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Thioether S-Ligation in a Side-on μ-η^2:η^2-Peroxo Dicopper(II) Complex[†]

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Abstract

$[(\mathrm{ANS})\mathrm{Cu}^{\mathrm{I}}(\mathrm{CH_3CN})]^+$ (1A), with $\mathrm{N_2S_{thioether}}$ ANS ligand, reacts with O_2 giving a side-on peroxodicopper(II) species $[\{(\mathrm{ANS})\mathrm{Cu}^{\mathrm{II}}\}_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-}\mathrm{O_2}^{2-})]^{2+}$ (1P), $\nu_{\mathrm{O\text{-}O}} = 731\ \mathrm{cm}^{-1}$. 1P is shown to possesses S-thioether ligation, following chemical-spectroscopic comparisons with analogues having all N-ligands or a –S(Ph) group. The finding is a rare occurrence and new for side-on $\mathrm{O_2}^{2-}$ binding.

Copper(I)–dioxygen adducts or derived species pertinent to copper protein O_2-binding and activation are currently of considerable interest in bioinorganic chemistry.[1-4] The focus of this paper relates to the discovery and influence of thioether sulfur ligation in copper(I)-dioxygen adducts, a topic which has attracted more recent attention. This is due to the existence of important copper monooxygenases, namely dopamine β-monoxygenase (DβM) and peptidyl glycine α-hydroxylating monooxygenase (PHM), which serve important roles in neurotransmitter or regulatory horomone biosynthesis.[5] The active-site in these proteins, where substrate binding and copper-dioxygen activation occur, is the so-called $\mathrm{Cu_M}$ site, which is ligated by two His and one Met ligands.[5-7] Biochemical and chemical evidence suggests that O_2 binds here and that a $\mathrm{Cu^{II}}$-superoxo ($\mathrm{O_2}^{\cdot-}$) dioxygen adduct or a derived $\mathrm{Cu^{II}}$-hydroperoxo or cupryl ($\mathrm{Cu^{II}\text{-}O^{\cdot}}$) entity initiates substrate oxidation chemistry.[5, 8-12] In

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[†]Electronic Supplementary Information (ESI) available: Experimental details of the structure determinations can be found in the Supplementary Information. Suitable single crystals of $[(\mathrm{ANS})\mathrm{Cu^I}(\mathrm{CH_3CN})]\mathrm{B}(\mathrm{C_6F_5})_4$ (**1A**) and $[(\mathrm{ANS})\mathrm{Cu^{II}}(\mathrm{Cl})_2]$ (**1B**) were mounted in Paratone-N oil on the end of a glass fiber and transferred to the N_2 cold stream of an Oxford Diffraction Xcalibur3 system equipped with Enhance optics and a CCD detector. The frames were integrated and a face indexed absorption correction and an inter-frame scaling correction were also applied with the Oxford Diffraction *CrysAlisRED* software package (CrysAlis CCD, Oxford Diffraction Ltd.,Version 1.171.27p5 beta). The structures were solved using direct methods and refined using the Bruker *SHELXTL* (v6.1) software package (Sheldrick, G.M. 2000). $[(\mathrm{ANS})\mathrm{Cu^I}(\mathrm{CH_3CN})]\mathrm{B}(\mathrm{C_6F_5})_4$ (**1A**): Crystal data. $\mathrm{C_{19}H_{33}CuN_3S{\cdot}C_{24}BF_{20}}$, M = 1078.13, Orthorhombic, *Pbca*, T = 110 K, a = 20.3371(4) A°, b = 16.4920(3) A°, c = 6.8598(6) A°, V (Å^3) = 9008.8(3), Z = 8, μ(Mo-Kα) = 0.65 mm^{-1}, Crystal size (mm) = 0.78 × 0.25 × 0.12, 55908 reflections measured, 10274 unique (R_{int} = 0.083). The final $R_1(I > 2\sigma(I))$ was 0.091. CCDC-738906. $[(\mathrm{ANS})\mathrm{Cu^{II}}(\mathrm{Cl})_2]$ (**1B**): Crystal data. $\mathrm{C_{17}H_{30}Cl_2CuN_2S}$, M = 428.93, Monoclinic, *P*2(1)/*n*, T = 110 K, a = 14.4850(6) Å, b = 9.3727(3) Å, c = 16.0378(6) Å, β = 115.278(5) °, V (Å^3) = 1968.86 (15), Z = 4, μ(Mo-Kα) = 1.47 mm^{-1}, Crystal size (mm) = 0.77 × 0.18 × 0.08, 12886 reflections measured, 4653 unique (R_{int} = 0.031). The final $R_1(I > 2\sigma(I))$ was 0.032. CCDC-738907. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/datarequest/cif.

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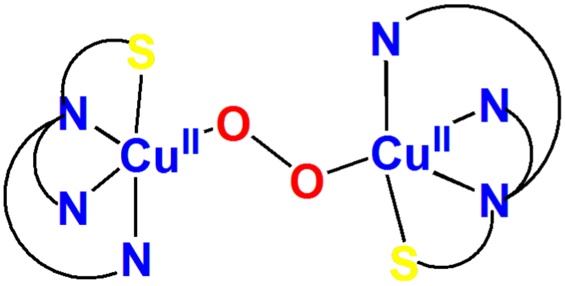
fact, the observance of an X-ray structure on a protein Cu^{II}-$O_2^{\cdot -}$ complex.[7] biochemical evidence.[5, 8-10] and theoretical calculations[9,10] that the Cu^{II}-superoxo species is the one effecting a substrate hydrogen-atom abstraction reaction.

The vast majority of the literature deals with copper(I)/dioxygen chemistry and adducts and reactivity with systems containing all nitrogen ligands, typically bi- tri- or tetradentate entities.[1-4, 13, 14] However, it is clearly important to develop an understanding of how thioether ligation influences the structure(s), spectroscopy, and reactivity of Cu^{I}_{n}-(O_2)-derived species.

Some work in this general area has occurred. A dicopper(I) complex with Met-based ligand was synthesized by Casella and co-workers;[15, 16] reaction with O_2 led to hydroxylation of a xylyl spacer group. Tolman and co-workers reported Cu^{I}-O_2 chemistry with a N_2S β-diketiminate ligand, but the S-donor does not coordinate to copper in derived O_2-adduct.[17] Quite recently, Nicholas and co-workers synthesized a bis-imidazole-thioether tridentate N_2S ligand while Cu^{I}-complex oxidation occurs, they did not observe Cu^{I}-O_2 adducts.[18-20]

Recently, we reported the first copper-dioxygen adduct with thioether ligation, an "end-on" μ-1,2-peroxodicopper(II) complex, each copper ion possessing a tetradentate N_3S ligand.[21, 22]



As DβM and PHM employ N_2S rather than N_3S protein ligand donors, we were interested to look further, at new tridentate ligands. In this report, we describe copper(I)/O_2 reactivity with ANS (Scheme 1), a linear N_2S tridentate ligand. We also had previously studied copper(I)/O_2 chemistry with the N_3 ligand MeAN (Scheme 1), which readily forms a side-on binuclear peroxo complex $[\{(MeAN)Cu^{II}\}_2(\mu\text{-}\eta^2{:}\eta^2\text{-}O_2^{2-})]^{2+}$ (**2P**), λ_{max} = 360 nm (ε=22,000 $M^{-1}cm^{-1}$) and 540 nm (ε = 2,500 $M^{-1}cm^{-1}$).[23] Our hypothesis was that an analogue, ANS, in which one alkylamine arm of MeAN is replaced by a thioether donor, might exhibit related chemistry. This turns out to be true, as we described here.

The copper(I) complex $[(ANS)Cu^{I}(CH_3CN)]^{+}$ (**1A**) (as $B(C_6F_5)_4^{-}$ salt) was generated from $[Cu^{I}(CH_3CN)_4]B(C_6F_5)_4$ addition to ANS, and characterized as a greenish white air-sensitive solid. $[(ANS)Cu^{II}(Cl)_2]$ (**1B**) was also synthesized. Both of these Cu^{I} and Cu^{II} complexes were characterized by X-ray diffraction (Fig. 1). Noteably, the S(thioether) coordination to copper ion occurs in both Cu^{I} and Cu^{II} complexes.

In order to describe the electronic environment of the ligand copper coordination complexes, while also comparing the environment of sulfur containing ANS $_{(N2}S)$ with MeAN (N_3), CO adducts of $[(ANS)Cu^{I}(CH_3CN)]^{+}$ (**1A**) and $[(MeAN)Cu^{I}]^{+}$ (**2A**) were generated and the electrochemistry via cyclic voltammetry of **1A** and **2A** were evaluated (Table 1). The IR spectrum of $[(ANS)Cu^{I}\text{-}CO]^{+}$ (**1-CO**) shows that ν_{CO} = 2092 cm^{-1}, significantly higher than that observed for $[(MeAN)Cu^{I}\text{-}CO]^{+}$ (**2-CO**, 2079 cm^{-1}). It is noteable that ν_{CO} for the Cu_M sites in PHM and DβM (Table 1)[25, 26] are essentially the same as that of $[(ANS)Cu^{I}$-

CO]$^+$ (**1-CO**), indicating that **1A** possesses a chemical environment reasonably mimicking that of protein active sites.

As for the ligand comparison, the results clearly indicate that MeAN is a better donor to copper(I) which then back-donates to its CO ligand to a greater extent, lowering ν_{CO}. The electrochemical behavior for **1A** vs **2A** is consistent with findings for CO ligation and ν_{CO} values, as the strong donor ligand MeAN better stabilizes the higher oxidation state, giving a more negative $E_{1/2}$ value (Table 1).

Oxygenation of **1A** at −94 °C in acetone gives a dark orange species, λ_{max} = 375 nm (ε =10,000 $cm^{-1}M^{-1}$) and 495 nm (ε =1,000 $cm^{-1}M^{-1}$) (Fig. 2), features consistent with those of an μ-η^2:η^2-peroxo-dicopper(II) species.[1] Thus, the complex is formulated as $[\{(ANS)Cu^{II}\}_2(\mu\text{-}\eta^2:\eta^2\text{-}O_2^{2-})]^{2+}$ (**1P**) Confirmation derives from resonance Raman spectroscopic data with λ_{ex}=379.5 nm employing either $^{16}O_2$ or $^{18}O_2$ for complex generation: $\nu_{Cu\text{-}Cu}$ = 273 cm^{-1} (Fig. 3A) and $\nu_{O\text{-}O}$ = 731 cm^{-1} ($\Delta\nu(^{18}O_2)$ = −40 cm^{-1}) (Fig. 3B). These vibrations are characteristic of a μ-η^2:η^2-peroxo-dicopper(II) species.[1,27]

These values are also similar to those observed for $[\{(MeAN)Cu^{II}\}_2(\mu\text{-}\eta^2:\eta^2\text{-}O_2^{2-})]^{2+}$ (**2P**) ($\nu_{O\text{-}O}$ = 721 cm^{-1} and $\nu_{Cu\text{-}Cu}$ = 268 cm^{-1}),[23] however the higher $\nu_{O\text{-}O}$ vibration frequency of $[\{(ANS)Cu^{II}\}_2(\mu\text{-}\eta^2:\eta^2\text{-}O_2^{2-})]^{2+}$ (**1P**) (731 cm^{-1}), compared to that for MeAN complex **2P** (721 cm^{-1}), indicates that the O-O bond in **1P** is stronger. Compared to MeAN, ANS is a weaker donor to copper resulting in increased peroxo π^*_σ donation to Cu and less backbonding into the peroxo σ^* resulting in a stronger peroxo O-O bond.[28]

The supposition that S(thioether) ligation occurs in $[\{(ANS)Cu^{II}\}_2(\mu\text{-}\eta^2:\eta^2\text{-}O_2^{2-})]^{2+}$ (**1P**) derives from observations discussed above and the following argument. If the thioether donor did not bind to copper in **1P** and was dangling, (as seen in Tolman's N_2S system),[17] the remainining "bidentate amine" ligand (N_2 portion of ANS) would result in formation of a bis-μ-oxo dicopper(III) species. As is already known, the copper(I) complex with *N*,*N*,*N*',*N*'-tetramethyl-(*1*,*3*)-propanediamine (TMPD), $[(TMPD)Cu^I(CH_3CN)]^+$ (**4A**), which was described by Stack and co-workers,[29] does exactly this (Scheme 1); $\nu_{Cu\text{-}O}$ = 609 cm^{-1}: $\Delta\nu(^{18}O_2)$ = −28 cm^{-1}. We also note that for a copper(I) complex with TMPD, $E_{1/2}$ is very negative (−393 mV, vs. $Fe(Cp)_2^{+/0}$), consistent with it's ability to form a bis μ-oxo complex, stabilizing a high oxidation state copper(III) environment.

To provide further support for thioether ligation in **1P**, we separately synthesized the ligand ANSPh (Scheme 1) and its Cu(I) complex $[(ANSPh)Cu^I(CH_3CN)]^+$ (**3A**). The large phenyl group of the ANSPh ligand, directly on the sulfur atom, inhibits sulfur coordination to copper ion in a Cu_2/O_2 adduct. This in fact is the case. The reaction of dioxygen with **3A** at −94 °C in acetone gives a yellow bis-μ-oxo dicopper(III) species (**3O**), λ_{max} = 409 nm (ε = 9,000 $cm^{-1}M^{-1}$) similar to typical bis-μ-oxo dicopper(III) species. Resonance Raman data for **3O** (Supporting Material) show only a characteristic core vibration, $\nu_{Cu\text{-}O}$ = 606 cm^{-1} ($\Delta\nu$ ($^{18}O_2$) = −28 cm^{-1}), suggesting a structure just like Stack's TMPD complex (Scheme 1)[29] and indicating the –SPh moiety does not coordinate. By inference, these results indicate that the S(thioether) donor in ANS must be able to coordinate to Cu(II) in $[\{(ANS)Cu^{II}\}_2(\mu\text{-}\eta^2:\eta^2\text{-}O_2^{2-})]^{2+}$ (**1P**).

In summary, a side-on μ-η^2:η^2-peroxodicopper(II) species has been generated from the oxygenation of LCu(I) complex with N_2S thioether ligand ANS. By comparison to the nature of the Cu_2O_2 species generated with closely related ligands where either the S(thioether) is unable to coordinate or is absent (a bis-μ-oxo dicopper(III) complex), we can conclude that coordination of the S(thioether) donor within $[\{(ANS)Cu^{II}\}_2(\mu\text{-}\eta^2:\eta^2\text{-}O_2^{2-})]^{2+}$ (**1P**) occurs. This is the first case of thioether coordination within a μ-η^2:η^2-peroxo-dicopper(II) structural type. This advance in copper-dioxygen chemistry further indicates that it is possible to study systems with S(thioether) ligation. Future investigations will focus on the effect of S(thioether) on reactivity of derived copper-dioxygen complexes,[30] and on the design and study of systems where only one copper ion is present.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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30. Following thermal decomposition of $[\{(ANS)Cu^{II}\}_2(O_2^{2-})]^{2+}$ (**1P**) and $[\{(ANSPh)Cu^{III}\}_2(O^{2-})_2]^{2+}$ (**3O**) and work-up including demetallation, oxygenated ligand products, i.e., sulfoxides of ANS and ANSPh, were isolated in moderate yield. Further details and expanded studies will be the subject of a future report.

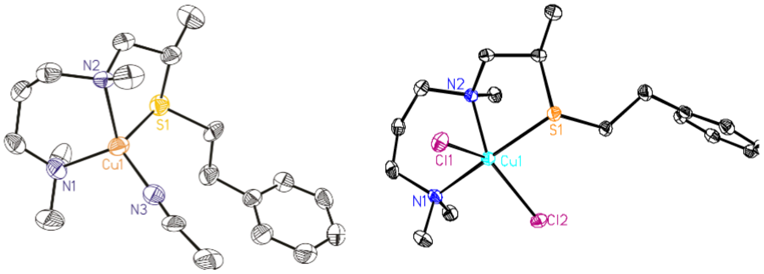


Fig. 1.

ORTEP diagram view (50% probability ellipsoids) of **1A** and **1B**. Left: X-ray structure of **1A**: Cu1-N1, 2.056 Å; Cu1-N2, 2.122 Å; Cu1-N3, 1.935 Å; Cu1-S1, 2.292 Å. Right: X-ray structure of **1B**: Cu1-N1, 2.071 Å; Cu1-N2, 2.136 Å; Cu1-S1, 2.387 Å, $\tau = 0.61$.[24]

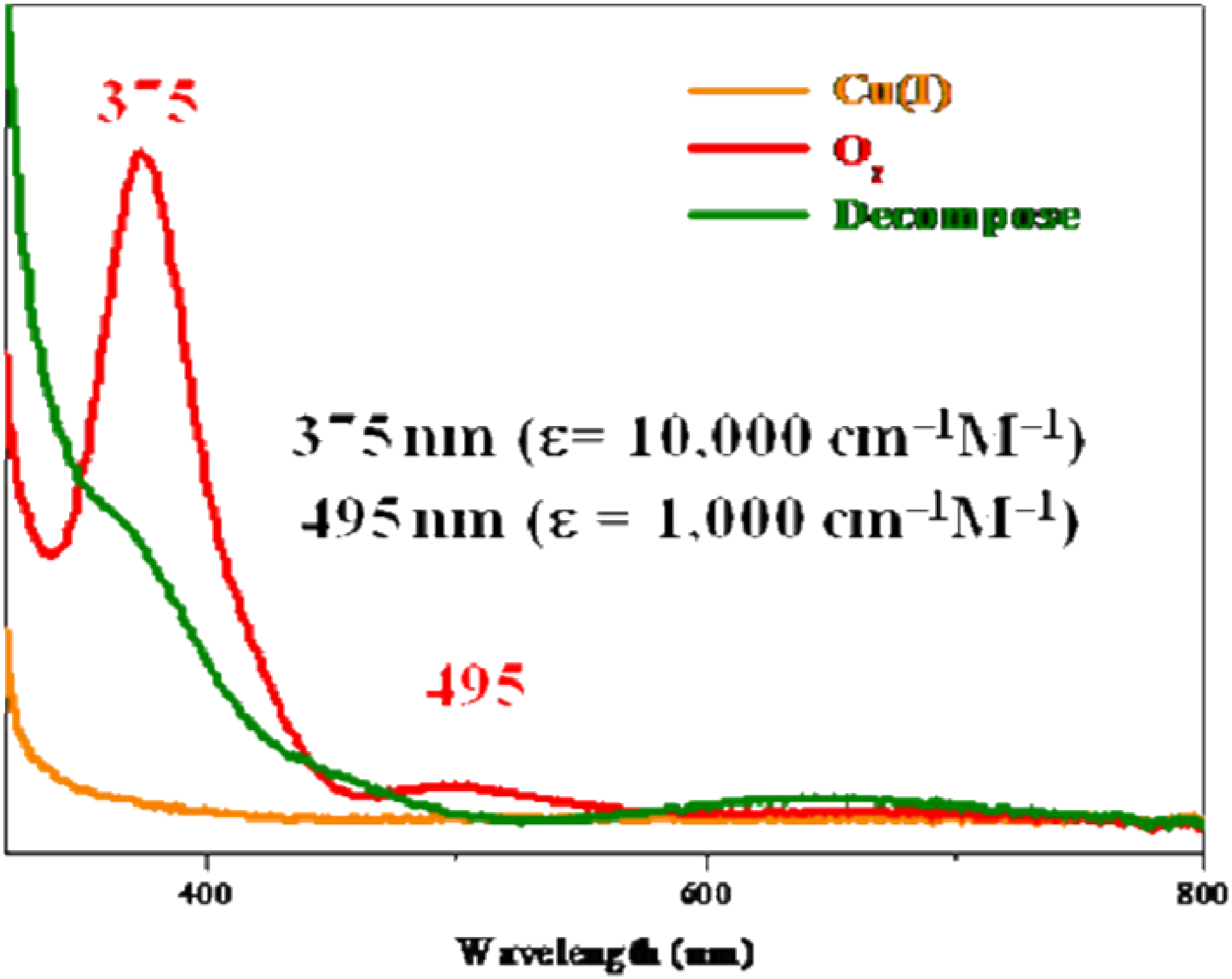


Fig. 2.

UV-Vis changes upon reaction of O_2 with $[(ANS)Cu(CH_3CN)]^+$ (**1A**) (**yellow**) in Acetone at −94 °C giving $[\{(ANS)Cu^{II}\}_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-}O_2)]^{2+}$ (**1P**) (**red**); warming to RT leads to a decomposition product (**green**).

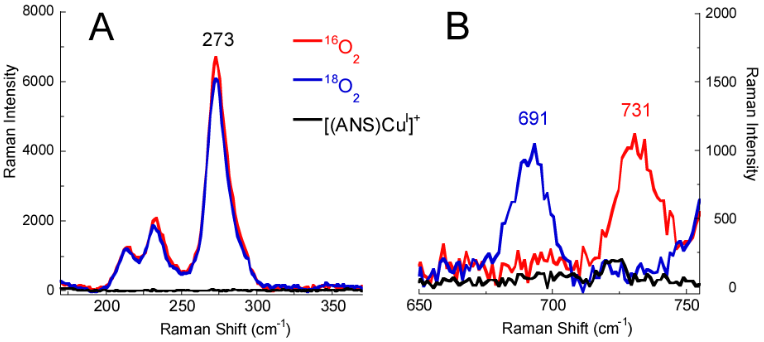
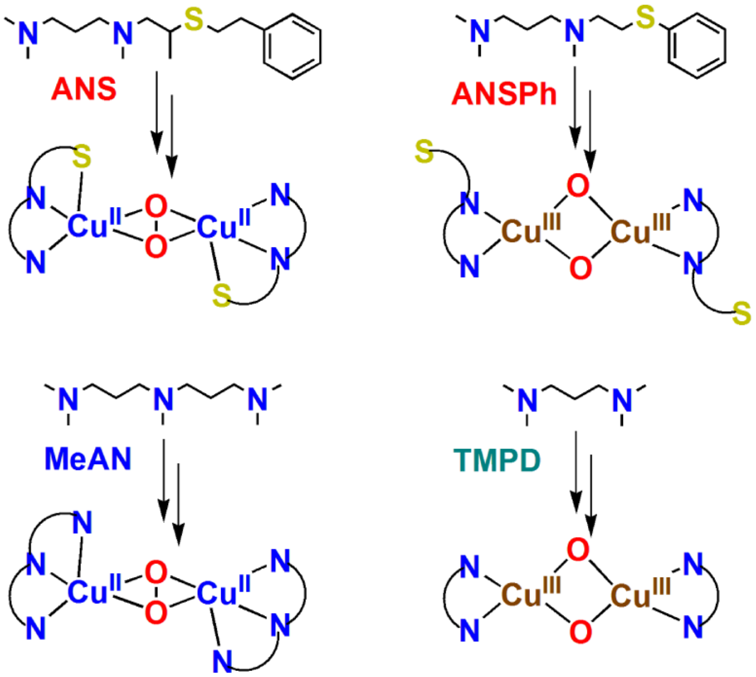


Fig. 3.

rR spectra of $[\{(ANS)Cu^{II}\}_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-}O_2^{2-})]^{2+}$ (**1P**) in acetone with $^{16}O_2$ (red) and $^{18}O_2$ isotopic substitution (blue) in the region of $\nu_{Cu\text{-}Cu}$ (A) and $\nu_{O\text{-}O}$ (B) (λ_{ex} = 379.5 nm, 77K, 5mW power).



Scheme 1.

Ligands and their Cu_2O_2 adducts.

Table 1

IR data for Cu^{I}-CO adducts and $E_{1/2}$ values of Cu^{I} complexes

	MeAN	**ANS**	**PHM**[a]	**DβM**[a]
Cu-CO ν_{CO} (cm^{-1}), THF solution	2079	2092	2093	2089
$E_{1/2}$ (mV) (vs. $Fe(Cp)_2^{+/0}$) DMF solution under Ar	−195	−180		

[a] data for the protein Cu_M site with His_2Met coordination.