# Synthesis of an Unsymmetrical Dinucleating Ligand That Leads to an Asymmetric Dicopper(II) Complex Having Different Donor Sets at Each Copper

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Asymmetry is an important feature of metalloproteins that contain at their active sites dinuclear iron complexes,[1] dinuclear copper complexes[2] (e.g., tyrosinase and molluscan hemocyanin), and trinuclear copper complexes[3] (e.g., multicopper oxidases). Few asymmetric biologically relevant dinuclear complexes of iron[4] and of copper[5,6,7a–e] have been synthesized. With few exceptions,[5,6] almost all model systems involving dinuclear copper complexes that have been studied so far have been derived from symmetrical ligands.[7] Accidentally unsymmetrical species have been characterized,[7a–c] for which the extent of asymmetry, as indicated by the difference in Cu–X–Cu' bond lengths, can be more than 0.3 Å. However, with symmetrical potentially dinucleating ligands or with bi- and tridentate ligands, asymmetry is not preordained for dinuclear species. Polydentate ligand systems that lead to obligately asymmetric dinuclear complexes remain very rare[6] and appear to be nonextant if (i) the metal sites remaining after coordination of the polydentate ligand are to differ in coordinative saturation and (ii) nonbiological, delocalized, coplanar, bidentate phenolato-(H)C=NR Schiff-base moieties are eschewed. We report here the synthesis of an unsymmetrical dinucleating ligand 2-[[bis(2-benzimidazolylmethyl)amino]-methyl]-4-methyl-6-[[(2-benzimidazolylmethyl)benzylamino]-methyl]phenol (hereafter referred to as N3O(H)N2-B),[8–10] a ligand that has –CH₂-spacers between donor groups and can offer a different suite of donor atoms to a pair of metal ions. The structure and solid-state magnetic properties are reported for an asymmetric dicopper(II) complex, [Cuᴵᴵ(N3-μ-O-N2-B)(μ-Cl)-Cuᴵᴵ(HOC₂H₅)](ClO₄)₂·4H₂O·C₂H₅OH, derived from this ligand.[11,12]

Scheme 1 summarizes the synthesis of the N3O(H)N2-B ligand. Figure 1 shows an ORTEP-type drawing of the cationic complex. The bridging chloro and phenolato ligands are located unsymmetrically between the two copper ions with Cu(2)–O(1) and Cu(1)–O(1) distances of 1.900(6) and 2.352(6) Å, respectively, and Cu(2)–Cl(1) and Cu(1)–Cl(1) distances of 2.649(3) and 2.274(2) Å, respectively. Coordination at Cu(1) is completed by one amine and two imine ligands (the N3 branch of the ligand) to give a distorted square pyramid, where the Cu–O(1) bond is axial and elongated; coordination at Cu(2) is completed by one imine and one amine ligand (the N2-benzyl branch of the ligand) and an ethanol moiety to give a very distorted five-coordinate stereochemistry, where the Cu(2)–Cl(1) bond is elongated and somewhat axial.

By way of comparison, a dicopper(II) complex with bridging hydroxo and phenolato groups has been characterized, featuring the unsymmetrical ligand 2-[[bis(2-pyridylmethyl)amino]-methyl]-6-[bis(2-pyridylmethyl)amino]phenol, a ligand that offers a similar suit of ligands but in a potentially stereochemically different manner to each copper ion.[5] However, in this complex the bridging O₍phenolato₎–Cu separations are identical [1.93(2) Å], as are the O₍hydroxo₎–Cu separations [2.02(2) Å]. Significant antiferromagnetic coupling between these two copper atoms exists. In contrast, in the solid state for the title complex, the magnetic moment is constant at 1.75(2) $\mu_B$ per copper in the range 77–295 K. The solid complex is EPR active ($g_x$ = 1.90, $g_z$ = 2.11, and $g_y$ = 2.28) both at room temperature and at 77 K (Figure 2). A low-field resonance at $g$ = 4.7 is indicative of copper atoms in close proximity. Consistent with the existence of an EPR signal at relatively high temperature is the absence of proton resonances associated with the complex in the ¹H NMR spectrum at room temperature. Together, these magnetic data indicate that the

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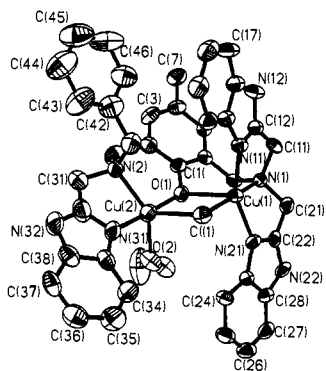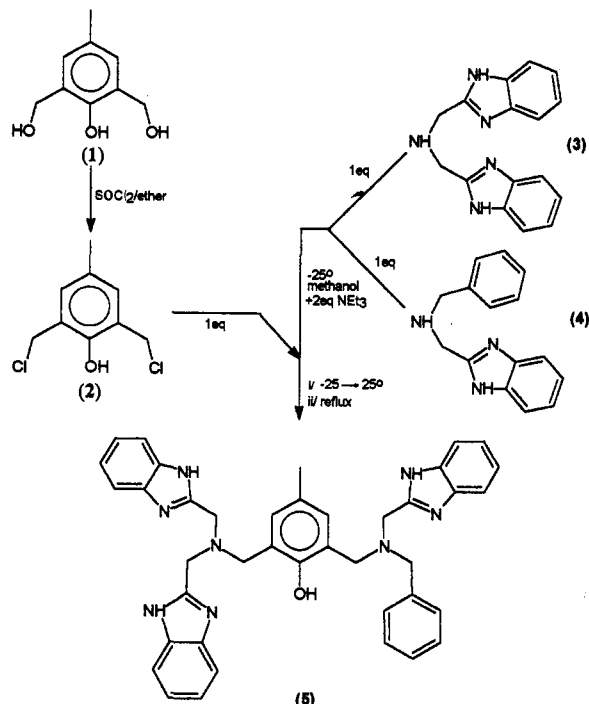
(8) 1 (17 g; 0.1 mol) was suspended in 300 mL of dry ether, and 23.8 g (0.2 mol) of thionyl chloride was added. After 2 h of stirring at room temperature, solvent was removed under reduced pressure and the solid residue of 2 was recrystallized from a mixture of 50% ether and 50% *n*-hexane; yield 89%. (b) Compound 3 was prepared according to ref 9, and compound 4 according to ref 10. (c) Compound 5 was prepared as follows: 1.0 g (0.005 mol) of 2 was added to a mixture of 1.18 g (0.005 mol) of 4, 1.35 g (0.005 mol) of 3, and 0.99 g (0.01 mol) of triethylamine in 50 mL of methanol, cooled to –20 °C. The solution was allowed to warm up to room temperature and then refluxed for 15 min. Stirring at room temperature for 24 h produced solid 5, which was purified by washing with several milliliters of cold methanol for a yield of 67%. Identity of the ligand was proven by NMR, IR, and mass spectrometries. FAB-MS determined the molecular weight to lie in the range 646–650 (calculated weight for C₄₀H₃₈N₈O is 646.799).

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(11) To a suspension of 105 mg (0.15 mmol) of 5 in 50 mL of absolute ethanol was added 111 mg (0.3 mmol) of Cu(ClO₄)₂·6H₂O. The complex crystallized by slow solvent evaporation. As crystals lost solvent very rapidly, they were examined at –20 °C and X-ray diffraction data were collected at –100 °C.

(12) (a) The complex crystallizes in space group P1̄, *a* = 13.066(7), *b* = 13.491(3) Å, *c* = 15.462(5) Å, α = 80.66(1)°, β = 89.89(4)°, γ = 85.98(4)°, *V* = 2682.67(18) Å.³ A total of 9445 reflections [8213 unique, $R_{merge}(F^2)$ = 0.045] was collected on a Siemens P4/RA diffractometer at –100 °C with graphite-monochromated Mo Kα radiation. The structure was solved by direct methods SHELXS-86 (Sheldrick, 1990) and refined on $F^2$ [all 8188 data, 706 variable parameters, 15 restraints using SHELXL-93 (Sheldrick, 1993)] to a weighted discrepancy index of 0.30 on $F^2$ [conventional $R$ on 5119 data with $F_0 \geq 4\sigma(F_0)$ of 0.088]. Hydrogen atoms were constrained to ride on their attached carbon atoms with appropriate geometry. The final $R$ is rather high due to disordered solvate species and substantial thermal motion of ethanol and benzyl moieties of the complex. (b) Magnetic susceptibility data were measured between 80 and 300 K on a computer-controlled Faraday system.

**Figure 1.** ORTEP-like diagram of the cationic part of [Cu$^{II}$N3-$\mu$-O-N2-B)($\mu$-Cl)Cu$^{II}$(HOC$_2$H$_5$)](ClO$_4$)$_2$·4H$_2$O·C$_2$H$_5$OH, showing the atom-labeling scheme. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (deg) are as follows: Cu(1)···Cu(2), 3.348(2); Cu(1)–O(1), 2.352(6); Cu(2)–O(1), 1.900(6); Cu(1)–Cl(1), 2.274(2); Cu(2)–Cl(1), 2.649(2); Cu(1)–N(1), 2.090 (6); Cu(1)–N(11), 1.965-(6); Cu(1)–N(21), 1.971(6); Cu(2)–O(2), 2.037(7); Cu(2)–N(2), 2.064-(7); Cu(2)–N(31), 1.955(7); O(1)–Cu(1)–Cl(1), 85.4(2); O(1)–Cu(2)–Cl(1), 85.6(2); Cu(1)–O(1)–Cu(2), 103.3(3); Cu(1)–Cl(1)–Cu(2), 85.31(8). Selected torsion angles (deg) are as follows: Cu(1)–O(1)–C(1)–C(6), 48.0; Cu(2)–O(1)–C(1)–C(2), –3.4.

**Scheme 1**





**Figure 2.** EPR spectrum of [Cu$^{II}$(N3-$\mu$-O-N2-B)($\mu$-Cl)Cu$^{II}$(HOC$_2$H$_5$)]-(ClO$_4$)$_2$·4H$_2$O·C$_2$H$_5$OH. Note the presence of the "forbidden" signal at $g$ = 4.7, indicating close proximity of two copper(II) ions.

For ascorbate oxidase a distinctive trinuclear copper complex with at least one Cu···Cu separation of about 3.5 Å has been revealed from an X-ray structure study,[3] and a similar active site is proposed for laccase and ceruloplasmin.[3] All of these proteins have EPR signals consistent with an apparent $S = ^1/_2$ system. Moreover, at least in the case of laccase, the EPR-active copper depends upon the nature of the exogeneous ligand.[13] That a pair of copper(II) ions in close proximity (<3.5 Å apart) exhibits spectroscopic and magnetic behavior apparently more typical of a mononuclear than a dinuclear system, as observed here (and also for some other dicopper(II) species where significant antiferromagnetic coupling exists[7b-d]), is a result of some cautionary significance in assigning the proximity of copper centers of multicopper oxidases less well characterized than those just cited. That is, well-separated, mononuclear copper(II) sites in a metalloprotein cannot be presumed from a constant magnetic moment and EPR activity.

The complex described here demonstrates the potential of this polydentate ligand, N3O(H)N2-B, to create asymmetric dinuclear complexes, at least of copper.[14] The synthetic scheme for the ligand is of some generality,[15] the non-phenolato bridging ligand of the dicopper(II) complex can be varied,[14] and the terminally coordinated solvent molecule is, in principle, replaceable.

**Acknowledgment.** We thank the National Science Foundation for Grant CHE-9115394 in support of the purchase of the diffractometer. We thank Professor M. A. Johnson from The George Washington University for facilitating the mass spectrometry measurement.

**Supplementary Material Available:** Complete tables of crystal data and structure refinement, atomic coordinates, bond lengths and angles, anisotropic displacement parameters, and hydrogen atom coordinates, complete bibliography for ref 7, listings of IR, $^1$H NMR, and satisfactory microanalytical data, and details of magnetic susceptometry (8 pages); listing of observed and calculated structure factors (19 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(14) For example, azido-, nitrato-, and acetato-bridged analogues have been isolated (Kamaras, P. Ph.D. Thesis, Georgetown University, Washington, DC, 1994).

(15) Similar ligands have been synthesized in which the benzyl group is replaced by cyclohexyl or 2-methoxybenzyl groups (unpublished results).

two copper(II) ions are neither significantly ferro- nor antiferromagnetically coupled. This is attributed in part to the asymmetric placement of the bridging ligands, in part to the placement of Cu(1) out of the nearly planar moiety defined by atoms Cu(2), O(1), Cl(1), and C(2) (see Figure 1), and in part to the stereochemistry of the complex that has Cu(1)–O(1) as an axial ligand of a distorted square pyramid and Cu(2)–O(1) as an equatorial ligand of a very distorted square pyramid. A similar EPR spectrum was observed for a singly and asymmetrically bridged dicopper(II) complex of the tetrabenzimidazole analogue of the N3O(H)N2-B ligand.[7d] In this complex, vacant sites at each copper are occupied by water, and a similar axial-equatorial arrangement 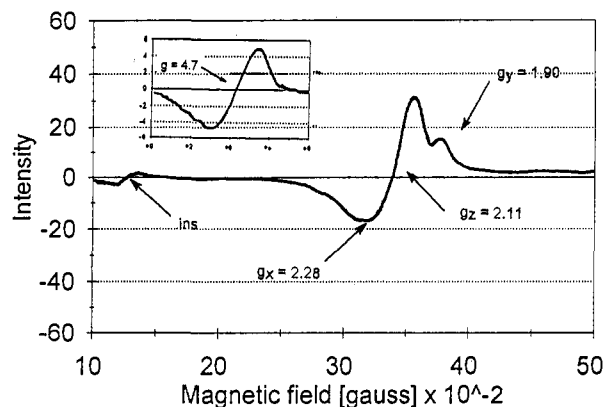of the Cu–O$_{phenolato}$ bonds is observed.