

A novel imidazolate-bridged heterodinuclear Cu(II)Zn(II) complex derived from a unique macrocyclic ligand with two hydroxyethyl pendants†

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[(CuimZnL_{-2H})(CuimZnL_{-H})](ClO₄)₃, the first imidazolate-bridged Cu(II)–Zn(II) complex of a unique single macrocyclic ligand with two flexible hydroxyethyl pendants, L (L = 3,6,9,16,19,22-hexaaza-6,19-bis(2-hydroxyethyl)tricyclo[22.2.2.2^{11,14}]triaconta-1,11,13,24,27,29-hexaene) has been obtained, in which the macrocyclic ligand with two hydroxyethyl arms possesses a markedly different conformation compared to its dicopper analogue.

The unique imidazolate-bridged Cu(II)–Zn(II) bimetallic core in the active site of copper–zinc superoxide dismutase (Cu₂Zn₂-SOD) has attracted much attention in the past two decades.¹ A number of imidazolate-bridged dicopper(II) complexes, as Cu₂Zn₂-SOD models, have been synthesized and characterized.² However, only a few successful examples of heterodinuclear copper(II)–zinc(II) complexes have been reported up till now because of difficulties with the syntheses.³ Very recently, we have designed and synthesized a new macrocyclic ligand with two hydroxyethyl pendants, L (L = 3,6,9,16,19,22-hexaaza-6,19-bis(2-hydroxyethyl)tricyclo[22.2.2.2^{11,14}]triaconta-1,11,13,24,27,29-hexaene),⁴ which may possess both rigidity and flexibility, and is expected to be a good candidate for Cu₂Zn₂-SOD model studies. Using the macrocyclic ligand, we have successfully obtained a new imidazolate-bridged dicopper(II) complex **1**, [(CuimCuL)-(ClO₄)₃·0.5H₂O], and a novel imidazolate-bridged heterodinuclear copper(II)–zinc(II) complex **2**, [(CuimZnL_{-2H})(CuimZnL_{-H})](ClO₄)₃. To our knowledge, the heterodinuclear complex **2** is the first imidazolate-bridged Cu(II)–Zn(II) complex of a single macrocyclic ligand. Additionally, the structures of the Cu–Zn and Cu–Cu complexes, obtained from the same macrocyclic ligand, are remarkably different. This is unlike the reported examples in which the structures of the heterodinuclear Cu–Zn complexes are always very similar to those of their dicopper analogs.³ Moreover, it is unexpected that the macrocyclic ligands in the two complexes possess two markedly different conformations, which can only be accomplished by stereochemical inversion at one (or more) of the nitrogen atoms (at least, one of the two tertiary nitrogen atoms) of the free macrocyclic ligand in the formation of the complexes.

The synthetic procedures are shown in Fig. 1, and the detailed preparations are given in ESI. The imidazolate-bridged dicopper complex **1** was obtained as bluish block crystals from CH₃OH/CH₃CN solution at pH ca. 6, while the heterodinuclear Cu–Zn complex **2** (Fig. 2) crystallized as greenish platelet crystals from H₂O/CH₃CN at pH ca. 9.5. The two complexes were characterized by elemental analysis, ICP, magnetism, ESR, and X-ray analysis.†

Complex **1** crystallizes in the orthorhombic space group *Pbca*. The asymmetric unit consists of a [(CuimCuL)]³⁺ cation,

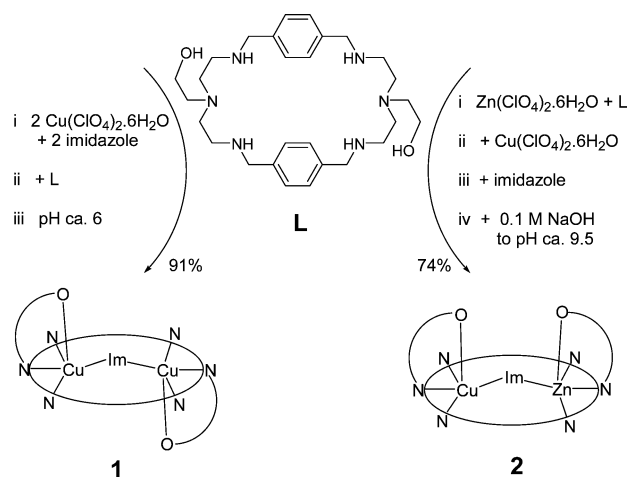


Fig. 1 Synthetic procedures and schematic structures of the cations of complex **1** and **2**.

three perchlorate anions and half of a water molecule. In the cation, two copper atoms are bridged by an imidazolate anion, forming a homodinuclear Cu(II)–Cu(II) complex (Fig. 3a). Each Cu(II) ion is pentacoordinated by a N4O environment; and analysis of the Cu coordination polyhedra⁵ gives values of the degree of distortion $\Delta = 0.38$ for Cu1 and $\Delta = 0.60$ for Cu2, indicating coordination geometries of distorted trigonal bipyramid (TBP) for Cu1 and distorted tetragonal pyramid (TP) for Cu2, respectively (for a definition of Δ see ref. 5). The distance between the two imidazolate-bridged Cu(II) ions is 5.999(2) Å, which is similar to those observed in other imidazolate-bridged dicopper(II) complexes.³ Note that the two hydroxyethyl arms of the macrocyclic ligand are located on different sides of the plane defined by the nitrogen atoms and the phenyl groups of the macrocyclic ligand, forming a chair-like (*anti*) conformation (Fig. 3a).

Unlike **1**, the heterodinuclear Cu(II)–Zn(II) complex **2** crystallizes in a different space group, triclinic *P1*, and the

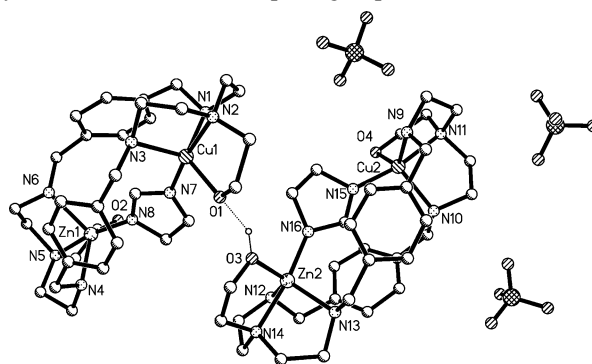


Fig. 2 Molecule structure of the Cu(II)–Zn(II) heterodinuclear complex [(CuimZnL_{-2H})(CuimZnL_{-H})](ClO₄)₃ **2**. Hydrogen atoms except H1 are omitted for clarity.

† Electronic supplementary information (ESI) available: detailed experimental section; Fig. S1–S3: temperature dependence of the magnetic susceptibility for **1** and ESR spectra for **1** and **2**. See <http://www.rsc.org/suppdata/cc/b3/b300013c/>

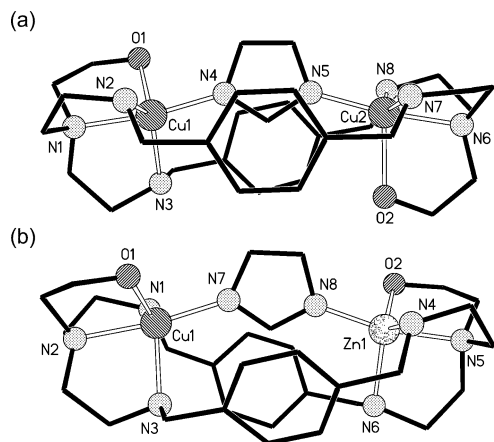
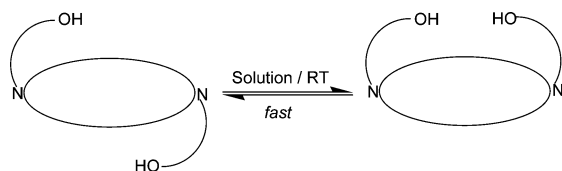


Fig. 3 Molecular structure of (a) homodinuclear cation $[(\text{CuimCu})\text{L}]^{3+}$ of **1**; (b) heterodinuclear cation **2A**, $[(\text{CuimZn})\text{L}_{-2\text{H}}]^+$. Hydrogen atoms and anions are omitted for clarity.

structure of **2** is also obviously different from that of **1**. In the asymmetric unit, there are two $\text{Cu}(\text{II})\text{-Zn}(\text{II})$ heterodinuclear cations, $[(\text{CuimZn})\text{L}_{-2\text{H}}]^+$ (cation **2A**) and $[(\text{CuimZn})\text{L}_{-\text{H}}]^{2+}$ (cation **2B**),⁶ joined together through a hydrogen bonding $\text{O1}\cdots\text{H1}\text{-O3}$ [$\text{O1}\cdots\text{O3}$, 2.403(3) Å; $\text{O1}\cdots\text{H1}\text{-O3}$, 152(4) $^\circ$] and forming a dihedral of 57.9(1) $^\circ$ based on the two $\text{Cu}\text{-im}\text{-Zn}$ planes, as well as three perchlorate anions (Fig. 2). The two cations are basically similar but somewhat different with respect to the coordination geometry, bond lengths and angles. Analysis of the Cu and Zn coordination geometry provides values of $\Delta = 0.31/0.31$ for $\text{Cu1}/\text{Cu2}$ and $\Delta = 0.15/0.12$ for $\text{Zn1}/\text{Zn2}$, indicating that the coordination geometries around the copper and zinc ions are all distorted trigonal bipyramidal (TBP); and the distortion of $\text{Cu1}/\text{Cu2}$ is more obvious than that of $\text{Zn1}/\text{Zn2}$, which is consistent with the tendency that the zinc(II) ion favors the trigonal-bipyramidal coordination geometry much more than the copper(II) ion.^{3b} In cation **2A** (Fig. 3b),⁷ both $\text{Cu}(\text{II})$ and $\text{Zn}(\text{II})$ atoms are coordinated in a N4O environment, in which three nitrogen and one oxygen atoms (N1 , N2 , N3 and O1 for Cu1 ; N4 , N5 , N6 and O2 for Zn1) are from the ligand **L**; one nitrogen atom is from imidazolate (N7 for Cu1 and N8 for Zn1) (Fig. 3b). The distance between the imidazolate-bridged $\text{Cu}(\text{II})$ and $\text{Zn}(\text{II})$ ions is 5.950(1) Å [for cation **2B**, the distance is 5.939(1) Å], which is slightly shorter than that in $\text{Cu}_2\text{Zn}_2\text{-SOD}$ ($\text{Cu}\cdots\text{Zn} = 6.3$ Å). Except for the obvious discrepancies in the coordination configuration of the metal ions, as well as the conformation of the two phenyl spacers and the position of the bridged imidazolate ring, the most distinctly different structural feature for cations **2A/2B** vs. complex **1** is that the two hydroxyethyl groups in **2** are located on the same sides (different sides in complex **1**) of the macrocycle, forming a boat-like (*syn*) conformation (Fig. 3b).

The remarkable differences between complexes **1** and **2** provide substantial evidence for the formation of the heterodinuclear imidazolate-bridged $\text{Cu}(\text{II})\text{-Zn}(\text{II})$ complex. We scrutinized the structures of the macrocyclic ligands in the two compounds and found that the two conformations can not be achieved only by bond rotations or twists of the macrocycle. The observed rapid interchange of the two conformations of the macrocyclic ligand (Scheme 1) which must be occurring in solution at room temperature requires stereochemical inversion at one of the two tertiary nitrogen atoms.⁸



Scheme 1

The variable-temperature magnetic susceptibility data for complex **1** reveal a typical antiferromagnetic interaction for imidazolate-bridged dicopper(II) complexes, and the $-2J$ (86.4 cm^{-1}) value of **1** falls in the range (0–163 cm^{-1}) for the imidazolate-bridged dicopper(II) complexes.^{2a} The ESR spectrum (110 K) of **2** in 50% water–DMSO solution ($g_{\parallel} = 1.94$, $g_{\perp} = 2.23$, $A_{\parallel} = 116$ G and $A_{\perp} = -105$ G) shows a line shape characteristic of mononuclear copper(II) ions in a trigonal-bipyramidal environment with a d_{z^2} ground state, but is very different from that of **1**, possessing typical features of antiferromagnetic coupled imidazolate-bridged dicopper(II) complexes.² The results clearly show that complex **2** is a heterodinuclear CuimZn complex, not a mixture of CuimCu and ZnimZn complexes, which is consistent with the crystal structure mentioned above.

The SOD-like activities of the two complexes were investigated by NBT assay^{2c,3} and the catalytic activity toward the dismutation of superoxide anion was measured. The IC_{50} values (50% inhibition of the reduction of NBT) of 0.62 and 0.26 μM [per $\text{Cu}(\text{II})$ ion] for complexes **1** and **2** show that they are among the most active model compounds,^{3b} but are somewhat less active than the native enzyme ($\text{IC}_{50} = 0.04$ μM). The good activities of the two complexes may be attributed to the flexible macrocyclic ligand. The difference in IC_{50} values for the two complexes should be ascribed to the evident discrepancy between their structures, especially in the conformation of the macrocyclic ligand with two pendants.

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Notes and references

† *Crystal data*: Compound **1**: $\text{C}_{31}\text{H}_{50}\text{N}_8\text{O}_{14.5}\text{Cl}_3\text{Cu}_2$, $M = 1000.22$, orthorhombic, space group $Pbca$, $a = 18.709(4)$, $b = 19.238(4)$, $c = 23.100(5)$ Å, $V = 8314(3)$ Å³, $Z = 8$, $D_c = 1.597$ g cm^{-3} , $\mu(\text{Mo-K}\alpha) = 1.290$ mm^{-1} . Of 8474 data collected, 7303 were independent ($R_{\text{int}} = 0.0216$). $R1 = 0.0735$ and $wR2 = 0.1679$ for $[I > 2\sigma(I)]$. Compound **2**: $\text{C}_{62}\text{H}_{87}\text{N}_{16}\text{O}_{16}\text{Cl}_3\text{Cu}_2\text{Zn}_2$, $M = 1684.71$, triclinic, space group $P\bar{1}$, $a = 14.172(2)$, $b = 16.673(2)$, $c = 21.284(3)$ Å, $V = 4665.0(11)$ Å³, $Z = 2$, $D_c = 1.199$ g cm^{-3} , $\mu(\text{Mo-K}\alpha) = 1.103$ mm^{-1} . Of 23946 data collected, 16118 were independent ($R_{\text{int}} = 0.0325$). $R1 = 0.0516$ and $wR2 = 0.1220$ for $[I > 2\sigma(I)]$. The data were collected on a Siemens P4 four-circle diffractometer and a Bruker SMART CCD diffractometer for **1** and **2**, respectively. The structures were solved by direct methods, and refined by least-squares treatment on F^2 using the SHELXTL software package. All non-hydrogen atoms were refined anisotropically by full-matrix least squares. Apart from H1 of O3 in **2**, found from a difference Fourier map, the other H atoms were computed and refined isotropically using a riding model. CCDC 200693 and 200694. See <http://www.rsc.org/suppdata/cc/b3/b300013c/> for crystallographic files in .cif or other electronic format.

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