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Isolation of a 2-Hydroxytetrahydrofuran Complex from Copper-Promoted Hydroxylation of THF

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Abstract

A complex of a binucleating macrocyclic ligand comprising a $[\text{Cu}^{\text{II}}(\mu\text{-OH})\text{Na}]^{2+}$ core reacts with CuI in THF/ CH_3CN to yield a novel species with a deprotonated 2-hydroxytetrahydrofuran (THF-2-ol) bridging between Cu(II) and Na(I) ions. The complexes were characterized by X-ray crystallography, EPR spectroscopy, and ESI-MS. ^{18}O -labeling studies support incorporation of the O-atom from the $\mu\text{-OH}$ into the coordinated THF-2-ol ligand.

In view of the significance of copper-catalyzed oxidations in biology¹ and for synthetic/ industrial applications,² a key goal in current research is to understand mechanisms of oxidation catalysis by studying copper-oxygen intermediates.³ In work aimed at addressing this goal, we recently reported the syntheses of **1** ($\text{R} = \text{Me}^4$ or iPr^5 , Scheme 1), examples of a new type of copper-oxygen species with a $[\text{Cu}^{\text{III}}\text{-OH}]^{2+}$ core, via 1-electron oxidation of $[\text{Cu}^{\text{II}}\text{-OH}]^+$ precursors. The thermally sensitive compounds **1** abstract hydrogen atoms from dihydroanthracene at high rates, on par with some of the most reactive iron- or – manganeseoxo/hydroxo complexes in the literature.⁶ As part of an effort to understand the basis for this reactivity and to develop even more useful oxidants, we asked: What would be the effect of a Lewis acid center in close vicinity to the $[\text{Cu}^{\text{III}}\text{-OH}]^{2+}$ core? Perturbation of the properties of this core might be expected on the basis of a number of recent observations, such as notable effects of (a) Sc^{3+} and Brønsted acids⁸ on the reactivity of $\text{Fe}^{\text{IV}}=\text{O}$ species, (b) Ca^{2+} ions on the properties of $\text{Co}^{\text{III/IV}}$ -aquo/hydroxo species,⁹ and (c) second-sphere hydrogen-bonding on the properties of a variety of metal-oxygen moieties.¹⁰

With the objective of sequestering a group IA metal ion in close proximity to $\text{Cu}^{\text{II/III}}\text{-OH}$ units akin to those in **1**, we focused on using prolignand LH_2 (Scheme 1), with the idea that the pyridine(dicarboxamide) like that in **1** would support the $\text{Cu}^{\text{II/III}}\text{-OH}$ unit and the triamine fragment would bind the group IA metal ion nearby. Building upon previous work showing that L^{2-} enables the synthesis of a variety of homo- and heterometallic complexes,¹¹ we report herein the synthesis and characterization of the desired complex **3**, comprising a $[\text{Cu}^{\text{II}}(\mu\text{-OH})\text{Na}]^{2+}$ core (Scheme 2). In a serendipitous discovery, we found that reaction of **3** with CuI yields a novel complex **4** containing a deprotonated 2-hydroxytetrahydrofuran (THF-2-ol) derived from apparent oxidation of a THF solvent molecule. Isotope labeling experiments indicate that the hydroxide in **4** is the source of the O atom in the product. The unique transformation yielding **4** complements the few previous reports of the hydroxylation of THF from species derived from reactions of Cu^{I} complexes with O_2 .^{12,13}

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ASSOCIATED CONTENT

Supporting Information. Experimental details, spectroscopic data (PDF) and X-ray crystallographic data (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

Treatment of the previously described complex Na[LCuCl] with excess NaOMe yielded the methoxide complex **2**, which was isolated as a purple solid (Scheme 2). Although definitive structural information was not obtained due to a lack of X-ray diffraction-quality crystals, the indicated formulation for **2** is supported by the results of elemental analysis, negative ion ESI-MS (peak envelope simulated as $[2 - \text{Na}^+]^-$; Figure S1), and EPR spectroscopy (axial signal with parameters similar to other reported pyridine(dicarboxamide)Cu(II) complexes; Figure S2). Exposure of **2** to H₂O in the presence of NaOMe or, in an alternate route, addition of H₂O to the preparation starting from Na[LCuCl], resulted in the formation of **3**, which was isolated as an analytically pure purple powder in moderate yield (45–55%). An X-ray crystal structure of **3** (Figure 1a) shows a hydroxide bridging between a 4-coordinate Cu(II) ion bound to the pyridine(dicarboxamide) and a Na(I) ion bound to the triamine portion of the macrocyclic ligand, with a Cu–Na distance of 3.568(2) Å. The metal-ligand bond distances, including the short Cu(II)–OH bond distance of 1.867(2) Å,¹⁴ are consistent with expectations. Interestingly, the complex crystallizes as a dimer, with the two symmetry-related macrocyclic LCu(OH)Na moieties linked via a pair of bonds from a carboxamide carbonyl in one ‘monomer’ to the Na⁺ ion in the other (Figure 1b). Thus, the Na(I) ion is 5-coordinate, with a distorted square pyramidal geometry ($\tau = 0.83$)¹⁵ and variable Na–N/O distances in the range 2.2–2.9 Å (Na–O < Na–N). The dimeric structure also appears in the negative ion ESI mass spectrum; peak envelopes for $[3 - \text{Na}^+]^-$ at m/z 564 and for $[(3)^2 - (\text{Na}^+)_2 - \text{OH}]^-$ at m/z 1111 were observed (Figure S3). The formulation of **3** was further supported by CHN analysis and EPR spectroscopy (axial signal similar to that of **2**; Figure S2).

In an attempt to substitute a Cu(I) ion for the Na(I) ion in **3** and prepare a mixed valent dicopper(I,II) complex, we treated a solution of **3** in CH₃CN/THF with CuI. A Cu⁰ mirror formed, however, suggesting that CuI acted as an oxidant,¹⁶ and the only discrete product we isolated was **4** (~20% yield). An X-ray crystal structure of **4** revealed 2-hydroxytetrahydrofuran (THF-2-ol), in deprotonated form, bridging the Cu(II) and Na(I) ions, with a weak interaction between Cu1 and O8 suggested by an interatomic distance of 2.513(9) Å (Figure 2). Like **3**, the complex crystallizes as a dimer via carboxamide O/Na interactions, such that the Na(I) ion is 5-coordinate, but in this case the two monomers are not symmetry related (Figure S4). Further support for the formulation of **4** came from CHN analysis and EPR spectroscopy (axial signal similar to that of **3**; Figure S2). Attempts to observe a parent ion in both positive and negative ion mode ESI mass spectra failed, but an ion corresponding to $[\text{Cu}(\text{O}-\text{THF})]^+$ (Figure S5) was identified as a major peak in the positive ion spectrum and was used as a marker for isotope labeling experiments (see below).

In order to determine the source of the O atom in the deprotonated THF-2-ol ligand in **4**, we first tested the purity of the THF solvent by GC/MS, reasoning that small amounts of THF-2-ol impurity (perhaps derived from autoxidation) might be the source of this ligand in the product. Comparison to standard samples of THF-2-ol in THF showed that no THF-2-ol was present in the THF used in the reaction to form **4** (0.5 mM detection limit, with a concentration of 11 mM being required to rationalize the isolated yield of **4** from THF-2-ol impurity). To evaluate if the O atom in the product arose from the hydroxide in **3**, the CuI reaction was repeated with ¹⁸O-labeled **3** (labeled at same level as H₂ ¹⁸O used in the synthesis, 97%, as shown by ESIMS; Figure S5). The positive ion ESI mass spectrum of the product showed a 79:21 mixture of $[\text{Cu}(\text{}^{18}\text{O}(\text{THF})\text{H})]^+ / [\text{Cu}(\text{}^{16}\text{O}-\text{THF})\text{H}]^+$ ions (Figure S6), consistent with the hydroxide ligand in **3** being the predominant source of the O atom in the deprotonated THF-2-ol in **4**.¹⁷

Attempts to reproduce the synthesis of **4** using various other oxidants¹⁸ failed, including I₂, acetylferrocenium hexafluoroantimonate, and tris(4-bromophenyl)aminium

hexachloridoantimonate. These results suggest that a more complicated role is played by CuI in the reaction, but in the absence of additional mechanistic data, we can only speculate about that role. One notion is that the oxidant contains a Cu-O(H[?])-Cu bridge generated by interaction of a [CuOH]ⁿ⁺ (n = 1 or 2) moiety with the added copper reagent. It is intriguing that THF hydroxylation was not observed in THF solutions of **1** or upon treatment of the Cu(II) precursor of **1** with CuI, implying involvement of the bound Na⁺ ion within the macrocyclic ligand framework (L²⁻) in the C-H activation process.

In conclusion, a complex with a [Cu^{II}(μ-OH)Na]²⁺ core (**3**) hydroxylates THF solvent via C-H bond activation upon reaction with CuI to yield a novel complex **4** that contains a deprotonated THF-2-ol ligand. Isotope labeling studies indicate that the hydroxide O-atom in **3** transfers to the THF-2-ol ligand in the product. This reaction is a rare example of THF hydroxylation by a copper moiety,^{12,13} and contrasts with previous reports insofar as it yields a copper complex of the product and does not involve Cu/O₂ chemistry.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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17. The reason for the presence of 21% ^{16}O -labeled product is unclear; we speculate that a small amount of leakage of H_2^{16}O into the reaction mixture during the experiment is to blame. In independent experiments, addition of H_2^{16}O to solutions of ^{18}O -labeled **3** resulted in rapid label exchange (ESI-MS), indicating high lability of the bound hydroxide ligand.
18. The cyclic voltammogram of **3** exhibited an irreversible oxidation at +0.077 V vs. Fc/Fc^+ (CH_3CN , 0.15 M Bu_4NPF_6 , Figure S7), similar to the E_{ox} for the reversible redox wave ($E_{1/2} = -0.076$ V) reported in ref. 5 for the $\text{Cu}^{\text{II/III}}$ couple for **1** (R = iPr) in acetone.

(a)

(b)

Figure 1.

Representations of the X-ray crystal structure of **3**, showing (a) the monomeric complex with all non-hydrogen atoms as 50% thermal ellipsoids and all hydrogen atoms omitted for clarity, except that on the bridging hydroxide, and (b) a portion of the dimer as a ball-and-stick model with the *N,N,N'*-trimethyltriamine fragments omitted for clarity; the carboxamide-Na interactions linking the monomer units are indicated by arrows and the involved Na and O atoms are labeled. Selected interatomic distances (Å) and angles (deg): Cu1-O1, 1.865(2); Cu1-N4 1.927(3); Cu1-N3 1.999(3); Cu1-N5, 2.010(3); Na1-O1, 2.292(3); Na1-N1, 2.447(3); Na1-N2, 2.731(3); Na1-O3A, 2.325(4); Na1-N6, 2.861(4);

Cu1 Na1, 3.568(2); O1-Cu1-N4, 178.19(12); O1-Cu1-N3, 100.37(11); N4-Cu1-N3, 79.82(12); O1-Cu1-N5, 100.05(11); N4-Cu1-N5, 79.82(13); N3-Cu1-N5, 159.49(12); O1-Na1-N1, 164.96(14); O1-Na1-N2, 103.07(10); N1-Na1-N2, 69.36(11); O1-Na1-N6, 104.31(11); N1-Na1-N6, 69.23(12); N2-Na1-N6, 115.01(11).

Figure 2.

Representations of the X-ray crystal structure of **4**, showing the monomeric complex with all nonhydrogen atoms as 40% thermal ellipsoids and all hydrogens omitted for clarity, (top) and the core with all C atoms except those in the THF-2-ol portion omitted (bottom). The “O₂ (amide)” refers to the carboxamide O atom from the other complex in the dimer. Selected interatomic distances (Å) and angles (deg): Cu1–O1, 1.909(9); Cu1–N7, 1.934(12); Cu1–N2, 2.000(11); Cu1–N6, 2.057(11); Cu1–O8, 2.513(9); Cu1–Na1, 3.609(5); Na1–O1, 2.320(11); Na1–N4, 2.463(13); Na1–N5, 2.662(13); Na1–N3, 2.768(14); Na1–O2(amide), 2.334(10); O1–Cu1–N7, 177.8(4); O1–Cu1–N2, 101.2(4); N7–Cu1–N2, 77.2(5); O1–Cu1–N6,

99.2(5); N7-Cu1-N6, 82.4(5); N2-Cu1-N6, 159.5(5); O1-Na1-N4, 164.5(5); O1-Na1-N5, 107.7(4); N4-Na1-N5, 67.4(4); O1-Na1-N3, 101.1(4); N4-Na1-N3, 70.2(4); N5-Na1-N3, 116.9(5).

Scheme 1.

Scheme 2.