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An Unusual Ligand Oxidation by a (μ-η^2:η^2-Peroxo)dicopper Compound: 1° > 3° C−H Bond Selectivity and a Novel Bis(μ-alkylperoxo)dicopper Intermediate

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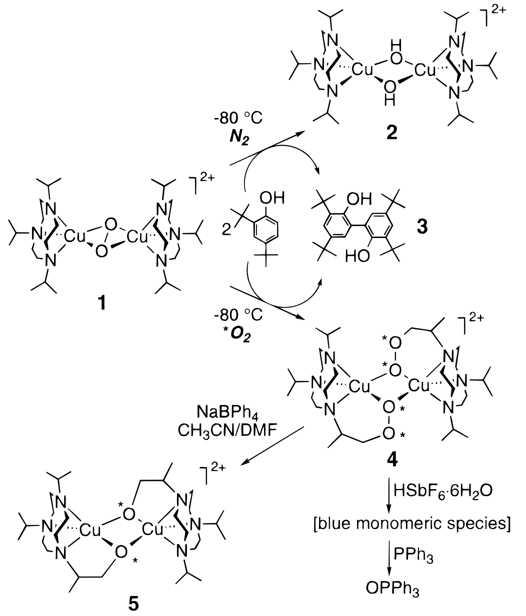
Active site peroxide and/or hydroperoxide complexes of iron and copper are key proposed intermediates in hydrocarbon hydroxylations promoted by metalloenzymes and other catalysts.[1] Notwithstanding the progress that has been made in synthetic modeling studies that have provided insight into the feasibility of some of the many conceivable mechanisms of oxygenase activity,[2] much remains to be learned about how M_nO_2, M_nOOR (M = Fe or Cu; R = H, alkyl, or acyl), or species derived therefrom effect C−H bond cleavage and oxidation. These issues have been addressed through examination of ligand hydrocarbyl group degradations that occur upon decay of metastable dioxygen or bis(μ-oxo) complexes of Cu,[3] Co,[4] Mn,[5] or Ni.[6] Although differences in the nature of the final products implicate divergent mechanisms for the various types of ligands and metals, attack of a (μ-η^2:η^2-peroxo)dimetal unit, or a species derived therefrom [e.g., a bis(μ-oxo)dimetal compound],[3b] at the most reactive methine or benzylic C−H bond of an alkyl substituent of a coordinated ligand is a commonly observed reaction pathway.

For example, research from our laboratory has shown that complex **1** decomposes to hydroxo-bridged **2** via selective, rate-determining cleavage of the isopropyl substituent methine C−H bond(s) (Scheme 1).[3a] In a different reaction that does not involve C−H bond activation, the same product **2** and diphenol **3** are formed in high yield (>90%) upon treatment of **1** with 2,4-di-*tert*-butylphenol (DTBP) at −78 °C under a N_2 atmosphere, presumably via H atom abstractions by the peroxo unit from the phenol to yield phenoxyl radicals that subsequently couple.[7] Here we report that, when performed in the presence of O_2, the reaction of **1** with DTBP takes a novel course involving oxygenation of isopropyl substituents, and at the methyl rather than the usual methine position. In addition, we surmise on the basis of available characterization data that the initial reaction product is an unprecedented bis(μ-alkylperoxo)dicopper(II) species.[8]

Scheme 1



Addition of DTBP (excess) to a red-brown solution of **1** (with SbF_6^- counterions) in CH_2Cl_2 at −78 °C with vigorous purging with O_2 caused a rapid color change to green. Warming and treatment with Et_2O induced precipitation of a green solid. A 96% yield (based on copper) of diphenol **3** was verified by GC/MS analysis of the filtrate, while new compound **4** was isolated in 63% yield as small green octahedrons upon recrystallization of the green solid (Scheme 1). Although repeated attempts to solve its X-ray crystal structure have not been successful due to extreme disorder and/or twinning problems, the formulation of **4** is supported by combined spectral, analytical, and chemical reactivity data.[9] The complex is EPR silent, consistent with a dinuclear structure with magnetically coupled Cu(II) ions, and exhibits $\lambda_{max} = 380$ nm (ϵ 2800 M^{-1} cm^{-1}) attributable to a ROO^-

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→ Cu^{II} LMCT transition.[8] Moreover, it gives an electrospray mass spectrum (ISP-MS) with the appropriate parent ion and daughter ion isotope patterns (Supporting Information) and yields a correct CHN analysis.[9] In further support of the presence of alkylperoxo units in **4**, coaddition of PPh_3 and $HSbF_6 \cdot 6H_2O$ (2 equiv) rapidly and quantitatively yielded $OPPh_3$, whereas in the absence of acid only trace oxidation of the phosphine was observed. These results are consistent with proton-induced cleavage of **4** into monomeric alkylhydroperoxide species competent to oxidize PPh_3,[10] a known reaction of simple alkylhydroperoxides.

In isotope labeling experiments, we found that treatment of **1**-$^{18}O_2$ with DTBP and $^{16}O_2$ yielded **4** having only ^{16}O present (ISP-MS). When $^{16}O_2$ was vigorously purged through a solution of **1**-$^{18}O_2$ in the absence of DTBP, no incorporation of ^{16}O into **1** was observed by resonance Raman monitoring of ν_{O-O} ($^{18}O_2$, 680 cm^{-1}; $^{16}O_2$, 722 cm^{-1}),[3a] ruling out simple exchange of bound and unbound O_2 as an explanation for the isotopic composition of **4** observed. These results show that the O_2 originally bound in **1** does *not* appear in the final alkylperoxo unit and that the exogenous O_2 is incorporated in the final product.

Attempts to prepare X-ray quality crystals of **4** with BPh_4^- counterions by slow metathesis with $NaBPh_4$ in CH_3CN/DMF instead yielded bis(μ-alkoxo)dicopper(II) compound **5** (Scheme 1),[9] presumably via a redox reaction between the counterion and **4**.[11] The X-ray structure of **5** (Figure 1)[12] reveals a typical $[Cu_2(\mu\text{-}OR)_2]^{2+}$ core and, importantly, attachment of the oxygen atoms to the methyl rather than the methine carbons of the functionalized isopropyl groups. We thus infer (but have yet to prove unambiguously) similar linking of the peroxo units to ligand methyl groups in **4**. Bis(μ-alkoxo)dimetal cores analogous to that found in **5** have been observed upon oxidation of isopropyl groups of various tridentate ligands when bound to Mn(II),[5] Ni(II),[6a] or Co(II),[4b] but only in a preliminary report[6b] for the case of Ni(II) was oxygenation observed at the methyl rather than the methine group. Bis(μ-alkoxo)dicopper compounds also resulted from the reaction of O_2 with Cu(I) complexes of polypyridyl ligands.[3e,f] In no instance, however, has the intermediacy of an alkylperoxide species been seen in $[Cu_2(\mu\text{-}OR)_2]^{2+}$ core formation.

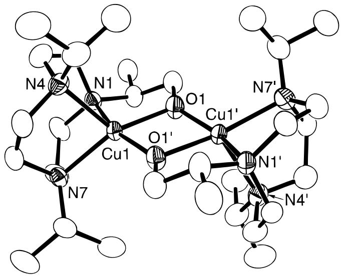

Figure 1. Representation of the dicationic portion of the X-ray crystal structure of $5 \cdot 2CH_3CN \cdot DMF$ (50% thermal ellipsoids; all hydrogen atoms omitted for clarity). Selected bond distances (Å) and angles (deg): Cu1···Cu1′, 3.0392(6); O1···O1′, 2.411(4); Cu1−O1, 1.940(3); Cu1−O1′, 1.937(3); Cu1−N1, 2.020(3); Cu1−N7, 2.095(3); Cu1−N4, 2.247(3); Cu1−O1−Cu1′, 102.8(1); O1−Cu1−O1′, 76.9(1); O1−Cu1−N1, 86.2(1); O1−Cu1−N7, 152.4(1); O1−Cu1−N4, 121.1(1); N1−Cu1−N7, 86.8(1); N1−Cu1−N4, 84.7(1); N7−Cu1−N4, 84.6(1).

To explain the production of biphenol **3** in the reactions of DTBP with **1**, H atom abstraction from DTBP by the (μ-η^2:η^2-peroxo)dicopper(II) core to yield a phenoxyl radical intermediate appears likely. While trapping of the resulting $[Cu_2(O)(OH)]^{2+}$ unit with a second molecule of DTBP ensues under N_2 to yield a bis(μ-hydroxo)dicopper(II) species,[3a] the fate of the resulting $[Cu_2(O)(OH)]^{2+}$ unit under O_2 differs for reasons that remain unclear. We suggest that, either directly or indirectly, perhaps after scission to a monomeric species and/or by a radical chain mechanism, a ligand-based 1° alkyl radical is generated regioselectively and is trapped by exogenous O_2 (as indicated by the isotope labeling experiments) to give an alkylperoxyl radical that, upon reduction (perhaps by a second DTBP molecule), ends up bridging the copper ions in the final isolated product **4**. The observation of oxidative attack at the less reactive 1° (methyl) rather than the more commonly targeted 3° (methine) position, α to the N-donor atom, of the ligand substituent is difficult to rationalize;[2g,3−5] evidently, an unusual oxidizing intermediate of unknown structure is produced when the **1**/DTBP reaction is carried out under O_2.[13]

In sum, although many mechanistic issues remain unresolved, we have conclusively demonstrated the core conversion $[Cu_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-}O_2)]^{2+}$ (**1**) → $[Cu_2(\mu\text{-}OR)_2]^{2+}$ (**5**) associated with the functionalization of the 1° rather than the 3° carbon positions of the coordinated ligand and have good evidence for the intermediate formation of the novel $[Cu_2(\mu\text{-}OOR)_2]^{2+}$ (**4**) unit. The conversions connecting these cores are remarkable (and complex!) and represent yet another illustration of the capability of Cu_nO_2 species to participate in novel hydrocarbon functionalization processes of potential relevance to those carried out by biological and other catalytic systems.

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Supporting Information Available: Full details of the X-ray crystal structure of $5 \cdot 2CH_3CN \cdot DMF$ and ISP-MS data and isotope pattern simulations for **4**, **5**, and the blue species generated from **4** + $HSbF_6 \cdot 6H_2O$ (21 pages). Ordering information is given on any current masthead page.

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[9] Data for **4**: FTIR (KBr, cm^{-1}) 2976, 2876, 1496, 1470, 1390, 1369, 1295, 1150, 1067, 970, 767, 718, 657 (SbF_6^-); UV−vis (DMF) [λ_{max}, nm (ϵ, M^{-1} cm^{-1})] 278 (6500), 380 (2800), 684 (270); EPR (9.46 GHz, 77K, 1:1 CH_3CN/toluene) silent; ISP-MS (CH_3CN) *m/z* 933 [M − SbF_6]$^+$, 917 [M − O − SbF_6]$^+$, 901 [M − O_2 − SbF_6]$^+$. Anal. Calcd for $C_{30}H_{64}N_6O_4Cu_2Sb_2F_{12}$: C, 30.82; H, 5.52; N, 7.19. Found: C, 30.72; H, 5.44; N, 7.13. Data for **5**: FTIR (KBr, cm^{-1}) 3054, 3034, 2980, 2871, 1580, 1479, 1424, 1394, 1261, 1129, 1067 (ν_{C-O}), 964, 840, 734, 706, 612; UV−vis (DMF) [λ_{max}, nm (ϵ, M^{-1} cm^{-1})] 382 (2700), 692 (390); EPR (9.46 GHz, DMF, 77 K) silent; ISP-MS (DMF) *m/z* 984 [M − BPh_4]$^+$. Anal. Calcd for $C_{78}H_{104}N_6O_2B_2Cu_2 \cdot 2H_2O$: C, 69.79; H, 8.11; N, 6.26. Found: C, 69.53; H, 7.89; N, 6.29. An O−H feature in the FTIR spectrum of the analysis sample corroborated inclusion of solvate water molecules (DMF was readily lost from the crystals, which after powdering were found to be hygroscopic).

[10] In support of this hypothesis, addition of $HSbF_6 \cdot 6H_2O$ alone to **4** caused immediate loss of the LMCT feature of **4** and generation of an unstable blue monomeric species characterized by a clean, axial EPR spectrum and ISP-MS data (see Supporting Information) indicative of the formulation $\{L^{iPr2iPrOOH}Cu(CH_3CN)(SbF_6)\}^+$: UV−vis ($CH_3CN$) [$\lambda_{max}$, nm ($\epsilon$, M^{-1} cm^{-1})] 306 (3800), 692 (120); EPR (1:1 CH_3CN/toluene, 9.46 GHz, 77 K) $g_\perp = 2.05$, $g_\parallel = 2.22$, $A_\parallel = 140$ G; ISP-MS (CH_3CN) *m/z* 626 [M − SbF_6]$^+$, 610 [M − O − SbF_6]$^+$, 585 [M − CH_3CN − SbF_6]$^+$, 569 [M − O − CH_3CN − SbF_6]$^+$. Addition of PPh_3 to this blue species quantitatively yielded $OPPh_3$.

[11] Strauss, S. H. *Chem. Rev.* **1993**, *93*, 927−942.

[12] Crystal data for $5 \cdot 2CH_3CN \cdot DMF$: $M = 1461.58$, $C_{85}H_{117}B_2Cu_2N_9O_3$, crystal dimensions 0.40 × 0.40 × 0.15 mm, monoclinic, space group $P2_1/c$ (No. 14), $a = 21.5867(5)$ Å, $b = 16.7724(4)$ Å, $c = 23.1655(5)$ Å, $\beta = 112.705(1)°$, $V = 7737.3(3)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.255$ g cm^{-1}, $2\theta_{max} = 50.00°$, Mo Kα radiation ($\lambda = 0.710\,73$ Å), $T = 153(2)$ K. Data were collected using the Siemens SMART system, and the structure was solved via direct methods. Full-matrix least-squares refinement on F^2 using SHELXS-Plus converged with final R1 = 0.0657 and wR2 = 0.1638 for 10 888 independent reflections with $I > 2\sigma(I)$ and 910 parameters. The DMF solvate exhibited large temperature factors indicative of disorder.

[13] So far we have not observed a bis(alkylperoxo)dicopper(II) species upon reaction of DTBP under O_2 with any of the other (μ-η^2:η^2-peroxo)- or bis(μ-oxo)dicopper complexes capped by 1,4,7-triazacyclononanes that we have prepared.