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Molecular Structure and Copper(II)-Mercaptide Charge-Transfer Spectra of a Novel $\text{Cu}_{14}[\text{SC}(\text{CH}_3)_2\text{CH}_2\text{NH}_2]_{12}\text{Cl}$ Cluster

Sir:

The intensely purple copper complexes of penicillamine $[\text{HSC}(\text{CH}_3)_2\text{CHN}^+\text{H}_3(\text{CO}_2^-)]$ and related ligands have possible relevance to the chemotherapeutic treatment of Wilson's^{1,2} and other³ diseases, and are a potential electronic-structural model for the Cu(II)-S(cysteine) chromophores present in the blue copper proteins. We report here the synthesis, unusual cluster structure, and selected electronic spectral properties of a complex best formulated as $([\text{Cu}^+]_8[\text{Cu}^{2+}]_6[\text{SC}(\text{CH}_3)_2\text{CH}_2\text{NH}_2]_{12}\text{Cl}) \cdot \sim 3.5\text{SO}_4 \cdot \sim 19\text{H}_2\text{O}$ (I). A closely related complex of composition $5\text{Ti} \cdot ([\text{Cu}]_{14}[\text{SC}(\text{CH}_3)_2\text{CHNH}_2(\text{CO}_2)]_{12}\text{Cl}) \cdot \sim 18\text{H}_2\text{O}$ (II) was structurally characterized recently by other workers.⁴

A mixture of 1.6 g of CuO, 5.7 g of $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$, 5.6 g of $\text{HSC}(\text{CH}_3)_2\text{CH}_2\text{NH}_2 \cdot \text{HCl}$,⁵ and 500 ml of H_2O was heated to 75 °C over a 15-min period; it yielded a gray solid and a purple filtrate. A stirred suspension of the gray solid in 300 ml of H_2O was transformed into an intensely purple solution, apparently by air oxidation (2 days, 25 °C). Addition of DMF caused precipitation of a purple solid, which was purified by three reprecipitations. Partial evaporation of a DMF/ H_2O solution of the purple material yielded 2.5 g (61% based on CuO) of purple-black crystals.⁶

Diffraction data were collected on a cleaved crystal⁷ using a Syntex P2₁ diffractometer and Mo K α radiation. After locating the copper positions via direct methods,⁸ the structure was solved and refined to convergence using 4790 reflections having $F \geq 3\sigma$; anisotropic temperature factors were refined for all Cu and S atoms. Crystal data and refinement results are as follows: monoclinic; $Z = 4$; $a = 18.318$ (3), $b = 21.826$ (5), $c = 28.829$ (6) Å; $\beta = 110.17$ (1)°; space group $C2/c$; $d_{\text{obsd}} = 1.79$ (1), $d_{\text{calcd}} = 1.745$ g/cm³; $R_F = 9.9\%$; $R_{wF} = 13.5\%$.^{9,10}

The structure (Figure 1) consists of discrete clusters in which 14 four-coordinate copper atoms are linked by 12 three-coordinate mercaptide ions and an eight-coordinate Cl^- ion¹¹ located at the center of symmetry. The Cl^- ion is bound in the antifluorite manner by an approximately cubic array of eight Cu atoms. The average Cl-Cu bond distance of 2.86 Å; Cu-Cl-Cu bond angles fall in the range 69.3–71.4° (70.53° is required for an idealized cubic arrangement). Four-coordination of these copper ions is completed by three triangularly oriented bonds to the bridging mercaptides; the average Cu-S (mercaptide) distance is 2.28 Å. A structural similarity of the pseudo-planar CuS_3 units to the cuprous ion sites in sulfide mineral structures¹³ indicates that Cu(1), Cu(2), Cu(3), and Cu(4) are Cu(I) species. The remaining six copper atoms have an approximately planar cis S_2N_2 ligand set (indicating divalency) with average Cu-N and Cu-S distances of 2.02 and 2.28 Å, respectively. These Cu(II) species are linked via bridges composed of a Cu(I) and two mercaptide sulfur atoms. Each mercaptide bridges two Cu(I) and one Cu(II) species; average Cu(I)···Cu(I) and Cu(I)···Cu(II) distances are 3.3 and 3.9 Å, respectively. Cu(I)···Cu(I) and Cu-S distances of ~ 2.78 and ~ 2.25 Å, respectively, have been reported¹⁴ for three Cu(I) complexes which have the Cu_8S_{12} substructure of I.

Our assignment of copper valences in I requires that the cluster have a net 7+ charge, a value consistent with the 5-charge observed for the cluster in complex II. Although elemental analysis⁶ indicate the presence of $\sim 3.5\text{SO}_4^{2-}$ species per cluster, only two SO_4^{2-} groups have been located crystallographically. The lattice H_2O molecules of both I and II are badly disordered; presumably, this problem also exists for some of the SO_4^{2-} .

Because the Cu(I) and Cu(II) ligand geometries differ greatly, mixed-valence transitions should require large energies¹⁵ relative to those observed for the Cu(I)/Cu(II)-acetate system,¹⁶ and are not expected to contribute to the visible absorptions of this rigid cluster. The broad absorption of the cluster at ~ 518 nm¹⁷ corresponds to an ϵ of ~ 3400 per Cu(II), and is assigned to the σ -component of S \rightarrow Cu(II) charge transfer (LMCT). The expected Cu(II) ligand-field absorptions may contribute to a poorly defined high energy shoulder at ~ 450 nm. Additional complexation of this tertiary mercaptide by two Cu(I) ions may explain the apparent absence of a weaker absorption in the 650–750-nm region otherwise expected for π -LMCT. The assignment¹⁸ of the intense absorption at ~ 600 nm of the blue copper proteins to S(cysteine) \rightarrow Cu(II) σ -LMCT is supported by our results. The observed blue shift of this band in the cluster to ~ 518 nm may result from mercaptide stabilization and/or the relatively high energy of the d vacancy in the pseudo-planar CuS_2N_2 unit. The $[\text{Cu}(\text{I})]_2$ -mercaptide unit does fall short of having thioether-like character; s(thioether) \rightarrow Cu(II) σ -LMCT has been ob-

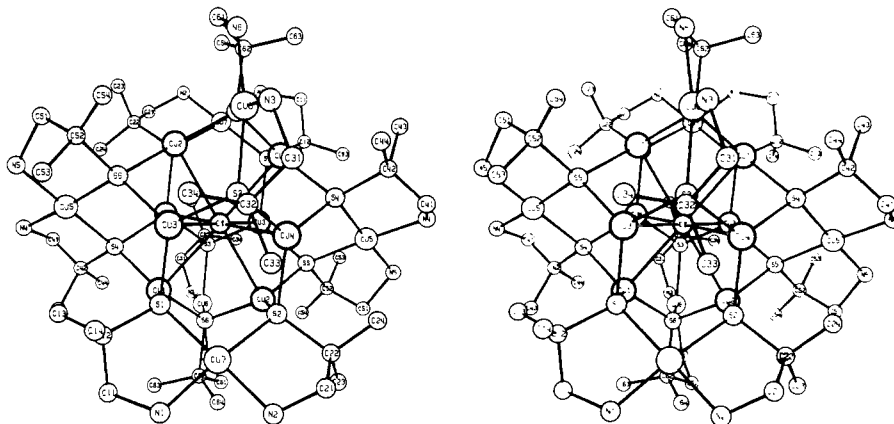


Figure 1. Stereoscopic view of $(\text{Cu}_{14}[\text{SC}(\text{CH}_3)_2\text{CH}_2\text{NH}_2]_{12}\text{Cl})^{7+}$. For clarity the lattice H_2O and SO_4^{2-} ions have been omitted.

served at ~ 390 nm for the trans CuS_2N_2 chromophore of $\text{Cu}(\text{H}_2\text{NCH}_2\text{CH}_2\text{SCH}_3)_2 \cdot 2\text{ClO}_4$.²⁰

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References and Notes

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- Anal. Calcd for $\text{Cu}_4[\text{SC}(\text{CH}_3)_2\text{CH}_2\text{NH}_2]_{12}\text{Cl} \cdot 3.5\text{SO}_4 \cdot 19\text{H}_2\text{O}$: Cu, 31.17; S, 17.41; N, 5.89; C, 20.20; H, 5.58; Cl, 1.24; S (as SO_4), 3.93; Zn, 0.0. Found: Cu, 31.35, 31.27, 31.88; S, 17.99, 17.80; N, 5.84, 6.05; C, 20.31, 21.08; H, 5.40, 5.31; Cl, 1.26, 1.28; S (as SO_4), 4.31; Zn, 0 to "trace".
- The crystals grow as twins, and apparently dehydrate if not sealed in a capillary with some DMF/ H_2O mother liquor.
- Program MULTAN, P. Main, M. M. Woolfson, and G. Germain, Department of Physics, University of York, England.
- The discrepancy between d_{obsd} and d_{calcd} has not been resolved by our attempts to minimize sample dehydration,⁷ the presence of additional H_2O , DMF, or other lattice species is not indicated by elemental analyses.⁸
- $R_F = \sum |F_d| - |F_d| / \sum |F_d|$; $R_{wF} = [\sum w(|F_d| - |F_d|)^2 / \sum w |F_d|^2]^{1/2}$.
- This formulation agrees with the results reported⁴ for complex II and is supported by the special chemical role of Cl^- in the formation of II.^{2,12} An alternate formulation with S^{2-} as the central ion and Cl^- as a disordered lattice species cannot be ruled out entirely.
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- C. Ou, B. Vasilou, V. Miskowski, J. A. Thich, R. A. Lalancette, J. A. Potenza, and H. J. Schugar, to be submitted for publication.

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SN2-Like Transition State for Methyl Transfer Catalyzed by Catechol-O-methyltransferase¹

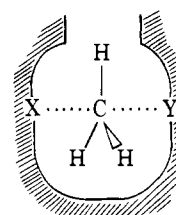
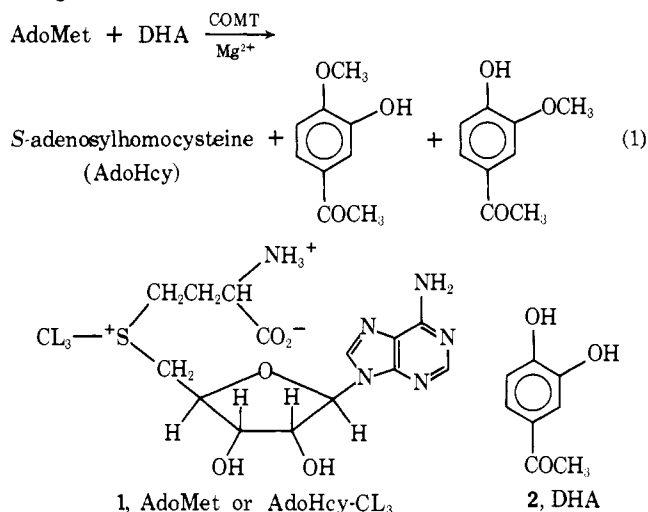
Sir:

The velocity of methyl transfer (eq 1) from *S*-adenosylmethionine (AdoMet or AdoHcy- CL_3 , **1**, L = H or D) to 3,4-dihydroxyacetophenone (DHA, **2**), catalyzed by rat-liver catechol-O-methyltransferase (COMT),² is increased substantially by trideuteration at the transferred methyl group ($V_{\text{H}}/V_{\text{D}} = 0.832 \pm 0.045$ at $37.00 \pm 0.05^\circ$). This inverse α -deuterium secondary isotope effect is exactly what is observed for many classical SN_2 reactions in organic-reaction systems,³ and constitutes a strong indication that COMT catalysis involves rate-limiting SN_2 methyl transfer with a trigonal-bipyramidal transition state of the type shown in structure 3. This information should prove critical

Table I.^a Velocities of Methyl Transfer to DHA from AdoHcy- CH_3 and AdoHcy- CD_3 , Catalyzed by COMT

$10^5[\text{AdoMet}]$, M	$10^9 V$ (M min^{-1}) ^b	
	AdoHcy- CH_3	AdoHcy- CD_3
3.86	$1335 \pm 7, 977 \pm 11$	—
7.73	$1922 \pm 7, 1854 \pm 7,$ 1823 ± 6	$2049 \pm 6, 2021 \pm 6,$ 1957 ± 8
11.59	$2011 \pm 5, 2024 \pm 5$	$2386 \pm 5, 2290 \pm 5$
15.45	$2282 \pm 5, 2307 \pm 5,$ 2280 ± 4	$2659 \pm 4, 2597 \pm 5,$ 2597 ± 5
38.63	$2436 \pm 6, 2545 \pm 6$	$2813 \pm 7, 2838 \pm 9$
103.0	$2728 \pm 11, 2361 \pm 8$	$3024 \pm 12, 3155 \pm 11$

^a Rates measured at 360 nm, $37.00 \pm 0.05^\circ$, phosphate buffer (0.125 M), pH 7.6, $[\text{Mg}^{2+}] = 1.5 \times 10^{-3}$ M, $[\text{DHA}] = 2.5 \times 10^{-4}$ M, $[\text{dithiothreitol}] = 4.5 \times 10^{-3}$ M, protein = 0.839 mg/ml. Velocities in M min^{-1} were calculated from $d(\text{absorbance})/dt$ using $\Delta_{360}^{\text{eff}} = 2877$. ^b Error limits are standard deviations within a single run.



3

for efforts now in progress⁴ to design transition-state-analogue inhibitors, in part for use as drugs, of this important enzyme and closely related enzymes of the liver and central nervous system.⁵

Table I shows velocities of methyl transfer by COMT at various concentrations of AdoHcy- CH_3 and AdoHcy- CD_3 . The data for the CH_3 cofactor generate the Michaelis-Menten expression of eq 2, while that of eq 3 is produced by the rates for the CD_3 cofactor.

$$10^9 V_{\text{H}} (\text{M min}^{-1}) = (2760 \pm 90)[\text{AdoMet}] / \{ [\text{AdoMet}] + (4.1 \pm 0.6) \times 10^{-5} \} \quad (2)$$

$$10^9 V_{\text{D}} (\text{M min}^{-1}) = (3220 \pm 60)[\text{AdoMet}] / \{ [\text{AdoMet}] + (4.3 \pm 0.4) \times 10^{-5} \} \quad (3)$$

Absorbance changes at $[\text{AdoMet}] \ll K_m$ were too small to permit an accurate determination of K_m . Although the mean values of K_m^{H} and K_m^{D} are essentially equal, the large experimental error precludes definite exclusion of a