

Exogenous Substrate Reactivity with a [Cu(III)₂O₂]²⁺ Core: Structural Implications

Viswanath Mahadevan,[†] Jennifer L. DuBois,[†]
Britt Hedman,^{*,†,‡} Keith O. Hodgson,^{*,†,‡} and T. D. P. Stack^{*,†}

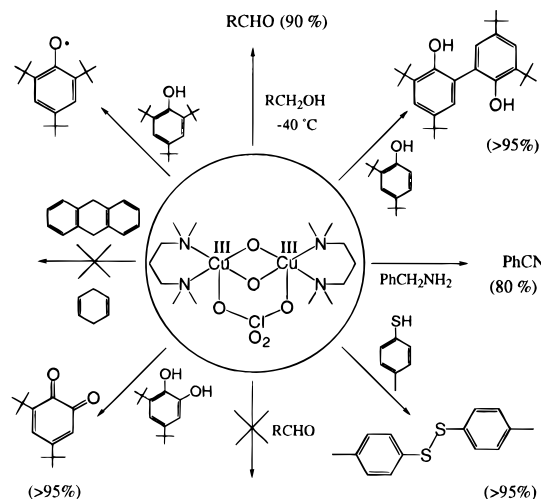
Department of Chemistry, Stanford University
Stanford, California 94305
Stanford Synchrotron Radiation Laboratory, SLAC
Stanford University, Stanford, California 94309

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Reactions of Cu(I) complexes with dioxygen are known to generate a structurally diverse array of oxidants in industrial and biological processes. Much effort has been directed toward the spectroscopic and structural characterization of the reactive species.^{1,2} The combination of low-temperature and bulky ligands has proven to be useful for successfully stabilizing and characterizing Cu/O₂ intermediates.^{3–7} However, the reactivities of these intermediates are usually limited to intramolecular ligand oxidation^{8–12} or intermolecular oxidation of readily oxidized substrates. In the latter case, the observed reactivity is plausibly explained by an atom-transfer mechanism involving the dioxygen derived ligands without precoordination of the substrate to the metal center. A balanced ligand design that precludes deleterious bimolecular reactions, yet allows substrate binding to the copper centers, is an attractive and intuitive means of converting these well-characterized Cu/O₂ intermediates into synthetically useful oxidants.¹³ Notable advances in the catalytic use of dioxygen as a terminal oxidant in alcohol oxidations with copper complexes has been the subject of several recent reports.^{14–16}

Recent work in [Cu(I)L] dioxygen chemistry has shown the prevalent formation of a bis- μ -oxo-dicopper(III) core, [L₂Cu(III)₂(O)₂]²⁺, at low temperatures and with weakly coordinating anions, where L is one of a wide variety of peralkylated-diamine or -triamine ligands.^{7,17,18} These high-valent metal-oxo species preferentially act as mild 2e⁻ oxidants and generally decompose

Scheme 1



upon warming (> -40 °C) by oxidizing an alkyl substituent of the ligand through a mechanism of NC^α-H hydrogen atom abstraction (HA).^{9,17} Consistent with this mechanism, [(L_{TMCHD})₂Cu(III)₂(O)₂]²⁺ (**1**) (TMCHD = *N,N,N',N'*-tetramethyl-(*1R,2R*)-cyclohexanediamine) proved to be the most thermally robust complex among the series of ligands examined in our previous report.¹⁷ Its limited reactivity with exogenous substrates prompted a more systematic study of the reactivity of other related complexes.¹⁹ *N,N,N',N'*-tetramethyl-(*1,3*)-propanediamine (L_{TMPD}) generates a thermally sensitive Cu/O₂/L_{TMPD} species, **2**,²⁰ spectroscopically similar to **1**.¹⁷ However unlike **1**, it readily oxidizes a variety of alcohols and benzylamines in respectable yields. A distinct structural difference between **1** and **2**, namely the ability to accommodate a fifth exogenous ligand in **2**, most readily explains this difference in reactivity.

Equimolar quantities of [Cu(I)(PhCN)₄](Y) (Y = CF₃SO₃⁻ or ClO₄⁻) and L_{TMPD} react rapidly in CH₂Cl₂ with dioxygen at -80 °C to generate [(L_{TMPD})₂Cu(III)₂(O)₂]²⁺ (**2**).²¹ The reactivity of **2** with readily oxidized substrates is largely similar to that of other [L₂Cu(III)₂(O)₂]²⁺ cores, as it rapidly and quantitatively (>95%) oxidizes 2,4-di-*tert*-butyl phenol, 3,5-di-*tert*-butyl catechol, and thiocresol at -80 °C (Scheme 1).²² Substrates with weak C-H bonds (e.g., 1,4-cyclohexadiene and 9,10-dihydroanthracene),²³ are not appreciably oxidized at -40 °C.²⁴

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(19) Five such [L₂Cu(III)₂(O)₂]²⁺ complexes do not react significantly ($\leq 2\%$) with benzyl alcohol at -80 °C or even on warming to 25 °C. (L = *N,N,N',N'*-tetramethyl-(*1R,2R*)CHD; *N,N'*-dimethyl *N,N'*-diethyl-(*1R,2R*)CHD; *N,N',N',N'*-tetraethyl-(*1R,2R*)CHD; *N,N'*-dimethyl *N,N'*-dibenzyl-(*1R,2R*)CHD and *N,N',N',N'*-tetraethylethylenediamine; CHD = cyclohexanediamine).

(20) [(L_{TMCHD})₂Cu(III)₂(O)₂](CF₃SO₃)₂ is ~5 times more stable ($t_{1/2}$ = 60 min) than [(L_{TMPD})₂Cu(III)₂(O)₂](CF₃SO₃)₂ ($t_{1/2}$ = 12 min) at -10 °C.

(21) (a) Optical spectroscopy shows characteristically intense ligand-to-metal charge-transfer (LMCT) bands at λ_{\max} = 290 nm (ϵ 16 000 M⁻¹ cm⁻¹) and 390 nm (ϵ 24 000 M⁻¹ cm⁻¹). (b) Resonance Raman data show an isotope sensitive feature at 609 cm⁻¹; $\Delta\nu$ (¹⁸O₂) = 28 cm⁻¹ (Henson, M. J.; Mahadevan, V.; Stack, T. D. P.; Solomon, E. I., unpublished results). (c) Electron paramagnetic resonance data at 77 K indicate a diamagnetic species. (d) Dioxygen binding is irreversible: dioxygen is not displaced upon warming either by evacuation or addition of CO(g). (e) An estimate of the reduction potential of **2** (~+500 mV versus SCE in CH₂Cl₂), is similar to that of **1** as established by titrations with suitable ferrocene derivatives: ~2 equiv of decamethylferrocene (-100 mV) are needed to fully quench the LMCT feature at 390 nm.

(22) Postulated structure of **2**(ClO₄)₂.

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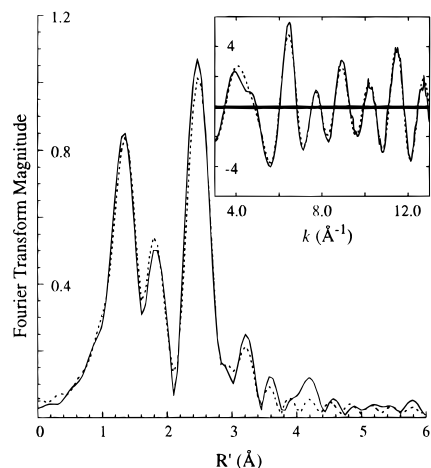


Figure 1. Fourier transform and (inset) EXAFS data and fit for $2(\text{CF}_3\text{SO}_3)_2$. Data are presented as solid lines, fits as dashed lines.

As X-ray quality crystals of **2** have been elusive, Cu K edge X-ray absorption spectroscopy (XAS) has been used to characterize the copper coordination. The spectrum for **2** exhibits a preedge feature at ~ 8980.5 eV, associated with the Cu(III) oxidation state in similar cores.²⁵ In contrast to other $[\text{L}_2\text{Cu(III)}_2\text{O}_2]^{2+}$ complexes with simple peralkylated-diamine ligands,¹⁷ the EXAFS data of **2** are best fit with penta- rather than tetra-coordinate copper centers (Figure 1).²⁶ The copper ligation consists of two oxygen scatterers at characteristically short distances ($\text{Cu}-\text{O}_{\text{ave}} = 1.81$ Å), two nitrogen scatterers ($\text{Cu}-\text{N}_{\text{ave}} = 2.01$ Å), and an additional oxygen scatterer at 2.32 Å.²⁷ The fifth ligand is metrically consistent with

(24) Reaction of 10 mM of $2(\text{ClO}_4)_2$ with 20 equiv of cyclohexadiene or dihydroanthracene at -40 °C for 20 h shows negligible substrate oxidation ($< 1\%$).

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(26) EXAFS data were collected at 10 K on two independently prepared solution (acetone) samples and one solid sample of $2(\text{CF}_3\text{SO}_3)_2$. Data were nearly identical within experimental uncertainty for all three samples. Fits to the data produced very similar structural models (See Supporting Information).

(27) Backscattering atoms which differ in Z by 1 are typically not distinguished by EXAFS (e.g., O and N) (Scott, R. A. *Methods Enzymol.* **1985**, *117*, 414). For the purposes of calculating phase and amplitude parameters, the copper ligation was modeled by two equivalent O, two equivalent N, and a longer axial O. Separate phase and amplitude parameters were calculated independently for each of these three ligand types. This is the basis for the distinction made between O and N backscatters in the EXAFS fit to the data.

(28) Solid $[(\text{Me}_3\text{TACN})_2\text{Cu}_2\text{O}_2](\text{CF}_3\text{SO}_3)_2$: $\text{Cu}-\text{Cu} = 2.77$ Å; $\text{Cu}-\text{O} = 1.81$ Å; $\text{Cu}-\text{N}_{\text{ave}} = 1.97$ Å; $\text{Cu}-\text{N} = 2.25$ Å. Results obtained from EXAFS data.

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(30) Yields for the oxidation of benzyl alcohol by $[(\text{L}_{\text{TMPD}})_2\text{Cu}_2\text{O}_2]^{2+}$ were higher for $[\text{Cu}(\text{PhCN})_4][\text{ClO}_4]$ or $[\text{Cu}(\text{PhCN})_4][\text{CF}_3\text{SO}_3]$ ($\sim 90\%$) as precursors rather than $[\text{Cu}(\text{MeCN})_4][\text{CF}_3\text{SO}_3]$ or $[\text{Cu}(\text{MeCN})_4][\text{ClO}_4]$ ($\sim 60\%$).

(31) **2** reacts with benzylamine at -80 °C to give benzonitrile (80%), and *N*-methyl benzylamine to give benzaldehyde (40%) but does not react with tertiary amines (all experiments performed under N_2).

(32) See Supporting Information.

(33) PhCHDO^- reacts upon mixing at -80 °C, whereas PhCHDOH requires -40 °C to react in a reasonable period of time ($t_{1/2} \approx 1$ h); $t_{1/2}$ for decay of **2** at -40 °C ~ 5 h. The oxidation of benzyl alcohol proceeds at -80 °C in the presence of 1.0 equiv of triethylamine in ~ 3 h (> 48 h in the absence of the amine).

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Table 1. Reaction of $2(\text{ClO}_4)_2$ with alcohols^a

alcohols	→	carbonyls	yield ³⁰
cinnamyl alcohol	→	cinnamaldehyde	90% (5) ^b
benzyl alcohol	→	benzaldehyde	90% (5)
α -methyl benzyl alcohol	→	acetophenone	60% (4)
cyclohexanol	→	cyclohexanone	70% (4)
1-octanol	→	1-octaldehyde	60% (4)

^a Reaction conditions: 10 mM of $2(\text{ClO}_4)_2$ with 2 equiv substrate at -40 °C in CH_2Cl_2 . ^b Number of experiments.

an axially ligated oxygen atom of a triflate anion. This expanded ligation is also consistent with a slight increase in the $\text{Cu}-\text{N}_{\text{ave}}$ (2.01 Å) and the $\text{Cu}-\text{Cu}$ distances (2.85 Å) relative to other $[(\text{L}_{\text{diamine}})_2\text{Cu(III)}_2(\text{O})_2]^{2+}$ complexes (e.g., $[(\text{L}_{\text{MECHD}})_2\text{Cu(III)}_2(\text{O})_2]^{2+}$ (**3**) $\text{MECHD} = N,N'$ -dimethyl N,N' -diethyl- $(1R,2R)$ -cyclohexanediamine, $\text{Cu}-\text{Cu} = 2.74$ Å, $\text{Cu}-\text{N}_{\text{ave}} = 1.94$ Å). Similar expansions of the $\text{Cu}-\text{Cu}$ and $\text{Cu}-\text{N}$ distances are observed in the 5-coordinate $[(\text{R}_3\text{TACN})_2\text{Cu(III)}_2(\text{O})_2]^{2+}$ ($\text{R} = \text{Me, Bn}$) species.^{28,29}

Complex **2** acts as a mild $2e^-$ oxidant which stoichiometrically converts alcohols (benzylic, allylic, and primary) to the corresponding aldehydes under mild conditions (-40 °C). Respectable yields are obtained in each case without measurable overoxidation (Table 1).^{30,31} Preliminary mechanistic data are most consistent with alcohol coordination, deprotonation, and finally oxidation. Nearly equivalent intramolecular primary kinetic isotope effects (KIE) using PhCHDOH or PhCHDO^- as substrates [$\text{KIE} = 4.8$ at 233 K]³² suggest that the product-determining steps of alkoxide and alcohol oxidation involve C–H bond cleavage. However, the dramatically different reaction rates between PhCH_2OH and PhCH_2O^- indicate that the rate-determining steps (RDS) are different.³³ For alcohols, deprotonation and C–H bond cleavage are not associated with the RDS since $k_{\text{PhCH}_2\text{OH}}/k_{\text{PhCH}_2\text{O}^-} = 1.1(1)$ at 253 K and $k_{\text{PhCH}_2\text{OH}}/k_{\text{PhCH}_2\text{O}^-} = 1.0(2)$ at 233 K. Further, the above results suggest that once the alcohol is bound, its dissociation is slow, relative to the C–H activation step. Further elucidation of the mechanism is underway.

The metrical and electronic features of the $[\text{Cu}_2(\text{O})_2]^{2+}$ core in **2** are similar to previously characterized bis-oxide-Cu(III) cores, yet the reactivity of **2** differs significantly. The subtle change in chelate-ring size from a 5-membered chelate in L_{TMCND} to a 6-membered chelate in L_{TMPD} provides sufficient flexibility in **2** to allow the proposed exogenous ligand coordination. This differential accessibility logically relates to the modulation of reactivity, reminiscent of hemocyanin (Hc) and tyrosinase (Tyr); the dioxygen intermediates of Hc and Tyr are electronically nearly identical, yet only Tyr oxidizes external substrates efficiently.^{2,34}

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Supporting Information Available: Synthetic details, optical spectrum of **2**, experimental details for kinetic, ligand product analysis and reaction of **2** with alcohols, amines (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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