Polyaza Macrobicyclic Cryptands: Synthesis, Crystal Structures of a Cyclophane Type Macrobicyclic Cryptand and of its Dinuclear Copper(I) Cryptate, and Anion Binding Features

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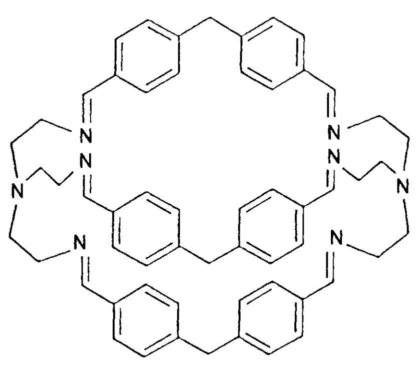
Multiple (amine + aldehyde) condensation gives the macrobicyclic cryptands (**1**) and (**3**) in high yield; (**1**) gave a dinuclear Cu^I cryptate and was reduced to a polyamine (**2**) which binds anions, when protonated.

Receptor molecules containing several subunits (polytopic) may complex several substrate species,[1] to form polynuclear metal complexes.[2] Thus, ditopic macropolycyclic ligands yield dinuclear cryptates of different types depending on the nature of the binding subunits incorporated in the structure.[2a] The bis-tren[3,4] ligand has been reported to form dinuclear cryptates of axial macrobicyclic type with a variety of metal ions[3,5] and to allow subsequent binding of substrate species, bridging the bound cations.[3,6]

We now report an efficient route to ditopic macrobicyclic polyamine ligands (**1**)—(**3**) *via* multiple (amine + aldehyde) condensation; we also describe the crystal structure of the



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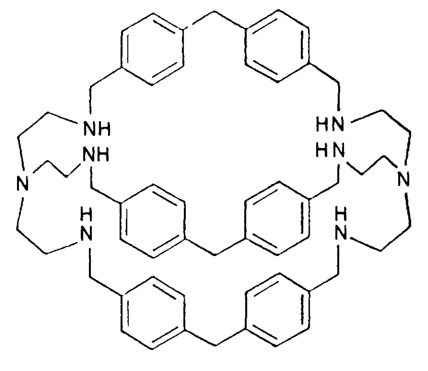

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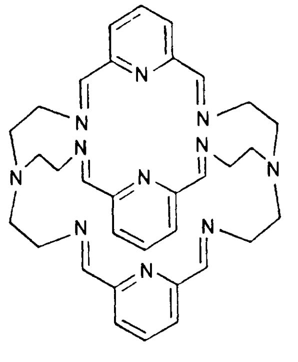

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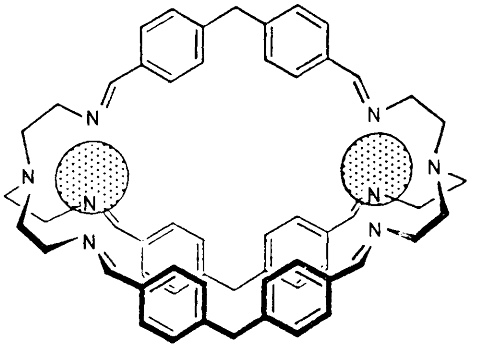

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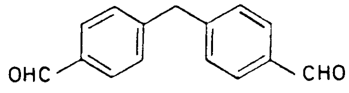

(5)

hexa-imine macrobicycle (**1**) and of its dinuclear Cu^{I} cryptate [Cu$_2$ ⊂ (**1**)]$^{2+}$, (**4**) as well as the binding properties of these new macrobicyclic ligands towards metal ions and anionic substrates.

A solution of dialdehyde (**5**)[7]† (1.71 mmol) in MeCN (20 ml) was added dropwise to a solution of tren [N(CH$_2$CH$_2$NH$_2$)$_3$] (1.14 mmol) in MeCN (25 ml) over a period of 15 min. A precipitate of almost pure macrobicycle hexaimine (**1**) was formed and was recrystallized from MeCN/CH$_2$Cl$_2$ (0.3 g, 60% yield; m.p. > 260 °C). Reduction of (**1**) (0.22 mmol) in tetrahydrofuran (THF) (10 ml) with LiAlH$_4$ (2.7 mmol) in THF (10 ml) (reflux for 1—3 h), gave the macrobicyclic polyamine (**2**), which was isolated as the hexahydrochloride and crystallized from aqueous methanol as white plates (0.18 g, 70%).

By analogy with the synthesis of compound (**1**), reaction of tren with pyridine-2,6-dicarbaldehyde gave the macrobicylic ligand (**3**) (crystallized from MeCN/THF; 80% yield; m.p. >260 °C.‡ The hexa-imine macrobicyclic cryptands (**1**) and (**3**) are sensitive to hydrolysis and are soluble in polar organic solvents. The octa-amine macrobicycle (**2**) is soluble in water when protonated.§

All three cryptands (**1**)—(**3**) may form metal ion complexes. Treatment of (**1**) in CH$_2$Cl$_2$ with [Cu(MeCN)$_4$]ClO$_4$ (2 equiv.) in MeCN gave the yellow dinuclear complex [(**1**), Cu$_2$] (ClO$_4$)$_2$ (94% yield, from MeCN/CH$_2$Cl$_2$; λ_{max} 352 nm, ε 12 500). The ^{1}H n.m.r. spectrum of the complex is markedly different from that of the ligand (**1**), the methylene, imino, and two aromatic protons being shifted downfield and the CH$_2$CH$_2$ signals upfield on complexation. Addition of AgPF$_6$ (2 equiv.) to (**1**) in MeCN/THF gave the colourless dinuclear complex [(**1**), Ag$_2$](PF$_6$)$_2$ (80% yield; λ_{max} 252 nm, ε 84 600).

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† Dialdehyde (**5**) was obtained *via* a Sommelet reaction (see S. J. Angyal, *Org. Reactions*, 1954, **7**, 197), by treating the bis-bromomethyl analogue of (**5**) with hexamethylenetetramine.

‡ Macrocycles have also been obtained from (**5**) by similar condensations.[8] For an example of polycondensation giving a polycyclic structure see ref. 9. For macrocycles derived from pyridine-2,6-dicarbaldehyde in the presence of metal ions see for instance ref. 10. For large macrobicyclic cryptands see also ref. 11.

§ The new compounds (**1**)—(**3**) and their complexes (see below) had spectral (^{1}H n.m.r., ^{13}C n.m.r., mass) and microanalytical data in agreement with the assigned structures.

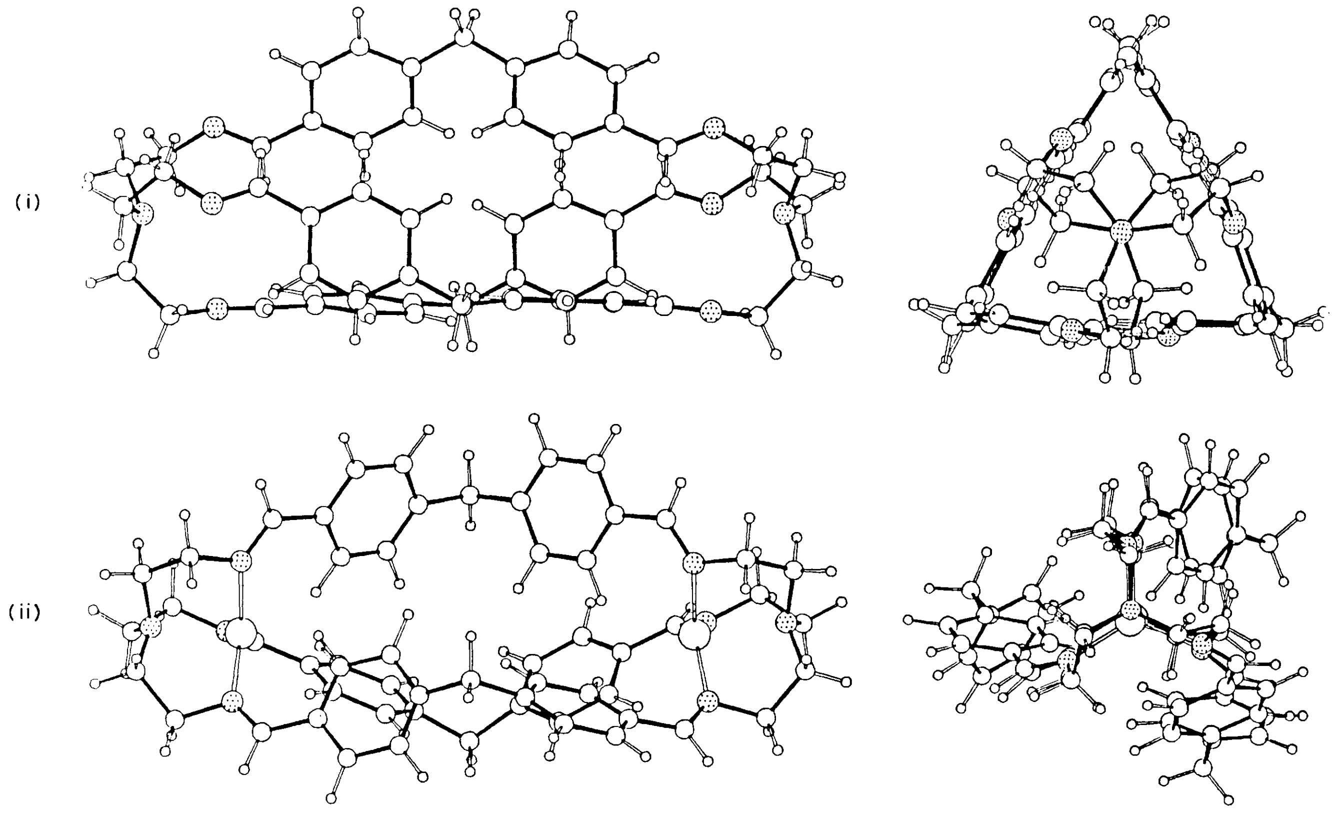

Figure 1. Structures of the macrobicyclic hexa-imine (**1**) (i) and of its dinuclear Cu^{I} cryptate [Cu$_2$ $\subset$ (**1**)]$^{2+}$ (ii), viewed from the side (left) and along the bridgehead N,N axis (right).

Treatment of macrobicycle (**3**) with Cu(MeCN)$_4$ClO$_4$ (2 equiv.) in THF/MeCN under argon gave a deep red, oxygen-sensitive dinuclear complex [(**3**), Cu$_2$](ClO$_4$)$_2$ (65% yield; λmax 385 nm, ε 3240). Similarly, the light yellow [(**3**), Ag$_2$]-(PF$_6$)$_2$ complex was obtained with AgPF$_6$ (79% yield; λ_{max} 290 nm, ε 15 400).

The crystal structures of both the macrobicyclic ligand (**1**) and of its dinuclear Cu^{I} complex were determined.¶

The macrobicyclic hexa-imine (**1**) has an elongated ellipsoidal shape possessing a ternary symmetry axis through the bridgehead nitrogens (Figure 1, top). The copper(I) complex of (**1**) is a dinuclear macrobicyclic cryptate [Cu$_2$ $\subset$ (**1**)]$^{2+}$ of axial type[2a] in which two Cu^{I} ions are contained inside the molecular cavity, each bound by one of the tripodal (amine, tri-imine) subunits located at the poles of the ligand (Figure 1, bottom).

The length of the macrobicyclic cage (distance between the bridgehead nitrogens) is the same (15.5 Å) in the free ligand and in the cryptate. The distances between any two methylene bridges, while the same in the ligand (7.5 Å), are different in the complex (7.83, 7.58, and 6.13 Å).

The complexation induces drastic changes in the conformation of the macrobicycle: the bridgehead N–C bonds are staggered in the free ligand, but are eclipsed in the dicopper complex. The approximate symmetry is D_3 (one ternary axis, with three 2-fold axes perpendicular to it and passing through the methylene bridges) for the free ligand, but the cryptate loses its ternary axis while exhibiting an approximate mirror plane. The cations attract the imino-nitrogens so that their average N–N distance, 4.4 Å in the free macrobicycle, decreases to 3.4 Å in the complex.

The two tetraco-ordinated Cu^{I} cations are situated at each end of the macrobicycle 11.07 Å apart. The co-ordination polyhedron has an unusual shape with the copper cation lying 0.2 Å *outside* the tetrahedron formed by the four nitrogens, towards the centre of the cavity. The macrobicyclic structure of ovoid shape defines three 'windows,' 2 large ones and a smaller one (see the CH$_2$, CH$_2$ distances given above), leading into a rather accessible cavity between the two copper ions. The N–Cu$_A$–Cu$_B$–N axis is bent (N–Cu$_A$–Cu$_B$ 174°, Cu$_A$–Cu$_B$–N 172°).

Binding of anionic substrates by the protonated macrobicyclic octa-amine (**2**) was detected by ^{1}H n.m.r. spectroscopy at 200 MHz. Addition of an aqueous solution of (**2**) to a

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¶ *Crystal data. Macrobicycle* (**1**), C$_{57}$H$_{60}$N$_8$·CHCl, from CHCl$_3$/MeCN; triclinic, space group $P\bar{1}$; a = 19.120(8), b = 15.550(6), c = 11.172(5) Å; α = 119.11(6), β = 98.95(5), γ = 101.60(5)°; U = 2716 Å^3; Z = 2. Data collection: Phillips PW 1100 diffractometer; scan speed: 0.05° s^{-1}, scan width 1.5° $\theta \leqslant 60°$; 7824 measured intensities, 3098 with $I \geqslant 3\sigma(I)$. Refinement conditions: hydrogens in calculated positions, anisotropic thermal parameters for all atoms except hydrogens; final R 7.0% (R_w 7.6%).

Copper(I) *complex of macrobicycle* (**1**), C$_{57}$H$_{60}$N$_8$Cu$_2$-(ClO$_4$)$_2$·2H$_2$O, crystallized by slow diffusion of ether into an acetonitrile solution of the complex; monoclinic, space group $C2/c$; a = 26.289(11), b = 12.122(5), c = 37.866(15) Å; β = 102.94(6)°; U = 11760 Å^3; Z = 8. Data collection: Philips PW 1100 diffractometer; scan speed: 0.12° s^{-1}, scan width: 1.3°, $\theta \leqslant 68°$; background measurement time equal to that of the intensities; 11 538 measured intensities, 5236 with $I \geqslant 3\sigma(I)$. Refinement conditions: two water molecules were localized, one with an occupation factor of 1, and the other split between two equivalently occupied positions; calculated hydrogen positions added to the refinement; all atoms with anisotropic thermal parameters except the hydrogens; final R = 8.6% (R_w = 8.9%). Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

solution of sodium succinate at pH 6.0 induced shifts in the signals of both the ligand and the substrate. Analysis of the titration data for $^-O_2CCH_2CH_2CO_2^-$ indicated formation of a 1:1 complex with a stability constant log K_s = 4.85 ± 0.2 (maximum low frequency shift of about 88 Hz). Binding of tartrate dianion also occurred. With terephthalate a similar analysis gave log $K_s \sim 4.0 \pm 0.3$, with probable participation of complexes of stoicheiometry different from 1:1. Thus, protonated (**2**) binds strongly molecular anions with, in view of the shielding shifts observed, inclusion into the macrobicyclic cavity, giving molecular cryptates (for molecular complexation see for instance ref. 12). The size of these difunctional substrates is compatible with interaction of each carboxylate group with a protonated $N(CH_2CH_2NH_2^+)_3$ subunit of the ditopic receptor molecule (**2**). A more extensive study of substrates of different shapes and dimensions will permit characterisation of the structural selectivity displayed by (**2**). Inclusion of substrates of appropriate size between the metal centres in the dinuclear cryptates (**4**) may also be envisaged,[2a,3,6] in particular when the bound metal ions are co-ordinatively unsaturated.

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