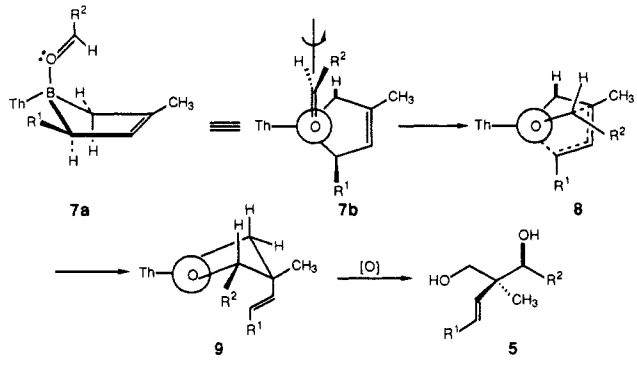
Table I. Regioselectivities Observed in Reactions of 3-Borolenes with Aldehydes

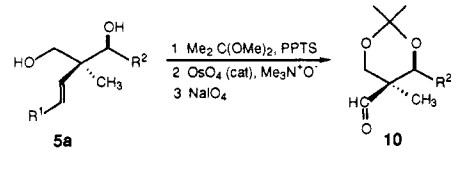
	3-borolene R	3-borolene R^1	R^2CHO R^2		ratio of diols[a,b] 5	6	yield (%)
1	thexyl	cyclohexyl	C_2H_5	a	98	2	70
			i-C_3H_7	b	97	3	85
			$CH_3CH{=}CH$	c	99	1	82
2	thexyl	cyclopentyl	C_2H_5	d	80	20	75
			i-C_3H_7	e	53	47	81
			$CH_3CH{=}CH$	f	94	6	85
3	thexyl	n-hexyl	C_2H_5	g	54	46	72
			$CH_3CH{=}CH$	h	53	47	84
4	cyclohexyl	cyclohexyl	C_2H_5	a	54	46	89

[a] The ratio of the diols **5** and **6** were determined by GLC analysis of the crude reaction mixtures on a 30 m DB-210 J & W glass capilary column. [b] The IR and ^1H NMR data are consistent with the assigned structures.

of the borolene. It should be noted in this connection that steric interactions between R^2 and R^1 become less pronounced as bonding takes place between the aldehyde and the borolene since R^1 turns outward as C-2 becomes a vinylic carbon. Finally, carbon–carbon bond formation between the trigonal centers of the aldehyde and the borolene with concomitant formation of the trans carbon–carbon double bond leads to the 1,2-oxaborolane intermediate **9**. Oxidation of **9** with alkaline hydrogen peroxide affords the diol **5**.[10]



From a purely synthetic point of view, the presently reported preparation of regioisomerically and diastereomerically pure unsaturated diols **5** is confined to those having a cyclohexyl substituent at the vinylic carbon. However, it should be noted that oxidative cleavage of the double bond in the diols **5a,b** using the Lemieux–Johnson procedure,[11] which results in loss of the cyclohexyl moiety, should provide access to the more general stereodefined aldol products, as exemplified by the conversion of **5a** into the 1,3-dioxa-5-cyclohexanecarboxaldehyde (**10**) in 78% yield. These have a quaternary center which is not readily obtained by current methodologies.[12]



Acknowledgment. We thank Professor H. Hope for the X-ray crystallographic analyses of compounds **5a–c**, Professor R. W. Hoffmann (University of Marburg) for helpful discussions, and the National Science Foundation for financial support of this work.

Supplementary Material Available: Experimental details for the synthesis of compounds **1–6** (9 pages). Ordering information is given on any current masthead page.

(10) We are grateful to a referee for valuable suggestions concerning the proposed mechanistic scheme.

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Palladium-Catalyzed Asymmetric 1,4-Disilylation of α,β-Unsaturated Ketones: Catalytic Asymmetric Synthesis of β-Hydroxy Ketones

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We wish to report here a novel approach to optically active α-unsubstituted and α-anti-substituted β-hydroxy ketones[1] through palladium-catalyzed asymmetric 1,4-disilylation of α,β-unsaturated ketones followed by oxidative cleavage of the carbon–silicon bond (Scheme I).

In hopes of developing a new catalytic silylation of α,β-unsaturated carbonyl compounds,[2] we examined a variety of silylating reagents and catalysts for the reaction of 4-phenyl-3-buten-2-one (**1a**) and found that 0.5 mol% of tertiary phosphine–palladium complexes such as tetrakis(triphenylphosphine)palladium(0) catalyze the 1,4-addition of 1,1-dichloro-1-phenyl-2,2,2-trimethyldisilane ($Cl_2PhSiSiMe_3$)[3] under mild conditions (at 40–80 °C for 5–40 h). Treatment of the 1,4-disilylation product **2a** with an excess of methyllithium in ether followed by acidic hydrolysis of the resulting β-phenyldimethylsilyllithium enolate gave 4-phenyl-4-(phenyldimethylsilyl)butan-2-one (**3a**) in 70–80% yield (Scheme II). The pallladium-catalyzed disilylation was also observed with $Cl_3SiSiMe_3$, but $(MeO)_3SiSiMe_3$, $X_2MeSiSiMe_3$ (X = Cl, F), and symmetrically substituted disilanes such as $XMe_2SiSiMe_2X$ (X = F, Cl, Ph) did not react with **1a**.[4,5]

Enantioselective disilylation was effected with $PdCl_2$[(+)-BINAP][6] as a catalyst where BINAP stands for 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl.[7] The reaction conditions and

(1) Although optically active α-syn-substituted β-hydroxycarbonyl compounds have been successfully prepared by the asymmetric aldol reaction, enantioselective synthesis of α-unsubstituted and α-anti-substituted β-hydroxy ketones remains to be explored. See, for example: (a) Narasaka, K.; Miwa, T.; Hayashi, H.; Ohta, M. *Chem. Lett.* **1984**, 1399. (b) Braun, M. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 24, and references cited therein. (c) Gennari, C.; Bernardi, A.; Colombo, L.; Scolastico, C. *J. Am. Chem. Soc.* **1985**, *107*, 5812. (d) Masamune, S.; Sato, T.; Kim, B.-M.; Wollmann, T. A. *J. Am. Chem. Soc.* **1986**, *108*, 8279 and references cited therein.

(2) Fleming and co-workers have developed conjugate silylation of α,β-unsaturated carbonyl compounds with $(PhMe_2Si)_2CuLi$, which does not require any catalysts. (a) Fleming, I.; Goldhill, J. *J. Chem. Soc., Chem. Commun.* **1978**, 176. (b) Ager, D. J.; Fleming, I.; Patel, S. K. *J. Chem. Soc., Perkin Trans I* **1981**, 2520. (c) Fleming, I.; Newton, T. W. *J. Chem. Soc., Perkin Trans I* **1984**, 1805.

(3) Prepared by the chlorodephenylation of $Ph_3SiSiMe_3$ with dry HCl in the presence of $AlCl_3$ in benzene: Hengge, E.; Bauer, G.; Brandstaetter, E.; Kollmann, G. *Monatsh. Chem.* **1975**, *106*, 887. For the palladium–$Cl_2PhSiSiMe_3$ chemistry, see: Hayashi, T.; Yamamoto, A.; Iwata, T.; Ito, Y. *J. Chem. Soc., Chem. Commun.* **1987**, 398.

(4) The disilylation with $Cl_2PhSiSiMe_3$ also occurred on different types of α,β-unsaturated ketones such as 3-methyl-4-phenyl-3-buten-2-one and 2-cyclohexenone: Hayashi, T.; Matsumoto, Y.; Ito, Y. *Tetrahedron Lett.*, in press.

(5) 1,4-Addition of $FMe_2SiSiMe_2F$ to methyl vinyl ketone in the presence of a palladium catalyst has been reported: Tamao, K.; Okazaki, S.; Kumada, M. *J. Organomet. Chem.* **1978**, *146*, 87.

(6) Prepared by mixing $PdCl_2(MeCN)_2$ with 1 equiv of (+)-BINAP in benzene and recrystallized from acetone/hexane: red crystal, mp 255–60 °C dec; $[\alpha]^{20}_D$ +682° (*c* 0.50, $CHCl_3$).

(7) Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Taketomi, T.; Akutagawa, S.; Noyori, R. *J. Org. Chem.* **1986**, *51*, 629 and references cited therein.

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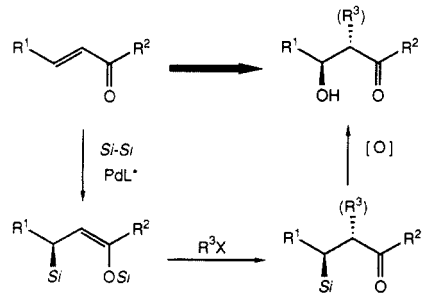
Table I. Asymmetric Disilylation of α,β-Unsaturated Ketones with $Cl_2PhSiSiMe_3$ Catalyzed by $PdCl_2$[(+)-BINAP][a]

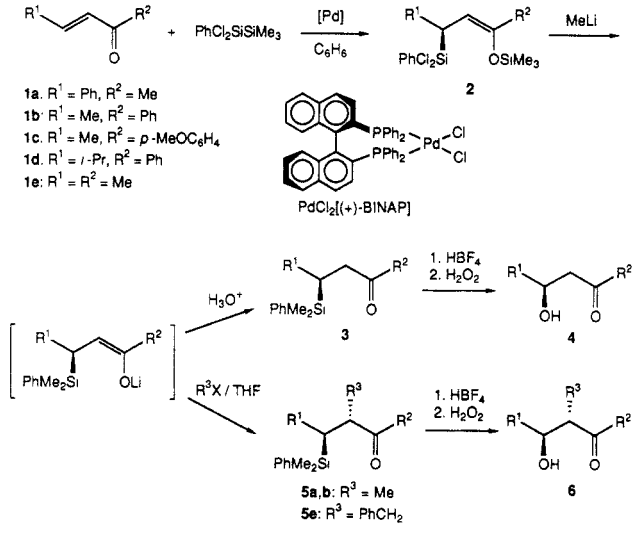
entry	substrate	reaction time (h)	isolation	silyl ketone yield[b] (%)	$[\alpha]_D^{20}$ ($CHCl_3$)[c] (deg)	% ee[d] (config)	hydroxy ketone yield (%)	$[\alpha]_D^{20}$ ($CHCl_3$)[e] (deg)
1	**1b**	2	1.MeLi/2.H_3O^+	**3b** (72)	+11.2	87 (*S*)[f]	**4b** (90)	+59.6[g]
2	**1b**	2	1.MeLi/2.MeI	**5b** (54)	+80.2	85 (2*S*,3*S*)[h]	**6b** (70)	+62.3
3	**1c**	0.5	1.MeLi/2.H_3O^+	**3c** (64)	+12.2	92	**4c** (81)	+56.7
4	**1d**	15	1.MeLi/2.H_3O^+	**3d** (42)	+11.7	86	**4d** (100)	+64.9
5	**1a**	17	1.MeLi/2.H_3O^+	**3a** (71)	+9.2	78 (*R*)[f]	**4a** (83)	+56.7[i]
6	**1a**	17	1.MeLi/2.MeI	**5a** (47)	−1.0	(78) (2*S*,3*R*)[h]	**6a** (45)	+47.9
7	**1e**	0.5	1.MeLi/2.H_3O^+	**3e** (65)	+21.0	(74) (*S*)[f]	**4e** (69)	+57.1[g]
8	**1e**	0.5	1.MeLi/2.$PhCH_2Br$	**5e** (42)	+120	74 (2*S*,3*S*)[h]	**6e** (66)	+68.2

[a] The reaction was carried out in refluxing benzene. Enone/$Cl_2PhSiSiMe_3$/catalyst = 1.0/(1.5–2.0)/0.005. [b] Isolated yield by preparative TLC on silica gel. [c] *c* 1.1–1.3. [d] Determined by HPLC analysis of **4b** (entry 1), **6b** (entry 2), **4c** (entry 3), **3d** (entry 4), **3a** (entry 5), and **5e** (entry 8) with a chiral column (Sumitomo Chemical Co., Sumipax OA-2000). The % ee values in parentheses (entries 6 and 7) were deduced from those in entries 5 and 8, respectively. [e] *c* 0.8–1.1 unless otherwise noted. [f] The configurations in entries 1, 5, and 7 were determined by the optical rotations of **4b** (ref 14), **4a** (ref 15), and **4e** (ref 16), respectively. [g] At 25 °C. [h] The anti selectivity is >20/1. The configurations of alkylated products were deduced from the anti stereochemistry and the absolute configurations at the 3-position of the protonated products. [i] At 23 °C.

Scheme I



Scheme II



results are summarized in Table I.[8] Disilylation of (*E*)-1-phenyl-2-buten-1-one (**1b**) with $Cl_2PhSiSiMe_3$ in the presence of the Pd-BINAP catalyst at 80 °C for 2 h followed by treatment with methyllithium and acidic hydrolysis gave a 72% yield of optically active 1-phenyl-3-(phenyldimethylsilyl)butan-1-one (**3b**) ($[\alpha]^{20}_D$ + 11.2° (*c* 1.3, $CHCl_3$)). The phenyldimethylsilyl group on β-silyl ketone **3b** was readily converted into a hydroxy group with retention of configuration by the method developed by Tamao[9] and Fleming.[10] Thus, fluorodephenylation (HBF_4·Et_2O/CH_2Cl_2) on the silyl group followed by oxidation of the silicon–carbon bond ($H_2O_2/KF/KHCO_3/MeOH/THF$) according to the procedure reported by Tamao[9] gave 90% yield of (*S*)-1-phenyl-3-hydroxybutan-1-one (**4b**)[11] ($[\alpha]^{25}_D$ +59.6° (*c* 0.8, $CHCl_3$)). The enantiomeric purity was determined to be 87% by HPLC analysis with a chiral stationary phase column (Sumipax OA-2000, hexane/dichloroethane/ethanol = 500/20/1) (entry 1). Highest enantioselectivity (92% ee) was obtained in the asymmetric disilylation of 4-methoxyphenyl ketone **1c** (entry 3). Other α,β-unsaturated ketones, (*E*)-4-phenyl-3-buten-2-one (**1a**) and (*E*)-3-penten-2-one (**1e**) also underwent the asymmetric disilylation catalyzed by Pd-(+)-BINAP at the same face of the carbon–carbon double bond as **1b** to give β-silyl ketones (*R*)-**3a** (78% ee) and (*S*)-**3c** (74% ee), respectively (entries 5 and 7). They were converted by the oxidation into β-hydroxy ketones (*R*)-**4a**[12] and (*S*)-**4e**,[13] respectively.

Methylation of the lithium enolate, generated by treatment of the disilylation product **2b** with methyllithium in ether, with methyl iodide in THF introduced methyl group anti selectively (>20/1) at the α-position to give a 54% yield of β-silyl ketone **5b** ($[\alpha]^{20}_D$ +80.2° (*c* 1.1, $CHCl_3$)), the oxidation of which gave anti β-hydroxy ketone **6b**[14] (entry 2). The enantiomeric purity determined by the HPLC analysis was 85%, essentially the same as that of protonation–oxidation product **4b**. The absolute configuration of **6b** is determined to be (2*S*,3*S*) since **6b** should have the same configuration at the 3-position as **4b**. Fleming has reported anti alkylation in a similar system[15] and has interpreted the anti stereochemistry by an electronic effect of the phenyldimethylsilyl group.[16] Similarly, the alkylation of lithium enolates resulting from **2a** and **2e** with methyl iodide or benzyl bromide proceeded anti selectively to give anti β-silyl ketones (2*S*,3*R*)-**5a**[15b] and (2*S*,3*S*)-**5c**, respectively. They were oxidized to anti β-hydroxy ketones **6** (entries 6 and 8).

(8) A typical procedure for the asymmetric disilylation is illustrated as follows. A mixture of 8.0 mg (0.01 mmol) of $PdCl_2$[(+)-BINAP] and 1.0 g (4.0 mmol) of $Cl_2PhSiSiMe_3$ in 2.0 mL of benzene was stirred at room temperature for 15 min under nitrogen. To the resulting clear yellow solution was added (*E*)-1-phenyl-2-buten-1-one (**1b**) (0.29 g, 2.0 mmol), and the mixture was heated to reflux for 2 h (monitoring by GLC). Ether (2.0 mL) was added, the mixture was cooled to −70 °C, and 6.2 mL (12 mmol) of 1.9 M methyllithium in ether was added. The reaction was stirred at −70 °C for 10 min and then quenched with diluted hydrochloric acid. Extraction with ether followed by preparative TLC on silica gel (hexane/ether = 5/1) gave 0.41 g (72% yield) of (*S*)-1-phenyl-3-(phenyldimethylsilyl)butan-1-one (**3b**) ($[\alpha]^{20}_D$ +11.2° (*c* 1.3, $CHCl_3$)).

(9) (a) Tamao, K.; Ishida, N.; Tanaka, T.; Kumada, M. *Organometallics* **1983**, *2*, 1694. (b) Tamao, K.; Ishida, N. *J. Organomet. Chem.* **1984**, *269*, C37. (c) Tamao, K.; Nakajo, E.; Ito, Y. *J. Org. Chem.* **1987**, *52*, 4412. (d) Tamao, K. In *Organosilicon and Bioorganosilicon Chemistry*; Sakurai, H., Ed.; Ellis Horwood: Chichester, 1985; p 231.

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(11) (*S*)-(+)-**4b**: $[\alpha]^{25}_D$ +50.5° (*c* 0.12, chloroform): Chenevert, R.; Thiboutot, S. *Can. J. Chem.* **1986**, *64*, 1599.

(12) (*R*)-(+)-**4b** (50% ee): $[\alpha]^{23}_D$ +37.8° (*c* 1, chloroform): Annuziata, R.; Cozzi, F.; Cinquini, M.; Colombo, L.; Gennari, C.; Poli, G.; Scolastico, C. *J. Chem. Soc., Perkin Trans. I* **1985**, 251.

(13) (*S*)-(+)-**4e**: $[\alpha]^{25}_D$ +55° (*c* 0.05, chloroform): Bolte, J.; Gourcy, J.-G.; Veschambre, H. *Tetrahedron Lett.* **1986**, *27*, 565.

(14) For (2*S**,3*S**)-**6b**, see: Curran, D. P. *J. Am. Chem. Soc.* **1983**, *105*, 5826.

(15) Alkylation of the enolates generated by the conjugate addition of a silylcuprate to α,β-unsaturated carbonyl compounds has been reported to give anti-alkylation products selectively: (a) Bernhard, W.; Fleming, I.; Waterson, D. *J. Chem. Soc., Chem. Commun.* **1984**, 28. (b) Bernhard, W.; Fleming, I. *J. Organomet. Chem.* **1984**, *271*, 281.

(16) Fleming, I.; Hill, J. H. M.; Parker, D.; Waterson, D. *J. Chem. Soc., Chem. Commun.* **1985**, 318.

Acknowledgment. We thank the Yamada Science Foundation for partial financial support of this work and Shin-etsu Chemical Industry Co., Ltd. for a gift of chlorosilanes. We are grateful to Dr. Kohei Tamao, Kyoto University, for valuable discussions.

Supplementary Material Available: ^1H NMR spectra and analytical data for silyl ketones and hydroxy ketones (1 page). Ordering information is given on any current masthead page.

Nickel and Iron EXAFS of Carbon Monoxide Dehydrogenase from *Clostridium thermoaceticum* Strain DSM

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Carbon monoxide dehydrogenase (CODH) from the acetogenic bacterium, *Clostridium thermoaceticum*, has been purified to apparent homogeneity.[1] The native enzyme which has an $\alpha_3\beta_3$ subunit stoichiometry was shown to contain 2Ni, 1-3Zn, 12Fe, and 14 acid labile sulfide per $\alpha\beta$ pair.[1-3] This enzyme catalyzes the reversible reduction of CO_2 to CO[4,5] and in addition catalyzes two isotope exchange reactions: (a) an exchange of labeled CoA with the CoA portion in unlabeled acetyl CoA[3] and (b) the exchange of labeled CO with the unlabeled acetyl CoA carbonyl group.[6] The enzyme is thought to catalyze the C–C bond formation step in the biosynthesis of acetate from C_1 precursors. When CO exchanges with the acetyl CoA carbonyl group in the presence of CODH, the chirality of the methyl group is retained.[20]

The EPR of carbon monoxide dehydrogenase in the presence of CO is due to a nickel–iron–carbon complex, according to hyperfine broadening when ^{61}Ni, ^{57}Fe, or ^{13}CO are present.[3,7] We here characterize the average ligand environments of nickel and iron in the Ni-EPR silent, CO-free form of this biological carbonylation catalyst.

EXAFS data have been collected on both the nickel and iron sites of CODH from *Clostridium thermoaceticum* strain DSM 521.[8,9] The CO dehydrogenase was purified under argon, in a state containing EPR silent nickel as previously described.[10,11]

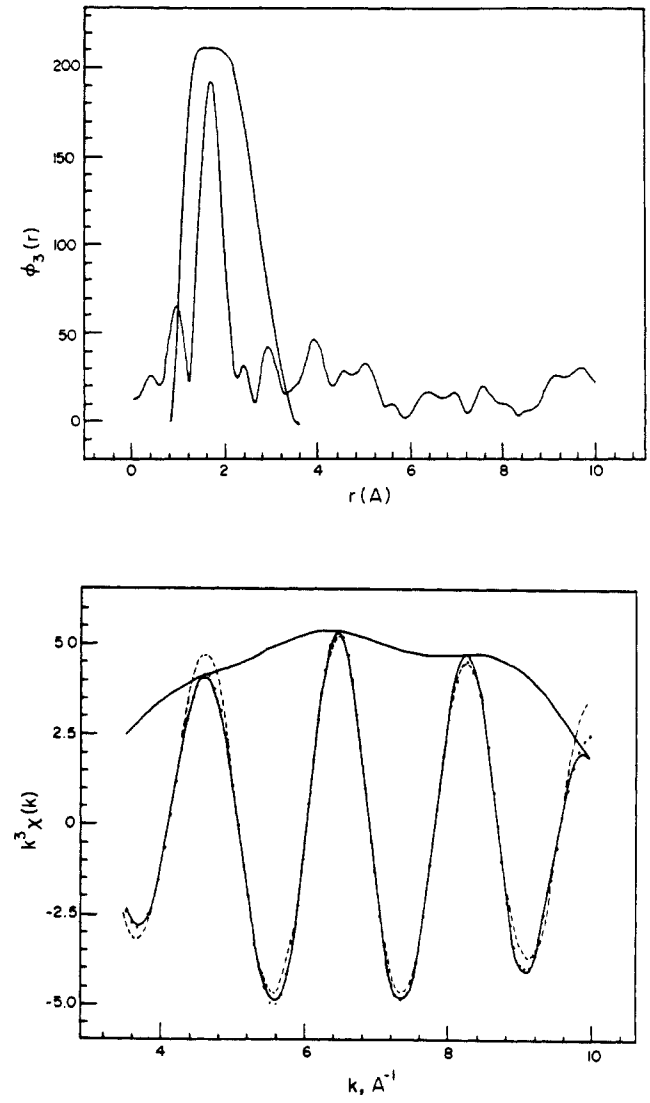

Figure 1. Fourier transform (a) and filtered data (b) of the $k^3\chi(k)$ vs k EXAFS spectrum from the nickel edge of CO dehydrogenase. The upper curve in (a) is the window function used in Fourier filtering. The dashed line in (b) is the one term sulfur fit to the Fourier filtered data (solid line) while the dotted line is the fit of one sulfur plus iron. The amplitude function for the filtered data is also shown.

Table I. Summary of CODH EXAFS Results

compound	bond	bond distance, Å	coord no.	Debye-Waller factor, Å
$Ni_2(TTH)_2$	Ni–S	2.16 ± 0.03	4	0.034 ± 0.005
CO dehydrogenase	Ni–S	2.16 ± 0.03	3.8	0.063 ± 0.004
$Ni_2(TTH)_2$	Ni–Ni	2.85 ± 0.04	1	0.0004 ± 0.003
CO dehydrogenase	Ni–Fe	3.25 ± 0.05	0.42	0.0005 ± 0.005
$(NEt_4)_3Fe_4S_4(SPh)_4$	Fe–S	2.27 ± 0.03	4	0.049 ± 0.004
CO dehydrogenase	Fe–S	2.27 ± 0.03	3.7	0.020 ± 0.003
$(NEt_4)_2Fe_4S_4(SPH)_4$	Fe–Fe	2.74 ± 0.03	3	0.059 ± 0.002
CO dehydrogenase	Fe–Fe	2.75 ± 0.03	2.6	0.030 ± 0.005

Table II. Summary of χ^2 for Different Fitting Models in the Analysis of Ni EXAFS of CODH

model	χ^2	model	χ^2
one term Ni–S	9.96	one term Ni–S plus Fe	2.82
two term Ni–S	6.63	two term Ni–S plus Fe	1.86

Metal content was determined by atomic absorption analysis by using a Perkin Elmer Model 2380 atomic absorption spectrophotometer with a programmable HGA-400 graphite furnace. The purified CODH (0.16 mM) containing 1 mM Ni and 5 mM Fe had a specific activity of 310 (μmol CO oxidized/min)/mg enzyme. Data analysis was performed according to the method

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⊥ Current address: Los Alamos National Laboratory, Los Alamos, NM.

(1) Ragsdale, S. W.; Clark, J. E.; Ljungdahl, L. G.; Lundie, L. L.; Drake, H. L. *J. Biol. Chem.* **1983**, *258*, 2364–2369.
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(7) Ragsdale, S. W.; Ljungdahl, L. G.; DerVartanian, D. V. *Biochem. Biophys. Res. Commun.* **1983**, *115*, 658–665.
(8) The EXAFS K-edge for both metals was measured by using the fluorescence technique at the Cornell High Energy Synchrotron Source on the C-1 beam line. Cobalt and manganese filters, for the nickel and iron edges, respectively, were used in conjunction with a Lytle cryostat and detector. The samples were kept at ca. 220 K during data acquisition. Batterman, B. W. In *EXAFS Spectroscopy: Techniques and Applications*; Teo, B. K.; Joy, D. C., Eds.; Plenum Press: New York; 1981; pp 197–204.
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(11) All buffers contained 5 mM dithiothreitol and 1 mM dithionite. Carbon monoxide dehydrogenase activity was determined by reduction of the artificial electron acceptor, methyl viologen, monitored spectrophotometrically at 600 nm. The exchange activity is inhibited by dithionite and thus was not measured on these samples directly.

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