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Structural Characterization of the First Example of a Bis(μ-thiolato)dicopper(II) Complex. Relevance to Proposals for the Electron Transfer Sites in Cytochrome *c* Oxidase and Nitrous Oxide Reductase

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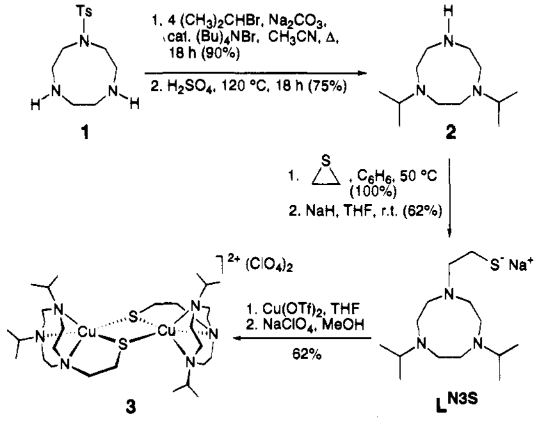
Stimulated by a desire to understand the basis for the unusual spectroscopic properties of type I copper sites in proteins, which have in common ligation of 2 N(His), 1 S(Cys), and 1 S(Met) to a single copper ion, many chemists have targeted mononuclear Cu(II)−thiolate complexes for synthesis.[1] Primarily because of difficulties associated with the redox decomposition shown in eq 1, the number of such compounds that have been isolated is rather limited. Nonetheless, study of these molecules

$$2\mathrm{Cu(II)} + 2\mathrm{SR}^- \rightarrow 2\mathrm{Cu(I)} + \mathrm{RSSR} \qquad (1)$$

has aided in the development of a detailed description of the electronic structural features of the type I sites that emphasizes the central role of the short Cu(II)−S(Cys) interaction.[2] Rapidly accumulating data (summarized elsewhere)[3−6] suggests that a second class of electron transfer centers exists in the enzymes cytochrome *c* oxidase (C*c*O) and nitrous oxide reductase (N$_2$OR). These sites have a dicopper unit (delocalized mixed valence in its resting state) ligated by 2 Cys, 2 His, and 1 Met in an unknown arrangement.[7] The possibility that cysteine thiolates bridge the copper ions has been suggested,[3b,4b,6,8] a doubly-bridged structure being particularly attractive because it could account for the short Cu···Cu distance implicated by EXAFS[4] and the high degree of electron delocalization in the mixed-valence site indicated by EPR.[9] Although Cu(I)−(μ-SR)$_x$−Cu(I) (x = 1 or 2) moieties are relatively common,[8,10,11] complexes containing thiolate bridges between Cu^{I}Cu^{II} [12] or Cu^{II}Cu^{II} [13] pairs are rare. Indeed, despite its prevalence in transition metal chemistry in general, to our knowledge the doubly-bridged M$_2$(μ-SR)$_2$ motif is unknown for M = Cu(II), presumably because of the tendency for operation of eq 1, for which the appropriate stoichiometry would be provided in attempted assembly reactions. Herein we report the use of a new, sterically hindered ligand for the isolation of the first example of such a complex, which has been subjected to structural investigations oriented toward relating its properties to those of the C*c*O and N$_2$OR electron transfer sites.

Scheme 1



The synthesis of ligand L^{N3S} began with 1-tosyl-1,4,7-triazacyclononane (**1**),[14] which was dialkylated and then detosylated to afford 1,4-diisopropyl-1,4,7-triazacyclononane (**2**, Scheme 1).[15] Functionalization with thiirane yielded the mercaptoethyl derivative,[16] which was deprotonated to give L^{N3S} as an air- and moisture-sensitive sodium salt. The title complex, [L^{N3S}Cu]$_2$(ClO$_4$)$_2$ (**3**), was isolated as dark green crystals in 62% yield by mixing L^{N3S} and cupric triflate in THF, removing solvent, exchanging anions (NaClO$_4$ in MeOH), and recrystallizing (MeOH/Et$_2$O).[15]

An X-ray crystal structural analysis (Figure 1)[17] showed that **3** [crystallized from MeOH/CH$_3$OC(CH$_3$)$_3$] contains two symmetry-related square pyramidal Cu(II) ions linked by the thiolate arms of the L^{N3S} ligands [N7 and N7′ in the axial positions].[18] The bis(μ-thiolato)dicopper(II) formulation is supported by the metal ion geometry [typical for Cu(II)] and the long S···S′ distance [3.093(2) Å], which, although shorter than the 3.7 Å van der Waals contact, argues against the presence of a *bona*

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(17) Crystal data for [L^{N3S}Cu]$_2$(ClO$_4$)$_2$·CH$_3$OC(CH$_3$)$_3$[**3**·CH$_3$OC(CH$_3$)$_3$]: MW = 959.07, C$_{33}$H$_{72}$Cl$_2$Cu$_2$N$_6$O$_9$S$_2$, crystal dimensions 0.45 × 0.32 × 0.22 mm, orthorhombic, space group *Pbcm*, a = 12.5618(8) Å, b = 13.4153(9) Å, c = 26.312(2) Å, V = 4434.1(5) Å^3, Z = 4, ρ_{calcd} = 1.437 g cm^{-3}, $2\theta_{\max}$ = 48.12°, Mo Kα radiation (λ = 0.710 73 Å), T = 193 K. Data were collected using the Siemens SMART system, and the structure was solved via direct methods. Full-matrix least squares refinement on F^2 using SHELXTL-V5.0 converged with final R = 0.0386 and wR^2 = 0.0893 for 3568 independent reflections with $I > 2\sigma(I)$ and 283 parameters.

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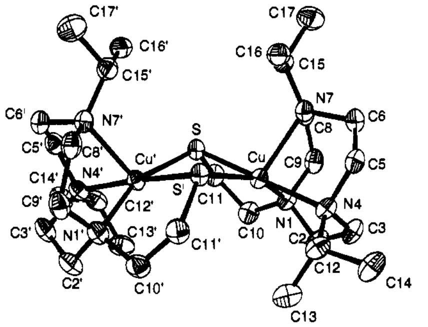

Figure 1. Representation of the cationic portion of the X-ray crystal structure of $[L^{N3S}Cu]_2(ClO_4)_2\cdot CH_3OC(CH_3)_3$ [**3**$\cdot CH_3OC(CH_3)_3$] (50% ellipsoids, hydrogen atoms not shown for clarity). Selected intramolecular distances (Å) and angles (deg): Cu−S, 2.3281(8); Cu−S′, 2.3341(8); Cu−N1, 2.064(2); Cu−N4, 2.102(2); Cu−N7, 2.261(2); Cu···Cu′, 3.340(2); S···S′, 3.093(2); S−Cu−S′, 83.14(3), Cu−S−Cu′, 91.52(3); S−Cu−N1, 86.90(7); S′−Cu−N4, 104.68(7); S−Cu−N7, 93.71(6); S′−Cu−N7, 115.01(6); N1−Cu−N4, 85.18(9); N1−Cu−N7, 85.31(9); N4−Cu−N7, 84.57(9).

fide disulfide bond.[19] The *cis* disposition of the axial N donors accompanies a distinct "butterfly" distortion of the $Cu_2(\mu\text{-}SR)_2$ core of the molecule that is characterized by a 146.5° angle between the S−Cu−S′/S−Cu′−S′ planes. Despite the shortening of the Cu···Cu distance that such a distortion induces, the combined result of a Cu−S−Cu angle of 91.52(3)° and an average Cu−S distance of 2.33 Å is a metal−metal separation of 3.340(3) Å that is notably greater than that typically found in $Cu_2(\mu\text{-}OR)_2$ moieties (ca. 2.9−3.1 Å).

Combined analytical and spectroscopic data suggest that compound **3** retains its integrity in MeOH solution. Evidence in support of this conclusion includes (i) a $[(M)(ClO_4)]^+$ envelope ($m/e = 771$) in the electrospray mass spectrum, (ii) conductance data indicative of a 1:2 electrolyte ($\Lambda_M = 200$ cm^{-1} mol^{-1} Ω^{-1}),[20] and (iii) EPR silence that is consistent with magnetic coupling between Cu(II) ions, the presence of which is supported by UV−vis spectroscopy [λ_{max} (ϵ/complex, M^{-1} cm^{-1}) 274 (sh, 3600), 338 (sh, 3100), 382 (3600), 676 (670) nm]. In CH_3CN, **3** decomposes to a species that exhibits a typical Cu(II) axial signal in its EPR spectrum ($g_\perp = 2.04$, $g_\parallel = 2.20$, $A_\parallel = 152 \times 10^{-4}$ cm^{-1}) and a different UV−vis spectrum [λ_{max} 396 (sh, 596), 490 (sh, 120), 698 (110) nm]. Electrochemical generation of a mixed-valence $[Cu^ICu^{II}]$ derivative of **3** has not been possible so far; only irreversible reductions at −0.23 and −0.73 V vs SCE appear in cyclic voltammograms of **3** in MeOH with 0.1 M $(Bu_4N)(PF_6)$.

X-ray absorption spectroscopic measurements on compound **3** have helped to define the EXAFS signatures associated with bis(thiolate)-bridged dicopper centers.[21] The Fourier transform (Figure 2) is dominated by the first-shell Cu−S component at 2.3 Å, with a barely resolved shoulder from the shorter Cu−N shell at the low R side. Two other resolved bands are seen due to Cu−C (2.9 Å) and Cu−Cu (3.3 Å). The metrical parameters associated with the fit (Figure 2, inset) correspond well with the details of the crystal structure. The well-resolved Cu−Cu peak in the Fourier transform [EXAFS 3.27(7) Å, crystallography 3.340(3) Å] is particularly significant, since it establishes that observable Cu−Cu interactions are expected from dicopper sites with bis(thiolate) connectivity at distances well in excess of 3 Å. This result is relevant to the interpretation of the EXAFS of the Cu_A sites in proteins where the Cu−Cu distance is believed to be much shorter (2.5 Å).

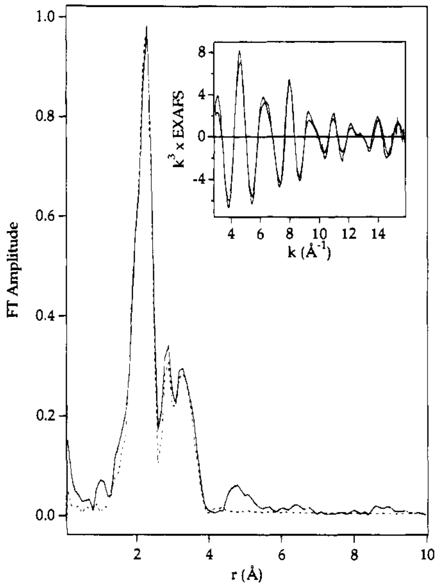

Figure 2. Experimental (solid) and simulated (dashed) Cu *K*-EXAFS (inset) and Fourier transforms of $[L^{N3S}Cu]_2(ClO_4)_2$ (**3**). The metrical parameters [coordination number, distance (Å)] used in the fit were as follows [Debye−Waller terms (Å^2) in parentheses]: 2 N at 2.04 (0.010); 2 S at 2.30 (0.012); 2 C at 2.85 (0.005); 1 Cu at 3.27 (0.012). Estimated errors are ±0.02 Å for first-shell distances and ±0.07 Å for the Cu−Cu interaction.

A folded core similar to that of **3** has been described for a bis(μ-thiolato)dicopper(I) complex $[Cu(SC_6H_4CH_3\text{-}o)(1,10\text{-phenanthroline})]_2$ (**4**) (149.9° fold angle),[10a] but the shapes of the $Cu_2(\mu\text{-}SR)_2$ rhombs in **3** and **4** differ significantly. Compound **4** has a much shorter Cu···Cu distance [2.613(3) Å] and a more acute Cu−S−Cu angle [68.0° (average)], despite similarities between the Cu(I)− and Cu(II)−S bond lengths [2.33 Å (average) and 2.34 Å (average) for **3** and **4**, respectively]. The geometric differences between these sites that have divergent copper oxidation states and coordination numbers illustrate the considerable flexibility of the $Cu_2(\mu\text{-}SR)_2$ unit and suggest that the configuration of such a motif in proteins such as *Cc*O and N_2OR will depend markedly on these factors. In particular, the small coligand set and mixed-valence nature of a $Cu_2[\mu\text{-}S(Cys)]_2$ core in the proteins may result in a short Cu···Cu distance like that implicated by EXAFS experiments, irrespective of the presence of the previously suggested Cu−Cu bond[4a] or additional bridging atom.[4b]

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Supporting Information Available: Experimental procedures and characterization data for all new compounds, UV−vis spectrum of **3** (Figure S1), and full details of the X-ray crystal structure of **3** including tables listing positional parameters, bond lengths and angles, and anisotropic displacement parameters (20 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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