

The Reactivity Landscape of Non-Heme Iron and Nitric Oxide: Fundamental Chemistry and Biological Relevance

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Nitric oxide (NO) is biosynthesized in mammals as a signaling molecule, and as an immune defense agent (by macrophages) to fight off invading pathogens. However, pathogenic bacteria use flavodiiron NO reductases (FNORs) as a protection against exogenous NO. These enzymes reduce two molecules of NO to non-toxic N₂O and water. FNORs are therefore implicated in bacterial pathogenesis as these enzymes equip these microbes with resistance against the mammalian immune defense agent NO. Despite this biomedical significance, the mechanism of these enzymes is not well understood. FNORs contain a typical non-heme diiron active site, which is in close proximity (~4 Å) of the flavin (FMN) binding domain of an adjacent subunit. We first prepared the diiron dinitrosyl model complex [Fe₂(BPMP)(OPr)(NO)₂]X₂ (X⁻ = BPh₄⁻, OTf⁻, BF₄⁻) and characterized it using a number of spectroscopic techniques. The crystal structure of this complex shows two end-on coordinated {FeNO}⁷ units in a coplanar arrangement. This complex undergoes quantitative N-N bond formation and N₂O release in the presence of 1 equivalent of reductant, via a semireduced {FeNO}⁷-{FeNO}⁸ intermediate. This complex therefore represents the first example of a functional model system for FNORs. Spectroscopic studies on the stable, mononuclear {FeNO}⁸ complex [Fe(TMGG₃tren)(NO)]⁺ show that reduction of a high-spin {FeNO}⁷ complex results in a weakening of the Fe-NO bond and an increase of radical character on the bound NO⁻ ligand, leading to the observed increase in reactivity. By tuning the redox potential of the non-heme diiron core, using the model complex [Fe₂((Py₂PhO₂)MP)(OPr)₂](OTf), we were further able to activate the direct NO reduction pathway, i.e. reaction of the corresponding diferrous complex with NO leads to direct N₂O generation without the need to add additional reducing equivalents. This represents the first demonstration of NO reduction by a diferrous non-heme diiron complex.

References:

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Biosketch: Nicolai Lehnert is a Professor of Chemistry and Biophysics at the Department of Chemistry, University of Michigan. He studied Chemistry at the Heinrich-Heine-University Düsseldorf, Germany, and obtained his Diploma in Chemistry in 1995. He then moved to the Johannes Gutenberg-University Mainz, Germany, where he received his Ph.D. in 1999 working on model systems for nitrogenase under supervision of Priv.-Doz. Dr. F. Tuczek and Prof. Dr. P. Gütllich. He then joined the group of Prof. Dr. E. I. Solomon at Stanford University, USA for postdoctoral research from 1999 to 2001. In November 2001, he started as a Habilitand (senior research assistant, includes the conduction of independent research) at the Institute of Inorganic Chemistry, Christian-Albrechts-University Kiel, Germany. After completion of his Habilitation (qualification for permanent faculty positions at German Universities) in 2006 he accepted a faculty position at the University of Michigan, where he started in September 2006

as an Assistant Professor. From 2007 – 2011 he was the Dow-Corning Assistant Professor of Chemistry. In 2012 he was promoted to Associate Professor with tenure, and in 2016 to the rank of Professor. His work is focused on the coordination chemistry of nitric oxide and its derivatives as it pertains to biological systems, especially NO sensing and detoxification. More recently he has also developed research programs in biocatalysis (artificial metalloenzymes) and electrocatalysis, the latter being focused on immobilization of molecular catalysts on electrode surfaces to drive energy-related reactions (especially proton reduction). A particular expertise of his group is the application of physical and theoretical methods to coordination compounds and corresponding catalysts. Lehnert has published more than 150 scientific papers in renowned journals and presented more than 100 invited conference and departmental seminar presentations.