acids. Our procedure differs from the classical approach,[13,14] in which the base (indicator) is used in a very small concentration. Benzene is used in our experiments in large, essentially stoichiometric concentrations. On the other hand, this very feature makes our method applicable to the compositions actually existing in the superacid catalysts and, as such, more relevant for potential correlation with the catalytic activity in hydrocarbon conversions.

Experimental Section

General Methods. Aluminum bromide (MC&B, 99%) was melted with pellets (3 mm) of pure aluminum metal[48] and sublimed inside a drybox. It was stored there in Teflon FEP bottles with Teflon caps. Hydrogen bromide (Matheson, 99.8%) was taken from a 1-lb metal cylinder (lecture bottle). The sources and handling of other materials were given in previous papers.[7b,25] A Vacuum/atmospheres Co. drybox was used. ^{13}C NMR spectra were recorded in the FT mode at 25.2 MHz (Varian XL-100 instrument).

Protonation of Benzene in HBr-$AlBr_3$. All the glassware was dried at 120 °C overnight and then transferred quickly to the drybox. Aluminum bromide (5 mmol) was weighed in a calibrated (8 mm o.d., 5.5 mm i.d.) Pyrex tube with a ground joint and Teflon stopper inside the drybox. Benzene (1.55–3.2 mmol) was added from a syringe with a long needle to the $AlBr_3$ at the bottom of the tube, cooled in liquid nitrogen. The amount of benzene was checked by weighing the tube after the addition. In order to avoid static electricity buildup, which would disturb the weighing operation, the tube was handled inside the drybox with aluminum foil connected to the ground. The stopper was then replaced with a vacuum-type stopcock, and the tube was taken out of the drybox and attached to the vacuum line which had been evacuated overnight with the hydrogen bromide cylinder attached. Hydrogen bromide was admitted into the vacuum line through a fritted glass disk in order to retain any solid particles coming from the metal cylinder or valve. It was condensed into a graduated centrifuge tube attached to the vacuum line and cooled in liquid nitrogen. The volume of HBr was measured at −80 °C (CH_2Cl_2–liquid N_2 bath),[49a] and then it was distilled slowly from the measuring tube maintained at −80 °C into the NMR tube submerged entirely in liquid nitrogen. At intervals the liquid nitrogen level was lowered slowly, the HBr frozen at the top of the tube was allowed to melt and flow down the wall to the bottom. This ensured that any $AlBr_3$ which might have adhered to the walls of the tube was washed down to the botton. When the desired volume of HBr (20–50 mmol) was introduced into the NMR tube, the latter was sealed with a torch and then warmed slowly to room temperature until the solids dissolved. This step served also to check the quality of the tube and seal. It was done with the tube behind a shield in a hood. After the NMR spectra were run, the tube was thermostated at 0 °C, the height of the upper layer was measured, and the volume was calculated. It was assumed that the upper layer consists of pure HBr.[49b] The quantity of HBr in the lower layer was determined by difference. The total quantity of HBr in each sample was checked by weighing the sealed tube at the end. The values measured by weight and by the volume distilled from the measuring tube differed by less than 7%.

Protonation of Benzene in HF-TaF_5 and HF-SbF_5. The samples in 30:1 acids were prepared in Teflon bottles and transferred to the NMR tubes as described previously.[7b] It was noticed, however, for the 4.9:1:(1/2.1) sample that at the temperature at which all solids disappeared, some HF was lost through evaporation during the transfer from the bottle to the NMR tube. Therefore, the other samples at low HF-TaF_5 ratios were prepared directly in the NMR tube. The TaF_5 was weighed first, the tube was cooled, and HF was added with a Teflon pipet. The excess of HF, if any, was allowed to evaporate at 20 °C until the weight was right. The tube was cooled again, benzene (preweighed in a vial) was added through a Teflon syringe needle directly to the lower part of the NMR tube, and the weight of the tube was measured again. If necessary, a few crystals of TaF_5 were added at the end to adjust the TaF_5/benzene ratio. In all cases the mixture became homogeneous at or slightly above room temperature; for the 2.5:1 TaF_5/benzene mixture, the tube had to be swirled at 26–30 °C for about 15 min.

Registry No. 1, 71-43-2; HF, 7664-39-3; HBr, 10035-10-6; SbF_5, 7783-70-2; TaF_5, 7783-71-3; $AlBr_3$, 7727-15-3.

(48) Robinson, J.; Osteryoung, R. A. *J. Am. Chem. Soc.* **1979**, *101*, 323.

(49) Density of HBr. (a) 2.2047 at 193.3 K: McIntosh, D. D.; Steele, B. D. *Z. Phys. Chem.* **1906**, *55*, 141. (b) 1.9365 at 0 °C: Russell, J.; Sullivan, W. E. *Proc. Trans. R. Soc. Can.* [3] **1926**, *20*, III, 301.

Synthesis and Acidity of Crown Ethers with Pendant Carboxylic Acid Groups[1]

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Ten crown ethers with pendant carboxylic acid groups are synthesized from corresponding hydroxy crown ethers. Within this series of crown ether carboxylic acids there is systematic variation of the following: (a) the crown ether cavity size, while holding the pendant carboxylic acid group constant, (b) the length of the linkage which joins the carboxylic acid group to a common polyether ring, and (c) the lipophilicity, while keeping the polyether ring and linkage which joins the carboxylic acid and polyether ring portions invariant. Dissociation constants of the crown ether carboxylic acids in water are determined.

Recently we reported the facile synthesis of hydroxy dibenzo crown ethers **1a–d** by the reaction of epichlorohydrin with diphenols in alkaline aqueous media.[2] The hydroxyl group "handles" of these functionalized crown ethers provide convenient sites for further structural elaboration.

For the study of ionizable crown ethers as agents for the solvent extraction of metal ions[3-6] or their active transport

(1) This research was supported by the Department of Energy (Contract DE-ASOS-80ER-10604) and the Texas Tech University Center for Energy Research.

(2) Heo, G. S.; Bartsch, R. A.; Schlobohm, L. L.; Lee, J. G. *J. Org. Chem.* **1981**, *41*, 3574-3575.

(3) Strzelbicki, J.; Bartsch, R. A. *Anal. Chem.* **1981**, *53*, 1894-1899.

(4) Strzelbicki, J.; Bartsch, R. A. *Anal. Chem.* **1981**, *53*, 2247-2250.

(5) Strzelbicki, J.; Heo, G. S.; Bartsch, R. A. *Sep. Sci. Technol.*, in press.

(6) Strzelbicki, J.; Bartsch, R. A. *Anal. Chem.* **1981**, *53*, 2251-2253.

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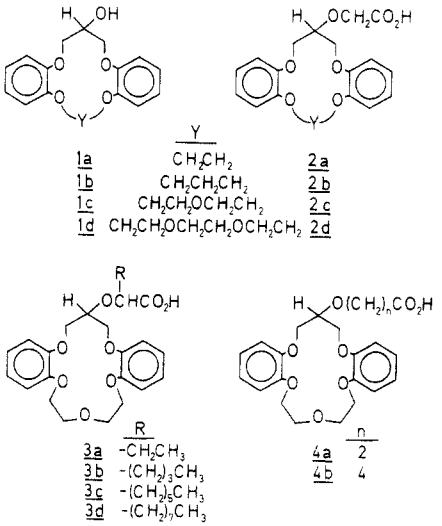
across liquid membranes,[7] we have prepared from these hydroxy crown ethers a series of 10 crown ethers, **2a–d**, **3a–d**, **4a–b**, which possess pendant carboxylic acid groups. In their ionized forms, these crown ether carboxlic acids offer the special advantage that metal ion extraction or transport does not require concomitant movement of aqueous phase anions into the organic phase.[3-7] The synthesis of these crown ether carboxylic acids and their dissociation constants in water are now reported.

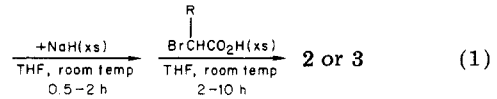


Results and Discussion

The crown ether carboxylic acids **2–4** are designed to give systematic structural variation of the polyether and carboxylic acid group portions of the molecules. Thus, **2a–d** are all oxyacetic acid derivatives in which the polyether cavity size and/or the number of alkyl ether oxygens are changed. For the series **2c**, **4a**, **4b**, the polyether portion is constant but the number of methylene units which connect the polyether and carboxylic acid portions is varied. Finally, with **3a–d**, one of the α-hydrogens of **2c** is replaced with different alkyl groups to systematically increase the lipophilicity of the crown ether carboxylic acid.

Crown Ether Oxyacetic Acids. Initially the hydroxy crown ether **1c** was converted into the crown ether carboxylic acid **2c** by the procedure of Cram and co-workers.[8] This method involved the initial formation of the methyl ester of **1c** and subsequent basic hydrolysis.

However, further experimentation led to the development of a simple, one-step method (eq 1). With bromoacetic acid, 76–82% yields of **2a–d** were isolated. From the higher α-bromo carboxylic acids, considerable lower yields (23–40%) of **3a–d** were obtained. These lower yields are attributed to difficulties in isolation and purification caused by the high lipophilicity of these crown ether carboxylic acids. Also no effort was made to maximize the yields of **3a–d**.



(1)

The identities of **2a–d** and **3a–d** were verified by infrared (IR) and proton magnetic resonance (^{1}H NMR) spectroscopy and by elemental analysis. The infrared spectra of **3a–d** exhibit some interesting differences. For **3a**, a single sharp carbonyl absorption at 1730 cm^{-1} is observed. For **3b**, a broad shoulder appears at approximately 1700 cm^{-1} in addition to a sharp absorption at 1740 cm^{-1}. Two sharp carbonyl absorptions at 1710 and 1685 cm^{-1} are noted for **3c** and **3d**. Absorption in the O–H stretching region for **3a** includes two sharp bands at 3560 and 3495 cm^{-1}. For **3b** these absorptions appear to collapse to a single broader band centered at 3250 cm^{-1}. Only very broad, ill-defined O–H stretching absorptions are noted in the IR spectra of **3c** and **3d**. Taken together these IR spectral changes indicate enhanced hydrogen bonding of the carboxylic acid groups in **3c** and **3d** compared with **3a** and **3b**. We suggest that this is due to intramolecular hydrogen bonding of the carboxylic acid group with the polyether oxygens.

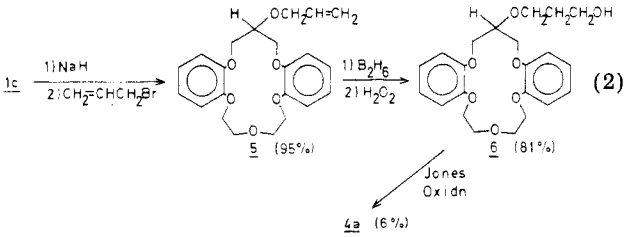
Table I. Acid Dissociation Constants and Solubilities of Crown Ether Carboxylic Acids in Water

compd	pK_a	solubility × 10^5, M
2a	3.69 ± 0.49 [a]	107
2b	4.36 ± 0.89	72.4
2c	4.59 ± 0.22 [b]	58.4
2d	3.89 ± 0.49	75.3
3a	5.30 ± 0.70	9.10
3b	5.90 ± 0.80	5.63
3c	7.19 ± 0.42	4.73
3d	7.35 ± 0.78	3.40
4a	4.89 ± 0.25	58.1
4b	6.41 ± 0.45	9.42

[a] Average value and standard deviations from three to five determinations. [b] A pK value of 4.56 ± 0.35 was reported in ref 3.

Crown Ether Carboxylic Acids 4a and 4b. Crown ether carboxylic acid **4b** was prepared from hydroxy crown ether **1c** by a two-step method. Room temperature reaction of **1c** with NaH in THF followed by the addition of ethyl 5-bromopentanoate produced 76% of the ethyl ester of **4b**. Basic hydrolysis of the ethyl ester with NaOH in EtOH at reflux gave **4b** in 91% yield.

Since treatment of the sodium alkoxide of **1c** in THF with ethyl 3-bromopropionate produced, after workup, only recovered **1c**,[9] it was necessary to develop a more elaborate route to the crown ether carboxylic acid **4a** (eq 2). Hydroxy crown ether **1c** was converted into the allyloxy crown ether **5** followed by hydroboration–oxidation to form the new hydroxy crown ether **6**. Jones oxidation of **6** gave the crown ether carboxylic acid **4a** in low yield.



(2)

The proposed structures of **4a** and **4b** are supported by IR and ^{1}H NMR spectra and by elemental analysis results.

Acid Dissociation Constants of Crown Ether Carboxylic Acids. Acid dissociation constants of the 10 crown ether carboxylic acids in water were determined by measuring the pH of aqueous solutions of known concentrations. Results are recorded in Table I.

Within the precision of the pK_a determinations, the values for the crown ether oxyacetic acids **2a–d** exhibit no systematic variation as the polyether cavity size and/or

(7) Strzelbicki, J.; Bartsch, R. A. *J. Membr. Sci.*, in press.
(8) Cram, D. J.; Helgeson, R. C.; Peacock, S. C.; Kaplan, L. J.; Domeir, L. A.; Moreau, P.; Koga, K.; Mayer, J. M.; Chao, Y.; Siegel, M. G.; Hoffman, D. H.; Sogah, G. D. *J. Org. Chem.* **1978**, *43*, 1930–1946.
(9) Apparently activated β-elimination is preferred to substitution.

number of dialkyl ether oxygen atoms are increased. The pK_a values for **2a–d** are all higher than the literature value of 3.57 for phenoxyacetic acid.[10] Thus, in agreement with the results of Newcomb and Cram,[11] the crown ether carboxylic acids are somewhat less acidic than closely related carboxylic acids which do not possess a polyether ring. These authors ascribe the lower acidities of the crown ether carboxylic acids to the following: (a) transannular hydrogen bonding of the carboxylic acid group with the crown ether oxygens and (b) steric inhibition to solvation of the crown ether carboxylate anion.[12] Since there should be little steric inhibition to solvation of the carboxylate groups in the anionic forms of **2a–d**, it appears that the former factor is dominant.

Increasing the lipophilicity of the crown ether carboxylic acids in the series **3a–d** markedly diminishes the acidity. An examination of CPK space-filling models indicates that when the R group of **3** becomes long it prefers to extend away from the polyether cavity. This would restrict the carboxylic acid group to the immediate vicinity of the polyether cavity where transannular hydrogen bonding of the carboxylic acid with the polyether oxygens would be maximized. Evidence for greater hydrogen bonding of the carboxylic acid groups of **3c** and **3d** compared with **3a** and **3b** is provided by their IR spectra (vide supra).

For the series **2c**, **4a**, **4b**, the systematic structural variation is increasing the number of methylene units between the polyether ring and the carboxylic acid group. In going from **2c** to **4a** the acidity remains constant within experimental error. However, the change from **4a** to **4b** causes a strong reduction in acidity. Clearly this acidity decrease cannot be attributed to steric inhibition of solvation of the carboxylate anion from **4b** which should be easier to solvate than the ionized form of **4a**. Inspection of CPK space-filling models suggests a very favorable conformation for **4b** in which the carboxylic acid group may hydrogen bond to the dialkyl ether oxygen of the polyether ring. For **2c** and **4a** the linkages which join the polyether and carboxylic acid portions of the molecules allow only for weaker hydrogen bonding with the less basic alkyl aryl oxygens of the crown ethers.

Experimental Section

Melting points were taken with either a Mel-Temp or Fisher Johns melting point apparatus and are uncorrected. IR spectra were obtained by using either a Beckman Acculab 8 or a Perkin-Elmer 457 spectrophotometer and are reported in reciprocal centimeters. ^1H NMR spectra were recorded with a Varian EM360 spectrometer and chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane. Mass spectra were obtained with a Varian MAT-311 instrument. Measurements of pH were made with a Fischer Scientific Accumet 620 pH meter using a Fisher Scientific 3-5A glass body combination electrode. Elemental analyses were performed by Integral Microanalytical Laboratories of Raleigh, NC.

Chemicals. The hydroxy crown ethers **1a–d** were available from earlier work.[2] Bromoacetic acid, 2-bromobutanoic acid, ethyl 5-bromopentanoate, allyl bromide, sodium borohydride, boron trifluoride etherate, and NaH (50% dispersion in mineral oil) were obtained from Aldrich and used directly. 2-Bromohexanoic acid, 2-bromooctanoic acid, and 2-bromodecanoic acid were prepared by a literature method.[13] Reagent grade THF and *n*-pentane were purified by distillation from $LiAlH_4$.

General Method for the Preparation of 2a–d. After removal of the protecting mineral oil from NaH (6 equiv) by washing with *n*-pentane under nitrogen, THF (400–1000 mL) and the hydroxy crown ether **1** (30–40 mmol) were added with stirring at room temperature. After the mixture was stirred for 30 min, 2 equiv of bromoacetic acid dissolved in 100–200 mL of THF was added dropwise during 0.5–2.0 h. Following completion of the addition, the reaction mixture was stirred for an additional 3–4 h at room temperature. After careful addition of water to destroy the excess NaH, the THF was evaporated in vacuo. The resulting alkaline aqueous solution was extracted with CH_2Cl_2 to remove unreacted **1** and was acidified to pH 1 with concentrated HCl. The acidic aqueous mixture was extracted with CH_2Cl_2 and the organic layer was dried with $MgSO_4$ and evaporated in vacuo leaving **2** as a white solid.

sym-Dibenzo-13-crown-4-oxyacetic acid, **2a** (mp 129 °C), was obtained from 11.5 g of **1a** in 76% yield: IR (KBr) 3400–2200 (COOH), 1700 (C=O); ^1H NMR ($CDCl_3$) δ 3.65–4.65 (m, 11), 6.98 (s, 8), 9.83 (br s, 1). Anal. Calcd for $C_{19}H_{20}O_7$: C, 63.32; H, 5.60. Found: C, 63.06; H, 5.60.

sym-Dibenzo-14-crown-4-oxyacetic acid, **2b** (mp 140–141 °C after recrystallization from Et_2O), was prepared from 9.5 g of **1b** in 80% yield: IR (KBr) 3500–2200 (COOH), 1700 (C=O); ^1H NMR (CD_3COCD_3) δ 2.25 (quintet, 2), 3.90–4.55 (m, 11), 5.60 (br s, 1), 6.97 (s, 8). Anal. Calcd for $C_{20}H_{22}O_7$: C, 64.17; H, 5.88. Found: C, 63.83; H, 6.08.

sym-Dibenzo-16-crown-5-oxyacetic acid, **2c** (mp 166–166.5 °C after recrystallization from EtOH–H_2O), was synthesized in 82% yield from 10.0 g of **1c**: IR (KBr) 3600–2400 (COOH), 1750 (C=O); ^1H NMR (CD_3SOCD_3) δ 3.45–4.28 (m, 13), 4.33 (s, 2), 6.89 (s, 8), COOH not observed. Anal. Calcd for $C_{21}H_{24}O_8$: C, 62.38; H, 5.94. Found: C, 62.43; H, 6.16.

sym-Dibenzo-19-crown-6-oxyacetic acid, **2d**, (mp 95–96 °C after crystallization of the oil from diethyl ether), was obtained in 66% yield from 7.8 g of **1d**: IR (KBr) 3400–2200 (COOH), 1720 (C=O); ^1H NMR ($CDCl_3$) δ 3.50–4.30 (m, 17), 4.50 (s, 2), 6.95 (s, 8), 8.70 (br s, 1). Anal. Calcd for $C_{23}H_{28}O_9$: C, 61.61; H, 6.25. Found: C, 61.37; H, 6.51.

General Method for the Preparation of 3a–d. After removal of the protecting mineral oil from 18 g of NaH (375 mmol) by washing with *n*-pentane under nitrogen, 50 mL of THF was added. After the mixture was stirred for 0.5 h at room temperature, 19.0 g (55 mmol) of **1c** dissolved in 100 mL of THF was added dropwise during 1–2 h. Following completion of the addition, the reaction mixture was stirred for 1 h at room temperature and then 83 mmol of the 2-bromo carboxylic acid dissolved in 100 mL of THF was slowly added dropwise over a period of 2–10 h. (The longer addition times were used for the higher molecular weight 2-bromo carboxylic acids.) After completion of the addition, the reaction mixture was stirred for 5–10 h at room temperature. The THF was evaporated in vacuo and the residue was carefully added to 250 mL of H_2O. The aqueous mixture was extracted with *n*-hexane or cyclohexane (4 × 50 mL) to remove unreacted **1c**. The pH of the resultant aqueous and organic oil mixture was adjusted to 3 by addition of 6 N HCl. The oily organic layer was separated, washed with 100 mL of H_2O, dissolved in 200 mL of CH_2Cl_2, and then dried with $MgSO_4$. The CH_2Cl_2 solution was passed through a (3 × 30 cm) column of silica gel (Sargent Welch, SC14608, 60–200 mesh) with cyclohexane and then CH_2Cl_2 as eluent. Concentration of the eluent to approximately 400 mL in vacuo and placement of the solution in a refrigerator overnight gave solid **3**, which was filtered and purified by recrystallization from petroleum ether (90–120 °C).

2-(*sym*-Dibenzo-16-crown-5-oxy)butanoic acid, **3a** (mp 93–95 °C), was synthesized in 40% yield: IR (KBr) 3560, 3495, 3490–2700 (COOH), 1730 (C=O); ^1H NMR ($CDCl_3$) δ 1.05 (t, 3), 1.90 (m, 2), 3.85–4.20 (m, 14), 6.83 (s, 8), 7.75 (s, 1). Anal. Calcd for $C_{23}H_{28}O_8 \cdot H_2O$: C, 61.32; H, 6.71. Found: C, 61.22; H, 6.40.

2-(*sym*-Dibenzo-16-crown-5-oxy)hexanoic acid, **3b** (mp 93–95 °C) was produced in 40% yield: IR (KBr) 3250 (br, COOH), 1740 (C=O); ^1H NMR ($CDCl_3$) δ 0.7–2.0 (m, 9), 3.8–4.8 (m, 16), 6.90 (s, 8), 9.45 (s, 1). Anal. Calcd for $C_{25}H_{32}O_8$: C, 65.20; H, 7.01. Found: C, 64.90; H, 7.01.

2-(*sym*-Dibenzo-16-crown-5-oxy)octanoic acid, **3c** (mp 75.5–77.5 °C), was prepared in 23% yield: IR (KBr) 3500–2700 (very br, COOH), 1710 and 1685 (C=O); ^1H NMR ($CDCl_3$) δ 0.7–2.2 (m,

(10) King, E. J. *J. Am. Chem. Soc.* **1960**, *82*, 3575–3578.
(11) Newcomb, M.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *97*, 1257–1259.
(12) Newman, M. S.; Fukunaga, T. *J. Am. Chem. Soc.* **1963**, *85*, 1176–1178.
(13) Vogel, A. I. "Textbook of Practical Organic Chemistry", 4th ed.; Longman: New York, 1978; p 529.

13), 3.8–4.6 (m, 14), 6.90 (s, 8), 9.35 (s, 1). Anal. Calcd for $C_{27}H_{36}O_8$: C, 66.37; H, 7.43. Found: C, 66.29; H, 7.35.

2-(*sym*-Dibenzo-16-crown-5-oxy)decanoic acid, **3d** (mp 87–88 °C), was obtained in 27% yield: IR (KBr) 3400–2700 (very br, COOH), 1710 and 1685 (C=O); ^{1}H NMR ($CDCl_3$) δ 0.7–2.2 (m, 17), 3.3–4.7 (m, 14), 6.90 (s, 8), 9.75 (s, 1). Anal. Calcd for $C_{29}H_{40}O_8$: C, 67.42; H, 7.81. Found: C, 67.34; H, 7.86.

Preparation of *sym*-(Allyloxy)dibenzo-16-crown-5 (5). After removal of the protecting mineral oil from 3.6 g of NaH (75 mmol) by washing with *n*-pentane under nitrogen, 400 mL of THF and 21.0 g (60 mmol) of **1c** were added, and the mixture was stirred for 0.5 h. Allyl bromide (8.81 g, 73 mmol) was added dropwise. After being stirred at room temperature for 6 h, the reaction mixture was filtered and 150 mL of H_2O was added to the filtrate. Evaporation of the THF in vacuo gave a tan solid, which was separated by decantation. The tan solid was successively suspended in portions of water and stirred until after 1 h the washing water remained colorless. After filtration and drying at 50 °C, 22.2 g (95%) of off-white solid with mp 110–111 °C was obtained: IR (KBr) 1640 (C=C; ^{1}H NMR ($CDCl_3$) δ 3.66–4.43 (m, 15), 5.03–6.20 (m, 3), 6.75 (br s, 8); mass spectrum, *m/e* 386 (M^+). Anal. Calcd for $C_{22}H_{26}O_6$: C, 68.39; H, 6.74. Found: C, 68.02; H, 6.70.

Preparation of 3-(*sym*-Dibenzo-16-crown-5-oxy)propanoic Acid (4a). Using Brown's procedure,[14] we added 0.92 g of $NaBH_4$ to a solution of **5** (9.4 g, 24.4 mmol) in 200 mL of THF. Boron trifluoride etherate (3.0 mL) was added at such a rate that the temperature could be maintained at 20–25 °C by a water bath. The reaction mixture was stirred at this temperature for 1.5 h and then 2 mL of H_2O was added to destroy the excess hydride. After the addition of 10 mL of 3 N aqueous NaOH and raising the temperature to 35 °C, 12 mL of 30% H_2O_2 was slowly added and the reaction mixture was stirred for 0.5 h at 40 °C. After the THF layer was decanted and addition of 30 mL of H_2O to it, the THF was evaporated in vacuo to give a pale brown oil which solidified when the aqueous mixture was kept in a refrigerator for 3 days. Filtration and drying gave 8.0 g of white solid: mp 64–67 °C; IR (KBr) 3500–3300 (OH); ^{1}H NMR ($CDCl_3$) δ 1.13–1.37 (m, 0.2, methyl group of the undesired 2-hydroxy isomer), 1.60–2.20 (m, 1.8, β-methylene group of **6**), 3.15–3.56 (m, 1), 3.60–4.65 (m, 17), 6.86 (s, 8). From the ^{1}H NMR spectrum of isomeric contamination of **6** by about 10% of the 2-hydroxy isomer was estimated.

The crude **6** was subjected to Jones oxidation.[15] The hydroboration product (24.0 g, 59 mmol) was dissolved in 110 mL of acetone and the solution was cooled to 5 °C in an ice–water bath. Jones's reagent[15] (25 mL) was slowly added while the temperature was maintained at 5 °C. After the mixture was stirred at this temperature for 5 h, sufficient $Na_2S_2O_5$ was added to produce a green mixture. The liquid was decanted, the pH was adjusted to 8 with Na_2CO_3 (13.5 g), 100 mL of H_2O was added, and most of the acetone was evaporated in vacuo. The resulting aqueous suspension was washed with 80 mL of diethyl ether. The brown aqueous layer was acidified with concentrated HCl to pH 1. The brown sticky solid which separated was collected and subjected to continuous column chromatography[16] (silica gel and activated carbon, eluted with CH_2Cl_2 and then CH_3COCH_3) to yield an oil which solidified to give 1.53 g (6%) of white **4a**: mp 116–119 °C; IR (KBr) 3600–2300 (COOH), 1720 (C=O); ^{1}H NMR ($CDCl_3$) δ 2.43–2.95 (m, 2), 3.10–4.63 (m, 15), 6.83 (s, 8). Anal. Calcd for $C_{22}H_{26}O_8$: C, 63.16; H, 6.22. Found: C, 63.36; H, 6.11.

Preparation of 5-(*sym*-Dibenzo-16-crown-5-oxy)pentanoic Acid (4b). After removal of the protecting mineral oil from 6.0 g of NaH (120 mmol) by washing with *n*-pentane under nitrogen, 500 mL of THF and 10.0 g (29 mmol) of **1c** were added. After the reaction mixture was stirred for 1 h at room temperature, ethyl 5-bromopentanoate (9 mL, 58 mmol) in 50 mL of THF was added dropwise over a 2-h period. After the addition was completed, the mixture was stirred for 15 h and then filtered with washing of the filtered material by additional THF. (**Caution**: The filtered material contains unreacted NaH which must be disposed of properly.) The filtrate was evaporated in vacuo. The residue was dissolved in CH_2Cl_2 and the CH_2Cl_2 solution was washed with H_2O, dried over $MgSO_4$, and evaporated in vacuo. Vacuum distillation of the resulting oil removed the unreacted ethyl 5-bromopentanoate and produced a residue (10.5 g, 76%) of the crude ethyl ester of **4b**: IR (neat) 1720 (C=O); ^{1}H NMR ($CDCl_3$) δ 1.25 (t, 3), 1.45–2.00 (m, 4), 2.10–2.55 (m, 2), 3.60–4.50 (m, 17), 6.95 (m, 8).

The oil (10.5 g, 22 mmol) was dissolved in 100 mL of EtOH and 3.6 g of NaOH (88 mmol) in 20 mL of H_2O was added. After refluxing for 12 h, the reaction solution was cooled, the EtOH was evaporated in vacuo, and 200 mL of H_2O was added. The resultant alkaline aqueous solution was washed with CH_2Cl_2 and acidified with concentrated HCl to pH 1. The aqueous mixture was extracted with CH_2Cl_2 and the CH_2Cl_2 solution was dried over $MgSO_4$ and then evaporated in vacuo. To the oily product was added 100 mL of Et_2O and the mixture was briefly refluxed. Decantation separated the ether-soluble product from some polymeric material. Upon cooling in ice–water, the product crystallized from the Et_2O solution to provide 9.0 g (91%) of **4b**: mp 97–98 °C; IR (KBr) 3600–2400 (COOH), 1770 (C=O); ^{1}H NMR ($CDCl_3$) δ 1.52–1.97 (m, 4), 2.13–2.60 (m, 2), 3.50–4.66 (m, 13), 6.90 (s, 8), 10.35 (br s, 1). Anal. Calcd for $C_{24}H_{30}O_8$: C, 64.57; H, 6.73. Found: C, 64.49; H, 6.90.

Acid Dissociation Constants and Solubilities of Crown Ether Carboxylic Acids. The acid dissociation constants of the crown ether carboxylic acids were determined by measuring the pH of aqueous solution of **2a–d**, **3a–d**, and **4a,b** of known concentrations. Average values and standard deviations from three to five independent determinations are listed in Table I.

Solubility determinations were performed by a combination of weighing and ultraviolet absorption measurements. The saturated solution of a crown ether carboxylic acids was prepared by stirring an excess of the crown ether in demineralized water at 80 °C for at least 12 h. The solution was allowed to cool, equilibrated at room temperature for 12 h, and filtered. The saturated solution was diluted with demineralized water and its ultraviolet absorption at 273–274 nm was compared with that of solutions formed by dissolving known amounts (but considerably less than that needed for saturation) of the crown ether carboxylic acid in demineralized water at 80 °C and cooling to room temperature. The extinction coefficients for the crown ether carboxylic acid absorption maxima at 273–274 nm in water for **2a–d**, **3a–d**, and **4a,b** are ($\times 10^3$): 3.60^4, 5.04^4, 5.10^3, 4.17^4, 4.14, 4.30, 4.38, 4.48, 4.45, and 4.66, respectively.

Registry No. **1a**, 78328-80-0; **1b**, 78328-81-1; **1c**, 78328-78-6; **1d**, 78328-79-7; **2a**, 79404-78-7; **2b**, 80186-73-8; **2c**, 78708-41-5; **2d**, 79404-79-8; **3a**, 79503-73-4; **3b**, 79519-67-8; **3c**, 79519-66-7; **3d**, 79519-65-6; **4a**, 80186-74-9; **4b**, 79503-72-3; **5**, 80186-75-0; **6**, 80186-76-1.

(14) Brown, H. C. "Organic Synthesis via Boranes"; Wiley-Interscience: New York, 1975; p 17.
(15) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley-Interscience: New York, 1967; p 142.
(16) Dewar, M. J. S.; Dewar, R. B. K.; Gaibel, Z. L. F. In "Organic Syntheses", Collect. Vol. 5; Wiley: New York, 1973; p 730.