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Dioxygen Activation by a Copper(I) Complex of a New Tetradentate Tripodal Ligand: Mechanistic Insights into Peroxodicopper Core Reactivity

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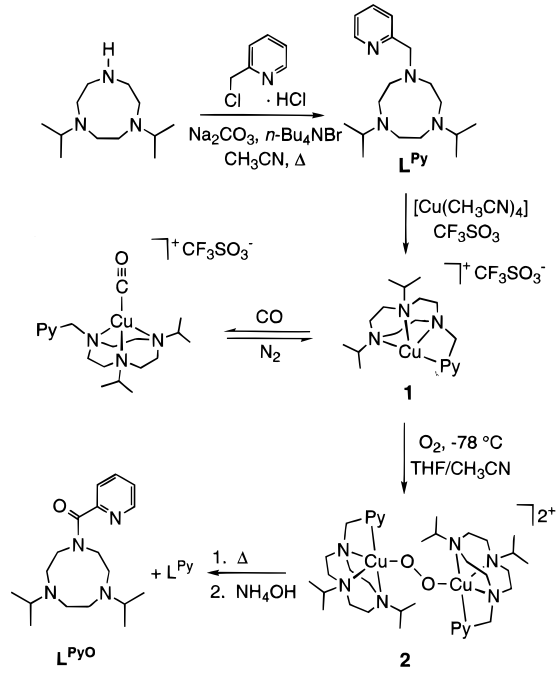
Oxidations mediated by copper and dioxygen in biological and synthetic systems generally proceed by initial formation of a Cu_n−O_2 adduct that then may attack a substrate directly or via intermediate steps (e.g., protonation, binding to an additional copper ion, or O−O bond scission). In efforts to elucidate the relationships between Cu_n−O_2 complex structure and function that underly oxidation pathways, we[1] and others[2] have endeavored to isolate, characterize, and examine the reactivity of superoxo-, peroxo-, and/or oxocopper complexes. Here we describe the CO and O_2 binding reactions of a copper(I) complex of a new N-donor ligand and our discovery of a novel oxidative reaction of a *trans*-1,2-peroxodicopper(II) complex that results in conversion of a ligand alkylamine group to an amide (a four-electron oxidation). A mechanism is proposed for this reaction involving an isomerization between *trans*-1,2- and μ-η^2:η^2-peroxo binding modes prior to C−H bond activation.

Scheme 1



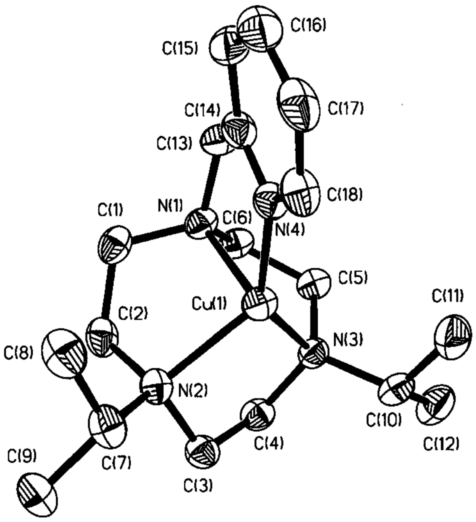


Figure 1. Thermal ellipsoid representation (50% probability; hydrogen atoms omitted for clarity) of one of the two crystallographically independent cations in the asymmetric unit of the X-ray crystal structure of $[L^{Py}Cu]CF_3SO_3$. Selected bond lengths (Å) and angles (deg) are as follows: Molecule 1, Cu(1)−N(1), 2.167(3); Cu(1)−N(2), 2.133(3); Cu(1)−N(3), 2.108(3); Cu(1)−N(4), 1.941(3); N(1)−Cu(1)−N(2), 85.75(11); N(1)−Cu(1)−N(3), 84.64(11); N(1)−Cu(1)−N(4), 86.21(12); N(2)−Cu(1)−N(3), 87.27(11); N(2)−Cu(1)−N(4), 131.05(12); N(3)−Cu(1)−N(4), 139.67(12). Molecule 2, Cu(2)−N(21), 2.175(3); Cu(2)−N(22), 2.090(3); Cu(2)−N(23), 2.133(3); Cu(2)−N(24), 1.939(3); N(21)−Cu(2)−N(22), 85.48(13); N(21)−Cu(2)−N(23), 85.69(13); N(21)−Cu(2)−N(24), 84.90(13); N(22)−Cu(2)−N(23), 86.98(12); N(22)−Cu(2)−N(24), 139.76(13); N(23)−Cu(2)−N(24), 130.97(12).

The copper(I) starting material $[L^{Py}Cu]CF_3SO_3$ (**1**) was isolated in 95% yield from the reaction of $[Cu(CH_3CN)_4]CF_3SO_3$ with L^{Py}, a sterically hindered tetradentate tripodal hybrid of the well-known 1,4,7-triazacyclononane (TACN) and tris(pyridylmethyl)amine (TMPA) ligand frames (Scheme 1).[3] An X-ray crystallographic analysis of the yellow complex [λ_{max} = 360 nm (ϵ 4100 M^{-1} cm^{-1}), assigned as a $Cu^I \rightarrow$ pyridyl metal-to-ligand charge transfer transition] revealed a trigonal pyramidal coordination geometry typical for copper complexes of tripodal ligands (Figure 1).[3] Reaction of $[L^{Py}Cu]CF_3SO_3$ with CO (1 atm) caused bleaching of the 360 nm absorption feature and growth of a ν_{CO} at 2067 cm^{-1}, consistent with binding of CO concomitant with displacement of the pyridyl arm to yield $[\eta^3$-$L^{Py}CuCO]CF_3SO_3$ (Scheme 1). Purging with N_2 cleanly reversed the process to regenerate **1**. Oxygenation of a solution of **1** in THF/CH_3CN (10:1 v/v) at −78 °C yielded a deep purple solution with spectroscopic properties indicative of a *trans*-1,2-peroxodicopper(II) complex having tetradentate L^{Py} coordination, $[(L^{Py}Cu)_2(O_2)](CF_3SO_3)_2$ (**2**). Complex **2** is EPR silent and exhibits UV-vis and resonance Raman spectral features closely analogous to those of Karlin's crystallographically characterized *trans*-1,2-peroxo complex capped by TMPA.[4,5]

Although stable for weeks at −78 °C, **2** decomposes upon warming both in the presence or absence of exogenous O_2 to yield a blue solution. Extraction of copper ions from this solution with NH_4OH yielded a mixture of L^{Py} and a new,

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(3) (a) Synthetic procedures and characterization data for all new compounds are provided as supporting information. (b) X-ray data for $[L^{Py}Cu]CF_3SO_3$, **1**: MW = 517.09, $C_{19}H_{32}CuF_3N_4O_3S$, crystal dimensions 0.50 × 0.28 × 0.09 mm, triclinic, space group *P*1, $a = 11.8518(1)$ Å, $b = 12.2046(2)$ Å, $c = 16.4397(1)$ Å, $\alpha = 89.264(1)°$, $\beta = 88.864(1)°$, $\gamma = 77.512(1)°$, $V = 2321.14(5)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.480$ g cm^{-3}, $2\theta_{max} = 50.02°$, Mo Kα radiation ($\lambda = 0.71073$ Å), T = 173 K. Data were collected using a Siemens SMART system, and the structure was solved via direct methods. A triflate anion and an isopropyl group were found to be disordered. Both groups were modeled using multiple rigid groups of occupancies 0.63:0.37 for the triflate and 0.144:0.404:0.452 for the 3-fold rotationally disordered isopropyl unit (see Supporting Information for details). Full-matrix least squares refinement on F^2 using SHELXTL V5.0 converged with final $R1 = 0.0490$ and $wR2 = 0.1000$ for 7845 independent reflections with $I > 2\sigma(I)$, 701 parameters, and 258 restraints.

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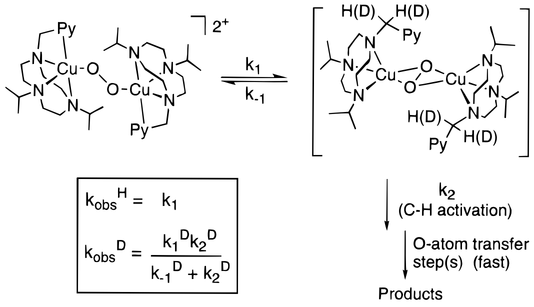
modified ligand L^{PyO} in a 4:1 ratio (∼75% total recovery).[3] When **2**-^{18}O derived from the reaction of $^{18}O_2$ with **1** was allowed to decompose, ^{18}O was incorporated into L^{PyO} (>95% by GC/MS). The conversion of L^{Py} to L^{PyO} thus represents a four-electron hydrocarbon oxidation, the novelty of which derives from the fact that it involves O atom transfer from a well-defined peroxodicopper species.[6]

We have begun to examine the mechanism of this oxidation reaction through a combination of kinetics and isotope labeling experiments. UV-vis monitoring of the decay of **2** in CH_3CN revealed a first-order dependence of the reaction rate on the concentration of **2** between −30 and 0 °C; $\Delta H^{\ddagger} = 12.6 \pm 0.5$ kcal mol^{-1} and $\Delta S^{\ddagger} = -23 \pm 2$ eu. The complex selectively deuterated at the pyridylmethyl position decomposed more slowly; $k_{obs}{}^{H}/k_{obs}{}^{D}$ (KIE) = 2.5(5) at −30 °C. In a double labeling experiment, equimolar solutions of $[(L^{Py}Cu)_2(O_2)]^{2+}$ and $[(d_{14}\text{-}L^{Py}Cu)_2(^{18}O_2)]^{2+}$ (deuterated at the isopropyl positions) were mixed at low temperature and allowed to decompose in the absence of exogenous O_2. A statistical mixture (1:1:1:1) of the isotopomeric amides L^{PyO}, L^{Py-18O}, d_{14}-L^{PyO}, and d_{14}-L^{Py-18O} was identified by GC/MS, indicating either that O-atom transfer is an intermolecular process or that peroxo ligands exchange between complexes faster than decomposition.

The first-order kinetics are consistent with the two rate-determining steps previously cited for peroxodicopper reactions: (i) O−O bond cleavage to monomeric $[CuO]^{1+}$ fragments[7] or (ii) direct intramolecular attack at the ligand C−H bond by the $[Cu_2(O_2)]^{2+}$ unit.[1] However, the observed negative $\Delta S^{\ddagger}$ argues against slow monomer generation, while the KIE much smaller than those typically seen for reactions in which cleavage of an aliphatic C−H bond by a Cu_2O_2 unit is unequivocably rate controlling (k^H/k^D = 20−30 at −30 °C)[1] argues against direct intramolecular C−H bond scission. Note also that geometric constraints prevent direct attack of the Cu_2O_2 unit at the benzylic C−H bond unless the pyridyl group first dissociates and rotates so as to allow the necessary C−H···O interaction to develop. We propose an alternative pathway involving a unimolecular isomerization followed by an as yet undefined C−H bond cleaving step (Scheme 2). Conversion of the *trans*-1,2-peroxide to a μ-η^2:η^2-peroxide (a "peroxide shift") accompanied by dissociation of the pyridylmethyl groups is an attractive hypothesis for the initial isomerization.[8] The feasibility of this notion is supported by the results of binding of CO to **1**, which induces pyridylmethyl arm dissociation (vide supra) as well as the additional finding that oxygenation of $[L^{iPr3}Cu(pyridine)]ClO_4$ (L^{iPr3} = 1,4,7-triisopropyl-1,4,7-triazacyclononane) in CH_2Cl_2 at −78 °C causes the ejection of pyridine and affords the known μ-η^2:η^2-peroxo complex $[(L^{iPr3}Cu)_2(O_2)](ClO_4)_2$.[1a,c] To explain the observation of a deuterium KIE of 2.5, which would be expected to be ∼1.0 if the "peroxide shift" were entirely rate-determining, we suggest that the rate-limiting step is influenced by the isotopic composition of the ligand. Thus, for the parent system we propose that the isomerization is slow ($k_{obs} = k_1$) and activation of the benzylic C−H bond ($k_2{}^H$) is fast. Upon ligand deuteration, however, the C−D bond cleavage step ($k_2{}^D$) becomes sufficiently slowed to become rate-determining, so that $k_{obs}{}^D = k_1{}^D k_2{}^D/(k_{-1}{}^D + k_2{}^D)$ (assuming a steady-state concentration for the μ-η^2:η^2-peroxo species).[9] As a result, the observed rate dependence $k_{obs}{}^H/k_{obs}{}^D$ = 2.5 is not a true primary KIE reflective of the nature of a single transition state.

Scheme 2



In sum, we have found a new reaction of a peroxodicopper complex of potential relevance to biological and catalytic hydrocarbon oxidations mediated by copper active sites. Preliminary mechanistic experiments implicate an intriguing, kinetically complex pathway for the four-electron oxidative transformation that we suggest involves a unimolecular isomerization of the peroxodicopper core as an initial step.

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Supporting Information Available: Experimental procedures and characterization data for all new compounds, kinetics data, and full details of the X-ray structure determination, including fully labeled thermal ellipsoid drawings of the cation in **1**, tables of bond lengths and angles, atomic positional parameters, and final thermal parameters (20 pages). See any current masthead page for ordering and Internet access instructions.

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[5] Spectroscopic data for **2**: UV-vis [λ_{max} (nm), ϵ (M^{-1} cm^{-1} per complex)] 550 (10,200), 600 (9700); Resonance Raman (λ_{ex} = 572 nm, 77K, 10:1 THF/CH_3CN) ν_{OO} = 822 cm^{-1} [$\Delta\nu(^{18}O)$ = 51 cm^{-1}], ν_{CuO} = 530 cm^{-1} [$\Delta\nu(^{18}O)$ = 24 cm^{-1}].

[6] For other four-electron oxidations of ligand pyridylmethyl or related groups promoted by copper ions, see: (a) Urbach, F. L.; Knopp, U.; Zuberbühler, A. D. *Helv. Chim. Acta* **1978**, *61*, 1097−1106. (b) Sprecher, C. A.; Zuberbühler, A. D. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 189. (c) Lee, D.-H.; Murthy, N. N.; Karlin, K. D. *Inorg. Chem.* **1996**, *35*, 804−805.

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[8] Precedent for isomerization of a *trans*-1,2-peroxo to a μ-η^2:η^2-peroxo complex exists, although the reported case was much more rapid, did not involve N-donor ligand dissociation, and was shown to proceed via the intermediacy of either monocopper-superoxo or dicopper(I) species. See: Jung, B.; Karlin, K. D.; Zuberbühler, A. D. *J. Am. Chem. Soc.* **1996**, *118*, 3763−3764.

[9] The change in the rate determining step due to deuteration is consistent with a KIE ($k_2{}^H/k_2{}^D$) of 20 as observed previously for isopropyl methine C−H bond cleavage by $[(L^{iPr3}Cu)_2(O_2)]^{2+}$ at −30 °C. From this estimated KIE we calculate $k_2{}^H = 1.6 \times 10^{-3}$ s^{-1}, which is an order of magnitude faster than the actual $k_{obs}{}^H$ (= 1.8×10^{-4} s^{-1}), in agreement with the hypothesis that the "peroxide shift" (k_1) step rather than the k_2 step is rate determining for the parent (nondeuterated) system.