133. Molecular Structure of the Ethylenediammonium Complex of a Tetracarboxy-macrocyclic Receptor Molecule

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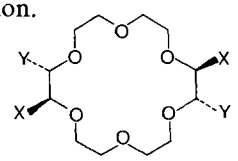
Summary

The crystal and molecular structure of the complex formed by the ionized bis-tartro-[18]-crown-6 receptor molecule **1** with the ethylenediammonium cation, is described. The macrocycle is roughly planar, the carboxy groups of each tartaric acid residue being in a diaxial relationship and extending above and below this plane. This conformation allows 'lateral' interactions with bound species to occur.

The substrate is sandwiched between two macrocycles, with one of its NH_3^+ heads anchored to the polyether core, and the other one in contact with the two carboxy groups of the neighboring molecule.

Introduction. – Since the discovery of the remarkable complexing properties of the macrocyclic polyethers towards cations [1], many compounds derived from the basic [18]-crown-6 structure **2** have been synthesized, which allow selective complexation of various substrates [2–7]. In the course of our investigations on the synthesis of new receptors for alkylammonium salts, we have prepared a tetracarboxylic [18]-crown-6 (**1**) incorporating two (*R, R*)-tartaric acid residues [3]. The affinity of this ligand for cations is at least three orders of magnitude higher than that of the unsubstituted macrocycle, forming very stable complexes even in aqueous solution [4]. The use of this basic unit (**1**) for the incorporation into macropolycyclic structures and for the design of molecular receptors, catalysts and carriers [3b] [4] [7] requires detailed knowledge of the geometry of the macrocycle and of its complexes with organic substrates. The present communication describes the crystal and molecular structure of the complex formed by this receptor molecule with the ethylenediammonium cation.



1 $X = Y = CO_2H$
2 $X = Y = H$
3 $X = CO_2^-$; $Y = CONHC_6H_5$

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Table 1. *Atomic coordinates* (with standard deviations) *and thermal parameters; for H-atoms $B = 5.0$ Å^2*

Atom	X	Y	Z
C(1)	0.2175(7)	0.1083(9)	0.0316(6)
H(11)	0.1599	0.1955	−0.0704
C(2)	0.1754(7)	0.2322(8)	0.1300(6)
H(21)	0.0414	0.2982	0.1030
O(3)	0.2552(6)	0.1112(7)	0.2622(5)
C(4)	0.2026(8)	0.2057(9)	0.3580(7)
H(41)	0.2174	0.3402	0.3573
H(42)	0.0712	0.2345	0.3290
C(5)	0.3076(8)	0.0804(9)	0.4992(7)
H(51)	0.2974	−0.0566	0.4993
H(52)	0.2625	0.1507	0.5693
O(6)	0.4807(6)	0.0492(7)	0.5412(5)
C(7)	0.5826(8)	−0.0509(9)	0.6814(6)
H(71)	0.5407	0.0380	0.7458
H(72)	0.5695	−0.1848	0.6961
C(8)	0.7650(8)	−0.0934(8)	0.7194(6)
H(81)	0.8405	−0.1671	0.8255
H(82)	0.7789	0.0397	0.7035
O(9)	0.8194(6)	−0.2140(7)	0.6349(5)
C(10)	0.9967(7)	−0.2979(8)	0.6745(6)
H(101)	1.0580	−0.2724	0.7743
C(11)	1.0388(7)	−0.2054(8)	0.5710(6)
H(111)	1.1730	−0.2590	0.5994
O(12)	0.9594(6)	−0.2507(7)	0.4445(5)
C(13)	1.0131(8)	−0.2135(9)	0.3432(7)
H(131)	0.9951	−0.0642	0.3268
H(132)	1.1454	−0.3059	0.3769
C(14)	0.9099(8)	−0.2534(9)	0.2129(7)
H(141)	0.9120	−0.3952	0.2330
H(142)	0.9621	−0.2476	0.1404
O(15)	0.7398(7)	−0.1123(8)	0.1581(6)
C(16)	0.6314(9)	−0.1577(11)	0.0399(7)
H(161)	0.6835	−0.1773	−0.0342
H(162)	0.6212	−0.2883	0.0706
C(17)	0.4586(9)	0.0084(11)	−0.0218(7)
H(171)	0.3750	−0.0203	−0.1112
H(172)	0.4689	0.1401	−0.0501
O(18)	0.3952(7)	0.0261(8)	0.0784(6)
C(19)	0.1455(8)	−0.0436(9)	0.0207(6)
O(20)	0.0 (0)	0.0 (0)	0.0 (0)
O(21)	0.2522(8)	−0.2168(8)	0.0324(7)
C(22)	0.2345(8)	0.3954(9)	0.1236(7)
O(23)	0.1446(8)	0.5258(8)	0.0166(6)
O(24)	0.3633(8)	0.3867(10)	0.2172(6)
C(25)	0.9739(8)	0.0131(8)	0.5640(7)
O(26)	0.8500(7)	0.1252(7)	0.4641(6)
O(27)	1.0575(7)	0.0584(7)	0.6715(6)
C(28)	1.0613(7)	−0.5167(8)	0.6818(6)
O(29)	1.2095(7)	−0.6096(7)	0.7057(6)
O(30)	0.9530(7)	−0.5885(7)	0.6649(6)
N(31)	0.6056(7)	−0.1370(8)	0.3520(6)
H(311)	0.6500	−0.1002	0.2802
H(312)	0.6855	−0.1317	0.4532

Table 1 (cont.)

Atom	X	Y	Z	
H(313)	0.4770	−0.0352	0.3228	
C(32)	0.6115(8)	−0.3341(9)	0.3515(6)	
H(321)	0.5316	−0.3393	0.2502	
H(322)	0.7401	−0.4359	0.3806	
C(33)	0.5495(8)	−0.3856(9)	0.4518(7)	
H(331)	0.4177	−0.2905	0.4172	
H(332)	0.6226	−0.3668	0.5508	
N(34)	0.5670(7)	−0.5873(8)	0.4640(6)	
H(341)	0.5215	−0.6187	0.5364	
H(342)	0.6986	−0.6835	0.4991	
H(343)	0.4937	−0.6072	0.3655	
WA(1)	0.4700(8)	−0.5472(9)	0.6758(7)	B= 5.09
WA(2)	0.6534(11)	−0.6624(13)	0.1586(9)	B= 8.79
WA(3)	0.7267(13)	−0.6421(15)	−0.0663(10)	B= 10.65

Crystal data and intensity measurements. – Crystals of composition $C_{16}H_{24}O_{14} \cdot C_2N_2H_8 \cdot 3\,H_2O$ were grown by slow cooling of a concentrated aqueous solution containing equimolar quantities of the tetracarboxylic acid **1** [3b] and ethylene diamine. They belong to the triclinic space group P_1 with lattice parameters $a = 9.372(3)$, $b = 7.604(3)$, $c = 10.847(3)$ Å, $\alpha = 87.06(3)$, $\beta = 112.47(3)$, $\gamma = 68.96(3)°$, $U = 650.6$ Å^3, $D_{calc} = 1.415$ for $Z = 1$, $\mu = 54$ m^{-1} for MoK_α radiation ($\lambda = 0.71069$ Å).

Intensities were measured up to $\theta = 28°$ with the help of a computer (PDP8)-controlled four-circle diffractometer (*Hilger and Watts* Y290) operating in the $\omega/2\theta$ scan mode and using Zr-filtered Mo-radiation.

Structure determination. – The structure was solved with the help of MULTAN-78 [8]. Refinement was performed by full-matrix least-squares using 2507 reflections with $I > 3\sigma$ (I). The non-hydrogen atoms were refined with anisotropic temperature factors leading to convergence at an R-index of 0.052. H-Atoms of the methylene and ammonium groups were included at calculated positions. No convincing evidence for the positions of the remaining H-atoms was found. During the refinement, three difference-map peaks were interpreted as O-atoms of water molecules and refined with isotropic temperature factors. Refinement and the associated calculations were carried out with the SHELX [9] programming system. Atomic positional parameters are listed in *Table 1*, bond lengths and angles in *Table 2*, while *Table 3* gives selected torsion angles, intermolecular contacts and the least-squares plane through the ether O-atoms.

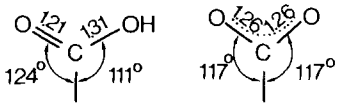
Description of the structure. – The structure of the complex is represented in *Figure 1* with the labelling used in the analysis. *Figure 2* gives a picture of the molecular packing. Since the compound was synthesized from (+)-(*R*, *R*)-tartaric acid without racemisation [3b], no attempt was made to establish its absolute configuration.

The asymmetric unit contains the expected [4] one-to-one substrate/receptor complex. The $^+H_3N{-}CH_2{-}CH_2{-}NH_3^+$ dication is in the *trans* conformation with normal bond lengths and angles [10] *(Table 2)*. Since the crystals were prepared by mixing equimolecular quantities of a tetraacid and a diamine, two acidic protons are used to form the substrate dication, so that the ligand in the complex must contain two carboxylate groups. A closer analysis of the structure is thus required in order to obtain information about the nature of the four carboxy residues and the location of the acidic protons.

Table 2. *Bond lengths* (in Å) *and bond angles* (in degrees) *with standard deviation*

Atoms	Length	Atoms	Length
C(2)–C(1)	1.530(0.011)	C(14)–C(13)	1.496(0.013)
O(18)–C(1)	1.413(0.010)	O(15)–C(14)	1.424(0.010)
C(19)–C(1)	1.522(0.010)	C(16)–O(15)	1.448(0.012)
O(3)–C(2)	1.419(0.008)	C(17)–C(16)	1.511(0.013)
C(22)–C(2)	1.538(0.010)	O(18)–C(17)	1.415(0.010)
C(4)–O(3)	1.434(0.009)	O(20)–C(19)	1.206(0.011)
C(5)–C(4)	1.498(0.011)	O(21)–C(19)	1.300(0.010)
O(6)–C(5)	1.429(0.009)	O(23)–C(22)	1.255(0.010)
C(7)–O(6)	1.432(0.009)	O(24)–C(22)	1.222(0.011)
C(8)–C(7)	1.499(0.011)	O(26)–C(25)	1.217(0.010)
O(9)–C(8)	1.431(0.008)	O(27)–C(25)	1.277(0.010)
C(10)–O(9)	1.421(0.008)	O(29)–C(28)	1.224(0.009)
C(11)–C(10)	1.539(0.009)	O(30)–C(28)	1.276(0.009)
C(28)–C(10)	1.539(0.009)	C(32)–N(31)	1.481(0.010)
O(12)–C(11)	1.416(0.009)	C(33)–C(32)	1.509(0.011)
C(25)–C(11)	1.537(0.009)	N(34)–C(33)	1.476(0.010)
C(13)–O(12)	1.426(0.009)		
Atoms	**Angle**	**Atoms**	**Angle**
O(18)–C(1)–C(2)	107.9(0.6)	C(14)–C(13)–O(12)	108.8(0.6)
C(19)–C(1)–C(2)	110.7(0.6)	O(15)–C(14)–C(13)	109.4(0.6)
C(19)–C(1)–O(18)	112.4(0.6)	C(16)–O(15)–C(14)	111.2(0.6)
O(3)–C(2)–C(1)	108.3(0.6)	C(17)–C(16)–O(15)	108.2(0.8)
C(22)–C(2)–C(1)	107.7(0.6)	O(18)–C(17)–C(16)	107.5(0.7)
C(22)–C(2)–O(3)	113.4(0.6)	C(17)–O(18)–C(1)	117.3(0.6)
C(4)–O(3)–C(2)	113.0(0.5)	O(20)–C(19)–C(1)	120.9(0.7)
C(5)–C(4)–O(3)	110.4(0.6)	O(21)–C(19)–C(1)	114.3(0.7)
O(6)–C(5)–C(4)	109.6(0.6)	O(21)–C(19)–C(20)	124.9(0.7)
C(7)–O(6)–C(5)	111.6(0.5)	O(23)–C(22)–C(2)	114.9(0.7)
C(8)–C(7)–O(6)	110.3(0.6)	O(24)–C(22)–C(2)	119.4(0.7)
O(9)–C(8)–C(7)	108.5(0.6)	O(24)–C(22)–O(23)	125.6(0.8)
C(10)–O(9)–C(8)	115.7(0.5)	O(26)–C(25)–C(11)	120.4(0.7)
C(11)–C(10)–O(9)	110.2(0.5)	O(27)–C(25)–C(11)	113.8(0.6)
C(28)–C(10)–O(9)	110.9(0.5)	O(27)–C(25)–O(26)	125.8(0.7)
C(28)–C(10)–C(11)	108.6(0.5)	O(29)–C(28)–C(10)	119.5(0.6)
O(12)–C(11)–C(10)	106.7(0.5)	O(30)–C(28)–C(10)	115.8(0.6)
C(25)–C(11)–C(10)	108.4(0.6)	O(30)–C(28)–O(29)	124.8(0.6)
C(25)–C(11)–C(12)	112.7(0.6)	C(33)–C(32)–N(31)	109.5(0.6)
C(13)–O(12)–C(11)	114.8(0.6)	N(34)–C(33)–C(32)	111.6(0.6)

The geometrical features of carboxylic and carboxylate groups in tartaric acid and in its salts are well documented [11] [12] and are indicated on the two following schemes as mean values (in Å and degrees) from different structures:



The O(20)C(19)O(21) fragment *(Table 2)* may thus be identified unambiguously as a carboxylic acid group; furthermore the synperiplanar O(18)C(1)C(19)O(21) conformation allows hydrogen bond formation in a five-membered cyclic

Table 3. *Selected data of interest*

Atoms	Torsion angle (°)	Atoms	Distance (Å)	Angle (°)
C(1)–C(2)–O(3)–C(4)	– 170.7	N(31)–H(311)–O(15)	2.86	163
C(2)–O(3)–C(4)–C(5)	– 172.4	N(31)–H(312)–O(9)	2.84	158
O(3)–C(4)–C(5)–O(6)	62.7	N(31)–H(313)–O(3)	2.87	172
C(4)–C(5)–O(6)–C(7)	173.2			
C(5)–O(6)–C(7)–C(8)	176.1	N(31)–O(6)	2.92	-
O(6)–C(7)–C(8)–O(9)	– 60.9	N(31)–O(12)	2.84	-
C(7)–C(8)–O(9)–C(10)	– 168.6	N(31)–O(18)	2.76	-
C(8)–O(9)–C(10)–C(11)	– 109.8			
O(9)–C(10)–C(11)–O(12)	– 63.4	N(34)–H(342)–O(26)	2.77	146
C(10)–C(11)–O(12)–C(13)	– 167.1	N(34)–H(343)–O(24)	2.70	173
C(11)–O(12)–C(13)–C(14)	– 175.7			
O(12)–C(13)–C(14)–O(15)	68.8	O(21)–O(23)	2.49	-
C(13)–C(14)–O(15)–C(16)	– 173.8	O(27)–O(30)	2.49	-
C(14)–O(15)–C(16)–C(17)	– 173.8			
O(15)–C(16)–C(17)–O(18)	– 60.9	$H_2O(1)$ O(29)	2.78	
C(16)–C(17)–O(18)–C(1)	– 153.5	$H_2O(1)$ N(34)	2.77	
C(17)–O(18)–C(1)–C(2)	– 143.0	$H_2O(1)$ $H_2O(3)$	2.75	
O(18)–C(1)–C(2)–O(3)	– 60.3	$H_2O(2)$ O(24)	2.92	
O(9)–C(10)–C(28)–O(29)	175.2	$H_2O(2)$ $H_2O(3)$	2.79	
O(12)–C(11)–C(25)–O(27)	– 172.0	$H_2O(3)$ O(20)	2.81	
O(18)–C(1)–C(19)–O(20)	170.0			
O(3)–O(2)–C(22)–O(23)	– 166.9			
N(31)–C(32)–C(33)–N(34)	– 175.0			

Best plane through O(3), O(6), O(9), O(12) and O(18).
Equation of this plane: $0.4365X + 0.8994Y - 0.0239Z = 1.9698$
Deviations from this plane: O(3): – 0.103; O(6): 0.330; O(9): – 0.285; O(12): 0.024; O(15): 0.195; O(18): – 0.161 and N(31): – 0.555A
Root mean square distance of the atoms from this plane is 0.210A

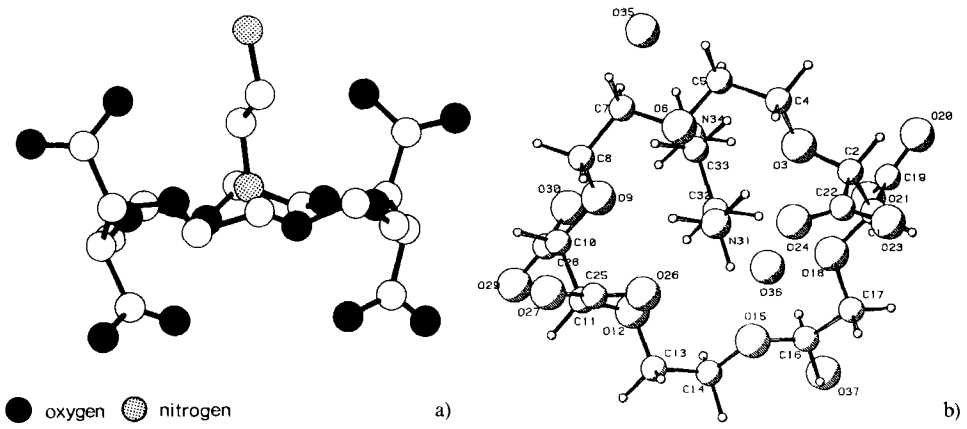


Fig. 1. a) *Side view of the molecular structure of the complex formed by the receptor molecule* **1** *with the* $^+H_3NCH_2CH_2NH_3^+$ *dication* (O-atoms are in black); b) *the same complex seen from the face opposite to the substrate.*

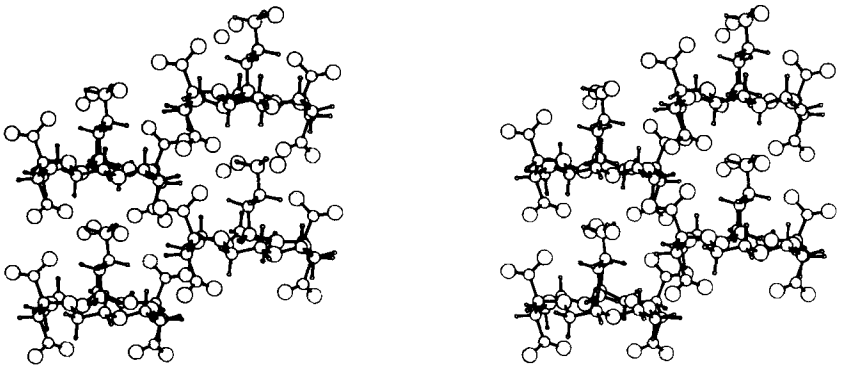


Fig. 2. *Stereoview of the molecular packing arrangement of the complexes in the crystal projected down the* c*-axis.*

O–C–C–O–H structure in a way similar to that found in secondary amide derivatives of **1** such as **3** [13]. It is much more difficult to identify the remaining three carboxy groups, because their geometries lie between those of CO_2H and CO_2^- units. The most likely CO_2H candidate is C(25)O(26)O(27) (see *Table 2*), but this assignment can only be tentative. The carboxy groups are involved in an intercomplex hydrogen bonding network with each other[2]) and with three water molecules *(Table 3)* which fill the space separating two adjacent macrocycles *(Figure 2).*

The substrate dication is sandwiched between two macrocycles, with one NH_3^+ site anchored to the 'top' of a ligand core. The other NH_3^+ group is in contact with the two carboxy groups at the 'bottom' of a neighbouring complex molecule *(Fig. 2),* thus contributing to the crystal packing forces along the *b* axis.

The macrocycle is in a roughly planar, relaxed conformation very similar to that found in other complexes of [18]-crown-6 [14–16] and of the non-symmetrical derivative **3** [13]. The C,C- and C,O-bond conformations are respectively *gauche* and *anti,* except for the *C*C–OC bonds (where *C denotes an asymmetric C-atom) *(Table 3).* The $g^+g^-g^+g^+g^-g^+$ C-framework has the approximate overall symmetry 2 (C_2). The conformation of the tartaric fragments in the macrocycle is the same as that found in crystalline tartaric acid itself [12]; the carboxy groups are in a diaxial relationship (torsion angles of 179.9 and 173.8°) allowing optimal interaction with the bound substrate to occur, and each O–*C–CO_2 fragment is nearly planar (deviations ranging from 6.3 to 15.3°). These results, together with molecular structure determinations on complexes of derivatives of **1** [13], show that such ligands display, at least when complexed, a remarkably constant conformation, a fact of much importance for the elaboration of more intricate receptor molecules based on this structural unit.

The substrate is anchored in the centre of one face and on top of the macrocycle by one of its NH_3^+ sites (0.56 Å away from the ether oxygen mean plane), within

[2]) The O(21)O(23) and O(27)O(30) distances (2.49 Å), are even shorter than those found in ammonium hydrogen tartrate (2.55 Å [11]).

hydrogen bonding distance to all ring O-atoms (2.76 to 2.92 Å, mean 2.85 Å). These distances are shorter than those determined in related complexes (for a review, see [16]), and are in line with the high stability of this complex [4]. The very strong electrostatic charge-charge interactions between the NH_3^+ and CO_2^- groups apparently pull the substrate deeper into the macrocyclic cavity, as may be judged from comparison with the NH_4^+ complex of [18]-crown-6 **2** itself, where the distance of the cation from the oxygen mean plane is appreciably larger (1.0 Å [15]).

In the complex, the macrocycle displays a cone like shape, the carboxy groups being further apart on the side where the substrate is bound (8.13 Å; 'open' face of the cone) than on the opposite face (6.17 Å) (see *Fig. 1*). Such a molecular shape may already preexist in the free tetracarboxy ligand. In the present complex several other factors may contribute to its stabilization: (i) stronger electrostatic interaction of the 'bottom' two carboxy groups with the bound NH_3^+ cation when these sites are drawn closer to the cationic centre; (ii) the carboxy groups on the same side as the substrate may be spread apart by steric repulsion with the bound molecule; (iii) intermolecular interaction with the terminal NH_3^+ group of the neighbouring complex, may pull together the 'bottom' carboxy groups of a given complex in the crystal packing environment. Effects (i) and (ii) may act in a cooperative fashion; the distortion resulting from one of them being transmitted to the opposite face of the macrocycle *via* the rotameric conformation along the *C, *C-bond. Thus, an increase in distance between the two carboxy groups on one side would result in a decrease of the distance between the two carboxy groups on the other side, in a sort of conformational 'reflex effect' [17]. In the structure of the Sr^{2+} complex of the non-symmetrically substituted *syn* macrocycle **3** derived from **1**, the two carboxylate groups are similarly closer together, whereas the $CONHC_6H_5$ residues are further apart [13]. The present structural features appear to indicate that the binding of a substrate molecule results in closing down one 'face' of the receptor molecule and opening up the other one, thus conferring *'toposelectivity'* to the complexation process, a property which may have significant implications for the design of ligands in which substrate binding is directed to a given location in the receptor molecule.

By extension, in 'face-discriminated' receptor units like **3** [13], a primary ammonium substrate $R-NH_3^+$ would bind to the face *opposite* to the axial carboxy groups and between the amide residues, thus allowing interactions and reactions to occur between the R group of the substrate and the functionalities of the lateral groups. Such toposelective binding appears indeed to be favoured in solution. Addition of a nicotinamide ammonium substrate to the bis-(L)-tryptophanato derivative of type **3** ($X=CO_2^-$; $Y=CONH(L)CH(CO_2^-)CH_2$-(3-indolyl)), following a procedure developed recently [18], leads to the appearance of an (indole)→(pyridinium) charge transfer band, indicating insertion of the substrate between the lateral amino-acid residues [19].

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