First Generation Analogues of the Binuclear Site in the Fe-Only Hydrogenases: $Fe_2(\mu\text{-}SR)_2(CO)_4(CN)_2^{2-}$
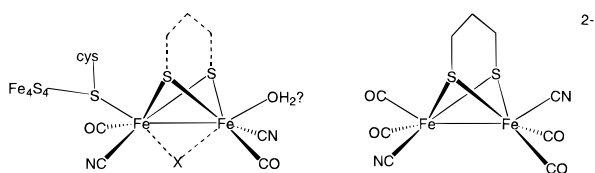
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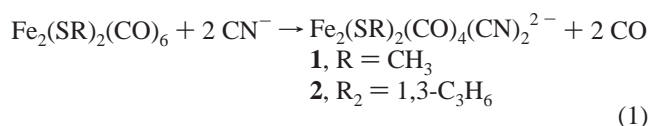*Urbana, Illinois 61801*

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Hydrogenase enzymes are utilized by numerous microorganisms to produce dihydrogen or to take up dihydrogen in support of their metabolic activities. The two families of metallohydrogenases feature $FeM(\mu\text{-}SR)_2(CO)_n(CN)_n$ cores.[1−3] Having cyanide and CO coligands as well as metal−metal bonding, the hydrogenase active sites represent a link between the otherwise disparate realms of organometallic and biological Fe−S chemistry.[4−6] The structure proposed[7] for the binuclear center of the Fe-only hydrogenases is depicted on the left of the following schematic next to the molecule prepared in this study:
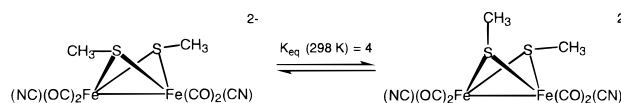

While a number of details remain uncertain, the active site structure is reproduced in crystallography of enzymes from two different genera.[7,8]

Initial preparative efforts targeted the series $Fe_2(SMe)_2(CO)_{6-n}(CN)_n^{n-}$. Solutions of $Fe_2(SMe)_2(CO)_6$[9] in methanol or acetonitrile react in minutes with Et_4NCN to give exclusively $Fe_2(SMe)_2(CO)_4(CN)_2^{2-}$ (**1**, eq 1). Analytically pure Et_4N^+ (**1a**) and Ph_4P^+ (**1b**) salts were precipitated in good yields.[10] We were unable to isolate monocyano species, even when a deficiency of Et_4NCN was used, indicating that the binding of the first CN^- enhances the rate of substitution at the second metal. On the other hand, excess Et_4NCN did not lead to the formation of higher

cyanides, i.e., $Fe_2(SMe)_2(CO)_{6-n}(CN)_n^{n-}$ ($n > 2$). Furthermore, the substitution is selective for placement of one CN^- on each Fe center, consistent with IR structural studies on the protein.[11] Crystallographic analysis[12] of $(PPh_4)_2[Fe_2(SMe)_2(CO)_4(CN)_2]$ confirmed the expected connectivity but suffered from disorder due to cocrystallization of the diequatorial and axial, equatorial isomers:

$$Fe_2(SR)_2(CO)_6 + 2\ CN^- \rightarrow Fe_2(SR)_2(CO)_4(CN)_2^{2-} + 2\ CO$$
$$\textbf{1}, R = CH_3$$
$$\textbf{2}, R_2 = 1,3\text{-}C_3H_6$$
$$(1)$$

An alternative approach to Fe−S−CO−CN$^-$ assemblies was pursued starting from $Fe_2S_2(CO)_6$ because we expected to be able to effect reactions of the S−S bond after CN^- for CO substitution.[13] This reaction afforded $(NEt_4)_2[Fe_6S_6(CO)_{12}]$,[14] indicating that the mildly reducing CN^- induces S-centered redox, not substitution, in contrast to the case for the μ-SR derivatives.

The crystallographic analysis of the *D. desulfuricans*-derived enzyme indicates that the Fe atoms are bridged via a 1,3-propanedithiol derivative.[7] Such a dithiolate is constrained to the diaxial geometry, obviating problems with isomerism at the μ-SR sites.[15] Red microcrystalline $(NEt_4)_2[Fe_2(S_2C_3H_6)(CO)_4(CN)_2]$ (**2a**, Figure 1) was obtained in 94% yield using methods for the preparation of **1a**. Compound **2a** is stable in solutions for extended periods but rapidly decomposes in air. Dynamic ^{13}C NMR studies on **2a** show that the trimethylene strap inverts rapidly on the NMR time scale at room temperature. Similarly, at room temperature, we observe only one ^{13}CN signal (50% enriched), while at −40 °C we observe two peaks attributed to the cessation of the ring-folding dynamics. Concomitant with the splitting of the CN^- signals, the trimethylene CH_2 signals split into two sets at −40 °C.

Crystallographic characterization of **2a**[16] confirms the resemblance of the $[Fe_2(S_2C_3H_6)(CO)_4(CN)_2]^{2-}$ dianion and the binuclear sites in the hydrogenases. The 1,3-propane dithiolate bridges a pair of Fe atoms, each coordinated by one CN^- and two CO ligands. The Fe−Fe distance (2.517 Å), which is clearly bonding, is comparable to that seen for both $Fe_2(SR)_2(CO)_6$ derivatives[15,17] but somewhat shorter than in both protein structures ($r_{Fe-Fe} \approx 2.6$ Å).[7,8] The crystallography confirms the presence of one CN^- on each Fe, as has been suggested for the *D. desulfuricans* protein.[7] The Fe−CX (X = O vs N) distances are

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(10) (PPh$_4$)$_2$[Fe$_2$(SCH$_3$)$_2$(CO)$_4$(CN)$_2$] (**1b**): ^{1}H NMR (CD$_3$CN, 400 MHz) δ 1.18 (s, SCH$_3$, a,e), 1.71 (s, SCH$_3$, e,e), 1.81 (s, SCH$_3$, a,e) (6 H, 79% a,e, 21% e,e), 7.4−8.0 (m, PPh$_4$, 40 H); IR (KBr, cm^{-1}) 2073 (m), 2057 (w), 1959 (s), 1915 (vs), 1882 (s), 1863 (s), 1839 (m). Anal. Calcd for C$_{56}$H$_{46}$Fe$_2$N$_2$O$_4$P$_2$S$_2$ (Found): C, 64.13 (64.03); H, 4.42 (4.44); N, 2.67 (2.50). The Et$_4$N$^+$ salt (**1a**): Anal. Calcd for C$_{24}$H$_{46}$Fe$_2$N$_4$O$_4$S$_2$: C, 45.72 (45.97); H, 7.35 (7.33); Fe, 17.72 (17.59); N, 8.89 (8.98); S, 10.17 (10.34). (PPh$_4$)$_2$[Fe$_2$(S$_2$C$_3$H$_6$)-(CO)$_4$(CN)$_2$] (**2b**): ^{1}H NMR (CD$_3$CN, 400 MHz) δ 1.65 (m, SCH$_2$*CH$_2$*CH$_2$S, 2H), 1.84 (m, S*CH$_2$*CH$_2$*CH$_2$*S, 4H), 7.4−8.0 (m, PPh$_4$, 40 H); IR (KBr, cm^{-1}) 2078 (s), 2029 (w), 1951 (s), 1917 (vs), 1880 (s), 1867 (sh); IR (CH$_2$Cl$_2$, cm^{-1}) 2071 (m), 2031 (w), 1964 (m), 1924 (s), 1884 (m). Anal. Calcd for C$_{57}$H$_{46}$Fe$_2$N$_2$O$_4$P$_2$S$_2$ (Found): C, 64.54 (64.79); H, 4.37 (4.47); N, 2.64 (2.97). The Et$_4$N$^+$ salt (**2a**): Anal. Calcd for C$_{25}$H$_{46}$Fe$_2$N$_4$O$_4$S$_2$ (Found): C, 46.74 (46.75); H, 7.22 (7.21); Fe, 17.38 (17.20); N, 8.72 (9.07); S, 9.98 (9.63). Fe$_2$(S$_2$C$_3$H$_6$)-(CO)$_4$(CN)$_2$(H$_2$O) (**3**): IR (KBr, cm^{-1}) 2119 (s), 2058 (s), 2038 (s), 2000 (s). Anal. Calcd for C$_9$H$_8$Fe$_2$N$_2$O$_4$S$_2$ (Found): C, 27.02 (27.15); H, 2.00 (1.89); N, 7.00 (7.26).

(11) IR study of the *D. vulgaris* Fe hydrogenase: Pierik, A. J.; Hulstein, M.; Hagen, W. R.; Albracht, S. P. J. *Eur. J. Biochem.* **1998,** *258,* 572−578.
(12) Crystallographic details for **1b**: space group P1 (Z = 2); a = 10.7271(8), b = 12.9116(10), and c = 21.1722(16) Å, α = 80.023(2), β = 79.553(2), and γ = 71.198(2)°.
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(16) Preparation of **2a**: Fe$_2$(S(CH$_2$)$_3$S)(CO)$_6$ and 2 equiv of Et$_4$NCN were combined at 0 °C in MeCN solution. The reaction mixture was brought to room temperature, and, after 1 h, the solvents were removed from the red solution. The residue was washed with hexanes (94% yield). Single crystals were obtained by layering CH$_2$Cl$_2$ solutions with hexanes. Crystal data for **2a**: triclinic; P1 (Z = 2); a = 7.9323(13), b = 10.0132(15), and c = 19.845-(3) Å, α = 90.867(4), β = 100.158(3), and γ = 95.603(3)°, R_1 = 0.0636, wR_2 = 0.1592; GOF = 0.976.
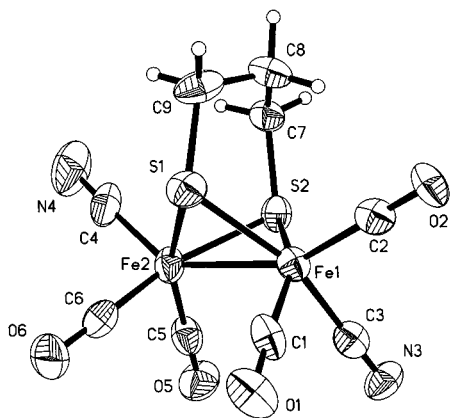(17) Dahl, L. F.; Wei, C. H. *Inorg. Chem.* **1963,** *2,* 328−334.

Figure 1. Structure of the dianion in $(Et_4N)_2[Fe_2(S_2C_3H_6)(CO)_4(CN)_2]$ (**2a**), with thermal ellipsoids set at the 50% probability level. Selected distances (Å) and angles (deg): Fe1−C1, 1.741(5); Fe1−C2, 1.769(6); Fe1−C3, 1.929(6); Fe1−S1, 2.2659(16); Fe1−S2, 2.2690(16), Fe1−Fe2, 2.5171(12); C1−Fe1−C2, 98.8(2); C1−Fe1−C3, 90.1(2); C2−Fe1−C3, 98.3(2); Fe1−S1−Fe2, 67.25(5); S1−Fe1−S2, 85.74(6).
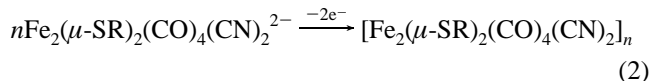
distinctly different: Fe−CO distances are ca. 0.2 Å shorter than the Fe−CN distances. It is interesting to note that the Fe−CO distances are ca. 0.08 Å shorter than in the hexacarbonyl Fe_2-$(SEt)_2(CO)_6$. The contraction of Fe−CO distances in mixed Fe−CO/CN complexes appears to be a general phenomenon.[5,18] The strengthening of the Fe−CO bonding by CN^- coordination may be related to the observed regioselective synthesis of **1** and **2** (see eq 1).

In contrast to the hexacarbonyls $Fe_2(SR)_2(CO)_6$, **2** is quite oxidatively sensitive.[19] Solutions of **2** react with $(NH_4)_2Ce(NO_3)_6$ (2 equiv) or, more conveniently, I_2 (1 equiv) to give neutral Fe_2-$(S_2C_3H_6)(CO)_4(CN)_2 \cdot H_2O$ (**3**). The oxidation of **2** to **3** was also effected, albeit less efficiently, using HOTf (2 equiv); the cogenerated H_2 (35% yield) was identified by NMR analysis ($\sim\delta$ 4.51) and quantified by gas volume measurements. The insolubil-

ity of **3** and the irreversible nature of the oxidations lead us to propose that **3** is polymeric, which would be consistent with the unsaturated 32e^- configuration for monomeric $Fe_2(S_2R)_2(CO)_4$-$(CN)_2$ (eq 2). While polymeric cyanometalates are well prece-

$$n\text{Fe}_2(\mu\text{-SR})_2(\text{CO})_4(\text{CN})_2^{2-} \xrightarrow{-2e^-} [\text{Fe}_2(\mu\text{-SR})_2(\text{CO})_4(\text{CN})_2]_n$$
(2)

dented (cf. Prussian Blue[20]), redox-induced polymerization of cyanometalate monomers is uncommon and merits further study, perhaps using solubilizing thiolato ligands. Not surprisingly, and as seen in the protein,[11] oxidation of **2** causes a significant shift in both the ν_{CO} and ν_{CN} bands[10] to higher frequencies.[21] Compound **3** is a promising synthetic entry into the $Fe^{II}_2(SR)_2$−CO−CN manifold, as demonstrated by its reaction with imidazoles and CN^- to give soluble $Fe_2(S_2C_3H_6)$−CO−CN−L derivatives, which will be the subject of a future report.

In summary, the electron-rich species $Fe_2(S_2C_3H_6)_2(CN)_2(CO)_4^{2-}$ bears a stoichiometric and structural resemblance to the Fe-only hydrogenases. The ready availability of these species should facilitate study of the molecular basis of hydrogenase catalysis.[22]

Note Added in Proof: Crystallographic analysis of the Fe-only hydrogenase (CpI) from *C. pasteurianum* reveals that the CO-inhibited enzyme has a $Fe(CO)_2(CN)$ site as seen in compounds **1** and **2** (Lemon, B. J.; Peters, J. W. *Biochemistry* **1999**, in press).

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