Synthesis of Lipophilic Crown Ethers with Pendant Phosphonic Acid or Phosphonic Acid Monoethyl Ester Groups

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Synthetic routes to fifteen lipophilic crown ether phosphonic acid monoethyl esters and nine lipophilic crown ether phosphonic acids are described. For both classes of crown ethers which have pendant, proton-ionizable groups, the crown ether ring sizes are systematically varied from 12-crown-4 and 24-crown-8.

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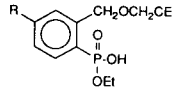
Crown ethers with a pendant proton-ionizable group are efficient reagents for the solvent extraction and transport of alkali metal cations across bulk liquid, liquid surfactant (emulsion), and polymer-supported liquid membranes [1-4]. Compared with crown ethers which do not possess such acidic groups, the proton-ionizable crown ethers have the distinct advantage that transport of the metal cation from the aqueous phase into the organic medium does not require concomitant transfer of an aqueous phase anion [5]. This factor is of immense importance to potential practical applications in which hard, hydrophilic, aqueous phase anions, such as chloride, nitrate and sulfate, would be involved.

Previously we have described the synthesis of lipophilic crown ethers which have a pendant carboxylic acid group [6-10]. Solvent extraction of alkali metal cations from aqueous solutions into organic solvents was found to be effective when the aqueous phase was basic [1,4]. For metal ion extraction from neutral or acidic aqueous solutions, a pendant group of greater acidity would be required. We now report the preparation of crown ethers with pendant phosphonic acid monoethyl ester groups which will have greater acidity than analogous compounds with carboxylic acid functions [11,12]. In addition, the synthesis of crown ether phosphonic acids provides di-ionizable ligands for the formation of one-to-one complexes with divalent metal ions.

Results and Discussion.

Two types of crown ether phosphonic acid monoethyl esters **1** and **2** in which CE = crown ether have been pre-



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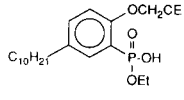

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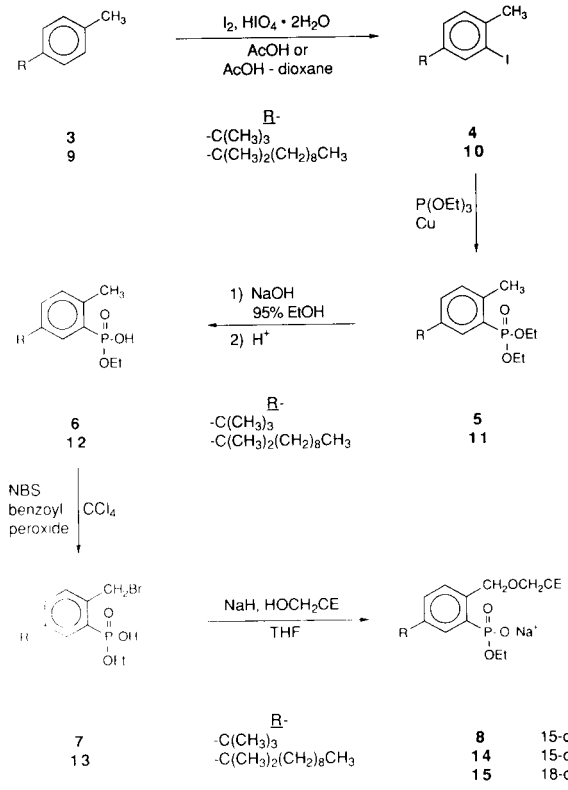
pared. The principal structural difference between the two types is the benzylic methylene group in the crown ether-containing side arm of **1**. The ^1H nmr spectroscopy of the diastereotopic benzylic hydrogens in **1** may be utilized to probe participation of an anionic side group in the complexation of a polyether-bound alkali metal cation in solution [13]. On the other hand, a more direct synthetic route to the lipophilic crown ether phosphonic acids **2** makes them more suitable for studies of the influence of crown ether ring size variation upon the efficiency and selectivity of alkali metal cation extraction and liquid membrane transport [1,14].

The preparative route to the lipophilic crown ether sodium monoethyl phosphonate **8**, which has a 15-crown-5 ring, is shown in Scheme 1. Following the procedure of Suzuki and coworkers for ring iodination of polyalkylbenzenes bearing bulky groups [15], reaction of commercially available 4-*tert*-butyltoluene (**3**) with iodine and periodic acid dihydrate in acetic acid gave selective iodination *or-*

Scheme 1



tho to the methyl group to form **4** in 76% yield. Reaction of **4** with triethylphosphite and freshly prepared, activated copper [16] provided a 72% yield of phosphonic acid diethyl ester **5** which gave an 82% yield of the corresponding phosphonic acid monoethyl ester **6** upon basic hydrolysis. For the benzylic bromination of **6**, refluxing with *N*-bromosuccinimide and benzoyl peroxide in carbon tetrachloride to produce **7** was found to be much more effective than reaction with bromine in carbon tetrachloride under irradiation. Conversion of up to 90% of **6** into **7** was determined by nmr for the benzoyl peroxide-initiated bromination. Due to difficulty in separating the brominated product from the reactant, the crude product was used for the next step.

Coupling of **7** with hydroxymethyl-15-crown-5 was accomplished by reaction of the crown ether alcohol with sodium hydride in tetrahydrofuran followed by the addition of **7** to produce a 64% yield of the lipophilic crown ether sodium monoethyl phosphonate **8**. The corresponding crown ether phosphonic acid monoethyl ester can be obtained by treatment of the sodium salt with hydrochloric acid.

When a chloroform solution of **8** was shaken with an aqueous solution of sodium chloride and hydroxide (*p*H = 10), it was determined by uv-visible spectroscopy of the chloroform phase that 85% of the extractant was lost to the alkaline aqueous layer. Hence the *tert*-butyl group in **8** was found to be insufficiently lipophilic to retain the ionized crown ether in the organic phase.

Since 4-alkyltoluenes with alkyl groups of greater lipophilicity than the *tert*-butyl group are not commercially available, the synthesis of 4-[(1,1-dimethyl)decyl]toluene was undertaken. By reaction of two equivalents of methylmagnesium iodide with ethyl decanoate, an 88% yield of 2-methyl-2-undecanol was realized. The alcohol was converted into 2-chloro-2-methylundecane in 96% yield by the procedure of Brown and Rei [17] in which a tertiary alcohol is exposed to a large molar excess anhydrous hy-

Table I

Metal Hydride Employed, Yields, Spectral Data and Elemental Analysis Data for Lipophilic Crown Ether Diethyl Phosphonates **20-30** and Model Compound **31** [a]

Compound No.	M of MH	Yield %	^{1}H NMR Spectra (60 MHz), ppm	IR Spectra, cm^{-1}	Molecular Formula	Elemental Analysis Theory/Found C	H
20	K	61	0.65-1.80 (m, 25H), 2.53 (t, 2H), 3.30-4.40 (m, 21H), 6.65-7.80 (m, 3H)	1255 (P=O), 1134, 1098 C–O), 1030 (P–O)	$C_{29}H_{51}O_8P\bullet 0.5H_2O$	61.36 61.48	9.23 9.25
21	K	40	0.65-2.10 (m, 27H), 2.55 (t, 2H), 3.40-4.45 (m, 21H), 6.65-7.85 (m, 3H)	1255 (P=O), 1130, 1090 (C–O), 1030 (P–O)	$C_{30}H_{53}O_8P$	62.92 63.00	9.33 9.18
22	K	61	0.65-2.11 (m, 29H), 2.56 (t, 2H), 3.30-4.40 (m, 21H), 6.65-7.90 (m, 3H)	1255 (P=O), 1126, 1091 (C–O), 1030 (P–O)	$C_{31}H_{55}O_8P$	63.46 63.67	9.45 9.25
23	K	43	0.65-2.20 (m, 28H), 2.55 (t, 2H), 3.30-4.40 (m, 22H), 6.65-7.90 (m, 3H)	1260 P=O), 1130, 1095 (C–O), 1035 (P–O)	$C_{31}H_{55}O_8P$	63.46 63.39	9.45 9.41
24	Na	59	0.70-1.80 (m, 25H), 2.55 (t, 2H), 3.30-4.40 (m, 25H), 6.65-7.85 (m, 3H)	1253 (P=O), 1128, 1089 (C–O), 1030 (P–O)	$C_{31}H_{55}O_9P\bullet 0.5H_2O$	60.86 61.15	9.23 9.09
25	K	35	0.70-2.00 (m, 25H), 2.30-2.80 (m, 3H), 3.40-4.40 (m, 26H), 6.70-7.90 (m, 3H)	1255 (P=O), 1122, 1091 (C–O), 1028 (P–O)	$C_{32}H_{57}O_9P$	62.32 62.03	9.31 9.14
26	Na	71	0.70-1.80 (m, 25H), 2.53 (t, 2H), 3.40-4.30 (m, 29H), 6.70-7.80 (m, 3H)	1253 (P=O), 1122, 1091 (C–O), 1030 (P–O)	$C_{33}H_{59}O_{10}P$	61.28 61.36	9.19 9.20
27	Na	73	0.65-2.35 (m, 27H), 2.53 (t, 2H), 3.40-4.30 (m, 29H), 6.70-7.80 (m, 3H)	1255 (P=O), 1120, 1090 (C–O), 1030 (P–O)	$C_{34}H_{61}O_{10}P$	61.80 61.51	9.30 9.49
28	Na	76	0.70-1.85 (m, 25H), 2.53 (t, 2H), 3.40-4.30 (m, 33H), 6.65-7.80 (m, 3H)	1253 (P=O), 1118 (C–O), 1029 (P–O)	$C_{35}H_{63}O_{11}P$	60.85 60.84	9.19 9.46
29	Na	69	0.60-1.70 (m, 25H), 2.55 (t, 2H), 3.40-4.25(m, 37H), 6.65-7.80 (m, 3H)	1253 (P=O), 1115 (C–O), 1028 (P–O)	$C_{35}H_{63}O_{12}P$	60.47 60.24	9.19 9.18
30	Na	50	0.70-1.80 (m, 25H), 2.55 (t, 2H), 3.60-4.40 (m, 25H), 6.90 (s, 4H), 6.65-7.85 (m, 3H)	1255 (P=O), 1130 (C–O), 1050 (P–O)		[b]	
31	Na	45	0.70-2.15 (m, 36H), 2.53 (t, 2H), 3.65-4.45 (m, 6H), 6.60-7.85 (m, 3H)	1253 (P=O), 1089 (C–O), 1030 (P–O)	$C_{27}H_{47}O_4P$	69.50 69.21	10.15 10.33

[a] Compounds **20-31** were colorless or pale yellow oils. [b] Hydrolyzed directly to phosphonic acid monoethyl ester **42** for which satisfactory elemental analysis was obtained.

drogen chloride.

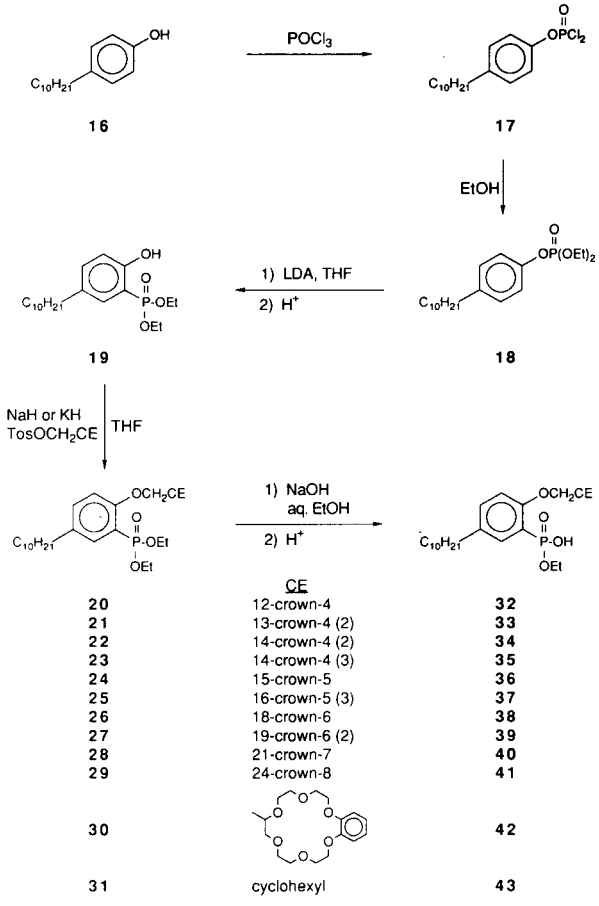
A Friedel-Crafts alkylation of toluene with 2-chloro-2-methylundecane was performed with tin(IV) chloride as the catalyst. Earlier work by Olah and coworkers in the *tert*-butylation of toluene [18] indicated that tin(IV) choride catalyst would offer the highest *para:meta* ratio without an excessive loss of reactivity. A series of reactions between 2-chloro-2-methylundecane and toluene with tin(IV) chloride at different temperatures was conducted. The percent of *para* isomer, as determined by gas chromatography, ranged from 96% at room temperature to 92% at 100°. At room temperature the *para:meta* ratio was higher, but the yield of product was low (~10%). At 100°, conversions of up to 81% were achieved, but the *para:meta* ratio was somewhat lower. As a compromise, the alkylation reaction was conducted at 50° for 48 hours to provide a 53% isolated yield of 4(3)-[(1,1-dimethyl)decyl]-toluene (**9**) with a *para* isomer content of 95%.

For conversion of **9** into lipophilic crown ether sodium monoethyl phosphonates **14** and **15** (Scheme 1) the synthetic route closely resembled that which was utilized to transform 4-*tert*-butyltoluene into **8**. For iodination of **9** to form **10**, a modified solvent system was required due to the poor solubility of **9** in acetic acid. With a solvent mixture of dioxane and acetic acid and an extended reaction time due to the lower solvent polarity, the reaction gave 72% of the ring-iodinated hydrocarbon **10**. Conversion of **10** into the diethyl phosphonate **11** then into the monoethyl phosphonate **12** was accomplished in 69 and 94% yields, respectively, under the same conditions that were employed to transform **4** into **6**. Benzylic bromination of **12** gave a crude product which was found by nmr to contain 85% of **13** and 15% of unreacted **12**. This crude product mixture was utilized without further purification for coupling with hydroxymethyl-15-crown-5 and hydroxymethyl-18-crown-6 to give the lipophilic crown ether sodium monoethyl phosphonates **14** and **15** in yields of 36 and 49%, respectively.

When tested under solvent extraction conditions, **14** and **15** were found to be sufficiently lipophilic to avoid loss from a chloroform phase into a highly basic aqueous phase.

The preparative route to eleven lipophilic crown ether phosphonic acid monoethyl esters of type **2** with varying crown ether ring sizes, as well as a model compound with a cyclohexane ring in place of the crown ether unit, is summarized in Scheme 2. Reaction of 4-decylphenol (**16**) with phosphorus oxychloride in the presence of cesium chloride gave a 92% yield of dichlorophosphonate **17** which was treated with ethanol to produce diethyl 4-decylphenyl phosphate (**18**) in 89% yield [19]. Reaction of **18** with lithium diisopropyl amide in tetrahydrofuran at low temperature [20] followed by acidification provided a 78% yield of diethyl 5-decyl-2-hydroxybenzenephosphonate (**19**). This key synthetic intermediate possesses a lipophilic group, a diethyl phosphonate function and a phenolic site for crown ether attachment.

Scheme 2



Reaction of sodium or potassium hydride in tetrahydrofuran with **19** followed by coupling of the resulting phenoxide ion with tosylates of (hydroxymethyl)crown ethers gave lipophilic crown ether diethyl phosphonates **20-30** in 35-77% yields. Similar coupling with the tosylate of (hydroxymethyl)cyclohexane produced the model phosphonate ester **31**, which contains a cyclohexane ring rather than a crown ether, in 45% yield. Table 1 provides a listing of the metal hydride reagents, yields, physical properties, spectral data and elemental analysis data for the lipophilic diethyl phosphonates **20-31**. Basic hydrolysis of diethylphosphonates **20-31** followed by acidification usually afforded the lipophilic monoethyl phosphonates **32-43** in 89-98% yields. Table 2 presents a listing of yields, physical properties, spectral data and elemental analysis data for lipophilic crown ether phosphonic acid monoethyl esters **32-42** and model compound **43**.

For investigation of the influence of the lipophilic group attachment site upon the efficiency and selectivity of metal ion extraction and transport across liquid membranes [14], lipophilic crown ether phosphonic acid mono-

Table 2

Yields, Physical Properties, Spectral Data and Elemental Analysis Data for Lipophilic Crown Ether Phosphonic Acid Monoethyl Esters **32-42** and Model Compound **43** [a]

Compound No.	Yield %	^{1}H NMR Spectra (60 MHz), ppm	IR Spectra, cm^{-1}	Molecular Formula	Elemental Analysis Theory/Found C	H
32	93	0.65-1.85 (m, 22H), 2.53 (t, 2H), 3.30-4.40 (m, 19H), 6.65-7.80 (m, 3H) 11.53 (s, 1H)	2310 (POH), 1255 (P=O), 1130, 1093 (C–O), 1047 (P–O)	$C_{27}H_{47}O_8P$	61.11 60.84	8.93 8.71
33	91	0.65-2.05 (m, 24H), 2.53 (t, 2H), 3.35-4.45 (m, 19H), 6.70-7.80 (m, 3H) 10.03 (s, 1H)	2312 (POH), 1255 (P=O), 1130, 1093 (C–O), 1047 (P–O)	$C_{28}H_{49}O_8P$	61.75 62.03	9.07 8.98
34	96	0.65-2.10 (m, 26H), 2.55 (t, 2H), 3.30-4.41 (m, 19H), 6.65-7.80 (m, 3H) 11.00 (br s, 1H)	2310 (POH), 1255 (P=O), 1124 (C–O), 1045 (P–O)	$C_{29}H_{51}O_8P\cdot 0.25\ H_2O$	61.85 61.78	9.22 9.26
35	90	0.65-2.05 (m, 25H), 2.51 (t, 2H), 3.35-4.40 (m, 20H), 6.70-7.80 (m, 3H) 11.60 (s, 1H)	2359 (POH), 1255 (P=O), 1124 (C–O), 1045 (P–O)	$C_{29}H_{51}O_8P$	62.35 62.09	9.20 9.23
36	92	0.65-1.80 (m, 22H), 2.52 (t, 2H), 3.30-4.40 (m, 23H), 6.60-7.75 (m, 3H) 11.43 (br s, 1H)	2350 (POH), 1250 (P=O), 1130, 1095 (C–O), 1050 (P–O)	$C_{29}H_{51}O_9P$	60.61 60.45	8.95 9.04
37	61 [b]	0.65-1.80 (m, 22H), 2.30-2.80 (m, 3H), 3.40-4.30 (m, 24H), 6.60-7.80 (m, 3H), 10.60 (br s, 1H)	2350 (POH), 1253 (P=O), 1118 (C–O), 1047 (P–O)	$C_{30}H_{53}O_9P$	61.21 60.92	9.07 8.83
38	96	0.60-1.70 (m, 22H), 2.53 (t, 2H), 3.30-4.25 (m, 27H), 6.70-7.70 (m, 3H), 9.55 (s, 1H)	2300 (POH), 1253 (P=O), 1120 (C–O), 1045 (P–O)	$C_{31}H_{55}O_{10}P$	60.18 60.24	8.96 8.95
39	93	0.65-2.10 (m, 26H), 2.53 (t, 2H), 3.30-4.40 (m, 27H), 6.65-7.80 (m, 3H), 11.50 (br s, 1H)	2300 (POH), 1250 (P=O), 1118 (C–O), 1040 (P–O)	$C_{32}H_{57}O_{10}P$	60.74 60.66	9.08 9.18
40	91	0.65-1.70 (m, 22H), 2.52 (t, 2H), 3.30-4.40 (m, 31H), 6.65-7.80 (m, 3H), 10.40 (br s, 1H)	2357 (POH), 1253 (P=O), 1118 (C–O), 1043 (P–O)	$C_{33}H_{59}O_{11}P$	59.80 59.58	8.97 8.94
41	89	0.65-1.75 (m, 22H), 2.53 (t, 2H), 3.30-4.30 (m, 35H), 6.65-7.80 (m, 3H),	2300 (POH), 1250 (P=O), 1120 (C–O), 1040 (P–O)	$C_{35}H_{63}O_{12}P$	59.47 59.31	8.98 9.20
42	98	0.70-1.80 (m, 22H), 2.55 (t, 2H), 3.60-4.35 (m, 23H), 6.90 (s, 4H), 6.65-7.85 (m, 3H), 9.15 (br s, 1H)	2600 (POH), 1255 (P=O), 1130 (C–O), 1050 (P–O)	$C_{35}H_{55}O_{10}P\cdot H_2O$	61.39 61.20	8.39 8.48
43	96	0.55-2.15 (m, 33H), 2.30-2.70 (m, 2H), 3.55-4.35 (m, 4H), 6.55-8.90 (m, 3H)	2328 (POH), 1253 (P=O), 1095 (C–O), 1047 (P–O)	$C_{25}H_{43}O_4P$	68.46 68.65	9.88 10.19

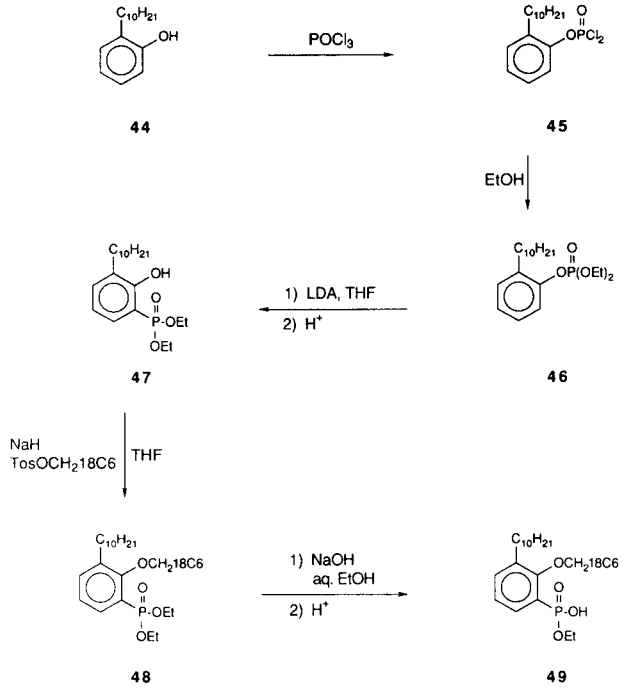
[a] Compounds **32-43** were colorless or pale yellow oils. [b] The initial impure product was chromatographed on alumina with ethyl acetate-methanol (10:1) as eluent. [c] Chloroform, rather than dichloromethane, is the recommended solvent for workup since the latter forms a strong solvate with **42**.

ethyl ester **49** was also synthesized (Scheme 3). In **49** the crown ether-containing group is positioned between lipophilic and proton-ionizable groups, whereas in structural isomer **38** the lipophilic group is distant from both the 18-crown-6 ring and the proton-ionizable group.

The 2-decylphenol (**44**) was converted into diethyl 2-hydroxy-3-decylphosphonate (**47**) in three steps by the same reaction sequence which was utilized previously to transform 4-decylphenol (**16**) into diethyl 2-hydroxy-5-decylphosphonate (**19**) in comparable yields. Reaction of **47** with sodium hydride in tetrahydrofuran and coupling with the tosylate of (hydroxymethyl)-18-crown-6 gave a 77% yield of lipophilic crown ether diethyl phosphonate **48** which afforded the corresponding phosphonic acid monoethyl ester **49** in 83% yield on hydrolysis.

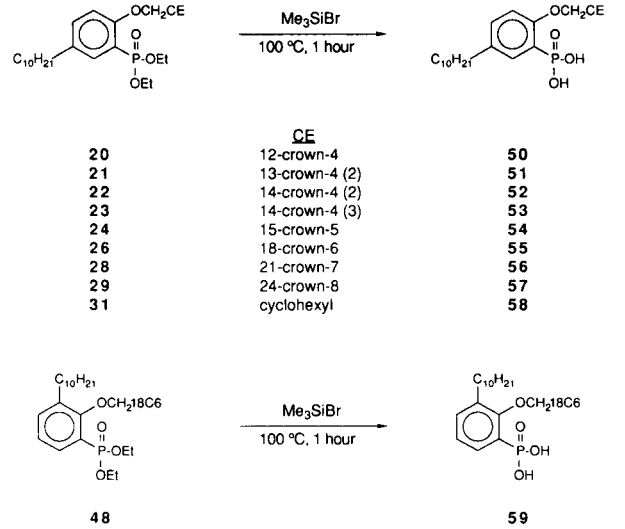
For the preparation of lipophilic crown ether phosphonic acids, acidic hydrolysis of monoethyl ester **33** was initially examined. Monoester **33** was recovered unchanged after stirring at room temperature in trifluoroacetic acid or heating with trifluoroacetic acid in benzene at 40-45°. However, reaction with trimethylsilyl bromide at 100° did hydrolyze the phosphonic acid monoethyl ester to the corresponding phosphonic acid. Subsequently, it was found that heating **21**, the diethyl phosphonate precursor to **33**,

Scheme 3



with trimethylsilyl bromide at 100° also produced the corresponding phosphonic acid. Since the phosphonate diethyl esters were usually easier to purify than the monoethyl esters, lipophilic crown ether diethyl phosphonates were utilized as precursors to lipophilic crown ether phosphonic acids (Scheme 4). For the lipophilic crown ether phosphonic acids **50-57** and **59** and the model compound **58**, yields, physical properties, spectral data and elemental analysis data are summarized in Table 3.

Scheme 4



CE		
20	12-crown-4	**50**
21	13-crown-4 (2)	**51**
22	14-crown-4 (2)	**52**
23	14-crown-4 (3)	**53**
24	15-crown-5	**54**
26	18-crown-6	**55**
28	21-crown-7	**56**
29	24-crown-8	**57**
31	cyclohexyl	**58**

EXPERIMENTAL

Melting points were taken on either a Mel-Temp or Fisher-Johns melting point apparatus and are uncorrected. The ir spectra were obtained with a Nicolet MS-X or Beckman Acculab 1 spectrometer and are reported in reciprocal centimeters. The ^{1}H nmr spectra were recorded with Varian EM360 or EM360A spectrometers in deuteriochloroform and chemical shifts are reported in parts per millions (δ) downfield from TMS. Elemental analysis was performed by Galbraith Laboratories (Knoxville, Tennessee).

Unless specified otherwise, reagent grade reactants and solvents were used as received from commercial suppliers. Tetrahydrofuran was purified by distillation from lithium aluminum hydride. Pentane was stored over potassium hydroxide pellets and distilled prior to use. The (tosyloxymethyl)crown ethers were available from earlier work [7,9]. The 2-decylphenol and 4-decylphenol [21] were prepared by adaptation of literature procedures [22,23].

Preparation of 4-*tert*-Butyl-2-iodotoluene (**4**).

To a solution of 4-*tert*-butyltoluene (30.03 g, 0.20 mole) in 123 ml of glacial acetic acid-water-concentrated sulfuric acid (100/20/3, respectively, by volume) was added iodine (20.00 g, 0.079 mole) and periodic acid dihydrate (9.43 g, 0.041 mole). The reaction mixture was stirred at 60-65° for 7 hours with occasional swirling of the flask to wash sublimed iodine back into the reaction mixture. The solvent was evaporated *in vacuo* and the residual oil was dissolved in diethyl ether. The ether solution was washed with 10% aqueous sodium thiosulfate (2 x 100 ml) then water (100 ml) and dried over magnesium sulfate. Evaporation of the filtrate *in vacuo* gave a pale yellow liquid which was distilled under vacuum (92-95°/1.0 torr) to give **4** (42.7 g, 76%) as a colorless oil; ir (neat): 1620, 1570 (aromatic ring) cm^{-1}; ^{1}H nmr: δ 1.25 (s, 9 H), 2.35 (s, 3 H), 7.00-7.20 (m, 2 H), 7.78 (d, 1 H).

Anal. Calcd. for $C_{11}H_{15}I$: C, 48.19; H, 5.52. Found: C, 47.97; H, 5.40.

Preparation of Diethyl 5-*tert*-Butyl-2-methylbenzenephosphonate (**5**).

A stirred mixture of **4** (20.00 g, 0.073 mole) and freshly prepared, activated copper metal [16] was heated to 155-160° under nitrogen and triethyl phosphite (36.39 g, 0.219 mole) was added dropwise (**caution**: vigorous foaming). The mixture was refluxed for 24 hours, cooled and filtered. Dichloromethane (100 ml) was added to the filtrate and the solution was washed with concentrated ammonium hydroxide (3 x 100 ml) then water (100 ml) and dried over magnesium sulfate). Evaporation *in vacuo* left a golden oil which was distilled under vacuum (123-125°/0.35 torr) to give **5** (14.93 g, 72%) as a colorless oil; ir (neat): 1249 (P=O), 1026 (P-O) cm^{-1}; ^{1}H nmr: δ 1.10-1.45 (m, 15 H), 2.55 (s, 3 H), 4.13 (pentet, 4 H), 7.05-7.57 (m, 2 H), 7.75-8.10 (m, 1 H).

Anal. Calcd. for $C_{15}H_{25}O_3P$: C, 63.36; H, 8.86. Found: C, 63.00; H, 8.70.

Preparation of Monoethyl 5-*tert*-Butyl-2-methylbenzenephosphonate (**6**).

To a solution of **5** (13.50 g, 0.048 mole) dissolved in 50 ml of 95% ethanol was added powdered sodium hydroxide (5.76 g, 0.144 mole). The solution was refluxed for 24 hours and evaporated *in vacuo*. The residue was dissolved in water and the aqueous solution was extracted with dichloromethane (3 x 50 ml).

Table 3

Yields, Physical Properties, Spectral Data and Elemental Analysis Data for Lipophilic Crown Ether Phosphonic Acids **50-57** and Model Compound **58** [a]

Compound No.	Yield %	^{1}H NMR Spectra (60 MHz), ppm	IR Spectra, cm^{-1}	Molecular Formula	Elemental Analysis Theory/Found C	H
50	54	0.60-1.70 (m, 19H), 2.90-4.68 (m, 19H), 6.40-7.80 (m, 3H), 8.62 (br s, 2H)	2360 (POH), 1123 (C–O)	$C_{25}H_{43}O_8P$• 0.2 $CHCl_3$	57.49 57.67	8.27 7.94
51	66	0.50-2.80 (m, 21H), 3.10-4.60 (m, 19H), 6.60-7.85 (m, 3H)	2370 (POH), 1126, 1090 (C–O)	$C_{26}H_{45}O_8P$	60.45 60.32	8.78 8.66
52	71	0.60-2.00 (m, 19H), 2.50 (br s, 2H), 3.00-4.65 (m, 18H), 6.60-7.85 (m, 3H), 9.40 (br s, 2H)	2357 (POH), 1120 (C–O)	$C_{27}H_{47}O_8P$• 0.5 CH_2Cl_2	57.63 57.22	8.44 8.59
53	49	0.50-2.00 (m, 22H), 2.45 (br s, 5H), 3.00-4.70 (m, 18H), 6.60-7.80 (m, 3H), 9.50 (br s, 2H)	2337 (POH), 1124, 1093 (C–O)	$C_{27}H_{47}O_8P$	61.11 61.39	8.93 8.85
54	97	0.80-1.70 (m, 19H) [b], 2.52 (t, 2H), 3.35-4.50 (m, 21H), 6.67 (t, 1H), 7.20-7.35 (m, 1H), 7.59 (d, 1H), 10.61 (s, 2H)	2350 (POH), 1125 (C–O)	$C_{27}H_{47}O_9P$• 0.4 CH_2Cl_2	56.69 56.62	8.30 8.29
55	90	0.75-1.70 (m, 19H) [b], 2.51 (t, 2H), 3.00-4.35 (m, 25H), 6.85 (t, 1H), 7.15-7.30 (m, 1H), 7.57 (d, 1H), 9.81 (s, 2H)	2362 (POH), 1114 (C–O)	$C_{29}H_{51}O_{10}P$• CH_2Cl_2	53.33 53.17	7.91 8.05
56	95	0.70-1.90 (m, 19H) [b], 2.53 (t, 2H), 2.90-4.40 (m, 29H), 6.88 (t, 1H), 7.20-7.35 (m, 1H), 7.59 (d, 1H), 8.83 (s, 2H)	2360 (POH), 1100 (C–O)	$C_{31}H_{55}O_{11}P$• CH_2Cl_2	53.40 53.36	7.98 8.08
57	64	0.50-2.00 (m, 19H), 2.53 (br s, 2H), 2.90-4.60 (m, 33H), 6.60-8.20 (m, 3H), 9.85 (br s 2H)	2341 (POH), 1109 (C–O)	$C_{33}H_{59}O_{12}P$• 1.1 CH_2Cl_2	53.04 52.88	7.99 8.21
58	90 [c]	0.65-2.80 (m, 32H), 3.55-3.95 (m, 2H), 6.55-7.90 (m, 3H)	2316 (POH)	$C_{23}H_{39}O_4P$	67.29 67.61	9.57 9.74
59	90	0.60-1.80 (m, 19H), 2.60 (br s, 2H), 3.00-4.30 (m, 25H), 6.60-7.90 (m, 3H)	2339 (POH), 1116 (C–O)	$C_{29}H_{51}O_{10}P$	58.97 59.28	8.70 8.50

[a] Except for **58**, all compounds were colorless, hygroscopic oils. [b] Spectrum taken at 200 MHz. [c] White amorphous solid with mp 147-148°.

The aqueous layer was acidified to *p*H = 2 with concentrated hydrochloric acid and extracted with dichloromethane (2 x 100 ml). The combined organic layers were dried over magnesium sulfate and the solvent was evaporated *in vacuo* to provide 10.00 g (82%) of **6** as a viscous, yellow oil; ir (neat): 2596, 2355 (POH), 1195 (P=O), 1039 (P-O) cm^{-1}; ^{1}H nmr: δ 1.10-1.45 (m, 12 H), 2.50 (s, 3 H), 4.00 (pentet, 2 H), 6.85-7.42 (m, 2 H), 7.65-8.05 (m, 1 H).

Anal. Calcd. for $C_{13}H_{21}O_3P$•0.4H_2O: C, 59.26; H, 8.34. Found: C, 59.21; H, 8.02.

Preparation of Sodium Monoethyl 5-*tert*-Butyl-1-(oxymethyl-15-crown-5)methylbenzenephosphonate (**8**).

A solution of **6** (10.00 g, 0.039 mole), *N*-bromosuccinimide (6.94 g, 0.039 mole) and benzoyl peroxide (0.05 g) in 50 ml of carbon tetrachloride was stirred at reflux for 8 hours. The mixture was cooled, allowed to stand at room temperature overnight, and filtered. The collected solid was washed with several small portions of cold carbon tetrachloride. The combined filtrate and washings were washed with water (100 ml) and dried over magnesium sulfate. The ^{1}H nmr analysis of the solution showed a 91% conversion into the bromomethyl compound **7**. The solvent was evaporated *in vacuo* to give a yellow oil. The crude product was used without further purification due to difficulty in separating **7** from **6**; ir (neat): 2590, 2352 (POH), 1190 (P=O), 1035 (P-O) cm^{-1}; ^{1}H nmr: δ 0.95-1.52 (m, 12 H), 2.50 (s, 0.20 H from residual **6**), 3.68-4.30 (pentet, 2 H), 4.75 (s, 2 H), 7.20-8.13 (m, 3 H), 13.72 (s, 1 H).

To 0.60 g of sodium hydride (15.0 mmole of 60% dispersion in mineral oil) under nitrogen was added dropwise a solution of hydroxymethyl-15-crown-5 [24] (1.00 g, 4.0 mmoles) in 10 ml of tetrahydrofuran and the mixture was stirred for 30 minutes. A solution of **7** (1.35 g of 91% pure compound, 15.0 mmoles) in 10 ml of THF was added dropwise which produced vigorous foaming. The mixture was refluxed for three days and the solvent was evaporated *in vacuo*. The red-brown solid residue was dissolved in 50 ml of water and extracted with dichloromethane (3 x 50 ml).

The combined organic layers were dried over magnesium sulfate and evaporated *in vacuo* to give an orange oil. Chromatography on silica gel with methanol as eluent gave 1.35 g (64%) of **8** as a tan solid; ir (potassium bromide): 1190 (P=O), 1120 (C-O), 1040 (P-O) cm^{-1}; ^1H nmr: δ 0.95-1.55 (m, 12 H), 3.10-4.55 (m, 25 H), 7.15-7.40 (m, 2 H), 7.82-8.18 (m, 1 H).

Anal. Calcd. for $C_{24}H_{40}O_9PNa \cdot 0.5H_2O$: C, 53.83; H, 7.72. Found: C, 54.02; H, 7.55.

Preparation for 4(3)-[(1,1-Dimethyl)decyl]toluene (**9**).

A Grignard reagent solution formed by dropwise addition of a solution of iodomethane (67.10 g, 0.47 mole) in 150 ml of anhydrous diethyl ether to 11.00 g (0.45 mole) of magnesium turnings was cooled in an ice bath. The ice bath was removed and a solution of ethyl decanoate (43.01 g, 0.22 mole) in 125 ml of anhydrous diethyl ether was added at such a rate that a mild reflux was maintained. Following completion of the addition, the mixture was refluxed for one hour. The mixture was cooled in an ice bath and 350 ml of saturated aqueous ammonium chloride was added dropwise with vigorous stirring. The white precipitate was filtered and the aqueous and organic layers were separated. The aqueous layer was extracted with diethyl ether (2 x 100 ml). The organic layer was washed successively with saturated aqueous ammonium chloride (100 ml), saturated aqueous sodium bicarbonate (100 ml) then water (2 x 100 ml). The washed organic layer and diethyl ether extracts of the original aqueous layer were combined, dried over magnesium sulfate and evaporated *in vacuo* to give a yellow oil which was refluxed in 10% aqueous sodium hydroxide for 24 hours. The mixture was cooled and the aqueous and organic layers were separated. The aqueous layer was extracted with diethyl ether (2 x 100 ml). The ether extracts and the organic layer were combined, washed with water (100 ml), dried over magnesium sulfate and evaporated *in vacuo*. Vacuum distillation (80-84°/0.4 torr) produced 36.00 g (88%) of 1,1-dimethyl-1-decanol as a colorless oil; ir (neat): 3360 (OH), 1131 (C-O) cm^{-1}; ^1H nmr: δ 0.60-0.90 (m, 3 H), 1.00-1.60 (m, 22 H), 1.70 (s, 1 H).

By a general procedure described by Brown and Rei [17], 1,1-dimethyl-1-decanol (20.00 g, 0.11 mole) was reacted with a large excess of gaseous hydrogen chloride. The organic layer was separated and dissolved in dichloromethane. The solution was dried over magnesium sulfate and evaporated *in vacuo* to give 2-chloro-2-methylundecane (21.16 g, 96%) as a pale yellow oil, ir (neat): 725 (C-Cl) cm^{-1}; ^1H nmr: δ 0.70-1.05 (m, 3 H), 1.10-1.50 (m, 14 H), 1.55-1.90 (m, 8 H).

Under nitrogen, tin(IV) chloride (16.05 g, 62 mmoles) was added by syringe through a septum to 65.25 g (0.71 mole) of toluene followed by 18.00 g (88 mmoles) of 2-chloro-2-methylundecane and the reaction mixture was stirred at 50° for 48 hours, cooled and poured into a mixture 25 ml of concentrated hydrochloride and 25 g of ice. After stirring for 15 minutes, the organic layer was separated, dissolved in petroleum ether (150 ml), washed with water (100 ml) and dried over magnesium sulfate. Evaporation *in vacuo* left a dark brown oil which was distilled under vacuum (128-130°/0.4 torr) to provide 12.08 g (53%) of **9** as a colorless oil; ir (neat): 1625 (benzene ring) cm^{-1}; ^1H nmr: δ 0.70-1.80 (m, 25 H), 2.25 (s, 3 H), 6.90-7.32 (m, 4 H). Gas chromatographic analysis established a 95/5 *para*/*meta* ratio in the product.

Anal. Calcd. for $C_{19}H_{32}$: C, 87.62; H, 12.38. Found: C, 87.89; H, 12.57.

Preparation of 4-[(1,1-Dimethyl)decyl]-2-iodotoluene (**10**).

By the procedure described previously for the conversion of **3** into **4** but with dioxane as an additional solvent, a mixture of 8.08 g (31.1 mmoles) of **9**, dioxane (80 ml), acetic acid (34 ml), water (1.2 ml), iodine (7.89 g, 31.1 mmoles) and periodic acid dihydrate (2.58 g, 31.1 mmoles) was refluxed for 48 hours. After workup, vacuum distillation (168-171°/0.35 torr) yielded 8.62 g (72%) of **10** as a pale orange oil; ir (neat): 1625 (benzene ring) cm^{-1}; ^1H nmr: δ 0.70-1.80 (m, 25 H), 2.35 (s, 3 H), 7.05-7.23 (m, 2 H), 7.72 (s, 1 H).

Anal. Calcd. for $C_{19}H_{31}I$: C, 59.07; H, 8.09. Found: C, 58.83; H, 8.06.

Preparation of Diethyl 5-[(1,1-Dimethyl)decyl]-2-methylbenzenephosphonate (**11**).

By the procedure given above for the transformation of **4** into **5**, a mixture of **10** (5.62 g, 14.6 mmoles) and freshly prepared, activated copper metal [16] (1.11 g, 17.5 mmoles) was heated at 160° and triethyl phosphite (7.25 g, 44 mmoles) was added. Reflux and workup as before gave the crude product which was purified by chromatography on silica gel with dichloromethane then dichloromethane/methanol (9/1) as eluents to provide 4.05 g (69%) of **11** as a pale green oil; ir (neat): 1168 (P=O), 1039 (P-O) cm^{-1}; ^1H nmr: δ 0.65-1.85 (m, 31 H), 2.50 (s, 3 H), 3.70-4.35 (pentet, 4 H), 6.80-7.45 (m, 2 H), 7.60-8.05 (m, 1 H).

Anal. Calcd. for $C_{23}H_{41}O_3P \cdot 0.8H_2O$: C, 67.22; H, 10.45. Found: C, 67.20; H, 10.40.

Preparation of Monoethyl 5-[(1,1-Dimethyl)decyl]-2-methylbenzenephosphonate (**12**).

To 4.00 g (10.00 mmoles) of **11** was added a solution of 1.20 g (30.0 mmoles) of powdered sodium hydroxide in 15 ml of 95% ethanol. Reaction and workup followed the procedure given for the preparation of **6**. The crude product, a viscous oil, was chromatographed on silica gel with ethyl acetate/methanol (3/1) as eluent to afford 3.50 g (94%) of **12** as a viscous tan oil; ir (neat): 2671, 2285 (POH), 1168 (P=O), 1039 (P-O) cm^{-1}; ^1H nmr: δ 0.65-1.95 (m, 28 H), 2.50 (s, 3 H), 3.70-4.35 (pentet, 2 H), 6.80-7.40 (m, 2 H), 7.55-8.05 (m, 1 H).

Anal. Calcd. for $C_{21}H_{37}O_3P$: C, 68.45; H, 10.12. Found: C, 68.23; H, 10.04.

Preparation of Sodium Monoethyl 5-[(1,1-Dimethyl)decyl]-2-(oxymethyl-15-crown-5)methylbenzenephosphonate (**14**).

A solution of **12** (3.00 g, 8.2 mmoles), 1.46 g (8.2 mmoles) of *N*-bromosuccinimide and 0.04 g of benzoyl peroxide in 25 ml of carbon tetrachloride was refluxed for 8 hours then allowed to stand at room temperature overnight. After filtration, the filtrate was washed with water (75 ml) and dried over magnesium sulfate. The ^1H nmr spectrum of the solution showed a 79% conversion of **12** into **13**. After evaporation *in vacuo*, the crude product was used without further purification; ir (neat): 2670, 2285 (POH), 1169 (P=O), 1140 (P-O) cm^{-1}; ^1H nmr: δ 0.65-1.95 (m, 28 H), 2.50 (s, 0.8 H from residual **12**), 3.70-4.32 (pentet, 2 H), 4.80 (s, 2 H), 7.00-8.15 (m, 3 H).

Potassium hydride (0.91 g, 35% dispersion in mineral oil, 8.0 mmoles) was washed with pentane under nitrogen and a solution of 0.90 g (3.6 mmoles) of hydroxymethyl-15-crown-5 [24] in 10 ml of tetrahydrofuran was added dropwise. The reaction mixture was stirred for 30 minutes and a solution of 1.93 g (3.6 mmoles) of **13** in 10 ml of tetrahydrofuran was added. The reaction mixture was refluxed for 24 hours and evaporated *in vacuo*. The residue was acidified to *p*H = 2 with 50% aqueous hydrochloric acid and

the aqueous solution was extracted with dichloromethane (3 x 50 ml). An excess of sodium carbonate was added to convert the phosphonic acid monoethyl into the sodium salt. The mixture was filtered and the filtrate was dried over magnesium sulfate and evaporated *in vacuo* to give a dark brown solid which was chromatographed on silica gel with ethyl acetate/methanol (5/2) then methanol as eluents to produce 0.80 g (36%) of **14** as a tan solid; ir (potassium bromide): 1170 (P=O), 1140 (P-O), 1107 (C-O) cm^{-1}; ^1H nmr: δ 0.65-1.90 (m, 28 H), 3.20-4.60 (m, 23 H), 4.65-5.30 (m, 2 H), 7.15-7.48 (m, 2 H), 7.75-8.20 (m, 1 H).

Anal. Calcd. for $C_{32}H_{56}O_9PNa$: C, 60.17; H, 8.84. Found: C, 59.92; H, 8.74.

Preparation of Sodium 5-[(1,1-Dimethyl)decyl]-2-(oxymethyl-18-crown-6)methylbenzenephosphonate (**15**).

Sodium hydride (0.32 g, 60% dispersion in mineral oil, 7.9 mmoles) was washed with pentane under nitrogen and a solution of hydroxymethyl-18-crown-6 [25] (0.51 g, 2.6 mmoles) in 10 ml of tetrahydrofuran was added dropwise. The mixture was stirred for 30 minutes and a solution of **13** (1.47 g, 2.6 mmoles) in 10 ml of tetrahydrofuran was added. The mixture was refluxed for 24 hours and evaporated *in vacuo*. The residue was dissolved in dichloromethane (50 ml) and the resulting solution was washed with water (2 x 50 ml), dried over magnesium sulfate, and evaporated *in vacuo* to leave a dark viscous oil. Chromatography on alumina with ethyl acetate/methanol (65/35) then methanol as eluents afforded 0.87 g (49%) of **15** as a tan solid; ir (potassium bromide): 1168 (P=O), 1110 (C-O), 1042 (P-O) cm^{-1}; ^1H nmr: δ 0.65-2.00 (m, 28 H), 3.20-4.35 (m, 27 H), 4.65-5.35 (m, 2 H), 7.10-7.40 (m, 2 H), 7.80-8.20 (m, 1 H).

Anal. Calcd. for $C_{34}H_{60}O_{10}PNa$: C, 59.81; H, 8.86. Found: C, 59.57; H, 8.84.

Preparation of 4-Decylphenyldichlorophosphate (**17**).

To a solution of 4-decylphenol (**16**) (40.2 g, 0.17 mole) in 100 ml of phosphorus oxychloride, 1.0 g of cesium chloride was added and the mixture was refluxed for 7 hours. The excess phosphorus oxychloride was removed by distillation and the residue was distilled under vacuum (166-168°/0.25 torr) to give 55.8 (92%) of **17** as a colorless oil; ir (neat): 1311 (P=O), 1186 (P-O) cm^{-1}; ^1H nmr δ 0.70-1.90 (m, 19 H), 2.58 (t, 2 H), 7.13 (s, 4 H).

Anal. Calcd. for $C_{16}H_{25}Cl_2O_2P$: C, 54.71; H, 7.17. Found: C, 54.54; H, 7.29.

Preparation of Diethyl 4-Decylphenylphosphate (**18**).

To 75.4 g (0.22 mole) of **17** cooled to 0°, 60 ml of ethanol was added slowly with stirring. The mixture was stirred overnight and the hydrogen chloride and excess ethanol were removed *in vacuo* to leave a residue which was distilled under vacuum (176-178°/0.3 torr) to provide 70.4 g (89%) of **18** as a colorless liquid; ir (neat): 1282 (P=O), 1219, 1167 (P-O) cm^{-1}; ^1H nmr: δ 0.88 (t, 3 H), 1.00-1.60 (m + t, 22 H), 2.56 (t, 2 H), 4.19 (pentet, 4 H), 7.12 (s, 4 H).

Anal. Calcd. for $C_{20}H_{35}O_4P$: C, 64.84; H, 9.52. Found: C, 65.03; H, 9.72.

Preparation of Diethyl 5-Decyl-2-hydroxybenzenephosphonate (**19**).

To a solution of 1.10 g (11.0 mmoles) of diisopropylamine in 20 ml of tetrahydrofuran at −78° was added slowly 11.0 mmoles of butyllithium in hexane. The lithium diisopropylamide solution was stirred for 15 minutes at −78° and a solution of **18** (3.70 g, 10.0 mmoles) in 20 ml of tetrahydrofuran was slowly added. The reaction mixture was stirred for 15 minutes at −78° and then overnight at room temperature. The mixture was poured into a mixture of 10% hydrochloric acid (100 ml) and diethyl ether (100 ml). The ether extract was dried over magnesium sulfate and evaporated *in vacuo* to provide 2.85 g (78%) of **19** as a white, waxy solid with mp 28-29°; ir (neat): 3149 (OH), 1253 (P=O), 1195 (P-O); ^1H nmr: δ 0.70-1.90 (m, 25 H), 2.51 (t, 2 H), 4.09 (pentet, 4 H), 6.65-7.40 (m, 3 H), 10.00 (s, 1 H).

Anal. Calcd. for $C_{20}H_{35}O_4P$: C, 64.84; H, 9.52. Found: C, 65.04; H, 9.30.

General Procedure for the Preparation of Lipophilic Crown Ether Diethyl Phosphonates **20-30** and Model Compound **31**.

Under nitrogen, sodium or potassium hydride dispersion in mineral oil as specified in Table 1 (1.1 equivalents) was suspended in 10 ml of tetrahydrofuran. (Sodium hydride was washed with pentane to remove the protecting mineral oil prior to use.) To the suspension was added dropwise a solution of **19** (2.7-10.0 mmoles) in 10 ml of tetrahydrofuran and the mixture was stirred for 1 hour at room temperature. A solution of the appropriate (tosyloxymethyl)crown ether or (tosyloxymethyl)cyclohexane [26] (1.1 equivalents) in 10 ml of tetrahydrofuran was added and the reaction mixture was refluxed for 3 days. The solvent was removed *in vacuo* and the residue was chromatographed on alumina with ethyl acetate as eluent to give the desired compounds as colorless or pale yellow oils. Yields, spectral data and elemental analysis data are given in Table 1.

General Procedure for the Preparation of Lipophilic Crown Ether Phosphonic Acids Monoethyl Esters **32-42** and Model Compound **43**.

To the diethyl phosphonate (1.1-3.2 mmoles) dissolved in ethanol was added 10 ml of 10% aqueous sodium hydroxide and the solution was refluxed overnight. The solvent was evaporated *in vacuo* and the residue was acidified to *p*H = 1 with 6 *N* hydrochloric acid. The mixture was extracted with dichloromethane (3 x 10 ml) and the combined extracts were washed with water and dried over magnesium sulfate. Evaporation of the dichloromethane *in vacuo* afforded the analytically pure phosphonic acid monoethyl esters as colorless or pale yellow oils. Yields, spectral data and elemental analysis data are recorded in Table 2.

Preparation of Diethyl 2-Decylphenyldichlorophosphate (**46**).

Under the conditions described above for the synthesis of **17** but with an extended reflux time of 3 days, 3.52 g (0.15 mole) of 2-decylphenol (**44**) and 100 ml of phosphorus oxychloride were reacted to give 45.8 g (87%) of **45** as a colorless liquid with bp 161-163°/0.3 torr; ir (neat): 1307 (P=O), 1163 (P-O) cm^{-1}; ^1H nmr: δ 0.65-2.00 (m, 19 H), 2.69 (t, 2 H), 7.05-7.50 (m, 4 H).

By the procedure provided earlier for the synthesis of **18**, reaction of ethanol (60 ml) and 74.0 g (0.21 mole) of **45** produced 75.6 g (92%) of **46** as a colorless liquid with bp 166-168°/0.3 torr; ir (neat): 1275 (P=O), 1226, 1035 (P-O) cm^{-1}; ^1H nmr: δ 0.70-2.00 (m, 25 H), 2.70 (t, 2 H), 4.20 (pentet, 4 H), 6.95-7.50 (m, 4 H).

Anal. Calcd. for $C_{20}H_{35}O_4P$: C, 64.84; H, 9.52. Found: C, 64.95; H, 9.56.

Preparation of Diethyl 3-Decyl-2-hydroxybenzenephosphonate (**47**).

By the procedure described above for the synthesis of **19**, phosphate **46** was treated with lithium diisopropylamide to give 16.60 g (64%) of **47** as a colorless oil with bp 168-170°/0.3 torr; ir (neat): 3092 (OH), 1246 (P=O), 1194 (P-O) cm^{-1}; ^1H nmr: δ 0.70-1.90 (m, 25 H), 2.65 (t, 2 H), 4.10 (pentet, 4 H), 6.60-7.45 (m, 3 H), 10.39 (s, 1 H).

Anal. Calcd. for $C_{20}H_{35}O_4P$: C, 64.84; H, 9.52. Found: C, 65.01; H, 9.56.

Preparation of Diethyl 3-Decyl-2-(oxymethyl-18-crown-6)benzenephosphonate (**48**).

With the general procedure cited above for the synthesis of **20-30**, 5.0 mmoles of **47** was reacted with sodium hydride and (tosyloxymethyl) 18-crown-6 to afford **48** in 77% yield as a colorless oil; ir (neat): 1249 (P=O), 1122 (C-O), 1026 (P-O) cm^{-1}; ^1H nmr: δ 0.65-2.00 (m, 25 H), 2.60 (t, 2 H), 3.30-4.40 (m, 29 H), 6.90-7.90 (m, 3 H).

Anal. Calcd. for $C_{33}H_{59}O_{10}P$: C, 61.28; H, 9.19. Found: C, 61.32; H, 8.99.

Preparation of Monoethyl 3-Decyl-2-(oxymethyl-18-crown-6)benzenephosphonic Acid (**49**).

By the procedure given above for the synthesis of **32-42**, 1.2 mmoles of **48** was hydrolyzed to produce an 83% yield of **49** as a colorless oil; ir (neat): 2230 (POH), 1222 (P=O), 1116 (C-O), 1045 (P-O) cm^{-1}; ^1H nmr: δ 0.65-1.90 (m, 22 H), 2.67 (t, 2 H), 3.30-4.30 (m, 27 H), 6.90-7.90 (m, 3 H).

Anal. Calcd. for $C_{31}H_{55}O_{10}P \cdot H_2O$: C, 58.47; H, 9.01. Found: C, 58.41; H, 8.67.

Preparation of Lipophilic, Crown Ether Phosphonic Acids **50-57** and **59** and Model Compound **58**.

The appropriate diethyl phosphonate (0.2-2.0 mmoles) was heated with 2.5 equivalents bromotrimethylsilane at 95° for 1 hour in a stoppered flask. Volatile materials were evaporated *in vacuo* and 10 ml of methanol was added to the residue. The solution was evaporated *in vacuo* and 10 ml of methanol was added to the residue again. Evaporation of the solution *in vacuo* gave the lipophilic phosphonic acids as hygroscopic, colorless oils (except for **58** which was a solid). The phosphonic acids were removed from the flask by dissolution in chloroform or dichloromethane. Yields, spectral data and elemental analysis data are given in Table 3.

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