Copper(I)/Dioxygen Reactivity with Dinuclear Compounds: Catalytic Oxygenation and Oxo-Transfer to a Ketone

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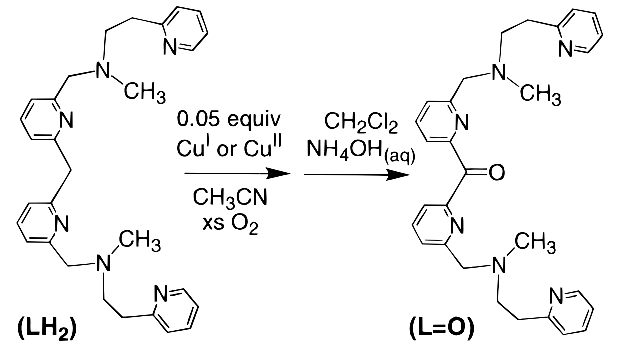
Received November 21, 1995

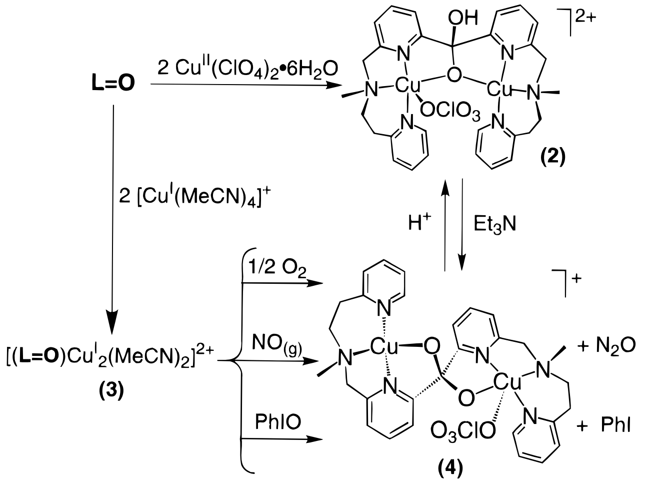
Investigations of copper(I)−O_2 interactions are of interest in the development of catalysts or reagents for oxidative transformations, and these may provide insights into copper−protein active-site structure, the nature of reactive intermediates, and oxidative mechanisms.[1] The use of dinucleating ligand complexes has been particularly useful in biomimetic studies of reversible O_2-binding in relation to the dicopper active site of the O_2-carrier protein hemocyanin and/or ligand−substrate oxidation by the monoxygenase tyrosinase.[1,2] Here, we describe new dinucleating ligands and their novel Cu(I)/O_2 reactivity.

Ketone **L═O** and reduced derivative **LH$_2$** were designed as new analogues of previously studied systems,[1,3] employing a linked set of tridentate chelates.[4] We find that the catalytic oxygenation of the methylene group of **LH$_2$** can be effected. Exposure of O_2 to an acetonitrile solution with **LH$_2$** containing 1/20 mole-equiv of either $[Cu^I(CH_3CN)_4](ClO_4)$ *or* $Cu^{II}(ClO_4)_2\cdot 6H_2O$ effects the rapid catalytic transformation to ketone **L═O** (20 turnovers; 86.1% and 90.2% isolated yields, respectively) (Scheme 1). Manometric O_2 uptake (0 °C) gives a **LH$_2$/O$_2$** = 1:1 ratio. The oxygenation reaction can be also effected noncatalytically, in a stoichiometric reaction, via O_2 reaction of isolated dicopper(I) complex $[(\mathbf{LH_2})Cu^I_2]^{2+}$ (**1**).[4] The yield of ketone is essentially quantitative, and utilization of $^{18}O_2$ in the **1**/O_2 reaction resulted in exclusive formation of **L═^{18}O**. To explore the possible role of Cu_2O_2 adducts (formally peroxodicopper(II) species) in its reactivity, **1(ClO$_4$)$_2$** was exposed to *1 equiv* of O_2 at −80 °C (via gastight syringe) in EtCN solvent.[5] However, warming to room temperature followed by workup resulted in *no* ketone formation, suggesting that direct oxygenation by a Cu(I)/O_2 derived species (i.e., "O_2-activation") is probably not involved. A separate observation is that use of excess Cu(II) ion with exposure to O_2 inhibits the oxygenation reaction; no ketone is formed. Thus, it appears that the presence of a base[6] is required, aiding carbanion formation from LH_2 (and/or one-electron oxidation), facilitating direct O_2-attack on the organic. The results and mechanistic suppositions are in accord with findings of Zuberbühler and co-workers,[7] who studied copper ion mediated oxygenation of related methylene containing bis(benzimidazol-2-yl)- or bis(2-pyridyl)methane compounds.[8]

Scheme 1



Scheme 2



We have further explored the chemistry of **L═O**, Scheme 2. Mixing this with two equiv $Cu^{II}(ClO_4)_2\cdot 6H_2O$ in CH_3CN solvent gives a blue solution, and the mono-alkoxide bridged product $[(\mathbf{L(OH)(O^-)})Cu^{II}_2(OClO_3^-)]^{2+}$ (**2**) is isolated in > 90% yield following precipitation with Et_2O.[9] The reaction represents a net hydration, also seen with various metal ions and with di-2-pyridyl or diimidazol-2-yl ketones.[10] In the present case, stabilization is provided by (monodeprotonation and) coordination to copper(II); we speculate that the hydration reaction is mediated by a juxtaposed $Cu^{II}_2OH_2$ or $Cu^{II}_2OH^-$ nucleophile.

To explore Cu(I)/O_2 reactivity, a dicopper(I) complex $[(\mathbf{L{=}O})Cu^I_2(CH_3CN)_2]^{2+}$ (**3**) was also isolated.[4] In CH_3CN, its reaction

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[1] For reviews see, (a) Kitajima, N.; Moro-oka, Y. *Chem. Rev.* **1994**, *94*, 737−757. (b) Fox, S.; Karlin, K. D. In *Active Oxygen in Biochemistry*; Valentine, J. S., Foote, C. S., Greenberg, A., Liebman, J. F., Eds.; Blackie Academic & Professional, Chapman & Hall: Glasgow, Scotland, 1995; pp 188−231. (c) Karlin, K. D.; Tyeklár, Z. In *Advances in Inorganic Biochemistry*; Eichhorn, G. L., Marzilli, L. G., Eds.; Prentice Hall: Englewood Cliffs, NJ, 1994; Vol. 9; pp 123−172.

[2] (a) Lee, D.-H; Wei, N.; Murthy, N. N.; Tyeklár, Z.; Karlin, K. D.; Kaderli, S.; Jung, B.; Zuberbühler, A. D. *J. Am. Chem. Soc.* **1995**, *117*, 12498−12513. (b) Sayre, L. M.; Nadkarni, D. *J. Am. Chem. Soc.* **1994**, *116*, 3157−3158.

[3] Karlin, K. D.; Tyeklár, Z.; Farooq, A.; Haka, M. S.; Ghosh, P.; Cruse, R. W.; Gultneh, Y.; Hayes, J. C.; Toscano, P. J.; Zubieta, J. *Inorg. Chem.* **1992**, *31*, 1436−1451 and references cited therein.

[4] See Supporting Information for synthesis, characterization, and X-ray structure information.

[5] Uptake of 1 equiv of O_2 by dicopper(I) complexes often results in the formation of Cu_2O_2 adducts which are stable at −80 °C.[1,3]

[6] The base may be either the polyamine ligand itself, or $O^{2-}/OH^-{-}Cu^{II}_n$ when formed from Cu(I)/O_2 chemistry.

[7] (a) Sprecher, C. A.; Zuberbühler, A. D. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 189. (b) Urbach, F. L.; Knopp, U.; Zuberbühler, A. D. *Helv. Chim. Acta* **1978**, *61*, 1097−1106.

[8] For a related Fe/O_2 mediated reaction, see: Guillot, G.; Mulliez, E.; Leduc, P.; Chottard, J.-C. *Inorg. Chem.* **1990**, *29*, 577−579.

[9] An X-ray analysis of **2** confirms the indicated structure.

[10] (a) Bandoli, G.; Dolmella, A.; Gerber, T. I. A.; du Preez, J. G. H.; Kemp, H. J. *Inorg. Chim. Acta* **1994**, *217*, 141−147. (b) Sommerer, S. O.; Baker, J. D.; Jensen, W. P.; Hamza, A.; Jacobson, R. A. *Inorg. Chim. Acta* **1993**, *210*, 173−176.

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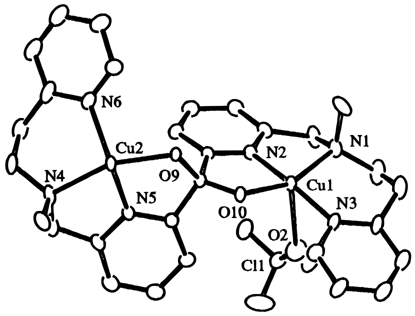
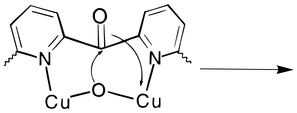


Figure 1. ORTEP (30% ellipsoids) view of cationic portion of $[(\mathbf{L(O^-)_2})\mathrm{Cu^{II}_2(OClO_3)}](\mathrm{ClO_4})\cdot 4\mathrm{CH_3CN}$ (**4(ClO₄)·4CH₃CN**).

with O_2 causes an immediate change to a green solution, from which $[(\mathbf{L(O^-)_2})\mathrm{Cu^{II}_2(OClO_3^-)}]^+$ (**4**) could be isolated in >95% yield (Scheme 2). An X-ray structure analysis[4] (Figure 1) reveals a μ-1,3-bridged *gem*-diolate unsymmetrical dicopper(II) complex with Cu···Cu = 5.583 (3) Å. *Thus, oxide (O^{2-}) addition to the ketone has been achieved with copper(I)-dioxygen reactivity.* $[(\mathbf{L(OH)(O^-)})\mathrm{Cu^{II}_2(OClO_3^-)}]^{2+}$ (**2**) and $[(\mathbf{L(O^-)_2})\mathrm{Cu^{II}_2(OClO_3^-)}]^+$ (**4**) are acid-base conjugate pairs (Scheme 2).

For the transformation $[(\mathbf{L{=}O})\mathrm{Cu^I_2(CH_3CN)_2}]^{2+}$ (**3**) + O_2 → $[(\mathbf{L(O^-)_2})\mathrm{Cu^{II}_2(OClO_3^-)}]^+$ (**4**), manometry indicates a reaction stoichiometry of **3**/O_2 = 2.0 (i.e., Cu/O_2 = 4:1), while mass spectrometric comparisons of samples of **3** reacted with $^{16}O_2$ vs $^{18}O_2$ are consistent with inclusion of *one* atom of O_2 into the product; the diolate oxygen atoms thus derive one from the original ketone and one from dioxygen. These observations point to the *complete* utilization and incorporation of both oxygen atoms from O_2, suggesting that it is *not* an initially formed Cu_2O_2 (peroxodicopper(II)) adduct, but rather an oxodicopper(II) species,[11-13] which effects the ketone oxygenation reaction. Initial formation of an unstable Cu_2O_2 adduct $[(\mathbf{L{=}O})\mathrm{Cu_2(O_2)}]^{2+}$ with subsequent attack by additional complex **3** (i.e., Cu/O_2 = 4:1)[14] could lead to a $\mathrm{Cu^{II}{-}O{-}Cu^{II}}$ species $\{[(\mathbf{L{=}O}))\mathrm{Cu^{II}_2(O^{2-})}]^{2+}\}$; this, however, must be unstable with respect to nucleophilic attack upon the proximate carbonyl group,[15] leading to dialkoxide $[(\mathbf{L(O^-)_2})\mathrm{Cu^{II}_2(OClO_3^-)}]^+$ (**4**).



(**4**)

Support for the proposition that a $\mathrm{Cu^{II}{-}O{-}Cu^{II}}$ species is involved comes from two other lines of evidence. Oxodicopper(II) complexes have also been generated by reacting copper(I) compounds with iodosylbenzene[12c,d] or nitric oxide.[12e] Indeed, reaction of $[(\mathbf{L{=}O})\mathrm{Cu^I_2(CH_3CN)_2}]^{2+}$ (**3**) with 1 equiv of PhIO under Ar gives $[(\mathbf{L(O^-)_2})\mathrm{Cu^{II}_2(OClO_3^-)}]^+$ (**4**) in 79% isolated yield; iodobenzene was detected qualitatively (e.g., by NMR spectroscopy) as the reaction byproduct (Scheme 2). Thus, an oxodicopper(II) species may form and react according to

$$[(\mathbf{L{=}O})\mathrm{Cu^I_2(CH_3CN)_2}]^{2+}\ (\mathbf{3}) + \mathrm{PhIO} \longrightarrow \{[(\mathbf{L{=}O})\mathrm{Cu^{II}_2(O^{2-})}]^{2+}\} + \mathrm{PhI}$$
$$\longrightarrow [(\mathbf{L(O^-)_2})\mathrm{Cu^{II}_2(OClO_3^-)}]^+\ (\mathbf{4})$$

Reaction of $[(\mathbf{L{=}O})\mathrm{Cu^I_2(CH_3CN)_2}]^{2+}$ (**3**) with NO(g) at −80 °C gives an intensely brown solution; removal of excess nitric oxide in vacuo followed by warming also gives **4** (86% yield). Nitrous oxide was detected (glc) in the head-space of the final reaction mixture,[12e] suggesting the mechanism

$$[(\mathbf{L{=}O})\mathrm{Cu^I_2(CH_3CN)_2}]^{2+}\ (\mathbf{3}) + 2\,\mathrm{NO(g)} \longrightarrow \{[(\mathbf{L{=}O})\mathrm{Cu_2(NO)_2}]^{2+}\}$$
$$\longrightarrow \{[(\mathbf{L{=}O})\mathrm{Cu^{II}_2(O^{2-})}]^{2+}\} + \mathrm{N_2O}$$
$$\longrightarrow [(\mathbf{L(O^-)_2})\mathrm{Cu^{II}_2(OClO_3^-)}]^+\ (\mathbf{4}).$$

The systems described further demonstrate how specific ligand design is important in defining the nature of observable chemistry. Here, copper(I)/O_2 reactivity is directed toward a substrate which is part of the dinucleating ligand, i.e., catalytic oxygenation of an activated methylene group or a novel ketone oxygenation reaction. In the latter chemistry, a reactive oxodicopper(II) species forms via Cu(I)/O_2 = 4:1 chemistry; the oxo group is subsequently "trapped" by the ligand carbonyl group. Higher nuclearity oxocopper(II) clusters are well described,[13,16] but no X-ray structures of discrete dinuclear $\mathrm{Cu(II){-}O^{2-}{-}Cu(II)}$ compounds exist.[17] Oxodicopper(II) species are known to transfer an oxygen atom to phosphines,[12a,d,e,18] and they are implicated in (catalytic) oxidative dehydrogenation reactions.[11,12b,18,19] We plan new syntheses and studies of the structure, physical properties, and scope of reactivity of oxo−Cu(II) complexes.

Acknowledgment. We thank Professor Susan Weintraub (U. Texas Health Sciences Center) for obtaining electrospray mass spectral data and analysis. We are grateful for the National Institutes of Health (Grant GM 28962) for research support.

Supporting Information Available: Text giving details of synthesis and physical characterization, an ORTEP diagram with complete atom labeling, and tables of crystal and refinement data, positional parameters, and bond lengths and angles for $[(\mathbf{L(O^-)_2})\mathrm{Cu^{II}_2(OClO_3^-)}](\mathrm{ClO_4})\cdot 4\mathrm{CH_3CN}$ (**4(ClO₄)·4CH₃CN**) (13 pages). The material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(15) Oxo−Cu(II) species are strongly basic.[11,13]

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