Inorganic Chemistry
Communication

Inorg. Chem. **2009**, *48*, 6359–6361 **6359**
DOI: 10.1021/ic900929u

Synthesis and Structure of Analogues for the Ni−Fe Site in Hydrogenase Enzymes

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Received May 12, 2009

Dithiolate bridging Ni−Fe complexes $[(dppe)Ni^{II}(\mu\text{-SEt})_2Fe^{II}(CN)_2(CO)_2]_6$ and $[(dppe)Ni^{II}(\mu\text{-pdt})Fe^{II}(CN)_2(CO)_2]$ [dppe = 1,2-bis(diphenylphosphino)ethane and pdt=1,3-propanedithiolate] have been synthesized and structurally characterized as structural analogues of the active site of Ni−Fe hydrogenase enzymes. The synthesis starts from key intermediate *fac*-$[Fe(CN)_2(CO)_3I]^-$. $[(dppe)Ni^{II}(\mu\text{-SEt})_2Fe^{II}(CN)_2(CO)_2]_6$, which features a near-planar diethanethiolate-bridged Ni−Fe rhomb, and the arrangement of $2CN^-$ ligands is cis to each other. In contrast, $[(dppe)Ni^{II}(\mu\text{-pdt})Fe^{II}(CN)_2(CO)_2]$ shows a much more folded NiS_2Fe rhomb, a short Ni−Fe distance, trans $2CN^-$ ligands, and a semibridging CN^- between Ni and Fe.

Hydrogenase enzymes, which occur in numerous microorganisms, catalyze the reversible formation and consumption of dihydrogen.[1−3]

$$2H^+ + 2e^- \rightleftharpoons H_2(g)$$

The crystal structures of several Ni−Fe hydrogenases have shown that the enzymes have a common but unique active site, namely, a dithiolate-bridged Ni−Fe center with two cyanides and a carbonyl ligand coordinated to the Fe atom (Figure 1). Crystallographic studies of the oxidized forms of enzymes indicate the presence of a third bridging ligand (X), which may be an O^{2-}, OH^-, or OOH^-;[4] this bridging ligand is replaced by a spectroscopically detected hydride in some reduced forms of the enzymes.[5]

The synthesis of analogues for this center has been very challenging because the active site contains not only two different metals but also five different ligands.[6−11] The closest synthetic analogue for the Ni−Fe center is $[Fe(CN)_2(CO)_2(\mu\text{-pdt})Ni(S_2CNR_2)]^-$ (**1**), which has been reported by Tatsumi et al.[11] Pointedly, one aspect in which **1** differs from the geometry of the Fe centers in the enzymes is the trans versus cis arrangement of the CN^- ligands. Complex **1** was synthesized from a starting complex, *trans*,*mer*-$[Fe(CN)_2(CO)_3Br]^-$ (**2**), in which the two CN^- ligands are mutually trans.[12] Herein, we report the synthesis of a new isomer of **2**, *fac*-$[Fe(CN)_2(CO)_3I]^-$ (**3**), in which the CN^- ligands are cis (as in the enzymes), and the use of **3** to prepare new Ni−Fe dimers (Scheme 1).

The reaction between *fac*-$[Fe(CO)_3I_3]^-$[13] and 2 equiv of CN^- affords **3**. The ligand arrangement in **3** was established by X-ray diffraction (Figure 2) and IR measurements. The IR spectrum of **3** in a methanol solution indicates that the facial arrangement of the CO ligands persists in a solution with peaks at 2144 cm^{-1} (w, CN), 2133 cm^{-1} (w, CN), 2104 cm^{-1} (s, CO), 2066 cm^{-1} (s, CO), and 2055 cm^{-1} (sh, CO). **3** is very sensitive to light both in solution and in the solid state.

IR spectra of reaction mixtures comprising **3** and 2 equiv of EtS^- in CH_3OH display two CO stretches of equal intensity at 1974 and 2022 cm^{-1}, indicating a *cis*-CO coordination, and suggest the formation of the *cis*,*cis*,*cis*-$[Fe(CN)_2(CO)_2(SEt)_2]^{2-}$ isomer (**4**). It is noted that Rauchfuss et al. have suggested the existence of $[Fe(CN)_2(CO)_2(SEt)_2]^{2-}$ as a reaction intermediate from the carbonylation of nonaqueous Fe^{II}/EtS^- solutions in the presence of CN^-.[14] There is no

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Published on Web 06/22/2009

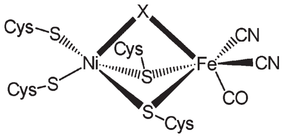


Figure 1. Active site structure of NiFe hydrogenase.

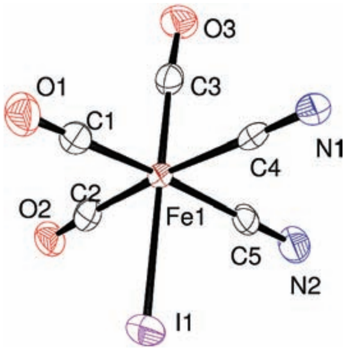
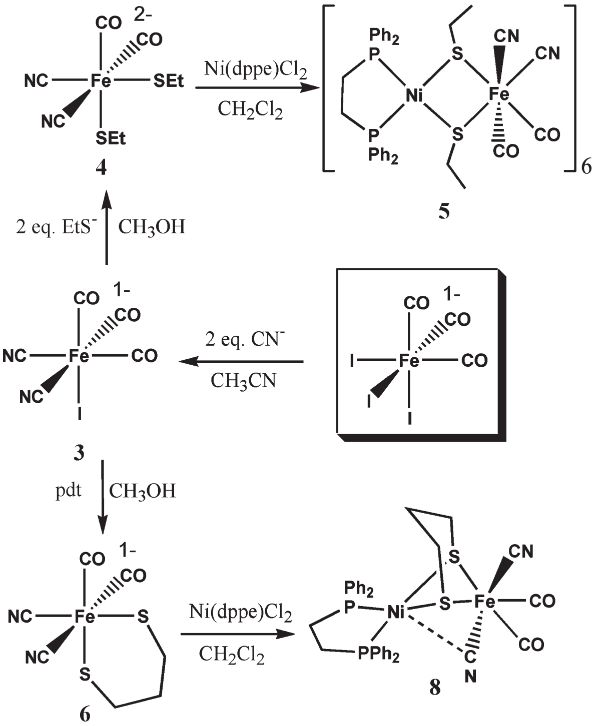


Figure 2. ORTEP drawing of **3** at a 50% probability level. Selected bond distances (Å) and angles (deg): Fe1–C1 1.836(5), Fe1–C2 1.835(5), Fe1–C3 1.797(5), Fe1–C4 1.939(5), Fe1–C5 1.929(5), Fe1–I1 2.634(1); C4–Fe1–C5 86.0(2).

Scheme 1. Synthetic Pathway to NiFe Analogues



observable change in the IR spectrum of **4** upon standing in a CH_3OH solution at room temperature for 8 h.

Although we have not crystallized **4**, its subsequent reaction with Ni(dppe)Cl_2 leads to the isolation of [(dppe)Ni^{II}-(μ-SEt)$_2$$Fe^{II}$$(CN)_2(CO)_2]_6$ (**5**) in high yield (Figure 3). In fact, the cis arrangement of the CN^- ligands in **5** indicates that **4** indeed has the cis,cis,cis geometry barring ligand rearrangement during its reaction with Ni(dppe)Cl_2. Complex **5** is stable at room temperature in a CH_2Cl_2 solution, even in air, for at least 8 h as monitored by IR spectroscopy. The IR spectrum of **5** in CH_2Cl_2 shows two equally intense CO peaks at 1998 and 2046 cm^{-1} and two CN peaks at 2110 and 2137 cm^{-1}.

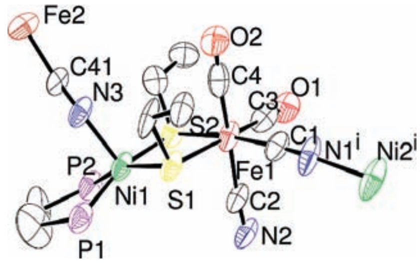


Figure 3. ORTEP drawing of one Ni–Fe unit from **5** at a 50% probability level. Phenyl groups from dppe and all H atoms have been removed for clarity. Selected bond distances (Å) and angles (deg): Fe1–C1 1.922(14), Fe1–C2 1.954(14), Fe1–C3 1.764(17), Fe1–C4 1.80(2), Fe1–S1 2.344(6), Fe1–S2 2.331(4), Ni1–S1 2.248(3), Ni1–S2 2.253(6), Ni1–P1 2.163(8), Ni1–P2 2.174(3), Ni1–N3 2.102(12); C1–Fe1–C2 85.2(6).

Complex **5** crystallizes in the hexagonal space group $P6_3$ with the asymmetric unit containing two Ni–Fe units. Six Ni–Fe units form a hexameric ring in the crystal lattice through an end-on bridging cyanide between the Fe and Ni atoms in adjacent units. Figure 3 shows the structure of one Ni–Fe unit with a CN from an adjacent Fe coordinated to Ni. The square-pyramidal coordination geometry of the Ni contrasts with the square-planar coordination found in **1**. Complex **5** has a nearly planar [NiS_2Fe] rhomb with a Ni1–S1–S2–Fe1 dihedral angle of 170.0(7)° and a Ni–Fe distance of 3.373(5) Å.

The two bridging ethanethiolate ligands have a syn, exo conformation, which is uncommon for unconstrained bridging thiolate ligands.[15] As in the enzyme, the Fe is coordinated to two CN^- ligands with a cis arrangement; however, in the enzymes, the CN^- ligands are both trans to the cysteine ligands. Even though the [NiS_2Fe] rhomb is nearly planar in **5**, it might undergo a conformation change upon removal of the extra CO ligand and substrate binding. Attempts to remove a CO ligand from these complexes are currently under active investigation.

The reaction between **3** and K_2pdt generates *cis,cis,cis*-[Fe-$(CN)_2(CO)_2(pdt)]^{2-}$ (**6**). The IR spectrum of **6** in a methanol solution shows two equally intense CO peaks at 1973 and 2023 cm^{-1}, indicating a *cis*-CO arrangement. The chelating nature of the pdt ligand and the cis arrangement of the two CO ligands require the cis,cis,cis structure for **6**. The only possible isomer with *cis*-CO ligands, *trans,cis,cis*-[Fe-$(CN)_2(CO)_2(pdt)]^{2-}$ (**7**), was previously reported from the reaction between **2**[12] and pdt.[11] IR measurements show that **6** exhibits CO vibrational frequencies distinctively different from those of **7**.

The reaction of **6** with Ni(dppe)Cl_2 produces monomeric [(dppe)Ni^{II}(μ-pdt)$Fe^{II}$$(CN)_2(CO)_2$] (**8**), whose stability is similar to that of **5**. The crystal structure of **8**, which is shown in Figure 4, indicates no bonding between the individual bimetallic units.

The chelating dithiolate ligand enforces the same syn, exo conformation of the thiolate bridge as that found in **5**. Nevertheless, the structure is significantly different from that of **5** or **1** (which also contains the pdt ligand). Contrary to our expectations, the structure shows that the two CN^- ligands are trans, which is the case for **1**. Because we started with the cis,cis,cis complex **6**, a ligand rearrangement must have occurred during its reaction with Ni(dppe)Cl_2. Complex **8**

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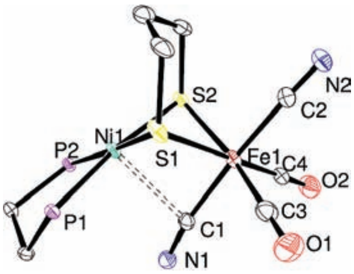

Figure 4. ORTEP drawing of **8** at a 50% probability level. Phenyl groups from dppe and all H atoms have been removed for clarity. Selected bond distances (Å) and angles (deg): Fe1−C1 1.968(3), Fe1−C2 1.920(3), Fe1−C3 1.790(3), Fe1−C4 1.785(3), Fe1−S1 2.339(1), Fe1−S2 2.343(1), Ni1−S1 2.229(1), Ni1−S2 2.210(1), Ni1−P1 2.181(1), Ni1−P2 2.196(1), Ni1−C1 2.421(1), C1−N1 1.153(4); C1−Fe1−C2 175.2(1), Fe1−C1−N1 169.9(3), Ni1−C1−N1 111.1(2).

has a significantly more folded [NiS$_2$Fe] rhomb than either **1** or **5** [Ni1−S1−S2−Fe1 dihedral angle 111.69(3)°], a short Ni1−Fe1 distance [2.809(1) Å], and an unusual semibridging CN^{-} [16] with a very short Ni1−C1 distance of 2.421(3) Å. The isomerization of the CN^{-} and CO ligands is not necessary for the occurrence of the semibridging CN^{-}. Despite the short Ni−C distance, the Ni−CN interaction has very little effect on the Fe1−C1 distance [1.968(3) Å], C1−N1 distance [1.153(4) Å], and the Fe1−C1−N1 angle [169.9(3)°]. The IR spectrum of **8** in a CH$_2$Cl$_2$ solution shows two equally intense CO peaks at 2005 and 2053 cm^{-1} and two CN peaks at 2081 and 2110 cm^{-1}. The low-energy CN^{-} vibration can be assigned to the semibridging CN^{-}.[17] For both **5** and **8**, the addition of the (dppe)Ni fragment results in a shift in the CO stretching frequencies to higher energies.

The structures of the new Ni−Fe complexes (**5** and **8**), together with **1**, demonstrate that small changes in the ligands can result in substantial structural changes at the metal centers. Of particular interest are the changes in the coordination geometry at the Ni centers: the increased coordination number in **5** is suggestive of possible substrate binding, while the semibridging CN^{-} in **8** is suggestive of the occurrence of the third bridging ligand in the hydrogenases. Work is ongoing to produce more realistic structural, spectroscopic, and reactivity analogues of the NiFe active site.

Acknowledgment. J.J. thanks Yeshiva University and Dr. Morton Lowengrub for financial and other support. S.A.K. acknowledges NSF Grant 0616392.

Supporting Information Available: Synthesis, characterization details, and crystallographic data for **3**, **5**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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