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Synthesis and structure of tribenzo-19-crown-6 lariat ethers

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Multistep preparative routes to a series of three new, proton-ionizable lariat ethers, *sym*-(R)tribenzo-19-crown-6-oxyacetic acids with R = H, C_3H_7, and C_8H_{17} have been developed. The crystal structure of the synthetic intermediate *sym*-(hydroxy)(propyl)-tribenzo-19-crown-6 has been determined. The compound crystallized in the monoclinic space group $P2_1/c$ with a = 8.902(4) Å, b = 10.296(5) Å, c = 27.631(9) Å, β = 97.41° with a volume of 2511.4 Å^3. The calculated density is 1.268 mg/mm^3 with Z = 4. The final R values are R = 7.99% and R_w = 5.17% using 1558 observed reflections [F>3.0 σ(F)].

INTRODUCTION

A wide variety of crown ether (macrocyclic polyether) compounds has been synthesized and employed for alkali and alkaline earth metal cation separations due to their superior binding ability for these metal ions.[1–3] When a side arm bearing one or more potential coordination sites is attached to the crown ether framework, the ligand is termed a lariat ether.[4]

Proton-ionizable lariat ethers are crown ethers which possess a pendent acidic group. Compared with neutral crown and lariat ethers, proton-ionizable lariat ethers have an important advantage for metal ion separation processes in that the transfer of a metal ion into an organic medium does not require concomitant transport of an aqueous phase anion.[5] This factor is immense importance in potential practical applications of lariat ether compounds for performing separations in which hard, hydrophilic aqueous phase anions, such as chloride, nitrate, or sulfate, would be involved.

Lipophilic lariat ethers with pendent acidic groups are effective and selective ligands for the solvent extraction of alkali metal cations and their transport across liquid membranes.[6,7] Among the lariat ethers with pendent acidic groups, *sym*-dibenzo-16-crown-5-oxyacetic acid derivatives (**1**)[6,8] and *sym*-dibenzo-19-crown-6-oxyacetic acid compounds (**2**)[8] have been studied to probe the effects of structural variations within the ligands upon the metal ion complexation process. Although high Na^+ selectivity was observed in competitive solvent extractions employing lipophilic *sym*-(alkyl)dibenzo-16-crown-5-oxyacetic acids (**1**, R = alkyl), the K^+ selectivity for analogous *sym*-(alkyl)dibenzo-19-crown-6-oxyacetic acids (**2**, R = alkyl) was only modest.[8] To determine if the K^+ selectivity could be enhanced by incorporation of a third benzo group into the 19-crown-6 ring, the synthesis of *sym*-tribenzo-19-crown-6 lariat ether carboxylic acids was undertaken. We now report the preparation of the *sym*-tribenzo-19-crown-6-oxyacetic acids **3–5**. The crystal structure of *sym*-(hydroxy)(propyl)tribenzo-19-crown-6 (**6**), a synthetic precursor to **4**, was determined which provides insight into the conformation of the tribenzo-19-crown-6 ring system.

RESULTS AND DISCUSSION

A. Preparation of *sym*-tribenzo-19-crown-6-oxyacetic acid (3)

The initial synthesis of a functionalized tribenzo-19-crown-6 compound involved formation of the macrocyclic ring and production of the functional group in a single step. Bisphenol **7**, which was prepared by Weber and Vögtle in five steps,[9] was reacted with aqueous KOH and epichlorohydrin[10] to form *sym*-(hydroxy)tribenzo-19-crown-6 (**8**). However, the yield of lariat ether alcohol **8** was only 35% and several steps had been required to obtain reactant bisphenol **7**. Therefore an alternative synthetic route to **8** was developed in which the alcohol group is first incorporated into a bisphenol unit followed by cyclization. This route is summarized in Scheme 1.

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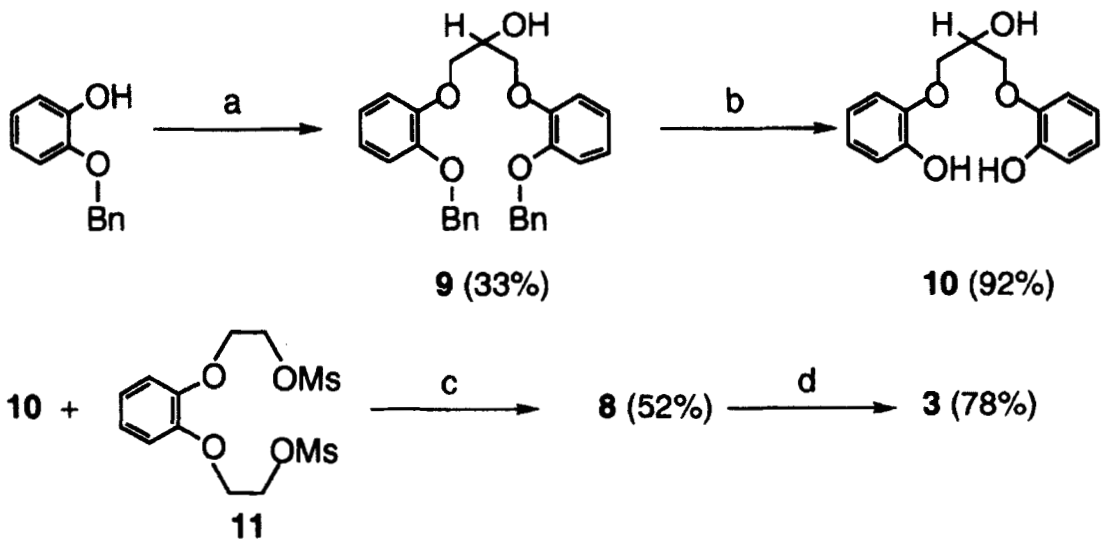
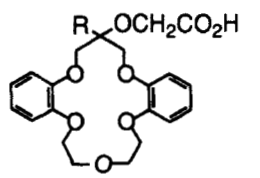


(a) NaOH, epichlorohydrin, aqueous THF. (b) H_2, 10% Pd/C, HOAc, EtOH. (c) Cs_2CO_3, DMF. (d) KH, $BrCH_2CO_2H$, THF.

Scheme I

Monobenzyl-protected catechol[11] was reacted with NaOH and epichlorohydrin in aqueous THF to provide polyether alcohol **9** in 33% yield. Despite several attempts to enhance the yield by variation of the epichlorohydrin addition rate, use of KOH instead of NaOH, etc., the yield of this step remained low. (When excess epichloridrin was utilized, the major reaction product was epoxide **12**.) However, the reactants are readily available and the reaction may be scaled up easily.

The benzyl protecting groups in **9** were removed by catalytic hydrogenolysis to give bisphenol alcohol **10** in 92 % yield. Dimesylate **11** was prepared in quantitative yield from reported 1,2-bis(2'-hydroxyethoxy)benzene (**13**),[12] which in turn was synthesized by converting commercially available catechol-O,O-diacetic acid into its diethyl ester followed by reduction of the diester with $LiAlH_4$ in THF. Ring formation by reaction of bisphenol alcohol **10** with Cs_2CO_3 and dimesylate **11** in DMF gave a 52% yield of *sym*-(hydroxy)tribenzo-19-crown-6 (**8**). Alkylation of lariat ether alcohol **8** with KH and bro-



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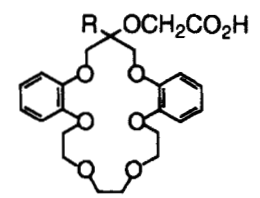

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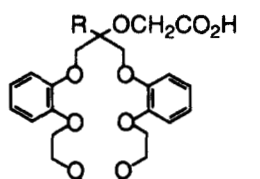
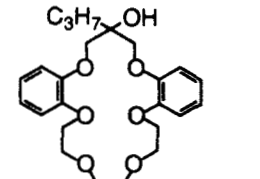


R	
3	H
4	C_3H_7
5	C_8H_{17}



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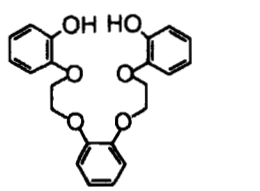

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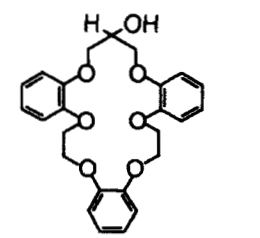

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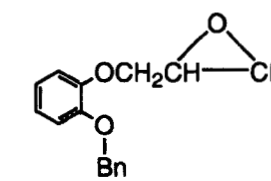

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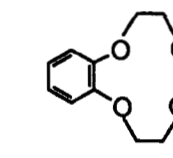

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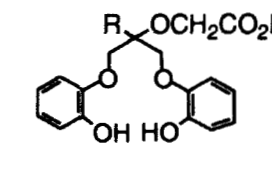
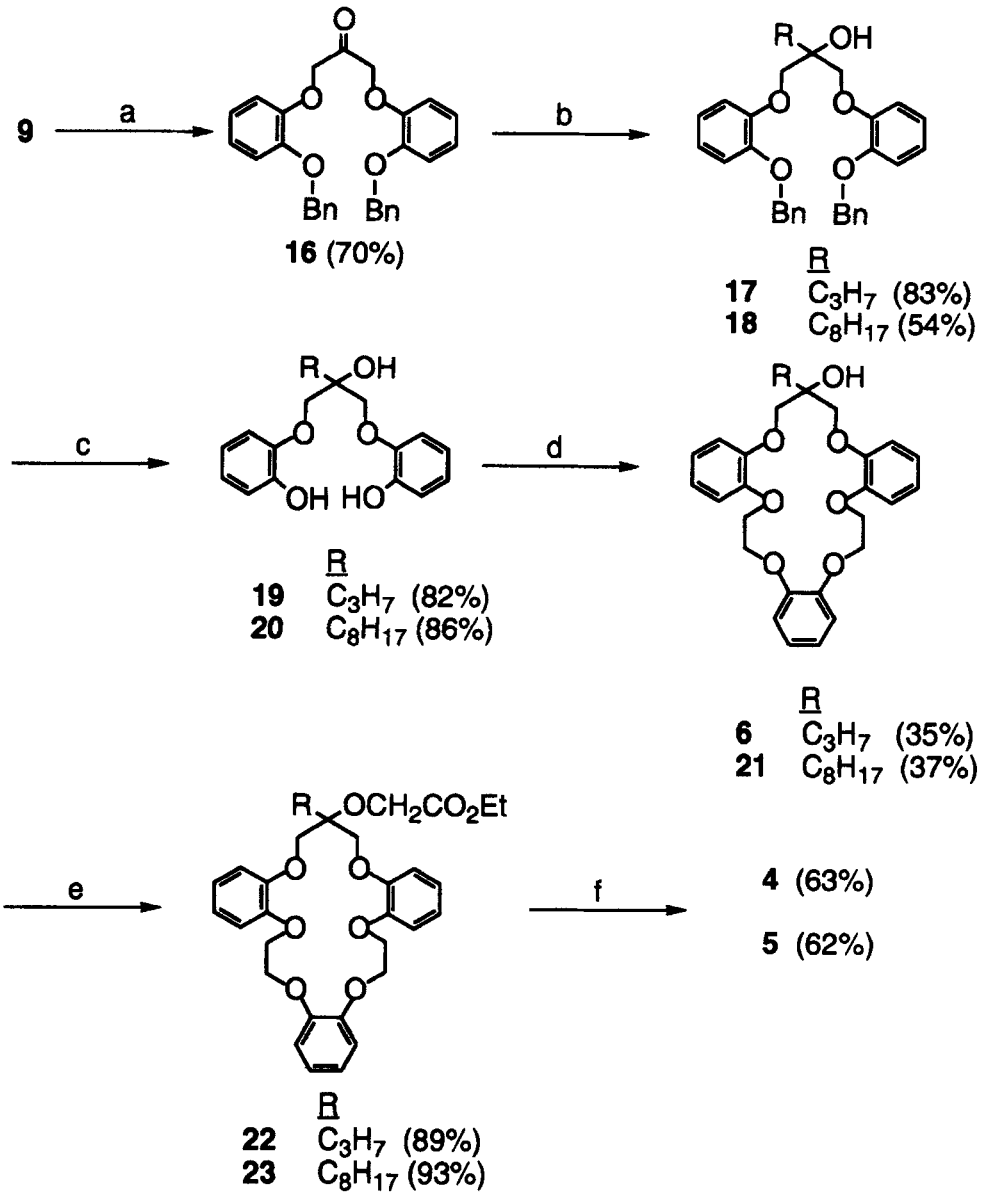


R	
14	H
15	C_2H_5



(a) Jones reagent, acetone. (b) Mg, RBr, THF. (c) H_2, 10% Pd/C, HOAc, EtOH. (d) Cs_2CO_3, **11**, DMF. (e) NaH, $BrCH_2CO_2Et$, THF. (f) NaOH, H_2O then HCl.

Scheme 2

moacetic acid in THF provided a 78 % yield of *sym*-tribenzo-19-crown-6-oxyacetic acid (**3**). When the alkylation was attempted with NaH as the base, the lariat ether alcohol **8** was recovered unchanged.

To determine if the acid-containing side arm could be introduced prior to the cyclization reaction, bisphenol carboxylic acid **14** and ester **15** were prepared from bisphenol alcohol **10**. From reactions of **14** and **15** with Cs_2CO_3 and dimesylate **11** in DMF, no cyclization products were isolated.

B. Preparation of *sym*-(alkyl)tribenzo-19-crown-6-oxyacetic acids 4 and 5

The preparation of *sym*-(propyl)tribenzo-19-crown-6-oxyacetic acid (**4**) and *sym*-(octyl)tribenzo-19-crown-6-oxyacetic acid (**5**) in six steps from polyether alcohol **9** is presented in Scheme 2.

Jones oxidation of **9** gave polyether ketone **16** in 70% yield. Reactions of **16** with propyl and octyl magnesium bromides in THF produced polyether tertiary alcohols **17** and **18** in 83 and 54% yields, respectively. Catalytic

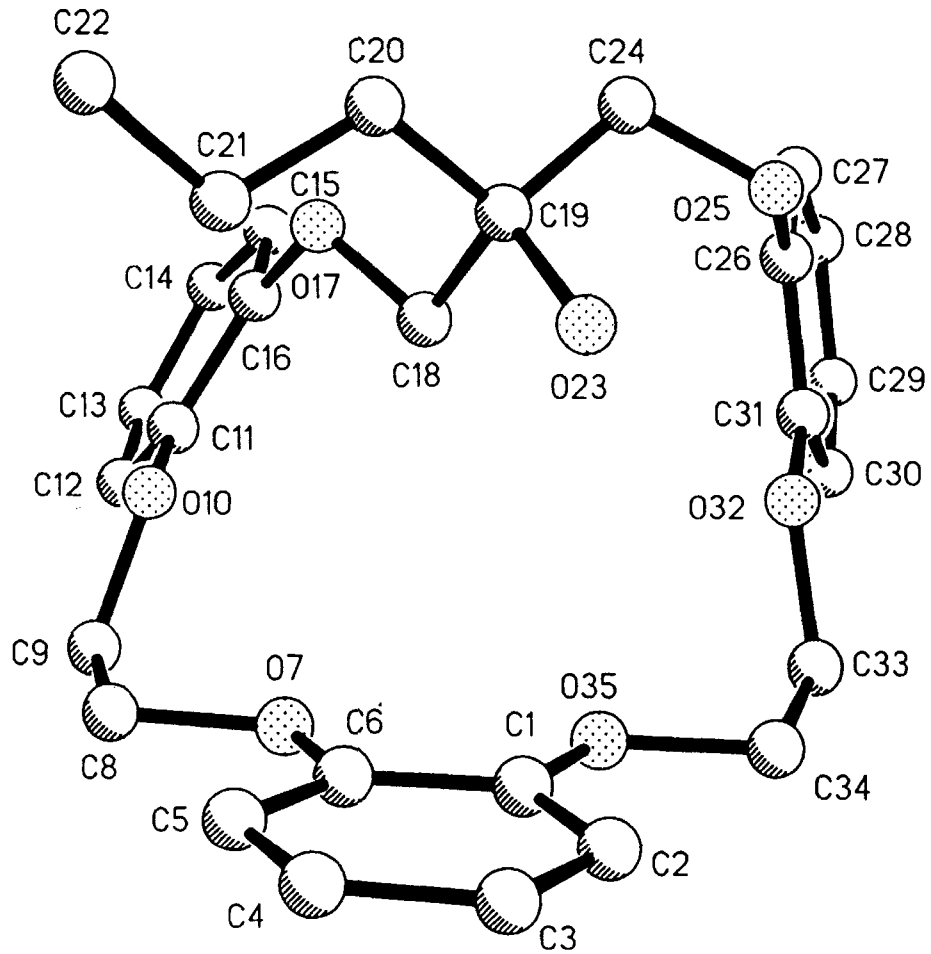


Figure 1 Computer drawing of the solid-state structure of *sym*-(hydroxy)(propyl)-tribenzo-19-crown-6 (**6**).

hydrogenolysis removed the benzyl-protecting groups from **17** and **18** to form bisphenol tertiary alcohols **19** and **20** in 82 and 86% yields, respectively. Cyclization by reaction of **19** and **20** with dimesylate **11** and Cs_2CO_3 in DMF provided 35 and 37% yields of lariat ether tertiary alcohols **6** and **21**, respectively. These cyclization yields are appreciably lower than that obtained with the bisphenol secondary alcohol **10** (Scheme 1).

Attempted alkylation of **6** with NaH or KH and bromoacetic acid in THF gave only recovered starting material. This necessitated attachment of the carboxylic acid-containing side arm by a two-step reaction sequence. Reaction of lariat ether alcohols **6** and **21** with NaH and ethyl bromoacetate in THF produced lariat ether esters **22** and **23** in 89 and 93% yields, respectively. Basic hydrolysis of the lariat ether esters gave 63 and 62% yields of *sym*-(propyl)tribenzo-19-crown-6-oxyacetic acid (**4**) and *sym*-(octyl)tribenzo-19-crown-6-oxyacetic acid (**5**), respectively.

Solid state structure of *sym*-(hydroxy)(propyl)tribenzo-19-crown-6 (6)

Although the lariat ether carboxylic acids **3–5** were oils, suitable single crystals of the lariat ether tertiary alcohol **6** were obtained and the structure was determined. A computer drawing of **6** is shown in Figure 1. The rigid benzo groups cause the cavity of the molecule to be open. The *geminal*-propyl group is directed away from the cavity, while the pendent alcohol group is directed into the cavity. There appears to be a hydrogen bond linking O23 and O32. However, it was not possible to locate the hydrogen which is bonded to O23 in any difference map. An attempt to calculate the position of that hydrogen atom resulted in a position that gave a reasonable hydrogen bond, but because of the uncertainty in the calculation, the position of the alcohol hydrogen atom was not included in the refinement. Other data which suggest the presence of a hydrogen bond involving O23 and O32 are the O23...O32 interatomic distance of 3.052 Å and the C19-O23...O32 angle of 97.3°.

Least-squares planes were calculated for the three benzene rings and for the six oxygen atoms of the crown ether ring. These planes are identified as A, B, C, and D for the least square planes involving C1-C6, C11-C16, C26-C31 and the six oxygen atoms of the crown ether ring, respectively. As expected, the least square planes for the benzene rings are essentially planar with average deviations from the planes of 0.0081 Å for A, 0.0127 Å

for B, and 0.0055 Å for C. The average deviation from the six-oxygen plane (plane D) is 0.3360 Å. The dihedral angles between A and D, B and D, and C and D are 121.3°, 120.3°, and 83.8°, respectively.

EXPERIMENTAL SECTION

General Methods

IR spectra were obtained with a Perkin Elmer Model 1600 FT-IR spectrophotometer. ^{1}H NMR spectra were recorded with a Bruker 200 MHz NMR spectrometer and chemical shifts are reported in parts per million (δ) downfield from TMS. Combustion analysis was performed by Desert Analytics (Tuscon, AZ).

Materials

Unless specified otherwise, reagent-grade reactants and solvents were used as received from chemical suppliers. DMF was distilled under vacuum and stored over molecular sieves. THF was purified by distillation from sodium ketyl. Polyether bisphenol **7**[9] and monobenzyl-protected catechol[11] were prepared by the reported methods.

1,3-Bis(*o*-benzyloxyphenoxy)-2-propanol (9)

To a solution of monobenzyl-protected catechol (39.7 g, 0.198 mol) in 2.7 L of 50% aqueous THF (v/v) was added NaOH (7.92 g, 0.198 mol). The mixture was stirred mechanically at 65 °C for 2 hours and the resulting solution was cooled to 50 °C. Epichlorohydrin (9.24 g, 0.099 mole) was added to the vigorously stirred solution during an 8-hour period with a syringe pump. After continued stirring for 2 days at 50 °C, the THF was evaporated *in vacuo* and 400 mL of CH_2Cl_2 was added to the aqueous residue. After shaking, the organic layer was separated, washed with 200 mL each of 5% aqueous HCL, brine, and water, dried over $MgSO_4$, and evaporated *in vacuo*. The resulting yellow oil was purified by column chromatography on silica get with benzene-hexane (1:1) as eluent to give a pale yellow oil. The oil was dissolved in 50 mL of Et_2O and cooled to give 12.25 g (33%) of **9** as a white solid, mp 55-56 °C. IR (KBr): 3492 (OH), 1256 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.31 (br d, 1H), 4.18-4.28 (d, 4H), 4.31-4.41 (m, 1H), 5.08 (s, 4H), 6.92 (s, 8H), 7.25-7.44 (m, 10H). Anal. Calcd for $C_{29}H_{28}O_5X0.1CH_2Cl_2$: C, 75.16; H, 6.11. Found: C, 75.32; H, 6.20.

1,3-Bis(*o*-hydroxyphenoxy)-2-propanol (10)

A mixture of **9** (6.35 g, 13.91 mmol), 10% Pd/C (0.20 g), acetic acid (4 drops) and 95% EtOH (80 mL) was shaken at room temperature in a Parr hydrogenator under 3 atmospheres of hydrogen for 24 hours. The mixture was filtered and evaporated *in vacuo* to give 3.28 g (92%) of **10** as a white solid, mp 174-175 °C. IR (KBr): 3362 (OH), 1264, 1036 (CO) cm^{-1}. ^{1}H NMR (acetone-d_6): δ 4.14-4.30 (m, 4H), 4.35-4.40 (m, 1H), 5.00-5.20 (br s, 1H), 6.73-6.86 (m, 6H), 6.97-7.02 (m, 2H), 7.82 (br s, 2H). Anal. Calcd for $C_{15}H_{16}O_5$: C, 65.21; H, 5.84. Found C, 64.99; H, 5.81.

Dimesylate of 1,2-bis(2'-hydroxyethoxy)benzene (11)

To a solution of 7.12 mL (51.3 mmol) of Et_3N and 3.90 g (19.7 mmol) of **13** in 300 mL of CH_2Cl_2 at 0 °C was added 3.35 mL (43.3 mmol) of methanesulfonyl chloride with a syringe pump during a 1-hour period. The reaction mixture was allowed to warm to room temperature during 2 hours and 20 mL of 5% aqueous HCl was added. After 30 minutes, the organic layer was separated, washed with 100 mL each of saturated aqueous $NaHCO_3$, brine, and water, dried over $MgSO_4$, and evaporated *in vacuo* to give a yellow solid which was recrystallized from 100 mL of hexane-CH_2Cl_2 (19:1) to afford 6.90 g (99%) of **11** as a white solid, mp 144-145 °C. IR (KBr): 1348, 1170 (SO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.15 (s, 6H), 4.25-4.30 (m, 4H), 4.57-4.62 (m, 4H), 6.94-6.97 (m, 4H). Anal. Calcd for $C_{12}H_{18}O_8S_2$: C, 40.67; H, 5.12. Found: C, 40.68; 5.00.

sym-(Hydroxy)tribenzo-19-crown-6 (8)

A mixture of **10** (3.00 g, 10.9 mmol) and Cs_2CO_3 (14.15 g, 43.4 mmol) in 120 mL of DMF was stirred at 120-125 °C for 3 hours under nitrogen. Over a 12-hour period, a solution of 3.85 g (10.9 mmol) of **11** in 50 mL of DMF was added with a syringe pump. The reaction mixture was refluxed for 24 hours and filtered. The filtrate was evaporated *in vacuo* to give a brown oil which was dissolved in 300 mL of CH_2Cl_2. The solution was washed with water (3 × 100 mL), dried over $MgSO_4$, and evaporated *in vacuo* to give a yellow oil which was chromatographed on silica gel with CH_2Cl_2 as eluent. The resulting white solid was washed with cold Et_2O to provide 2.47 g (52%) of **8** with mp 145-147 °C. IR (KBr): 3547 (OH), 1229, 1057 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.16 (br d, 1H), 4.20-4.24 (m, 5H), 4.37 (m, 8H), 6.88-7.00 (m, 12H). Anal. Calcd for $C_{25}H_{26}O_7$: C, 68.48; H, 5.98. Found: C, 68.09; H, 5.70.

sym-Tribenzo-16-crown-5-oxyacetic acid (3)

The protecting mineral oil was removed from KH (1.78 g of 35% dispersion in mineral oil, 15.50 mmol) by washing with dry pentane under nitrogen. To the dry powder was added 2.27 g (5.18 mmol) of **8** in 150 mL of THF and the mixture was stirred at room temperature for 2 hours. A solution of bromoacetic acid (1.08 g, 7.77 mmol) in 40 mL of THF was added at room temperature with a syringe pump during a 2-hour period and the mixture was stirred overnight. The mixture was cooled to 0 ° and ice-water was carefully added to consume the

excess of KH. The solvent was evaporated *in vacuo* and 300 mL of water was added to the residue. The aqueous solution was washed with EtOAc (4 × 50 ML), acidified to pH = 1 with 6 N HCl, and extracted with CH_2Cl_2 (3 × 100 mL). The combined extracts were dried over $MgSO_4$, filtered, and evaporated *in vacuo* to afford 2.01 g (78%) of **3** as an oil. IR (neat): 3696 (OH), 1756 (C=O), 1255, 1127 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 4.23-4.29 (m, 7H), 4.39 (s, 8H), 6.90-7.04 (m, 12H), 7.40-7.60 (br s, 1H). Anal. Calcd for $C_{27}H_{28}O_9$: C, 65.32; H, 5.68. Found: C, 65.04; H, 5.77.

1,3-Bis(*o*-benzyloxyphenoxy)-2-propanone (16)

To a stirred solution of **9** (7.08 g, 15.5 mmol) in 200 mL of acetone at °C was slowly added 20 mL of Jones reagent[13] and the mixture was allowed to stir overnight at room temperature. The solution was filtered and the filtered green residue was washed with acetone (2 × 50 mL). The combined filtrate and washings were evaporated *in vacuo* and the residue was dissolved in CH_2Cl_2 (300 mL). The solution was washed with water (3 × 100 mL), dried over $MgSO_4$, and evaporated *in vacuo* to give a brown oil which was chromatographed on alumina with benzene as eluent to provide a yellow oil. The oil was dissolved in 50 mL of Et_2O and cooled to give 4.45 g (70%) of **16** as a white solid with mp 104-105 °C. IR (KBr): 1744 (C=O), 1258, 1124, 1046 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 4.91 (s, 4H), 5.10 (s, 4H), 6.79-6.95 (m, 8H), 7.24-7.40 (m, 10H). Anal. Calcd for $C_{29}H_{26}O_5$: C, 76.63; H, 5.77. Found: C, 76.83; H, 5.63.

1-(*o*-Benzyloxyphenoxy)-2-[methylene(*o*-benzyloxyphenoxy)]-2-pentanol (17)

A mixture of magnesium turnings (0.53 g, 21.8 mmol), 1-bromopropane (2.68 g, 21.8 mmol) and THF (150 mL) was refluxed under nitrogen until the magnesium turnings had nearly disappeared. The reaction mixture was cooled to 0 °C and a solution of 3.30 g (7.26 mmol) of **16** in 40 mL of THF was added during a 3-hour period with a syringe pump. The reaction mixture was refluxed overnight and cooled to 0 °C and 30 mL of 5% aqueous NH_4Cl was added. The reaction mixture was stirred at room temperature for 1 hour and the THF was evaporated *in vacuo*. To the aqueous residue was added 300 mL of CH_2Cl_2. After shaking, the organic layer was separated, dried over $MgSO_4$, and evaporated *in vacuo* to give a yellow oil which was chromatographed on alumina with CH_2Cl_2 as eluent to give 3.00 g (83%) of **17** as an oil. IR (neat): 3487 (OH), 1256, 1122, 1023 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.87-0.95 (t, 3H), 1.45-1.54 (m, 2H), 1.70-1.78 (m, 2H), 3.04 (br s, 1H), 3.99-4.04 (d, 2H), 4.10-4.15 (d, 2H), 5.05 (s, 4H), 6.85-6.92 (m, 8H), 7.25-7.42 (m, 10H). Anal. Calcd for $C_{32}H_{34}O_5$: C, 77.08; H, 6.87. Found: C, 76.70; H, 6.73.

1-(*o*-Benzyloxyphenoxy)-2-[methylene(*o*-benzyloxyphenoxy)]-2-decanol (18)

By the procedure given for the preparation of **17** but with 1-bromopropane replaced by 1-bromooctane, **18** was synthesized as an oil in 54% yield. IR (neat): 3492 (OH), 1256, 1122, 1024 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.85-0.92 (t, 3H), 1.20-1.50 (m, 12H), 1.68-1.71 (m, 2H), 3.11 (br s, 1H), 4.00-4.05 (d, 2H), 4.10-4.15 (d, 2H), 5.04 (s, 4H), 6.89-6.90 (m, 8H), 7.29-7.39 (m, 10H). Anal. Calcd for $C_{37}H_{44}O_5$: C, 78.14; H, 7.80. Found: C, 78.20; H, 7.74.

1-(*o*-Hydroxyphenoxy)-2-[methylene(*o*-hydroxyphenoxy)]-2-pentanol (19)

A mixture of **17** (3.51 g, 7.04 mmol), 10% Pd/C (0.20 g), acetic acid (4 drops) and 95% EtOH (80 ML) was shaked at room temperature in a Parr hydrogenator under 3 atmospheres of hydrogen for 24 hours. The reaction mixture was filtered and evaporated *in vacuo* to give a white oil which was dissolved in Et_2O (50 mL) and cooled to give 1.83 g (82%) of **19** as a white solid, mp 167-168 °C. IR (KBr): 3362 (OH), 1264, 1111, 1037 (CO) cm^{-1}. ^1H NMR (acetone-d_6): δ 0.89-0.96 (t, 3H), 1.46-1.58 (m, 2H), 1.79-1.87 (m, 2H), 2.85-3.10 (br s 2H), 4.09-4.25 (q, 4H), 6.71-6.84 (m, 6H), 6.94-7.01 (m, 2H), 7.10-7.70 (br s, 1H). Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.96. Found: C, 68.00; H, 6.82.

1-(*o*-Hydroxyphenoxy)-2-[methylene(*o*-hydroxyphenoxy)]-2-decanol (20)

By the same procedure given above for the preparation of **19** but with **18** in place of **17**, an 86% yield of **20** was obtained as an oil. IR (neat): 3362 (OH), 1264, 1111, 1037 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.80-0.86 (t, 3H), 1.09-1.23 (m, 12 H), 1.76-1.88 (m, 2H), 3.93-4.05 (m, 4H), 5.55 (br s, 1H), 6.50-6.55 (d, 2H), 6.22-6.28 (m, 2H), 6.69-6.78 (m, 2H), 6.82-6.99 (m, 2H), 8.02 (br s, 2H). Anal Calcd for $C_{23}H_{32}O_5$: C, 71.11; H, 8.30. Found: C, 71.10; H, 8.23.

***sym*-(Hydroxy)(propyl)tribenzo-19-crown-6 (6)**

A mixture of **19** (0.97 g, 3.05 mmol), Cs_2CO_3 (3.97 g, 12.19 mmol) and DMF (50 mL) was stirred at 120-125 °C for 3 hours under nitrogen. With a syringe pump, a solution of **11** (1.08 g, 3.05 mmol) in 40 mL of DMF was added during a 12-hour period. The reaction mixture was stirred for an additional 24 hours at 120-125 °C, cooled to room temperature, and filtered. The filtrate was evaporated *in vacuo* and 300 mL of CH_2Cl_2 was added to the residue. The solution was washed with water (3 × 100 mL), dried over $MgSO_4$ and evaporated *in vacuo* to give a yellow oil which was chromatographed on silica gel with CH_2Cl_2 as eluent to afford a pale yellow oil. Dissolution of the oil in 50 mL of Et_2O and cooling gave

0.85 g (35%) of **6** as a white solid, mp 115-116 °C. IR (KBr): 3498 (OH), 1253, 1114, 1043 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.79-0.87 (t, 3H), 1.45-1.49 (m, 2H), 1.62-1.67 (m, 2H) 2.80-3.20 (br s, 1H), 4.11 (s, 4H), 4.31-4.35 (s, 8H), 6.86-6.94 (m, 12H). Anal. Calcd for $C_{28}H_{32}O_7X0.2CH_2Cl_2$: C, 68.08; H, 6.56. Found: C, 67.77; H, 6.81.

***sym*-(Hydroxyl)(octyl)tribenzo-19-crown-6 (21)**

By the same procedure as described above for **6** except with **20** in place of **19**, a 37% yield of **21** was obtained as a white solid, mp 67-68 °C. IR (KBr): 3503 (OH), 1256, 1117, 1044 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.83-0.88 (t, 3H), 1.20-1.42 (m, 12H), 1.64-1.72 (m, 2H), 3.13 (s, 1H), 4.12 (s, 4H), 4.35 (s, 8H), 6.89-6.95 (m, 12H) Anal. Calcd for $C_{33}H_{42}O_7X0.1H_2O$: C, 71.74; H, 7.70. Found: C, 71.39; H, 7.51.

Ethyl *sym*-(propyl)tribenzo-19-crown-6-oxyacetate (22)

The protecting mineral oil was removed from NaH (0.27 g of 60% dispersion in mineral oil, 6.76 mmol) by washing with dry pentane under nitrogen. To the dry powder was added a solution of 0.65 g (1.35 mmole) of **6** in 80 mL of THF and the mixture was stirred for 2 hours at room temperature. Ethyl bromoacetate (0.34 g, 2.03 mmol) in 10 mL of THF was added during a 2-hour period with a syringe pump. The reaction mixture was stirred overnight at room temperature and then cooled to 0 °C. Ice-water was slowly added to destroy the excess of NaH. The THF was evaporated *in vacuo* and 100 mL of CH_2Cl_2 was added to the aqueous residue. After shaking, the organic layer was separated, washed with water (3 × 100 mL), dried over $MgSO_4$, and evaporated *in vacuo*. The resulting pale yellow oil was chromatographed on silica gel with CH_2Cl_2 then EtOAc as eluents to provide 0.68 g (89%) of **22** as an oil. IR (neat): 1754, 1731 (C=O), 1256, 1218, 1117 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.78-0.85 (t, 3H), 1.10-1.17 (t, 3H), 1.40-1.50 (m, 2H), 1.70-1.77 (m, 2H), 4.00-4.08 (q, 2H), 4.23-4.39 (m, 14H), 6.85-6.96 (m, 12H). Anal. Calcd for $C_{32}H_{38}O_9$: C, 67.83; H, 6.76. Found: C, 68.23; H, 6.60.

Ethyl *sym*-(octyl)tribenzo-19-crown-6-oxyacetate (23)

By the same procedure given for the preparation of **22** but with **21** in place of **6**, a 93% yield of **23** was obtained as an oil. IR (neat): 1756, 1726 (C=O), 1256, 1219, 1126 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.83-0.89 (t, 3H), 1.10-1.19 (m, 15H), 1.74-1.83 (m, 2H), 4.00-4.09 (q, 2H), 4.23-4.25 (m, 4H), 4.30-4.38 (m, 10H), 6.85-6.93 (m, 12H). Anal. Calcd for $C_{37}H_{48}O_9$: C, 69.79; H, 7.60. Found: C, 69.96; H, 7.50.

***sym*-(Propyl)tribenzo-19-crown-6-oxyacetic acid (4)**

A solution of 0.88 g (1.59 mmol) of **22** and 0.38 g (9.54 mmol) of NaOH in 50 mL of H_2O was refluxed overnight. The aqueous solution was cooled to room temperature, washed with Et_2O (3 × 100 mL), acidified with 6N HCl to pH 1, and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over $MgSO_4$ and evaporated *in vacuo*. The resulting brown oil was chromatographed on silica gel with EtOAc then MeOH as eluents to give 0.54 g (63%) of **4** as an oil. IR (neat): 3355 (OH), 1772, 1731 (C=O), 1255, 1218, 1126 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.85-0.92 (t, 3H), 1.35-1.47 (m, 2H), 1.72-1.80 (m, 2H), 4.10-4.15 (d, 2H), 4.26-4.41 (m, 12H), 6.81-7.03 (m, 12H). Anal. Calcd for $C_{30}H_{34}O_9$: C, 66.90; H, 6.36. Found: C, 67.13; H, 6.32.

***sym*-(Octyl)tribenzo-19-crown-6-oxyacetic acid (5)**

By the same produce described for the preparation of **4** except using **23** instead of **22**, a 62% yield of **5** was realized as an oil. IR (neat): 3367 (OH), 1773, 1731 (C=O), 1256, 1219, 1127 (CO) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.85-0.91 (t, 3H), 1.20-1.41 (m, 12H), 1.72-1.82 (m, 2H), 4.09-4.15 (d, 2H), 4.26-4.36 (m, 12H), 6.86-6.97 (m, 12H). Anal. Calcd for $C_{35}H_{44}O_9$: C, 69.06; H, 7.29. Found: C, 69.27; H, 7.21.

Structure determination for *sym*-(hydroxy)(propyl)-tribenzo-19-crown-6 (6)

A suitable single crystal of **6** was grown from hexane-CH_2Cl_2 (2:1). Crystal data, intensity data collection and structure solution information are included in the supplementary material. Positions for hydrogen atoms bonded to carbons were calculated and U values for these atoms were set at 0.080 $Å^2$. It was not possible to locate the alcohol hydrogen bonded to O23 in the final difference map. Because of the small number of observed data, the structure was refined to two sections.

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