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Virtual & In-Person Section Meeting

Friday, December 2, 3:30 PM

at University of Miami, Coral Gables, Cox Science Building, Rm 318

or join via Zoom Meeting

https://miami.zoom.us/j/94394458498?pwd=MjNVZkFLMFgycldQQjBUQXVyTnpjUT09 Meeting ID: 943 9445 8498 Passcode: 704056

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Investigation of the Reaction Mechanism of Flavodiiron Nitric Oxide Reductases Using Synthetic Model Complexes

Abstract: 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 $[Fe_2(BPMP)(OPr)(NO)_2]X_2$ (**1**, $X^- = BPh_4^-$, OTf^-, BF_4^-) and characterized it using a number of spectroscopic techniques. The crystal structure of this complex shows two end-on coordinated high-spin (hs-) $\{FeNO\}^7$ units in a coplanar arrangement. This complex undergoes quantitative N-N bond formation and N_2O release in the presence of 1 equivalent of reductant, via a semireduced hs-$\{FeNO\}^7$/hs-$\{FeNO\}^8$ intermediate. This complex therefore represents the first example of a functional model system for FNORs.

We further investigated how a distortion of the active site affects the ability of the diiron core to mediate N_2O formation. For this purpose, we prepared several analogs of **1** that contain two monodentate ligands in place of the bridging carboxylate, $[Fe_2(BPMP)(X)_2(NO)_2]^{3+/1+}$ (**2-X**; X = triflate, 1-methylimidazole, or methanol). Structural data of **2-X** show that without the bridging carboxylate, the diiron core expands, leading to elongated (O)N-N(O) distances (from 2.80 Å in **1** to 3.00-3.96 Å in **2-X**) and distorted (O)N-Fe-Fe-N(O) dihedral angles (from coplanarity (5.9°) in **1** to 52.9-85.1° in **2-X**). Whereas **1** produces quantitative amounts of N_2O upon one-electron reduction, N_2O production is substantially impeded in **2-X**, to an initial 5-10% N_2O yield. The main products after reduction are unprecedented hs-$Fe^{II}/\{Fe(NO)_2\}^{9/10}$ dinitrosyl iron complexes (DNICs). The reactivity of these products was further investigated. Finally, we also investigated whether NO reduction can be mediated by hs-$\{FeNO\}^7$ complexes in the absence of additional, reducing equivalents. By tuning the reduction potentials of the complexes, we were able to show that direct NO reduction can indeed be induced, via the formation of highly activated hs-$\{FeNO\}^7$ intermediates. Using steric bulk, we were able to isolate a corresponding mononuclear complex, and we characterized it by X-ray crystallography and with a number of spectroscopic methods.

Dr. Lehnert earned his Ph.D. in Bioinorganic Chemistry in 1999 at Johannes Gutenberg-University Mainz, Germany, followed by a postdoctoral associate at Stanford University, 1999-2001, and at Christian-Albrechts-University Kiel, Germany, 2001-2006. He joined the University of Michigan faculty in 2006 and rose to full professor by 2016. His awards and honors include an NSF CAREER award, 2009, award for Outstanding Contributions to Undergraduate Education, College of Literature, Science, and the Arts, University of Michigan, 2014, John Dewey Teaching Award, College of Literature, Science, and the Arts, University of Michigan, 2016, Harold R. Johnson Diversity Service Award, University of Michigan, 2018, and Carol Hollenshead Inspire Award for Excellence in Promoting Equity & Social Change, University of Michigan, 2021.

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