A Comparison between the Solid State Structures and Solution Behaviour of Molecular Complexes formed between Primary Alkylammonium Salts and Chiral Crown Ethers incorporating 1,2:4,6-Diacetals of D-Mannitol

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The results of an X-ray crystallographic study of D-(1)-$Me_2CHNH_3ClO_4$ and D-(2)-$PhCH_2NH_3ClO_4$ reveal conformational features and a hydrogen bonding pattern in the 1:1 complexes which may be correlated with the complexation behaviour of the 20-crown-6 derivatives D-(1), D-(2), and (3) in solution towards a range of cationic guest species.

The complexing properties of the 20-crown-6 derivative D-(1) incorporating a 1,3:4,6-di-O-methylene-D-mannitol residue towards $RNH_3^+X^-$ salts (where R = Me, Me_2CH, Me_3C, $PhCH_2$, PhCHMe, $PhCHCO_2Me$, or $PhCH_2CHCO_2$-Me, and X = SCN or ClO_4) in $CDCl_3$ and CD_2Cl_2 solutions have been discussed by us[1] previously. In addition to the anticipated *primary* hydrogen bonding interaction between the $(OCH_2CH_2)_5O$ portion of D-(1) and the NH_3^+ centres in the RNH_3^+ ions of the 1:1 complexes, [1]H n.m.r. spectroscopic evidence was obtained for the existence of a much weaker *secondary* interaction between some RNH_3^+ ions and D-(1). This interaction was only observed (i) when the RNH_3^+ ion contained a phenyl group and (ii) when X = ClO_4 (*i.e.*, not when X = SCN). It has been attributed[1] to a

dipole-induced dipole interaction between one of the 1,3-dioxan rings in D-(1) and the phenyl ring in the RNH_3^+ ions. In particular, the dramatic and preferential shieldings of H_{1a} and H_B observed in the low-temperature [1]H n.m.r. spectra of some 1:1 complexes of the type D-(1)-$PhCHR^1$-$NH_3^+(ClO_4^-)$† provide compelling evidence for proposing

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† The conformational representation shown in the formula for D-(1)-$PhCHR^1NH_3^+(ClO_4^-)$ is one we have employed previously (ref. 1). However, it now has to be modified (ref. 2) with respect to the relative conformational dispositions of the two 1,3-dioxan rings on the basis of the crystal structure data reported herein. We can also be more precise regarding the nature of the hydrogen bonding pattern between the NH_3^+ centre and the macrocyclic oxygen atoms.

this additional stabilising and structuring interaction.[2] Hence, we were surprised to discover from the X-ray crystal structure (Figure 1) of the 1:1 complex formed between $PhCH_2NH_3{}^+ClO_4{}^-$ and the 20-crown-6 derivative‡ D-(2) incorporating a 1,3:4,6-di-O-benzylidene-D-mannitol residue that, in the solid state, the phenyl group in the $PhCH_2NH_3{}^+$ ion is oriented over the $(OCH_2CH_2)_5O$ loop of D-(2) and away from the 1,3-dioxan rings of the carbohydrate unit. Here, we discuss the stabilities and possible structures of 1:1 complexes formed in solution between $RNH_3{}^+$ ions and the 20-crown-6 derivatives D-(1) and D-(2) in the knowledge of the solid state structures of D-(1)-$Me_2CHNH_3ClO_4$ (Figure 2) and D-(2)-$PhCH_2NH_3ClO_4$ (Figure 1).§

X-Ray crystallography of D-(2)-$PhCH_2NH_3ClO_4$ reveals (Figure 1) that the $(OCH_2CH_2)_5O$ loop in D-(2) adopts a conformation in which the sequence of torsional angles (O–C, C–C, C–O) from O(1) to O(16) reads ag^+ a ag^- a ag^+ a ag^- a g^- g^- a with values for *anti* (*a*) bonds of *ca.* 175° and for *gauche* (*g*) bonds of *ca.* ± 65°. This pattern shows that the only major departures from a characteristic complexing conformation are about (i) the O(13)–C(14) bond with a value of −66° (*cf.* a normal value of *ca.* 175°) and (ii) the C(14)–C(15) bond where the helicity is reversed. This perturbation may be a consequence of having to accommodate the carbohydrate residue within the macrocycle. The two 1,3-dioxan rings of this residue are oriented approximately normal to each other (72° between their mean planes) with a torsional angle of 62° for O(21)–C(22)–C(23)–O(24). All the oxygen atoms in the $(OCH_2CH_2)_5O$ loop are directed inwards towards the $NH_3{}^+$ group which enters into two-point binding to D-(2) with strong hydrogen bonds formed between H_b and O(7) and H_a and O(13). However, there is a third very much weaker hydrogen bond from H_c to O(1) though the $H_c \ldots$ O(1) distance is rather long (2.36 Å) and the $N–H_c \ldots$ O angle (155°) appreciably smaller compared with
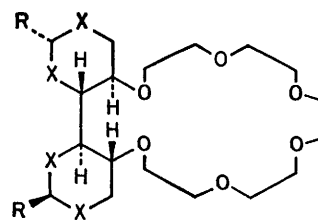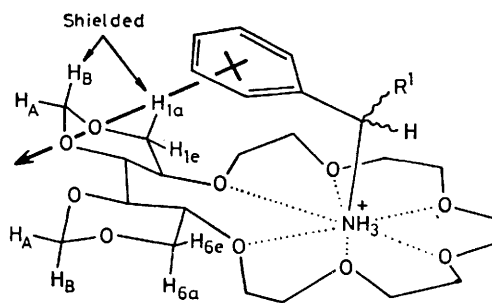
‡ D-(2), $[\alpha]_D$ −5.4° (*c* 1.0, $CHCl_3$), was obtained (55%) as an oil after chromatography (Et_2O) on SiO_2 of the products resulting from a reaction between 1,3:4,6-di-O-benzylidene-D-mannitol (N. Baggett and P. Stribblehill, *J. Chem. Soc., Perkin Trans.* 1, 1977, 1123), $Ts(OCH_2CH_2)_5OTs$ (Ts = tosyl), and NaH in Me_2SO at 60 °C for 20 h. This new compound gave a satisfactory elemental analysis, and mass ($M\cdot^+$, 560) and ^1H n.m.r. (ref. 2) spectral data.

§ Crystals of D-(2)-$PhCH_2NH_3ClO_4$ were obtained from dichloromethane–hexane. *Crystal data*: monoclinic, space group $P2_1$, a = 9.370(2), b = 20.479(5), c = 10.431(2) Å, β = 105.05(2)°, U = 1933 Å^3, Z = 2. Of the 2694 independent reflections ($\theta \leqslant 57°$) measured on a diffractometer using Cu-K_α radiation, 78 were classified as unobserved. The structure was solved by direct methods and refined anisotropically to give a current R = 0.047. The $NH_3{}^+$ hydrogen atoms were clearly resolved in a difference electron density map and the group was refined as a rigid body. The $ClO_4{}^-$ ion was not within interactive distance of the cationic complex.

Crystals of D-(1)-$Me_2CHNH_3ClO_4$ were obtained from dichloromethane–light petroleum (b.p. 60—80 °C). *Crystal data*: monoclinic, space group $P2_1$, a = 9.200(2), b = 9.580(2), c = 15.878(3) Å, β = 90.83(1)°, U = 1399 Å, Z = 2. Of the 2021 independent reflections ($\theta \leqslant 58°$) measured on a diffractometer using Cu-K_α radiation, 129 were classified as unobserved. The structure was solved by direct methods and refined anisotropically to give a current R = 0.055. The $NH_3{}^+$ hydrogen atoms were clearly resolved in a difference electron density map and the group was refined as a rigid body. The $ClO_4{}^-$ ion is disordered with two principal orientations of the oxygen atoms about the chlorine atom being identified. The ion was not within interactive distance of the cationic complex.

The atomic co-ordinates for these investigations are available on request from the Director of 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.

D-(1) X = O, R = H

D-(2) X = O, R = Ph

(3) X = CH_2, R = H

D-(1)-PhCHR^{1}NH$_3^+$ (ClO$_4^-$)

the other two which constitute almost linear hydrogen bonds. In view of the reduced basicity[3] of O(1), on account of the *anti* disposition of O(24) and O(26), it is hardly surprising that this oxygen atom is associated with the weakest hydrogen bond.¶ What is surprising is the disposition of the phenyl ring of the benzyl group relative to D-(2). Confronted with a choice of one of three rotational isomers about the N(41)–C(42) bond, the phenyl ring adopts a conformation in which the torsional angle H_a–N(41)–C(42)–C(43) is 56° and the phenyl group is staggered between H_a and H_b. By referring to this conformation as the H_a/H_b isomer, and to the other two possible stable staggered conformations for the phenyl ring as the H_b/H_c and H_a/H_c isomers, we can recognise the opportunity for an equilibrium $H_a/H_b \rightleftharpoons H_b/H_c \rightleftharpoons H_a/H_c$ involving these diastereoisomeric complexes in solution provided the hydrogen bonding pattern involving the $NH_3{}^+$ centre and the $(OCH_2CH_2)_5O$ loop is essentially the same in solution as that in the solid state. In the following communication,[2] we present evidence that indeed such an equilibrium exists in CD_2Cl_2 solution and that, as the temperature of the solution is lowered, the H_a/H_c conformation becomes increasingly highly populated.

The X-ray crystal structure of D-(1)-$Me_2CHNH_3ClO_4$ also reveals (Figure 2) that the two 1,3-dioxan rings are oriented approximately normal to each other (82° between their mean planes) with a torsional angle of 55° for O(21)–C(22)–C(23)–O(24). However, other features of this solid state structure differ quite considerably from that (Figure 1) of

¶ Bell (ref. 3) has drawn attention to the fact that O(1) and O(16) in D-(1) would be expected to suffer a two-thirds reduction in basicity relative to the corresponding oxygen atoms in (3) since 1,4-dioxan (β = 0.369) is known (M. Kamlet, A. Solomonovici, and R. W. Taft, *J. Am. Chem. Soc.*, 1979, **101**, 3734) to be *ca.* one third less basic than tetrahydropyran (β = 0.544) on the β-scale of hydrogen bond acceptor basicities.
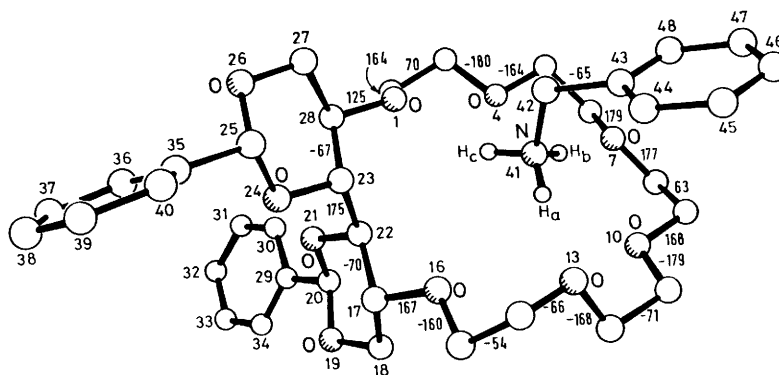
Figure 1. The solid state structure of D-(2)-PhCH$_2$NH$_3$$^+$. C–O bond lengths (Å) in the (OCH$_2$CH$_2$)$_5$O loop of D-(2) range from 1.404(7) for O(10)–C(11) to 1.447(6) for O(1)–C(28) and C–C lengths from 1.460(8) for C(8)–C(9) to 1.529(6) for C(17)–C(22). Bond angles (°) at O atoms range from 110.1(4) for O(7) to 115.5(4) for O(16). Torsional angles (°) (O–C–C–O and C–C–O–C) associated with the 20-membered ring are shown beside the relevant C–C and C–O bonds in the structure. Hydrogen bond distances, R[N · · · O](Å), R[H · · · O](Å), angles (θ$_N$ and θ$_H^0$) between COC planes and (a) NO vectors and (b) HO vectors, N–H · · · O angles (°) at H atoms: [N(41)–O(1)], 3.25, [H$_c$–O(1)], 2.36, (a) 30, (b) 37, H$_c$, 155; [N(41)–O(7)], 2.90, [H$_b$–O(7)], 1.95, (a) 25, (b) 29, H$_b$, 170; [N(41)–O(13)], 3.05, [H$_a$–O(13)], 2.10, (a) 37, (b) 40, H$_a$, 170. Torsional angle, H$_a$–N(41)–C(42)–C(43), 56°.
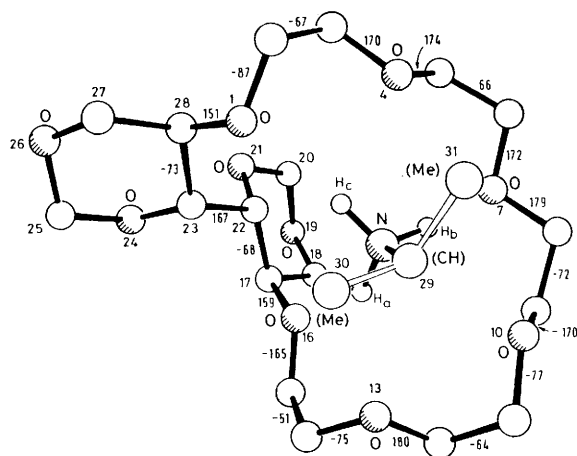

Figure 2. The solid state structure of D-(1)-Me$_2$CHNH$_3$$^+$. C–O bond lengths (Å) in the (OCH$_2$CH$_2$)$_5$O loop of D-(1) range from 1.401(7) for C(9)–O(10) to 1.457(9) for C(12)–O(13) and C–C lengths from 1.448(11) for C(11)–C(12) to 1.515(7) for C(17)–C(22). Bond angles (°) at O atoms range from 111.8(4) for O(4) to 116.5(4) for O(1). Torsional angles (°) (O–C–C–O and C–C–O–C) associated with the 20-membered ring are shown beside the relevant C–C and C–O bonds in the structure. Hydrogen bond distances, R[N · · · O](Å), R[H · · · O](Å), angles (θ$_N$ and θ$_H^0$) between COC planes and (a) NO vectors and (b) HO vectors, N–H · · · O angles (°) at H atoms: [N–O(1)], 3.11, [H$_c$–O(1)], 2.15, (a) 26, (b) 26, H$_c$, 175; [N–O(7)], 2.98 [H$_b$–O(7)], 2.04, (a) 39, (b) 43, H$_b$, 166; [N–O(13)], 2.97, [H$_a$–O(13)], 2.15, (a) 40, (b) 48, H$_a$, 142; [N–O(16)], 3.10, [H$_a$–O(16)], 2.30, (a) 3, (b) 3, H$_a$, 140. Torsional angle, H$_c$–N–C(29)–C(30), 58°.

Table 1. The association constants (K_a × 10^{-3}/dm^3 mol^{-1})^a for formation of 1 : 1 complexes between D-(1), D-(2), and (3) and some selected picrate salts in CDCl$_3$ at 25 °C.

Host/Guest	Li$^+$	Na$^+$	K$^+$	Rb$^+$	NH$_4$$^+$	MeNH$_3$$^+$	Bu^{t}NH$_3$$^+$
D-(1)	23	33	450	260	630	12	0.4
D-(2)	30	80	300	210	480	9.6	0.6
(3)^b	73	160	4800	1000	1500	52	4.4

^{a} The K_a values were determined by a u.v. spectroscopic method following extraction of aqueous picrate solutions of the guests with CDCl$_3$ solutions of the hosts (S. S. Moore, T. L. Tarnowski, M. Newcombe, and D. J. Cram, *J. Am. Chem. Soc.*, 1977, **99**, 6398). ^{b} Values from ref. 3.

D-(2)-PhCH$_2$NH$_3$ClO$_4$. The differences can be summarised as follows: (i) The sequence of the torsional angles (O–C, C–C, C–O) associated with the conformation of the (OCH$_2$-CH$_2$)$_5$O loop in D-(1) reads g^- g^- a ag^+ a ag^- a g^- g^- ag^- g^- a from O(1) to O(16). (ii) H$_a$ is involved in bifurcated hydrogen bonding to O(13) and O(16). In common with the direct hydrogen bond (length, 3.11 Å) formed by H$_c$ to O(1) that involving H$_a$ to O(16) is also a long (3.10 Å) hydrogen bond. The torsional relationship between the two 1,3-dioxan rings about the interannular bond in both D-(1)-Me$_2$CHNH$_3$ClO$_4$ and D-(2)-PhCH$_2$NH$_3$ClO$_4$ in the solid state is similar and

probably also corresponds to the conformational type preferred in solution.

The association constants (K_a) for 1 : 1 complex formation between D-(1), D-(2), and (3) and a range of picrate salts in CDCl$_3$ solution are listed in Table 1. These K_a values demonstrate that the cation binding abilities of D-(1) and D-(2) are similar but markedly less than those of the corresponding 1,1'-bicyclohexyl-20-crown-6 derivative (3) in which four oxygen atoms (X = O) in the 1,3-dioxan rings of D-(1) are replaced by methylene groups (X = CH$_2$). The lower basicities of O(1) and O(16) in D-(1) and D-(2) probably account (*cf.* ref. 3) in part for this observation. Indeed, if the hydrogen bonds involving these oxygen atoms are also weak in solution, then competition for hydrogen bonding to the anion would be expected to manifest itself. On the basis of this model we can explain our earlier observation[1] that only in the case of phenyl-containing RNH$_3$$^+$ cations of ClO$_4$ salts is a secondary interaction observed in solution at low temperatures.[2] In the case of the RNH$_3$SCN salts, the relatively good hydrogen bonding anion[4] probably competes very effectively with O(1) and O(16) for H$_c$ on the NH$_3$$^+$ centre, thus preventing an efficient stabilising interaction between the phenyl and 1,3-dioxan rings. Finally, the fact that the cation selectivities revealed by the K_a values in Table 1 are not nearly so high with D-(1) and D-(2) as they are with (3) may arise because of the destructuring of complexes in the O(1) and O(16) region of the macrocycles in D-(1) and D-(2) rather than as a result of major conformational differences about the interannular bonds between (i)

the 1,3-dioxan rings in D-(1) and D-(2) and (ii) the cyclo-hexyl rings in (3).

Received, 11th June 1982; Com. 668

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