NMR studies on the Li$^+$ and Na$^+$ complexes of dibenzo-14-crown-4 lariat ethers†

Zhihong Chen,[a] Peter J. Moehs[b] and Richard A. Sachleben*[a]

[a] *Chemical and Analytical Sciences Division, Oak Ridge National Laboratory, PO Box 2008, Oak Ridge, TN 37831-6119, USA*

[b] *Department of Chemistry, Saginaw Valley State University, 7400 Bay Road, University Center, MI 48710, USA*

The Li$^+$ and Na$^+$ complexes of a series of substituted dibenzo-14-crown-4 ethers bearing alkyl, ether, hydroxylic and carboxylic functional groups have been investigated in solution by ^{1}H and ^{13}C NMR spectroscopy. As was found previously for the uncomplexed ligands, the orientation of the sidearm relative to the crown cavity in the complexes depends on the nature of the atom linking the sidearm to the macrocyclic ring. Most significantly, when the sidearm is attached to the macrocyclic ring through an ether linkage the sidearm is oriented towards the cavity, resulting in intramolecular interactions between the bound carbon and secondary donor groups on the sidearm, which appear to be stronger for sodium than for lithium.

Introduction

Advances in the ionic recognition of Group 1 and 2 metals by synthetic ionophores[1,2] owes much to the discovery of crown ethers[3] and related macrocyclic compounds.[4–6] The subsequent development of lariat ethers and ionizable lariat ethers was driven by efforts to increase both binding strength and ion-specificity.[7–9] Despite the proliferation of research in this area, the factors that influence interactions between a coordinated cation and secondary donor groups of lariat ethers are not well-understood.[8] This is due in part to the flexibility of most crown ethers;[1,10] the introduction of substituent groups can strongly influence the preferred conformations of lariat ethers,[8,11] while the nature of the linkage of the sidearm has a significant effect on the interaction of secondary donor groups with the macrocyclic cavity.[8,12,13] Both inter- and intra-molecular interactions can compete for binding with a complexed cation.[12,13] In a continuing effort to better understand cation binding by ionizable lariat ethers, we have been investigating the conformational preferences of lariat ethers based on the rigid dibenzo-14-crown-4 framework;[12,13] specifically, the effect of sidearm orientation on the discrimination between lithium and sodium cations.

The significant interest in crown ethers as lithium ionophores has resulted from the important applications of lithium in science, medicine and technology.[14] The 14-crown-4 system has received particular attention[9,15–21] because of its nearly optimal cavity size for complexation of the lithium cation.[3,9,16,20] Within the 14-crown-4 ether family, dibenzo-14-crown-4 (DB14C4) and its derivatives are known to be highly preorganized for cation complexation;[21b,22] these molecules adopt a V-shape, where the two planar halves intersect at an angle of 118–138° and the oxygens are arranged to form the base of a square pyramid when complexed to a guest molecule or ion (*e.g.* H_2O, Li$^+$ or Na$^+$).[12,21,22] This arrangement provides a particularly attractive environment for complexation of Li$^+$, since most Li$^+$ complexes are four- or five-fold coordinate and the most selective Li$^+$ ionophores exhibit either four-fold tetrahedral or five-fold square pyramidal coordination.[23]

Numerous *sym*-DB14C4 lariat ethers bearing proton-ionizable sidearms have been studied for the selective complexation and extraction of lithium.[9,24–26] The extraction properties of these compounds are expected to be strongly influenced by the orientation of the ionizable sidearm relative to the crown cavity.[8,11] Structural studies of substituted DB14C4 ethers in solution[13a] and of DB14C4 ethers and their complexes in the solid state,[12,21] have indicated that the preferred orientation of the sidearm is determined by the linkage between the sidearm and the ring. When the sidearm is attached to the macrocycle *via* an ether oxygen, it adopts a conformation which orients it towards the cavity of the macrocycle. Conversely, substituents attached by a carbon linkage prefer a conformation where the sidearm is directed away from the cavity. Solvent extraction studies have shown that the mode of attachment of the sidearm to the dibenzo-14-crown-4 ether ring has a significant effect on the cation selectivity and the extraction efficiency of these ligands; for example, bis-*tert*-octylbenzo-14-crown-4-acetic acid (*tert*-octyl = 1,1,3,3-tetramethylbutyl) exhibits lithium selectivity, whereas bis-*tert*-octylbenzo-14-crown-4-oxyacetic acid extracts sodium and potassium preferentially over lithium[26] (compounds **5** and **9**, respectively). Studies of related dibenzo-14-crown-4-oxyacetic acids have also suggested a dependence of the lithium selectivity on the conformation of the sidearm.[16b] Previous work has shown NMR to be a powerful tool for studying the conformations of lariat ethers and their complexes in solution.[13,27] In a continuation of our previous conformational study of DB14C4 lariat ethers,[13a] we have investigated the complexation of the lariat ethers **1–9** with lithium and sodium ions in solution by ^{1}H and ^{13}C NMR spectroscopy.

Results and discussion

The ^{1}H and ^{13}C NMR spectra of the compounds **1–9** were recorded in [^{2}H$_6$]acetone, with and without added alkali metal salts. The proton resonances were partially assignable by simple inspection; 2D COSY and TOCSY experiments were performed to complete the assignments. The chemical shifts for protons on C1, C2, C9, C10, C11 and C12 are reported in Table 1. The proton coupling constants between protons on C9 and C10 (Table 2) were obtained by direct measurement from 1D spectra where possible, and the remaining measurements were obtained using computer simulation.[28] 2-D ROESY experiments were used to obtain the dipolar proton coupling data shown in Table 3. The complete ^{13}C assignments (Table 4) were made using DEPT and/or HETCOR.

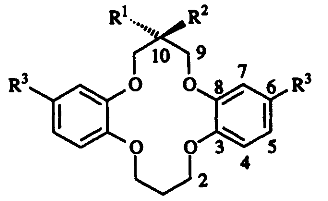
---

† Abbreviations: 14-crown-4: 1,4,8,11-tetraoxacyclotetradecane; dibenzo-14-crown-4: 6,7,8,15,16,17-hexahydrodibenzo[*b*,*i*][1,4,8,11]-tetraoxacyclotetradecine.

Table 1 ^1H chemical shifts of 1–9 and their complexes with $LiClO_4$ and $NaClO_4$ in [$^1H_6$]acetone at 303 K

Compound	1-H[a]	2-H[a]	9-H[a]	10-H	11-H	12-H
1	2.18	4.24	*b*	*b*	—	—
1–Na	2.39	4.32	*b*	*b*	—	—
1–Li	2.52	4.48	*b*	*b*	—	—
2	2.19	4.21/4.25	4.04/4.16	2.34	1.14	—
2–Na	2.28/2.48	4.21/4.36	4.06/4.23	2.57	1.13	—
2–Li	2.40/2.59	4.34/4.58	4.16/4.42	2.78	1.18	—
3	2.18	4.22	4.18	2.43	1.81	3.75
3–Na	2.28/2.48	4.20/4.42	4.07/4.38	2.70	1.74	3.74
3–Li	2.68/2.49	4.36/4.60	4.25/4.59	2.92	1.80	3.81
4	2.21	4.23	4.23	2.67	2.67	—
4–Na	2.38/2.27	4.25/4.32	4.19/4.34	2.85	2.65	—
4–Li	2.53	4.36/4.62	4.34/4.57	3.14	2.69	—
5	2.19	4.25	4.16/4.25	2.67	2.67	—
5–Na	2.31/2.22	4.24/4.26	4.22/4.35	2.80	2.65	—
5–Li	2.54/2.40	4.34/4.53	4.36/4.59	3.07	2.68	—
6	2.21	4.20/4.24	4.16/4.26	4.25	—	—
6–Na	2.38/2.69	4.13/4.54	4.33/4.53	4.62	—	—
6–Li	2.38/2.60	4.34/4.52	4.43/4.47	4.56	—	—
7	2.22	4.22	4.16/4.26	3.85	3.50	—
7–Na	2.39/2.63	4.13/4.54	4.30/4.72	4.20	3.61	—
7–Li	2.36/2.62	4.32/4.61	4.47/4.73	4.22	3.48	—
8	2.22	4.22	4.18/4.28	4.02	3.77	3.69
8–Na	2.36/2.58	4.13/4.50	4.31/4.68	4.36	3.87	3.75
8–Li	2.38/2.65	4.29/4.60	4.54/4.72	4.49	3.84	3.78
9	2.30	4.26	4.33/4.43	4.14	4.42	—
9–Na	2.39	4.09/4.54	4.39/4.79	4.46	4.48	—
9–Li	2.39	4.09/4.54	4.39/4.79	4.46	4.48	—

[a] Separate resonances for axial and equatorial protons are given when resolved. [b] H-1 ≡ H-10 and H-2 ≡ H-9 in **1**.



1

1 $R^1 = R^2 = R^3 = H$

2 $R^1 = \overset{11}{CH_3}, R^2 = R^3 = H$

3 $R^1 = \overset{11}{CH_2}\overset{12}{CH_2}OH, R^2 = R^3 = H$

4 $R^1 = \overset{11}{CH_2}\overset{12}{CO_2H}, R^2 = R^3 = H$

5 $R^1 = \overset{11}{CH_2}\overset{12}{CO_2H}, R^2 = H,$
$R^3 = \overset{13}{C}(\overset{14}{CH_3})_2\overset{15}{CH_2}\overset{16}{C}(\overset{17}{CH_3})_3$

6 $R^1 = H, R^2 = OH, R^3 = H$

7 $R^1 = H, R^2 = O\overset{11}{CH_3}, R^3 = H$

8 $R^1 = H, R^2 = O\overset{11}{CH_2}\overset{12}{CH_2}OH, R^3 = H$

9 $R^1 = H, R^2 = O\overset{11}{CH_2}\overset{12}{CO_2H},$
$R^3 = \overset{13}{C}(\overset{14}{CH_3})_2\overset{15}{CH_2}\overset{16}{C}(\overset{17}{CH_3})_3$

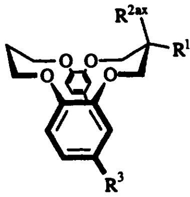
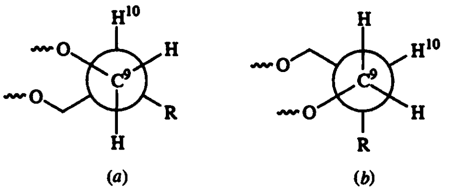


Fig. 1 Conformation of substituted dibenzo-14-crown-4 ethers



(*a*) (*b*)

Fig. 2 Newman projections along C-9 and C-10 of substituted DB14C4 ethers

Recently,[13a] we reported that the substituted DB14C4 ethers **1–9** are highly rigid molecules in solution. As found in the solid state,[12,21,22] the benzo groups form the two planar halves of a V with the bridge propylene units oriented in a pseudo-boat conformation (Fig. 1). Substituent groups on C10 can reside in either a pseudo-equatorial position, where the dihedral angle formed with the O–C9 bond of the macrocyclic ring is anti [Fig. 2(*a*)], or a pseudo-axial position where the dihedral angle is gauche [Fig. 2(*b*)]. The preferred position in the uncomplexed crown ethers is determined by the atom attached to C10. The substituent occupies the pseudo-axial position when this atom is oxygen; when this atom is carbon, the pseudo-equatorial conformer is observed. The first objective of the current study was to determine the corresponding conformations of **1–9** in the presence of Li^+ and Na^+.

Previously, we used ^1H–^1H coupling constants and NOE to establish the conformation of the sidearms in **1–9**.[13a] Analysis of the coupling constant data listed in Table 2 and the NOE data in Table 3 leads to similar conclusions for the lithium and sodium complexes of **1–9**. Referring to the Newman projections shown in Fig. 2, we examined the vicinal coupling constants between the proton on C10 with the two protons on C9. The complexes of **2–5** exhibit one larger coupling ($J > 5$ Hz), as expected for an anti relationship, and one smaller coupling ($J < 5$ Hz), as expected for a gauche interaction. The ROESY data for the complexes of **2** and **3** exhibit crosspeaks between the proton on C10 and the equatorial proton on C9, but not to the axial proton on C9. These results are consistent with con-

Table 2 ^1H NMR vicinal coupling constants (J/Hz) of *sym*-dibenzo-14-crown-4 ethers and their complexes with $LiClO_4$ and $NaClO_4$ in [$^2H_6$]acetone at 303 K

Compound	R	J_{9e-10}	J_{9a-10}	Compound	R	J_{9e-10}	J_{9a-10}
2	CH_3	4.9	7.1	**6**	OH	4.7	6.5
2–Na	CH_3	3.9	8.8	**6–Na**	OH	0.8	3.7
2–Li	CH_3	3.2	9.5	**6–Li**	OH	2.4	4.8
3	CH_2CH_2OH	4.8	6.6	**7**	OCH_3	4.9	6.1
3–Na	CH_2CH_2OH	3.5	9.2	**7–Na**	OCH_3	1.0	3.6
3–Li	CH_2CH_2OH	2.9	9.5	**7–Li**	OCH_3	1.2	4.4
4	CH_2CO_2H	*a*	*a*	**8**	OCH_2CH_2OH	5.1	6.2
4–Na	CH_2CO_2H	3.9	7.8	**8–Na**	OCH_2CH_2OH	1.1	4.0
4–Li	CH_2CO_2H	3.2	9.5	**8–Li**	OCH_2CH_2OH	1.0	4.2
5	CH_2CO_2H	*a*	*a*	**9**	OCH_2CO_2H	5.4	5.4
5–Na	CH_2CO_2H	4.2	9.5	**9–Na**	OCH_2CO_2H	1.0	3.8
5–Li	CH_2CO_2H	3.2	9.3	**9–Li**	OCH_2CO_2H	1.6	4.1

[a] Not resolved.

Table 3 Dipolar proton coupling observed in 2-D ROESY spectra of *sym*-dibenzo-14-crown-4 ether complexes with $LiClO_4$ and $NaClO_4$ in [$^2H_6$]acetone at 303 K

Compound	Resonance	Observed ROE cross-peaks[a]	Compound	Resonance	Observed ROE cross-peaks[a]
2–Li	11-H	10 (w)	**2–Na**	11-H	10 (i)
	10-H	9e (w), 11 (w)		10-H	9e (w), 11 (i)
	9e-H	9a (s), 10 (w)		9e-H	9a (s), 10 (w)
	9a-H	9e (s)		9a-H	9e (s)
3–Li	12-H	9e (w), 11 (w)	**3–Na**	12-H	11 (s)
	11-H	12 (w)		11-H	10 (i), 12 (s)
	10-H	9e (w)		10-H	9e (i), 11 (i)
	9e-H	9a (s), 10 (w)		9e-H	9a (s), 10 (i)
	9a-H	9e (s)		9a-H	9e (s)
7–Li	11-H	—	**7–Na**	11-H	—
	10-H	9a (s), 9e (i)		10-H	9a (i), 9e (i)
	9e-H	9a (s), 10 (i)		9e-H	9a (s), 10 (i)
	9a-H	9e (s), 10 (s)		9a-H	9e (s), 10 (i)
8–Li	12-H	9a (w), 11 (s)	**8–Na**	12-H	11 (i)
	11-H	12 (s)		11-H	12 (i)
	10-H	9a (i), 9e (i)		10-H	9a (s), 9e (i)
	9e-H	9a (s), 10 (i)		9e-H	9a (s), 10 (i)
	9a-H	9e (s), 10 (i), 12 (w)		9a-H	9e (s), 10 (s)

[a] s, strong; i, intermediate; w, weak.

former (*a*) and indicate that the substituent on C10 occupies the pseudo-equatorial position. The complexes of **6–9** exhibit two small couplings ($J < 5$ Hz), consistent with two gauche interactions as in conformer (*b*) where the sidearm occupies a pseudo-axial position, which is supported by the ROESY data for the complexes of **7** and **8** which exhibit crosspeaks between the proton on C10 and both protons on C9.

In our earlier report,[13a] we noted that a similarity existed between the conformation of the oxypropylene bridge of DB14C4 and the chair form of cyclohexane and 1,3-dioxane. We demonstrated that despite the differences in the overall ring structure of cyclohexane and DB14C4, a correlation between ^{13}C chemical shifts of C10 with the substituent position for **1–9** could be made, similar to those for axial and equatorial substituents on chair cyclohexane. The ^{13}C chemical shift correlation for C10 in **2**, **3**, **5**, **6** and **9**, relative to C1 of **1**, with and without added $LiClO_4$ or $NaClO_4$, are listed in Table 5, along with the corresponding chemical shift correlations for substituted cyclohexanes. Once again, these data are consistent with our conclusion of a pseudo-axial orientation for **6–9** which have an oxygen atom attached at C10, and a pseudo-equatorial orientation for **2–5**, which have a carbon substituent at C10.

Having established that the overall conformation of the ligands does not change in the presence of added alkali salts, we directed our attention to investigating the effect that the sidearm has on the cation–macrocycle interaction and on the interaction between the sidearm and a complexed cation. Examination of the ^1H chemical shift data (Table 1) shows that all of the hydrogens of the macrocyclic ring exhibit a shift to lower field upon addition of $LiClO_4$ or $NaClO_4$. This down-field shift can be interpreted in terms of decreasing electron density in the macrocyclic ring due to the electron-withdrawing effect of cation complexation by the oxygens of the crown ether. In general, the magnitude of the downfield-shifts should correlate with the strength of the interaction between the cations and crown ethers.[29] For ligands **1–5**, the ^1H chemical shift changes are greater for the lithium complexes than for the corresponding sodium complexes, indicating stronger binding of lithium ion. For compounds **6–9**, however, the ^1H chemical shift changes are similar for lithium and sodium complexes, suggesting similar binding for these two cations.

Interpretation of the ^{13}C chemical shift data is complicated by the fact that ^{13}C resonances are more sensitive to conformation than ^1H resonances.[30] Variations in the observed ^{13}C chemical shifts (Table 3) can be indicative of ligand conformational changes as well as electronic effects due to cation binding. As in the case of the ^1H chemical shifts, a downfield shift of ^{13}C signals will result from decreasing electron density on the carbon atom upon cation complexation. However, an upfield shift can result if the C–C and C–O bonds undergo distortional stresses upon complexation.[30] The different trends for the ^{13}C resonances for **1–9** and their complexes, evident in the data given in Table 2, indicate competing effects on the ^{13}C chemical shifts. The ^{13}C resonances of C1, C3, C4, C7, C8, C10 and C11 are shifted upfield for all these ligands upon complexation with either lithium or sodium ion. The resonances of C2

Table 4 ^{13}C chemical shifts of *syn*-dibenzo-14-crown-4 ethers and the chemical shift changes that occur upon complexation with $LiClO_4$ and $NaClO_4$ in [$^2H_6$]acetone at 303 K; $\Delta\delta < 0$ depicts a shift to higher field[a]

	δ_C											
Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12
1	30.18	67.96	150.76	117.35	122.69	—	—	—	—	—	—	—
1–Na	−0.78	**1.15**	−1.57	−2.83	−0.24	—	—	—	—	—	—	—
1–Li	−1.66	**2.06**	−3.53	−4.85	0.27	—	—	—	—	—	—	—
2	30.30	67.76	150.54	117.40	122.75	122.87	117.95	150.87	73.07	34.65	14.24	—
2–Na	−0.69	**0.90**	−1.10	−2.02	−0.21	−0.26	−2.26	−1.19	**0.82**	−0.60	−0.35	—
2–Li	−1.55	**1.85**	−2.87	−4.10	0.14	0.09	−4.49	−3.05	**1.54**	−1.27	−0.96	—
3	30.27	67.86	150.68	117.30	122.70	122.87	117.89	150.91	71.70	37.13	32.62	60.64
3–Na	−0.97	**1.30**	−1.62	−2.87	−0.27	−0.36	−3.17	−1.72	**1.50**	−0.92	−0.38	−0.42
3–Li	−1.74	**2.07**	−3.43	−4.67	0.20	0.03	−5.11	−3.55	**2.14**	−1.63	−1.04	−0.74
4	30.31	67.89	150.32	116.97	122.59	123.07	118.04	150.92	70.87	36.12	33.15	173.60
4–Na[b]	—	—	—	—	—	—	—	—	—	—	—	—
4–Li	−1.83	**2.01**	−3.20	−4.27	−0.28	0	−5.17	−3.62	**2.21**	−1.01	−0.71	−0.20
5	30.38	67.83	148.69	117.40	120.77	144.53	117.31	149.50	70.89	36.81	33.30	173.63
5–Na	−0.39	**0.52**	−0.70	−1.13	−0.26	−0.07	−1.44	−0.56	**0.58**	−0.37	−0.06	−0.19
5–Li	−1.43	**1.64**	−3.69	−4.01	−0.36	0.47	−4.66	−2.43	**1.80**	−1.27	−0.47	−0.68
6	30.18	68.19	150.73	117.30	122.70	122.90	117.90	151.25	73.06	69.57	—	—
6–Na	−1.02	**1.30**	−2.70	−5.71	−0.95	−1.30	−6.32	−2.73	**−1.16**	−2.10	—	—
6–Li	−1.91	**1.85**	−3.51	−5.14	−0.19	−0.42	−6.04	−3.62	**−0.39**	−2.77	—	—
7	30.22	67.79	150.06	117.21	122.76	123.47	118.71	151.01	70.54	79.03	57.99	—
7–Na	−1.11	**1.08**	−2.30	−5.43	−0.76	−1.25	−6.47	−2.67	**−0.91**	−2.55	−0.15	—
7–Li	−2.14	**1.97**	−3.13	−4.89	−0.01	−0.39	−6.23	−3.59	**−0.37**	−3.69	−0.75	—
8	30.30	67.78	150.04	117.20	122.19	123.51	118.74	151.00	70.90	77.91	72.84	62.34
8–Na	−1.26	**1.36**	−2.45	−5.29	−0.28	−1.47	−6.34	−2.79	**−1.30**	−3.21	−1.99	−0.79
8–Li	−2.02	**2.07**	−3.16	−4.79	0.34	−0.71	−6.29	−3.57	**−1.05**	−4.20	−2.99	−0.65
9	30.18	67.67	148.38	115.97	120.97	144.45	117.13	148.91	70.88	78.24	68.05	171.97
9–Na	−1.02	**1.35**	−2.30	−5.46	−1.57	−0.41	−5.47	−1.77	**−1.24**	−2.28	−1.44	0.69
9–Li	−1.61	**2.02**	−2.86	−4.35	−0.66	−0.40	−5.05	−2.18	**−0.89**	−3.28	−1.64	0.89

[a] $\Delta\delta_C$ for C-2 and C-9 of the Na and Li complexes are shown in bold. [b] ^{13}C chemical shifts were not obtained due to the low solubility of the complex in [$^2H_6$]acetone.

Table 5 ^{13}C NMR substituent shift correlations for cyclohexanes, dibenzo-1-4-crown-4 ethers and dibenzo-14-crown-4 ether complexes

			Cyclohexane[a]		
Compound	R	Solvent	ax	eq	Dibenzo-14-crown-4[b]
2	CH_3	$CDCl_3$	1.5	6.0	4.5
2	CH_3	[$^2H_6$]Acetone			4.5
2–Na	CH_3	[$^2H_6$]Acetone			4.7
2–Li	CH_3	[$^2H_6$]Acetone			4.9
3	CH_2CH_2OH	$CDCl_3$			6.6
3	CH_2CH_2OH	[$^2H_6$]Acetone			6.9
3–Na	CH_2CH_2OH	[$^2H_6$]Acetone			6.8
3–Li	CH_2CH_2OH	[$^2H_6$]Acetone			7.0
4	CH_2CO_2H	$CDCl_3$			6.5
4	CH_2CO_2H	[$^2H_6$]Acetone			6.0
4–Na	CH_2CO_2H	[$^2H_6$]Acetone			*c*
4–Li	CH_2CO_2H	[$^2H_6$]Acetone			6.6
5	CH_2CO_2H	$CDCl_3$			5.9
5	CH_2CO_2H	[$^2H_6$]Acetone			6.6
5–Na	CH_2CO_2H	[$^2H_6$]Acetone			7.0
5–Li	CH_2CO_2H	[$^2H_6$]Acetone			7.0
6	OH	$CDCl_3$	39.0		38.6
6	OH	[$^2H_6$]Acetone		43.0	39.4
6–Na	OH	[$^2H_6$]Acetone			38.1
6–Li	OH	[$^2H_6$]Acetone			38.3
7	OCH_3	$CDCl_3$	47.0		48.0
7	OCH_3	[$^2H_6$]Acetone		52.0	48.9
7–Na	OCH_3	[$^2H_6$]Acetone			47.1
7–Li	OCH_3	[$^2H_6$]Acetone			46.8
8	OCH_2CH_2OH	$CDCl_3$	47.0		48.1
8	OCH_2CH_2OH	[$^2H_6$]Acetone		52.0	47.7
8–Na	OCH_2CH_2OH	[$^2H_6$]Acetone			45.3
8–Li	OCH_2CH_2OH	[$^2H_6$]Acetone			45.2
9	OCH_2CO_2H	$CDCl_3$	46.0		48.5
9	OCH_2CO_2H	[$^2H_6$]Acetone		52.0	48.1
9–Na	OCH_2CO_2H	[$^2H_6$]Acetone			46.6
9–Li	OCH_2CO_2H	[$^2H_6$]Acetone			46.4

[a] $\Delta\delta$ from unsubstituted cyclohexane. [b] $\Delta\delta$ from dibenzo-14-crown-4. [c] ^{13}C chemical shifts were not obtained due to the low solubility of the complex in [$^2H_6$]acetone.

and C9 in the lithium and sodium complexes of **1**–**5** all exhibit downfield shifts. In **6**–**9**, an upfield shift of C9 was observed in contrast to the downfield shifts of C2, and this upfield shift is greater for the sodium complexes than for the lithium complexes.

These results suggest that **6**–**9** undergo conformational changes upon complexation that are having a unique effect at C9. An obvious source of this effect is the sidearm attached to C10. In each of **6**–**9**, the sidearm occupies the pseudo-axial position and contains an ether group linking it to the macrocyclic ring at C10. This ether group presents a potential coordination site for an ion bound in the crown ether cavity and is, in fact, coordinated to the sodium cation in the crystalline complex of sodium dibenzo-14-crown-4-oxyacetate.[12b] It is reasonable to conclude from these NMR data that in solution the ether oxygen on C10 in **6**–**9** is interacting with the cation complexed in the crown cavity and that it interacts more strongly with Na^+ than with Li^+.

Finally, the question remains whether the functionality (hydroxylic or carboxylic) at C12 in **3**, **4**, **5**, **8** and **9** interacts with the complexed cation. The pseudo-equatorial orientation of the sidearm in **3**, **4** and **5** precludes intramolecular coordination.[12b] On the other hand, it is not unreasonable to look for interactions with a complexed cation by the terminal functionality in **8** and **9**. The upfield shifts of C11 in **8** and **9** are larger than the corresponding shifts in **2**–**5** and **7**. In addition, the carboxylate carbon in **9** (C12) exhibits a downfield shift, in contrast to the upfield shift observed for C12 in **5**. Thus, the hydroxy group in **8** or the carboxylic acid group in **9** may be coordinating directly to the cation through oxygen, or alternatively, interacting *via* hydrogen-bonding to the perchlorate anion of a complexed ion-pair. In either case, participation of the sidearm in cation complexation is expected to influence both the selectivity and strength of cation binding by these lariat ethers.

Conclusion

All the results we have obtained from both ^1H and ^{13}C NMR studies indicate that no overall conformational changes of the crown ring occur upon complexation of **1**–**9** with lithium or sodium perchlorate, and the orientation of the sidearm is the same in both the free ligands and in the complexes. The preference for lithium binding by **1**–**5** in acetone, as indicated by the ^1H chemical shift results, is consistent with the selectivities reported for DB14C4 ethers in the literature. On the other hand, the ether oxygen on C10 in **6**–**9** provides a secondary donor group which is known to coordinate to Na^+ in the solid state.[11] The results presented here provide structural evidence that the ether oxygen on C10 in **6**–**9** coordinates to the complexed cation in solution and that the cation interacts with the terminal functionality of the sidearm when it is in the pseudo-axial position, but does not do so when the sidearm is in the pseudo-equatorial position. The larger size of the sodium ion, combined with ability of the sidearm in **8** and **9** to wrap around the complexed cation and provide a larger coordination environment, provides a basis for rationalizing the selectivity differences reported for **5** and **9**.

Experimental

The preparations of the crown ethers have been reported elsewhere.[12,13,26] $[^2H_6]$Acetone (99.9%) was purchased from the Cambridge Isotope Laboratory and Aldrich Chemical Company. Solvents were dried over molecular sieves before use. $LiClO_4$ and $NaClO_4$ salts (Aldrich) were recrystallized from deionized water and dried *in vacuo* for 24 h at 110 °C before use.

NMR experiments on **1**–**3** and **5**–**9** were performed on 100 mM solutions of the crown ethers in $[^2H_6]$acetone in 5 mm tubes on a Bruker MSL-400. Spectra of **4** were obtained on 20 mM solutions in $[^2H_6]$acetone. Samples of the complexes were prepared by dissolution of an equimolar quantity of salt in a 100 mM solution of crown ether (20 mM for **4**) in $[^2H_6]$acetone; the solution of **2**·$NaClO_4$ was filtered to remove precipitated complex. Chemical shifts were referenced to tetramethylsilane (TMS). All experiments were conducted at 303 K. 1-D ^1H NMR spectra were obtained at 400.13 MHz using a spectral width of 4000 Hz over 32 K data points. 1-D ^{13}C spectra were obtained at 100.613 MHz using a spectral width of 20 kHz over 32 K data points.

Acknowledgements

This research was sponsored by the Division of Chemical Sciences, Office of Basic Energy Sciences, US Department of Energy, under contract number DE-AC05-96OR22464 with Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. and by an appointment (Z. H. C.) to the ORNL Postgraduate Research Program administered by the Oak Ridge Institute for Science and Education.

References

1 M. Dobler, *Ionophores and Their Structures*, Wiley, New York, 1981.

2 N. S. Poonia and A. V. Bajaj, *Coord. Chem. Rev.*, 1988, **87**, 55.

3 (*a*) C. J. Pedersen, *J. Am. Chem. Soc.*, 1967, **89**, 2495; (*b*) C. J. Pedersen, in *Synthetic Multidentate Macrocyclic Compounds*, eds. R. M. Izatt and J. J. Christensen, Academic Press, New York, 1978, p. 1; (*c*) C. J. Pedersen, *J. Inclusion Phenom.*, 1988, **6**, 337.

4 (*a*) J.-M. Lehn, *Structure and Bonding*, 1973, **16**, 1; (*b*) J.-M. Lehn, *J. Inclusion Phenomon.*, 1988, **6**, 351.

5 D. J. Cram, *J. Inclusion Phenomon.*, 1988, **6**, 397.

6 G. W. Gokel, *Crown Ethers and Cryptands*, ed. J. F. Stoddart, The Royal Society of Chemistry, Cambridge, 1990.

7 (*a*) D. M. Dishong, C. J. Diamond, M. I. Cinoman and G. W. Gokel, *J. Am. Chem. Soc.*, 1983, **105**, 586; (*b*) R. A. Schultz, B. D. White, D. M. Dishong, K. A. Arnold and G. W. Gokel, *J. Am. Chem. Soc.*, 1985, **107**, 6659.

8 G. W. Gokel and J. E. Trafton, in *Cation Binding by Macrocycles. Complexation of Cationic Species by Crown Ethers*, eds. Y. Inoue and G. W. Gokel, Marcel Dekker, New York, 1990, p. 253.

9 R. A. Bartsch, *Solvent Extr. Ion Exch.*, 1989, **7**, 829.

10 I. Goldberg, in *Crown Ethers and Analogs*, eds. S. Patai and A. Rappaport, Wiley, New York, 1989, ch. 6 and 7.

11 Y. Nakatsuji, T. Nakamura, M. Okahara, D. M. Dishong and G. W. Gokel, *J. Org. Chem.*, 1983, **48**, 1237.

12 (*a*) R. A. Sachleben, J. H. Burns and G. M. Brown, *Inorg. Chem.*, 1988, **27**, 1787; (*b*) J. H. Burns and R. A. Sachleben, *Inorg. Chem.*, 1990, **29**, 788; (*c*) R. A. Sachleben and J. H. Burns, *Acta Cryst.*, 1991, **C47**, 1968; (*d*) J. H. Burns and R. A. Sachleben, *Acta Cryst.*, 1991, **C47**, 3339.

13 (*a*) Z. H. Chen and R. A. Sachleben, *J. Chem. Soc., Perkin Trans. 2*, 1994, 537; (*b*) Z. Chen, R. A. Sachleben and B. A. Moyer, *Supramol. Chem.*, 1994, **3**, 219.

14 (*a*) *Lithium—Current Application in Science, Medicine and Technology*, ed. R. O. Bach, Wiley, New York, 1985; (*b*) *Lithium: Inorganic Pharmacology and Psychiatric Use*, ed. N. J. Birch, IRL Press, Oxford, 1988.

15 U. Olsher, *J. Am. Chem. Soc.*, 1982, **104**, 4006.

16 (*a*) B. P. Czech, D. A. Babb, B. Son and R. A. Bartsch, *J. Org. Chem.*, 1984, **49**, 4805; (*b*) R. A. Bartsch, B. P. Czech, S. I. Kang, L. E. Stuart, W. Walkowiak, W. A. Charewicz, G. S. Heo and B. Son, *J. Am. Chem. Soc.*, 1985, **107**, 4997.

17 (*a*) S. Kitazawa, K. Kimura, H. Yano and T. Shono, *J. Am. Chem. Soc.*, 1984, **106**, 6978; (*b*) K. Kimura, H. Yano, S. Kitazawa and T. Shono, *J. Chem. Soc., Perkin Trans. 2*, 1986, 1945; (*c*) K. Kimura, M. Tanaka, S.-I. Iketani and T. Shono, *J. Org. Chem.*, 1987, **52**, 836.

18 K. Suzuki, H. Yamada, K. Sato, K. Watanabe, H. Hisamoto, Y. Tobe and K. Kobiro, *Anal. Chem.*, 1993, **65**, 3404.

19 R. Kataky, P. E. Nicholson and D. Parker, *J. Chem. Soc., Perkin Trans. 2*, 1990, 321.

20 Y. Inoue, T. Hakushi, Y. Liu and L. H. Tong, *J. Org. Chem.*, 1993, **58**, 5411.

21 (*a*) N. K. Dalley, W. M. Jiang and U. Olsher, *J. Incl. Phenom. Mol. Recogn.*, 1992, **12**, 305; (*b*) G. Shoham, W. N. Lipscomb and U. Olsher, *J. Chem. Soc., Chem. Commun.*, 1983, 208; (*c*) G. Shoham, D. W. Christianson, R. A. Bartsch, G. S. Heo, U. Olsher and W. N. Lipscomb, *J. Am. Chem. Soc.*, 1984, **106**, 1280;

(*d*) U. Olsher, F. Frolow, R. A. Bartsch, M. J. Pugia and G. Shoham, *J. Am. Chem. Soc.*, 1989, **111**, 9217; (*e*) U. Olsher, F. Frolow, N. K. Dalley, J. Weiming, Z.-Y. Yu, J. M. Knobeloch and R. A. Bartsch, *J. Am. Chem. Soc.*, 1991, **113**, 6750.
22 R. A. Sachleben and J. H. Burns, *J. Chem. Soc.*, *Perkin Trans. 2*, 1992, 1971.
23 U. Olsher, R. M. Izatt, J. S. Bradshaw and N. K. Dalley, *Chem. Reviews*, 1991, **91**, 137.
24 E. Uhlemann, H. Bukowsky, F. Dietrich, K. Gloe, P. Muhl and H. Mosler, *Anal. Chim. Acta*, 1989, **224**, 47.
25 Y. Habata, M. Ikeda and S. Akabori, *J. Chem. Soc.*, *Perkin Trans. 1*, 1992, 2651.
26 R. A. Sachleben, B. A. Moyer and J. L. Driver, *Sep. Sci. Technol.*, 1995, **30**, 1157.
27 A. Kaifer, H. D. Durst, L. Echegoyen, D. M. Dishong, R. A. Schultz and G. W. Gokel, *J. Org. Chem.*, 1982, **47**, 3195; (*b*) A. Kaifer, L. Echegoyen and G. W. Gokel, *J. Org. Chem.*, 1984, **49**, 3029; (*c*) A. Kaifer, L. Echegoyen, H. D. Durst, R. A. Schultz, D. M. Dishong, D. M. Goli and G. W. Gokel, *J. Am. Chem. Soc.*, 1984, **106**, 5100; (*d*) Y. Li, G. W. Gokel, J. Hernandez and L. Echegoyen, *J. Am. Chem. Soc.*, 1994, **116**, 3087; (*e*) Y. Li and L. Echegoyen, *J. Am. Chem. Soc.*, 1994, **116**, 6832.
28 PANIC: NMR Simulation/Iteration Program, Version 850501, Bruker Instruments Inc., Zurich, 1986.
29 D. Live and S. Chan, *J. Am. Chem. Soc.*, 1976, **98**, 3769.
30 J. B. Stohers, *Carbon-13 NMR Spectroscopy*, Academic Press, New York, 1972.

Paper 6/00175K
Received 4*th January* 1996
Accepted 26*th June* 1996