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Coordination Chemistry and Reactivity of a Cupric Hydroperoxide Species Featuring a Proximal H-Bonding Substituent

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Supporting Information

ABSTRACT: At −90 °C in acetone, a stable hydroperoxo complex $[(BA)Cu^{II}OOH]^+$ (**2**) (BA, a tetradentate N_4 ligand possessing a pendant $-N(H)CH_2C_6H_5$ group) is generated by reacting $[(BA)Cu^{II}(CH_3COCH_3)]^{2+}$ with only 1 equiv of H_2O_2/Et_3N. The exceptional stability of **2** is ascribed to internal H-bonding. Species **2** is also generated in a manner not previously known in copper chemistry, by adding 1.5 equiv of H_2O_2 (no base) to the cuprous complex $[(BA)Cu^{I}]^+$. The broad implications for this finding are discussed. Species **2** slowly converts to a *μ*-1,2-peroxodicopper(II) analogue (**3**) characterized by UV−vis and resonance Raman spectroscopies. Unlike a close analogue not possessing internal H-bonding, **2** affords no oxidative reactivity with internal or external substrates. However, **2** can be protonated to release H_2O_2, but only with $HClO_4$, while 1 equiv Et_3N restores **2**.

In this Communication, we describe the generation, characterization, and reactivity of a copper(II) hydroperoxide complex bearing a new tripodal tetradentate chelating ligand, which confers unusual thermal stability and where its synthesis and reactivity are distinctive. In the biochemistry of copper enzymes which process molecular oxygen, mononuclear copper species derived from copper(I) and dioxygen, such as cupric superoxide, cupric hydroperoxide, and even high-valent copper oxo species,[1] have all been considered as possible important intermediates in certain copper monooxygenases (inserting one or two atoms from O_2 into a C−H substrate) and oxidases (effecting substrate dehydrogenations where O_2 is reduced to either H_2O_2 or water). Examples are peptidyl-glycine-*α*-hydroxylating monooxygenase and copper amine oxidases.[2]

It is critical to elucidate fundamental aspects of the formation and structural/spectroscopic and reactivity characteristics of all these intermediates. A part of our research program includes such investigations, especially for $Cu^{II}O_2^{\bullet-}$ and $Cu^{II}OOH$ complexes. Although a number of well-characterized[3] and even structurally defined[4] $Cu^{II}OOH$ complexes have been described, there is still a considerable deficit in our understanding of the fundamental properties of copper(II) hydroperoxide species, such as the means for their formation from $Cu^{II}O_2^{\bullet-}$ precursors[5] and their intrinsic scope of reactivity and mechanism(s).

Tris(2-pyridylmethyl)amine (TMPA) and copper(I)/O_2 chemistry lead to the now well-studied *trans*-*μ*-1,2-peroxodicopper(II) complex $[\{(tmpa)Cu^{II}\}_2(O_2^{2-})]^{2+}$ (Figure 1a).[7] Earlier, Masuda and Yamaguchi[3a] elaborated on the TMPA scaffold by inputting H-bonding moieties on one or more of the 6-pyridyl positions, i.e., using a pivalamide group py-NHC(O)-*t*-Bu (Figure 1b). In ongoing studies where we systematically alter the pendant substrate group to aid in the elucidation of reaction mechanism(s), we designed and synthesized a new ligand (BA), possessing a potential H-bonding group (Figure 1d). Herein, we report the synthesis, characterization and reactivity of the complex $[(BA)Cu^{II}OOH](ClO_4)$, which exhibits different behavior than many other $Cu^{II}OOH$ containing complexes, providing new insights and new questions for the future.

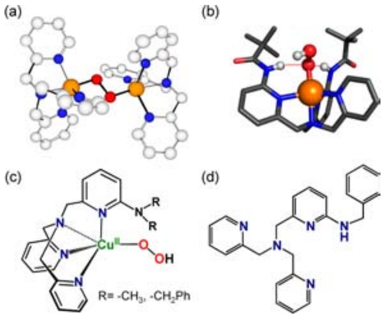

Figure 1. (a) *trans*-*μ*-1,2-peroxodicopper(II) complex with the ligand TMPA, (b) Masuda's $[(bppa)Cu^{II}OOH]^+$ complex stabilized by ligand-derived H-bonding,[4] (c) $Cu^{II}OOH$ species which undergo ligand-based oxidative N-dealkylation chemistry,[6] and (d) the new ligand, BA, the subject of the current study. See the text.

As a starting point, we synthesized the copper(II) complex $[(BA)Cu^{II}(CH_3COCH_3)](ClO_4)_2$ (**1**) by simple combination of the ligand and $Cu(ClO_4)_2 \cdot 6H_2O$ in acetone.[8] Single crystal X-ray diffraction analysis determined its structure, revealing a slightly distorted trigonal-bipyramidal (TBP) coordination ($\tau = 0.83$; $\tau = 1.00$ for idealized TBP geometries; Figure 2). EPR measurements reveal a signature "reverse" axial ($g_{\parallel} = 2.07$, $g_{\perp} = 2.22$) spectrum known for TBP, and the two readily apparent d−d envelopes seen in a UV−vis spectrum also have the relative intensities known to be associated with solution TBP coordination geometries.[9]

The new mononuclear copper(II) hydroperoxide species, formulated as $[(BA)Cu^{II}OOH]^+$ (**2**), could be generated at −90 °C in acetone by reacting complex **1** with 1 equiv of H_2O_2 (50% aq) in the presence of Et_3N (1 equiv) under Ar (Figure 2). Complex **2** is bright green and exhibits a LMCT band at 393 nm ($\varepsilon = 1600$ M^{-1} cm^{-1}) which is characteristic of known ligand−

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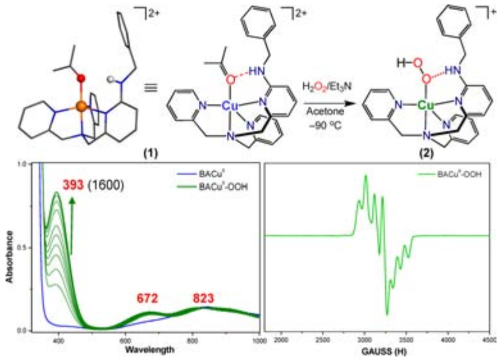

Figure 2. Displacement ellipsoid plot (50% probability) and ChemDraw representation of $[(BA)Cu^{II}(CH_3COCH_3)]^{2+}$ (**1**) and reaction with 1 equiv H_2O_2/Et_3N to generate **2** in ~7 min. Also shown are UV−vis spectra illustrating the formation of **2** (0.6 mM) at 393 (ε = 1600 M^{-1} cm^{-1}), 672 (ε = 260 M^{-1} cm^{-1}), and 823 (ε = 310 M^{-1} cm^{-1}) nm from **1** and an EPR spectrum of **2** (2 mM; X-band, ν = 9.186 GHz; acetone at 70 K): $g_{\|}$ = 2.00, $A_{\|}$ = 90 G, $g_{\perp}$ = 2.21, $A_{\perp}$ = 93 G.

$Cu^{II}OOH$ complexes. Again, solution TBP coordination is indicated for **2**, with the two d−d bands at 672 and 823 nm and the observed EPR spectral characteristics (Figure 2). Ligand−$Cu^{II}OOH$ complexes with TBP coordination are in fact common.[3a] A highly notable characteristic of **2** is that its formation requires only the addition of 1 equiv of H_2O_2; in all other examples reported, excesses of hydrogen peroxide and base (typically Et_3N) are required for full formation.[3a,d] This indicates exceptional stability for **2**, which we propose to be due to H-bonding taking place (see also below).

Complex **2** is very stable at −90 °C in acetone but converts to a new *trans*-μ-1,2-peroxodicopper complex $[\{(BA)Cu^{II}\}_2(O_2^{2-})]^{2+}$ (**3**) at −50 °C (Figure 3a). This could also be directly generated by reacting $[(BA)Cu^{I}]^{+}$ with O_2 in acetone/THF at −50 °C. Complex **3** was characterized by UV−vis, EPR ("silent"), and resonance Raman (rR) spectroscopies (Figure 3b,c). The latter reveals an (O−O) stretch at 843 cm^{-1} ($\Delta^{18}O_2$ = −46 cm^{-1}) and ν(Cu−O) = 540 cm^{-1} ($\Delta^{18}O_2$ = −27 cm^{-1}). On the basis of prior work of Masuda et al.[3c,10] and by comparison to what is observed for $[\{(tmpa)Cu^{II}\}_2(O_2^{2-})]^{2+}$, lacking any H-bonding,[7] the UV−vis blue shift (525 to 498 nm) and rR shift of ν(O−O) to higher frequency (831 to 843 cm^{-1}) indicate that H-bonding to the peroxo O atoms occurs in **3** (see Figure S8[8]).

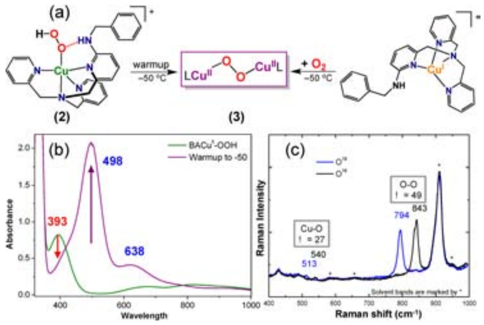

Figure 3. (a) Transformation of **2** (0.6 mM) to a *trans*-μ-1,2-peroxodicopper complex **3** or by reacting a $[(BA)Cu^{I}]^{+}$ complex with O_2. (b) UV−vis spectra at −50 °C in acetone, where **2** (green) transforms to **3** (purple), **2** → **3** + H_2O_2. (c) rR spectrum of **3** (0.6 mM) measured in THF at −80 °C ($\lambda_{excitation}$ = 515 nm).[8]

With the finding of H-bonding in **3**, it follows that ligand−NH to hydroperoxo H-bonding also occurs in **2**, as supported by the following: (i) The crystal structure of **1** reveals the existence of intramolecular H-bonding between the ligand side arm N−H and O atom of acetone (Figure 2 and SI[8]), and the acetone O atom is in the same position with respect to copper and the ligand, as is the proximal O atom in the $Cu^{II}\underline{\mathbf{O}}OH$ moiety. (ii) DFT calculations[8] confirm this assumption. In fact, the angle ∠O−H−N relaxes from ~162° in **1**[8] to 167° and 168° in the optimized structure of **2** (calculated with the B3LYP or BP86 DFT functionals, respectively). The DFT-calculated values are closer to the H-bonding ideal value of 180°.[11] In addition, the O···N distance is shortened in **2** compared to in **1**, indicating that H-bonding is stronger in **2**; (Figure S4 and Table S2).[8] Moreover, both the ∠O−H−N angle and the O···N distance in **2** compare closely to those in Masuda's $[(bppa)Cu(OOH^{-})]^{+}$ (see Figure 1b) complex (see Table S2).

Interestingly, **2** can be generated from the reaction of the copper(I) complex $[(BA)Cu^{I}]B(C_6F_5)_4$[8] with 1.5 equiv of H_2O_2 in the absence of Et_3N at −90 °C in acetone (eq 1).

$$[(BA)Cu^{I}]^{+} + 3/2H_2O_2 \rightarrow [(BA)Cu^{II}{-}OOH]^{+} + H_2O \tag{1}$$

The yield, based on comparison of the absorptivity (at 393 nm) of **2**, compared to that made via the $\mathbf{1}/H_2O_2/Et_3N$ syntheses, is ≥85% for 1.5 equiv of H_2O_2 and essentially quantitative with 4 equiv of H_2O_2. In fact, this is a new approach in copper chemistry, to generate a $Cu^{II}OOH$ species by hydrogen peroxide oxidation of the reduced metal complex. However, in nonheme iron (nh-Fe) chemistry, such reactions, i.e., ligand−Fe^{II} + H_2O_2 giving $Fe^{III}OOH$ species (which may go on to $Fe^{IV}O$ complexes), are relatively common.[12] By analogy, a set of reactions, eqs 2−4, can be proposed for our copper case. The sequence of reactions required necessarily includes a high-valent copper oxo product (best described as a $Cu^{II}O^{\bullet}$ species)[13] generated by a "Fenton" type reaction (but formal peroxide heterolytic cleavage)[14] in the first step (eq 2).

$$Cu^{I} + H_2O_2 \rightarrow Cu^{II}O^{\bullet} + H_2O \tag{2}$$

$$Cu^{II}O^{\bullet} + Cu^{I} \rightarrow Cu^{II}OCu^{II} \tag{3}$$

$$Cu^{II}OCu^{II} + 2H_2O_2 \rightarrow 2Cu^{II}OOH + H_2O \tag{4}$$

$$Cu^{I} + 3/2H_2O_2 \rightarrow Cu^{II}OOH + H_2O \tag{5}$$

The analogous nh-Fe product would be the now well-known $Fe^{IV}{=}O$ complex; in one case from Que and co-workers,[15] it does only require 1 equiv of H_2O_2 plus a catalytic "base". This high-valent $Cu^{II}O^{\bullet}$ species would immediately react with the starting copper(I) complex to give a highly basic $Cu^{II}OCu^{II}$ compound (eq 3), which further combines with H_2O_2 to give the observed final products in the correct stoichiometry (eq 5). In the Supporting Information, we show an alternative sequence of reactions (a mechanism) where the more classic first reaction produced is copper(II) + hydroxyl radical ($^{\bullet}OH$). However, this may[15a] or may not occur in nh-Fe chemistry.

The importance of this finding, eq 1, is that unusual (e.g., $Cu^{II}OCu^{II}$) and unknown (e.g., $Cu^{II}O^{\bullet}$) species are likely formed in the reaction sequence (eqs 2−4). The characterization of such entities is critically important to a full understanding of Cu^{I}/O_2 (bio)chemistry. Future high priority investigations include trapping and characterization of such intermediates accompanied by detailed mechanistic inquiries.

The enhanced relative stability of **2** compared to the close analogues shown in Figure 1c, ascribed to H-bonding within **2**, and also reflected by the need for only 1 equiv of H_2O_2 for formation (vide supra), in fact does inhibit oxidative N-dealkylation chemistry within **2**. In other words, prolonged standing of **2** at −90 °C or warming gives no detectable benzaldehyde. Furthermore, no spectral change occurs upon the reaction of **2** with exogenous substrates such as a 2,6-di-*tert*-butyl-4-methoxyphenol, 1-benzyl-1,4-dihydronicotinamide,[1c] 10-methyl-9,10-dihydroacridine,[1c] reducing agents (decamethylferrocene and cobaltocene), and 1-hydroxy-2,2,6,6-tetramethylpiperidine (TEMPO-H).[5a]

However, interesting acid−base chemistry occurs. Upon addition of $HClO_4$ (1 equiv) to a solution of **2** in acetone at −90 °C; a light green to pale blue color change occurs immediately. H_2O_2 is produced (NaI titration and formation of I_3^-) essentially quantitatively. With the addition of 1 equiv of Et_3N, the full spectrum associated with **2** is restored (Scheme 1).

Scheme 1. Reversible Acid−Base Reactivity

This reversible acid−base reaction was carried out for three cycles showing the full recovery of the $Cu^{II}OOH$ complex **2**.[8] The use of other acids such as HCl and CF_3COOH also afforded Cu^{II} and H_2O_2.[8] Here, however, the reactions cannot be reversed upon the addition of a base (Et_3N). We suggest that the stronger coordination ability of the conjugated bases (Cl^- and CF_3COO^-) precludes hydroperoxo ligation and regeneration of **2**. Further support of this supposition is the detection of $[(BA)Cu^{II}Cl]^+$ and $[(BA)Cu^{II}OOCF_3]^+$ complexes using electrospray ionization mass spectrometry (ESI-MS).[8] This is the first example of such clean acid−base on−off behavior in copper hydroperoxo chemistry, again of particular note because only 1 equiv of acid and/or base is required. We should point out that in nh-Fe chemistry, a somewhat related kind of acid−base reactivity is known, wherein iron(III) hydroperoxo complexes with η^1 end-on binding can be treated with base to convert to a side-on bound η^2-peroxoiron(III) species.[12]

In summary, a $Cu^{II}OOH$ species with enhanced stability can be reversibly generated by reacting a ligand−copper(II) complex $[(BA)Cu^{II}]^{2+}$ with 1 equiv of H_2O_2/Et_3N. This finding is a synthetic advance. Alternatively, it can be synthesized by a new method, oxidizing the reduced complex $[(BA)Cu^I]^+$ with H_2O_2 in the absence of a base. Strong evidence for ligand 2° amine N−H H-bonding (rather than a more commonly used py-NHC(O)-*t*-Bu pyridyl pendant[3d,10]) to the proximal O atom in the $Cu^{II}OOH$ moiety is presented. Future studies will include investigations centered on the subject matter of eqs 2−5 (vide supra) and the elucidation of the inherent reactivity of $Cu^{II}OOH$ species which may also include H-bonding.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Synthetic and analytical details, UV−vis and EPR spectra, X-ray structural details, and a cif file. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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