient nature of the heme-O_2 adduct.[1,2] Additionally, these systems are not amenable to flash photolysis, as Fe(II)-CO adducts are not photolabile in our experience, making it extremely difficult to trap the dioxygen adduct of heme-Aβ. In this study we report the first instance of rapid freeze quench trapping and characterizing the heme(III)-$O_2^{\bullet-}$ intermediate involved in the heme-Aβ induced formation of partially reduced oxygen species (PROS) in physiologically relevant aqueous medium using absorption and resonance Raman spectroscopy. The kinetics of this process indicates a key role of the Tyr10 residue, unique to human Aβ, in the generation of H_2O_2 from O_2.



1. M. Seal, S. Mukherjee, D. Pramanik, K. Mittra, A. Dey and S. G. Dey, *Chem. Commun.*, 2013, **49**, 1091-1093.

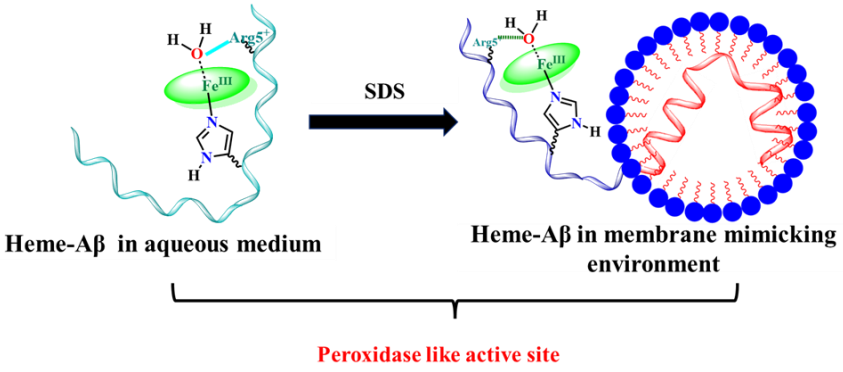
2. M. Seal, S. Mukherjee and S. G. Dey, *Metallomics*, 2016, **8**, 1266-1272.

Heme-Aβ in SDS micellar environment: Active site environment and reactivity

Chinmay Dey, Madhuparna Roy, Abhishek Dey*, Somdatta Ghosh Dey*

School of Chemical Sciences
Indian Association for the Cultivation of Science
2A & 2B, Raja SC Mullick Road, Kolkata, WB, India 700032
*E-mail: icsgd@iacs.res.in

Alzheimer's disease (AD), the most common cause of dementia, is a progressive neurodegenerative disorder that causes brain cell death. Oxidative stress derived from the accumulation of redox cofactors like heme in amyloid plaques originating from amyloid β (Aβ) peptides has been implicated in the pathogenesis of AD. In the past our group has studied the interactions and reactivities of heme with soluble oligomeric and aggregated forms of Aβ. In this manuscript we report the interaction of heme with Aβ that remains membrane bound using membrane mimetic SDS (sodium dodecyl sulfate) micellar medium. Employing different spectroscopic techniques, we find that Aβ binds heme using one of its three His (preferentially His13) in SDS micellar medium. We also find that Arg5 is an essential distal residue responsible for higher peroxidase activity of heme bound Aβ in this membrane mimetic environment than free heme. This peroxidase activity exerted by even membrane bound heme-Aβ can potentially be more detrimental as the active site remains close to membranes and can hence oxidise the lipid bilayer of the neuronal cell, which can induce cell apoptosis. Thus, heme-Aβ in solution as well as in membrane-bound form are detrimental.



Keywords: Amyloid β, Heme, SDS micelle, Alzheimer's disease, peroxidase activity

References

1. D. Pramanik and S. G. Dey, *J. Am. Chem. Soc.*, 2011, **133** , 81 —87.

Synthetically Tuneable Suprahybrid Nanoparticles for Efficacious Delivery of Therapeutics

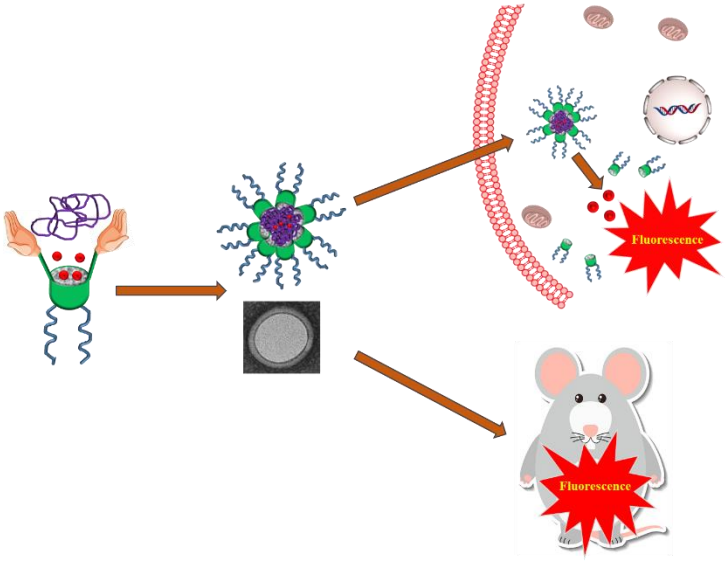
Arka Banerjee[a], Kajol[b], Geetika Bajaj[c], Dr. Nitin K. Singhal[c], Dr. Rakesh K. Pathak*[a]

[a]Department of Chemical Sciences, [b]Department of Biological Sciences, Indian Institute of Science Education and Research, Odisha.

[c]National Agri-Food Biotechnology Institute, Sec 81, Mohali, Punjab.

Email. arkab@iiserbpr.ac.in

Polymeric and lipid-hybrid nano-systems have emerged as potential tools for addressing modern drug delivery[1] and theranostic challenges. However, multicomponent lipid hybrid nano-scaffolds often face several challenges including solubility, immune compatibility, poor bioavailability, and synthetic functionalization. Hence, there is a gap between synthetic tunability and introducing stabilizing components on a single platform which often lacks in several nano medicines. In order to address these issues a single molecular platform with a multifaceted synthetic approach is required which can minimize the requirement to use several stabilizers to make nano-formulations. Supramolecular systems such as calix[4]arenes are capable of encapsulating different drugs and biomolecules in a non-covalent fashion[2]. Moreover, this platform can be tuned extensively upon tailor-made synthetic modifications to make self-assembled nanoparticles upholding a wide range of treatment modalities which does not require external stabilization. In the current work, we have synthetically modified the lower rim of calix[4]arene with polyethylene glycol chains of different molecular weights. Upon synergistic blending of this system with FDA-approved PLGA the resulting nanoparticles are stable in the physiological environment[3]. Interestingly, cellular toxicity studies revealed negligible toxicity even at the highest concentration of the polymeric core. To demonstrate the utility of this platform as a successful delivery carrier we have utilized hydrophobic nile red encapsulated nanoparticles to track cellular internalization and biodistribution in animal model. We have found extended retention of dye *in-vivo* whereas, almost no toxicity is found in major organs of these nanoparticles. Further, these modified supra-hybrid nano-scaffolds can open innovative avenues that hold great promise in the advancement of modern drug delivery strategies and therapeutic outcomes.



Keywords. Supramolecular chemistry, Calixarenes, Lipids-Polymeric Hybrid Nanoparticles, Drug Delivery, Nanomedicine.

References and Notes:

1. Huang, Y. and coworkers *Nano Lett*, **2020**, 20, 3039.
2. Shi, Y.P and coworkers *Anal. Chem*, **2021**, 93, 15080.
3. Pathak, R.K. and coworkers *ACS Appl. Mater. Interfaces* **2023**, 15, 45, 52207.

Evaluating Anti-Alzheimer's Potential of Selected Synthetic and Natural Multifunctional Molecules

Priyal Malpani, Monika Rana, Anuj K. Sharma*
Department of Chemistry, Central University of Rajasthan, NH-8, Bandarsindri, Kishangarh, Ajmer, RJ, 305817

E-mail: *2022phdch003@curaj.ac.in*, *monikarana21894@gmail.com* , *anuj.sharma@curaj.ac.in*

Alzheimer's Disease (AD) is a result of several pathological factors like amyloid protein deposition, oxidative stress and metal-ion dyshomeostatis (imbalance) in brain etc.[1,2] The development of multifunctional molecules that can efficiently target multiple factors simultaneously without disturbing the other biological phenomenon are expected to be beneficial. To suppress the excessive metal-ion concentration and to interact with amyloid protein, we have designed, synthesized and characterized a new class of compounds having Azo-Stilbene moieties with metal chelating arms with hetero-atoms. Stilbene framework is well known for Amyloid interaction whereas the presence of N and O atoms makes them suitable for metal-chelation. Their metal chelation properties are established using various spectroscopic techniques. Myricetin and Epigallocatechin are some familiar examples of natural products that have been thoroughly studied for their anti-AD potential. Apart from synthetic molecules, a series of polyphenolic compounds like flavonoids, flavanones, etc. have been investigated for metal-chelation properties and their anti-Alzheimer's potential.[4,6]

The Cholinesterase enzymes (AChE and BuChE) play a key role to control the levels of important neurotransmitters like acetylcholine that is found in significantly low levels in AD affected patients. All the molecules under our investigation were tested for their AChE inhibition activity in-vitro. The obtained IC_{50} values were compared with the standard references (Rivastigmine and Donepezil) and found to exhibit AChE inhibitory activity. Overall, a summary of above investigations will be presented.[3,5,6]

References

[1] Sharma, A.K.; Pavlova, S. T.; Kim, J.; Finkelstein, D.; Hawco, N.J.; Rath, N. P.; Kim, J.; Mirica, L. M. *J. Am. Chem. Soc.* **2012**, 134, 6625−6636.
[2] Kepp, K.P. *Chem. Rev.* 2012, 112, 10, 5193–5239
[3] Rana, M.; Sharma A K. *Metallomics*. **2019**, 11, 64–84
[4] Rana, M.; Roy, T. K.; Sharma, A. K.* Inorg. Chim. Acta, **2018**, 471, 419.
[5] Rana, M.; Cho, H. J.; Arya, H.; Bhatt, T. K.; Bhar, K.; Bhatt, S.; Mirica, L. M.; Sharma, A. K. *Inorg. Chem.* **2022**, 61, 10294−10309
[6] Nam, G.; Hong, M.; Lee, J.; Lee, H. J.; Ji, Y.; Kang, J.; Baik, M.-H.; and Lim, M. H. *Chem. Sci.,* **2020**, 11, 10243

Red light-assisted modulation of the cytotoxic activity of iron(III) complex functionalized selenium nanowires through glutathione (GSH) depletion

Rintu Bhowmik[a], Maynak Pal[a], Aarti Upadhyay[b], Mithun Roy*[a]

[a.] Department of Chemistry, National Institute of Technology Manipur, Langol 795004, Imphal (Manipur), INDIA, [b.] Department of Inorganic and Physical Chemistry, Indian Institute of Science, Bangalore-560012 (INDIA).

E-mail: rintubhowmik1111@gmail.com; mithunroy.iisc@gmail.com

Photoredox chemistry caused by the ligand-to-metal charge transfer (LMCT) in red light activable iron(III)-phenolate/carboxylate complexes leads to the reactive oxygen species (ROS) generation. This property could be implemented as a potent strategic tool for photochemotherapeutic applications. Again, the association of nanomaterials to these types of complexes tends to increase the potency of the system as a chemotherapeutic drug. Herein we have synthesized an iron(III) complex with molecular formula [Fe(L^1)(L^2)] (**Fe**) (L^1 is bis(3,5 di-tert-butyl-2-hydroxybenzyl)glycine and L^2 is 5-(1,2-dithiolan-3-yl)-N-(1,10-phenanthroline-5-yl)pentanamide) functionalized selenium nanowires (**Fe-SeNWs**) and characterized the nanohybrid by UV-visible, FT-IR, DLS, powder XRD, and TEM analysis. We found a significant red shift in the developed nanocomposite (**Fe-SeNWs**) (λ_{max} = 625 nm) with respect to the bare iron(III) complex (**Fe**) (λ_{max} = 573 nm), rendering the nanocomposite an ideal candidate for the photochemotherapeutic application. Furthermore, the nanocomposite exhibited a significant glutathione depletion capacity (0.1 mg/mL **Fe-SeNWs** depleted 35.53 μM of GSH), which was beneficial for the high cytotoxicity towards alveolar basal epithelial (A549) cancer cells. The cellular uptake studies of both the complex (**Fe**) and the nanocomposite (**Fe-SeNWs**) were probed in A549 cells and revealed that the nanocomposite exhibited better uptake than the complex. Confocal imaging microscopy of the nanocomposite (**Fe-SeNWs**) in A549 cells indicated that the compound was localized partly in mitochondria and significantly in the endoplasmic reticulum. The photocytotoxicity evaluation of the nanocomposite in HeLa and A549 cells was done by MTT assay in red light (600-720 nm, 30 J/cm^2). The IC_{50} values for the nanocomposite were determined to be 72.0 and 23.9 μg/mL in HeLa and A549 cells respectively in red light. Mechanistic studies revealed that intracellular generation of ROS on red light

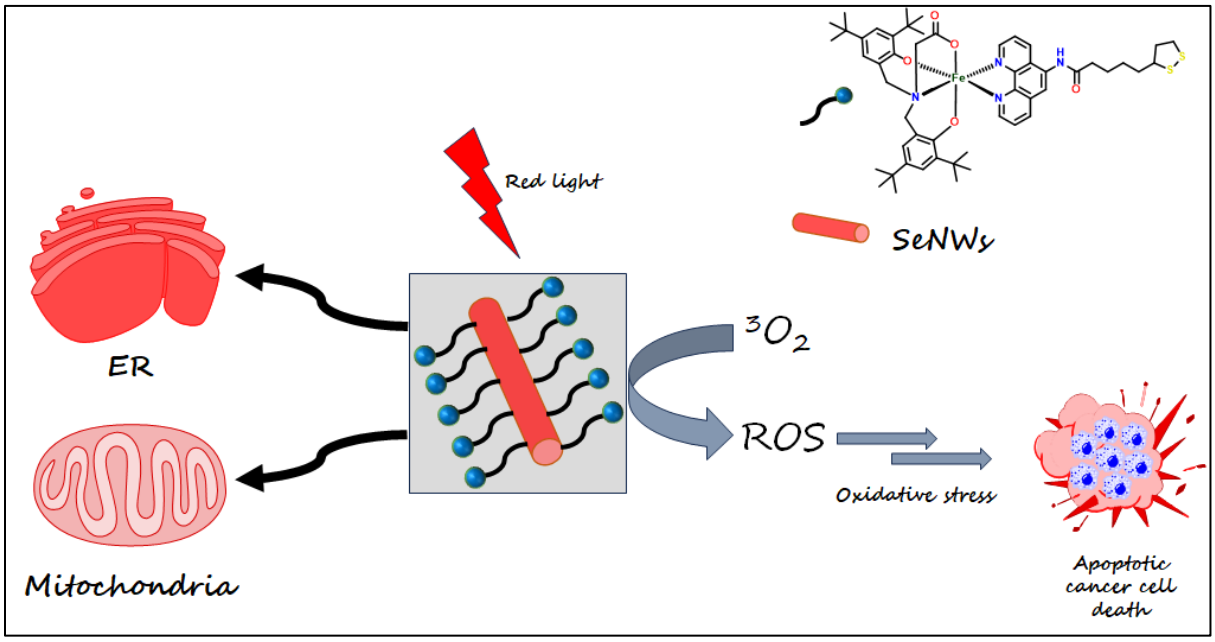
activation leads to apoptotic cell death of A549 cells. Overall we developed a red light activable iron(III) complex functionalized selenium nanowires (Fe-SeNWs) as a potential strategic tool for photochemotherapeutic applications.

References.

1. Pal, M., Ramu, V., Musib, D., Kunwar, A., Biswas, A. and Roy, M., 2021. Iron (III) Complex-Functionalized Gold Nanocomposite as a Strategic Tool for Targeted Photochemotherapy in Red Light. Inorganic Chemistry, 60(9), 6283-6297.

2. Basu, U., Khan, I., Hussain, A., Kondaiah, P. and Chakravarty, A.R., 2012. Photodynamic Effect in Near-IR Light by a Photocytotoxic Iron (III) Cellular Imaging Agent. Angewandte Chemie International Edition, 51(11), 2658-2661.

3. Wu, Y., Guo, T., Qiu, Y., Lin, Y., Yao, Y., Lian, W., Lin, L., Song, J. and Yang, H., 2019. An inorganic prodrug, tellurium nanowires with enhanced ROS generation and GSH depletion for selective cancer therapy. Chemical science, 10(29), 7068-7075.



Regulation of Tyrosinase Enzyme Activity by Glutathione Peroxidase Mimics

Rakesh Kumar Rai and Gouriprasanna Roy*

Department of Chemistry, Indian Institute of Technology Tirupati, Tirupati – 517619, India;
Email: gproy@iittp.ac.in

Tyrosinase (Tyr), a copper-containing enzyme, is widely present in plants, bacteria, and humans, where it is involved in the biosynthesis of melanin-type pigments. Biosynthesis of melanin is known to cause serious skin lesions and melanoma in humans and unfavorable browning in fruits, vegetables, and seafood. The development of a potent Tyr−inhibitor is of huge economic and industrial impact and will have applications in the food industry, cosmetics, and therapeutics. Kojic acid (IC_{50} 25 µM) is a well-known marketed tyrosinase inhibitor. However, its use is limited due to problems associated with irritation and dermatitis. Again, the regulation of tyrosinase enzymes is highly controlled by the cellular redox level. It is reported that under the condition of oxidative stress, tyrosinase activity increases, and glutathione peroxidase (GPx), a Se-containing antioxidative enzyme, is downregulated. Therefore, an effective tyrosinase inhibitor that also has a substantial capability to degrade hydrogen peroxide (GPx-like mimic) will be of tremendous value as a therapeutic and anti-browning agent. A lot of research progress has also been made to discover an efficient and safe tyrosinase inhibitor. In this regard, an effort has been made to develop a selone/thione of naturally occurring heterocycles with dual functionality (tyrosinase inhibitor and GPx-like mimic). It is found that the selones of naturally occurring heterocycles are not only potent tyrosinase inhibitors but also have a strong hydrogen peroxide degradation ability (antioxidative activity like Gpx). The IC_{50} value for a selone of a naturally occurring non-toxic heterocycle with excellent GPx-like activity is found to be 0.47 µM which is 53 times more than the well-known and widely used tyrosinase inhibitor kojic acid (IC_{50} 25 µM).

References:

(1) Buitrago, E.; Vuillamy, A.; Boumendjel, A.; Yi, W.; Gellon, G.; Hardré, R.; Philouze, C.; Serratrice, G.; Jamet, H.; Réglier, M.; Belle, C. *Inorg. Chem.* **2014**, *53*, 12848-12858.

(2) Rai, R. K.; Karri, R.; Dubey, K. D.; Roy, G. *J. Agric. Food Chem.* **2022**, *70*, 9730–9747.

(3) Jiménez, M.; García-Carmona, F. *Arch. Biochem. Biophys.* **2000**, *373*, 255–260.

Yaqine BEN HADJ HAMMOUDA

Oxidative stress is known to play a major role in the pathogenesis of inflammatory bowel diseases (IBDs) and, in particular, superoxide dismutase (SODs) defenses were shown to be weakened in patients suffering from IBDs. SOD mimics, also called SOD mimetics, as low molecular weight complexes reproducing the activity of SOD, constitute promising antioxidant catalytic metallodrugs in the context of IBDs. A Mn(II) complex SOD mimic (Mn1) based on an open-chain diamino-ethane ligand exerting antioxidant and anti-inflammatory effects on an intestinal epithelial cellular model was shown to be experience metal exchanges between the manganese center and metal ions present in the biological environment. We report here the study of three new SOD mimics designed to improve the kinetic inertness of Mn1. They result from Mn1 functionalization with a cyclohexyl and/or a propyl group with the aim of limiting respectively (a) metal exchanges and (b) deprotonation of an amine from the 1,2-diaminoethane central scaffold. The new manganese-based SOD mimics displayed a higher intrinsic SOD activity, and also improved kinetic inertness in metal ion exchange processes (with Zn(II), Cu(II), Ni(II) and Co(II)). They were shown to provide anti-inflammatory and antioxidant effects in cells at lower doses than Mn1 (down to 10 µM). To understand if the origin of this improvement was limited to their higher inertness or if their intracellular localization may come into play, Synchrotron Radiation X-ray Fluorescence (SXRF) imaging experiments were carried out in intestinal epithelial model cells HT29-MD2 that were also incubated with a rhenium-based multimodal mitochondrial-targeted probe created by our team. Imaging results show a low level of intracellular localization and a homogeneous distribution, suggesting that the improvement of the second generation of mimics can rather be attributed to their higher kinetic inertness.

This improvement was due to their higher inertness against metalassisted dissociation and not to different cellular overall accumulation. Based on its higher inertness, the SOD mimic containing both the propyl and the cyclohexyl moiety was suitable for intracellular detection and quantification by mass spectrometry, quantification, that was achieved by using a 13C-labelled Co-based analog of the SOD mimics as an external heavy standar

Biological studies of low-molecular weight manganese complexes mimicking the superoxide dismutase activity

Namita Raju JOHN, Nicolas DELSUC, Clotilde POLICAR

Laboratoire des Biomolécules, LBM, Département de chimie, Ecole Normale Supérieure, PSL University,Sorbonne Université,CNRS, 75005 Paris, France

namita-raju.john@ens.psl.eu

Several biochemical reactions occurring in living organisms lead to the formation of reactive oxygen species (ROS) as a by-product. In order to regulate the intracellular concentration of these species, there exist certain antioxidant defences. Any disturbance in this finely tuned balance between ROS and the anti-oxidant defences result in oxidative distress, which is associated with a number of diseases. Policar's group has developed a low molecular weight manganese complex called Mn1, mimicking the active site of Manganese superoxide dismutase enzyme which is responsible for the dismutation of the superoxide radical. Studies have shown that Mn1 has both anti-oxidant as well as anti-inflammatory activity and thus it could be a potential drug against inflammatory bowel diseases, which at the moment have no treatment.

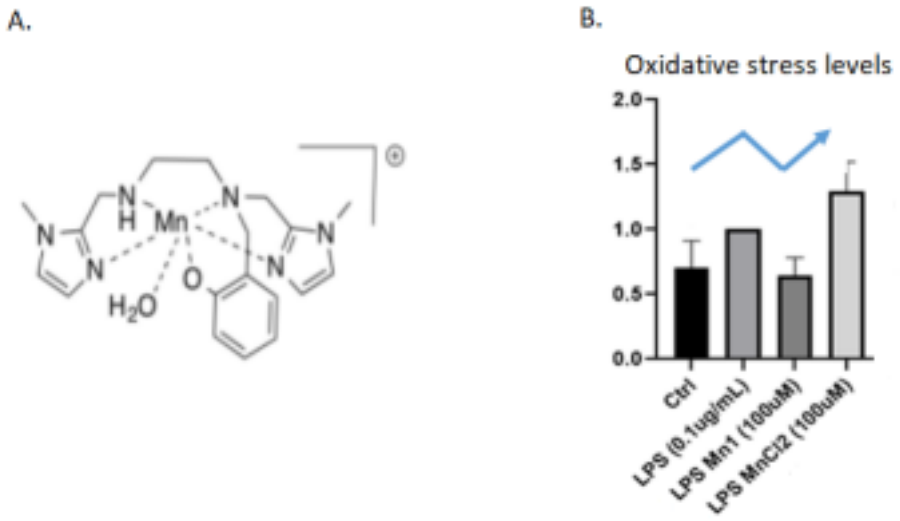


Figure 1 A. Structure of Mn1 and B. Change in oxidative stress levels upon the action of Mn1 analysed as a measure of number of oxidised cysteines

This study mainly involves biological assays on intestinal epithelial cells on which inflammation has been induced by activation with LPS and its treatment with Mn1. The level of oxidative stress was quantified with a cysteine-labelling method. Additionally, the level of expression of several proteins under the influence of Mn1 was investigated using the Western blot technique.

References

1. Cisnetti, F.; Lefèvre, A.-S.; Guillot, R.; Lambert, F.; Blain, G.; Anxolabéhère-Mallart, E.; Policar, C. A New Pentadentate

Ligand Forms Both a Di- and a Mononuclear MnII Complex: Electrochemical, Spectroscopic and Superoxide

Dismutase Activity Studies. *Eur. J. Inorg. Chem.* **2007**, *2007* (28), 4472– 4480. https://doi.org/10.1002/ejic.200601236.

2. Policar, C. Mimicking SOD, Why and How: Bio-Inspired Manganese Complexes as SOD Mimic. In *Redox Active Therapeutics*; Batinić-Haberle, I., Rebouças, J. S., Spasojević, I., Eds.; Oxidative Stress in Applied Basic Research and Clinical Practice; Springer International Publishing: Cham, 2016; pp 125–164. https://doi.org/10.1007/978-3-319-30705-3_7.

3. Mathieu, E.; Bernard, A.-S.; Delsuc, N.; Quévrain, E.; Gazzah, G.; Lai, B.; Chain, F.; Langella, P.; Bachelet, M.; Masliah, J.; Seksik, P.; Policar, C. A Cell-Penetrant Manganese Superoxide Dismutase (MnSOD) Mimic Is Able To Complement MnSOD and Exerts an Antiinflammatory Effect on Cellular and Animal Models of Inflammatory Bowel Diseases. *Inorg. Chem.* **2017**, *56* (5), 2545–2555.

https://doi.org/10.1021/acs.inorgchem.6b02695.

In situ v.s. Frozen: Effects on X-ray Absorption Spectroscopy of Soluble Methane Monooxygenase

Olivia McCubbin Stepanic,[A] Kara Zielinski,[B] Derek Rice,[A] Chris Pollock,[C] Rahul Banerjee,[D,E] John Lipscomb,[D] Lois Pollack,[B] Serena DeBeer[A]

A: Department of Inorganic Spectroscopy, Max Planck Institute for Chemical Energy Conversion, Mülheim a.d. Ruhr, Germany 45470; B: Cornell Applied Engineering and Physics, Cornell University, Ithaca, NY, USA 14853; C: Cornell High Energy Synchrotron Source, Cornell University, Ithaca, NY, USA 14853; D: College of Biological Sciences, University of Minnesota, Minneapolis, MN, USA 55455; E: Department of Chemistry and Biochemistry, Auburn University, Auburn, AL, USA 36849

Abstract

Methanol, a potential low-emission energy source and a key building block in the production of paints, pharmaceuticals, plastics and other chemicals, is produced on the order of approximately 100 million tons annually, largely from natural gas, biomass, or coal. Methane, a greenhouse gas, is thought to have contributed to 30% of global warming seen so far.[1] The current industrial production of methanol from methane requires a syngas process, high temperatures (>900 °C) and pressures (>50 bar). As methane capture processes become commercialized,[2] more efficient systems to convert methane into methanol are required. Soluble methane monooxygenase (sMMO), a di-iron protein, is capable of highly selective C-H bond activation reactions at ambient temperatures and pressures, and gaining mechanistic and structural insight from theseenzymes will aid in the goal of creating more green routes for the production of methanol and other valuable chemicals. sMMO has been the subject of study for decades, and the structure of intermediate Q, which occurs upon the breakage of the O-O bond and directly prior to the conversion of methane to methanol, is hotly debated.[3–5] Spectroscopic techniques and even crystallographic data performed under different conditions have provided varied pictures of even the more easily isolated sMMO-red and -ox states.[6,7] Such structural differences may be explored and understood by using a spectroscopic probe that is feasible in multiple experimental conditions, such as X-ray absorption spectroscopy (XAS). Here, frozen solution data of

MMO-ox and red are compared with *in situ* HERFD XAS and UV/Vis using a microfluidic mixer. Preliminary findings on pre-edge differences between frozen and *in situ* sMMO-Qare also shown.

References

(1) IEA (2022), Global Methane Tracker 2022, IEA, Paris https://www.iea.org/reports/global-methane-tracker-2022, License: CC BY 4.0

(2) Hu, G.; May, E. F.; Li, K. G. We Commercialized a Methane Capture Technology in Ten Years — Here's How. *Nature* **2022**, *604* (7905), 242–245.

(3) Cutsail, G. E.; Banerjee, R.; Zhou, A.; Jr, L. Q.; Lipscomb, J. D.; DeBeer, S. High-Resolution Extended X-Ray Absorption Fine Structure Analysis Provides Evidence for a Longer Fe···Fe Distance in the Q Intermediate of Methane Monooxygenase. *J Am Chem Soc* **2018**, 14.
(4) Jacobs, A. B.; Banerjee, R.; Deweese, D. E.; Braun, A.; Babicz, J. T.; Gee, L. B.; Sutherlin, K. D.; Böttger, L. H.; Yoda, Y.; Saito, M.; Kitao, S.; Kobayashi, Y.; Seto, M.; Tamasaku, K.; Lipscomb, J. D.; Park, K.; Solomon, E. I. Nuclear Resonance Vibrational Spectroscopic Definition of the Fe(IV) $_2$ Intermediate Q in Methane Monooxygenase and Its Reactivity. *J. Am. Chem. Soc.* **2021**, *143* (39), 16007–16029. https://doi.org/10.1021/jacs.1c05436.
(5) Schulz, C. E.; Castillo, R. G.; Pantazis, D. A.; DeBeer, S.; Neese, F. Structure–Spectroscopy Correlations for Intermediate Q of Soluble Methane Monooxygenase: Insights from QM/MM Calculations. *J. Am. Chem. Soc.* **2021**, *143* (17), 6560–6577. https://doi.org/10.1021/jacs.1c01180.
(6) Rosenzweig, A. C.; Nordlund, P.; Takahara, P. M.; Frederick, C. A.; Lippard, S. J. Geometry of the Soluble Methane Monooxygenase Catalytic Diiron Center in Two Oxidation States. *Chem. Biol.* **1995**, *2* (6), 409–418. https://doi.org/10.1016/1074-5521(95)90222-8.
(7) Srinivas, V.; Banerjee, R.; Lebrette, H.; Jones, J. C.; Aurelius, O.; Kim, I.-S.; Pham, C. C.; Gul, S.; Sutherlin, K. D.; Bhowmick, A.; John, J.; Bozkurt, E.; Fransson, T.; Aller, P.; Butryn, A.; Bogacz, I.; Simon, P.; Keable, S.; Britz, A.; Tono, K.; Kim, K. S.; Park, S.-Y.; Lee, S. J.; Park, J.; Alonso-Mori, R.;Fuller, F. D.; Batyuk, A.; Brewster, A. S.; Bergmann, U.; Sauter, N. K.; Orville, A. M.; Yachandra, V. K.; Yano, J.; Lipscomb, J. D.; Kern, J.; Högbom, M. High-Resolution XFEL Structure of the Soluble Methane Monooxygenase Hydroxylase Complex with Its Regulatory Component at Ambient Temperature in Two Oxidation States. *J. Am. Chem. Soc.* **2020**, *142* (33), 14249–14266. https://doi.org/10.1021/jacs.0c05613.

Spectroscopic and catalytic features of a novel O2-stable M2-type [FeFe]-Hydrogenase

Subhasri Ghosh, Thomas Happe

Photobiotechnology, Faculty of Biology and Biotechnology, Ruhr-University Bochum

The increasing interest in the use of H2 as a "clean" alternative to fossil fuels, promotes the use of [FeFe]- hydrogenases as efficient biocatalysts for H2 production and uptake (2H+ + 2e- ⇔ H2) in regenerative bio-based fuel cells. The unique features of their active site (H-cluster) allow [FeFe]-hydrogenases to attain very high production rates of up to 10,000 H2 molecules per second. The H-cluster comprises a conventional [4Fe4S]-sub-cluster ([4FeH]) that enables intermittent storage and rapid supply of electrons for the reversible reduction of protons to H2 occurring at a covalently coupled [2Fe2S]-sub-cluster ([2FeH]). Unfortunately, this promising biocatalyst is highly sensitive to molecular oxygen (O2). Previous studies suggest that O2 irreversibly reacts with the distal iron center (Fed) of the [2FeH]-cluster and as a consequence of subsequent protonation steps is converted into the reactive oxygen species (ROS) which degrades the [2FeH]-cluster and the [4FeH]-cubane[1-2]. This O2 sensitivity of [FeFe]-hydrogenase poses an immense challenge for stabilizing the enzyme under aerobic conditions. By addressing this issue, we performed an extensive database search for [FeFe]-hydrogenases and identified an M2-type bacterial hydrogenase for detailed study. Our initial results show presence of an O2 protected state, although the hydrogenase has substantial dissimilarity in its sequence in comparison to the recently known O2 stable [FeFe]-hydrogenase CbA5H[3]. Interestingly, it also has shown different enzymatic features in FTIR-spectroscopy in contrast to the model hydrogenases known so far.

References:

1. Winkler *et. al., Biochim. Biophys. Acta* **2013**, *1827*, 974
2. Esselborn *et. al., J. Am. Chem. Soc.* **2019**, 141, 44, 17721–17728
3. Winkler *et. al., Nat. Commun.* **2021**, 12, 756

Exploring the Acid-induced Reduction of η^2-bound Nitrite on Copper(II)-Cobalt(II) Centres in a Bimetallic Complex

Jyotiprokash Biswas,[a‖] Kulbir,[b‖] Prabhakar Bhardwaj,[b‖] Somnath Ghosh,[b†] Carola Schulzke,[c] Ulf-Peter Apfel,*[a,d] Pankaj Kumar*[b]

[a]Inorganic Chemistry I – Industrial Electrochemistry Ruhr-Universität Bochum, Universitätsstrasse 150, NC 1/71a 44801 Bochum, Germany.

[b]Department of Chemistry, Indian Institute of Science Education and Research (IISER), Tirupati 517507, India.

[c]Institute for Biochemistry, University of Greifswald, Felix-Hausdorff-Straße 4, 17489 Greifswald, Germany

[d]Department of Electrosynthesis, Fraunhofer UMSICHT, Osterfelder Str. 3, 44607 Oberhausen, Germany

[‖]Equally contributing authors

Correspondences: ulf.apfel.rub.de; pankaj@iisertirupati.ac.in

Nitrite (NO_2^-) delivers nitric oxide (NO) in biological system in the moments of hypoxia via nitrite reductase enzymes (NIRs) under acidic conditions. Synthetically produced monometallic model systems of 3d-transition metals (*e.g.* Cu, Fe)[1,2,3] have shown acid-induced NO_2^- reduction, generating metal-nitrosyls or $NO_{(g)}$ with H_2O or H_2O_2 as side products. Herein, we report on the acid-induced reduction of η^2-bound NO_2^- in a hetero-bimetallic Cu^{II}-Co^{II} system to understand the effect of a bimetallic system.

Initially, a new hetero-bimetallic Cu^{II}-NO_2^--Co^{II} complex, $[(LN_8H)Cu^{II}(NO_2^-)Co^{II}]^{3+}$ bearing octadentate N_8-cryptand ligand (LN_8H), was prepared. Upon reaction with 1 equiv. acid the $[(LN_8H)Cu^{II}(NO_2^-)Co^{II}]^{3+}$ complex produces NO(g) via a proposed nitrous acid intermediate $[(LN_8H)Cu^{II}$-ONOH-$Co^{II}]^{4+}$, $[Cu(ONOH)Co]^{4+}$. In addition to NO(g), we observed as side product H_2O, which is believed to be formed via the decomposition of H_2O_2.

To verify that the observed NO is originating from the bound NO_2^-, the released gas mixture from the above mentioned NO_2^- reduction reaction was tracked using real-time headspace gas analysis using a gas mass analyzer and $NO_{(g)}$ formation was observed. Further mechanistic investigations, using ^{15}N-labeled-$^{15}NO_2^-$, ^{18}O-labeled-$^{18}O^{14}N^{16}O^-$ and D^+ source, revealed that the N-atom and O-atom in the $^{14/15}NO$ & $^{14}N^{18}O$ gases are derived from NO_2^- ligand and H-atom in H_2O derived from H^+-source, respectively. Previous reports on biomimetic modelling of NiRs & H^+-induced NO_2^- reduction reactions suggest cleavage of N-O bond of the ON-OH moiety in the proposed $[M^{n+}$-ONOH$]^{n+}$ intermediate to generate NO with H_2O[4,5] and in some cases •OH (H_2O_2)[6] or metal hydroxides.[7] To gain more insight about the reaction course, we performed •OH radical trapping experiment using a radical scavenger (2,4-DTBP), which confirmed the reaction sequences in which N-O bond homolysis generates •OH free radical from the ON-OH moiety, resulting in different products that were monitored with GC-MS and thus indirectly supporting the presence of proposed $[Cu(ONOH)Co]^{4+}$ intermediate in the 1 equiv. H^+ induced NO_2^- reduction reaction. Additionally, formation of •OH (H_2O_2) was confirmed and quantified via UV-Vis spectro-iodometric titration.

1. M. Kumar, N. A. Dixon, A. C. Merkle, M. Zeller, N. Lehnert, E. T. Papish, *Inorg. Chem.,* **2012**, *51*, 7004-7006.
2. S. Hong, J. J. Yan, D. G. Karmalkar, K. D. Sutherlin, J. Kim, Y. M. Lee, Y. Goo, P. K. Mascharak, B. Hedman, K. O. Hodgson,K. D. Karlin, E. I. Solomon, W. Nam, *Chem. Sci.,* **2018**, *9*, 6952-6960.
3. R. C. Maji, S. K. Barman, S. Roy, S. K. Chatterjee, F. L. Bowles, M. M. Olmstead, A. K. Patra, *Inorg Chem,* **2013**, *52*, 11084-11095.
4. B. A. Averill, *Chem. Rev.,* **1996**, *96*, 2951-2964.
5. S. Maekawa, T. Matsui, K. Hirao, Y. Shigeta, *J. Phys. Chem. B,* **2015**, *119*, 5392-5403.
6. W. M. Ching, P. P. Chen, C. H. Hung, *Dalton Trans.,* **2017**, *46*, 15087-15094.
7. M. Lintuluoto, J. M. Lintuluoto, *Metallomics,* **2018**, *10*, 565-578.

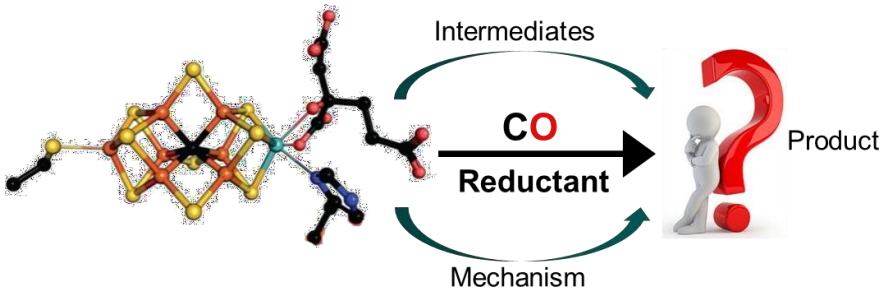
A Detailed Mechanism Investigation of CO Binding TO Molybdenum Nitrogenase Enzymes

Atanu Rana,[1] Casey Van Stappen,[1] Laure Decamps,[1] Serena DeBeer*[1]Affiliation:

Postdoctoral researcher

[1]Address: Max Planck Institute for Chemical Energy Conversion, Stiftstrasse 34-36,45470 Mülheim an der Ruhr, Germany.

Abstract: Nitrogenase (N2ase) is a microbial enzyme that converts inert atmospheric dinitrogen (N2) to bioavailable ammonia (NH3) under ambient conditions, a process essential for all life on the earth to build central metabolites, such as nucleotides and amino acids.[1] Three types of N2ases have been described, named after the heterometal of their catalytic cofactors, i.e., Mo N2ase (cofactor: [MoFe7S9C]), V N2ase (cofactor: [VFe7S8C(CO3)]), and Fe N2ase (putative cofactor composition: [Fe8S9C]).[2] While all three enzymes natively catalyse the reduction of N2 with varyingefficiencies, they exhibit low substrate specificity, promiscuously reducing a range of small molecule substrates like CO, CN-, C2H2 etc.[3] My work is dedicated to understanding the mechanism of CO reduction by Mo-N2ase. There are five differentspecies that have been characterized during the turnover condition with sodium dithionite as a reductant and CO as a substrate using EPR spectroscopy and stopped-flow FTIR, simultaneously (Scheme 1). Both are excellent tools for interrogating CO binding in N2ases; they provide orthogonal perspectives. To get certainty in our findings, we have monitored six different reaction conditions in terms of electron flux and substrate concentration. Based on these experimental results, we have constructed a plausible mechanism for CO binding to FeMoco where CO can only bindupon one e- reduction of the cofactor.



Scheme 1: Schematic representation of Mo-Nitrogenase reactivity towards CObinding.

References:

[1] Van Stappen, C.; Decamps, L.; Cutsail, G. E.; Bjornsson, III, R.; Henthorn, J. T.; Birrell J. A.;DeBeer, S. *Chem. Rev.*, **2020**, *120*, 5005.

[2] Chisnell, J. R.; Premakumar, R.; Bishop, P. E. *Journal of Bacteriology*, **1988**, *170*, 27-33.

[3] Seefeldt, L. C.; Yang, Z. Y.; Lukoyanov, D. A.; Harris, D. F.; Dean, D. R.; Raugei, S.; Hoffman, B.M. *Chem. Rev.* **2020**, *120*, 5082-510.

Reactive High-Spin Iron(IV)-Oxo Sites through Dioxygen Activation in a Metal-Organic Framework

Kaipeng Hou, Jonas Börgel, Henry Z. H. Jiang, **Daniel J. SantaLucia**,[1,2] Hyunchul Kwon, Hao Zhuang, Khetpakorn Chakarawet, Rachel C. Rohde, Jordan W. Taylor, Chaochao Dun, Maria V. Paley, Ari B. Turkiewicz, Jesse G. Park, Haiyan Mao, Ziting Zhu, E. Ercan Alp, Jiyong Zhao, Michael Y. Hu, Barbara Lavina, **Sergey Peredkov**,[1] Xudong Lv, Julia Oktawiec, Katie R. Meihaus, **Dimitrios A. Pantazis**,[2] Marco Vandone, Valentina Colombo, **Eckhard Bill**,[1] Jeffrey J. Urban, R. David Britt, Fernande Grandjean, Gary J. Long, **Serena DeBeer**,[1] **Frank Neese**,[2] Jeffrey A. Reimer, Jeffrey R. Long

[1] Max Planck Institute for Chemical Energy Conversion, 45470, Mülheim an der Ruhr, Germany

[2] Max-Planck-Institut für Kohlenforschung, 45470, Mülheim an der Ruhr, Germany

Natural nonheme Fe-containing enzymes utilize dioxygen from the atmosphere to produce high-valent Fe(IV)=O (i.e. ferryl oxo) intermediates capable of various hydrocarbon oxidation reactions, such as C–H bond oxygenations.[1,2] There is therefore great interest in developing bioinspired systems that can use O_2 to produce Fe(IV)=O species that can oxidize light hydrocarbons to make platform chemicals (e.g. the oxygenation of ethane to produce ethanol). In natural systems, ferryl oxo intermediates exhibit S = 2 (i.e. high-spin) states, which enables such reactivity. In contrast, the vast majority of synthetic Fe(IV)=O systems studied to date are S = 1 (i.e. intermediate-spin), and generally are formed with oxidants other than O_2, such as *m*CPBA, N_2O, and iodosobenzene, among others. Only a small number of synthetic compounds have been formed from dissolved molecular O_2.[3-6] Furthermore, compared to their S = 1 counterparts, there are not many examples of synthetic S = 2 ferryl oxo species reported in the literature.[7-15] There have been no examples of synthetic S = 2 ferryl oxo species produced from O_2 as the O-atom source until now. We report the first example of such a system, a metal-organic framework (MOF), bioinspired by taurine α-ketoglutarate dioxygenase (TauD)[16] capable of catalytic cyclohexane oxidation at room temperature and with demonstrated stoichiometric ethane oxidation. The catalytic cycle of the MOF system is proposed to be analogous to that of the TauD cycle, where intermediate *J* (TauD-*J*) is similar to the S = 2 Fe(IV)=O intermediate formed in the MOF catalytic cycle. The focus of this investigation is on the spectroscopic characterization of this high-spin ferryl oxo species via variable-temperature/variable-field (VTVH) Mössbauer spectroscopy as well as Fe Kβ X-ray emission spectroscopy (XES), both of which unambiguously show that the Fe(IV)=O intermediate is S = 2, in agreement with theoretical methods that suggested that the structure and spin state are similar to TauD-*J*.[17]

References:

1. Hohenberger, J.; Ray, K.; Meyer, K. The biology and chemistry of high-valent iron–oxo and iron–nitride complexes. *Nat. Commun.* **2012**, *3*, 720.
2. Guo, M.; Corona, T.; Ray, K.; Nam, W. Heme and Nonheme High-Valent Iron and Manganese Oxo Cores in Biological and Abiological Oxidation Reactions. *ACS Cent. Sci.* **2019**, *5*, 13-28.

3. Thibbon, A.; England, J.; Martinho, M.; Young, V. G., Jr.; Frisch, J. R.; Guillot, R.; Girerd, J.-J.; Münck, E.; Que, L., Jr.; Banse, F. Proton- and Reductant-Assisted Dioxygen Activation by a Nonheme Iron(II) Complex to Form an Oxoiron(IV) Intermediate. *Angew. Chem. Int. Ed.* **2008**, *47*, 7064-7067.
4. Li, F.; Van Heuvelen, K. M.; Meier, K. K.; Münck, E.; Que, L., Jr. Sc^{3+}-Triggered Oxoiron(IV) Formation from O_2 and its Non-Heme Iron(II) Precursor via a Sc^{3+}–Peroxo–Fe^{3+} Intermediate. *J. Am. Chem. Soc.* **2013**, *135*, 10198-10201.
5. Kass, D.; Corona, T.; Warm, K.; Braun-Cula, B.; Kuhlmann, U.; Bill, E.; Mebs, S.; Swart, M.; Dau, H.; Haumann, M.; Hildebrandt, P.; Ray, K. Stoichiometric Formation of an Oxoiron(IV) Complex by a Soluble Methane Monooxygenase Type Activation of O_2 at an Iron(II)-Cyclam Center. *J. Am. Chem. Soc.* **2020**, *142*, 5924-5928.
6. Dedushko, M. A.; Greiner, M. B.; Downing, A. N.; Coggins, M.; Kovacs, J. A. Electronic Structure and Reactivity of Dioxygen-Derived Aliphatic Thiolate-Ligated Fe-Peroxo and Fe(IV) Oxo Compounds. *J. Am. Chem. Soc.* **2022**, *144*, 8515-8528.
7. England, J.; Martinho, M.; Farquhar, E. R.; Frisch, J. R.; Bominaar, E. L.; Münck E.; Que, L., Jr. A Synthetic High-Spin Oxoiron(IV) Complex: Generation, Spectroscopic Characterization, and Reactivity. *Angew. Chem. Int. Ed.* **2009**, *48*, 3622-3626.
8. England, J.; Guo, Y.; Van Heuvelen, K. M.; Cranswick, M. A.; Rohde, G. T.; Bominaar, E. L.; Münck, E.; Que, L., Jr. A More Reactive Trigonal-Bipyramidal High-Spin Oxoiron(IV) Complex with a cis-Labile Site. *J. Am. Chem. Soc.* **2011**, *133*, 11880-11883.
9. Lacy, D. C.; Gupta, R.; Stone, K. L.; Greaves, J.; Ziller, J. W.; Hendrich, M. P.; Borovik, A. S. Formation, Structure, and EPR Detection of a High Spin Fe(IV)–Oxo Species Derived from Either an Fe(III)–oxo or Fe(III)–OH Complex. *J. Am. Chem. Soc.* **2010**, *132*, 12188-12190.
10. Xue, G.; Fiedler, A. T.; Martinho, M.; Münck, E.; Que, L., Jr. Insights into the P-to-Q conversion in the catalytic cycle of methane monooxygenase from a synthetic model system. *Proc. Natl. Acad. Sci. U.S.A.* **2008**, *105*, 20615-20620.
11. Bigi, J. P.; Harman, W. H.; Lassalle-Kaiser, B.; Robles, D. M.; Stich, T. A.; Yano, J.; Britt, R. D.; Chang, C. J. A High-Spin Iron(IV)–Oxo Complex Supported by a Trigonal Nonheme Pyrrolide Platform. *J. Am. Chem. Soc.* **2012**, *134*, 1536-1542.
12. Biswas, A. N.; Puri, M.; Meier, K. K.; Oloo, W. N.; Rohde, G. T.; Bominaar, E. L.; Münck, E.; Que, L., Jr. Modeling TauD-*J*: A High-Spin Nonheme Oxoiron(IV) Complex with High Reactivity toward C–H Bonds. *J. Am. Chem. Soc.* **2015**, *137*, 2428-2431.
13. Gordon, J. B.; Albert, T.; Dey, A.; Sabuncu, S.; Siegler, M. A.; Bill, E.; Moënne-Loccoz, P.; Goldberg, D. P. A Reactive, Photogenerated High-Spin (S = 2) Fe^{IV}(O) Complex via O_2 Activation. *J. Am. Chem. Soc.* **2021**, *143*, 21637-21647.
14. Oswald, V. F.; Lee, J. L.; Biswas, S.; Weitz, A. C.; Mittra, K.; Fan, R.; Li, J.; Zhao, J.; Hu, M. Y.; Alp, E. E.; Bominaar, E. L.; Guo, Y.; Green, M. T.; Hendrich, M. P.; Borovik, A. S. Effects of Noncovalent Interactions on High-Spin Fe(IV)–Oxido Complexes. *J. Am. Chem. Soc.* **2022**, *142*, 11804-11817.
15. Hill, E. A.; Weitz, A. C.; Onderko, E.; Romero-Rivera, A.; Guo, Y.; Swart, M.; Bominaar, E. L.; Green, M. T.; Hendrich, M. P.; Lacy, D. C.; Borovik, A. S. Reactivity of an Fe^{IV}-Oxo Complex with Protons and Xxidants. *J. Am. Chem. Soc.* ***2016, 138***, 13143-13146.
16. Krebs, C.; Galonić Fujimori, D.; Walsh, C. T.; Bollinger, J. M., Jr. Non-Heme Fe(IV)–Oxo Intermediates. *Acc. Chem. Res.* **2007**, *40*, 484-492.
17. Hou, K.; Börgel, J.; Jiang, H. Z. H.; SantaLucia, D. J.; Kwon, H.; Zhuang, H.; Chakarawet, K.; Rohde, R. C.; Taylor, J. W.; Dun, C.; Paley, M. V.; Turkiewicz, A. B.; Park, J. G.; Mao, H.; Zhu, Z.; Alp, E. E.; Zhao, J.; Hu, M. Y.; Lavina, B.; Peredkov, S.; Lv, X.; Oktawiec, J.; Meihaus, K. R.; Pantazis, D. A.; Vandone, M.; Colombo, V.; Bill, E.; Urban, J. J.; Britt, R. D.; Grandjean, F.; Long, G. J.; DeBeer, S.; Neese, F.; Reimer, J. A.; Long, J. R. Reactive high-spin iron(IV)-oxo sites through dioxygen activation in a metal–organic framework. *Science* **2023**, *382*, 547-553.

Structure and Function of the Photosynthetic Cytochrome c550: Insights from QM/MM Calculations

Sinjini Bhattacharjee, Frank Neese, Dimitrios A. Pantazis

Max-Planck-Institut für Kohlenforschung, Mülheim an der Ruhr, Germany

Redox processes involving transition metal systems play pivotal roles in chemistry and biology, spanning from bioinspired catalysts to fundamental energy conversion processes in nature. One notable example is found in photosynthesis, where Photosystem II (PSII) catalyses the oxidation of H_2O into molecular O_2 and initiates an electron transfer (ET) cascade, ultimately generating a proton gradient across the thylakoid membrane.[1] Cytochromes (Cyt) are known to serve as prominent redox active cofactors facilitating ET. Within cyanobacterial PSII, Cyt c550 (PsbV) is a membrane-extrinsic soluble domain featuring a distinctive heme-c active site. However, discrepancies in reported midpoint potentials (E_m) for the soluble versus PSII-bound forms of Cyt c550 raise intriguing questions regarding its potential role in photosynthetic ET.[2, 3] A theoretical investigation of this system is challenging due to the coupling between the electronic changes at the heme active site and the conformational changes of the surrounding protein matrix. This places heavy demands on computational approaches, both in terms of an accurate representation of the coordination environment and in the choice of electronic structure method.[4] In this study, we employ a multiscale modeling approach within the MM/MD and QM/MM framework, complemented by DFT and high-level wave function based quantum chemical methods to accurately determine the redox potentials of Cyt c550. This approach takes into account local structural changes and secondary sphere interactions around the heme active site to assess their possible influence on the redox potential of Cyt c550 in distinct environments. Our results highlight the role of explicit solvation and global protein electrostatics in modulating the redox properties of metallocofactors within complex biological systems.

References

1. N. Cox, D. A. Pantazis and W. Lubitz, *Annu. Rev. Biochem.*, 2020, **89**, 795-820.
2. M. Roncel, D. Kirilovsky, F. Guerrero, A. Serrano and J. M. Ortega, *Biochim. Biophys. Acta*, 2012, **1817**, 1152-1163.
3. F. Guerrero, A. Sedoud, D. Kirilovsky, A. W. Rutherford, J. M. Ortega and M. Roncel, *J. Biol. Chem.*, 2011, **286**, 5985-5994.
4. S. Bhattacharjee, M. Isegawa, M. Garcia-Ratés, F. Neese and D. A. Pantazis, *J. Chem. Theory Comput.*, 2022, **18**, 1619-1632.

ENDOR Spectroscopy and Analysis of Copper Oxygen Adductsof a Model Complex

Sarmistha Bhunia,[1] Blaise Geoghegan,[1] George E. Cutsail[1]*

Affiliation: Post-doctoral Researcher,

[1]Max Planck Institute for Chemical Energy Conversion, Stiftstrasse 34–36,45470 Mülheim an der Ruhr, Germany

Abstract: Numerous biomimetic copper complexes have been employed to identify the oxygen bound adducts and to explore the reaction mechanism towards dioxygen and peroxide.[1,2,3] So far, the copper(II)-hydroperoxo intermediate is known to play a crucial role inbiological oxidations of certain Cu containing monooxygenases.[4] However, the question remains about the structure function relationship in terms of the electronic nature, bonding interactions of the surrounding nuclei with the paramagnetic metal center. Our goal is to utilize advanced EPR techniques like electron nuclear double resonance (ENDOR) spectroscopy tomeasure the orientational hyperfine couplings (HFC) and also the spin densities of the oxygenatoms of $[Cu(Me_6\text{-tren})(X)]^{2+}$(X = H_2O, OH^-, OOH^-) complexes having different axial ligation. Two complexes have been prepared with water (Cu-OH_2) and hydroxide (Cu-OH) ligands to examine the structural variation, metal-ligand covalency for a neutral vs anionic ligand by thepulse EPR, ENDOR spectroscopic studies using their corresponding ^2H and ^{17}O isotopic analogues. By the ^1H Davies and ^2H Mims ENDOR measurements, we can get information about the nature of bonding and coupling of protons from the ligand backbone as well as axialH_2O/OH^- coordination. Additionally, the EPR parameters from our results also matches well with the Density functional theory calculations. The generation of isotopically labelled (^{17}O) peroxide species from $[Cu(Me_6\text{-tren})(MeCN)]^{2+}$ complex is proceeding followed by the ^{17}O ENDOR measurement and thereby, a correlation between oxygen atomic charge, HFC and spin population associated with the reactivity can be obtained.

Reference:

[1] Siegfried Schindler*, Eur. J. Inorg. Chem. 2000, 231122326.

[2] Michael Becker, Frank W. Heinemann, and Siegfried Schindler*, Chem. Eur. J. 1999, 5, 3124-3129.

[3] Yu Jin Choi,[a] Kyung-Bin Cho,[b] Minoru Kubo,[c] Takashi Ogura,c Kenneth D. Karlin,[b,d] Jaeheung Cho*[a]and Wonwoo Nam*[a,b] Dalton Trans., 2011, 40, 2234–2241.

[4] Katlyn K. Meier,[†,‡] Stephen M. Jones,[†,‡] Thijs Kaper,[§] Henrik Hansson,[∥] Martijn J. Koetsier,[⊥] Saeid Karkehabadi,[∥] Edward I. Solomon,[*,†] Mats Sandgren,[*,∥] and Bradley Kelemen[*,§], Chem. Rev. 2018, 118, 2593−2635.

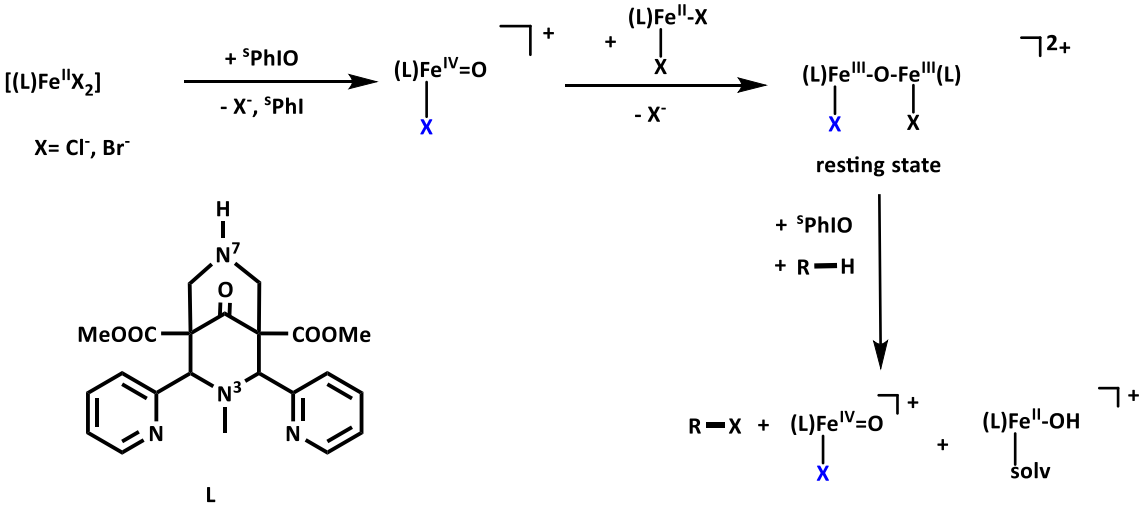
A μ-oxo diiron(III) bispidine-mediated selective halogenation of alkanes

Rejith Radhamani, Gunasekaran Velmurugan, Peter Comba*

Universität Heidelberg, Anorganisch-Chemisches Institut, Im Neuenheimer Feld 270, 69120 Heidelberg, Germany

E-Mail: rejithraj.radhamani@aci.uni-heidelberg.de

Non-heme iron enzymes are known to oxidize a range of substrates by catalyzing the activation of dioxygen. The Fe(IV)-oxido species are generally believed to be key reactive intermediates in non-heme iron enzymes for performing different natural transformations like halogenation, hydroxylation and olefin epoxidation. Spectroscopic studies implicate high-valent diiron species as intermediates in the oxidation chemistry of the diiron centers in methane monooxygenase (MMO) and ribonucleotide reductase (RNR), while mononuclear Fe(IV)-oxido units have been proposed as the oxidant for several mononuclear nonheme iron enzymes.[1,2] Our synthetic efforts to obtain models for such high-valent intermediates have yielded $[Cl(L)Fe^{III}\text{-}O\text{-}Fe^{III}(L)Cl]^{2+}$ as a resting state, where L is a bispidine ligand.[3] This resting state complex has been successfully synthesized by the stoichiometric oxidation of $[(L)Fe^{II}Cl_2]$ with iodosylbenzene and is fully characterized. Experimental data indicate that with $[Cl(L)Fe^{III}\text{-}O\text{-}Fe^{III}(L)Cl]^{2+}$ and cyclohexane or cyclopentane as substrate, there is selective formation of chlorocyclohexane or chlorocyclopentane, respectively. For a detailed understanding of the mechanism of the selective halogenation of alkanes, a thorough computational study was conducted.



References

1. P. C. Bruijnincx, G. van Koten, R. J. K. Gebbink, *Chem. Soc. Rev.* **2008**, *37*, 2716-2744.
2. K. Bleher, P. Comba, D. Faltermeier, A. Gupta, M. Kerscher, S. Krieg, B. Martin, G. Velmurugan, S. Yang, *Chem. Eur. J.* **2022**, *28*, e202103452.
3. M. Abu-Odeh, K. Bleher, N. Johnee Britto, P. Comba, M. Gast, M. Jaccob, M. Kerscher, S. Krieg, M. Kurth, *Chem. Eur. J.* **2021**, *27*, 11377-11390.

Second sphere residue effects on K-edge X-ray absorption spectroscopy and reactivity in Lytic Polysaccharide Monooxygenases: a computational study.

Ashish Tamhankar[1], Sergio A. V. Jannuzzi[1], Kelsi R. Hall[2], Chris Joseph[1], Iván Ayuso-Fernández[2], Lukas Rieder[3], Rannei Skaali[2], Ole Golten[2], Frank Neese[4], Åsmund K. Røhr[2], Vincent G. H. Eijsink[2]*, Morten Sørlie2*, Serena DeBeer[1]*

[1]Max Planck Institute for Chemical Energy Conversion, Stiftstraße 34-36, 45470 Mülheim an der Ruhr, Germany.

[2] Faculty of Chemistry, Biotechnology and Food Science, Norwegian University of Life Sciences (NMBU), Ås, Norway.

[3] Institute for Molecular Biotechnology, Graz University of Technology, Graz, Austria.

[4] Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, 45470 Mülheim an der Ruhr, Germany.

Abstract body: Lytic polysaccharide monooxygenases (LPMOs) are monocopper enzymes which activate strong C–H bonds through a mechanism that remains a matter of debate. The LPMO active site is largely conserved and features a “histidine brace” motif as the primary coordination sphere ligating a mononuclear copper center. However, the secondary sphere around the copper site has large variations through the LPMO subfamilies, which may allow for tailoring of the copper site and substrate binding pockets. In this study, by mutating this residue we investigated the role of a conserved glutamine residue (Gln164) in the second coordination sphere of *Nc*AA9C LPMO on the reoxidation rate of the Cu(I) enzyme with H_2O_2 (co-substrate) in the absence of polysaccharide substrate.

Experimental reaction rates showed that the nature of the headgroup of the second-sphere residue, Gln164 fine tunes LPMO functionality and copper reactivity. Mutation to Glu lowered the reduction potential and decreased the ratio between reduction and reoxidation rates. Quantum mechanical calculations suggested mechanistic differences in the H_2O_2 splitting pathway between the wild type and Gln164Glu mutant LPMO. Comparison between calculated and experimental XAS spectra indicated potential protonation state variation in the Glu residue. Reactivity calculations with varying Glu164 protonation states might explain the differences in the experimental reoxidation rate and indicate an altered reaction mechanism with a Cu(III)-hydroxide species being formed after H_2O_2 activation. This study highlights the crucial role of the second sphere residue in LPMO catalytic functioning, suggesting potential for LPMO-inspired synthetic catalysts targeting various C-H bond activation reactions.

Probing the General Base for DNA Polymerization in Telomerase: A QM/MM Molecular Dynamics Investigation

Chandan K. Das[1], *Abhinav Gupta*[2], *& Nisanth N. Nair*[2]

[1]Computational Biotechnology, RWTH Aachen University, Germany

[2]*Department of Chemistry, IIT Kanpur, India*
email id: c.das@biotec.rwth-aachen.de, nnair@iitk.ac.in

Nucleic acid polymerization catalyzed by nucleic acid polymerase lies at the core of genetic inheritance. Often nucleic acid polymerases are considered as effective drug targets for the treatment of cancer. Telomerase which is involved in the incorporation of telomeric DNA sequence at the 3' end of the eukaryotic chromosome, has particularly gained interest in the anti–cancer therapeutic research because of their hyperactivity found in cancer cells. The molecular mechanism of telomerase catalyzednucleic acid polymerization, especially the general base in deprotonation of 3'-hydroxyl, remains unclear. To shed light on this, we perform extensive DFT-based QM/MM molecular dynamics (MD) simulation combined with a powerful enhanced sampling technique, namely metadynamics, based on which, we present here a novel mechanistic insight into the telomerase catalyzed DNA polymerization, in particular, the role of bulk water in deprotonation of 3'-hydroxyl will be discussed. We will also show that our findings are in agreement with the results from time-resolved X-ray crystallography and the kinetic experiments.

References:

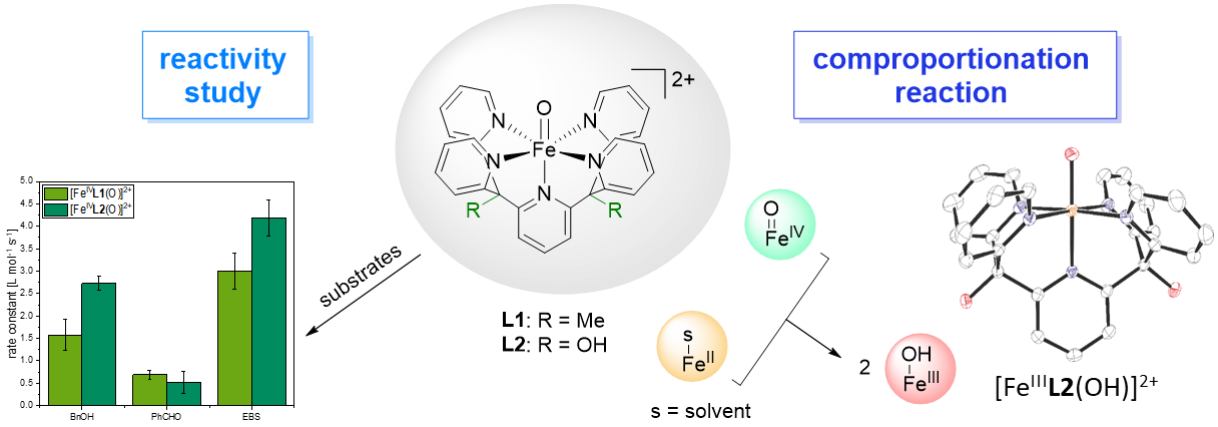
Phys. Chem. Chem. Phys., **2023**, 25, 14147-14157 *DOI:10.1039/D3CP00521F*

Two plus four equals three – iron(II)/iron(IV) comproportionationreactions and iron(IV)-oxido reactivity studies

Annika Menke, Niko S. W. Lindlar né Jonasson, Laura Senft, Andrea Squarcina, David Schmidl, Jan C. Kruse, Thomas Josephy, Peter Mayer, Peter Comba, FrancMeyer, Ivana Ivanović-Burmazović, Lena J. Daumann*

Heinrich-Heine-Universität, Institut für Bioanorganische Chemie,Universitätsstraße 1, 40225 Düsseldorf, lena.daumann@hhu.de.

Iron enzymes are ubiquitous in nature and perform a vast variety of reactions.Especially for those enzymes bearing iron-oxygen compounds as active sites, varioussynthetic model complexes have been developed such as iron(III)-hydroxido[1] (lipoxygenase) or iron(IV)-oxido complexes[2] (various iron(II)/α-KG-dependent enzymes). Different derivatives of pentapyridyl (PY5/Py_5) ligand systems are commonly used for this purpose as iron complexes thereof often can be handled undernearly physiological conditions (soluble in water, stable at room temperature). The iron(IV)-oxido complex $[Fe^{IV}(O)\mathbf{L1}]^{2+}$ (or $[Fe^{IV}(O)Py_5Me_2H]^{2+}$ developed by Chang et al.[3] was recently established as good model complex for TET enzymes by us.[2]



In this work, the repertoire of literature-known iron complexes containing Py_5-ligands was expanded. Two complete series of iron(II), iron(III) and iron(IV) species of the Py_5Me_2 (**L1**) and $Py_5(OH)_2$ (**L2**) ligand systems are presented here, including two newmononuclear iron(III)-hydroxido and a new iron(IV)-oxido species. All synthesized compounds were characterized using electron paramagnetic resonance, Mößbauer and UV-vis spectroscopy as well as cyclic voltammetry and high-resolution mass spectrometry. It was found that iron(II) and iron(IV)-oxido complexes comproportionateto afford the corresponding iron(III) species. In addition, a comparative reactivity studycontaining several substrates with C-H moieties was performed.

References:

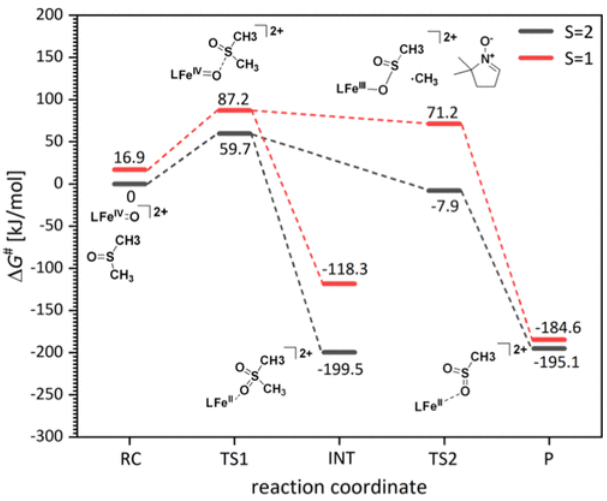
[1] Stack and coworkers *J. Am. Chem. Soc*. **2002**, *124* (1), 83–96.
[2] Daumann and coworkers. *Angew. Chem. Int. Ed*. **2021**, *60* (39), 21457–21463.
[3] Chang and coworkers *Inorg. Chem*. **2015**, *54* (12), 5879–5887.

Exploring the mechanism of nonheme bispidine-iron-oxo catalyzed C_1 and C_2 compound formation from various organic substrates

Gunasekaran Velmurugan[a], Jonas Hädeler[b], Rebekka Lauer[b], Rejith Radhamani[a], Frank Keppler[b], and Peter Comba[a]

[a]*Institute of Inorganic Chemistry, Heidelberg University, Heidelberg, Germany*
[b]*Institute of Geosciences, Heidelberg University, Heidelberg, Germany*
E-mail: peter.comba@aci.uni-heidelberg.de

Methane (CH_4) is the most abundant organic trace gas in the atmosphere and has a significant role in tropospheric and stratospheric chemistry. Most natural sources are associated with microorganisms living under anaerobic conditions in wetlands, rice fields, landfills or the gastrointestinal tracts of ruminants and termites. However, recent studies have revealed direct CH_4 release from eukaryotes, including plants, animals, fungi, and lichens, even in the absence of microbes and in the presence of oxygen. These novel aerobic CH_4 production routes differ from the well-known anaerobic pathway that involves catalytic activity by methanogenic enzymes. We have explored a range of nonheme oxo-iron(IV) model systems with tetra- or pentadentate bispidine ligands that to produce methane from organic material with methyl-substituted heteroatoms, e.g., methionine.[1] This model reaction for the natural aerobic production of methane is shown to proceed via two sulfoxidation steps involving the oxo-iron(IV) complexes, with a bifurcation in the second step that either produces the sulfone or leads to demethylation with similar probabilities. The resulting methyl radicals lead to C_1 and C_2 compounds in all possible oxidation states.



Together with ^2H, ^{13}C and ^{18}O labeling studies and product analyses, density functional theory (DFT) has helped to understand the reaction mechanisms. A main objective is to include all relevant substituted organic compounds as substrates for the formation of methane and other C_1 and C_2 compounds in various oxidation states. There are three possible pathways for the product formation, i.e. hydrogen atom abstraction (HAA), oxygen atom transfer (OAT) and outer sphere electron transfer. The combination of DFT shows that for thioethers and sulfoxides, methyl radicals are produced by OAT,[2] while other routes prevail for other substrates.[3] This study is shown to give deeper insights into the reaction mechanism for the formation of methane and other volatile organic compounds that are of importance in the carbon cycling and the atmospheric physics and chemistry.

References

1. Benzing, K.; Comba, P.; Martin, B.; Pokrandt, B.; Keppler, F. *Chem. - Eur. J.* **2017**, *23*, 10465.
2. Hädeler, J.; Velmurugan, G.; Lauer, R.; Radhamani, R.; Keppler, F.; Comba, P. *J. Am. Chem. Soc.* **2023**, https://doi.org/10.1021/jacs.3c06709.
3. Velmurugan, G.; Comba, P. *J. Comput. Chem.* **2023** (under revision).

Dioxygen Activation at a Co(II) Centre Supported by a Redox Non-innocent Guanidine Based NNN Pincer type ligand

Dibya Jyoti Barman, Prof. Dr. Kallol Ray*

Institut für Chemie, Humboldt-Universität zu Berlin, Brook-Taylor-Straße 2, 12489Berlin, Germany

Abstract: Transition metal mediated dioxygen activation is crucial for numerous biological metalloenzymes and industrial related synthetic catalysts.[1] Employing different first row transition metal centres surrounded by biologically inspired and goaloriented ligand systems has emerged as one of the definitive directions to understandthe fundamental in-between steps of dioxygen activation.[2] Namely, one electron reduction of dioxygen to generate metal superoxo species is believed to be the first key step[3] towards dioxygen transformation and catalysis. In spite of extensive studiesin the past,[4] only a small subset of these metal complexes with special ligand architecture enabled the trapping of reactive metal(III)-superoxo intermediate prior to O–O bond cleavage to form high valent metal(IV)-oxo species.

In most cases, the cobalt(II) complexes either remain oxygen inert or form comparatively less reactive low spin cobalt(III)-superoxo and μ-peroxo species upondonating one electron to dioxygen. However, a very few cobalt complexes has lately emerged, after carefully tailoring of the ligand systems (amidophenyl amine, thiolate, aminophenolate etc.),[5] capable of donating electrons to dioxygen to form versatile cobalt(II)-superoxo intermediate.

In this poster, a novel guanidine based NNN pincer type cobalt(II) complex will be presented that forms interesting superoxo and hydroperoxo species, upon oxygen reduction by taking advantage of the ligand non-innocence, thereby keeping the Cobalt oxidation state unchanged at +2. Furthermore, reactivity studies demonstrate that the cobalt(II)-superoxo species form a cobalt(II)-nitrate moiety upon reaction withnitrogen monoxide, possibly via the involvement of a peroxynitrite intermediate. The systematic research and reactivity studies to be presented will be in contingence within-depth spectroscopic and crystallographic analyses to understand the role of ligandinfluence, metal oxidation and spin states.

References:

[1] M. Costas, M. P. Mehn, M. P. Jensen, L. Que, *Chemical Reviews* **2004**, *104*, 939-986.
[2] E. G. Kovaleva, J. D. Lipscomb, *Nature Chemical Biology* **2008**, *4*, 186-193.
[3] J. P. T. Zaragoza, D. P. Goldberg, in *Dioxygen-dependent Heme Enzymes* (Eds.: M. Ikeda- Saito, E. Raven), The Royal Society of Chemistry, **2018**, p. 0.
[4] aG. A. Rodley, W. T. Robinson, *Nature* **1972**, *235*, 438-439; bE. C. Niederhoffer, J. H. Timmons, A. E. Martell, *Chemical Reviews* **1984**, *84,* 137-203; cD. H. Busch, N. W. Alcock, *Chemical reviews* **1994**, *94,* 585-623.

[5] aA. R. Corcos, O. Villanueva, R. C. Walroth, S. K. Sharma, J. Bacsa, K. M. Lancaster, C. E. MacBeth, J. F. Berry, *Journal of the American Chemical Society* **2016**, *138*, 1796-1799; bJ. B.Gordon, A. C. Vilbert, M. A. Siegler, K. M. Lancaster, P. Moënne-Loccoz, D. P. Goldberg, *Journal of the American Chemical Society* **2019**, *141*, 3641-3653; cP. Kumar, S. V. Lindeman, A. T. Fiedler, *Journal of the American Chemical Society* **2019**, *141*, 10984-10987.

Electrocatalytic Nitrite Reduction by Fe-Porphyrin Based Metal-Organic Framework with High Rate and Selectivity in Presence of Secondary Sphere Interaction

Arnab Ghatak, Idan Hod*

Post-Doctoral Research Scientist, Ben Gurion University of the Negev, Israel

Email: ghatak@post.bgu.ac.il / ghatak65arnab@gmail.com

The challenge with six electron nitrite reduction process is selectivity as well as slow kinetics in presence of competitive hydrogen evolution reaction owing to low Faradaic efficiency (FE), and hence proper design of suitable catalyst is the need of the hour. Heme (Fe-porphyrin) embedded Zr_6-oxo based 2D MOF(Zr-BTB)[1], has been used as an efficient selective nitrite reduction catalyst, taking advantage of the chemical robustness and mass transport properties of the MOF, where for the first time in MOF system post synthetic tethering with hydroxy benzoic acid is done to mimic the H-bond donor ability and proton translocation of the Tyr residue present in the native enzyme. Generating second sphere H-bonding and proton relay interaction with the iron porphyrin in presence of MOF's inherent properties enables to achieve more than 90% selectivity in terms of FE of NH_3 from nitrite in aqueous solution under heterogeneous electrochemical condition. Spectroelectrochemical analysis shows the formation of reactive intermediate Fe bound NO during the course of the reaction, which gets stabilized in presence of hydroxy groups to increase the rate (~5 times) and selectivity (>30%). This depicts an alternative NH_3 synthesis method with clean reagent from wastewater nitrite having high selectivity and reactivity.

References

[1] Shimoni, R.; Shi, Z.; Binyamin, S.; Yang, Y.; Liberman, I.; Ifraemov, R.; Mukhopadhyaya, S.; Zhang, L.; Hod, I. *Angew.chemie*. **2022**, *61* (32).

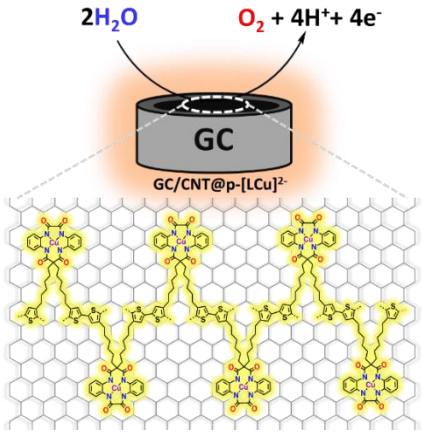
Robust Molecular Anodes for Electrocatalytic Water Oxidation Based on Electropolymerized Molecular Cu Complexes

Koushik Ranu[1], Sebastian Amthor[1], Carlos. G. Bellido[1], Fernando. F. Salomon[1], Marcos Gil-Sepulcre[1*], Antoni Llobet[1,2*]

[1] Institute of Chemical Research of Catalonia (ICIQ), Barcelona Institute of Science and Technology (BIST), Tarragona, Spain, Avinguda Països Catalans 16, 43007 Tarragona, Spain

[2] Departament de Química, Universitat Autònoma de Barcelona, 08193 Cerdanyola del Vallès, Barcelona, Spain. kranu@iciq.es

Artificial photosynthetic systems have gained attention to produce solar fuels in a sustainable way. Solar-driven water oxidation reaction (WOR) is an essential reaction to understand these systems. However, as this process is thermodynamically uphill, catalysts play important role to overcome the barrier. Towards this goal, d-block metals show unprecedented efficiency in different forms, from oxides to molecular systems.[1] From past decades, several synthetic molecular water oxidation catalysts (WOCs) have been developed in order to get insight to the mechanism of O-O bond formation which involves multielectron and multiproton catalytic processes.[2] Nonetheless, water oxidation reaction is still practically a big challenge. This work reports a Cu based molecular WOC based on TAML ligands $[LCu]^{2-}$.[3] This system has been modified with thiophene moieties that can polymerize on different graphitic surfaces [4] under oxidative conditions. The versatility of this approach is to increase a loading of the catalyst as a film on heterogeneous surfaces. The resulting hybrid electroanode shows excellent performance to catalyse water to dioxygen at neutral pH achieving current density of 22 mA/cm^2 at 1.45 V vs NHE and working at an onset overpotential around 250 mV. Regarding the stability in long run, we achieved TONs in the range of 5000 during 24h in CPE with no apparent loss of activity and keeping its integrity as molecular catalyst.



References

[1] Hunter. B.M, Gray. H.B, Muller A.M, *Chem. Rev.* **2016**, *116*, 22, 14120–14136

[2] Siegbahn. E.M. , Biochimica et Biophysica Acta 1827 (2013) 1003–1019

[3] P. Garrido-Barros, I. Funes-Ardoiz, S. Drouet, J. Benet-Buchholz, F. Maseras, A. Llobet, *J. Am. Chem. Soc.* **2015**, 137, 21, 6758–6761

[4] P. Garrido-Barros, C. Gimbert-Suriñach, D. Moonshiram, A. Picón, P. Monge, V. S. Batista, A. Llobet, *J. Am. Chem. Soc.* **2017**, 139, 37, 12907–12910

Elucidating the Mechanism of CO2 Reduction by Mn/Re Catalysts: A Time-resolved Spectroscopic Investigation

Samir Chattopadhyay, Reiner Lomoth, * Leif Hammarström* Department of Chemistry

Angstrom Laboratory, Uppsala University, Box 523,
75120 Uppsala, Sweden

Electrocatalytic and photocatalytic CO_2 reduction (CO_2RR) hold great promise for addressing climate change and reducing reliance on fossil fuels in various industries.[1] Molecular CO_2RR catalysts offer benefits like tunability, selectivity, and efficiency, [2] butenhancing their suitability for industrial use requires a more profound understanding of their underlying mechanisms, an area where current CO_2RR research falls short.

Re and Mn bipyridine tricarbonyl complexes ($M(bpy)(CO)_3X$, X= -Cl/-Br, M= Re/Mn) are known for their CO_2 reduction capabilities.[3,4] The Re complex can reduce CO_2 to CO without the need for a Brønsted acid, whereas the Mn counterpart requires an acidsource to activate CO_2.[4] Current renewable energy research is focused on developing molecular CO_2RR catalysts with 2nd sphere residues (providing H+ transfer, electrostatic interaction, H-bonding, and Lewis acid residues for intermediates stabilization) around their active sites.[5] This approach enhances efficiency and productselectivity. To design efficient catalysts for producing formate, CO, CH_4, and other products from CO_2, understanding the mechanistic cycle is crucial. However, there remains a lack of comprehensive understanding of the CO_2RR mechanistic cycle catalyzed by Re/Mn-bipyridine complexes.[6] A recently proposed cycle combines density functional theory calculations with experimental evidence.[7]

This work aims to uncover the mechanistic cycle by synthesizing intermediatesindependently and examining the effects of adding reducing equivalents and protons.We will employ time-resolved FTIR and a stopped-flow mixing system to track CO vibrational frequency changes within catalysts at a sub-millisecond scale. Few in- depth analyses of intermediate formation and decay exist. Our objective is to explorethe catalytic cycle through various intermediates, thoroughly investigating their kineticsof formation and decay.

References:

1. Zhang, S.; Fan, Q.; Xia, R.; Meyer, T. J. *Accounts of Chemical Research* **2020**, 53 (1), 255.

2. Amanullah, S.; Saha , P.; Nayek , A.; Ahmed, M. E.; Dey, A. *Chem. Soc. Rev.*, **2021**, **50** , 3755

3. Hawecker, J.; Lehn, J.-M.; Ziessel, R. *Journal of the Chemical Society, Chemical Communications* 1**984***,* (6)*,* 328

4.Bourrez, M.;Molton,F.;Chardon Noblat,S.;Deronzier,.*Angew.Chem.,Int. Ed*. **2011**,50,9903

5. Nichols, A.W.; Machan, C.W. *Frontiers in Chemistry*, **2019**, 2296

6. Riplinger, C.; Carter, E. A.; *ACS Catalysis*, **2019**, 5, 900

7. Riplinger, C.; Sampson, M. D.; Ritzmann, A. M.; Kubiak, C. P.; Carter, E. A. *J. Am. Chem. Soc*. **2014**,136 (46), 16285

A Rare Ni(II)-Monomethyl Complex as a Model for Acetyl-CoA Synthase

Shounak Nath†, Leonel Griego† and Liviu Mirica†

†Department of Chemistry, University of Illinois at Urbana-Champaign, Urbana IL61801

Acetyl-CoA Synthase (ACS), also known as Nature's Monsanto acetic acid catalyst, isa Ni enzyme that plays a central role in the biosynthesis of acetyl-CoA.[1] Despite the importance of this enzyme, there exists a lot of debate in literature about its mechanism. Synthetic systems that model the structure and/or the function of the enzyme active site can aid in providing insights about the mechanism and pave the way for subsequent catalyst design for industrial applications.[2] We aim to design a model system that can model the proposed intermediates in the enzyme pathway: oneof the main focuses being a Ni(methyl)(CO), the intermediate formed prior to migratoryCO insertion, that has neither been detected in the enzyme nor has been modelled byprevious synthetic model systems.

Accordingly, we have developed a Ni(II) monomethyl complex supported by the tridentate macrocyclic ligand 1,4,7-triisopropyltriazacyclononane (iPr3tacn) (a ligand that is known to stabilize both odd and even oxidation states of Ni)[3] as a functional model for ACS. This complex was found to be competent for reaction with CO to forma Ni(methyl)(CO) and subsequently a Ni(acetyl)(CO) complex via a migratory insertionreaction. A detailed kinetic evaluation of the migratory insertion step was performed. In addition, DFT calculations were employed to support the proposed mechanism for this elementary step. The Ni(II)(methyl)(CO) and the Ni(II)(acetyl)(CO) complexes were both reactive towards a spectrum of thiolates to generate the corresponding thioesters (acetyl-CoA analogues), a step that mimics the final step of the enzyme mechanism. In addition, we have been able to spectroscopically characterize a Ni(I)- CO species supported by iPr3tacn, thus demonstrating that Ni complexes supported with this ligand framework can also access odd oxidation state intermediates relevantto the mechanism of ACS.

References:

1. Can, M.; Armstrong, F. A.; Ragsdale, S. W. Structure, Function, and Mechanism of the Nickel Metalloenzymes, CO Dehydrogenase, and Acetyl-CoA Synthase. *Chem. Rev.* 2014**,** *114*, 4149- 4174.
2. Company, A.; McDonald, A. R. Bio-Relevant Chemistry of Nickel, In *Comprehensive Coordination Chemistry III*; Elsevier, 2021; pp 846-877.
3. Griego, L.; Chae, J. B.; Mirica, L. M. Triisopropyl-1,4,7-Triazacyclononane, a Goldilocks Ligand for Probing the Role of Ni(III) and Ni(I) Centres in Cross-Coupling Catalysis 2023, *accepted*.

Thermodynamics of Proton-Coupled Electron Transfer at Tricopper *μ*-oxo/hydroxo/aqua Complexes

Saikat Mondal, Weiyao Zhang, and Shiyu Zhang*

Department of Chemistry & Biochemistry, The Ohio State University, 100 West 18th Avenue, Columbus, Ohio 43210, United States

Abstract body: Multicopper oxidases (MCOs) are enzymes that efficiently reduce dioxygen through proton-coupled electron transfer (PCET) while avoiding the formation of harmful reactive oxygen species (ROS).[1] Understanding the thermodynamics of PCET at tricopper oxo/hydroxo/aqua intermediates during oxygen reduction is crucial for elucidating how MCOs harness the oxidative power of O_2. In this study, we determined the O-H and N-H bond dissociation free energies (BDFE) and pK_a values of a series of tricopper hydroxo/aqua complexes at various oxidation and protonation states.[2,3] We found that the O-H and N-H BDFEs of nine tricopper complexes falls in a range of 44.7-78.9 kcal/mol. The tricopper species with evenly matched proton and electron numbers have mild BDFEs around 55 kcal/mol, while those with either more protons or electrons exhibit more extreme BDFE values. Additionally, the pK_a of O-H motifs close to the tricopper center (ca. 1.92 Å) change by ca. 8-16 pKa unit per oxidation state, while the N-H motif further away from the tricopper center (ca. 3.98 Å) changes by ca. 5 pK_a unit per oxidation state.[4] The steeper increases of the O-H pK_a as the tricopper center is reduced promote intramolecular proton transfer from the N-H motif in secondary coordination sphere. Overall, our study shed light on how MCOs could employ tricopper active sites to facilitate efficient PCETs during dioxygen reduction while preventing ROS formation and oxidative damage of the surrounding protein scaffold.

References:

(1) Solomon, E. I.; Sundaram, U. M.; Machonkin, T. E. Multicopper Oxidases and Oxygenases. *Chem. Rev.* **1996**, *96*, 2563–2605.

(2) Zhang, W.; Moore, C. E.; Zhang, S. Encapsulation of Tricopper Cluster in a Synthetic Cryptand Enables Facile Redox Processes from CuICuICuIto CuIICuIICuIIstates. *Chem. Sci.* **2021**, *12*, 2986–2992.

(3) Zhang, W.; Moore, C. E.; Zhang, S. Multiple Proton-Coupled Electron Transfers at a Tricopper Cluster: Modeling the Reductive Regeneration Process in Multicopper Oxidases. *J. Am. Chem. Soc.* **2022**, *144*, 1709–1717.

(4) Reed, C. J.; Agapie, T. A Terminal FeIII-Oxo in a Tetranuclear Cluster: Effects of Distal Metal Centers on Structure and Reactivity. *J. Am. Chem. Soc.* **2019**, *141*, 9479–9484.

On SOMs, Supramolecular interactions and Determining H-bond Strength optically and their applications.

Nidhi Kumari and Soumyajit Roy*

EFAML, Material Science Centre, Department of Chemical Science, Indian Institute of Science Education and Research – Kolkata, Mohanpur 741246, India

Email id: roy.soumyajit@googlemail.com, *nidhi02kumari@gmail.com*

Condensation polymerization is a known reaction in coordination chemistry. Extensive condensation of a metal-oxo salt leads to the formation of extended networks in a dispersion commonly known as sols. These are colloidal states of oxometalate, having diffused boundary known as Soft-oxometalates which open avenues for various applications in catalysis, active matter, water oxidation, and CO2RR. Reduction of CO_2 to value-added fuels is important for developing a sustainable energy source and fulfilling the demand of the energy crisis. In this context, our group had designed chalcogenides-based photocatalysts like softoxometalate $[\{K_{6.5}Cu(OH)_{8.5}(H2O)_{7.5}\}_{0.5}@\{K_3PW_{12}O_{40}\}]_n$ (n= 1348–2024) **[1]**, softoxometalates Mix type metal (Mo_{154}, $Mn_6P_3W_{34}$, Mo_{132}) **[2]**, Mo based Polyoxometates **[3]**, $\{MoV_9\}_n$ (n= 1332–3600) based soft-oxometalate **[4]** where formic acid, formaldehyde (C1 based carbon reduced product) are formed on reduction of carbon dioxide. Further, porphyrinoid-based electrocatalysts i.e. Mn-corrole and Co-corrole were used to convert CO_2 to acetic acid (F.E = 63%) and ethanol (F.E.= 48%) respectively (C_2-based carbon product) [5-6]. Further, we show the direct optical determination of H-bond strength by varying the dielectric constant of the medium and its application in forming a glassy crystal phase as Meta-material.

References:

1. S. Das, S. Kumar, S. Garai, R. Pochamoni, S. Paul, and S. Roy, ACS applied materials & interfaces 9, no. 40 (2017): 35086-35094.

2. S. Das, S. Biswas, T. Balaraju, S. Barman, R. Pochamoni, and S. Roy, Journal of Materials Chemistry A 4, no. 22 (2016): 8875-8887.

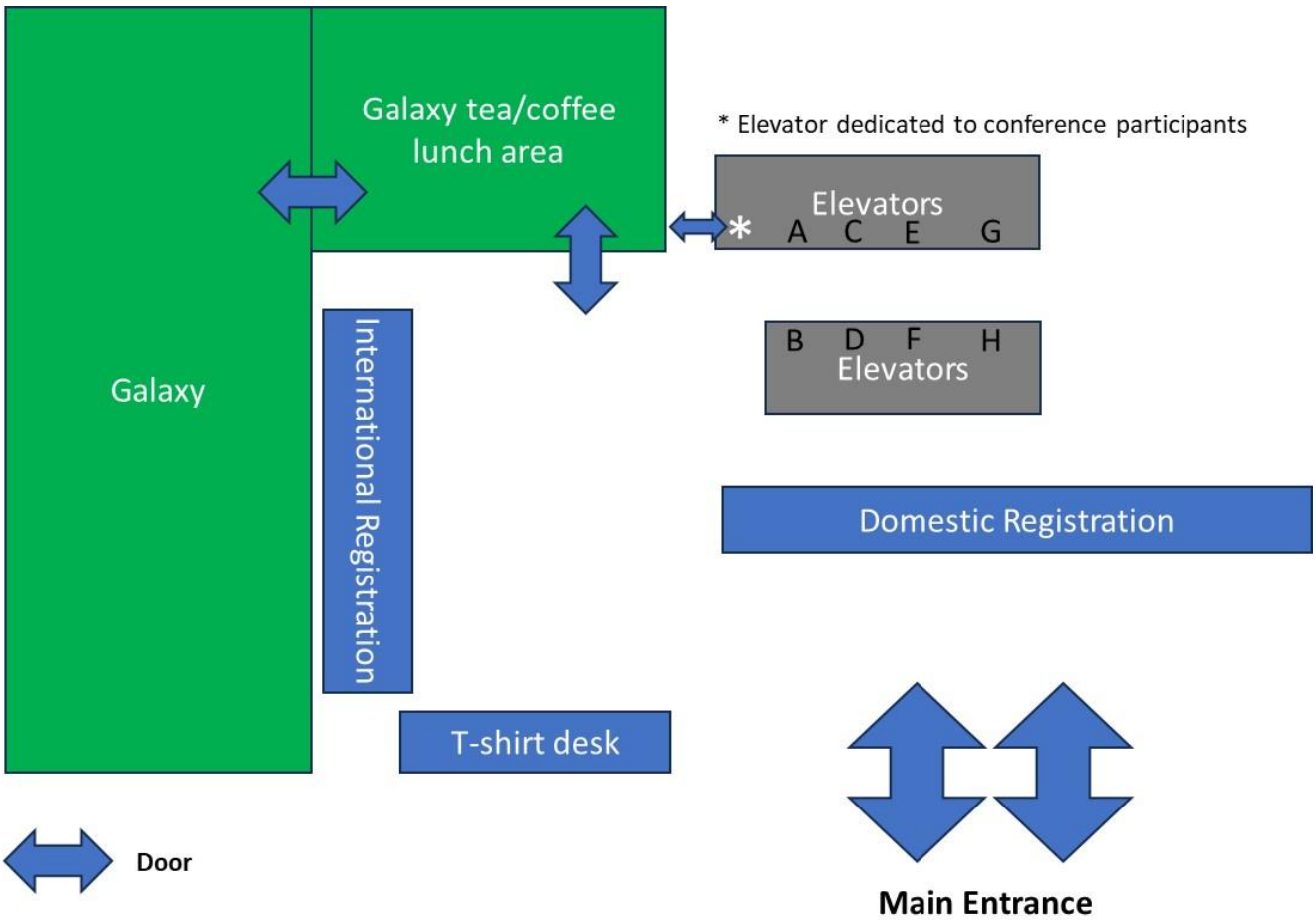
3. S. Barman, S. S. Sreejith, S Garai, R. Pochamoni, and S. Roy, ChemPhotoChem 3, no. 2 (2019): 93-100.

4.. S. Barman, S. Das, S. S. Sreejith, S. Garai, R. Pochamoni, and S. Roy, Chemical Communications 54, no. 19 (2018): 2369-2372.

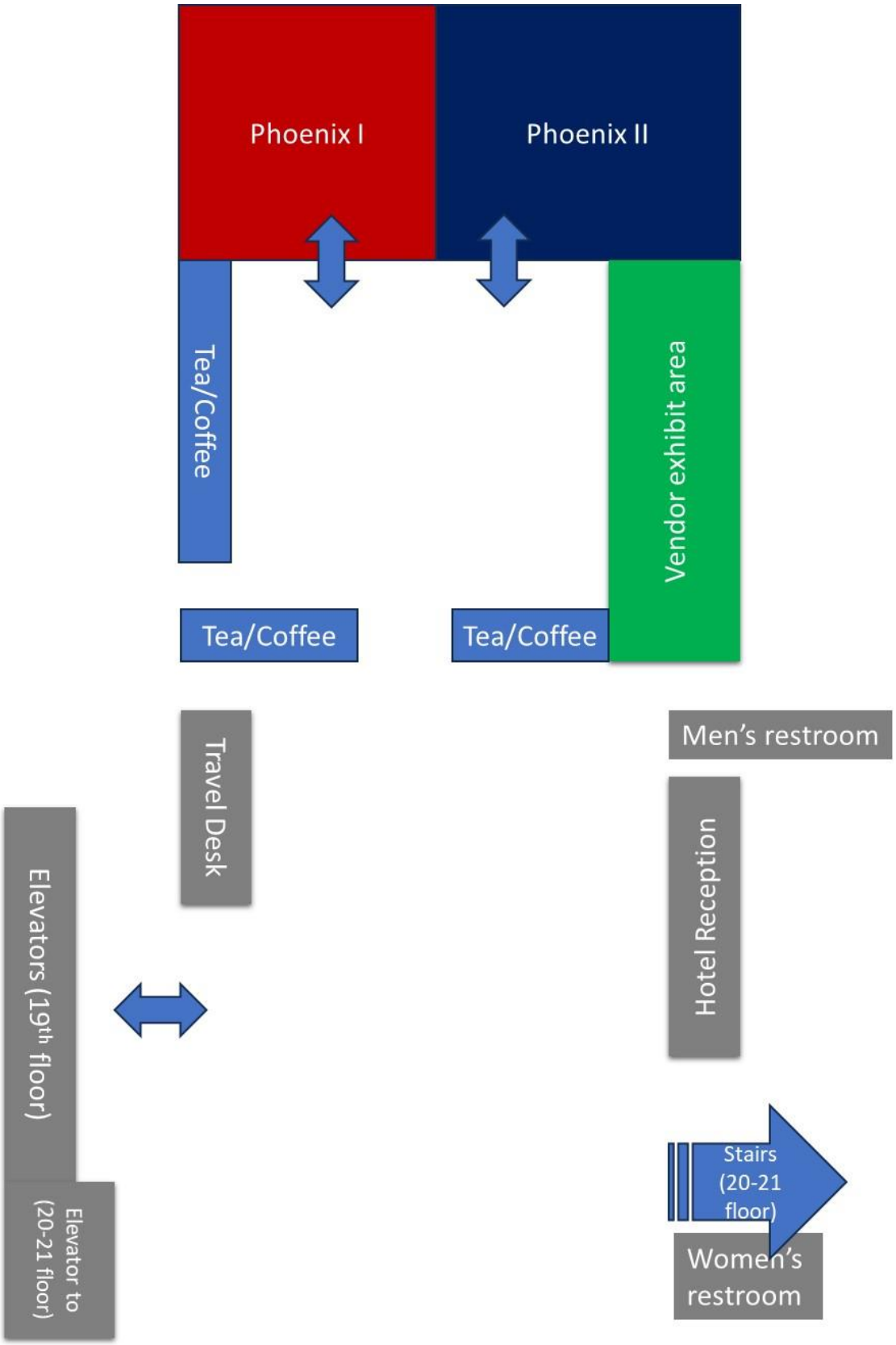
5. S. Gonglach, S. Paul, M. Haas, F. Pillwein, S. S. Sreejith, S. Barman, R. De, et.al, Nature communications 10, no. 1 (2019): 1-10.

6. R. De, S. Gonglach, S. Paul, M. Haas, S. S. Sreejith, P. Gerschel, U-P. Apfel, T.H. Vuong, J. Rabeah, S.Roy, W. Schofberger, Angewandte Chemie 132, no. 26 (2020): 10614-10621.

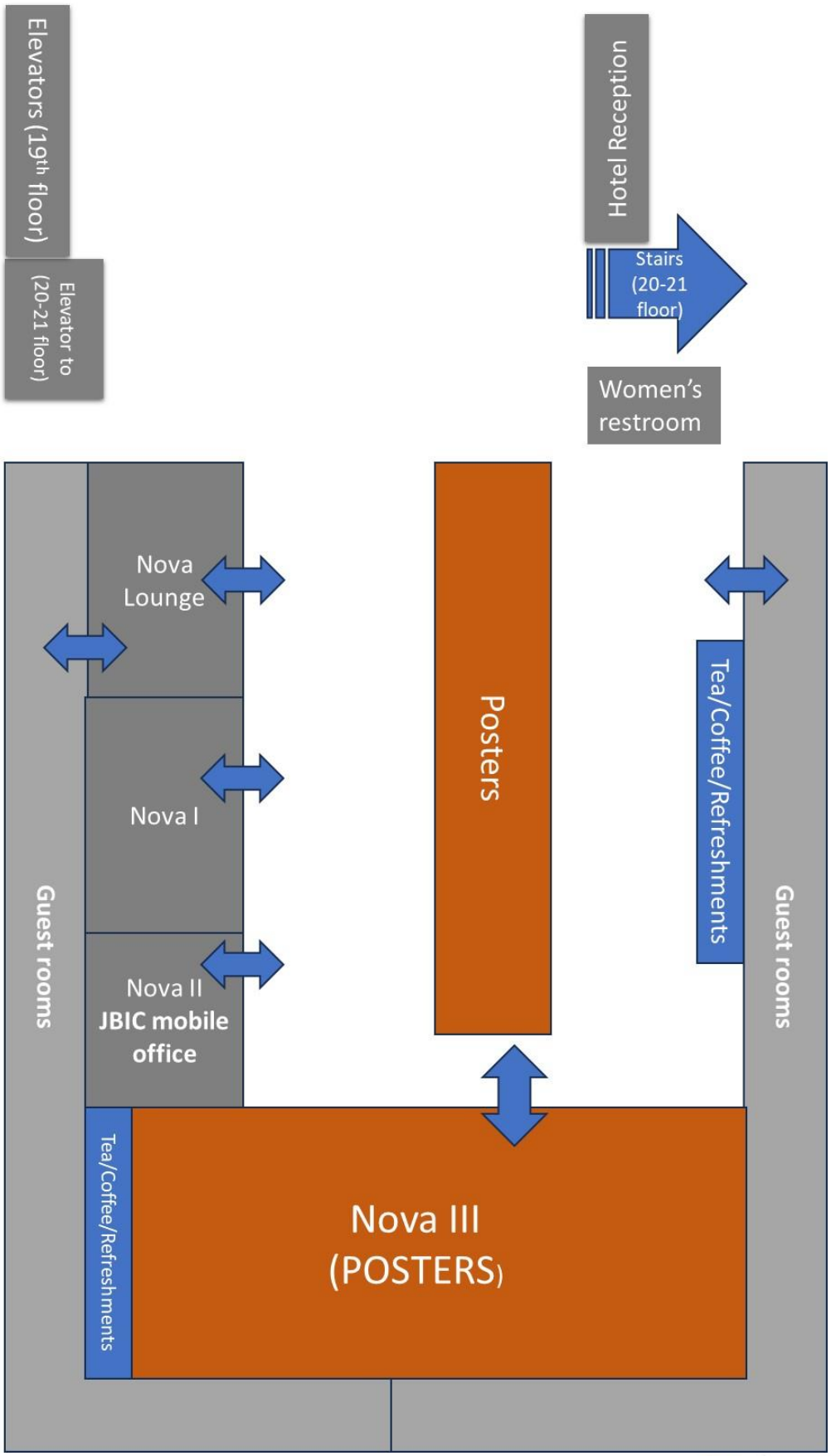
Floor Plan: Ground Floor



Floor plan: 19th Floor (I, seminar area)



Floor plan: 19th Floor (II, poster area)



Sponsored by

Sponsored by

ROYAL SOCIETY OF CHEMISTRY

Sponsored by

Sponsored by

ACS
Chemistry for Life®

Sponsored by

Sponsored by

BRUKER

MERCK

ADD Cool

Sponsored by

WILEY

SBIC

The Society of
Biological Inorganic Chemistry
Bringing inorganic chemistry to life

SABIC

7 - 11 JANUARY 2024 . KOLKATA