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Side arm participation in lariat ether carboxylate-alkali metal cation complexes in solution

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Abstract—Lariat ether carboxylic acids of structure $CECH_2OCH_2C_6H_4$–2-CO_2H with crown ether (CE) ring sizes of 12-crown-4, 15-crown-5 and 18-crown-6 are prepared and converted into alkali metal–lariat ether carboxylate complexes. Absorptions for the diastereotopic benzylic protons in the ^1H NMR spectra of the complexes in $CDCl_3$ are utilized to probe the extent of side arm interaction with the crown ether-complexed metal ion as a function of the crown ether ring size and identity of the alkali metal cation.

1. Introduction

For more than three decades, macrocyclic polyether compounds (crown ethers) have been synthesized and utilized in alkali and alkaline earth metal cation determinations due to their superior binding ability for these metal ions.[1] Attachment of a side arm with potential metal ion coordination sites produces complexing agents called lariat ethers.[2] Such lariat ethers are designed to enhance the cation binding ability or selectivity of crown ethers by providing the potential of three-dimensional complexation, thereby mimicking the dynamic complexation processes exhibited by natural macrocyclic ionophores. When the side arm contains an acidic group, a proton-ionizable lariat ether is produced in which the ligand provides not only a polyether binding site for metal ion complexation, but also the requisite anion for formation of an electroneutral complex.[3] Such proton-ionizable lariat ethers exhibit markedly enhanced solvent extraction of alkali and alkaline earth metal cations and their transport across liquid membranes compared to non-ionizable analogs when the source aqueous solutions contain metal chlorides, nitrates and sulfates.[4]

Side arm participation in metal ion complexation by lariat ethers has been demonstrated in solid-state structures and inferred by increased stability constants in solution compared with corresponding crown ether ligands.[2] More convincing evidence for side arm participation in metal ion complexation by lariat ethers in solution was provided by ^{13}C NMR relaxation time (T_1) measurements.[5] In these studies, the mobility of carbons within dialkyl and alkyl aryl ether-containing side arms of non-ionizable lariat ethers was reduced when a complex was formed.

Some time ago, we designed and synthesized the lariat ether phosphonic acid monoethyl ester **1** with a 15-crown-5 ring (Scheme 1) and prepared from this proton-ionizable lariat ether the lithium, sodium, and potassium lariat ether phosphonate monoethyl ester complexes.[6] In $CDCl_3$, the ^1H NMR signals for the benzylic protons were broadened singlets for the lithium and potassium salts. However, the signal for the benzylic protons in the sodium salt was an AB quartet. The differences between the proton NMR spectra for the sodium salt on the one hand and the lithium and potassium salts on the other are readily interpretable in terms of the relationship between the diameters of the polyether cavity (1.7–2.2 Å) and lithium (1.20 Å), sodium (1.90 Å), and potassium (2.66 Å) cations. Thus, Na^+ is of an appropriate size to bind tightly within the polyether cavity. Simultaneous coordination of the phosphonate function markedly restricts the mobility of the side group and the diastereotopic benzylic protons in the sodium complex.

To explore the influence of ring size variation upon such side arm participation, the series of lariat ether carboxylic acids **2**–**4** (Scheme 1) has been prepared. In this series, the crown ether ring size is systematically varied from 12-crown-4 to 15-crown-5 to 18-crown-6. Five alkali metal carboxylate salts were produced from each of these three proton-ionizable lariat ethers and their ^1H NMR spectra in deuteriochloroform were determined to assess the level of side arm participation. Results of this study are now reported.

Keywords: Proton-ionizable lariat ether; Metal ion complexation.

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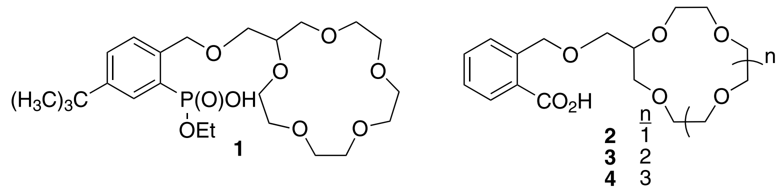


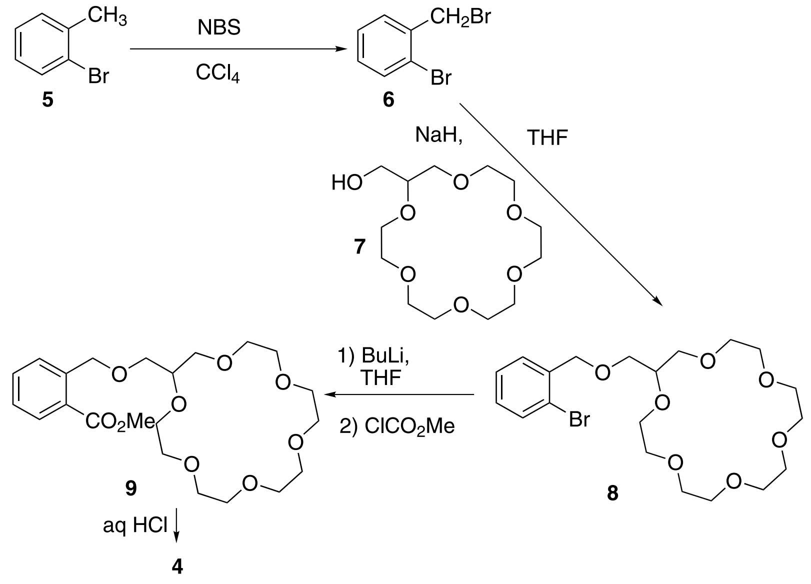
Scheme 1. Structures of a lariat ether phosphonic acid monoethyl ester **1** and lariat ether carboxylic acids **2**–**4**.

2. Results and discussion

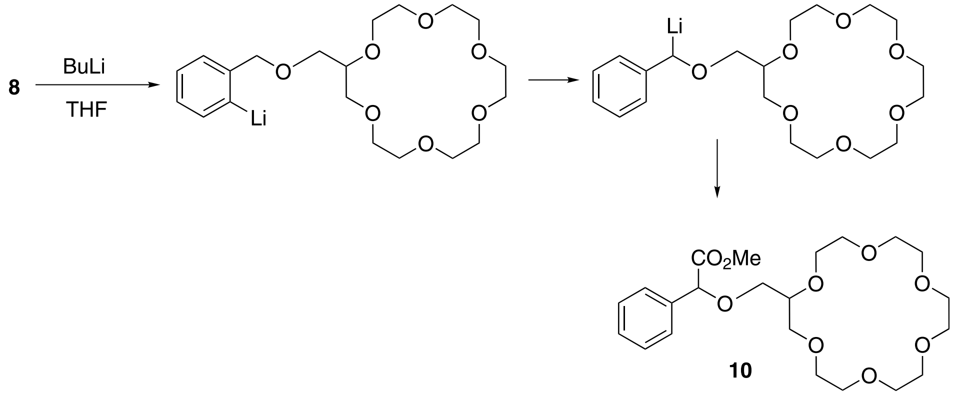
2.1. Synthesis of lariat ether carboxylic acids

For the original preparative approach to lariat ether carboxylic acids **2**–**4**, the 18-crown-6 compound **4** was the target, as illustrated in Scheme 2. Bromination of 2-bromotoluene (**5**) with NBS in CCl_4 gave 2-bromobenzyl bromide (**6**) in 84% yield. Reaction of **6** with the sodium alkoxide of hydroxymethyl-18-crown-6 (**7**) in THF gave key intermediate **8**. However, when **8** was treated with *n*-BuLi in THF at −78 °C followed by quenching with methyl chloroformate, problems were encountered. While it appeared that some of the desired methyl benzoate crown ether **9** was formed, a by-product was produced in an approximately equal amount. Thin layer chromatographic analysis showed two compounds with very similar R_f values. The IR spectrum of the mixture exhibited two strong carbonyl stretching absorptions of equal intensity. One absorption at 1756 cm^{-1} was consistent with an aliphatic ester, while the other absorption at 1736 cm^{-1} corresponded to the aromatic ester carbonyl group of **9**. Although no attempt was made to separate the two products, these observations together with the ^1H NMR spectrum of the mixture led to the conclusion that the two compounds were structural isomers. It is postulated that the undesired product is the structural isomeric ester **10** resulting from a transmetallation reaction of the initially formed aryllithium compound (Scheme 3).

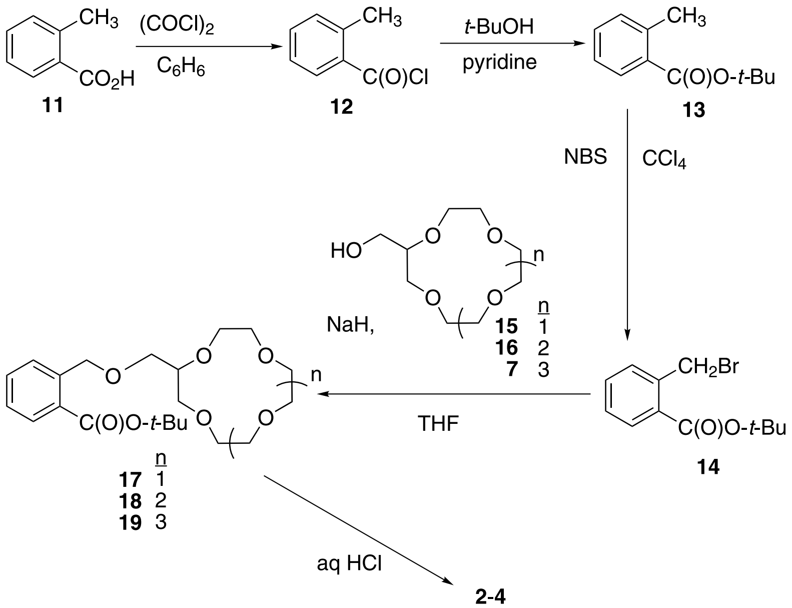
The successful preparative route to lariat ether carboxylic



Scheme 2. Initial synthetic scheme for preparation of lariat ether carboxylic acid **4**.



Scheme 3. Rationalization for formation of a second isomeric 18-crown-6 ester.



Scheme 4. Synthetic scheme for preparation of lariat ether carboxylic acids **2**–**4**.

acids **2**–**4** is shown in Scheme 4. Reaction of 2-methylbenzoic acid (**11**) with oxalyl chloride in benzene gave a quantitative yield of the corresponding acid chloride **12**. Reaction of **12** and *t*-BuOH gave *t*-butyl ester **13**. Benzylic bromination of **13** with NBS in CCl$_4$ provided a 61% yield of *t*-butyl 2-bromomethylbenzoate (**14**). Coupling of **14** with the sodium alkoxides derived from hydroxymethyl-12-crown-4 (**15**), hydroxymethyl-15-crown-5 (**16**) and hydroxymethyl-18-crown-6 (**7**) in THF gave lariat ether esters **17**–**19** in 68, 81, and 90% yields, respectively. (A model study performed with methyl 2-bromomethylbenzoate showed competing attack of the sodium alkoxide derived from (hydroxymethyl)cyclohexanol at both the benzylic and carbonyl carbons. To suppress the latter, the *t*-butyl ester **14** was utilized for reaction with the (hydroxymethyl)crown ethers **15**, **16**, and **7**.) Acidic hydrolysis gave the lariat ether carboxylic acids **2**–**4** in 96, 86, and 89% yields, respectively.

Table 1. Chemical shift (δ) the chemical shift difference ($\Delta\upsilon$) data for diastereotopic, benzylic protons of the lariat ether carboxylic acids **2**–**4** and their alkali metal carboxylate salts in CDCl$_3$

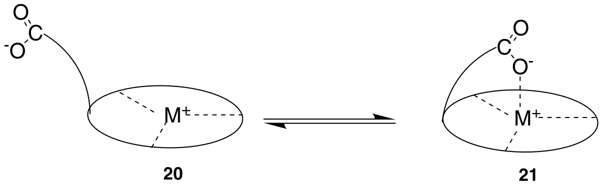
Compound	δ (ppm)[a]	$\Delta\upsilon$ (Hz)[b]
2	4.91	[c]
Li$^+$	4.73	[d]
Na$^+$	4.85	11.4
K$^+$	4.80	32.8
Rb$^+$	4.81	[d]
Cs$^+$	4.82	[d]
3	4.93	[c]
Li$^+$	4.85	[c]
Na$^+$	4.89	15.9
K$^+$	4.92	31.3
Rb$^+$	4.91	25.7
Cs$^+$	4.93	18.2
4	4.94	[d]
Li$^+$	4.92	[d]
Na$^+$	4.84	45.9
K$^+$	4.89	56.9
Rb$^+$	4.94	63.2
Cs$^+$	4.96	21.5

[a] Chemical shift for the singlet or the average chemical shift for the benzylic protons in the AB pattern.
[b] Calculated based upon the center of gravity for the AB quartet.
[c] Absorption was a sharp singlet.
[d] Absorption was a broad singlet.

2.2. NMR spectroscopic studies

Chemical shift (δ) and chemical shift difference ($\Delta\upsilon$) data for the AB quartets exhibited by the diastereotopic benzylic protons in lariat ether carboxylic acids **2**–**4** and their alkali metal carboxylate salts in CDCl$_3$ are presented in Table 1. The chemical shift values for the AB quartets were based on calculations for the center of gravity.[7]

It is readily evident from the data presented in Table 1 that the ^{1}H NMR absorptions for the benzylic protons in the lariat ether carboxylate salts exhibit a strong dependence on the identity of the alkali metal cation and the crown ether ring size. This dependence can be rationalized using the conformational equilibrium shown in Scheme 5. In structure **20**, the pendant carboxylate group does not interact with the polyether-bound metal ion. Rotation about the single bonds in the side arm is facile and the diastereotopic benzylic protons are magnetically equivalent, leading to a singlet absorption in the ^{1}H NMR spectrum. In structure **21**, the carboxylate group coordinates with the polyether-bound metal ion. This restricts the side arm and the diastereotopic benzylic protons are non-equivalent producing an AB



Scheme 5. Depiction of lariat ether carboxylates in which the ionized side arm is: (a) conformationally mobile in **20**; and (b) conformationally restricted due to its interaction with the polyether-complexed metal ion in **21**.

pattern in the ^{1}H NMR spectrum. The greater is the carboxylate–metal ion interaction in **21**, the more this form will contribute to the equilibrium mixture. A greater proportion of conformer **21** will produce greater restriction of the side arm in the 'averaged' structure for the equilibrium. This will enhance the level of non-equivalency for the diastereotopic benzylic protons and result in a larger chemical shift difference, $\Delta \upsilon$.

For crown ethers with 12-crown-4, 15-crown-5 and 18-crown-6 rings, averaged cavity sizes are 1.44, 1.84, and 2.90 Å, respectively.[8] For the alkali metal cations, the diameters for Li^+, Na^+, K^+, Rb^+, and Cs^+ are 1.56, 1.96, 2.66, 2.98, and 3.30 Å, respectively.[8]

For the lariat ether carboxylates derived from **2**, the cavity of 12-crown-4 is too small to accommodate even the smallest alkali metal cation. Therefore, perching[9] complexes would be formed with the alkali metal cation located somewhat above the plane of the crown ether oxygens. The chemical shift differences recorded in Table 1 reveal little restriction of the side arm for the lithium, rubidium, and cesium carboxylates. However, ^{1}H NMR absorptions for the benzylic protons in the sodium and potassium carboxylate salts exhibit pronounced AB patterns. The larger $\Delta \upsilon$ value for the potassium carboxylate salt indicates greater side arm restriction than in the sodium carboxylate complex. It is envisioned that the potassium ion perches on the crown ether ring and interacts with both the carboxylate terminus and the dialkyl ether oxygen in the side arm.

Although Li^+ can form a nesting[9] complex, the other alkali metal cations are too large to fit within the 15-crown-5 cavity of lariat ether carboxylates obtained from **3**. For the Li^+ complex, the benzylic proton absorption is a sharp singlet, revealing a conformationally mobile side arm. The $\Delta \upsilon$ values in Table 1 show that the side arm restriction increases as the metal ion is varied $Na^+ < Cs^+ < Rb^+ < K^+$. This ordering indicates that K^+ is the most appropriate size to perch on the polyether oxygens, while interacting with both the carboxylate and ether oxygens in the side arm.

For the carboxylates derived from lariat ether **4**, Li^+, Na^+, and K^+ can all form nesting complexes, with formation of perching complexes for Rb^+ and Cs^+. The broadened singlet observed for the benzylic protons in the complex with Li^+, shows a slight conformational restriction of the side arm. From the data in Table 1, it is seen that the $\Delta \upsilon$ values for the AB quartets increase as the alkali metal cation is varied in the order $Cs^+ < Na^+ < K^+ < Rb^+$. Once again the cation with the greatest side arm restriction in the complex is that in which the metal ion can perch on the oxygens of the polyether ring and interact with both the carboxylate and ether oxygens in the side arm.

3. Conclusions

For the alkali metal carboxylates obtained from lariat ether carboxylic acids **2–4**, the complexes with the greatest side arm restrictions are those in which the metal ion is large enough to perch on the crown ether oxygens yet small enough to interact well with the ether and carboxylate oxygens in the side arm.

4. Experimental

4.1. General

Melting points were determined with a Fisher-Johns melting point apparatus. ^{1}H and ^{13}C NMR spectra were obtained with an IBM AF-200 or AF-300 spectrometer. Spectra were taken in $CDCl_3$ and chemical shifts are reported in parts per million (ppm) downfield from TMS. IR spectra were obtained with a Perkin-Elmer 1600 Series FT-IR spectrophotometer and are given in wave numbers (cm^{-1}).

THF was distilled from sodium metal. Pyridine was dried over KOH pellets and *t*-BuOH was distilled from CaH_2.

Hydroxymethyl-12-crown-4 (**15**), hydroxymethyl-15-crown-4 (**16**) and hydroxymethyl-18-crown-6 (**7**) were prepared by reported procedures.[10,11]

4.1.1. 2-Bromobenzyl bromide (6). 2-Bromotoluene (10.00 g, 59 mmol) was dissolved in CCl_4 (100 mL) followed by addition of NBS (10.41 g, 59 mmol) and a catalytic amount of benzoyl peroxide. The mixture was stirred at reflux for 6 h. The mixture was allowed to cool to room temperature and was filtered. The filtrate was washed with water and dried over Na_2SO_4. Removal of the solvent in vacuo gave a light yellow liquid, which was distilled under vacuum (bp 80–85 °C/0.85 Torr, literature[12] bp 120–123 °C/16 Torr) to give 12.39 g (84%) of **6** as a colorless oil. ^{1}H NMR ($CDCl_3$): δ 4.54 (s, 2H), 7.10 (d of t, 1H), 7.23 (d of t, 1H), 7.38 (d of d, 1H), 7.51 (dd, 1H).

4.1.2. Bromo-2-(oxymethyl-18-crown-6)methylbenzene (8). A solution of hydroxymethyl-18-crown-6 (**7**) (1.50 g, 5.10 mmol) in THF (10 mL) was added dropwise to a flask containing NaH (0.31 g of 60% dispersion in mineral oil, 7.65 mmol). The mixture was stirred for 5 min at room temperature and a solution of bromide **6** (1.40 g, 5.10 mmol) in THF (10 mL) was added dropwise over a 10 min period. The mixture was stirred overnight at room temperature and the solvent was evaporated in vacuo. The residue was dissolved in CH_2Cl_2 and the solution was dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was chromatographed on silica gel with CCl_4/EtOAc (1:1) as eluent to give 1.83 g (77%) of **8** as a colorless, viscous oil. ^{1}H NMR ($CDCl_3$): δ 3.62–3.74 (m, 25H), 4.60 (s, 2H), 7.14 (d of t, 1H), 7.30 (d of t, 1H), 7.50 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 69.93, 70.64, 70.76, 70.83, 71.56, 72.32, 72.50, 78.33, 122.40, 127.22, 128.70, 128.8, 132.31. Anal. Calcd for $C_{18}H_{27}O_6Br$: C, 51.56; H, 6.49. Found: C, 51.44; H, 6.46.

4.1.3. 2-Methylbenzoyl chloride (12). *o*-Toluic acid (5.00 g, 36.7 mmol) was suspended in dry benzene (30 mL) and oxalyl chloride (9.32 g, 73.4 mmol) was added in one portion. The reaction mixture was stirred at room temperature for 14 h under nitrogen. The solvent and excess of oxalyl chloride were evaporated in vacuo to provide a quantitative yield of **12** as a pale green oil. IR (neat): 1770 (C=O) cm^{-1}.

4.1.4. *tert*-Butyl 2-methylbenzoate (13).[13] Pyridine (8.9 mL, 110 mmol) and *t*-BuOH (10.4 mL, 110 mmol) were added to a flask containing acid chloride **12** (5.67 g, 36.7 mmol). Upon stirring the solution overnight at room temperature, a white precipitate formed. After addition of CH_2Cl_2, the resulting solution was washed with water and 5% aq HCl. The organic layer was dried over Na_2SO_4 and the solvent was evaporated in vacuo. The residue was passed through a short column of alumina with petroleum ether as eluent to give 6.02 g (85%) of ester **13** as a colorless oil. IR (neat): 1718 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.59 (s, 9H), 2.57 (s, 3H), 7.18–7.24 (m, 2H), 7.33 (d of d, 1H), 7.83 (d of d, 1H).

4.1.5. *tert*-Butyl 2-(bromomethyl)benzoate (14).[14] To a solution of ester **13** (1.68 g, 8.76 mmol) in CCl_4 (20 mL) was added NBS (1.81 g, 10.52 mmol) and benzoyl peroxide (0.20 g). The solution was irradiated for 2 h with a 500 watt tungsten lamp, allowed to cool to room temperature and washed with water. The organic layer was dried over $MgSO_4$ and evaporated in vacuo to provide a viscous oil. Chromatography on silica gel with CCl_4 as eluent gave **14** (1.46 g, 61%) as a colorless, viscous oil. ^1H NMR ($CDCl_3$): δ 1.62 (s, 9H), 4.93 (s, 2H), 7.29–7.48 (m, 3H), 7.87 (d of d, 1H).

4.1.6. *tert*-Butyl 2-[(oxymethyl-12-crown-4)methyl]-benzoate (17). A solution of hydroxymethyl-12-crown-4 (**15**) (0.41 g, 2.00 mmol, dried at 90 °C under high vacuum for 24 h) in THF (10 mL) was added to a flask containing NaH (0.09 g, 2.2 mmol, 60% dispersion in mineral oil). After stirring the mixture for 10 min, a solution of ester **14** (0.54 g, 2.00 mmol) in THF (10 mL) was added. The mixture was stirred for 5 h at room temperature and the solvent was evaporated in vacuo. To the residue were added CH_2Cl_2 and water. The organic layer was dried over $MgSO_4$, concentrated, and chromatographed on deactivated alumina with EtOAc as eluent to yield **17** (0.55 g, 68%) as a colorless oil. IR (neat): 1705 (C=O), 1134 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.58 (s, 9H), 3.50–4.00 (m, 17H), 4.91 (s, 2H), 7.25–7.90 (m, 4H). Anal. Calcd for $C_{21}H_{32}O_7$: C, 63.60; H, 8.14. Found: C, 63.42; H, 7.83.

4.1.7. 2-[Oxymethyl-12-crown-4)methyl]benzoic acid (2). To ester **17** (0.55 g, 1.40 mmol) was added 6 N HCl (5 mL) and the mixture was stirred at room temperature under nitrogen for 3 h. The acidic solution was made basic (pH ~ 12) with 20% aq NaOH. The basic solution was extracted with CH_2Cl_2 (3×10 mL) and acidified to pH 1 with 6 N HCl. The acidic solution was extracted with CH_2Cl_2 (3×25 mL). The combined organic layers were dried over $MgSO_4$ and evaporated in vacuo to give **2** (0.45 g, 96%) as a pale yellow oil. IR (neat): 2864 (COOH), 1715 (C=O), 1136 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.40–3.95 (m, 17H), 4.92 (s, 2H), 6.70 (br s, 1H), 7.35 (t, 1H), 7.55 (m, 2H), 7.99 (d, 1H). ^{13}C NMR ($CDCl_3$): δ 70.07, 70.18, 70.51, 70.93, 70.93, 71.49, 71.56, 76.57, 77.00, 77.42, 78.48, 127.20, 127.63, 127.75, 130.15, 131.36, 132.93, 140.80, 171.44. Anal. Calcd for $C_{17}H_{24}O_7$: C, 59.96; H: 7.11. Found: C, 59.95; H, 7.23.

4.1.8. *tert*-Butyl 2-[(oxymethyl-15-crown-5)methyl]-benzoate (18). By the procedure recorded above for preparation of **17**, hydroxymethyl-15-crown-5 (**16**) (0.50 g, 2.00 mmol, dried at 80 °C under high vacuum for 24 h) was reacted with ester **14** to give **18** (0.71 g, 81%) as a colorless oil. IR (neat): 1706 (C=O), 1134 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.58 (s, 9H), 3.60–3.88 (m, 21H), 4.91 (s, 2H), 7.20–7.90 (m, 4H). Anal. Calcd for $C_{23}H_{36}O_8$: C, 62.71; H, 8.23. Found: C, 62.92; H, 7.96.

4.1.9. 2-[Oxymethyl-15-crown-5)methyl]benzoic acid (3). By the procedure given above for the preparation of **2**, ester **18** (0.71 g, 1.60 mmol) was hydrolyzed to provide **3** (0.53 g, 86%) as a pale yellow oil. IR (neat): 2870 (COOH), 1713 (C=O), 1119 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.55–3.95 (m, 21H), 4.93 (s, 2H), 6.70 (br s, 1H), 7.35 (t, 1H), 7.55 (t, 1H) 7.65 (t, 1H), 8.05 (d, 1H). ^{13}C NMR ($CDCl_3$): δ 70.08, 70.36, 70.53, 70.69, 71.03, 71.09, 71.25, 76.57, 77.00, 77.42, 78.55, 126.88, 127.02, 127.37, 127.69, 131.00, 131.15, 132.75, 141.06, 170.93. Anal. Calcd for $C_{19}H_{28}O_8$: C, 59.39; H, 7.34. Found: C, 59.44; H, 7.26.

4.1.10. *tert*-Butyl 2-[(oxymethyl-18-crown-6)methyl]-benzoate (19). A solution of hydroxymethyl-18-crown-6 (**7**) (0.89 g, 2.96 mmol, dried at 80 °C under high vacuum for 24 h) in THF (10 mL) was added to a flask containing NaH (0.14 g, 3.55 mmol, 60% dispersion in mineral oil). After the mixture was stirred for 5 min, a solution of ester **14** (0.80 g, 2.95 mmol) in THF (10 mL) was added. The mixture was stirred for 5 h at room temperature and the solvent was evaporated in vacuo. To the residue, CH_2Cl_2 and water were added. The organic layer was dried over $MgSO_4$, concentrated, and chromatographed on silica gel with CH_2Cl_2/MeOH (10:1) as eluent to give **19** (1.26 g, 89%) as a viscous, colorless oil. IR (neat): 1710 (C=O), 1126 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.59 (s, 9H), 3.61–3.86 (m, 25H), 4.91 (s, 2H), 7.30 (d of t, 1H), 7.48 (d of t), 7.65 (d of t), 7.86 (d of d, 1H). Anal. Calcd for $C_{25}H_{40}O_9$: C, 61.97; H, 8.32. Found: C, 62.20; H, 8.16.

4.1.11. 2-[Oxymethyl-18-crown-6)methyl]benzoic acid (4). By the procedure given above for the preparation of **2**, ester **19** (0.71 g, 1.60 mmol) was hydrolyzed to provide **4** (0.53 g, 86%) as a pale yellow oil. IR (neat): 2850 (OH); 1712 (C=O), 1125 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.65–3.74 (m, 22H), 3.83–3.86 (m, 3H), 7.35 (d of t, 1H), 7.53 (d of t, 1H), 7.64 (d of d, 1H), 8.02 (d of t, 1H) 10.90 (br s, 1H). ^{13}C NMR ($CDCl_3$): δ 69.59, 70.41, 70.54, 70.66, 70.75, 71.35, 71.40, 76.57, 77.00, 77.42, 78.13, 127.00, 127.64, 128.12, 131.06, 132.46, 140.57, 170.71. Anal. Calcd for $C_{21}H_{32}O_9$: C, 58.87, H, 7.53. Found: C, 58.92; H, 7.48.

4.2. ^1H NMR investigations of lariat ether carboxylic acids and their alkali metal carboxylates

Lariat ether sodium, potassium, rubidium, and cesium carboxylates were produced by stirring **2–4** with an excess of the alkali metal carbonate in $CDCl_3$ at room temperature followed by filtration with the filtrate passing directly into the NMR tube. The lithium lariat ether carboxylates were prepared by reaction of solutions of **2–4** in THF with 1 equiv of *n*-BuLi in THF at −78 °C. The THF was evaporated in vacuo. After addition of $CDCl_3$, the resultant solutions were transferred to NMR tubes.

^1H NMR spectra of **2–4** and their alkali metal carboxylate salts in $CDCl_3$ were measured at 300 MHz. Chemical shift values were determined to be independent of the sample concentration. The chemical shift differences were calculated for the AB quartets based on the center of gravity.[7] The coupling constants J_{AB} for all observed doublets were approximately 12 Hz, which is consistent with normal bond angles for a tetrahedral methylene group.

Acknowledgements

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References and notes

1. Bradshaw, J. S.; Izatt, R. M.; Bordunov, A. V.; Zhu, C. Y.; Hathaway, J. K. Crown ethers. In *Comprehensive Supramolecular Chemistry*; Gokel, G. W., Ed.; Pergamon: New York, 1996; pp 35–95.
2. Gokel, F. W.; Schall, O. F. Lariat ethers. In *Comprehensive Supramolecular Chemistry*; Gokel, G. W., Ed.; Pergamon: New York, 1996; pp 97–152.
3. Strzelbicki, J.; Bartsch, R. A. *Anal. Chem.* **1981**, *53*, 1894–1899.
4. Bartsch, R. A. *Solvent Extr. Ion Exch.* **1989**, *7*, 829–854.
5. Echegoyen, L.; Kaiser, A.; Durst, H.; Schultz, R. A.; Dishong, D. M.; Goli, D. M.; Gokel, G. W. *J. Am. Chem. Soc.* **1984**, *106*, 5100–5103.
6. Robison, T. W.; Bartsch, R. A. *J. Chem. Soc., Chem. Commun.* **1985**, 990–991.
7. Siverstein, G. C.; Bassler, G. C.; Morrill, T. C. *Spectroscopic Identification of Organic Compounds*, 4th ed.; Wiley: New York, 1991; pp 171.
8. Vögtle, F.; Weber, E. In *Crown Ethers and Analogs*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1989; pp 250–251.
9. Cram, D. J.; Trueblood, K. N. Concept, structure, and binding in complexation. *Host Guest Complex Chemistry Macrocycles. Synthesis, Structures, Applications*; Vögtle, F., Weber, E., Eds.; 1985, 128.
10. Czech, B. P.; Czech, A.; Son, F.; Lee, H. K.; Bartsch, R. A. *J. Heterocycl. Chem.* **1986**, *23*, 465–471.
11. Hu, H.; Bartsch, R. A. *J. Heterocycl. Chem.* **2004**, *41*, 557–562.
12. Amati, A.; Dosualdo, G.; Zhao, L.; Bravo, A.; Fontana, F.; Minisci, F.; Bjorsvik, H.-R. *Org. Process Res. Dev.* **1998**, *2*, 261–269.
13. Paul, S.; Schmidt, R. R. *Synlett* **2002**, 1107–1108.
14. Reinmann, E.; Grasberger, F.; Polborn, K. *Monatsh. Chem.* **2003**, *134*, 991–1014.