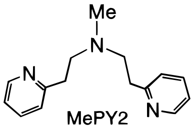
Peroxo-, Oxo-, and Hydroxo-Bridged Dicopper Complexes: Observation of Exogenous Hydrocarbon Substrate Oxidation

Honorio V. Obias,[†] Yin Lin,[†] N. N. Murthy,[†] Elna Pidcock,[‡] Edward I. Solomon,[‡] Martina Ralle,[§] Ninian J. Blackburn,[§] Yorck-Michael Neuhold,[‖] Andreas D. Zuberbühler,[‖] and Kenneth D. Karlin*,[†]

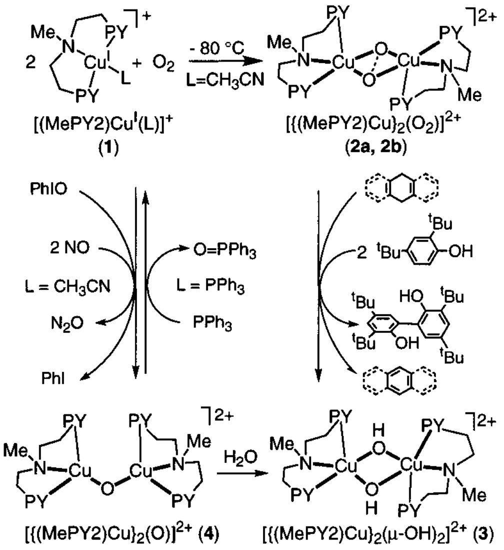
Department of Chemistry
The Johns Hopkins University
Baltimore, Maryland 21218
Department of Chemistry, Stanford University
Stanford, California 94305
Department of Chemistry, Biochemistry, and Molecular
Biology, Oregon Graduate Institute of
Science & Technology, Portland, Oregon 97291
Institut für Anorganische Chemie
University of Basel, CH-4056 Basel, Switzerland

Received May 29, 1998

Recent investigations of copper(I)/O_2 reactivity relevant to oxidative chemical processes and metalloenzyme active-site chemistry have led to considerable advances.[1] Nitrogen donor ligands are utilized in studies of $Cu_n-(O_2)$ or $Cu_n-(O)_2$ species, emphasizing kinetics−thermodynamics,[2] structures,[1] correlations to spectroscopy, and substrate reactivity. A number of X-ray crystal structures are now available,[1,3] including peroxo−dicopper(II) complexes either with μ-1,2 (end-on)[3a] or μ-η^2:η^2 (side-on)[1] coordination. $Cu^I{}_n/O_2$ reactions can directly give μ-oxo (O^{2-})−Cu(III) species, $Cu_n-(O)_2$ ($n = 2^{3b-e}$ or $n = 3^{3f}$), and Tolman and co-workers[3c] have shown that the interconversion of the μ-η^2:η^2-peroxo and bis-μ-oxo cores can occur. The nature of the ligand (i.e., denticity, flexibility, steric, or electronic factors) critically influences the structure formed and resulting reactivity patterns; the controlling factors are under both experimental and theoretical[4] scrutiny. Here, we describe new insights with copper complexes with MePY2.[5] We observe *both* side-on peroxo and bis-μ-oxo species in a single L-Cu^I/O_2 reaction, with novel reactivity toward *exogenous* substrates. A related mono-μ-oxo dicopper complex is also described, and its properties contrasted.


MePY2

Scheme 1



The side-on μ-η^2:η^2-peroxo−dicopper(II) ligation observed in the O_2-carrier protein hemocyanin[6] was first proposed in studies of O_2-adducts $[Cu_2(Nn)(O_2)]^{2+}$ {Nn are binucleating analogues of MePY2, with $-(CH_2)_n-$ (n = 3−5) linkers}.[7] Kitajima and co-workers firmly established this binding mode in an X-ray structure using pyrazolylborate ligands.[1a,8] Mononucleating ligands RPY2 (R = Me, Ph, $PhCH_2$,[9] or $PhCH_2CH_2$[10]) can also be utilized to generate similar complexes, $[\{(RPY2)Cu\}_2(O_2)]^{2+}$. Here, significant new insights are obtained by examination of reactions of $[(MePY2)Cu^I(CH_3CN)]BArF$ (**1**−BArF)[5,11] (Scheme 1; PY = 2-pyridyl). This reacts with O_2 at −80 °C in CH_2Cl_2 giving a solution species formulated as $[\{(MePY2)Cu\}_2(O_2)](BArF)_2$ (**2**−$(BArF)_2$) (but, see below) {manometry (3 trials) $Cu/O_2 = 2{:}1 \pm 15\%$; λ_{max} = 360 (ϵ = 14400), 410 (sh, 2500), 530 (400), 654 (300) nm; EPR silent; ^1H NMR spectrum, diamagnetic}. Stopped-flow kinetics measurements[11] reveal that the rate of *inter*molecular O_2-binding to copper in **2**−$(BArF)_2$ is considerably reduced compared to that seen for analogues with binucleating ligands, i.e., $[Cu_2(N4)(O_2)]^{2+}$ and $[Cu_2(XYL)(O_2)]^{2+}$ (XYL, with m-xylyl linker),[2,12] with $k_{on} = 1.91\ (\pm\ 0.03) \times 10^4\ M^{-2}\ s^{-1}$ at −20 °C in acetone ($\Delta H^\ddagger = -0.7 \pm 1$ kJ M^{-1}, $\Delta S^\ddagger = -164 \pm 4$ J K^{-1} M^{-1}); no intermediates are observed. Compared to *intra*molecular O_2-binding in those binuclear complexes, **2**−$(BArF)_2$ exhibits the strongest binding (enthalpically) yet seen for a Cu_2-O_2 species ($\Delta H_{on}° = -89 \pm 3$ kJ mol^{-1}), but is entropically destabilized {$\Delta S_{on}° = -240 \pm 9$ J K^{-1} M^{-1}.[2] **2**−$(BArF)_2$ is stable for days at

---

[†] Johns Hopkins University.

[‡] Stanford University.

[§] Oregon Graduate Institute.

[‖] University of Basel.

(1) (a) Kitajima, N.; Moro-oka, Y. *Chem. Rev.* **1994**, *94*, 737−757. (b) Karlin, K. D.; Zuberbühler, A. D. In *Bioinorganic Catalysis, 2nd ed.*, revised and expanded; Reedijk, J., Bouwman, E., Eds.; Marcel Dekker: New York, 1999, in press. (c) Kopf, M.-A.; Karlin, K. D. In *Biomimetic Oxidations*; Meunier, B., Ed.; Imperial College Press: London, 1999, Ch. 7, in press.

(2) Karlin, K. D.; Kaderli, S.; Zuberbühler, A. D. *Acc. Chem. Res.* **1997**, *30*, 139−147.

(3) (a) Tyeklár, Z.; Jacobson, R. R.; Wei, N.; Murthy, N. N.; Zubieta, J.; Karlin, K. D. *J. Am. Chem. Soc.* **1993**, *115*, 2677−2689. (b) Mahapatra, S.; Young, J. V. G.; Kaderli, S.; Zuberbühler, A. D.; Tolman, W. B. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 130−133. (c) Halfen, J. A.; Mahapatra, S.; Wilkinson, E. C.; Kaderli, S.; Young, V. G., Jr.; Que, L., Jr.; Zuberbühler, A. D.; Tolman, W. B. *Science* **1996**, *271*, 1397−1400. (d) Mahapatra, S.; Halfen, J. A.; Wilkinson, E. C.; Pan, G.; Wang, X.; Young, J. V. G.; Cramer, C. J.; Que, L., Jr.; Tolman, W. B. *J. Am. Chem. Soc.* **1996**, *118*, 11555−11574. (e) Mahadevan, V.; Hou, Z.; Cole, A. P.; Root, D. E.; Lal, T. K.; Solomon, E. I.; Stack, T. D. P. *J. Am. Chem. Soc.* **1997**, *119*, 11996−11997. (f) Cole, A. P.; Root, D. E.; Mukherjee, P.; Solomon, E. I.; Stack, T. D. P. *Science* **1996**, *273*, 1848−1850.

(4) (a) Cramer, C. J.; Smith, B. A.; Tolman, W. B. *J. Am. Chem. Soc.* **1996**, *118*, 11283−11287. (b) Liu, X.-Y.; Palacios, A. A.; Novoa, J. J.; Alvarez, S. *Inorg. Chem.* **1998**, *37*, 1202−1212. (c) Bérces, A. *Inorg. Chem.* **1997**, *36*, 4831−4837.

(5) Abbreviations used: PY2 = bis[2-(2-pyridyl)ethyl]amine; BArF = $B[3,5\text{-}(CF_3)_2C_6H_3]_4^-$; EXAFS, Extended X-ray Absorption Fine Structure.

(6) Magnus, K. A.; Ton-That, H.; Carpenter, J. E. *Chem. Rev.* **1994**, *94*, 727−735.

(7) (a) Blackburn, N. J.; Strange, R. W.; Farooq, A.; Haka, M. S.; Karlin, K. D. *J. Am. Chem. Soc.* **1988**, *110*, 4263−4272. (b) Pidcock, E.; Obias, H. V.; Karlin, K. D.; Solomon, E. I. *J. Am. Chem. Soc.*, in press.

(8) This research group also characterized mono-μ-oxo and corresponding bis-μ-hydroxo−dicopper(II) compounds which could be used to generate their peroxo species, thus relating the three complexes. See ref 1a.

(9) Sanyal, I.; Mahroof-Tahir, M.; Nasir, S.; Ghosh, P.; Cohen, B. I.; Gultneh, Y.; Cruse, R.; Farooq, A.; Karlin, K. D.; Liu, S.; Zubieta, J. *Inorg. Chem.* **1992**, *31*, 4322−4332.

(10) Itoh, S.; Nakao, H.; Berreau, L. M.; Kondo, T.; Komatsu, M.; Fukuzumi, S. *J. Am. Chem. Soc.* **1998**, *120*, 2890−2899.

(11) See Supporting Information.

(12) Jung, B.; Karlin, K. D.; Zuberbühler, A. D. *J. Am. Chem. Soc.* **1996**, *118*, 3763−3764.

10.1021/ja981878h CCC: $15.00

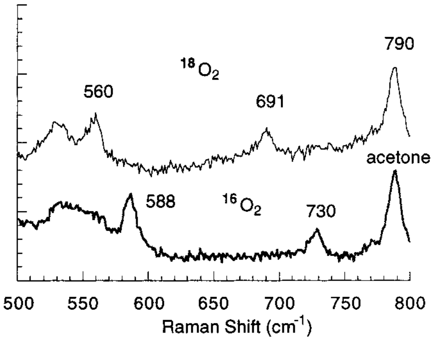


Figure 1. Solution resonance raman spectrum of dioxygen adduct of **1** in acetone at −90 °C (386 nm excitation).

−80 °C in CH_2Cl_2, but decomposition (decrease in UV−vis intensity) occurs after 100 min for the corresponding ClO_4^- analogue, whereas the PF_6^- derivative degrades quickly.[16] The intense absorption at 360 nm is characteristic of the side-on peroxo ligation,[3d,15] as is the very low energy resonance Raman band (Figure 1), ν(O−O) = 730 cm^{-1}, to 691 cm^{-1} with $^{18}O_2$ substitution. However, the UV−vis and resonance Raman signatures[3d,e] for the bis-μ-oxo−dicopper(III) core (**2b**) are also observed; ν = 588 cm^{-1} ($^{16}O_2$; 560 cm^{-1} with $^{18}O_2$), and preliminary profile studies indicate that the UV−vis 410 nm shoulder is associated with $[\{(MePY2)Cu\}_2(O)_2]^{2+}$ (**2b**). We estimate this form (**2b**) to be present to the extent of 1−10% relative to that of the side-on peroxo species $[\{(MePY2)Cu\}_2(\mu\text{-}\eta^2{:}\eta^2\text{-}O_2)]^{2+}$ (**2a**).

Precipitation of **2**−(BArF)$_2$ by addition of heptane at ≤−80 °C affords a dark purple solid, which is stable for weeks when stored cold. Redissolution in cold CH_2Cl_2 gives the same UV−vis spectrum observed in the **1**/O_2 reaction. Thus, peroxo (**2a**) and bis-μ-oxo (**2b**) complexes may be in rapid equilibrium, as seen in Tolman's systems.[3c,16] Factor analysis of the **1**/O_2 reaction kinetics (i) excludes the independent formation of two species, whereas (ii) the subsequent decay of **2** is not wavelength dependent.

The dioxygen adduct mixture **2** is most stable as a cold solution in CH_2Cl_2 solvent, but **2**−(BArF)$_2$ and **2**−(ClO$_4$)$_2$ decompose upon warming in all solvents, cleanly affording the blue-green bis-μ−hydroxo−dicopper(II) complex $[\{MePY2)Cu^{II}\}_2(\mu\text{-}OH^-)]^{2+}$ (**3**) (Scheme 1), (λ_{max}($CH_2Cl_{2)}$ = 366 (ϵ = 4000), 640 (150) nm; $\nu_{(O-H)}$ = 3659 cm^{-1}; μ_{eff}/Cu = 1.49 μ_B; paramagnetically shifted ^{1}H NMR spectrum). An X-ray structure[11] of the perchlorate salt defines this often observed (ligand)/Cu^I/O_2 degradation product and structure type.[3d−f,14b] Cu···Cu = 3.012 (1) Å, Cu−O = 1.953 (3)$_{ave}$.

Reaction of **2**−(BArF)$_2$ (−80 °C; excess O_2 removed) with added substrates is observed (Scheme 1): (i) Addition of 2,4-di(*tert*-butyl)phenol gives **3** plus the phenoxyl radical derived coupling product 3,3′,5,5′-tetra-*tert*-butyl-2,2′-dihydroxybiphenyl. This reaction is complete in minutes (−80 °C), as followed by UV−vis (640 nm) spectroscopic formation of **3**. (ii) The thermal decomposition of **2**−(BArF)$_2$ in tetrahydrofuran (THF) solvent cleanly affords **3**; monitoring of this pseudo-first-order reaction (−80 °C) in THF-d_8 yields a k_H/k_D = 3.2. (iii) Reaction of dihydroanthracene and 1,4-cyclohexadiene (∼1 equiv) gives complete conversion of **2** to **3** after ∼16 h at −80 °C, on a UV−vis scale. On a synthetic scale, reaction with 1 equiv of substrate gave anthracene (>80%) and benzene (>70%), respectively. These results point to the ability of **2** to effect clean hydrogen-atom abstraction reactions, seen elsewhere[1b,c,3d,e,10,17] as *intra*molecular processes for peroxo or bis-μ-oxo complexes on the copper-ligand as substrate,[18] but here observed for exogenously added hydrocarbon substrates.[3e,19]

Another type of μ-oxo−copper complex, with contrasting behavior, can be generated by reaction of $[(MePY2)Cu^I(CH_3CN)]^+$ (**1**) with $NO_{(g)}$ in THF solution, producing $[\{MePY2)Cu^{II}\}_2(\mu\text{-}O)]^{2+}$ (**4**) (λ_{max} = 345 (4000), 680 (100) nm) (Scheme 1); N_2O product was detected qualitatively by gas chromatography (GC).[20] Reaction of **1** with 1 equiv of iodosylbenzene (PhIO) as the O-atom donor also produces **4** along with 1 equiv of PhI (GC and NMR). Contrasting with the physical properties of $[\{MePY2)Cu^{II}\}_2(\mu\text{-}OH^-)]^{2+}$ (**3**), those of **4** have a $\nu_{(O-H)}$ vibration which is absent, whereas its magnetic properties indicate stronger antiferromagnetic coupling between Cu(II) ions, μ_{eff}/Cu = 1.10 μ_B, and a ^{1}H NMR spectrum of **4** is nearly identical to that of **1**. Structural insight comes from EXAFS spectroscopy[11] carried out on frozen THF solutions of **4**−(BArF)$_2$, revealing a best fit for 3 N atoms (from MePY2, with multiple scattering from two pyridines) at 2.023 Å, plus a strong single Cu-ligand interaction at 1.906 Å. This is consistent with a Cu−O (oxo) bond, shorter than that observed for Cu^{II}−μ-OH$^-$ moieties, although longer than in Cu^{III}−(μ-O)−Cu^{III},[3d,e] Cu^{II}−(μ-O)−Fe^{III},[21] or for Cu(II)−peroxo[1a] bond distances. Also consistent with the Cu^{II}−O−Cu^{II} formulation for **4** are its observed reactions. Addition of 3 equiv of PPh_3 rapidly produces 1 equiv O=PPh_3 and 2 equiv of $[(MePY2)Cu^I(PPh_3)]^+$ (**1**, L = PPh_3, Scheme 1); by contrast, reaction of PPh_3 with **2** does not occur, and with **3**, it is very sluggish. Titration of $[\{MePY2)Cu^{II}\}_2(\mu\text{-}O)]^{2+}$ (**4**) with water (in THF) leads directly to $[\{MePY2)Cu^{II}\}_2(\mu\text{-}OH^-)]^{2+}$ (**3**). By further contrast, **4** does not oxidize phenols or dihydroanthracene.

In summary, new insights into copper(I)/O_2 reactivity include the observation that the low-temperature product of reaction of O_2 with mononuclear complex $[(MePY2)Cu^I\text{−}(CH_3CN)]^+$ (**1**) is $[\{(MePY2)Cu\}_2(O_2)]^{2+}$ (**2**), which exisits as a mixture of μ-η^2:η^2-peroxo−dicopper(II) and some bis-μ-oxo−dicopper(III) species.[22] Finding of the latter confirms this possibility for the first time when using ligands other than purely triazacycloalkane-[3b−d] or etheylenediamine-containing donors,[3e,f] and further points to the likely general importance of a side-on peroxo/bis-μ-oxo equilibrium. The facile hydrogen-atom abstraction reactions described for **2** are rare examples of Cu^I/O_2 derived Cu_2−O_2 (or Cu_2−(O)$_2$, vide supra) oxidations of exogenous hydrocarbon substrates.[19] Further studies are needed to understand how the nature of the ligand differentially influences the structure and reactivity of Cu$_n{}^I$/O_2 derived species.

Acknowledgment. We are grateful to the National Institutes of Health (K.D.K., GM 28962; E.I.S., DK 31450; N.J.B., NS 27583;) and Swiss National Science Foundation (A.D.Z.) for research support.

Supporting Information Available: Procedures for compound synthesis, details of the kinetics study, resonance Raman spectroscopy, EXAFS spectroscopy, and X-ray structure report for **3** (25 pages, print/PDF). See any current masthead page for ordering and Web access instructions.

JA981878H

---

(13) 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.

(14) (a) The product is $[\{MePY2)Cu^{II}\}_2(\mu\text{-}F)_2]^{2+}$, previously[9] formulated as a bis-μ-(OH$^-$)$_2$ complex. (b) See also: Lee, S. C.; Holm, R. H. *Inorg. Chem.* **1993**, *32*, 4745−4753.

(15) Baldwin, M. J.; Root, D. E.; Pate, J. E.; Fujisawa, K.; Kitajima, N.; Solomon, E. I. *J. Am. Chem. Soc.* **1992**, *114*, 10421−10431.

(16) The 360 to 410 nm intensity ratio appears to be invariant with solvent, anion, or temperature; the low percentage of **2b** present may make shifts in the equilibrium difficult to observe.

(17) Mahapatra, S.; Halfen, J. A.; Tolman, W. B. *J. Am. Chem. Soc.* **1996**, *118*, 11575−11586.

(18) Intramolecular aromatic hydroxylations, see: refs 1 and 2.

(19) Using discrete copper(III) complexes Mayer and co-workers also observe oxidations (most likely hydrogen atom abstraction reactions) with added substrates. Blubaugh, T. J.; Collier, A. M.; Lockwood, M. A.; Lovell, S.; Mayer, J. M. *Angew. Chem., Int. Ed. Engl.*, **1998**, in press.

(20) Paul, P. P.; Karlin, K. D. *J. Am. Chem. Soc.* **1991**, *113*, 6331−6332.

(21) Karlin, K. D.; Nanthakumar, A.; Fox, S.; Murthy, N. N.; Ravi, N.; Huynh, B. H.; Orosz, R. D.; Day, E. P. *J. Am. Chem. Soc.* **1994**, *116*, 4753−4763.

(22) Surprisingly, no bis-μ-oxo form of the copper−dioxygen adduct has been observed in the closely related complex, $[\{(PhCH_2CH_2PY2)Cu\}_2(O_2)]^{2+}$.[10]