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Coordination Chemistry and Reactivity of a Cupric-hydroperoxide Species Featuring a Proximal H-bonding Substituent

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Abstract

At −90 °C in acetone, a stable hydroperoxo complex [(BA)Cu^{II}-OOH]⁺ (**2**) (**BA**, a tetradentate N₄ ligand possessing a pendant −N(H)CH₂C₆H₅ group) is generated by reacting [(BA)Cu^{II}(CH₃COCH₃)₂]²⁺ with only one equiv H₂O₂/Et₃N. 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 3/2 equiv H₂O₂ (no base) to the cuprous complex [(BA)Cu^I]⁺. The broad implications for this finding are discussed. **2** slowly converts to a μ-1,2-peroxo dicopper(II) analogue (**3**) characterized by UV-Vis and resonance Raman spectroscopies. Unlike a close analogue not possessing internal H-bonding, [(BA)Cu^{II}-OOH]⁺ (**2**) affords no oxidative reactivity with internal or external substrates. However, **2** can be protonated to release H₂O₂, but only with HClO₄, while one equiv Et₃N restores **2**.

In this report, we describe the generation, characterization and reactivity of a Cu^{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 (Chart 1)¹ have all considered as possible important intermediates in certain copper monooxygenases (inserting one or two atoms from O₂ into a C-H substrate) and oxidases (effecting substrate dehydrogenations where O₂ is reduced either to H₂O₂ or water). Examples are peptidyl-glycine-α-hydroxylating monooxygenase and copper amine oxidases.²

It is critical to elucidate fundamental aspects of the formation, structural/spectroscopic and reactivity characteristics of all these intermediates. A part of our research program includes such investigations, especially for Cu^{II}-O₂^{•−} and Cu^{II}-OOH complexes. Although a number of well-characterized³ and even structurally defined⁴ 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}-O₂^{•−} precursors⁵ and their intrinsic scope of reactivity and mechanism(s).

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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>.

TMPA {tris(2-pyridylmethyl)amine} and copper(I)/O₂ chemistry lead to the now well-studied *trans*-μ-1,2-peroxo dicopper(II) complex [$\{(\text{tmpa})\text{Cu}^{\text{II}}\}_2(\text{O}_2^{2-})\}^{2+}$] (Figure 1a).⁷ Earlier, Masuda and coworkers^{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 $[(\text{BA})\text{Cu}^{\text{II}}\text{-OOH}](\text{ClO}_4)$, which exhibits different behavior than many other Cu^{II}-OOH containing complexes, providing new insights and new questions for the future.

As a starting point, we synthesized the copper(II) complex $[(\text{BA})\text{Cu}^{\text{II}}(\text{CH}_3\text{COCH}_3)](\text{ClO}_4)_2$ (**1**) by simple combination of ligand and Cu(ClO₄)₂•6H₂O 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 $[(\text{BA})\text{Cu}^{\text{II}}\text{-OOH}]^+$ (**2**) could be generated at −90 °C in acetone by reacting complex **1** with one equiv H₂O₂ (50 % *aq*) in the presence of Et₃N (1 equiv) under Ar (Figure 2). Complex **2** is bright green and exhibits a LMCT band at 393 nm ($\epsilon = 1,600 \text{ M}^{-1}\text{cm}^{-1}$) which is characteristic of known (ligand)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 $[(\text{BA})\text{Cu}^{\text{II}}\text{-OOH}]^+$ (**2**) is that its formation requires only the addition of one equiv H₂O₂; in all other examples reported an excess of hydrogen peroxide and base (typically Et₃N) are required for full formation.^{3a,3e} This indicates exceptional stability for **2**, 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-peroxo-dicopper complex $[(\text{BA})\text{Cu}^{\text{II}}]_2(\text{O}_2^{2-})^{2+}$ (**3**) at −50 °C (Figure 3a). This could also be directly generated by reacting $[(\text{BA})\text{Cu}^{\text{I}}]^+$ with O₂ in acetone/THF at −50 °C. Complex **3** was characterized by UV-Vis, EPR (‘silent’) and resonance Raman (rR) spectroscopies (Figure 3b, 3c). The latter reveals an (O-O) stretch at 843 cm^{−1} ($\Delta^{18}\text{O}_2 = -46 \text{ cm}^{-1}$) and $\nu(\text{Cu-O}) = 540 \text{ cm}^{-1}$ ($\Delta^{18}\text{O}_2 = -27 \text{ cm}^{-1}$). Based on prior work of Masuda,^{3d,10} and by comparison to what is observed for $[\{(\text{tmpa})\text{Cu}^{\text{II}}\}_2(\text{O}_2^{2-})]^{2+}$, lacking any H-bonding,⁷ the UV-Vis blue-shift (525 to 498 nm) and rR shift of $\nu\text{O-O}$ to higher frequency (831 to 843 cm^{−1}), indicate that H-bonding to the peroxo-O-atoms occurs in **3** (See Figure S8⁸).

With the finding of H-bonding in **3**, it follows that ligand NH to hydroperoxo H-bonding also occurs in $[(\text{BA})\text{Cu}^{\text{II}}\text{-OOH}]^+$ (**2**), as supported by the following: (i) The crystal structure of **1** reveals the existence of intramolecular H-bonding between the ligand sidearm N-H and O-atom of acetone (Figure 2 and SI⁸), and the acetone O-atom is in the same position with respect to Cu and the ligand as is the proximal oxygen-atom in the Cu^{II}-OOH moiety. (ii) DFT calculations⁸ confirm this assumption. In fact, the angle $\angle\text{O-H-N}$ 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-bond 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 $[(\text{BA})\text{Cu}^{\text{II}}\text{-OOH}]^+$ (**2**) (Figure S4 and Table S2).⁸ Moreover,

both the $\angle\text{O-H-N}$ angle and the $\text{O}\cdots\text{N}$ distance in **2** compare closely to those in Masuda's $[(\text{bppa})\text{Cu}(\text{OOH})]^+$ (see Fig. 1b) complex (See Table S2).

Interestingly, $[(\text{BA})\text{Cu}^{\text{II}}\text{-OOH}]^+$ (**2**) can be generated from the reaction of the copper(I) complex $[(\text{BA})\text{Cu}^{\text{I}}]\text{B}(\text{C}_6\text{F}_5)_4$ ⁸ with 3/2 equiv H_2O_2 in the absence of Et_3N at -90°C in acetone (Eq. 1).

The yield, based on comparison of the absorptivity (at 393 nm) of (**2**), compared to that made *via* the (**1**)/ H_2O_2 / Et_3N syntheses, is 85 % for 1.5 equiv H_2O_2 and essentially quantitative with 4 equiv H_2O_2 . In fact, this is a new approach in copper chemistry, to generate a $\text{Cu}^{\text{II}}\text{-OOH}$ species, by hydrogen peroxide oxidation of the reduced metal complex. However, in non-heme iron (nh-Fe) chemistry, such reactions, *i.e.*, $\text{ligand-Fe}^{\text{II}} + \text{H}_2\text{O}_2$ giving $\text{Fe}^{\text{III}}\text{-OOH}$ species (which may go on to $\text{Fe}^{\text{IV}}\text{-oxo}$ 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 $\text{Cu}^{\text{II}}\text{-O}^\bullet$ species)¹³ generated by a “Fenton” type reaction (but formal peroxide heterolytic cleavage)¹⁴ in the first step (Eq. 2).

The analogous nh-Fe product would be the now well-known $\text{Fe}^{\text{IV}}=\text{O}$ complex; in one case from Que and coworkers,¹⁵ it does only require one equiv H_2O_2 plus a catalytic ‘base’. This high-valent $\text{Cu}^{\text{II}}\text{-O}^\bullet$ species would immediately react with starting copper(I) complex to give a highly basic $\text{Cu}^{\text{II}}\text{-O-Cu}^{\text{II}}$ compound (Eq. 3), which further combines with H_2O_2 to give the observed final products observed 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 ($\bullet\text{OH}$). However, this may^{15a} or may not occur in nh-Fe chemistry.

The importance of this finding, Eq. 1, is that it is quite likely that unusual (e.g., $\text{Cu}^{\text{II}}\text{-O-Cu}^{\text{II}}$) and even unknown (e.g., $\text{Cu}^{\text{II}}\text{-O}^\bullet$) species form in the reaction sequence (Eqs. 2–4). The characterization of such entities is critically important to a full understanding of $\text{Cu}^{\text{I}}/\text{O}_2$ (bio)chemistry. Future high priority investigations would include trapping and characterization of such intermediates accompanied by detailed mechanistic inquiries.

The enhanced relative stability of $[(\text{BA})\text{Cu}^{\text{II}}\text{-OOH}]^+$ (**2**) compared to the close analogs shown in Figure 1c, ascribed to H-bonding within **2**, and also reflected by the need for only one equiv 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 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-dihydro-acridine,^{1c} reducing agents (decamethylferrocene and cobaltocene) and 1-hydroxy-2,2,6,6-tetramethyl-piperidine (TEMPO-H).^{5a}

However, interesting acid-base chemistry occurs. Upon addition of HClO₄ (1 equiv) to a solution of [(BA)Cu^{II}-OOH]⁺ (**2**) in acetone at -90 °C, a light green to pale blue color change occurs immediately. H₂O₂ is produced (NaI titration and formation of I₃⁻) essentially quantitatively. With addition of one equiv Et₃N, the full spectrum associated **2** is restored (Scheme 1).

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, CH₃COOH and CF₃COOH also afforded the formation of Cu^{II} and H₂O₂.⁸ Here, however, the reactions cannot be reversed upon addition of a base (Et₃N). We suggest that the stronger coordination ability of the conjugated bases (Cl⁻, CH₃COO⁻, CF₃COO⁻) precludes hydroperoxo ligation and regeneration of [(BA)Cu^{II}-OOH]⁺ (**2**). Further support of this supposition is the detection of [(BA)Cu^{II}-Cl]⁺ and [(BA)Cu^{II}-OOCF₃]⁺ 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 one equiv 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 Fe^{III}-hydroperoxo complexes with η¹-end-on binding can be treated with base to convert to a side-on bound η²-peroxo-Fe^{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 H₂O₂/Et₃N. This finding is a synthetic advance. Alternatively, it can be synthesized by a new method, oxidizing the reduced complex [(BA)Cu^I]⁺ with H₂O₂ in the absence of a base. Strong evidence for ligand 2°-amine N-H hydrogen 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. Thus far, we have not observed oxidative capability that can be ascribed to [(BA)Cu^{II}-OOH]⁺ (**2**). 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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Synopsis

A Cu(II)-OOH species, generated from either a Cu(II) complex with 1eq H₂O₂/1eq Et₃N or a Cu(I) complex with 1.5eq H₂O₂ without Et₃N, shows reversible acid-base reactivity with 1eq HClO₄/1eq Et₃N.

Figure 1.

(a) a *trans*- μ -1,2-peroxo dicopper(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 text.

Figure 2.

Displacement ellipsoid plot (50 % probability level) and ChemDraw representation of $[(BA)Cu^{II}(CH_3COCH_3)]^{2+}$ (**1**) and reaction with one equiv H_2O_2/Et_3N to generate $[(BA)Cu^{II}-OOH]^+$ (**2**) in ~7 min. Also shown are UV-Vis spectra illustrating the formation of **2** (0.6 mM) at 393 ($\epsilon = 1,600\text{ M}^{-1}\text{cm}^{-1}$), 672 ($\epsilon = 260\text{ M}^{-1}\text{cm}^{-1}$) and 823 ($\epsilon = 310\text{ M}^{-1}\text{cm}^{-1}$) nm from **1**, and an EPR spectrum of **2** (2 mM) (right; X-band, $\nu = 9.186\text{ GHz}$; acetone at 70 K): $g_{||} = 2.00$, $A_{||} = 90\text{ G}$, $g_{\perp} = 2.21$, $A_{\perp} = 93\text{ G}$.

Figure 3.

(a) Transformation of $[(BA)Cu^{II}-OOH]^+$ (**2**) (0.6 mM) to a *trans*-μ-1,2-peroxo-dicopper complex $[(BA)Cu^{II}]_2(O_2^{2-})^{2+}$ (**3**) or by reacting $[(BA)Cu^I]^+$ complex with O₂. Also see Supporting Information. (b) UV-Vis spectra at -50 °C in acetone, where **2** (green) transforms to **3** (purple), $2 \text{ (2)} \rightarrow 3 + H_2O_2$. (c) rR spectrum of **3** (0.6 mM) measured in THF at -80 °C ($\nu_{excitation} = 515 \text{ nm}$).⁸

Scheme 1.
Reversible Acid-Base Reactivity

Chart 1.