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An Unusual Copper(I) Complex of a New Macrocyclic Ligand

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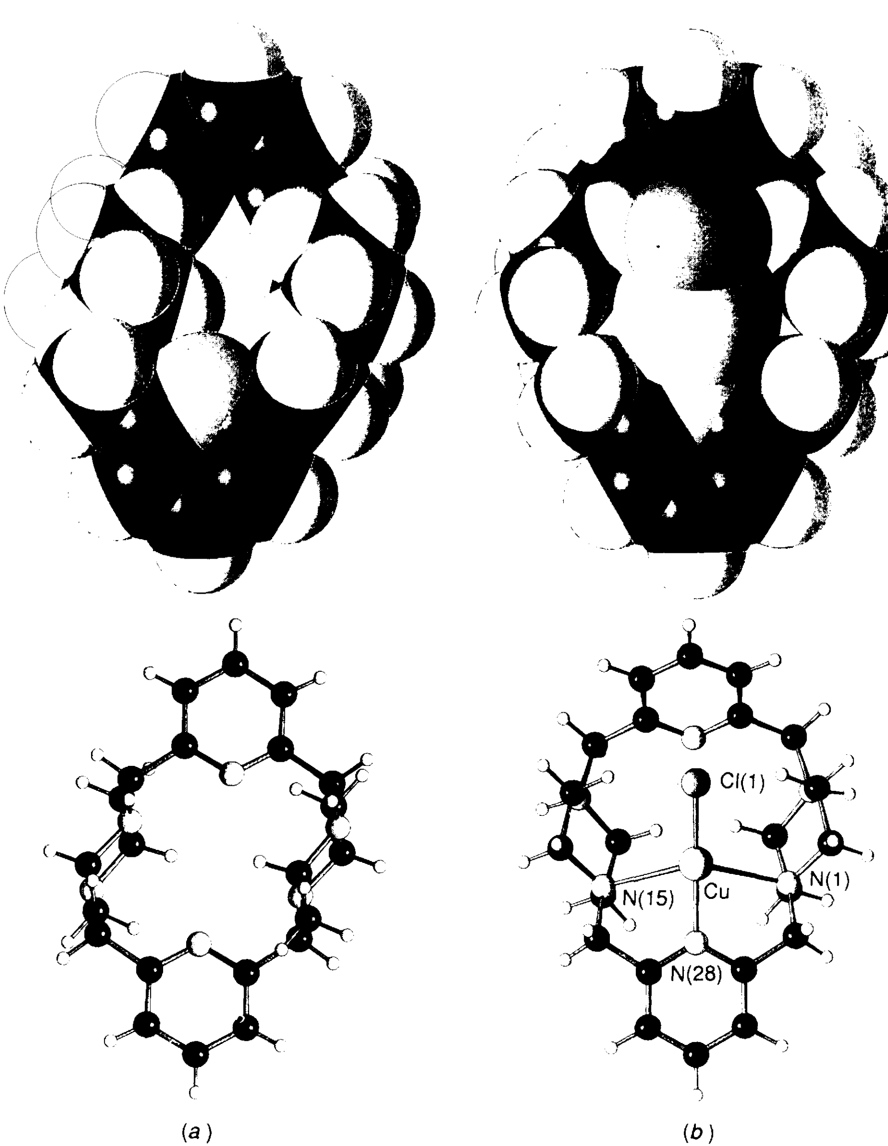
The new 18-membered macrocyclic ligand 1,5(2,6)dipyridina-3,7(1,4)dipiperazinaoctacyclophane,† shows an allosteric effect upon complexation with copper(I) chloride in aqueous ethanol resulting in an extraordinary copper complex, the structure of which has been established by X-ray diffraction analysis.

Recently we have reported a concept for the synthesis and inclusion properties of large macrocycles which contain piperazine units as essential building blocks.[1] The synthesis of macrocyclic ligands as receptors for either ions or uncharged organic molecules is an important field in examination of complexation abilities and complex formation. Ligands forming suitable cavities have been used for catalytic reactions.[2] One of the most interesting features in supramolecular complex chemistry is the allosteric effect,[2a] where a conformational change caused by complexation of a metal ion makes a second complexation of another metal ion possible. Especially, the capability of macrocycles and cryptands to show allosteric effects and their ability to act as hosts for anions and cations,[3] intrigued us to question if piperazines could be used as donor spacers in the synthesis of macrocyclic ligands. Piperazine offers an aliphatic nitrogen-containing building block in which the ring is preorganized.[4] Piperazine itself is a good hydrogen-bond acceptor, which together with its metal complexing capabilities makes it interesting for supramolecular complex chemistry.[5] The favoured conformation of *N*,*N*-alkyl disubstituted piperazines is the chair conformation with the *N*-substituents in equatorial positions, but in some



(*a*) (*b*)

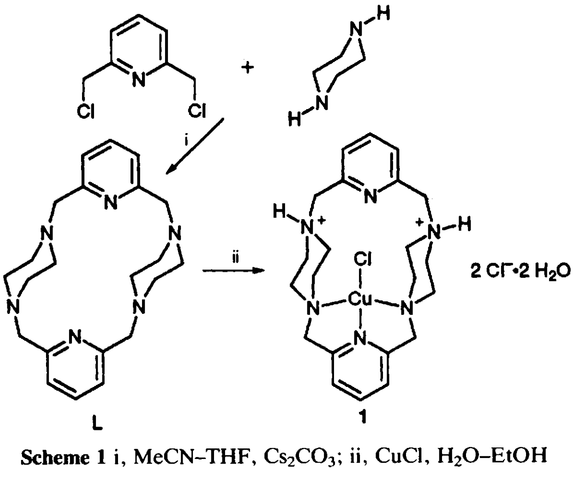
Fig. 1 A SCHAKAL[7] plot for L (*a*) and $[Cu(H_2L)Cl]^{2+}$ (*b*) based on X-ray studies. The Cl anions and the water molecules for the latter are not shown. Bond distances (Å) and angles (°) around the copper ion: Cu–Cl(1) 2.137(1), Cu–N(1) 2.495(4), Cu–N(15) 2.504(4), Cu–N(28) 1.947(4), Cl(1)–Cu–N(1) 109.9(1), Cl(1)–Cu–N(15) 109.1(1), Cl(1)–Cu–N(28) 164.5(1), N(1)–Cu–N(15) 129.1(1), N(1)–Cu–N(28) 75.2(1), N(15)–Cu–N(28) 75.9(1).

small- or medium-sized azacrown–metal complexes piperazine has been found to exist in the boat conformation.[6] Piperazine-containing compounds have been reported to form weak complexes with Cu^{2+}, Ni^{2+}, Zn^{2+}, Cd^{2+} and Pb^{2+} ions.[6d] Some of those, mostly Cu- and Ni-complexes, have been characterised by X-ray diffraction.[6a,c]

The synthesis of L (Scheme 1) was performed under high dilution conditions.‡ The physical data§ and the X-ray analysis¶ shows the high symmetry (inversion) of the uncomplexed ligand [Fig. 1(*a*)]. The cavity is very crowded and complex formation is sterically hindered. However complexation with suitable metal ions could be possible after appropriate conformational changes altering the spatial orientation of the free electron pairs of the coordinating nitrogen atoms. CuCl was selected as a probe for complex formation due to the size and coordination properties of the copper(I) ion. In order to achieve better control for complex formation aqueous ethanol was used as a solvent. In this solvent CuCl is nearly insoluble, but is readily solubilised in the presence of the ligand. The colour changed from pale yellow to dark yellowish green indicating that a reaction has occurred.||

The X-ray analysis¶ of the copper(I) complex reveals an unusual structure consisting of diprotonated ligand H_2L and CuCl [Fig. 1(*b*)] with two additional Cl^- anions hydrogen bonded to the protonated nitrogen atoms and to two water molecules. The complex can thus be formulated as $[Cu(H_2L)Cl]Cl_2 \cdot 2H_2O$ **1**. The conformational change observed for L upon complexation not from the chair to the boat form as has been observed in known piperazine complexes,[6] but instead at 180° rotation of one of the piperazine units occurs. The rotation can be explained by a rapid protonation of two piperazine nitrogen atoms of the basic ligand L in acidic media (CuCl + H_2O). Protonation at N(4) and N(12) [or N(1) and N(15)], rather than symmetrical diprotonation at N(1) and N(2), leads to a conformational change as a consequence of steric hindrance between the piperazine hydrogens and the NH atoms. The rotation of one piperazine moiety creates a suitably sized pocket-shaped coordination site which is now accessible to Cu^I. Thus an allosteric effect [protonation → complexation] is observed. The coordination sphere consists of three nitrogen atoms (one pyridine and two piperazine moieties) and one chlorine atom. The coordinating atoms surround the copper atom unsymmetrically in a 2 + 2 fashion thus exhibiting a very unusual coordination geometry (Scheme 2 and Fig. 1) for Cu^I which, when four-coordinate, prefers a tetrahedral geometry.

The current study presents a relatively simple but preorganised ligand showing an allosteric effect caused by pH, rather than previous complexation with another metal ion. The complexation due to this effect demonstrates the versatility of piperazine as a building block[1] and in addition the copper(I) complex shows an extraordinary coordination geometry. We are currently preparing unsymmetrical analogues of L and testing their complexation abilities with other metal ions.



Scheme 1 i, MeCN–THF, Cs_2CO_3; ii, CuCl, H_2O–EtOH

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Footnotes

† Named using the forthcoming new, IUPAC approved, system for phane nomenclature due to be published in near future, see ref. 1. IUPAC name: 1,4,12,15,27,28-hexaazapentacyclo-$[18.2.2.2.^{12,15}1.^{6,10}1.^{17,21}]$-octadodeca-6,8,10(27),17,19,21(28)-hexane.

‡ *Synthesis of* L: Solutions of 2,6-di(chloromethyl)pyridine (6 g, 34 mmol) in MeCN (250 cm^3) and piperazine (2.93 g, 34 mmol) in THF–MeCN (250 cm^3) (1 : 1.5) are simultaneously dropped into a refluxing, well stirred solution of Cs_2CO_3 (10 g, 34 mmol) in MeCN–THF (500 cm^3; 4 : 1 v/v) over 8 h. After the addition was complete the mixture is kept refluxing for an additional 3 h. The inorganic residue is filtered off and the solvent is evaporated. The remaining yellow residue was chromatographically separated on aluminum oxide using MeCN-EtOH (15 : 1, v/v) as eluent giving L in 1.6 g (25%) yield. A minor product (yield <2%) was the cyclic trimer as established by MS. Crystals for X-ray analysis were obtained by slow evaporation of a MeCN–EtOH solution after chromatographic purification.

§ *Physical and spectroscopic data for L.* $R_f = 0.48$ (MeCN–EtOH; 10 : 1, v/v), mp. 276°C (decomp.). MS (35 eV, VG Autospec HRMS): *m/z* 378 (M^+, 58), 190 (50), 107 (100%). NMR (JEOL GSX-270, CD_2Cl_2): ^1H (270.1 MHz), δ 2.34 (s, 16H, NCH_2CH_2), 3.5 (s, 8H, NCH_2), 7.15 (t, 4H, H of pyridine), 7.54 (d, 2H, H of pyridine); ^{13}C (67.9 MHz), δ 52.62, 64.14, 122.14, 136.00, 157.09.

¶ *X-Ray crystal structure analysis of L and* $[Cu(H_2L)Cl]Cl_2 \cdot 2H_2O$ **1**: L, colourless, $C_{22}H_{30}N_6$, $M_r = 378.52$, monoclinic, space group *C2/c* (no. 15), $a = 17.615(2)$, $b = 9.696(1)$, $c = 12.654(1)$ Å, $\beta = 111.69(1)°$, $V = 2008.3(4)$ Å^3, $Z = 4$, $D_c = 1.252$ g cm^{-3}, Cu-Kα radiation [λ(Cu-Kα) = 1.5418 Å], μ(Cu-Kα) = 0.571 mm^{-1}, 2265 measured, 2012 unique reflections ($R_{int} = 0.009$), 1657 with $I > 3\sigma I$, $R = 0.036$ and $R_w = 0.035$. **1**, greenish yellow, $C_{22}H_{32}Cl_3CuN_6 \cdot 2H_2O$, $M_r = 586.47$, monoclinic, space group $P2_1/n$ (no. 14), $a = 10.762(1)$, $b = 13.714(2)$, $c = 17.802(5)$ Å, $\beta = 98.16(2)°$, $V = 2600.7(8)$ Å^3, $Z = 4$, $D_c = 1.498$ g cm^{-3}, Mo-Kα radiation [λ(Mo-Kα) = 0.7107 Å], μ(Mo-Kα) = 1.183 mm^{-1}, 4012 measured, 3597 unique reflections ($R_{int} = 0.015$), 2133 with $I > 3\sigma I$, $R = 0.035$ and $R_w = 0.032$. CAD4 diffractometer (Enraf-Nonius). Atomic coordinates, bond lengths and angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

|| Crystal of **1** for X-ray analysis were obtained by recrystallization; ligand L and CuCl (1 : 1) were dissolved in water (25 cm^3) giving a dark yellowish green coloration. The unsealed 50 cm^3 flask was then placed into a 250 cm^{-3} beaker containing EtOH (50 cm^3). The system was sealed tightly and left to stand at room temperature. After nine months greenish yellow crystals emerged on the wall of the flask just above the solvent surface and were used for X-ray analysis. Owing the very small amount of **1** obtained no spectroscopic data were obtained.

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