Syntheses and Crystal Structures of 'Encapsulated' Guanidinium Complexes of 27-Membered Macrocyclic Ligands

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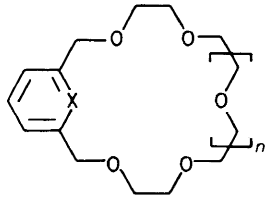
X-Ray structures of complexes of 2,6-pyrido-27-crown-9 and 1,3-xylyl-27-crown-8 with guanidinium perchlorate show a complementary hydrogen bonding relationship between host and guest; in the former complex the pyridyl nitrogen is used preferentially as a hydrogen binding site; the structures found are compared with those of the protonated 27-membered macrocycle and with 2,6-pyrido-24-crown-8.

Most of the work on crown ether complexation so far has been focussed on the interaction of crown ethers with monofunctional guests, *e.g.* metal or alkylammonium ions.[1] Complexes of *polyfunctional* organic guests which can use all their hydrogen atoms in hydrogen bonding between host and guest have been reported for benzo-27-crown-9, dibenzo-27-crown-9, and dibenzo-30-crown-10 with guanidinium cations.[2] In solution, such an 'encapsulated' complex has been postulated for a 27-crown-9 hexacarboxylate with guanidinium chloride.[3] Recently we have reported a similar complex of benzo-27-crown-9 and uronium perchlorate.[4]

The macrocyclic ligands in these complexes have exclusively oxygen atoms as hydrogen binding sites. Hitherto the effect of other acceptors for hydrogen bonds in this type of complex has not been investigated, although Cram and co-workers[5,6] have shown that, in complexes of smaller crown ethers with $Bu^tNH_3^+$ cations, the pyridyl nitrogen atom is a better hydrogen binding site than the ether oxygens.

As part of our work on proton transfer reactions in complexation of organic guest species by macrocyclic ligands, we are currently studying systematically the effect of the pyrido group as a hydrogen binding site in a series of crown ethers with a ring size of 15—33 atoms.



(**1a**—**g**) X = N
(**2**) X = CH
(**3e,f**) = (**1e,f**)·guanidium perchlorate
(**4**) = (**2**)·guanidium perchlorate
(**5**) = (**1e**)·picric acid

The pyrido macrocycles (**1a**—**g**) and the model system (**2**) were synthesized *via* the method used by Wagner and Rastetter[7] for the synthesis of (**1b**). Yields and melting points are summarized in Table 1.

Complex formation of the 18- to 33-membered rings was studied by equilibrating solutions of the crown ether (1 mmol) in $CDCl_3$ (2 ml) with a solution of $LiClO_4$ (2 mmol) and guanidinium sulphate (2 mmol) in water (2 ml). Subsequently

Table 1

Compound (ref.)	n	Yield (%)	M.p. (°C)	$GuClO_4$[a] extracted (equiv.)
(1a) (8)	0	5	oil	—[b]
(1b) (7)	1	55	37—39	0.35
(1c) (9)	2	59	oil	0.23
(1d) (9)	3	37	48—50	0.35
(1e)	4	72	oil	1.00
(1f)	5	60	oil	1.00
(1g)	6	55	oil	0.85
(2) (10)	4	65	oil	1.00

[a] $GuClO_4$ = Guanidinium perchlorate. In the case of the smaller rings some $LiClO_4$ was co-extracted: **(1b)** 0.04, **(1c)** 0.15, **(1d)** 0.02 equiv. For the larger macrocycles **(1e—g)** the amount of $LiClO_4$ extracted was negligible ($\leqslant$ 0.002 equiv). [b] Not investigated.

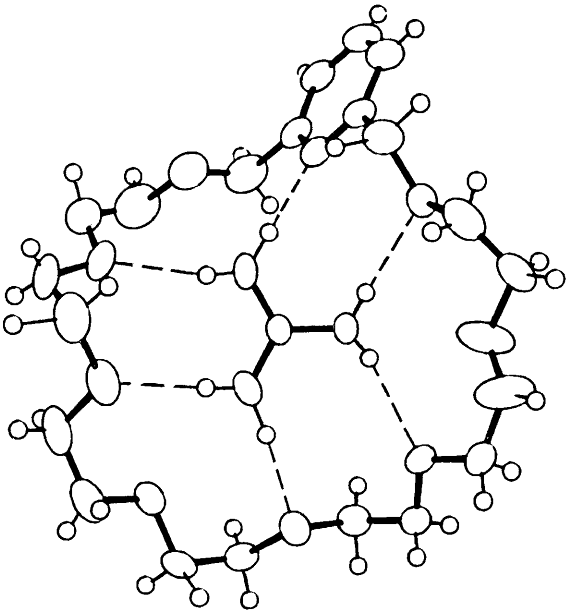


Figure 1. ORTEP[11] view of 2,6-pyrido-27-crown-9·guanidinium perchlorate (1 : 1) **(3e)**. *Crystal data:* $C_{22}H_{41}O_{12}N_4Cl$, triclinic, space group $P\bar{1}$, a = 14.186(6), b = 12.134(6), c = 9.229(3) Å, α = 105.26(5), β = 82.36(3), γ = 109.69(3)°, U = 1441 Å^3, Z = 2, D_c = 1.361 g cm^{-3}, μ(Mo-K_α) = 1.7 cm^{-1}. 5057 Reflections were measured (at 193 K) using the ω–2θ scan mode ($4 < \theta < 25°$) on a Philips PW 1100 diffractometer with graphite-monochromated Mo-K_α radiation. 4218 Reflections with $I > \sigma(I)$ (from counting statistics) were used for the solution by direct methods.[12] The structure is slightly disordered. All hydrogen atoms but one were located in a difference Fourier map. The structure was refined by least-squares methods[13] to a final weighted R-factor of 10.6% (513 parameters refined: scale factor, isotropic extinction parameter, positional parameters, anisotropic thermal parameters for non-H atoms, isotropic for H).

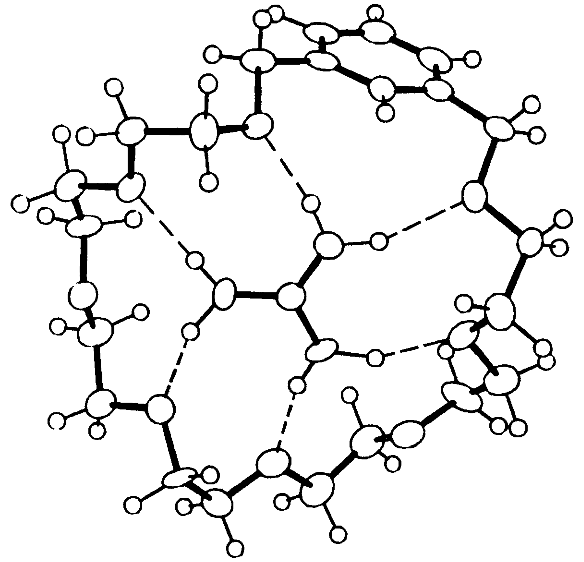


Figure 2. ORTEP[11] view of 1,3-xylyl-27-crown-8·guanidinium perchlorate (1 : 1) **(4)**. *Crystal data:* $C_{23}H_{42}O_{12}N_3Cl$, orthorhombic, space group $Pbcn$, a = 24.549(7), b = 12.630(5), c = 18.608(6) Å, U = 5769 Å^3, Z = 8, D_c = 1.358 g cm^{-3}, μ(Mo-K_α) = 1.7 cm^{-1}. 2666 Reflections were measured (at 144 K) as for **(3e)** ($4 < \theta < 20°$). 2386 Reflections with $I > \sigma(I)$ (from counting statistics) were used for the solution by direct methods.[12] All hydrogen atoms were located in a difference Fourier map. The structure was refined as before (see Figure 1 caption) to a final weighted R-factor of 3.5% (521 parameters refined).

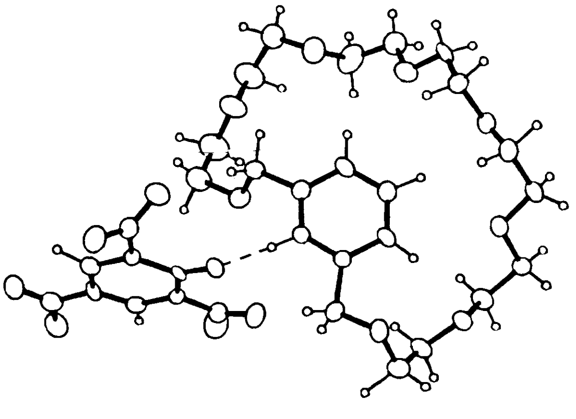


Figure 3. ORTEP[11] view of 2,6-pyrido-27-crown-9·picric acid (1 : 1) **(5)**. *Crystal data:* $C_{27}H_{38}O_{15}N_4$, monoclinic, space group $C2/c$, a = 30.760(23), b = 8.725(3), c = 23.450(12) Å, β = 97.43(4)°, U = 6241 Å^3, Z = 8, D_c = 1.406 g cm^{-3}, μ(Mo-K_α) = 1.1 cm^{-1}. 4187 Reflections were measured (at 145 K) as for **(3e)** ($4 > \theta > 22.5°$). 3410 Reflections with $I > \sigma(I)$ (from counting statistics) were used for the solution by direct methods.[12] All hydrogen atoms were located in a difference Fourier map. The structure was refined as before (see Figure 1 caption) to a final weighted R-factor of 5.3% (568 parameters refined).

the chloroform layer was dried and the amount of guanidinium perchlorate transferred to the organic phase was determined by ^1H n.m.r. spectroscopy. The results are summarized in Table 1.

Solid molecular 1 : 1 complexes of **(1e)**, **(1f)**, and **(2)** with guanidinium perchlorate were obtained after evaporation of the solvent. The products were recrystallized from ethanol–diethyl ether: **(3e)** (m.p. 112—115 °C), **(3f)** (m.p. 64—67 °C), and **(4)** (m.p. 74—75 °C)† respectively.

The crystal structures of the complexes of the 27-membered

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† Satisfactory elemental analyses were obtained.

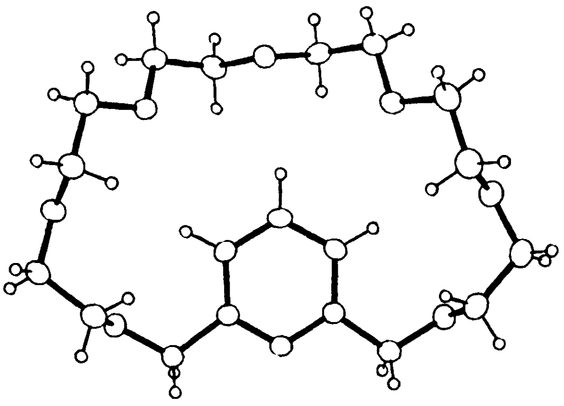

Figure 4. ORTEP[11] view of 2,6-pyrido-24-crown-8 (**1d**). *Crystal data:* $C_{19}H_{31}O_7N$, triclinic, space group $P\bar{1}$, $a = 11.274(1)$, $b = 10.141(1)$, $c = 9.137(1)$ Å, $\alpha = 101.41(2)$, $\beta = 98.90(2)$, $\gamma = 92.75(1)°$, $U = 1008$ Å^3, $Z = 2$, $D_c = 1.2727$ g cm^{-3}, $\mu(\text{Mo-}K_\alpha) = 0.9$ cm^{-1}. 3337 Reflections were measured (at 145 K) as for (**3e**) ($3 < \theta < 25°$). 3038 Reflections with $I > \sigma(I)$ (from counting statistics) were used for the solution by direct methods.[12] All hydrogen atoms were located in a difference Fourier map. The structure was refined as before (see Figure 1 caption) to a final weighted R-factor of 3.3% (369 parameters refined).

rings [*i.e.* (**3e**) and (**4**)] were determined by X-ray crystallography,‡ see Figures 1 and 2.

Corey–Pauling–Koltun molecular models show that the guanidinium cation can not be encapsulated by (**1b**—**d**); consequently it can only form a perpendicular type of complex.[14] This explains the poor extraction by the 18-, 21-, and 24-membered macrocycles, because a perpendicular type of complex will be highly hydrated, as can be seen from the ^{1}H n.m.r. spectra.

The 27-membered rings show a complementary hydrogen bonding relationship to the guanidinium cation. In complexes (**3e**) and (**4**) the guanidinium cation uses all six hydrogen atoms for hydrogen bonds between host and guest, yielding a highly structured encapsulated complex.

The difference between the two complexes is due to the preferential formation of a hydrogen bond with the pyridyl nitrogen in complex (**3e**). This indicates that the pyridyl nitrogen is a better hydrogen bond acceptor than the ether oxygens for the guanidinium cation. In complex (**3e**) the proton is *not* transferred from the guanidinium ion to the pyridyl nitrogen. This is obviously due to the greater basicity of guanidine.

In complex (**4**) the aromatic ring is almost perpendicular to the plane of the macrocyclic ring to avoid steric interaction with the guanidinium cation. The 30-membered ring (**1f**) also extracts guanidinium perchlorate quantitatively, whereas for the 33-membered ligand (**1g**) the increased difference in size between host and guest leads to a lowering of the efficiency of extraction.

In order to study the effect of the complexation reaction on the conformation of the pyrido macrocycles, the structure of (**3e**) was compared with the protonated 27-membered macrocycle (**5**) and the solid free 24-membered crown ether (**1d**) [(**1e**) could not be obtained in the crystalline form]. Reports on the structural data of free macrocyclic polyethers are limited.

The picrate salt (**5**) of (**1e**) was prepared by dissolving (**1e**) (1 mmol) and picric acid (1 mmol) in ethanol. The crystalline salt precipitated upon slow evaporation of the solvent at 25 °C, and was recrystallized from ethanol (m.p. 69—70 °C).†

Both in the protonated ligand (**5**) and in the free ligand (**1d**) the pyridyl unit fills the cavity of the macrocyclic ring, with the pyridyl nitrogen pointing outwards (see Figures 3 and 4).‡ Newkome *et al.*[15] have reported a similar effect in a spherical cryptand. This means that the cavity of the macrocyclic ligand is formed only upon complexation with an appropriate guest species. Dunitz and co-workers[16] have shown an analogous difference between 18-crown-6 and the corresponding complexes.

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‡ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.