Complexing Properties of a Bisdianhydro-D-mannitolo-30-crown-10 Derivative in the Solution and Solid States; X-Ray Crystal Structure

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Summary X-Ray crystallography has revealed that the chiral 30-crown-10 derivative DD-(2) adopts a basket-like conformation when it forms a 1:1:1 complex with (S)-[PhCHMeNH$_3$]$^+$ ClO$_4$$^-$ and H$_2$O in the solid state; ^{1}H n.m.r. spectroscopy suggests that 1:1:1 complexes of this type between (i) DD-(2), R^{1}NH$_3$$^+$ cations, and H$_2$O, and (ii) DD-(2), R^{1}NH$_3$$^+$ cations, and R^{2}NH$_2$ are also stable in solution.

In the preceding communication the chiral 30-crown-10 derivative DD-(2), prepared from 1,4:3,6-dianhydro-D-

DD – (2)
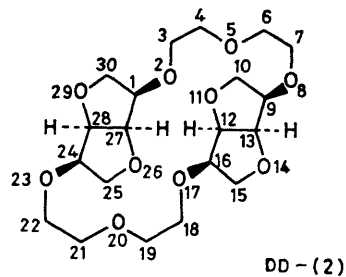
mannitol D-(1), was reported[1] to complex with organic, inorganic, and metal cations despite X-ray crystallographic and n.m.r. spectroscopic evidence that DD-(2) adopts a folded 'face-to-back' conformation in both the solid and solution states. Since this conformation lacks a hydrophilic cavity suitable for binding cationic species, DD-(2) must experience a major conformational change as a prelude to complexation. Indeed, an X-ray structural analysis† (Figure) reveals that DD-(2) unfolds and adopts the expected 'face-to-face' conformation with a hydrophilic interior and an essentially hydrophobic exterior when it forms a 1 : 1 : 1 complex with an (S)-PhCHMeNH₃⁺ cation and a water molecule. The crystals employed in this investigation were obtained from a mixed solvent system after EtOH and light petroleum (b.p. 60—80 °C) had been added to a CD₂Cl₂ solution containing equimolar quantities of DD-(2) and (S)-PhCHMeNH₃ClO₄. This CD₂Cl₂ solution had previously been employed (Table 1) in a low-temperature ¹H n.m.r. experiment. Whilst no special precautions (other than the use of plastic-stoppered tubes) were taken to exclude moisture during (i) the preparation of the n.m.r. sample and (ii) subsequent crystallisation, it was noted that even the CD₂Cl₂ (supplied by Fluorochem Ltd.) employed in the
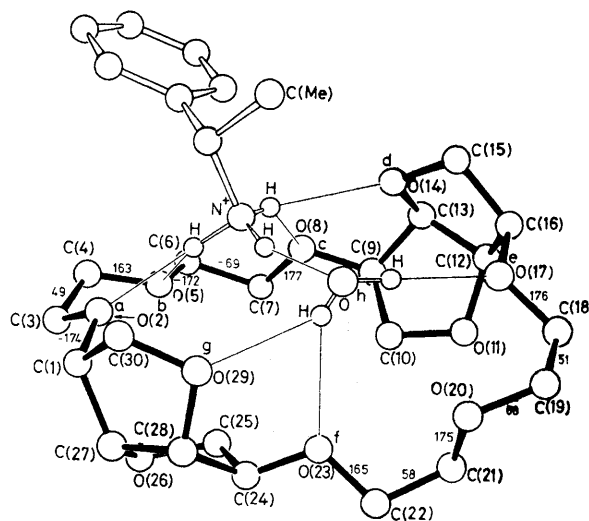

FIGURE. Structure of the 1 : 1 : 1 complex between DD-(2), (S)-PhCHMeNH₃ClO₄, and water. Torsion angles (°) for some selected bonds are shown.

TABLE 1. ¹H N.m.r. spectral data[a] and kinetic and thermodynamic parameters for selected 1 : 1 : 1 complexes formed by DD-(2) in CD₂Cl₂.

R¹ in R¹NH₃⁺ClO₄⁻	H₂O or R²NH₂	δ[b] (Host)	Chemical Shifts at 30 °C δ[c] [Guest(s)]	T_c[d]/°C (±3 °C)	Δν(°C)[b,d] (±2 Hz)	k_c[d]/s⁻¹	ΔG‡c[d] (±0·3 kcal mol⁻¹)
Me₃C	H₂O	4·58	1·44 (s, CMe₃); 6·88 (br. s, NH₃⁺, H₂O)	—[e]	—[e]	—[e]	—[e]
PhCH₂	H₂O	4·56	4·20,4·33(AB system, J_{AB} = 15 Hz, CH₂); 7·15 (br. s, NH₃⁺, H₂O); 7·46 (m, Ph)	—65	73(—80)	102	9·9
(R)-PhCHMe	H₂O	4·58	1·75 (d, J = 7 Hz, Me); 4·57 (q, J = 7 Hz, CH); 7·47 (m, Ph)	—50	91(—90)[f]	202	10·6
(S)-PhCHMe	H₂O	4·57	1·74 (d, J = 7 Hz, Me); 4·57 (q, J = 7 Hz, CH); 7·48 (m, Ph)	—50	88(—80)[f]	196	10·6
Me₃C	Me₃CNH₂[g,h]	4·57	1·28 (s, CMe₃); 4·67 (br. s, NH₃⁺, NH₂)	—101	66(—108)	147	8·2
PhCH₂	Me₃CNH₂[g,h,i]	4·55	1·26 (s, CMe₃); 4·05 (s, CH₂); 4·82 (br. s, NH₃⁺, NH₂); 7·38 (Ph)	—76	84(—95)	187	9·3
(S)-PhCHMe	Me₃CNH₂[g,h,j]	4·56	1·32 (s, CMe₃); 1·47 (d, J = 7 Hz, Me); 4·26 (q, J = 7 Hz, CH); 4·77 (br. s, NH₃⁺, NH₂); 7·33 (m, Ph)	—84	94(—100)[f]	209	8·9
(R)-PhCHMe	PhCH₂NH₂[g,i,j]	4·56	1·45 (d, J = 7 Hz, Me); 4·22 (q, J = 7 Hz, CH); 4·51 (br. s, NH₃⁺, NH₂); 7·38 (m, Ph)	—70	77(—80)[f]	171	9·6
(S)-PhCHMe	PhCH₂NH₂[g,i,j]	4·55	1·42 (d, J = 7 Hz, Me); 4·21 (q, J = 7 Hz, CH); 4·42 (br. s, NH₃⁺, NH₂); 7·37 (m, Ph)	—65	78(—80)[f]	173	9·9

[a] All spectra were recorded at 220 MHz on a Perkin Elmer R34 spectrometer with Me₄Si as 'lock' and internal standard. [b] The only host signal which is listed is the multiplet for H-12, -13, -27, and -28 in DD-(2). It is this signal which exhibits temperature dependence in the 1 : 1 : 1 complexes. [c] All guest signals which are not obscured by host signals are listed. [d] Abbreviations used are: T_c, coalescence temperature; Δν, frequency separation of H-12, -13, -27, and -28 with the temperature at which it was measured indicated in parentheses; k_c, exchange-rate constant at T_c calculated from the expression $k_c = \pi\Delta\nu/2^{\frac{1}{2}}$; ΔG‡c, free energy of activation calculated from the Eyring equation. [e] No spectral changes other than line broadening down to —90 °C. [f] Only two signals were observed at low temperatures although in principle up to four might be expected in these asymmetric 1 : 1 : 1 complexes. [g] The salts (R¹NH₃ClO₄) and the amine (R²NH₂) are listed as they were employed and do not necessarily reflect the nature of the two bound guest species in the 1 : 1 : 1 complexes. For example, since Me₃CNH₂ (pK_a 10·68) is more basic than PhCH₂NH₂ (pK_a 9·35), the proton will prefer to be associated with the former amine. [h] Me₃CNH₂ : δ (CD₂Cl₂) 1·09 (s, CMe₃) and 1·27 (br. s, NH₂). [i] PhCH₂NH₂ : δ (CD₂Cl₂) 1·48 (br. s, NH₂), 3·82 (s, CH₂), and 7·31 (m, Ph). [j] (R)- and (S)-PhCHMeNH₂ : δ (CD₂Cl₂) 1·33 (d, J = 7 Hz, Me), 1·60 (br. s, NH₂), 4·12 (q, J = 7 Hz, CH), and 7·30 (m, Ph).

† Crystal data for the 1 : 1 : 1 complex; C₂₀H₃₂O₁₀.C₈H₁₂ClNO₄.H₂O, orthorhombic, space group $P2_12_12_1$, a = 12·560(1), b = 22·048(2), c = 11·694(1) Å, U = 3238 Å³, Z = 4, D_c = 1·38 g cm⁻³. Of the 3119 independent reflections (θ < 65°) measured on a diffractometer using Cu-K_α radiation, 487 were classified as unobserved. The structure was solved by direct methods and refined to give R = 0·049. The ClO₄⁻ anion is ordered and quite separate from the cationic complex moiety in the crystal form. 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.

[1]H n.m.r. experiment contained H_2O. Although the chemical shift (δ 1·80) of this H_2O signal remained unchanged when DD-(2) was dissolved in the CD_2Cl_2, it shifted to a much lower field (Table 1) with the other exchangeable protons (NH_3^+) when an $R^1NH_3ClO_4$ salt was added, indicating that H_2O is involved in complexation in solution as well as in the solid state. Rapid dissolution of 1 mol. equiv. of any of the $R^1NH_3ClO_4$ salts in CD_2Cl_2 solutions of DD-(2) was accompanied by significant changes in the [1]H n.m.r. spectrum of the host as well as the appearance of additional signals for the guest species. In particular, the previously enantiotopic methylene protons in $PhCH_2NH_3ClO_4$ become diastereotopic in the chiral complex as demonstrated by their appearance as an AB system. The bridgehead protons (H-12, -13, -27, and -28) between the cis-fused five-membered rings in DD-(2) provide a suitable [1]H n.m.r. probe to study the ease with which the guest species dissociate away from the host allowing it to undergo the necessary conformational change before association of the guest species occurs at the opposite face. Free energies of activation ($\Delta G_c^{\ddagger}$) for this sequence of events at the coalescence temperatures are listed in Table 1.

The successful location of all the hydrogen atoms in the structure (Figure) of the 1:1:1 complex has enabled a detailed analysis to be made of the hydrogen bonding in the complex. In all, seven (a–g) of the ten oxygen atoms of DD-(2) are involved in hydrogen-bond formation. One of the NH_3^+ hydrogen atoms of the (S)-PhCHMeNH$_3^+$ cation is bonded to the oxygen atom of the H_2O molecule with both species residing side-by-side in the hydrophilic cavity of the host. The other two NH_3^+ hydrogen atoms, and one of the H_2O hydrogen atoms, are involved in bifurcated hydrogen bonds to three pairs (a and b, c and d, and f and g) of oxygen atoms leaving the other H_2O hydrogen atom to participate in hydrogen bonding to the seventh (e) oxygen atom. Two other conformational features characterising the structure of the 1:1:1 complex merit highlighting. (i) In the solid state structure of one (A) of the molecules of the free crown ether,[1] one of the dianhydromannitol residues has one of its oxygen atoms oriented towards the face of the cis-fused five-membered rings. In the 1:1:1 complex, it is this conformation which is adopted by both dianhydromannitol residues enabling oxygen atoms (d) and (g) to form hydrogen bonds with the guest species. (ii) Since there is sufficient flexibility in DD-(2) for hydrogen-bond geometry not to be dictated predominantly by the need for the free crown to minimise its own strain energy, we have listed in Table 2 the angles (ϕ) of approach of the H · · · ·O

TABLE 2. Hydrogen-bond lengths (R) and angles (ϕ) between hydrogen-bond vectors and corresponding C–O–C planes.

X—H · · · ·O	$R(X \cdots O)$ Å	$\phi/°$
N^+—H · · · ·O(a)	3·03	11
N^+—H · · · ·O(b)	3·00	42
N^+—H · · · ·O(c)	2·98	31
N^+—H · · · ·O(d)	3·00	18
N^+—H · · · ·O(h)	2·83	55
O(h)—H · · · ·O(e)	2·96	10
O(h)—H · · · ·O(f)	2·99	11
O(h)—H · · · ·O(g)	2·90	15

vectors to the associated COC planes as well as the hydrogen-bond distances $R(X \cdots O)$ between 'heavy' atoms (X and O). Although a wide range (ϕ 10—42°) of angles of approach is observed, there is clearly a tendency[2] (ϕ_{avg}. 20°) for the adoption of a trigonal approach (ϕ 0°) of hydrogen bonds to ether oxygen atoms in preference to a tetrahedral one (ϕ ca. 55°).

The incorporation of an H_2O molecule in a 1:1:1 complex with DD-(2) and an $R^1NH_3^+$ cation suggested to us that it should be possible to replace H_2O by R^2NH_2 and so bind two organic species side-by-side in the same cavity. Indeed, preliminary [1]H n.m.r. spectroscopic evidence (Table 1) points to the formation of 1:1:1 complexes between DD-(2), $R^1NH_3^+$ cations, and amines R^2NH_2. The consequences of being able to form complexes of this type are obvious in the context of catalysis.

[1] J. C. Metcalfe, J. F. Stoddart, G. Jones, T. H. Crawshaw, A. Quick, and D. J. Williams, preceding communication.
[2] A. C. Coxon, D. A. Laidler, R. B. Pettman, and J. F. Stoddart, J. Am. Chem. Soc., 1978, 100, 8260; J. F. Stoddart, Chem. Soc. Rev., 1979, 8, 85; J. F. Stoddart in 'Enzymic and Non-Enzymic Catalysis,' eds. P. Dunnill, A. Wiseman, and N. Blakebrough, Ellis Horwood, Chichester, 1980, p. 84.