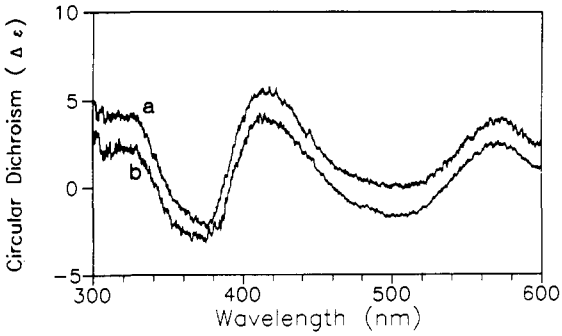

Figure 1. Circular dichroic spectra of 33 μM (a) *C. pasteurianum* Fd and (b) synthetic Fd in 0.1 M NaCl and 50 mM Tris, pH 8. Spectra are offset 0.1 deg/(M cm).

The 55 amino acid sequence, which was confirmed immediately after synthesis, was that of the *Clostridium pasteurianum* Fd:[5]

1 11 21 31
AYKIADSCVS CGACASECPV NAISQGDSIF VIDADTCIDC

41 51
GNCANVCPVG APVQE.

The native apoprotein, prepared as previously described,[6] and synthetic apoprotein eluted to identical positions on high-resolution PAGE gels. In a modification of a previously reported protocol to reconstitute the iron–sulfur clusters,[6] the synthetic apoprotein was incubated anaerobically in a 20-fold molar excess of DTT and 50-fold molar excess of both $FeCl_3$ and Na_2S at 25 °C for 3 h. All synthetic holoprotein used throughout this study was purified by salt gradient chromatography.

The synthetic Fd differs significantly from previous $[4Fe\text{-}4S]^{2-/3-}$ analogues which contain 12 or fewer amino acids.[7] The major differences are that the apoprotein ligates two clusters and that one of the four cysteine residues which chelates each cluster is from a separate and distant segment of the polypeptide chain. Lastly, proper folding of the synthetic Fd may be critical in cluster formation since the synthetic peptide is synthesized from the C → N terminus, in contrast to the native protein which is synthesized in vivo from the N → C terminus.

The visible spectra of the oxidized native and synthetic ferredoxins were virtually identical (figure not shown). Similarly, the circular dichroic spectra of the oxidized native and synthetic holoprotein were identical as shown in Figure 1, indicating that the synthetic holoprotein is folded properly. The EPR spectra of reduced synthetic ferredoxin provides additional evidence for two spin-coupled [4Fe-4S] clusters (figure not shown). The principal *g* values determined for reduced synthetic Fd (1.89, 1.94, 2.05) are in excellent agreement with the *g* values (1.91, 1.94, 2.06) previously determined for reduced native *C. pasteurianum* Fd.[8] The partial reduction of the synthetic ferredoxin by *C. pasteurianum* hydrogenase at pH 8 and its full reduction by dithionite (see Figure 2) demonstrate its electron-transferring competence.

The reduction potential of both the synthetic and native Fd was −400 mV vs NHE at pH 8. Both reduction potentials were pH independent as determined directly at an edge pyrolytic graphite electrode[9] using square-wave voltammetry as previously described.[10] The reduction potential for previous analogue clusters, which are isoelectronic with Fd's, are characteristically 100 mV more negative than native Fd clusters. The difference between the reduction potential of previous analogues and that of native clusters has been attributed to the protein matrix of native Fd's[11] and is further confirmed by this study.

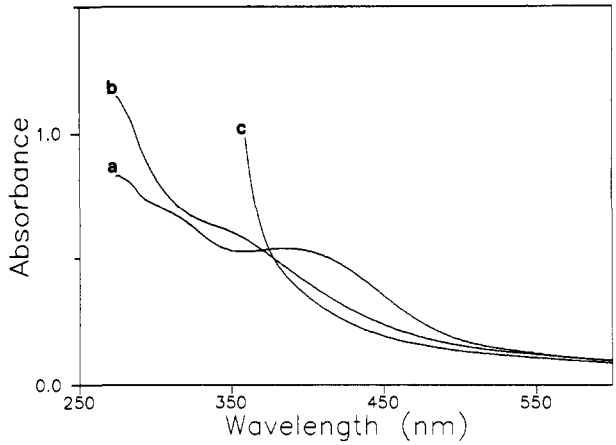

Figure 2. UV–visible spectra of 20 μM synthetic Fd in 0.5 M NaCl and 50 mM Tris, pH 8, where the Fd is (a) fully oxidized, (b) partially reduced by hydrogenase, and (c) fully reduced by dithionite.

We are presently using the above methods to examine ferredoxin variants, including a tyrosine-2 → histidine-2 variant which should result in a ferredoxin with a pH-dependent reduction potential as previously suggested.[10] While site-directed mutagenesis is a powerful tool for investigating the influence of the polypeptide on functionality, in this communication we have demonstrated for the first time that totally synthetic methods can be used successfully and with comparable ease to study a naturally occurring and biologically important metalloprotein.

Acknowledgment. Research at UW—Milwaukee was supported by NIH Grant GM41927 to B.A.F. We thank Dr. M. J. Benecky, Mount Sinai Hospital, Milwaukee, WI, for his assistance in obtaining the CD spectra.

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Dimolybdenum and Ditungsten Derivatives of the Trisilanol $[(c\text{-}C_6H_{11})_7Si_7O_9(OH)_3]$: $[(c\text{-}C_6H_{11})_7Si_7O_{12}]_2Mo_2$ (M≡M) and $[(c\text{-}C_6H_{11})_7Si_7O_{12}]_2W_2(\mu\text{-}H)(O\text{-}t\text{-}Bu)$

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The trisilanol $(c\text{-}C_6H_{11})_7Si_7O_9(OH)_3$, represented by I, is a potential source of a −3 siloxy ligand with interesting steric and electronic requirements.[2] Metal ions bound to I or a −1, −2, or

(1) (a) University of California, Irvine. (b) Indiana University.
(2) (a) Feher, F. J.; Newman, D. A.; Walzer, J. F. *J. Am. Chem. Soc.* **1989**, *111*, 1741. (b) Feher, F. J.; Newman, D. A. *J. Am. Chem. Soc.* **1990**, *112*, 1931. (c) Feher, F. J.; Budzichowski, T. A.; Weller, K. J. *J. Am. Chem. Soc.* **1989**, *111*, 7288. (d) Feher, F. J.; Weller, K. J. *Organometallics* **1990**, *9*, 2638. (e) Feher, F. J. *J. Am. Chem. Soc.* **1986**, *108*, 3850. (f) Feher, F. J.; Gonzales, S. L.; Ziller, J. W. *Inorg. Chem.* **1988**, *27*, 3440. (g) Feher, F. J.; Walzer, J. F. *Inorg. Chem.* **1990**, *29*, 1604.

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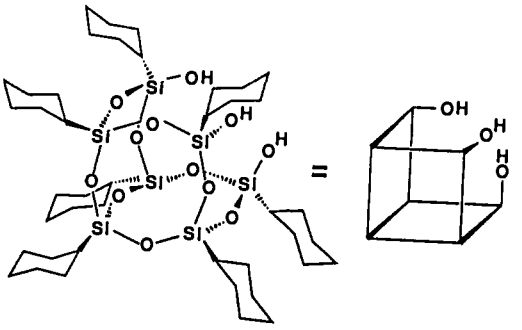
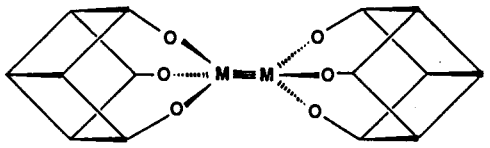
−3 siloxide derivative (formed by successive hydroxyl group deprotonations) may serve as models for metal ions covalently linked to silica supports. The tripodal, cagelike nature of I led us to investigate the possibility of obtaining "dumbbell" dinuclear compounds, of type II, whose electronic structure and reactivity should differ significantly from those of the now "normal" ethane-like $X_3M{\equiv}MX_3$ compounds,[3] or bridged compounds such as M_2(pinacolate)$_3$.[4] We describe here our initial attempts to prepare a "dumbbell" complex of type II supported by the −3 anion of trisilanol I.



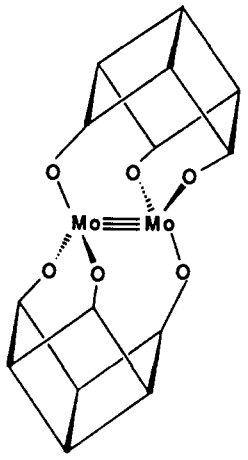
I



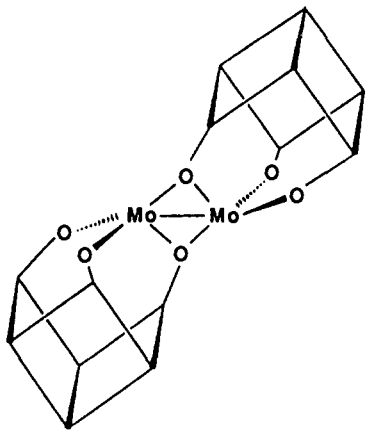
II

The reaction between Mo_2(O-*t*-Bu)$_6$ and I (2 equiv) in benzene or toluene at room temperature leads to a rapid replacement of all six alkoxide ligands and the formation of orange crystals in 80% yield by crystallization from toluene at −15 °C.[5] This new compound possesses the proper stoichiometry for the expected product, but ^{13}C and ^{29}Si NMR spectra are far too complicated for a D_{3d} symmetric dimer. At low temperature, both the ^{29}Si NMR spectrum (−15 °C) and the methine region of the ^{13}C NMR spectrum (−30 °C) exhibit five resonances with relative integrated intensities of 2:2:1:1:1, indicating that the dimer possesses two equivalent Si_7O_{12} ligand frameworks which are bisected by a molecular plane of symmetry. Three structures that are consistent with the low-temperature ^{29}Si and ^{13}C NMR data are represented by III, IV, and V. Structure III retains a $\sigma^2\pi^4$ electronic configuration for the M≡M bond, while oxygen-bridged structures IV and V maximize M—O bonding at the expense of M—M bonding.[6]

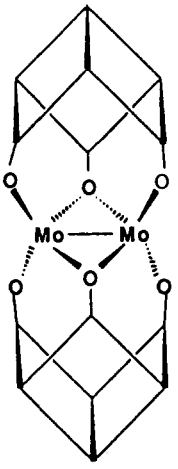
A single-crystal X-ray diffraction study established the ground-state structure as that depicted by III. The unit cell contains two molecules of III, each at a crystallographic center



III



IV



V

of symmetry, and six molecules of benzene, with Mo–Mo = 2.215 (2) Å (av), Mo–O = 1.90 (1) Å (av), and Mo–Mo–O = 99–105°.[7]

Upon warming, the low-temperature ^{29}Si and ^{13}C NMR spectra of III gradually coalesce toward high-temperature limiting spectra with three resonances with relative integrated intensities of 3:3:1. Two ^{29}Si resonances with relative intensities of 2:1 broaden and coalesce between 23 and 45 °C, while at the high-temperature limit of the solvent (toluene-d_8) two other resonances with relative intensities of 2:1 are broadened into the base line. The ^{29}Si resonance for the apical Si atom is unaffected by these changes and remains sharp. The methine region of the ^{13}C NMR spectrum exhibits similar behavior, but three resonances with relative integrated intensities of 3:3:1 are clearly observable at 125 °C. On the basis of these data, we propose that III is in a dynamic equilibrium with the dumbbell isomer II and that their interconversion most likely involves an oxygen-bridged species with a type IV structure.

The corresponding reaction between W_2(O-*t*-Bu)$_6$ and I (2 equiv) in toluene gives a brown solution, which affords a yellow microcrystalline material upon cooling to −15 °C. Room-temperature ^{13}C and ^{29}Si NMR spectra reveal 14 different (three partially overlapping) ^{29}Si and methine ^{13}C signals for two symmetry-inequivalent Si_7O_{12} frameworks.[8] Resonances attributable

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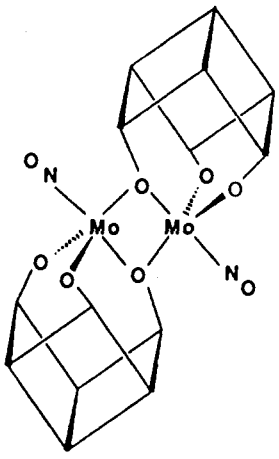
(5) All reactions were carried out under an N_2 atmosphere and with dried and deoxygenated solvents. The following elemental analyses have been obtained. For III, calcd for $C_{84}H_{154}Mo_2O_{24}Si_{14}$: C, 47.30; H, 7.28. Found: C, 47.22; H, 7.19. For VI, calcd for $C_{84}H_{154}Mo_2N_2O_{26}Si_{14}$: C, 46.00; H, 7.08; N, 1.29. Found: C, 45.20; H, 6.80; N, 1.29. For $[(c\text{-}C_6H_{11})_7Si_7O_{12}]_2(\mu\text{-}H)$(O-*t*-Bu), calcd for $C_{88}H_{164}O_{25}Si_{14}W_2$: C, 44.35; H, 6.94. Found: C, 42.93; H, 6.54. Selected NMR data for III: $^{13}C\{^1H\}$ NMR (126 MHz, toluene-d_8) (15 °C) δ 25.16, 24.32, 24.26, 23.67, 23.61 (1:2:2:1:1 for CH) (15 °C) δ 25.16, 24.32, 24.26, 23.67, 23.61 (1:2:2:1:1 for CH), (125 °C) δ 24.6 ($W_{1/2}$ = 25 Hz), 24.1 ($W_{1/2}$ = 12 Hz), 23.7 (3:3:1 for CH); $^{29}Si\{^1H\}$ NMR (99 MHz, −15 °C, toluene-d_8) δ −51.0, −58.1, −62.2, −62.8, −63.5.

(6) (a) The molecular structures of $[(c\text{-}C_6H_{11})_7Si_7O_{12}]_2M_2$ (M = Ti, V)[2f,g] and $[(c\text{-}C_6H_{11})_7Si_7O_{12}]_2Al_2$[2c] are based on structure V. The bond connectivity patterns for $[(c\text{-}C_6H_{11})_7Si_7O_{12}]_2(VO)_2$[6b] and $[(c\text{-}C_6H_{11})_7Si_7O_{12}]_2B_2$[6b] are based on structure III. (b) Feher, F. J.; Budzichowski, T. A., manuscripts in preparation.

(7) Crystal data at −154 °C: a = 16.201 (3) Å, b = 25.415 (5) Å, c = 16.078 (3) Å, α = 102.78 (1)°, β = 112.84 (1)°, γ = 90.79 (1)°, Z = 2, d_{calcd} = 1.322 g cm^{-2}, and space group $P\bar{1}$; 17030 reflections were collected by using Mo Kα, 6° ≤ 2θ ≤ 45°, and 13583 reflections having $F > 3\sigma(F)$ were used in the refinement. The molecules have a crystallography-imposed center of symmetry. Residues are $R(F)$ = 0.070 and $R_w(F)$ = 0.078.

to one *tert*-butoxide ligand are also observed, as well as a resonance at δ 14.33 in the ^{1}H NMR spectrum, which shows coupling to two inequivalent ^{183}W nuclei (^{183}W, $I = {}^1/_2$, 14.5% natural abundance). We formulate this new ditungsten compound as $[(c\text{-}C_6H_{11})_7Si_7O_{12}]_2W_2(\mu\text{-}H)(O\text{-}t\text{-}Bu)$, an analogue of $[W_2(\mu\text{-}H)(O\text{-}i\text{-}Pr)_7]_2$.[9]

The reaction between III and NO (2 equiv) gives a dinitrosyl complex that possesses (by ^{29}Si and ^{13}C NMR) two equivalent Si_7O_{12} frameworks that are bisected by a molecular plane of symmetry.[10] By analogy to the known reaction chemistry of $Mo_2(OR)_6$ compounds with NO,[11] we formulate this compound as $[(c\text{-}C_6H_{11})_7Si_7O_{12}]_2Mo_2(NO)_2$, of structural type VI, which is formed by cleavage of the M≡M bond. Quite interestingly, ν(NO) for VI occurs at 1670 cm^{-1} in the IR spectrum. This is approximately 30 cm^{-1} higher than ν(NO) observed for analogous alkoxide complexes, indicating that the trisiloxide ligand is a poorer electron donor than three independent alkoxide ligands.[12]



VI

In conclusion, the use of I as a ligand for dinuclear Mo and W complexes has allowed two aspects of the chemistry of the $(M{\equiv}M)^{6+}$ unit to be seen for the first time. First, the dynamic NMR data for III suggest that the energy required to transform an ethane-like $X_3M{\equiv}MX_3$ compound to a bridged species may be between 11 and 14 kcal/mol. Second, the facile oxidative addition of an O—H bond to a $(W{\equiv}W)^{6+}$ center occurs in the absence of a Lewis base.[13] Both of these observations may reflect a bridge-stabilizing ability of the $[(c\text{-}C_6H_{11})_7Si_7O_{12}]^{3-}$ ligand, but further speculation is not warranted at this time. Further studies of the reactivity of these interesting trisiloxy dinuclear compounds are planned.

Acknowledgment. We thank the National Science Foundation for support. T.A.B. thanks the John and Fannie Hertz Foundation for a predoctoral fellowship.

(8) Selected NMR data for $[(c\text{-}C_6H_{11})_7Si_7O_{12}]_2W_2(\mu\text{-}H)(O\text{-}t\text{-}Bu)$: ^{1}H NMR (500 MHz, C_6D_6, 25 °C) δ 14.33 [1 H, $J_{W\text{-}H}$ = 88 Hz (14%), 120 Hz (16%)]; ^{13}C{^{1}H} NMR *(126 MHz, toluene-d_8, 22 °C) δ 26.3, 25.8, 25.6, 24.6, 24.4, 24.3, 24.0, 23.9, 23.8, 23.7, 23.6, 23.5 (1:1:1:1:1:3:1:1:1:1:1:1: for CH), 92.7 (OCMe$_3$), 30.8 (C*Me*$_3$); ^{29}Si{^{1}H} NMR (99 MHz, C_6D_6, 22 °C): δ −60.0, −61.4, −62.0, −62.9, −63.8, −67.3, −67.4, −67.5, −67.6, −68.1, −68.4, −69.2 (1:1:1:1:1:1:1:1:3:1:1:1).

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(10) Selected NMR data for VI: ^{13}C{^{1}H} NMR (126 MHz, toluene-d_8, 22 °C) δ 24.6, 24.3, 24.2, 24.0, 23.7 (1:1:2:2:1 for CH); ^{29}Si{^{1}H} NMR (99 MHz, C_6H_6, 22 °C): δ −55.4, −61.4, −63.1, −66.3, −66.8 (2:1:1:2:1).

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(12) (a) The electron-withdrawing capabilities of a Si_8O_{12} silasesquioxane framework are comparable to those of a trifluoromethyl (i.e., CF_3) group.[12b] (b) Feher, F. J.; Budzichowsi, T. A. *J. Organomet. Chem.* **1989**, *379*, 33.

(13) This is in contrast to the oxidative addition of *i*-PrOH to $W_2(O\text{-}i\text{-}Pr)_6$ to yield $[W_2(H)(O\text{-}i\text{-}Pr)_7]_2$. See ref 9b.

Supplementary Material Available: Listing of atomic coordinates and isotropic thermal parameters, bond angles, and bond distances for $[(c\text{-}C_6H_{11})_6Si_7O_{12}]_2Mo_2$ (M≡M) (14 pages). Ordering information is given on any current masthead page.

Requirements for Houben–Hoesch and Gattermann Reactions. Involvement of Diprotonated Cyanides in the Reactions with Benzene

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Friedel–Crafts acylation with nitriles and HCl (and/or Lewis acids) is called the Houben–Hoesch reaction (eq 1).[1] The

$$\mathrm{ArH} + \mathrm{RC{\equiv}N} \xrightarrow{\mathrm{H^+}} \mathrm{ArC(=NH)R} \xrightarrow{\mathrm{H_2O}} \mathrm{ArC(=O)R} \qquad (1)$$

Gattermann reaction is a special case in which the nitrile is hydrogen cyanide (R = H).[2] These reactions are generally useful only with phenols, phenolic ethers, and some heterocyclic compounds. The reaction mechanism seems to be complex and is not completely settled.[3] The first stage consists of protonation of a nitrile to a nitrilium ion (**1**) or nitrile–Lewis acid complex. Generally these are regarded as being the electrophilic species attacking the phenols or other activated aromatics.[3] The protonated form (**2**) of the chloro imine is also a candidate electrophile.

$$\underset{\mathbf{1}}{\mathrm{RC{\equiv}N^+H} \leftrightarrow \mathrm{RC^+{=}NH}} \qquad \underset{\mathbf{2}}{\mathrm{RC(Cl){=}N^+H_2}}$$

The reactions of nitriles with benzene itself have been studied less thoroughly. The original procedure of Gattermann was improved by Hinkel et al:[4] the reaction of hydrogen cyanide with benzene was attained in the presence of an excess amount of HCl and $AlCl_3$ at refluxing temperature. The reaction in the presence of $Zn(CN)_2$–HCl–$AlCl_3$ was examined by Olah et al.[5] In these reactions the monoprotonated species or other stable cationic species such as **1** and **2** cannot be the attacking electrophile toward benzene. In this paper, a simple and generalized procedure and requirements for the Gattermann and Houben–Hoesch reactions are described.

Sodium cyanide and benzene did not react in the presence of 23% trifluoromethanesulfonic acid (TFSA)–77% trifluoroacetic acid (TFA) (H_0 = −10.6, 450 equiv with respect to the cyanide).[6] Heightening of the acidity was required for the reaction to occur. In TFSA (H_0 = −13.7), the reaction proceeded within 30 min and the yield reached 44% (determined after aqueous acid hydrolysis to benzaldehyde). Addition of 1% SbF_5 to TFSA (H_0 = −16.8) speeded up the reaction. In the presence of 5% SbF_5, the reaction was instantaneous and the yield was excellent (Table I).

In order to eliminate the complexity arising from the use of sodium cyanide, trimethylsilyl cyanide was chosen as the cyanide.

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(6) The acidity function H_0 of TFA–TFSA was determined by a modification of the procedure previously described using a set of nitroanilines and nitrobenzenes as Hammett's indicators with UV detection. Experimental details will be reported elsewhere.

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