Hydrogenase Models and Studies Based on Iron Carbonyl Chelate Complexes

Phillip I. Volkers Final Seminar July 24, 2007

The hydrogenase (H_2ase) family of enzymes catalyzes the reduction of protons to dihydrogen or the reverse reaction of dihydrogen oxidation to protons. The two main classes of H_2ases are named based on the metal content of the active site: FeFe or NiFe. A minor, third class of H_2ase bears a single Fe center in the active site and is referred to as the iron-sulfur-cluster-free H_2ase, or Hmd.[1] Studies of H_2ases have been ongoing since their discovery in the 1930's by Stephenson and Stickland, but sophisticated small molecule chemical modeling studies did not flourish until the elucidation of X-ray crystal structures of [NiFe]- and [FeFe]-H_2ases within the past few years.[2]

Crystallographic analyses of the [FeFe]-H_2ases' active site structures revealed a biologically unprecedented subferrous-containing Fe_2S_2 butterfly core ligated by: a cysteine-ligated Fe_4S_4-cubane; two cyano and three carbonyl ligands; and a substrate (H, H_2) binding site (Figure 1). Also, the bridging thiolates are connected by a three-member chain, likely $(CH_2)_2NH$ (Figure 1). The diiron portion of the active site bears structural similarities to the long-known $Fe_2(SR)_2(CO)_6$ class of organometallic compounds.[3] Indeed, $Fe_2(SR)_2(CO)_6$ complexes have often served as the starting point for synthesizing structural and catalytically functional mimics[4] of the [FeFe]- H_2ase active site, which predominantly reduces protons to dihydrogen.

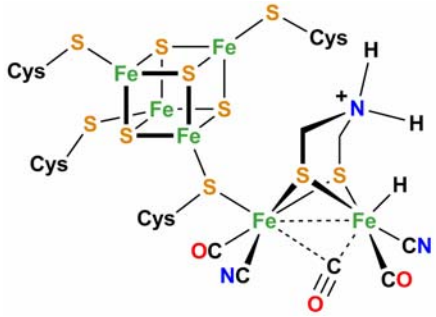

Figure 1: Composite schematic of the H_{red} state of the [FeFe]–H_2ase active site, based on X-ray studies of H_2ases from *Desulfovibrio desulfuricans* and *Clostridium pasteurianum*.[2d,e]

H_2ase models, like other active site models, are designed to replicate structural, spectroscopic, or functional features of the enzyme. The dithiolate cofactor has recently attracted much attention as a convenient means to functionalize diiron model complexes. Alternatively, little work has examined the possibility of replacing the thiolates with other bridging groups to enhance catalytic activity or structural control.[5] Ultimately, improved models and catalysts may be derived from a better understanding of the enzyme, and such knowledge may be gained from advanced spectroscopic models.

Fe_2S_2 complexes featuring pendant-functionalized dithiolate ligands were synthesized. Functionalities include a carboxylic acid and a maleimidyl moiety. Such functionalities are amenable to derivatization, enabling surface-anchoring of the complexes.[6] Maleimide-functionalized complexes have permitted bioconjugation of the non-planar, subferrous motif within the apo heme pocket of myoglobin.[7]

Fe_2N_2 complexes were examined as candidates for H_2ase modeling to explore the scope of the basic catalytic motif with respect to the steric and electronic properties of the bridging ligand. Specifically, $Fe_2(N_2C_{12}H_8)(CO)_4L_2$ species were examined for ligand substitution reactivity and proton reduction catalysis. Metal hydride formation afforded an isomer, attributed to the minimal steric profile of the bridging ligand, that is without analog in the Fe_2S_2 system. Overall, the Fe_2N_2 motif is now established as a new class of structural and catalytically functional models of [FeFe]-H_2ase.[8] As such, the diversity of azo ligands will allow greater steric and electronic control of model complexes.

New routes to $Fe_2(SR)_2(CO)_4L_2$ complexes have been elucidated, starting from the CO-free iron sources of $FeCl_2$ or iron powder. Such routes utilize oxidative carbonylation, reductive carbonylation, or comproportionation. The routes readily allow isotopic-labeling of model complexes with ^{57}Fe for study by specialized techniques, e.g. Mössbauer or NRVS, generating new insights into [FeFe]- and Hmd-H_2ases.[9] A comproportionation route permits selective labeling of one iron center of the diiron unit with ^{57}Fe (Figure 2).[10] Also, the comproportionation route is finding further utility in generating heterometallic dinuclear complexes.

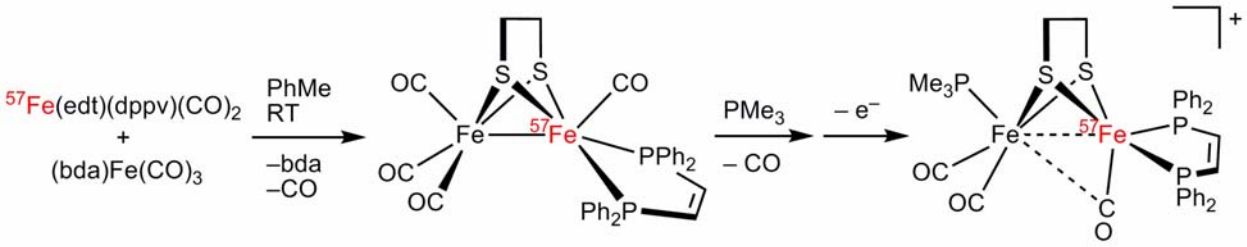

Figure 2. Comproportionation route to diiron complexes selectively-labeled with ^{57}Fe.

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