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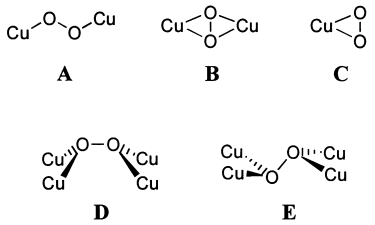
μ_4-Peroxo versus Bis(μ_2-Hydroxo) Cores in Structurally Analogous Tetracopper(II) Complexes**

Franc Meyer* and Hans Pritzkow

In biological systems, nature often uses the combined redox power of several adjacent metal ions for mediating multi-electron redox transformations. In particular, oligonuclear copper enzymes play a pivotal role in the reversible binding and in the activation of O_2 for oxidation and oxygenation reactions, respectively,[1]—well known representatives include the O_2 carrier protein hemocyanin[2] as well as the enzymes catechol oxidase and tyrosinase.[3] In view of the interest in the use of O_2 in catalytic oxidation reactions, extensive research has been devoted to the search of stable copper – dioxygen adducts[4, 5] to gain insight into the binding of O_2 at oligonuclear copper sites and to understand the function of such metalloenzymes.[6] In this context, structural investigations of copper – peroxo systems are of prime importance.

To date, copper – dioxygen adducts characterized by X-ray crystallography are a set comprised of a complex with *trans*-μ-1,2-peroxo bridge (type **A**),[7] two model complexes for the O_2-binding protein hemocyanin that feature a μ-η^2:η^2-peroxo group (**B**),[5, 8] and a mononuclear η^2-superoxo copper(II) compound (**C**).[9] In addition, a μ_4-peroxo coordination mode



unique in copper chemistry, in which a peroxo group spans four copper(II) ions (**D**), has been described by Krebs et al.[10] Herein, we report a novel example of such unusual μ_4-peroxo coordination (**E**), as well as the X-ray crystallographic characterization of a structurally analogous complex in which the O–O linkage is formally cleaved and replaced by two OH units, while at the same time the overall tetranuclear framework is fully conserved.

The new copper complexes are based on a multidentate pyrazolate ligand L^-.[11] Ligands of this type have proven suitable to hold two metal ions in close proximity and to therefore enable cooperative action of the two metal centers.[12] The metal – metal separation can be tuned by the lengths of the chelating side arms attached to the heterocycle: In complexes of L^- bearing "short" side arms, long metal – metal distances are enforced and small ions like OH^- are

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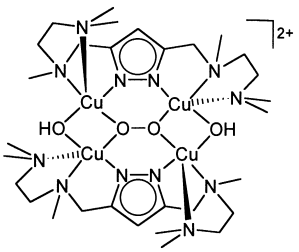
prevented from occupying a secondary bridging position.[13] For the O_2 binding by a dicopper(I) complex with L^-, an initial *cis*-μ-1,2-peroxo coordination is predicted from molecular models.



1

Diffusion of O_2 into a solution of $L^-/2[Cu(MeCN)_4]PF_6$ in EtCN that has previously been layered with Et_2O at $-80\,^{\circ}C$ affords dark green crystals of the peroxo complex $\mathbf{1}\cdot 2\,PF_6$. The molecular structure of **1** has been resolved crystallographically[14] and is depicted in Figure 1. Figure 2 shows details of its central coordination core.

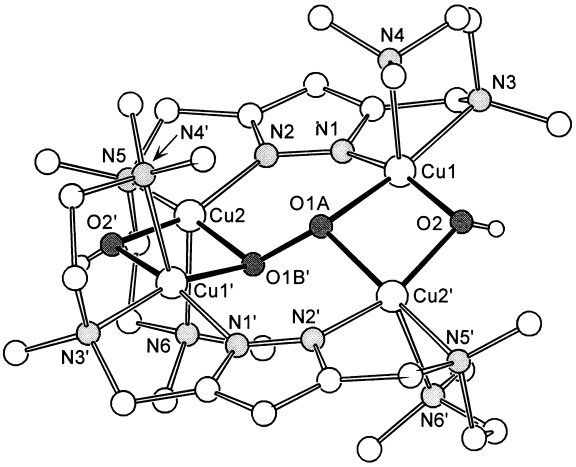


Figure 1. Molecular structure of **1** in the solid state. Only one position of the disordered peroxo group is shown. Selected distances [Å] and angles [°]: Cu1-N1 1.920(3), Cu1-N3 2.149(3), Cu1-N4 2.323(4), Cu1-O1A 2.040(4), Cu1′-O1B′ 1.950(4), Cu1-O2 1.934(3), Cu2-N2 1.911(2), Cu2-N5 2.153(3), Cu2-N6 2.351(3), Cu2-O1B′ 2.015(4), Cu2′-O1A′ 1.968(4), Cu2-O2′ 1.919(3), N1-N2 1.357(3), O1A-O1B′ 1.497(5), Cu1···Cu2 3.902, Cu1···Cu2′ 2.986, O2···F2 3.013; Cu1-O2-Cu2′ 101.6(2), Cu1-O1A-Cu2′ 96.3(2), Cu1-O1A-O1B′ 121.6(3), Cu2′-O1A-O1B′ 115.4(2), Cu2-O1B′-Cu1′ 97.7(2), Cu2-O1B′-O1A 123.8(3), Cu1′-O1B′-O1A 113.0(2).

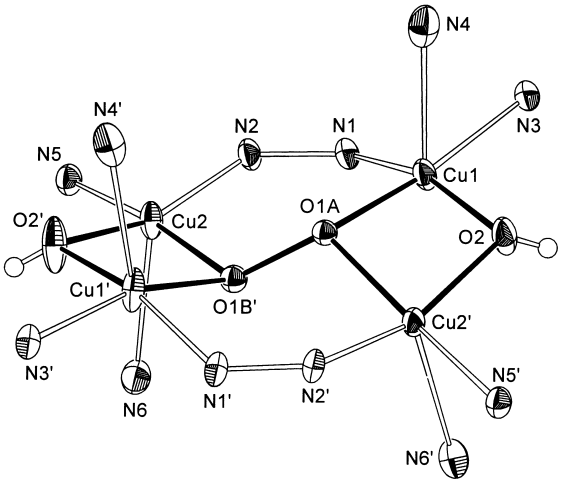
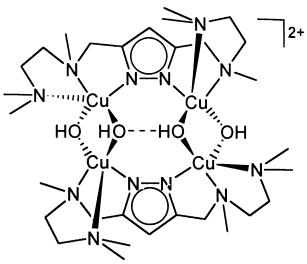


Figure 2. Central coordination core of **1**.

Compound **1** is a tetranuclear complex with a central O_2^{2-} peroxo ligand. As expected from the geometric constraints imposed by the ligand matrix L^-, the diatomic peroxo unit bridges the copper ions Cu1 and Cu2 of a bimetallic LCu_2 entity in the *cis*-μ-1,2-fashion. However, this peroxo binding mode is stabilized by a second dicopper(II) moiety and leads to the formation of an overall tetranuclear framework with a μ_4-coordination of the O_2^{2-} unit in **1**. The two shorter edges of the nonplanar rectangle of four copper(II) ions (dihedral angle 23.6°) are each spanned by an additional hydroxide, the H atom of which could be located in a bridge to the PF_6^- counteranion. The accompanying O–H stretching mode gives rise to a sharp band at 3641 cm^{-1} in the IR spectrum.

The copper(II) ions in **1** are nested in Jahn–Teller-distorted square–pyramidal environments, where the terminal N-donors of the L^- ligand side arms (N4 and N6) are found in the apical positions at expected, albeit long, Cu–N distances (2.323(4) and 2.351(3) Å, respectively). The center of the tetranuclear cation is located on a two-fold crystallographic axis and the peroxo ligand is disordered over two positions. The O1A–O1B′ bond length (1.497(5) Å) lies well within the range characteristic for an O_2^{2-} ligand, although it is the longest O–O distance of all copper–peroxo complexes characterized crystallographically to date. The geometry of the $\{Cu_4(O_2)\}$ core in **1** differs from those of the related μ_4-peroxo tetracopper(II) complex reported by Krebs et al.:[10] In that compound, the peroxo ligand caps a nearly planar Cu_4 rectangle and thus adapts an ecliptic orientation with respect to the O–O bond (*cis*-μ_4-peroxo, type **D**). Such features have also been found in three other complexes (of Fe, Mo, and Sb) which show μ_4-coordination of a peroxo ligand.[15] In addition, planar μ_4-O_2^{2-} coordination has been observed in the case of a hexanuclear iron complex.[16] In contrast, the oxygen atoms of the O_2^{2-} group in **1** are situated on different sides of the Cu_4 framework and the peroxo group is surrounded by the metal centers in an approximately *trans*-staggered arrangement (*trans*-μ_4-peroxo, type **E**).

The peroxo complex $\mathbf{1}\cdot 2\,PF_6$ is stable at room temperature. Its composition is further confirmed by mass spectrometry: The fast atom bombardment (FAB) mass spectrum (matrix = nitrobenzylalcohol) shows a signal at m/z 1055 with an isotopic distribution pattern characteristic for the $[L_2Cu_4(O_2)(OH)_2(PF_6)]^+$ ion.



2

When a solution of $\mathbf{1}\cdot 2\,PF_6$ exposed to air is stored at room temperature some, blue crystals of a second compound $\mathbf{2}\cdot 2\,PF_6$ form over a few days. The molecular structure of **2**, as determined by X-ray crystallography, is depicted in Figure 3.[14] Figure 4 gives a detailed view of its central coordination unit.

In complex **2**, the tetranuclear core, built of two bimetallic LCu_2 fragments and two linking OH bridges (O1 and O4) as is found in **1**, is fully conserved. However, two further hydroxo bridges (O2 and O3), instead of the central peroxo ligand, are present in **2**. The H atoms of all four hydroxo bridges could be

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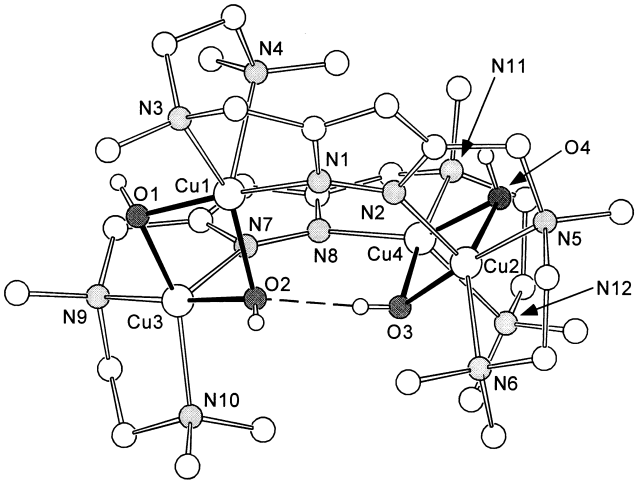

Figure 3. Molecular structure of **2** in the solid state. Selected distances [Å] and angles [°]: Cu1-N1 1.939(4), Cu1-N3 2.138(4), Cu1-N4 2.384(4), Cu1-O1 1.928(4), Cu1-O2 1.989(4), Cu2-N2 2.142(4), Cu2-N5 2.071(4), Cu2-N6 2.116(4), Cu2-O3 1.917(4), Cu2-O4 1.995(3), Cu3-N7 2.197(4), Cu3-N9 2.065(4), Cu3-N10 2.069(4), Cu3-O1 1.954(4), Cu3-O2 1.937(4), Cu4-N8 1.980(4), Cu4-N11 2.081(4), Cu4-N12 2.323(5), Cu4-O3 1.915(4), Cu4-O4 1.993(3), N1-N2 1.364(5), N7-N8 1.365(5), Cu1 ··· Cu2 4.348, Cu3 ··· Cu4 4.530, Cu1 ··· Cu3 2.925, Cu2 ··· Cu4 2.925, O2 ··· O3 2.747; Cu1-O1-Cu3 97.8(2), Cu1-O2-Cu3 96.3(2), Cu2-O3-Cu4 99.5(2), Cu2-O4-Cu4 94.4(2).

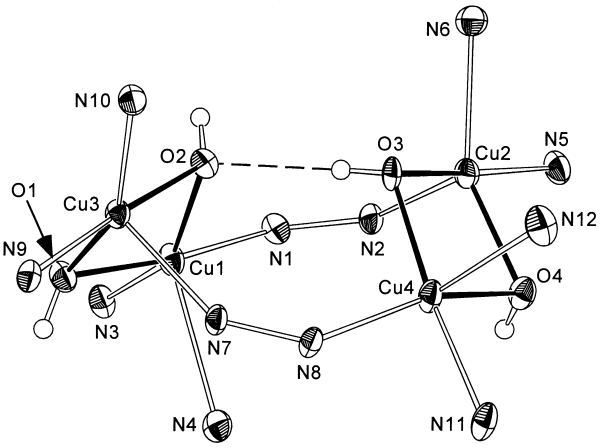

Figure 4. Central coordination core of **2**.

located: The H atom bound to O3 forms a short hydrogen bridge between the central O atoms (d(O2 ··· O3) = 2.747 Å), all other oxygen-bound H atoms are found in bridges to PF_6^- counteranions or to a EtCN solvent molecule. Three of the four terminal N donor atoms of the chelating side arms of the ligands L are located on one side of the Cu_4 framework (N6, N10, and N12), thus shielding three quadrants of the central (H)O ··· HO-group surroundings. Only atom N4 is situated on the opposite side of the Cu_4 framework and leaves sufficient space for the H atom bound to O2. The IR spectrum of **2** shows two bands in the range typical for the O–H stretch (3644, 3589 cm^{-1}).

The Cu_4 core, which consists of two LCu_2 fragments, is present in both **1** and **2**. The tetranuclear framework thereby allows for variability of the central O–O distance (1.497 Å for the peroxo group in **1** versus 2.747 Å for the (H)O ··· HO bridge in **2**) in two ways. First, different Cu ··· Cu separations are adopted in each LCu_2 bimetallic moiety (3.902 Å in **1** versus 4.348/4.530 Å in **2**) and, second, the planes of the two Cu_2O_2 four-membered rings are tilted severely with respect to each other in **2** (99.4°). From a purely structural point of view, a mutual transformation of the $\{Cu_4(O_2)\}$ and $\{Cu_4(OH)_2\}$ units of such tetrametallic cores should obviously be feasible; the formation of the central $\{Cu_4(OH)_2\}$ fragment in **2** formally reflects a two electron reduction and concomitant double protonation of the $\{Cu_4(O_2)\}$ fragment in **1**. Complex **2** thus indicates to what the reductive cleavage of dioxygen, after it is first captured as a μ_4-peroxo ligand on a Cu_4 surface, might eventually lead. The question whether compound **2** results from reductive cleavage of the peroxo group in **1** or whether **2** forms by a different pathway is presently under investigation.

Experimental Section

1: HL[11] (0.18 g, 0.61 mmol) was dissolved in THF (20 mL) and was deprotonated by addition of $[NBu_4]OH$ (0.61 mL, 1.0 M in methanol) at 0 °C. After evaporation of all volatile material under reduced pressure, the residue was extracted into EtCN (20 mL). A solution of $[Cu(MeCN)_4]PF_6$ (0.45 g, 1.21 mmol) in EtCN (10 mL) was then added under argon at – 80 °C. After stirring for 10 min at – 80 °C, the yellow reaction mixture was layered with Et_2O (100 mL) and air was let to diffuse into the remaining space of the Schlenk tube. The closed Schlenk tube was then stored – 80 °C. The solution gradually turned green and, after two weeks, a precipitate containing small crystals of $\mathbf{1}\cdot 2PF_6$ formed. This was filtered and dried at room temperature (yield: 0.14 g, 0.12 mmol, 38 %). Recrystallization was achieved by layering an EtCN solution of the product with Et_2O. UV/Vis (EtCN) $\lambda_{max}(\varepsilon)$: 360 nm (3100), 631 nm (260 $M^{-1}cm^{-1}/Cu_4$); elemental analysis: calcd. for $C_{30}H_{64}Cu_4F_{12}N_{12}O_4P_2$ (1201.0): C 30.00, H 5.37, N 13.99; found: C 30.53, H 5.40, N 13.54. When the solution containing $\mathbf{1}\cdot 2PF_6$ was stored at room temperature, blue crystals of $\mathbf{2}\cdot 2PF_6\cdot$EtCN gradually formed.

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[14] Crystal data of $\mathbf{1}\cdot 2PF_6$ ($C_{30}H_{64}Cu_4F_{12}N_{12}O_4P_2$, $M=1201.0$): monoclinic, space group $C2/c$, $a=21.309(1)$, $b=11.421(1)$, $c=19.174(1)$ Å, $\beta=97.562(1)^\circ$, $V=4625.8(5)$ Å^3, $Z=4$, $\rho_{calcd}=1.725$ g cm^{-3}, $\mu(Mo_{K\alpha})=1.981$ mm^{-1}, $2\theta_{max}=52.7^\circ$, 4720 independent reflections, 3342 observed with $I>2\sigma(I)$, 417 refined parameters; all H atoms have been localized and refined isotropically, $R1=0.037$ ($I>2\sigma(I)$), $wR2=0.088$ (all data), GOF = 0.924 (refinement on F^2), max./min. residual electron density 0.661/ – 0.300 e Å^{-3}. Crystal data of $\mathbf{2}\cdot 2PF_6$ ($C_{30}H_{66}Cu_4F_{12}N_{12}O_4P_2\cdot EtCN$, $M=1258.1$): monoclinic, space group $P2_1/c$, $a=11.985(1)$, $b=26.728(3)$, $c=16.114(2)$ Å, $\beta=100.505(2)^\circ$, $V=5075.3(8)$ Å^3, $Z=4$, $\rho_{calcd}=1.647$ g cm^{-3}, $\mu(Mo_{K\alpha})=1.810$ mm^{-1}, $2\theta_{max}=49.4^\circ$, 8656 independent reflections, 5111 observed with $I>2\sigma(I)$, 644 refined parameters; the O-bound H atoms have been localized and refined isotropically, all other H atoms have been included in calculated positions, $R1=0.046$ ($I>2\sigma(I)$), $wR2=0.108$ (all data), GOF = 0.878 (refinement on F^2), max./min. residual electron density 0.892/ – 0.434 e Å^{-3}. Data have been collected on a Bruker AXS CCD diffractometer, $Mo_{K\alpha}$ radiation ($\lambda=0.71073$ Å), $T=173$ K, ω scan, structures have been solved using direct methods (SHELXS-86 and SHELXL-97). Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-138151 ($\mathbf{1}\cdot(PF_6)_2$) and CCDC-138152 ($\mathbf{2}\cdot(PF_6)_2$. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk)..
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The Use of Immobilized Templates—A New Approach in Molecular Imprinting

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Molecular imprinting is a technique that allows specific recognition sites for target molecules to be formed in synthetic polymers through the use of templates. Customary protocols for molecularly imprinted polymers (MIPs) are based on one of two distinct approaches: the "covalent approach" and the "noncovalent approach". The covalent approach was pioneered by the group of Wulff[1] and uses covalent bonds between the imprint molecules and functional monomers. The other approach, which is based on noncovalent interactions, was introduced by Mosbach and coworkers.[2] More recently, a hybrid system was proposed that comprises a covalent imprinting step and subsequent rebinding of the imprint molecule by noncovalent interactions.[3]

Molecular imprinting of small molecules has until now only been done with the template (imprint) molecules in free solution. These polymers will be referred to here as classical MIPs. Herein we present a novel imprinting method based on oriented immobilization of the template onto a solid support. After polymerization, the support is dissolved and thus sacrificed (Figure 1). Our aim is to demonstrate the feasibility

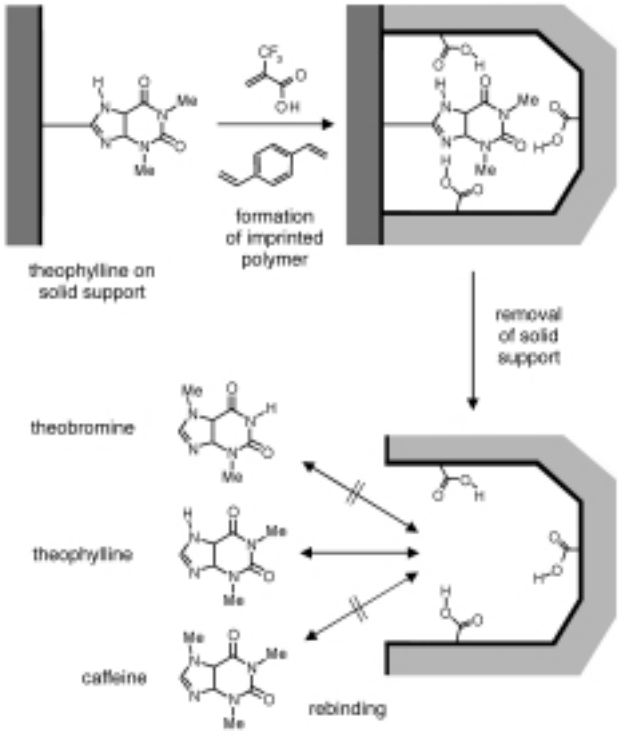

Figure 1. Schematic representation of the molecular-imprinting approach employing immobilized templates and a sacrificial solid support.

of this approach, which extends molecular imprinting technology to a new dimension. The bronchodilating drug theophylline was investigated as a model template by immobilizing its 8-carboxypropyl derivative onto a support of aminopropyl-derivatized silica gel. Immobilization of 8-carboxypropyltheophylline was achieved through the formation of amide bonds by using carbodiimide chemistry adapted from protocols used for solid-phase peptide synthesis.[4] The amount of template coupled was determined at the end of the reaction by elemental analysis (Table 1). Approximately 75% of the free aminopropyl groups on the silica surface could be coupled with 8-carboxypropyltheophylline. Acetic anhydride was added at the end of the coupling

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