Three-Coordinate Cu(II) Complexes: Structural Models of Trigonal-Planar Type 1 Copper Protein Active Sites

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Members of the type 1 class of copper protein active sites are common redox reagents in biochemistry, and extensive studies of them have been crucial to the development of modern bioinorganic chemistry.[1] A trigonally disposed His₂Cys ligand complement is found in all of these sites, with a short, highly covalent Cu–S(Cys) interaction being the primary determinant of their unique spectroscopic features.[2] Despite their categorization as a single type of copper center, the type 1 coppers exhibit variable coordination geometries whose relationships to spectroscopic and redox properties are under intense study.[2,3] These geometries mainly differ in additional ligand(s) provided to the copper atom by the protein: two donors at long distances (>3.0 Å), giving a 3 + 2 trigonal bipyramid (azurin);[4] one donor at a shorter distance (2.6–2.9 Å), giving a distorted tetrahedron (e.g., plastocyanin);[5] or no donating residues, leaving a three-coordinate trigonal-planar copper (fungal laccase,[6a] ceruloplasmin,[6b,c] and certain azurin mutants[6d]).[7] The trigonal-planar structure is an arrangement for Cu(II) that has no precedent, to our knowledge, in the coordination chemistry of this ion. Here, we report the first examples of synthetic Cu(II) complexes with such a geometry, including a thiolate complex that closely mimics the structures of the trigonal fungal laccase and ceruloplasmin type 1 sites.[8]

The lithium salt of 2,4-bis(2,6-diisopropylphenylimido)pentane (L⁻)[9] was reacted with CuCl₂ to give red-purple LCuCl (**1**).[10] An X-ray crystal structure (Figure S1, Supporting Information)[11] revealed only three ligands coordinated to the metal ion, two nitrogen atoms from L⁻ at 1.870(3) Å and a chloride at 2.127(1) Å, in an almost perfectly planar geometry (the metal lies only 0.005 Å from the N₂Cl plane). The Cu(II) oxidation level was confirmed from charge-balance considerations, a bond-valence

sum analysis,[12] and EPR spectroscopy (1 spin/Cu by integration; Figure S2, Supporting Information).

Reaction of **1** with sodium 4-methylthiophenolate resulted in oxidation of the thiolate to a disulfide.[8a] However, treating **1** with sodium triphenylmethylthiolate gave thermally stable, deep blue-purple LCuSCPh₃ (**2**).[10] The X-ray crystal structure (Figure 1b) shows that the bulky diimine L⁻ continues to enforce three-coordination in **2**, despite the tendency of thiolate ligands to form bridges.[8a] One isopropyl methine hydrogen atom approaches the copper from each side of the plane at a distance of 2.8–2.9 Å, but we cannot distinguish whether this geometry is a result of weak bonding to the copper atom or from ligand constraints. The short Cu–N and Cu–S bond lengths [1.922(3) and 2.124(1) Å, respectively] are very similar to the distances in the crystal structures of the trigonal-planar sites in the blue copper proteins fungal laccase (1.9, 2.2 Å; Figure 1a)[6a] and ceruloplasmin (∼2.1 Å),[6b] as well as other type 1 copper sites.[7] Interestingly, the Cu geometry is distorted slightly toward pyramidal; the metal ion lies 0.220(1) Å from the N₂S plane, comparable to the deviation in azurin (0.1 Å)[4] but not as large as in the more tetrahedral plastocyanin active site (0.4 Å).[5] The pyramidalization in **2**, which lacks an axial ligand, should lead to reevaluation of claims that weak (2.9 Å or greater) axial "bonding" in type 1 copper sites leads to movement of the metal out of the N₂S plane. This distortion from planarity, as well as the Cu–S–C angle of 119.43(8)° that is more obtuse than that in the proteins (∼110°), may result from steric crowding in **2**.

The axial signal in the X-band EPR spectrum of **2** (Figure 2a) corroborates its Cu(II) formulation, but the $g_\parallel = 2.17$ and $A_\parallel =$

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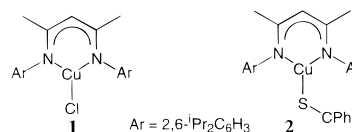
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(10) Data for **1** (yield 51%): UV/vis (CH₂Cl₂) [λmax, nm (ε, mM⁻¹ cm⁻¹)] 340 (∼25), 507 (4.1), 657 (1), 840 (1); EPR (9.61 GHz, CH₂Cl₂/toluene, 20 K) $g_\parallel = 2.20$, $A_\parallel = 130 \times 10^{-4}$ cm⁻¹, $g_\perp = 2.05$, $A_\perp = 8 \times 10^{-4}$ cm⁻¹. Anal. Calcd for C₂₉H₄₁CuClN₂: C, 67.42; H, 8.00; N, 5.42. Found: C, 67.36; H, 8.05; N, 5.46. Data for **2** (yield 51%): UV/vis (heptane) [λmax, nm (ε, mM⁻¹ cm⁻¹)] 340 (∼20), 427 (1.1), 487 (1.0), 561 (1.3), 749 (5.8); EPR (9.61 GHz, toluene, 20 K) $g_\parallel = 2.17$, $A_\parallel = 111 \times 10^{-4}$ cm⁻¹, $g_\perp = 2.04$, $A_\perp = 13 \times 10^{-4}$ cm⁻¹. Anal. Calcd for C₄₈H₅₆CuSN₂: C, 76.20; H, 7.46; N, 3.70. Found: C, 76.21; H, 7.58; N, 3.68.

(11) X-ray data for **1**: monoclinic, space group P2₁/n, a = 12.5239(2) Å, b = 16.6649(1) Å, c = 13.9652(1) Å, β = 104.521(1)°, V = 2821.59(5) Å³, Z = 4, ρcalcd = 1.216 g/cm³. For **2**: monoclinic, space group C2/c, a = 38.799-(8) Å, b = 13.156(3) Å, c = 17.577(4) Å, β = 109.82(3)°, V = 8441(3) Å³, Z = 8, ρcalcd = 1.191 g/cm³. Nonhydrogen atoms were refined with anisotropic thermal parameters, and hydrogen atoms were in idealized positions with riding thermal parameters. Full-matrix least-squares refinement on F² converged for **1** (R1 = 0.0335, wR2 = 0.0782, GOF = 1.043 for 4036 independent reflections with I > 2σ(I) and 308 parameters) and **2** (R1 = 0.0418, wR2 = 0.0867, GOF = 1.019 for 5417 independent reflections with I > 2σ(I) and 479 parameters).

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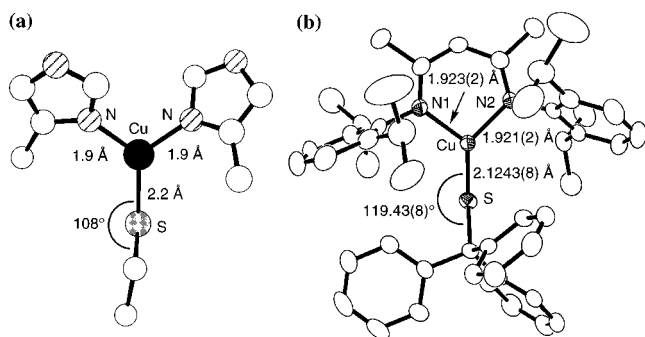
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(a)   **(b)**

Figure 1. (a) Type 1 copper site in fungal laccase as determined by X-ray crystallography (ref 6a). (b) Thermal ellipsoid (50%) diagram of the X-ray structure of **2** (hydrogen atoms omitted).
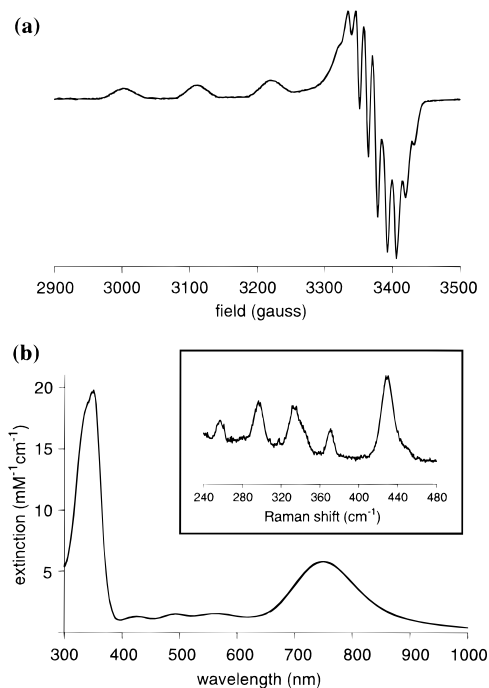
(a)

(b)

Figure 2. (a) X-band EPR spectrum of **2** in toluene (9.61 GHz, 20 K): $g_{\parallel} = 2.17$, $A_{\parallel} = 111 \times 10^{-4}$ cm^{-1}, $g_{\perp} = 2.04$, $A_{\perp} = 13 \times 10^{-4}$ cm^{-1}. (b) UV−vis spectrum of **2** in heptane solution (298 K). Inset: Resonance Raman spectrum of **2** in C$_6$D$_6$ ($\lambda_{ex} = 632.8$ nm, $T = 77$ K).

111×10^{-4} cm^{-1} values differ significantly from those typical for type 1 copper protein sites ($g_{\parallel} = 2.2-2.3$ and $A_{\parallel} < 70 \times 10^{-4}$ cm^{-1}). It is noteworthy, however, that EPR spectra of the trigonal-planar sites in fungal laccase and ceruloplasmin are exceptional for type 1 copper, displaying axial signals with lower $g_{\parallel}$ values near 2.20 and higher $A_{\parallel}$ values ($\sim 90 \times 10^{-4}$ cm^{-1}) that have been related to a stronger Cu−S(cys) interaction.[13−15] Thus, the EPR spectrum of **2**, like its structure, is quite similar to those of the trigonal-planar type 1 sites. The optical absorption spectrum of **2** in heptane (Figure 2b) has multiple features, of which the one with $\lambda_{max} = 749$ nm ($\epsilon = 5800$ M^{-1} cm^{-1}) is of particular interest. It is reminiscent of, but at longer wavelength than, the intense feature near 600 nm ($\epsilon \approx 5000$ M^{-1} cm^{-1}) responsible for the deep blue color of the type 1 sites, including the trigonal-planar ones.[2,3,14] By analogy to the protein data and on the basis of its high extinction coefficient, we ascribe the 749-nm band in **2** to a thiolate → Cu(II) charge-transfer transition

(d−d bands may be buried under this feature[2,3,14]). The disparity between the energies of this transition in the model and in the proteins is under study.

The resonance Raman spectrum ($\lambda_{ex} = 632.8$ nm) of **2** in C$_6$D$_6$ exhibits multiple features (Figure 2b, inset), with a band at 430 cm^{-1} being most prominent. Similar spectra have been reported for type 1 copper sites, and major bands between 340 and 435 cm^{-1} in these cases have been assigned as predominantly Cu−S vibrations (ν_{Cu-S}).[3,16,1716,17] Higher ν_{Cu-S} values imply a stronger Cu−S bond, but interpretation is complicated by vibrational coupling with S−C and C−C thiolate vibrations. Preliminary assignment of the 430-cm^{-1} band in **2** to ν_{Cu-S} is supported by the similarity of its frequency to those reported in other model complexes (e.g., 422 cm^{-1} for one with the same Ph$_3$CS$^-$ ligand).[8e] Also, its high energy is consistent with the strong Cu−S bonding expected in this trigonal complex and compares well with the major ν_{Cu-S} bands between 428 and 435 cm^{-1} in fungal laccases from several organisms.[14,16]

In view of the function of the type 1 sites as electron-transfer agents, it is generally believed that the unusual trigonal or tetrahedral Cu(II) coordination geometry exists to minimize ligand reorganization upon reduction to Cu(I).[18] Thus a Cu(I)-like coordination geometry is enforced, giving the copper ion a high redox potential (+0.2−0.6 V vs NHE). At the extreme are the three-coordinate fungal laccase and ceruloplasmin centers, which have the highest redox potentials of the type 1 coppers (in some cases, >+0.7 V).[6c,14,19] The redox potential of **2** in THF is much lower ($E_{1/2} = -0.18$ V vs NHE, Figure S6, Supporting Information),[20] at least in part because of charge donation by the anionic L$^-$.

In summary, using a relatively simple synthetic approach, we have characterized the first three-coordinate complexes of Cu(II), including a close structural analogue of the trigonal type 1 copper protein active sites. This work demonstrates that appropriate protecting ligands can give this unusual Cu(II) geometry in the absence of protein-enforced geometric constraints.[21] There are spectroscopic similarities between the synthetic model and the protein centers, but important differences in absorption, Raman, and electrochemical properties need to be explained through further studies.

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