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Rearrangement of Symmetrical Dicubane Clusters into Topological Analogues of the P Cluster of Nitrogenase: Nature's Choice?

Yugen Zhang, Jing-Lin Zuo, Hong-Cai Zhou, and R. H. Holm*

Department of Chemistry and Chemical Biology, Harvard University, Cambridge, Massachusetts 02138

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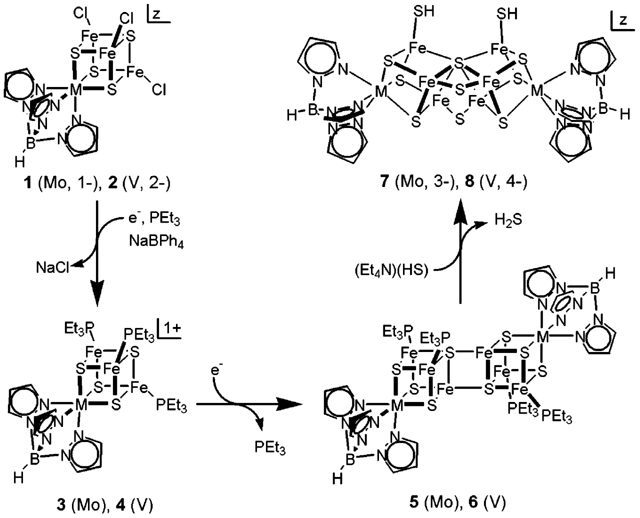
The electron-transfer P cluster (Fe_8S_7) and the catalytic cofactor cluster (MFe_7S_9; M = Mo, V) of the MoFe protein of nitrogenase[1−3] have been assembled only by biosynthesis. Noting spectroscopic evidence that the protein as normally isolated contains substantially reduced clusters (majority of Fe(II)),[4−6] we are investigating the reactivity of reduced Fe−S[7] and M−Fe−S[8−12] clusters, often with tertiary phosphine ligation as a device to stabilize low oxidation states. We describe here the use of reduced clusters in the synthesis of the initial molecular topological analogues of the P cluster in the crystallographically defined P^N state.[13,14] The synthetic procedure, outlined in Scheme 1, includes both molybdenum- and vanadium-containing clusters; heterometal M and charge *z* are specified. To ensure regioselective reactions and avoidance of potentially isomeric final products, tris(pyrazolyl)hydroborate(1−) (Tp) at the heterometal site is a protecting group and in single cubanes a stipulator of trigonal symmetry. All structures have been proven by X-ray structure determinations.[11,12,15]

Scheme 1



Treatment of $[(Tp)MoFe_3S_4Cl_3]^{1-}$ [11] (**1**, $[MoFe_3S_4]^{3+}$) with 5 equiv each of PEt_3 and $NaBPh_4$ for 12 h results in reductive substitution and formation of $[(Tp)MoFe_3S_4(PEt_3)_3]^{1+}$ (**3**, $[MoFe_3S_4]^{2+}$), isolated as the BPh_4^- salt[15] (80%). Reduction of **3** with 1.3 equiv of $(Bu_4N)(BH_4)$ for 16 h gives the neutral edge-bridged double cubane $[(Tp)_2Mo_2Fe_6S_8(PEt_3)_4]$ (**5**, 70%). Its structure[15] resembles that of $[(Cl_4cat)_2(Et_3P)_2Mo_2Fe_6S_8(PEt_3)_4]$[8,9] (**9**) but is more reduced, being the first example of an isolated $[MoFe_3S_4]^{1+}$ cluster. Reaction of a slurry of **5** with 4 equiv of $(Et_4N)(HS)$ causes the solid to dissolve immediately with formation of $[(Tp)_2Mo_2Fe_6S_9(SH)_2]^{3-}$ (**7**). Slow diffusion of ether into the reaction mixture leads to separation of $(Et_4N)_3[\mathbf{7}]\cdot 9MeCN$ (73%). The reaction sequence **2** → **4** → **6** of vanadium-containing clusters has been demonstrated recently.[12] The double cubane $[(Tp)_2V_2Fe_6S_8(PEt_3)_4]$ (**6**) is isostructural with **5** and is also strongly reduced ($2[VFe_3S_4]^{1+}$). It reacts similarly with 4 equiv of $(Et_4N)(HS)$ to form $[(Tp)_2V_2Fe_6S_9(SH)_2]^{4-}$ [**8**], isolated as $(Et_4N)_4[\mathbf{8}]\cdot 6MeCN$ (70%).

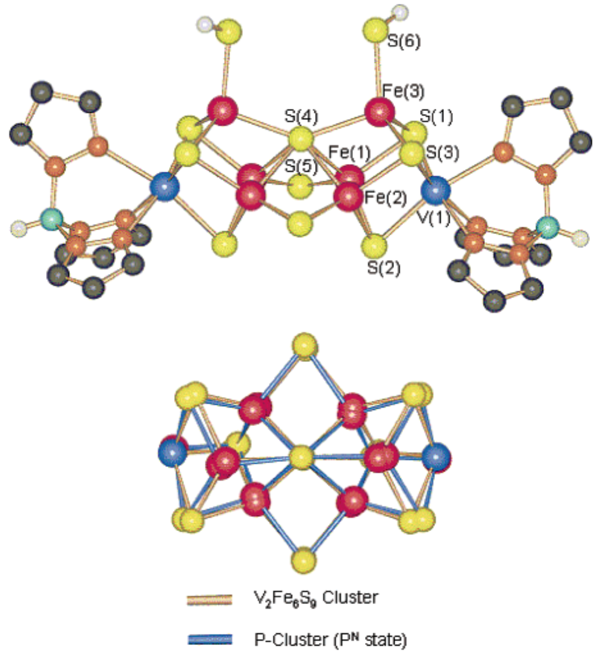


Figure 1. (Upper) Structure of cluster **8** in which a crystallographic C_2 axis passes through μ_6-S(4) and the center of square Fe(1,1′)(2,2′) and relates primed and unprimed atoms. (Lower) Best-fit superposition of the $V_2Fe_6S_9$ core of **8** and the $Fe_8S_7(\mu_2\text{-}S_{Cys})_2$ core of the *Klebsiella pneumoniae* P^N cluster,[14] which in its entirety is $Fe_8S_7(\mu_2\text{-}S_{Cys})_2(S_{Cys})_4$. The bridging cysteinate atoms are simulated by S(5,5′) and two terminal cysteinates by S(6,6′) of **8**.

Clusters **7** and **8** are isostructural and nearly isometric.[15] The structure of vanadium cluster **8**, which has crystallographically imposed C_2 symmetry, is set out in Figure 1. The core exhibits the bridging pattern $[V_2Fe_6(\mu_2\text{-}S)_2(\mu_3\text{-}S)_6(\mu_6\text{-}S)]$, which reduces to two distorted cuboidal fragments $VFe_3(\mu_3\text{-}S)_3$ sharing the common bridge atom μ_6-S(4) and externally bridged by μ_2-S(5,5′). Each iron atom has distorted tetrahedral stereochemistry, with terminal hydrosulfide ligands at Fe(3,3′) and trigonally distorted octahedral coordination at the vanadium atoms with parameters typical of Tp binding.[11,12] The most conspicuous individual feature of **7** and **8** is the infrequently encountered μ_6-S atom, at which there are nine independent Fe−S−Fe angles. Three of these are notably obtuse, Fe(3)−S(4)−Fe(1′,2′,3′) = 136−141°, and convey the open nature

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* To whom correspondence should be addressed. E-mail: holm@chemistry.harvard.edu.

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of the structure along the Fe(3,3′)S(4) edge at which the angle is 140.8(1)°. In **7** the range is similar (135−141°), and the edge angle is 141.0(1)°. Other parameters in both structures occur in the intervals normally found for cubane-type Fe_4S_4 and MFe_3S_4 structures.[7,11,12,16] However, the most important result is that the core shapes of **7** and **8** are clearly similar to that of the P^N cluster as determined in two different enzymes.[13,14] Shown in Figure 1 is a best-fit superposition of the 17 atoms of the $V_2Fe_6S_9$ core of **8** and the $Fe_8S_7(\mu_2\text{-}S_{Cys})_2$ core of the P^N cluster, described by a weighted rms deviation of 0.33 Å. For the $Mo_2Fe_6S_9$ core of **7** and the P^N cluster, the corresponding value is 0.38 Å. Notwithstanding the less precise protein data, obtained at resolutions of 2.0 and 1.6 Å for the proteins from *Azotobacter vinelandii*[13] and *Klebsiella pneumoniae*,[14] respectively, we conclude that *the synthetic and native cluster cores approach congruency*. Other than the presence of six-coordinate heterometals, a number of apparent differences contribute to the structural deviations. Among these is a much larger edge-bridge angle (158° in the P cluster) and its attendant effect on atom positions. Of lesser influence is the presence of two $Fe-(\mu_2\text{-}S)-Fe$ bridges at the periphery of **7** and **8** (74.6−77.6°) instead of two $Fe-(\mu_2\text{-}S_{Cys})-Fe$ bridges (73°, 76°) as in the protein.

The core structure of **7** has been observed before as sulfide-bridged fragments in the high-nuclearity clusters $[(Cl_4cat)_6(Et_3P)_6Mo_6Fe_{20}S_{30}]^{8-}$ [17] and $[(Cl_4cat)_2(Et_3P)_4Mo_4Fe_{12}S_{20}K_3(DMF)]^{5-}$.[10] These clusters were prepared by the reaction of edge-bridged **9** with $(Et_4N)(SH)$ under specific reaction and workup conditions. Their formation also illustrates the value of reduced double cubanes as precursors to new structures. However, because of the complicated and tight sulfide-bridged cluster structures, properties intrinsic to the fragments of interest, such as oxidation level, charge distribution, and redox states, cannot be deconvoluted from those of the whole clusters. *Molecular* clusters **7** and **8** provide that opportunity. Oxidation states of metal atoms in heterometal clusters are often difficult to assess. Terminal Fe−SR bond lengths increase as the oxidation level of Fe_4S_4 clusters decreases. The Fe−SH distances in **7** (mean 2.291 Å) and **8** (2.327(3) Å, when compared with the values in $[Fe_4S_4(SH)_4]^{2-}$ (mean 2.262 Å)[18] and $[Fe_4S_4(SH)_4]^{3-}$ (2.317(2) Å),[16] are consistent with substantial Fe(II) character at these sites. The Mössbauer spectrum[15] of **8** at 4.2 K consists of two overlapping doublets fitted in an intensity ratio of 3:1. The majority/minority doublet has $\delta = 0.52/0.59$ mm/s (mean 0.54 mm/s) and $\Delta E_Q = 1.23/0.65$ mm/s. The spectrum of **7** is a broadened quadrupole doublet with $\delta = 0.55$ mm/s and $\Delta E_Q = 0.62$ mm/s. While comparison with isomer shifts of other reduced clusters[7,9−12] is not precise because of differences in structure and terminal ligands, we do note the values for $[Fe_4S_4(SEt)_4]^{3-}$ (0.59 mm/s), double cubane $\{(Tp)_2Mo_2Fe_6S_8(SPh)_4\}^{4-}$ (0.64 mm/s), and the P^N cluster (∼0.64 mm/s)[4] and conclude that **7** and **8** are substantially reduced clusters. In keeping with its reduced nature, **7** shows three quasireversible oxidations at $E_{1/2} = -1.09$, -0.71, and -0.43 V; redox steps of **8** appear to be irreversible. Electronic structural properties of these clusters will be described subsequently.

The apparent means of formation of **7** and **8** can be summarized by the reaction $[(Tp)_2M_2Fe_6S_8(PEt_3)_4] + 4HS^- \rightarrow [(Tp)_2M_2Fe_6S_9(SH)_2]^{4-} + H_2S + 4PEt_3$. In the case of **7** (for which $E_{1/2}$ (4−/3−) < -1.1 V), the cluster is isolated in a one-electron oxidized form; the oxidant is currently unknown. While clusters **5** and **6** have nonphysiological Tp ligands and a core structure yet to be found in a protein-bound condition, this reaction does raise a provocative question in biosynthesis. Can two closely juxtaposed Fe_4S_4 clusters be induced to coalesce into the P^N topology by reaction with hydrosulfide? Further, is the P cluster a precursor to the all-iron nitrogenase cofactor, and are one Fe_4S_4 cluster and one MFe_3S_4 cluster component building blocks to the FeMo- and FeV-cofactor clusters of nitrogenase? Last, we note the contributions of others in the synthesis of clusters relevant to nitrogenase clusters by use of reduced Mo−Fe−S double cubanes.[19,20]

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Supporting Information Available: Crystallographic data in CIF format of the compounds in footnote 15. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) *Experimental Details:* All reactions were carried out under strictly anaerobic conditions in acetonitrile; products were isolated as black, air-sensitive solids. X-ray diffraction data ($\theta = 1.2-22.5°$) were collected at 213 K on a Siemens SMART CCD-based diffractometer; structures were solved and refined by standard methods. [**2**](BPh_4): rhombohedral (*R3*); $a = 15.4332(8)$ Å, $c = 44.421(5)$ Å; $Z = 6$, R1(wR2) = 0.066(0.198). **5**: monoclinic ($P2_1/n$); $a = 11.2863(9)$ Å, $b = 25.282(2)$ Å, $c = 12.8320(9)$ Å; $\beta = 112.743(1)°$, $Z = 4$, R1(wR2) = 0.049(0.120). $(Et_4N)_3$[**7**]·9MeCN: monoclinic ($P2_1/n$); $a = 18.358(1)$ Å, $b = 17.534(1)$ Å, $c = 29.424(2)$ Å; $\beta = 96.619(1)°$, $Z = 4$, R1(wR2) = 0.066(0.151). $(Et_4N)_4$[**8**]·6MeCN: monoclinic ($I2/a$); $a = 22.981(7)$ Å, $b = 16.858(5)$ Å, $c = 24.753(7)$ Å; $\beta = 96.441(5)°$, $Z = 4$, R1(wR2) = 0.074(0.160). The ^1H NMR spectra of **1**−**4** and **5**−**8** in CD_3CN are consistent with three-fold and two-fold symmetry, respectively. Isomer shifts δ of ^{57}Fe are referenced to Fe metal at room temperature; all quoted values are at 4.2 K.
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