Small Molecule Mimics of Hydrogenases Enzymes: Synthesis, Protonation, and Electrocatalysis

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In nature, H_2 is processed by enzymes called hydrogenases, which catalyze the reduction of protons to dihydrogen, as well as the reverse reaction. The active sites of the two most prevalent hydrogenases contain NiFe or FeFe cores, bound to thiolates, cyanide, and carbon monoxide ligands. These enzymes are also rich in Fe-S clusters to allow the necessary redox chemistry of hydrogen oxidation and production.[1] Both enzymes operate at rates and overpotentials comparable with the best synthetic Pt catalysts.[2,3] Due to growing concern over the climate effects of burning fossil fuels, there is a push to replace these fuels with carbon free alternatives, one option being H_2. However, this would require catalysts for H_2 production that are based on cheap, easily accessible metals. This problem inspired extensive research on the development of functional small molecule mimics of the hydrogenase enzymes.[4] The work presented herein is motivated by the goal of understanding the mechanism of hydrogenase enzymes, in order to design better catalysts for hydrogen production.

The [FeFe]-hydrogenases feature an amino-dithiolate cofactor that bridges the two Fe centers (Figure 1). One Fe center is in a rotated geometry, leaving an open coordination site adjacent to the amine, which is the proposed site of substrate binding. Many active site models undergo protonation to form hydride complexes and catalyze proton reduction. However, the thermodynamic product of protonation is a bridging hydride, which is not biologically relevant. A number of phosphine substituted diiron complexes form terminal hydrides at very low temperatures.[5-7]

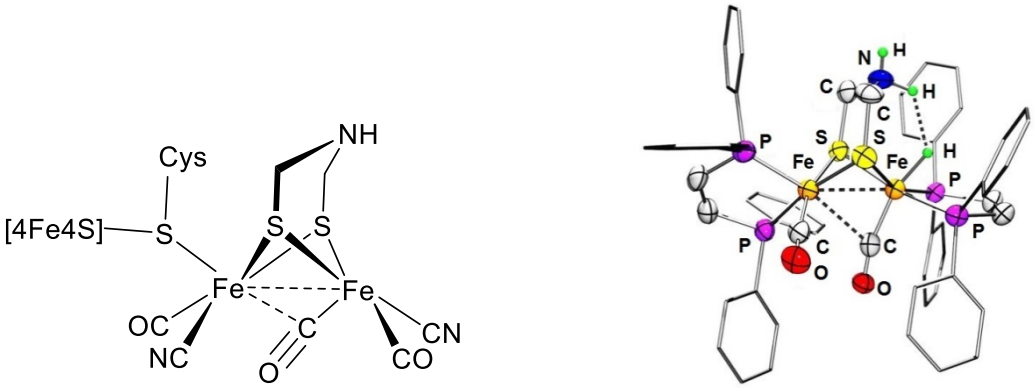

Figure 1: Active site of [FeFe]-hydrogenase (left) and ORTEP of FeFe model (right)

Protonation of complexes of the type $Fe_2(xdt)(CO)_4(dppv)_2$ (xdt= pdt ($[S_2C_3H_6]^{2-}$) or adt^{NH} ($[NH(SCH_2)_2]^{2-}$); dppv= $Ph_2PC_2H_2PPh_2$), results in the formation of terminal hydrides that are stable at 0 °C for ~ 30 minutes.[7,8] In the presence of excess acid, $Fe_2(adt^{NH})(CO)_4(dppv)_2$ sustains double protonation to form a terminal hydride ammonium species. This complex, [*t*-$HFe_2(adt^{NH2})(CO)_4(dppv)_2](BF_4)_2$, is the first example of a crystallographically characterized

terminal hydride produced by protonation, a route that is biologically relevant (Figure 1).[8] The structure displays a short NH--HFe distance of 1.88 Å, indicative of dihydrogen bonding. The molecule is hence positioned to release H_2, and represents a key intermediate in the mechanism of proton reduction catalysis.

For both the adt^{NH} and the pdt derivatives, the terminal hydride species are reduced at potentials ~150 mV milder than the corresponding bridging hydrides. The adt^{NH} terminal hydride complexes catalyze proton reduction at rates up to 58,000 s^{-1} and overpotentials (the deviation from the thermodynamic reduction potential of the acid) of 0.5 - 0.7 V. Both replacing the adt^{NH} cofactor pdt ($[S_2C_3H_6]^{2-}$) and the replacing terminal hydride with a bridging hydride, lowers the rate of catalysis significantly (TOF= 5 - 20 s^{-1}) and results in an inefficient overpotential (0.9 - 1.3 V). This indicates hydrogen evolution by biomimetic diiron dithiolates is accelerated by the amine cofactor, to which the hydride ligand must be adjacent.[8]

Unlike models for [FeFe]-hydrogenase, hydride containing models of [NiFe]-hydrogenase were unknown until our group reported the complex [(dppe)Ni(pdt)(μ-H)Fe(CO)$_3$]BF_4 (dppe= $PPh_2C_2H_4PPh_2$), and its derivatives in which CO was substituted with phosphine ligands.[9,10] Most importantly, these NiFe hydrides were found to catalyze proton reduction at mild overpotentials. A new route to NiFe models was developed, enabling the synthesis of new derivatives, varying in the identity of the dithiolate, the diphosphine, and the ligands on the Fe center (Figure 2).[11]

Figure 2: Active site of [NiFe]-hydrogenase (left) and ORTEP of NiFe model (right)

With a range of derivatives, we probed the roles of Ni and Fe in catalysis. The acidity of the hydride is more strongly affected by changes at the Fe center (ΔpK_a^{MeCN} of 4 for L= PPh_3 vs L= CO) than changes at the Ni center (ΔpK_a^{MeCN} of 2.5 for R = Ph vs Cy). The reduction potential appears to be more strongly affected by changes at Ni (ΔE_{red} of 250 mV for R = Ph vs Cy) than at Fe (ΔE_{red} of 200 mV for L = CO vs PPh_3). Changes in the dithiolate have a minimal effect on the reduction potentials of the hydrides, although the rates of hydrogen evolution are strongly affected by the dithiolate. The catalysts operate at overpotentials of 0.4 V and the rates up to 300 s^{-1}, which are in the upper range for model complexes although modest by the standards of the enzymes.[11]

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