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Redox Inversion of Helicity in Propeller-Shaped Molecules Derived from *S*-Methyl Cysteine and Methioninol

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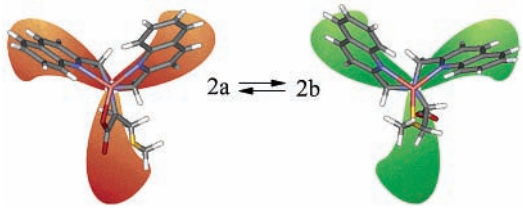
ABSTRACT



One-electron reduction inverts the helicity of copper complexes formed from derivatives of *S*-methylcysteine and methioninol. The change in conformation of the organic ligand is followed in the exciton-coupled circular dichroism (ECCD) spectra of the complexes.

Much interest has been directed to the developing field of molecular switches, where the possibility of creating molecule-based technology is anticipated to advance the miniaturization of computer devices.[1] As these materials are realized, they exhibit promising properties for technologies based on organic electrooptic materials. Among this class of compounds are molecules that have the ability to invert helicity in a reversible manner.[2] These chiroptical switches are often photoresponsive, and the handedness of the molecules allows distinct interactions with left and right circularly polarized light. This birefringent property enables well-defined, nondestructive signal readout. Thus far, interconversion of molecules from one chiral state to another has been achieved by photochromism,[3] thermal isomerism,[4] and reduction/oxidation.[5]

We reported recently a system in which one-electron oxidation or reduction resulted in the inversion of helicity in a coordination complex.[6] This system, shown in Figure 1, involved a derivative of the amino acid methionine. In the copper(II) oxidation state, the ligand formed a pentacoordinate complex with the metal ion and either solvent or counterion. Upon one-electron reduction to copper(I), the ligand underwent reorganization and the carboxylate was replaced by thioether as one of four ligands to the metal ion.

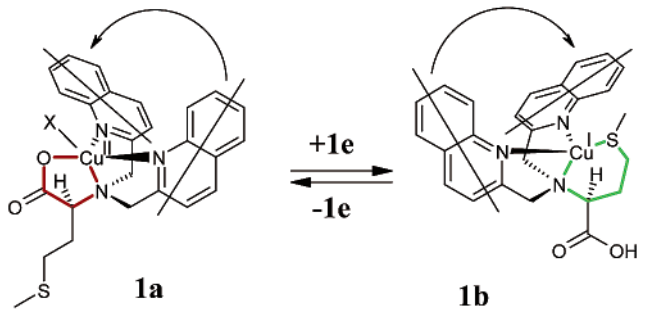


Figure 1. Chiroptical molecular switch based on methionine (X = solvent or counterion).

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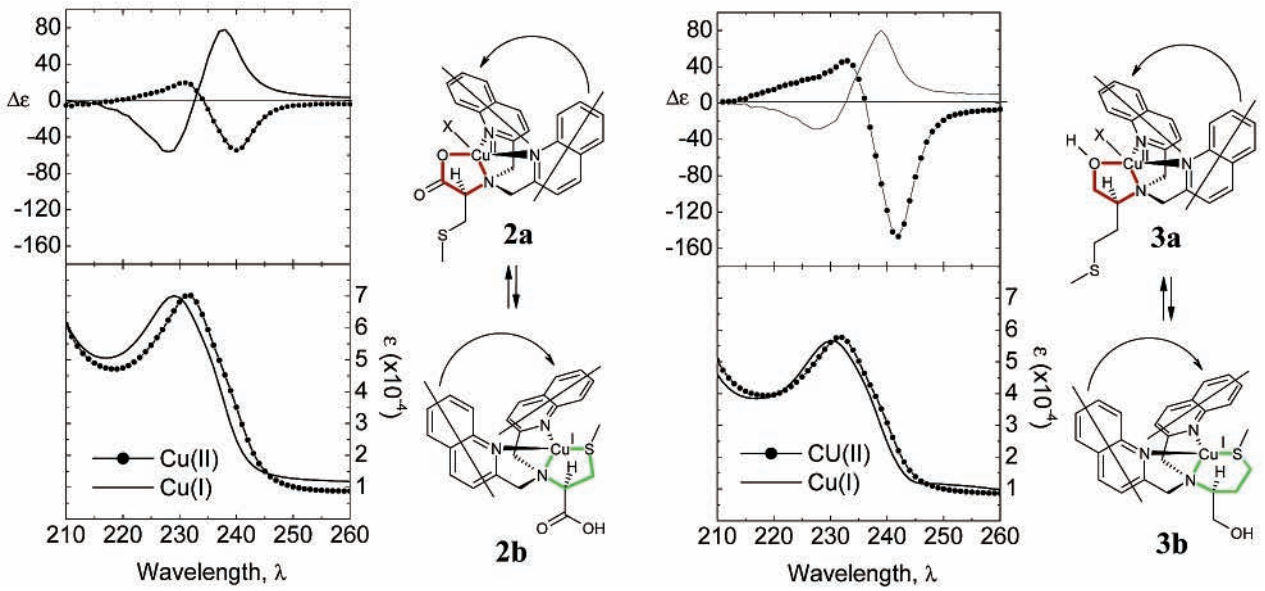
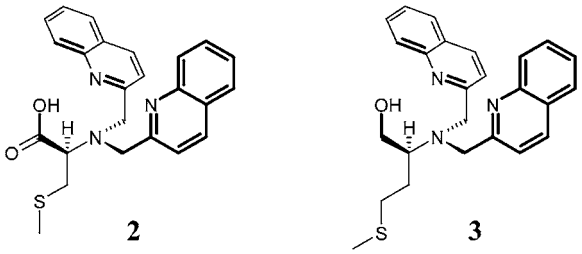


Figure 2. Exciton-coupled CD spectra of **2a**,**b** and **3a**,**b**. The two oxidation states of copper produce opposite Cotton effects (X = solvent or counterion).

In this paper, we report two new systems that show redox inversion of molecular helicity. Ligand **2** is a derivative of *S*-methyl-(L)-cysteine that may coordinate a metal via three nitrogen atoms and either carboxylate or thioether functional groups. Ligand **3** is derived from (*S*)-methioninol (i.e., the product from reduction of (L)-methionine). This ligand offers the metal a choice between thioether or alcohol ligation. These two ligands were selected for study due to their similarity to the methionine system, yet each varied the inner ligation sphere significantly. Previously, the two ligands were reported as putative intermediates in an analytical assay to determine absolute configurations of amino acids and amino alcohols.[7,8]



The requisite ligand for the complex **2a** [Cu(**2**)ClO_4] was prepared from commercially available *S*-methylcysteine. The ester was formed as described,[9] and the product was alkylated in 82% yield with bromomethylquinoline[10] in DMF in the presence of sodium bicarbonate. After saponification of the ester, the carboxylic acid was dissolved in methanol with $Cu(ClO_4)_2 \cdot 6H_2O$, affording blue crystals. The ligand for **3a** [Cu(**3**)ClO_4] was similarly prepared from (L)-methioninol and bromomethylquinoline. The free ligands were characterized by NMR and elemental analysis. The complex **2a** gave satisfactory elemental analysis, but **3a** did not, even after repeated attempts with different counterions. In this complex, the hydroxyl group may be partially protonated, resulting in fractional counterion occupancy. Copper(I) complexes of ligands **2** and **3** were formed by chemical reduction of **2a** and **3a** in situ with ascorbic acid.[11] Independent preparation of Cu(I) complexes by mixing solutions of the ligands with $CuPF_6$ gave solutions with identical spectra, but the data reported here were gathered from solutions prepared using the in situ method. Various attempts to obtain X-ray quality crystals of these complexes produced only amorphous solids.

The absorption spectra of ligands **2**−**3** and their copper complexes in methanol display bands characteristic for quinoline chromophores. The spectra display two major transitions of practically equal intensities (207 and 232 nm) and a band of poorly resolved peaks at 280−330 nm. An analysis of these transitions was discussed elsewhere.[12] Shown in Figure 2 are the transitions near 232 nm, which have been assigned as ^1B_b transitions with transition dipoles oriented in the longitudinal direction crossing both rings.[13]

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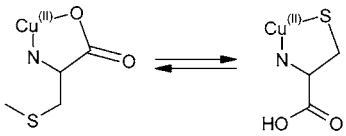
There is a small dependence of λ_{max} upon the presence of metal ion and its oxidation state.

The circular dichroism spectra of the ligands and complexes are shown in Figure 2. While the UV spectra of the free ligands are very similar to those of the complexes, the CD spectra are negligible on the scale observed for the complexes. The significant difference in amplitude of the metal-complexed ligands indicates that a conformational change results in a favorable interchromophore orientation for coupling of the transition moments, giving rise to exciton-coupled circular dichroism (ECCD).[6,14,15] The other telltale indicators of ECCD are the bisignate shape of the spectra and the correspondence of the null in the CD spectra to λ_{max} in the UV spectra. Both the Cu(II) and the Cu(I) spectra satisfy the criteria for ECCD spectra.[16] The Cu(II) complexes give negative couplets (negative and then positive CE, reading from longer to shorter wavelength). The sign of the couplet is consistent with that observed for other derivatives of (L)-amino acids[6,17] and (L)-amino alcohols.[7]

The Cu(II) and Cu(I) complexes give ECCD couplets with inverted signs. Reduction of the oxophilic copper(II) to the thiophilic copper(I) induces ligand reorganization within the complex from a metallochelate involving the carboxylate to a five- (**2b**) or a six-membered ring (**3b**) involving the thioether group. The methylene and methine carbons attached to the tertiary amine nitrogen adopt a conformation in which they are "geared", and the presence of a chiral center on the methionine arm biases the helicity of **2a**. With an L-configuration at the carbon center, an M helix is adopted in the Cu(II) oxidation state. The helicity inverts upon reduction of the metal center because exchange of the carboxylate and thioether groups requires a pivot of the chiral arm about the C−N bond, which in turn induces the two methylene groups to invert. Optical properties of **2a** and **2b** are easily distinguishable by ECCD, which offers advantages such as an infallible (±) readout for each state, as well as increased sensitivity due to signal amplification associated with ECCD.



(1)

The relative amplitudes (defined as $\Delta\epsilon_{peak} - \Delta\epsilon_{trough}$) of the CD spectra are notable. The amplitudes of the two Cu(I) complexes **2b** and **3b** are similar to one another and also to **1b** (A = 110−160 M^{-1} cm^{-1}). However, the amplitude of **2a** (A = 80 M^{-1} cm^{-1}) is only half that of **1a** (180 M^{-1} cm^{-1}) and **3a** (155 M^{-1} cm^{-1}). This is surprising in that the postulated structures of these three complexes are very similar. The likely explanation is the presence of an equilibrium between carboxylate and sulfide ligation in the Cu(II) oxidation state, giving a mixture of $Cu^{II}N_3OX$ and $Cu^{I}N_3S$ coordination, as shown in eq 1. Both **1a** and **3a** offer five-membered metallochelates for carboxylate coordination and six-membered chelate rings for sulfide coordination. For copper(II) complexes, five-membered rings are preferred.[18] Compound **2a**, however, gives five-membered metallochelates regardless of which arm coordinates. Thus, an equilibrium between carboxylate and sulfide coordination in **2a** would result in partial cancellation of ECCD amplitude. Prior studies of a similar derivative of serine also showed reduced amplitude, although not as pronounced.[17]

Variable-temperature CD measurements were used to examine this issue in more detail. *N*,*N*-Bis(2-quinolylmethyl) derivatives of aspartic acid, methionine, alanine, glutamic acid, and leucine showed a pronounced dependence of CD amplitude on temperature (between −30 and 50 °C) with ΔA = 20−45. Reduction of temperature reduces the occupancy of alternative conformations lacking the chromophore orientation that gives rise to strong ECCD couplets.[15] However, derivatives of *S*-methylcysteine and serine show a significantly different temperature dependence, with $\Delta A \leq 10$. The lower dependence of CD amplitude observed for **2a** suggests that the free energies of the two states suggested in eq 1 are closer in energy to one another than those observed for the amino acid derivatives lacking side chains capable of forming five-membered metallochelate rings.

In summary, three systems derived from methionine and cysteine have now been shown to display redox-induced inversion of molecular helicity. Circular dichroism has greatly facilitated this study because of the dependence of CD sign and amplitude on molecular conformation. Indeed, unexpected molecular dynamic aspects of competitive coordination were observed here and would have been difficult or impossible to observe otherwise.

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Supporting Information Available: Experimental procedures and spectroscopic characterization of compounds and variable-temperature circular dichroism data. This material is available free of charge via the Internet at http://pubs.acs.org.

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