**Encapsulated Cluster**

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# A Ferromagnetic $[Cu_3(OH)_2]^{4+}$ Cluster Formed inside a Tritopic Nonaazapyridinophane: Crystal Structure and Solution Studies**

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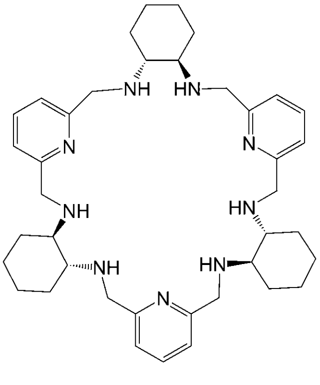
Chemists working in coordination and/or supramolecular chemistry find a continuous source of inspiration in biomolecules and enzyme active sites.[1] In this respect, trinuclear $Cu^{II}$ centers have attracted a lot of interest due to their resemblance to multicenter blue copper oxidases like ascorbate oxidase, ceruloplasmin, lacase oxidase, and particulate methane monooxygenase.[2] These enzymes contain at least four copper centers, which are necessary for four-electron reduction of molecular oxygen to water. For instance, the high-resolution structure of ascorbate oxidase shows that the mononuclear electron-transfer copper site of type 1 (T1) is connected to the trinuclear site through a patch formed by a cysteine residue from which two histidine residues diverge to bind the T3 copper ions. In the oxidized form of the enzyme, the T3 $Cu^{II}$ atoms, apart from the imidazole moiety of the histidine residues of the patch, are coordinated by another two imidazole units and by an OH group that bridges the two atoms, which are 3.71 Å far apart from each other. The geometry around each metal ion can be best described as a trigonal bipyramid with a vacant equatorial position oriented towards the T2 copper atom, which completes the trinuclear center. In the T2 site the $Cu^{II}$ center is coordinated in a very particular T-shaped geometry by two histidine residues and a monodentate hydroxo group or a water molecule.

The mechanism by which these centers catalyze the four-electron reduction of molecular dioxygen to water and the magnetic properties of these particular arrangements of copper ions have attracted great interest from both the biochemical and magnetochemical points of view. Therefore, small-molecule studies aimed at mimicking their properties are of great relevance in this respect.[3]



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Here we report one of the first examples[4] in which a $Cu_3(OH)_2$ ensemble is formed within a macrocyclic framework. Macrocycle **1** consists of three (*R*,*R*)-1,2-cyclohexyldiamine residues linked through 2,6-dimethylpyridine spacers.[5] This ligand shows very interesting features, for example, chiral $D_3$ symmetry with nine potentially coordinating nitrogen atoms around a macrocyclic cavity with enough space for several transition metal atoms. We report on its crystal structure, magnetic behavior, and characterization in solution by potentiometric measurements and paramagnetic $^1H$ NMR spectroscopy.

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First, to determine the speciation of the $Cu^{II}$–**1** system in aqueous solution, pH-metric titrations were carried out for metal:ligand molar ratios between 1:1 and 3:1.[6] At a $Cu^{II}$:**1** ratio of 3:1 trinuclear species predominate over the entire studied pH range. The monohydroxylated species $[Cu_3(\mathbf{1})(OH)]^{5+}$ starts to prevail in solution at pH 3.6, and dihydroxylated $[Cu_3(\mathbf{1})(OH)_2]^{4+}$ is the major species in aqueous solution in the pH range 6–9. At higher pH values, trihydroxylated species are formed (Figure S1, Supporting Information). Formation of the trihydroxo trinuclear species is also supported by electrospray ionization mass spectrometry (ESI-MS) of aqueous solutions of $Cu(AcO)_2$ and **1**·6 HCl recorded at pH 10. The spectra show peaks at $m/z$ 297.8, 464.1, and 476.1 corresponding to the cationic species $[Cu_3(\mathbf{1})(OH)_3]^{3+}$, $[Cu_3(\mathbf{1})(OH)_3Cl]^{2+}$, and $[Cu_3(\mathbf{1})(OH)_3(AcO)]^{2+}$, respectively (Figure S2, Supporting Information). Formation of hydroxylated species at such low pH values indicates very strong Lewis acidity of the trinuclear site.

Crystals of $[Cu_3(\mathbf{1})(OH)_2](ClO_4)_2Cl_2\cdot 5H_2O$ (**2**) were grown by slow evaporation of aqueous solutions containing $Cu(ClO_4)_2\cdot 6H_2O$ and **1**·6 HCl at pH 7.0. The asymmetric unit of **2** consists of a $[Cu_3(\mathbf{1})(OH)_2]^{4+}$ cation (Figure 1), two $ClO_4^-$ and two $Cl^-$ counteranions, and five lattice water molecules.[7]

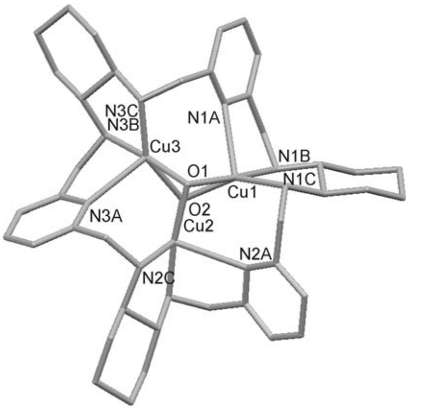

***Figure 1.*** Stick representation of the structure of the cation $[Cu_3(\mathbf{1})(OH)_2]^{4+}$. Hydrogen atoms, solvent molecules, and counterions are omitted. Cu–N distances [Å]: Cu1–N1A 2.394(8), Cu1–N1B 1.992(7), Cu1–N1C 1.987(8), Cu2–N2A 2.440(7), Cu2–N2B 1.964(6), Cu2–N2C 2.001(6), Cu3–N3A 2.363(7), Cu3–N3B 1.960(7), Cu3–N3C 2.007(7).

The three $Cu^{II}$ centers and the hydroxo bridges define a very interesting trimeric moiety with Cu-O-Cu angles very close to 90° (Figures 1 and 2), and the largest deviation from right angles is 86.6° for Cu2-O2-Cu3. The Cu–Cu distances are about 2.8 Å. Although the three $Cu^{II}$ coordination sites are similar, some slight differences can be found in bond lengths and angles (see Table S1, Supporting Information). For instance, the displacements of the $Cu^{II}$ centers from the mean equatorial planes are 0.216, 0.167, and 0.253 Å for Cu1, Cu2, and Cu3, respectively. The Cu1-O1-O2-Cu2, Cu1-O1-O2-Cu3, and Cu2-O1-O2-Cu3 dihedral angles are 119.6, 121.3, and 119.1°, respectively.

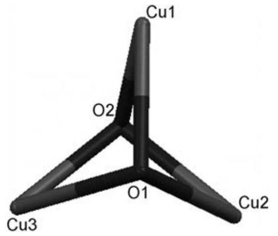

***Figure 2.*** $Cu_3(OH)_2$ trimer in **2**. Distances [Å]: Cu1–O1 2.0321(3), Cu1–O2 2.030(4), Cu2–O1 1.988(3), Cu2–O2 2.028(3), Cu3–O1 1.973(3), Cu3–O2 2.072(3), Cu1–Cu2 2.822(2), Cu1–Cu3 2.862(2), Cu2–Cu3 2.812(2). Angles [°] Cu1-O1-Cu2 89.5, Cu1-O1-Cu3 91.5, Cu2-O1-Cu3 90.4, Cu1-O2-Cu2 88.1, Cu1-O2-Cu3 88.5, Cu2-O2-Cu3 86.6.

The magnetic behavior of compound **2**, in the form of a $\chi_M T$ versus $T$ plot, is shown in Figure 3. At room temperature the $\chi_M T$ value of 1.17 $cm^3 mol^{-1} K$ is as expected for three magnetically isolated spin doublets. On cooling, $\chi_M T$ increases monotonically to attain a value of 1.57 $cm^3 mol^{-1} K$ at 3.5 K and decreases further to 1.54 $cm^3 mol^{-1} K$. The shape of this plot clearly shows the occurrence of intramolecular ferromagnetic interactions; the slight decrease at very low temperatures is due to zero-field splitting effects of the low-lying spin quartet ($S = 3/2$).

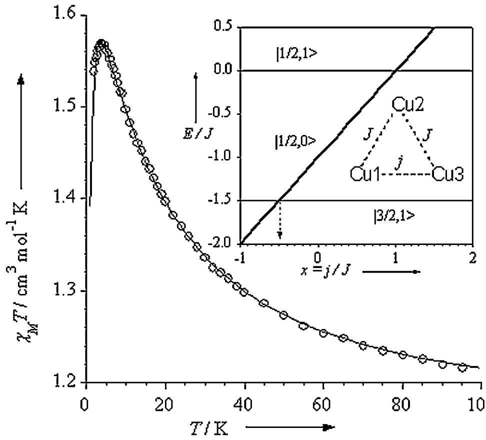

***Figure 3.*** Dependence of $\chi_M T$ of **1** on temperature. The solid line is the theoretical curve based on Equation (1). The inset shows the variation of the spin-state energies for an isosceles triangle with local spins $S_1 = S_2 = S_3 = 1/2$ versus the ratio $x = j/J$.

The Q-band ($h\nu \approx 35$ GHz $\approx 1.2$ cm$^{-1}$) EPR spectra of a powder sample of **2** as a function of temperature (Figure 4) provide clear evidence of the presence of a ground spin quartet with a zero-field splitting $2D \leq h\nu$,[8] where $2D$ is the energy gap between the $\pm 3/2$ and $\pm 1/2$ Kramers doublets arising from the low-lying spin quartet.

Owing to the triangular arrangement of the three crystallographically independent copper atoms in **2**, three different exchange pathways through double hydroxo bridges are expected ($J_{12}$, $J_{13}$, and $J_{23}$; see inset of Figure 3). The $J$ values in doubly hydroxo bridged dicopper(II) species are strongly dependent on angle $\alpha$ at the hydroxo bridge. A

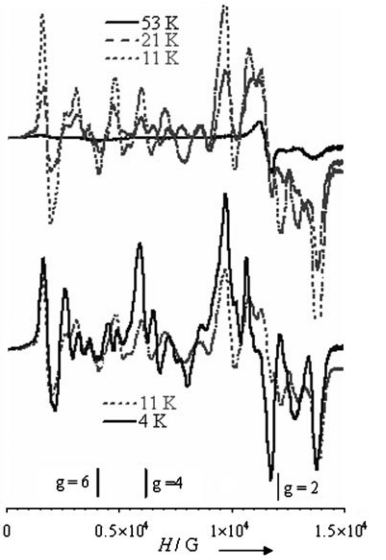

***Figure 4.*** Q-Band EPR spectra of a powder sample of **1** at different temperatures.

tentative fit of the magnetic data of **2** to these three magnetic couplings as variable parameters did not provide a unique solution because of the strong correlation among them. Inspection of the tricopper core shows that the average angle at the hydroxo bridge ($\alpha_{ij}$) and copper–copper distance ($d_{ij}$) are $\alpha_{13} = 90°$ and $d_{13} = 2.86$ Å, $\alpha_{12} = 88.8°$ and $d_{12} = 2.82$ Å, and $\alpha_{23} = 88.5°$ and $d_{23} = 2.81$ Å.

Thus, the magnetic interaction model can be simplified by assuming that $j_{12} = j_{23} = J$ and $j_{13} = j$, as indicated in the inset of Figure 3. Taking into account this coupling scheme and considering that the zero-field splitting of the spin quartet is axial, the the magnetic susceptibility of **2** is given by Equation (1)

$$\chi_M = \frac{N\beta^2 g^2}{4kT}\left\{\frac{(3+2/d)+(3-2/d)\exp(-2d)+\exp(-x/2-y)+\exp(-3x/2)}{1+\exp(-2d)+\exp(-x/2-y)+\exp(-3x/2)}\right\} \tag{1}$$

where $d = D/kT$, $x = J/kT$, $y = j/kT$, we assumed the same value of $g$ for all three copper atoms, and $g_{\parallel} = g_{\perp} = g$. Least-squares fitting of the magnetic data of **1** through Equation (1) leads to two set of values: 1) $J = +10.2(2)$, $j = -2.7(2)$ cm$^{-1}$ and 2) $J = +1.3(1)$, $j = +17.2(3)$ cm$^{-1}$, with $g = 2.06(1)$ and $D = 0.5(1)$ cm$^{-1}$ in both cases. The calculated curve reproduces the magnetic data very well in both cases. An energy diagram as $E/J$ versus the $j/J$ ratio ($x$) is shown in the inset of Figure 3, with the common notation $|S,S^*\rangle$, where $S$ is the total spin ($S = S_1 + S_2 + S_3$) and $S^* = S_1 + S_3$. The low-lying level is $S = 3/2$ when $J > 0$ and $j/J > -0.5$. Cases 1) and 2) both fulfill these conditions. Magnetostructural correlations and theoretical studies on doubly hydroxo bridged dicopper(II) complexes have shown that ferromagnetic interactions are expected for values of $\alpha$ less than 97.5°,[9] and its magnitude increases with decreasing $\alpha$. This trend has been observed for values of $\alpha$ greater than 90°. As far as we know, examples with $\alpha \leq 90$ have not been reported. However, with decreasing $\alpha$, the copper–copper distance decreases, and this leads to metal–metal interactions that would enhance the antiferromagnetic contribution. Consequently, the ferromagnetic coupling would be decreased and even the antiferromagnetic term could be dominant for smaller values of $\alpha$. Although the geometry of the hydroxo bridge in **2** ($\mu_3$-OH) is not the same as that investigated in other doubly hydroxo bridged dicopper(II) species ($\mu_2$-OH), the small values of the magnetic couplings computed in **2** reveal that the antiferromagnetic contribution is quite significant and that it would be larger for smaller values of $\alpha$. In this sense, we propose parameter set 2) as more realistic. To validate the approaches used in the fitting process, we performed DFT calculations on the experimental geometry of the trinuclear complex. More details on the methodology is given in the Supporting Information or in previous works.[10] In agreement with the $J$ values obtained from the experimental data, the theoretical calculations provide the following results: $J_{13} = +9.7$, $J_{12} = +9.4$, and $J_{23} = -6.2$ cm$^{-1}$. In agreement with our previous comments, while smaller angles $\alpha$ lead to antiferromagnetic coupling ($J_{23}$), stronger ferromagnetic interactions are observed when this angle takes on larger values ($J_{13}$).

Application of paramagnetic $^1$H NMR spectroscopy to multinuclear copper sites has proved to be useful to evaluate the electronic properties and magnetic characteristic in solution. The magnitude of the electronic relaxation times of magnetically coupled dinuclear or trinuclear Cu$^{II}$ systems allow the observation of relatively sharp isotropically shifted signals.[11] A number of studies have characterized the electronic properties of dinuclear Cu$^{II}$ systems in the last two decades.[11a,12] However, to our knowledge few paramagnetic $^1$H NMR studies on trinuclear Cu$^{II}$ complexes have been reported up to now.

The $^1$H NMR spectrum recorded in D$_2$O at pH 8 (Figure 5), where the trinuclear $[Cu_3(\mathbf{1})(OH)_2]^{4+}$ species predominates, shows, in the downfield region, four well-resolved hyperfine-shifted signals (a–d) and one unresolved signal (g). The spectrum additionally shows two well-resolved signals (e, f) and one unresolved signal (E) shifted upfield. The isotropically shifted signals have line widths, measured at half-height, of less than 100 Hz, except signal (a), which has a line width of 550 Hz.

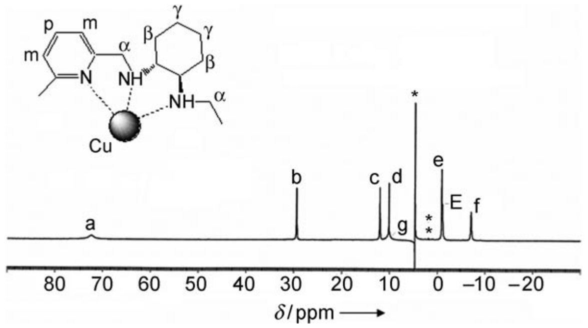

***Figure 5.*** 400 MHz $^1$H NMR spectra in D$_2$O at 298 K and pH 8 of the system Cu$^{2+}$-**1** in 3:1 molar ratio. The asterisks mark the residual solvent and impurity signals (*, H$_2$O; **, HOD).

Longitudinal relaxation times vary from as short as 0.66 ms for signal a, to 22 ms for signal b; see Table S4, Supporting Information. The relatively long longitudinal relaxation times and relatively sharp isotropically shifted signals are characteristic of magnetic interactions in coupled trinuclear copper(II) complexes.[13] The proton signals for $[Cu_3(\mathbf{1})(OH)_2]^{4+}$ can be assigned on the basis of the longitudinal relaxation times and the integrated protons (see Table S4, Supporting Information and Figure 5).

The existence of dipolar connectivity in the NOESY spectrum (Figure S3, Supporting Information), between signals b and e, c and d, e and f, and d and f confirms the assignment given in Table S4 (Supporting Information). Moreover, variable-temperature $^1$H NMR studies of $[Cu_3(\mathbf{1})(OH)_2]^{4+}$ from 288 to 323 K show not only Curie behavior for some signals, but also anti-Curie and temperature-independent behavior for signals d and c respectively (see Table S3, Supporting Information).

The existence of a magnetically coupled trinuclear copper(II) system is manifested in the anti-Curie behavior. It has been reported that, in magnetically coupled dicopper systems, which imply modulation of the zero-field splitting (ZFS), antiferro- or ferromagnetic couplings could provide similar effects.[11a] The paramagnetic NMR studies are consistent with the magnetic studies described and show that $[Cu_3(\mathbf{1})(OH)_2]^{4+}$ in solution has similar electronic properties to those observed in the solid state.

These results open up the possibility to prepare a range of trinucleating $Cu^{II}$ receptors in which the magnetic properties can be modulated by means of constitutional parameters of the systems. Currently we are exploring this line.

## Experimental Section

Further experimental details concerning the pH-metric titrations,[6] NMR studies, magnetic susceptibility measurements, and X-ray[7] and EPR studies can be found in the Supporting Information.

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**Keywords:** cluster compounds · copper · macrocyclic ligands · magnetic properties · N ligands

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[6] pH-Metric studies were carried out at 298.1 K in aqueous solution containg 0.15 mol dm$^{-3}$ $NaClO_4$ as source of ionic strength by using previously described equipment. The data were analyzed by means of the HYPERQUAD set of programs (P. Gans, A. Sabatini, A. Vacca, *Talanta* **1996**, *43*, 1739) to derive the ligand basicity constants and the formation constants of the $Cu^{2+}$ complexes (see Supporting Information).

[7] Data were collected on a X-Calibur Nova single crystal diffractometer with $Cu_{K\alpha}$ radiation ($\lambda = 1.54180$ Å). Crystallographic data for **2**: $C_{39}H_{69}Cl_4Cu_3N_9O_{15}$, $M = 1236.45$, triclinic, $P1$ (no. 1), $a = 9.863(4)$, $b = 11.670(5)$, $c = 12.458(7)$ Å, $\alpha = 111.22(5)$, $\beta = 90.62(4)$, $\gamma = 91.31(3)°$, $V = 1336.1(12)$ Å$^3$, $\mu = 3.820$ mm$^{-1}$, $T = 293(2)$ K, 59216 collected reflections, 10197 unique reflections, $R_{int} = 0.081$, $R1 = 0.055$ $[I > 2\sigma(I)]$, $wR2 = 0.156$ (all data). CCDC 723744 (**2**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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