[FeFe]-Hydrogenase Synthetic Models: Case Studies Incorporating Nitrosyl Ligands and Pendant Bases

Matthew Olsen Final Seminar November 22, 2010

Hydrogenases are enzymes that catalyze the reversible interconversion of protons, electrons, and dihydrogen ($2H^+ + 2e^- \rightleftharpoons H_2$). Because of the potential utility of H_2 as an energy carrier, the detailed understanding of hydrogenases has received considerable attention and funding.[1] In particular, hydrogenases are fascinating because they employ inexpensive first row transition metals, while operating at overpotentials and rates comparable with the industrial standard, Pt metal.[2]

Of the three classes of hydrogenases, the [FeFe]-hydrogenases are reported to operate the fastest.[3] For the enzyme from *Desulfovibrio desulfuricans*, turnover frequencies of 55,000 s^{-1} for H_2 uptake and 7,500 s^{-1} for H_2 production have been reported.[3] The active site of [FeFe]-hydrogenase features a diiron dithiolate core that is covalently linked to a Fe_4S_4 cluster via a cysteine residue, the sole link to the remainder of the protein. The diiron portion is coordinated by several cyanide and carbonyl ligands. Two catalytically active states are observed for [FeFe]-hydrogenase; an H_2 oxidizing state (H_{ox}) and a proton reducing state (H_{red}) (Figure 1).[4] These two states rapidly interconvert throughout the catalytic cycle.

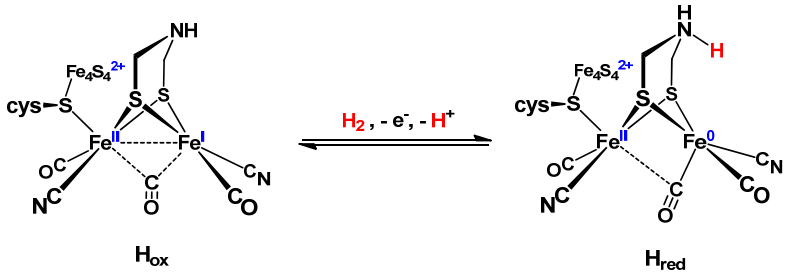

Figure 1. Interconversion of the active states of [FeFe]-hydrogenase.

Non-protein cofactors are especially important to the active site. The identity of the bridging dithiolate cofactor is thought to be 'azadithiolate' ($[(SCH_2)_2NH]^{2-}$). This azadithiolate is proposed to serve as a relay for protons to and from the active site, as well as assist in the heterolysis of H_2.[5] Similarly, the covalently tethered Fe_4S_4 cluster may act as an electron relay. The majority of work supporting these proposals is based on computational evidence.[6] Synthetic model complexes that study the role of these cofactors have only emerged recently. Importantly, model complexes do not reproduce the geometry of the active site.[7] While models display pseudo C_{2v} symmetry, the active site is rotated such that a carbonyl is located in the bridging position and a vacant site is exposed.

Synthetic models bearing redox-active ligands are scarce and their effects are unexplored. The treatment of various $34e^-$ diiron dithiolato carbonyl complexes with $NOBF_4$ afforded NO^+

substituted derivatives.[8] Electrochemical studies indicate that the nitrosyl ligand is redox-active; mild, reversible, and ligand-based reductions are observed. However, diiron nitrosyl complexes display unique properties prior to reduction. Structural characterization indicates that the diiron nitrosyl complexes undergo dramatic distortions which are unprecedented for $34e^-$ diiron dithiolates (Figure 2). These distortions make them first-generation *structural* models for the geometry of the active site. The structural distortions are due to the π-acceptor ability of the nitrosyl, which partially oxidizes Fe. This is supported by the reactivity of these complexes, which *functionally* resembles the oxidized state. Diiron nitrosyl complexes of sufficient electronic asymmetry and basicity are found to reversibly bind CO, as does the oxidized state of the enzyme. Interestingly, these CO adducts contain bridging nitrosyl ligands (Figure 2).[8]

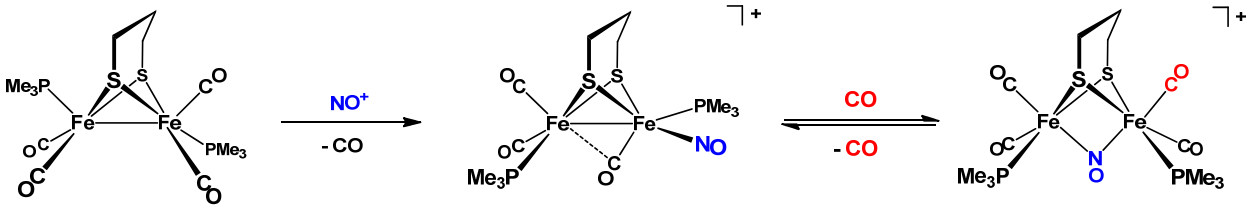

Figure 2. Structural and reactivity effects imparted by substitution of NO^+ on $34e^-$ diiron dithiolate complexes.

Although the majority of [FeFe]-hydrogenase model compounds are capable of proton reduction, no examples of H_2 oxidation were known prior to this work. No reactivity with H_2 was observed for the above diiron nitrosyl complexes. Unlike typical reduced models ($34e^-$), oxidized models ($33e^-$) geometrically resemble the active site of the enzyme. However, none of these models contain pendant bases. A first generation of *aza*dithiolate-bearing models was synthesized by oxidation of the $34e^-$ precursor $Fe_2[(SCH_2)_2NCH_2C_6H_5](CO)_3(dppv)(PMe_3)$ with $FcBAr^F{}_4$ (dppv = *cis*-1,2-bis(diphenylphosphino)ethylene, $BAr^F{}_4$ = tetrakis(bis-3,5-trifluorophenyl)borate).[9] Like the H_{ox} state, these H_{ox} models bind CO. Treatment of the same H_{ox} model with 1800 psi H_2 for 26 h yielded the corresponding hydride complex, and represented the first example of H_2 oxidation by a model complex.[9] The extreme conditions required indicate that H_2 activation suffers a large barrier, which is linked to the ability of traditional H_{ox} models to only accept $1e^-$. In contrast, H_2 is a $2e^-$ reagent.

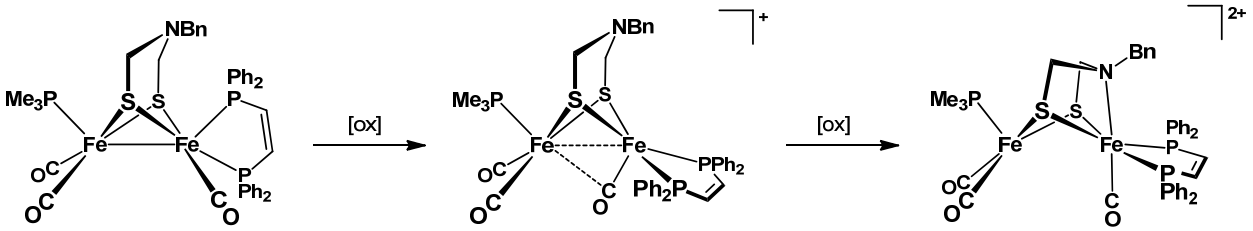

Figure 3. Illustration of redox-induced structural effects for diiron azadithiolates.

This problem was addressed by the attempted synthesis of $32e^-$ model complexes. Treatment of $[Fe_2\{(SCH_2)_2NBn\}(CO)_3(dppv)(PMe_3)]^+$ with a second equivalent of $FcBAr^F{}_4$

afforded the dication $[Fe_2[\kappa_3\text{-}(SCH_2)_2NCH_2C_6H_5](CO)_3(dppv)(PMe_3)]^{2+}$. In this unusual complex, the amine is proposed to coordinate to Fe (Figure 3). An MeCN-adduct of this dication was crystallographically characterized.[9] The amine-bound complex was not observed to react with 1 atm H_2, in agreement with saturation of the previously vacant site. Preliminary results indicate that the ^{t}Bu azadithiolate derivative displays hindered amine binding.

References

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