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Dithiolato-Bridged Dinuclear Iron−Nickel Complexes $[Fe(CO)_2(CN)_2(\mu\text{-}SCH_2CH_2CH_2S)Ni(S_2CNR_2)]^-$ Modeling the Active Site of [NiFe] Hydrogenase

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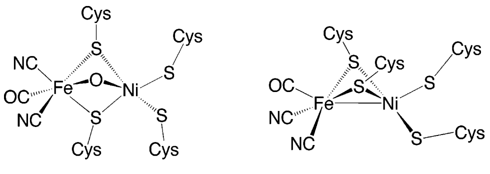
Hydrogenase is essential to hydrogen metabolism by catalyzing the reversible interconversion of proton and molecular hydrogen.[1] The enzyme has been found in many microorganisms of biotechnological interest, which can be grouped into two classes based on the type of metal-containing active sites, namely, [Fe]-only[2] and [NiFe][3] hydrogenases. For the [NiFe] hydrogenase, X-ray structure determination has been carried out for *Desulfovibrio* (*D.*) *gigas*,[3a,b] *D. fructosovorans*,[3c] *D. vulgaris* (Miyazaki),[3d,e] and *Desulfomicrobium* (*Dm.*) *baculatum*.[3f] Two forms of the active sites are known. One is referred to as the oxidized form, where Fe and Ni are bridged by two cysteine S and one O atoms with relatively long Fe−Ni distances of ca. 2.9 Å. The other is the reduced form, with short Fe−Ni bonds of 2.5−2.6 Å and only two bridging cysteine S atoms or perhaps with an additional H-bridge. An exception may be the oxidized form of *D. vulgaris* (Miyazaki), in which the triply bridged Fe−Ni distance is as short as 2.6 Å. Despite the geometrical diversity, interesting common features can be seen in the structure of [NiFe] hydrogenases; the Fe center carries both CO and CN ligands, and the four cysteine S atoms (or three cysteine S atoms and one selenocysteine Se for *Dm. baculatum*) are coordinated to Ni in a distorted tetrahedral geometry.



oxidized form *reduced form*

The intriguing dinuclear structure of [NiFe] hydrogenases has been a challenging target for inorganic/organometallic chemists,[4] and several thiolate-bridged dinuclear Ni−Fe complexes have been prepared: [Ni{1,5-bis(mercaptoethyl)-1,5-diazacyclooctane}Fe$(CO)_4$],[5] [{Fe{N$(CH_2CH_2S)_3$}$(CO)_2$-*S*,*S′*}NiCl(dppe)],[6a] [{Fe{N$(CH_2CH_2S)_3$}(CO)-*S*,*S′*}Ni$(S_2CN^iPr_2)$]],[6b] [$(C_6H_4S_2)$Ni(μ-S$(C_6H_4)_2S_2$)Fe(CO)$(PMe_3)_2$],[7] [{Ni(*N*,*N′*-diethyldiazanonane-1,9-dithiolate)}Fe$(NO)_2$],[8] and [(NO)Ni(μ-S$(CH_2)_2$S$(CH_2)_2$S)Fe$(NO)_2$].[9] However, these complexes do not possess the crucial CO/CN ligand set on iron. The reason for this is the absence of CO/CN complexes of iron, which are suitable for construction of Fe−Ni dinuclear structures. Difficulty also comes from the strong affinity of nickel for CN^-, and therefore, a new synthetic method is required to link the $[Fe(CO)_x(CN)_y]$ fragments to appropriate Ni complexes. The recent synthesis of Fe^{II} carbonyl/cyanide/thiolate complexes, for example, $[Fe(CO)(CN)_2(bdt)]^{2-}$ (bdt = benzenedithiolate), $[Fe(CO)_2(CN)_3(SR)]^{2-}$, and $[Fe(CO)_3(CN)_2(SR)]^-$,[10] prompted us to examine the reactions of preformed Fe^{II} precursors with Ni^{II} complexes. Herein, we report the first synthesis of the dithiolato-bridged Fe−Ni complexes, in which Fe carries both CO and CN ligands.

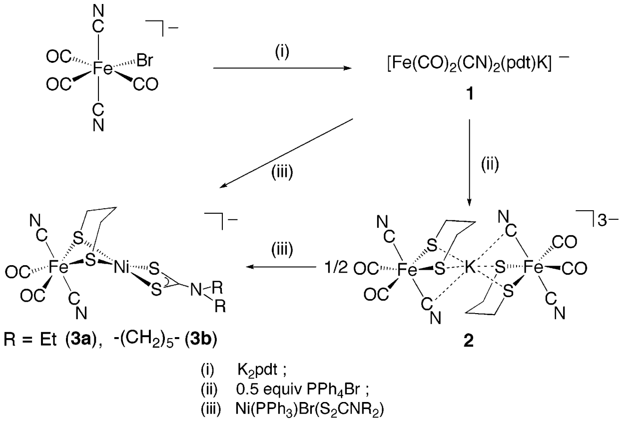
The reaction of $(PPh_4)[Fe(CO)_3(CN)_2Br]$[10c] with 1 equiv of K_2(pdt) (pdt = 1,3-propanedithiolate) afforded $(PPh_4)[Fe(CO)_2(CN)_2(pdt)K]$ (**1**) (Scheme 1). Complex **1** was characterized by means of ESI−MS and IR spectroscopy. Although crystallization of **1** was not successful, further treatment with 0.5 equiv of PPh_4Br gave $(PPh_4)_3[Fe_2(CO)_4(CN)_4(pdt)_2K]$ (**2**) in 88% yield. The IR spectrum of **2** in KBr consists of two relatively weak bands at 2102 (w) and 2085 cm^{-1} (m), assignable to CN stretching vibrations, and two intense CO stretching bands at 2002 and 1938 cm^{-1}. These IR signals closely resemble those of **1**. The Raman spectrum of **2**, in the solid state, shows one CN band at 2101 cm^{-1} and two CO bands at 2002 and 1936 cm^{-1}. The disappearance of one CN band in the Raman spectrum indicates a trans configuration of two CN ligands, in accordance with the X-ray derived structure.

Treatment of a CH_3OH solution of **1** with $Ni(PPh_3)Br(S_2CNR_2)$[11] (S_2CNR_2 = dithiocarbamate) in acetone led to an immediate color change from light red to greenish brown. After stirring for 3 h at −40 °C and for further 1 h at 0 °C, the thiolate-bridged dinuclear Ni−Fe complexes $(PPh_4)[(CO)_2(CN)_2Fe(\mu\text{-}pdt)Ni(S_2CNR_2)]$ (**3a**; R = Et, **3b**; $R_2 = -(CH_2)_5-$) were obtained in 74 and 90% yields, respectively. Alternatively, complex **3a** was also prepared from **2**, but due to a necessary crystallization step, the yield was 31%. In solution, both **3a** and **3b** are thermally unstable at ambient temperature and moderately sensitive to oxygen. Thus, maintaining an acetonitrile solution of **3a** at room temperature resulted in the precipitation of a brown solid and gradual formation of $[Ni(CN)_2(S_2CNEt_2)]^-$ in the solution, as monitored by ESI−MS. According to the ^1H NMR spectrum, **3a** and **3b** are diamagnetic, presumably consisting of low-spin Ni^{II} and Fe^{II} ions. The six methylene protons of the pdt ligand are observed as four sets of ^1H NMR signals (2:2:1:1), indicating the formation of a thiolate-bridged dinuclear structure. The Raman spectrum of **3a** in CH_3OH reveals one CN stretching band at 2113 cm^{-1} and two relatively broad CO stretching bands (ν(CO)) at 2040 and 1991 cm^{-1}. The IR spectrum in CH_3OH shows two CN bands at 2110 and 2094 cm^{-1}, and this together with the Raman signature suggests a trans disposition of two CN ligands on Fe. The ν(CO) region of the IR spectrum is somewhat complicated, exhibiting two intense bands at 2044 and 1994 cm^{-1}, one with moderate intensity at 2031 cm^{-1}, and a shoulder on the low-energy side of the 1994 cm^{-1} band. Likewise, there are four CO bands in the IR spectrum in KBr; 2031 (s), 2015 (m), 1977 (s), 1959 (m) cm^{-1}. The reason for the extra pair of CO bands is not clear, but the systematic shift to higher wavenumbers, relative to those of **2** (2002 and 1938 cm^{-1} in KBr), points to S-bridging between Fe and Ni, by which π-donation from S to Fe, and then to CO, is weakened.

X-ray analyses of **3a** and **3b** confirmed that the two S atoms of pdt bridge iron to nickel, and that two CN ligands on Fe are trans to each other. Since the coordination geometries of **3a** and **3b** are

10.1021/ja051590+ CCC: $30.25

Scheme 1



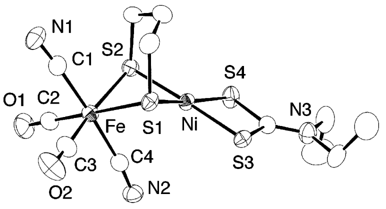


Figure 1. Anion part of **3a** with thermal ellipsoids at 50% probability level.

practically the same, only the ORTEP drawing of **3a** is shown in Figure 1. A distinction between CO and CN was unequivocally made by a clear difference in Fe−CN and Fe−CO distances (av 1.927 versus av 1.779 Å). Complexes **3a** and **3b** reproduce well the structural feature of the active site of [NiFe] hydrogenase in that the two thiolate S atoms link Fe and Ni, the Ni is coordinated by four S atoms, and the Fe carries both CO and CN ligands. Important geometrical parameters of **3a** and **3b** are compared with those of the oxidized forms of *D. gigas* and *D. fructosovorans* in Table 1. The Fe(Ni)−S and Fe−Ni distances are all comparable, except for the unusually long Ni−S(bridge) bond length in *D. gigas*. One obvious difference between our model complexes and the oxidized forms is the number of bridging ligands. The triply bridged structure of the oxidized form of *D. gigas* results in a smaller Fe−S−Ni angle, and yet the Fe−Ni distance remains long, whereas the doubly bridged Fe−Ni bond of the reduced form of either *D. vulgaris* (Miyazaki) or *Dm. baculatum* is substantially short. It is not likely that the Ni−Fe distance is dictated by the number of bridging atoms, but is rather controlled by the oxidation state and/or spin state of metal centers. The coordination geometry of Ni in **3a** and **3b** is close to square planar with the dihedral angles of 8.0 and 4.0 (av)°, respectively, between the [NiS1S2] and [NiS3S4] planes. This is in contrast to the highly distorted NiS_4 geometry of the oxidized and reduced forms of [NiFe] hydrogenases.

It is known that carbon monoxide acts as a reversible inhibitor of hydrogenases,[12] and the incoming CO is thought to be bound to Ni, on the basis of spectroscopic and X-ray crystallographic study.[13] However, the six-coordinate nature of Fe in **3a**,**b** with two CO ligands implies that extra CO on iron could be another possibility. Although there are some discrepancies between the structures of **3a**,**b** and the active sites of [NiFe] hydrogenases, they are the closest yet structural models containing many important features, and this should facilitate better understanding of physicochemical properties and the structure−function relationship of hydrogenases.

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Table 1. Comparison of Selected Bond Distances (Å) and the Fe−S−Ni Angle of **3a**, **3b**, and the Oxidized Form of *D. gigas* and *D. fructosovorans*

	3a	3b	*D gigas*	*D. fructosovorans*
Fe−Ni	3.0587(6)	3.0364(8)	2.9	2.9
Fe−S−Ni[a]	84.43	84.71	73.7	*b*
Fe−S(bridge)[a]	2.337	2.338	2.2	2.4
Ni−S(bridge)[a]	2.213	2.111	2.6	2.4
Ni−S(terminal)[a]	2.206	2.209	2.2	2.3

[a] Averaged. [b] Data not deposited in the protein data bank (PDB).

Supporting Information Available: Details of synthesis and characterization and crystallographic data for **2**·2THF, **3a**, and **3b** (PDF and CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Cammack, R. *Nature* **1999**, *397*, 214−215. (b) Adams, M. W. W.; Stiefel, E. I. *Science* **1998**, *282*, 1842−1843. (c) Thauer, R. K.; Klein, A. R.; Hartmann, G. C. *Chem. Rev.* **1996**, *96*, 3031−3042. (d) Albracht, S. P. J. *Biochim. Biophys. Acta* **1994**, *1188*, 167−204. (e) Evans, D. J.; Pickett, C. J. *Chem. Soc. Rev.* **2003**, *32*, 268−275.

(2) (a) Peters, J. W.; Lanzilotta, W. N.; Lemon, B. J.; Seefeldt, L. C. *Science* **1998**, *282*, 1853−1858. (b) Nicolet, Y.; Piras, C.; Legrand, P.; Hatchikian, C. E.; Fontecilla-Camps, J. C. *Structure* **1999**, *7*, 13−23. (c) Lemon, B. J.; Peters, J. W. *Biochemistry* **1999**, *38*, 12969−12973.

(3) (a) Volbeda, A.; Charon, M. H.; Piras, C.; Hatchikian, E. C.; Frey, M.; Fontecilla-Camps, J. C. *Nature* **1995**, *373*, 580−587. (b) Volbeda, A.; Garcin, E.; Piras, C.; de Lacey, A. L.; Fernandez, V. M.; Hatchikian, E. C.; Frey, M.; Fontecilla-Camps, J. C. *J. Am. Chem. Soc.* **1996**, *118*, 12989−12996. (c) Rousset, M.; Montet, Y.; Guigliarelli, B.; Forget, N.; Asso, M.; Bertrand, P.; Fontecilla-Camps, J. C.; Hatchikian, E. C. *Proc. Natl. Acad. Sci. U.S.A.* **1998**, *95*, 11625−11630. (d) Higuchi, Y.; Yagi, T.; Yasuoka, N. *Structure* **1997**, *5*, 1671−1680. (e) Higuchi, Y.; Ogata, H.; Miki, K.; Yasuoka, N.; Yagi, T. *Structure* **1999**, *7*, 549−556. (f) Garcin, E.; Vernede, X.; Hatchikian, E. C.; Volbeda, A.; Frey, M.; Fontecilla-Camps, J. C. *Structure* **1999**, *7*, 557−566.

(4) Happe, R. P.; Roseboom, W.; Pierik, A. J.; Albracht, S. P. J.; Bagley, K. A. *Nature* **1997**, *385*, 126.

(5) Lai, C.-H.; Reibenspies, J. H.; Darensbourg, M. Y. *Angew. Chem., Int. Ed.* **1996**, *35*, 2390−2393.

(6) (a) Smith, M. C.; Barclay, J. E.; Cramer, S. P.; Davies, S. C.; Gu, W.-W.; Hughes, D. L.; Longhurst, S.; Evans, D. J. *J. Chem. Soc., Dalton Trans.* **2002**, 2641−2647. (b) Smith, M. C.; Barclay, J. E.; Davies, S. C.; Hughes, D. L.; Evans, D. J. *Dalton Trans.* **2003**, 4147−4151.

(7) Sellmann, D.; Geipel, F.; Lauderbach, F.; Heinemann, F. W. *Angew. Chem., Int. Ed.* **2002**, *41*, 632−634.

(8) Osterloh, F.; Saak, W.; Hasse, D.; Pohl, S. *Chem Commun.* **1997**, 979−980.

(9) Liaw, W.-F.; Chiang, C.-Y.; Lee, G.-H.; Peng, S.-M.; Lai, C.-H.; Darensbourg, M. Y. *Inorg. Chem.* **2000**, *39*, 480−484.

(10) (a) Rauchfuss, T. B.; Contakes, S. M.; Hsu, S. C. N.; Reynolds, M. A.; Wilson, S. R. *J. Am. Chem. Soc.* **2001**, *123*, 6933−6934. (b) Sellmann, D.; Geipel, F.; Heinemann, F. W. *Chem.*−*Eur. J.* **2002**, *8*, 958−966. (c) Liaw, W.-F.; Lee, N.-H.; Gau, H.-B.; Chen, C.-H.; Jung, S.-J.; Hung, C.-H.; Chen W.-Y.; Hu, C.-H.; Lee, G.-H. *J. Am. Chem. Soc.* **2002**, *124*, 1680−1688. (d) Chen, C.-H.; Chang, Y.-S.; Yang, C.-Y.; Chen, T.-N.; Lee, C.-M.; Liaw, W.-F. *Dalton Trans.* **2004**, 137−143. (e) Liaw, W.-F.; Lee, N.-H.; Chen, C.-H.; Lee, C.-M.; Lee, G.-H.; Peng, S.-M. *J. Am. Chem. Soc.* **2000**, *122*, 488−494. (f) Hsu, H.-F.; Koch, S. A. *J. Am. Chem. Soc.* **1997**, *119*, 8371−8372.

(11) (a) Nikolov, G. S.; Tyutyulkov, N. *Inorg. Nucl. Chem. Lett.* **1970**, *6*, 697−700. (b) Pastorek, R.; Kamenicek, J.; Brezina, F.; Hamrusova, M.; Sindelar, Z.; Lasovaky, J. *Chem. Pap.* **1993**, *47*, 210−214.

(12) (a) Thauer, R. K.; Kaufer, B.; Zahringer, M.; Jungermann, K. *Eur. J. Biochem.* **1974**, *42*, 447−452. (b) Yagi, T.; Honya, M.; Tamiya, N. *Biochim. Biophys. Acta* **1968**, *153*, 699−705. (c) Daday, A.; Lambert, G. R.; Smith, G. D. *Biochem. J.* **1979**, *177*, 139−144. (d) Adams, M. W.; Hall, D. O. *Biochem. J.* **1979**, *183*, 11−22. (e) Yagi, T.; Kimura, K.; Daidoji, H.; Sakai, F.; Tamura, S. *J. Biochem.* **1976**, *79*, 661−671.

(13) (a) Van der Zwaan, J. W.; Coremans, J. M.; Bouwens, E. C.; Albracht, S. P. *Biochim. Biophys. Acta* **1990**, *1041*, 101−110. (b) Ogata, H.; Mizoguchi, Y.; Mizuno, N.; Miki, K.; Adachi, S.; Yasuoka, N.; Yagi, T.; Yamauchi, O.; Hirota, S.; Higuchi, Y. *J. Am. Chem. Soc.* **2002**, *124*, 11628−11635. (c) Frey, M.; Fontecilla-Camps, J. C. In *Handbook of Metalloproteins*; Messerschmidt, A., Huber, R., Poulos, T., Wieghardt, K., Eds.; John Wiley & Sons: Chichester, U.K., 2001; Volume 2, pp 880−896. (d) DeLacey, A. L.; Stadler, C.; Fernandez, V. M.; Hatchikian, E. C.; Fan, H.-J.; Li, S.; Hall, M. B. *J. Biol. Inorg. Chem.* **2002**, *7*, 318−326.

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