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

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Several themes motivate the synthetic modeling of the active sites of the hydrogenase enzymes: interest in complexes of dihydrogen and hydride ligands,<sup>1</sup> novel biochemistry implied by structurally unusual active sites,<sup>2–4</sup> and the potential for utilizing hydrogen as an energy carrier.<sup>5</sup> Through recent intense efforts, synthetic models for the active site of the [FeFe]-H<sub>2</sub>ases are yielding useful mechanistic insights.<sup>6,7</sup> Modeling the more prevalent [NiFe]-H<sub>2</sub>ases, however, has proven more challenging.<sup>8</sup> The functional core of this enzyme features a nickel tetrathiolate wherein two thiolates are bridging to an Fe(CN)<sub>2</sub>(CO) center. Several states of the [NiFe]-H<sub>2</sub>ases 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).<sup>9</sup> Despite intensive efforts, compounds featuring the NiFeS<sub>2</sub>(μ-H) core have resisted synthetic modeling, although progress with related RuNiS<sub>2</sub>(μ-H) has recently been described.<sup>10</sup> 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)<sub>2</sub>(dppe)<sup>11</sup> (**1**) with NiCl<sub>2</sub>(dppe) in hot acetone solution to give the μ-chloro bimetallic cation [(CO)-(dppe)Fe(pdt)(μ-Cl)Ni(dppe)]<sup>+</sup> ([**2Cl**]<sup>+</sup>), isolated as its BF<sub>4</sub><sup>−</sup> salt (pdt= 1,3-propanedithiolate; dppe = 1,2-C<sub>2</sub>H<sub>4</sub>(PPh<sub>2</sub>)<sub>2</sub>; OTs<sup>−</sup> = CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>-4-SO<sub>3</sub><sup>−</sup>) (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)<sub>2</sub>(dppe),” generated from [Ni(H<sub>2</sub>O)<sub>6</sub>](OTs)<sub>2</sub><sup>12</sup> and dppe. Treatment of a CH<sub>2</sub>Cl<sub>2</sub> solution of Ni(OTs)<sub>2</sub>(dppe) with **1** rapidly gave the salt of the dicationic dicarbonyl [(CO)<sub>2</sub>(dppe)Fe(pdt)Ni(dppe)]<sup>2+</sup> ([**2CO**]<sup>2+</sup>), 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)<sup>2+</sup> module binds to the dithiolate without

perturbing the coordination sphere of the Fe(II) center. The dicationic nickel–iron complex  $[\mathbf{2}(\text{CO})]^{2+}$  is observed as an intermediate in the reaction of **1** and  $\text{NiCl}_2(\text{dppe})$ . Solutions of  $[\mathbf{2}(\text{CO})]^{2+}$  in  $\text{CH}_2\text{Cl}_2$  were found to react with  $\text{NBu}_4\text{BH}_4$  to give a complex mixture. Analysis of this mixture revealed the presence of the targeted cationic hydride  $[(\text{CO})(\text{dppe})\text{Fe}(\text{pdt})(\mu\text{-H})\text{Ni}(\text{dppe})]^+ [\mathbf{2H}]^+$ : a molecular ion was observed in the ESI-MS, and the  $^1\text{H}$  NMR spectrum revealed two high-field triplets consistent with two isomers depending on the stereochemistry of the Fe(dppe) center. Solutions of crude  $[\mathbf{2H}]^+$  are more robust than the dicationic precursor consistent with a complex that has three bridging ligands (like the  $\mu$ -chloride  $[\mathbf{2Cl}]^+$ ).

Because of the inefficiency of the hydride routes but encouraged by the stability of crude samples of  $[\mathbf{2H}]^+$ , we investigated an alternative route to  $[\mathbf{2H}]^+$  starting from more reduced reagents. The Fe(I) complex  $(\text{CO})_3\text{Fe}(\text{pdt})\text{Ni}(\text{dppe})$  (**3**)<sup>13</sup> readily protonated with  $\text{HBF}_4\cdot\text{Et}_2\text{O}$  in  $\text{CH}_2\text{Cl}_2$  solution to give the corresponding hydride  $[\mathbf{3H}]^+$  (Scheme 1). When monitored by FT-IR spectroscopy, protonation induces a shift in  $\nu_{\text{CO}}$  of  $54\text{ cm}^{-1}$ . The retention of the  $\nu_{\text{CO}}$  pattern suggests that the protonation occurs at the Ni–Fe bond. Consistent with this assignment, the hydride region of the  $^1\text{H}$  NMR spectrum for  $[\mathbf{3H}]\text{BF}_4$  displays a triplet ( $\delta$ –3.53,  $J_{\text{PH}} \sim 6\text{ Hz}$ ), and the  $^{31}\text{P}$  NMR spectrum shows a singlet. Excess acid is not deleterious; i.e.  $[\mathbf{3H}]^+$  does not protonate further, even with a large excess of  $\text{HBF}_4\cdot\text{Et}_2\text{O}$ . Solutions of  $[\mathbf{3H}]\text{BF}_4$  are stable in air for days.

Representing the first example of a nickel–iron thiolato hydride,<sup>14</sup>  $[\mathbf{3H}]\text{BF}_4$  was characterized crystallographically (Figure 2). Including the bridging hydride ligand, the Fe center is quasi-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.<sup>2,9</sup> Completing the synthetic cycle outlined in the scheme,  $[\mathbf{3H}]^+$  reacts with dppe under photochemical conditions to give the hydride  $[\mathbf{2H}]^+$ , which exhibits spectroscopic properties seen in the crude samples (high field  $^1\text{H}$  NMR, ESI/MS, FT-IR). This substitution method should allow the synthesis of related complexes with a range of ligands on Fe.

The complex  $[\mathbf{3H}]^+$  resembles the 34e diiron dithiolato hydrides  $[\text{Fe}_2(\text{pdt})(\mu\text{-H})(\text{CO})_{6-x}(\text{PR}_3)_x]^+$ , which are considered to be useful models for the [FeFe]-hydrogenases.<sup>6</sup> Deprotonation of methylene chloride solutions of  $[\mathbf{3H}]^+$  with  $\text{NEt}_3$  ( $[\text{HNEt}_3]\text{BF}_4$ ,  $\text{p}K_{\text{a}} = 18$ ) were found to rapidly give **3**. Complex  $[\mathbf{3H}]^+$  is an active catalyst for the reduction of protons to  $\text{H}_2$ , as indicated by electrochemical measurements. For a  $\text{CH}_2\text{Cl}_2$  solution of  $\text{CF}_3\text{CO}_2\text{H}$  ( $\text{p}K_{\text{a}}$  in  $\text{CH}_3\text{CN} = 12.65$ ;  $E^\circ \sim -0.90\text{ V}$  vs  $\text{Fc}/\text{Fc}^+$ ),<sup>15</sup> a catalytic current is observed near  $-1.37\text{ V}$  vs  $\text{Fc}/\text{Fc}^+$ , 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.<sup>6,16</sup>

Complex **3** is also easily oxidized to the monocation,  $E_{1/2} \sim -520\text{ V}$  (vs  $\text{Fc}/\text{Fc}^+$ ). Using ferrocenium as the oxidant ( $\text{FcBF}_4$ ), we generated the salt  $[\mathbf{3}]\text{BF}_4$ . This cation exists in the same oxidation state ( $\text{FeNi}^{3+}$ ) assigned to the Ni–L state of the enzyme.<sup>4</sup> The IR spectrum shows that oxidation shifts  $\nu_{\text{CO}}$  by  $\sim 29\text{ cm}^{-1}$ . Although the argument is qualitative, the

values for  $\nu_{\text{CO}}$  indicate that one-electron oxidation affects the  $\text{Fe}(\text{CO})_3$  center less than protonation, which formally corresponds to a  $\text{Fe}(\text{II})$  ion. A frozen 8:2  $\text{CH}_2\text{Cl}_2/\text{THF}$  solution of  $[\mathbf{3}]\text{BF}_4$  exhibits an intense nearly axial EPR spectrum lacking phosphine hyperfine coupling. The EPR and FT-IR properties are similar to those for square pyramidal  $\text{Fe}(\text{I})$  species.<sup>17</sup> It is likely that replacement of CO ligands in  $\mathbf{3}$  will enable access to higher oxidation states of the  $\text{NiFe}(\text{SR})_2$  system beyond the  $(\text{FeNi})^{3+}$  state.

The methods described above provide access to functional models for the  $[\text{NiFe}]$ -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.

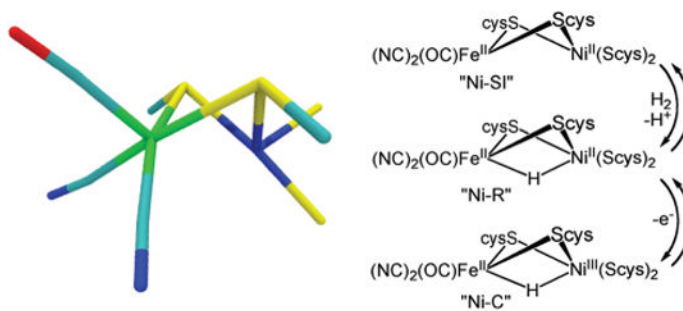
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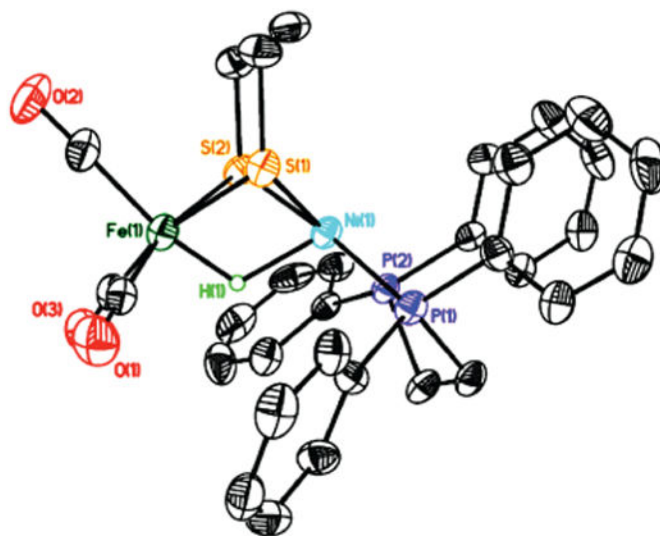
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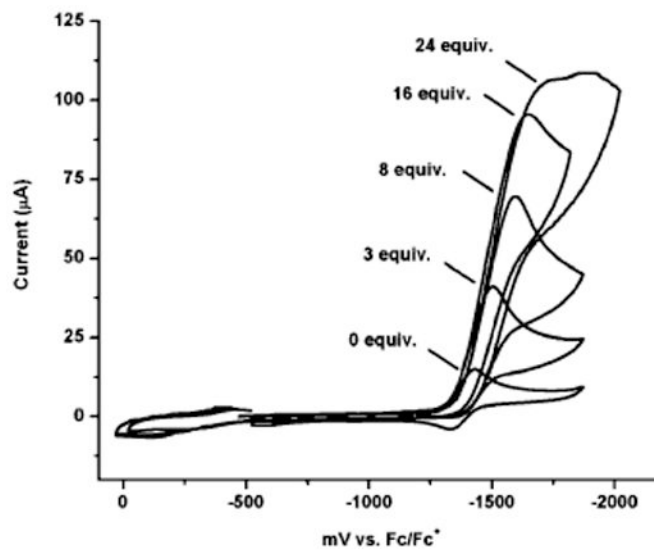


**Figure 1.** Structure of the active site in [NiFe]-hydrogenase (left, PDB #1WUL) and its key conversions (right).<sup>9</sup>

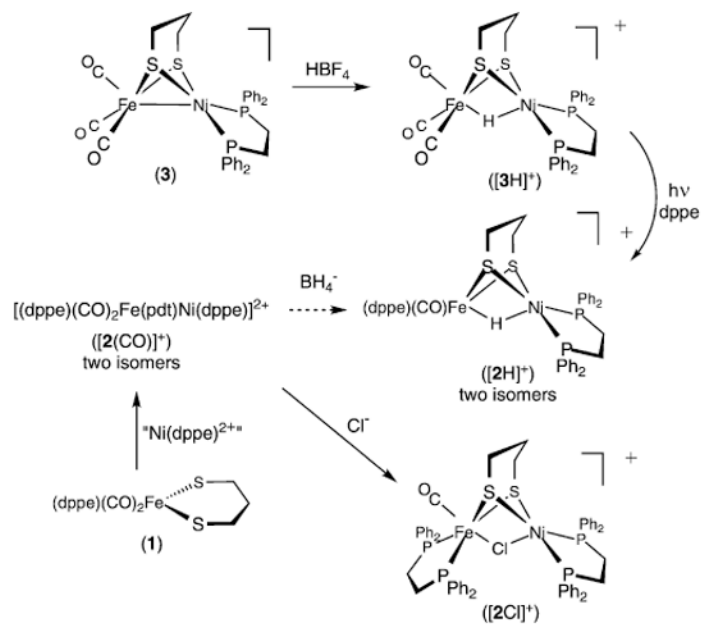


**Figure 2.**

Structure of the cation in  $[(dppe)NiFe(pdt)(H)(CO)_3]BF_4$  ( $[3H]BF_4$ ). Key distances ( $\text{\AA}$ ): 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( $\cdots$ )S, 3.101. The Ni–Fe distance in  $[(CO)(dppe)Fe(pdt)(\mu\text{-Cl})Ni(dppe)]BF_4$  is 3.076  $\text{\AA}$ .



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



**Scheme 1. Synthetic Approaches to Nickel–Iron Dithiolato Hydrides**