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Novel Single and Double Diiron Oxadithiolates as Models for the Active Site of [Fe]-Only Hydrogenases

Li-Cheng Song,^{*,†} Zhi-Yong Yang,[†] Hong-Zhu Bian,[†] and Qing-Mei Hu^{†,‡}

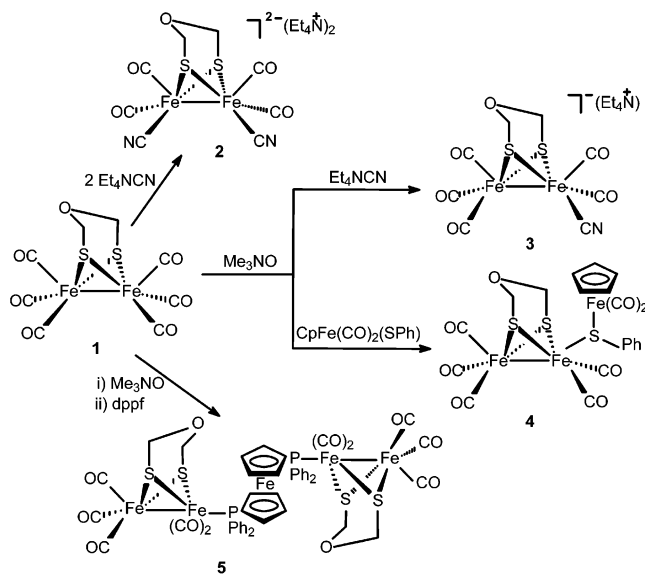
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Summary: The series of diiron oxadithiolate model complexes for the active site of [Fe]-only hydrogenases $\text{Fe}_2(\mu\text{-SCH}_2\text{OCH}_2\text{S-}\mu)(\text{CO})_6$ (**1**), $[\text{Fe}_2(\mu\text{-SCH}_2\text{OCH}_2\text{S-}\mu)(\text{CN})_2(\text{CO})_4](\text{Et}_4\text{N})_2$ (**2**), $[\text{Fe}_2(\mu\text{-SCH}_2\text{OCH}_2\text{S-}\mu)(\text{CN})(\text{CO})_5](\text{Et}_4\text{N})$ (**3**), $\text{Fe}_2(\mu\text{-SCH}_2\text{OCH}_2\text{S-}\mu)(\text{CO})_5[\text{CpFe}(\text{CO})_2(\text{SPh})]$ (**4**), and $[\text{Fe}_2(\mu\text{-SCH}_2\text{OCH}_2\text{S-}\mu)(\text{CO})_5]_2[(\eta^5\text{-Ph}_2\text{PC}_5\text{H}_4)_2\text{Fe}]$ (**5**) have been synthesized and fully characterized by elemental analysis, spectroscopy, and X-ray diffraction analysis. The structural features for some of the model complexes are compared with the corresponding features for the active site of [Fe]-only hydrogenases.

Hydrogenases are highly effective enzymes which can catalyze the reversible redox reaction $\text{H}_2 \rightleftharpoons 2\text{H}^+ + 2\text{e}^-$ in a wide variety of microorganisms.¹ On the basis of the metals involved in the enzymes, hydrogenases may be divided into two major classes: [Fe]-only hydrogenases and [NiFe]-hydrogenases.² The [Fe]-only hydrogenases (denoted as [Fe]H₂ases) have been subjected to extensive study, largely because of their unusual structures and their capacity to produce dihydrogen, an alternative “clean” energy source.³ The crystallographic⁴ and IR spectroscopic⁵ studies revealed that the active site of [Fe]H₂ases (so-called H cluster) consists of a butterfly Fe_2S_2 subcluster that bears three unusual ligands, CO, CN^- , and $\text{Fe}_4\text{S}_4(\text{SCys})_4$, and a less defined three-atom linker (possibly composed of carbon or any combination of C, N, and O atoms) bridged between two S atoms of the butterfly Fe_2S_2 subcluster. Since then, numerous modeling studies on the active site of [Fe]H₂ases have been successfully carried out. However, it is noteworthy that such studies have, so far, mainly been limited to single diiron 1,3-propanedithiolate derivatives⁶ and single diiron azadithiolate derivatives.⁷ To further understand the active site of [Fe]H₂ases, we recently carried out a study concerning the syntheses and structures of single and double diiron oxadithiolate derivatives, since the structural studies on the active

Scheme 1



site of [Fe]H₂ases indicated, as mentioned above, the possible presence of an oxygen atom in the three-atom linker bridged between two S atoms.^{4,5} Now, we report the interesting results obtained from this investigation.

Treatment of the parent diiron oxadithiolate complex $\text{Fe}_2(\mu\text{-SCH}_2\text{OCH}_2\text{S-}\mu)(\text{CO})_6$ (**1**),⁸ prepared from $(\mu\text{-LiS})_2\text{Fe}_2(\text{CO})_6$ ⁹ and $(\text{ClCH}_2)_2\text{O}$,¹⁰ with 2 equiv of Et_4NCN afforded the corresponding dicyano derivative $[\text{Fe}_2(\mu\text{-SCH}_2\text{OCH}_2\text{S-}\mu)(\text{CN})_2(\text{CO})_4](\text{Et}_4\text{N})_2$ (**2**) in 94% yield, whereas complex **1** reacted with 1 equiv of $\text{Me}_3\text{NO} \cdot 2\text{H}_2\text{O}$ followed by treatment with 1 equiv of Et_4NCN to give the monocyno derivative $[\text{Fe}_2(\mu\text{-SCH}_2\text{OCH}_2\text{S-}\mu)(\text{CN})(\text{CO})_5](\text{Et}_4\text{N})$ (**3**) in 62% yield (Scheme 1). Model compounds **1–3** were fully characterized by elemental analysis and spectroscopy¹¹ as well as by X-ray diffraction techniques.¹² The X-ray structural study of **3**

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(8) This complex was previously prepared by another method in 32% yield,^{7b} but our method is more simple and convenient and gives a much higher yield (60%). In addition, we confirmed its structure by X-ray diffraction.

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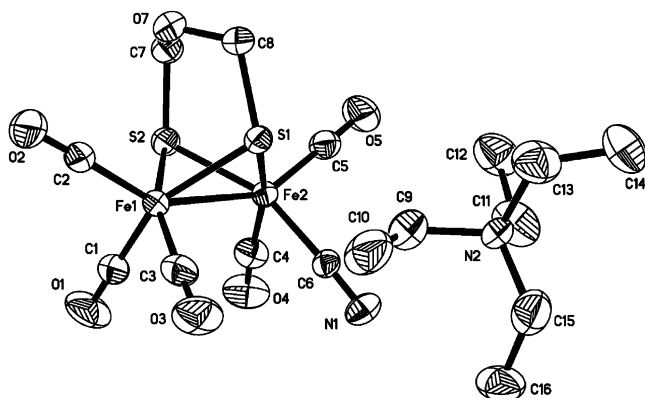


Figure 1. Molecular structure of **3** (30% probability displacement ellipsoids). Selected bond lengths (Å) and angles (deg): Fe2–S1 = 2.2461(17), Fe1–S2 = 2.2699(18), Fe1–Fe2 = 2.5121(13); Fe1–S1–Fe2 = 67.70(5), Fe2–S2–Fe1 = 67.72(5), C8–O7–C7 = 112.6(5).

(Figure 1) showed that the CN^- ligand occupies an equatorial coordination site of one Fe atom, which is consistent with its position in the H cluster of $[\text{Fe}]_{\text{H}_2}\text{-ases}$.⁴ In addition, the bridgehead oxygen atom in **3**, in contrast to that in its parent complex **1** (for its molecular structure, see Supporting Information), is not 50% disordered between the two Fe atoms of the butterfly Fe_2S_2 cluster core but is fixed completely opposite to the Fe atom attached to the CN^- ligand, which could be attributed to the strong electrostatic repulsion between the negatively charged CN^- ligand and the electro-negative O atom.

(11) **1**: to a solution of $(\mu\text{-LiS})_2\text{Fe}_2(\text{CO})_6$, prepared from $(\mu\text{-S}_2)\text{Fe}_2(\text{CO})_6$ (0.172 g, 0.5 mmol), Et_3BHLi (1 M, 1 mL), and THF (20 mL) at -78°C , was added bis(chloromethyl) ether (0.173 g, 1.5 mmol), and then the mixture was warmed to room temperature and stirred for 3 h. Solvent was removed and the residue was subjected to TLC using CH_2Cl_2 /petroleum ether (1/4 v/v) as eluent to give **1** as a red solid. Yield: 0.117 g. ^1H NMR (200 MHz, CDCl_3): δ 4.21 (s, 4H, 2CH_2). IR (KBr disk): $\nu_{\text{C=O}}$ 2077, 2035, 1989 cm^{-1} . **2**: a solution of **1** (0.194 g, 0.5 mmol) in MeCN (20 mL) at 0°C was treated with a solution of Et_4NCN (0.156 g, 1.0 mmol) in MeCN (10 mL). After it was warmed to room temperature, the mixture was stirred for 1 h. Solvent was removed, and the residue was washed thoroughly with CH_2Cl_2 /Et₂O to give **2** as a red solid. Yield: 0.303 g. ^1H NMR (200 MHz, CD_3CN): δ 3.98 (s, 4H, 2CH_2), 3.18 (br. s, 16H, $8\text{CH}_2\text{CH}_3$), 1.20 (br. s, 24H, $8\text{CH}_2\text{CH}_3$). IR (KBr): ν_{CN} 2077, 2028; $\nu_{\text{C=O}}$ 1965, 1928, 1899, 1888, 1872 cm^{-1} . **3**: a solution of **1** (0.194 g, 0.5 mmol) in MeCN (15 mL) was treated with a solution of $\text{Me}_3\text{NO}\cdot 2\text{H}_2\text{O}$ (0.056 g, 0.5 mmol) in MeCN (10 mL) at room temperature. After 5 min, the mixture was cooled to -40°C and treated with a solution of Et_4NCN (0.078 g, 0.5 mmol) in MeCN (10 mL). After 0.5 h, the mixture was warmed to room temperature and stirred for 1 h. The same workup as for **2** gave **3** as a red solid. Yield: 0.160 g. ^1H NMR (200 MHz, CDCl_3): δ 4.09 (s, 4H, 2CH_2), 3.31 (q, 8H, $4\text{CH}_2\text{CH}_3$), 1.34 (br. s, 12H, $4\text{CH}_2\text{CH}_3$). IR (KBr): ν_{CN} 2088; $\nu_{\text{C=O}}$ 2030, 1987, 1968, 1945, 1907 cm^{-1} . Similarly, when $\text{CpFe}(\text{CO})_2(\text{SPh})$ (0.143 g, 0.5 mmol) or dppf (0.139 g, 0.25 mmol) was used instead of Et_4NCN , **4** and **5** were obtained as red solids. **4**: yield 0.233 g. ^1H NMR (200 MHz, CDCl_3): δ 7.19–7.68 (m, 5H, C_6H_5), 4.99 (s, 5H, C_5H_5), 3.80–4.28 (m, 4H, 2CH_2). IR (KBr): $\nu_{\text{C=O}}$ 2034, 1992, 1974, 1964, 1914 cm^{-1} . **5**: yield 0.288 g. ^1H NMR (200 MHz, CDCl_3): δ 7.38–7.60 (m, 20H, $4\text{C}_6\text{H}_5$), 4.25 (d, 8H, $2\text{C}_5\text{H}_4$), 3.50, 3.65 (d, d, 8H, 4CH_2). ^{31}P NMR (81.0 Hz, CDCl_3): δ 54.16 (s). IR (KBr): $\nu_{\text{C=O}}$ 2047, 1983, 1933; $\nu_{\text{C-O-C}}$ 1163 cm^{-1} .

(12) Crystal data are as follows. **3**: monoclinic, space group C2/c , $a = 32.554(12)$ Å, $b = 11.294(4)$ Å, $c = 13.655(5)$ Å, $\beta = 114.653(11)^\circ$, $F(000) = 2128$, $V = 4563(3)$ Å³, $Z = 8$, $D_c = 1.503$ g cm^{-3} , $\mu(\text{MoK}\alpha) = 1.486$ mm⁻¹, $R = 0.0552$, $R_w = 0.1071$, GOF = 1.009. **4**: orthorhombic, space group $\text{P2}_12_12_1$, $a = 11.021(7)$ Å, $b = 13.173(8)$ Å, $c = 16.851(10)$ Å, $\alpha = \beta = \gamma = 90^\circ$, $F(000) = 1296$, $V = 2446(2)$ Å³, $Z = 4$, $D_c = 1.754$ g cm^{-3} , $\mu(\text{MoK}\alpha) = 2.055$ mm⁻¹, $R = 0.0362$, $R_w = 0.0599$, GOF = 0.974. **5**: triclinic, space group P1 , $a = 10.422(6)$ Å, $b = 13.454(86)$ Å, $c = 14.360(8)$ Å, $\alpha = 117.430(12)^\circ$, $\beta = 106.307(10)^\circ$, $\gamma = 94.840(10)^\circ$, $F(000) = 770$, $V = 1660.4(14)$ Å³, $Z = 1$, $D_c = 1.529$ g cm^{-3} , $\mu(\text{Mo K}\alpha) = 1.534$ mm⁻¹, $R = 0.0576$, $R_w = 0.1432$, GOF = 1.015.

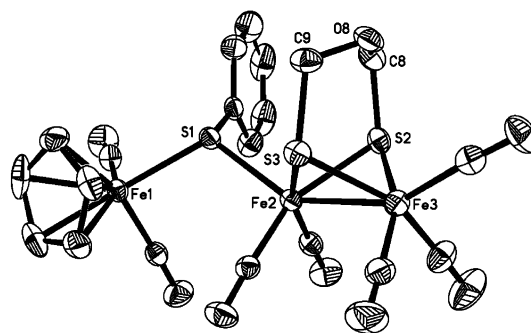


Figure 2. Molecular structure of **4** (30% probability displacement ellipsoids). Selected bond lengths (Å) and angles (deg): Fe1–S1 = 2.3016(14), Fe2–S2 = 2.2556(14), Fe2–Fe3 = 2.5026(14); Fe1–S1–Fe2 = 114.33(5), Fe2–S2–Fe3 = 67.19(4), C8–O8–C9 = 112.8(3).

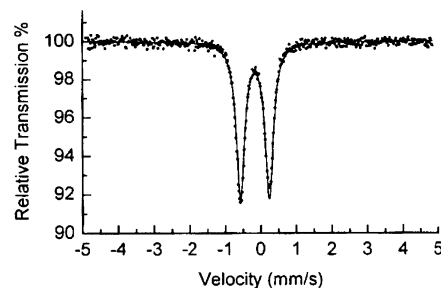


Figure 3. ^{57}Fe spectrum of **1**.

Further treatment of **1** with 1 equiv of $\text{Me}_3\text{NO}\cdot 2\text{H}_2\text{O}$ and 1 equiv of $\text{CpFe}(\text{CO})_2(\text{SPh})$ in MeCN resulted in formation of the metallo-thioether-substituted derivative $\text{Fe}_2(\mu\text{-SCH}_2\text{OCH}_2\text{S-}\mu)(\text{CO})_5[\text{CpFe}(\text{CO})_2(\text{SPh})]$ (**4**) in 72% yield (Scheme 1), which was characterized by elemental analysis and spectroscopy¹¹ as well as by X-ray diffraction techniques.¹² While the $[\text{2Fe3S}]$ assemblies related to the diiron subsite of the H cluster were previously reported,¹³ complex **4** is the first $[\text{3Fe3S}]$ assembly related to the active site of $[\text{Fe}]_{\text{H}_2}\text{-ases}$, in which one of the Fe atoms of the butterfly Fe_2S_2 cluster is ligated to the S atom of a metallo-thioether ligand. The simple metallo-thioether $\text{CpFe}(\text{CO})_2(\text{SPh})$ is obviously a good ligand for mimicking the real, complicated metallo-thioether ligand $\text{Cys-SFe}_4\text{S}_4(\text{SCys})_3$ in the H cluster of $[\text{Fe}]_{\text{H}_2}\text{-ases}$, and thus complex **4** is more structurally analogous to the H cluster of $[\text{Fe}]_{\text{H}_2}\text{-ases}$ than those reported $[\text{2Fe3S}]$ assemblies. The crystallographic study of **4** (Figure 2) indicated that the bridgehead O atom points opposite to the axially substituted metallo-thioether $\text{CpFe}(\text{CO})_2(\text{SPh})$, which is possibly in order to avoid the strong steric repulsion between the bulky ligand $\text{CpFe}(\text{CO})_2(\text{SPh})$ and the bridgehead O atom when it points to the bulky ligand.

The Mössbauer spectrum of parent complex **1** shows one doublet (IS = -0.02 mm/s; QS = 0.81 mm/s) (Figure 3) attributed to the two identical Fe atoms in its butterfly Fe_2S_2 cluster core, while the spectrum of **4** displays two doublets (Figure 4): the outer doublet (IS = 0.13 mm/s, QS = 1.66 mm/s) is assigned to the one Fe atom in the $\text{CpFe}(\text{CO})_2(\text{SPh})$ ligand, and the inner doublet is assigned to the two Fe atoms in its butterfly

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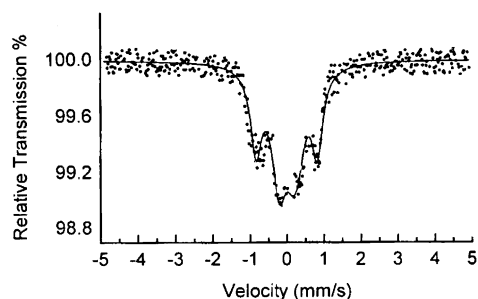


Figure 4. ^{57}Fe spectrum of **4**.

Fe_2S_2 cluster core. In fact, the inner doublet was formed by overlapping another two doublets (IS = 0.17 mm/s, QS = 0.55 mm/s; IS = 0.11 mm/s, QS = 0.33 mm/s) attributed to the slightly different two Fe atoms in the butterfly Fe_2S_2 cluster core of complex **4**, respectively. The Mössbauer data for the 2Fe subcluster of $[\text{Fe}]\text{H}_2\text{-ases}$ from two organisms were previously reported. The reduced 2Fe subcluster from *C. Pasteurianum* has IS and QS values, respectively, of 0.08 and 0.87 mm/s.¹⁴ The oxidized, CO-inhibited 2Fe subcluster of *D. Vulgaris* has IS values of 0.13 and 0.17 mm/s and QS values of 0.65 and 0.70 mm/s.¹⁵ It follows that the IS and QS values of the two Fe atoms in the butterfly Fe_2S_2 cluster of our $[\text{3Fe3S}]$ assembly **4** are close to those observed in the reduced and the oxidized, CO-inhibited 2Fe subcluster, respectively.

Another novel complex, $[\text{Fe}_2(\mu\text{-SCH}_2\text{OCH}_2\text{S-}\mu)(\text{CO})_5]_2\text{-}[(\eta^5\text{-Ph}_2\text{PC}_5\text{H}_4)_2\text{Fe}]$ (**5**), was similarly prepared by reaction of complex **1** with 1 equiv of $\text{Me}_3\text{NO}\cdot 2\text{H}_2\text{O}$ and subsequent treatment with 0.5 equiv of 1,1'-bis(diphenylphosphino)ferrocene (dppf) in 90% yield (Scheme 1). This complex was characterized by elemental analysis and IR, ^1H NMR, and ^{31}P NMR spectroscopy,¹¹ as well as by X-ray diffraction.¹² As can be seen in Figure 5, this model complex, in contrast to the single diiron oxadithiolate **4**, consists of two diiron oxadithiolate moieties, which are joined together through a dppf ligand. The dppf ligand in **5** is somewhat similar to the aforementioned $\text{CpFe}(\text{CO})_2(\text{SPh})$ in complex **4**, for example, both being a CpFe-containing species and being

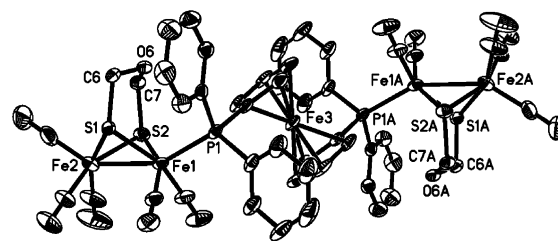


Figure 5. Molecular structure of **5** (30% probability displacement ellipsoids). Selected bond lengths (Å) and angles (deg): Fe1–S1 = 2.2612(19), Fe1–Fe2 = 2.5430(16), Fe1–P1 = 2.265(2); Fe1–S1–Fe2 = 68.32(6), Fe2–Fe1–P1 = 152.19(5), C6–O6–C7 = 113.3(5).

axially coordinated to the iron atom of diiron oxadithiolate through the heteroatom S or P. The bond length of Fe1–Fe2 (= Fe1A–Fe2A = 2.5430(16) Å) in **5** is slightly longer than that of Fe2–Fe3 (2.5026(14) Å) in **4** and thus is even closer to the corresponding lengths in the oxidized form (2.62 and 2.60 Å)^{4a,b} and the reduced form (2.55 Å)^{4c} of the enzymes.

In summary, we have synthesized and structurally characterized the oxadithiolatodiiron-containing model compounds **1–5**. Particularly noteworthy is that the single oxadithiolatodiiron $[\text{3Fe3S}]$ assembly **4** is the first model to mimic not only the Fe_2S_2 subsite but also the cysteine-S- $[\text{Fe}_4\text{S}_4]$ subsite in the active site of $[\text{Fe}]\text{H}_2\text{-ases}$. **5** contains two oxadithiolatodiiron structural units, which could be regarded structurally as a double model for the active site of $[\text{Fe}]\text{H}_2\text{-ases}$. This is similar to the case of the double-cubane MoFe_3S_4 model for the Mo/Fe cofactor of nitrogenases.¹⁶

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Supporting Information Available: X-ray crystallographic files for **1**, **3**, **4**, and **5** in CIF format and text giving details for the synthesis and characterization of **1–5**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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