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Fluorine Encapsulation and Stabilization of Biologically Relevant Low-Valence Copper-Oxo Cores

Zhengbo Hu,[†] **Graham N. George,**[‡] **and Sergiu M. Gorun***[,†]

Department of Chemistry, Brown University, Providence, Rhode Island 02912, and Stanford Synchrotron Radiation Laboratory, SLAC, Menlo Park, California 94025

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The rational design of metalloenzyme active site models is an area of both scientific and technological interest. The preparation of robust copper complexes has been stimulated by similar biological motifs, whose functionalities range from reversible O_2 binding (hemocyanine, Hc[1]) to oxygenation of external substrates (tyrosinase[2]). Steric and electronic parameters are currently varied in hydrocarbon-based ligands.[3] Replacing all C−H bonds adjacent to a metal by C−F bonds resulted in a dinuclear μ-η^2:η^2 peroxo complex, $[(\mathrm{CuTp}^{\mathrm{CF_3,CH_3}})_2\mathrm{O_2}]$, **1a**, which, to our knowledge, appears to be the most stable to date, both in solid state and solution, while reversibly binding O_2 at ambient temperature.[4] While amorphous **1a** was obtained by the *rapid* evaporation of its solutions, *slow* evaporation results in the formation of crystals, **1b**, of a different composition.

We report herein the structural deconvolution of **1b** into **1a** and a bis(hydroxo) complex, **2,** and insights into the apparent paradoxical effect of fluorine groups upon their valence state and structural stability. This is the first structurally characterized metal-bonded peroxo group in a fluorine-rich environment.

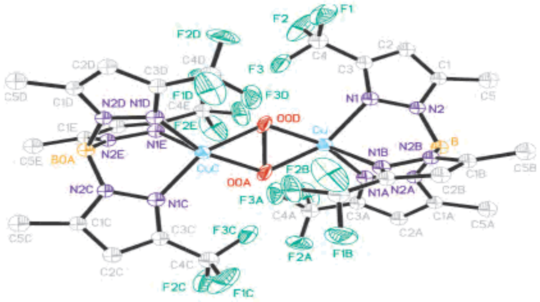

Figure 1. X-ray structure at 40% probability of **1b.** Hydrogen atoms and disordered CF_3 groups are omitted. The Cu, O, and F atoms were refined anisotropically. Selected bond length (Å) and angles (deg): Cu- -CuC 3.365(3), O(0A)−O(0D) 1.73(3), Cu−O(0A) 1.88(2), Cu−O(0D) 1.90(2), Cu−N(1) 2.018(15), Cu−N(1A) 1.992(14), Cu−N(1B) 2.420(4), Cu−O0A−CuC 125.6(7), O(0D)−Cu−O(0A) 54.4(5), O(0D)−Cu−N(1A) 157.2(9), O(0A)−Cu−N(1A) 105(1), O(0D)−Cu−N(1) 103(2), O(0A)−Cu−N(1) 157.3(9), N(1A)−Cu−N(1) 96.5(2), O(0D)−Cu−N(1B) 108.4(9), O(0A)−Cu−N(1B) 104(2), N(1A)−Cu−N(1B) 84.8(3), N(1)−Cu−N(1B) 84.3(3).

The evaporation of a toluene solution of **1a** yields crystals, which, unlike the starting purple solid, are bicolor with distinct, orientation-independent blue and purple regions. The X-ray analysis[5] of a mostly purple specimen reveals a crystallographically unique $\mathrm{CuTp}^{\mathrm{CF_3,CH_3}}\mathrm{O}$ fragment, which generates by symmetry a disordered dinuclear complex. Each metal, three-fold disordered about the ligand three-fold axis (and slightly off it), defines an equilateral triangle with Cu- -Cu distances of 0.615 Å, whereas six oxygen sites define a central regular hexagon. Each copper exhibits equatorial Cu−N distances of 1.99(1) and 2.02(1) Å, and a long, 2.420(4) Å, axial one. The choice of the unique copper pair is limited to two options: (i) Cu−N axial vectors oriented syn (N_{ax}−Cu−N_{ax} torsion angle 66°, Cu- -Cu = 3.308(2) Å), or (ii) anti (N_{ax}−Cu−N_{ax} torsion angle 180°, Cu- -Cu = 3.365(3) Å). The choice of the two unique oxygen atoms of the oxygen hexagon is limited to either a "meta" (O−O = 1.50(3) Å) or "para" (O−O = 1.73(3) Å) pair, since the "ortho" contacts are 0.865 Å. The "meta" choice exhibits the expected peroxo O−O distance, but its combination with either the syn or anti copper option results in (i) "butterfly" Cu_2O_2 cores, inconsistent[6] with the UV−Vis spectrum[4] of **1a**, and (ii) at least one very short (1.767 Å or below) Cu−O distance, inconsistent with Cu(II) (see below). The "para" (oxygen)−anti (copper) combination, Figure 1, exhibits a strictly planar Cu_2O_2 unit and 1.9 Å Cu−O distances. A bond valence sum (BVS) analysis, using parameters calibrated to 2.00 ± 0.05 for the $\mathrm{CuN_3O_2}$ chromophores of $[\mathrm{CuTp}^{\mathrm{CF_3,CH_3}}(\mathrm{O_2CCH_3})]$ and $[\mathrm{CuTp}^{\mathrm{CF_3,CH_3}}(\mathrm{CO_3})]$,[7] gives a 2.2 value, which is consistent with the 2.2 value calculated for the μ-η^2:η^2 peroxo cores of $[\mathrm{Cu_2(L)O_2}]^{2+}$, L = 1,2-bis[2-(bis(6-methyl-2-pyridyl)-methyl)-6-pyridyl]ethane[8a] and $[(\mathrm{CuTp}^{^i\mathrm{Pr},^i\mathrm{Pr}})_2\mathrm{O_2}]$.[8b,9] In contrast, we calculate a high BVS of ∼2.4 for at least one metal center of the "meta"−anti combinations. Furthermore, the coordination equatorial planes exhibit the highest degree of planarity, the (N_{eq}−

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* To whom correspondence should be addressed.

[†] Department of Chemistry, Brown University.

[‡] Stanford Synchrotron Radiation Laboratory.

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(5) Unit cell: a = 11.6539(6) Å, c = 26.154(1) Å, V = 3076.2(3) $Å^3$ at 213(2) K. Z = 3, ρ_{calc} = 1.745 g/cm^3. Space group R-3, trigonal; 104 parameters refined on F^2 gave R1 = 0.0554, wR2 = 0.1208 using 5835 reflections (1402 independent).

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(9) A related structure[10] also contains a μ-η^2:η^2 peroxo core but was omitted in the BVS calculation due to inaccurate metal−ligand distances.

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Cu−N$_{eq}$)−(O−Cu−O) dihedral angles (11.4−79.9° observed range) having the minimum value. This feature, in conjunction with the Cu_2O_2 core planarity, favors the strong (over 600 cm^{-1}) intramolecular antiferromagnetic coupling established by the lack of a room-temperature ESR signal for both **1a**[4] and **1b**.

The Cu- -Cu and O−O distances in **1b**, 3.365 and 1.73 Å, respectively, are, however, shorter and longer, respectively, relative to the corresponding (3.55 ± 0.05 and 1.45 ± 0.05 Å) distances observed in oxyHc[1] and μ-η^2:η^2 peroxo models,[8,10] despite their overall structural resemblance. Similar distortions in $[\{Cu(MePY2)\}_2O_2]^{2+}$ (MePY2 = methyl bis(2-pyridylethyl) amine)[11] have been ascribed to the admixture of a $[Cu(III)O]_2$ component in the Cu(II) structure. A similar possibility was considered for **1b**, which is consistent with the lack of intramolecular ligand repulsion (see below), long Cu−N$_{ax}$ axial bonds, viewed to favor $[Cu(III)O]_2$ over $Cu(II)_2O_2$ cores,[10] and the lack of an ESR signal. The K-edge XAS of **1b**, however, lacks the diagnostic[12] 1s−3d Cu(III) 8981 eV band, yet shows the Cu(II) 8979 eV transition. Thus, both XAS and UV−vis data eliminate the possibility of the presence of Cu(III).

We ascribe the elongation and contraction of the *average* O−O and Cu- -Cu contacts, respectively, to a small amount of cocrystallized $[(Cu(II)Tp^{CF_3,CH_3})_2(OH)_2]$, **2**. Indeed, a detailed analysis of the electronic density contour map of **1b,** which reveals asymmetric peaks consistent with the overlapping of two types of copper-oxo cores (see Figure S1, Supporting Information), and a preliminary X-ray analysis[13] of a mostly blue crystal from the same batch as **1b** show the $Cu(II)_2(OH)_2$ core in **2**. Assuming that the observed Cu- -Cu and O−O distances in **1b** are a weighted average of typical[14] bis(hydroxo) (2.93(5), 2.51(8) Å) and peroxo (3.52, 1.45 Å) values,[8] we estimate that **1b** contains about 80% **1a** and 20% **2**, but no Cu(III).[15] Complex **1b** does not disproportionate to $[Cu(Tp^{CF_3,CH_3})_2]$, the classical thermodynamic sink for Tp dinuclear complexes. Steric reasons might explain this observation since the CF_3 group is considered to be at least as sterically demanding as isopropyl,[16] and $[(CuTp^{^iPr,^iPr})_2(O_2)]$ is more stable than $[(CuTp^{CH_3,CH_3})_2(O_2)]$,[8b] whereas $[Cu(Tp^{R,R'})_2]$ complexes have been reported for R, R′ = CH$_3$ but not *i*-propyl.[17] Indeed, when R, R′ = *i*-propyl, H, respectively, a 3 → 5 steric relief isomerization is observed,[18] but in all cases the Cu(II) valence state is maintained. For comparison purposes, we prepared and structurally characterized $[Cu(Tp^{CF_3,CH_3})_2]$, **3**[19] (Figure S3). Its facile formation and stability (no isomerization) in noncoordinating solvents suggests that in $[Cu(Tp^{R,R'})_2]$ complexes the CF_3 group is, surprisingly, *less* sterically demanding compared with *i*-propyl. Unlike its nonfluorinated counterparts, however, **3** is redox unstable in coordinating solvents; acetonitrile reduces it quantitatively (based on copper) to $[Cu(I)Tp^{CF_3,CH_3}(ACN)]$, **4**.[4,20] The latter, which resists air oxidation both in solid-state and CH_2Cl_2 solutions, also forms when **1a** is dissolved in acetonitrile. The reductions of **1a** and **3** are consistent with the fluorine-induced higher value of the onset of electrochemical reduction potential of **3** in CH_2Cl_2, −0.21V compared with −1.55V (versus Ag/AgCl) for $[Cu(Tp^{CH_3,CH_3})_2]$. Thus, there are no steric reasons to prevent a shortening of Cu- -Cu distances in **1a** and, therefore, its collapse to a dinuclear Cu(III)bis(oxo) or Cu(II)bis(hydroxo) complex. We conclude that the steric protection the CF_3 groups may impart to the peroxo group in **1a** via encapsulation may stabilize it, while the robustness of C−F bonds and fluorine inductive effects facilitate the reversibility of O_2 binding by favoring Cu(I) over Cu(III) and ensuring the ligand integrity, respectively. Notably, ligand electronic deficiency is generally insufficient to impart stability. Thus, while the copper-peroxo complex of a tris(pyridine) ligand is unstable, covalently linking two such units into a dinucleating ligand improves its stability.[8a] The above illustrate the apparent paradoxical consequences of fluorination. The hard−soft acid base theory suggests that the "hardening" of a ligand should favor *higher* metal oxidation states and enhance its Lewis acidity, in contrast with our observations. In addition, B−N cleavage of Tp complexes, which is ascribed to the high Lewis acidity of Cu(II),[21] is not observed for **3** or during the solvent-induced reduction or oxygenation chemistry of **1a**.

Complexes **1b** and **2** form in toluene, even in the absence of water, possibly via H abstraction by **1a**, or by an unknown precursor, perhaps containing Cu(II). While the detailed mechanism remains to be established, the simultaneous formation and cocrystallization of **1a** and **2** suggests a minimum reorganizational energy upon H addition to **2** (likely a multistep process) and opens the possibility of using Cu(I)/Cu(II) systems protected from internal oxidative damage for the bioinspired oxygenation of external substrates.

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Supporting Information Available: Crystallographic tables for **1b** and **3**; figures S1, S2, and S3. This material is available free of charge at http://pub.acs.org.

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(13) Unit cell: $a = 11.582(2)$ Å, $c = 25.977(5)$ Å, $V = 3018.0(8)$ Å^3 at 173(2) K. $Z = 3$, $\rho_{calc} = 1.782$ g/cm^3. Space group *R*-3, trigonal; 159 parameters refined on F^2 gave R1 = 0.0492, wR2 = 0.1211 using 5421 reflections (1193 independent). A minor peroxide component is also present. Hu, Z.; Young, V. G., Jr.; Gorun, S. M., manuscript in preparation.

(14) Cambridge Crystallographic Database, October 2000 release.

(15) In a control calculation, by using the appropriate oxygen−copper bond lengths and the XAS Cu(II)/Cu(III) ratio, the weighted average procedure can also reproduce the X-ray determined Cu- -Cu and O−O distances of the Cu(II)/(Cu(III) solid solution.[11]

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(19) **3** was prepared by reacting stoichiometrically the ligand and $CuCl_2$ in acetone, filtering, evaporating the solvent, and recrystallizing the residue from CH_2Cl_2. X-ray quality crystals were obtained in 65% yield. Correct elemental analysis. Unit cell: $a = 10.2686(2)$ Å, $b = 10.8280(1)$ Å, $c = 11.4112(1)$ Å, $\alpha = 113.564(1)°$, $\beta = 99.739(1)°$, $\gamma = 111.220(1)°$, $V = 1008.35(2)$ Å^3 at 298(2) K. $Z = 2$, $\rho_{calc} = 1.617$ g/cm^3. Space group *P*1, triclinic. 576 parameters were refined on F^2 to R1 = 0.0483, wR2 = 0.1267 using 9598 reflections (7387 independent).

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