Tuning of the Copper–Thioether Bond in Tetradaentate N₃S₃(thioether) Ligands; O–O Bond Reductive Cleavage via a [CuII₂(μ-1,2-peroxo)]²⁺/[CuIII₂(μ-oxo)]²⁺ Equilibrium

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ABSTRACT: Current interest in copper/dioxygen reactivity includes the influence of thioether sulfur ligation, as it concerns the formation, structures, and properties of derived copper-dioxygen complexes. Here, we report on the chemistry of {L-CuI}_2(O_2) species \( L = \text{DMMESE}, \text{DMMESD}, \text{and DMMESE}_2 \), which are N₃O₃(S(thioether)-based ligands varied in the nature of a substituent on the S atom, along with a related N₃O₃(O(ether)) (EOE) ligand. Cu²⁺ and Cu²⁺ complexes have been synthesized and crystallographically characterized. Copper(I) complexes are dimeric in the solid state, \( \{\text{L-CuI}\}_2[B(C_6F_5)_4]_2 \), however are shown by diffusion-ordered NMR spectroscopy to be mononuclear in solution. Copper(II) complexes with a general formulation \( \{\text{L-CuII}(X)\}_n \) results in the formation of \( \text{trans-μ-1,2-peroxodicopper(II)} \) species \( \{\text{L-CuII}(X)\}_2(\mu-1,2-O_2) \}^{2+} \) \( (1^\circ) \). Weakening the Cu–S bond via a change to the thioether donor found in DMMESE leads to the initial formation of \( \{\text{L-CuII}(X)\}_2(\mu-1,2-O_2) \}^{2+} \) \( (2^\circ) \) that subsequently isomerizes to a bis-μ-oxodicopper(III) complex, \( \{\text{L-CuII}(X)\}_2(\mu-\text{oxo}) \}^{2+} \) \( (3^\circ) \). Reactivity for these Cu/O₂ adducts were confirmed by resonance Raman (rR) spectroscopy. This solution mixture is sensitive to the addition of methylsulfonate, which shifts the equilibrium toward the bis-μ-oxo isomer. Further weakening of the Cu–S bond in DMMESE or substitution with an ether donor in DMMSEOE leads to only a bis-μ-oxo species (3⁰ and 4⁰, respectively). Reactivity studies indicate that the bis-μ-oxodicopper(III) species \( (2^\circ, 3^\circ) \) and not the \( \text{trans-perxo} \) isomers \( (1^\circ, 2^\circ) \) are responsible for the observed ligand sulfoxidation. Our findings concerning the existence of the \( 2^\circ/2^0 \) equilibrium contrast with previously established ligand-Cu/O₂ reactivity and possible implications are discussed.

INTRODUCTION

Copper ion-mediated dioxygen activation studies have focused on understanding the kinetics and thermodynamics of reactive intermediate formation and their subsequent diverse oxidative reactivity.¹ Such work is inspired by the known utility of copper in oxidative transformation of organic substrates. Additionally, the probing of ligand-copper(I)-O₂ chemistry is motivated by the presence of copper enzymes which mediate O₂-processing.² The detailed nature of the copper(s) active site environment (i.e., ligand type, coordination number and geometry, etc.) dictates the observed chemical reactivity, such as functioning as an O₂-carrier, an oxygenase incorporating O atom(s) into a substrate, or an oxidase effecting substrate dehydrogenation chemistry.³ In chemical studies geared toward either practical oxidations or elucidation of fundamental aspects of copper-dioxygen chemistry, it is a chelating polydentate ligand which controls the (L)Cu/O₂ reactivity.

The majority of the Cu—I/O₂ literature on adduct formation and reactivity involves systems containing all nitrogen ligands, primarily bi-, tri-, or tetradeentate entities.³ However, certain copper metalloproteins utilize sulfur-containing ligand residues, such as cysteine and methionine (Met) in “blue” copper electron-transfer proteins⁴ and in certain monoxygenases,⁴ (vide infra), (Figure 1).²

Figure 1. Copper enzymes/proteins with S-ligands: (a) Peptidylglycine-α-hydroxylating monoxygenase (PHM), C–H oxygenation, (b) Azurin, electron transfer.

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Thioether S-ligation is important in the dioxygen activating monoxygenases peptidylglycine-α-hydroxylating monoxygenase (PHM) (Figure 1a) and dopamine β-monooxygenase (DβM). These enzymes contain unique “non-coupled” binuclear copper centers, separated by ~11 Å, one copper center with three histidine ligands (CuM), and the other with two histidines and one methionine (Met)/(CuM). The CuM center is where O₂-activation and substrate hydroxylation occur, while CuMet receives reducing equivalents from ascorbate and is thought to serve as an electron transfer relay source to the CuM center as needed for monoxygenase activity.

Undoubtedly, the thioether ligand plays a major role in setting the electronic structure and coordination required for CuM O₂-binding and activation leading to peptide pro-hormone (for PHM) oxidative N-dealkylation. However, the precise role of Met coordination and the actual PHM reaction mechanism have yet to be fully determined. A crystal structure obtained by Amzel and co-workers reveals dioxygen bound to CuM in an end-on superoxo fashion as depicted in Figure 1a. Computational or biochemical arguments suggest that this Cu<sup>II</sup>-O₂*- intermediate initiates the chemistry via substrate hydrogen-atom abstraction. Other O₂-derived species have been suggested as the H atom abstracting intermediate; these include a cupric hydroperoxide (Cu<sup>III</sup>-OOH) complex formed from reduction-protonation of the initially formed Cu<sup>II</sup>-O₂*- complex or a cupryl (Cu<sup>III</sup>-O↔Cu<sup>II</sup>-O) entity generated after even further reduction—protonation.¹

Inspired by this biochemistry and with the motivation to elucidate the role of the Met ligand in PHM and DβM, a variety of ligand scaffolds with thioether donors have been synthesized, and their O₂-reactivity has been interrogated. Within the N<sub>2</sub>S<sub>(thioether)</sub> family of ligands, copper(I) complexes with anionic ligands (Chart 1a) react to give bis-µ-oxo dicopper(III) products, however, thioether ligation was ruled out. Cu<sup>I</sup> complexes with imidazolyl ligands (Chart 1b) were oxidized, but no discrete CuO<sub>2</sub> intermediates formed. With tertiary amine donors (Chart 1c) we demonstrated that a µ-η<sup>2</sup>:η<sup>2</sup>-peroxodicopper(II) complex could be generated.⁸

In the investigations described in this present report, we explored the chemistry of three N<sub>2</sub>S<sub>(thioether)</sub> ligands. Salient features of these new ligands are that they all contain more electron-rich 4-methoxy-3,5-dimethylpyridyl (DMM) donors (relative to ESE, Chart 1d) and the ethyl linked thioether moieties. The thioether donor was tuned across a series of ligands by using a variety of substituents (either ethyl in DMM<sub>2</sub>ESE, phenyl in DMMESP, or 2,4-dimethylphenyl in DMM<sub>2</sub>ESDP, Chart 1). As will be detailed in this report, addition of dioxygen to the Cu(I) complex of DMM<sub>2</sub>ESE leads to the formation of a µ-1,2-trans-peroxodicopper(II) complex similar to the pyridine containing ESE. Weakening of the Cu–S interaction by substituting a phenyl or dimethylphenyl group (DMMESP and DMM<sub>2</sub>ESDP) stabilizes a copper(III) bis-µ-oxo isomer as determined from UV–vis and resonance Raman (rR) spectroscopy. In the case of DMMESP, both CuI<sub>2</sub>O<sub>2</sub> core isomers are present at equilibrium, the first example of such an equilibrium reaction in the presence of a thioether donor. The results have also been compared to those observed for the N<sub>2</sub>O ligand DMM<sub>2</sub>ESE (Chart 1) that contains an ether donor, to further assess the effect the thioether donor has on the activation of dioxygen in these complexes.

**EXPERIMENTAL SECTION**

**General.** All materials used were commercially available analytical grade from Sigma-Aldrich chemicals and TCL. Acetone was distilled under an inert atmosphere over CaSO₄ and degassed under argon prior to use. Diethyl ether was used after being passed through a 60 cm long column of activated alumina (Innovative Technologies) under argon. Acetonitrile was stored under N₂ and purified via passage through 2 × 60 cm columns of activated alumina (Innovative Technologies Inc.). Inhibitor free tetrahydrofuran (THF) and 2-methyltetrahydrofuran (MeTHF) were purchased from Sigma-Aldrich and distilled under argon from sodium/benzophenone and degassed with argon prior to use. Pentane was freshly distilled from calcium hydride under an inert atmosphere and degassed prior to use. Cu(η<sup>2</sup>)(CH<sub>3</sub>CN)₂(B(C,F<sub>3</sub>)<sub>4</sub>) was synthesized according to literature protocols,¹³ and its identity and purity were verified by elemental analysis and/or H NMR. Synthesis and manipulations of copper salts were performed according to standard Schlenk techniques or in an MBraun glovebox (with O₂ and H₂O levels below 1 ppm).

**Instrumentation:** Bench-top low-temperature UV–vis experiments were carried out on a Cary Bio-50 spectrophotometer equipped with a liquid nitrogen chilled Unisoku USP-203-A cryostat using a 1 cm modified Schlenk cuvette. NMR spectroscopy was performed on Bruker 300 and 400 MHz instruments with spectra calibrated either to internal tetramethylsilane (TMS) standard or to a residual protio solvent. EPR measurements were performed on an X-Band Bruker

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**Chart 1**

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A number of N<sub>2</sub>S<sub>(thioether)</sub> type ligands have also been studied. In the case of two pyridyl and one amine donors (Chart 1d), we showed that Cu'/O<sub>2</sub> reactivity leads to a µ-1,2-trans-peroxodicopper(II) species.⁹ In addition, evidence for a Cu(II)–S bond in this species was observed in the extended X-ray absorption fine structure (EXAFS) spectra. For a number of N<sub>2</sub>S<sub>(thioether)</sub> benzimidazole containing ligands (Chart 1e), Castilla and co-workers tested O₂ reactivity with copper(I) derivatives, but no copper-dioxygen intermediates (as might be detected by spectroscopic interrogation) were observed during the complexes’ oxidation to copper(II).¹⁰ Depending on the identity if the Ar and R substituents, superoxide anion could be detected by a radical trapping agent.¹⁰ With guanidine donors (Chart 1f), Schindler and co-workers recently reported the formation of a side-on µ-η<sup>2</sup>:η<sup>2</sup>-peroxodicopper(II) complex that subsequently isomerized to an equilibrium mixture with a bis-µ-oxodicopper(III) product.
Gaussian transitions using Peak positions were determined from power, and samples were hand spun for data collected at 380 nm. Peak (Coherent I90C by an argon ion laser (Innova Sabre 25/7) and a krypton ion laser chilled in a pentane/N2(l) bath. Oxygenation of the copper samples was prepared in MeTHF. A 500 μL aliquot of this copper(1) solution was added to the 5 mm NMR sample tube, capped with a septum, and chilled in a −135° backscattering configuration, and excitation was provided by an argon ion laser (Innova Sabre 25/7) and a krypton ion laser (Coherent 190C−K). Data were collected for 5 min at 20 mW of power, and samples were hand spun for data collected at 380 nm. Peak positions were determined from fitting the experimental data with Gaussian transitions using Peakfit Version 4. For the DMS/ESR spectra, the Cu spectrum was subtracted from both the 16O2 and 18O2 spectra, the CuI spectrum was subtracted from both the 16O2 and 18O2 spectra.

Synthesis of Ligands. DMS/ES. 2-(Chloromethyl)-4-methoxy-3,5-dimethylpyridine hydrochloride (5.50 g, 24.76 mmol), 2-(ethylthio)-3,5-dimethyl-pyridine hydrochloride (8.910 g, 40.12 mmol), and potassium carbonate (11.09 g, 80.21 mmol) in CH3CN (120 mL) were stirred in 100 mL methylene chloride in a 250 mL round-bottom flask at room temperature under Ar. After removal of the solvent, crude yellow oil was dissolved in 100 mL dichloromethane and washed with water three times. After drying over MgSO4, the solution was filtered and removed by rotary evaporation. The resulting yellow oil was purified by column chromatography (alumina, 100% ethyl acetate, Rf = 0.67) yielding a pale yellow oil (2.36 g, 59% yield). 1H NMR (400 MHz, CDCl3): δ 8.11 (s, 2H), 6.93−6.81 (m, 2H), 3.77 (s, 4H), 3.70 (s, 4H), 2.89−2.86 (t, 2H), 2.79−2.75 (t, 2H), 2.25−2.13 (m, 12H), 2.13 (s, 6H). ESI-MS, m/z: 480.50 (M + H+).

DMS/EOE. 2-(Chloromethyl)-4-methoxy-3,5-dimethylpyridine hydrochloride (2.26 g, 10.19 mmol), 2-ethoxyl ethanamine (0.41 g, 4.63 mmol), and K2CO3 (3.22 g, 23.30 mmol) were stirred in 100 mL methylene chloride in a 250 mL round-bottom flask, and then this mixture was refluxed for 4 days under Ar. After removal of the solvent, crude yellow oil was dissolved in 100 mL dichloromethane and washed with water three times. After drying over MgSO4, the solution was filtered and removed by rotary evaporation. The resulting yellow oil was purified by column chromatography (alumina, ethyl acetate/hexane = 2:1, Rf = 0.52) yielding a pale oil (1.52 g, 85% yield). 1H NMR (400 MHz, CDCl3): δ 8.14 (s, 2H), 3.77 (s, 4H), 3.70 (s, 4H), 3.38−3.33 (q, 2H), 2.72−2.70 (t, 2H), 2.16 (s, 6H), 2.08 (s, 6H), 1.20−1.10 (t, 3H). ESI-MS, m/z: 388.42 (M + H+).

Synthesis of Copper(I) Complexes. DMS/ES/Cu[(B(C6F5)4)2]. In a 100 mL Schlenk flask in the glovebox, 258 mg (0.285 mmol) of [Cu(CsCH3CN)2][B(C6F5)4] was dissolved in 7 mL of THF. 115 mg (0.285 mmol) of DMS/ES ligand dissolved in 5 mL of THF was added to the copper solution yielding a pale yellow solution. This yellow solution was allowed to stir for 10 min at which time 100 mL of degassed pentane was added to the solution. After 1 h, the supernatant was decanted, and the oil removed from the glovebox and dried under vacuum for 20 min affording 288 mg of a white powder (88% yield). Single crystals were obtained by topping of dry pentane into a solution of the complex in THF. 1H NMR (300 or 400 MHz, THF-d8): δ 8.41 (s, 2H), 4.34−4.28 (d, 2H), 4.04−4.04 (d, 2H), 3.81 (s, 6H), 3.33−3.30 (b, 4H), 2.42−2.37 (q, 2H), 2.29 (s, 6H), 2.23 (s, 6H), 1.27−1.22 (t, 3H). Elemental analysis: (C52H37BCuF20N3O2S) Calcd: C (51.06), H (3.08), N (3.34). Found: C (51.06), H (3.08), N (3.34).

DMS/ES/Cu[(B(C6F5)4)2] (2). 1H NMR (300 MHz, THF-d8): δ 8.34 (s, 2H), 7.48−7.31 (m, 3H), 4.25 (d, 2H), 4.09 (d, 2H), 3.73 (s, 6H), 3.50 (s, 2H), 2.99 (s, 2H), 2.24 (s, 6H), 2.17 (s, 6H). Elemental analysis: (C52H37BCuF20N3O2S) Calcd: C (50.29), H (2.97), N (3.52). Found: C (50.39), H (2.92), N (3.52). DMS/ES/Cu[(B(C6F5)4)2] (3). 1H NMR (300 MHz, THF-d8): δ 8.21 (s, 2H), 7.14−6.90 (m, 6H), 4.22 (d, 2H), 4.01 (d, 2H), 3.73 (s, 6H), 3.42 (s, 2H), 3.02 (s, 2H), 2.41−2.18 (m, 18H). Elemental analysis: (C52H37BCuF20N3O2S) Calcd: C (51.10), H (3.05), N (3.44). Found: C (51.06), H (3.08), N (3.34).

DMS/EOE/Cu[(B(C6F5)4)2] (4). 1H NMR (300 MHz, THF-d8): δ 8.28 (s, 2H), 4.17−4.11 (d, 2H), 3.75 (s, 6H), 3.71−3.67 (d, 2H), 3.12−3.03 (m, 4H), 2.41−2.35 (d, 2H), 2.25(s, 6H), 2.22(s, 6H), 1.00−0.97
RESULTS AND DISCUSSION

Synthesis and Characterization of Copper(I) Complexes, 1, 2, and 3. Reaction of ligand DMMSE and Cu

The description of experimental procedures for generating and handling the copper-dioxygen adducts in order to carry out UV-vis, IR, CV, ESI-MS, and NMR analyses and the reactivity study where examination of ligand thioether sulfoxidation is probed are further described in the Supporting Information (SI).

Figure 2. Representations of the dimeric Cu(I) complexes described in the crystal structures of (a) \([\{\text{DMMESE} \text{CuI}\}_2](\text{B(C}_6\text{F}_5\text{I})_4)_2\) (1), (b) \([\{\text{DMMESDP} \text{CuI}\}_2](\text{B(C}_6\text{F}_5\text{I})_4)_2\) (2), and (c) \([\{\text{DMMESDP} \text{CuI}\}_2](\text{B(C}_6\text{F}_5\text{I})_4)_2\) (3). Selected bond distances (Å) and bond angles (deg) are also listed. The H atoms and counterions were omitted for clarity.

\[\text{C}_2\text{H}_2\text{Cl}_2\text{Cu}_2\text{Ni}_4\text{O}_8\text{S}\] Calcd: C (39.67), H (4.99), N (6.31); Found: C (38.95), H (5.09), N (5.98). EPR spectrum (Figure S18): X-band (2 mM, \(\nu = 9.186 \text{ GHz}\)) spectrometer in acetone at 70 K: \(g_{\parallel} = 2.034\), \(g_{\perp} = 2.036\), \(A = 168 \text{ G}\).

\[\text{C}_2\text{H}_2\text{Cl}_2\text{Cu}_2\text{Ni}_4\text{O}_8\text{S}\] Calcd: C (44.24), H (5.17), N (5.53); Found: C (44.24), H (5.48), N (5.54). EPR spectrum (Figure S18): X-band (2 mM, \(\nu = 9.986 \text{ GHz}\)) spectrometer in acetone at 70 K: \(g_{\parallel} = 2.034\), \(A = 168 \text{ G}\).

\[\text{C}_2\text{H}_2\text{Cl}_2\text{Cu}_2\text{Ni}_4\text{O}_8\text{S}\] Calcd: C (48.87), H (3.11), N (4.21). EPR spectrum (Figure S18): X-band (2 mM, \(\nu = 9.186 \text{ GHz}\)) spectrometer in acetone at 70 K: \(g_{\parallel} = 2.034\), \(g_{\perp} = 2.036\), \(A = 168 \text{ G}\).

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From this value, we calculate a hydrodynamic diameter of $1.13 \times 10^{-9}$ m, which agrees closely ($1.08 \times 10^{-9}$ m) with that obtained from X-ray structural parameters for the mononuclear copper(II) complex $\text{[(DMMESE)CuII(ClO}_4\text{)]}^+$ ($1a$), see SI. Further, our diffusion constant for $1$ closely matches that determined via DOSY measurements for the well-known mononuclear Cu species $\text{[(TMPA)CuI(CH}_3\text{CN)}](B-(C}_6\text{F}_5)_4\text{)}$,20 however log $D$ varies considerably from that determined for the discrete dicopper complexes $\text{[(N}_5\text{)(CuI)}_2\text{](B-(C}_6\text{F}_5)_4\text{)}_2$ and $\text{[(XYL-H)CuI}_2\text{](B-(C}_6\text{F}_5)_4\text{)}_2$, see SI including Table S1.

Additionally, variable-temperature (VT) $^1$H NMR experiments on (I) in THF-$d_8$, acetone-$d_6$, or DMF-$d_7$ ($25^\circ \text{C}$ to $-60^\circ \text{C}$) show minimal temperature dependence resulting from chemical dynamics (see Figures S7$-$S11 for details). This is in contrast to systems where the dimer is in equilibrium with the monomer, resulting in significant chemical shift changes with temperature.6,16 Further, DMF and acetone are reasonably good ligands for copper(I), 21 and even weak solvent coordination would be expected to break up any dimeric structure.22

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Synthesis and Characterization of Copper(II) Complexes. To experimentally probe the effect of the thioether substituent on the Cu(II)$-$S interaction, which would also be expected to occur in copper-dioxygen adducts where the copper is either CuII or Cu III (vide infra), copper(II) perchlorate complexes (Chart 2) were synthesized for each ligand. $\text{[(DMMESE)CuII(ClO}_4\text{)]}^+$ $\text{[(DMMESE)CuII(ClO}_4\text{)]}^+$, $\text{[(DMMESP)CuII(H}_2\text{O)}](ClO}_4\text{)}_2$ ($2a$), and $\text{[(DMMESDP)CuII(H}_2\text{O)}](ClO}_4\text{)}_2$ ($3a$). Selected bond distances ($\AA$) and bond angles (deg) are also listed. The H atoms (except for those of the water ligands found in $2a$ and $3a$) and noncoordinating counterions were omitted for clarity.

**Figure 3.** Representations of the monomeric Cu(II) complexes described in the crystal structures of (a) $\text{[(DMMESE)CuII(ClO}_4\text{)]}^+$ ($1a$), (b) $\text{[(DMMESP)CuII(H}_2\text{O)}](ClO}_4\text{)}_2$ ($2a$), and (c) $\text{[(DMMESDP)CuII(H}_2\text{O)}](ClO}_4\text{)}_2$ ($3a$). Selected bond distances ($\AA$) and bond angles (deg) are also listed. The H atoms (except for those of the water ligands found in $2a$ and $3a$) and noncoordinating counterions were omitted for clarity.
group), while steric factors are clearly relevant, even with comparing the Cu–S bond lengths 2a directly with 3a, the latter with its o-methylaryl substituent. We carried out cyclic voltammetry experiments on 1a, 2a, and 3a (see the SI). A slightly more negative $E_{1/2}$ value observed for 1a compared to 2a and 3a indicates that the ethylthio arm of 1a is at least a marginally better donor than the thiophenyl-type arms in 2a and 3a. Overall, however, it is difficult to tease out the differences in electronic vs steric factors in these and related complexes.24

The EPR spectra for all of these complexes in solution are of the axial type (Figure S18) indicating that these mononuclear Cu(II) complexes are found in a distorted SP environment. This observation that the S(thioether) atom binds axially in these copper(II) complexes suggests that such binding can occur in the copper-dioxygen adducts described below.

**Oxygenation Reactions of Cu(II) complexes.** [DMMESE]-Cu$^{II}$ (1) + O$_{2(1)}$. Dioxygen reacts with [DMMESE]Cu$^{III}$ (1) in MeTHF at −130 °C, forming the low-temperature stable intense indigo blue species (1$^\mathbf{3}$)(see Chart 2). The UV–vis spectrum of 1$^\mathbf{3}$ is characterized by three transitions at 445 (2150 M$^{-1}$ cm$^{-1}$), 521 (8640 M$^{-1}$ cm$^{-1}$), and 615 nm (10 850 M$^{-1}$ cm$^{-1}$; Figure S23) and is similar to other trans-peroxo species such as [(TMPA)Cu$^{II}_2$($\mu$-1,2-O$_2$)$^\mathbf{2+}$].25 Yet, the lower energy charge transfer (CT) transition at 615 nm for 1$^\mathbf{3}$ is more intense than the higher energy transition. This intensity ratio was previously observed in [(ESE)Cu$^{II}_2$($\mu$-1,2-O$_2$)$^\mathbf{2+}$] (Chart 1d, Figure 4b) and was ascribed to a geometric distortion from the trigonal bipyramidal coordination environment in TMPA (Figure 4a) toward a SP geometry in ESE. This geometric distortion would increase the overlap of the $\pi^*$ orbital with the Cu(II) hole, resulting in a higher intensity CT transition.26 The similar intensity ratio of the CT transitions in 1$^\mathbf{3}$ and [(ESE)Cu$^{II}_2$($\mu$-1,2-O$_2$)$^\mathbf{2+}$] indicate it also possesses a distorted SP geometry, similar to the coordination environment observed in the X-ray structure of [DMMESE]-Cu$^{II}_2$(ClO$_4$)$_2$ (1a) (vide supra).

[(DMESP)Cu$^{II}$] + O$_{2(1)}$. Upon oxygenation in MeTHF at −130 °C, a trans-peroxodicopper(II) species [(DMESP)-Cu$^{II}_2$($\mu$-1,2-O$_2$)$^\mathbf{2+}$]$^\mathbf{2+}$ with UV–vis features at 504 and 644 nm was initially formed. Over time (∼30 min) these features decay, and a new species (2$^\mathbf{0}$) with an absorption feature at 388 nm forms (Figure 5).

However, the absorption features of 2$^\mathbf{0}$ do not completely convert to 2$^\mathbf{0}$ (Figure S), indicating an equilibrium between these complexes (Figure 6a, upper), with $K_{eq} = [2^\mathbf{0}]/[2^\mathbf{0}] = 2.6$ at −130 °C.26 The rate constant for the trans-peroxo to bis-µ-oxo interconversion can be well estimated from the data in Figure S, $k_{trans\rightarrow bis-oxo} = 9.6$ s$^{-1}$ (−130 °C). Further evidence that the low-temperature combination of 2$^\mathbf{0}$ and 2$^\mathbf{0}$ represents a dynamic equilibrium mixture can be readily seen from examination of a series of spectra we recorded for the 2 + O$_2$ reaction at a variety of temperatures, in some cases then also warming. These spectra and explanatory comments are given in Figures S19–S20.

We have previously characterized a similar trans-peroxo/bis-µ-oxo equilibrium with the all nitrogen tetradeutrar donor (BQPA) ligand (BQPA = bis(2-quinoxyethyl) (2-pyridylmethyl)-amine). Similarly, [(BQPA)Cu$^{II}_2$] reacts with dioxygen to first form a Cu$^{III}_2$($\mu$-1,2-O$_2$)$^\mathbf{2+}$ species that converts to a Cu$^{III}_2$(µ-O$_2$)$^\mathbf{2+}$ complex, $k_{trans\rightarrow bis-oxo} = 0.16$ s$^{-1}$ (−90 °C); $K_{eq} = 3.2$ (−90 °C).27 The observation of a trans-peroxo/bis-µ-oxo equilibrium in these systems differs from what has typically been presumed, that only a side-on µ-η$^1$-η$^1$-peroxodicopper(II) could be in (rapid) equilibrium with a bis-µ-oxodicopper(III) complex (Figure 6b, upper).2

The Cu$^{III}_2$($\mu$-O$_2$)$^\mathbf{2+}$/[Cu$^{III}_2$($\mu$-1,2-O$_2$)$^\mathbf{2+}$] equilibrium with DMMESE (Figure S and 6a) is also sensitive to the addition of the coordinating anion methylsulfonate. A spectroscopically pure (UV–vis) bis-µ-oxo species 2$^\mathbf{0}$ ((CH$_3$SO$_3$)$_{\mathbf{2+}}$), $\lambda_{max} = 386$ nm (13 000) (Figure S22), is obtained with one equiv of (NBu$_4$)($\mathbf{2+}$)(CH$_3$SO$_3$) (Figure 6a, lower part).28 Stack and co-workers29 previously demonstrated that addition of methylsulfonate or other chelating anions converts a mixture of side-on µ-η$^1$-η$^1$-peroxodicopper(II) and bis-µ-oxodicopper(III) species with bidentate ligands to an anion bridged side-on peroxo species (Figure 6b). Masuda and co-workers30 also observed conversion of a Cu$^{III}_2$($\mu$-O$_2$)$^\mathbf{2+}$ complex to a side-on peroxo species bridged by a benzoate donor with addition of the latter,
indicating coordinating anions stabilize the side-on peroxo isomer relative to the bis-μ-oxo.

$[\text{DMMESDP} \text{Cu}^\text{II}]^+ (3) + \text{O}_2 \text{gms}$. The reaction of $[\text{DMMESDP} \text{Cu}^\text{II}]^+ (3)$ with $\text{O}_2$ only gives a bis-μ-oxodicopper(III) species (UV−vis criterion), $[\text{DMMESDP} \text{Cu}^\text{II}]_2^2+ (\text{O}_2 \text{O}^-)_2 (3^0)$ ($\lambda_{\max} = 388$ nm, 13 000 M$^-1$ cm$^1$), see Figure S23. This species (3$^0$) is stable for hours at $-130 \degree C$ with only minimal decomposition occurring (UV−vis criterion). The increased size of the dimethylphenyl group weakens the Cu−S interaction (as evident from the longer Cu(II)−S bond in the structure of 3a) with the result that DMME ESP acts like a tridentate ligand, which favors the bis-μ-1,2-peroxo dicopper(III) analogue; in the structure of $[\text{TMPA} \text{Cu}^\text{II}]_2(\text{μ-1,2-} \text{O}_2 \text{O}^-)_2$ (Figure 4), the ligand arms are interdigitated.

The influence of the Cu−S interaction on the oxygenated products was further probed in comparison to a ligand lacking the thioether donor atom. Oxygenation of the Cu(II) complex (4) of DMME OE, possessing the same three N-donors but having an ether O atom replacing the sulfur (Charts 1 and 2), leads to the formation of a new species with prominent optical absorption at 382 nm (20 000 M$^-1$ cm$^1$, Chart 2), nearly identical in $\lambda_{\max}$ and absorptivity to the bis-μ-oxo complexes 2$^0$ and 3$^0$. The further comparison of the UV−vis spectrum of 4$^0$ with those of 2$^0$ and 3$^0$ and other literature examples$^{15e,31}$ clearly shows this is a bis-μ-oxodicopper(III) complex, $[\text{DMMEOE} \text{Cu}^\text{III}]_2(\text{O}_2 \text{O}^-)_2$ (4$^0$). This suggests that as the fourth donor is weakened, the bis-μ-oxo isomer is stabilized, and the ligand behaves like a N$_3$ donor. Since the oxygen atom of the ether arm in DMME OE has an extremely weak to nonexistent interaction with the copper, this also strongly suggests that the thioether is coordinated to the Cu(II)−O isomer relative to the bis-μ-oxo isomers. 27

Resonance Raman Spectroscopic Characterization of 1$^0$, 2$^0$, 2$^0$, 2$^0$−(CH$_2$SO$_3$)$^-$, and 3$^0$. Resonance Raman spectroscopy confirms the assignment of 1$^0$ and 2$^0$ as trans-peroxo isomers and 2$^0$, 2$^0$−(CH$_2$SO$_3$)$^-$, and 3$^0$ as bis-μ-oxo isomers. Laser excitation of oxygenated samples of 2 that were frozen after $-1$ min contains mostly 2$^0$ and yields Raman spectra (Figure 7a) with four isotope sensitive bands that are consistent in energy and isotope shift with the $\nu_{\text{O-O}}$ ($\text{^18O}_2$: 830 and 810 cm$^-1$; $\text{^16O}_2$: 784 and 772 cm$^-1$) and the symmetric $\nu_{\text{Cu-O}}$ ($\text{^18O}_2$: 545 and 531 cm$^-1$; $\text{^16O}_2$: 518 and 500 cm$^-1$) of previously characterized end-on peroxo species. 14 The presence of two $\nu_{\text{O-O}}$ is similar to the R spectra of $[\text{BQPA} \text{Cu}^\text{II}]_2(\text{O}_2 \text{O}^-)_2$ and results from two end-on peroxo isomers in both systems. 27 These two species likely arise from the asymmetric coordination environment present in DMME ESP, which yields two different arrangements of the ligand around the Cu$^\text{II}$-O$_2$O$^-$. 28b In one isomer, the thioether ligands would be anti to each other and in the other syn (Scheme 1). Also present in the R spectra is an isotope insensitive vibration at 415 cm$^-1$. A band at similar energy and intensity is observed in the R spectra of $[\text{TMPA} \text{Cu}^\text{III}]_2(\text{O}_2 \text{O}^-)_2$ and has been previously assigned as the Cu−Namine stretch. 25b The R spectra of 1$^0$ are also characteristic of an end-on peroxo species (Figure S24) and are consistent with the presence of both syn and anti trans-peroxo isomers.

Laser excitation of an oxygenated sample of $[\text{DMMESDP} \text{Cu}^\text{II}]^+$ (2) that was frozen after $-90$ min and contains mostly 2$^0$ produces one isotope sensitive stretch ($\text{^18O}_2$: 597 cm$^-1$; $\text{^16O}_2$: 570 cm$^-1$, Figure 7b) that is similar to the R spectra of the structurally characterized $[\text{Me}_3\text{tpa} \text{Cu}^\text{III}]_2(\mu-\text{O}_2 \text{O}^-)_2$ complex$^{34}$ and the bis-μ-oxo isomer of BQPA.$^{27}$ This vibration has been previously assigned as the symmetric Cu$_2$(μ-2O$_2$O$^-)_2$ core-breathing mode. The addition of dioxygen and 1 equiv of tetrabutylammonium methanesulfonate (CH$_3$SO$_3$)$^-$ (per copper dimer) to a solution of the Cu(I) salt 2 results in an absorption spectrum that only contains features arising from a bis-μ-oxo species (vide infra). The R spectra of this complex is indistinguishable (2 cm$^-1$ resolution) from the R spectrum of 2$^0$, which was synthesized with a B(C$_6$F$_5$)$_4$ counterion (Figure S25). Additionally, similar R spectra were observed for 3$^0$ (Figure S26). This further indicates that while 1$^0$ and 3$^0$ are pure trans-peroxo and bis-μ-oxo species, respectively, the oxygenated products of 2 in the presence of B(C$_6$F$_5$)$_4$$^-$ (and not CH$_3$SO$_3$)$^-$ are an equilibrium mixture of these two isomers.

The combination of the absorption and R spectra indicate that the coordination environment of 1$^0$ and 2$^0$ is distorted toward SP (Scheme 1). Not only is this coordination geometry observed in the perchlorate crystal structures 1a and 2a but also the lower energy $\pi^\text{a}$ CT transition in both 1$^0$ and 2$^0$ is more intense than the higher energy $\pi^\text{a}$ CT transition. This is in contrast to the structure of $[\text{TMPA} \text{Cu}^\text{III}]_2(\mu-1,2-\text{O}_2 \text{O}^-)_2$ (Figure 4a) where a trigonal bipyramidal coordination geometry (τ = 0.9) is observed$^{25a,32}$ The ligand environment..
is rather flexible since $2^\mu$ can readily equilibrate to give bis-$\mu$-oxo species ($2^\mu_3$), adopting a Cu$^{II}_3$($\mu$-O)$_2$ core with a square planar geometry (Scheme 1) analogous to the crystallographically characterized complex [((Me$_2$tpa)Cu$^{III}_2$($\mu$-$\delta$-O)$_2$)$_2$]$_2^+$ where Me$_2$tpa has two of the three pyridyl donors (of TMPA) possessing ortho (6-position) methyl groups.33 In this case, the methylypyridines are axial (Cu–N = 2.5 Å). By analogy, the apical amine and one pyridyl ligand arm are equatorial in $2^\mu_3$ and $3^\mu_3$, with the other pyridyl and thiophenyl arms interacting axially with the Cu(III) ion. However, due to the potential lability of this interaction, it is possible that $2^\mu_3$ and $3^\mu_3$ do not possess even a weak, axial thioether–Cu(III) interaction as we have depicted in Scheme 1.

**Ligand Substrate Reactivity of $1^\mu$, $2^\mu$, and $3^\mu$ Species.** To seek further insight into Cu-dioxo bonding and reactivity in the presence of a thioether donor, the copper(I) complexes were oxygenated at slightly warmer temperatures to probe for the possibility of ligand sulfoxidation chemistry. Cu$^{I}$(B(C$_6$F$_5$)$_4$)$_2$ ($2^\mu$) was bubbled with dioxygen gas in MeTHF at $-120 \pm 2$ °C, forming as described above a mixture of [(DMMESP)Cu$^{III}_2$($\mu$-1,2-O$_2$)$^{2+}$ ($2^\mu_2$)] and [(DMMESP)Cu$^{III}_2$($\mu$-O$_2$)$^{2+}$ ($2^\mu$)]. Further hour-long incubation at $-120 \pm 2$ °C led to decomposition of both intermediates resulting in a color change from dark indigo blue to green. Workup of this reaction product solution at low temperature (see SI) and analysis of the organic products, the ligands, and any oxidized species showed that approximately one out of two DMMESP sulfoxidation chemistry. 

The same behavior was observed for the room temperature oxygenation of [(ESE)Cu$^{I}]+$.9b Here, two electrons provided by two copper(I) complexes lead to a sulfoxidation. However, the theoretical yield is a maximum of 50%. By comparison, under $2^\mu$-peroxo/bis-$\mu$-oxo equilibrium observed in other systems. Additionally, only ligands with an accessible bis-$\mu$-oxo isomer oxidize the thioether to the corresponding sulfoxide at low temperatures indicating this isomer is the oxidant responsible for this electrophilic reactivity. The observation of this $\mu$-$\eta^2$-$\eta^2$-peroxodicopper(II) species. These systems demonstrate a new strategy to reversibly cleave an O–O bond, which has new potential implications for the development of a synthetic, copper-based water splitting catalyst.44

**ASSOCIATED CONTENT**

# Supporting Information

Details concerning X-ray crystallographic analyses including cif files, variable-temperature NMR, DOSY NMR, UV–vis, IR and rR spectroscopies, cyclic voltammetry, ESI mass spectrometry, and the procedures for carrying out the sulfoxidation reactivity. 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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