New Lipophilic Crown Ethers with Intraannular Carboxylic Acid Groups: Synthesis and Alkali Metal Cation Extraction

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A six-step synthetic route to four lipophilic crown ethers with intraannular carboxylic acid groups and ring sizes of 15-crown-4, 18-crown-5, 21-crown-6 and 24-crown-7 is described. Eight new polyether compounds that bear inward-facing bromo and formate ester substituents are prepared as synthetic intermediates. Selectivities and efficiencies of the four new lipophilic crown ether carboxylic acids in competitive alkali metal cation extraction from aqueous solutions into chloroform are evaluated.

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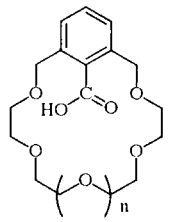
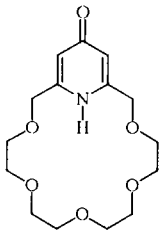
Introduction.

Crown ether compounds containing acidic functions may be separated into three general categories. In the first type (*e.g.*, in **1** [1]), the ionizable group projects into the crown ether cavity. The ionizable function is incorporated into the macrocylic ring itself in the second type (*e.g.*, in **2** [2]). In the third type, the ionizable group is part of a side arm that is attached to the crown ether ring (*e.g.*, in **3** [3]).



1 (n = 0-3)



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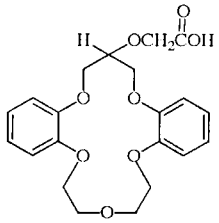
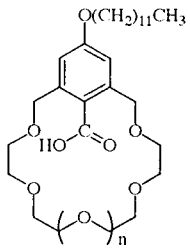


3

Crown ethers with pendant proton-ionizable groups are efficient agents for the solvent extraction of alkali and alkaline earth metal cations and their transport across various types of liquid membranes [4-13]. These ionizable macrocyclic ligands have a distinct advantage over non-ionizable crown ethers in that transport of the metal cation from the aqueous phase into the organic phase does not require concomitant transfer of the aqueous phase anion. Hydrophilic anions, such as chloride, nitrate and sulfate, distribute poorly into organic media [3].

Previously, we described the preparation of lipophilic crown ethers with pendant acid-containing side arms [14-22]. Incorporation of a lipophilic group was necessary to prevent loss of the extractant from the organic phase during the solvent extraction of metal ions [4].

We now report the synthesis of lipophilic crown ethers **4-7** with intraannular carboxylic acid groups in which the crown ether ring size is varied systematically and evaluation of their alkali metal cation complexation behavior in solvent extraction.



	n
4	0
5	1
6	2
7	3

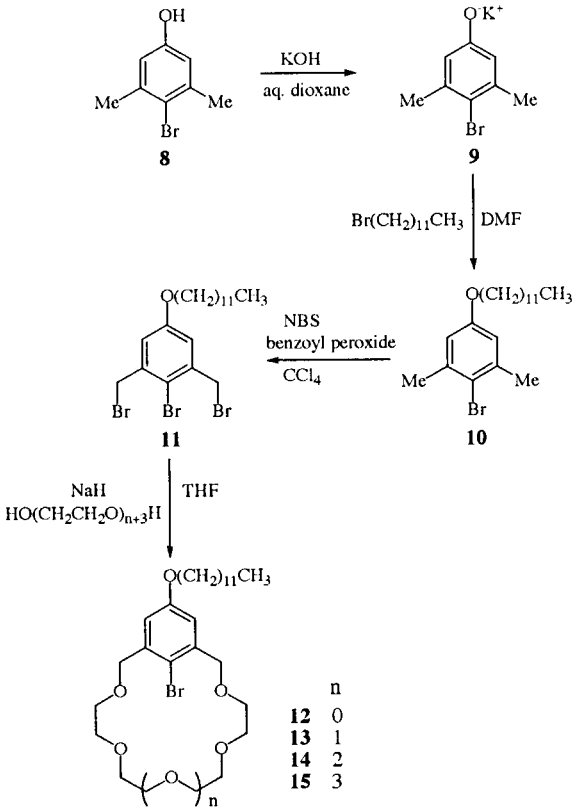
Results and Discussion.

Synthesis of Lipophilic Crown Ether Carboxylic Acids **4-7**.

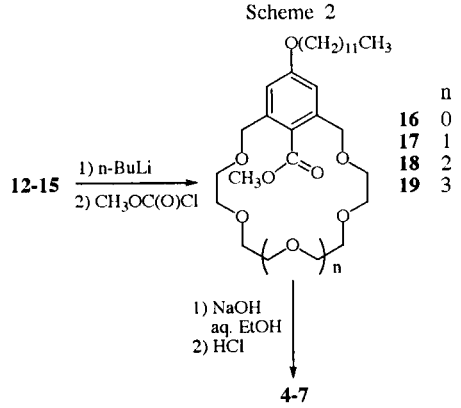
The preparative procedure for lipophilic crown ether carboxylic acids **4-7** was patterned after those reported for the synthesis of the non-lipophilic analogues **1** [1,23]. The synthetic strategy was the preparation of a lipophilic crown ether with an intraannular bromo group (Scheme 1) to be followed by replacement of the bromo group with a carboxylic acid function (Scheme 2).

A procedure for the alkylation of 4-bromo-3,5-dimethylphenol was developed using 4-bromophenol as a model compound. From reaction of 4-bromophenol with potassium carbonate in acetone [24] or sodium hydride in tetrahydrofuran [25] followed by the addition of 1-bromododecane and refluxing, none of the desired alkyl aryl ether product was obtained. Similarly, reaction of 4-bromophenol with sodium hydroxide and 1-bromododecane in a two-phase water-dichloromethane (1:1) system at room temperature with cetyldimethylammonium bromide as the phase transfer catalyst failed to produce the target compound. However, when potassium 4-bromophenoxide was isolated from the reaction of 4-bromophenol and potassium hydroxide in water and then reacted with 1-bromododecane in dimethylformamide at reflux, 4-bromophenyl dodecyl ether was realized.

Scheme 1



Scheme 2



Potassium 4-bromo-3,5-dimethylphenoxide (**9**) was isolated from the reaction of commercially available 4-bromo-3,5-dimethylphenol (**8**) with potassium hydroxide in aqueous dioxane (Scheme 1). Reaction of **9** with 1-bromododecane in dimethylformamide at reflux gave lipophilic ether **10** in 78% yield.

For conversion of the two benzylic groups in **10** into α-bromobenzyl groups, reaction with *N*-bromosuccinimide using benzoyl peroxide as initiator [1] was utilized to produce the di(bromomethyl) product **11** (Scheme 1). The low yield for this step (30%) was due to concomitant formation of the monobrominated compound and the *gem*-dibrominated product. Replacement of *N*-bromosuccinimide with 1,3-dibromo-5,5-dimethylhydantoin did not enhance the yield of compound **11**.

Ring closure was accomplished by reaction of the appropriate oligoethylene glycol with sodium hydride in tetrahydrofuran followed by reaction with the di(bromomethyl) compound **11** under high dilution conditions to afford crown ethers **12-15** with inward-facing bromo substituents in 58-61% yields.

Due to a lack of success with the reaction of an aryl lithium reagent derived from the bromo crown-6 compound **13** with carbon dioxide, a two-step reaction pathway [22] was utilized (Scheme 2). In the first step, the bromo crown ethers **12-15** were reacted with *n*-butyllithium in tetrahydrofuran to form the aryllithium intermediates, which were subsequently treated with methyl chloroformate to give the crown ether formate esters **16-19**, respectively, in 63-76% yields. In the final step, saponification of the crown ether esters with sodium hydroxide in aqueous ethanol, followed by acidification, gave the target lipophilic crown ether carboxylic acids **4-7** in yields exceeding 80%.

For the crown-4 compounds **4**, **12** and **16** which bear intraannular carboxylic acid, bromo and methyl ester groups, respectively, at the 2-position, AB quartets for the benzylic methylene protons were observed between 4.1 and 5.1 δ in the proton nuclear magnetic resonance spectra. In contrast, the proton nuclear magnetic resonance spectra for the crown-5, -6 and -7 analogues showed only singlets for the benzylic methylene hydrogens. Thus for the crown-4 compounds, the metacyclophane bridge is too short to allow easy passage of the substituent through the crown ether ring cavity, resulting in the formation of a rather rigid system in which the two hydrogens on a benzylic carbon are non-equivalent and diastereotopic.

Solvent Extraction of Alkali Metal Cations by Lipophilic Crown Ether Carboxylic Acids **4-7**.

The metal ion complexing behavior of the new lipophilic proton-ionizable crown ether compounds was evaluated by competitive alkali metal cation extraction from aqueous solutions into chloroform. Data from the competitive extractions of aqueous solutions of alkali metal chlorides with hydroxide for pH adjustment (0.25 *M* in each) with 0.050 *M* chloroform solutions of the lipophilic crown ether carboxylic acids **4-7** are summarized in Table 1. Although complete profiles of metal ion concentrations in the chloroform phase versus the equilibrium pH of the aqueous phase for pH 4-12 were obtained (*e.g.*, see [19,20]), only the data obtained at the highest pH are presented.

The total metal ion loading for the four extractants is 93-100% which attests to the formation of 1:1 metal ion-ionized crown ether extraction complexes. This observation also demonstrates that the ligands are sufficiently lipophilic to prevent their significant loss from the organic phase when in contact with a highly basic aqueous phase during solvent extraction.

The selectivity order for alkali metal cation extraction by lipophilic crown ether carboxylic acids **4-7** is seen to vary with the ring size. For the crown-4 extractant **4**, the selectivity order is Li > Na > K > Rb > Cs. This is the ordering of the charge densities of the alkali metal cations which indicates that the metal ion associates primarily with the carboxylate group in the ionized ligand. This can be attributed to the small crown ether ring size and to the location of the carboxylate group above the plane of the crown ether ring as suggested by the proton magnetic resonance spectrum of **4** (*vide supra*).

For the crown-5 compound **5**, the extraction selectivity order is Li > K > Na > Rb > Cs. Reversal in the Na/K selectivity compared with the crown-4 extractant **4**, suggests that the complexed metal cation is interacting with both the crown ether ring and the carboxylate group in the ionized form of **5**.

With the crown-6 and crown-7 extractants **7** and **8**, respectively, the selectivity order is Cs > Rb > K > Na ≥ Li. Preference for extraction of the larger alkali metal cations by the larger ring extractants is consistent with predominant association of the metal cation with the crown ether unit in the lipophilic crown ether carboxylate.

Table 1

Effect of Crown Ether Ring Size Variation on the Selectivity and Efficiency of Competitive Alkali Metal Cation Extraction from Aqueous Solutions into Chloroform by Lipophilic Crown Ether Carboxylic Acids **4-7**

compound	ring size	pH	selectivity order andloading selectivity coefficients*	maximal metal (%)
1	15C4	11.5	Li > Na > K > Rb > Cs 1.3 4.4 14 24	100
2	18C5	11.0	Li > K > Na > Rb > Cs 1.8 3.8 7.2 13	100
3	21C6	11.7	Cs > Rb > K > Na > Li 2.3 3.2 3.9 13	100
4	24C7	11.7	Cs > Rb > K > Li,Na 1.7 1.8 5.1	97

EXPERIMENTAL

Melting points were determined with either a Mel-Temp or a Fisher-Johns melting point apparatus and are uncorrected. Infrared (ir) spectra were recorded with Beckman Acculab 8 or Nicolet MX-S FT-IR spectrometers for samples on sodium chloride plates (neat or a film deposited from deuteriochloroform solution) or as potassium bromide pellets and are reported in wave numbers (cm^{-1}). Proton nuclear magnetic resonance (^1H NMR) spectra were recorded with Varian EM360 or Bruker AF-200 spectrometers and chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded with the Bruker AF-200 instrument with chemical shifts (ppm) reported using the center line of the deuteriochloroform peak as an internal standard. Elemental analysis was performed by Galbraith Laboratories, Inc. of Knoxville, Tennessee. Dimethylformamide was purified by distillation from calcium hydride and stored over molecular sieves (5 angstroms). Tetrahydrofuran and pentane were purified by distillation from lithium aluminum hydride under nitrogen. Reagent-grade reactants and solvents were obtained from chemical suppliers and used as received.

4-Bromo-1-dodecyloxy-3,5-dimethylbenzene (**10**).

To a suspension of 4-bromo-3,5-dimethylphenol (**8**) (5.00 g, 24.9 mmoles) in 50 ml of a 50% solution of 1,4-dioxane in water was added potassium hydroxide (1.40 g, 24.9 mmoles). The reaction mixture was stirred at room temperature for 2 hours. The solvents were evaporated *in vacuo* and the residual water was removed by azeotropic distillation with benzene for 24 hours. The solvent was evaporated to give a solid, which was triturated in cold dichloromethane, filtered and dried to afford 5.66 g (95%) of crude potassium 4-bromo-3,5-dimethylphenoxide (**9**) as an off-white solid.

A solution of **9** (5.60 g, 23.6 mmoles), 1-bromododecane (5.84 g, 23.6 mmoles) and 200 ml of anhydrous dimethylformamide was refluxed for 48 hours. The reaction mixture was filtered and the filtrate was evaporated *in vacuo* to give a residue, which was added to a mixture of water and diethyl ether (30 ml of each). The separated aqueous phase was extracted with three 30-ml portions of diethyl ether. The organic layer and extracts were combined, dried over magnesium sulfate and evaporated *in vacuo*. Column chromatography of the residue on silica gel with benzene as eluent afforded 6.78 g (78%) of **10** as a colorless oil; ir (deposit from deuteriochloroform solution on a sodium chloride plate): 1168 (C-O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.70-2.10 (m, 23H), 2.32 (s, 6H), 3.83 (t, J = 6.0 Hz, 2H), 6.60 (s, 2H).

Anal. Calcd. for $C_{20}H_{33}OBr$: C, 65.03; H, 9.00. Found: C, 65.00; H, 9.18.

4-Bromo-1-dodecyloxy-3,5-di(bromomethyl)benzene (**11**).

A mixture of **10** (2.07 g, 5.6 mmoles), *N*-bromosuccinimide (2.21 g, 12.4 mmoles), benzoyl peroxide (0.10 g) and 50 ml of carbon tetrachloride was refluxed for 12 hours. The mixture was filtered to remove the succinimide and the filtrate was evaporated. Column chromatography of the residue on silica gel with pentane:carbon tetrachloride (2:1) as eluent gave 0.89 g (30%) of **11** as a white solid with mp 52-54°; ir (deposit from dichloromethane solution on a sodium chloride plate): 1174 and 1213 (C-O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.50-2.00 (m, 23H), 3.90 (t, J = 7.5 Hz, 2H), 4.55 (s, 4H), 6.90 (s, 2H).

Anal. Calcd. for $C_{20}H_{31}OBr_3$: C, 45.57; H, 5.93. Found: C, 45.73; H, 5.93.

4-Bromo-1-dodecyloxy-3,5-xylyl-15-crown-4 (**12**).

To a mixture of sodium hydride (0.61 g, 15.2 mmol, 60% dispersion in mineral oil) and 350 ml of tetrahydrofuran at reflux was added a solution of triethylene glycol (0.57 g, 3.8 mmoles) and **11** (2.00 g, 3.8 mmoles) in 50 ml of tetrahydrofuran over a period of 24 hours. Upon completion of addition, the reaction mixture was stirred at reflux for an additional 24 hours, allowed to cool to room temperature, filtered and evaporated *in vacuo* to give a solid which was extracted with

three 60-ml portions of hot petroleum ether. After evaporation of the combined organic extracts *in vacuo*, the residue was chromatographed on an alumina column with dichloromethane-ethyl acetate (4:1) as eluent to afford 1.14 g (58%) of **12** as a pale yellow solid with mp 31-32°; ir (deposit from deuteriochloroform on a sodium chloride plate): 1257, 1168, and 1105 (C-O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.85 (t, J = 6.1 Hz, 3H), 1.27 (s, 18H), 1.79 (pentet, 2H), 3.20-3.80 (m, 12H), 3.94 (t, J = 6.5 Hz, 2H), 4.20 (d, J = 12.3 Hz, 2H), 5.10 (d, J = 12.6 Hz, 2H), 6.85 (s, 2H).

Anal. Calcd. for $C_{26}H_{43}O_5Br$: C, 60.58; H, 8.41. Found: C, 60.35; H, 8.41.

4-Bromo-1-dodecyloxy-3,5-xylyl-18-crown-5 (**13**).

Reaction of sodium hydride, **11** (2.00 g, 3.8 mmoles) and tetraethylene glycol (0.74 g, 3.8 mmoles) by the procedure described for the preparation of **12** gave 1.27 g (60%) of **13** as a white solid with mp 55-57°; ir (deposit from deuteriochloroform on a sodium chloride plate): 1257, 1168, and 1105 (C-O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.90 (t, J = 6.2 Hz, 3H), 1.30 (s, 18H), 1.75 (pentet, 2H), 3.40-3.80 (m, 16H), 3.95 (t, J = 8.3 Hz, 2H), 4.65 (s, 4H), 6.95 (s, 2H).

Anal. Calcd. for $C_{28}H_{47}O_6Br$: C, 60.10; H, 8.47. Found: C, 60.37; H, 8.76.

4-Bromo-1-dodecyloxy-3,5-xylyl-21-crown-6 (**14**).

Reaction of sodium hydride, **11** (1.74 g, 3.3 mmoles) and pentaethylene glycol (0.79 g, 3.3 mmoles) by the procedure described for the preparation of **12** provided 1.21 g (61%) of **14** as a white solid with mp 40-43°; ir (deposit from deuteriochloroform solution on a sodium chloride plate): 1168, 1105, and 1255 (C-O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.90 (t, J = 6.4 Hz, 3H), 1.30 (s, 18H), 1.80 (pentet, 2H), 3.50-3.85 (m, 20H), 3.95 (t, J = 8.2 Hz, 2H), 4.65 (s, 4H), 6.95 (s, 2H).

Anal. Calcd. for $C_{30}H_{51}O_7Br$: C, 59.69; H, 8.52. Found: C, 59.82; H, 8.71.

4-Bromo-1-dodecyloxy-3,5-xylyl-24-crown-7 (**15**).

Reaction of sodium hydride, **11** (1.74 g, 3.3 mmoles) and hexaethylene glycol (0.90 g, 3.3 mmoles) by the procedure described for the preparation of **12** produced 1.25 g (60%) of **15** as a colorless oil; ir (deposit from deuteriochloroform on a sodium chloride plate): 1248 and 1118 (C-O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.90 (t, J = 6.1 Hz, 3H), 1.29 (s, 18H), 1.80 (pentet, 2H), 3.50-3.80 (m, 24H), 4.95 (t, J = 6.5 Hz, 2H), 4.65 (s, 4H), 7.00 (s, 2H).

Anal. Calcd. for $C_{32}H_{55}O_8Br$: C, 59.34; H, 8.56. Found: C, 59.74; H, 8.63.

2-Carbomethoxy-5-dodecyloxy-1,3-xylyl-15-crown-4 (**16**).

To a solution of **12** (1.75 g, 3.4 mmoles) in 15 ml of tetrahydrofuran cooled to -78° in an acetone-dry ice bath was added 2.08 ml of *n*-butyllithium (2.5 *M* in hexane, 5.2 mmoles). The reaction mixture was stirred at -78° for 8 hours after which 0.80 ml of methyl chloroformate (10.3 mmoles) was added. Stirring was continued as the reaction mixture was allowed to warm to room temperature. Following evaporation of the solvent *in vacuo*, the residue was subjected to column chromatography on alumina with dichloromethane-ethyl acetate (1:1) as eluent to give 1.14 g (67%) of **16** as a colorless oil; ir (deposit from deuteriochloroform on a sodium chloride plate): 1726 (C=O), 1161, 1114, 1120 and 1089 (C-O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.80 (t, J = 6.7 Hz, 3H), 1.20 (s, 18H), 1.70 (pentet, 2H), 3.10-3.70 (m, 12H), 3.75 (s, 3H), 3.90 (t, J = 6.5 Hz, 2H), 4.15 (d, J = 12.8 Hz, 2H), 4.96 (d, J = 12.7 Hz, 2H), 6.75 (s, 2H).

Anal. Calcd. for $C_{28}H_{46}O_7$: C, 67.99; H, 9.37. Found: C, 67.95; H, 9.51.

2-Carbomethoxy-5-dodecyloxy-1,3-xylyl-18-crown-5 (**17**).

Reaction of **13** (1.23 g, 2.2 mmoles), *n*-butyllithium and methyl chloroformate by the procedure described for the preparation of **16** gave 0.80 g (68%) of **17** as a colorless oil; ir (neat): 1722 (C=O), 1122, 1161, and 1091 (C-O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.85 (t, J = 6.8 Hz, 3H), 1.25 (s, 18H), 1.75 (pentet, 2H), 3.40-3.80 (m, 16H), 3.85 (s, 3H), 4.00 (t, J = 8.4 Hz, 2H), 4.60 (s, 4H), 6.90 (s, 2H).

Anal. Calcd. for $C_{30}H_{50}O_8$: C, 66.89; H, 9.35. Found: C, 67.21; H, 9.42.

2-Carbomethoxy-5-dodecyloxy-1,3-xylyl-21-crown-6 (**18**).

Reaction of **14** (1.03 g, 1.7 mmoles), *n*-butyllithium and methyl chloroformate by the procedure described for the preparation of **16** provided 0.75 g (76%) of **18** as a colorless oil; ir (neat): 1724 (C=O), 1113 and 1039 (C-O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.85 (t, J = 6.7 Hz, 3H), 1.25 (s, 18H), 1.80 (pentet, 2H), 3.55 (m, 20H), 3.90 (s, 3H), 3.95 (t, J = 6.5 Hz, 2H), 4.60 (s, 4H), 6.90 (s, 2H).

Anal. Calcd. for $C_{32}H_{54}O_9$: C, 65.95; H, 9.34. Found: C, 66.24; H, 9.43.

2-Carbomethoxy-5-dodecyloxy-1,3-xylyl-24-crown-7 (**19**).

Reaction of **15** (2.07 g, 3.2 mmoles), *n*-butyllithium and methyl chloroformate by the procedure described for the preparation of **16** produced 1.26 g (63%) of **19** as a colorless oil; ir (neat): 1724 (C=O), 1114 and 1039 (C-O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.90 (t, J = 6.9 Hz, 3H), 1.25 (s, 18H), 1.75 (pentet, 2H), 3.60 (m, 24H), 4.00 (m, 5H), 4.65 (s, 4H), 6.85 (s, 2H).

Anal. Calcd. for $C_{34}H_{58}O_{10} \cdot 0.35\ CH_2Cl_2$: C, 62.84; H, 9.01. Found: C, 62.77; H, 9.10.

2-Carboxy-5-dodecyloxy-1,3-xylyl-15-crown-4 (**4**).

A mixture of **16** (0.85 g, 1.7 mmoles), sodium hydroxide (0.20 g, 5.1 mmoles) and 95% ethanol (36 ml) was heated at reflux for 24 hours. The reaction was monitored by TLC and additional sodium hydroxide was added as needed (one pellet at a time) until all of the starting material **16** was consumed. The solvent was evaporated *in vacuo* and the residue was dissolved in 20 ml of dichloromethane and washed with three 20 ml portions of 4 *N* hydrochloric acid and then with water. The organic layer was dried over magnesium sulfate and evaporated *in vacuo* to give 0.69 g (84%) of **4** as a white solid with mp 71-73°; ir (potassium bromide): 3600-2600 (COOH), 1722 (C=O), 1167, 1140, 1107, and 1080 (C-O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.90 (t, J = 6.0 Hz, 3H), 1.25 (s, 18H),

1.80 (pentet, 2H), 3.35-3.80 (m, 12H), 3.95 (t, J = 6.3 Hz, 2H), 4.15 (d, J = 14.1 Hz, 2H), 5.05 (d, J = 12.4 Hz, 2H), 6.80 (s, 2H); ^{13}C nmr (deuteriochloroform): δ 169.8, 158.7, 137.7, 128.4, 115.9, 71.4, 70.1, 70.0, 68.1, 68.0, 31.8, 29.5, 29.2, 29.0, 25.8, 22.6, 14.0.

Anal. Calcd. for $C_{27}H_{44}O_7$: C, 67.47; H, 9.23. Found: C, 67.26; H, 9.42.

2-Carboxy-5-dodecyloxy-1,3-xylyl-18-crown-5 (**5**).

Basic hydrolysis and acidification of **17** (0.80 g, 1.5 mmoles) by the procedure described for the preparation of **4** produced 0.65 g (83%) of **5** as a yellow-white solid with mp 66-68°; ir (neat): 3600-2600 (COOH), 1724 (C=O), 1167, 1118, and 1099 (C-O) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 0.90 (t, J = 6.2 Hz, 3H), 1.25 (s, 18H), 1.75 (pentet, 2H), 3.60-3.85 (m, 16H), 3.95 (t, J = 6.5 Hz, 2H), 4.65 (s, 4H), 6.65 (s, 2H); ^{13}C nmr (deuteriochloroform): δ 169.4, 157.6, 137.0, 125.7, 112.7, 71.3, 70.1, 69.3, 68.5, 67.1, 30.9, 28.7, 28.6, 28.3, 28.1, 24.9, 21.7, 13.1.

Anal. Calcd. for $C_{29}H_{48}O_8$: C, 66.39; H, 9.22. Found: C, 66.26; H, 9.18.

2-Carboxy-5-dodecyloxy-1,3-xylyl-21-crown-6 (**6**).

Basic hydrolysis of **18** (0.70 g, 1.2 mmoles) and acidification by the procedure described for the preparation of **4** produced 0.56 g (82%) of **6** as a white solid with mp 46-48°; ir (deposit from deuteriochloroform solution on a sodium chloride plate): 3700-3177 (COOH), 1722 (C=O), 1167 and 1107 (C-O) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 0.90 (t, J = 5.7 Hz, 3H), 1.25 (s, 18H), 1.75 (pentet, 2H), 3.60-3.85 (m, 20H), 3.95 (t, J = 8.1 Hz, 2H), 4.70 (s, 4H), 6.80 (s, 2H); ^{13}C nmr (deuteriochloroform): δ 169.9, 159.0, 138.1, 125.7, 114.1, 71.8, 71.0, 70.6, 70.3, 70.1, 67.8, 31.7, 29.5, 29.4, 29.2, 28.9, 25.8, 22.5, 14.0.

Anal. Calcd. for $C_{31}H_{52}O_9$: C, 65.47; H, 9.22. Found: C, 65.17; H, 9.26.

2-Carboxy-5-dodecyloxy-1,3-xylyl-24-crown-7 (**7**).

Basic hydrolysis of **19** (1.30 g, 2.0 mmoles) and acidification by the procedure described for the preparation of **4** gave 0.99 g (81%) of **7** as a yellow oil; ir (neat): 3600-2600 (COOH), 1722 (C=O), 1103 (C-O) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 0.85 (t, J = 6.1 Hz, 3H), 1.25 (s, 18H), 1.75 (pentet, 2H), 3.60-3.85 (m, 24H), 3.95 (t, J = 6.1 Hz, 2H), 4.65 (s, 4H), 6.85 (s, 2H); ^{13}C nmr (deuteriochloroform): δ 169.6, 159.3, 138.5, 124.8, 113.6, 71.5, 70.9, 70.7, 70.3, 69.8, 67.9, 31.8, 29.5, 29.4, 29.2, 29.0, 25.8, 22.5, 14.0.

Anal. Calcd. for $C_{33}H_{56}O_{10}$: C, 64.68; H, 9.21. Found: C, 64.36; H, 9.31.

Extraction Procedure.

An aqueous solution of the alkali metal chlorides with hydroxides for pH adjustment (5.0 ml, 0.25 *M* in each) and 5.0 ml of a chloroform solution of the complexing agent (0.050 *M*) were shaken for 30 minutes in a 30-ml separatory funnel at room temperature [19]. The phases were separated and equilibrium pH of the aqueous phase was measured. Of the organic phase, 4.0 ml was removed and shaken with 5.0 ml of 0.1 *N* hydrochloric acid for 30 minutes to strip the metal cations from the organic phase into an aqueous solution for analysis with a Dionex Model 2000 ion chromotograph.

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