Structural and conformational studies of alcohol, diol and methyl ether derivatives of dibenzo-14-crown-4. Implications for ligand and tecton design

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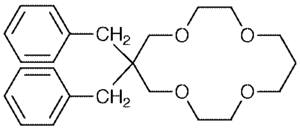
Molecular structures are determined for six dibenzo-14-crown-4 derivatives that have one or two substituents on the central carbon(s) of the three-carbon bridge(s). The series of compounds includes three crown ether alcohols, one crown ether *trans*-diol, and two methoxy crown ether compounds. The crystal structures for these six crown ethers reveal that due to hydrogen-bonding and steric interactions, a hydroxy substituent is directed, at least partially, toward the crown ether cavity and an unusual intra- and intermolecular hydrogen bond network is formed between the hydroxy group protons and the ether oxygens of the crown ether ring. On the other hand, an ether group or a substituent with carbon as the first atom is oriented away from the polyether ring. The structure of *sym*-(methoxy)(methyl)dibenzo-14-crown-4 is markedly different from that of *sym*-(hydroxy)(methyl)dibenzo-14-crown-4 both in terms of the substituent orientation and very significant distortion from planarity of the four crown ether oxygens in the former. Support for an unusual conformation for *sym*-(methoxy)(methyl)dibenzo-14-crown-4 in solution is derived from ^{13}C NMR measurements. Crown ether alcohols are hydrogen-bonding "tectons" that participate in strong, specific and directional intermolecular interactions.

Introduction

Although many commonly encountered crown ethers have only two-carbon bridges between the oxygen atoms, several crown ether compounds which exhibit high selectivity in alkali metal cation complexation possess one or two three-carbon units.[1] Thus the disubstituted 14-crown-4 derivative **1** and dibenzo-14-crown-4 **2** exhibit pronounced Li^+ selectivity in ion-selective electrodes.[2,3] For competitive solvent extraction of alkali metal cations from water into chloroform, 14-crown-4 carboxylic acids **3** and **4** transfer only Li^+ and Na^+ into the organic medium and the Li^+/Na^+ selectivity is high.[4,5] Dibenzo-16-crown-5 amides (**5** with $X = NR_2$) exhibit high Na^+ selectivity in solvent polymeric membrane electrodes[6] and dibenzo-16-crown-5 carboxylic acids (**5** with X = OH) show excellent Na^+ selectivity in competitive solvent extraction of alkali metal cations,[7] as well as competitive transport of such species across polymer-supported liquid membranes.[8]

Recently, we reported that alcohol derivatives of dibenzo-14-crown-4 are selective complexing agents for hydronium ions over alkali metal and alkaline earth cations in solvent polymeric membrane electrodes.[9–11] Therefore, such compounds are potential ionophores for hydronium ions in solvent extraction and liquid membrane transport processes. These crown ether alcohols are also excellent host molecules for neutral guest molecules, such as water and methanol.[10,11] In another investigation, it was shown that these crown ether alcohols may function as bifunctional ligands in complexation of lithium salts by providing simultaneous cation complexation and anion solvation.[12]

With a combination of ether and hydroxy groups, these crown ether alcohols provide multifunctional binding diversity. The hydrophilic ether oxygens of the crown ether and the



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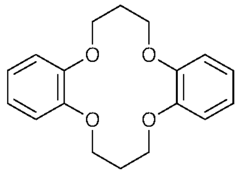

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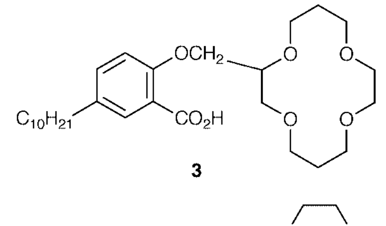

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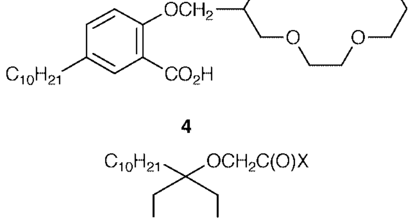

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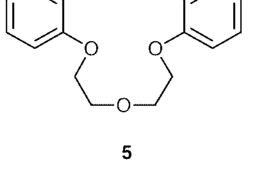

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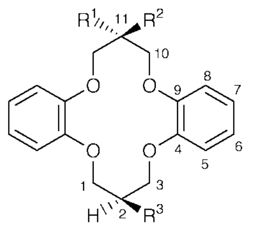

	R¹	R²	R³
6	OH	H	H
7	CH_2OH	H	H
8	OH	Me	H
9	OH	H	OH
10	OMe	H	H
11	OMe	Me	H
12	$OCH_2CO_2^-Li^+$	H	H

Fig. 1 Molecular numbering schemes for dibenzo-14-crown-4-alcohols **6**–**8**, diol **9** and methyl ethers **10** and **11**.

oxygen and acidic proton of the alcohol moiety, on the one hand, and the hydrophobic hydrocarbon skeleton of the crown ether, on the other, generate versatile hosts for both charged and neutral guest species which are candidates as building block units in supramolecular architecture. Crown ether alcohols are hydrogen-bonding tectons in that they participate in strong, specific and directional interactions.[10,13–15]

In the solid-state structure of dibenzo-14-crown-4 **2**, the four ether oxygens are coplanar.[16] Two major planes are formed by all of the atoms on each side of the molecule with the middle carbon of the three-carbon bridge being included in both planes. The dihedral angle formed by the two benzene rings in the V-shaped molecule is 122.8°. The dibenzo-14-crown-4 molecule provides an ideal base of square-planar coordination in LiNCS,[17] LiPicrate, $LiClO_4$ and LiI[18,19] complexes.

To probe the structural influence of attaching hydroxy, hydroxymethyl, methoxy, and geminal methyl groups to the central carbon of a three-carbon bridge in dibenzo-14-crown-4, the crystal structures of crown ether alcohols **6**–**8**, diol **9** and methyl ethers **10** and **11** (Fig. 1) have now been determined by X-ray diffraction. For this series, the substituents are varied from one hydroxy group in **6** to a hydroxymethyl group ($-CH_2OH$) in **7** to geminal hydroxy and methyl groups in **8** to a *trans*-diol with one hydroxy group on each three-carbon bridge in **9** to a methoxy group in **10** and to geminal methoxy and methyl groups in **11**. Structures for this series of mono- and disubstituted dibenzo-14-crown-4 compounds are now reported and analyzed.

Experimental

Materials

Substituted dibenzo-14-crown-4 compounds **6**,[10] **7**,[11] and **9**[11,20] were prepared by the reported procedures. Crystals of substituted dibenzo-14-crown-4 compounds **6**–**11** were grown from acetonitrile solutions.

Synthesis

***sym*-(Hydroxy)(methyl)dibenzo-14-crown-4 8.**[21] To 1.07 g (44.0 mmol) of magnesium turnings in dry Et_2O (140 cm^3) under nitrogen at room temperature was added dropwise a solution of iodomethane (5.68 g, 40.0 mmol) in dry Et_2O (10 cm^3). Stirring of the mixture for 1 h formed a white emulsion which was cooled in an ice bath. A solution of *sym*-(keto)dibenzo-14-crown-4[10] (6.28 g, 20.0 mmol) in dry THF (100 cm^3) was added dropwise. The ice bath was removed and the reaction mixture was stirred at room temperature for 12 h. Water (20 cm^3) was added and the mixture was stirred for 30 min. After evaporation of the organic solvents *in vacuo*, the residue was extracted with CH_2Cl_2 (2 × 100 cm^3). The combined CH_2Cl_2 layers were washed with water, dried over $MgSO_4$ and evaporated *in vacuo*. The crude product was crystallized from EtOAc–hexanes (1 : 1) and washed with Et_2O to give 3.99 g (61%) of white solid with mp 146–147 °C (lit.[22] mp 142.5–143 °C); $\delta_H(CDCl_3)$ 1.38 (3 H, s), 2.13–2.41 (2 H, m), 3.59 (1 H, s), 4.02 (2 H, d, *J* 9.0), 4.12–4.22 (2 H, m), 4.24–4.33 (2 H, m), 6.86–6.98 (2 H, m); δ_C 21.6, 29.3, 67.6, 71.2, 75.5, 115.1, 116.8, 121.7, 122.5, 149.3, 149.6.

***sym*-(Methoxy)dibenzo-14-crown-4 10.** To a stirred suspension of NaH (0.61 g, 25.3 mmol) in dry THF (20 cm^3), a solution of **6** (4.00 g, 12.66 mmol) in dry THF (80 cm^3) was added at room temperature. After 1 h, a solution of iodomethane (3.59 g, 2.53 mmol) in dry THF (10 cm^3) was added and the mixture was stirred for 16 h at room temperature. Water (5 cm^3) was added to destroy the excess NaH and the solution was evaporated *in vacuo*. To the residue CH_2Cl_2 was added and the organic layer was washed with water (3 × 50 cm^3), dried over $MgSO_4$ and evaporated *in vacuo*. The crude product was purified by column chromatography on alumina with EtOAc–pentane (1 : 1) as eluent to give 3.18 g (76%) of white crystals with mp 124–125 °C (Found: C, 68.9; H, 6.7. Calc. for $C_{19}H_{22}O_5$: C, 69.1; H, 6.7%); $\delta_H(CDCl_3)$ 2.15–2.45 (2 H, m), 3.57 (3 H, s), 3.98 (1 H, m), 4.15–4.34 (8 H, m), 6.87–7.03 (8 H, m); δ_C 29.3, 58.2, 66.9, 69.7, 78.2, 78.2, 116.1, 117.5, 122.0, 122.7, 148.8, 149.8.

***sym*-(Methoxy)(methyl)dibenzo-14-crown-4 11.** In a similar fashion, NaH (0.48 g, 20 mmol), **8** (3.00 g, 9.1 mmol) and iodomethane (2.84 g, 20.0 mmol) were reacted in THF. Following workup, the residue was subjected to flash chromatography on silica gel with CH_2Cl_2–EtOAc (9 : 1) as eluent and then crystallized from hexanes to afford 0.89 g (28%) of **11** as a white solid with mp 90–91 °C (Found: C, 69.8; H, 7.3. Calc. for $C_{20}H_{24}O_5$: C, 69.8; H, 7.0%); $\delta_H(CDCl_3)$ 1.45 (3 H, s), 2.28 (2 H, pen, *J* 5.5), 3.46 (3 H, s), 4.08 (2 H, d, *J* 9.2), 4.13–4.30 (6 H, m), 6.85–7.01 (8 H, m); δ_C 17.8, 29.3, 50.3, 67.4, 72.4, 76.4, 115.4, 117.9, 121.7, 122.7, 149.3, 150.0.

Structure determination

Solid-state structures of the six compounds were obtained using direct methods. The crystal data and refinement results are summarized in Table 1. Compounds **6** and **8** lie on mirror planes and both molecules contain some disorder. In **6** there was orientational disorder consisting of a fractional oxygen O5 bonded to C2 with a population parameter of 0.70 and a fractional oxygen O5′ bonded to C11 with a population parameter of 0.30. In **8** the carbon and oxygen atoms bonded to C11 (a carbon on the mirror plane) were also considered to be on the mirror plane, although the thermal parameters indicated that these atoms were slightly off that plane. This disorder could not be resolved.

All non-hydrogen atoms for the six structures were refined anisotropically with the exception of the disordered oxygen O5′ in **6**. Hydrogen atoms bonded to oxygen atoms and the carbon atoms on the mirror planes were located in difference maps while positions of the remaining hydrogens were calculated.

Results

Synthesis

The synthetic routes to the three new dibenzo-14-crown-4 compounds **8**, **10** and **11** are shown in Scheme 1.

Solid-state structures

Molecular numbering schemes for the six functionalized dibenzo-14-crown-4 compounds are given in Fig. 1. Repeated attempts to prepare single crystals of *cis*-diol **9** in an anhydrous form provided only the monohydrate. The high melting point of the *cis*-diol **9** monohydrate is consistent with a very stable monohydrate structure.[15,22]

The molecular structures of the substituted dibenzo-14-crown-4 compounds **6**–**11** are shown in Figs. 2–7, respectively.†

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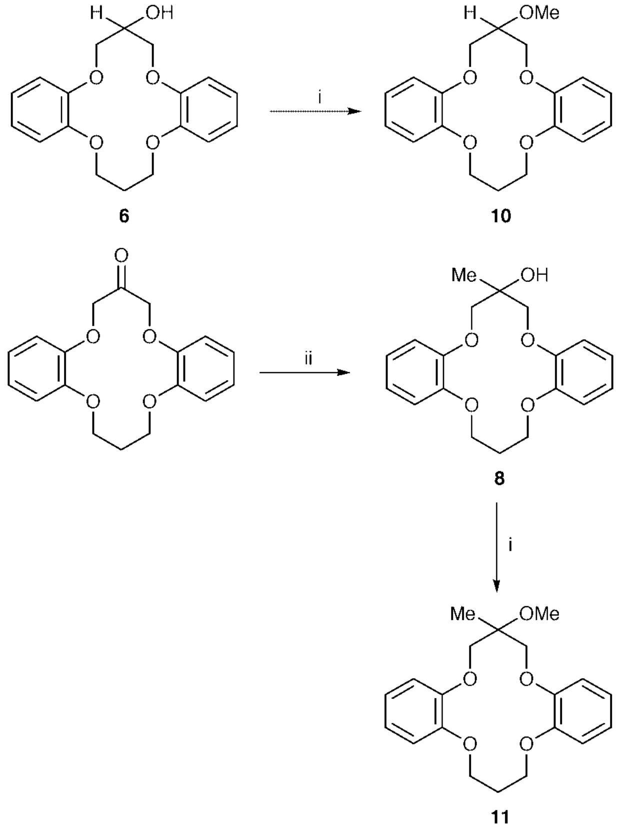
† CCDC reference number 188/186. See http://www.rsc.org/suppdata/p2/1999/2557 for crystallographic files in .cif format.

Table 1 Crystal data and refinement results for dibenzo-14-crown-4 compounds **6**–**11**

Compound	**6**	**7**	**8**	**9**	**10**	**11**
Formula	$C_{18}H_{20}O_5$	$C_{19}H_{22}O_5$	$C_{19}H_{22}O_5$	$C_{18}H_{20}O_6$	$C_{19}H_{22}O_5$	$C_{20}H_{24}O_5$
Formula weight	316.34	330.37	330.37	332.34	330.37	344.39
Crystal system	Orthorhombic	Monoclinic	Orthorhombic	Monoclinic	Monoclinic	Monoclinic
Space group	*Pnma*	$P2_1$	$Cmc2_1$	$C2/c$	$P2_1/c$	$P2_1/c$
Crystal[a] size/mm	0.45 × 0.38 × 0.30	0.50 × 0.10 × 0.08	0.45 × 0.20 × 0.15	0.40 × 0.20 × 0.15	0.30 × 0.12 × 0.08	0.33 × 0.30 × 0.25
a/Å	21.005(13)	9.621(10)	17.060(7)	33.139(8)	17.160(3)	20.295(6)
b/Å	14.453(8)	9.499(11)	17.922(5)	5.0640(10)	4.8770(10)	8.139(3)
c/Å	5.099(2)	10.262(7)	5.552(2)	20.155(3)	21.453(4)	11.205(5)
β/deg	90	115.39(6)	90	108.30(2)	112.64(10)	101.19(2)
V/Å^3	1551.7	847.3	1697.5	3211.3	1657.0	1815.7
Z	4	2	4	8	4	4
R^1, wR^2 ($I > 2\sigma(I)$)[b]	0.059, 0.136	0.084, 0.207	0.049, 0.110	0.049, 0.102	0.067, 0.113	0.067, 0.126
GOF on F^2	0.968	1.007	0.916	0.981	1.025	1.032

[a] All crystals were colorless. [b] $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$, $wR^2 = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{\frac{1}{2}}$.



Scheme 1 *Reagents*: i, NaH, MeI, THF; ii, Mg, MeI, Et$_2$O.

In crown ether secondary alcohol **6** (Fig. 2), the hydroxy group is disordered in two sites. In one site (Fig. 2a), the hydroxy group is directed away from the polyether cavity (70% partial occupancy); while in the second site (Fig. 2b), the hydroxy group is oriented toward the polyether cavity (30% partial occupancy). When a geminal methyl group is added in crown ether tertiary alcohol **8** (Fig. 3), the hydroxy group is directed toward the polyether cavity, while the methyl group is oriented away. In the crown ether *trans*-diol **9** (Fig. 4), one hydroxy group is oriented toward the macrocyclic cavity, while the second points away from it. For the hydroxymethyl crown ether **7** (Fig. 5), the CH$_2$OH group is directed away from the polyether cavity. In crown ether methyl ether **10** (Fig. 6), the methoxy group is directed away from the polyether cavity. For crown ether **11** (Fig. 7) which has geminal methoxy and methyl groups, the former is directed away from the polyether cavity and the latter is oriented toward the polyether cavity.

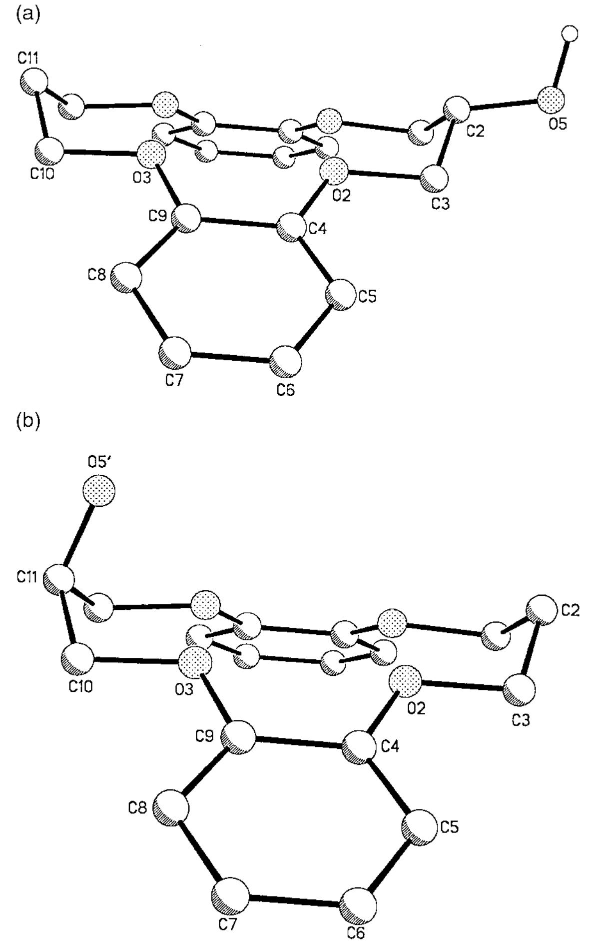


Fig. 2 Crystal structure for crown ether alcohol **6** with the hydroxy group disordered in two sites.

The structures of substituted dibenzo-14-crown-4 compounds **6**–**11** may also be defined in terms of the dihedral angle between the two major planes.[22] For functionalized dibenzo-14-crown-4 compounds **6**–**11**, these "hinge" angles are 129.6, 135.0, 118.9, 132.0, 126.6 and 130.0°, respectively. The least-squares planes for compound **11** show considerably more deviation from planarity than do those for compounds **6**–**10** (compare Fig. 7 with Figs. 2–6).

For crown ethers **6**–**11**, it is interesting to examine the O–C–C$_x$–Y torsion angles where O is an ether oxygen of the cyclic polyether unit, C$_x$ is the central carbon of the three-carbon bridge and Y is the first atom of the substituent. These torsion angles are presented in Table 2. When Y is a carbon atom in **7**

Table 2 Significant torsion angles in dibenzo-14-crown-4 compounds **6**–**11**

Compound	O	C	C_X	Y	O–C–C_X–Y
6	O2	C3	C2	O5	165.8(3)
	O3	C10	C11	O5′	−53.5(7)
7	O3	C10	C11	C19	167.9(8)
	O4	C12	C11	C19	−168.8(8)
8	O3	C10	C11	C19	−167.1(6)
	O3	C10	C11	O5	−48.4(6)
9	O1	C1	C2	O6	169.9(2)
	O2	C3	C2	O6	−168.2(2)
	O3	C10	C11	O5	54.5(3)
	O4	C12	C11	O5	−55.4(3)
10	O3	C10	C11	O5	−169.4(5)
	O4	C12	C11	O5	164.3(5)
11	O3	C10	C11	O5	−175.0(4)
	O3	C10	C11	C19	65.4(5)
	O4	C12	C11	O5	56.2(5)
	O4	C12	C11	C19	−178.4(4)

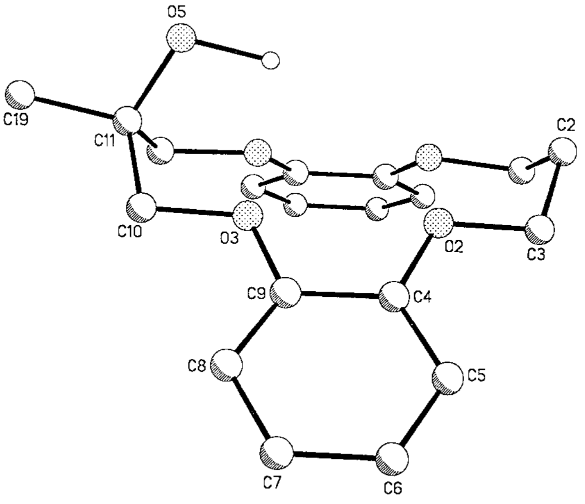


Fig. 3 Crystal structure for crown ether alcohol **8**.

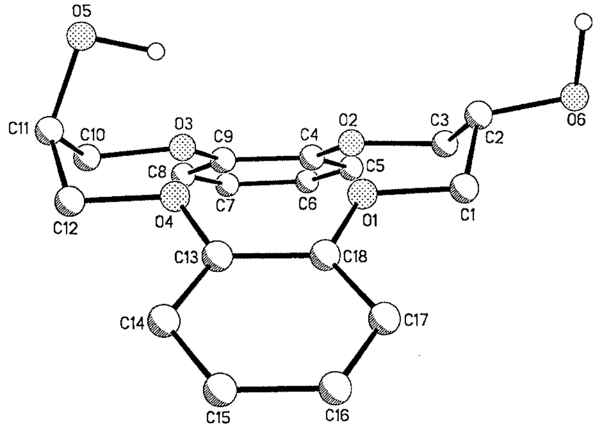


Fig. 4 Crystal structure for crown ether diol **9**.

and **8**, the torsion angles approach 180° (*i.e.*, a *trans* conformation). If Y is an oxygen, there is a *gauche* conformation in some of the structures, but a *trans* conformation in others. Thus, in crown ether secondary alcohol **6**, the oxygen in the more populated site is *trans* and in the less populated site is *gauche*. The oxygen is *trans* in the methoxy crown ether **10**. For disubstituted dibenzo-14-crown-4 compounds, the oxygen is *gauche* in crown ether tertiary alcohol **8**; while one oxygen is *gauche* and the other is *trans* in crown ether *trans*-diol **9**. Based upon this pattern, it was anticipated that the oxygen in methoxy crown ether **11** would be *gauche* because of the presence of a methyl group also bonded to C_x (C11). However due to

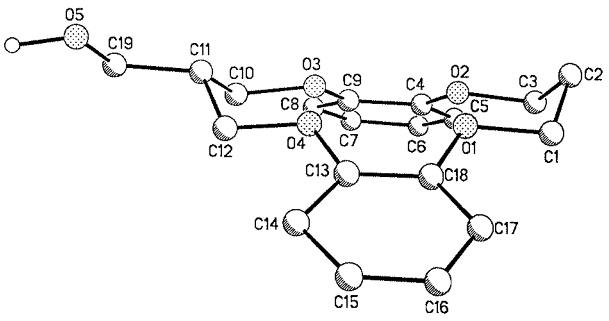


Fig. 5 Crystal structure for crown ether alcohol **7**.

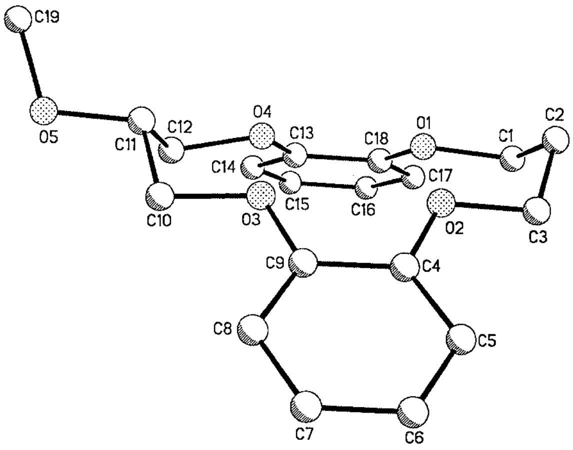


Fig. 6 Crystal structure for crown ether methyl ether **10**.

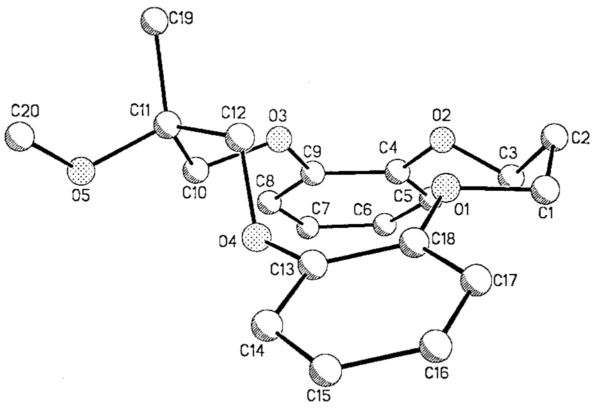


Fig. 7 Crystal structure for crown ether methyl ether **11**.

distortion in the dibenzo-14-crown-4 ring system in **11**, the methoxy oxygen has both *gauche* and *trans* arrangements (Fig. 7), as does C19, the methyl carbon atom. This distortion is evident in the arrangement of the crown ether oxygens. The crystallographic mirror planes present in **6** and **8** cause the four crown ether oxygens to be planar. These four oxygens are also planar in **7**, **9** and **10** with average deviations of an oxygen atom from the least-squares planes of 0.018, 0.013 and 0.009 Å, respectively. However for **11**, the average deviation of an oxygen atom from the least-squares plane is 0.184 Å with a 0.746 Å deviation of O4 from the plane described by O1, O2 and O3.

Intramolecular hydrogen bonds are possible in the *gauche* conformations of **6** and **8** and for one of the hydroxy groups in **9**. Possible hydrogen-bonding interaction distances in crown ether alcohols **6**–**9** are listed in Table 3. When the alcohol oxygen is *gauche*, intramolecular hydrogen bonding occurs. However, when an alcohol oxygen or the carbon of a hydroxymethyl group is *trans*, intermolecular hydrogen bonds are formed. These two different possibilities for hydrogen bond formation are illustrated for crown ether diol **9** and the

Table 3 Possible H-bond interaction distances in compounds **6**–**9**

Compound	D	H	A	H···A/Å	D···A/Å	D–H···A/deg	Symmetry translation of A
6	O5	H5A	O2	2.27	3.133	142	$x, y, -1 + z$
	O5	H5A	O2	2.27	3.133	142	$x, 0.5 - y, -1 + z$
	O5′		O3		2.647		x, y, z
7	O5	H5A	O3	2.12	3.031	140	$1 - x, 0.5 + y, 1 - z$
	O5	H5A	O4	2.31	3.226	141	$1 - x, 0.5 + y, 1 - z$
8	O5	H5A	O3	2.27	2.679	95	x, y, z
	O5	H5A	O3	2.27	2.679	95	$-x, y, z$
9	O5	H5A	O3	2.27	2.719	104	x, y, z
	O5	H5A	O4	2.22	2.746	109	x, y, z
	O6	H6A	O1	1.96	3.158	167	$x, -1 + y, z$
	O6	H6A	O2	2.42	3.124	114	$x, -1 + y, z$

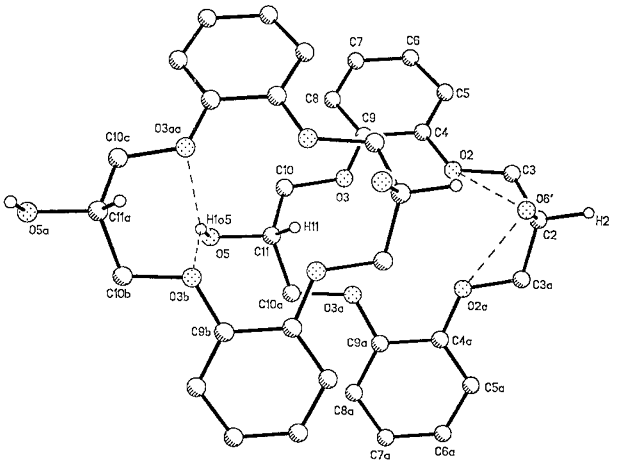


Fig. 8 Hydrogen-bond pattern for crown ether diol **9** and the isostructural crown ether alcohol **6**.

isostructural alcohol **6** in Fig. 8. The O–H···O angles close to 90° in **8** and **9** suggest that the intramolecular hydrogen bonds are weak. Angles for the intermolecular hydrogen bonds in **6** and **7** and for the second alcohol group in **9** are more normal.

Discussion

Solid-state structures

For the crown ether secondary alcohol **6** in which the hydroxy group is attached to the central carbon of the three-carbon bridge, the hydroxy oxygen is disordered with respect to the polyether cavity. In the more populated site (Fig. 2a), the hydroxy group oxygen is *trans* to the neighboring ethereal oxygens in the polyether ring; while in the other site (Fig. 2b), the hydroxy group oxygen is *gauche* to these ethereal oxygens. Of these two forms, one may consider the *gauche* form (Fig. 2b) to be the less stable since it is subject to nonbonded repulsions which are minimized in the *trans* arrangement (Fig. 2a). Since both the hydroxy and ether oxygens are polar functions, the *trans* conformation should also be more stable since it reduces the dipolar repulsion present in the *gauche* conformation. On this basis, the *gauche* structure should be disfavored in **6**. Nevertheless, a partial occupancy of 30% of the *gauche* conformation is observed. Thus, the orientation of the hydroxy group with respect to the dibenzo-14-crown-4 unit appears to be also affected by intramolecular hydrogen bonds between the hydroxy hydrogen and the neighboring ether oxygens.[11] The partial occupancy ratio between the *gauche* and *trans* conformations of 3 : 7 indicates that the two conformations have very similar energies.

To probe the effect on the *gauche* : *trans* ratio caused by replacing the hydroxy hydrogen in **6** with a methyl group, the solid-state structure of *sym*-(methoxy)dibenzo-14-crown-4 **10** was determined (Fig. 6). In **10**, the methoxy oxygen is *trans* to the neighboring ether oxygens of the polyether ring. Thus replacement of the hydroxy proton in compound **6** by a methyl group in compound **10** produces only the *trans* conformation for the substituent. Compound **10** differs from **6** primarily in two aspects. The small proton in **6** has been substituted by a bulky methyl group and the protic hydroxy group is replaced by a non-protic ether function. It appears that the methoxy group in **10** causes pronounced nonbonding and dipolar repulsions with the crown ether unit which are minimized in the *trans* arrangement. In crown ether alcohol **6**, there is also the possibility for intramolecular hydrogen bonding[10,11] which would stabilize the *gauche* conformation. Such hydrogen bonding interactions are not possible in the crown ether methyl ether **10**.

There are two possible limiting conformations for the crown ether tertiary alcohol *sym*-(hydroxy)(methyl)dibenzo-14-crown-4 **8**. In the first, the hydroxy group is *gauche* to the ether oxygens and the methyl group is *trans*. In the other, the hydroxy group is *trans* and the methyl group *gauche*. In the crystal structure of **8** (Fig. 3), only the former conformation is observed. Apparently intramolecular hydrogen bonding between the hydroxy hydrogen and the neighboring ether oxygens stabilizes the *gauche* conformation. This finding is of particular interest and importance. Orientation of the hydroxy group in **8** inward with the O–H bond parallel to the crown ether ring forms a preorganized binding site which should stabilize a metal ion complex of **8** compared with that of the secondary alcohol analog **6**.

For the crown ether *trans*-diol **9**, one hydroxy group is *gauche* to the neighboring ether oxygens and the other is *trans* (Fig. 4). Intramolecular hydrogen bonding between the hydroxy proton and the neighboring ether oxygens will stabilize the *gauche* hydroxy group. The solid-state structure of crown ether alcohol **6** is isostructural with the disordered crystal structure of crown ether *trans*-diol **9**. In both structures, there is a hydroxy group *gauche* to the neighboring ether oxygens. It should be noted that a *gauche*–*gauche* conformation, but no *trans*–*trans* arrangement, is reported in *cis*-diol **9** monohydrate.[11,15] These experimental data provide additional support for the important contribution of hydrogen-bonding interactions to the preferred substituent conformation in these crown ether alcohols.

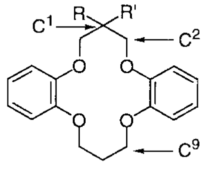
For *sym*-(hydroxymethyl)dibenzo-14-crown-4 **7**, the attachment of the alcohol-containing substituent to the crown ether ring is through a carbon atom. Orientation of the substituent with respect to the neighboring ethereal oxygens is *trans* (Fig. 5). This finding is consistent with conformational analysis studies which show repulsion between oxygen and carbon atoms in the 1,4-positions.[23–28] These results are supported by the crystal structure of *sym*-(methyl)dibenzo-14-crown-4 in which 1,4 oxygen–carbon atom repulsion is observed.[29]

It might be anticipated that the attachment of one or more substituents to the central carbon(s) of the three-carbon bridge(s) in dibenzo-14-crown-4 would change the dihedral angle between the major planes formed by the two benzene rings in the V-shaped molecules.[16] The reported[16] hinge angle for dibenzo-14-crown-4 (**2**) is 122.8°. For monosubstituted dibenzo-14-crown-4 compounds **6**, **7** and **10**, these "hinge" angles are 129.6, 135.0 and 126.6°, respectively. Thus, for crown ether alcohol **6** and methyl ether **10**, the hinge angle is larger than that in the parent crown ether **2**. For the hydroxymethyl crown ether **7**, the hinge angle is appreciably larger. For the disubstituted dibenzo-14-crown-4 compounds, the effect of substituents on the hinge angle is noted to depend upon their attachment site(s) and identity. The hinge angle is 132.0° for diol **9** in which one hydroxy group is attached to each three-carbon bridge. In contrast, for the crown ether tertiary alcohol **8**, the hinge angle is only 118.9° which reveals a substantial narrowing of the hinge angle when the two substituents are geminal and one is a hydroxy group. On the other hand, for the geminal methoxy-substituted crown ether **11**, the hinge angle is 130.0° which is a more usual value for a substituted dibenzo-14-crown-4 compound.

For the crown ether alcohols **6** and **7** and *trans*-diol **9**, the ligand molecule has been shown to interact with the counter-anion of a complexed cation *via* hydrogen bonding.[12] There are two types of hydrogen bonds in crown ether compounds **6**–**9**. The first consists of an intramolecular hydrogen bond (in **6**, **8** and **9**), while the second involves intermolecular hydrogen bonding (in **7** and **9**). In both cases, the interaction is between a proton-donor hydroxy group and a proton-acceptor ether oxygen. When the hydroxy group is *gauche* to the neighboring oxygens of the polyether unit, the hydrogen atom is oriented towards the cavity so it can interact with an ether oxygen by intramolecular hydrogen bonding. When the hydroxy group is *trans* and directed away from the polyether unit, the hydrogen atom interacts with the ether oxygens of a neighboring molecule. These orientations for intra- and intermolecular hydrogen bonding are shown for crown ether *trans*-diol **9** and the isostructural crown ether alcohol **6** in Fig. 8. Intermolecular hydrogen bonding between the hydroxy groups of two crown ether alcohol molecules is not observed. The unique hydrogen-bond pattern of crown ether alcohols controls whether intracomplex or intercomplex hydrogen bonding will take place between the hydroxy group and the anion of the complexed cation. Intercomplex hydrogen bonds are produced when the hydroxy groups are unavailable for intracomplex hydrogen bond formation due to conformational restrictions (*i.e.*, for compound **7** and one of the hydroxy groups in **9**).

A very significant result of this study is the unexpected molecular structure of geminally disubstituted crown ether **11**. It was anticipated that the structure of methoxy crown ether **11** would closely resemble the conformation of crown ether alcohol **8** due to the rigidity of the dibenzo-14-crown-4 system (which produces a V-shaped structure with planar ether oxygens) and the presence of a geminal methyl group in both systems. However, replacement of the hydroxy proton in **8** by a methyl group in **11** produces a reversal in the positioning of the geminal substituents (*i.e.*, the hydroxy group in **8** is directed toward the polyether cavity, but the methoxy group in **11** points away) and also markedly alters the conformation of the crown ether ring. Apparently, the presence of the methoxy methyl group engenders steric repulsions which cause one ring oxygen (O4) to be twisted in the opposite direction to the other three ring oxygens to produce a structure which resembles that for the four ether oxygens in benzo-13-crown-4.[30] *To our knowledge, this is the first example of a substituted dibenzo-14-crown-4 compound which diverges from the planar arrangement of the four crown ether oxygens found in the parent crown ether* **2**.[16]

Table 4 ^{13}C NMR chemical shifts for selected carbon atoms in substituted dibenzo-14-crown-4 compounds **6**, **8**, **10** and **11**



			Chemical shift in CDCl$_3$, δ				
Compound	R	R′	*C*–C^1	*C*–O–C^1	*C*^{1}	*C*^{2}	*C*^{9}
6	H	OH	—	—	68.6	71.5	67.3
8	CH$_3$	OH	21.6	—	71.2	75.5	67.6
10	H	OCH$_3$	—	58.2	78.2	69.7	66.9
11	CH$_3$	OCH$_3$	17.8	50.3	76.4	72.4	67.4

Although both *gauche* and *trans* conformations are observed in the solid-state structure for crown ether secondary alcohol **6**, only the former is observed in the monohydrate form[10,11,15] and in lithium salt complexes.[16] Similarly, the *gauche* conformation is reported for the lithium crown ether oxyacetate derivative **12**.[31]

The conformation observed for hydroxymethyl crown ether **7** is similar to that reported for complexes of **7** with LiSCN and LiNO$_3$.[12] The conformation of crown ether diol **9** is essentially the same as that for **9** in its LiSCN complex, as well as in its monohydrate form.[12,15]

Conformational study by ^{13}C NMR

^{13}C NMR chemical shifts are useful for structural studies in solution.[32] Compounds exist as a set of equilibrating conformations in solution and the signals observed in the NMR spectra are due to the average-weighted conformations (provided exchange is fast on the NMR timescale). The lower energy conformations have greater populations, so the observed δ values approach those for these preferred conformations.

To probe for similarities or differences between the conformations of substituted dibenzo-14-crown-4 compounds **6**, **8**, **10** and **11** in solution and the solid-state, a ^{13}C NMR investigation was undertaken. The ^{13}C NMR chemical shifts for selected nuclei in compounds **6**, **8**, **10** and **11** are presented in Table 4. It is noted that the chemical shifts for C^9, which is remote from the substituent(s), are very nearly the same for the four compounds.

Since the change from a hydroxy substituent in **6** to a methoxy group in **10** should not produce an appreciable electronic effect at C^1, the downfield shift for C^1 in going from **6** to **10** is ascribed to a conformational effect. In studies of cyclohexane derivatives,[33] movement of a substituent from an equatorial to an axial position was found to produce a similar change in the ^{13}C NMR chemical shift for the carbon to which the substituent was attached. This change was attributed to a larger number of *anti* H–H interactions in the equatorial structure. By analogy, we deduce that the preferred conformations for the substituents in **6** and **10** are to be directed toward the ring in the former and away from the ring in the latter.

Steric repulsion between the geminal methoxy and methyl substituents attached to C^1 in **11** (a γ-*gauche* effect) is evident from the upfield chemical shift for the side arm carbons in **11** compared with those in compounds **8** and **10**. Apparently such repulsion is responsible for the distorted dibenzo-14-crown-4 ring in the solid-state structure of **11**.

Due to the same γ-*gauche* effect, the signal for C^2 in **10** is shifted upfield from that in **6** as a result of steric interaction between the C^2 (or C$^{2'}$) methylene group and the γ carbon (*i.e.*, the methyl of the methoxy group). Although a conformation with the substituent pointed away from the ring in **10** is preferred (*vide supra*), the change of δ for C^2 in **10** is smaller than the γ-*gauche* effect observed for the side arm carbons in **11**. This can be explained by the presence of fewer rotamers in **10** for which the γ-*gauche* interaction takes place, as well as distribution of the interactions between C^2 and $C^{2'}$.

The similar upfield shifts for C^2 in **11** compared with **8** are noteworthy. For this pair of disubstituted compounds, the shift of the C^2 signal is even larger than for **10** *vs.* **6**. From Newman projections, it is clear that γ-*gauche* interactions are more effective (realized in a larger number of conformations) if the methoxy group points away from the ring. Since it was concluded that the methoxy group in **10** points away from the ring (*vide supra*), it follows that it also points away from the ring in **11**. This is consistent with the solid-state conformation of **11** (Fig. 7).

Now we focus our attention upon the solution structure of crown ether tertiary alcohol **8**. Since there is no hydrogen attached to C^1 in **8**, no *anti* H–H interactions are possible. Also there is no possibility for γ-interactions with the substituents. Now comparing the C^1 chemical shifts for all four compounds, it can be seen that there is only a small change for **8** *vs.* **6** and for **10** *vs.* **11**. As deduced above, both **10** and **11** have the methoxy substituent oriented away from the ring and the difference is the replacement of a hydrogen directed toward the ring in **10** with a methyl group in **11**. For **8** *vs.* **6**, the only difference is the replacement of a geminal hydrogen with a geminal methyl group. Therefore, it seems reasonable that in both **8** and **6** the hydroxy group is oriented towards the ring. It is unlikely that only electronic effects are responsible for the large upfield change in chemical shift for C^1 in going from **11** to **8**. From a comparison of the C^1 chemical shifts for **8** *vs.* **6** and for **10** *vs.* **11**, it is deduced that the methoxy group in **11** and the hydroxy group in **8** have opposite orientations. Thus, it is concluded that the preferred conformation for **8** is one with the hydroxy group oriented towards the ring and the methyl group away from it. The solution structure deduced for **8** is consistent with the solid-state structure (Fig. 3).

For crown ethers **8**, **10** and **11**, there is agreement between the conformational arrangement of their substituent(s) in solution and in the solid-state structures.

Implications for ligand and tecton design

This conformational analysis study describes a step on the way to molecules which are capable of holding simultaneously cations and anions at sites determined solely by the molecular architecture.[12] Results of this study have an important bearing on the design of new substituted dibenzo-14-crown-4 ligands. For a substituent attached to the central carbon of a three-carbon bridge, the conformation is affected by 1,4-interactions of the substituent attachment atom and the neighboring ethereal oxygens. Due to intramolecular hydrogen bonding, a hydroxy substituent will be directed at least partially toward the crown ether cavity. On the other hand, a carbon attachment atom or replacing the hydroxy proton of an alcohol with an alkyl group will orient the substituent away from the polyether ring. Thus for instances in which involvement of a side arm in intramolecular interaction with the counter-anion of a crown ether-complexed cation is desired, the substituent should be an alcohol group. On the other hand, for intermolecular interactions of the side arm with another crown ether molecule the first substituent atom should be carbon.

Attachment of a geminal alkyl group to the central carbon of the three-carbon bridge orients the hydroxy substituent towards the crown ether ring. Such an arrangement preorganizes the binding site and maximizes interactions between the side arm and the counter-anion of a crown ether-complexed cation. The type of hydrogen bond with the counter-anion is dictated by the ligand conformation. Intracomplex hydrogen bonds are formed by oxygen attachment to the central carbon of the three-carbon bridge.

Tectons are molecules that can participate in strong, specific, and directional intermolecular interactions. Hydrogen bonding is reasonably strong and directional, and its effectiveness is beyond question.[13,14] Hydrogen bonding tectons can interact with one another to form three-dimensional structures of predictable geometry. The principle of molecular tectons can be used to construct a wide variety of three-dimensional structures from organic building blocks.[13,14] In general, crown ether alcohols possess both proton-donor and proton-acceptor functional groups and can provide such organic building blocks.[10–12,15] Because of their structural rigidity, dibenzo-14-crown-4 alcohols and diols are particularly attractive construction units. Working with these crown ether alcohol tectons as building blocks for three-dimensional construction is enabling us to use the powerful tools of organic synthesis to design subunits and then allow them to assemble to make a wide variety of structures, like the water–methanol channels.[10]

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