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Solution structures of alkali metal *sym*-(R)dibenzo-14-crown-4-oxyacetates[1]

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Solution structures of alkali metal *sym*-(R)dibenzo-14-crown-4-oxyacetates with R = $C_{10}H_{21}$ (**L1**X) and R = H (**L2**X) have been probed by ^{1}H and ^{13}C NMR spectroscopy. Analysis of the diastereotopic nonequivalence changes, $\Delta\delta_{AB}$, especially for atoms remote from the sidearm attachment site, provides insight into the preferred orientation of the sidearm in solution. Cooperative metal ion complexation by the crown ether portion of the ligand and the sidearm is evident for all of the salts in $CDCl_3$. Solvent dependence of the structure is noted for the **L2**X salts. In DMSO-d_6 and D_2O, the degree of interaction between the cation and the crown ether moiety varies with the identity of the alkali metal cation. Three different metal ion coordination arrangements are deduced for **L2**Li in $CDCl_3$, DMSO-d_6, and D_2O. The Li^+ is complexed by both the polyether unit and the carboxylate group of the sidearm in $CDCl_3$. In D_2O, the Li^+ is coordinated to the polyether unit and through one or more water molecules to the carboxylate group of the sidearm. In DMSO-d_6, the Li^+ does not associate with the crown ether unit.

Introduction

Lariat ethers (LEs),[2] crown ethers bearing sidearms with potential coordination sites, are an important class of macrocyclic multidentate ligands. Compared to the parent crown ethers, their complexation ability may be enhanced by formation of three-dimensional cavities through sidearm participation. In contrast to rigid three-dimensional ligands, such as cryptands, LEs are flexible and can provide a different array of donor atoms depending on the position of the sidearm. Whether the macrocyclic polyether ring and/or the sidearm participate in metal ion complexation determines the binding properties of the LE. The ability to regulate sidearm participation is central to the development of LE chromogenic and fluorogenic metal ion sensors.[3] Therefore, the assessment of sidearm participation in metal ion complexation is important for the design of new LE reagents with improved properties.

Although X-ray crystallography provides insight into the solid-state structure of a metal ion complex, the structure of the complex in solution might differ due to interaction with solvent molecules. Since complexation and extraction of metal ion complexes take place in the liquid phase, solution structures are of special importance.

Beginning with the work of Live and Chan,[4] NMR spectroscopy has been used widely to study the solution structures of crown ether complexes. Sidearm participation in metal ion complexation by LEs has been assessed by measuring ^{13}C NMR relaxation times,[5] using a lanthanide shift reagent,[6] or studying changes of chemical shifts induced by complexation.[7]

The objective of this investigation was to probe solution structures of metal ion complexes for dibenzo-14-crown-4 (DB14C4) compounds with pendant ionized groups (Fig. 1). In the solid-state structure of lithium *sym*-dibenzo-14-crown-4-oxyacetate (**L2**Li) solvated with 7.5 H_2O molecules,[8] Li^+ was complexed by the crown ether moiety and a water molecule that formed a bridge between the cation and the carboxylate anion. Similar structures with a polar solvent molecule residing between the complexed cation and an anion in the sidearm were found for sodium *sym*-dibenzo-14-crown-4-oxyacetate (**L2**Na) (solvated with 3 EtOH and 0.5 H_2O molecules)[9] and sodium *sym*-dibenzo-14-crown-4-oxymethylphenylphosphinate (solvated with 2 EtOH and 2 H_2O molecules).[10] From the absence of direct interaction between the cation and the ionized sidearm in these solid-state structures it was deduced that the sidearm does not play a role in metal complexation by such DB14C4 compounds,[2a,11] even though they have been shown[12] to be much more effective reagents in metal ion separations by solvent extraction and membrane transport compared to the corresponding unsubstituted crown ethers. Recent NMR studies for complexes of a lipophilic derivative of unionized **L2**H with lithium and sodium perchlorates in solution[13] suggest that "the carboxylic acid group may be coordinating directly to the cation".

We now report the results of our study of solution structures for five alkali metal *sym*-(decyl)dibenzo-14-crown-4-oxyacetates (**L1**X) and five alkali metal *sym*-dibenzo-14-crown-4-oxyacetates (**L2**X) by NMR spectroscopy.

Results and discussion

The ^{1}H NMR spectra for the alkali metal LE carboxylates in $CDCl_3$ differ dramatically from those of the corresponding LE carboxylic acid (Fig. 2). Although the entire spectrum changes significantly, attention is focused primarily on the proton signals for the methylene groups of the macrocyclic polyether unit (2-CH_2, 9-CH_2, and 10-CH_2) and the oxyacetic sidearm (11-CH_2). (See Fig. 1 for the atom numbering scheme.)

sym-(Decyl)dibenzo-14-crown-4-oxyacetates†

Signal assignments and determination of conformation. Each of the **L1**X salts exhibits a different ^{1}H NMR spectrum (Fig. 2). Although the signal shapes are the same for the five alkali metal salts **L1**X, the chemical shifts for their signals vary. Since all five salts are derived from the same ionized species (**L1**$^-$), the spectral differences are attributed to variations in the salt structures. In each spectrum, there is only one single set of signals. This means that conformational transformations in solution are fast on the NMR time scale and the observed signals are due to a

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† IUPAC name is (4-decyl-1,7(1,2)-dibenzena-2,6,8,12-tetraoxacyclododecaphan-4-yloxy)acetates.

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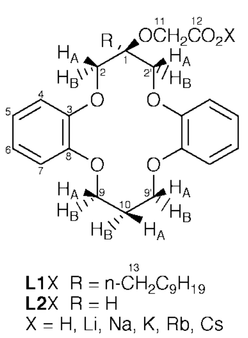

Fig. 1 Atom numbering scheme for the *sym*-(R)dibenzo-14-crown-4-oxyacetates.

weighted average (or, simply, average) conformation.[14a] The conformation of the DB14C4 unit in its LE derivatives in solution as deduced[15] from NMR spectra is wedge shaped, similar to that found in solid-state structures. The average conformation of the DB14C4 unit in salts **L1X** is proposed to be very close to that shown in Fig. 3, conformer A.‡

Since the carbon atom of the macrocyclic ring to which the sidearm is attached is a prochiral center, hydrogens of all methylene groups in the ring are diastereotopic. The nonequivalency of diastereotopic groups in NMR spectra is well known.[14b] Signal assignments in the ^{1}H NMR spectra of the **L1X** salts were made by inspection and verified by ^{1}H–^{13}C HETCOR spectra. In addition to establishing connections between hydrogen and carbon atoms, the HETCOR spectra exhibited a large nonequivalence for the diastereotopic hydrogens bound to the same carbon atom. Together with the ^{13}C spectra, they confirmed the absence of differences between the left and the right hand portions of the salt molecules in solution.

Assignment of signals for diastereotopic hydrogens H_A and H_B was based on NOE experiments. The downfield 2-H doublets have NOE connections with hydrogens on both sidearms, 11-H and 13-H. The upfield doublets have a NOE connection only with the 13-H signals. Therefore, the downfield doublets were assigned to 2-H_A and the upfield doublets to 2-H_B. This is consistent with a structure in which the oxyacetic sidearm occupies a pseudo-axial position. When irradiated at any of the four signal positions for the 9-H and 10-H atoms, NOE signals were observed for the other three positions. In a locked conformation, there would be no significant NOE between vicinal hydrogens in pseudo-axial positions since they are directed away from each other. Also the broadened signals for 9-H and 10-H, indicate a conformational mobility of the unsubstituted three-carbon bridge with interconversion of the 9-H and 10-H atoms in both pseudo-equatorial and pseudo-axial positions (Fig. 3). However, in any conformation only 9-H_A and 10-H_A are located close to the oxyacetic sidearm. Therefore, the downfield signals are assigned to H_A atoms since they should be more affected by a coordinated cation and the ionized sidearm. Although conformational interconversion for this unsubstituted three-carbon atom bridge is evident, the appearance of

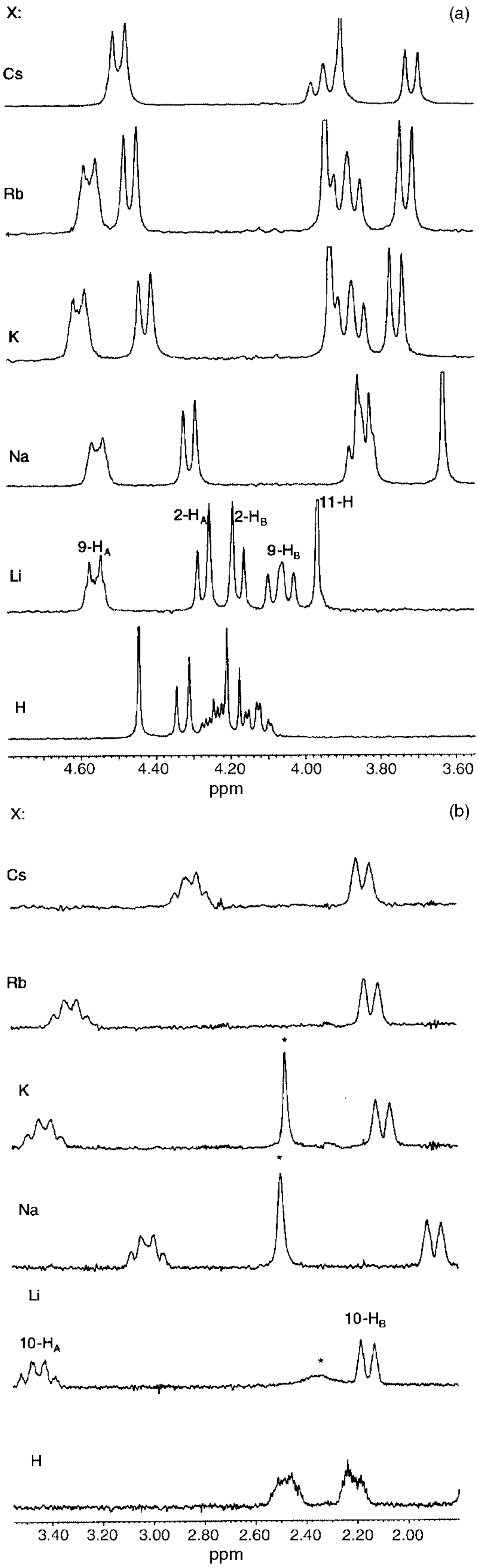

Fig. 2 ^{1}H NMR spectra of the **L1X** salts in $CDCl_3$ (a) for the 4.80–3.55 ppm region and (b) for the 3.50–1.90 ppm region (* identifies the water signal in the latter).

the signals makes it possible to suggest the average conformation. Since the 10-H_A signal is observed as a pseudo-quartet (see Fig. 2b), the atom evidently occupies a pseudo-axial position, thus having large coupling constants with geminal 10-H_B and two vicinal 9-H_B atoms in *anti*-positions. The 10-H_B atom adopts a pseudo-equatorial position, since it appears as a broad

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‡ We feel that it is more correct to refer to the deduced conformation as the weighted average rather than "the only one present in solution",[15] since conformational interconversion does occur at ambient temperature. However, the population of the preferred, wedge-shaped conformation A (Fig. 3), is so dominant that the average conformation is very close to it. Evidence for conformational dynamics of the crown ether ring was obtained by measuring the half-widths of signals in the ^{13}C NMR spectra at different temperatures. In **L1K**, the C-1 signal had half-widths of 2.3 and 1.9 Hz (75.469 MHz) at 293 K and 233 K, respectively. In the same spectra, the C-10 signal had half-widths of 5.4 and 8.9 Hz, respectively. This indicates that C-10 is in fast conformational exchange and C-1 is in slow exchange at 293 K. Thus, differing dynamic conformational behavior was demonstrated for the two three-carbon bridges in the ligand.

Table 1 ^{1}H NMR chemical shifts for selected nuclei of **L1X** in CDCl$_3$

	δ			δ			δ			δ	
X	2-H$_A$	2-H$_B$	$\Delta\delta 2_{AB}$[a]	9-H$_A$	9-H$_B$	$\Delta\delta 9_{AB}$[a]	10-H$_A$	10-H$_B$	$\Delta\delta 10_{AB}$[a]	11-H	13-H
H	4.33	4.20	0.13	4.25	4.13	0.12	2.47	2.21	0.26	4.45	1.77
Li	4.27	4.18	0.09	4.56	4.06	0.50	3.45	2.15	1.30	3.97	1.70
Na	4.31	3.85	0.46	4.56	3.86	0.70	3.02	1.89	1.13	3.63	1.53
K	4.43	3.76	0.67	4.60	3.88	0.72	3.42	2.09	1.33	3.93	1.63
Rb	4.47	3.73	0.74	4.57	3.89	0.68	3.32	2.14	1.18	3.94	1.63
Cs	4.49	3.71	0.78	4.49	3.95	0.54	2.84	2.17	0.67	3.90	1.63

[a] $\Delta\delta_{AB} = \delta H_A - \delta H_B$.

Table 2 ^{13}C NMR chemical shifts for selected nuclei of **L1H** and chemical shift changes[a] for the alkali metal salts **L1X** in CDCl$_3$

X	C-12	C-3	C-8	C-5	C-6	C-4	C-7	C-1	C-2	C-9	C-11	C-13	C-10
H	171.5	150.0	148.1	123.0	121.1	117.1	113.4	80.0	71.5	68.0	61.9	32.3	29.1
Li	2.1	−3.2	−2.3	−1.0	0.3	−6.4	−3.0	−3.7	0.1	1.1	0.1	0.1	−1.7
Na	1.9	−2.5	−1.5	−1.6	−0.5	−5.7	−3.3	−4.0	−0.3	1.2	0.3	0.2	−1.5
K	1.8	−2.1	−0.7	−1.9	−0.5	−5.6	−2.8	−4.2	0.2	1.2	0.3	0.1	−1.4
Rb	1.9	−2.1	−0.5	−2.0	−0.4	−5.6	−2.5	−4.1	0.5	1.0	0.4	0.0	−1.6
Cs	1.9	−2.0	−0.2	−1.8	−0.2	−4.9	−1.5	−3.7	0.6	0.4	0.5	−0.2	−1.3

[a] $\Delta\delta = \delta_{salt} - \delta_{acid}$ and $\Delta\delta > 0$ is a downfield shift.

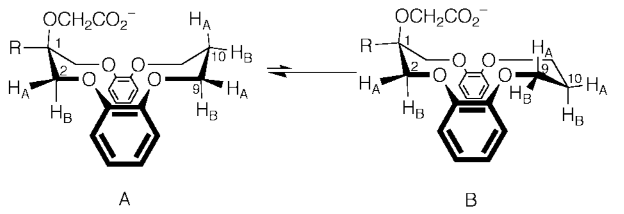


Fig. 3 Two major conformations of the dibenzo-14-crown-4 unit in salts **L1X** and **L2X**.

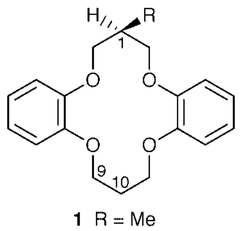
doublet with only one large coupling constant with a geminal hydrogen atom. Similarly, the 9-H$_A$ atoms, which produce a doublet of unresolved multiplets (Fig. 2a), occupy pseudo-equatorial positions and the 9-H$_B$ atoms which produce an overlapped doublet of doublets (observed as a pseudo-triplet) occupy a pseudo-axial position. Thus, the average structure of this three-carbon bridge closely resembles that in conformer A in Fig. 3.[15] The ^{1}H NMR spectral data are presented in Table 1. For the ^{13}C NMR spectral data for salts **L1X** shown in Table 2, the signal assignments were based on the ^{1}H–^{13}C HETCOR and NOE spectra, as well as on literature data.[13,15,16]

Determination of sidearm participation in complexation. Alkali metal cation complexation by the crown ether unit of the ligand is readily evident from the changes in proton and carbon chemical shifts upon salt formation (Tables 1 and 2). However, it is not obvious if the ionized sidearm takes part in the complexation or the shifts in its signals are simply due to its ionization. Therefore, the ^{1}H NMR spectra were examined in detail to determine if the sidearm participates in metal ion complexation.

Chemical shift differences ($\Delta\delta$) for diastereotopic groups depend upon how different are their environments. Although the observance of diastereotopic nonequivalence in salts of proton ionizable LE was interpreted in terms of sidearm participation in metal ion complexation some time ago,[17] this approach was not developed.

In **L1X**, distinctions between the top and bottom of the ligand are produced by the two different sidearms attached to the prochiral center C-1. The location of the sidearms and the cation relative to the cyclic polyether unit and the conformation of the macrocyclic polyether itself contribute to environmental differences for diastereotopic protons and, therefore, to the $\Delta\delta$ values. By analysis of changes in the magnitude of $\Delta\delta$ for hydrogens on different carbons of the crown ether unit with metal ion variation, and taking into account the size of the ions and the conformation of the crown ether unit, insight was provided into the structures of the salts in solution.

Positioning of the cation relative to the crown ether cavity should vary in accordance with the cation-to-macrocycle size fit.[18] For the series of alkali metal ions, only Li$^+$ matches the cavity size of DB14C4. However, it has been shown that in the solid state, even Li$^+$ is positioned slightly above the plane of the four oxygens in **L2Li**.[8] Since the other alkali metal ions are too large to fit within the crown ether cavity, perching complexes must be formed. Accordingly, the metal cation influence upon the $\Delta\delta$ values should increase in order: Li$^+$ < Na$^+$ < K$^+$ < Rb$^+$ < Cs$^+$. For metal ion complexes with DB14C4 LEs, metal ions are positioned with almost equal distances to all four oxygen atoms of the cyclic polyether unit.[8–10] This should produce an equal cation effect on the $\Delta\delta 2_{AB}$ and $\Delta\delta 9_{AB}$ values for conformer A in Fig. 3. On the other hand, the influence of the sidearm upon $\Delta\delta$ will be restricted to neighboring atoms. Its effect on the hydrogens on transannular C-9 and C-10 atoms will be seen only if the sidearm is situated close to these atoms. An indication of the magnitude of the $\Delta\delta 9_{AB}$ and $\Delta\delta 10_{AB}$ values expected to be induced by complexed cations may be obtained from the literature.[13] The effect of short sidearms (R–OH, Me, OMe) in complexes of lithium and sodium perchlorates with DB14C4 LEs (**1**–**3**, respectively) on the remote positions should be minimal, although the position of the anion could contribute to some extent. The $\Delta\delta 9_{AB}$ and $\Delta\delta 10_{AB}$



1 R = Me
2 R = OH
3 R = OMe

Table 3 ^{1}H NMR data for selected nuclei of **L2**X in $CDCl_3$

	δ					δ			δ			δ
X	1-H	2-H$_A$	2-H$_B$	$\Delta\delta 2_{AB}$[a]	$^3J_{1-2}$/Hz	9-H$_A$	9-H$_B$	$\Delta\delta 9_{AB}$[a]	10-H$_A$	10-H$_B$	$\Delta\delta 10_{AB}$[a]	11-H
H	4.22	4.38	4.26	0.12	[b]	4.24		[b]	2.32		[b]	4.39
Li	4.26	4.46 dd	4.28 d	0.18	4.6 (A) 0 (B)	4.46	4.11	0.35	2.98	2.23	0.75	4.18
Na	4.00	4.52 dd	4.00 d	0.52	3.5 (A) 0 (B)	4.18	3.75	0.43	3.03	1.68	1.35	4.02
K	3.78	4.47 dd	3.86 d	0.61	3.0 (A) 0 (B)	4.50	3.84	0.66	3.25	2.11	1.14	4.01
Rb	3.85	4.48 dd	3.88 d	0.70	[b]	4.55	3.86	0.69	3.10	2.14	0.96	4.04
Cs	3.77	4.55 dd	3.85 d	0.70	3.2 (A) 0 (B)	4.38	3.87	0.51	2.73	2.10	0.63	4.00
NMe_4[c]	4.08	4.21 d		0	5.0	4.12		[b]	2.18		[b]	4.05

[a] $\Delta\delta_{AB} = \delta H_A - \delta H_B$. [b] Not determinable. [c] The NMe_4 singlet is at 3.16.

Table 4 ^{13}C NMR chemical shifts for selected nuclei of **L2**H and chemical shift changes[a] for the salts **L2**X in $CDCl_3$

X	C-12	C-3	C-8	C-5	C-6	C-4	C-7	C-1	C-2	C-9	C-11	C-10
H	172.6	149.8	148.2	123.4	121.9	118.3	115.3	78.9	70.4	67.2	67.9	29.3
Li	1.5	−2.4	−1.5	−1.3	−0.2	−5.8	−3.1	−6.0	−1.6	1.2	−0.9	−1.3
Na	1.8	−2.1	−1.2	−2.4	−1.1	−6.9	−4.9	−4.4	−1.5	0.9	1.7	−1.8
K	1.0	−1.8	−0.7	−2.4	−1.3	−6.7	−4.8	−5.4	−1.3	0.8	1.8	−1.3
Rb	1.1	−1.7	−0.4	−2.4	−1.2	−6.6	−4.6	−4.7	−1.5	1.1	2.5	−1.3
Cs	1.4	−1.4	−0.1	−2.3	−0.9	−5.6	−3.0	−3.7	−1.7	1.1	2.9	−1.1
NMe_4	2.1	−0.6	0.7	−1.2	0.2	−1.8	0.3	−3.0	−0.6	−0.1	2.6	−0.1

[a] $\Delta\delta = \delta_{salt} - \delta_{acid}$ and $\Delta\delta > 0$ is a downfield shift.

values observed for these complexes were in the range of 0.15–0.44 ppm.

For **L1**Li, $\Delta\delta 9_{AB}$ is significantly larger than $\Delta\delta 2_{AB}$. The $\Delta\delta 10_{AB}$ value is among the largest in the **L1**X series, which reveals close proximity of the sidearm to the remote positions 9 and 10 of the crown ether ring. Consequently, participation of the carboxylate group of the sidearm in metal ion complexation by the ligand is deduced. As the metal ion size increases, the $\Delta\delta 2_{AB}$ and $\Delta\delta 9_{AB}$ values first become almost equal for **L1**K; then the former becomes larger. This indicates a diminished influence of the sidearm on the $\Delta\delta 9_{AB}$ value, since the larger cations do not allow the sidearm to reach over to remote positions of the crown ether ring. Large $\Delta\delta 10_{AB}$ values (more than 1 ppm for all but the caesium salt), which result from the positions of both the metal ion and the sidearm, provide evidence for the cooperative complexation of all alkali metal ions by the crown ether unit and the sidearm. The decrease in the $\Delta\delta 9_{AB}$ and $\Delta\delta 10_{AB}$ values for **L1**Cs may result not only from a diminished influence of the sidearm, but also by a shift in the conformational equilibrium (Fig. 3). If large Cs^+ produces steric interactions in conformer A, its population might diminish slightly, thereby affecting the average conformation. However, the shapes of the NMR signals for 9-H and 10-H in this salt are essentially the same, indicating that the average conformation is not changed very much.

sym-Dibenzo-14-crown-4-oxyacetates §

Determination of sidearm participation in complexation. The alkali metal *sym*-dibenzo-14-crown-4-oxyacetates **L2**X, in which the geminal alkyl group has been removed, were also investigated. Signal assignments were made in a similar fashion to that described above for the **L1**X salts. The ^{1}H NMR spectral data for **L2**X in $CDCl_3$ are presented in Table 3 and the ^{13}C NMR chemical shift data are given in Table 4.

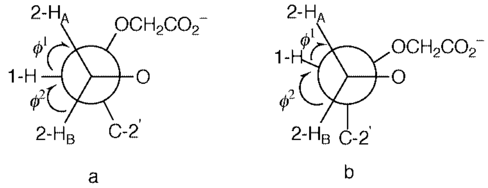


Fig. 4 Newman projection along C-2–C-1 for acid **L2**H and salts **L2**X.

In addition to alkali metal salts, the tetramethylammonium salt **L2**NMe_4 was also studied. This cation was chosen for comparison, since it cannot coordinate with the crown ether portion of the molecule. In agreement, the ^{13}C NMR data show negligible $\Delta\delta$ values for C-9 and C-10, which are remote from the sidearm. This verifies the absence of interaction between NMe_4^+ and the macrocyclic polyether unit. Therefore, it is particularly significant to compare the ^{1}H NMR spectral data for this salt with those for the alkali metal salts.

For this series of LE salts, a hydrogen atom is geminal to the proton-ionizable sidearm. This feature allows information about the sidearm orientation to be obtained from the coupling constants of 1-H with 2-H$_A$ and 2-H$_B$ ($^3J_{1-2A}$ and $^3J_{1-2B}$, respectively), since they are determined by the magnitudes of the corresponding dihedral angles φ^1 and φ^2, respectively, between the coupled atoms (Fig. 4). For the LE carboxylic acid **L2**H, the coupling constants could not be determined in $CDCl_3$ due to strongly overlapping signals. In DMSO-d_6 (Table 5), the equal coupling constants revealed that $\varphi^1 = \varphi^2$, in agreement with the results of a previous study.[15]

From the Karplus equation,[14c] $^3J_{1-2B} = 0$ for the alkali metal salts **L2**X (Table 3) establishing that the corresponding dihedral angle φ^2 is 80–90°, which results from a greater orientation of the sidearm toward the crown ether cavity than in the acid **L2**H. For dihedral angles from 0 to 90°, a larger angle decreases the J value. The $^3J_{1-2A}$ value decreases in the order **L2**Li > **L2**Na > **L2**K (Table 3). This reveals that φ^1 increases in the

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§ IUPAC name is 1,7(1,2)-dibenzena-2,6,8,12-tetraoxacyclododecaphan-4-yloxy)acetates.

Table 5 ^{1}H NMR data for selected nuclei of **L2**X in DMSO-d_6

	δ					δ			δ			δ
X	1-H	2-H_A	2-H_B	$\Delta\delta 2_{AB}$[a]	$^{3}J_{1\text{–}2}$/Hz	9-H_A	9-H_B	$\Delta\delta 9_{AB}$[a]	10-H_A	10-H_B	$\Delta\delta 10_{AB}$[a]	11-H
H	4.03	4.21 d		0	5.5	4.14 m		[b]	2.15 m		[b]	4.29
Li	4.03	4.25 dd	4.15 dd	0.10	4.3 (A) [b] (B)	4.15 m		[b]	2.16[c]		0	3.85
Na	4.08	4.37 dd	4.13 d	0.24	3.5 (A) 0 (B)	4.37	3.97	0.40	2.52	2.16	0.36	3.78
K	3.95	4.46 dd	3.98 d	0.48	3.4 (A) 0 (B)	4.36	3.88	0.48	2.58	2.07	0.51	3.79
Rb	3.93	4.46 dd	3.97 d	0.49	3.6 (A) 0 (B)	4.36	3.90	0.46	2.47	2.11	0.36	3.79
Cs	3.96	4.29 dd	4.10 d	0.19	[b]	4.24	4.05	0.19	2.25	2.15	0.10	3.81

[a] $\Delta\delta_{AB} = \delta H_A - \delta H_B$. [b] Not determinable. [c] Pentet with $^{3}J_{10\text{–}9} = 5.3$ Hz.

Table 6 ^{13}C NMR chemical shifts for selected nuclei of **L2**H and chemical shift changes[a] for the alkali metal salts **L2**X in DMSO-d_6

X	C-12	C-3	C-8	C-5	C-6	C-4	C-7	C-1	C-2	C-9	C-11	C-10
H	171.8	149.4	148.3	122.5	121.5	117.3	115.4	76.2	69.5	67.0	66.8	28.6
Li	0.5	−0.3	0.1	−0.4	0.1	−0.8	−0.1	−1.3	−0.1	0.1	2.5	−0.1
Na	−0.3	−1.9	−1.2	−1.6	−0.6	−5.3	−3.8	−2.3	−1.1	1.2	2.5	−0.9
K	−0.9	−1.5	−0.6	−1.8	−1.0	−5.5	−3.9	−3.0	−1.2	1.3	3.5	−1.2
Rb	−0.9	−1.3	−0.4	−1.8	−0.8	−5.1	−3.4	−2.6	−1.0	1.2	4.0	−1.0
Cs	0.4	−0.7	0.1	−1.1	−0.3	−2.8	−1.3	−1.7	−0.3	0.5	3.6	−0.5

[a] $\Delta\delta = \delta_{salt} - \delta_{acid}$ and $\Delta\delta > 0$ is a downfield shift.

same order. Thus the greatest orientation of the sidearm toward the macrocyclic polyether cavity is observed for the lithium salt. This is consistent with joint participation of the sidearm and the macrocyclic polyether unit in metal ion coordination. It should be noted that this change in the sidearm orientation in alkali metal salts **L2**X compared to the acid **L2**H is not observed for the **L2**NMe_4 salt.

Diastereotopic nonequivalence values, $\Delta\delta_{AB}$, for the **L2**X salts in $CDCl_3$ are given in Table 3. The large $\Delta\delta 10_{AB}$ values observed for the alkali metal salts demonstrate cooperative complexation of all alkali metal ions by the crown ether unit and the sidearm in this series as well. In the **L2**NMe_4 salt, the cation is not complexed by the crown ether unit, so neither the cation nor the sidearm is near the crown ether moiety. The absence of signal separation for the diastereotopic hydrogens observed for this salt illustrates the case in which the effects of both the cation and the sidearm are negligible. This feature will be utilized later. The data obtained for this salt provide another example of how useful the analysis of $\Delta\delta_{AB}$ values can be in probing the solution structures of LEs.

Effect of solvent polarity on LE salt structure. In a comparison of the $\Delta\delta 9_{AB}$ and $\Delta\delta 10_{AB}$ data for the alkali metal salts of **L2**H (Table 3) with those for the salts of **L1**H (Table 1), the magnitude of $\Delta\delta 10_{AB}$ for **L2**Li is somewhat divergent. Probably this results from minor structural differences for the salt, with the cation still coordinated by both the crown ether unit and the sidearm. However, it might also result from a change in the coordination mode to that observed[8] in the solid-state structure for **L2**Li·7.5H_2O in which a water molecule is inserted between the metal ion and the carboxylate group of the sidearm. To check this possibility, and also to probe the effect of solvent polarity on the LE salt structure, the NMR spectra of alkali metal salts **L2**X were measured in the more polar solvents of DMSO-d_6 and D_2O. Upon dissolution of the salts in D_2O, opalescent solutions were produced indicating micelle formation. This opalescence was minor for **L2**Li and **L2**Na, greater for **L2**K and **L2**Rb, and much greater for the **L2**Cs. Broadening of the ^{1}H NMR spectrum for the **L2**Cs in D_2O to an extent that $\Delta\delta_{AB}$ values could not be determined is attributed to this phenomenon. The ^{1}H NMR spectral data for **L2**X in DMSO-d_6 and D_2O are recorded in Tables 5 and 7, respectively. The ^{13}C NMR data in DMSO-d_6 are presented in Table 6.

Significant differences in ^{1}H NMR spectral data for the alkali metal salts **L2**X in the three solvents are clearly evident. Therefore, we conclude that structures of the LE salts may be altered by a change of solvent. The $\Delta\delta_{AB}$ values for the salts are smaller in DMSO-d_6 and D_2O than in $CDCl_3$. In particular, the smaller $\Delta\delta 10_{AB}$ values imply that the oxyacetate sidearm is no longer in close proximity to the 10-H atoms. Also, the data for **L2**Li and **L2**Cs in DMSO-d_6 contrast with those for the other alkali metal salts. The following structure is proposed for **L2**Na, **L2**K, and **L2**Rb in DMSO-d_6 and D_2O and for **L2**Li in D_2O. The metal ion is coordinated by the macrocyclic polyether unit and through one or more solvent molecules to the carboxylate group of the sidearm. The fact that carboxylate group still participates in cation coordination, though *via* one or more bridging solvent molecules, is evident from the $^{3}J_{1\text{–}2B}$ coupling constants. As noted in $CDCl_3$, the change in magnitude of this coupling constant in alkali metal salts **L2**X compared to the acid **L2**H establishes a corresponding change in the sidearm orientation toward the macrocyclic cavity. Thus, the proposed structure is consistent with the observed solid-state structures for solvated **L2**Li and **L2**Na.[8,9]

Marked changes of the NMR spectra for **L2**Li in DMSO-d_6 from that in $CDCl_3$ indicate a different structure. The negligibly small chemical shift changes, $\Delta\delta$, for C-9 and C-10 in the ^{13}C spectrum and very small or undefinable $\Delta\delta_{AB}$ values in the ^{1}H spectrum resemble those observed for the **L2**NMe_4 salt in $CDCl_3$ solution (*vide supra*). Consequently, it is proposed that Li^+ is not coordinated by the crown ether unit of **L2**Li in DMSO-d_6.

For **L2**Cs in DMSO-d_6, an equilibrium between closely populated structures with and without crown ether–cation interaction is suggested in view of the small $\Delta\delta_{AB}$ values and the $\Delta\delta$ values for the C-9 and C-10 atoms observed in the ^{1}H and ^{13}C NMR spectra, respectively. Such equilibria are presumed to occur for solutions of all of the **L2**X salts. For **L2**Cs in DMSO-d_6, there is a special case in which both structures are populated

Table 7 ^{1}H NMR data for selected nuclei of **L2**X in D_2O

	δ					δ			δ			δ
X	1-H	2-H_A	2-H_B	$\Delta\delta 2_{AB}$[a]	$^3J_{1\text{–}2}$/Hz	9-H_A	9-H_B	$\Delta\delta 9_{AB}$[a]	10-H_A	10-H_B	$\Delta\delta 10_{AB}$[a]	11-H
Li	4.12	4.38 dd	4.13 d	0.25	4.2 (A) 0 (B)	4.23	3.98	0.25	2.26		[b]	4.15
Na	4.14	4.51 dd	3.99 d	0.52	3.5 (A) 0 (B)	4.36	3.80	0.56	2.36	2.20	0.16	4.14
K	4.05	4.56	3.94	0.62	[b]	3.94	3.55	0.39	2.25	1.90	0.35	3.94
Rb	4.06	4.56	3.97	0.59	[b]	3.97	3.60	0.37	2.26	1.94	0.32	4.00

[a] $\Delta\delta_{AB} = \delta H_A - \delta H_B$. [b] Not determinable.

appreciably. For the other **L2**X salts, the structures proposed on the basis of the spectral data are adopted by a majority of the molecules.

For **L2**Li in DMSO-d_6, the signal for the 10-H hydrogens is a pentet, which implies that both the 10-H_A and 10-H_B protons have the same chemical shifts and the same coupling constants with both the 9-H_A and 9-H_B. This is consistent with a fast conformational interconversion between different conformations of the unsubstituted three-carbon bridge so the 10-H_A and 10-H_B hydrogens have equal probabilities to occupy pseudo-equatorial and pseudo-axial positions. This results in an averaging of the coupling constants of the 10-H protons with all four 9-H nuclei.

Concluding remarks

Analysis of diastereotopic nonequivalence changes, $\Delta\delta_{AB}$, is shown to be a valuable method for probing the solution structures of LEs. In particular, $\Delta\delta_{AB}$ values for atoms remote from the sidearm attachment site provide information concerning the sidearm location relative to the crown ether cavity.

The NMR structural investigations demonstrate cooperative metal ion complexation by the crown ether portion of the molecule and the sidearm for *sym*-(R)dibenzo-14-crown-4-oxyacetates in $CDCl_3$.

A solvent dependence of structure is observed for the lithium–caesium *sym*-dibenzo-14-crown-4-oxyacetates. In DMSO-d_6 and D_2O, the degree of interaction between the cation and the crown ether moiety varies with the identity of the alkali metal ion. The change in the solution structure with solvent variation found for lithium *sym*-DB14C4-oxyacetate, **L2**Li, provides a particularly striking example. For each of the three solvents studied, $CDCl_3$, DMSO-d_6 and D_2O, a different structure was indicated. The structure deduced for the **L2**Li in D_2O is consistent with that determined for crystals of the **L2**Li·7.5H_2O.[8] This result demonstrates that the solid-state structure determined for the compound complexed with solvent molecules will most likely be the preferred structure in that solvent, but not necessarily in other solvents.

Experimental

^{1}H NMR spectra were measured at 298 K with an IBM AF-300 spectrometer at 300.13 MHz using a spectral width of 6 kHz over 64 K data points. ^{13}C NMR spectra were measured at 298 K with an IBM AF-200 spectrometer at 50.324 MHz using a spectral width of 14 kHz over 32 K data points. ^{13}C NMR spectra at variable temperature and those for the ^{1}H–^{13}C HETCOR experiments were measured with an IBM AF-300 spectrometer at 75.469 MHz using a spectral width of 29 kHz over 64 K data points. ^{1}H–^{13}C HETCOR and NOE experiments were performed with an IBM AF-300 spectrometer using the standard programs. Chemical shifts (δ) are expressed in ppm from tetramethylsilane (TMS) and J values are given in Hz. TMS was used as an internal standard in $CDCl_3$ and DMSO-d_6. Sodium 3-(trimethylsilyl)tetradeuteropropanate (TSP) was used as an internal standard for **L2**Na in D_2O. For the other **L2**X salts in D_2O, the residual OH signal (4.87 ppm for **L2**Na) was used as a standard.

Lariat ethers **L1**H[19] and **L2**H[8] were prepared by reported procedures.

Preparation of L1X and L2X salts

A 0.05 mol dm^{-3} stock solution of the lariat ether carboxylic acid was prepared in $CDCl_3$. A 0.8 mL sample of the stock solution was added to a vial together with the appropriate powdered alkali metal carbonate (5–7 fold excess). After magnetic stirring for 8 h at room temp., the mixture was filtered and the solution was used for the NMR spectral measurement.

For spectral measurements in DMSO-d_6 and D_2O, the **L2**X salt was prepared in $CHCl_3$, the solvent was evaporated to dryness and the solid was dissolved in DMSO-d_6 or D_2O to give a concentration of 0.05 mol dm^{-3}.

The **L2**NMe_4 salt was prepared by reaction of **L2**H with an equivalent amount of 25% aqueous NMe_4OH, followed by evaporation to dryness.

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