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# Selective Syntheses of Iron−Imide−Sulfide Cubanes, Including a Partial Representation of the Fe−S−X Environment in the FeMo Cofactor

Xu-Dong Chen,[†] Jeremiah S. Duncan,[‡,§] Atul K. Verma,[‡,∥] and Sonny C. Lee*,[†]

*Department of Chemistry, Princeton University, Princeton, New Jersey 08540, United States, and Department of Chemistry, University of Waterloo, Waterloo, ON, Canada N2L 3G1*

Received July 22, 2010; E-mail: sclee@uwaterloo.ca

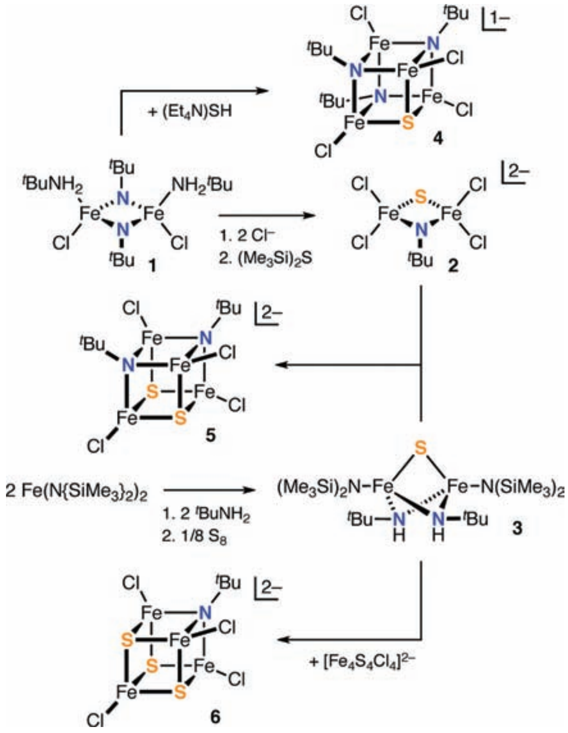
***Abstract:*** The dinuclear precursors $Fe_2(N^tBu)_2Cl_2(NH_2{}^tBu)_2$, $[Fe_2(N^tBu)(S)Cl_4]^{2-}$, and $Fe_2(NH^tBu)_2(S)(N\{SiMe_3\}_2)_2$ allowed the selective syntheses of the cubane clusters $[Fe_4(N^tBu)_n(S)_{4-n}Cl_4]^z$ with $[n, z] = [3, 1-], [2, 2-], [1, 2-]$. Weak-field iron−sulfur clusters with heteroleptic, nitrogen-containing cores are of interest with respect to observed or conjectured environments in the iron−molybdenum cofactor of nitrogenase. In this context, the present iron−imide−sulfide clusters constitute a new class of compounds for study, with the $Fe_4NS_3$ core of the [1, 2−] cluster affording the first synthetic representation of the corresponding heteroligated $Fe_4S_3X$ subunit in the cofactor.

The iron−molybdenum cofactor (FeMo cofactor) is the structurally complex, weak-field iron−sulfur (Fe−S) cluster responsible for nitrogen fixation in molybdenum-dependent nitrogenase enzymes.[1] The core of the cofactor is currently formulated as $[MoFe_7S_9X]$ in the resting state, with X assigned as a monatomic, hexairon-coordinated, interstitial ligand of uncertain identity.[2] Crystallographic analysis suggests that X is a 2p element, either carbon, nitrogen, or oxygen, with nitrogen as the favored fit,[2] and computational models predict geometries and redox potentials that support X = N;[3] ENDOR and ESEEM experiments, however, have not detected hyperfine couplings indicative of X = (C/N).[4]

The heteroleptic composition of the cofactor core is unique in biological Fe−S chemistry, and its synthesis, significance, and properties are unknown. The heteroleptic core environment may extend beyond the resting-state structure: although the mechanism of cofactor action is an open problem, several proposals integrate substrate-derived nitrogenous moieties into the Fe−S core framework during catalysis.[5] In synthetic Fe−S chemistry, heteroleptic weak-field cluster cores occur rarely and only in limited circumstances. For heterodonors that bridge solely iron, as is the case for X, the non-sulfide ligands are either organosubstituted monoanions [thiolates, bis(trimethylsilyl)amide, methoxide] or other chalcogenide dianions (selenide, oxide), and all structurally characterized examples involve $\mu_2$ bridging.[6]

The construction of relevant heteroleptic Fe−S cores is potentially useful in the study of cofactor chemistry both for the development of synthetic approaches to the cofactor cluster and for the definition of intrinsic properties associated with this environment. We have a standing interest in the cluster chemistry of weak-field iron and nitrogen anions (N-anions), particularly as it may relate to the FeMo cofactor, and we describe here its application to the selective assembly of weak-field Fe−S−X cores, where X is either an organoamide or organoimide (NR) donor (Scheme 1).

***Scheme 1***



Our syntheses began with the preparation of dinuclear complexes containing mixed sulfide and N-anion bridges (Figure 1).[7] One of the imides in $Fe_2(N^tBu)_2Cl_2(NH_2{}^tBu)_2$ (**1**)[8] can be replaced with sulfide by reaction with 2:1 $Cl^-/(Me_3Si)_2S$ to give deep-brown $[Fe_2(N^tBu)(S)Cl_4]^{2-}$ (**2**, 55%, as the $Et_4N^+$ salt). Complex **2** is the mixed-core congener of the known dimers $[Fe_2S_2Cl_4]^{2-}$ and $[Fe_2(N^tBu)_2Cl_4]^{2-}$.[8,9] A different dinuclear sulfide/N-anion complex can be prepared from the sequential treatment of $Fe(N\{SiMe_3\}_2)_2$ with $^tBuNH_2$ (1 equiv, THF, 45 °C) followed by sulfur (0.5 equiv, benzene, room temperature) to yield black $Fe_2(NH^tBu)_2(S)(N\{SiMe_3\}_2)_2$ (**3**, 40%). The dinuclear confacial bitetrahedral geometry of **3** is unusual, having been observed elsewhere only in a handful of late-transition-metal $d^{8-10}$ systems.[6] All of the complexes in this report exhibited characteristic isotropically shifted (paramagnetically induced) $^1H$ NMR spectra that facilitated solution identification.[10]

Dinuclear species **1**−**3** served as precursors for the syntheses of the tetranuclear clusters $[Fe_4(N^tBu)_n(S)_{4-n}Cl_4]^z$. Thus, separate binary equimolar reactions of **1** with $(Et_4N)SH$, **2** with **3**, and **3** with $[Fe_4S_4Cl_4]^{2-}$ formed the $[n, z] = [3, 1-]$ (**4**), [2, 2−] (**5**), and [1, 2−] (**6**) clusters, respectively. Each individual cluster is the principal metal-containing product of its designated reaction system;

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[†] University of Waterloo.
[‡] Princeton University.
[§] Current address: Department of Atmospheric Science and Chemistry, Plymouth State University, Plymouth, NH 03264.
[∥] Current address: Avecia Biotechnology, Inc., Milford, MA 01757.

10.1021/ja106478k

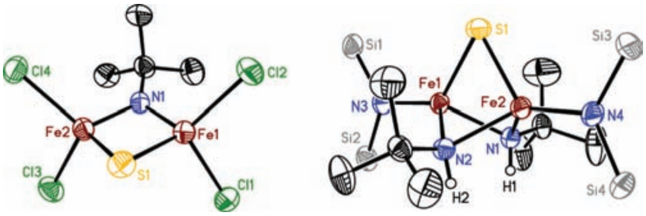

***Figure 1.*** Structures of (left) $[Fe_2(N^tBu)(S)Cl_4]^{2-}$ (**2**) and (right) $Fe_2(NHtBu)_2(S)(N\{SiMe_3\}_2)_2$ (**3**) with thermal ellipsoids at the 50% probability level; silylamide methyl substituents have been omitted for clarity. Selected mean metrics for **2**/**3** (Å or deg): $Fe-N_b$, 1.842(5)/2.054(8); Fe−S, 2.233(8)/2.234(5); $Fe-Cl/N_t$, 2.277(1)/1.882(3); Fe•••Fe, 2.5653(9)/2.4557(8); $N_b\cdots S$, 3.141(4)/3.103(8); $N_b\cdots N_b$, −/2.731(5); $N_b-Fe-S$, 100.4(4)/92.6(3); $N_b-Fe-N_b$, −/83.3(4); $Fe-N_b-Fe$, 88.3(2)/73.4(1); Fe−S−Fe, 70.12(4)/66.69(4). $N_b$ and $N_t$ refer to bridging and terminal nitrogen donors, respectively. In all of the figures, uncertainties are the larger of the standard deviation of all the observations or the largest individual estimated standard deviation within the set of observations.

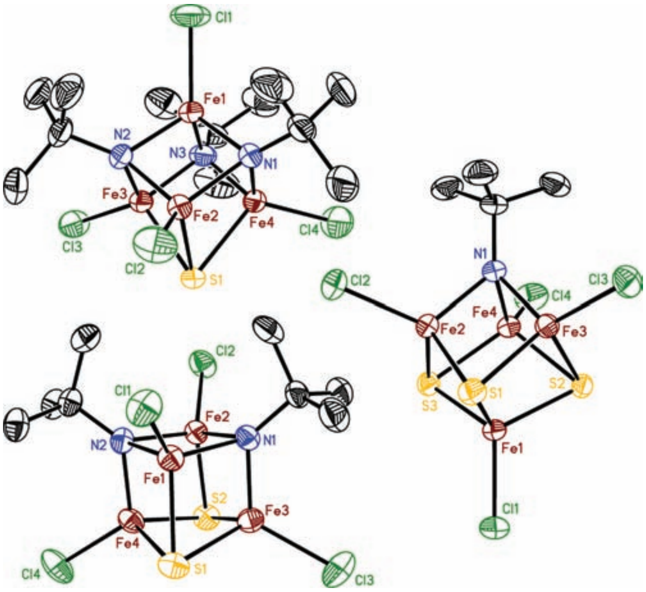

***Figure 2.*** Structures of $[Fe_4(N^tBu)_n(S)_{4-n}Cl_4]^z$ with thermal ellipsoids at the 50% probability level: (top left) $[n, z] = [3, 1-]$ (**4**); (bottom left) $[n, z] = [2, 2-]$ (**5**); (right) $[n, z] = [1, 2-]$ (**6**). Selected mean metrics for **4**/**5**/**6** (Å or deg): Fe−N, 1.946(8)/1.95(4)/1.953(9); Fe−S, 2.306(7)/2.32(2)/2.300(9); Fe−Cl, 2.197(9)/2.238(5)/2.227(8); Fe•••Fe (NN face), 2.59(2)/2.6718 (7)/−; Fe•••Fe (NS face), 2.683(6)/2.63(1)/2.655(3); Fe•••Fe (SS face), −/ 2.7962(8)/2.77(1); N•••N, 2.910(13)/2.887(4)/−; N•••S, 3.25(1)/3.302 (4)/3.30(1); S•••S, −/3.611(1)/3.61(2); N−Fe−N, 96.7(7)/94.22(8)/−; N−Fe−S, 99.5(5)/101.8(5)/101.2(2); S−Fe−S, −/101.63(6)/103.4(6); Fe−N−Fe, 85(2)/85.5(2)/85.7(2); Fe−S−Fe, 71.1(3)/71(2)/73(2).

in the crude reaction mixtures, the only additional NMR-detectable[10] paramagnetic species above trace levels were other members of the set **4**−**6**, which occurred as minor coproducts that totaled <5 to 20% yield relative to the dominant complex. Under the assumption that the dinuclear reactants contributed both irons to the final tetranuclear products, the in situ combined yields ranged from 50−70% for the three reactions by NMR assay. All of the clusters were isolated as analytically pure, black crystalline $Et_4N^+$ salts in up to 50% yield.

Crystallographic analyses[7] (Figure 2) established that clusters **4**−**6** possess congeneric cubane structures that complete the compositional series previously observed only at the $[n, z] = [0, 2-/3-]$ and $[4, 0/1-]$ end points.[9,11,12] The heteroleptic cores merge structural features from the homoleptic end points: the Fe−S bond distances are much longer than Fe−N distances, the Fe−S−Fe angles are more acute than the Fe−N−Fe angles, and the donor separations in the rhombic faces are ordered as S•••S > S•••N > N•••N. The core of **5** is replicated in nitrosyl-ligated $[Fe_4(N^tBu)_2S_2(NO)_4]^{0/1-}$, which was previously prepared by self-assembly from $Hg[Fe(CO)_3NO]_2$ and $(^tBuN)_2S$;[13] these earlier clusters, however, are strong-field species, and their properties differ significantly from those of the present system. The nitrogen−sulfur core configurations of **4** and **6** are unprecedented for any metal/ligand combination.

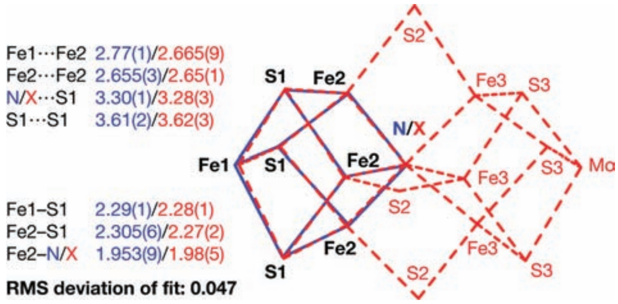

***Figure 3.*** Superposition of the $Fe_4(N/X)S_3$ cores of **6** (solid blue) and the FeMo cofactor (dashed red) with root-mean-square (RMS) deviation and selected mean distances (Å). Selected mean angles for **6**/cofactor (deg): S1−Fe1−S1, 103.7(5)/105(1); S1−Fe2−S1, 102.9(6)/105.9(5); S1−Fe2−N/X, 101.2(2)/101(1); Fe1−S1−Fe2, 74.1(3)/71.8(6); Fe−S1−Fe2, 70.3(1)/71.6(6); Fe2−N/X−Fe2, 85.7(2)/84(1). Means were calculated assuming idealized $C_{3v}$ symmetry and represent averages over all independent observations.

In solution, pure samples of **4**−**6** are stable with respect to disproportionation by core ligand exchange, and mixtures of **4** and **6** do not produce **5**. Cyclic voltammetry[14] revealed the systematic effect of the ligand substitution sequence $n = 0-4$ on the redox properties, with each replacement of sulfide by imide incrementally shifting the potentials of equivalent redox couples by ca. −400 mV; this pattern reflects the greater donor ability of the N-anion ligand and explains the formation of **4** in a more oxidized state relative to **5** or **6**.

The reduction of dinuclear diferric species is known to yield cubanes in Fe−S[9] and Fe−NR[15] chemistry, and the syntheses of **4**−**6** were devised on the basis of this behavior; a similar tactic has been investigated for the preparation of heterometallic Mo−Fe−S clusters.[16] Hypothetical balanced reactions for the syntheses can be constructed using the experimental stoichiometries (see the Supporting Information), with azo-*tert*-butane and disulfide offered as possible oxidized coproducts on the basis of the chemistry of related cluster systems.[8,15,17] We emphasize that these stoichiometries are notional: the spectroscopic cluster yields indicate that a significant portion of the reaction mass is either insoluble or otherwise NMR-silent, and we detected only trace quantities of azobutane in GC assays. The actual mechanisms of cluster formation are likely to be complex: beyond reduction and nuclearity expansion, other significant transformations must occur, including core ligand substitution for the synthesis involving $\mathbf{1} + SH^-$ and protonolysis and rearrangement for reactions employing triply bridged dimer **3**. Despite the mechanistic complexities, the cubane assembly reactions are selective, yielding a single predominant core composition in all cases. Efforts to elucidate and further direct the course of cluster assembly are in progress.

The complexes reported here permit the first study of weak-field Fe−NR−S clusters and their potential connection to the chemistry of the FeMo cofactor. *tert*-Butylimide, of course, is neither nitride nor any of the other monatomic ligands proposed as X, and the present clusters do not replicate the full cofactor structure. Nevertheless, the $Fe_4NS_3$ core of **6** affords a structural representation nearly isometric with the analogous eight-atom $Fe_4S_3X$ subunit of the cofactor cluster,[2] as demonstrated by the superposition in Figure 3. Most of the mean core metrics for the two cluster fragments differ by less than 2%; the largest deviations are for the Fe1•••Fe2 contacts, which are 4% shorter on average in the cofactor as a result of a small displacement of Fe1 along the idealized $C_3$ axis. Inasmuch as structural criteria currently supply the only observational evidence for X, cluster **6** offers, in partial form, the closest synthetic approximation to date for the conjectured Fe−S−(X = N) environment in the FeMo cofactor. Further detailed physical and chemical investigations of cubanes **4**−**6** and related clusters will be the subjects of future reports.

**Acknowledgment.** This research was supported by the Beckman Foundation and NSF CHE-9984645 (initial studies) and by NSERC, CFI, and ORF.

**Supporting Information Available:** Synthetic details and additional characterization (elemental analysis, ESI-MS, and UV−vis data), proposed balanced reactions, additional references, and crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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## References

(1) Burgess, B. K.; Lowe, D. J. *Chem. Rev.* **1996**, *96*, 2983.
(2) Einsle, O.; Tezcan, F. A.; Andrade, S.; Schmid, B.; Yoshida, M.; Howard, J. B.; Rees, D. C. *Science* **2002**, *297*, 1696.
(3) Noodleman, L.; Lovell, T.; Han, W.-G.; Li, J.; Himo, F. *Chem. Rev.* **2004**, *104*, 459.
(4) Lukoyanov, D.; Pelmenschikov, V.; Maeser, N.; Laryukhin, M.; Yang, T. C.; Noodleman, L.; Dean, D. R.; Case, D. A.; Seefeldt, L. C.; Hoffman, B. M. *Inorg. Chem.* **2007**, *46*, 11437.
(5) Peters, J. W.; Szilagyi, R. K. *Curr. Opin. Chem. Biol.* **2006**, *10*, 101.
(6) Specific examples and citations are provided in the Supporting Information.
(7) Crystallographic data (Mo Kα, 200 K), listed as *a*, *b*, *c*, *β* (Å or deg); space group, *Z*; $2\theta_{max}$ (deg), GOF, R1/wR2 for $I > 2\sigma(I)$ (%): **2**: 9.3855(3), 15.6669(8), 20.7398(11), 95.827(3); $P2_1/n$, 4; 52.2, 1.03, 5.34/13.3. **3**: 16.4939(8), 9.0249(5), 23.5935(13), 101.945(2); $P2_1/n$, 4; 52.0, 1.03, 6.04/10.5. **4**: 23.4155(10), 20.7305(9), 17.8411(13), 130.1660(10); *C*2/*c*, 8; 60.8, 1.02, 3.30/7.22. **5**: 17.8185(12), 11.3121(7), 22.1301(14), 108.7950(10); $P2_1/c$, 4; 45.6, 0.98, 4.98/10.20. **6**: 26.4805(11), 10.7835(4), 12.7847(5), 90; $Pca2_1$, 4; 57.4, 1.07, 3.79/8.05.
(8) Duncan, J. S.; Zdilla, M. J.; Lee, S. C. *Inorg. Chem.* **2007**, *46*, 1071.
(9) Wong, G. B.; Bobrik, M. A.; Holm, R. H. *Inorg. Chem.* **1978**, *17*, 578.
(10) $^1$H NMR data (300 MHz, ca. 22 °C, $C_6D_6$ for **3**, MeCN-$d_3$ for all others), $\delta$ (ppm): **2**, 6.84; **3**, 8.89, 2.31, 1.80; **4**, 10.58; **5**, 7.01; **6**, 5.47; $Et_4N^+$ (when present), ca. 3.2, 1.2.
(11) Hagen, K. S.; Uddin, M. *Inorg. Chem.* **2008**, *47*, 11807.
(12) (a) Verma, A. K.; Nazif, T. M.; Achim, C.; Lee, S. C. *J. Am. Chem. Soc.* **2000**, *122*, 11013. (b) Link, H.; Decker, A.; Fenske, D. *Z. Anorg. Allg. Chem.* **2000**, *626*, 1567.
(13) (a) Chu, C. T.-W.; Gall, R. S.; Dahl, L. F. *J. Am. Chem. Soc.* **1982**, *104*, 737. (b) Gall, R. S.; Chu, C. T.-W.; Dahl, L. F. *J. Am. Chem. Soc.* **1974**, *96*, 4019.
(14) Reversible or quasireversible (qrev) redox couples (0.1 M TBAP/MeCN, 100 mV/s), $E_{1/2}$ (V vs SCE) (z/z+1): $Fe_4(N^tBu)_4Cl_4$, +0.17 (1−/0),−0.96 (2−/1−, qrev); **4**,−0.53 (2−/1−, qrev); **5**,−0.09 (2−/1−),−1.55 (3−/2−, qrev); **6**,−1.16 (3−/2−, qrev); $[Fe_4S_4Cl_4]^{2-}$,−0.82 (3−/2−, qrev).
(15) Duncan, J. S.; Nazif, T. M.; Verma, A. K.; Lee, S. C. *Inorg. Chem.* **2003**, *42*, 1211.
(16) (a) Koutmos, M.; Georgakaki, I. P.; Tsiolis, P.; Coucouvanis, D. *Z. Anorg. Allg. Chem.* **2008**, *634*, 255. (b) Han, J.; Koutmos, M.; Al Ahmad, S.; Coucouvanis, D. *Inorg. Chem.* **2001**, *40*, 5985.
(17) Sharp, C. R.; Duncan, J. S.; Lee, S. C. *Inorg. Chem.* **2010**, *49*, 6697.

JA106478K