Dicopper(I) Complexes of Unsymmetrical Binucleating Ligands and Their Dioxygen Reactivities

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The design, synthesis, and characterization of binuclear copper(I) complexes and investigations of their dioxygen reactivities are of interest in understanding fundamental aspects of copper/O_2 reactivity and in modeling copper enzyme active-site chemistry. In the latter regard, unsymmetrical binuclear systems are of interest. Here, we describe the chemistry of new unsymmetrical binuclear copper complexes, starting with the binucleating ligand UN2-H, possessing a *m*-xylyl moiety linking a bis[2-(2-pyridyl)ethyl]amine (PY2) tridentate chelator and a 2-[2-(methylamino)ethyl]pyridine bidentate group. Dicopper(I) complexes of UN2-H, $[Cu_2(\text{UN2-H})]^{2+}$ (**1**), as PF_6^- and ClO_4^- salts, are synthesized. These react with O_2 (Cu:O_2 = 2:1, manometry) resulting in the hydroxylation of the xylyl moiety, producing the phenoxohydroxodicopper(II) complex $[Cu_2(\text{UN2-O}^-)(OH^-)(CH_3CN)]^{2+}$ (**2**). Compound **2**$(PF_6)_2$ is characterized by X-ray crystallography, which reveals features similar to those of a structure described previously (Karlin, K. D.; et al. *J. Am. Chem. Soc.* **1984**, *106*, 2121−2128) for a symmetrical binucleating analogue having two tridentate PY2 moieties; here a CH_3CN ligand replaces one pyridylethyl arm. Isotope labeling from a reaction of **1** using $^{18}O_2$ shows that the ligand UN2-OH, extracted from **2**, possesses an ^{18}O-labeled phenol oxygen atom. Thus, the transformation **1** + O_2 → **2** represents a monooxygenase model system. $[Cu^I_2(\text{UN2-OH})(CH_3CN)]^{2+}$ (**3**), a new binuclear dicopper(I) complex with an unsymmetrical coordination environment is generated either by reduction of **2** with diphenylhydrazine or in reactions of cuprous salts with UN2-OH. Complex **3** reacts with O_2 at −80 °C, producing the (μ-1,1-hydroperoxo)dicopper(II) complex $[Cu^{II}_2(\text{UN2-O}^-)(OOH^-)]^{2+}$ (**4**) (λ_{max} 390 nm (ϵ 4200 M^{-1} cm^{-1}), formulated on the basis of the stoichiometry of O_2 uptake by **3** (Cu:O_2 = 2:1, manometry), its reaction with PPh_3 giving O═PPh_3 (85%), and comparison to previously studied close analogues. Discussions include the relevance and comparison to other copper bioinorganic chemistry.

Introduction

Copper−dioxygen reactivity studies are relevant to the utilization of atmospheric O_2 in stoichiometric or catalytic oxidative organic transformations mediated by copper ion complexes,[1−4] as well as to understanding dioxygen utilization by copper proteins.[1,5−7] The latter class includes hemocyanins (arthropodal and molluscan blood O_2-transport proteins),[6] as well as monooxygenases such as tyrosinase (*o*-phenols → *o*-quinones),[6] dopamine β-monooxygenase (DβM; benzylic β-amino hydroxylation),[7] peptidylglycine α-hydroxylating monooxygenase (PHM; oxidative N-dealkylation),[7,8] and particulate (membrane-bound) copper-dependent methane monooxygenase.[6] In addition, copper oxidases effect substrate oxidations with concomitant reduction of dioxygen to hydrogen peroxide or water; these include galactose oxidase (alcohol oxidation),[7,9−11] amine oxidases (amine oxidative deamination),[7] catechol oxidase (catechol → quinone),[12] multicopper "blue" oxidases (e.g., laccase, ascorbate oxidase, and ceruloplasmin, which encompass trinuclear copper centers),[6,13] and heme−copper oxidases (proton pumps).[5,14,15]

Our own interests have in particular focused on the design and syntheses of ligands that provide stabilization of copper(I) in low-coordination (two, three, or four) nitrogen donor ligand environments yet allow facile dioxygen activation and reactivity. Mono-, bi-, and trinucleating[16] ligands and copper(I) complexes have been studied, emphasizing structures of copper(I) complexes, kinetics/thermodynamics of O_2 reactions,[17] characterization of dioxygen adducts (superoxo-, peroxo-, or hydroperoxo-

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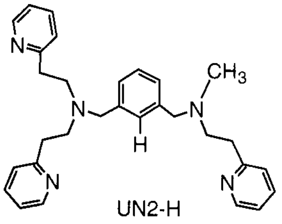
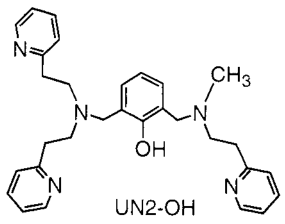
copper complexes),[1,5,18] and determination of oxygenation or oxidation products.[1] Included in the last category are monooxygenase model systems, wherein binuclear copper(I) complexes react with O_2, with subsequent attack on and hydroxylation of an arene (i.e., *m*-xylyl) moiety within the binuclear complex. Detailed mechanistic studies have revealed that dicopper(I) oxygenation produces an electrophilic μ-η^2:η^2-peroxo intermediate in close proximity to the arene substrate.[1,19−21]

Following these studies, we were interested in designing analogue ligands and their binuclear complexes that are unsymmetrical, where each copper ion is in a different coordination environment. As pointed out by Sorrell,[22] such unsymmetrical dicopper sites are of bioinorganic interest because they occur in the active sites of metalloproteins, shown by either direct X-ray structural or protein sequence homology studies for molluscan hemocyanins,[6,23] tyrosinases,[6,22] and catechol oxidase[12] and within the trinuclear centers of multicopper oxidases.[6,13] Another example is the monooxygenase PHM, in which the dicopper site is the active functional unit, even though the Cu ions are ∼11 Å apart, and the Cu ions possess very different ligations, one with a methionine sulfur ligand and the other without.[8]

While there has not been a great deal of research activity in this area, a number of groups,[24−33] including ours,[34−36] have striven to generate binucleating ligands that yield unsymmetrical dicopper complexes. Related studies have been conducted to generate unsymmetrical diiron[37,38] or dinickel[39,40] complexes because of the known unsymmetrical biological active sites for hemerythrin (non-heme diiron O_2 carrier)[41] or urease (urea hydrolysis at a dinickel active site),[42] respectively. In dicopper chemistry, most of the previous studies have involved the syntheses and characterizations of unsymmetrical dicopper(II) complexes,[24−33] while we have emphasized dicopper(I) compound generation and O_2 reactivity.[34−36]

Here, we describe the synthesis of the new binucleating ligand UN2-H. A dicopper(I) complex of this ligand is synthesized, and its reaction with O_2 is shown to result in ligand hydroxylation, producing a dicopper(II) complex, whose X-ray structure is reported. From this product is isolated the new unsymmetrical binucleating ligand UN2-OH, and its dicopper(I) complex oxygenation chemistry is also described.

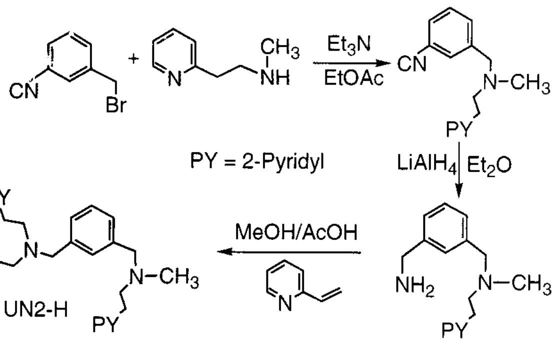

UN2-H


UN2-OH

Results and Discussion

Syntheses of UN2-H and Its Dicopper(I) Complex. The unsymmetrical binucleating ligand UN2-H containing two pendant tri- and bidentate groups with amine and pyridyl donors attached to the 1,3-positions of the *m*-xylyl spacer was synthesized in three steps, as represented in Scheme 1.

Scheme 1



The dicopper(I) complex **1** was synthesized by the reaction of UN2-H and 2 equiv of the copper(I) precursor $[Cu(CH_3CN)_4]^+A^-$ ($A^- = PF_6^-$ or ClO_4^-) in CH_2Cl_2; it was isolated as a yellow solid, followed by precipitation with Et_2O, giving $[Cu_2(UN2\text{-}H)]^{2+}$ (**1**) (Scheme 2), on the basis of analytical and spectroscopic data.

The ^1H NMR spectrum of $[Cu_2(UN2\text{-}H)](PF_6)_2$ (**1a**) displays two benzylic protons at two different chemical positions (see Experimental Section), as expected from its unsymmetrical nature. The ^{13}C NMR spectrum also indicates chemical inequivalence for the benzylic carbons, while the methylene carbons on the tridentate arms appear equivalent. These observations are consistent with the unsymmetrical coordination environments of the two coppers. In the absence of X-ray structural information, the coordination environments about the

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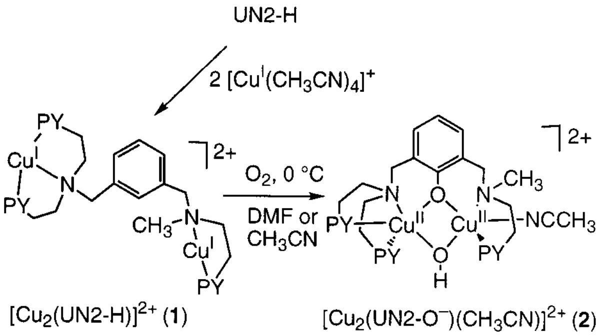
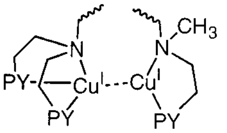
Scheme 2



two copper(I) centers in **1** can be speculated. The fact that the complex does not contain any solvates (on the basis of elemental analysis and NMR spectroscopy) suggests that the copper(I) bearing the pendent ligand with one pyridyl unit can only have 2-coordinated near-linear geometry or have intramolecular Cu···Cu interactions with the tricoordinate (binding the tridentate moiety) Cu(I) ion:



Casella[43−45] and Feringa[46,47] have described copper(I) complexes with similar bidentate moieties. Complexes having Cu(I)···Cu(I) interactions, or at least cases with clearly short Cu(I)···Cu(I) distances, are well-known,[48−56] including a closely related dicopper(I) complex with tpen (tpen = *N*,*N*,*N*′,*N*′-tetrakis(2-pyridylmethyl)ethylenediamine).[49] We have reported many examples of three-coordinate Cu(I) with the bis[2-(2-pyridyl)-ethyl]amine tridentate group.[57−59]

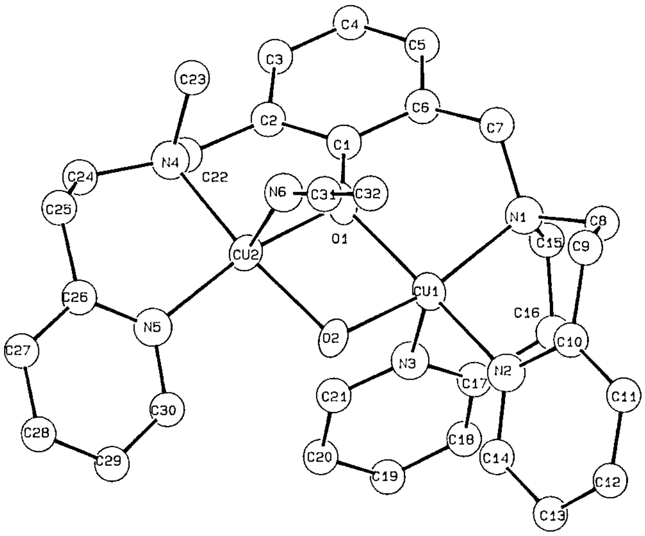


Figure 1. ORTEP view of the cationic portion of [Cu$^{II}_2$(UN2-O$^-$)(OH$^-$)(CH$_3$CN)](PF$_6$)$_2$ (**2**(PF$_6$)$_2$).

Dioxygen Reactivity of [Cu$_2$(UN2-H)]$^{2+}$ (1): Hydroxylation Reaction. The dinuclear copper(I) complex [Cu$_2$(UN2-H)]$^{2+}$ (**1**) reacts readily with O$_2$, in either DMF or CH$_3$CN at or below room temperature, causing an instantaneous change to a green color. The product obtained in >90% yield is identified as the phenoxo- and hydroxo-bridged dicopper(II) complex [Cu$_2$(UN2-O$^-$)(OH$^-$)(CH$_3$CN)]$^{2+}$ (**2**) (Scheme 2), which results from hydroxylation of the arene ring that was part of the ligand framework. The X-ray structure of **2** is described below. The oxygenation reaction **1** + O$_2$ → **2** was monitored spectrophotometrically at low temperature (−78 °C) in an attempt to observe the formation of any dioxygen−copper complex intermediate, as has been seen occasionally[20,34] without the need for fast time scale (i.e., stopped-flow kinetics) measurements. In fact, only the spectrum corresponding to the final product **2** could be observed after benchtop mixing (~10 s) of O$_2$ with **1** at −78 °C, because of its short lifetime and/or instability. However, formation of a dioxygen adduct is proposed in part on the basis of analogies to other systems (vide infra) and of the observed stoichiometry of O$_2$ uptake. Monometric measurements (Experimental Section) in DMF at 0 °C show that that 1 mol of dioxygen is consumed/mol of complex **1**, i.e., Cu:O$_2$ = 2:1, which is the stoichiometry expected for a monooxygenase model reaction. Furthermore, FAB mass spectral analysis of the product phenol ligand that is obtained by the reaction of **1** with ^{18}O$_2$ and isolation by leaching the copper ions out of **2** using aqueous NH$_3$ added to CH$_2$Cl$_2$ (Experimental Section) shows that it is UN2-^{18}OH. This demonstrates that one atom of the dioxygen molecule has been incorporated into the aryl ring of the binucleating ligand.

X-ray Structure and Other Characterizations of [Cu$_2$(UN2-O$^-$)(OH$^-$)(CH$_3$CN)]$^{2+}$ (2). A perspective view of the cationic portion of **2**(PF$_6$)$_2$ is shown in Figure 1. Selected crystal and refinement data are given in Table 1, and selected bond distances and angles are summarized in Table 2. The two copper atoms are bridged by a common exogenous hydroxo and an endogenous phenoxo oxygen atom. However, as expected, the binuclear complex possesses distinctly unsymmetrical coordination environments about the two coppers ion centers. Cu1 is coordinated to the tridentate (bis[2-(2-pyridyl)ethyl]amine) N$_3$ donor set resulting in a facial geometry, while Cu2 is coordinated to the bidentate N$_2$ donor set and to an additional ligand, a molecule of acetonitrile. The geometry about each copper can be best described as slightly distorted square pyramidal (Cu1, $\tau = 0.09$; Cu2, $\tau = 0.05$; based on Addison[60] analysis where $\tau = 0.0$ for a perfect square pyramid and $\tau = 1.0$ for a trigonal

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Table 1. Selected Crystallographic Data for **2**(PF'_6)$_2$

empirical formula	$C_{32}H_{38}Cu_2F_{12}N_6O_2P_2$
MW	955.71
crystal color, shape	green, parallelpiped
crystal dimens, mm	0.1 × 0.2 × 0.3
crystal system	monoclinic
a, Å	14.927(3)
b, Å	13.581(2)
c, Å	18.872(3)
β, deg	90.58(1)
V, Å^3	3826(1)
D_{calcd}, g/cm^3	1.66
space group	$P2_1/c$
Z	4
radiation *λ*(Mo Kα), Å	0.710 69
temp, K	296
abs coeff, cm^{-1}	12.92
no. of refined parameters	295
R^a	0.078
$R_w{}^b$	0.081

[a] $R = \sum|F_o| - |F_c|/\sum|F_o|]$. [b] $R_w = [\sum w(|F_o| - |F_c|)^2/\sum w|F_o|^2]^{1/2}$, $w = 4F_o{}^2/\sigma^2(F_o{}^2)$.

Table 2. Selected Distances and Angles for **2**(PF_6)$_2$

Intramolecular Distances (Å)			
Cu1−Cu2	3.060(3)	Cu2−O2	1.94(1)
Cu1−O1	1.97(1)	Cu2−N4	2.03(1)
Cu1−O2	1.93(1)	Cu2−N5	2.02(1)
Cu1−N1	2.06(2)	Cu2−N6	2.36(2)
Cu1−N2	2.00(1)	N4−C23	1.48(2)
Cu1−N3	2.19(2)	N6−C31	1.13(2)
Cu2−O1	1.97(1)	C31−C32	1.47(3)

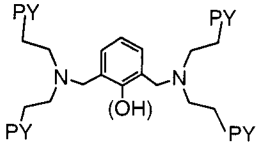
Intramolecular Angles(deg)			
O1−Cu1−O2	76.9(4)	O1−Cu2−N5	166.9(6)
O1−Cu1−N1	93.7(5)	O1−Cu2−N6	94.6(5)
O1−Cu1−N2	159.9(5)	O2−Cu2−N4	163.9(5)
O1−Cu1−N3	98.8(5)	O2−Cu2−N5	94.8(5)
O2−Cu1−N1	165.5(6)	O2−Cu2−N6	90.0(5)
O2−Cu1−N2	91.2(5)	N4−Cu2−N5	96.7(6)
O2−Cu1−N3	97.6(6)	N4−Cu2−N6	100.0(6)
N1−Cu1−N2	94.4(6)	N5−Cu2−N6	95.4(6)
N1−Cu1−N3	94.8(6)	Cu1−O1−Cu2	102.0(5)
N2−Cu1−N3	98.7(6)	Cu1−O2−Cu2	104.3(5)
O1−Cu2−O2	76.7(5)	C22−N4−C23	109(1)
O1−Cu2−N4	89.8(5)	Cu2−N6−C31	149(2)

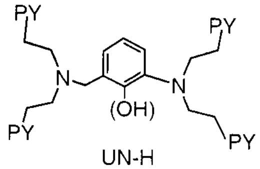
bypyramid) with the basal plane around Cu1 comprising N1, N2, O1, and O2 and that around Cu2 comprising N4, N5, O1, and O2. The N3 atom of pyridyl and the N6 atom of acetonitrile occupy the axial sites of the two coppers. The Cu1 and Cu2 atoms lie 0.26 and 0.18 Å out of their respective basal planes.

The unusual feature of the structure is that the neutral CH_3CN molecule is bound to one of the copper(II) ions. This molecule, in fact, compensates for the lack of coordination due to the missing pyridyl arm in the designed UN2-H (and thus also UN2-O$^-$) ligand. The axial Cu−N_{CCH_3} bond distance of 2.36 Å is longer than the Cu−PY_{axial} distances, which are ~2.25 Å. However, it is in the range observed for Cu(II) complexes containing multidentate chelating ligands (2.02−2.50 Å) but is longer than those found in the mononuclear complexes $[Cu^{II}(TMPA)(CH_3CN)]^{2+}$ (~1.98 Å) (TMPA = tris(2-pyridylmethyl)amine)[61,62] and $Cu(NO_3)_2(CH_3CN)_2$ (1.92 Å).[63] Another unusual feature is that the Cu2−N6−C31 angle about acetonitrile is 149°, in contrast to an expected value of ~180° for a linear structure. This may be attributed to crystal packing or steric hindrance imposed by the neighboring phenyl and methyl groups. Other structural parameters, such as the Cu···Cu separation, ∠Cu1−O−Cu2, and ∠O1−Cu−O2 (see Table 2), are almost identical to those of the "parent" complex $[Cu_2(XYL\text{-}O^-)(OH^-)]^{2+}$;[58] thus, the absence of one pyridyl arm does not seem to cause any significant effects on the structure. The structure of $[Cu_2(UN2\text{-}O^-)(OH^-)(CH_3CN)]^{2+}$ (**2**) also compares very closely with those of related symmetrical compounds studied by Mukherjee[64,65] or Feringa[46] and their co-workers: (*μ*-hydroxo)- and (*μ*-phenoxo)dicopper(II) complexes formed by oxygenation of xylyl-type dicopper(I) analogues having two equivalent bidentate N_2 donor arms, the latter being either an alkylamine plus a pyridyl arm[64,65] or a Schiff-base plus a pyridyl arm.[46,66]

Further characterization of $[Cu_2(UN2\text{-}O^-)(OH^-)(CH_3CN)]^{2+}$ (**2**) was also carried out. Electrospray mass spectrometry (ESI-MS) performed in acetonitrile solution reveals a major peak at *m/z* 769, $(M + H)^+$, corresponding to $[\mathbf{2}\cdot PF_6 - CH_3CN]^+$, in which a molecule of CH_3CN found in the solid is lost; other notable peaks observed correspond to $[\mathbf{2}\cdot CH_3CN]^+$ and $[Cu_2(UN2\text{-}O^-)]^+$, possibly formed by reduction of copper(II) under electrospray mass spectral conditions. Complex **2** exhibits a strong IR vibration at 3610 cm^{-1}, indicating the presence of an O−H group, in this case bridging the two copper(II) ions. The reduced room-temperature magnetic moment of 0.95 μ_B per copper ion suggests antiferromagnetic coupling between the two copper centers, also consistent with the observed EPR silence at 77 K. A cyclic voltammogram of **2**, in either acetonitrile or DMF, does not show sequential two-electron reversible behavior; instead, a cathodic wave at −0.49 V and two anodic waves at −0.37 and −0.25 V are observed. This behavior has also been seen for analogous dicopper(II) complexes with XYL-OH and UN-OH ligands,[58,67] and is probably due to the presence of the bridging hydroxo (*μ*-OH) ligand, which does not readily support both copper oxidation states.

Aspects of the Monooxgyenase Reaction. The observed monoxygenase reactivity in the conversion $\mathbf{1} + O_2 \rightarrow \mathbf{2}$ is very reminiscent of our previous dioxygen reactivity studies with binucleating ligand complexes of XYL and UN (L) (see the following diagram), $[(L)Cu^I{}_2]^{2+}$, which give phenoxo- and


XYL-H
(XYL-OH)


UN-H
(UN-OH)

$$[(L)Cu^I{}_2]^{2+} + O_2 \longrightarrow [(L\text{-}O^-)Cu^{II}{}_2(OH^-)]^{2+}$$

L = XYL-H or UN-H

hydroxo-bridged binuclear products $[(L\text{-}O^-)Cu^{II}{}_2(OH^-)]^{2+}$.[21,34,58] In particular, for the XYL system, detailed mechanistic studies have been carried out, and stopped-flow kinetic[1,17,20] and resonance Raman spectroscopic[19] studies have revealed the formation of an intramolecular side-on (*μ*-η^2:η^2-peroxo)di-

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copper(II) intermediate upon oxygenation of $[(XYL)Cu^I_2]^{2+}$; in a succeeding step, electrophilic attack on the arene (xylyl) substrate occurs, giving the hydroxylated product $[(XYL\text{-}O^-)Cu^{II}_2(OH^-)]^{2+}$.[1] It is interesting that $[Cu_2(UN2\text{-}H)]^{2+}$ (**1**), even though it has a 2-coordinate Cu(I) center (with a bidentate ligand) and/or perhaps a Cu(I)•••Cu(I) interaction (vide supra), is still able to undergo the hydroxylation reaction. However, the oxygenation reactions with **1** were carried out in coordinating solvents (DMF, CH_3CN) and the possibility of solvent coordination to the second 2-coordinate copper is likely. It should be noted that CH_3CN is known to have an inhibitory effect on O_2 binding to copper complexes with (pyridylalkyl)amine ligands, on the basis of low-temperature stopped-flow kinetic studies (millisecond to minute time scale).[68,69] In the present synthetic benchtop experiments using acetonitrile as the reaction solvent, CH_3CN inhibition was not noticeable.

A number of other research groups subsequently also studied related xylyl-hydroxylating sytems.[43−47,64−66,70−73] Investigations by Sorrell[71] have shown that partial replacement of pyridine moieties by an imidazole or pyrazole donor group completely inhibits oxygen insertion into these xylyl ligands with two tridentates, while, in related systems, the presence of other donors such as benzimidazole,[74] imidazole,[43] thioether,[45] or alkylamino (e.g., triazacyclononane)[73] ligands does allow for the activation of O_2 and hydroxylation reactions. The strong influence of changes in the ligand donors upon reactivity leads to the conclusion that electronic effects are crucial in determining whether oxygen atom insertion reactions occur.

Dioxygen Reactivity of the Dicopper(I) Complex $[Cu_2(UN2\text{-}OH)(CH_3CN)]^{2+}$ (3) with an Unsymmetrical Phenol Ligand: Formation of a Hydroperoxo Species. We have previously studied the chemistry of dicopper(I) complexes and their O_2 reactivities utilizing binucleating ligands that possess a phenolic function, e.g., XYL-OH and UN-OH (see preceding diagram); these ligands were obtained by hydroxylation reactions with their parent ligands XYL and UN. In fact, our first authenticated copper dioxygen adduct was obtained in a study of $[Cu^I_2(XYL\text{-}O^-)]^+$, which reversibly forms a stable (at −80 °C) adduct, the peroxodicopper(II) complex $[Cu^{II}_2(XYL\text{-}O^-)(O_2^{2-})]^+$.[75,76] Either protonation of the latter species or, alternatively, reaction of O_2 with the protonated percursor complex $[Cu^I_2(XYL\text{-}OH)]^{2+}$ affords the (μ-1,1-hydroperoxo)dicopper(II) complex $[Cu^{II}_2(XYL\text{-}O^-)(OOH^-)]^{2+}$.[77,78] Analogous chemistry occurs with UN-OH, and species with greater thermal stability, $[Cu^{II}_2(UN\text{-}O^-)(O_2^{2-})]^+$ and $[Cu^{II}_2(UN\text{-}O^-)(OOH^-)]^{2+}$ have been characterized.[35]

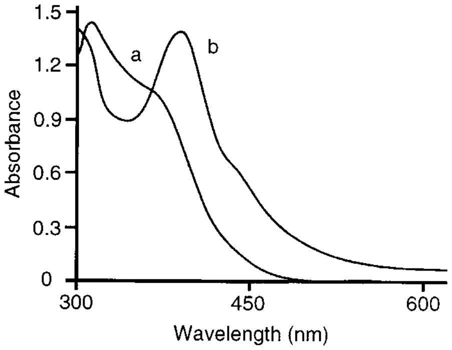
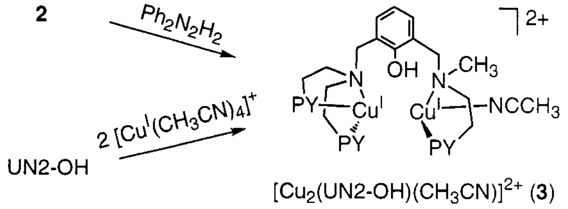


Figure 2. UV−vis spectra of (a) $[Cu^I_2(UN2\text{-}OH)(CH_3CN)]^{2+}$ (**3**) and (b) its dioxygen adduct $[Cu^{II}_2(UN2\text{-}O^-)(OOH^-)]^{2+}$ (**4**) in CH_2Cl_2 at ∼−80 °C.

Scheme 3



With the ability to generate synthetic quantities of UN2-OH via the oxygenation reaction $\mathbf{1} + O_2 \rightarrow \mathbf{2}$, we were interested in exploring further dicopper(I) chemistry with UN2-OH. The dicopper(I) complex $[Cu^I_2(UN2\text{-}OH)(CH_3CN)]^{2+}$ (**3**) was either generated directly by diphenylhydrazine reduction of the dicopper(II) complex $[Cu_2(UN2\text{-}O^-)(OH^-)(CH_3CN)]^{2+}$ (**2**) or obtained by reacting 2 equiv of the copper(I) precursor $[Cu(CH_3CN)_4]^+$ with UN2-OH (Scheme 3).

Analytical and spectroscopic data for $[Cu^I_2(UN2\text{-}OH)(CH_3CN)]^{2+}$ (**3**) indicate the presence of an additional donor ligand, CH_3CN, suggested to be coordinated to the copper(I) center bound to the bidentate ligand pendent within UN2-OH (Scheme 3). This leads to unsymmetrical tricoordination about both copper(I) centers, one having an N_3 donor set from two pyridyl groups and a tertiary amine and the other having the same donor set except that the third nitrogen is from acetonitrile rather than from a pyridyl group. Schindler and co-workers[79] have also described a dicopper(I) complex where CH_3CN binds to only one of the two copper ions, whereas there are many examples of binuclear copper(I) complexes with nitrogenous chelators where CH_3CN coordinates to each copper ion.[65,80,81] For **3**, we do not know if there is an interaction of either or both copper(I) ions with the nearby phenol oxygen atom; however, our previous studies[78] of a related complex indicate that such interactions are likely.

Hydroperoxo Formation. The reaction of the dicopper(I) complex $[Cu^I_2(UN2\text{-}OH)(CH_3CN)]^{2+}$ (**3**) (312 nm, ϵ 3800 M^{-1} cm^{-1}; 366 nm, ϵ 2500 M^{-1} cm^{-1}) with O_2 was monitored by UV−vis spectroscopy at low-temperature, −78 °C (Figure 2). A dark green solution, with a characteristic strong absorption

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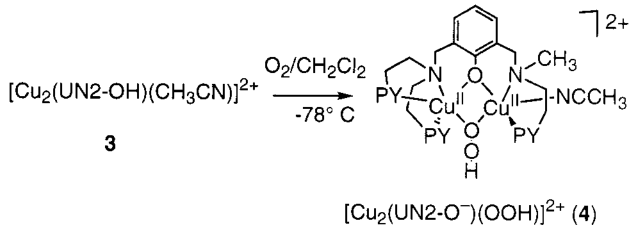
Scheme 4



band at λ_{max} 390 nm (ϵ 4200 M^{-1} cm^{-1}) is observed to form immediately (Figure 2). In addition, a shoulder at ~450 nm (ϵ 1630 M^{-1} cm^{-1}) and additional weaker absorptions (observable at higher concentrations) occur at ~630 nm (ϵ 400 M^{-1} cm^{-1}) and 1000 nm (ϵ 90 M^{-1} cm^{-1}). The low-energy bands are assigned to d−d transitions typical for a Cu(II) ion with a d^9 electronic configuration. Dioxygen uptake measurements show that the stoichiometry of the reaction is $Cu:O_2 = 2:1$ (Experimental Section), and thus we formulate the green oxygenation product as the hydroperoxo complex $[Cu^{II}_2(UN2\text{-}O^-)(OOH^-)]^{2+}$ (**4**) (Scheme 4), The transition at ~390 nm is assigned to an $HOO^- \rightarrow Cu(II)$ LMCT transition; however, an absorption due to a $PhO^- \rightarrow Cu(II)$ LMCT band may also be buried underneath. Furthermore, **4** reacts with PPh_3 to cleanly transfer an oxygen atom to yield $PPh_3{=}O$ (85%), a reaction also characteristic of the hydroperoxo complexes.[35,78] In contrast, the "parent" peroxodicopper(II) complexes show only dispacement of O_2 (giving (phosphine)dicopper(I) complexes), rather than phosphine oxidation.[35,76]

The formulation of $[Cu^{II}_2(UN2\text{-}O^-)(OOH^-)]^{2+}$ (**4**) as a (hydroperoxo)dicopper(II) complex, as already noted above, in large part is proposed on the basis of the analogy and similarity to the chemistry of $[Cu^{II}_2(XYL\text{-}O^-)(OOH^-)]^{2+}$ [77,78] and $[Cu^{II}_2(UN\text{-}O^-)(OOH^-)]^{2+}$.[35] Both of these well-characterized species also have strong charge-transfer absorptions near 390 nm, values which are blue-shifted compared to the ~505 nm absorptions found in the spectra of their unprotonated peroxodicopper(II) "parent" complexes $[Cu^{II}_2(XYL\text{-}O^-)(O_2^{2-})]^+$ and $[Cu^{II}_2(UN\text{-}O^-)(O_2^{2-})]^+$. All of the hydroperoxo species, including $[Cu^{II}_2(UN2\text{-}O^-)(OOH^-)]^{2+}$ (**4**), are thought to possess μ-1,1-OOH^- ligation on the basis of the X-ray structure obtained for the acylperoxo complex $[Cu^{II}_2(XYL\text{-}O^-)(m\text{-}ClC_6H_4C(O)\text{-}OO^-)]^{2+}$ [82] and Extended X-ray Absorption Fine Structure (EXAFS) spectroscopic studies carried out on $[Cu^{II}_2(XYL\text{-}O^-)\text{-}(OOH^-)]^{2+}$ [78] and $[Cu^{II}_2(UN\text{-}O^-)(OOH^-)]^{2+}$.[35] Sorrell and coworkers[83] have reported that analogous unsymmetrical complexes, $[Cu_2(Py2Pz2)(N_6OH)]^{2+}$ and $[Cu_2(Py2(DMP)_2)(N_6OH)]^{2+}$ (Py = pyridyl, Pz = pyrazole, DMP = 3,5-dimethyl-1-pyrazole), also reacted at low temperature with dioxygen ($Cu:O_2 = 2:1$), presumably forming copper−hydroperoxo (Cu−OOH) complexes with spectroscopic features very similar to the ones described here. It is clear from the present and past studies that changes in ligand environments have drastic effects on the formations, stabilities, and reactivities of copper (hydro)peroxo complexes derived from dioxygen.[1] Continuing investigations employing systematic variations in donor atom type, coordination number, and geometry can lead to a better understanding of dioxygen reactions in both biological and abiological systems.

Copper−hydroperoxo (Cu_n−OOH) species have been implicated in enzyme actions. Such Cu−OOH species, derived from O_2 reactions and proton transfer chemistry originating from copper(I) precursors, have been suggested to be important intermediates in the reactions of dopamine β-monooxygenase and peptidylglycine α-hydroxylating monooxygenase.[7] A Cu−OOH species has also been proposed to be involved in the disproportionation of superoxide ($2O_2^- + 2H^+ \rightarrow O_2 + H_2O_2$) mediated by the copper−zinc superoxide dismutase (SOD) enzyme.[84,85] Solomon and co-workers have proposed a Cu(II)−hydroperoxo species as an intermediate in the reduction of dioxygen to water, $O_2 \rightarrow 2H_2O$, catalyzed by laccase and other multicopper oxidases.[6] The generation and understanding of the chemistry of copper−hydroperoxo species warrant further attention.

Summary

The new unsymmetrical binucleating ligand UN2-H, with *m*-xylyl-linked tridentate and bidentate moieties, has led to the generation of two new unsymmetrical dicopper(I) complexes. The first, $[Cu_2(UN2\text{-}H)]^{2+}$ (**1**), provides a new monooxygenase model system reaction ($Cu:O_2 = 2:1$), leading to the incorporation of an oxygen atom derived from O_2 into the xylyl linker; the products are a (phenolato)dicopper(II) complex, $[Cu^{II}_2(UN2\text{-}O^-)(OH^-)(CH_3CN)]^{2+}$ (**2**), and a new phenol binucleating ligand, UN2-OH, by way of extraction. From either of these, another unsymmetrical dicopper(I) complex, $[Cu^I_2(UN2\text{-}OH)\text{-}(CH_3CN)]^{2+}$ (**3**), was produced, This reacts with O_2 ($Cu:O_2 = 2:1$), giving a (μ-1,1-hydroperoxo)dicopper(II) complex, $[Cu^{II}_2(UN2\text{-}O^-)(OOH^-)]^{2+}$ (**4**), formulated on the basis of its similarity to previously studied analogues. These studies show the versatility of copper−dioxygen chemistry involving the bis-[2-(2-pyridyl)ethyl]amine (PY2) tridentate chelator or the 2-[2-(methylamino)ethyl]pyridine bidentate group[86] and that the design of unsymmetrical analogues of previously studied symmetrical systems (i.e., XYL and XYL-OH) can lead to rich dicopper(I)/O_2 chemistries.

As discusssed above, it is of interest to continue the development of hydroperoxo−copper chemistry, including the input of systematic ligand variations. Further mechanistic studies on the complexes described here could involve stopped-flow kinetics of the reactions of **1**, **3**, and a deprotonated phenoxo analogue of **3** with O_2. Planned reactivity studies with exogenous oxidizable substrates may be of considerable interest, as O_2 adducts involving dicopper complexes with UN2-H or UN2-O(H) possess a labile site (e.g., the exchangeable CH_3CN ligand in **2** and **4**), which may facilitate substrate binding and reactivity.

Experimental Section

Materials and Methods. Reagents and solvents used were of commercially available reagent grade quality. All of the manipulations of copper(I) species and their dioxygen adducts were carried out under argon atmosphere using Schlenk techniques. Freshly distilled solvents dried under argon from appropriate drying agents were used. UV−vis spectra were measured on a Hewlett-Packard 8452 A diode array spectrophotometer equipped with a Neslab low-temperature circulator. The methods of manipulation and solution preparation for low-temperature UV−vis spectroscopy have been described previously.[87,88] Infrared spectra were recorded on a Mattson Galaxy 4030 FT-IR

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spectrometer for samples in Nujol mulls on NaCl. FAB-MS spectra were obtained on a VG Instruments 70S gas chromatograph−mass spectrometer operating in the positive mode using nitrobenzyl alcohol as the matrix, and ESI-MS spectra were obtained on a Finnigan LCQ trap mass spectrometer equipped with a standard electrospray source. Room-temperature magnetic moments were determined with the use of a Johnson Matthey magnetic susceptibility balance. Cyclic voltammetry was performed on a Bioanalytical Systems (BAS) electrochemical analyzer at 25 °C under an argon atmosphere. These measurements were carried out on 2−4 mM copper complexes with 0.1 M (n-Bu$_4$N)ClO$_4$ or (n-Bu$_4$N)PF$_6$ as the supporting electrolyte in either dry CH$_3$CN or DMF at scan rates of 20−50 mV s^{-1}. A conventional H-type cell was used with a platinum disk (3 mm) as the working electrode, a platinum coil as the counter electrode, and Ag/AgNO$_3$ (0.1 N in CH$_3$CN) as the reference electrode.

Synthesis of UN2-H. The ligand was synthesized in three steps. *N*-Methyl-*N*-[2-(2-pyridyl)ethyl]-*m*-tolunitrile was synthesized by mixing a solution of α-bromo-*m*-tolunitrile (20 g, 102 mmol) in ethyl acetate (250 mL) with 2-[2-(methylamino)ethyl]pyridine (13.9 g, 102 mmol) containing triethylamine (13 g, 129 mmol). Purification was effected by column chromatography on alumina/ethyl acetate, yielding 19 g (74%). In the second step, *N*-methyl-*N*-[2-(2-pyridyl)ethyl]-α,α′-diamino-*m*-xylene was prepared by the reduction of the nitrile derivative with LiAlH$_4$ in diethyl ether. The product was purified by column (5 H 25 cm) chromatography on alumina/ethyl acetate, which removed unreacted starting material; the product was obtained by eluting with methanol. ^{1}H NMR (CDCl$_3$, 80 MHz): δ 2.2 (s, 3 H), 2.6−3.15 (m, 4 H), 3.50 (s, 2 H), 3.70 (br s, NH$_2$, 2 H), 3.75 (s, 2 H), 6.90−7.70 (m, 7 H), 8.45 (d, 1 H). In the final step, the above amine (15 g, 59 mmol), acetic acid (15 g, 250 mmol), and 2-vinylpyridine (26 g, 248 mmol) were reacted in methanol (150 mL) for 5 days at ∼45 °C. The methanol and excess 2-vinylpyridine were removed by high-vacuum rotary evaporation. The product was purified by column (6 H 30 cm) chromatography on alumina/diethyl ether to remove traces of vinylpyridine and then by elution of the product ligand with ethyl acetate to give 12.2 g (45%) of a brown-yellow oil, $R_f = 0.38$ (alumina/ethyl acetate). ^{1}H NMR (CD$_3$CN, 300 MHz): δ 2.25 (s, 3 H), 2.83 (t, 2 H), 2.90−3.04 (m, 10 H), 3.47 (s, 2 H), 3.65 (s, 2 H), 7.00−7.20 (m, 10 H), 7.45 (m, 3 H), 8.45 (d, 3 H). ^{13}C NMR (CD$_3$CN, 300 MHz): δ 35.60, 35.96, 41.73, 53.53, 57.08, 58.11, 61.78, 121.06, 121.12, 123.15, 123.27, 127.28, 127.33, 127.91, 129.28, 136.01, 136.08, 139.22, 139.79, 149.09, 149.11, 160.69, 160.75.

Synthesis of [Cu$^{I}_2$(UN2-H)](A$^-$)$_2$ (A$^-$: PF$_6^-$, 1a; ClO$_4^-$, 1b). Under an Ar atmosphere, the ligand UN2-H (0.50 g, 1.07 mmol) dissolved in degassed CH$_2$Cl$_2$ (20 mL) was added dropwise with stirring to solid [Cu(CH$_3$CN)$_4$]ClO$_4$ (0.77 g, 2.06 mmol). After 20 min, the product was precipitated using saturated diethyl ether (150 mL). The precipitate was then dissolved in CH$_2$Cl$_2$ (15 mL), diethyl ether was added until the solution became cloudy, and the resulting solution was filtered through a medium-porosity frit. Precipitation by diethyl ether (100 mL) afforded a yellow microcrystalline material. The solvent was decanted, and the solid was washed with diethyl ether and dried under vacuum (yield 0.69 g, 85%). Anal. Calcd for C$_{30}$H$_{35}$Cl$_2$Cu$_2$N$_5$O$_8$: C, 45.51; H, 4.42; N, 8.85. Found: C, 45.07; H, 4.53; N, 8.76. ^{1}H NMR (CD$_3$CN, 300 MHz): δ 2.39 (s, 3 H), 2.66−3.04 (m, 12 H), 3.88 (s, 2 H), 4.20 (s, 2 H), 7.29−7.44 (m, 10 H), 7.75−7.88 (m, 3 H), 8.44 (d, 1 H), 8.53 (d, 2 H). ^{13}C NMR (CD$_3$CN, 300 MHz): 33.04, 33.28, 42.88, 51.95, 55.77, 59.07, 62.30, 122.22, 122.56, 124.32, 124.61, 127.71, 130.16, 130.68, 131.62, 132.63, 133.48, 137.60, 137.68, 149.32, 149.35, 160.65, 160.70. IR (Nujol; cm^{-1}): 2010 (m, br, ClO$_4$-), 1600, 1570 (C═C), 1090 (vs, br, ClO$_4^-$). The PF$_6^-$ analogue **1a** was similarly synthesized, using [Cu(CH$_3$CN)$_4$]PF$_6$. Anal. Calcd for C$_{30}$H$_{35}$N$_5$P$_2$F$_{12}$Cu$_2$: C, 40.81; H, 3.97; N, 7.94. Found: C, 41.66; H, 4.22; N, 8.25.

Reaction of [Cu$^{I}_2$(UN2-H)](PF$_6$)$_2$ (1a) with O$_2$: Isolation of [Cu$^{II}_2$(UN2-O$^-$)(OH$^-$)(CH$_3$CN)](PF$_6$)$_2$ (2(PF$_6$)$_2$). Under an argon atmosphere, the ligand UN2-H (12.21 g, 26.26 mmol) dissolved in DMF (250 mL) was introduced to solid [Cu(CH$_3$CN)$_4$]PF$_6$ (19.16 g, 51.43 mmol). After 30 min of stirring, the resulting yellow solution was added to precooled (in air) 0 °C DMF (1400 mL), and then the mixture was stirred for 3 days at room temperature. The resulting dark green solution was rotoevaporated under reduced pressure to remove DMF, the green residue was dissolved in a mixture of CH$_3$CN and CH$_2$Cl$_2$ (20:80, v/v), and the solution was passed through a short column (5 × 8 cm) packed with silica gel. The green fraction was collected, concentrated to 300 mL, and layered with diethyl ether (600 mL). After a few days, X-ray-quality crystals were obtained. The crystals were washed with diethyl ether and dried under vacuum to give 19 g (77%) of **2**(PF$_6$)$_2$. Anal. Calcd for C$_{32}$H$_{38}$Cu$_2$F$_{12}$N$_6$O$_2$P$_2$: C, 40.21; H, 3.98; N, 8.80. Found: C, 40.30; H, 4.05; N, 8.70. Room-temperature UV−vis [CH$_3$CN; $\lambda_{\max}$, nm (ϵ, M^{-1} cm^{-1})]: 216 (7400), 243 (20 000), 259 (20 300), 336 (2300), 375 (3550), 635 (200). IR (Nujol; cm^{-1}): 3610 (s, OH), 2300 (br, CH$_3$CN), 2262 (s, CH$_3$CN), 1605 (s, C═C), 1505 (s, C═C), 840 (s, PF$_6^-$). Molar conductivity, Λ_M (DMF): 300 Ω^{-1} cm^2 mol^{-1}. Magnetism (solid, room temperature): $\mu_{\text{eff}} = 0.95 \pm 0.10\ \mu_B$/Cu. EPR (DMF, 77 K): silent. Manometry, as described below, and in previous publications,[81,89,90] was carried out in DMF at 0 °C, showing that Cu:O$_2$ = 2:1.

Reaction of [Cu$^{I}_2$(UN2-H)](ClO$_4$)$_2$ (1b) with ^{18}O$_2$. A solution of [Cu$^{I}_2$(UN2-H)](ClO$_4$)$_2$ (**1b**) (0.30 g, 0.38 mmol) dissolved in 30 mL of argon-saturated DMF was exposed to an atmosphere of ^{18}O$_2$ (ICON, 96 atom %, 100 mL) at 0 °C in an ice−water bath and stirred overnight at room temperature. The solvent was then removed under reduced pressure (40 °C). The residue was dissolved in CH$_2$Cl$_2$, the solution was filtered through filter paper, and the crude product was precipitated by the addition of diethyl ether. The precipitate was washed with ether and dried in air to give 0.28 g (85%) of green product. The UV−vis and IR spectra were similar to those of an authentic sample of **3**(ClO$_4$)$_2$. The complex was reduced by KCN, and the ligand extracted showed 100% hydroxylation according to thin-layer chromatography. Mass spectrometry (FAB) showed incorporation of ^{18}O (97% ^{18}O, 3% ^{16}O) into the ligand: UN2-^{18}OH, m/z 484 (100%; M + 1); UN2-OH with ^{16}O, m/z 482.

Synthesis of [Cu$^{I}_2$(UN2-OH)(CH$_3$CN)](PF$_6$)$_2$ (3(PF$_6$)$_2$). A degassed solution of 0.41 g (2.23 mmol) of diphenylhydrazine in 20 mL of CH$_3$CN was added to 1 g (1.05 mmol) of green crystalline complex **2**(PF$_6$)$_2$. The mixture was stirred for 6 h at room temperature, after which the resulting orange-yellow solution was treated with dry, degassed diethyl ether (250 mL) to give a light yellow oily precipitate. This precipitate was then dissolved in dry degassed CH$_3$CN (15 mL), the solution was filtered through a medium-porosity frit, and diethyl ether (250 mL) was added to the filtrate, again giving an oily precipitate. This was washed twice with dry diethyl ether, further stirred with ether for ∼30 min, and then dried under vacuum to give 0.78 g (76%) of highly air-sensitive product. Anal. Calcd for C$_{32}$H$_{38}$Cu$_2$F$_{12}$N$_6$OP$_2$: C, 40.89; H, 4.05; N, 8.95. Found: C, 41.00; H, 4.59; N, 8.80. UV−vis (CH$_2$Cl$_2$; $\lambda_{\max}$, nm (ϵ, M^{-1} cm^{-1})): 312 (3800), 366 (2500). ^{1}H NMR (CD$_3$CN, 300 MHz): δ 1.98 (s, CH$_3$CN, 3 H), 2.35 (s, 3 H), 2.70−2.90 (m, 10 H), 3.10 (t, 2 H), 3.75 (s, 2 H), 4.12 (s, 2 H), 6.72 (t, 1 H), 6.98 (d, 1 H), 7.05−7.15 (m, 2 H), 7.25−7.35 (m, 5 H), 7.65 (t (d−d), 1 H), 7.80 (t (d−d), 2 H), 8.42 (d, 1 H), 8.50 (d, 2 H). ^{13}C NMR (CD$_3$CN, 75.4 MHz): δ 33.67, 34.74, 39.90, 52.26, 52.89, 55.54, 60.13, 119.65, 121.74, 121.97, 122.25, 122.46, 123.99, 124.52, 128.71, 129.04, 131.03, 131.78, 137.27, 137.57, 149.31, 159.21, 160.67. IR (Nujol; cm^{-1}): 2310, 2272 (CN of CH$_3$CN), 846 (PF$_6^-$).

Measurement of Gas (O$_2$) Uptake by [Cu$^{I}_2$(UN2-OH)(CH$_3$CN)]$^{2+}$ (3) To Form [Cu$^{II}_2$(UN2-O$^-$)(OOH$^-$)]$^{2+}$ (4). O$_2$ gas uptake measurements were carried out at −82 °C in a gas buret system, as previously described.[81,89,90] A 50 mL Schlenk flask with a mark on the neck was charged with complex **3**(PF$_6$)$_2$ (0.450 g, 0.479 mmol) under Ar. The complex was dissolved in Ar-saturated CH$_2$Cl$_2$, and the solution was diluted up to the mark on the neck of the reaction flask. The sidearm of the flask was attached to the buret assembly, and the flask was immersed in a cold bath at −82 °C. After temperature equilibration, the flask was evacuated for 20 min while the contents were stirred.

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The stopcock leading to the reaction flask was then closed, and the buret system was equilibrated to 1 atm of O_2 pressure by vacuum/O_2 cycles. After equilibration, the stopcock leading to the reaction flask was opened. The volume of gas was read by adjusting the Hg reservoir height in the U-tube of the buret assembly. The volume changes in the buret were recorded after every 20−30 min, and the final reading was recorded when no further change in volume was observed over a period of 1.5−2.5 h. The volume of O_2 taken up by the solvent was determined by a blank run performed under similar conditions. The number of moles of gas taken up by the complex was calculated by using the ideal gas law. The stoichiometry of the reaction was **3**:O_2 = 1.06:1 (average of two trials).

Reaction of $[Cu^{II}_2(UN2\text{-}O^-)(OOH^-)]^{2+}$ (4) with PPh_3: Oxidation of PPh_3. To a green solution of **4**$(PF_6)_2$, obtained by introducing dioxygen into a CH_2Cl_2 solution of **3**$(PF_6)_2$ (0.140 g, 0.149 mmol) at −80 °C, was added a slight excess of 1 equiv of PPh_3; the solution was stirred at −80 °C for 12 h. The resulting mixture was warmed to room temperature, and the solvent was removed by rotary evaporation. The residue was washed thoroughly with several portions of diethyl ether. Gas chromatographic analysis of the ether extracts showed the formation of $PPh_3{=}O$ in 85% yield.

X-ray Structure Determination of $[Cu^{II}_2(UN2\text{-}O^-)(OH^-)(CH_3CN)](PF_6)_2$ (2$(PF_6)_2$). Green crystals of **2**$(PF_6)_2$ suitable for X-ray analysis were obtained from a solution of CH_3CN/CH_2Cl_2 (1:4, v/v) layered with diethyl ether. A crystal covered with epoxy was mounted on a Rigaku AFC6S diffractometer. Automatic centering and least-squares routines were carried out on 25 reflections to obtain the unit cell parameters. A $\omega-2\theta$ scan mode was employed for the collection of intensity data. Three check reflections measured after every 150 reflections exhibited no significant crystal decay. The data were collected ($3.5 \leq 2\theta \leq 50°$) at a scan speed of 32.0° $\min^{-1}$. Corrections for Lorentz and polarization effects were applied. The linear absorption coefficients for Mo Kα radiation were low, and azimuthal scans of several reflections indicated no need for absorption correction. The positional parameters of the copper and phosphorus atoms were located by direct methods and the remaining non-hydrogen atoms were located by subsequent difference Fourier maps and least-squares refinements. Only the copper, phosphorus, and oxygen atoms were refined anisotropically by full-matrix least-squares techniques. All measurements were made at room temperature on a Rigaku AFC6S diffractometer using Mo Kα radiation and a graphite monochromator. All calculations were performed on a VAX 3520 computer using the TEXSAN crystallographic software package. Selected crystal and refinement data are given in Table 1. Further details of the crystal data refinement, the positional and thermal displacement parameters, and complete bond distances and angles are given in the Supporting Information.

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Supporting Information Available: Listings of X-ray crystal data and refinement details, atomic coordinates and isotropic temperature factors, anisotropic temperature factors, and bond distances and angles for **2**$(PF_6)_2$. This material is available free of charge via the Internet at http://pubs.acs.org.

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