Nuclear Magnetic Resonance Study of the Solution Structures of Some Crown Ethers and Their Cation Complexes[1]

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Abstract: Proton (^1H) and carbon (^{13}C) nuclear magnetic resonance (NMR) have been used to elucidate the solution structure of a number of "crown" cyclic polyethers. We have examined benzo-18-crown-6 (B18C6), dibenzo-18-crown-6 (DB18C6), and dibenzo-30-crown-10 (DB30C10) and their interactions with Na^+, K^+, Cs^+, and Ba^{2+}. These studies were undertaken in water, water–acetone, acetone, and chloroform as a function of cation crown ether concentration and of the anion (I^-, SCN^-, and ClO_4^-). Structural information was deduced from detailed analysis of the ^1H and ^{13}C spectra, proton–proton vicinal coupling constants, and the salt-induced chemical shifts. The complexes of B18C6 and DB18C6 were shown to have the same structures in the various solvents as was previously reported for complexes of DB18C6 in the crystalline state. However, the solution conformation of the uncomplexed molecules differs from that of DB18C6 in the crystal. The K^+, Cs^+, and Ba^{2+} complexes of DB30C10 in solution were found to have the same configuration as that reported for the K^+ complex in the crystal. The Na^+ complex does not, and we have proposed an alternate structure. Evidence is presented for complete removal of the solvation sphere of the cation upon complexation to DB30C10, but this is apparently not the situation in the case of the 18-membered rings. The existence of a previously postulated "sandwiched" complex with a Cs^+ ion between two dibenzo-18-crown-6 molecules has been demonstrated in solution in the present work.

Introduction

Since the synthesis of "crown" ether compounds by Pedersen several years ago, and his observation of their ion binding properties,[3] a great deal of interest has been focused on them. This is because of the possible chemical and biological applications of their unusual ion complexation, solvation, and transport effects.[4] A number of investigations of the thermodynamics of these processes have been carried out,[5] as well as studies of their molecular structure using infrared[6] and ^{23}Na nuclear magnetic resonance spectroscopy,[7] and x-ray crystallography.[8] However, in view of the polar nature of the crown ethers and the importance of cation solvation, it is necessary to have structural information in a variety of solvents for both the free molecules and their complexes if the ion selectivity of these interesting compounds is to be understood.

We are reporting here a study of dibenzo-18-crown-6 (DB18C6), benzo-18-crown-6 (B18C6), and dibenzo-30-crown-10 (DB30C10) (Figure 1) and their interactions with various cations and ion pairs in several solvents. Proton magnetic resonance (^1H NMR) and carbon-13 magnetic resonance (^{13}C NMR) are techniques which should be well suited for such an investigation. The ^1H NMR spectra of cyclic ethers can be complex, and for this reason it has been suggested that ^1H NMR is not very effective for studies of these compounds.[7b] But by appropriate choice of molecules and through the use of a high-field NMR spectrometer, it is possible to overcome this difficulty. The benzo-substituted crown ethers mentioned above are obvious choices, not only because of the wealth of information on them and related molecules,[5-8] but also because the aromatic moieties, due to their ring current magnetic anisotropy,[9] lead to a convenient spectroscopic resolution of the multiplets in the ether region of the ^1H NMR spectrum. From this ring current effect one can deduce the spatial relations of the ether protons and the aromatic groups, and hence the assignment of the ether resonances. Another consequence of the increased spectral resolution is that the ether vicinal coupling constants, which are important in conformation determination, can now be readily extracted. Moreover, through the use of off-resonance heteronuclear decoupling,[10] the assignment of the ^{13}C spectrum can be made.

A study of DB18C6 and B18C6 allows the comparison of two molecules of similar size and ion binding properties, but with vastly different solubility properties in both the free and complexed forms. From these studies, the role of ring substituents on the structure and properties can be examined. DB30C10 should be representative of larger cyclic ethers, which would be expected to be more flexible and have greater ion adaptability upon formation of a complex. The x-ray structure for the complex K^+-DB30C10[8d] is quite different from that for Na^+-DB18C6[8a] and is reminiscent of the arrangement of the naturally occurring nonactin complex, making for an interesting comparison.

The solubilities of these molecules place some restriction on the choice of solvents. For this reason pure water could only be used when studying B18C6. However, by employing mixed water–acetone solvents, information on the effect of water on the properties of the other cyclic ethers in question could be obtained. Acetone was chosen as the primary solvent because it is a polar solvent with a high dielectric constant in which all of the species of interest were sufficiently soluble for ^1H NMR studies. Chloroform provides a low dielectric constant solvent of the type used in extraction studies and is a possible approximation for the interior of lipid membranes.

Experimental Section

DB18C6, B18C6, DB30C10, and the complex $(DB18C6)_2$-CsI were a generous gift of H. K. Frensdorff of the Du Pont Company. These compounds were used as received.

KCNS, $KClO_4$, and NaSCN were reagent grade from Mallinkrodt Co.; KI and NaI were reagent grade from Baker Chemical Co.; reagent grade $NaClO_4$ was from ROC/RIC Co. $Ba(ClO_4)_2$ was prepared by George Rossman at Caltech and was in excess of 99% pure.

Acetone-d_6 was purchased from Diaprep and Merck Co.; chloroform-d was purchased from Merck and D_2O was from Columbia Organic Co. Initially, care was taken to dry the acetone-d_6 with $CaSO_4$ or over molecular sieves. It was found, however, that using this solvent directly from the manufacturers' sealed vials gave the same results. Any contribution of water from the salts was negligible. When acetone and chloroform are mentioned as NMR solvents in this work, it is the deuterated form that is being referred to.

All crown ethers and salts were independently soluble enough in

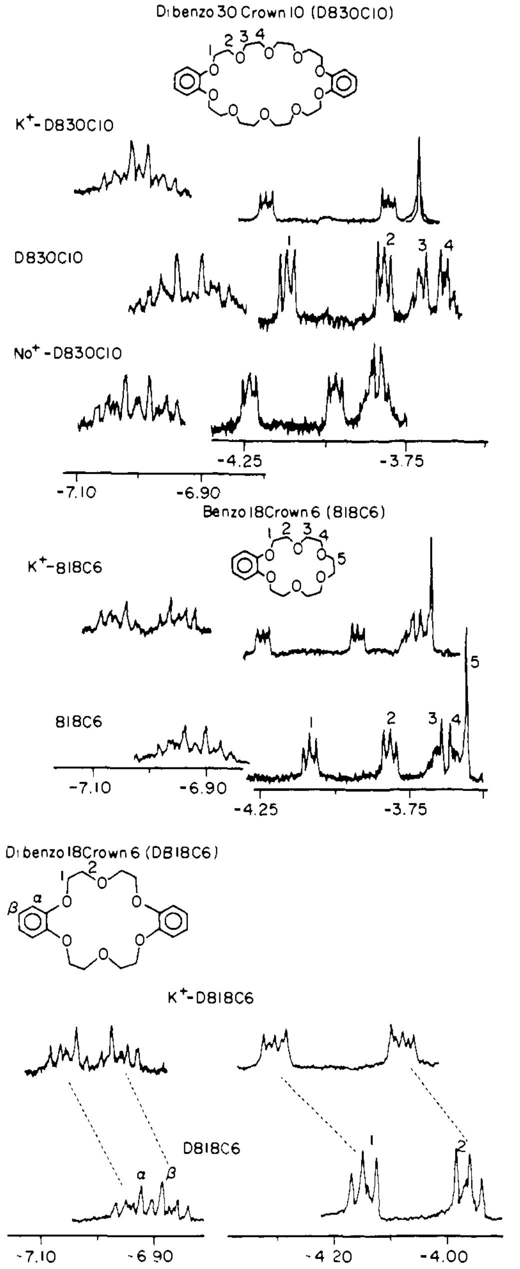


Figure 1. ^{1}H NMR spectra of dibenzo-18-crown-6 (DB18C6), benzo-18-crown-6 (B18C6), and dibenzo-30-crown-10 (DB30C10), and their KSCN or NaClO$_4$ complexes in acetone-d_6. Shifts are relative to Me$_4$Si.

acetone to perform the ^{1}H NMR experiments. Complexes in CDCl$_3$ were made by evaporating the acetone and redissolving the crystalline complex in CDCl$_3$ where possible.

With the exception of the DB18C6/Cs$^+$ binding curve, where the Cs$^+$ concentration was held constant and the ether concentration varied, all other binding curves were determined at constant ether concentration by varying the concentration of the salt in question.

All NMR spectra were taken on a Varian HR-220 equipped with a Fourier transform accessory for ^{1}H and ^{13}C. The proton spectra were taken at 220 MHz, either in the CW or FT mode at ~15 °C. The ^{13}C spectra were all done in the FT mode at 55.3 MHz and at ~47 °C. Noise and single frequency proton decoupling were used.[10] Assignments of the ^{13}C spectra were made from both resonance and off-resonance decoupling. A Varian 620i computer with 16K memory (8K for FT data) was employed to carry out the Fourier transform. T_1's were determined by progressive saturation and (90°-180°-90°) inversion recovery sequence.[11] Peak intensities were determined by weighing cut-out spectra and the accuracy of T_1 values is estimated to be ±10%. Chemical shifts are good to within ±0.5 Hz for protons and ±1 Hz for carbons; vicinal proton-proton coupling constants are good to ±0.2 Hz. A negative shift indicates a downfield shift.

Results and Discussion

Uncomplexed Crown Ethers. DB18C6 has the simplest spectrum of the cyclic ethers studied (Figure 1). However, all of the crown ethers we examined exhibit the same basic spectral characteristics. The ^{1}H NMR spectra of DB18C6 in acetone and CDCl$_3$ consist of two multiplets in the ether region at about 4.1 ppm downfield from Me$_4$Si, and another multiplet due to the aromatic protons at about 7.0 ppm downfield from Me$_4$Si. The spectra of B18C6 and DB30C10 in the ether region are more complex due to the greater number of chemically nonequivalent ether fragments (Figure 1). The proton chemical shifts of the various crown ethers in the various solvent systems studied are summarized in Table I.

The main reason for the separation of the ether resonances is the chemical shift anisotropy of the benzo group. However, comparing the shifts of the individual ether protons relative to internal Me$_4$Si, we found that there is also an upfield shift of these resonances in acetone relative to that in CDCl$_3$. This shift is more pronounced at position 2 of DB18C6 and at positions 2, 3, and 4 in the cases of B18C6 and DB30C10, the magnitude for these shifts all being about the same (0.06-0.09 ppm). Because of the strong distance dependence of the ring current effect,[9] we feel that this rules out a benzo group reorientation effect. The behavior is attributed to chemical shift anisotropy of the acetone solvent molecules.[12] The effect is stereospecific presumably either because there is preferential orientation of the acetone molecules in the proximity of the ether linkages, or these parts of the crown ether molecule are more exposed to the solvent.

Both the multiplets for the ether and aromatic protons are characteristic of a four-spin AA'BB' coupled system.[13] The aromatic region is typical of the spectra found for 1,2-disubstituted benzenes ($J_{AA'} = 0.2$, $J_{AB} = 8.0$, $J_{A'B} = 1.6$, $J_{BB'} = 7.4$ Hz).[13] These coupling constants show no variation between the various compounds studied or upon ion complexation. The ether multiplet of DB18C6 is typical of what is observed for a XCH$_2$CH$_2$Y fragment undergoing rapid rotamer conversion.[14] On analysis of the coupling constants (Table II) with relations for such systems,[15] it is concluded that the ether fragments are undergoing conversion between the syn- and anti-gauche rotamers. 1,4-Dioxane, which is known to undergo ring inversion resulting in similar rotamer interconversion, exhibits analogous coupling constants.[14] A comparison of the proton vicinal coupling constants for the (C(1), C(2)) and (C(3), C(4)) either fragments of B18C6 and DB30C10 with those of DB18C6 (Table II) show them to be the same, and hence we surmise that the ether fragments in those two molecules are in gauche conformation with rapid interconversion as well.

A lower limit to the rate of interconversion between the gauche rotamers can be estimated from the possible chemical shift difference between the methylene protons within a geminal pair assuming that the crown ring system is frozen in one configuration. Under these circumstances, we expect a chemical shift difference between these protons due to the slightly different juxtaposition of the two methylene protons relative to the benzo groups. The chemical shift difference can be estimated from Johnson and Bovey's[9] theory on the ring current shifts and was found to be ~100 Hz. For these calculations we have used the interatomic distances derived from x-ray data for DB30C10[8d] and DB18C6[8a] and a Dreiding model with all gauche rotamers for DB18C6. Since only narrow resonances are observed in our experiments with uncomplexed molecules, these results indicate that the interconversion between the syn- and anti-gauche rotamers must be faster than 10^3 s^{-1}.

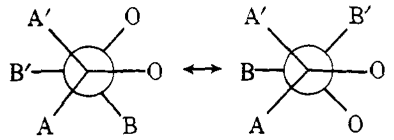
Table I. Proton Chemical Shifts of Uncomplexed Crown Ethers in Various Solvents[a]

Crown ether	Solvent	Ether protons[b] 1	2	3	4	5	Aromatic protons[b] β	α
DB18C6	Acetone	−4.147	−3.965				−6.876	−6.944
	$CDCl_3$	−4.177	−4.041				−6.877	−6.899
B18C6	Acetone	−4.124	−3.852	−3.700	−3.633	−3.596	−6.882	−6.950
	$CDCl_3$	−4.163	−3.930	−3.776	−3.722	−3.692	−6.887	−6.905
	29 mol % D_2O in acetone	−4.149	−3.879	−3.752	−3.688	−3.688	−6.996	−7.032
	D_2O	−4.223	−3.900	−3.727	−3.709	−3.661	−6.898	−6.953
DB30C10	Acetone	−4.131	−3.826	−3.712	−3.632		−6.879	−6.953
	$CDCl_3$	−4.153	−3.887	−3.799	−3.698		−6.881	−6.899
	29 mol % D_2O in acetone	−4.148	−3.859	−3.734	−3.661		−6.896	−6.976

[a] All chemical shifts are given in parts per million and are referred to internal Me_4Si, except in the case of D_2O, where they are referred to DSS. [b] Protons are designated by the number of the carbon to which they are attached (see Figure 1).

Table II. Vicinal Coupling Constants for Ether Fragments (Hz)

Crown ether	Solvent	C(1)–C(2) fragment[a] $J_{A'B}$	J_{AB}	C(3)–C(4) fragment[a] $J_{A'B}$	J_{AB}
DB18C6	Acetone	3.5	5.8		
	$CDCl_3$	3.3	5.7		
B18C6	Acetone	3.3	6.1	3.2	6.2
	$CDCl_3$	3.2	6.1	3.3	6.1
	29 mol % D_2O in acetone	2.5	6.1	3.0	6.1
	D_2O	1.8	6.2		
DB30C10	Acetone	3.1	6.2	3.3	6.0
	$CDCl_3$	3.0	6.0	3.3	6.0
	29 mol % D_2O in acetone	3.0	6.1	3.2	6.0
1,4-Dioxane		2.7	6.05		



[a] $J_{A'B} = J_{AB'}$, $J_{AB} = J_{A'B'}$

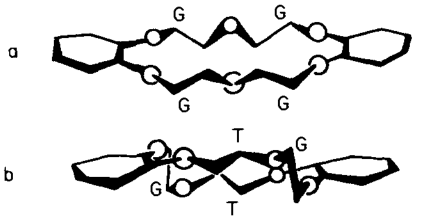


Figure 2. (a) Proposed solution conformation, and (b) x-ray structure (ref 8a) of DB18C6.

Rapid rotamer interconversion of the ether linkage is found in this study for complexed crown molecules, except for some of the ion complexes in $CDCl_3$. In the latter cases, slight broadening is observed in the ether spectrum, suggesting that the rate of rotamer interconversion has become more comparable to the NMR time scale, no doubt a reflection of the slower dissociation rate for the ion complexes in this solvent system.

In contrast to the above conclusion, the x-ray results for the free DB18C6[8a] indicate the presence of both trans and gauche rotamers. Similar studies of DB30C10,[8d] however, show only syn- and anti-gauche rotamers with dihedral angles about 60°, in agreement with our present NMR observations. In the case of DB18C6, aside from the coupling constant data which we have presented above, detailed ring current calculations assuming various configurations also indicate that the observed experimental data here are best accounted for by a rapid interconversion with gauche rotamers. In Table III, for example, we compare the chemical shift difference between C(1) and C(2) (or C(3) and C(4)) protons predicted by two structures, one provided by the x-ray data[8a] and the other, the syn ↔ anti-gauche structural model proposed here (Figure 2), with the observed ether multiplet separation. The experimental result is in closer agreement with our proposed structure. The reliability of these computations can be assessed by performing similar calculations, based on the all-gauche crystallographic structural data for DB30C10.[8d] Excellent agreement is obtained between the calculated and experimental shift difference for the ether multiplet in the C(1)-C(2) fragment here.

A further confirmation of the similarity of the DB18C6, B18C6, and DB30C10 structures is found by combining the shifts of the ether protons in the latter two cases $((\delta_{H_1} + \delta_{H_4}) - (\delta_{H_2} + \delta_{H_3}))$, to estimate the result for ether multiplet separation in DB18C6. This means of combining the shifts compensates for the presence of only one aromatic group in B18C6 and the negligible effect of the more distant aromatic group on the ether proton shifts in DB30C10. Thus H_1 in DB18C6 sees an effect similar to the H_1's in B18C6 and DB30C10 from the proximal benzo group and an additional contribution similar to that seen for the H_4's from the distal aromatic moiety. A similar argument holds for H_2 and H_3. The results for DB30C10 are 50 and 38 Hz in $CDCl_3$ and acetone, respectively, and for B18C6, 46 and 39 Hz for $CDCl_3$ and acetone. There is a close correspondence between these numbers and ether multiplet separation for DB18C6 in Table III.

The spectral parameters for B18C6 and DB30C10 in 29 mol

Table III. Ether Multiplet Separation

Crown ether	Solvent	Experimental $\delta_{H_2}-\delta_{H_1}$	$\delta_{H_3}-\delta_{H_2}$	$\delta_{H_4}-\delta_{H_3}$	Calculated $\delta_{H_2}-\delta_{H_1}$ From proposed structure	From x-ray structure
DB18C6	Acetone	40.0			49	62
	$CDCl_3$	30.0				
B18C6	Acetone	59.8	33.4	14.0		
	$CDCl_3$	57.2	33.8	12.0		
DB30C10	Acetone	67.0	25.2	16.1		61
	$CDCl_3$	58.4	21.6	20.0		

Table IV. Limiting Cation-Induced Shifts for DB18C6 Complexes in Acetone (Hz)

Salt	H_1	H_2	H_α	H_β
KI	-30.3	-23.0	-17.5	-22.6
KSCN	-32.8	-26.2	-18.7	-25.8
$KClO_4$	-32.5	-21.2	-18.9	-25.8
NaI	-23.7	-9.5	-19.1	-14.0
NaSCN	-16.5	-16.6	-11.9	-8.8
$NaClO_4$	-23.7	-8.1	-19.9	-14.8
$Ba(ClO_4)_2$	-77.1	-41.8	-47.8	-37.1

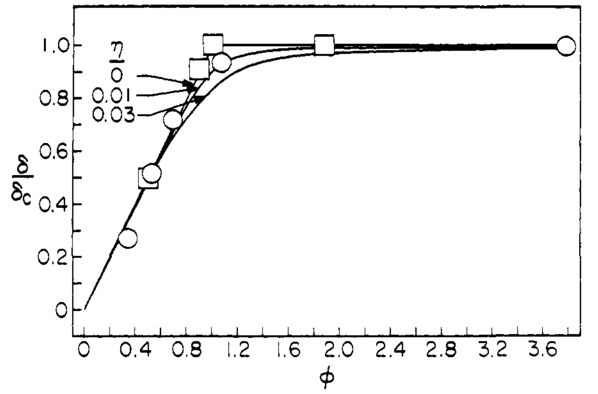


Figure 3. Normalized cation-induced shifts for K^+ (squares) and Na^+ (circles) at various relative concentrations with DB18C6 in acetone-d_6. The average of the normalized shifts for all the protons in the molecule is plotted. For the K^+ plot, KSCN was the salt and the DB18C6 concentration was 6.67×10^{-3} M. $K_{K^+} > 2 \times 10^4$ M^{-1}. For the Na^+ plot, $NaClO_4$ was the salt, and the DB18C6 concentration was 2.5×10^{-3} M. $K_{Na^+} \sim 4 \times 10^4$ M^{-1}. The solid lines are solutions to the equation $\delta/\delta_c = \frac{1}{2}\{(1 + \eta + \Phi) - [(1 + \eta + \Phi)^2 - 4\Phi]^{1/2}\}$ for particular values of η. This equation represents the weighted average of the chemical shifts of the products and reactants for the reaction $I^+ + \text{crown} \rightleftharpoons I^+ \text{crown}$. δ_c is the shift of a particular resonance in the product, δ is observed shift for the same resonance at a given concentration of reactants added, $\eta = 1/(K[\text{crown}_{tot}])$ where K is the equilibrium constant for the reaction, and $[\text{crown}_{tot}]$ is the total concentration of crown ether present. $\Phi = [I_{tot}^+]/[\text{crown}_{tot}]$, where $[I_{tot}^+]$ is the total concentration of the cation present.

% D_2O in acetone are not a great deal different from those observed in acetone (Tables I and II), but when B18C6 is studied in D_2O, the ether coupling constants were found to be significantly different from those observed in the other media (Table II) used in this work. The results in D_2O are much more typical of those found in the ion complexes (vide infra). The formation of a complex with H_3O^+, previously reported for dicyclohexyl-18-crown,[6a] is unlikely here, since the pH of the solution in our studies was neutral. A more likely possibility is the hydration of the ether oxygens.

For DB30C10 and DB18C6 in $CDCl_3$ and B18C6 in $CDCl_3$ and acetone, we have observed no spectral changes over a concentration range of 2×10^{-3} to 2×10^{-1} M, and thus have no evidence for aggregation of the molecules in these solvent systems.

Crown Ether–Ion Complexes in Acetone. K^+. The addition of potassium to DB18C6 in acetone induces two major spectral changes. These are seen in Figure 1 and Table IV. First, although the spectrum retains the AA'BB' character and the feature of gauche rotamer interconversion, the coupling constants change: $J_{A'B} = 2.2 \pm 0.2$ Hz and $J_{AB} = 6.3 \pm 0.2$ Hz. From the well-known relationship between vicinal coupling constants and dihedral angles,[15] it can be deduced that the observed changes in ether coupling constants are consistent with a small increase in the dihedral angle of the OCH_2CH_2O fragment. The ether vicinal coupling constants are the same for all the K^+ complexes of the three cyclic ethers examined in the work.

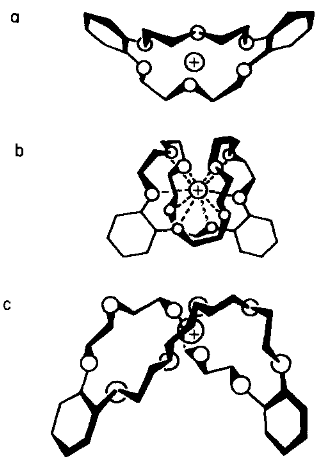


Figure 4. (a) X-ray structure of the (Rb, NaSCN)(DB18C6) complex (ref 8a), (b) X-ray structure of the KI-DB30C10 complex (ref 8d), and (c) proposed solution structure of Na^+-DB30C10 complex.

Secondly, the resonances all shift downfield. The K^+ induced shifts are linear up to a 1:1 K^+-crown ratio, above which no further changes are observed. This is illustrated in the binding curve plotted in Figure 3. On the basis of this result, we conclude that a 1:1 K^+-DB18C6 complex is formed with a binding constant greater than 2×10^4 M^{-1}. Three anions, ClO_4^-, SCN^-, and I^-, were used in these studies and it was found for K^+ complexes that they had little effect on the spectral characteristics of the complexes, indicating that ion pairing is unimportant in this case (Table IV).

The change in dihedral angle upon ion complexation, referred to above, affects the position of the ether protons relative to the benzo groups; this could contribute to the observed salt-induced chemical shifts. This contribution is small, however, compared to the electric field effects arising from the presence of an ion. The chemical shift induced by the presence of an electric field can be calculated using a slightly modified version of an equation first derived by Buckingham.[16]

$$\delta_E = -12.5 \times 10^{-6} \frac{q}{\mathbf{r}^2} \cos\theta + 17.0 \times 10^{-6} \frac{q^2}{\mathbf{r}^4} \qquad (1)$$

where δ_E is the electric field induced chemical shift, q is the ionic charge of the ion, $\mathbf{r}$ is vector measuring the distance between the ion and the proton in question, and θ is the angle between the vector $\mathbf{r}$ and the C–H bond. An estimate of the ion-induced shifts was made for the DB18C6 complexes using the atomic coordinates provided by the x-ray data[6a] (Figure 4). However, such a calculation yielded shifts several times greater than observed. To ascertain if the discrepancy was due to inaccuracies in the theory the incremental shift for substituting an ion +2 in charge for one bearing a +1 charge was calculated and compared with the experimentally observed salt-induced shift between the Ba^{2+} and K^+ complexes of DB18C6. Ba^{2+} was chosen because its ionic radius is only 0.04 Å greater than K^+, and the ion-binding characteristics including the ether coupling constants are the same for both complexes. In addition, virtually identical incremental shifts were observed in acetone and methanol for the substitution, thus ruling out ion pairing and solvent effects. The calculated incremental shift was found to be in reasonable agreement with experiment, (Table V) assuming that the cation is situated in the center of the ether ring. This is the position that Na^+ and K^+ were found to occupy in DB18C6 complexes in Me_2SO.[6b] The lack of agreement between the initial electric field calculation and experiment is thus attributed to a change in the solvent interaction upon complexation of a cation and any change in field due to the reorientation of the ether dipoles.

The K^+ complexes of B18C6 show very similar spectral

Table V. Incremental Shift for Replacing K^+ with Ba^{2+} (Hz)

		H_1	H_2
Observed	DB18C6	−45	−19
	B18C6	−42[a]	−29[a]
Calculated	Cation position relative to ring center, Å		
	0.94	−71.0	21.7
	0.54	−69.6	3.5
	0.0	−63.9	−23.7
	−0.54	−54.5	−41.9
	−0.94	−85.0	−50.0

[a] Average shifts of H_1 and H_4 for H_1 and H_2 and H_3 for H_2.

Table VI. Cation-Induced Shifts for Complexes of B18C6 in Acetone (Hz)

Salt	H_1	H_2	H_3	H_4	H_5	H_β	H_α
KI	−37.2	−24.6	−21.1	−24.8	−27.3	−22.9	−27.5
KSCN	−34.0	−23.5	−19.5	−22.2	−25.8	−19.8	−29.8
$KClO_4$	−33.8	−20.7	−17.8	−21.5	−25.4	−22.4	−27.4
NaI	−21.8	−17.4	−8.1	−15.8	−16.1	−12.7	−14.7
NaSCN	−20.8	−26.1	−9.7	−14.4	−14.8	−16.5	−18.5
$NaClO_4$	−21.5	−16.2	−7.6	−12.5	−15.4	−12.3	−14.3
$Ba(ClO_4)_2$	−69.6	−48.0	−54.1	−69.0	−77.0	−42.1	−57.1

Table VII. Concentration Dependence of Shifts and Coupling Constants for $(CsI)_1(DB18C6)_2$ (Hz)

Solvent	Concn, M	H_1	H_2	H_3	H_4	$J_{A'B}$	J_{AB}
Acetone	9.9×10^{-3}	12.1	−0.2	−11.5	−1.5	2.4	6.4
	4.95×10^{-3}	10.0	−1.6	−13.5	−3.5	2.3	6.3
	1.02×10^{-3}	0.2	−10.2	−9.0	−7.0	2.3	6.3
$CDCl_3$	4.87×10^{-2}	42.7	40.4	7.4	−24.1		
	1.02×10^{-3}	18.2	9.0	7.0	−8.0	2.5	6.0

characteristics in all respects to those of DB18C6 (particularly when the absence of one benzo group is taken into account). The induced shifts are almost the same (Table VI), the ether vicinal couplings are the same, and the incremental shift for replacing K^+ with Ba^{2+} are similar (Table V).

Na^+. The binding of sodium to DB18C6 induces the same general spectral patterns observed for K^+ complexation (Table IV, Figure 3). The ether vicinal coupling constants remain the same as for the K^+ complexes, indicating the same conformation. The salt-induced shifts in the case of the Na^+ complexes tend to be smaller than those observed for the K^+ complexes. There is, for Na^+ complexes, a greater anion dependence than found in the K^+ cases. Complexes with I^- and ClO_4^- anions give one set of results and those with SCN^- give another. It is known that $NaClO_4$ is completely dissociated in acetone while NaI and NaSCN can form ion pairs.[17] We conclude, therefore, that the difference in the shifts is due to ion pairs, only when the SCN^- ion is present.

For B18C6 the Na^+ complexes exhibit the same features as the corresponding DB18C6 complexes, although there is less of an anion effect (Table VI).

The greater solubility of B18C6 complexes has allowed an investigation of those with NaSCN and $NaClO_4$ over a range of 2×10^{-3} to 2×10^{-1} M in acetone. No spectral differences were observed as a function of concentration.

Cs^+. The binding of Cs^+ to DB18C6 in acetone shows unusual behavior compared to those previously examined, as can be seen upon a comparison of the salt-induced shifts presented in Figures 3 and 5 and the data summarized in Tables IV and VII. The nonlinearity of the curves indicates the presence of more than one complex. It was suggested by Pedersen that various stoichiometries might be present for crown ether complexes.[18] These complexes are thought to have a cation sandwiched between two crown ether molecules, but only in cases where the cationic radius is larger than the center cavity of the crown ether ring have such structures been observed. The latter is the case here, as opposed to the situation for Na^+ and K^+.

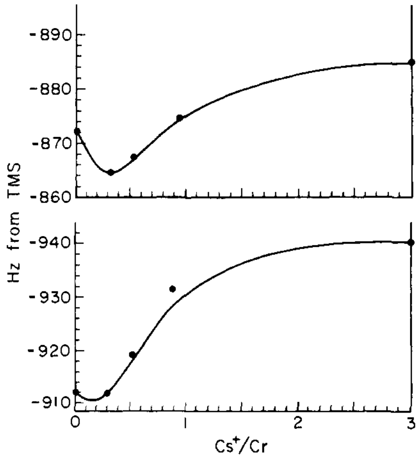


Figure 5. Chemical shift behavior of the ether protons (H_1 lower, H_2 upper graph) on complexation of DB18C6 with Cs^+. Solid curves were calculated from reported equilibria (ref. 5b) as described in the text.

Frensdorff has shown that Cs^+ forms 1:1 and 1:2 Cs^+/crown complexes with DB18C6 in methanol and has obtained equilibrium constants for the formation of these complexes. Assuming this equilibrium is transferable to the present solvent system, namely acetone, we used these data to estimate the relative quantities of DB18C6, $(Cs)_1$ $(DB18C6)_1$, and $(Cs)_1$ $(DB18C6)_2$ under our experimental conditions. By an iterative fitting procedure we derived the following proton chemical shifts for 1:1 and 1:2 Cs^+/crown complexes relative to the free crown ether.

These induced shifts for the 1:1 complex are $H_1 = -40.0$, $H_2 = -19.7$, $H_\alpha = -16.9$, and $H_\beta = -20.1$ Hz, and for the 1:2 complex $H_1 = 6.0$, $H_2 = 10.0$, $H_\alpha = 0.0$, and $H_\beta = -20.0$ Hz. The similarity of the limiting shifts for the K^+ and for the 1:1 Cs^+ DB18C6 complexes would be expected if the Cs^+ occupied a position slightly below the ether ring in the direction of the molecular curvature, and if the conformation is the same as the K^+ complex. This can be concluded by examining trends in the calculated electric field shifts. The upfield salt-induced limiting shifts for the ether protons in the 1:2 Cs^+-crown complex can be explained by sandwiching a Cs^+ between two DB18C6 molecules in the configuration found in the K^+ complex, with one DB18C6 molecule rotated 90° relative to the other. This would place the ether protons of one DB18C6 molecule in the shielding region of the aromatic groups of the other. The upfield chemical shifts of the 1:2 complex relative to the 1:1 complex are in reasonable agreement with the additional ring current effect expected, assuming interatomic distances determined using a CPK molecular model and the absence of appreciable relative rotation of the two crown ether molecules.

The lack of concentration dependence in the ether vicinal coupling constants for $(CsI)_1$ $(DB18C6)_2$ (Table VII) suggests the same ether ring conformation for both 1:1 and 1:2 Cs-crown complexes, and the similarity of these coupling constants with those found for K^+ complexes implies a similar crown ether ring conformation to the other complexes as well.

Crown Ether-Ion Complexes in $CDCl_3$. In $CDCl_3$, the spectra of DB18C6 complexes of K^+ and Na^+ show similar features to those observed in acetone when I^- is the counterion, but different behavior when SCN^- and ClO_4^- are present (Table VIII). In the latter two cases, the C(2) proton reso-

Table VIII. Cation-Induced Shifts for DB18C6 Complex in $CDCl_3$ (Hz)

	H_1	H_2	H_β	H_α
KI	−27.0	−33.0	8.0	−9.0
KSCN	−2.0	−28.2	5.2	−7.8
NaI	−36.2	−28.0	3.5	−11.5
NaSCN	0.8	−29.4	1.5	−9.5
$NaClO_4$	5.4	−24.6	9.9	−5.1

Table IX. Cation-Induced Shifts for B18C6 Complexes in $CDCl_3$ (Hz)

	H_t	H_2	H_3	H_4	H_5	H_β	H_α
KI	−12.2	−25.2	−17.8	−1.2	−10.6	8.7	−10.3
KSCN	−11.2	−8.4	−5.7	1.3	−5.2	3.9	−8.1
$KClO_4$	−7.2	−0.8	3.2	1.3	−3.4	4.8	−3.2
NaI	−13.8	−40.8	−22.6	−2.5	−7.3	8.7	−10.3
NaSCN	−1.6	−21.4	−4.2	3.8	1.8	6.1	−6.9
$NaClO_4$	−7.2	−17.4	−4.2	3.8	1.3	2.7	−6.3

nances shift upfield, but the shifts for protons at C(1) remain essentially unchanged on complexation. This has the effect of collapsing the ether resonances. By contrast, the aromatic resonances of the complexes exhibit about the same separation in $CDCl_3$ as in acetone (cf. Tables I, IV, and VIII).

The salt-induced shift of the ether resonances are a linear function of the ratio of the cation to crown concentration up to the concentration ratio of 1:1, indicating 1:1 stoichiometry as well as rapid cation exchange on the proton NMR time scale. There is some broadening of the KI-DB18C6 resonances, which we attribute to the onset of slow ring inversion. Since the process of ring inversion for the complex would require transient partial release of the ion to the solvent, and $CDCl_3$ is a rather hostile environment for K^+, the most probable mechanism for inversion is collisional exchange between free and complex molecules. It has been found that this exchange process is much slower than that with a favorable solvent.[7c]

The variation of observed shifts with anion is attributed to ion pairing. This effect on the salt-induced chemical shifts can be treated in terms of (i) a DB18C6-cation complex rotating isotropically in a solvent cage with the accompanying anion positioned randomly on the surface of the cage, or (ii) maintaining some fixed position relative to the complex. If we use eq 1 to calculate the contribution of the electric field effect from the anion in the first case, the first term will go to zero, while the second term will go as the average of $\mathbf{r}^{-4}$ over all orientations (here $\mathbf{r}$ is the proton-anion vector). This latter term produces a small upfield shift for both protons. If an anion is positioned for equal times directly above and below the center of the ether ring, then we find a differential effect on the resonances of the ether proton with the C(1) proton having a greater upfield shift than the C(2) protons. The results for complexes with I^- ions approach that for the first model, while the SCN^- and ClO_4^- results are consistent with their center of charge being fixed 4 Å above and below the center of the ether ring.

The coalescence of the ether resonances or broadening discussed above obscure the ether vicinal coupling constants in all cases except the NaI-DB18C6 complex. Here the coupling constants were found to be consistent with what is observed for other complexes.

For B18C6 complexes in $CDCl_3$ the variation of shift with anion is observed (Table IX), though the shifts in the presence of I^- are less like those in acetone than was the case for DB18C6. The changes in the shifts when SCN^- and ClO_4^- are present, relative to those with I^-, do not readily match the calculated effects. This can be due to the asymmetry of the B18C6 molecule, which will affect the anion distribution around it. The ether vicinal couplings are the same as for other complexes.

The KI and NaI complexes of B18C6 have been studied from 2×10^{-3} to 2×10^{-1} M and no noticeable differences were observed.

The ether vicinal coupling constants of $(CsI)_1(DB18C6)_2$ dissolved in $CDCl_3$ are similar to those found in acetone (Table VII), indicating similar complex structures in both media. The concentration dependence of the chemical shifts in $CDCl_3$ suggest multiple stoichiometries. The relatively large shifts on complexation in this media may be due to the presence of additional 2:3 and 1:3 Cs^+/crown complexes.

Crown Ether–Ion Complexes in D_2O–Acetone and D_2O. The induced shifts (Table X) and coupling constants for K^+ and Na^+ complexes of B18C6 in 29 mol % D_2O in acetone were found to be essentially identical with those in pure acetone. In pure D_2O, the shifts are similar although, perhaps, not directly comparable, because of a small solvent effect. The ether coupling constants are also about what is expected for these complexes.

The formation constants for the K^+ and Ba^{2+} complexes in D_2O are approximately 1×10^2 and 5×10^3 M^{-1}, respectively.

Crown Ether–Ion Complexes of DB30C10 in Acetone. K^+. Although there is a great deal of similarity between the observed structural and spectral features of B18C6 and DB30C10 in the uncomplexed form, their potassium complexes show large spectral differences (Figure 1, Table XI). Instead of the downfield salt-induced shifts observed for all the ether resonances in the K^+-B18C6 complex, we find for DB30C10 that only the C(1) and C(4) proton resonances move downfield appreciably upon K^+ complexation, with the C(2) proton peaks actually moving upfield. In addition, the H_3 and H_4 chemical shifts become indistinguishable. This latter result must be due to effects particular to the structure of this complex. We found no appreciable anion effect on the shifts.

The structure derived from x-ray data for the K^+-DB30C10[8d] complex is substantially different from what is found for Na^+-DB18C6[8a] and what we have concluded for the B18C6 complexes. In the DB30C10 case, the cation is completely surrounded by the ether molecule (Figure 4). If we calculate the ring current and electric field contributions to the induced shifts on the basis of the x-ray data for the K^+-DB30C10 complex, we obtain poor agreement with experiment, although the experimental and calculated incremental shift for replacing K^+ and Ba^{2+} do agree well with this structure (Table XII). In the Ba^{2+} complex the "chemical shift equivalence" for the C(3) and C(4) proton persists, although it is slightly broadened, indicating a small inequivalence. This result is consistent with the x-ray structure determination, since the calculated incremental shifts are nearly the same for both C(3) and C(4) protons.

For the Cs^+ complex the same general features as those in the K^+ complex are observed; for this case, however, the H_3 and H_4 resonances are separated by about 7 Hz. This must reflect a small change in the structure needed to accommodate the larger Cs^+ ion in the same general complex conformation.

The coupling constants change on complexation just as they did for the 18-membered ring compounds, as is suggested by the X-ray structure, which shows an increase in the dihedral angle of the OCH_2CH_2O fragment to a little more than 60° in the complex.[8d]

The binding of K^+, Ba^{2+}, and Cs^+ to DB30C10 follow 1:1 stoichiometry with equilibrium constants of $(2.0 \pm 0.5) \times 10^4$ M^{-1} for K^+ and $(1.7 \pm 0.5) \times 10^4$ M^{-1} for Cs^+.

Na^+. Unlike the previous crown ethers examined, the spectrum of the Na^+-DB30C10 complex in acetone does not resemble the one for K^+. The binding constant is substantially lower, being $(3.5 \pm 0.75) \times 10^2$ M^{-1}. The induced shifts for

Table X. Cation-Induced Shifts for B18C6 Complexes in D_2O–Acetone and D_2O (Hz)

Solvent	Salt	H_1	H_2	H_3	H_4	H_5	H_β	H_α
29 mol % D_2O in acetone	KSCN	−29.0	−14.0	−19.6	−24.3	−27.0	−14.1	−30.1
	$NaClO_4$	−15.2	−9.4	−12.0	−12.0	−15.6	−10.0	−19.0
D_2O	KCl	−9.7	−4.0	−8.6	−4.6	−3.5	−15.9	−7.9
	$Ba(ClO_4)_2$	−23.5	−22.0	−29.0	−25.0	−16.0	−21.5	−14.5

Table XI. Induced Shifts for DB30C10 Complexes in Acetone (Hz)

Salt	H_1	H_2	H_3	H_4	H_β	H_α
KI	−14.2	4.8	−1.6	−19.2	−21.4	−16.1
KSCN	−16.2	3.6	−1.6	−19.2	−21.1	−16.1
$KClO_4$	−14.6	4.2	−1.4	−19.0	−20.9	−15.9
$NaClO_4$	−22.3	−31.2	−34.5	−40.3	−19.1	−18.1
$CsClO_4$	−2.5	4.8	−1.6	−12.8	−20.9	−17.9
$Ba(ClO_4)_2$	−80.1	−39.9	−65.1	−82.7	−65.4	−89.4

Table XII. Calculated and Observed Incremental Shifts for DB30C10 Complexes (Hz)

Incremental Shift (Ba^{2+}–K^+)	H_1	H_2	H_3	H_4
Calculated[a]	68	33	48	41
Observed	64	44	63	63

[a] From x-ray structure (ref 8d).

Table XIII. Induced Shifts for DB30C10 Complexes in $CDCl_3$ (Hz)

	H_1	H_2	H_3	H_4	H_β	H_α
KI	−21.6	−26.7	−16.8	3.2	17.6	−4.4
KSCN	−20.6	−27.2	−16.4	3.6	16.3	−4.7
$KClO_4$	−6.6	−6.2	−8.6	1.6	0.3	−0.7

the Na^+ complex are similar to those observed for the 18-membered ring systems (cf. Table IV and XI). Here, however, the magnitudes of the salt-induced shifts are in the order $H_4 > H_3 > H_2 > H_1$. The Na^+ ion is therefore probably closer to H_4 than it is to H_3, and so forth for H_2 and H_1. These differences in spectra suggest different structures for K^+ and Na^+ complexes. This might be expected since the cavity formed by the DB30C10 molecule in the K^+ complex conformation cannot be made small enough to hold the Na^+ ion tightly. On the basis of our spectral data we propose a configuration shown schematically in Figure 4. In this arrangement the cation is always in contact with the two oxygen atoms connected to the C(4)'s and in contact half the time, assuming ring inversion, with each of the oxygens between C(2) and C(3). This provides tetrahedral coordination, and does not require the large conformational changes on complexation that are responsible for the unusual shifts observed for the K^+ complexes.

Our structures for the DB30C10 complexes indicate complete stripping of ion solvation. This is consistent with the result that the binding constant for DB30C10 complexes of K^+, Cs^+, and Na^+ drop by approximately an order of magnitude in 40 mol % D_2O in acetone from what they were in pure acetone. By contrast, the binding of K^+ and Na^+ to DB18C6 in 40 mol % D_2O in acetone and the binding of K^+ and Na^+ to B18C6 in 29 mol % D_2O in acetone remains unchanged (the most meaningful case is Na^+-DB18C6, since for the others we can only set a lower limit to the binding constant). Since one and possibly two molecules of water are coordinated with the Na^+, K^+, and Cs^+ ions in solution for the ratio of D_2O to acetone used here,[19] one expects a decrease of the formation constant of the complex if total stripping of the shell occurs during complexation. On the other hand, DB18C6 and B18C6 would, in the proposed complex configuration, permit coordination of up to two solvent molecules, so that the water molecules need not be stripped from the cation. Accordingly, for the 18-membered ring crown ethers, the formation constant of the complexes may not depend strongly on the water content in the solvent at these levels.

Crown Ether–Ion Complexes of DB30C10 in $CDCl_3$. The chemical shifts of K^+ complexes of DB30C10 in $CDCl_3$ are given in Table XIII. The similarity of the coupling constants in acetone and $CDCl_3$, as well as the retention of shift equivalence for the H_3 and H_4 resonances suggest the same structure in both solvents. The upfield induced shifts of the ether protons for these cases are in contrast to the downfield shifts found for the K^+-DB18C6 and K^+-B18C6 complexes in $CDCl_3$. We attribute this difference to the effect of the counter ion as the I^- and SCN^- complexes give one set of results and the ClO_4^- complexes another. In view of our previous conclusion for DB18C6 we infer that I^- and SCN^- are distributed randomly around these complexes, while the ClO_4^- anion can occupy positions within the four bends of the ether chains and at the top and bottom of the molecule (Figure 4).

^{13}C NMR of Crown Ethers. ^{13}C chemical shifts are known to be sensitive to conformation, and relatively less sensitive to perturbations such as solvent effects, than are proton chemical shifts.[8] Although the understanding of the ^{13}C shifts is not sufficient to establish the details of small structural changes on the basis of those spectral positions of the ^{13}C resonances alone, there are distinctive shifts characteristic of the complexed forms of the crown ethers which present a more simplified picture than the proton results.

The chemical shifts, spectra and peak assignments for the ether region of B18C6 and some of its complexes in $CDCl_3$ and acetone are given in Table XIV and Figure 6. As can be seen, the spectra of the uncomplexed molecule are similar in both solvents. The KI-B18C6 spectra indicate changes on complexation that are alike in both solvents, and are shared by the other complexes in $CDCl_3$ and acetone. From these results we can reaffirm the similarity of the K^+ and Na^+ complexes and of B18C6 itself in both solvents. The chemical shifts of the ether carbons of DB18C6 in $CDCl_3$ are very similar to those for positions 1 and 2 of B18C6 (Table XIV). They also match closely those reported for DB18C6 in CD_2Cl_2.[20] The KSCN-DB18C6 complex indicates the same changes on complexation[20] as B18C6. From this we again conclude that the two ether ring conformations, in the uncomplexed and complexed forms, are the same for both of these molecules.

When free B18C6 is observed in D_2O, we find a spectrum similar to that for the complexed molecule in other solvents (Figure 6), as was also suggested by the ether proton coupling constants. The K^+ complex of B18C6 in D_2O shows almost the same ^{13}C NMR spectrum as the uncomplexed molecule, giving the typical pattern for a B18C6 complex. We can then conclude that the same bound conformation persists in all solvents studied. The D_2O result indicates the rather minor role that the cation plays in the ^{13}C NMR shift as opposed to the effect of conformational changes.

The ^{13}C spectra of B18C6 and DB30C10 (Table XIV) are very similar (Figures 6 and 7), as were the respective ^1H NMR spectra. However, when these molecules are complexed with K^+, the ^{13}C NMR spectra are grossly different, an observation which is consistent with our earlier conclusion of radically different structures in the complexed form.

The ^{13}C spin-lattice relaxation times (T_1's) of DB30C10

Table XIV. ^{13}C NMR Shifts from Me_4Si for B18C6, DB18C6, and DB30C10 in Free and Complexed Form

Crown ether	Solvent	C(1)	C(2)	C(3)	C(4)	C(5)	α	β
B18C6	Acetone[a]	−70.25	−70.49	−71.57	−71.50	−71.50	−115.60	−122.30
B18C6	$CDCl_3$[a]	−69.44	−69.87	−70.20	−70.20	−70.20	−114.50	−121.60
KSCN−B18C6	$CDCl_3$[a]	−67.10	−68.90	−70.14	−70.14	−70.14		
DB18C6	$CDCl_3$	−69.39	−70.19					
DB18C6[b]		−68.80	−70.20				−113.50	−121.30
KSCN−DB18C6[b]	CD_2Cl_2	−67.50	−69.20				−111.60	−121.50
DB30C10	$CDCl_3$[a]	−69.50	−70.30	−71.06	−70.89		−115.20	−121.75
KSCN−DB30C10	$CDCl_3$[a]	−69.40	−69.07	−68.84	−68.80		−116.50	−123.00

[a] Specific assignments for C(3), C(4), and C(5) not made. [b] From ref. 20.

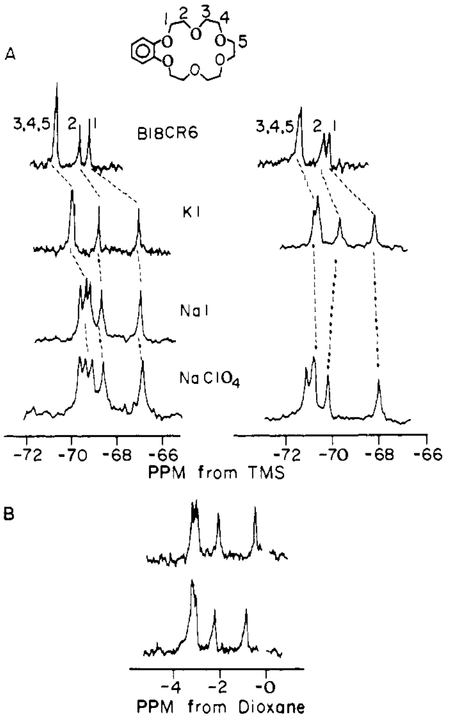


Figure 6. (a) ^{13}C NMR spectra of the ether region of B18C6 and some of its complexes in acetone (right side) and $CDCl_3$ (left side). Shifts are relative to internal Me_4Si. (b) ^{13}C NMR spectra of B18C6 (upper) and KCl-B18C6 (lower) in D_2O. Shifts are relative to dioxane.

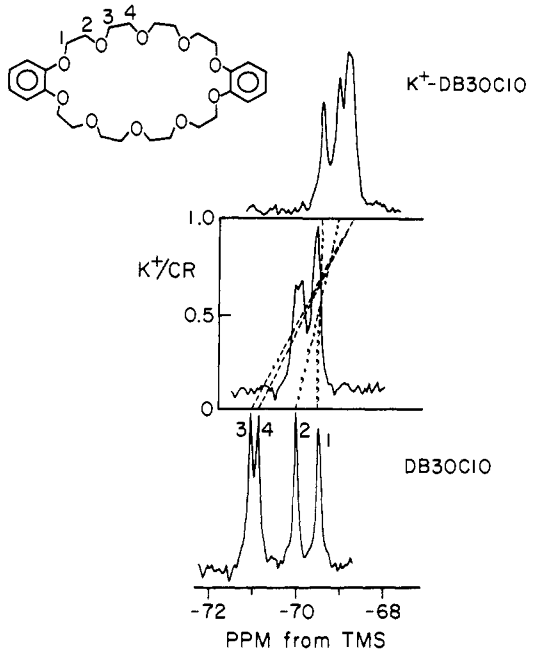


Figure 7. ^{13}C NMR spectra of the ether region of DB30C10 (bottom), 50% K^+ complexed DB30C10 (middle), and KSCN-DB30C10 in $CDCl_3$. Shifts are relative to internal Me_4Si.

have been measured in both free and complexed forms. For uncomplexed DB30C10, the T_1's of all the protonated carbons are very similar, while in the complex the ether carbons relax about twice as fast as the protonated aromatic carbons (Table XV). If the molecule is rigid, and can tumble rapidly and isotropically, the carbon T_1's should be proportional to the number of protons attached.[21] These results thus imply segmental motion in the ether fragments of the free crown ether on a time scale of 10^{-11} s, while on this time scale the complex appears rigid. Fedarko has come to the same conclusions for DB18C6 and its K^+ complex.[20] The ether segmental motion of the uncomplexed molecules may well be related to the inversion of gauche rotamers observed in the proton spectra. This process slows down in the complex to a point where it can no longer contribute to the relaxation process.

Conclusion

We have examined the NMR spectrum of several cyclic ethers and their cation complexes in a number of solvents and have been able to derive a great deal of information on their properties. A summary of the formation constants derived for the various cation complexes is presented in Table XVI.

The chemical shifts and vicinal coupling constants observed for the free crown ethers in the various organic solvents studied here indicate that the OCH_2CH_2O fragments are in an all gauche configuration with rapid conversion between the anti- and syn-gauche rotamers. This is consistent with the crystallographic data for DB30C10,[8d] but not for DB18C6.[8a] There is also apparently some interaction between water molecules and the ether ring, which can affect the dihedral angle of the gauche rotamers. The presence or absence of rigid benzo substituents on the crown ether ring do not seem to affect these structural characteristics. The similarity of the conformation of DB18C6 and B18C6 in the organic and mixed solvents used in this study suggests that the solubility variations between them are due primarily to the ring substituents. This result is consistent with the interpretation of previous extraction studies using dicyclohexyl-18-crown-6 and di(*tert*-butylcyclohexyl)-18-crown-6,[5d] and suggests the possibility of producing crown ethers with specific solubilities without affecting the cation-crown interaction.

The configuration of the complexes of DB18C6 are essentially the same in all solvents used. The complexes exhibit rapid gauche-rotamer interconversion also, although probably at a slower rate than for the free molecule. The solution structure of the complexes of DB18C6 is consistent with the x-ray structure of Na^+-DB18C6,[8a] when the cation is smaller than the ring cavity size. Under these circumstances, only monomeric complexes were found in bulk solution. If the ion-dipole interactions are the dominant force in the crown-cation complexation, then for solvents where the Born relation is at least qualitatively correct, the ion affinity should increase with size in the range of constant complex configuration. This is what has been observed for the 18-membered crown ethers in

Table XV. Carbon T_1's for DB30C10 and DB18C6[a] in Seconds

	Solvent	C(1)	C(2)	C(3),C(4)	α	β
DB30C10	$CDCl_3$	1.18	1.05	0.95	1.01	1.96
KSCN–DB30C10	$CDCl_3$	0.82	0.77	0.73	1.40	1.40
DB18C6	CD_2Cl_2	1.24	1.19		1.72	1.73
KSCN–DB18C6	CD_2Cl_2	0.50	0.50		0.90	1.00

[a] DB18C6 data from ref 20.

Table XVI. Summary of Formation Constants for Various Cation Complexes of Several Crown Ethers

Ion	Crown ether	Solvent	Formation constants, M^{-1}	Ref.
K^+	DB18C6	Acetone	$>2 \times 10^4$	*a*
Na^+	DB18C6	Acetone	$\sim 4 \times 10^4$	*a*
K^+	DB18C6	Methanol	1×10^5	*b*
Na^+	DB18C6	Methanol	2.3×10^4	*b*
Cs^+	DB18C6	Methanol	3.55×10^3 (K_1) 8.32×10^2 (K_2)	*b*
K^+	B18C6	Acetone	$>10^4$	*a*
Na^+	B18C6	Acetone	$>10^4$	*a*
K^+	B18C6	D_2O	1×10^2	*a*
Ba^{2+}	B18C6	D_2O	5×10^3	*a*
K^+	DB30C10	Acetone	2×10^4	*a*
Na^+	DB30C10	Acetone	3.5×10^2	*a*
Cs^+	DB30C10	Acetone	1.7×10^4	*a*
K^+	DB30C10	Methanol	3.98×10^4	*b*
Cs^+	DB30C10	Methanol	1.7×10^4	*b*

[a] Present work. [b] H. K. Frensdorff, *J. Am. Chem. Soc.*, 93, 600 (1971).

acetone, methanol, and water up to Rb^+ (ionic diameter 2.94 Å),[4a] which is in the range of the ether ring diameter for these rings (2.6–3.2 Å).[4a] When the cations are too big to be accommodated within the 18-membered ring, there can exist complexes of various stoichiometries, depending on the solvent.

The K^+, Cs^+, and Ba^{2+} complexes of DB30C10 have conformations in solution that are consistent with the KI-DB30C10[8d] complex in the crystal, but the arrangement of the Na^+-DB30C10 complex is not the same as the others. This indicates the ability of this crown ether to adapt itself to different-sized cations. In all these complexes the cations are shielded from direct access to the solvent. These latter two features are in contrast to what was observed for the 18-membered crown complexes.

Much of the interest in crown ethers stems from their ability to solubilize salts into media where they normally cannot exist. The application of ion-affinity data obtained in high dielectric constant solvents to predict the specificities of extraction into low dielectric constant media is not straightforward. Even though the cation–crown conformation may be the same in both types of solvents, there can be a range of ion pairing tendencies which can modify the extraction, depending on the specific salt and solvent in question, as we have shown. Others have also reported similar ion-pairing effects.[5f,g] Ion pairing should be particularly important for the 18-membered cyclic ethers, since in the monomeric complexes the anion can be in direct contact with the complexed cation. In order to predict the influence of the anion, it is necessary to consider the anion–solvent and anion–complex interactions on the extraction equilibrium.

Carrier-mediated conductance studies with di(*tert*-butylcyclohexyl)-18-crown-6 in model membrane bilayers have suggested that the active species were 3:1 and 2:1 crown–ion complexes for Cs^+, Rb^+, K^+, Na^+, and Li^+.[5d] The presence of such species for K^+ and Na^+ in bulk solution does not seem likely from our results. There is, however, a potentially important difference between the nature of a neutralized complex in a bulk phase and as ion carrier in a bilayer. In the latter medium, particularly at sufficiently low complex concentration, an accompanying anion need not be present.[22] Under these conditions, a charged crown–carrier complex may interact with free crown molecules present via stacking. Further, if the size of the complex were increased by formation of a sandwich-type complex, the Born term in the solvation energy for the complex would be reduced, particularly in a hydrocarbon-like medium. Such "sandwich" complexes are expected for larger ions anyway, and for Cs^+, we have obtained evidence for such stoichiometry in a bulk medium. This hypothesis could explain the contrasting bilayer conductance selectivity ($Cs^+ > Rb^+ > K^+ > Na^+ > Li^+$) and solution ion-affinity data ($K^+ > Na^+ > Cs^+ > Li^+$ in H_2O) for di(*tert*-butylcyclohexyl)-18-crown-6.[5d]

The general structural properties of DB30C10 make it the best choice for comparison with the two naturally occurring ionophores valinomycin and nonactin. From ^{13}C spin relaxation data that we and others[20] have obtained, it is found that there is a greater flexibility of the ring in the uncomplexed cyclic ether than in the natural ionophores. Proton NMR results of DB30C10 complexes in low dielectric solvents indicate that there is fast cation exchange between ether molecules ($>10^3\ s^{-1}$). For valinomycin and nonactin in low dielectric constant solvents, this exchange is too slow for measurement by NMR ($0.0 \pm 0.25\ s^{-1}$ for valinomycin).[23] We, therefore, conclude that the activation energies for complexation and decomplexation in the case of DB30C10 is substantially lower than they are for the two natural ionophores in low dielectric media. In methanol the rates of both complexation and decomplexation for DB30C10 are about an order of magnitude greater than they are for valinomycin. This difference in kinetic behavior may have important implications regarding the biological action of DB30C10 and other cyclic ethers in membrane systems.

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References and Notes

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Carbon-13 Chemical Shifts of the Pentamethylene Heterocycles

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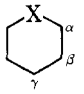
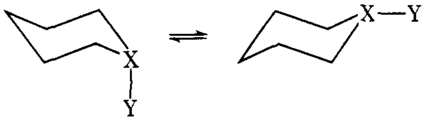
Abstract: Carbon-13 chemical shifts have been measured for the pentamethylene heterocycles from groups 4, 5, and 6. The chemical shifts of the α and γ carbons are governed almost entirely by the electronegativity of the heterogroup at the 1 position, with small direct perturbations due to substituents on the heteroatom. The chemical shift of the β carbons also depends on the heteroatom electronegativity, but the orientation of the substituent at the 1 position (axial or equatorial) provides another major contribution. Thus the β chemical shift is a useful determinant for the conformational preference at the 1 position. Increased heteroatom electronegativity causes a downfield shift for the α carbon but an upfield shift for the β and γ carbons, in the ratio $20/-1/-2$, as derived from the slopes of the chemical shift vs. electronegativity plots. Thus polarization of charge apparently reverses sign between the first (α) and second (β) carbons, with a large dropoff in magnitude, in agreement with the Pople–Gordon theory that requires an alternation of sign. The increase in magnitude of the shift without change of sign between the second (β) and third (γ) carbons is the result of a direct (steric) γ interaction similar to that between a 1-axial group and the β carbon.

Among the pentamethylene heterocycles (**1**) are found the fundamental building blocks for many alkaloids (piperidine) and for the pyranose sugars (oxane[2] or tetrahydropyran).



1

The series provides an outstanding platform for the study of conformational, structural, and electronic effects by variation of the atom X.[3] Although there have been many studies of the carbon-13 spectra of saturated heterocycles,[4] no investigation has centered on the parent heterocycles, with substituents only on the heteroatom. Systematic studies have been reported on some phosphorinanes,[5] piperidines,[6] and 1,3-dioxanes.[7] With so few data, there have been no attempts to compare effects from group to group and from row to row in the periodic table. This study was designed to survey the full range of pentamethylene heterocycles, with silicon and germanium as representatives from group 4, nitrogen, phosphorus, and arsenic from group 5, and oxygen, sulfur, selenium, and tellurium from group 6. The objective was to assess the factors that influence the chemical shifts of the ring carbons. Changes in bond lengths and bond angles alter the overall shape of the ring. Substituents on the heteroatom influence the ring reversal conformational equilibrium (eq 1). Inductive effects depend on the electronegativity of X and of its substituent(s) Y. The presence of axial substituents on X can affect the shielding of the β carbon. We have gathered chemical shift and relaxation time[8] data and report herein on the interpretation of the shielding parameters.



(1)

Experimental Section

Carbon-13 chemical shifts were measured on a Bruker HFX-90 nuclear magnetic resonance spectrometer operating at 22.628 232 MHz in a single-coil, pulsed mode. Hexafluorobenzene provided a fluorine-19 heteronuclear lock. A Schomandl frequency synthesizer Model ND30M produced the carbon-13 frequency. Pulses were obtained from a Bruker B-SV2 power amplifier, and a second Bruker B-SV2 power amplifier was used for broadband and off-resonance decoupling of protons. Frequency offsets were measured with a Hewlett-Packard Model 5216A frequency counter. A pulse width of 7 μs was found to be optimal for a frequency range of 5000 Hz.

The free induction decay signal was stored in a Fabri-tek (Nicolet) 1074 signal averager with 4095 channels. The dwell time per channel was normally set at 100 μs with zero delay. The 4K free induction decay signal was converted by Fourier transformation to a 2K frequency domain spectrum by a Digital PDP-8/L computer with 4K memory. Data were recorded as the magnitude spectra.

Some carbon-13 spectra were obtained on 5-mm samples fitted by two spacers into 10-mm tubes containing the external lock C_6F_6. The lower Teflon spacer also served as a vortex plug. When sufficient sample was available, the roles were reversed, and the sample was placed in the 10-mm tube and the lock signal in the 5-mm tube. All chemical shifts were referred to internal tetramethylsilane, with allowance for sample geometry.

The number of pulses necessary to obtain a good spectrum varied from 128 to 8000, depending on the concentration of the sample. Time between pulses was normally 0.5 s, but for some samples with long relaxation times the delay time was extended to 20 s.

Most of the samples were available from previous work, or were prepared according to reported procedures.[9-15] Details may be found elsewhere.[4b] 1,1-Dimethylsilinane was obtained from Aldrich. 1,1-Dimethylgerminane was prepared by the method of Mazerolles.[16]