Proton Control of the Conformation of a Macrobicyclic Ligand

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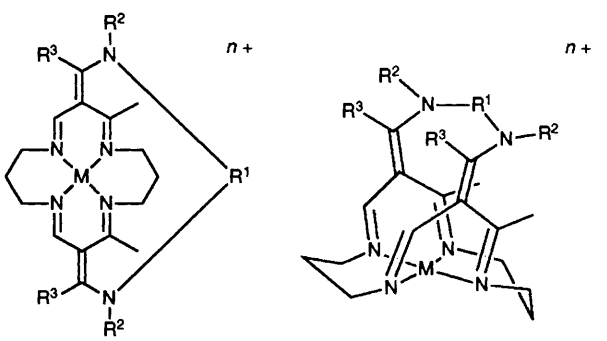
Crystal structure determinations for two salts show that the structures of metal-free cyclidene ligand salts are critically dependent on the degree of protonation, showing either a structure close to those found for corresponding metal complexes, or an entirely different conformation stabilised by N–H···Cl hydrogen bonds in an 'ion quartet', a cluster formed by the $[LH_5]^{5+}$ ion interacting with 3 Cl^- ions.

The formation of metal complexes from macrocyclic ligands is generally favoured thermodynamically over similar complexes containing open-chain ligands. This advantage, labelled the macrocyclic effect, arises from the topological constraints associated with the cyclic structure.[1] Specifically, chelation of the macrobicyclic ligand to a metal ion produces the distinctive saddle-shaped conformations[2] that provide cyclidene macrobicyclic metal complexes **I** with their remarkable behaviour as dioxygen carriers and artificial oxygenase enzymes.[3] The detailed shape of the cavity has been shown to be controlled by the ligand substituents, and in particular when R^1 is $[CH_2]_n$, the width of the void is controlled by the chain length.[4] The notion of preorganization directs interest towards the tendency of the ligand to adopt the conformation required by chelation, but in the absence of the metal ion.



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1 $R^1 = [CH_2]_6$, $R^2 = R^3 =$ Me; no metal; 2 H^+
2 $R^1 = [CH_2]_3NH[CH_2]_3$, $R^2 =$ H, $R^3 =$ Me; no metal; 5 H^+
3 Co^{3+} complex of **1**

We have now determined the X-ray structures of two metal-free lacunar cyclidene ligands **1** ($R^1 = [CH_2]_6$, $R^2 = R^3$ = Me) and **2** ($R^1 = [CH_2]_3NH[CH_2]_3$, R^2 = H, R^3 = Me) as their protonated salts.‡ Their conformations can be compared to that of **3**, the Co^{2+} complex of **1** (**6a** in ref. 4). Chemically, the difference between the two ligands is small, the inclusion of an NH group in the polymethylene bridge in **2**, and the replacement of two N–Me groups by N–H. Although their formation conditions are essentially identical, using anhydrous HCl gas, **1** forms as a di-protonated and **2** as a penta-protonated salt; the slightly greater basicity expected for **2** and the specific solubility properties of these salts are presumably responsible for this striking difference.

Fig. 1 shows the remarkable result of the change in protonation. In **1** the ligand conformation is very similar to

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‡ Both **1** and **2** were prepared by demetallation with anhydrous HCl of the corresponding Ni^{II} salt in methanol (**1**) or acetonitrile (**2**), followed by the addition of NH_4PF_6 to precipitate the salts. The preparation of the Ni^{II} salt and the demetallation for **1** are described in C. J. Cairns and D. H. Busch, *Inorg. Synth.*, 1990, **27**, 261; for **2** they are in P. Jackson, Ph.D. Thesis, Ohio State University, 1981. Both have previously been considered to be $[PF_6]_3$ salts.

Crystal data: **1**, $C_{26}H_{46}N_6F_{12}P_2$, $M = 732.6$, orthorhombic, $Pca2_1$; $a = 17.584(11)$, $b = 12.075(10)$, $c = 15.990(14)$ Å, $U = 3395$ Å^3, $Z = 4$, $T = 290$ K, $R = 0.075$ for 1764 unique observed $[I/\sigma(I) \geqslant 2.0]$ reflections; 509 parameters. **2**, $C_{24}H_{41}N_7F_{12}P_2Cl_3$, $M = 823.9$, monoclinic, $P2_1/n$; $a = 11.843(2)$, $b = 20.599(4)$, $c = 15.615(3)$ Å, $\beta = 95.48(3)$, $U = 3792$ Å^3, $Z = 4$, $T = 220$ K, $R = 0.089$ for 1921 unique observed $[I\sigma(I) \geqslant 2.0]$ reflections; 469 parameters. Both complexes showed disordered $[PF_6]^-$ groups while in **1** one carbon atom had two alternative positions (50 : 50 occupancy), and **2** contained a highly disordered solvent molecule. Despite the low data : parameter ratios, both refinements were well behaved, giving good definition of positional and thermal parameters.

Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Center. See Notice to Authors, Issue No. 1.

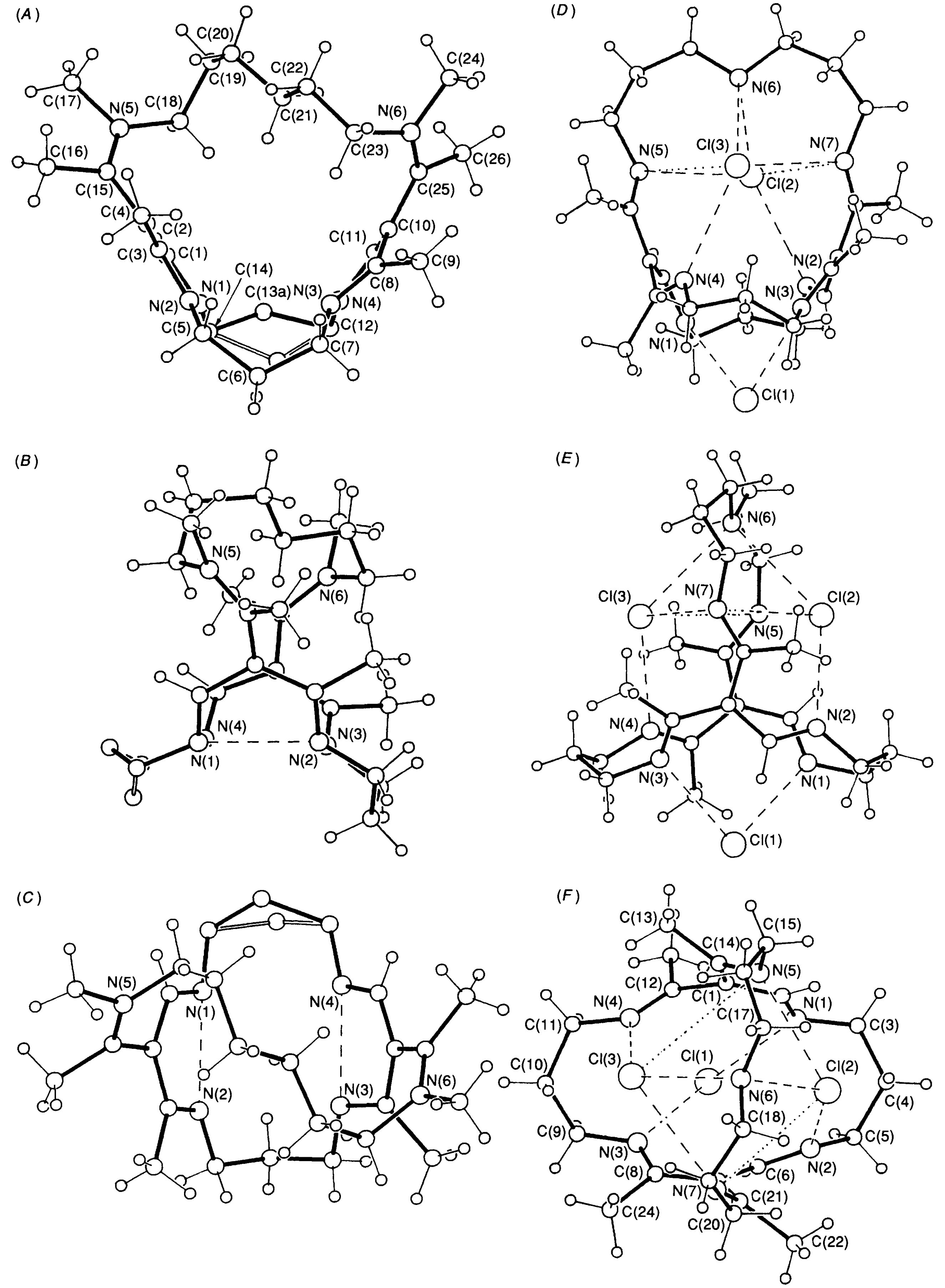

Fig. 1 Views of the cations of ligand salts **1** (*A–C*) and **2** (*D–F*). Dashed lines indicate probable hydrogen bonds, and dotted lines the other short N···Cl contacts in **2**. The positions of N–H protons are inferred from geometry at N and hydrogen bond contacts; in **1** one is presumed to be associated with N(1) or N(2), the other with N(3) or N(4); in **2** they are assigned to N(1), N(3), N(5), N(6) (additional to the proton present in the neutral ligand) and N(7).

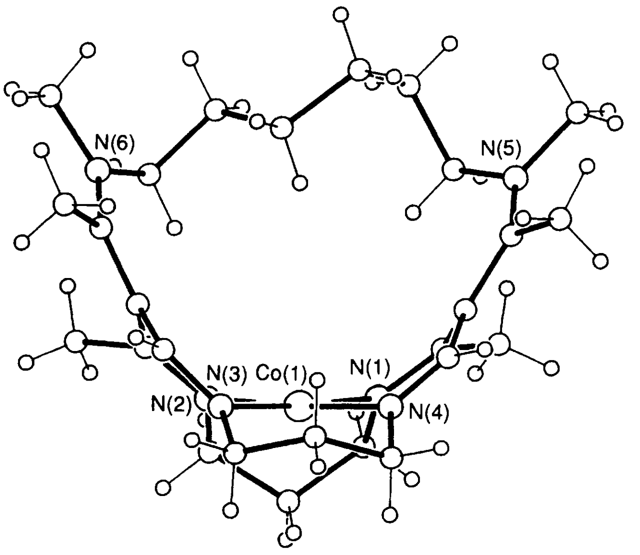

Fig. 2 View of the cation of the Co^{2+} complex **3** of ligand **1** (from ref. 4)

that of the metal complexes (Fig. 2). The cyclidene unit is saddle-shaped with the four nitrogen atoms coplanar. Although the $-[CH_2]_3-$ links are no longer incorporated into six-membered rings, they retain equivalent 'boat' and 'chair' conformations (the latter disordered as in several cyclidene complexes, *e.g.* **12** in ref. 4). The positions of the two protonated nitrogen atoms are not directly identifiable but two of the N$\cdots$N distances across the ring (close to 2.62 Å) are significantly shorter than the others (2.98 Å). This strongly suggests that the protons form hydrogen bonds between N(1)/N(2) and N(3)/N(4); their repulsion will be minimised if they are attached to diagonally opposed nitrogen atoms. Effectively, two protons have replaced M^{2+} within the 16-membered ring.

Structure **2** provides a complete contrast. Four of the added protons are attached to the nitrogen atoms of the 16-membered ring (the fifth being on the nitrogen at the centre of the bridge).§ Each cation is associated in an 'ion quartet' with three Cl$^-$ ions through a network of N–H$\cdots$Cl hydrogen bonds (lengths 3.07–3.25 Å); although such bonds are not frequently encountered, they are regularly found in appropriate systems (*e.g.* amine salts of $[CuCl_4]^{2-}$).[5] No N$\cdots$N hydrogen bonds cross the 16-membered ring, but instead the N–H$\cdots$Cl bonds cause the four nitrogen atoms in the ring to turn outwards, pointing alternately up and down. On one side of the ring N(1) and N(3) are linked to Cl(1), while on the other side, the ring containing the five remaining nitrogen atoms is capped by Cl(2) and Cl(3). This unit is sufficiently compact that the two N$\cdots$Cl contacts not containing H-atoms (3.42 and 3.77 Å) are only slightly longer than the N–H$\cdots$Cl bonds.

Considered in detail, the conformation of **1** leads to a rather steeper-sided cavity than found for the metal complexes. Unlike metal ions, the two protons do not enforce square-planar geometry on the ring. As a result, the lone pairs on nitrogen can be directed somewhat below the N$_4$-plane. Simultaneously, the larger N(1)/N(4) and N(2)/N(3) distances (2.98 Å compared to 2.7 Å in **3**) allow the sides of the cavity to become more vertical; the angle between the {NCCN} planes on each side [N(1),C(1),C(3),N(2)/N(3),C(8),C(11),N(4)] has the uniquely low value of 74.3° (98.8° in **3**; angle γ in ref. 4). This leads to the one major conformational difference between **1** and **3**. All normal [16]-cyclidene complexes have a *cis*-arrangement of the bridge ends [attached to C(15) and C(25) in Fig. 1(*A*)]. Such an arrangement in **1**, with the short N(5)$\cdots$N(6) distance, would be unsatisfactory for bridging by a $-[CH_2]_6-$ chain. As a result, the methyl groups on C(15) and C(25) are *trans*, with the chain taking a diagonal path across the cavity [Fig. 1(*C*)], and with C$\cdots$C distances across the cavity almost the same in **1** as in **3**.

The conclusion from the structures of **1** and **2** is that in the absence of a metal ion, these ligands can adopt the same conformation as that found in stable metal complexes, probably with little energy penalty. However, this favourable geometry for complexation occurs only under very specific conditions, requiring the formation of appropriate intramolecular links. The structure of **2** shows that under other conditions very different conformations can arise.

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§ Although the protons were not located directly, N(5) and N(7) both appear to be sp^2 hybridised, with 120° C–N–C angles. They each make one N–H$\cdots$Cl hydrogen bond in the presumed direction of their attached hydrogen atoms.

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