Irreversible Reduction of Dioxygen by Simple Peralkylated Diamine–Copper(I) Complexes: Characterization and Thermal Stability of a [Cu₂(μ-O)₂]²⁺ Core

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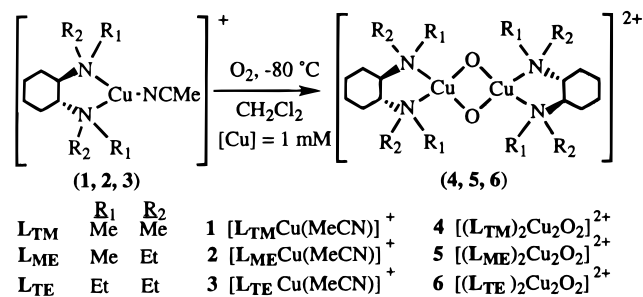David E. Root, Tapan K. Lal, Edward I. Solomon, and
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The reaction of O_2 with copper(I) plays a vital role in biological and synthetic oxidative catalysis.[1–6] Recent efforts have been directed toward elucidating the structure–reactivity relationship of these Cu/O_2 species through synthetic model systems.[2,7–13] Many of these systems are based on the well-characterized binuclear copper protein hemocyanin (Hc) in which each Cu is ligated by three histidine residues in both the oxidized and reduced form.[14] In an attempt to emulate this natural system, most studies have focused on sterically encumbered tridentate nitrogen ligands to the exclusion of simple diamine ligands.[2,15–18] Yet, in both OxyHc and all structurally characterized model Cu/O_2 intermediates employing such tridentate ligands,[2,13,16–18] a single axial nitrogen atom is always weakly bound, suggesting that bidentate N-ligation of each copper alone may be capable of stabilizing Cu/O_2 intermediates.

Presented here is a study of the characterization and reactivity of the Cu/O_2 species generated from the reaction of O_2 and a series of Cu(I) peralkylated-1,2-cyclohexanediamine[19] complexes at −80 °C (Scheme 1). The species produced are 2:1 Cu:O_2 complexes in which the O_2 bond is fully cleaved—a recurring theme in the reactivity of simple Cu(I) peralkylated-diamine complexes with O_2.[7,9] Subtle variations of the ligand N-alkyl substituents dramatically alter the thermal stability of the resulting complexes, with the least sterically bulky ligand (L_{TM}) generating the most stable complex. Since these complexes primarily degrade by a mechanism most consistent with a hydrogen atom abstraction (HA) of accessible NC^{α}–H bonds of the alkyl substituents (*vide infra*), complexes containing substituents with stronger C–H bonds (Me) are more stable.

The reaction of each ligand with $[Cu(MeCN)_4](CF_3SO_3)$ yields a trigonal-planar Cu(I) complex with MeCN as a labile auxiliary.[20] These copper(I) complexes, **1**–**3** (Scheme 1), react with O_2 at −80 °C in CH_2Cl_2 to afford the yellow-brown, thermally unstable, diamagnetic[21] species **4**–**6**, respectively. The UV/Vis and resonance Raman (rR) spectroscopic features (Table 1) of **4**–**6** are characteristically intense and similar, consistent with a series of isostructural complexes. Their intense optical absorptions are attributed to ligand-to-metal charge transfer (LMCT) based on the relatively low energy and associated rR enhancement of these transitions. A 2:1 (Cu:O_2) stoichiometry has been directly established in the case of **5** and **6** by manometry.[22] The incorporated O_2 is not displaced from the adducts by CO(g) or PPh_3, or by evacuation and heating. These complexes decompose upon warming, with partial N-dealkylation of the ligand and formation of aldehydic products.[23]

Thermally sensitive crystals of **5** were characterized by X-ray diffraction.[24] The extremely well-ordered ($R = 0.052$) unit cell contains a binuclear $[(L_{ME})_2Cu_2(\mu_2\text{-}O)_2]^{2+}$ cluster in which the O–O bond is cleaved, consistent with the observed irreversibility of O_2 binding (Figure 1). The $[Cu_2(\mu_2\text{-}O)_2N_4]^{2+}$ unit is nearly planar,[25] and each Cu is ligated in a square-planar N_2O_2 environment. Although the ligand alkyl substituents could potentially adopt a number of different conformations, a highly ordered, *pseudo-C_2-symmetric* alternation of ethyl and methyl substituents within each ligand and between each ligand is observed. This arrangement maximizes the steric protection of the $[Cu_2(\mu_2\text{-}O)_2]^{2+}$ core. The most striking metrical parameters are the extremely short Cu–O bonds to both metals (average

Scheme 1

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(19) The (1*R*,2*R*)-cyclohexanediamine backbone was chosen for both its preorganized nature and its chirality. The enantiomeric purity of the ligand significantly reduces the probability of forming diastereomeric binuclear metal complexes.

(20) **3** has been characterized by single-crystal X-ray diffraction.[9]

(21) By solution EPR and NMR susceptibility measurements at −80 °C.

(22) In our hands, manometric measurements required concentrated (40 mM) solutions of the Cu(I) precursors. In the case of **1**, oxygenation of a concentrated (>5 mM) CH_2Cl_2 solution results in formation of a 3:1 species.[9] Formally, the 3:1 Cu:O_2 complex could result from the equimolar reaction of $[(L_{TM})_2Cu_2(\mu_2\text{-}O)_2]^{2+}$ with $[L_{TM}Cu(MeCN)]^+$; however, titrations of the Cu(I) complex with the dimer under N_2 atmosphere results in the reduction of the dimer to $[(L_{TM})_2Cu_2(\mu_2\text{-}OH)_2]^{2+}$. Therefore, $[(L_{TM})_2Cu_2(\mu_2\text{-}O)_2]^{2+}$ is not an intermediate in the pathway leading to the formation of the 3:1 complex.

(23) Similar reactivities has been documented for the TACN derivatives.[7]

(24) Crystal data for [**5**]·(CF₃SO₃)₂·4CH₂Cl₂: yellow-brown rhombic blocks from cold (−80 °C) CH_2Cl_2/ether; monoclinic $P2_1$ (No. 4), $a = 12.1336(2)$ Å, $b = 11.9387(3)$ Å, $c = 18.4717(3)$ Å, $\beta = 108.387(1)°$, $V = 2539.19(8)$ Å³, $Z = 4$, $R(R_w) = 5.2(6.1)$.

(25) The $Cu_2O_2N_4$ unit is planar to within 0.07 Å rms deviation.

Figure 1. ORTEP representation (50% probability) of the crystal structure of [**5**]·(CF$_3$SO$_3$)$_2$·4CH$_2$Cl$_2$. Unlabeled ellipsoids represent carbon atoms, and open circles represent hydrogen atoms. Selected interatomic distances (Å): Cu(1)−O(1), 1.814(6); Cu(1)−O(2), 1.809(6); Cu(2)−O(1), 1.796(6); Cu(2)−O(2), 1.804(6); Cu(1)···Cu(2), 2.743(1); O(1)···O(2) 2.344(1).

Table 1. Selected Spectroscopic and Kinetic Data for the Cu/O$_2$ Complexes

Complex	Cu···Cu distance (Å)	LMCT bands (nm) (M^{-1}cm^{-1}) per dimer	rR shift (cm^{-1}) ^{16}O$_2$ (^{18}O$_2$) Δ (^{18}O$_2$)	$\Delta H^{\ddagger}$ (kcal/mol) $\Delta S^{\ddagger}$ (cal/mol)	k (sec^{-1}) ($t_{1/2}$ [sec]) at -10 °C
[(L$_{TM}$)$_2$Cu$_2$O$_2$]$^{2+}$ * **4**		296 (20,000) 392 (25,000)	605 (581) Δ = 23 cm^{-1}	13.4(2) −24(1)	0.0002 (3500)
[(L$_{ME}$)$_2$Cu$_2$O$_2$]$^{2+}$ * **5**	2.743 (X-ray)	306 (21,000) 401 (28,000)	610 (587) Δ = 23 cm^{-1}	11.8(3) −25(1)	0.004 (170)
[(L$_{TE}$)$_2$Cu$_2$O$_2$]$^{2+}$ * **6**		312 (17,000) 406 (23,000)	616 (590) Δ = 26 cm^{-1}		0.033 (20)
[L$_2$Cu$_2$O$_2$]$^{2+}$ * L=TACN^{Me_3}		300 (12,000) 405 (11,000)	604 (581) Δ = 23 cm^{-1}	12.7(1) −18(3)	0.017 (40)
[L$_2$Cu$_2$O$_2$]$^{2+}$ **11** L=TACN^{Bn_3}	2.794 (X-ray)	318 (12,000) 430 (14,000)	602/608(583) Δ = 23 cm^{-1}	13.0(2) −13(2)	0.096 (7)
[LCu$_2$O$_2$]$^{2+}$ **13** L=*i*Pr$_4$dtne	2.783 (X-ray)	316 (14,000) 414 (13,000)	600 (582) Δ = 18 cm^{-1}	13.5(5) −14(2)	0.029 (24)

* This work

Cu−O: 1.81 Å). The core is nearly isostructural[26] with that of [(TACN^{Bn}3)$_2$Cu$_2$O$_2$]$^{2+}$,[13,17] although the Cu···Cu distance is shorter by 0.05 Å, possibly due to the reduced steric repulsion between the two organic ligands. A Cu absorption K-edge study of **5** indicates a formal +3 oxidation state for the coppers.[27] Therefore, the isostructural species **4−6** are best described as bis(μ-oxo)dicopper(III) complexes.

In **4−6**, the Cu(III) oxidation state is greatly stabilized by the bridging oxide ligands and the overall square-planar coordination geometry around each copper.[28] Accordingly, these complexes behave as *mild* one-electron oxidants, with reduction potentials near +500 mV vs SCE as assessed by titrations with ferrocene derivatives.[29] However, these complexes are unable to oxidize oxygen-atom transfer substrates (PPh$_3$ and organic sulfides) even upon warming.

Despite their structural similarity, **4−6** are starkly differentiated by their rates of thermal decomposition. At −10 °C (1.0 mM, N$_2$), **4−6** undergo spontaneous decomposition accompanied by ligand dealkylation, a process that obeys first-order kinetics.[30] The thermal stability of **4−6** is inversely correlated to the number of *N*-ethyl substituents: **4** is nearly 200 times more stable than **6**. It is clear that for the purpose of stabilizing these [Cu$_2$(μ_2-O)$_2$]$^{2+}$ cores, *N*-methyl substituents are preferable to bulkier *N*-alkyl substituents with NC$^{\alpha}$−H bonds. Bidentate nitrogen ligation also enhances thermal stability relative to tridentate ligation (Me$_3$TACN), as indicated by the ~100-fold difference in the half-lives of the corresponding permethylated derivatives (entries 1 and 4, Table 1).

Kinetic measurements and ligand product analysis suggest that decomposition of **4−6** is initiated by activation of an NC$^{\alpha}$−H bond of an alkyl substituent.[7] The thermal degradation of **5** provides the most refined insight into the process, as this complex incorporates equally accessible ethyl and methyl substituents. Product analysis indicates a clean selectivity among these groups: an *N*-ethyl substituent is removed exclusively, with formation of acetaldehyde. Substitution of the *N*-ethyl α-hydrogens in **5** with deuterium results in a k_H/k_D of 3.0[31] for the decomposition; hence, the rate determining step must involve cleavage of an *N*-ethyl C$^{\alpha}$−H bond. Examination of the relevant activation parameters (Table 1)[32] reveals that the 20-fold disparity in decomposition rates between **4** and **5** arises solely from the differing enthalpies of activation

($\Delta\Delta H^{\ddagger}_{TM-ME}$ = 1.6 kcal/mol). This value matches the anticipated difference in NC$^{\alpha}$−H bond energies for methylene and methyl groups (~1.5 kcal/mol)[33,34] and is consistent with an HA mechanism. Further evidence supports the involvement of radicals in this mechanism: (i) the decomposition rate is slowed ~2-fold in the presence of 1 atm of O$_2$ and (ii) reaction of **4−6** with 2,4,6-tri-*tert*-butylphenol yields the phenoxyl radical and the corresponding bis(μ-hydroxo)dicopper(II) complex [L$_2$Cu$_2$-(μ_2-OH)$_2$]$^{2+}$, as characterized by optical and EPR spectroscopy.

A family of simple diamine−Cu(I) complexes have been synthesized and their corresponding low-temperature oxygen adducts structurally and spectroscopically characterized as bis-(μ-oxo)dicopper(III) species. The square-planar geometry and bridging dianionic oxide ligands in the [Cu$_2$(μ_2-O)$_2$]$^{2+}$ core provide a nearly ideal coordination environment for Cu(III), facilitating the 4e$^-$ reduction of dioxygen by only two Cu(I) centers. Such reactivity involving O−O bond cleavage is ubiquitous among all chelating diamine Cu(I) complexes characterized to date[35] (>15), indicating that the [L$_2$Cu$_2$(μ_2-O)$_2$]$^{2+}$ structural motif constitutes a large class of Cu/O$_2$ species. The character of this core is that of a mild oxidant that preferentially reacts through a HA mechanism. Fortuitously, the least bulky *N*-alkyl substituent (Me) affords the most stable [Cu$_2$(μ_2-O)$_2$]$^{2+}$ complex due to the relatively higher strength of the accessible NC$^{\alpha}$−H bonds, preserving the potential for reactivity with exogenous organic substrates. Such reactivity is currently being investigated.[36]

Supporting Information Available: Synthetic details and spectroscopic data for **1−6**, crystallographic data for **5**, and experimental details for the kinetic and ligand product analysis (16 pages). See any current masthead page for ordering and Internet access information.

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(36) The lithium salt of cinnamyl alcohol reacts quantitatively with [(**L**$_{TM}$)$_2$Cu$_2$(μ_2-O)$_2$]$^{2+}$ at −80 °C, to yield cinnamaldehyde.