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FULL PAPER

Preparation, characterisation and structures of copper(II) complexes of an asymmetric anti-cancer drug analogue†

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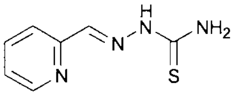
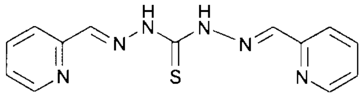
A series of copper(II) complexes of the anti-cancer drug analogue 1,5-bis(2-pyridylmethylene)thiocarbonohydrazide (H_2L) was synthesized from acid solution. The single crystal structures of two asymmetric, binuclear, complexes $[\{Cu_2(HL)(H_2PO_4)_2\}_2][NO_3]_2\cdot 2H_2O$ and $[\{Cu_2(HL)(CF_3CO_2)_3\}_2]$ and two mononuclear, monomeric complexes $[Cu(H_3L)(H_2O)][ClO_4]_3\cdot 2H_2O$ and $[Cu(H_3L)(NO_3)_2]NO_3$ were solved. The binuclear complexes are dimeric with three-atom anion bridges. Selective removal of one copper ion gives mononuclear monomers. The primary magnetic exchange is between copper(II) centres within a planar binuclear unit with weaker interactions *via* anion or sulfur bridges.

Since their biological activities were first reported[1] in 1946, thiosemicarbazones and their complexes have been studied intensely. Research focused on the pyridine-2-carbaldehyde thiosemicarbazone (Hpt) when anti-leukemia activity was observed in mice.[2] Later, it was found that the copper(II) complex was more active than the metal free ligand.[3,4] Proposed modes of action involved inhibition of DNA synthesis and oxidative phosphorylation,[3] and inactivation of tumour viruses by *N*-methylisatin-β-thiosemicarbazone.[5] Besides studies on biological properties, the co-ordination chemistry of these potential tridentate chelators has attracted attention. Stable model thiolato and nitrogen Lewis-base adduct complexes of $[Cu(pt)]^+$ have been isolated from aqueous solution.[6] Crystallographic studies have revealed ternary nitrogen adduct formation,[6,7] complexation of dihydrogenphosphate[8] and pyrophosphate[9] and the system's remarkable ability to form complexes of both the anionic and neutral ligand.[6–11]



Hpt



H_2L

The ligand 1,5-bis(2-pyridylmethylene)thiocarbonohydrazide (H_2L) can be considered as an extended, symmetrical analogue of Hpt. Although the antifungal properties of a monocopper(II) complex of H_2L were noted,[12] little structural work and physical properties has been reported previously on the H_2L system. Recently we reported[13] the asymmetric, bis-copper(II), dimeric complex $[\{Cu_2(HL)(H_2PO_4)_2\}_2][NO_3]_2\cdot 2H_2O$ and its variable temperature magnetic properties. One copper(II) centre is bonded to an NNS, tridentate domain, as is seen for Hpt complexes. The ligand does not symmetrically bridge the metals *via* the S, instead furnishing an NNN donor set for the other Cu^{II}, employing a deprotonated thioamide N. Owing to the ligand's potential to bind two copper(II) ions and the enhanced bioactivity of this ligand type with copper, we present detailed studies on the synthesis and characterization of a series of mono- and bi-nuclear copper(II) complexes of H_2L from acid solution. Four single crystal structures, $[\{Cu_2(HL)(H_2PO_4)_2\}_2][NO_3]_2\cdot 2H_2O$, $[\{Cu_2(HL)(CF_3CO_2)_3\}_2]$, $[Cu(H_3L)(H_2O)][ClO_4]_3\cdot 2H_2O$ and $[Cu(H_3L)(NO_3)_2]NO_3$ are presented along with spectroscopic and magnetic studies.

Experimental

Instrumentation

The electronic transmittance spectra were recorded on a Shimadzu UV-1601 UV-Vis spectrophotometer using Nujol mulls and in DMSO solution, infrared spectra on a Shimadzu IR 470 spectrophotometer as KBr disks in the range 4000–400 cm^{-1}. Microanalyses were performed by the Microanalytical Laboratory at the National University of Singapore. Room temperature magnetic susceptibility measurements were carried out on a Johnson-Matthey Magnetic Susceptibility Balance with $Hg[Co(SCN)_4]$ as standard. Corrections for diamagnetism were made by using Pascal's constants. Molar conductance measurements were made using a Kyoto Electronics CM-115 Conductivity meter with a Kyoto Electronics conductivity cell on *ca.* 1 mM solutions. Dropping mercury electrode (DME) and hanging mercury drop electrode (HMDE) analyses were carried out on a EG&G Polarographic Analyzer, model 174A, with 0.1 M $[N(C_2H_5)_4]ClO_4$ as electrolyte in DMF at room temperature and degas time 12 min. Conditions: scan rate 5 mV s^{-1}; current range 0.2 mA; reference electrode, Ag–AgCl; counter electrode, platinum foil; working electrode, platinum wire.

Syntheses

CAUTION: perchlorate salts are potentially explosive. The compound H_2L (recrystallized from DMF–water (1:7), yield 92%, mp 194–195 °C)[14] and $[Cu_2L(NO_3)_2]\cdot 3H_2O$[13] were synthesized following published procedures. All other chemicals were used as obtained.

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† *Supplementary data available*: rotatable 3-D crystal structure diagram in CHIME format. See http://www.rsc.org/suppdata/dt/1999/3573/

Binuclear copper(II) complexes. *$[Cu_2(HL)Cl_3]\cdot 2H_2O$ 1, $[Cu_2(HL)(NO_3)][NO_3]_2$ 3 and $[Cu_2(HL)Br_2]Br\cdot 3H_2O$ 4.* To a solution of H_2L (142 mg, 0.5 mmol) in hot ethanol (30 ml), $CuCl_2\cdot 2H_2O$ (171 mg, 1.00 mmol), $Cu(NO_3)_2\cdot 3H_2O$ (242 mg, 1.00 mmol) or $CuBr_2$ (224 mg, 1.00 mmol) in hot ethanol (5 ml) was added, followed by HCl (1 M, 1.0 ml), concentrated HNO_3 (2 ml) or HBr (48%, 2.85 ml) respectively. The solution was stirred for 30 min at room temperature and filtered, the product washed with ethanol before drying *in vacuo*. Yields: **1** 244 mg (89%); **3** 221 mg (74%); **4** 299 mg (82%).

$[Cu_2(HL)(HSO_4)(SO_4)]\cdot 4H_2O$ 2. To a solution of H_2L (284 mg, 1.00 mmol) in hot ethanol (50 ml), $CuSO_4\cdot 5H_2O$ (506 mg, 2.00 mmol) in water (10 ml) was added, followed by concentrated sulfuric acid (4 ml). The solution was stirred for 30 min at room temperature. The product was filtered off and washed with water then ethanol before drying *in vacuo*. Yield: 627 mg (93%).

$[Cu_2(HL)I_3]\cdot HI\cdot 1.5H_2O$ 5. To a filtered solution of $[Cu_2L(NO_3)_2]\cdot 3H_2O$ (294 mg, 0.50 mmol) in hot water (40 ml), HI (55–58%, 5 ml) in water (10 ml) was added. The solution was stirred for 30 min at room temperature, the product filtered off and washed with water before drying *in vacuo*. Yield: 425 mg (50%).

$[Cu_2(HL)F_3]\cdot 2HF\cdot 3H_2O$ 6. To a solution of H_2L (284 mg, 1.00 mmol) in hot ethanol (50 ml) in a plastic beaker, $CuF_2\cdot 2H_2O$ (275 mg, 2.00 mmol) in HF (40%, 1 ml) and water (5 ml) were added. The solution was stirred for 1 h at room temperature then filtered. After two months a crystalline precipitate had separated. Yield: 130 mg (23%).

$[\{Cu_2(HL)(H_2PO_4)_2\}_2][NO_3]_2\cdot 2H_2O$ 7. See ref. 13.

$[Cu_2(HL)(H_2PO_4)_3]\cdot 2H_2O$ 8. The complex $[Cu_2L(NO_3)_2]\cdot 3H_2O$ (294 mg, 0.50 mmol) and NaH_2PO_4 (69 mg, 0.50 mmol) were dissolved in H_3PO_4 (2 M, 15 ml). After 10 d, a precipitate appeared which was filtered off and washed with diethyl ether. Yield: 160 mg (49%).

$[Cu_2(HL)(ClO_4)_2]ClO_4\cdot 5H_2O$ 9. To a solution of H_2L (142 mg, 0.50 mmol) in hot ethanol (20 ml), $Cu(ClO_4)_2\cdot 6H_2O$ (371 mg, 1.00 mmol) in hot ethanol (5 ml) and $HClO_4$ (70%, 3 ml) were added. The green solution was filtered and a crystalline precipitate appeared after 2 months. Yield: 190 mg (48%).

$[\{Cu_2(HL)(CF_3CO_2)_3\}_2]$ 10. To a solution of H_2L (142 mg, 0.50 mmol) in hot ethanol (20 ml), $Cu(CF_3CO_2)_2\cdot 2H_2O$ (358 mg, 1.10 mmol) was added, followed by CF_3CO_2H (98%, 0.2 ml). The solution was stirred for 30 min at room temperature. The product was filtered off and washed with water before drying *in vacuo*. Yield: 135 mg (36%). Single crystals suitable for X-ray analysis were obtained from a saturated ethyl acetate solution after one week.

Mononuclear copper(II) complexes. *$[Cu(H_2L)Cl_2]\cdot 3.5H_2O$ 11, $[Cu(H_2L)Br_2]\cdot 1.5H_2O$ 12 and $[Cu(HL)(NO_3)]\cdot H_2O$ 13.* To a solution of H_2L (142 mg, 0.50 mmol) in hot ethanol (20 ml), $CuCl_2\cdot 2H_2O$ (341 mg, 1.00 mmol), $CuBr_2$ (224 mg, 1.00 mmol) or $Cu(NO_3)_2\cdot 3H_2O$ (242 mg, 1.00 mmol) in ethanol (10 ml) was added respectively. The solution was stirred for 30 min at room temperature. The product was filtered off and washed with ethanol before drying *in vacuo*. Yields: **11** 253 mg (52%); **12** 440 mg (82%); **13** 331 mg (77%).

$[Cu(HL)I]\cdot H_2O$ 14. To an aqueous solution (30 ml) of $[Cu(HL)(NO_3)]\cdot H_2O$ (427 mg, 1.00 mmol), KI (180 mg, 1.00 mmol) in water (5 ml) was added. The solution was stirred for 30 min at room temperature. The product was filtered off and washed with ethanol before drying *in vacuo*. Yield: 245 mg (50%).

$[Cu(H_3L)(NO_3)_2]NO_3$ 15 and $[Cu(H_3L)(H_2O)][ClO_4]_3\cdot 4.5H_2O$ 16. The complex $[Cu_2L(NO_3)_2]\cdot 3H_2O$ (588 mg, 1.00 mmol) or $[Cu_2L(ClO_4)(OH)]\cdot H_2O$ ‡ (535 mg, 1.00 mmol) were dissolved in hot ethanol (20 ml) with concentrated HNO_3 (0.2 ml) or $HClO_4$ (70%, 0.5 ml). The solution was filtered and after a week dark green crystals suitable for X-ray diffraction analysis were obtained. Yields: **15** 125 mg (23%); **16** 140 mg (22%).

Crystallography

Crystal data and basic information about the data collection and structure refinement are listed in Table 2. Single crystals of complexes **10**, **15** and **16** were mounted and sealed in a glass capillary tube. The diffraction experiments were carried out on a Siemens Smart CCD diffractometer with a Mo-Kα sealed tube. The software SMART[15] was used for collection of data frames, indexing reflections and determination of lattice parameters, SAINT[15] for integration of intensity of reflections and scaling, SADABS[16] for absorption correction and SHELXTL[17] for space group and structure determination, refinements, graphics and structure reporting.

For complex **16** individual isotropic thermal parameters were refined for disordered perchlorate oxygen atoms. The positional and isotropic thermal parameters of the H atoms attached to water O atoms were refined. For **10** the F atoms of CF_3 groups in all the trifluoroacetato anions showed large thermal activity indicating the possibility of disorder. The fluorine atoms attached to C15 were refined anisotropically. Attempts to refine the anisotropic thermal parameters of the rest of the fluorine atoms were not satisfactory.

A single crystal of complex **7** was mounted and sealed in a quartz capillary. The X-ray data were collected using a Siemens P4 X-ray diffractometer with Mo-Kα radiation. The intensity data were reduced and corrected for Lorentz polarization factors. The crystal structure was solved using SHELXS 86[18] and refined with full matrix least squares on F^2 using SHELXL 93.[18]

CCDC reference number 186/1633.

See http://www.rsc.org/suppdata/dt/1999/3573/ for crystallographic files in .cif format.

Results and discussion

The bis-copper(II) complexes of H_2L prepared (Table 1) with the ligand co-ordinating as a monoanion, $[Cu_2(HL)]^{3+}$, were all from acidic solution and are very stable towards concentrated mineral acids. This was also observed for the Hpt system. However, in contrast to $[Cu(Hpt)]^{2+}$ which was oxidatively decomposed by >0.33 M HNO_3 or $HClO_4$,[10a] $[Cu_2(HL)]^{3+}$ is stable in *ca.* 1 M HNO_3 or $HClO_4$ and yields the respective complexes of these anions, $[Cu_2(HL)(NO_3)][NO_3]_2$ **3** and $[Cu_2(HL)(ClO_4)_2]ClO_4\cdot 5H_2O$ **9**. In order to bind two copper(II) ions the ligand must have the amide deprotonated. Therefore, when $CuSO_4$ and H_2SO_4 are treated with H_2L the product $[Cu_2(HL)(HSO_4)(SO_4)]\cdot 4H_2O$ **2** is formulated as having a hydrogen-sulfate ion in order to balance the charges. The exact location of the proton is not certain, however spectroscopic data are consistent with the formulation.

What is apparent is that the two copper(II) centres are chemically distinct, and under certain conditions one may selectively be displaced. This can be seen from the isolation of the two mononuclear monomers $[Cu(H_3L)(NO_3)_2]NO_3$ **15** and $[Cu(H_3L)(H_2O)][ClO_4]_3\cdot 4.5H_2O$ **16** (see below) which were obtained by dissolving their binuclear parents in the appropriate ethanolic mineral acid. The stability of the NNS bonded copper(II) centre is higher than the NNN site, consistent with copper's affinity for the softer S donor, and it is therefore the latter which is displaced first.

Structure descriptions

$[\{Cu_2(HL)(H_2PO_4)_2\}_2][NO_3]_2\cdot 2H_2O$ 7. A preliminary description of complex **7** has been reported.[13]

$[\{Cu_2(HL)(CF_3CO_2)_3\}_2]$ 10. An ORTEP[19] diagram of

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‡ Preparation is identical to that for $[Cu_2L(NO_3)_2]\cdot 3H_2O$ using $Cu(ClO_4)_2\cdot 6H_2O$, as reported in ref. 13.

Table 1 Colours, analytical and magnetic data for the complexes

Complex	Colour	Analyses (%)[a]				μ_{eff}/μ_B[b]
		C	H	N	Other	
1 $[Cu_2(HL)Cl_3]\cdot 2H_2O$	Brown	28.5(28.2)	2.5(2.7)	14.5(15.2)	19.7(19.3)[c]	1.66
2 $[Cu_2(HL)(HSO_4)(SO_4)]\cdot 4H_2O$	Green	23.1(23.1)	3.0(2.9)	12.4(12.4)	14.2(14.2)[d]	1.15
3 $[Cu_2(HL)(NO_3)][NO_3]_2$	Green	26.8(26.2)	2.0(1.9)	21.1(21.1)	—	1.55
4 $[Cu_2(HL)Br_2]Br\cdot 3H_2O$	Dirty green	22.2(22.2)	1.7(2.4)	11.7(11.9)	34.2(34.0)[e]	1.54
5 $[Cu_2(HL)I_3]\cdot HI\cdot 1.5H_2O$	Dirty green	16.5(16.5)	1.6(1.6)	8.9(8.9)	55.1(53.7)[f]	1.37
6 $[Cu_2(HL)F_3]\cdot 2HF\cdot 3H_2O$	Dark green	27.4(27.4)	2.9(3.5)	14.3(14.7)	15.5(16.6)[g]	1.10
7 $[\{Cu_2(HL)(H_2PO_4)_2\}_2][NO_3]_2\cdot 2H_2O$	Dark green	22.7(22.5)	2.4(2.5)	13.8(14.0)	9.1(9.3)[h]	1.30
8 $[Cu_2(HL)(H_2PO_4)_3]\cdot 2H_2O$	Green	21.1(21.2)	2.9(3.0)	11.2(11.4)	13.2(12.6)[h]	1.40
9 $[Cu_2(HL)(ClO_4)_2]ClO_4\cdot 5H_2O$	Dark green	19.5(19.5)	2.4(2.7)	10.5(10.5)	13.7(13.3)[c]	1.35
10 $[\{Cu_2(HL)(CF_3CO_2)_3\}_2]$	Green	30.3(3.04)	1.7(1.5)	11.1(11.2)	—	1.54
11 $[Cu(H_2L)Cl_2]\cdot 3.5H_2O$	Dirty green	32.6(32.4)	3.2(4.0)	17.7(17.5)	14.3(14.7)[c]	1.88
12 $[Cu(H_2L)Br_2]\cdot 1.5H_2O$	Dirty green	29.1(29.2)	3.2(2.8)	15.4(15.7)	11.1(11.9)[i]	1.84
13 $[Cu(HL)(NO_3)]\cdot H_2O$	Dark green	36.4(36.6)	3.1(3.1)	22.8(23.0)	14.6(14.9)[i]	1.85
14 $[Cu(HL)I]\cdot H_2O$	Brown	31.6(31.8)	2.4(2.7)	17.0(17.1)	26.6(25.8)[f]	2.30
15 $[Cu(H_3L)(NO_3)_2]NO_3$	Dark green	29.4(29.2)	2.3(2.5)	23.4(23.6)	—	1.80
16 $[Cu(H_3L)(H_2O)][ClO_4]_3\cdot 4.5H_2O$[j]	Dark green	20.8(20.9)	2.5(3.2)	11.1(11.3)	14.7(14.3)[c]	1.87

[a] Calculated values are given in parentheses. [b] At 300 K per copper(II) ion. [c] %Cl. [d] %S. [e] %Br. [f] %I. [g] %F. [h] %P. [i] %Cu. [j] Molecules of hydration vary; crystal structure shows 3 but microanalytical data indicate 5.5; %Cu, 8.1(8.5).

Table 2 Crystal data and refinement details for complexes **7**, **10**, **15** and **16**

	7	**10**	**15**	**16**
Empirical formula	$C_{13}H_{17}Cu_2N_7O_{12}P_2S$	$C_{19}H_{11}Cu_2F_9N_6O_6S$	$C_{13}H_{12}CuN_9O_9S$	$C_{13}H_{19}Cl_3CuN_6O_{15}S$
T/K	295(2)	293(2)	293(2)	293(2)
Crystal system	Triclinic	Triclinic	Monoclinic	Triclinic
Space group	$P\bar{1}$	$P\bar{1}$	$P2_1/c$	$P\bar{1}$
M(g mol^{-1})	684.4	749.48	534.92	701.29
a/Å	8.604(2)	9.500(1)	8.238(1)	7.491(1)
b/Å	10.719(2)	12.237(1)	18.092(1)	8.395(1)
c/Å	14.268(3)	12.577(1)	13.285(2)	21.967(1)
α/°	109.57(3)	76.88(1)	—	98.63(1)
β°	90.11(3)	78.94(1)	95.60 (1)	90.81(1)
γ/°	110.62(3)	67.72(1)	—	107.12(1)
U/Å^3, Z	1149.6(4), 2	1308.37(5), 1	1970.40 (4), 4	1320.67(9), 2
Reflections collected	4799	7281	12952	8285
Independent reflections	3930	5179	4935	5909
R(int)	0.0211	0.0150	0.0218	0.0128
$R1/wR_2$ (all data)	0.0576/0.1217	0.0644/0.1631	0.0551/0.1028	0.0566/0.1312
$(I > 2\sigma)$	0.0411/0.1041	0.0573/0.1574	0.0384/0.0932	0.0462/0.1238
μ/mm^{-1}	2.157	1.818	1.287	1.307

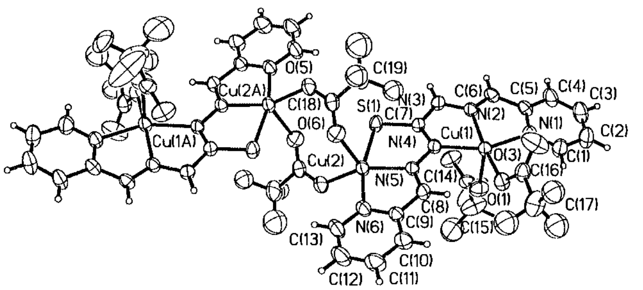

Fig. 1 View of the binuclear dimer $[\{Cu_2(HL)(CF_3CO_2)_3\}_2]$ **10**, showing the numbering scheme.

complex **10** is depicted in Fig. 1. Selected bond distances and angles are listed in Tables 3 and 4 respectively. The complex is a centrosymmetric dimer of bimetallic units, bridged by two bidentate trifluoroacetato ligands with the remaining four trifluoroacetate anions being monodentate and binding to the non-bridging metals. The copper centres are five-co-ordinate with distorted square pyramidal environments. For Cu(2), HL^- furnishes an NNS tridentate equatorial donor set, with the fourth position occupied by a bridging trifluoroacetato O, Cu(2)–O(5A) 1.924(4) Å. The apical site is from another trifluoroactetato O, Cu(2)–O(6) (2.349(4) Å), with a weaker interaction due to Jahn–Teller distortions. Atom Cu(1) has an NNN donor set from the ligand and is displaced out of the mean plane, which consists of N(2), N(1), N(4), Cu(1) by 0.029 Å towards the axial oxygen O(1). The metal associated distances about Cu(1) are *ca.* the same as for **7** whereas those for Cu(2) are all reduced for **10**, presumably a result of a stronger apical donor interaction in **10** (Cu(2)–O(11) 2.860(4), Cu(2)–S(1A) 3.242(2) Å **7**; Cu(2)–O(6) 2.349(4) Å **10**). It is interesting that of the two tridentate copper centres in the complex the one involved in bridging has the NNS donor set, as seen in Hpt complexes.[8,10,11] The ligand is approximately planar, and the remaining co-ordination and ligand parameters are nearly the same as for **7**.

The average bond lengths and angles for the $CF_3CO_2^-$ anions agree well with those reported.[20] The monodentate $CF_3CO_2^-$ shows two essentially equivalent C–O distances (C(14)–O(1) 1.240(6) and C(16)–O(3) 1.262(7) Å). The smaller than expected difference between them results from the hydrogen bond on N(3) (O(2)···N(3) 2.685(6) Å), which increases the delocalization effect. The two bidentate $CF_3CO_2^-$ anions co-ordinate with Cu(2) and Cu(2A) to form an eight membered ring with the two C–O bonds equivalent (1.237(6) and 1.229(7) Å) due to delocalization. The distances between Cu(2A)··· Cu(2) and Cu(2)···Cu(1) are 4.5 and 4.9 Å respectively. There is one hydrogen bonding contact from the amide N to lattice water, N(3)···O(2) 2.685(6) Å.

$[Cu(H_3L)(H_2O)][ClO_4]_3\cdot 2H_2O$ 16. An ORTEP diagram for

Table 3 Selected bond lengths (Å) for complexes **7** and **10**

	7	**10**		**7**	**10**
Cu(1)–O(11)	1.933(3)	—	C(7)–N(3)	1.353(6)	1.358(6)
Cu(1)–N(2)	1.954(4)	1.958(4)	C(7)–N(4)	1.340(6)	1.340(6)
Cu(1)–N(1)	2.053(4)	2.038(5)	N(5)–N(4)	1.369(5)	1.369(6)
Cu(1)–N(4)	2.076(4)	2.045(4)	C(9)–C(8)	1.461(6)	1.458(7)
Cu(1)–O(21)	2.159(3)	—	C(7)–S(1)	1.706(4)	1.715(5)
Cu(2)–O(1)	1.890(3)	—	P(2)–O(1)[a]	1.485(3)	—
Cu(5)–N(5)	1.966(3)	1.970(4)	P(2)–O(21)	1.501(3)	—
Cu(2)–N(6)	2.004(4)	2.029(5)	P(2)–O(23)	1.544(4)	—
Cu(2)–S(1)	2.263(2)	2.292(2)	P(2)–O(22)	1.548(4)	—
Cu(2)–O(11)	2.860(4)	—	P(1)–O(12)	1.495(3)	—
C(5)–C(6)	1.461(6)	1.459(8)	P(1)–O(11)	1.516(3)	—
N(2)–C(6)	1.270(6)	1.279(7)	P(1)–O(13)	1.560(4)	—
N(3)–N(2)	1.356(5)	1.360(6)	P(1)–O(14)	1.564(4)	—
Cu(1)–O(3)	—	1.937(4)	O(1)–C(14)	—	1.240(6)
Cu(1)–O(1)	—	2.220(4)	O(2)–C(14)	—	1.225(7)
Cu(2)–O(5)	—	1.924(4)	O(3)–C(16)	—	1.262(7)
Cu(2)–O(6A)	—	2.349(4)	O(4)–C(16)	—	1.208(8)
O(5)–C(18)	—	1.237(6)			

[a] Symmetry relation: $-x + 1, -y + 1, -z + 1$.

Table 4 Selected bond angles (°) for complexes **7** and **10**

7		**10**	
O(11)–Cu(1)–N(1)	95.4(2)	N(4)–Cu(1)–O(3)	102.0(2)
N(1)–Cu(1)–N(2)	78.9(2)	O(3)–Cu(1)–N(1)	99.7(2)
N(2)–Cu(1)–N(4)	77.4(2)	O(1)–Cu(1)–N(2)	101.8(2)
N(4)–Cu(1)–O(11)	140.5(1)	N(4)–Cu(1)–O(1)	94.5(2)
O(21)–Cu(1)–N(1)	97.4(2)	O(3)–Cu(1)–O(1)	91.6(2)
O(21)–Cu(1)–N(2)	104.2(2)	N(1)–Cu(1)–N(4)	157.0(2)
O(21)–Cu(1)–N(4)	95.8(2)	O(3)–Cu(1)–N(2)	166.5(2)
O(21)–Cu(1)–O(11)	95.0(1)	O(5)[1]–Cu(2)–N(6)	90.7(2)
N(1)–Cu(1)–N(4)	155.1(1)	N(5)–Cu(2)–N(6)	80.5(2)
N(2)–Cu(1)–O(11)	160.5(2)	O(5)[1]–Cu(2)–S(1)	103.4(2)
O(1)–Cu(2)–N(6)	92.8(2)	Cu(1)–N(1)–C(5)	112.4(4)
N(6)–Cu(2)–N(5)	81.1(2)	Cu(1)–N(2)–N(3)	116.7(3)
S(1)–Cu(2)–O(1)	100.7(1)	Cu(1)–N(2)–C(6)	119.0(4)
Cu(1)–N(1)–C(5)	112.6(3)	C(7)–N(3)–N(2)	114.7(4)
Cu(1)–N(2)–N(3)	117.2(3)	Cu(1)–N(4)–C(7)	113.3(3)
Cu(1)–N(2)–C(6)	119.6(3)	N(5)–N(4)–C(7)	112.1(4)
C(7)–N(3)–N(2)	116.0(4)	S(1)–C(7)–N(4)	126.5(4)
Cu(1)–N(4)–C(7)	113.5(3)	Cu(2)–N(5)–C(8)	116.3(4)
N(5)–N(4)–C(7)	110.9(4)	Cu(2)–N(5)–N(4)	122.6(3)
S(1)–C(7)–N(4)	127.4(4)	Cu(2)–N(6)–C(9)	112.3(3)
Cu(2)–N(5)–C(8)	115.8(3)	N(5)–Cu(2)–S(1)	84.5(1)
Cu(2)–N(5)–N(4)	122.4(3)	O(5)[1]–Cu(2)–N(5)	156.4(2)
Cu(2)–N(6)–C(9)	112.4(5)	N(6)–Cu(2)–S(1)	165.04(14)

Symmetry relation:[1] $-x - 1. -y + 1, -z + 1$.

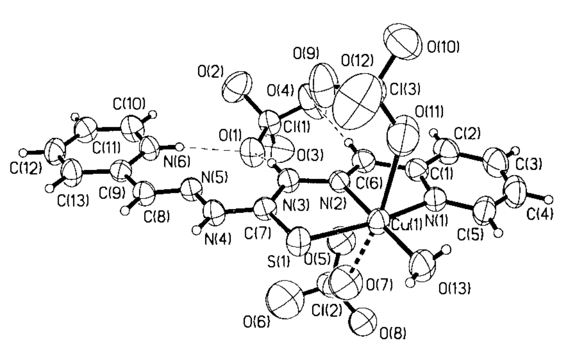

Fig. 2 View of the monomer $[Cu(H_3L)(H_2O)][ClO_4]_3{\cdot}2H_2O$ **16**, showing the numbering scheme.

complex **16** is depicted in Fig. 2. Selected bond distances and angles are listed in Tables 5 and 6 respectively. The complex crystallizes as a monometallic monomer with four tightly bonded in-plane donors around the copper atom, comprised of N(1), N(2), S(1) from the cationic ligand and a co-ordinated water, O(13). There are significantly weaker axial interactions to perchlorate ions at 2.58 (Cu–O(11)) and 2.85 Å (Cu–O(7)) giving an overall tetragonal co-ordination geometry for copper. Bonding parameters are comparable to those of **7** and **10**, and $[Cu(Hpt)]^+$ complexes.[6–11] The whole ligand is planar, as seen by the biggest deviation from the copper associated least-squares plane formed by N(2), N(1), S, C(1)–C(7) being 0.10 Å. Under the acidic conditions employed the non-co-ordinated pyridine is protonated and the thioamide has not deprotonated, therefore the ligand co-ordinates as the cation H_3L^+. In spite of this, and the reduced conjugation resulting from the pyridine being protonated, the geometry is very similar to those of $[Cu(HL)]^{3+}$ in **7** and **10**.

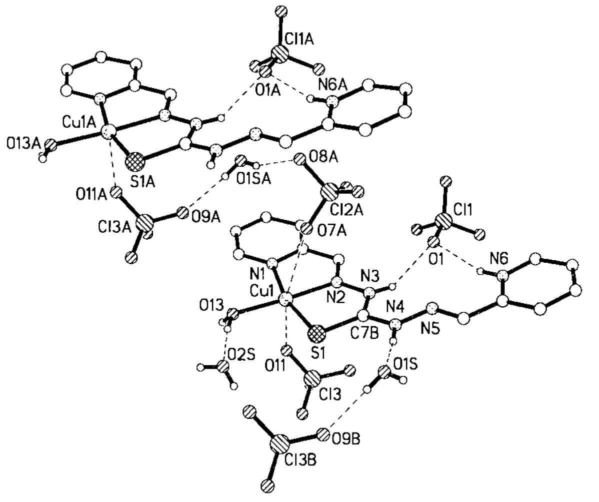

Fig. 3 View of $[Cu(H_3L)(H_2O)][ClO_4]_3{\cdot}2H_2O$ **16**, showing hydrogen-bonding interactions.

Two non-bonded water molecules and three perchlorate ions occupy the space between monomers and interact weakly with them through hydrogen bonds (Fig. 3), which are O(1SA)··· N(4A) 2.720(4), O(1B)···N(3B) 2.896(3), O(1B)···N(6B) 2.948(4), and O(1SA)···O(9A) 2.857(4) Å.

$[Cu(H_3L)(NO_3)_2]NO_3$ 15. An ORTEP diagram for complex **15** is depicted in Fig. 4. Selected bond distances and angles are listed in Tables 5 and 6 respectively. The complex crystallizes as a monomer with a distorted square pyramidal co-ordination sphere around the copper centre. The co-ordination mode of H_3L^+ is the same as found in **16** and bonding parameters are similar. Three of the five co-ordination sites are occupied by NNS from H_3L^+ and the other two oxygen atoms are from

Table 5 Selected bond lengths (Å) for complexes **15** and **16**

	16	**15**		**16**	**15**
Cu(1)–S(1)	2.284(1)	2.284(1)	Cu(1)–N(1)	2.016(3)	2.013(2)
Cu(1)–N(2)	1.941(2)	1.960(2)	Cu(1)–O(13)	1.936(3)	1.951(2)[a]
Cu(1)–O(11)	2.580(3)	2.369(3)[b]	Cu(1)–O(7)	2.859(3)	—
C(1)–N(1)	1.349(4)	1.356(3)	C(1)–C(2)	1.393(5)	1.377(3)
C(1)–C(6)	1.459(4)	1.463(3)	C(2)–C(3)	1.405(6)	1.385(4)
C(3)–C(4)	1.361(6)	1.377(4)	C(4)–C(5)	1.375(6)	1.382(4)
C(5)–N(1)	1.339(4)	1.331(3)	C(6)–N(2)	1.277(4)	1.278(3)
N(2)–N(3)	1.364(3)	1.365(3)	N(3)–C(7)	1.342(4)	1.344(3)
C(7)–N(4)	1.334(4)	1.335(3)	C(7)–S(1)	1.708(3)	1.701(2)
N(4)–N(5)	1.372(3)	1.372(3)	N(5)–C(8)	1.275(4)	1.272(3)
C(8)–C(9)	1.459(4)	1.463(3)			

[a] Cu(1)–O(1). [b] Cu(1)–O(4).

Table 6 Selected bond angles (°) for complexes **15** and **16**

	15	**16**	
O(1)–Cu(1)–N(1)	101.11(19)	97.01(2)	O(13)–Cu(1)–N(1)
O(1)–Cu(1)–N(2)	174.47(10)	177.04(12)	O(13)–Cu(1)–N(2)
O(1)–Cu(1)–S(1)	95.15(7)	96.43(9)	O(13)–Cu(1)–S(1)
O(1)–Cu(1)–O(4)	85.78(11)	90.7	O(13)–Cu(1)–O(11)
N(2)–Cu(1)–N(1)	80.39(8)	80.85(10)	
S(1)–Cu(1)–N(1)	160.79(7)	165.78(8)	
S(1)–Cu(1)–N(2)	84.40(6)	85.55(7)	
O(4)–Cu(1)–N(1)	99.20(9)	84.7	O(11)–Cu(1)–N(1)
O(4)–Cu(1)–N(2)	88.73(10)	91.1	O(11)–Cu(1)–N(2)
O(4)–Cu(1)–S(1)	92.06(7)	99.7	O(11)–Cu(1)–S(1)
O(7)–Cu(1)–S(1)	—	85.0	
O(7)–Cu(1)–N(2)	—	70.0	
O(7)–Cu(1)–N(1)	—	86.5	
O(7)–Cu(1)–O(13)	—	107.9	
O(7)–Cu(1)–O(11)	—	160.3	
C(9)–C(8)–N(5)	117.4(2)	117.9(3)	
C(8)–N(5)–N(4)	116.8(2)	116.2(2)	
N(5)–N(4)–C(7)	117.96(19)	118.1(2)	
N(4)–C(7)–N(3)	118.4(2)	118.2(3)	
C(7)–N(3)–N(2)	115.58(19)	116.0(2)	
N(3)–N(2)–C(6)	122.1(2)	122.1(3)	
N(2)–C(6)–C(1)	114.4(2)	114.5(3)	
N(3)–N(2)–Cu(1)	120.05(14)	120.2(2)	
C(7)–S(1)–Cu(1)	95.60(8)	94.95(10)	

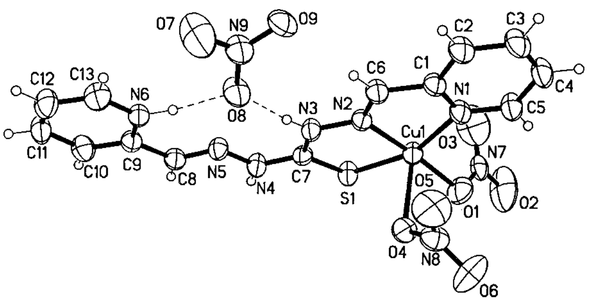

Fig. 4 View of the monomer $[Cu(H_3L)(NO_3)_2]NO_3$ **15**, showing the numbering scheme.

monodentate nitrato ions with the axial nitrato group weaker as expected (Cu–O(4) 2.369(3) Å).

Oxygen atoms in two of the nitrate ions (N(8), N(9)) are not involved in strong hydrogen bonding and are seriously disordered. Atom O(8) does form hydrogen bonds with the protonated pyridine nitrogen N(6) (O(8)···N(6) 2.740(3) Å), and the protonated thioamide nitrogen N(3) (O(8)···N(3) 2.779(3) Å).

Electrochemical studies

Table 7 Redox potential data for selected compounds[a]

Compound	$E_{1/2}$/V		
	⟨1⟩	⟨2⟩	⟨3⟩
H_2L	0.02	—	—
Hpt	0.14	—	—
$CuCl_2$	0.07	−0.08(sh)	—
$[\{Cu(pt)(CH_3CO_2)\}_2]$	0.21	—	−0.58
11 $[Cu(H_2L)Cl_2]\cdot3.5H_2O$	0.14	−0.10	
12 $[Cu(H_2L)Br_2]\cdot1.5H_2O$	0.22	−0.27	—
13 $[Cu(HL)(NO_3)]\cdot H_2O$	0.12	−0.16	−0.49
1 $[Cu_2(HL)Cl_3]\cdot2H_2O$	0.29	−0.12	−0.29
2 $[Cu_2(HL)(HSO_4)(SO_4)]\cdot4H_2O$	0.18	−0.14	−0.40
3 $[Cu_2(HL)(NO_3)][NO_3]_2$	0.16	−0.14	−0.43
4 $[Cu_2(HL)Br_2]Br\cdot3H_2O$	0.18	−0.19	−0.48
7 $[\{Cu_2(HL)(H_2PO_4)_2\}_2][NO_3]_2\cdot2H_2O$	0.29	−0.28	−0.39
9 $[Cu_2(HL)(ClO_4)_2]ClO_4\cdot5H_2O$	0.15	−0.22	−0.40

[a] Scan rate, 5 mV s^{-1}; reference electrode, Ag–AgCl; counter electrode, platinum foil; working electrode, platinum wire: 0.1 M $[NEt_4]ClO_4$ electrolyte in DMF at room temperature: degas time, 12 min; sh, shoulder.

As the biological mechanism(s) of action for the related Hpt copper(II) complexes are related to their electrochemical properties,[4a] DME and HMDE voltammetric studies of the complexes and the ligand were conducted. In the differential pulse polarogram of H_2L there is only one strong peak at *ca.* 0.02 V. The dicopper(II) complexes exhibit redox processes in the range of 0.2 to −1.3 V. Results for selected compounds are given in Table 7.

The binuclear complexes exhibit three reduction processes from 0.4 to −0.6 V, as given in eqns. (1) to (3). In the first,

$$[Cu_2(HL)]^{3+} + e^- \longrightarrow [Cu_2(HL)]^{2+} \quad (1)$$

$$[Cu_2(HL)]^{2+} + e^- \longrightarrow [Cu_2(HL)]^{+} \quad (2)$$

$$[Cu_2(HL)]^{+} + n\,e^- \longrightarrow [Cu_2(HL)]^{1-n} \quad (3)$$

$[Cu_2(HL)]^{3+}$ is reduced to form a dication, with the range of this process being between 0.29 and 0.15 V. Compared with the monocopper compounds **11**–**13**, the binuclear complexes have similar $E_{1/2}$ values at *ca.* 0.25 V, suggesting it is the Cu^{II} co-ordinated to sulfur which is first reduced. The second process has $E_{1/2}$ values in the range −0.22 to 0.12 V and the third from −0.29 to −0.48 V. From the cyclic voltammetry HMDE studies, the first two processes are one electron and reversible, whereas the third is quasireversible, and it is difficult to determine *n*. Extending the potential range to −1.1 V revealed two irreversible reduction processes considered as ligand centred.

It was difficult to determine all sites of reduction. The first two reductions were regarded as metal based as copper(I) complexes of H_2L can be prepared, and stable copper(I) complexes of Hpt have been isolated.[4c] The copper(I) complexes of H_2L are air oxidized rapidly and significant geometry changes are likely for Cu^I when compared to Cu^{II}.

Table 8 Electronic absorption and conductivity data for complexes

Complex	Absorption bands (nm)[a]			
	Charge transfer		d–d	Λ[b]
1 $[Cu_2(HL)Cl_3]\cdot 2H_2O$	*c*	490	640	35
2 $[Cu_2(HL)(HSO_4)(SO_4)]\cdot 4H_2O$	*c*	*c*	690	56
3 $[Cu_2(HL)(NO_3)][NO_3]_2$	380	440	640	114
4 $[Cu_2(HL)Br_2]Br\cdot 3H_2O$	400	479	670	55
5 $[Cu_2(HL)I_3]\cdot HI\cdot 1.5H_2O$	390	560	709	117
6 $[Cu_2(HL)F_3]\cdot 2HF\cdot 3H_2O$	390	470	660	9
7 $[\{Cu_2(HL)(H_2PO_4)_2\}_2][NO_3]_2\cdot 2H_2O$	390	480	640	32
8 $[Cu_2(HL)(H_2PO_4)_3]\cdot 2H_2O$[d]	390	480	630	—
9 $[Cu_2(HL)(ClO_4)_2]ClO_4\cdot 5H_2O$	430	520	680	68
10 $[\{Cu_2(HL)(CF_3CO_2)_3\}_2]$	390	470	710	47
11 $[Cu(H_2L)Cl_2]\cdot 3.5H_2O$	370	440	620	25
12 $[Cu(H_2L)Br_2]\cdot 1.5H_2O$	360	450	640	30
13 $[Cu(HL)(NO_3)]\cdot H_2O$	370	440	*c*	23
14 $[Cu(HL)I]\cdot H_2O$	360	460	640	17
15 $[Cu(H_3L)(NO_3)_2]NO_3$	360	430	630	112
16 $[Cu(H_3L)(H_2O)][ClO_4]_3\cdot 4.5H_2O$	360	430	630	115

[a] Nujol mull transmittance results. [b] In DMSO, S cm^{-2} mol^{-1}. [c] Not resolved. [d] Insoluble in DMSO.

Electronic spectra

Mull transmittance spectra for dicopper(II) complexes exhibit two charge transfer transitions at *ca.* 390 and 470 nm which are assigned to $N\rightarrow Cu^{II}$ and $S\rightarrow Cu^{II}$ respectively.[21] Compared with dicopper complexes, the monocopper species have higher energy CT transitions, due to the decrease of delocalization as seen by the transitions at *ca.* 360–370 ($N\rightarrow Cu^{II}$) and *ca.* 430–460 nm ($S\rightarrow Cu^{II}$) (Table 8). The d–d transitions for all complexes at *ca.* 640 nm indicate the copper centre geometry is 4 + 1 distorted square pyramidal, or 4 + 2 tetragonal as observed in the crystal structures of **7**, **10**, **15**, and **16** and related Hpt complexes of Cu^{II}.[8–10]

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