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Structurally related dibenzo-16-crown-5 lariat ethers with pendant ester and ether groups are prepared. Structural variations within the series of alkyl lariat ether esters include changes in the O-alkyl group, attachment site and nature of the lipophilic group, and length of the spacer, which connects the ester group to the polyether framework. Also synthesized are bis(crown ether) diesters with two dibenzo-16-crown-5 or two dicyclohexano-16-crown-5 units and two ester groups connected to each other by a linker of varying length. Synthetic strategies for the preparation of these lariat ethers with pendant ester- and ether-containing side arms are described.

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Introduction.

A wide variety of macrocyclic polyether ligands (crown ethers) has been synthesized and utilized in alkali and alkaline earth metal cation separations due to their superior binding ability for these metal ions [1]. Attachment of one or more side arms, with potential metal ion coordination sites, to a crown ether framework produces complexing agents known as lariat ethers [2]. These macrocycles have been designed to enhance the cation binding ability of crown ethers and to partially mimic the dynamic complexation processes shown by natural macrocyclic ligands [2].

In earlier work, we prepared lariat ether derivatives based upon a dibenzo-16-crown-5 scaffold in which oxyacetic acid [3-8], oxyacetohydroxamic acid [7], monoethyl oxymethylphosphonic ester [9], or *N*-(X)sulfonyl oxyacetamide groups [10] were attached to the central carbon of the three-carbon bridge in the polyether ring. In their ionized forms, such proton-ionizable lariat ethers are efficient and selective agents for the solvent extraction of alkali metal, alkaline earth metal, and lanthanide ions and for their transport across liquid membranes [7,9-23].

To complement studies of metal ion separations by crown ethers with pendant proton-ionizable groups, investigations of metal ion complexation by analogous macrocyclic polyethers with neutral potential chelating functions in the side arms were undertaken. Examples include dibenzocrown ethers with pendant amide groups, whose synthesis was reported earlier [24], and dibenzo-16-crown-5 compounds with pendant ester and ether functions, whose complexation behavior was investigated in solvent polymeric membrane electrodes [25]. Also, a few macrocyclic compounds with pendant ester groups have served as precursors for the preparation of lariat ether carboxylic acids [5,8].

We now report preparative routes to 61 new crown ethers with pendant ester and ether groups based on a

dibenzo-16-crown-5 scaffold, as well as 6 new bis(crown ether) esters. Structures of these compounds and their physical, spectroscopic and combustion analysis data are given in Tables 1-8. Compounds **1**, **10**, **12**, **25**, **26**, **50-52**, and **54**, which were reported previously in the literature, are included in the tables for comparison.

Results and Discussion.

For the preparation of dibenzo-16-crown-5 compounds with pendant ester groups, several traditional synthetic approaches were employed. In addition, a new preparative route to lariat ether ethyl esters was developed.

Attached side arm functionalities are an increasingly common design consideration for macrocyclic complexing agents because they may provide three-dimensional complexation of metal ions. Marked enhancement in Na⁺ extraction over the other alkali metal cations by *sym*-(R)dibenzo-16-crown-5-oxyacetic acids when a linear alkyl group is attached to the same polyether ring carbon that bears the ionizable side arm was reported [5,14]. Recently, it was found that preorganization of the binding site by intramolecular hydrogen bonding of a carboxylic acid function to one or more polyether oxygen atoms in such compounds is facilitated by a geminal alkyl group [26].

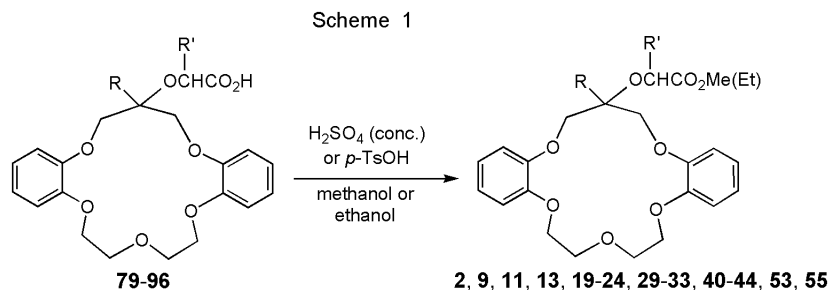
For investigation of metal ion complexation properties of ester derivatives of such lariat ether carboxylic acids in solvent polymeric membrane electrodes, lariat ether esters **2**, **9**, **11**, **13**, **19-24**, **27**, **29-33** (Table 1) and **37**, **40-43** (Table 3) were prepared from the corresponding carboxylic acids by acid-catalyzed esterification (Scheme 1). The lariat ether carboxylic acid was refluxed in absolute methanol or ethanol with sulfuric acid or *p*-toluenesulfonic acid as catalyst. The water, which formed during the esterification process, was removed by passing the condensate through a Soxhlet thimble containing anhydrous sodium

sulfate. The desired esters were obtained in excellent yields.

In this series of lariat ether esters, the substituent attached geminal to the coordinating side arm is varied to include hydrogen and linear alkyl, branched alkyl, alkynyl, perfluoroalkyl, and phenyl groups. Thus this series of lariat ether esters allows for further examination of the influence of structural variation in methyl or ethyl *sym*-(R)dibenzo-16-crown-5-oxyacetate compounds beyond those in which R = hydrogen or a linear alkyl group.

oxyacetic acids followed by esterification with ethanol by the method described above gave the title macrocycles.

A different synthetic route to lariat ether ethyl esters **2** and **13** was developed in which *sym*-(hydroxy)-(R)dibenzo-16-crown-5 compounds **99** and **100** were treated with ethyl diazoacetate [29] and boron trifluoride in benzene to produce lariat ether esters **2** and **13** in 51 and 41% yields, respectively (Scheme 3). This new method may be useful when the starting lariat ether alcohol contains a functional group that is unstable to



	R	R'		R	R'
79	H	C ₆ H ₅	88	C ₁₂ H ₂₅	H
80	C ₂ H ₅	H	89	C ₁₄ H ₂₉	H
81	CH(CH ₃) ₂	H	90	C ₁₆ H ₃₃	H
82	C ₃ F ₇	H	91	C ₁₈ H ₃₇	H
83	C ₄ H ₉	H	92	C ₂₀ H ₄₁	H
84	C ₆ H ₁₃	H	93	CH ₂ =CH(CH ₂) ₈	H
85	C ₆ F ₁₃	H	94	C ₆ H ₁₃ C=C	H
86	C ₈ H ₁₇	H	95	C ₆ H ₅	H
87	C ₁₀ H ₂₁	C ₆ H ₅	96	C ₆ H ₅	C ₆ H ₅

To probe the influence of replacing benzo groups in the macrocyclic rings of ethyl *sym*-(R)dibenzo-16-crown-5-oxyacetate compounds with two cyclohexano units, lariat ether esters **34** and **35**, were prepared (Scheme 2). The precursor *sym*-(R)dicyclohexano-16-crown-5-oxyacetic acids **97** and **98** were prepared by catalytic hydrogenation of the corresponding known *sym*-(R)dibenzo-16-crown-5-

the conditions employed in more facile synthesis of esters.

Refluxing lariat ether carboxylic acid **101** containing a geminal alkenyl group with *p*-toluenesulfonic acid as catalyst in ethanol did not produce the anticipated lariat ether ethyl ester. Instead, product **102** was obtained for which a possible mechanism for its formation is shown in

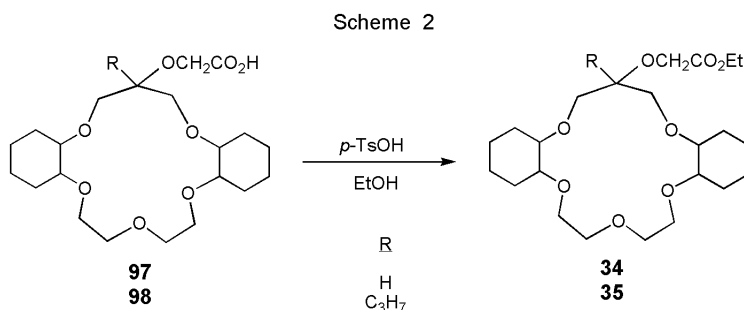


Table 1
Data for Dibenzo 16-crown-5 Lariat Ether Esters **1-35**

Compound	R	R'	R''	Yield (%)	Mp (°C)	¹ H NMR (deuteriochloroform) δ (ppm)	IR (cm ⁻¹) [a]	Molecular Formula	Analysis % Calcd./Found C H
1	H	H	CH ₃	82[b]	oil	1.25-1.33 (t, 3H, J=6.2Hz), 3.91-4.58 (m, 17H)	1750 (C=O),	C ₂₃ H ₂₈ O ₈	63.88 6.53
2	H	H	C ₂ H ₅	98		6.82-7.03 (m, 8H) 1257 (C-O)			64.19 6.83
3	H	H	C ₆ H ₁₃	62	89-91	0.85-0.95 (t, 3H, J=6.3Hz), 1.25-1.45 (s, 6H), 1.55-1.70 (m, 2H), 3.93-4.40 (m, 15H), 4.59 (s, 2H), 6.83-7.01 (m, 8H)	1712 (C=O), 1258 (C-O)	C ₂₇ H ₃₆ O ₈	66.38 7.43 66.03 7.43
4	H	H	C ₈ H ₁₇	86	82-84	0.84-0.90 (t, 3H, J=6.4Hz) 1.15-1.48 (br s, 10H), 1.55-1.77 (m, 2H), 3.83-4.06 (m, 4H), 4.06-4.50 (m, 11H), 4.59 (s, 2H), 6.79-7.08 (m, 8H)	1752 (C=O), 1258 (C-O)	C ₂₉ H ₄₀ O ₈	67.42 7.80 67.47 7.83
5	H	H	C ₁₀ H ₂₁	84	70-72	0.85-0.91 (t, 3H, J=6.4Hz), 1.13-1.45 (br s, 14H), 1.54-1.75 (m, 2H), 3.83-4.06 (m, 4H), 4.08-4.48 (m, 11H), 4.59 (s, 2H), 6.80-7.08 (m, 8H)	1752 (C=O), 1258 (C-O)	C ₃₁ H ₄₄ O ₈	68.36 8.14 68.61 7.84
6	H	H	C ₁₂ H ₂₅	78	oil	0.80-1.50 (s, 23H), 3.40-4.40 (m, 13H), 4.45 (s, 2H), 4.72 (s, 2H), 6.81-7.02 (m, 8H)	1755 (C=O), 1256 (C-O)	C ₃₃ H ₄₈ O ₈	67.24 7.91 67.56 7.61
7	H	H	CH(CH ₃) ₂	94	oil	1.26-1.29 (d, 6H, J=6Hz), 3.92-4.42 (m, 13H), 4.54 (s, 2H), 5.05-5.25 (m, 1H), 6.83-7.02 (m, 8H)	1744 (C=O), 1258 (C-O)	C ₂₄ H ₃₀ O ₈	64.56 6.77 64.67 6.67
8	H	H	C(CH ₃) ₃	62	oil	1.50 (s, 9H), 3.93-4.41 (m, 13H), 4.47 (s, 2H), 6.83-7.02 (m, 8H) 1255 (C-O)	1737 (C=O),	C ₂₅ H ₃₂ O ₈	65.20 7.00 64.94 6.87
9	H	C ₆ H ₅	CH ₃	100	118-119	3.73 (s, 3H), 3.84-3.97 (m, 4H), 4.11-4.16 (m, 4H), 4.34-4.49 (m, 4H), 5.66 (s, 2H), 6.79-7.00 (m, 8H), 7.36-7.39 (m, 3H), 7.53-7.56 (m, 2H)	1748 (C=O), 1257 (C-O)	C ₂₈ H ₃₀ O ₈	68.00 6.11 68.29 6.11
10	CH ₃	H	C ₂ H ₅	91[c]	102-104	1.04-1.10 (t, 3H, J=6Hz) 1.17-1.23 (t, 3H, J=6Hz), 2.01-2.04 (m, 2H), 3.86-4.24 (m, 12H), 4.40-4.45 (d, 2H, J=10Hz), 4.73 (s, 2H), 6.81-6.98 (m, 8H)	1756, 1728 (C=O), 1257 (C-O)	C ₂₅ H ₃₂ O ₈	65.20 7.00 65.15 6.87
11	C ₂ H ₅	H	C ₂ H ₅	93		0.99-1.05 (t, 3H, J=6Hz), 1.17-1.23 (t, 3H, J=6Hz), 1.54-1.59 (m, 2H), 1.94-2.01 (m, 2H), 3.91-4.19 (m, 12H), 4.40-4.45 (d, 2H, J=10Hz), 4.73 (s, 2H), 6.80-6.94 (m, 8H)	1756, 1727 (C=O), 1257 (C-O)	C ₂₆ H ₃₄ O ₈	65.81 7.22 65.75 7.13
12	C ₃ H ₇	H	CH ₃	94[d]	72-74	0.87-0.93 (t, 3H, J=6Hz), 1.25-1.29 (m, 6H), 1.48-1.62 (m, 6H), 1.95-2.05 (m, 2H), 3.88-4.25 (m, 12H), 4.43-4.48 (d, 2H, J=10Hz), 4.74 (s, 2H), 6.84-6.95 (m, 8H)	1756 (C=O), 1257 (C-O)	C ₃₀ H ₄₂ O ₈	67.90 7.98 67.50 8.03
13	C ₃ H ₇	H	C ₂ H ₅	94					
14	C ₃ H ₇	H	C ₆ H ₁₃	85	oil				

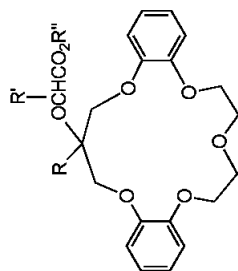


Table 1 (continued)

Compound	R	R'	R''	Yield (%)	Mp (°C)	¹ H NMR (deuteriochloroform) δ (ppm)	IR (cm ⁻¹)[a]	Molecular Formula	Analysis % Calcd./Found
15	C ₃ H ₇	H	C ₈ H ₁₇	80	oil	0.83-0.90 (t, 3H, J=7.2Hz), 0.98-1.05 (t, 3H, J=7.2Hz), 1.12 (br s, 10H), 1.42-1.70 (m, 4H), 1.91-2.08 (m, 2H), 3.83-4.28 (m, 12H), 4.40-4.45 (d, 2H, J=10Hz), 4.74 (s, 2H), 6.77-7.03 (m, 8H)	1758 (C=O), 1257 (C-O)	C ₃₂ H ₄₆ O ₈	68.79 8.30 68.99 8.43
16	C ₃ H ₇	H	C ₁₀ H ₂₁	77	oil	0.85-0.91 (t, 3H, J=6.4Hz), 0.99-1.06 (t, 3H, J=7.2Hz), 1.14 (br s, 10H), 1.43-1.70 (m, 4H), 1.91-2.10 (m, 2H), 3.84-4.28 (m, 6H), 4.40-4.45 (d, 2H, J=10Hz), 4.74 (s, 2H), 6.76-7.03 (m, 8H)	1758 (C=O), 1257 (C-O)	C ₃₄ H ₅₀ O ₈	69.60 8.59 69.68 8.38
17	C ₃ H ₇	H	CH(CH ₃) ₂	90	oil	0.95-1.01 (t, 3H, J=6Hz), 1.17-1.20 (d, 6H, J=6Hz), 1.47-1.60 (m, 2H), 1.92-2.03 (m, 2H), 4.07-4.14 (m, 10H), 4.41-4.46 (d, 2H, J=10Hz), 4.70 (s, 2H), 4.95-5.05 (m, 1H), 6.83-6.90 (m, 8H)	1752 (C=O), 1257 (C-O)	C ₂₇ H ₃₆ O ₈	66.38 7.43 66.54 7.32
18	C ₃ H ₇	H	C(CH ₃) ₃	56	oil	0.98-1.05 (t, 3H, J=7.2Hz), 1.40-1.60 (m, 11H), 1.93-2.0 (m, 2H), 3.92-4.20 (m, 10H), 4.42-4.47 (d, 2H, J=10Hz), 4.62 (s, 2H), 6.80-6.96 (m, 8H)	1758 (C=O), 1257 (C-O)	C ₂₈ H ₃₈ O ₈	66.91 7.62 66.96 7.54
19	CH(CH ₃) ₂	H	C ₂ H ₅	89	135-136	1.14-1.21 (m, 9H), 2.56-2.59 (m, 1H), 3.90-4.20 (m, 12H), 4.51-4.56 (d, 2H, J=10Hz), 4.79 (s, 2H), 6.79-6.97 (m, 8H)	1755 (C=O), 1257 (C-O)	C ₂₆ H ₃₄ O ₈	65.81 7.22 65.63 7.21
20	C ₃ F ₇	H	C ₂ H ₅	90	oil	1.13-1.20 (t, 3H, J=7.2Hz), 3.80-4.30 (m, 10H), 4.32-4.40 (d, 2H, J=16Hz), 4.65-4.73 (d, 2H, J=16Hz), 5.05 (s, 2H), 6.80-7.02 (m, 8H)	1761 (C=O), 1258 (C-O)	C ₂₃ H ₂₇ O ₈ F ₇ 0.3C ₆ H ₁₄	53.31 5.02 53.50 4.95
21	C ₄ H ₉	H	C ₂ H ₅	92	75-76	0.94-1.00 (t, 3H, J=7.2Hz), 1.17-1.24 (t, 3H, J=7.2Hz), 1.44 (m, 4H), 1.80-2.04 (t, 2H, J=6.4Hz), 3.91-4.19 (m, 12H), 4.41-4.46 (d, 2H, J=10Hz), 4.75 (s, 2H), 6.80-6.97 (m, 8H)	1756, 1726 (C=O), 1256 (C-O)	C ₂₇ H ₃₆ O ₈	66.38 7.43 66.36 7.37
22	C ₆ H ₁₃	H	C ₂ H ₅	94	109-111	0.87-0.94 (t, 3H, J=7.2Hz), 1.18-1.25 (t, 3H, J=7.2Hz), 1.33-1.36 (m, 8H), 1.97-2.03 (t, 2H, J=6Hz), 3.90-4.19 (m, 12H), 4.40-4.45 (d, 2H, J=10Hz), 4.74 (s, 2H), 6.79-6.98 (m, 8H)	1756, 1726 (C=O), 1256 (C-O)	C ₂₉ H ₄₀ O ₈	67.42 7.80 67.28 7.94
23	C ₆ F ₁₃	H	C ₂ H ₅	90	oil	1.10-1.20 (t, 3H, J=7.2Hz), 3.90-4.30 (m, 10H), 4.33-4.45 (d, 2H, J=24Hz), 4.68-4.80 (d, 2H, J=24Hz), 5.04 (s, 2H), 6.80-7.00 (m, 8H)	1762 (C=O), 1258 (C-O)	C ₂₉ H ₂₇ O ₈ F ₁₃	46.41 3.63 46.83 3.63
24	C ₈ H ₁₇	H	C ₂ H ₅	93	116-117	0.89-0.96 (t, 3H, J=7.2Hz), 1.20-1.27 (t, 3H, J=7.2Hz), 1.30-1.33 (m, 12H), 2.00-2.06 (t, 2H, J=6Hz), 3.87-4.19 (m, 12H), 4.40-4.45 (d, 2H, J=10Hz), 4.74 (s, 2H), 6.81-6.97 (m, 8H)	1757, 1734 (C=O), 1256 (C-O)	C ₃₁ H ₄₄ O ₈	68.36 8.14 68.13 7.98
25	C ₁₀ H ₂₁	H	CH ₃	79[e]		0.85-0.90 (t, 3H, J=6.3Hz), 1.07-1.12 (t, 3H, J=7.2Hz), 1.22 (s, 16H), 2.04-2.08 (m, 2H), 3.88-4.27 (m, 11H), 4.48-4.52 (d, 1H, J=10Hz), 5.88 (s, 1H), 6.73-6.92 (m, 8H), 7.26-7.31 (m, 3H), 7.53-7.56 (m, 2H)	1748 (C=O), 1256 (C-O)	C ₃₉ H ₅₂ O ₈	72.19 8.08 72.05 8.16
26	C ₁₀ H ₂₁	H	C ₂ H ₅	91[e]					
27	C ₁₀ H ₂₁	C ₆ H ₅	C ₂ H ₅	99	oil	1.16-2.05 (m, 21H), 3.61-3.67 (t, 2H, J=6Hz), 4.01-4.49 (m, 14H), 4.75 (s, 2H), 6.89-7.00 (m, 8H)	3412 (OH), 1754 (C=O), 1256 (C-O)	C ₃₂ H ₄₆ O ₈	67.32 8.23 67.54 8.32

Table 1 (continued)

Compound	R	R'	R''	Yield (%)	Mp (°C)	¹ H NMR (deuteriochloroform) δ (ppm)	IR (cm ⁻¹)[a]	Molecular Formula	Analysis % Calcd./Found
29	C ₁₂ H ₂₅	H	C ₂ H ₅	95	91-92	0.88-0.95 (t, 3H, J=7.2Hz), 1.20-1.27 (t, 3H, J=7.2Hz), 1.28-1.35 (m, 20H), 2.00-2.06 (t, 2H, J=6Hz), 3.91-4.19 (m, 12H), 4.40-4.45 (d, 2H, J=10Hz), 4.74 (s, 2H), 6.81-6.94 (m, 8H)	1758, 1728 (C=O), 1256 (C-O)	C ₃₃ H ₅₂ O ₈	69.97 70.12 8.72 8.85
30	C ₁₄ H ₂₉	H	C ₂ H ₅	96	88-90	0.88-0.95 (t, 3H, J=7.2Hz), 1.20-1.27 (t, 3H, J=7.2Hz), 1.23-1.27 (m, 24H), 1.99-2.05 (t, 2H, J=6Hz), 3.91-4.19 (m, 12H), 4.40-4.45 (d, 2H, J=10Hz), 4.74 (s, 2H), 6.81-6.97 (m, 8H)	1758, 1728 (C=O), 1257(C-O)	C ₃₇ H ₅₆ O ₈	70.67 70.43 8.98 9.13
31	C ₁₆ H ₃₃	H	C ₂ H ₅	94	86-87	0.88-0.95 (t, 3H, J=7.2Hz), 1.20-1.27 (t, 3H, J=7.2Hz), 1.22-1.26 (m, 28H), 1.99-2.05 (t, 2H, J=6Hz), 3.91-4.19 (m, 12H), 4.40-4.45 (d, 2H, J=10Hz), 4.74 (s, 2H), 6.81-6.97 (m, 8H)	1758, 1728 (C=O), 1257(C-O)	C ₃₉ H ₆₀ O ₈ [*] 0.1CH ₂ Cl ₂	70.58 70.85 9.12 9.12
32	C ₁₈ H ₃₇	H	C ₂ H ₅	97	87-88	0.88-0.95 (t, 3H, J=7.2Hz), 1.20-1.27 (t, 3H, J=7.2Hz), 1.21-1.26 (m, 32H), 2.00-2.06 (t, 2H, J=6Hz), 3.91-4.19 (m, 12H), 4.40-4.45 (d, 2H, J=10Hz), 4.74 (s, 2H), 6.81-6.94 (m, 8H)	1758, 1728 (C=O), 1257(C-O)	C ₄₁ H ₆₄ O ₈	71.90 71.69 9.42 9.40
33	C ₂₀ H ₄₁	H	C ₂ H ₅	95	90-91	0.88-0.95 (t, 3H, J=7.2Hz), 1.20-1.27 (t, 3H, J=7.2Hz), 1.23-1.27 (m, 36H), 2.00-2.06 (t, 2H, J=6Hz), 3.91-4.19 (m, 12H), 4.40-4.45 (d, 2H, J=10Hz), 4.74 (s, 2H), 6.81-6.98 (m, 8H)	1758, 1727 (C=O), 1256 (C-O)	C ₄₃ H ₆₈ O ₈	72.44 72.23 9.61 9.80

[a] Deposit from dichloromethane solution onto a sodium chloride plate. [b] Reference 27. [c] Reference 28. [d] Reference 29. [e] Reference 5.

Table 2

Data for Dicyclohexano-16-crown-5 Lariat Ether Esters **34** and **35**

Compound	R	Yield (%)	Mp (°C)	¹ H NMR (deuteriochloroform) δ (ppm)	IR (cm ⁻¹) [a]	Molecular Formula	Analysis % Calcd./Found
34	H	93	oil	1.03-2.14 (m, 20H), 3.03-4.02 (m, 16H), 4.03-4.52 (m, 4H)	1754 (C=O)	C ₂₃ H ₄₀ O ₈ 1202 (C-O)	62.12 62.42 9.07 8.86
35	C ₃ H ₇	96	oil	0.68-0.96 (m, 3H), 0.97-2.08 (m, 23H), 2.98-3.84 (m, 16H), 3.99-4.62 (m, 4H)	1758 (C=O), 1199 (C-O)	C ₂₆ H ₄₆ O ₈	64.16 63.94 9.53 9.40

[a] Deposit from dichloromethane solution onto a sodium chloride plate.

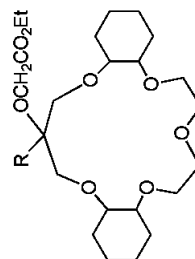
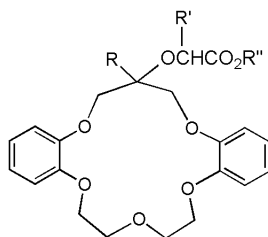


Table 3
Data for Dibenzo-16-crown-5 Lariat Ether Esters **36-43**



Compound	R	R'	R''	Yield (%)	Mp (°C)	¹ H NMR (deuteriochloroform) δ (ppm)	IR (cm ⁻¹) [a]	Molecular Formula	Analysis % Calcd./Found C H	
36	(CH ₃) ₂ C=CH	H	C ₂ H ₅	53	85-86	1.19-1.26 (t, 3H, J=7.2Hz), 1.83 (s, 3H), 1.98 (s, 3H), 3.92-3.99 (m, 4H), 4.10-4.44 (m, 10H), 4.65 (s, 2H), 5.56 (s, 1H), 6.82-6.95 (m, 8H)	1755 (C=O), 1257 (C-O)	C ₂₇ H ₃₄ O ₈	66.65 66.68	7.04 6.98
37	CH ₂ =CH(CH ₂) ₈	H	C ₂ H ₅	90	85-86	1.16-2.05 (m, 19H), 3.90-4.49 (m, 14H), 4.75 (s, 2H), 4.90-5.04 (m, 2H), 5.70-5.90 (m, 1H), 6.89-7.00 (m, 8H)	1757 (C=O), 1640 (C=C), 1256 (C-O)	C ₃₃ H ₄₆ O ₈	69.45 69.50	8.13 8.02
38	CH ₂ =CH-C ₆ H ₄	H	C ₂ H ₅	72	115-116	1.22-1.29 (t, 3H, J=7.2Hz), 3.97-4.23 (m, 10H), 4.47-4.63 (m, 4H), 4.70 (s, 2H), 5.22-5.29 (d, 1H, J=14Hz), 5.73-5.81 (d, 2H, J=16Hz), 6.65-6.95 (m, 8H), 7.44-7.49 (d, 2H, J=10Hz), 7.80-7.84 (d, 2H, J=8Hz)	1760 (C=O), 1629 (C=C), 1256 (C-O)	C ₃₁ H ₃₄ O ₈	69.45 69.50	8.13 8.02
39	CH ₂ =C(CH ₃)C ₆ H ₄	H	C ₂ H ₅	80	104-105	1.21-1.28 (t, 3H, J=7.2Hz), 2.17 (s, 3H), 3.96-4.22 (m, 10H), 4.48-4.64 (m, 4H), 4.70 (s, 2H), 5.09 (s, 1H), 5.40 (s, 1H), 6.78-6.89 (m, 8H), 7.50-7.54 (d, 2H, J=8Hz), 7.79-7.83 (d, 2H, J=8Hz)	1755 (C=O), 1628 (C=C), 1257 (C-O)	C ₃₂ H ₃₆ O ₈	70.04 70.16	6.61 6.74
40	C ₆ H ₁₃ C=C	H	C ₂ H ₅	80	74-76	0.79-0.85 (t, 3H, J=6Hz), 1.18-1.47 (m, 11H), 2.16-2.23 (t, 2H, J=6Hz), 3.67-3.90 (m, 4H), 4.08-4.20 (m, 6H), 4.29-4.41 (m, 4H), 4.54 (s, 2H), 6.75-6.98 (m, 8H)	1757 (C=O), 1258 (C-O)	C ₃₁ H ₄₀ O ₈	68.87 68.89	7.46 7.35
41	C ₆ H ₅	H	CH ₃	97	154-155	3.94 (s, 3H), 3.96-4.01 (m, 4H), 4.14-4.17 (m, 4H), 4.52-4.60 (m, 4H), 4.75 (s, 2H), 6.75-6.94 (m, 8H), 7.32-7.45 (m, 5H)	1758 (C=O), 1256 (C-O)	C ₂₈ H ₃₀ O ₈	68.00 67.96	6.11 6.19
42	C ₆ H ₅	H	C ₂ H ₅	84	117-118	1.21-1.28 (t, 3H, J=7.2Hz), 3.79-4.02 (m, 6H), 4.56-4.58 (m, 4H), 4.72 (s, 2H), 6.78-6.90 (m, 8H), 7.32-7.43 (m, 3H), 7.83-7.88 (m, 2H)	1754 (C=O), 1256 (C-O)	C ₂₉ H ₃₂ O ₈	68.49 68.39	6.34 6.25
43	C ₆ H ₅	C ₆ H ₅	C ₂ H ₅	96	58-60	1.04-1.09 (t, 3H, J=7.2Hz), 3.92-4.15(m, 11H), 4.63-4.69 (t, 2H, J=9Hz), 4.83-4.87 (d, 1H, J=10.2Hz), 5.66 (s, 1H), 6.70-6.92 (m, 8H), 7.28-7.54 (m, 6H), 7.56-7.57 (d, 2H, J=1.8Hz), 7.86-7.88 (d, 2H, J=6.9Hz)	1764 (C=O), 1256 (C-O)	C ₃₅ H ₃₆ O ₈	71.90 71.61	6.20 6.49

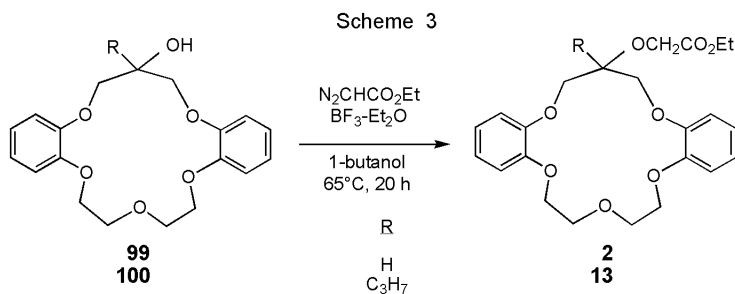
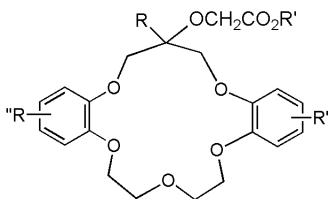


Table 4
Data for Dibenzo-16-crown-5 Lariat Ether Esters **44-48**



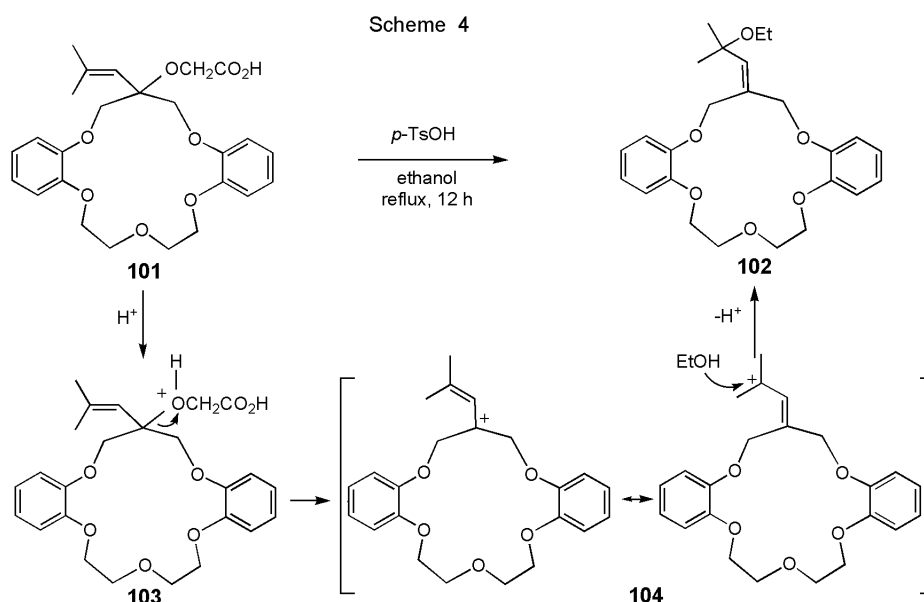
Compound	R	R'	R''	Yield (%)	Mp (°C)	¹ H NMR (deuteriochloroform) δ (ppm)	IR (cm ⁻¹) [a]	Molecular Formula	Analysis %		
									Calcd./Found	C	H
44	H	C ₂ H ₅	NO ₂	95	oil	1.27-1.35 (m, 3H), 3.96-4.00 (m, 4H), 4.24-4.53 (m, 13H), 6.86-7.02 (m, 2H), 7.71-7.96 (m, 4H)	1734 (C=O), 1257 (C-O)	C ₂₃ H ₂₆ O ₁₂	52.88 52.56	5.02 4.81	
45	H	CH ₃	NH ₂	92	168-170	3.60-4.25 (m, 16H), 4.50-4.55 (d, 2H, J=10Hz), 4.65-5.00 (br s, 4H), 6.00-6.40 (m, 4H), 6.60-6.75 (m, 2H) [b]	3437, 3356, 3225 (NH ₂), 1764 (C=O)	C ₂₂ H ₂₈ N ₂ O ₈	58.92 58.90	6.29 6.51	6.25 6.32
46	H	C ₂ H ₅	NH ₂	93	51-56	1.20-1.30 (t, 3H, J=7.3Hz), 3.45 (br s, 4H), 3.75-4.65 (m, 17H), 6.10-6.45 (m, 4H), 6.65-6.95 (m, 2H)	3437, 3361, 3225 (NH ₂), 1747 (C=O)	C ₂₃ H ₃₀ N ₂ O ₈	59.73 60.04	6.54 6.69	6.06 5.85
47	C ₃ H ₇	CH ₃	NH ₂	93	59-60	0.92-0.99 (t, 3H, J=7.2Hz), 1.33-1.60 (m, 2H), 1.80-2.10 (m, 2H), 3.50 (br s, 4H), 3.66 (s, 3H), 3.75-4.85 (m, 14H), 6.10-6.45 (m, 4H), 6.65-6.85 (m, 2H)	3433, 3358, 3221 (NH ₂), 1753 (C=O)	C ₂₅ H ₃₄ N ₂ O ₈	61.21 61.57	6.99 7.12	5.71 5.30
48	C ₃ H ₇	C ₂ H ₅	NH ₂	89	60-70	0.92-1.05 (t, 3H, J=7.5Hz), 1.20-1.30 (t, 3H, J=7.4Hz), 1.33-1.60 (m, 2H), 1.80-2.10 (m, 2H), 3.46 (br s, 4H), 3.80-4.85 (m, 16H), 6.10-6.80 (m, 6H)	3430, 3356, 3216 (NH ₂), 1749 (C=O)	C ₂₆ H ₃₆ N ₂ O ₈	61.89 61.57	7.19 7.12	5.55 5.30

[a] Deposit from dichloromethane solution onto a sodium chloride plate. [b] Perdeuteriodimethyl sulfoxide.

Scheme 4. In this mechanism, formation of the protonated intermediate **103** gives the allylic carbocation intermediate **104**, which subsequently reacts with ethanol to produce **102**. The target lariat ether ester was eventually realized

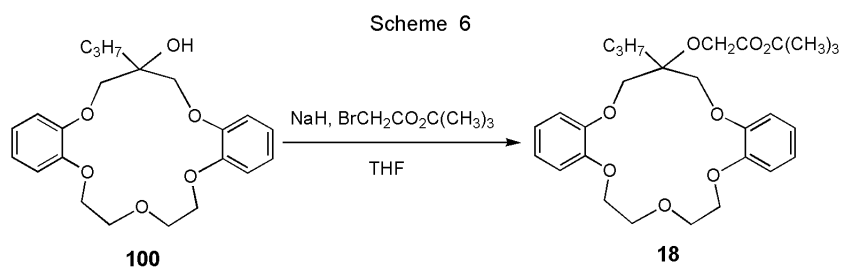
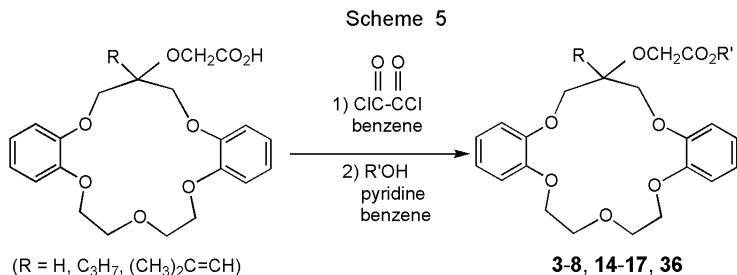
by a different approach (Scheme 5).

To probe the influence of ester alkyl group variation in polymeric membrane electrodes, a series of alkyl *sym*-dibenzo-16-crown-5-oxyacetate esters **3-8**, **14-17**, and **36**



was prepared (Scheme 5). The lariat ether carboxylic acids were treated with oxalyl chloride to form acid chlorides followed by reaction with the appropriate alcohol in the presence of pyridine usually gave the desired ester in good yield.

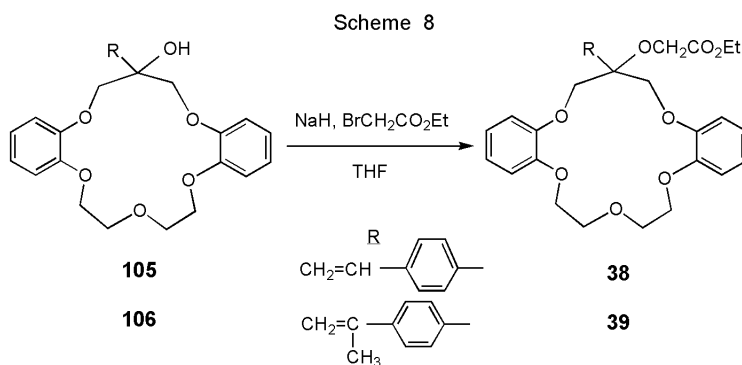
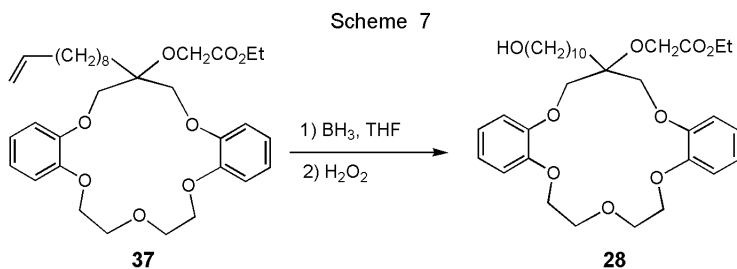
Lariat ether ester **28** was synthesized for coupling with chloromethylated polystyrene [30]. The preparative route to this compound is shown in Scheme 7. Thus hydroboration-oxidation of lariat ether ester **37** with borane-tetrahydrofuran complex and hydrogen peroxide [31] gave the



However, the *tert*-butyl ester of *sym*-(propyl)dibenzo-16-crown-5-oxyacetic acid (**18**) could not be obtained by the method shown in Scheme 5. Apparently, steric hindrance between the acid chloride and the alcohol prevented the reaction. Therefore, an alternative synthetic route to **18** was investigated (Scheme 6)

desired product containing a hydroxyl group at the terminus of the long aliphatic chain.

Lariat ether esters **38** and **39** (Table 3) were prepared by reaction of the corresponding lariat ether alcohols **105** and **106** with sodium hydride and ethyl bromoacetate in tetrahydrofuran (Scheme 8).



Lariat ether esters **44-48** containing either a nitro or amino group on both benzene rings were prepared as shown in Scheme 9. Reduction of di(nitrobenzo)-16-crown-5-oxyacetic acids **107** and **108** to the corresponding diamino compounds was first attempted by catalytic hydrogenation with Pd/C as the catalyst and 60 psi of hydrogen in ethanol at room temperature. However, poor solubility of *sym*-di(nitrobenzo)-16-crown-5-oxyacetic acid (**107**) in ethanol resulted in sluggish reaction. Substitution of hydrogen with hydrazine as the hydrogen source under reflux reduced the nitro groups to amine functions, but the carboxylic acid group was converted concomitantly into a hydrazide function. Infrared and nuclear magnetic resonance spectra provided strong evi-

dence for acyl hydrazide formation. Treatment of **109** and **110** with the appropriate alcohol and excess sulfuric acid provided esters **45-48**.

Lariat ether esters **49**, **53** and **55** with longer pendant arms than the macrocycles described previously were prepared as shown in Schemes 10 and 11. Nitrile **111** was refluxed in ethanol-benzene (1:2) through which gaseous hydrochloric acid was passed to produce the corresponding ester **49** (Scheme 10). Lariat ether esters **53** and **55** were prepared by refluxing the corresponding carboxylic acids in ethanol with sulfuric acid as catalyst (Scheme 11).

A series of dibenzo-16-crown-5 derivatives with acyloxy side arms attached to the central carbon of the three-carbon bridge was prepared for examination of their

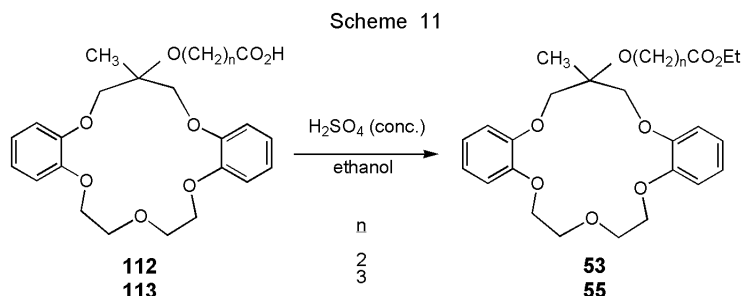
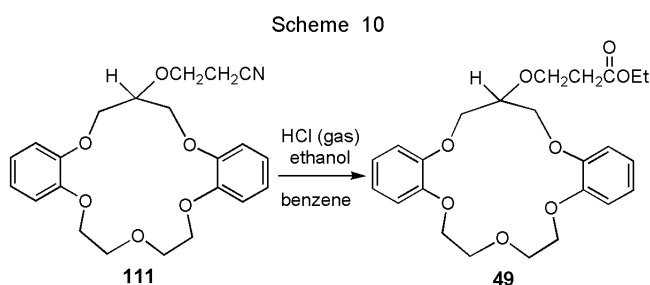
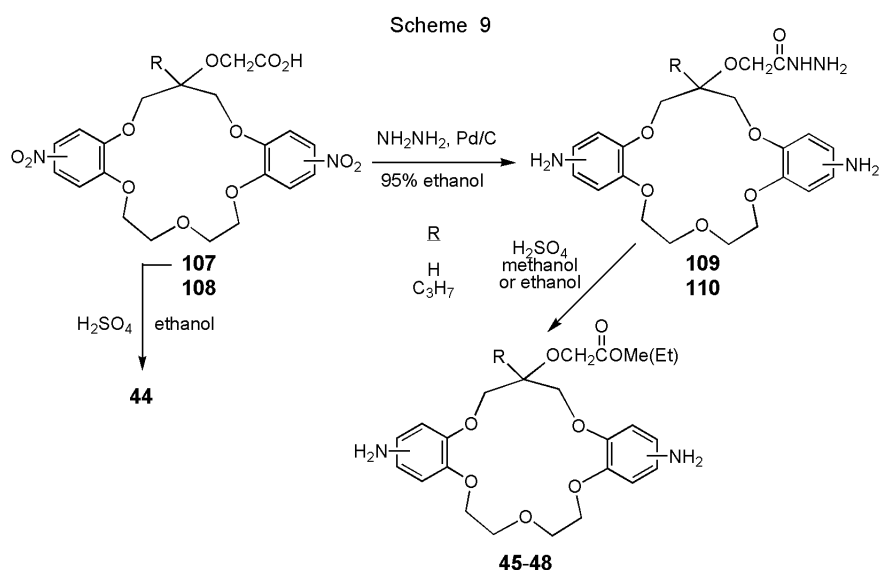
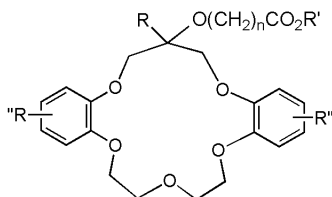


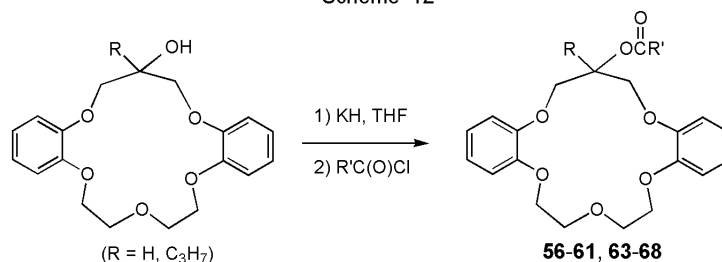
Table 5
Data for Dibenzo-16-crown-5 Lariat Ether Esters **49-55**



Compound	R	R''	R'	n	Yield (%)	Mp (°C)	¹ H NMR (deuteriochloroform) δ (ppm)	IR (cm ⁻¹) [a]	Molecular Formula	Analysis % Calcd./Found C H
49	H	C ₂ H ₅	H	2	28	oil	1.21-1.27 (t, 3H, J=6Hz), 3.82-4.60 (m, 19H), 6.85-7.01 (m, 8H)	1752 (C=O), 1258 (C-O)	C ₂₄ H ₃₀ O ₈	64.56 6.77 64.45 6.53
50	H	CH ₃	(CH ₃) ₃ C	2	74[b]					
51	H	CH ₃	H	3	79[b]					
52	CH ₃	CH ₃	H	2	65[b]					
53	CH ₃	C ₂ H ₅	H	2	92	oil	1.22-1.29 (t, 3H, J=7.2Hz), 1.55 (s, 3H), 2.55-2.65 (t, 2H, J=7.5 Hz), 3.83-4.30 (m, 16H), 6.80-7.00 (m, 8H)	1729 (C=O), 1257 (C-O)	C ₂₅ H ₃₂ O ₈ ^a 0.2CH ₂ Cl ₂	63.38 6.84 63.31 6.64
54	CH ₃	CH ₃	H	3	94[b]					
55	CH ₃	C ₂ H ₅	H	3	94	oil	1.19-1.27 (t, J=7.5Hz), 1.50 (s, 3H), 1.88-2.00 (m, 2H), 2.42-2.51 (t, 2H, J=8Hz), 3.77-4.23 (m, 16H), 6.82-7.00 (m, 8H)	1731 (C=O), 1257 (C-O)	C ₂₆ H ₃₄ O ₈	65.81 7.22 65.90 7.10

[a] Deposit from dichloromethane solution onto a sodium chloride plate. [b] Reference 28.

Scheme 12



behavior in solvent polymeric membrane electrodes. The synthetic route is given in Scheme 12 and the structural variation is shown in Table 6. The lariat ether alcohol was treated with potassium hydride, followed by addition of the appropriate acid chloride to produce the lariat ether esters.

Lariat ether ester **62**, which served as a spin-labeled lariat ether [32] was prepared by another method (Scheme 13). Reaction of *sym*-(hydroxyl)dibenzo-16-crown-5 (**99**) and carboxylic acid nitroxide **114** with *N,N'*-dicyclohexylcarbodiimide in tetrahydrofuran formed crown ether nitroxide **62** in 5% yield. The low yield was attributed to

Scheme 13

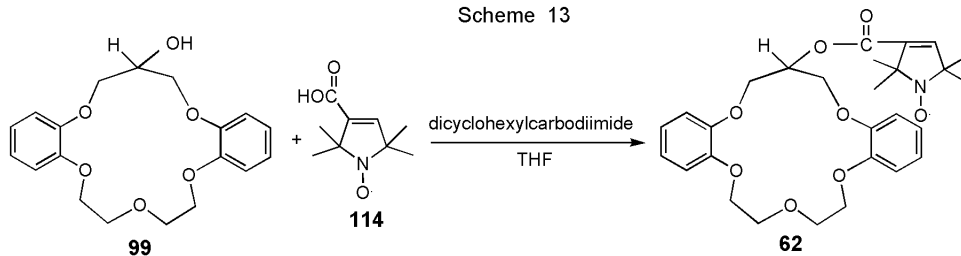
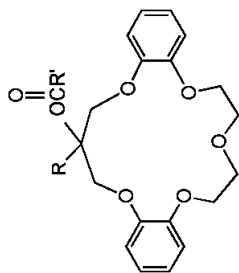


Table 6
Data for Dibenzo-16-crown-5 Lariat Ether Esters **56-68**



Compound	R	R'	Yield (%)	mp (°C)	¹ H NMR (deuteriochloroform) δ (ppm)	IR (cm ⁻¹)[a]	Molecular Formula	Analysis % Calcd./Found	H
56	H	CH ₃	77	118-120	2.13 (s, 3H), 3.92-3.96 (m, 4H), 4.15-4.19 (m, 4H), 4.38-4.40 (d, 4H, J=4Hz), 4.95-5.05 (m, 1H), 6.83-6.98 (m, 8H)	1738 (C=O), 1257 (C-O)	C ₂₁ H ₂₄ O ₇	64.94 64.89	6.23 6.36
57	H	C ₃ H ₁₁	87	oil	0.86-0.93 (t, 3H, J=7.2 Hz), 1.30-1.45 (m, 6H), 2.35-2.42 (t, 2H, J=7.2Hz), 3.92-3.96 (m, 4H), 4.10-4.21 (m, 4H), 4.36-4.39 (m, 4H), 5.45-5.53 (m, 1H), 6.82-7.00 (m, 8H)	1735 (C=O), 1258 (C-O)	C ₂₅ H ₃₂ O ₇	67.55 67.81	7.26 7.00
58	H	C(CH ₃) ₃	66	113-114	1.26 (s, 9H), 3.90-4.50 (m, 12H), 5.45-5.55 (m, 1H), 6.80-7.02 (m, 8H)	1726 (C=O), 1258 (C-O)	C ₂₄ H ₃₀ O ₇	66.96 67.19	7.02 7.12
59	H	C ₆ H ₅	77	101-103	3.95-4.02 (m, 4H), 4.17-4.22 (m, 4H), 4.50-4.54 (m, 4H), 4.98-5.30 (m, 1H), 6.82-6.97 (m, 8H), 7.42-7.59 (m, 3H), 8.08-8.13 (m, 2H)	1718 (C=O), 1258 (C-O)	C ₂₆ H ₂₆ O ₇	69.32 69.18	5.82 5.75
60	H	4-(CH ₃) ₂ C ₆ H ₄	59	42-44	3.82-4.60 (m, 15H), 5.65-5.75 (m, 1H), 6.79-7.05 (m, 10H), 8.02-8.10 (d, 2H, J=16Hz)	1710 (C=O), 1257 (C-O)	C ₂₇ H ₂₈ O ₈ [*] 0.1C ₃ H ₁₄	67.78 68.13	6.06 5.66
61	H	4-(O ₂) ₂ N ₂ C ₆ H ₄	70	155-156	3.95-4.21 (m, 8H), 4.54-4.58 (d, 4H, J=8Hz), 5.70-5.80 (m, 1H), 6.82-7.05 (m, 8H), 8.20-8.35 (m, 4H)	1726 (C=O), 1258 (C-O)	C ₂₆ H ₂₅ O ₉	63.03 63.15	5.09 5.05
62	H	TPO[b]	5	170-171	1.22 (s, 6H), 1.50 (s, 6H), 3.81-4.18 (m, 13H), 5.30 (s, 1H), 6.79 (m, 8H)	1742 (C=O), 1258 (C-O)	C ₂₈ H ₃₄ N ₂ O ₈	65.65 65.94	6.64 6.93
63	C ₃ H ₇	CH ₃	46	114-115	0.94-1.01 (t, 3H, J=7.2Hz), 1.38-1.53 (m, 2H), 2.05 (s, 3H), 2.14-2.22 (m, 2H), 3.91-3.95 (m, 4H), 4.13-4.17 (m, 4H), 4.37-4.42 (d, 2H, J=10Hz), 4.63-4.68 (d, 2H, J=10Hz), 6.82-6.95 (m, 8H)	1732 (C=O), 1258 (C-O)	C ₂₄ H ₃₀ O ₇	66.96 67.03	7.02 6.90
64	C ₃ H ₇	C ₃ H ₁₁	50	82-83	0.88-1.00 (m, 6H), 1.25-1.70 (m, 8H), 2.05-2.35 (m, 4H), 3.91-3.95 (m, 4H), 4.13-4.17 (m, 4H), 4.37-4.42 (d, 2H, J=10Hz), 4.63-4.68 (d, 2H, J=10Hz), 6.82-6.95 (m, 8H)	1731 (C=O), 1258 (C-O)	C ₂₈ H ₃₈ O ₇	69.11 69.39	7.87 7.99
65	C ₃ H ₇	(CH ₃) ₃ C	81	105-106	0.90-0.97 (t, 3H, J=7.2Hz), 1.25 (s, 9H), 1.40-1.60 (m, 2H), 2.10-2.21 (m, 2H), 3.85-4.00 (m, 4H), 4.10-4.20 (m, 4H), 4.35-4.40 (d, 2H, J=10Hz), 4.60-4.65 (d, 2H, J=10Hz), 6.80-6.92 (m, 8H)	1724 (C=O), 1258 (C-O)	C ₂₇ H ₃₆ O ₇	68.62 68.69	7.68 7.65

Table 6 (continued)

Compound	R	R'	Yield (%)	mp (°C)	¹ H NMR (deuteriochloroform) δ (ppm)	IR (cm ⁻¹)[a]	Molecular Formula	Analysis % Calcd./Found	
								C H	
66	C ₃ H ₇	C ₆ H ₅	99	114-116	0.96-1.03 (t, 3H, J=7.2Hz), 1.52-1.70 (m, 2H), 2.31-2.39 (m, 2H), 3.92-4.30 (m, 8H), 4.55-4.60 (d, 2H, J=10Hz), 4.76-4.82 (d, 2H, J=12Hz), 6.82-6.98 (m, 8H), 7.38-7.52 (m, 3H), 8.00-8.10 (m, 2H)	1714 (C=O), 1257 (C-O)	C ₂₉ H ₃₇ O ₇ •0.7C ₂ H ₅ Cl ₂	64.62 64.31	6.10 5.87
67	C ₃ H ₇	4-(CH ₃ O)C ₆ H ₄	72	41-43	0.95-1.02 (t, 3H, J=7.2Hz), 1.50-1.65 (m, 2H), 2.30-2.45 (m, 2H), 3.38-4.22 (m, 11H), 4.23-4.26 (d, 2H, J=6Hz), 4.27-4.33 (d, 2H, J=12Hz), 6.80-7.04 (m, 10H), 7.92-8.05 (d, 2H, J=26Hz)	1707 (C=O), 1256 (C-O)	C ₃₀ H ₃₄ O ₉	68.95 68.75	6.56 6.30
68	C ₃ H ₇	4-(O ₂ N)C ₆ H ₄	86	58-60	0.95-1.02 (t, 3H, J=7.2Hz), 1.50-1.70 (m, 2H), 2.30-2.42 (m, 2H), 3.90-4.25 (m, 8H), 4.55-4.80 (m, 4H), 6.80-7.00 (m, 8H), 8.09-8.25 (m, 4H)	1721 (C=O), 1258 (C-O)	C ₂₉ H ₃₁ NO ₉	64.80 64.79	5.81 5.49

[a] Deposit from dichloromethane solution onto a sodium chloride plate. [b] TPO = 3-(2,2,5,5-tetramethyl-3-pyrrolinyloxy).

the difficulty in separating **62** from the byproduct, *N,N'*-dicyclohexylurea.

Shortly after his initial report on the discovery of crown ethers, Pedersen published a paper in which the ability of two crown ether rings to coordinate with a single metal ion was described [33]. This phenomenon occurs when the cation is too large to fit into the cavity of the crown ether and, therefore, positions itself between two crown ether units. Pedersen called these coordinations "sandwich complexes", or "club sandwich complexes" for the rarer 3:2 (crown ether:cation) complexes.

Reports of such stable 2:1 complexes of crown ethers with cations led to the synthesis of a wide variety of molecules containing two pendant crown ether units [34]. Structural variations were applied to determine the best distance between the two crown ether units for cooperative interaction. Then Shono and coworkers incorporated bis(crown ether) diesters [35] and diamides [36] into PVC membrane ion-selective electrodes with excellent results.

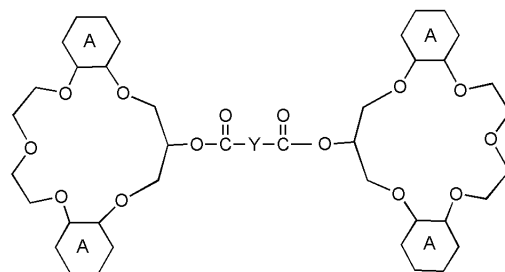
The bis(crown ether) esters **69-74** (Table 7) were prepared by reaction of lariat ether alcohol **99** or **115** with the appropriate di(acid chloride), as depicted in Scheme 14. Bis(crown ether) esters **69-74** contain two crown ether units and two ester groups, which are connected by Y. The length of Y was varied to investigate the optimal distance between the two linked crown ether units for cooperative interaction.

The lariat ethers **75-78** (Table 8) with ether side arms were prepared for assessment of their behavior in polymeric membrane electrodes. Their preparation is shown in Scheme 15. Lariat ether alcohols **99**, **100**, **116** and **117** were treated with sodium hydride in tetrahydrofuran to give the alkoxide intermediate, which was subsequently reacted with 2-methoxyethyl bromide to produce the desired products **75-78**, respectively.

As mentioned previously, selectivities of several dibenzo-16-crown-5 compounds with pendent ester groups for alkali metal, alkaline earth metal, and ammonium ions have been determined with solvent polymeric membrane electrodes [25]. The ionophores include alkyl *sym*-(R)dibenzo-16-crown-5-oxyacetates where R = hydrogen, linear alkyl, branched alkyl, fluoroalkyl, alkenyl, alkynyl, and phenyl groups. For lariat ethers with a hydrogen, linear alkyl function, or branched alkyl group geminal to the side arm with the ester-containing side arm, the Na⁺/K⁺ selectivity increased as the bulkiness of the geminal substituent was enhanced, whereas the Na⁺/Li⁺ selectivity exhibited a weaker inverse relationship to the size of R. On the other hand, the Na⁺/K⁺ and Na⁺/Li⁺ selectivities were insensitive to variations in the size and shape of the side arm containing the ester group. For lariat ether ester ionophores **2**, **3**, **5**, **7**, **8**, **36**, **40**, and **42**, very high Na⁺/Li⁺ selectivities of 10^{3.8}-10^{3.9} were observed [25b].

In addition to their use as complexing agents, several

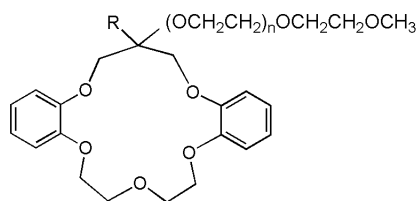
Table 7
Data for Bis(crown ether) Esters **69-74**



Compound	A	Y	Yield (%)	mp (°C)	¹ H NMR (deuteriochloroform) δ (ppm)	IR (cm ⁻¹) [a]	Molecular Formula	Analysis Calcd./Found C H	
69	1,2-benzo	none	70	145-147	3.65-4.65 (m, 24H), 5.45-5.80 (m, 2H), 6.65-7.15 (m, 16H) 1257 (C-O)	1735 (C=O),	C ₄₀ H ₄₂ O ₁₄ • H ₂ O	62.81 62.53	5.80 5.88
70	1,2-benzo	CH ₂	65	70-72	3.45-4.60 (m, 26H), 5.55 (s, 2H), 6.90 (s, 16H)	1740 (C=O), 1258 (C-O)	C ₄₁ H ₄₄ O ₁₄ • 0.1CH ₂ Cl ₂	64.17 64.23	5.79 5.81
71	1,2-cyclohexano	none	81	oil	1.45 (br s, 32H), 3.60-3.65 (m, 34H)	1763 (C=O), 1118 (C-O)	C ₄₀ H ₆₆ O ₁₄ • 2H ₂ O	59.53 59.51	8.74 8.97
72	1,2-cyclohexano	CH ₂	78	oil	1.45 (br s, 32H), 3.65 (s, 36H)	1745 (C=O), 1125 (C-O)	C ₄₁ H ₆₈ O ₁₄ • 1.5H ₂ O	60.64 60.46	8.81 8.93
73	1,2-cyclohexano	CH ₂ CH ₂	72	oil	1.50 (br s, 32H), 2.65 (s, 4H), 3.65 (s, 34H)	1740 (C=O), 1126 (C-O)	C ₄₂ H ₇₀ O ₁₄ • 2.5H ₂ O	59.76 59.87	8.96 9.00
74	1,2-cyclohexano	CH ₂ OCH ₂	74	oil	1.45 (br s, 32H), 3.50-3.55 (m, 38H)	1736 (C=O), 1132 (C-O)	C ₄₂ H ₇₀ O ₁₅ • 2H ₂ O	59.27 59.40	8.77 9.08

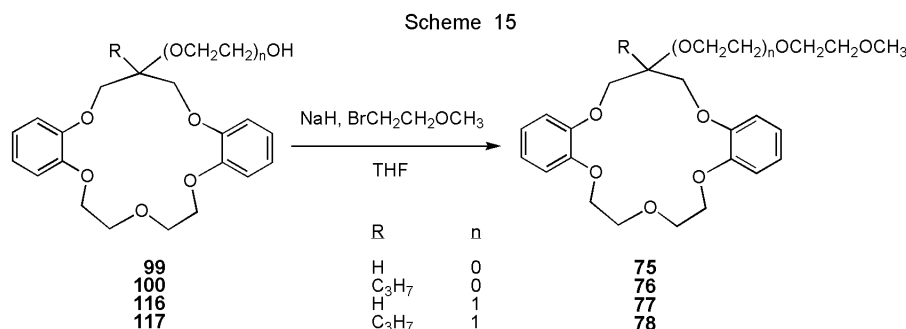
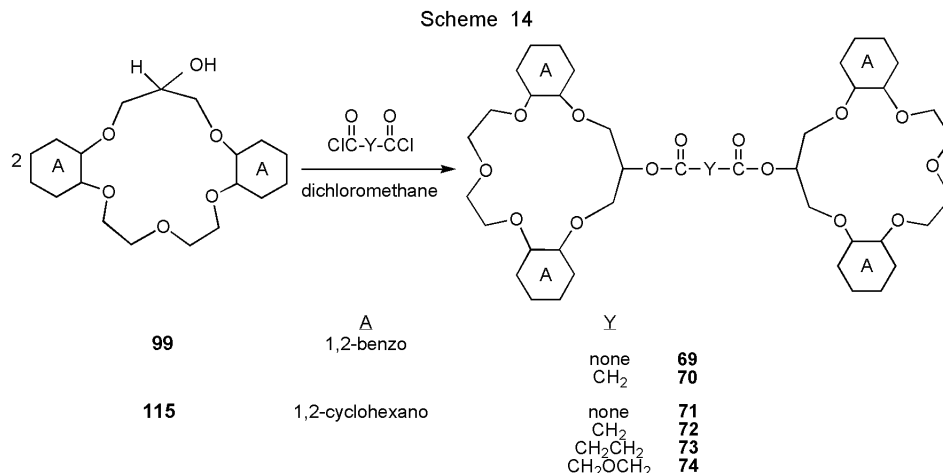
[a] Deposit from dichloromethane solution onto a sodium chloride plate.

Table 8
Data for Dibenzo-16-crown-5 Compounds **75-78** with Ether Side Arms



Compound	R	n	Yield (%)	mp (°C)	¹ H NMR (deuteriochloroform) δ (ppm)	IR (cm ⁻¹) [a]	Molecular Formula	Analysis % Calcd./Found C H	
75	H	0	77	62-63	3.50 (s, 3H), 3.62-4.40 (m, 17H), 6.83-7.05 (m, 8H)	1256 (C-O)	C ₂₂ H ₂₈ O ₇	65.35 65.56	6.93 6.96
76	C ₃ H ₇	0	83	oil	0.94-1.01 (6, 3H, J=7.2Hz), 1.40-1.55 (m, 2H), 1.88-2.00 (m, 2H), 3.40 (s, 3H), 3.55-3.62 (t, 2H, J=7.2Hz), 3.90-4.35 (m, 14H), 6.81-6.96 (m, 8H)	1257 (C-O)	C ₂₅ H ₃₄ O ₇	67.24 67.46	7.67 7.77
77	H	1	30	oil	3.39 (s, 3H), 3.55-4.40 (m, 21H), 6.82-7.02 (m, 8H)	1257 (C-O)	C ₂₄ H ₃₂ O ₈	64.27 64.41	7.19 6.90
78	C ₃ H ₇	1	32	oil	0.94-1.01 (6, 3H, J=7.2Hz), 1.40-1.55 (m, 2H), 1.87-1.96 (m, 2H), 3.38 (s, 3H), 3.51-4.32 (m, 20H), 6.80-6.97 (m, 8H)	1257 (C-O)	C ₂₇ H ₃₈ O ₈	66.10 65.99	7.81 7.84

[a] Deposit from dichloromethane solution onto a sodium chloride plate.



lariat ether esters were employed as precursors for the preparation of lariat ether carboxylic acids [5,8], as monomers for the preparation of polyamide polymers [37], and as a spin-labeled lariat ether [32] to provide structural and dynamic information about crown ether-metal ion complexes.

Identities of all new compounds were confirmed by ir and ¹H nmr spectroscopy, and combustion analyses.

EXPERIMENTAL

Unless specified otherwise, reagent grade reactants and solvents were used as received from commercial suppliers. Tetrahydrofuran was dried and distilled from sodium with benzophenone ketyl as indicator. Starting compounds **79**, **87**, **91**, **95**, **96** [7], **80**, **84** [6], **100** [15], **83**, **86**, **89**, **115** [4], **81**, **82**, **85**, **88**, **90**, **92-94**, **101**, **107**, **108**, **112**, **113** [8], **99** [38], **105**, **106**, **116**, **117** [28] were available from our previous work.

The infrared (ir) spectra were obtained with a Perkin Elmer Model 1600 spectrophotometer and are reported in reciprocal centimeters (cm⁻¹). The proton nuclear magnetic resonance (¹H nmr) spectra were recorded with an IBM AF-200 spectrometer in deuteriochloroform and chemical shifts are reported in parts per million downfield (δ) from tetramethylsilane. Melting points were measured with a Mel-Temp melting point apparatus and are uncorrected. Combustion analyses were performed by Desert Analytics Laboratory, Tucson, AZ. Unless stated otherwise,

physical properties and spectral and combustion analysis data are recorded in Tables 1-8.

General Procedure for the Preparation of Lariat Ether Esters **2**, **9**, **11**, **13**, **19-24**, **27**, **29-33**, **37**, **40-44**, **53** and **55**.

A solution of 5.0 mmoles of the appropriate lariat ether carboxylic acid and 6 drops of concentrated sulfuric acid in 150 ml of methanol or ethanol (absolute) in a flask configured so that the condensate passed through a Soxhlet thimble containing anhydrous sodium sulfate was refluxed for 12 hours. After the alcohol was evaporated *in vacuo*, 50 ml of 5% aqueous potassium carbonate solution and 150 ml of dichloromethane were added to the residue. The organic layer was separated and washed with water (2 x 50 ml), dried over magnesium sulfate, and concentrated *in vacuo* to give the desired product.

General Procedure for the Preparation of Lariat Ether Esters **3-8**, **14-17** and **36**.

A solution of the appropriate lariat ether carboxylic acid (1.80 mmoles) and 0.32 ml (3.6 mmoles) of oxalyl chloride in 40 ml of anhydrous benzene was stirred at room temperature under nitrogen for 10 hours. The solvent and excess oxalyl chloride was evaporated *in vacuo* to give the crude acid chloride, which was used without purification in the next step. To a stirred solution containing 1.80 mmoles of the lariat ether acid chloride in 40 ml of dry tetrahydrofuran was slowly added 1.80 mmoles of the appropriate alcohol and 7.2 mmoles of pyridine under nitrogen at room temperature. The mixture was stirred for an additional 3

hours. After the tetrahydrofuran was evaporated *in vacuo*, 200 ml of dichloromethane was added, followed by washing by 10% hydrochloric acid (2 x 50 ml) and water (2 x 50 ml). The dichloromethane layer was dried over magnesium sulfate and concentrated *in vacuo* to give the crude product, which was purified by recrystallization or column chromatography.

Preparation of *tert*-Butyl[*sym*-(Propyl)dibenzo-16-crown-5-oxy]acetate (**18**).

After removal of the protecting mineral oil from 0.33 g of sodium hydride (8.3 mmoles, 60% dispersion) by washing with pentane, 0.80 g (2.1 mmoles) of *sym*-(hydroxy)(propyl)dibenzo-16-crown-5 (**100**) in 50 ml of tetrahydrofuran was added and the mixture was stirred for 30 minutes at room temperature. *tert*-Butyl bromoacetate (0.33 ml, 4.2 mmoles) was added slowly and the mixture was stirred for 12 hours at room temperature. The excess sodium hydride was decomposed by careful addition of water. After the tetrahydrofuran was evaporated *in vacuo*, dichloromethane (200 ml) and water (100 ml) were added. The organic layer was separated, washed with water (2 x 50 ml), dried over magnesium sulfate, and evaporated *in vacuo* to give a colorless oil. Chromatography of the crude product on silica gel with dichloromethane as eluent provided 1.05 g (56%) of **18** as a colorless oil.

General Procedure for the Synthesis of Lariat Ether Esters **2** and **13** by Reaction of Lariat Ether Carboxylic Acids with Ethyl Diazoacetate.

The *sym*-(*R*)dibenzo-16-crown-5-oxyacetic acid (1.44 mmoles) in 100 ml of benzene was dried by azeotropic distillation with the use of a Dean-Stark apparatus until 20 ml of solution remained. The solution was cooled to 0 °C and then 0.15 ml of ethyl diazoacetate (1.44 mmoles) and 5 drops of boron trifluoride etherate were added. The reaction mixture was stirred at room temperature overnight. The solvent was evaporated *in vacuo* and the residue was chromatographed on silica gel with ethyl acetate-hexane (1:3) and (1:2) as eluents to give the title compounds **2** and **13**, respectively. **WARNING: Ethyl diazoacetate is explosive at high temperatures!**

Preparation of Lariat Ether Ester **28**.

To the unsaturated lariat ether ester **37** (1.0 mmol) was added 0.70 ml of a cold (0 °C) solution of 0.5 M borane (0.35 mmol) in tetrahydrofuran. The reaction mixture was stirred at 0 °C for 2 hours and then at room temperature for 2 hours. A 1 N sodium hydroxide solution (0.21 ml) and 0.14 ml of 30% hydrogen peroxide solution were added. The reaction mixture was extracted with dichloromethane, the organic layer was dried over magnesium sulfate, and evaporated *in vacuo* to give the desired product.

General Procedure for the Preparation of *sym*-(*R*)Dicyclohexano-16-crown-5-oxyacetic Acids **97** and **98**.

A mixture of the *sym*-(*R*)dibenzo-16-crown-5-oxyacetic acid (24.73 mmoles), 5% rhodium on alumina catalyst (1.00 g), and acetic acid (1.00 g) in 300 ml of 1-butanol was stirred under hydrogen (500-600 psi) at 65 °C for 20 hours. The reaction mixture was filtered through filter paper and evaporated *in vacuo*. The residue was dissolved in 100 ml of methanol and the mixture was filtered through a Teflon filter (0.22 μm) and then the filtrate was evaporated *in vacuo* to give the title compounds.

sym-Dicyclohexano-16-crown-5-oxyacetic Acid (**97**).

This compound was obtained in 99% yield as a colorless oil; ir (deposit from dichloromethane solution on a sodium chloride plate): ν 3423 (COOH), 1765 (C=O), 1110 (C-O) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.10-2.22 (m, 16H), 3.20-4.61 (m, 19H).

Anal. Calcd. for $\text{C}_{21}\text{H}_{36}\text{O}_8$: C, 60.56; H, 8.71. Found: C, 60.41; H, 8.73.

sym-(Propyl)dicyclohexano-16-crown-5-oxyacetic Acid (**98**).

This compound was obtained in 98% yield as a colorless oil; ir (deposit from dichloromethane solution on a sodium chloride plate): ν 3500-2500 (COOH), 1760 (C=O), 1109 (C-O) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 0.99-1.02 (m, 3H), 1.12-2.25 (m, 20H), 3.10-4.62 (m, 18 H).

Anal. Calcd. for $\text{C}_{24}\text{H}_{42}\text{O}_8$: C, 62.86; H, 9.23. Found: C, 62.84; H, 9.00.

General Procedure for the Preparation of Lariat Ether Esters **38** and **39**.

Under nitrogen, 1.78 g of sodium hydride (44.6 mmoles, 60% dispersion in mineral oil) was washed with dry hexane and then 100 ml of dry tetrahydrofuran was added. A solution of the appropriate crown alcohol (8.90 mmoles) in 100 ml of dry tetrahydrofuran was added dropwise. The mixture was stirred for 1 hour at room temperature and then cooled in ice water. A solution of 1.79 g of ethyl bromoacetate (10.7 mmoles) in 10 ml of dry tetrahydrofuran was added by use of a syringe pump over a period of 1 hour and the reaction mixture was stirred overnight at room temperature. The reaction mixture was cooled in an ice-water bath and then ice-water was carefully added to quench the excess sodium hydride. Tetrahydrofuran was removed *in vacuo* and the aqueous residue was extracted with dichloromethane. The organic solution was dried over magnesium sulfate and evaporated *in vacuo* to give a viscous yellow oil. The oil was chromatographed on silica gel with dichloromethane-hexane (4:1), followed by ethyl acetate-hexane (2:3) as eluent to give the desired products **38** and **39**.

Preparation of *sym*-Di(aminobenzo)-16-crown-5-oxyacetyl Hydrazide (**109**).

sym-Di(nitrobenzo)-16-crown-5-oxyacetic acid (**107**) (10.00 g, 20.2 mmoles), 10% Pd/C (1.00 g), and 60 ml of anhydrous hydrazine were added to 300 ml of 95% ethanol. The mixture was refluxed for 24 hours and then filtered through Celite. The filtrate was concentrated *in vacuo* to 30-50 ml and placed in a refrigerator overnight to afford a white solid. The white solid was filtered, washed with cold ethanol (5 x 50 ml) and diethyl ether (2 x 50 ml), and dried in a vacuum oven at 60 °C to provide 7.81 g (86%) of product with a mp of 178-190 °C; ir (potassium bromide): ν 3370, 3290 and 3180 (NH_2 and NHNH_2), 1680 (C=O); cm^{-1} ; ^1H nmr (dimethyl sulfoxide- d_6): δ 3.30-5.40 (m, 21H), 5.90-6.40 (m, 4H), 6.60-6.75 (m, 2H), 8.93 (s, 1H).

Anal. Calcd. for $\text{C}_{21}\text{H}_{28}\text{N}_4\text{O}_7$: C, 56.24; H, 6.29; N, 12.49. Found: C, 56.02; H, 6.04; N, 12.35.

Preparation of *sym*-(Propyl)di(aminobenzo)-16-crown-5-oxyacetyl Hydrazide (**110**).

sym-(Propyl)di(nitrobenzo)-16-crown-5-oxyacetic acid (**108**) (5.00 g, 9.32 mmoles), 10% Pd/C (0.60 g), and 25 ml of anhy-

drous hydrazine were added to 150 ml of 95% ethanol. The reaction mixture was refluxed for 36 hours and then filtered through Celite. After removal of the ethanol *in vacuo*, 200 ml of brine was added and then the mixture was extracted with dichloromethane (3 x 100 ml). The organic extracts were combined, dried over sodium carbonate, and evaporated *in vacuo* to provide a white solid, which was dried in a vacuum oven at 60 °C to give 3.88 g (85%) of white solid with mp 45-70 °C; ir (deposit from chloroform solution on a sodium chloride plate): ν 3413, 3334 and 3216 (NH₂ and NHHN₂), 1668 (C=O) cm⁻¹; ¹H nmr (dimethyl sulfoxide-d₆): δ 0.85 -1.05 (t, 3H, J=7.5 Hz), 1.30-1.60 (m, 2H), 1.65-1.90 (m, 2H), 3.65-5.20 (m, 18H), 5.95-7.10 (m, 6H), 8.50-8.65 (t, 3H, J=7.3 Hz).

Anal. Calcd. for C₂₄H₃₄N₄O₇: C, 58.76; H, 6.99; N, 11.42. Found: C, 58.40; H, 7.10; N, 11.65.

General Procedure for the Preparation of Lariat Ether Esters **45-48**.

The appropriate *sym*-di(aminobenzo)-16-crown-5-oxyacetyl hydrazide **109** or **110** (6.69 mmoles) and 3.0 ml of concentrated sulfuric acid were added to 300 ml of dry methanol or ethanol. The reaction mixture was refluxed for 24 hours with the condensate passing through a Soxhlet extraction thimble containing anhydrous magnesium sulfate. The solvent was evaporated *in vacuo* to give a residue, which was dissolved in water and extracted with 100 ml of dichloromethane to remove organic impurities. The aqueous phase was carefully adjusted to pH >7 with saturated aqueous sodium bicarbonate and then extracted with dichloromethane (4 X 100 ml). The combined organic layers were washed with brine (100 ml), dried over sodium carbonate, and evaporated *in vacuo* to afford a white solid. The solid was dried in a vacuum oven at 60 °C to afford the title compound.

Preparation of Ethyl 3-(*sym*-Dibenzo-16-crown-5-oxy)propionate (**49**).

Hydrogen chloride gas was bubbled through a boiling solution of **111** (1.00 g, 2.50 mmoles) in 120 ml of ethanol-benzene (1:2) for 8 hours. A Dean-Stark trap was used to remove the water formed in the reaction. Subsequently, 15 ml of water was added to the mixture to hydrolyze the imidic ether hydrochloride intermediate to the ester. The mixture was concentrated *in vacuo* and then the residual aqueous layer was extracted with dichloromethane. The organic layer was washed with water, dried over magnesium sulfate, and evaporated *in vacuo* to give the crude product, which was purified by chromatography on silica gel with diethyl ether-dichloromethane (1:7) as eluent to provide the title compound as an oil.

General Procedure for the Preparation of Lariat Ether Esters **56-61** and **63-68**.

Potassium hydride (0.24 g, 6.1 mmole, 35% dispersion in mineral oil) was washed with pentane to remove the oil. A solution of the corresponding lariat ether alcohol (3.0 mmol) in 50 ml dry tetrahydrofuran was added. The mixture was stirred for 30 minutes at room temperature and then the appropriate acid chloride (6.0 mmole) was added. The reaction mixture was stirred for 5 hours at room temperature and then filtered. The filtrate was evaporated *in vacuo* to give the crude product, which was purified by chromatography on silica gel with dichloromethane to provide the title compounds.

Preparation of (*sym*-Dibenzo-16-crown-5-yl)-2,2,5,5-tetramethyl-3-pyrrolinyl-1-oxyl-3-carboxylate (**62**).

At room temperature, lariat ether alcohol **99** (1.70 g, 4.9 mmoles) and 2,2,5,5-tetramethyl-3-pyrrolinyl-1-oxyl-3-carboxylic acid (0.84 g, 4.5 mmol) were added with stirring to 30 ml of tetrahydrofuran. *N,N'*-Dicyclohexylcarbodiimide (1.10 g, 5.3 mmoles) was then added, resulting in the immediate formation of a precipitate. The mixture was stirred for 2 days. The solvent was evaporated *in vacuo* and the residue was dissolved in dichloromethane. The organic solution was washed with 5% sodium hydroxide (2 X 50 ml), dried over magnesium sulfate, and evaporated *in vacuo* to give a residue, which was chromatographed on silica gel with dichloromethane-diethyl ether as eluent to produce 0.13 g of yellow needles.

General Procedure for the Preparation of Bis(crown ether) Esters **69-74**.

To a boiling solution of lariat ether alcohol **99** or **115** (10.0 mmole) in 200 ml of dichloromethane was added a solution of the appropriate di(acid chloride) (5.0 mmoles) in dichloromethane (20 ml) over 2.5 hours by use of a syringe pump. The reaction mixture was refluxed for 2 hours, cooled to room temperature, and then washed with a 1 M solution of sodium bicarbonate in saturated sodium chloride (3 X 75 ml). The dichloromethane solution was dried over magnesium sulfate and evaporated *in vacuo*. The residue was extracted with ethanol for 24 hours in a Soxhlet extractor. The volume of ethanol was then reduced to 50 ml and the solution was cooled in an ice bath until the product crystallized (for compounds **69** and **70**). The crystalline product was collected, washed with cold cyclohexane, and left under vacuum overnight. For compounds **71-74**, the solvent was evaporated to give oils.

General Procedure for the Preparation of Lariat Ethers **75-78**.

Potassium hydride (1.02 g, 9.0 mmole, 35% dispersion in mineral oil) was washed with pentane to remove the oil and then a solution of the corresponding lariat ether alcohol in tetrahydrofuran (100 ml) was added and the mixture was stirred for 30 minutes. Then 0.56 ml of 1-bromo-2-methoxyethane (6.0 mmole) was added. After refluxing the mixture for 4 hours, the excess potassium hydride was carefully quenched with water. The tetrahydrofuran was evaporated *in vacuo* to give a residue to which 150 ml of dichloromethane and 100 ml of water were added. The organic layer was washed with water (2 X 50 ml), dried over magnesium sulfate, and evaporated *in vacuo* to give the crude product, which was purified by recrystallization from hexanes for **75** or chromatography on alumina with dichloromethane, ethyl acetate, and diethyl ether as eluents for **76-78**, respectively.

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