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Electrochemical Behavior of an Aminotrithioether Ligand: Copper(II)-Mediated Oxidative C–C Bond Formation

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A neutral aminotrithioether interacts with Cu^I, generating a coordination polymer in the solid state. Electrochemical studies indicate that the ligand is prone to oxidation by Cu^{II}, which results in a novel C–C bond formation reaction.

Thioether ligands have raised interest in recent years because of their involvement in several types of metalloenzyme active sites.[1−4] Among the inorganic models developed to mimic the properties of these enzymes, polythioethers provide a sulfur-rich environment around biologically relevant metal centers.[5−17] In the specific case of trithioethers, the ethylene-bridged tripodal NS_3 ligands employed by the group of Rorabacher form stable complexes with copper,[18−20] and their electronic properties resemble those of type 1 copper sites in metalloenzymes.[21,22] Related anionic and neutral tripodal trithioethers have been used to prepare monomeric, oligomeric, and polymeric Cu^I complexes (Chart 1).[10−17] In contrast, attempts to prepare cupric analogues have been unsuccessful, and the observed reduction of Cu^{II} to Cu^I indicates ligand-based oxidation.[11] This raises the question of whether the differences in coordination properties between the ethylene- and methylene-bridged trithioethers toward Cu^{II} are due to the lack of a bridgehead N donor in the latter or to the intrinsic reactivity of the $E-CH_2-S$ linker ($E = B$, C, Si). In order to discriminate between the two scenarios, we herein report the synthesis of a methylene-bridged aminotrithioether ligand, its reactivity toward Cu^I and Cu^{II}, and the spectroscopic and structural characterization of the products.

The aminotrithioether ($\mathbf{L^{Me}}$) was obtained by acid-catalyzed condensation of 2,4-dimethylbenzenethiol and hexamethylenetetramine (eq 1). The reaction of $\mathbf{L^{Me}}$ with an equimolar amount of $[Cu(CH_3CN)_4]PF_6$ results in a yellow microcrystalline material formulated as $[\mathbf{L^{Me}}Cu]PF_6$ (**1**) based on combustion analysis. ^1H NMR spectra of acetonitrile-d_3 solutions of $\mathbf{L^{Me}}$ with increasing amounts of $[Cu(CH_3CN)_4]PF_6$ (0.5−2.0 equiv) reveal only one set of resonances that do not change significantly, even at -40 °C, consistent with the presence of several coexisting and rapidly exchanging species.[23] Some of the complexes present in solution were detected by mass spectrometry; electrospray ionization mass spectrometry (ESI-MS) spectra of **1** contain peaks corre-

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(23) See the Supporting Information.

10.1021/ic7009429 CCC: $37.00

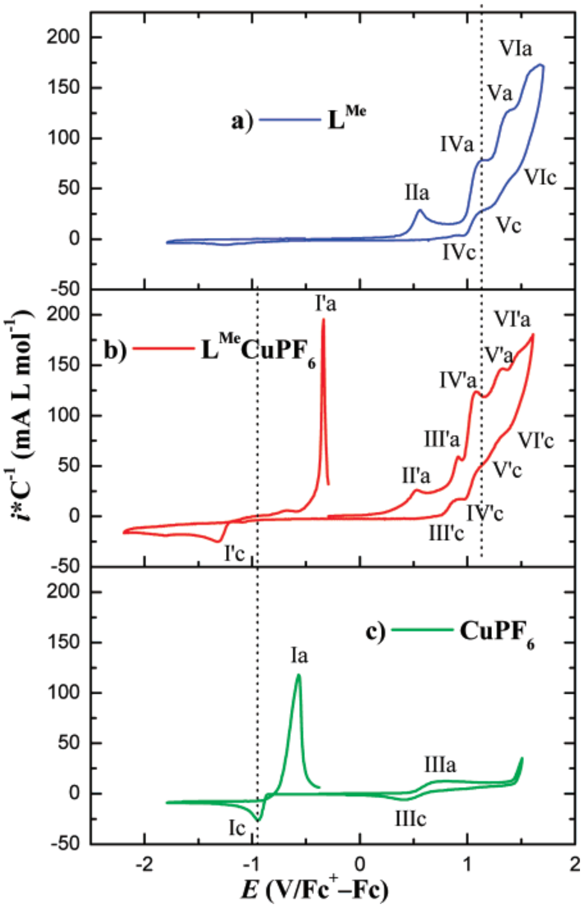
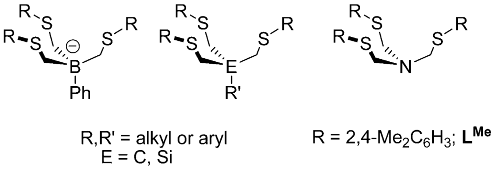
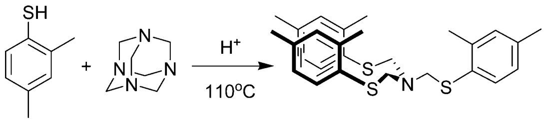


Figure 1. Cyclic voltammograms of (a) $\mathbf{L^{Me}}$, (b) **1**, and (c) $[Cu(CH_3CN)_4]PF_6$ in CH_3CN with $(Bu_4N)PF_6$ as the supporting electrolyte.

Chart 1



sponding to copper-containing species at *m/z* 997 $[\mathbf{L^{Me}}_2Cu]^+$, and the base peak at *m/z* 530 $[\mathbf{L^{Me}}Cu]^+$, as well as ligand-derived fragments.[23]



(1)

The electrochemical behavior of **1** in acetonitrile is characterized by six redox processes (I′−VI′ in Figure 1b), four of which are ligand-centered, based on cyclic voltammetry studies of **1** and $\mathbf{L^{Me}}$. All but one of the processes of **1** are quasi-reversible, with the irreversible anodic peak corresponding to ligand-based oxidation at 0.53 V (II′a, Figure 1b; IIa at 0.56 V for $\mathbf{L^{Me}}$, Figure 1a). The other ligand-centered processes are also displaced to lower potentials upon coordination of Cu^I.[23] The redox process at $E_{1/2} = 0.84$ V (III′, Figure 1b), which is absent in $\mathbf{L^{Me}}$, was assigned to the Cu^{II}/Cu^I couple and is shifted to a considerably higher potential compared to that of $[Cu(CH_3CN)_4]PF_6$, $E_{1/2} = 0.56$ V (III, Figure 1c). Oxidative degradation of $\mathbf{L^{Me}}$ (see below) precludes measurement of the $\mathbf{L^{Me}}/Cu^{II}$ stability constant, which determines the redox potentials in related tripodal ligand/Cu systems.[18,24−26] Nonetheless, the high redox potential of the Cu^{II}/Cu^I couple of **1** can be attributed to the thioether donors, which raise the potential relative to N donors, and the S−Cu−S chelate ring size of 6.[18] Because the Cu^{II}/Cu^I redox potential of 0.84 V is higher than the ligand-centered oxidation at 0.53 V, coordination of Cu^{II} to $\mathbf{L^{Me}}$ could induce an intramolecular redox reaction (see below).

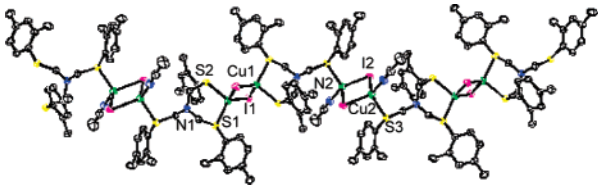


Figure 2. ORTEP diagram of a fragment of the polymeric structure of **3** at the 50% probability level. H atoms and a molecule of acetonitrile are omitted for clarity. Selected bond lengths (Å) and angles (deg): Cu1−I1, 2.636(1); Cu1−I#1, 2.674(1); Cu1−S1, 2.304(1); Cu1−S2, 2.326(1); Cu2−I2, 2.651(1); Cu2−I#2, 2.599(1); Cu2−S3, 2.330(1); Cu2−N2, 2.004(2); I1−Cu1−I#1, 120.57(1); Cu1−I1−Cu#1, 59.43(1); S1−Cu1−S2, 103.12(3); I2−Cu2−I#2, 117.29(2); Cu2−I2−Cu#2, 62.72(2); S3−Cu2−N2, 109.55(7). Color code: C, gray; N, blue; Cu, green; I, pink; S, yellow.

To probe further the donor properties of $\mathbf{L^{Me}}$ toward Cu^I, $\mathbf{L^{Me}}$ was treated with 1 equiv of CuI to yield $[\mathbf{L^{Me}}CuI]$ (**2**), as determined by combustion analysis. ESI-MS spectra of **2** display one copper-containing species $[\mathbf{L^{Me}}Cu]^+$ at *m/z* 530.[23]

Despite repeated attempts to structurally characterize **1** and **2**, X-ray-quality crystals were obtained from the reaction of $\mathbf{L^{Me}}$ with 2 equiv of CuI, which afforded $\{[\mathbf{L^{Me}}Cu_2I_2(CH_3CN)]\cdot CH_3CN\}_n$ (**3**). Its solid-state structure consists of a coordination polymer with bridging iodides and $\mathbf{L^{Me}}$ acting in a μ-κ^1,κ^2 fashion (Figure 2).[27] The independent Cu1 and Cu2 centers are related to additional Cu^I ions by a crystallographic inversion center, generating rhomboidal Cu_2I_2 cores with average Cu−S and Cu−I bond lengths similar to those of reported complexes of trithioethers with Cu^I.[15,28] The lack of bonding between the nearly planar N1 atom (sum of angles = 358°) and the Cu centers can be attributed to the highly strained four-membered chelate ring that would result. In addition, the presence of the strongly coordinating iodo ligands could also preclude Cu−N1 bonding.

The solution behavior of **3** is similar to that of **1** and **2**, although the presence of heavier copper-containing species was evidenced by mass spectrometry.[23] Thus, the peaks at

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(27) Crystal data for **3**: $C_{31}H_{39}Cu_2I_2N_3S_3$, MW = 930.71 g·mol^{-1}, crystal 0.34 × 0.18 × 0.17 mm^3, triclinic, space group $P\bar{1}$, $a = 10.686(2)$ Å, $b = 13.399(3)$ Å, $c = 14.177(3)$ Å, $\alpha = 84.473(3)°$, $\beta = 68.200(3)°$, $\gamma = 73.740(3)°$, $V = 1809.2(7)$ Å^3, $Z = 2$, $T = 173(2)$ K, R1 = 0.0221 for $I > 2\sigma(I)$, wR2 = 0.0566 for 6646 reflections.

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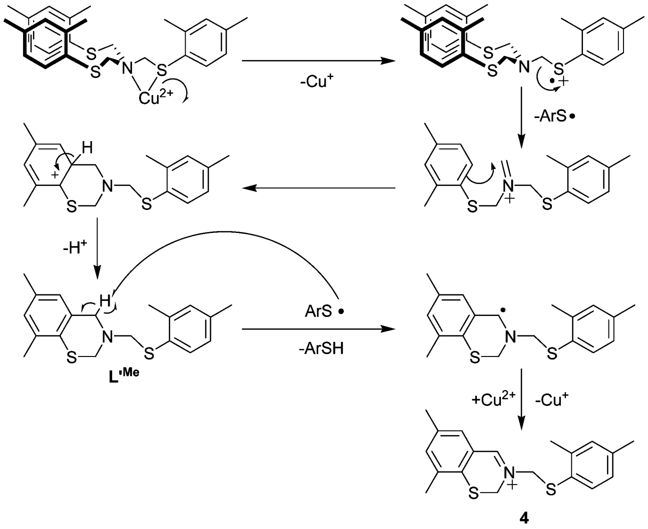
Scheme 1



m/z 1189 and 997 were assigned to the dicopper species $[\mathbf{L^{Me}}_2Cu_2I]^+$ and the previously identified $[\mathbf{L^{Me}}_2Cu]^+$.

Complexes **1**−**3** are stable toward oxidation by O_2 in the solid state: after exposure to air for 7 days, no sign of oxidation to Cu^{II} was found by electron paramagnetic resonance (EPR) spectroscopy. In an aerobic acetonitrile solution, **1** decomposes over a period of 5 days, yielding ArSH (m/z 138, $[ArSH_2]^+$), ArSSAr (m/z 274), and unidentified copper-containing products.[23] Similarly, exposure of acetonitrile solutions of **3** to air led to decomposition, based on UV−vis spectra acquired over 3 weeks.[23] Spectral changes are consistent with ligand-based oxidation, with no bands in the visible region that could be ascribed to d−d transitions of Cu^{II}.

The reduction of Cu^{II} to Cu^{I} by $\mathbf{L^{Me}}$ was evidenced by the bleaching of solutions of $[Cu(H_2O)_6](ClO_4)_2$ and $[Cu(H_2O)_6]Cl_2$. Thus, Cu^{II} complexes of $\mathbf{L^{Me}}$ are not accessible, as is inferred from electrochemical data, in contrast with the reported Cu^{II} complexes of ethylene-bridged NS_3 ligands.[18,19] This behavior had previously been observed in the reaction of trithioether borates with Cu^{II},[11] which leads to unidentified Cu^{I} products. The reaction of $\mathbf{L^{Me}}$ with 1 equiv of $[Cu(H_2O)_6](ClO_4)_2$ in acetonitrile by ESI-MS shows peaks at m/z 883, tentatively assigned to $[Cu(ArSSAr)_3]^+$, at m/z 802 for the copper-containing species $[\mathbf{L'^{Me}}_2Cu(CH_3CN)_2]^+$, at m/z 747 for an unidentified complex, and at m/z 721 for $[\mathbf{L'^{Me}}_2Cu]^+$; fast atom bombardment MS revealed the presence of ArSH and ArSSAr.[23]

Although the ligand derivative $\mathbf{L'^{Me}}$ was not isolated (Scheme 1),[23] the reaction of $\mathbf{L^{Me}}$ with 1−2 equiv of $[Cu(H_2O)_6](ClO_4)_2$ afforded a new compound (**4**) with two inequivalent aromatic groups, based on the four Ar*Me* singlets in the δ 2.28−2.50 ppm region of ^1H NMR spectra (ESI-MS: m/z 328). The solid-state structure of **4** revealed a novel C−C bond formation reaction between one of the aromatic rings and a methylene group (Figure 3).[29] Few examples of copper-mediated C−C bond formation have been reported, and it appears that the presence of an electrochemically active methylene group is essential.[30]

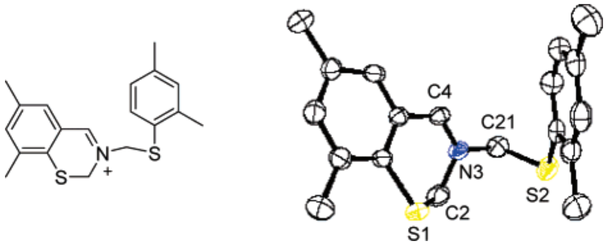


Figure 3. Schematic diagram and ORTEP view of the cation of **4** at the 50% probability level. Selected bond lengths (Å) and angles (deg): N3−C2, 1.479(5); N3−C21, 1.467(5); N3−C4, 1.284(5); S1−C2, 1.767(5); S2−C21, 1.791(4); C2−N3−C4, 119.7(4); C2−N3−C21, 117.6(4); C4−N3−C21, 122.6(4).

The low oxidation potential of $\mathbf{L^{Me}}$ allows intramolecular electron transfer upon coordination of Cu^{II}. Subsequent heterolytic C(methylene)−S bond cleavage would yield a sulfur-based radical and a nitrogen-stabilized carbocation. Electrophilic aromatic substitution at the 6 position would then lead to C−C bond formation to afford $\mathbf{L'^{Me}}$ (Scheme 1). $\mathbf{L'^{Me}}/Cu^{I}$ complexes detected by ESI-MS could not be isolated, and $[Cu(CH_3CN)_4]ClO_4$ was recovered. On the basis of the redox potentials determined for the electrochemically generated $\mathbf{L'^{Me}}$, further oxidation by a second equiv of Cu^{II} is prohibited. Instead, H-atom abstraction (by the limited amount of $ArS^\bullet$ available) followed by oxidation by excess Cu^{II} would yield the observed product **4**.

In summary, $\mathbf{L^{Me}}/Cu^{I}$ represents a dynamic system with rapidly interconverting complexes in solution. The chelate ring size of 4 does not support Cu^{II} complexation, in line with previously reported stability trends for related complexes of tripodal ligands.[18−20,24−26] Instead, oxidation of $\mathbf{L^{Me}}$ by Cu^{II} results in an intramolecular C−C bond formation reaction. Efforts to adapt this novel Cu^{II}-promoted transformation to other organic compounds with electrochemically active methylene groups are currently underway.

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Supporting Information Available: Crystal structure information (CIF) and experimental details (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(29) Crystal data for **4**: $C_{19}H_{22}ClNO_4S_2$, MW = 427.95 g·mol^{-1}, crystal 0.20 × 0.06 × 0.05 mm^3, monoclinic, space group $P2_1/c$, a = 8.887(3) Å, b = 14.107(4) Å, c = 16.121(5) Å, β = 98.751(5)°, V = 1997.6(10) Å^3, Z = 4, T = 173(2) K, R1 = 0.0605 for $I > 2\sigma(I)$, wR2 = 0.1119 for 3643 reflections.

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