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Mixed Valence, Tricopper(I,II,I) Complexes with Thiolate Bridges. Progress toward Synthetic Models of the Putative $\{Cu_2\}^{3+}$ Sites in Nitrous Oxide Reductase and Cytochrome *c* Oxidase

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Nitrous oxide reductase (N_2OR) is a copper-containing bacterial enzyme that catalyzes the reduction of N_2O to N_2 during denitrification.[1−5] It has been suggested on the basis of spectroscopic studies that the paramagnetic copper center associated with electron transfer in the enzyme is an unusual mixed valence [Cu(1.5)•••Cu(1.5)] binuclear cluster, the presence of a seven-line hyperfine splitting pattern in EPR spectra being indicative of delocalization of unpaired spin density over the two copper ($I = {}^3/_2$) atoms.[2] Ligation of the novel cluster by two cysteine, two histidine, and one methionine residue has been proposed on the basis of the conserved nature of these groups among proteins from different sources,[3] the ability to engineer the center by incorporating these residues into a protein,[4] and spectroscopic data.[5] Similarities among the amino acid sequences and multiple frequency EPR spectroscopic data for N_2OR and the Cu_A site in cytochrome c oxidase (CcO) have led to the controversial proposal that the latter may also be a mixed valence dicopper unit.[6] It has been proposed that electron delocalization between the copper ions occurs either via an unsupported Cu−Cu bond[7] or via one or more bridging thiolates.[2c,6a] While model complexes corroborating the hypothesis of a direct Cu•••Cu interaction have been prepared,[8] mixed valence thiolate-bridged dicopper compounds that might provide precedence for the latter structural proposal are, to our knowledge, unknown.[9,10] In initial progress toward the goal of constructing such species, we report the synthesis and characterization of novel mixed valence tricopper(I,II,I) complexes with thiolate bridges. Despite clear drawbacks as accurate N_2-OR or Cu_A active site models, these unusual compounds nevertheless demonstrate the feasibility of a N-donor ligand-supported Cu^I-(μ-SR)-Cu^{II} motif.

Our synthetic strategy for the assembly of the mixed valence complexes involved combination of monomeric copper(II) dithiolates L^1Cu^{II} (**1**)[11,12] or L^2Cu^{II} (**2**)[11,13] with either of the copper(I) bis(pyrazolyl)dihydroborates $\{[H_2B(3,5\text{-}RR'pz)_2]Cu\}_n$ (**3**: R = *t*-butyl, R′ = H, *n* = 2; **4**: R = R′ = Me, *n* unknown) (Scheme 1).[13] The copper(I) starting materials were prepared by mixing either $Tl[H_2B(t\text{-}Bupz)_2]$[11,14] or $K[H_2B(Me_2pz)_2]$[11,15] with CuCl in THF. An X-ray crystal structure of **3** revealed bridging $[H_2B(t\text{-}Bupz)_2]^-$ ligands between linear two-coordinate Cu^I ions (Figure S5), a geometry similar to that of $\{[HB(t\text{-}Bupz)_3]Cu\}_2$.[16,17] The copper(II) thiolate starting materials were synthesized from the free thiols[12,18] and $Cu(acac)_2$ under an N_2 atmosphere; **1** was reported previously[12] but **2** is a new compound.[13]

Addition of colorless CH_2Cl_2 solutions of the copper(I) complexes to solutions of purple **1** or burgundy **2** induced color changes to dark green. Monitoring by UV−vis absorption spectroscopy indicated that 1 equiv of **3** or **4** [i.e., two Cu^I ions] was needed in order to reach the reaction endpoint (cf. Figure S1). The substantial red shifts and intensity changes of the optical absorption features of the copper(II) precursors upon

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(11) Abbreviations used: L^1 = bis(mercapto-1,1-dimethylethyl)-*trans*-1,2-diaminocyclohexane; L^2 = bis(mercaptoethyl)diazacyclooctane; *t*-Bupz = 3-*tert*-butylpyrazolyl; Me_2pz = 3,5-dimethylpyrazolyl.

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(13) Spectroscopic and analytical data for all new compounds are provided in the supplementary material. Pertinent data for **2** and **6** are as follows. **2**: UV−vis (CH_2Cl_2) [λ_{max}, nm, (ϵ, M^{-1} cm^{-1})] 350 (4500), 404 (sh, 2100), 538 (550); EPR (1:1 toluene/CH_2Cl_2, 9.24 GHz, 10 K) $g_\perp = 2.021$, $g_\| = 2.125$, $A_\|^{Cu} = 173.6 \times 10^{-4}$ cm^{-1}. **6**: UV−vis (CH_2Cl_2) [λ_{max}, nm, (ϵ, L mol^{-1} cm^{-1})] 346 (2400), 425 (sh, 1300), 594 (730); EPR (50:50 toluene/CH_2Cl_2, 9.46 GHz, 77 K) $g_\perp = 2.017$, $g_\| = 2.129$, $A_\|^{Cu} = 166.0 \times 10^{-4}$ cm^{-1}.

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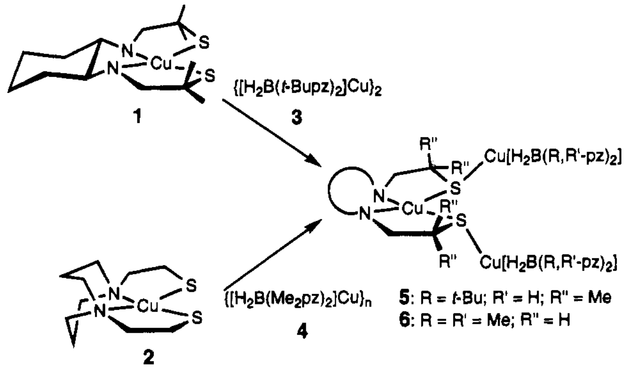
Scheme 1



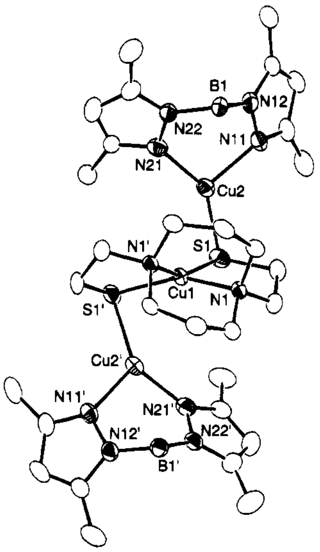


Figure 1. ORTEP representation of the X-ray structure of $\{L^2\text{-}Cu([H_2B(Me_2pz)_2]Cu)_2\}\cdot C_7H_8$ (**6**$\cdot C_7H_8$) with atom labels shown for all noncarbon atoms (35% ellipsoids, hydrogen atoms not shown for clarity). Selected bond distances (Å) and angles (deg): Cu1−S1, 2.247(3); Cu1−N1, 2.019(8); Cu2−S1, 2.181(4); Cu2−N11, 2.056(9); Cu2−N21, 1.935(8); S1−Cu1−S1′, 99.5(2); Cu1−S1−Cu2, 85.1(1); S1−Cu2−N11, 118.3(3); S1−Cu2−N21, 143.3(3); N11−Cu2−N21, 98.4(4); N1−Cu1−N1′, 87.8(4); N1−Cu1−S1, 91.5(2); N1−Cu1−S1′, 154.8(3).

treatment with **3** or **4** support complexation to the thiolate ligands by the added Cu^I ions,[13] an hypothesis that was confirmed by X-ray crystal structure determinations of the dark green products $\{L^1Cu([H_2B(t\text{-}Bupz)_2]Cu)_2\}\cdot C_7H_{16}$ (**5**$\cdot C_7H_{16}$)[19] and $\{L^2Cu([H_2B(Me_2pz)_2]Cu)_2\}\cdot C_7H_8$ (**6**$\cdot C_7H_8$) (Figure 1).[16b] Two symmetry-related, three-coordinate, planar Cu^I ions are linked via thiolate sulfur atoms to the central four-coordinate Cu^{II} ion in the topologically similar tricopper complexes [Cu1···Cu2 = 3.163(5) Å for **5** and 2.996(5) Å for **6**], the geometric differences between the metal coordination spheres within each complex being clearly indicative of a localized oxidation state description (class I).[20] The structure of the central $Cu^{II}N_2S_2$ core of **6** is nearly identical to that of **5** and its parent Cu^{II} compound **1**, as evinced by similar $Cu^{II}N_2/Cu^{II}S_2$ dihedral angles [34(1)° for **6**, 36(1)° for **5**, and 32.77(6)° for **1**] and like Cu^{II}−S distances [2.247(3) Å for **6**, 2.260(9) Å for **5**, and 2.231(7) Å for **1**] that are within the known range of copper(II)−thiolate bond lengths.[12,21] The Cu^I−S bond distances [2.182(9) Å for **5**, 2.181(4) Å for **6**] are shorter than typical ones reported for trigonal sites in copper(I)−thiolate clusters (2.27 Å),[22] but are comparable to that in $K\{[HB(Me_2pz)_3]Cu(p\text{-}NO_2C_6H_4S)\}$ [2.19(1) Å].[23]

In addition to the structural evidence, preliminary EPR spectroscopic data support localized mixed valence formulations for the tricopper complexes. They exhibit axial signals (one spin per trimer by integration) with parameters obtained by spectral simulation that are closely similar to those of their monomeric precursors **1** and **2** (Figures S1−S4).[13] These similarities and a lack of hyperfine features that would result from spin interactions with more than one copper nucleus provide further support for little, if any, structural alteration of the $Cu^{II}N_2S_2$ cores upon complexation by the Cu^I fragments and argue against valence delocalization in the trimers.

The nuclearity of the tricopper complexes, the significantly different coordination geometries of the copper ions, and the resulting lack of electron delocalization as shown by EPR spectroscopy are clear indications of shortcomings of these compounds as accurate models of the putative N_2OR or CcO clusters. Nevertheless, the isolation and characterization of the new compounds shows that a Cu^I−(μ-SR)−Cu^{II} unit with additional N-donor ligation can be accessed and thus should be given further consideration as a possible protein active site structure. Future work will focus on using the new compounds as benchmarks for future comparative spectroscopic studies (e.g. EXAFS) and on the construction of more symmetrical thiolate-bridged model complexes that might better stabilize a spin-delocalized ground state.

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Supplementary Material Available: Spectroscopic and analytical data for **2**−**6**, UV−vis titration data for the **1** → **5** conversion (Figure S1), EPR spectra and simulations for **2** (Figure S2), **5** (Figure S3), and **6** (Figure S4), and fully labeled ORTEP drawings (Figures S5−S7) and tables of bonds lengths, bond angles, atomic coordinates, and thermal parameters for **3**, **5**, and **6** (22 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(19) Preliminary crystal data for **5**$\cdot C_7H_{16}$: $C_{42}H_{76}N_{10}S_2B_2Cu_3$, fw 995.38, tetragonal, space group $P4_32_12$ (No. 96), at 177 K, $a = b = 15.64(2)$ Å, $c = 28.79(3)$ Å, $V = 7039(25)$ Å^3, $Z = 8$, $R = 0.103$, and $R_w = 0.092$ for 1581 reflections with $I > 2\sigma(I)$ and 161 parameters. The high *R* indices for this structure result from disorder in the included solvent molecule (heptane) which could not be adequately modeled, in part because of the low number of data from the poorly diffracting crystal. See Figure S6.

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