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Binuclear Copper Complexes: An Open and Shut Case. A Strong Antiferromagnetically Coupled μ-Monohydroxo Bridged Complex

Patrick L. Burk, John A. Osborn,* and
Marie-Thérèse Youinou

Laboratoire de Chimie Inorganique Moléculaire et de
Catalyse (ERA 721)
Institut Le Bel, Université Louis Pasteur
67070 Strasbourg Cedex, France

Yvette Agnus, Rémy Louis, and Raymond Weiss*

Laboratoire de Christallochimie et de
Chimie Structurale (ERA 008)
Institut Le Bel, Université Louis Pasteur
67070 Strasbourg Cedex, France

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Binuclear copper systems are implicated in a wide variety of biochemical processes, especially in transport and multielectron redox reactions of molecular oxygen. Recent interest has focused on the oxygen carrier, hemocyanin[1] and the oxidase enzymes, tyrosinase,[2] laccase,[3] and ceruloplasmin.[4] Particularly intriguing are the changes in spectroscopic, magnetic, and electron resonance data with reactions at the binuclear site.[5] For example, oxy- and methemocyanin,[6] although both formally $Cu(II)_2$ species, are ESR silent, and magnetic susceptibility studies place a lower limit of -550 cm^{-1} for the antiferromagnetic exchange interaction in the oxy form.[7] Chemical, spectroscopic, and EXAFS[8] studies suggest that the two coppers are held by an unknown[9] endogenous ligand at a distance of 3.4–3.7 Å. However, reaction of hemocyanin with NO or $NaNO_2$ (pH $\sim$6)[10] causes conversion to a dimer form which, despite the similarity of its optical properties to the met form, is EPR active, and the Cu–Cu distance is estimated as $\sim$6 Å. In this communication, we present studies on and X-ray structures of a binuclear copper system which demonstrates like properties.

We have previously described the ligand L (or $\langle\cdots\rangle$)[11] and the binuclear copper(I) complex **1**, $[\langle Cu(I)\cdots Cu(I)\rangle](BF_4)_2$, which in propylene carbonate (PC) solution absorbs CO (reversibly) and O_2 (partly reversibly).[12] Treatment of **1**, (in nitromethane) with NO yields a dark-green solution from which, on addition of THF, **2** crystallizes as the dark-green BF_4^- salt. The X-ray structure of **2** consists of discrete binuclear cations $[\langle Cu(II)NO_2\cdots Cu(II)NO_2\rangle]^{2+}$ (Figure 1) and BF_4^- anions.[13] Each Cu(II) has a distorted octahedral environment consisting of the ONS_2 donor set of the ligand and, surprisingly, a chelating NO_2^- group.[14] The approximate symmetry of the cation is C_{2v} with the crystallographic plane of symmetry containing the following atoms: 2 Cu, 2 NO_2, O(7), O(27), N(1), N(21), C(13), C(14), C(17), and C(20). Elongation along one axis produces asymmetrically coordinated NO_2^- groups, as reflected by the longer Cu–O distances 2.38 (3) and 2.50 (3) Å compared to the shorter ones 1.91 (3) and 1.95 (3) Å. The $Cu(II)\cdots Cu(II)$ intramolecular distance is 11.264 (6) Å since L is in an open configuration.

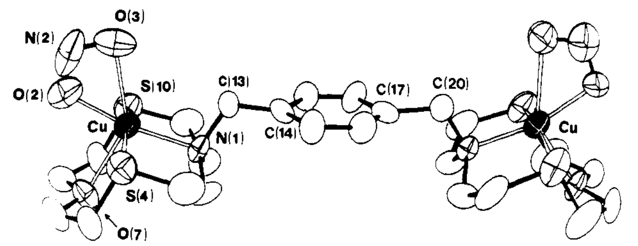

Figure 1. Structure of the $[\langle Cu(II)(NO_2)\cdots Cu(II)(NO_2)\rangle]^{4+}$ cation. The $Cu\cdots Cu$ interatomic distance is 11.264 (6) Å. Selected bond distances (in Å) (the second value corresponds to the related distances or angles for the unlabeled half of the molecule): Cu–O(2), 1.91 (3), 1.95 (3); Cu–O(3), 2.38 (3), 2.50 (3); Cu–N(1), 2.06 (3), 2.02 (3); Cu–S(4), 2.342 (6), 2.377 (6); Cu–O(7), 2.34 (2), 2.22 (2). Selected bond angles (in deg): N(1)–Cu–O(2), 169.6 (2), 163.8 (1); N(1)–Cu–S(4), 88.7 (5), 88.4 (5); N(1)–Cu–O(7), 100.8 (7), 103.6 (8); S(4)–Cu–O(2), 92.6 (6), 93.7(6); S(4)–Cu–O(7), 82.6 (5), 82.6 (4); O(7)–Cu–O(2), 89.6 (8), 92.6 (8).

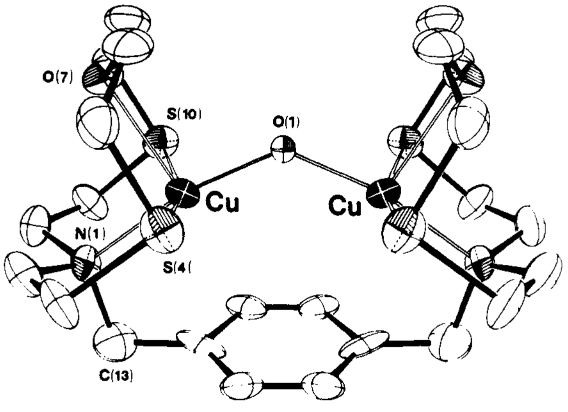

Figure 2. Structure of the $[\langle Cu(II)\cdots(OH)\cdots Cu(II)\rangle]^{3+}$ cation. The $Cu\cdots Cu$ interatomic distance is 3.384 (9) Å and the bond angle Cu–O(I)–Cu is 132.2 (4)°. Selected bond distances (in Å): Cu–O(1), 1.85 (2); Cu–N(1), 2.06 (5); Cu–S(4), 2.35 (2); Cu–O(7), 2.37 (4); Cu–S(10), 2.39 (2). Selected bond angles (in deg): O(1)–Cu–N(1), 167.2 (9); O(1)–Cu–S(4), 95.5 (8); O(1)–Cu–O(7), 98.1 (9); O(1)–Cu–S(10), 95.4 (8); N(1)–Cu–O(7), 94.8 (9); S(4)–Cu–S(10), 159.5 (7).

$[\langle Cu(II)(H_2O)_3\cdots Cu(II)(H_2O)_3\rangle](BF_4)_4$ (**3**) was prepared by addition of $Cu(BF_4)_2\cdot 6H_2O$ (2 mol) to L (1 mol) in PC. The resultant green crystals dissolved in PC show absorptions at 670 (ϵ_{Cu} $\sim$500), 390 (ϵ_{Cu} $\sim$4300), 315 (ϵ_{Cu} $\sim$2000 cm^{-1} mol^{-1} L) and 275 nm (sh). The magnetic moment at 20 °C is 1.85 μ_B/Cu, and the solid-state ESR spectrum at 20 °C shows a resonance at $g_{av} = 2.099$ with no detectable $\Delta m = 2$ transition. Hence a normal

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(1) (a) Himmelwright, R. S.; Eickman, N. C.; Solomon, E. I. *J. Am. Chem. Soc.* **1979**, *101*, 1576. (b) Himmelwright, R. S.; Eickman, N. C.; Lubien, C. D.; Solomon, E. I. *Ibid.* **1980**, *102*, 5378 and references therein.

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(6) It has recently been suggested[1b] that the "dimer" and "met" nomenclature used here be replaced by "EPR-detectable met" and "EPR-nondetectable met".

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(9) In the oxy protein, the coordination around the Cu^{2+} ions is, as yet, unknown; however, recent EXAFS (cf. ref 8) and other studies suggest the presence of three imidazole groups, O_2, and a further bridging ligand.

(10) (a) Schoot Uiterkamp, A. J.; *FEBS Lett.* **1972**, *20*, 93. (b) Schoot Uiterkamp, A. J.; van der Deen, H.; Berendsen, H. C.; Boas, J. F. *Biochim. Biophys. Acta* **1974**, *372*, 407.

(11) L is 1,4-bis[(1-oxa-4,10-dithia-7-azacyclododecan-7-yl)methyl]benzene which can bind two metal ions in an ear-muff configuration clearly demonstrated in Figure 2.

(12) Bulkowski, J. E.; Burk, P. L.; Ludmann, M. F., Osborn, J. A. *J. Chem. Soc., Chem. Commun.* **1977**, 498.

(13) **2** crystallizes in the monoclinic space group $P2_1/m$ with $a = 14.471$ (4), $b = 17.201$ (5), $c = 8.835$ (3) Å; $\beta = 106.19(2)°$; $M_r = 909.56$, $\rho_{calcd} = 1.430$ g cm^{-3} with $Z = 2$ formula units per cell. A total of 1910 independent nonzero reflections were measured on a Picker FACS 3 diffractometer, and 1220 reflections with $I > 3\,\sigma(I)$ were used in subsequent structure solution and least-squares refinement. $R_f = 0.09$ and $R_{wf} = 0.10$.

(14) The origin of the additional oxygen atom is unclear but may come from adventitious traces of oxygen or by disproportionation of NO on the complex.

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Cu(II) complex is indicated, showing no interaction between Cu(II) ions, in which an open conformation of L as found for **2** is presumed for **3**.

When dissolved in water at pH ~6, **3** is transformed into a closely related complex which can be isolated independently.[15] This new complex **4** shows optical transitions (in PC) at 685 (ϵ_{Cu} ~475), 585 (sh), 447 (ϵ_{Cu} ~8000), 375 (ϵ = ~4200), and 315 nm (ϵ ~1600). Analysis and infrared data indicate the presence of the complex $[\langle Cu(II)\cdots(OH)\cdots Cu(II)\rangle](BF_4)_3$ as well as solvate molecules of PC, H_2O, and ethyl acetate. The preliminary X-ray structure of **4**[16] is shown in Figure 2. The two copper atoms, each in a distorted five-coordinate geometry, are bridged by a single hydroxo group. The dimer unit possesses a symmetry plane which is perpendicular to the phenyl ring and contains the oxygen atom of the bridge. The geometry around each Cu(II) ion is approximately square pyramidal. The basal plane defined by O(1), S(4), N(1), and S(10) is distorted toward a tetrahedral configuration as indicated by the angles S–Cu–S = 159.5 (7) and N–Cu–O = 167.2 (9)°. The apical position is occupied by the ether O(7). Most important, L is now in its "ear-muff" or closed conformation with the single bridging hydroxo group holding the two Cu(II) atoms at a distance of 3.384 (9) Å. The Cu-O-Cu angle of 132.2 (4)° is much larger than those previously observed in planar di-μ-hydroxo copper complexes which range from 95 to 105°.[17]

Despite the similar optical properties of **3** and **4**, **4** has entirely different magnetic and ESR behavior. The ESR spectrum of powdered samples of **4** at 293 K shows typical triplet state features, with $\Delta m = \pm 1$ transitions at $g = 2.094$ and a much weaker $\Delta m = 2$ transition at half-field characteristic of the dimeric unit.[18]

The temperature dependence of the magnetic susceptibility was monitored through measurements of changes in the area of the $\Delta m = 2$ ESR signal with temperature[19] in the range 333 to 103 K. A plot of log IT against $1/T$, where I is the product of the intensity of the signals and the line width square, is linear with a slope of $|2J|/k$. The average $-2J$ value thus obtained by three measurements on three different samples is 850 cm^{-1}. Similarly, the temperature variation of the magnetic susceptibility has been studied to determine the magnitude of the exchange integral by using a Faraday-type magnetometer from 300 to 1.3 K. The data are typical of two strongly antiferromagnetically coupled ($S = {}^1/_2$) systems which exhibit a subnormal magnetic moment of 0.48 μ_B/Cu at room temperature. Furthermore, the magnetic susceptibilities measured from 300 to 1.3 K allow the singlet–triplet separation energy of −2J to be calculated[20] as 820 cm^{-1}, which is in good agreement with the ESR data.

Binuclear copper complexes bridged by a single hydroxo group are rare.[21-26] Complex **4** is the first example for which the X-ray structure as well as the detailed magnetic measurements have been reported. The very strong antiferromagnetic interaction observed in **4** would seem to be related to the large Cu–O–Cu angle as well as to the presence of the bridging OH group in both basal planes of the binuclear unit thus allowing good overlap with the $d_{x^2y^2}$ orbitals of both Cu atoms.[27] These results lead to two important conclusions: (a) the conformational flexibility of this type of ligand and the "face-to-face" approach of the two nucleating centers allow the observation of sensitive structural and physical changes at the binuclear site; (b) a single bridging phenolate from a tyrosine residue could adequately satisfy the structural and magnetic requirements of binuclear type III copper system. We are currently trying to synthesize such a structural unit.

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(15) By treatment of **3** in PC with 3-Å molecular sieves and slow addition of ethyl acetate, small and poorly formed crystals of **4** were obtained.

(16) **4** crystallizes in the monoclinic space group $P2/m$ with $a = 18.899$ (6), $b = 13.016$ (5), $c = 8.763$ (3) Å; $\beta = 98.98(2)°$; $V = 2129.5$ Å^3; $\rho_{expt} = 1.65$, $\rho_{calcd} = 1.64$ g cm^{-3}; $Z = 2$ formula units per cell. A total of 2917 independent nonzero reflections were measured on a Philips PW 1100 diffractometer. 2394 reflections with $I > 3\,\sigma(I)$ were used for solving the structure. At the present stage of refinement the value of the conventional discrepancy index is $R_f = 0.16$. The macrocyclic binuclear cation is clearly defined and separated form the solvate molecules (PC, H_2O, ethyl acetate) and BF_4^- anions which are very disordered at statistically occupied positions. This extensive disorder, however, does not affect the structural details of the complex cation. Further refinement is in progress.

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(19) See: Wasson, J. R.; Shyr, C. I.; Trapp, C. *Inorg. Chem.* **1968**, *7*, 469.

(20) The experimental data closely follow the Bleaney–Bowers equation giving the molecular susceptibility as a function of the temperature for a Cu(II) dimer.

$$\chi_M = \frac{2g^2\beta^2N}{3kT}\left[\frac{1}{1 + \frac{1}{3}\exp(-2J/kT)}\right] + 2N\alpha$$

where $2N\alpha = 120$ and g is determined from the ESR measurements. The magnetic data have been corrected for monomeric paramagnetic impurities which were detected from the variable-temperature ESR studies (maximum amount = 5%).

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Photoreduction of 5-Bromouracil. Ionic and Free-Radical Pathways

Barry J. Swanson, J. Christopher Kutzer, and Tad H. Koch*

Department of Chemistry, University of Colorado
Boulder, Colorado 80309

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Replacement of thymine in DNA by 5-bromouracil (BU) yields DNA with enhanced photosensitivity with respect to single strand breaks[1] and DNA–protein photocrosslinking.[2] Little, however, is known about the chemistry of crosslinking to proteins. Sulfhydryl compounds such as cysteine[3] and indole containing compounds such as tryptophan derivatives[4] have been shown to couple photochemically with 5-bromouracil and 5-bromouradine. Reaction with tryptophan derivatives is sensitized by acetone, quenched by 1,3-pentadiene, and proposed to occur via an electron-transfer mechanism.[4]

We have investigated the photoreduction of 5-bromouracil to uracil in deuterium labeled 2-propanol solvents to clarify the primary photochemical processes of 5-bromouracil which lead to DNA photosensitivity. The literature often describes the primary photochemical event as homolysis of the vinyl carbon–bromine bond.[5] We report here evidence which suggests that 5-bromouracil is reduced to uracil via a radical pathway in the singlet

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