DALTON

Crystal structures and superoxide dismutase mimetic activity of $[CuL_2(Him)_2]\cdot MeOH$ and $[CuL_2(mim)_2]\cdot H_2O$ [HL = 4-amino-*N*-(thiazol-2-yl)benzenesulfonamide, Him = imidazole, mim = *N*-methylimidazole]†

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The complexes $[CuL_2(Him)_2]\cdot MeOH$ **1** and $[CuL_2(mim)_2]\cdot H_2O$ **2** [HL = 4-amino-*N*-(thiazol-2-yl)-benzenesulfonamide, Him = imidazole, mim = *N*-methylimidazole] have been prepared and their crystal structures determined. In **1** the metal centre has a very irregular stereochemistry, being co-ordinated by six nitrogen atoms, two of them from the imidazole ligands and the other four from three sulfonamides, one belonging to an adjacent asymmetric unit. The crystal packing shows stacking interactions between the imidazole and phenyl rings of the sulfonamide. In **2** the co-ordination polyhedron is intermediate between square pyramidal and trigonal bipyramidal. Spectroscopic and electrochemical data are in accord with the crystal structures. The *in vitro* O_2^- scavenger activity of the complexes shows that they exhibit high superoxide-dismutase mimetic activity.

Copper(II) complexes have possible medical uses in the treatment of many diseases including cancer.[1,2] The anticancer activity may be based on the ability of the complexes to inhibit DNA synthesis. Another possible mechanism involves the scavenging of superoxide anions.[1] Recently, kinetic and thermodynamic considerations have shown that Cu,Zn-superoxide dismutase (SOD) is unique in its ability to catalyse dismutation of O_2^- *in vivo* in contrast to copper compounds which have this feature *in vitro* due to the different reactivities towards dioxygen (low for SOD and high for copper complexes).[3] It is suggested that the copper compounds may efficiently replace SOD only in those pathological processes in which the local concentrations of O_2^- are rather high. It is not clear which parameters are involved in the differing dismutation abilities shown by different copper complexes *in vitro*. A limited steric hindrance to the approach of the superoxide (hyperoxide, O_2^-) anion is considered an essential requirement for the successful binding of the superoxide radical.[4] In a previous study we tested the superoxide dismutase-like activity of some 4-amino-*N*-(thiazol-2-yl)benzenesulfonamide (HL) copper complexes.[5] The higher geometrical distortion of the co-ordination polyhedron of Cu^{II} in the $[Cu(HL)_2Cl_2(MeOH)]$ with respect to $[Cu(HL)_2Cl_2(EtOH)]$ shows a direct relation to the higher SOD-like activity. However, the recently reported $[CuL(Cl)(py)_3]$ complex (py = pyridine),[6] having a minor co-ordination polyhedron distortion, showed higher SOD-like activity. It has been reported that the presence of co-ordination sites belonging to nitrogen heteroatomic rings such as imidazoles or pyridines is important for high SOD activity.[7] In our attempt better to understand the correlation between these structural factors and the scavenger ability of the copper compounds and the implications they may have for the synthesis of physiologically active complexes, we have synthesised, characterised and tested the SOD-like activity of the copper complexes of HL with imidazole (Him) and *N*-methylimidazole (mim). Imidazole is a ubiquitous ligand in chemical and biological systems.

† *Non-SI unit employed:* $\mu_B \approx 9.27 \times 10^{-24}$ J T^{-1}.

Experimental

Materials

Copper chloride dihydrate, Him, mim and HL were reagent grade used without further purification.

Synthesis

The compound $CuCl_2\cdot 2H_2O$ (0.17 g, 1 mmol) was added to a solution of HL (0.5 g, 2 mmol) in hot methanol (75 cm^3). Then, to the resulting yellowish mixture Him (0.68 g, 10 mmol) was added and the solution turned dark green. It was stirred for 15 min and then propan-2-ol (35 cm^3) was added. The final solution was left to stand at 4 °C. After 14 d prismatic green crystals of $[CuL_2(Him)_2]\cdot MeOH$ **1** were obtained in 32% yield (Found: C, 40.7; H, 3.6; Cu, 8.8; N, 19.2. $C_{25}H_{28}CuN_{10}O_5S_4$ requires C, 40.6; H, 3.8; Cu, 8.6; N, 18.9%). IR: $\tilde{\nu}_{max}$/cm^{-1} 3440s and 3350s (N–H sulfonamide); 3120s (N–H imidazole); 1500s (thiazole ring); 1310s, 1150s and 560w (SO_2); 950s (S–N). UV/VIS: λ_{max}/nm 590, 410 and 290. EPR; $g_\perp = 2.06$, $g_\parallel \approx 2.35$.

The synthesis of the mim complex was similar but mim (797 μl, 10 mmol) was added instead of Him. Prismatic brown crystals of $[CuL_2(mim)_2]\cdot H_2O$ **2** (24% yield) appeared after 4 d (Found: C, 41.5; H, 3.8; Cu, 8.5; N, 18.7. $C_{26}H_{30}CuN_{10}O_5S_4$ requires C, 41.4; H, 4.0; Cu, 8.4; N, 18.6%). IR: $\tilde{\nu}_{max}$/cm^{-1} 3440s and 3350s (N–H sulfonamide); 3120s (N–H imidazole); 1500s (thiazole ring); 1310s, 1150s and 560w (SO_2); 950s (S–N). UV/VIS: λ_{max}/nm 650 (sh), 450 and 330. EPR: $g_\perp = 2.06$, $g_\parallel \approx 2.29$, $A_\parallel \approx 132 \times 10^{-4}$ cm^{-1}.

Physical measurements

Analytical data (C, H, N), IR, UV/VIS and EPR spectra, magnetic susceptibility measurements and electrochemical experiments were carried out as described previously.[6]

Crystallography

Complex 1. *Crystal data.* $C_{25}H_{28}CuN_{10}O_5S_4$, $M = 740.36$, monoclinic, space group *Cc* (no. 9), $a = 10.286(3)$, $b =$

13.701(3), c = 21.974(4) Å, β = 93.24(2)°, U = 3092(1) Å^3 (by least-squares refinement on diffractometer angles for 25 automatically centred reflections, λ = 1.541 84 Å), Z = 4, D_c = 1.590 g cm^{-3}, $F(000)$ = 1524, μ(Cu-Kα) = 39.3 cm^{-1}. Prismatic dark green. Crystal size: 0.08 × 0.10 × 0.22 mm.

Data collection and processing. Data were measured at 293(2) K with a CAD-4 diffractometer using the ω–2θ scan mode with ω-scan width = 0.7 + 0.14tan θ, ω-scan speed = 1.2° min^{-1}, graphite-monochromated Cu-Kα radiation; 3069 unique reflections ($30 < \theta < 45°$, hkl, $hk-l$, $0 < h < 12$, $0 < k < 16$, $-26 < l < 26$), giving 2321 with $I \geqslant 3\sigma(I)$. Corrections for Lorentz-polarisation, decay (maximum 13.5%) and empirical absorption[8] (transmission: minimum = 83.3%, maximum = 99.9%) were made during processing.

Structure analysis and refinement. The structure was solved by Patterson methods. All non-hydrogen atoms were refined anisotropically by full-matrix least squares. The amine and methanol hydrogen atoms were not found in the Fourier-difference map and were disregarded. The other hydrogen atoms, geometrically positioned (at 0.95 Å from their neighbouring atoms) were not refined, but their thermal parameters were taken as proportional (× 1.3) to those of their neighbouring non-hydrogen atoms. Secondary extinctions[9] were applied. Atomic scattering factors were taken from ref. 10. The weighting scheme $w = 4F_o^2/[\sigma(I)^2 + (0.04F_o^2)^2]$ gave satisfactory agreement analyses. Final R and R' values were 0.055, 0.064. Calculations were performed with the SDP and MOLEN software[11,12] on a Micro-Vax-3100 computer.

Complex 2. *Crystal data.* $C_{26}H_{30}CuN_{10}O_5S_4$, M = 754.36, orthorhombic, space group *Pbca* (no. 61), a = 12.175(3), b = 19.160(8), c = 27.332(10) Å, U = 6376(4) Å^3 (by least-squares refinement on diffractometer angles for 25 automatically centred reflections, λ = 1.541 84 Å), Z = 8, D_c = 1.439 g cm^{-3}, μ(Cu-Kα) = 31.4 cm^{-1}. Prismatic dark brown. Crystal size: 0.50 × 0.10 × 0.10 mm.

Data collection and processing. Data were measured and corrected as above except that ω-scan width = 0.9 + 0.14 tan θ, ω-scan speed = 2.1° min^{-1}; 5826 unique reflections ($40 < \theta < 48°$, hkl, $hk-l$, $0 < h < 14$, $0 < k < 23$, $0 < l < 33$), giving 1934 with $I \geqslant 1.5\sigma(I)$, maximum decay = 12.2%, minimum transmission = 50.9%, maximum = 99.9%.

Structure analysis and refinement. The structure was solved by direct methods.[13] All non-hydrogen atoms were refined anisotropically by full-matrix least squares. The occupancy of the water oxygen atoms was refined and converged to 0.5. Hydrogen atoms were not refined (thermal factor proportional, × 1.3, to that of the neighbouring atom was imposed); the N–H hydrogen atoms were found in the Fourier-difference maps, the O–H ones were not and therefore disregarded, and the positions of the other hydrogen atoms were calculated. The weighting scheme was of the form $w = \sigma(F_o)^{-2}$. Other details as for complex **1**. Final R and R' values were 0.061, 0.058. Calculations were performed with the SDP software[11] on a Micro-Vax-3100 computer.

Atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1996, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 186/39.

Table 1 Selected bond distances (Å) and angles (°) with estimated standard deviations (e.s.d.s) in parentheses

Complex **1**			
Cu–N(1B)	2.032(8)	Cu–N(3B)	2.635(8)
Cu–N(1A)	2.026(8)	Cu–N(4A)	2.005(8)
Cu–N(2B)	2.682(7)	Cu–N(4B)	1.980(8)
N(1B)–Cu–N(1A)	154.1(3)	N(1B)–Cu–N(2B)	55.8(3)
N(1B)–Cu–N(4A)	90.3(3)	N(1B)–Cu–N(4B)	89.5(4)
N(1B)–Cu–N(3B^I)	105.3(3)	N(1A)–Cu–N(2B)	98.4(3)
N(1A)–Cu–N(4A)	87.9(3)	N(1A)–Cu–N(4B)	91.8(3)
N(1A)–Cu–N(3B^I)	100.5(3)	N(2B)–Cu–N(4A)	91.9(3)
N(2B)–Cu–N(4B)	87.1(3)	N(4A)–Cu–N(4B)	178.9(3)
N(2B)–Cu–N(3B^I)	156.3(3)	N(4B)–Cu–N(3B^I)	91.4(3)
N(4A)–Cu–N(3B^I)	89.7(3)		
Complex **2**			
Cu–N(1A)	2.00(1)	Cu–N(4A)	2.000(9)
Cu–N(1B)	2.001(8)	Cu–N(4B)	1.983(9)
Cu–N(2A)	2.57(1)		
N(1A)–Cu–N(1B)	166.3(4)	N(1B)–Cu–N(4A)	90.0(4)
N(1A)–Cu–N(4A)	90.0(4)	N(1B)–Cu–N(4B)	91.3(4)
N(1A)–Cu–N(4B)	88.9(3)	N(4A)–Cu–N(4B)	178.5(3)

Superoxide dismutase assay

The superoxide dismutase activity of metal complexes was determined according to Oberley and Spitz[14] with minor modifications.[6]

Results and Discussion

Crystal structure of $[CuL_2(Him)_2]$·MeOH 1

Selected bond distances and angles are given in Table 1. Fig. 1 shows the numbering scheme and thermal ellipsoids drawn at the 30% probability level, Fig. 2 a view of the strand parallel to *a*.

The copper(II) ion is six-co-ordinated by two nitrogens furnished by the imidazole ligands, and four nitrogen atoms from three sulfonamide ligands, one of which belongs to an adjacent asymmetric unit. The stereochemistry of the metal centre is very irregular, and it can be considered a distorted octahedron, with the equatorial plane defined by the N(1A), N(1B), N(4A) and N(4B) atoms and the axial positions occupied by the N(3B^I) (I $x-1, y, z$) and N(2B) atoms. The mean equatorial metal–ligand distance (2.011 Å) is markedly shorter than the mean axial one (2.659 Å) according to a model of tetragonal distortion of octahedral copper(II) complexes.[15] The angles at the metal centre are however quite far from those at an octahedron, because of the short bite of the chelating sulfonamide ligand. It is worth noting

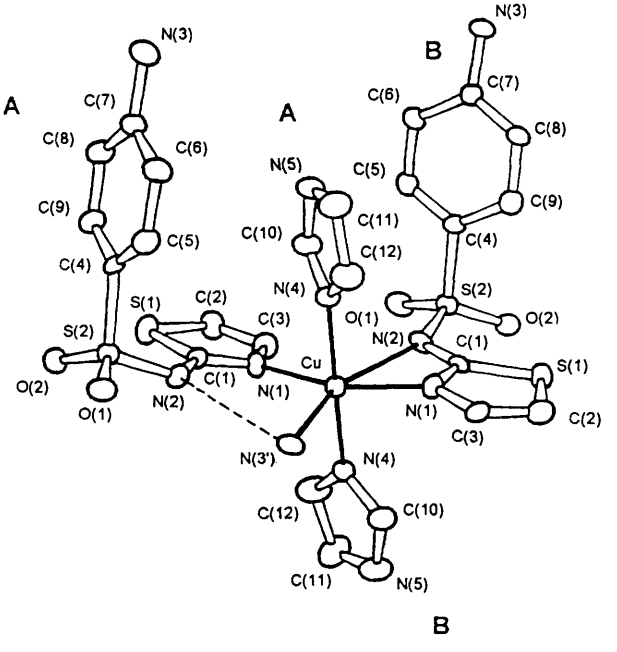

Fig. 1 Numbering scheme of $[CuL_2(Him)_2]$·MeOH complex and thermal ellipsoids drawn at the 30% probability level

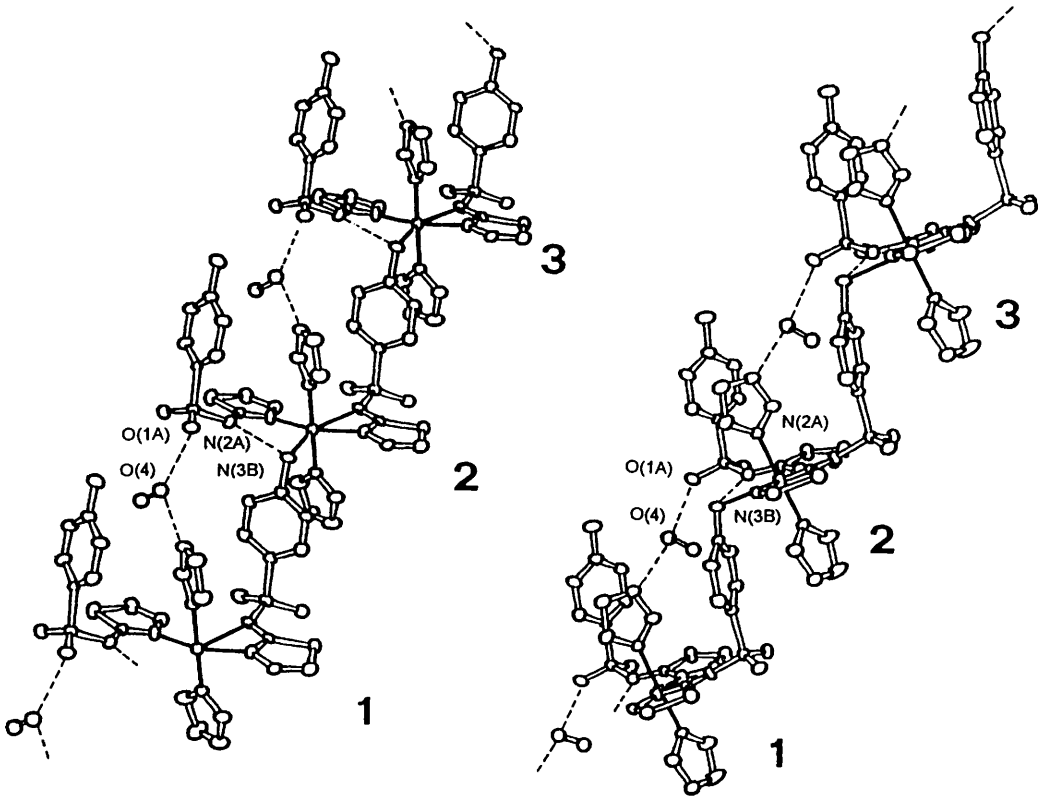

Fig. 2 View of the strand parallel to *a* for the $[CuL_2(Him)_2]$·MeOH complex

that N(2B)–Cu–N(1B) has a small value of 55.8°, similar to those observed for *cis*-distorted octahedral copper(II) complexes.[15]

One of the sulfonamide ligands chelates the metal cation through the sulfonamidato N(2B) and thiazole N(1B) atoms, forming a tetraatomic ring, and is also bound to an adjacent copper(II) ion through the amino N(3B) atom. The other sulfonamide ligand is monodentate through the thiazole N(1A) atom. In this ligand, atom N(2A) is not co-ordinated [Cu · · · N(2A) is 3.257(7) Å, too long for bonding]. This N(2A) atom participates in a hydrogen bond with $N(3B^I)$ [N(2A) · · · $N(3B^I)$ 3.06(1) Å]. The orientation of the monodentate sulfonamide ligand depends, at least in part, on stacking interactions between the phenyl ring A and the imidazole ring A [the planes defined by these rings form an angle of 18.8(1.0)°; the shortest distance, C(6A) · · · N(5A) is 3.54(1) Å].

The copper–imidazole co-ordinative bonds are significantly different [1.980(8) and 2.005(5) Å, respectively], however both values fall in the observed range for this kind of bond,[16] and their difference does not cause significant distortion of the two imidazole rings.[17] The different bonding to the metal cation may be due to packing effects: the imidazole ligands are involved in different intermolecular contacts.

The two ligands present in the asymmetric unit, despite their different structural behaviours, have nearly equivalent bond distances and angles but quite different ones from those of the free sulfonamide.[18,19]

Owing to the presence of a sulfonamide ligand bridging two adjacent metal cations, the crystal structure is characterised by a strand parallel to *a*. The energetics of this structural element is quite complex. Besides the co-ordinative bond Cu–$N(3B^I)$, each monomer is joined to the other by a stacking interaction between the imidazole ring N(4B), C(10B), N(5B), C(11B), C(12B) and the phenyl ring $C(4B^I)$, $C(5B^I)$, $C(6B^I)$, $C(7B^I)$, $C(8B^I)$, $C(9B^I)$ [angle between the planes, 27.9(9)°; shortest bond distance C(8B) · · · C(10B) 3.23(2) Å]. Moreover, a methanol molecule bridges *via* hydrogen bonds two adjacent monomers [N(5A) · · · $O(4^I)$ 2.80(1), O(4) · · · $O(1^{III})$ 2.81(1) Å, N(5A)–$O(4^{II})$–$O(1A^{III})$ 133.2(4)°; II $x + 2$, y, z; III $x + 3$, y, z].

Neighbouring strands parallel to *a* are connected only by hydrogen bonds per monomer [O(2A) · · · $N(3A^{IV})$ 3.10(1), O(1B) · · · $N(3B^{IV})$ = 3.00(1) Å; IV $x - \frac{1}{2}$, $y - \frac{1}{2}$, z]. A third one is connected to the first through a single hydrogen bond per monomer [O(1A) · · · $N(5B^V)$ 3.09(1) Å; V x, y, $-\frac{1}{2} + z$].

It is noteworthy that we present in this paper a proof of the interaction of the imidazole with a phenyl ring through the ligand–ligand effect in the solid state. Few examples of this, so important in biological systems, have been reported.[20]

Crystal structure of $[CuL_2(mim)_2]$·H_2O 2

Bond distances and angles are listed in Table 1. Fig. 3 shows the co-ordination polyhedron around Cu^{II}. The copper atom is five-co-ordinated with a geometry intermediate between square pyramidal (*SPY*) and trigonal bipyramidal (*TBPY*). The equatorial plane is defined by two thiazole N(1A) and N(1B) atoms of the two sulfonamides in *trans* position at distances of 2.00(1) and 2.001(8) Å, and by two imidazole N(4A) and N(4B) atoms at distances of 2.000(9) and 1.983(9) Å. The axial site is occupied by a sulfonamidato N(2A) atom at longer distance [2.57(1) Å] than the equatorial ones. On the contrary, atom N(2B) is not co-ordinated [Cu · · · N(2B) 3.119(9) Å]. As in complex **1**, there is a very small angle at copper of 57.8° and a larger one of 108.5°; the others are close to 90°. The copper(II) ion is 0.1134 Å above the equatorial plane.

The extent of geometrical distorsion from regular *SPY* and *TBPY* stereochemistries can be quantified by the ratio between the basal angles, defined as $\tau = [(\alpha - \beta)/60] \times 100$.[22] The relevant angles in complex **2**, α = 178.5 and β = 166.3°, yield a τ value of 20% which indicates a small distortion of the complex from *SPY* geometry. Comparison of this value with those of other copper sulfonamide complexes reported by us recently,[5,6,23] Table 2, shows similar distortion to that found for the $[CuL(Cl)(py)_3]$ complex.

No intramolecular stacking interactions between the

methylimidazole and the phenyl rings are observed, in contrast to those detected in complex **1**. No other stacking interactions, intra- or inter-molecular, were observed. The molecules interact only weakly through a water molecule O(3) (refined occupancy 0.5) which bridges by hydrogen bonds two adjacent units: $O(1A^{I}) \cdots O(3^{I})$ 2.69(3), $O(3^{I}) \cdots O(1A^{II})$ 2.62(4) Å, $O(1A^{I})$–$O(3^{I})$–$O(1A^{II})$ 97(1)° (symmetry codes: I x, y, z; II $1 - x, -y, 1 - z$).

Infrared spectra

Upon co-ordination, the bands at 1550 and 920 cm^{-1} assigned to the thiazole ring and stretching S–N vibrations are shifted to 1500 and 950–940 cm^{-1}, respectively.

EPR spectra and magnetic data

The solid-state EPR spectrum of compound **1** is anisotropic having a $g_{\perp}$ parameter value of 2.06. The parallel component is very weak, $g_{\parallel} \approx 2.35$. The lack of copper(II) hyperfine coupling in this complex is likely due to dipole–dipole interactions between the copper(II) ions of neighbouring molecules connected through the sulfonamidato N(3B) atom.

The EPR spectrum of complex **2** is also axial with two weak signals in the parallel region: $g_{\parallel} \approx 2.29$ and $g_{\perp} = 2.06$. The value of $A_{\parallel} \approx 132 \times 10^{-4}$ cm^{-1} is consistent with an intermediate geometry between square pyramidal and trigonal bipyramidal.[24]

Both complexes exhibit 'normal' values of the room-temperature solid-state magnetic moments for an orbitally non-degenerate ground state (1.92 and 1.75 μ_B for **1** and **2**, respectively[25]).

Electronic absorption spectra

The solid reflectance spectrum of compound **1** shows three strong bands. The band at 590 nm corresponds to a ligand-field transition, characteristic of elongated tetragonal octahedral or square-coplanar stereochemistries.[15] The band at 410 nm can be considered a charge-transfer transition and that at 290 nm is attributed to sulfonamide ligand–ligand transitions. The d–d band is similar in intensity to those of the other two bands probably due to the strong asymmetry of the co-ordination polyhedron of the copper(II) ion.

The UV/VIS spectrum of complex **2** shows a strong maximum at 450 nm and a weaker one at 330 nm which are due to ligand $\pi \longrightarrow \pi^*$ transitions as well as ligand-to-metal charge-transfer transitions from the π-type orbitals of the sulfonamide or Him ring to the π^*-type copper-based orbitals.[26] The shoulder at 650 nm is a ligand-field transition. The differences in the absorption spectra of the complexes can be attributed to the σ-donor abilities of the axial ligands and steric effects of the equatorial imidazole ligands.[27,28]

Electrochemistry

The cyclic voltammetric behaviour of complex **1** at $v = 0.25$ V s^{-1} in the potential range +0.5 to −1.5 V *vs.* saturated calomel electrode (SCE) is shown in Fig. 4. The compound exhibits two well defined one-electron reduction peaks A_1 (0.06 V) and A_2 (0.45 V). For the first redox step the potential difference ΔE_p between the anodic and the corresponding cathodic peak (A_1') is 0.16 V, according to a quasi-reversible process corresponding to $Cu^{2+} \longrightarrow Cu^{+}$. This redox couple seems not to be totally reversible, according to $\Delta E_p = E_p(A_1) - E_p(A_1')$, probably as a consequence of a chemical reaction coupled to the electrochemical process. However, the ratio $i_p(A_1):i_p(A_1')$ close to 1 indicates relative stability of the copper(I) intermediate species. The second reduction process can be tentatively assigned to the reduction to copper(I) species which generate metallic copper, and which is easily reoxidised in the reverse sweep (peak A_2') The value of $E_{\frac{1}{2}}$ determined by averaging the anodic and cathodic peak potentials, of the reduction of Cu^{2+} is 0.14 V. The $E_{\frac{1}{2}}$ can be expressed as $E = E^{0}_{Cu^{II}-Cu^{I}} + 0.059 \log [K(Cu\text{–}Him)^{+}/K(Cu\text{–}Him)^{2+}]$. Using $E = -0.104$ V (*vs.* NHE)[29] and $E^{0}_{Cu^{II}-Cu^{I}} = 0.155$ V (ref. 30) we obtain the stability constant ratio $K(Cu\text{–}Him)^{+}/K(Cu\text{–}Him)^{2+} = 4 \times 10^{-5}$.

The voltammetric behaviour of complex **2** (see Fig. 4) presents some differences with respect to that of **1**. Only one reduction peak [$E_p(A_1) = 0.09$ V] is clearly observed corresponding to the step $Cu^{2+} \longrightarrow Cu^{+}$, while the second peak is

Table 2 Values of τ for five-co-ordinated complexes

Compound	τ
$[Cu(HL)_2Cl_2(MeOH)]$	0.36
$[Cu(HL)_2Cl_2(EtOH)]$	0.28
$[CuL(Cl)(py)_3]$	0.19
$[CuL_2(mim)_2]\cdot H_2O$	0.20

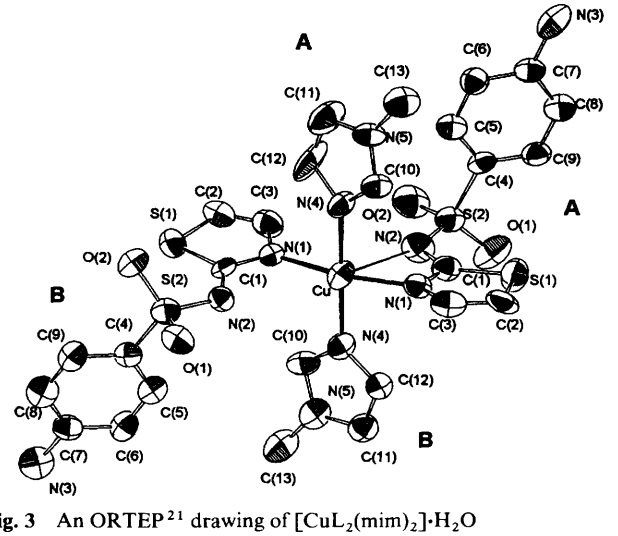

Fig. 3 An ORTEP[21] drawing of $[CuL_2(mim)_2]\cdot H_2O$

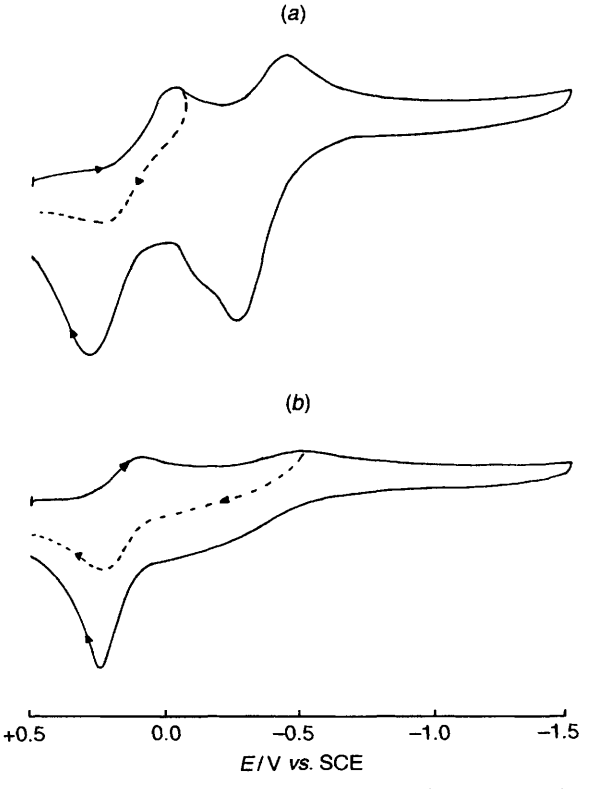

Fig. 4 Cyclic voltammograms for (*a*) $[CuL_2(Him)_2]\cdot MeOH$ **1** and (*b*) $[CuL_2(mim)_2]\cdot H_2O$ **2** complexes in Me_2SO

Table 3 Superoxide dismutase-mimetic activity

Compound	IC_{50}*/μmol dm^{-3}	$-\log IC_{50}$	Axial bond length/Å
$[Cu(HL)_2Cl_2(MeOH)]$	2.510	5.60	2.33
$[Cu(HL)_2Cl_2(EtOH)]$	5.170	5.28	2.28
$[CuL(Cl)(py)_3]$	1.310	5.88	2.50
$[CuL_2(Him)_2]\cdot MeOH$	0.664	6.18	—
$[CuL_2(mim)_2]\cdot H_2O$	0.429	6.37	2.57
Superoxide dismutase	0.006	8.21	—

* IC_{50} is defined as the concentration of complex or enzyme which produces 50% inhibition of nitroblue tetrazolium reduction. A molecular weight of 31 200 was considered for calculating the enzyme concentration. The axial bond distance of the Him complex is not included because the complex has 4 + 1 + 1 geometry.

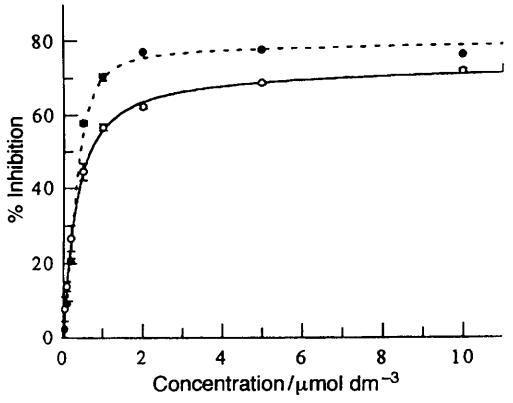

Fig. 5 Percentage inhibition of nitroblue tetrazolium reduction plotted against the concentration of the copper complexes (● for the Him complex and ○ for the mim complex). Each point represents the mean ± standard deviation of triplicate determinations

unobserved, suggesting the copper(I) complex is very unstable. In the reverse sweep the anodic peak must be assigned to the oxidation of copper metal.

The stability-constant ratios for the copper-(I) and -(II) sulfonamide complexes previously reported establish the following stability order of the intermediate copper(I) complexes: Him (4×10^{-5}) < py (1×10^{-4}) < EtOH (1.6×10^{-4}) < MeOH (2.3×10^{-4}). The corresponding mim complex is the least stable.

Superoxide dismutase mimetic activity

The superoxide dismutase activity of the complexes was assayed by their ability to inhibit the reduction of nitroblue tetrazolium. Fig. 5 shows the % inhibition plotted against the concentration of the copper complexes. Table 3 shows the IC_{50} of the copper complexes. From these data we can appreciate that the present complexes, having a similar activity to that of other copper complexes described in the literature,[31,32] are more active than other reported copper sulfonamide complexes. It is worth noting that **2** has an activity 77 times less than that of SOD.

The different behaviour of the species toward the O_2^- radical ion may be due to differences in their structures.[33–35] Following several authors,[36,37] in previous papers we intended to relate the geometrical distortion of the co-ordination polyhedron with the superoxide dismutase activity. For the $[Cu(HL)_2Cl_2(ROH)]$ compounds (R = Me or Et) a direct relation was established.[5] However, the $[CuL(Cl)(py)_3]$ complex,[6] with a minor distortion in the co-ordination polyhedron, has a lower IC_{50} value suggesting that other factors must be taken into account. The values obtained for the present compounds are lower than that of $[CuL(Cl)(py)_3]$ in spite of the fact that the mim complex has a similar co-ordination number and similar distortion. This fact is probably due to the different σ-donor abilities of mim and pyridine. The distorted geometry of these complexes must stabilise the copper(I) oxidation state. In this sense, taking into account the experimental conditions, our electrochemical results indicate that the stability of copper(I) has little influence on the superoxide dismutase-like activity.

A comparison of axial ligand bond distances in the four five-co-ordinate complexes establishes the following relation: the longer the axial bond distance the lower is IC_{50} (Table 3). This correlation is in agreement with the hypothesis which indicates that one of the factors which increases the superoxide dismutase activity is the rapid exchange of molecules axially linked to the metal centre.[38]

Acknowledgements

We thank Dr. J. Latorre (University of Valencia) for his help in the electrochemical measurements and Dr. J. Server (University of Valencia) for assistance with the crystal structure analyses. We greatly appreciate financial support from Comisión Interministerial de Ciencia y Tecnologia (SAF 94-075). J. C. thanks the Generalitat Valenciana (Spain) for a doctoral fellowship.

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Received 22*nd December* 1995; *Paper* 5/08332J