10p: IR (neat) 2955, 1718, 1450, 1200, 1180, 1122, 1080, 778 cm^{-1}; NMR (CCl_4) δ 1.93–2.84 (m, 2 H), 3.26–3.84 (m, 2 H), 3.39 (s, 3 H), 3.74 (s, 3 H), 4.16 (br d, J = 5 Hz, 1 H), 5.09–5.34 (m, 1 H). Anal. Calcd for $C_7H_{12}NO_3Br$: C, 35.31; H, 5.08; N, 5.88; Br, 33.56. Found: C, 35.52; H, 5.07; N, 5.59; Br, 33.81.

β-Iodo-α-methoxy-*N*-(methoxycarbonyl)pyrrolidine (10q): 38% yield at 5.0 faradays/mol (supporting electrolyte NH_4I); IR (neat) 2960, 1715, 1452, 1380, 1112, 1080, 958, 780 cm^{-1}; NMR (CCl_4) δ 2.03–2.81 (m, 2 H), 3.20–3.80 (m, 2 H), 3.34 (br s, 3 H), 3.74 (s, 3 H), 4.16 (br d, J = 5 Hz, 1 H), 5.16–5.43 (m, 1 H). Anal. Calcd for $C_7H_{12}NO_3I$: C, 29.49; H, 4.24; N, 4.91; I, 44.52. Found: C, 29.67; H, 4.30; N, 4.97; I, 44.52.

β-Bromo-α-methoxy-*N*-(methoxycarbonyl)piperidine (11p): 81% yield at 3.5 faradays/mol (supporting electrolyte NaBr); IR (neat) 2952, 1708, 1448, 1272, 1160, 1082, 968, 952, 778 cm^{-1}; NMR (CCl_4) δ 1.29–2.45 (m, 4 H), 2.95 (br t, J = 12 Hz, 1 H), 3.27 and 3.36 (2 s, $^5/_2$ H and $^1/_2$ H), 3.63–4.63 (m, 2 H), 3.74 (s, 3 H), 5.44 (br s, 1 H); mass spectrum, m/e 253 (M^+ + 2), 251 (M^+), 222 ($M^+ - OCH_3 + 2$), 220 (100%, $M^+ - OCH_3$); exact mass calcd m/e 251.0157, found 251.0146.

β-Iodo-α-methoxy-*N*-(methoxycarbonyl)piperidine (11q): 81% yield at 4.0 faradays/mol (supporting electrolyte NaI); IR (neat) 2950, 1712, 1448, 1258, 1200, 1152, 1072, 940 cm^{-1}; NMR (CCl_4) δ 1.34–2.24 (m, 4 H), 2.97 (br t, J = 12 Hz, 1 H), 3.26 (s, 3 H), 3.75 (s, 3 H), 3.79–4.14 (m, 1 H), 4.41 (br s, 1 H), 5.44 (br s, 1 H); mass spectrum, m/e 268 ($M^+ - OCH_3$), 172 (M^+ - I), 158 (100%); exact mass calcd m/e 267.9837 (M - OCH_3), found 267.9856 ($M^+ - OCH_3$).

β-Bromo-α-methoxy-*N*-(methoxycarbonyl)azacycloheptane (12p): 70% yield at 5.0 faradays/mol (supporting electrolyte: NaBr); IR (neat) 2948, 2855, 1703, 1438, 1335, 1118, 1095, 1085, 1010, 955, 776 cm^{-1}; NMR (CCl_4) δ 1.13–2.31 (m, 6 H), 2.59–3.96 (m, 3 H), 3.28 (s, 3 H), 3.74 (s, 3 H), 5.25–5.61 (m, 1 H); mass spectrum, m/e 267 (M^+ + 2), 265 (M^+), 236 ($M^+ + 2 - OCH_3$), 234 ($M^+ - OCH_3$), 208, 206, 186 (M^+ - Br), 154, 144, 128 (100%); exact mass calcd m/e 265.0314, found 265.0302.

β-Iodo-α-methoxy-*N*-(methoxycarbonyl)azacycloheptane (12q): 66% yield at 4.5 faradays/mol (supporting electrolyte NaI); IR (neat) 2940, 2850, 1700, 1436, 1338, 1137, 1105, 1088, 1068, 1003, 943, 770 cm^{-1}; NMR (CCl_4) δ 1.23–2.51 (m, 6 H), 2.69–3.09 (m, 1 H), 3.18–4.13 (m, 2 H), 3.32 (s, 3 H), 3.79 (s, 3 H), 5.36–5.73 (m, 1 H); mass spectrum, m/e 313 (M^+), 282 ($M^+ - OCH_3$), 254, 196, 186 (100%, M^+ - I); exact mass calcd m/e 313.0176, found 313.0151.

Reduction of 4a and 9b. A general procedure is exemplified by reduction of **9b**. Into a solution of **9b** (0.238 g, 0.97 mmol) in acetic acid (4 mL) was added in portions 90% $NaBH_4$ (0.184 g, 4.36 mmol). After 1.5 h, aqueous $NaHCO_3$ (60 mL) was poured into the reaction mixture and the organic portion was extracted with CH_2Cl_2 (20 mL × 4). After the extract was dried over $MgSO_4$ and the solvent was removed in vacuo, the residue was chromatographed on silica gel ($AcOC_2H_5$:hexane = 1:2) to afford **β-acetoxy-*N*-(methoxycarbonyl)pyrrolidine (13)** in 82% yield.

13: IR (neat) 2955, 2890, 1741, 1710, 1458, 1395, 1248, 1202, 775 cm^{-1}; NMR (CCl_4) δ 1.83–2.29 (m, 2 H), 2.07 (s, 3 H), 3.09–3.84 (m, 4 H), 3.66 (s, 3 H), 5.15–5.49 (m, 1 H); mass spectrum, m/e 127 (100%, M^+ - AcOH). Anal. Calcd for $C_8H_{13}NO_4$: C, 51.33; H, 7.00; N, 7.48. Found: C, 51.05; H, 6.99; N, 7.20.

The reduction of **4a** under the similar conditions gave **14**.

β-Chloro-*N*-(methoxycarbonyl)piperidine (14): 80% yield from **4a**; IR (neat) 2972, 2880, 1718, 1481, 1454, 1419, 1270, 1248, 1202, 1162, 1138, 972, 778, 770 cm^{-1}; NMR (CCl_4) δ 1.23–2.49 (m, 4 H), 2.76–3.30 (m, 2 H), 3.53–4.30 (m, 3 H), 3.68 (s, 3 H); mass spectrum, m/e 179 (M^+ + 2), 177 (M^+), 164, 162, 142 (M^+ - Cl), 102 (100%); exact mass calcd m/e 177.0556, found 177.0543.

Transformation of 6a and 11p to 15 and 16. A mixture of **6a** (0.332 g, 1.85 mmol) and NH_4Cl (0.01 g, 0.19 mmol) was heated (100 °C) under an atmosphere of nitrogen with reduced pressure (22 mm) for 3 h. After the reaction was completed, **β-chloro-α,β-didehydro-*N*-(methoxycarbonyl)pyrrolidine (15)** was isolated by Kugelrohr distillation in 94% yield. **β-Bromo-α,β-didehydro-*N*-(methoxycarbonyl)piperidine (16)** was prepared in 96% yield by heating (225 °C) **12p** under reduced pressure (45 mm).

15: bp 140 °C (22 mm); IR (neat) 2970, 2915, 1718, 1459, 1390, 1200, 1132 cm^{-1}; NMR (CCl_4) δ 2.85 (br t, J = 10 Hz, 2 H), 3.73 (s, 3 H), 3.87 (br t, J = 10 Hz, 2 H), 6.62 (br s, 1 H); mass spectrum, m/e 163 (M^+ + 2), 161 (100%, M^+); exact mass calcd m/e 161.0244, found 161.0250.

16: bp 225 °C (42 mm); IR (neat) 3100, 2950, 1708, 1654, 1440, 1382, 1342, 1302, 1250, 1190, 1120, 982, 968, 762, 748 cm^{-1}; NMR (CCl_4) δ 1.97 (tt, J = 6 and 6 Hz, 2 H), 2.46 (t, J = 6 Hz, 2 H), 3.59 (t, J = 6 Hz, 2 H), 3.75 (s, 3 H), 7.12 (br s, 1 H). Anal. Calcd for $C_7H_{10}NO_2Br$: C, 38.21; H, 4.58; N, 6.36; Br, 36.31. Found: C, 38.31; H, 4.56; N, 6.19; Br, 36.04.

Oxidation Potentials. Oxidation potentials were measured at room temperature by using an H-type cell, potentiostat HA-104, and function generator HB-107A (Hokuto Denko Ltd.). Oxidation was carried out in dry acetonitrile containing 0.1 N $LiClO_4$ as a supporting electrolyte at platinum electrode using an aqueous saturated calomel reference electrode. The scan rate was 100 mV/s. The concentrations of **8a** and **8b** were 4 mmol/L.

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Synthesis and Alkali-Metal Complexing Abilities of Crown Ether Tertiary Alcohols

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Twenty-three crown ethers with a hydroxyl and an alkyl or aryl group linked directly to the central carbon of a three-carbon bridge were synthesized in one-step reactions of glycol and bisphenol dianions with substituted 2-(chloromethyl)oxiranes. Crown ether tertiary alcohols with methyl, *n*-decyl, *n*-tetradecyl, phenyl, and *p*-(*n*-decyl)phenyl substituents and four ring sizes are prepared. The effect of substituent on Na^+ and K^+ complexation is assessed by the picrate extraction method for closely related tertiary crown ether alcohols with 16-crown-5 and 15-crown-5 rings.

Crown ether alcohols are versatile synthetic intermediates for the preparation of ionophores with pendant arms,[1] bis crowns,[2] and polymer-bound crowns.[3] Pendant arms with additional neutral or anionic coordination sites often provide substantially increased metal ion binding

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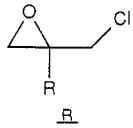
0022-3263/87/1952-0541$01.50/0

compared with the parent crown ether. Attachment of an alkyl group to the crown ether carbon that bears the pendant arm may further facilitate metal ion complexation.[4,5] This enhancement has been ascribed to steric interactions that orient the pendant arm over the polyether cavity.

Presently available methods for the preparation of crown ether tertiary alcohols from glycol or bisphenol precursors are multistep reactions or produce undesirable side products.[6,7] We now report a one-step synthesis of crown ether tertiary alcohols in which an alkyl or aryl substituent and the hydroxyl group are attached to the central carbon of a three-carbon bridge. To assess the cation binding efficiencies of such crown ether tertiary alcohols, picrate extractions have been conducted with 16-crown-5 compounds and closely related 15-crown-5 derivatives. This study establishes basic complexation data for comparison when the compounds are modified by attachment of pendent side arms.

Results and Discussion

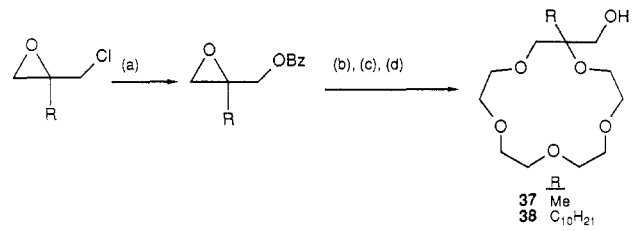
Synthesis. In earlier work, we and others utilized the reaction of 2-(chloromethyl)oxirane with glycolate and bisphenolate dianions to prepare crown ether secondary alcohols.[8] We have now discovered that this ring-closure method may be extended to the synthesis of crown ether tertiary alcohols when 2-substituted 2-(chloromethyl)oxiranes 1–5 are utilized.



R	
1	Me
2	Ph
3	n-$C_{10}H_{21}$
4	n-$C_{14}H_{29}$
5	p-($C_{10}H_{21}$)C_6H_4

The requisite 2-substituted 2-(chloromethyl)oxiranes **1–5** were prepared by two synthetic approaches. Several methods for the synthesis of 2-methyl-2-(chloromethyl)-oxirane (**1**) are reported in the literature.[9] The most convenient bench scale procedure employed an aqueous solution of KBr–Br_2 to quantitatively convert methylallyl chloride to 3-bromo-1-chloro-2-methyl-2-propanol, which upon azeotropic distillation from $Ca(OH)_2$ gave **1** in an 85% yield.[10] With a method developed by Johnson,[11] 2-phenyl-2-(chloromethyl)oxirane (**2**) was prepared by the reaction of PhMgBr with 1,3-dichloro-2-propanone at −60 °C to give 1,3-dichloro-2-phenyl-2-propanol in an 77% yield, which upon treatment with NaOH produced **2** in an 85% yield.

Scheme I[a]



R	
37	Me
38	$C_{10}H_{21}$

[a] Key: (a) BzOH, 50% NaOH, Bu_4NBr, C_6H_6; (b) $HO(CH_2CH_2O)_3H$, NaH, THF; (c) TsCl, NaOH, dioxane; (d) H_2, 10% Pd/C, PTSA, EtOH.

New substituted 2-(chloromethyl)oxiranes **3–5** were prepared by reaction of the appropriate alkyl- or arylmagnesium bromide with 1,3-dichloro-2-propanone at −60 °C to give the dichlorohydrins in 61–70% yields, which were converted to the epoxides **3–5** in 79–98% yields by NaOH. Attempts to synthesize 2-*n*-hexadecyl-, 2-*sec*-butyl-, and 2-*tert*-butyl-2-(chloromethyl)oxiranes by analogous procedures were unsuccessful. Product analysis by GLC showed that instead of carbonyl addition, reduction and enolization predominated. Alkyllithium reagents are often used to increase the degree of carbonyl addition.[12] From the addition of *t*-BuLi to 1,3-dichloro-2-propanone at −60 °C only a 1–2% yield of the desired addition product was obtained. Steric factors are undoubtedly responsible for the difficulty of carbonyl addition.

The synthesis of 2-[*p*-(*n*-decyl)phenyl]-2-(chloromethyl)oxirane (**5**) required the preparation of 1-bromo-4-*n*-decylbenzene. This was accomplished by the conversion of *p*-(*n*-decyl)aniline to its diazonium tetrafluoroborate salt,[13] followed by a PTC reaction[14] with $BrCCl_3$ and KOAc in THF in the presence of 18-crown-6.

Dianions from glycols **6–9** were cyclized with 2-substituted 2-(chloromethyl)oxiranes **1–5** in THF to form crown ether tertiary alcohols **14–26** with ring sizes of 13-crown-4, 14-crown-4, 16-crown-5, and 19-crown-6. The glycolates were generated from metal hydrides, and a metal ion template effect was utilized to facilitate cyclization. Thus, a 1:1 mixture of LiH and NaH was found to produce the highest yields of 13-crown-4 and 14-crown-4 compounds; whereas NaH and KH were used to prepare the 16-crown-5 and 19-crown-6 derivatives, respectively. In general, the yields of crown ether tertiary alcohols were higher in cyclizations with 2-*n*-decyl-2-(chloromethyl)oxirane and 2-*n*-tetradecyl-2-(chloromethyl)oxirane (48–74%) than with 2-phenyl-2-(chloromethyl)oxirane and 2-[*p*-(*n*-decyl)-phenyl]-2-(chloromethyl)oxirane (14–63%) or 2-methyl-2-(chloromethyl)oxirane (26–62%). The highest cyclization yields were obtained for formation of 16-crown-5 rings. Spectra and capillary GLC retention times for samples of **18** made by this method and the procedure reported by Tomoi and co-workers[6] were identical. The 13- and 14-crown-4 compounds formed strong solvates with CH_2Cl_2. Mass spectral analysis of such solvates demonstrated that the chlorocarbon was freed only upon heating at 200 °C under a vacuum of 10^{-5} torr. In agreement, elemental analysis of these compounds shows small amounts of CH_2Cl_2 even after heating at 150 °C (0.1 torr) for 24 h.

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(13) Procedure taken from: *Org. React. (N.Y.)* **1949**, *5*, 198–206.
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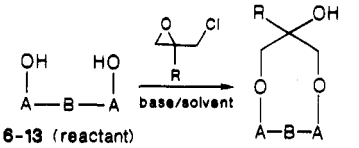
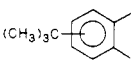
Table I. Preparation of Substituted Hydroxy Crown Ethers



compd	A	B	base/solvent	compd	R	yield, %
6	CH_2CH_2	OCH_2CH_2O	LiH-NaH/THF	14	CH_3	26
6	CH_2CH_2	OCH_2CH_2O	LiH-NaH/THF	15	n-$C_{10}H_{21}$	48
6	CH_2CH_2	OCH_2CH_2O	LiH-NaH/THF	16	Ph	14
7	CH_2CH_2	$OCH_2CH_2CH_2O$	LiH-NaH/THF	17	n-$C_{14}H_{29}$	52
8	CH_2CH_2	$O(CH_2CH_2O)_2$	NaH/THF	18	CH_3	67
8	CH_2CH_2	$O(CH_2CH_2O)_2$	NaH/THF	19	n-$C_{10}H_{21}$	74
8	CH_2CH_2	$O(CH_2CH_2O)_2$	NaH/THF	20	n-$C_{14}H_{29}$	71
8	CH_2CH_2	$O(CH_2CH_2O)_2$	NaH/THF	21	Ph	56
8	CH_2CH_2	$O(CH_2CH_2O)_2$	NaH/THF	22	p-(n-$C_{10}H_{21}$)C_6H_4	63
9	CH_2CH_2	$O(CH_2CH_2O)_3$	KH/THF	23	CH_3	37
9	CH_2CH_2	$O(CH_2CH_2O)_3$	KH/THF	24	n-$C_{10}H_{21}$	51
9	CH_2CH_2	$O(CH_2CH_2O)_3$	KH/THF	25	n-$C_{14}H_{29}$	55
9	CH_2CH_2	$O(CH_2CH_2O)_3$	KH/THF	26	Ph	31
10	o-C_6H_4	$OCH_2CH_2CH_2O$	LiOH/H_2O	27	CH_3	52
10	o-C_6H_4	$OCH_2CH_2CH_2O$	LiOH/H_2O	28	Ph	52
11	o-C_6H_4	$O(CH_2CH_2O)_2$	NaOH/H_2O	29	CH_3	63
11	o-C_6H_4	$O(CH_2CH_2O)_2$	NaOH/H_2O	30	Ph	77
12	o-C_6H_4	$O(CH_2CH_2O)_3$	KOH/H_2O	31	CH_3	38
12	o-C_6H_4	$O(CH_2CH_2O)_3$	KOH/H_2O	32	Ph	79
10	o-C_6H_4	$OCH_2CH_2CH_2O$	LiH-NaH/THF-DMF	33	n-$C_{10}H_{21}$	45
11	o-C_6H_4	$O(CH_2CH_2O)_2$	NaH/THF-DMF	34	n-$C_{10}H_{21}$	65
12	o-C_6H_4	$O(CH_2CH_2O)_3$	KH/THF/DMF	35	n-$C_{10}H_{21}$	50
13		$O(CH_2CH_2O)_2$	NaH/THF	36	CH_3	64

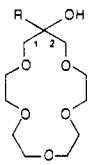
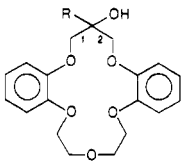
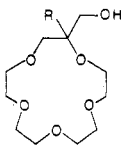
Facile syntheses of dibenzo crown ether tertiary alcohols **27–32** were accomplished in 31–79% yields by slow addition of 2-phenyl- and 2-methyl-2-(chloromethyl)oxirane to aqueous solutions of bisphenols **10–12** and the appropriate alkali-metal hydroxides. Due to the high lipophilicity of 2-*n*-decyl-2-(chloromethyl)oxirane, ring closures with bisphenols in aqueous base were unsuccessful. However cyclizations to form **33–35** in 45–65% yields were effected in THF–DMF when appropriate metal hydrides were utilized to generate the bisphenolates. Synthesis of the highly lipophilic crown ether tertiary alcohol, *sym*-hydroxymethylbis[4(5)-*tert*-butylbenzo]-16-crown-5 (**36**) in 64% yield resulted from the reaction of bisphenol **13** with NaH in THF followed by addition of 2-methyl-2-(chloromethyl)oxirane.

For comparison of cation complexing properties, the 2-alkyl-2-(hydroxymethyl)-15-crown-5 compounds **37** and **38** were prepared from the corresponding 2-alkyl-2-(chloromethyl)oxiranes **1** and **3** by the route shown in Scheme I. Thus, **1** and **3** were converted into 1-(benzyloxy)-2-alkyl-2,3-epoxypropanes by the reaction with BzOH and 50% aqueous NaOH under PTC conditions. Subsequent reaction with the sodium alkoxide of tetraethylene glycol in THF gave 2-alkyl-2-[(benzyloxy)methyl]pentaethylene glycols, which were cyclized by the Okahara procedure[15] to provide the 2-alkyl-2-[(benzyloxy)methyl]-15-crown-5 compounds. Debenzylation of the latter produced **37** and **38**.

The structures and purities of all new compounds were verified by IR, ^1H NMR, and mass spectra and by GLC and elemental analyses.

Extraction Studies. Binding abilities of the substituted 16-crown-5 and 15-crown-5 compounds for Na^+ and K^+ were assessed by solvent extraction of aqueous solutions of sodium and potassium picrates with deuteriochloroform solutions of the crown ethers at room temperature. Extraction constants, K_{ex}, and association constants, K_a, were evaluated in the customary manner.[16,17] The data for substituted hydroxy-16-crown-5 ethers, hydroxydibenzo-16-crown-5 ethers, and hydroxymethyl-15-crown-5 ethers are presented in Table II and show that changes occurs in both Na^+ and K^+ binding upon substituent variation.

Table II. Extraction Constants (K_{ex}) and Association Constants (K_a) for Cation Complexation with 16-Crown-5 and 15-Crown-5 Compounds at 22–23 °C

			K_{ex}		K_a	
	compd	R	Na^+	K^+	Na^+	K^+
		H	2.40		5.16	
	18	CH_3	3.35	3.30	6.09	5.89
	19	n-$C_{10}H_{21}$	3.56	2.90	6.30	5.49
	21	Ph	3.31	2.78	6.07	5.36
	22	p-($C_{10}H_{21}$)-C_6H_4	2.60	2.69	5.36	5.28
		H	2.51	2.42	5.27	5.01
	29	CH_3	3.08	2.22	5.84	4.81
	34	n-$C_{10}H_{21}$	3.03	2.41	5.78	5.01
	32	Ph	2.34	1.64	5.08	4.24
		H	3.21		5.96	
	37	CH_3	4.19	3.08	6.95	5.67
	38	n-$C_{10}H_{21}$	3.33	2.76	6.08	5.34

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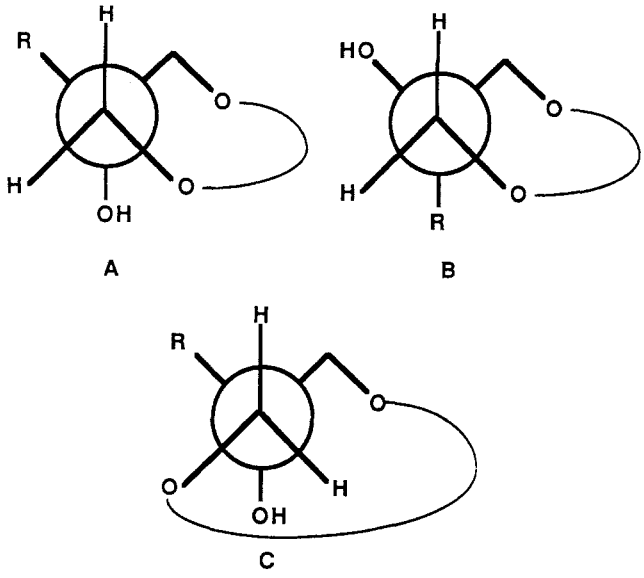

Figure 1. Crown ether conformers.

For the (ethyleneoxy)-16-crown-5 compounds, alkyl substitution increases Na^+ association and extraction constants by 1 order of magnitude. Phenyl group substitution also causes substantial enhancement in Na^+ association and extraction constants, but the increases for the *p*-(*n*-decyl)phenyl substituent are much smaller. Association and extraction constants for K^+ decrease uniformly with increasing size and lipophilicity of the substituent.

These results may be rationalized by the conformational effect that a substituent will have on host preorganization. Since the formation of a complexing cavity requires conformational reorganization and desolvation of binding sites, the preorganization of the host geometry to fit the guest geometry facilitates complexation.[18] The rotational profile about bond 1 (Table II) of the *sym*-hydroxy-16-crown-5 compounds may be represented by the staggered conformers **A**–**C** in Figure 1. Changes of the substituent group R will vary the total steric and solvation energies of the six possible conformations about bonds 1 and 2, which will influence the minimal potential energy conformation of the host. In **A**–**C**, a gauche interaction is destabilizing, but less so if the gauche groups are OH and OR for which hydrogen bonding is possible.

For unsubstituted *sym*-hydroxy-16-crown-5 (R = H), conformer **A** has two gauche interactions and conformers **B** and **C** have one each. However, for conformer **C**, the gauche interaction permits hydrogen bonding. Thus, conformer **C** in which the methylene group is directed into the potential cavity is predicted to be the most stable.

For the substituted *sym*-(alkyl or arylhydroxy-16-crown-5 compounds (R = alkyl, aryl), each of the conformers has two gauche interactions. However, for conformers **A** and **C**, one set of gauche interactions is of the hydrogen-bonding type. If the substituent R has larger spatial demands than a methylene group, then conformer **A** is predicted to be the most stable. Thus, the change for preferred conformation **C** to **A** upon introduction of the substituent explains the enhanced binding of Na^+ by the crown ether tertiary alcohols when compared with a crown ether secondary alcohol.

For the *sym*-hydroxydibenzo-16-crown-5 compounds, introduction of an alkyl group again enhances cation complexation but to a lesser extent than found for the previous series due to the rigidifying benzo groups. However, when the sterically demanding phenyl substituent is present, cation binding is inferior to that of the corresponding crown ether secondary alcohol. Insight into this apparent anomaly is provided by the ^1H NMR spectra for *sym*-hydroxyphenyldibenzo-crown compounds **28**, **30**, and **32** in the region δ 3.0–5.0 (Figure 2). For each compound, a downfield singlet for two hydrogens is separated from the remainder of the ring methylene hydrogen signals. This suggests nonequivalence of the two methylene groups on the three-carbon bridge and is consistent with an **A**–**C** conformation (Figure 3) in which one methylene group points into the polyether cavity. Shielding by the phenyl group substituent causes one pair of the methylene hydrogens to resonate at lower field than the other. The anomalous resonances disappear upon metal ion complexation by **28**, **30**, and **32**.

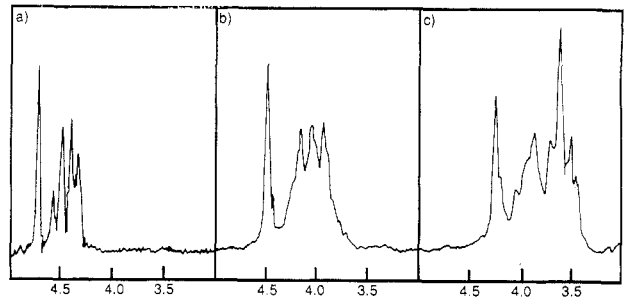

Figure 2. ^1H NMR spectra (60 MHz) for dibenzo crown ether tertiary alcohols (a) **28**, (b) **30**, and (c) **32**.

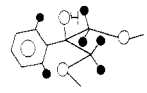

Figure 3. **A**–**C** conformation for phenyl-substituted dibenzo crown ether alcohols.

Crown ether tertiary alcohols **37** and **38** are structural isomers of **18** and **19**. For the former, the ring size is 15-crown-5; whereas the latter are 16-crown-5 derivatives. It is interesting to note that only for the complexation of Na^+ by **37** (compared with **18**) does the binding of the more symmetric 15-crown-5 compound surpass that of the structurally isomeric 16-crown-5 derivative. Thus, for crown ether tertiary alcohols, the incorporation of a three-carbon bridge is not detrimental to complexation efficiency.

Experimental Section

IR spectra were obtained on neat samples (unless specified otherwise) with a Nicolet MX-S infrared spectrophotometer and are recorded in reciprocal centimeters. ^1H NMR spectra were recorded with Varian EM 360A or EM 360 spectrometers in deuteriochloroform, and chemical shifts are reported in parts per million (δ) downfield from Me_4Si. Visible spectra were recorded with a Perkin-Elmer Lambda 5 UV–vis spectrophotometer. GLC analysis was performed with a Varian Model 3700 flame ionization gas chromatograph on a SE-30 capillary column, and purity was determined on the basis of peak area. Mass spectra were obtained with a Hewlett-Packard 5995B GC/MS. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. Unless specified otherwise reagent-grade reactants and solvents were obtained from chemical suppliers and used as received. THF was purified by distillation from $LiAlH_4$ under nitrogen, and DMF was freshly distilled and placed over molecular sieves. The reagents 1,9-dihydroxy-3,7-dioxanonane[19] (**9**), bisphenols **10**–**12**,[8]

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sym-bis[2-[4(5)-*tert*-butyl-2-hydroxyphenoxy]ethyl] ether[20] (**13**), *sym*-hydroxy-16-crown-5,[8] *sym*-hydroxydibenzo-16-crown-5,[8] and hydroxymethyl-15-crown-5[21] were prepared by literature methods.

2-Methyl-2-(chloromethyl)oxirane (1). A solution of Br_2 (320 g, 109 mL, 2.0 mol) and KBr (140 g, 1.25 mol) in 300 mL of water was added dropwise over 4 h to a cooled mixture of methylallyl chloride (190 g, 202 mL, 2.1 mol) in 1 L of water. The reaction mixture was stirred at 20 °C for 12 h. The organic layer was separated, and the aqueous layer was extracted with 500 mL of Et_2O. The combined organic layers were dried over $MgSO_4$ and distilled twice under vacuum to afford 391 g (98%) of 1-bromo-3-chloro-2-methyl-2-propanol as a colorless liquid: bp 84–86 °C (20 mm); IR (film) 3470 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.00 (s, 4 H), 1.90 (s, 3 H). Into a three-necked round-bottom flask equipped with a distillation condenser and charged with $Ca(OH)_2$ (90.8 g) in 360 mL of water was added 1-bromo-3-chloro-2-methyl-2-propanol (75.0 g, 0.4 mol) over 1 h via a pressure-equilibrating addition funnel. The azeotropic mixture of epoxide and water [bp 55–57 °C (135 mm)], which distilled as the addition proceeded, was added to 50 mL of brine and extracted with Et_2O (2 × 100 mL). The combined organic layers were dried ($MgSO_4$) and distilled to afford 29.7 g (82%) of 2-methyl-2-(chloromethyl)oxirane as a colorless liquid: bp 122–123 °C (lit.[10] bp 122 °C); IR (film) 1250 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.65 (s, 2 H), 2.81 (s, 2 H), 1.40 (s, 3 H).

General Procedure for the Preparation of 2-Substituted 2-(Chloromethyl)oxiranes 2–5. The appropriate Grignard reagent was produced by dropwise addition of the alkyl or aryl halide (0.175 mol) in 25 mL of anhydrous Et_2O to a mixture of magnesium turnings (2.4 g, 0.175 mol) and a few iodine crystals in 50 mL of anhydrous Et_2O under nitrogen at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred until all of the magnesium was consumed. The Grignard reagent was added over 1.5 h to a solution of 1,3-dichloro-2-propanone (22.6 g, 0.175 mol) in 100 mL of anhydrous Et_2O under nitrogen at −60 °C. The reaction mixture was stirred for 0.5 h at −60 °C, after which a solution of HOAc (11.0 g) in 16 mL of anhydrous Et_2O was added and the mixture was warmed to room temperature. Water (100 mL) and 100 mL of Et_2O were added, and the Et_2O layer was separated, dried ($MgSO_4$), and evaporated in vacuo. The residue was distilled under vacuum. The resultant 2-substituted 1,3-dichloro-2-propanol (0.10 mol) in 100 mL of MeOH and 25 mL of CH_2Cl_2 was added dropwise to 40.0 mL of 1 N NaOH, and the mixture was stirred under nitrogen for 24 h. Water (100 mL) was added, and the organic solvent was removed in vacuo. Extraction with CH_2Cl_2 (100 mL), drying ($MgSO_4$), evaporation in vacuo, and vacuum distillation gave a clear oil of sufficient purity for synthetic use. Analytical samples were purified by chromatography on deactivated silica gel with petroleum ether (bp 30–60 °C) as eluent.

1,3-Dichloro-2-phenyl-2-propanol was realized as a colorless oil (72%): bp 80–85 °C (0.1 mm); IR (film) 3537, 3427 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.39 (s, 5 H), 3.87 (s, 4 H), 3.10 (br s, 1 H). Ring closure gave **2** (98%) as a colorless oil: bp 109–110 °C (6 mm) [lit.[11] bp 109–109.5 °C (6.0 mm)]; IR (film) 3100 (Ar H), 1249 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.42 (s, 5 H), 3.07 (q AB, J = 6.3 Hz, 2 H), 3.07 (q AB, J = 8.7 Hz, 2 H); capillary GLC, purity 99.5%.

2-*n*-Decyl-1,3-dichloro-2-propanol was obtained as a colorless oil: 71%; bp 115–116 °C (0.9 mm); IR (film) 3423 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.31 (s, 4 H), 2.24 (br s, 1 H), 1.5–0.8 (m, 21 H). Ring closure gave **3** (98%) as a colorless oil: bp 127–128 °C (1.5 mm); IR (film) 1250 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.51 (s, 2 H), 2.54 (s, 2 H), 1.5–0.8 (m, 21 H); capillary GLC, purity 99.2%. Anal. Calcd for $C_{13}H_{25}OCl$: C, 67.07; H, 10.82. Found: C, 67.48; H, 10.94.

1,3-Dichloro-2-*n*-tetradecyl-2-propanol was produced as a colorless oil: 61%; bp 130–132 °C (0.8 mm); IR (film) 3420 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.81 (s, 4 H), 3.07 (br s, 1 H), 1.5–0.8 (m, 29 H). Ring closure gave **4** (97%) as a colorless oil: bp 142–145 °C (1.4 mm); IR (film) 1250 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.71 (s, 2 H), 2.84 (s, 2 H), 1.5–0.8 (m, 29 H); capillary GLC, purity 99.7%. Anal. Calcd for $C_{17}H_{33}OCl$: C, 69.86; H, 11.38. Found: C, 69.57; H, 10.98.

2-[*p*-(*n*-Decyl)phenyl]-1,3-dichloro-2-propanol was synthesized as a colorless oil: 66%; bp 125–126 °C (0.1 mm); IR (film) 3540 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.2–7.8 (m, 4 H), 3.95 (s, 4 H), 2.15 (t, 2 H), 1.8–0.8 (m, 19 H). Ring closure gave **5** (79%) as a colorless oil: bp 147–148 °C (2.0 mm); IR (film) 1250 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.1–7.7 (m, 4 H), 3.89 (s, 4 H), 2.95 (m, 2 H), 2.17 (t, 2 H), 1.8–0.8 (m, 19 H); capillary GLC, purity 99.0%. Anal. Calcd for $C_{19}H_{29}OCl$: C, 73.88; H, 9.46. Found: C, 73.44; H, 9.41.

1-Bromo-4-*n*-decylbenzene. To a mixture of 100 mL of 3 N HCl and 4-*n*-decylaniline (25.0 g, 0.10 mol) at 0 °C was added a solution of sodium nitrite (7.0 g, 0.10 mol) in 15 mL of water dropwise, while the temperature was maintained at 0–5 °C. An ice-cold 48% solution of fluoroboric acid (55 mL) was added, followed by stirring for 20 min and filtering. The product was washed with 15 mL of ice-cold 48% fluoroboric acid, 50 mL of 95% EtOH, and 25 mL of Et_2O to give 25.3 g (71%) of 4-*n*-decylbenzenediazonium tetrafluoroborate as a white solid: mp 83–86 °C; IR (KBr) 2304 (N≡N) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.21 (s, 4 H), 2.20 (t, 2 H), 1.8–0.8 (m, 19 H).

To a 33% solution of bromotrichloromethane (440 g, 2.1 mol) in 440 mL of dry THF was added 4-*n*-decylbenzenediazonium tetrafluoroborate (25.0 g, 0.075 mol) along with KOAc (15.2 g, 0.154 mol) and 18-crown-6 (1.0 g, 0.0038 mol), and the mixture was stirred at room temperature for 3 h. After filtration the solution was dried ($MgSO_4$), the solvent was removed in vacuo, and the crude product was purified by chromatography on silica gel with CH_2Cl_2 as eluent to give 14.7 g (61%) of 1-bromo-4-*n*-decylbenzene as an oil: ^1H NMR ($CDCl_3$) δ 6.3–6.7 (q AB, 4 H), 2.20 (t, 2 H), 1.45–0.8 (m, 19 H).

General Procedure for the Preparation of Crown Ether Tertiary Alcohols 14–26. The appropriate metal hydride (0.05 mol) was suspended in 100 mL of dry THF under nitrogen. A solution of glycol **6–9** (0.02 mol) in 25 mL of dry THF was added dropwise, followed by stirring at 40 °C for 0.5 h, addition of 2-substituted 2-(chloromethyl)oxirane **1–5** (0.02 mol), gradually heating to reflux over 4 h, and refluxing for 20 h. The reaction mixture was cooled to 0 °C, neutralized with 1:1 concentrated HCl–EtOH, and filtered, and the solvents were evaporated in vacuo. The resultant oil was dissolved in 150 mL of water, and the aqueous mixture was extracted with CH_2Cl_2 (3 × 100 mL). The combined Ch_2Cl_2 extracts were washed with water (3 × 100 mL), dried ($MgSO_4$), and evaporated in vacuo to give the crude product, which was purified by chromatography on two alumina columns with CH_2Cl_2–MeOH (25:1) as eluent to give the products as yellow oils.

***sym*-Hydroxymethyl-13-crown-4 (14)**: oil; 26%; IR (film) 3406 (OH), 1111 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.2 (br s, 1 H), 3.56 (s, 16 H), 1.05 (s, 3 H); capillary GLC, purity 99.0%; MS, 220.3 (M^+). Anal. Calcd for $C_{10}H_{20}O_5 \cdot 0.6CH_2Cl_2$: C, 46.86; H, 7.87. Found: C, 46.77; H, 8.01.

***sym*-Hydroxy-*n*-decyl-13-crown-4 (15)**: oil; 48%; IR (film) 3445 (OH), 1120 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.60 (s, 16 H), 1.35–0.8 (m, 21 H); MS 346.5 (M^+). Anal. Calcd for $C_{19}H_{38}O_5 \cdot H_2O$: C, 62.60; H, 10.80. Found: C, 62.36; H, 11.06.

***sym*-Hydroxyphenyl-13-crown-4 (16)**: oil; 14%; IR (film) 3400 (OH), 1110 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.3 (s, 5 H), 3.41–4.24 (m, 16 H), 2.8 (br s, 1 H); capillary GLC, purity 99.7%; MS, 282.3 (M^+). Anal. Calcd for $C_{15}H_{22}O_5 \cdot 0.15CH_2Cl_2$: C, 61.66; H, 7.61. Found: C, 61.44; H, 7.88.

***sym*-Hydroxy-*n*-tetradecyl-14-crown-4 (17)**: oil; 52.0%; IR (film) 3421 (OH), 1120 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.63 (s, 16 H), 2.35 (m, 2 H), 1.3–0.8 (m, 29 H); MS, 416.4 (M^+). Anal. Calcd for $C_{24}H_{48}O_5 \cdot 0.25CH_2Cl_2$: C, 68.57 H, 11.16. Found: C, 68.71; H, 10.84.

***sym*-Hydroxymethyl-16-crown-5 (18)**: oil; 67%; IR (film) 3400 (OH), 1110 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.2 (br s, 1 H), 3.31–3.62 (m, 20 H), 1.12 (s, 3 H); capillary GLC, purity 99.9%; MS, 264.3 (M^+).

***sym*-Hydroxy-*n*-decyl-16-crown-5 (19)**: oil; 74%; IR (film) 3445 (OH), 1120 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.60 (s, 20 H), 1.35–0.8 (m, 21 H); MS, 390.5 (M^+). Anal. Calcd for $C_{21}H_{42}O_6$: C, 64.58; H, 10.84. Found: C, 64.37; H, 10.62.

***sym*-Hydroxy-*n*-tetradecyl-16-crown-5 (20)**: oil; 71%; IR (film) 3421 (OH), 1120 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.82 (br

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s, 1 H), 3.63 (s, 20 H), 1.4–0.8 (m, 29 H); MS, 446.4 (M^+). Anal. Calcd for $C_{25}H_{50}O_6$: C, 67.23 H, 11.28. Found: C, 67.50; H, 11.10.

***sym*-Hydroxyphenyl-16-crown-5 (21)**: oil, 59%; IR (film) 3440 (OH), 1110 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.12–7.56 (m, 5 H), 3.57 (s, 20 H), 3.2 (br s, 1 H); capillary GLC, purity 99.6%; MS, 326.3 (M^+). Anal. Calcd for $C_{17}H_{26}O_6$: C, 62.56; H, 8.03. Found: C, 62.22; H, 7.61.

***sym*-Hydroxy[*p*-(*n*-decyl)phenyl]-16-crown-5 (22)**: oil; 63%; IR (film) 3450 (OH), 1110 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.21 (m, 4 H), 4.00 (br s, 1 H), 3.62 (s, 20 H), 2.14 (t, 3 H), 1.4–0.8 (m, 19 H). Anal. Calcd for $C_{27}H_{46}O_6$: C, 70.40; H, 10.07. Found: C, 70.37; H, 10.41.

***sym*-Hydroxymethyl-19-crown-6 (23)**: oil; 67%; IR (film) 3400 (OH), 1110 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.2 (br s, 1 H), 3.41–3.62 (m, 24 H), 1.20 (s, 3 H); capillary GLC, purity 99.8%. Anal. Calcd for $C_{21}H_{42}O_6$: C, 54.53; H, 9.15. Found: C, 54.96; H, 9.21.

***sym*-Hydroxy-*n*-decyl-19-crown-6 (24)**: oil; 51%; IR (film) 3443 (OH), 1120 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.60 (s, 24 H), 1.4–0.8 (m, 21 H); MS, 434.5 (M^+). Anal. Calcd for $C_{23}H_{46}O_7$: C, 64.25; H, 10.67. Found: C, 63.94; H, 10.92.

***sym*-Hydroxy-*n*-tetradecyl-19-crown-6 (25)**: oil; 55%; IR (film) 3400 (OH), 1120 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.91 (br s, 1 H), 3.60 (s, 24 H), 1.35–0.8 (m, 29 H); MS, 490.4 (M^+). Anal. Calcd for $C_{27}H_{54}O_7 \cdot 2.0H_2O$: C, 61.56; H, 11.10. Found: C, 61.23; H, 10.82.

***sym*-Hydroxyphenyl-19-crown-6 (26)**: oil; 31%; IR (film) 3400 (OH), 1110 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.16–7.60 (m, 5 H), 4.2 (br s, 1 H), 3.57 (s, 24 H); MS, 370.4 (M^+). Anal. Calcd for $C_{19}H_{30}O_7 \cdot 0.3CH_2Cl_2$: C, 58.55; H, 7.79. Found: C, 58.58; H, 7.73.

General Procedure for the Preparation of Dibenzo Crown Ether Tertiary Alcohols 27–32. A mixture of metal hydroxide (1.2 mol) and bisphenol **10–12** (0.6 mol) in 1400 mL of water was heated at 90 °C under nitrogen until a solution formed. The solution was cooled to 50 °C and 2-substituted 2-(chloromethyl)oxirane **1** or **2** (0.6 mol) was added over 3 h followed by additional stirring for 10 h. Additional metal hydroxide (0.6 mol) was added in one portion, the 2-substituted 2-(chloromethyl)-oxirane (0.3 mol) added over 3 h, followed by stirring for 10 h, and the sequence was repeated. The product was filtered and purified by chromatography on a short silica gel column with CH_2Cl_2 as eluent to give a white solid.

***sym*-Hydroxymethyldibenzo-14-crown-4 (27)**: mp 142.5–143 °C; 52%; IR (KBr) 3489 (OH), 1246, 1120 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.87 (s, 8 H), 4.34–3.80 (m, 8 H), 3.67 (br s, 1 H), 2.47 (m, 2 H), 1.35 (s, 3 H). Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 68.79; H, 6.70.

***sym*-Hydroxyphenyldibenzo-14-crown-4 (28)**: mp 72–74 °C; 52%; IR (KBr) 3440 (OH), 1250, 1132 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.00–7.55 (m, 5 H), 7.15 (s, 8 H), 4.77 (s, 2 H), 4.65–4.34 (m, 6 H), 2.51 (m, 2 H); MS, 392.4 (M^+). Anal. Calcd for $C_{24}H_{24}O_5 \cdot 0.75H_2O$: C, 71.01; H, 6.37. Found: C, 71.23; H, 6.33.

***sym*-Hydroxymethyldibenzo-16-crown-5 (29)**: mp 109–110 °C; 63%; IR (KBr) 3400 (OH), 1240, 1120 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.95 (s, 8 H), 4.15–3.65 (m, 12 H), 1.41 (s, 3 H). Anal. Calcd for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.44; H, 6.75.

***sym*-Hydroxyphenyldibenzo-16-crown-5 (30)**: mp 37.5–40 °C; 77%; IR (KBr) 3400 (OH), 1250, 1120 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.00–7.25 (m, 5 H), 6.95 (s, 8 H), 4.50 (s, 2 H), 4.32–3.65 (m, 10 H); MS, 422.3 (M^+). Anal. Calcd for $C_{25}H_{26}O_6$: C, 71.08; H, 6.20. Found: C, 70.09; H, 6.21.

***sym*-Hydroxymethyldibenzo-19-crown-6 (31)**: mp 52.5–53.5 °C; 38%; IR (KBr) 3335 (OH), 1251, 1125 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.93 (s, 8 H), 4.21–3.55 (m, 16 H), 3.37 (br s, 1 H), 1.40 (s, 3 H). Anal. Calcd for $C_{22}H_{28}O_7 \cdot H_2O$: C, 62.55; H, 7.15. Found: C, 62.63; H, 7.04.

***sym*-Hydroxyphenyldibenzo-19-crown-6 (32)**: mp 25–28 °C; 79%; IR (KBr) 3400 (OH), 1250, 1132 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.84–7.12 (m, 5 H), 6.95 (s, 8 H), 4.42 (s, 2 H), 4.30–3.47 (m, 14 H); MS, 466.4 (M^+). Anal. Calcd for $C_{27}H_{30}O_7$: C, 69.51; H, 6.48. Found: C, 69.28; H, 6.43.

General Procedure for the Preparation of Dibenzo Crown Ether Tertiary Alcohols 33–35. To a suspension of metal hydride (16 mmol) in 100 mL of dry THF/DMF (1:1) was added bisphenol **10–12** (8.0 mmol), and the mixture was stirred at room temperature under nitrogen for 0.5 h. The resultant solution was heated to 50 °C and 2-*n*-decylepichlorohydrin (**3**; 8.0 mmol) was added during 3 h, followed by refluxing for 5 h. Subsequent addition of the metal hydride (8.0 mmol) in one portion and **3** (4.0 mmol) during 3 h, followed by refluxing for 5 h, was repeated twice. The reaction mixture was refluxed for 20 h, cooled to 0 °C, neutralized with a solution of 1:1 concentrated HCl/EtOH, and filtered. The solvents were evaporated in vacuo, and the resultant oil was dissolved in CH_2Cl_2 (50 mL) and washed with water (50 mL). The CH_2Cl_2 layer was dried ($MgSO_4$) and evaporated in vacuo to give the crude product, which was purified by chromatography on two silica gel columns with CH_2Cl_2 as eluent.

***sym*-Hydroxy-*n*-decyldibenzo-14-crown-4 (33)**: mp 71.5–72 °C; 45%; IR (KBr) 3460 (OH), 1250, 1120 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.90 (s, 8 H), 4.54–3.80 (m, 8 H), 3.45 (br s, 1 H), 2.45 (m, 2 H), 1.5–0.8 (m, 21 H); MS, 456.3 (M^+). Anal. Calcd for $C_{28}H_{40}O_5 \cdot H_2O$: C, 70.87; H, 8.88. Found: C, 70.53; H, 8.38.

***sym*-Hydroxy-*n*-decyldibenzo-16-crown-5 (34)**: mp 82–83 °C; 78%; IR (KBr) 3450 (OH), 1240, 1120 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.95 (s, 8 H), 4.37–3.72 (m, 12 H), 3.2 (s, 1 H), 1.50–0.8 (s, 21 H); MS, 486.5 (M^+). Anal. Calcd for $C_{29}H_{42}O_6 \cdot 0.5H_2O$: C, 70.28; H, 8.73. Found: C, 70.54; H, 8.29.

***sym*-Hydroxy-*n*-decyldibenzo-19-crown-6 (35)**: colorless oil; 50%; IR (KBr) 3431 (OH), 1253, 1120 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.95 (s, 8 H), 4.51–3.50 (m, 16 H), 3.30 (br s, 1 H), 1.5–0.8 (s, 21 H); MS, 530.4 (M^+). Anal. Calcd for $C_{31}H_{46}O_7 \cdot 0.5H_2O$: C, 69.00; H, 8.78. Found: C, 69.22; H, 9.03.

Preparation of 36. Under nitrogen, 1.0 g (25.0 mmol) of NaH (60% dispersion in mineral oil) was washed with dry pentane to remove the protecting oil and was suspended in 100 mL of dry THF. To the stirred mixture was added **13** (5.0 g, 12.5 mmol), and the mixture was stirred for 1 h. A solution of **1** (1.37 g, 12.5 mmol) in 25 mL of dry THF was added dropwise followed by stirring at 40 °C for 2 h and refluxing for 20 h. Water (150 mL) was added to the cooled reaction mixture, the THF was removed in vacuo, and the resultant basic mixture was extracted with CH_2Cl_2 (3 × 100 mL). The combined CH_2Cl_2 extracts were washed with H_2O, dried ($MgSO_4$), and evaporated in vacuo to give the crude product, which was purified by chromatography on silica gel with CH_2Cl_2 and Et_2O as eluents to give 3.7 g (64%) of **36** as a yellow oil: IR (KBr) 3383 (OH), 1253, 1120 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.21–6.82 (s, 6 H), 4.78 (br s, 1 H), 4.23–3.52 (m, 12 H), 1.4–0.8 (m, 21 H); MS, 472.4 (M^+). Anal. Calcd for $C_{28}H_{40}O_6$: C, 71.16; H, 8.53. Found: C, 70.91; H, 8.53.

Preparation of *sym*-Alkyl(hydroxymethyl)-15-crown-5 Compounds 37 and 38. To BzOH (0.04 mol) and *n*-Bu_4NBr (0.004 mol) in 20 mL of C_6H_6 were added **1** (0.04 mol) and 10 mL of 10% aqueous NaOH, and the mixture was heated to 70 °C for 24 h. The organic layer was evaporated in vacuo, and the resultant oil was dissolved in CH_2Cl_2 (50 mL) and washed with H_2O (50 mL). The CH_2Cl_2 extract was dried ($MgSO_4$) and evaporated in vacuo to give a crude product that was purified by chromatography on alumina with CH_2Cl_2 as eluent to give 3-(benzyloxy)-1,2-epoxy-2-methylpropane as an oil: 68%; IR (film) 1255 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.34 (s, 5 H), 4.53 (m, 2 H), 3.46 (q AB, 2 H), 2.56 (q AB, 2 H), 1.38 (s, 3 H). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.09; H, 8.10.

Under nitrogen, 0.76 g (19.0 mmol) of sodium hydride (60% dispersion in mineral oil) was washed with dry pentane to remove the protecting oil and was suspended in 100 mL of dry THF. Tetraethylene glycol (19.0 mmol) in 25 mL of dry THF was added dropwise, followed by stirring for 1.0 h, addition of 3-(benzyloxy)-1,2-epoxy-2-methylpropane (19.0 mmol), and refluxing for 24 h. The reaction mixture was cooled to 0 °C, neutralized with 10% HCl, and filtered. The solvent was evaporated in vacuo, to give a crude product that purified by chromatography on alumina with Et_2O–EtOH (9:1) as eluent to give 2-[(benzyloxy)-methyl]-2-methylpentaethylene glycol (mixture of two isomers) as a colorless oil: 66%; IR (film) 3450 (OH), 1251, 1114 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30 (s, 5 H), 4.55 (s, 2 H), 4.00–3.21 (m, 22 H), 1.18 (s, 3 H); MS, 372.2 (M^+). Anal. Calcd for $C_{19}H_{32}O_7$: C, 61.27; H, 8.66. Found: C, 60.96; H, 8.74.

A solution of the resultant substituted glycol (12.5 mmol) and *p*-TsCl (12.5 mmol) in 50 mL of dry dioxane was added over 6 h to a mixture of powdered NaOH (50.0 mmol) in 150 mL of dry dioxane at 60 °C. The reaction mixture was stirred for 12 h at

60 °C and filtered, and the solvent was evaporated in vacuo, to give the crude product, which was purified by chromatography on alumina with EtOAc as eluent to give 2-[(benzyloxy)-methyl]-2-methyl-15-crown-5 as a colorless oil: 79%; IR (film) 1249, 1114 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30 (s, 5 H), 4.53 (s, 2 H), 4.30–3.26 (m, 20 H), 1.20 (s, 3 H); MS, 354.2 (M^+). Anal. Calcd for $C_{19}H_{32}O_7 \cdot 0.25H_2O$: C, 63.57; H, 8.56. Found: C, 63.65; H, 8.29.

The 2-[(benzyloxy)methyl]-2-methyl-15-crown-5 (2.38 g, 9.0 mmol) and 0.25 g of 10% Pd–C in 100 mL of absolute EtOH were shaken in a Parr hydrogenator under H_2 (40 psi) for 24 h. The reaction mixture was filtered, and the solvent was evaporated in vacuo, to yield 85% of 2-(hydroxymethyl)-2-methyl-15-crown-5 (**37**) as a colorless oil: IR (film) 3296 (OH), 1118 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.70 (s, 20 H), 3.03 (br s, 1 H), 1.13 (s, 3 H); MS, 264.2 (M^+). Anal. Calcd for $C_{12}H_{24}O_6 \cdot 0.25H_2O$: C, 53.61; H, 9.18. Found: C, 53.54; H, 8.90.

The 2-*n*-decyl-2-(hydroxymethyl)-15-crown-5 (**38**) was realized in an analogous fashion from **3** as an colorless oil: IR (film) 3400 (OH), 1110 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.65 (s, 20 H), 3.05 (br s, 1 H), 1.4–0.8 (m, 21 H); MS, 390.4 (M^+). Anal. Calcd for $C_{21}H_{42}O_6 \cdot 0.75H_2O$: C, 62.42; H, 10.85. Found: C, 62.48; H, 10.80.

Picrate Extraction into Deuteriochloroform. Extractions of potassium and sodium picrates into deuteriochloroform by crown ether alcohols were conducted as before.[19] Extraction and association constants were calculated by the literature methods.[16,17]

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Chiral Biphenyl Bis(crown ethers): Synthesis and Resolution

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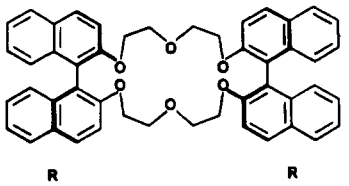
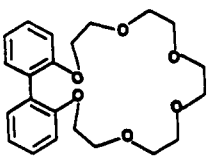
New chiral bis(crown ethers) with a central 2,2′,6,6′-tetraoxybiphenyl unit have been prepared and resolved. Their complexing properties and absolute configuration are discussed.

Crown ethers form complexes not only with simple alkali metal cations but also with ammonium ions and the conjugate acids of primary amines. Much work has been done to refine the selectivity of the ligand to the extent that selection between enantiomers of chiral primary amines is now possible.[1] A ligand that discriminates enantiomers must itself be chiral, a good example[2] being **1**. The binaphthyl moieties are asymmetric due to hindered rotation about the pivot bond and the ligand as a whole is chiral because the binaphthyls have the same absolute configuration.

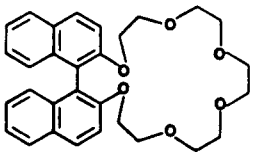


1

Ligands with two complexing sites, such as the bis(crown ethers) are of special interest since the two sites may cooperate. In a suitable bis(crown ether), complexation with a metal ion can induce a conformational change which is transferred to the second crown ether ring and crown ethers with biaryl units are interesting in this respect. Cram and co-workers[3] have reported the preparation of the biphenyl–crown ether **2**, although it was used only as a prototype for the preparation of the binaphthyl–crown ether **3**.

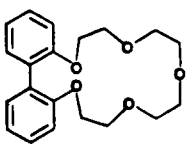


2



3

More recently, the biphenyl–crown ether **4** has been prepared,[4] and Rebek and Wattley[5] have used a bipyridyl system (**5**) to study the effect of coordination of a metal to the nitrogens on the binding ability of the crown ether.



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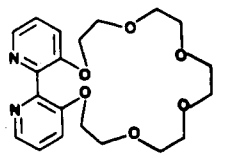

5

All these biphenyl–crown ethers have one C_2 axis of symmetry, i.e., the molecules have two identical sides, and a guest ion thus experiences the same environment regardless of which side it encounters. Introduction of a second C_2 axis, perpendicular to the first one, automatically introduces a third which is perpendicular to the first two,

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