

A Giant-size Azamacrocycle: Synthesis and Crystal Structure of its Dinuclear Cadmium Complex

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The synthesis of a giant-size polyazamacrocycle 4,34-dimethyl-1,4,7,10,13,16,19,22,25,28,31,34,37,40,43,46,49,52,55,58-icosazapentacyclo[56.2.2.2.27.10.228.31.237.40]octahexacontane (L) is reported together with the crystal structure of its dinuclear cadmium(II) complex $[\text{Cd}_2(\text{H}_2\text{L})][\text{ClO}_4]_6 \cdot 5\text{H}_2\text{O}$.

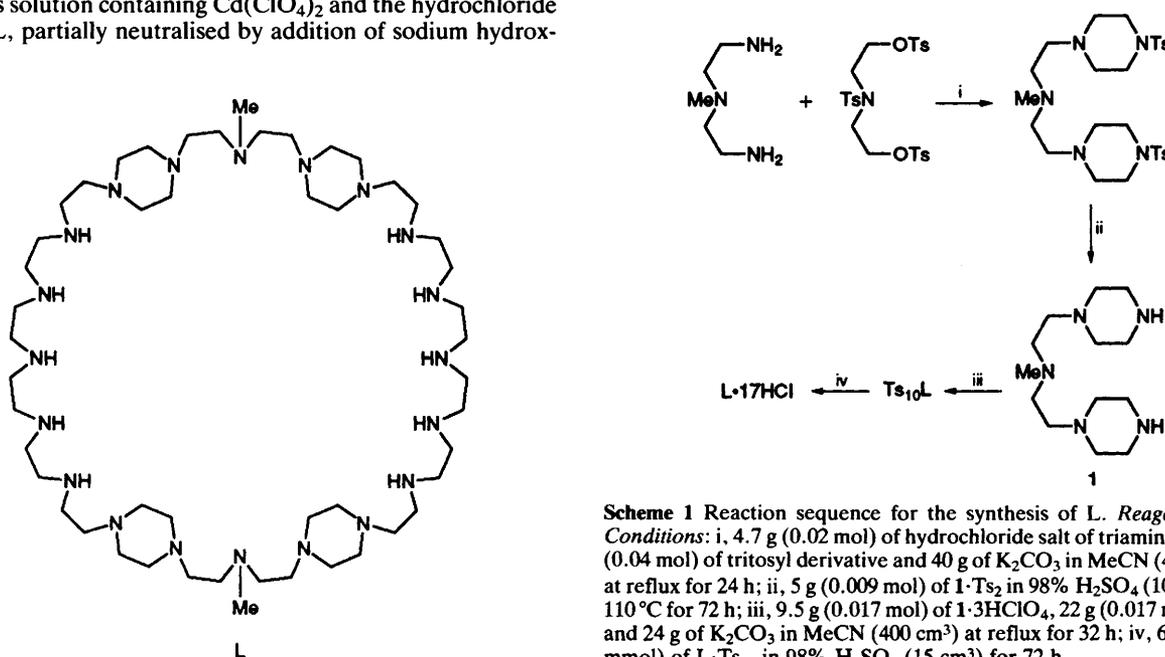
Large, up to 30–40 membered azamacrocycles, are a class of compound extensively studied in the last few years.^{1,2} Most of the polyazamacrocycles so far synthesised have been prepared by using the method of Richman and Atkins³ or its modifications. In this method the cyclization reaction takes place in DMF or MeCN in the presence of metal carbonates,⁴ 1:1 reactions usually occur also when reactants are characterized by large, saturated and flexible structures.⁵ More complex synthetic pathways are observed when aromatic moieties are present in the building blocks for the assembly of the macrocyclic frameworks.⁶ Until now very few reports have appeared on very large macrocyclic compounds, *i.e.* with an overall atomicity >40.⁷ In our laboratories great effort has been made to obtain macrocycles with large cavities.⁸ We report on the synthesis and preliminary ligating properties of a giant-size azamacropolycycle 4,34-dimethyl-1,4,7,10,13,16,19,22,25,28,31,34,37,40,43,46,49,52,55,58-icosazapentacyclo[56.2.2.2.27.10.228.31.37.40]hexacontane, L.

This partially reinforced macrocycle is obtained in quite high yield (29%) by reaction of bis(2-piperazinylethyl)amine **1** (Scheme 1) with *O,O'*-bis(methylsulfonyl)-3,6,9,12,15-pentakis(*p*-tolylsulfonyl)-3,6,9,12,15-pentazaheptadecane-1,17-diol **2**. The surprising result is the formation of a 60-membered ring rather than the expected 30-membered ring. The incorporation of a piperazine ring in **1** which increases its rigidity and therefore the probability of intramolecular reaction, is most likely responsible for the observed reaction pathway. The absence of any cation-template effect strengthens this hypothesis. Preliminary results indicate that the same synthetic pathway can produce, in good yield, other giant-size macrocycles by substitution of **2** by other reagents.

The structure of L has been confirmed by X-ray analysis of a crystal of its dinuclear cadmium(II) complex. Crystals, suitable for X-ray analysis were obtained by slow evaporation of an aqueous solution containing $\text{Cd}(\text{ClO}_4)_2$ and the hydrochloride salt of L, partially neutralised by addition of sodium hydroxide.

The molecular structure of $[\text{Cd}_2(\text{H}_2\text{L})][\text{ClO}_4]_6 \cdot 5\text{H}_2\text{O}$ consists of discrete dinuclear $[\text{Cd}_2(\text{H}_2\text{L})]^{6+}$ cations, perchlorate anions and lattice water molecules. The dinuclear complex cation is disposed around a crystallographic inversion centre with the two Cd^{II} ions in an identical environment (Fig. 1).[†] The symmetry-related metal ions are separated by 10.233(1) Å. Each cadmium ion is coordinated by five secondary nitrogen atoms and by one nitrogen atom belonging to a piperazinic ring, with Cd–N bond distances in the range 2.345(9)–2.438(9) Å. The coordination geometry of the cadmium can be described as distorted trigonal-prismatic in which the basal faces are defined by atoms N(1), N(7), N(8) and N(6), N(9), N(10). Two basal and three lateral edges of this prism are spanned by $\text{NCH}_2\text{CH}_2\text{N}$ chains. The present molecular structure can be compared with that of the dinuclear cadmium(II) complex of the thirty-membered macrocycle 1,4,7,10,13,16,19,22,25,28-decaazacyclotriacotane,⁹ in which the smaller and less hindered macrocycle gives rise to a dinuclear complex where the two metal ions are in different coordination environments and are separated by 5.75 Å. In this structure one of the two cadmium ions is octahedrally surrounded by two chloride ions and four adjacent nitrogen atoms of the ligand while the other is coordinated by the remaining six secondary nitrogen atoms connected by ethylenic chains and adopts a distorted trigonal-prismatic coordination, very similar to that found in $[\text{Cd}_2(\text{H}_2\text{L})]^{6+}$.

In the $[\text{Cd}_2(\text{H}_2\text{L})]^{6+}$ cation, the two metal ions engage in coordination with the most flexible parts of the macrocycle which assumes an overall Z-conformation [Fig. 1(b)]. The rigid piperazine rings produce an elongated macrocyclic cavity of approximate dimensions 4×16 Å. The acidic proton H(3) interacts, *via* hydrogen-bonding with the N(4) piperaza-



Scheme 1 Reaction sequence for the synthesis of L. *Reagents and Conditions:* i, 4.7 g (0.02 mol) of hydrochloride salt of triamine, 23.4 g (0.04 mol) of tritosyl derivative and 40 g of K_2CO_3 in MeCN (400 cm^3) at reflux for 24 h; ii, 5 g (0.009 mol) of **1**·Ts₂ in 98% H_2SO_4 (10 cm^3) at 110 °C for 72 h; iii, 9.5 g (0.017 mol) of **1**·3HClO₄, 22 g (0.017 mol) of **2** and 24 g of K_2CO_3 in MeCN (400 cm^3) at reflux for 32 h; iv, 6.3 g (2.5 mmol) of L·Ts₁₀ in 98% H_2SO_4 (15 cm^3) for 72 h.

zinc nitrogen and with O(13) belonging to a perchlorate anion [H(3)⋯N(4) 2.44(7), H(3)⋯O(13) 2.68(5) Å]. A considerable hydrogen-bond network involving hydrogens bound to the secondary nitrogen atoms [N(6), N(7), N(8), N(9)], water oxygens [O(1), O(2), O(3)] and some oxygen atoms of the perchlorate anions [O(33), O(13), O(11), O(21)], is also present in the unit cell.

A question which arises when dealing with such large flexible cyclic molecules, is whether chemical properties associated with its cyclic nature are retained. To begin to

answer to this question we have carried out potentiometric measurements in order to investigate the basicity behaviour of L. Preliminary results indicate that the basicity constants are grouped in two different sets, as typically found for saturated azamacrocycles.⁸

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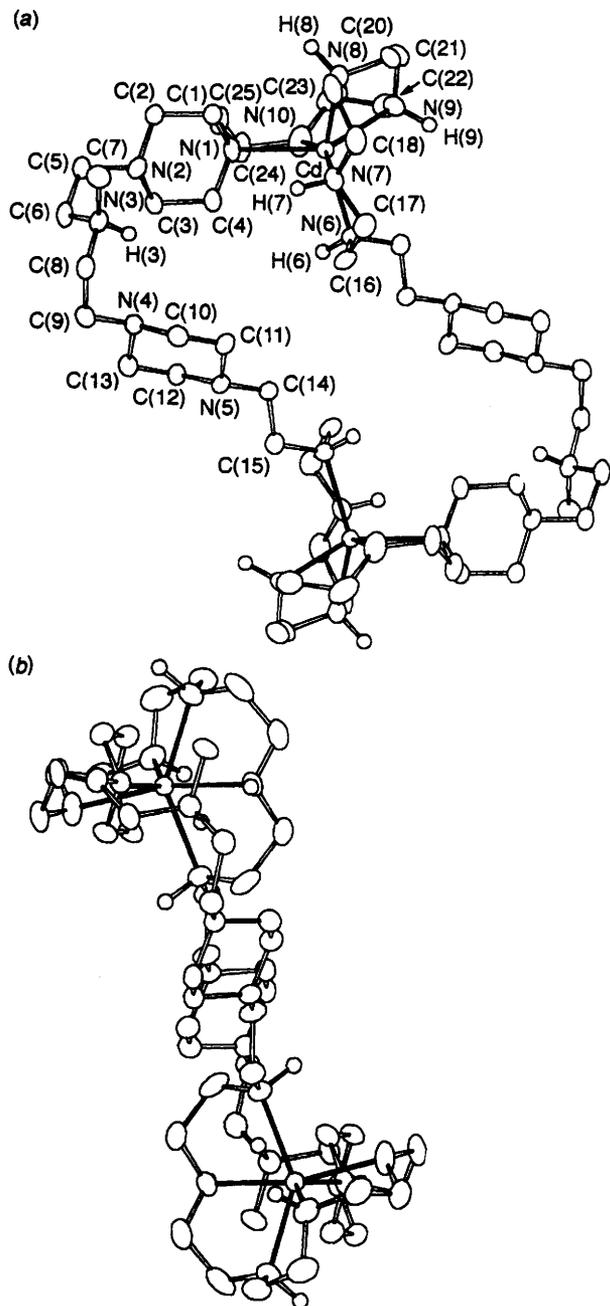


Fig. 1 Top (a) and side-view (b) of the centrosymmetric cation $[\text{Cd}_2(\text{H}_2\text{L})]^{6+}$. Only symmetry-independent atoms for the ORTEP-generated structure are labelled.

Footnote

† Crystal data: $\text{C}_{50}\text{H}_{124}\text{Cd}_2\text{Cl}_6\text{N}_{20}\text{O}_{29}$, $M_r = 1907.16$, monoclinic, space group $P2_1/c$, $a = 19.173(1)$, $b = 9.667(2)$, $c = 23.561(2)$ Å, $\beta = 109.81(1)^\circ$, $V = 4109(1)$ Å³, $Z = 2$. A total of 7351 reflections ($2 < 2\theta < 50^\circ$, Mo-K α radiation) were collected on an Enraf-Nonius CAD4 diffractometer. 3767 Reflections having $I > 3.0\sigma(I)$ were used in the structure solution and refinement. The structure was solved by the heavy-atom technique. The complex cation is disposed around a crystallographic inversion centre, thus the asymmetric unit contains only half the molecular formula. All the non-hydrogen atoms, except the water oxygen atoms, were refined anisotropically. The oxygen atom of a water molecule, affected by disorder, was refined with population parameter 0.5. A ΔF map revealed the acidic protons, which were introduced and isotropically refined, while the remaining hydrogen atoms of the ligand were introduced in calculated positions and their coordinates refined accordingly to those of the linked atoms, with an overall thermal parameter $U = 0.08$ Å². Two different sites were found for the ethylenic carbon atoms C(24) and C(25), each with occupancy of 0.5. Final refinement, for 494 parameters, converged at $R = 0.067$ and $R_w = 0.067$. 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.

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