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Nickel−Iron Dithiolato Hydrides Relevant to the [NiFe]-Hydrogenase Active Site

Bryan E. Barton, C. Matthew Whaley, Thomas B. Rauchfuss,* and Danielle L. Gray

School of Chemical Sciences, University of Illinois, Urbana, Illinois 61801

Received March 31, 2009; E-mail: rauchfuz@uiuc.edu

Several themes motivate the synthetic modeling of the active sites of the hydrogenase enzymes: interest in complexes of dihydrogen and hydride ligands,[1] novel biochemistry implied by structurally unusual active sites,[2−4] and the potential for utilizing hydrogen as an energy carrier.[5] Through recent intense efforts, synthetic models for the active site of the [FeFe]-H_2ases are yielding useful mechanistic insights.[6,7] Modeling the more prevalent [NiFe]-H_2ases, however, has proven more challenging.[8] The functional core of this enzyme features a nickel tetrathiolate wherein two thiolates are bridging to an $Fe(CN)_2(CO)$ center. Several states of the [NiFe]-H_2ases have been detected, although only two oxidation states are catalytically significant, Fe(II)Ni(III) (Ni−C, with a hydride) and Fe(II)Ni(II) (Ni−R, with a hydride, and Ni−SI, without; see Figure 1).[9] Despite intensive efforts, compounds featuring the $NiFeS_2(\mu$-H) core have resisted synthetic modeling, although progress with related $RuNiS_2(\mu$-H) has recently been described.[10] We now report successful and potentially generalizable routes to the long-sought nickel−iron dithiolato hydrides.

In our initial approach to biomimetic models, we treated the iron dithiolato complex $Fe(pdt)(CO)_2(dppe)$[11] (**1**) with $NiCl_2$(dppe) in hot acetone solution to give the μ-chloro bimetallic cation [(CO)(dppe)Fe(pdt)(μ-Cl)Ni(dppe)]$^+$ ([**2**Cl]$^+$), isolated as its BF_4^- salt (pdt = 1,3-propanedithiolate; dppe = 1,2-$C_2H_4(PPh_2)_2$; OTs^- = $CH_3C_6H_4$-4-SO_3^-) (Scheme 1). The brown-red colored complex is diamagnetic, consistent with low spin Fe(II) and Ni(II) centers. Attempts to replace the chloride ligand with hydrides proved unfruitful. Nonetheless, with three bridging ligands, the structure of the bimetallic complex verified that the ligand set is geometrically compatible with the corresponding targeted μ-hydrido complexes.

Seeking chloride-free precursors, we next examined the related condensation of **1** with "$Ni(OTs)_2$(dppe)," generated from $[Ni(H_2O)_6](OTs)_2$[12] and dppe. Treatment of a CH_2Cl_2 solution of $Ni(OTs)_2$(dppe) with **1** rapidly gave the salt of the dicationic dicarbonyl [$(CO)_2$(dppe)Fe(pdt)Ni(dppe)]$^{2+}$ ([**2**(CO)]$^{2+}$), obtained as a mixture of symmetric and unsymmetric stereoisomers. A pair of isomers (in a similar ratio) are also seen in the iron precursor. Thus, it appears that the Ni(dppe)$^{2+}$ module binds to the dithiolate without perturbing the coordination sphere of the Fe(II) center. The dicationic nickel−iron complex [**2**(CO)]$^{2+}$ is observed as an intermediate in the reaction of **1** and $NiCl_2$(dppe). Solutions of [**2**(CO)]$^{2+}$ in CH_2Cl_2 were found to react with NBu_4BH_4 to give a complex mixture. Analysis of this mixture revealed the presence of the targeted cationic hydride [(CO)(dppe)Fe(pdt)(μ-H)Ni(dppe)]$^+$ [**2**H]$^+$: a molecular ion was observed in the ESI-MS, and the ^{1}H NMR spectrum revealed two high-field triplets consistent with two isomers depending on the stereochemistry of the Fe(dppe) center. Solutions of crude [**2**H]$^+$ are more robust than the dicationic precursor consistent with a complex that has three bridging ligands (like the μ-chloride [**2**Cl]$^+$).

Because of the inefficiency of the hydride routes but encouraged by the stability of crude samples of [**2**H]$^+$, we investigated an alternative route to [**2**H]$^+$ starting from more reduced reagents. The Fe(I) complex $(CO)_3$Fe(pdt)Ni(dppe) (**3**)[13] readily protonated with $HBF_4 \cdot Et_2O$ in CH_2Cl_2 solution to give the corresponding hydride [**3**H]$^+$ (Scheme 1). When monitored by FT-IR spectroscopy, protonation induces a shift in ν_{CO} of 54 cm^{-1}. The retention of the ν_{CO} pattern suggests that the protonation occurs at the Ni−Fe bond. Consistent with this assignment, the hydride region of the ^{1}H NMR spectrum for [**3**H]BF_4 displays a triplet (δ −3.53, J_{PH} ~6 Hz), and the ^{31}P NMR spectrum shows a singlet. Excess acid is not deleterious; i.e. [**3**H]$^+$ does not protonate further, even with a large excess of $HBF_4 \cdot Et_2O$. Solutions of [**3**H]BF_4 are stable in air for days.

Representing the first example of a nickel−iron thiolato hydride,[14] [**3**H]BF_4 was characterized crystallographically (Figure 2). Including the bridging hydride ligand, the Fe center is quasi-

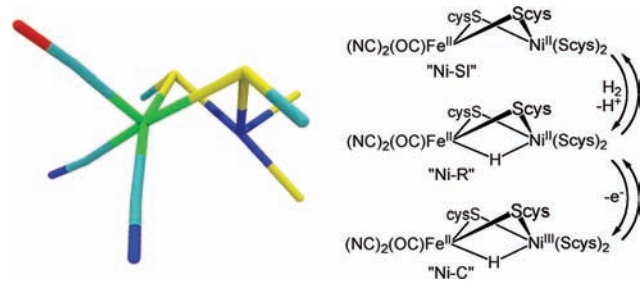
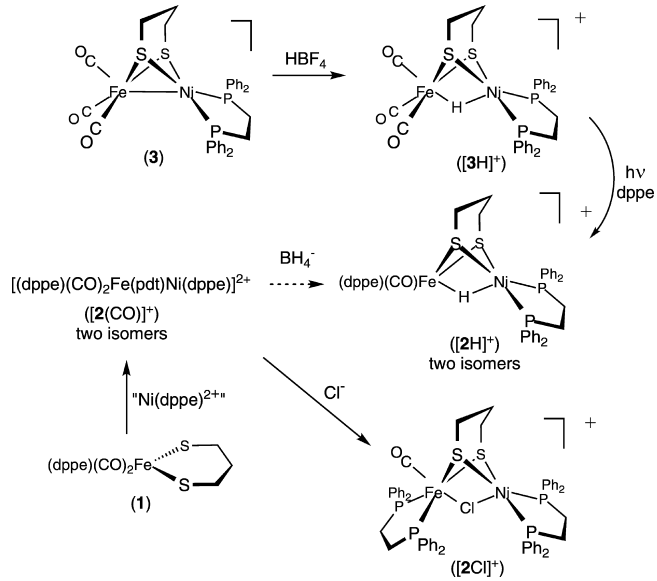


Figure 1. Structure of the active site in [NiFe]-hydrogenase (left, PDB #1WUL) and its key conversions (right).[9]

Scheme 1. Synthetic Approaches to Nickel−Iron Dithiolato Hydrides



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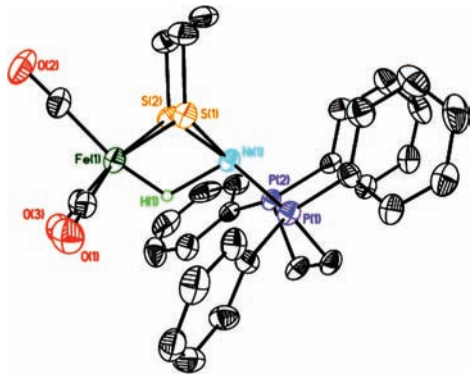

Figure 2. Structure of the cation in [(dppe)NiFe(pdt)(H)$(CO)_3$]BF_4 ([**3**H]BF_4). Key distances (Å): Ni−Fe, 2.6131(14); Ni−S(1), 2.210(2); Ni−S(2), 2.219(2); Fe−S(1), 2.321(2); Fe−S(2), 2.322(2); Ni−H, 1.64(6); Fe−H, 1.46(6); S···S, 3.101. The Ni−Fe distance in [(CO)(dppe)Fe(pdt)(μ-Cl)Ni(dppe)]BF_4 is 3.076 Å.

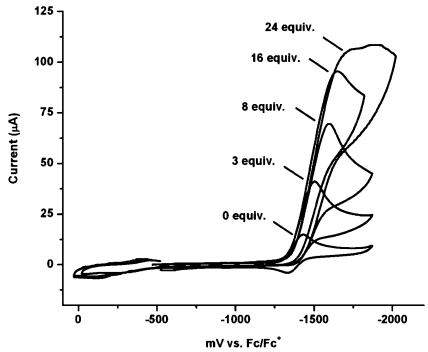

Figure 3. Cyclic voltammetry of [**3**H]BF_4 in the presence of varying equivalents of CF_3CO_2H. Conditions: 0.001 M [**3**H]BF_4 in CH_2Cl_2 solution, 0.1 M NBu_4PF_6, scan rate of 100 mV/s.

octahedral and Ni is approximately square pyramidal. The hydride connectivity, the metal coordination numbers, and the presence of three diatomic terminal ligands on Fe match features of the active site of the enzyme in the Ni−R state.[2,9] Completing the synthetic cycle outlined in the scheme, [**3**H]$^+$ reacts with dppe under photochemical conditions to give the hydride [**2**H]$^+$, which exhibits spectroscopic properties seen in the crude samples (high field ^{1}H NMR, ESI/MS, FT-IR). This substitution method should allow the synthesis of related complexes with a range of ligands on Fe.

The complex [**3**H]$^+$ resembles the 34e diiron dithiolato hydrides $[Fe_2(pdt)(\mu\text{-}H)(CO)_{6-x}(PR_3)_x]^+$, which are considered to be useful models for the [FeFe]-hydrogenases.[6] Deprotonation of methylene chloride solutions of [**3**H]$^+$ with NEt_3 ([$HNEt_3$]BF_4, pK_a = 18) were found to rapidly give **3**. Complex [**3**H]$^+$ is an active catalyst for the reduction of protons to H_2, as indicated by electrochemical measurements. For a CH_2Cl_2 solution of CF_3CO_2H (pK_a in CH_3CN = 12.65; $E° \sim -0.90$ V vs Fc/Fc$^+$),[15] a catalytic current is observed near −1.37 V vs Fc/Fc$^+$, which is milder than that seen for the diiron complexes (Figure 3). The proposed catalytic cycle begins with protonation of **3** and probably follows the mechanistic pattern described for the substituted diiron catalysts, i.e., a cycle that involves reduction of the hydride followed by protonation.[6,16]

Complex **3** is also easily oxidized to the monocation, $E_{1/2} \sim -520$ V (vs Fc/Fc$^+$). Using ferrocenium as the oxidant ($FcBF_4$), we generated the salt [**3**]BF_4. This cation exists in the same oxidation state $(FeNi)^{3+}$ assigned to the Ni−L state of the enzyme.[4] The IR spectrum shows that oxidation shifts ν_{CO} by ~29 cm^{-1}. Although the argument is qualitative, the values for ν_{CO} indicate that one-electron oxidation affects the $Fe(CO)_3$ center less than protonation, which formally corresponds to a Fe(II) ion. A frozen 8:2 CH_2Cl_2/THF solution of [**3**]BF_4 exhibits an intense nearly axial EPR spectrum lacking phosphine hyperfine coupling. The EPR and FT-IR properties are similar to those for square pyramidal Fe(I) species.[17] It is likely that replacement of CO ligands in **3** will enable access to higher oxidation states of the $NiFe(SR)_2$ system beyond the $(FeNi)^{3+}$ state.

The methods described above provide access to functional models for the [NiFe]-hydrogenases. The models are amenable to extensive modifications by variations of the ligands. Our results should encourage the development of a host of biomimetic hydrides, leading to new mechanistic insights relevant to Nature's most pervasive catalysts for processing hydrogen.

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Supporting Information Available: Preparative, spectroscopic, and crystallographic details. This material is available free of charge via the Internet at http://pubs.acs.org.

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