

## Molecular Receptors. Synthesis and X-Ray Crystal Structure of an 18-Crown Ether Phenol Complex of 1,2-Diaminoethane

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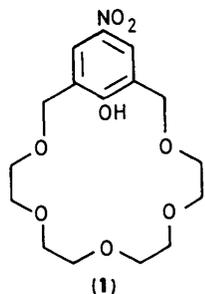
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Treatment of 18-crown-5 *p*-nitrophenol (1) with 1,2-diaminoethane produces a 1:2 cage-like complex (2) in which proton transfer has occurred to both amino groups. The crystal structure of (2) has been determined. Crystals of (2)·2EtOH are monoclinic, space group  $P2_1/n$  with two formula units in a cell of dimensions  $a = 11.903(2)$ ,  $b = 14.361(3)$ ,  $c = 13.014(2)$  Å,  $\beta = 95.98(2)^\circ$ . The structure was solved by direct methods and refined by full-matrix least-squares calculations;  $R = 0.058$  for 961 reflections with  $I > 2\sigma(I)$ . The diammonium cation lies about a crystallographic inversion centre and the asymmetric crystal unit contains half a dication, one crown-ether phenolate, and one ethanol. Reception of the  $\text{NH}_3^+$  moiety by the crown-ether phenolate after proton transfer involves  $\text{N-H} \cdots \text{O}$  hydrogen bonding to three ethereal oxygen atoms [ $\text{N} \cdots \text{O}$  2.952(8), 2.789(8), and 2.899(8) Å]; the phenolate oxygen atom does not participate in receptor binding *via* hydrogen bonding, but instead is linked to ethanol of solvation *via* an  $\text{O-H} \cdots \text{O}$  hydrogen bond [ $\text{O} \cdots \text{O}$  2.820(8) Å]. The structure is thus unlike that of the monoammonium salt of (1) in that the N-H moieties hydrogen bond to the macrocycle only and in an *endo* rather than an *exo* fashion.

The ability of macrocyclic crown ethers to form well defined stoichiometric complexes with a variety of cationic guests is now a well established phenomenon in receptor chemistry. There is also considerable interest in designing molecular receptors capable of receiving neutral guests,<sup>1</sup> *e.g.* amines, and we have been examining the possibility of binding molecules selectively by means of a proton transfer from host to guest thus increasing the binding forces between the two. In 1977<sup>2</sup> we described the first example of such a receptor with the synthesis of 18-crown-5 *p*-nitrophenol (21-hydroxy-18-nitro-2,5,8,11,14-



pentaoxa[15]metacyclophane) (1) in which the protonionisable group extends towards the macrocyclic cavity in an intra-annular relationship (Figure 1). When treated with ammonia, phenol (1) undergoes proton transfer to form an ammonium phenoxide in which the cation is solvated within the cavity with the phenoxide ion, which forms part of the macro ring, acting electrostatically as the primary binding site. In the literature since then a few examples of such proton-transfer receptor complexes have been reported for amines, *viz.* proton transfer from 2,2'-bis(carboxymethoxymethyl)-1,1'-binaphthyl crown-ethers to L-valine,<sup>3</sup> and a crystalline complex of 2-carboxy-1,3-xylyl-18-crown-5 and t-butylamine.<sup>4,5</sup> The formation of a 1:1 complex between 1,2-diaminoethane and a tetracarboxy macrocyclic receptor is associated with the transfer of two protons from the acid residues to the diamine guest.<sup>6</sup> Proton

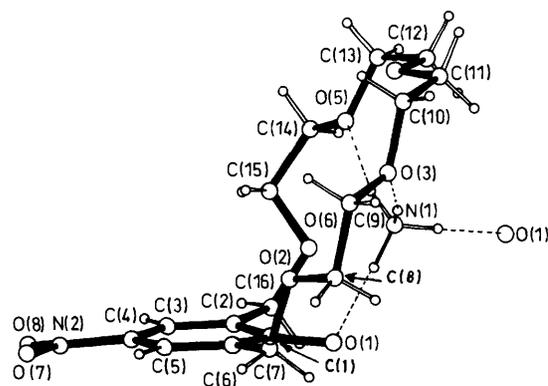


Figure 1. View of the structure of the ammonium salt of (1) showing the hydrogen-bonding scheme which holds the  $\text{NH}_4^+$  ion

transfer has also been demonstrated from a triazole ring to (*R*)-(1-naphthyl)ethylamine in complexation of the latter by a crown ether of which the former is a constituent part,<sup>7</sup> and Reinhoudt and his co-workers<sup>8</sup> have conducted a detailed study of the protonation and reception of urea by crown ethers with intra-annular carboxylate groups

*X*-Ray diffraction of the complex obtained from crown phenol (1) and ammonia revealed a high degree of synergism between the intra-annular phenolic group and the macrocycle. In particular, proton transfer has occurred and the resulting  $\text{NH}_4^+$  cation is centred in the cavity supported by three  $\text{N-H} \cdots \text{O}$  hydrogen bonds, one to the phenoxy oxygen atom (the shortest), and two to transannular ethereal oxygen atoms (Figure 1).

We have extended this type of investigation to difunctional guests and now describe the crystal and molecular structure of the complex (2) obtained from (1) and 1,2-diaminoethane. Sutherland has conducted a comprehensive study of factors controlling the complexation of diammonium salts by neutral

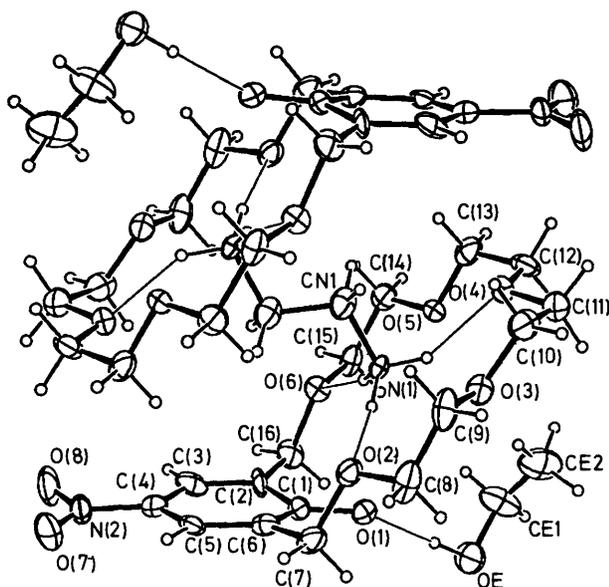


Figure 2. ORTEP<sup>14</sup> plot of the centrosymmetric complex (2)·2EtOH showing our numbering scheme and hydrogen bonds (thin lines)

hosts.<sup>9</sup> The design of receptors for neutral diamine guests may be of general interest in view of the biological significance of such systems. Treatment of (1) with 1,2-diaminoethane in methanol produced a yellow precipitate from which yellow crystals of (2), m.p. 164–167 °C, were obtained on crystallisation from ethanol. Our X-ray analysis showed that these were an ethanol solvate of composition (2)·2EtOH, which occurs in the unit cell as discrete centrosymmetric globular moieties, separated by normal van der Waals distances.

Crystals of (2)·2EtOH are monoclinic, space group  $P2_1/n$  with two formula units in a cell of dimensions  $a = 11.903(3)$ ,  $b = 14.361(3)$ ,  $c = 13.014(2)$  Å,  $\beta = 95.98(2)^\circ$ . The structure was solved by direct methods and refined by full-matrix least-squares calculations;  $R = 0.058$  for 961 reflections with  $I > 2\sigma(I)$ .

A view of (2)·2EtOH is shown in Figure 2 and molecular dimensions are in Table 1. Proton transfer has occurred to both amino groups and the diammonium cation lies about a crystallographic inversion centre which is at the mid-point of the  $-\text{CH}_2-\text{CH}_2-$  bond. The crown ether molecule has an essentially undistorted conformation with all ring C–O–C–C torsion angles close to 180°, and all O–C–C–O values close to *gauche*. All six N···O distances in the complex lie in the narrow range 2.789(8)–2.952(8) Å; fortunately, the assignment of N–H···O hydrogen bonding was made unequivocal by the clear location of the three hydrogen atoms on the ammonium nitrogen atom N(1) (Figure 3) which establishes that oxygens O(2), O(4), and O(6) participate in N–H···O hydrogen bonding. Clearly the most interesting, and unexpected, feature of the structure is the fact that the phenolate oxygen atom O(1) is *not* involved in receptor binding *via* hydrogen bonding, but is instead linked by an O–H···O hydrogen bond to ethanol of solvation [O···O 2.820(8) Å]. This is quite unlike the monoammonium salt of (1) (Figure 1) where the phenolate is involved in hydrogen bonding in two modes with the  $\text{NH}_4^+$  ion both intra- and inter-molecularly, the ethereal oxygens involved being O(3) and O(5) and complex formation being *exo*. In (2)·2EtOH, complex formation is *endo*, which results in the dication being encapsulated by two crown-ether ligands. The result is a complex with an overall globular appearance. The dihedral angle between the aromatic and

Table 1. Molecular dimensions

Interatomic distances (Å)

O(1)–C(1)	1.290(10)	C(5)–C(6)	1.376(12)
O(2)–C(7)	1.443(12)	C(6)–C(7)	1.457(13)
O(2)–C(8)	1.442(11)	C(8)–C(9)	1.463(15)
O(3)–C(9)	1.400(11)	C(10)–C(11)	1.495(14)
O(3)–C(10)	1.417(12)	C(12)–C(13)	1.488(14)
O(4)–C(11)	1.417(11)	C(14)–C(15)	1.492(14)
O(4)–C(12)	1.394(11)	CN(1)–CN(1) <sup>a</sup>	1.448(11)
O(5)–C(13)	1.376(12)	OE–CE(1)	1.331(15)
O(5)–C(14)	1.394(11)	CE(1)–CE(2)	1.26(2)
O(6)–C(15)	1.435(10)	OE···O(1) <sup>b</sup>	2.820(8)
O(6)–C(16)	1.417(11)	N(1)···O(1)	2.823(8)
O(7)–N(2)	1.240(11)	N(1)···O(2) <sup>b</sup>	2.952(8)
O(8)–N(2)	1.246(12)	N(1)···O(3)	2.882(9)
N(1)–CN(1)	1.471(11)	N(1)···O(4) <sup>b</sup>	2.789(8)
N(2)–C(4)	1.435(11)	N(1)···O(5)	2.908(8)
C(1)–C(2)	1.409(13)	N(1)···O(6) <sup>b</sup>	2.899(8)
C(1)–C(6)	1.425(12)	HN(1)···O(4) <sup>b</sup>	1.93
C(2)–C(3)	1.332(12)	HN(2)···O(2) <sup>b</sup>	2.02
C(2)–C(16)	1.491(13)	HN(3)···O(6) <sup>b</sup>	1.96
C(3)–C(4)	1.409(13)	HO···O(1) <sup>b</sup>	1.87
C(4)–C(5)	1.385(13)		

Bond angles (°)

C(7)–O(2)–C(8)	114.8(7)	C(3)–C(4)–C(5)	117.2(8)
C(9)–O(3)–C(10)	112.1(7)	C(4)–C(5)–C(6)	121.7(8)
C(11)–O(4)–C(12)	115.2(7)	C(1)–C(6)–C(5)	118.6(8)
C(13)–O(5)–C(14)	109.4(7)	C(1)–C(6)–C(7)	117.0(8)
C(15)–O(6)–C(16)	112.3(6)	C(5)–C(6)–C(7)	124.4(8)
O(7)–N(2)–O(8)	123.0(7)	O(2)–C(7)–C(6)	109.6(7)
O(7)–N(2)–C(4)	119.7(8)	O(2)–C(8)–C(9)	111.0(8)
O(8)–N(2)–C(4)	117.2(8)	O(3)–C(9)–C(8)	109.0(8)
O(1)–C(1)–C(2)	118.4(7)	O(3)–C(10)–C(11)	110.8(8)
O(1)–C(1)–C(6)	122.1(8)	O(4)–C(11)–C(10)	109.7(7)
C(2)–C(1)–C(6)	119.3(7)	O(4)–C(12)–C(13)	111.7(7)
C(1)–C(2)–C(3)	118.6(8)	O(5)–C(13)–C(12)	109.7(8)
C(1)–C(2)–C(16)	123.0(7)	O(5)–C(14)–C(15)	108.8(7)
C(3)–C(2)–C(16)	118.5(9)	O(6)–C(15)–C(14)	110.5(7)
C(2)–C(3)–C(4)	123.7(9)	O(6)–C(16)–C(2)	107.1(7)
N(2)–C(4)–C(3)	124.5(9)	N(1)–CN(1)–CN(1) <sup>a</sup>	112.0(8)
N(2)–C(4)–C(5)	118.4(8)	OE–CE(1)–CE(2)	125(1)

<sup>a</sup> This atom is obtained from the co-ordinate list by applying the transformation:  $-x, -y, -z$ . <sup>b</sup> Denotes a distance involving a hydrogen bond.

macrocyclic ring planes is reduced to 43° from the 58° found for the *exo* monoammonium complex; presumably the 15° reduction in interplanar angle allows more effective encapsulation of the dication. An essentially identical *endo* hydrogen-bonded complex has recently been reported<sup>10</sup> for the 1,3-xylyl-18-crown-5 macrocycle with the bulky *t*-butylammonium cation, where the same N–H···O hydrogen bonding scheme as in (2)·2EtOH occurs, and the dihedral angle between the mean crown and aromatic ring planes is 44°.

Although the accuracy is not high because of the paucity of data (associated with the loose packing and relatively large thermal parameters of the globular entity), the dimensions of the 18-crown-5 ring in (2)·2EtOH are in accord with values reported previously for (1),<sup>2</sup> with C–O 1.376–1.443(12), mean 1.414 Å, and C–C 1.457–1.495(14), mean 1.481 Å. The C–O(phenolate) distance is 1.290(10) Å [1.287(3) Å in (1)], and the dimensions of the nitrophenolate system follow the same trend as note in (1) with some suggestion of quinonoid character. The  $\text{C}_2\text{H}_5$  group of the ethanol of solvation is undergoing large librational motion and its dimensions [C–C 1.26(2), C–O 1.33(2) Å] reflect this. Complexation of the diammonium cation is thus associated with a major reorganisation in the host, the most striking

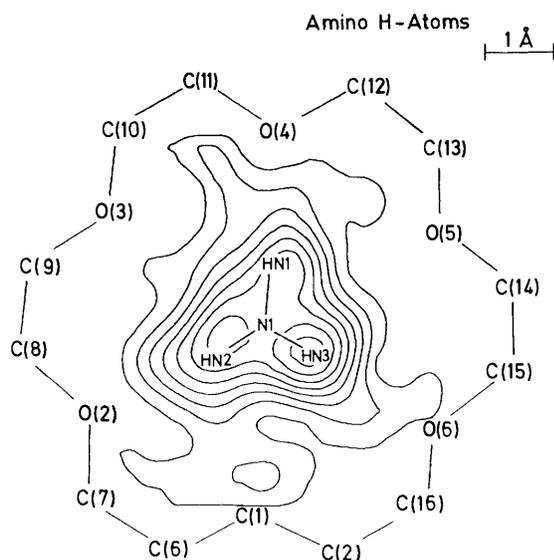


Figure 3. Section of a difference map computed to locate the  $\text{NH}_3^+$  atoms. Contour levels are of approximately  $0.05 \text{ e } \text{\AA}^{-3}$ . Also shown is the projection of the crown ether ring atoms

Table 2. Positional parameters and their estimated standard deviations

Atom	x	y	z
O(1)	0.313 5(5)	-0.125 4(4)	0.063 0(4)
O(2)	0.094 4(5)	-0.231 1(4)	0.022 5(4)
O(3)	0.028 6(5)	-0.189 6(4)	0.222 7(4)
O(4)	0.038 4(5)	-0.003 4(4)	0.297 6(4)
O(5)	0.191 1(5)	0.123 3(4)	0.222 8(4)
O(6)	0.270 4(5)	0.089 1(4)	0.028 4(4)
O(7)	0.178 7(7)	-0.155 9(6)	-0.408 7(5)
O(8)	0.246 7(6)	-0.014 5(6)	-0.399 9(5)
N(1)	0.109 8(5)	-0.039 2(5)	0.104 0(5)
N(2)	0.223 3(6)	-0.089 6(6)	-0.359 0(5)
C(1)	0.286 7(7)	-0.116 2(6)	-0.035 1(6)
C(2)	0.312 4(7)	-0.031 6(7)	-0.082 1(6)
C(3)	0.293 1(7)	-0.024 4(7)	-0.184 5(7)
C(4)	0.241 4(7)	-0.094 7(7)	-0.248 4(7)
C(5)	0.205 5(7)	-0.173 8(7)	-0.200 2(6)
C(6)	0.223 4(7)	-0.185 2(6)	-0.094 8(7)
C(7)	0.180 9(8)	-0.263 3(7)	-0.038 8(7)
C(8)	0.059 8(9)	-0.298 1(7)	0.095 5(7)
C(9)	-0.023 7(9)	-0.258 0(7)	0.157 5(7)
C(10)	-0.044 5(8)	-0.154 4(7)	0.292 7(8)
C(11)	0.012 8(8)	-0.080 1(7)	0.359 5(7)
C(12)	0.081 1(8)	0.074 7(7)	0.352 0(7)
C(13)	0.107 3(8)	0.151 3(6)	0.281 3(7)
C(14)	0.215 3(8)	0.195 4(6)	0.156 9(7)
C(15)	0.307 7(8)	0.164 8(6)	0.095 4(7)
C(16)	0.359 4(7)	0.050 7(7)	-0.022 4(7)
CN(1)	0.002 3(8)	-0.000 9(7)	0.055 8(6)
OE	0.480 7(6)	-0.115 3(5)	0.232 8(5)
CE(1)	0.449 0(11)	-0.048 5(9)	0.294 5(10)
CE(2)	0.372 3(11)	-0.055 8(8)	0.353 4(11)

change involving the non-complexation of the phenolate oxygen atom. The crown-ether ring which adopted an irregular conformation when complexed in an *exo* fashion with an

\* Supplementary data (see section 5.6.3 Instructions for Authors, in the January issue). Hydrogen-atom co-ordinates, thermal parameters, torsion angles, and mean plane data have been deposited at the Cambridge Crystallographic Data Centre.

ammonium ion, now adopts a regular 18-crown conformation on *endo*-complexation with the diammonium cation.

In earlier examples of complexation coupled with proton transfer, hydrogen bonding between the anionic and cationic sites has been a significant feature of the total binding. It is now clear that this is not a requirement for receptor activity. This discovery should assist in the design of new receptors for neutral guests in which proton transfer contributes to the binding energy.

## Experimental

**Crystal Data.**—(2)·2EtOH,  $\text{C}_{38}\text{H}_{66}\text{N}_4\text{O}_{18}$ ,  $M = 867.0$ . Monoclinic,  $a = 11.903(3)$ ,  $b = 14.36(3)$ ,  $c = 13.014(2)$  Å,  $\beta = 95.98(2)^\circ$ ,  $U = 2213(1)$  Å<sup>3</sup>,  $Z = 2$ ,  $D_c = 1.30$  g cm<sup>-3</sup>,  $F(000) = 932$ . Mo- $K_\alpha$  radiation  $\lambda = 0.71073$  Å,  $\mu(\text{Mo-}K_\alpha) = 1.0$  cm<sup>-1</sup>. Space group  $P2_1/n$  uniquely from the systematic absences ( $h0l$  absent if  $h + l = 2n + 1$ ,  $0kl$  absent if  $k = 2n + 1$ ). A yellow crystal of dimensions  $0.13 \times 0.18 \times 0.38$  mm was used for the analysis.

**Data Collection and Processing.**—Accurate cell data and crystal orientation matrix were determined on a CAD-4 diffractometer by a least-squares treatment of the setting angles of 24 reflections in the range  $10 < \theta < 12^\circ$ . Intensities of reflections with  $2 < 2\theta < 40^\circ$  were measured by the  $\omega/2\theta$  scan technique [ $\omega$  scan width  $(0.70 \times 0.35 \tan \theta)$ ] using graphite-monochromatized Mo- $K_\alpha$  radiation. There was no evidence of crystal decay during the course of the data collection. Data collection was stopped at  $2\theta = 40^\circ$  when it became apparent that there were very few reflections being measured as 'observed' beyond this angle. 2364 Reflections were measured, of which 2051 were unique ( $R$ -factor on averaging = 0.022); the 961 with  $I > 2\sigma(I)$  were labelled 'observed' and used in structure solution and refinement after correction for Lorentz and polarisation factors.

**Structure Analysis and Refinement.**—The structure was solved with the aid of Multan-82<sup>11</sup> which revealed all non-hydrogen atoms. Refinement was by full-matrix least-squares calculations, initially with isotropic and then with anisotropic thermal parameters. At an intermediate stage of the refinement, difference maps showed maxima in positions consistent with the expected locations of the hydrogen atoms; in the final rounds of calculations the hydrogen atoms were positioned on geometrical grounds (N-H, C-H 0.95 Å) and included (as riding atoms) in the structure factor calculations with an overall  $B(\text{iso})$  of 6.0 Å<sup>2</sup>. At convergence, the maximum shift/error ratio was 0.03 with  $R = 0.058$  and  $R_w = 0.070$ . Weights were derived from the counting statistics [ $w = 1/\sigma^2 F_o + 0.040(F_o)^2$ ] and scattering factors were taken from International Tables for X-Ray Crystallography.<sup>12</sup> All calculations were performed on our PDP11/73 computer using SDP-Plus.<sup>13</sup> Details of molecular geometry are in Table 1, and atomic co-ordinates are in Table 2.\*

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