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Different types of macrocyclic polyethers with partially fluorinated side arms are prepared. These new macrocyclic ligands are based on *sym*-dibenzo-16-crown-5 and *sym*-dicyclohexano-16-crown-5 scaffolds.

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Introduction

Due to their unique complexation capabilities, macrocyclic polyethers (crown ethers) are widely used for complexation and selective extraction of a wide variety of metal ions, such as alkali and alkaline earth metal cations and trivalent lanthanides [1]. Many different modifications have been made to the parent crown ether structure to probe the influence of ligand structure on the cation-complexing properties of these macrocycles [1]. In recent years, macrocyclic compounds with fluorine atoms in their cavities or fluorinated side arms have received increasing attention. Macrocyclic ligands with one or more fluorine-containing side arms have potential applications in metal ion separations involving a fluorous phase [2] or supercritical carbon dioxide [3]. Also, macrocycles with a fluorine label on the macrocyclic framework have potential application as ^{19}F nmr probes [4].

In 1984, Cram and coworkers attempted to assess interactions between fluorine atom-containing macrocycles and metal cations [5]. However, cavitands composed of fluorobenzene units did not exhibit any complexation ability toward alkali metal ions [5]. Perfluorocrown ethers and cryptands have been prepared by Lagow and coworkers using direct fluorination of the corresponding crown ethers and cryptands [6]. As a result of the strong electron-withdrawing nature of the CF_2 units, the oxygen atoms in these polyethers no longer exhibit Lewis basicity and the macrocycles do not form stable metal complexes [7]. However, these compounds may have some medical applications as ^{19}F nmr imaging agents [8] and oxygen carriers [6c].

Partially fluorinated macrocycles prepared by Farnham and coworkers formed complexes with anions, particularly fluoride ion [9]. Kimura and coworkers synthesized a series of mono-, di- and tetrafluorinated cyclams and demonstrated that these ligands form stable copper and nickel complexes [10]. In a series of papers, Plenio and coworkers showed that partially fluorinated crown ethers and cryptands prepared from small fluorine-containing building blocks form stable complexes with alkali and alkaline earth metal cations [11]. ^{13}C and ^{19}F nmr spectral data, X-ray crystallographic analysis, and determinations of stability constants provide strong experimental evidence for fluorine atom-metal cation interactions. Takemura and coworkers have

prepared fluorine-containing macrocyclic compounds in which only the fluorine atom acts as a donor [12]. The K^+ complex formation with the ligands was confirmed by ^1H , ^{13}C and ^{19}F nmr spectra. X-ray crystallographic analysis showed that the six fluorine atoms are coordinated to K^+ in a distorted octahedral geometry. Several different types of macrocyclic ligands with fluorine-containing side arms have been prepared, as well [13-15].

Recently, we have reported the preparation of a series of N-substituted aza, diaza, and tetraaza macrocycles with partially fluorinated side arms and determined their efficiencies and selectivities in alkali metal and silver picrate extractions from aqueous solutions into chloroform [16]. Macrocycles with longer spacers between the macro-ring and the perfluoroalkyl group were found to exhibit greater extraction efficiencies than analogues with shorter spacers. Also, we have reported the preparation of lariat ether carboxylic acids [17], *O*-benzylhydroxamates [17a], and hydroxamic acids [17a] with fluorine-containing substituents. In general, the presence of fluorine-containing substituents was found to increase the solubility of the lariat ethers in supercritical carbon dioxide [17a].

We now report the synthesis of crown ethers with partially fluorinated side arms based on *sym*-dibenzo-16-crown-5 and *sym*-dicyclohexano-16-crown-5 scaffolds. As previously stated [16], we are interested in the preparation of partially fluorinated macrocycles that possess good solubility in non-polar, partially fluorinated and chlorofluorinated hydrocarbon solvents or in supercritical carbon dioxide yet provide strong metal ion complexing ability.

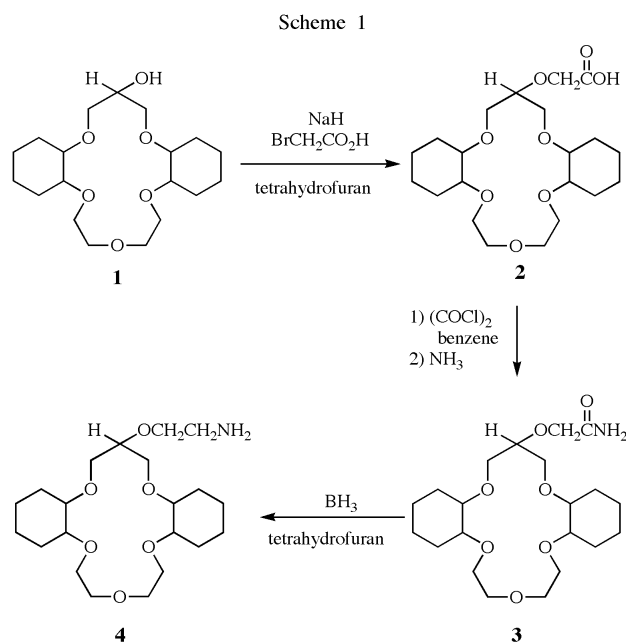
Results and Discussion.

For the preparation of macrocyclic ligands with partially fluorinated side arms, several different synthetic strategies were utilized.

In our earlier work [16], macrocycles with partially fluorinated side arms were prepared by coupling a fluorine-containing acid chloride with an azacrown ether and subsequent reduction of the resultant amide to an amine. Now we extend this strategy for the preparation of macrocyclic amines with partially fluorinated side arms.

The synthesis of lariat ether amine **4**, a precursor to a lariat ether amine with a partially fluorinated side arm is

presented in Scheme 1. Hydrogenation of *sym*-(hydroxy)dibenzo-16-crown-5 with 5% rhodium on alumina catalyst in 1-butanol under 500-600 psi of hydrogen gave *sym*-(hydroxy)dicyclohexano-16-crown-5 (**1**) in 91% yield. The efficiency for this catalytic hydrogenation was improved from the 50% yield in a reported method [18] that utilized ruthenium on carbon as the catalyst. Reaction of lariat ether alcohol **1** with sodium hydride and bromoacetic acid in tetrahydrofuran provided *sym*-dicyclohexano-16-crown-5-oxyacetic acid (**2**) in 74% yield. Reaction of **2** with oxalyl chloride gave the corresponding acid chloride that was treated with ammonia in acetonitrile to produce a 77% yield of lariat ether amide **3**. Reduction of **3** with borane-tetrahydrofuran complex gave an 86% yield of lariat ether amine **4**.



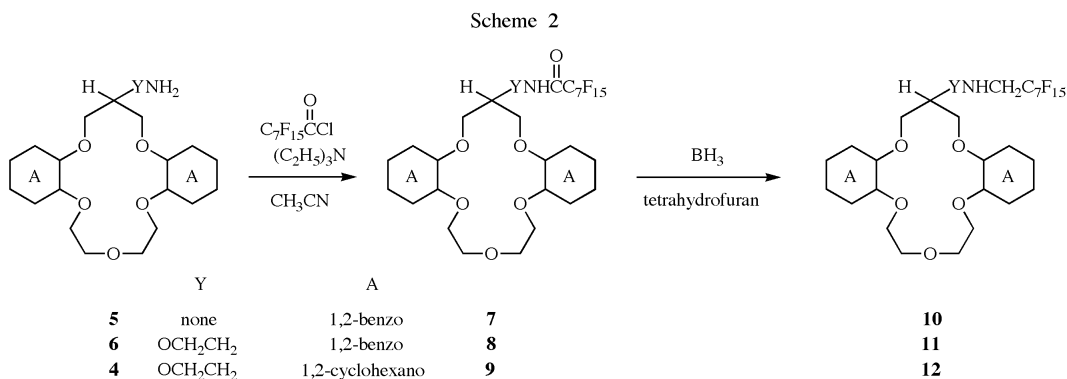
Synthesis of lariat ether amines **5** and **6** was reported previously [19]. Reactions of commercially available perfluorooctanoyl chloride with lariat ether amines **4-6** and

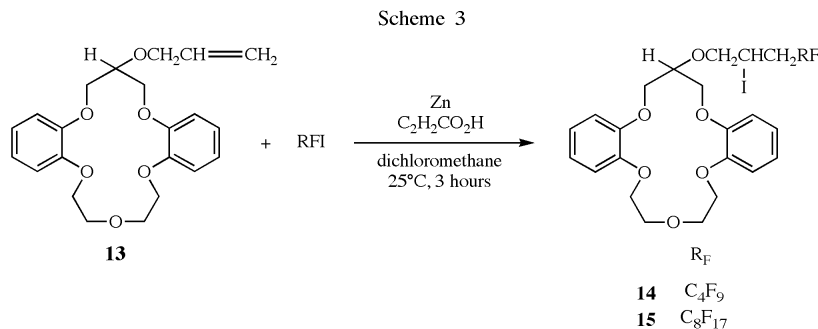
triethylamine in acetonitrile produced 90-92% yields of the corresponding lariat ether amides **7-9** (Scheme 2). Reduction of **7-9** with borane-tetrahydrofuran complex in tetrahydrofuran gave the corresponding lariat ether amines **10-12** with partially fluorinated substituents in 61-94% yields.

Macrocycles **10** and **11** both have 1,2-benzo groups on the macroring and the same perfluoroalkyl group length, but different spacers between the macroring and the perfluoroalkyl moiety. Macrocycle **12** has the same spacer between the macroring and perfluoroalkyl moiety and the same perfluoroalkyl group length as **11**, but with 1,2-cyclohexano substituents instead of 1,2-dibenzo groups. Previously we found that macrocycles with longer spacers between the macroring and perfluoroalkyl group exhibited greater extraction efficiencies than did analogues with shorter spacers [16]. The spacers between the macroring and perfluoroalkyl moieties in **11** and **12**, and to some extent in **10**, should be long enough to effectively attenuate the electron-withdrawing effects of the perfluoroalkyl group. Since cation complexation by crown ethers increases when alkyl aryl ether oxygens are replaced by dialkyl ether oxygens [20], the primary structural difference between **11** and **12** should be an enhancement of the oxygen basicity in the latter.

The second synthetic strategy involved reactions of perfluoroalkyl iodides with *sym*-(allyloxy)dibenzo-16-crown-5 (**13**), propionic acid, and zinc in dichloromethane to provide the partially fluorinated macrocycles **14** and **15** in 69 and 24% yields, respectively (Scheme 3).

Blancou and coworkers report that reaction of perfluoroalkyl iodides with allyl alcohol in different solvents catalyzed by zinc gave only the addition product [21]. On the other hand, reaction of methylenebutanedioic acid with perfluoroalkyl iodides, propionic acid, and zinc in dichloromethane produced the addition-reduction product [22]. In our case, as determined by elemental analyses, the iodine was not reduced under the latter reaction conditions and only the addition product was formed. At this time, no effort has been made to remove the iodine by reduction. It is noteworthy that in the absence of propionic acid, under





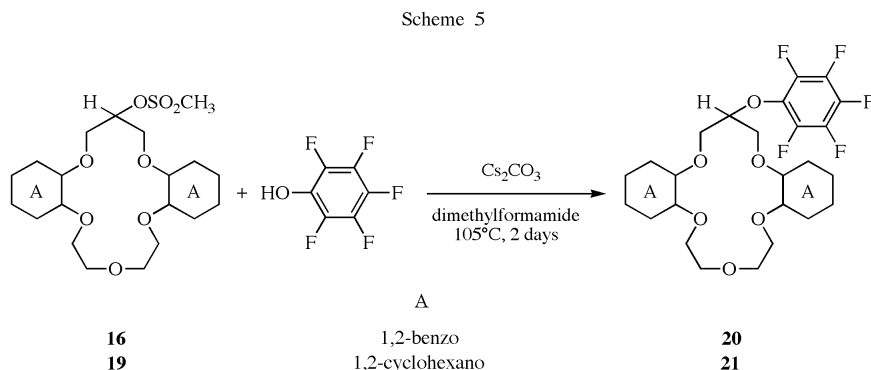
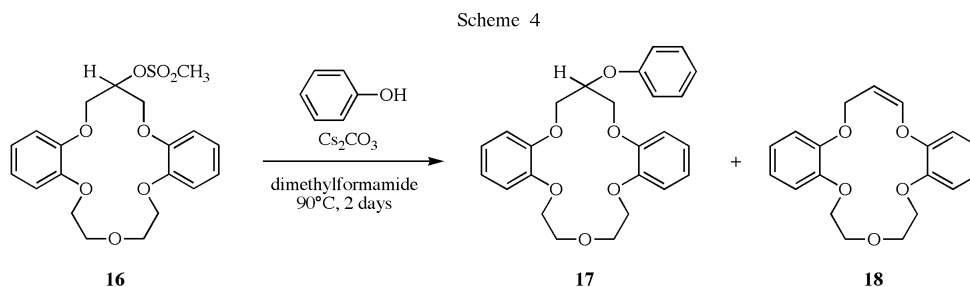
the same reaction conditions, no reaction took place. Only unchanged starting material **13** was recovered.

The third synthetic strategy was to prepare new lariat ethers with a pentafluorophenoxy side arm. To determine if substitution by phenoxide anion were feasible, reaction of lariat ether mesylate **16** [19] with phenol and cesium carbonate in dimethylformamide was performed (Scheme 4). After two days at 90°, the spot corresponding to the starting material had disappeared and two new spots appeared on tlc. The two major products were identified as the desired substitution product **17** (36% yield) and the elimination product **18** (27% yield). It should be noted that **18** was not observed in an analogous reaction with thiophenoxide as the nucleophile in the synthesis of *sym*-(thiophenoxy)-dibenzo-16-crown-5 [23]. Thus it appears that the elimination reaction became competitive with the substitution reaction for the harder phenoxide ion nucleophile.

Reaction of the lariat ether alcohol **1** with methanesulfonyl chloride and triethylamine in dichloromethane pro-

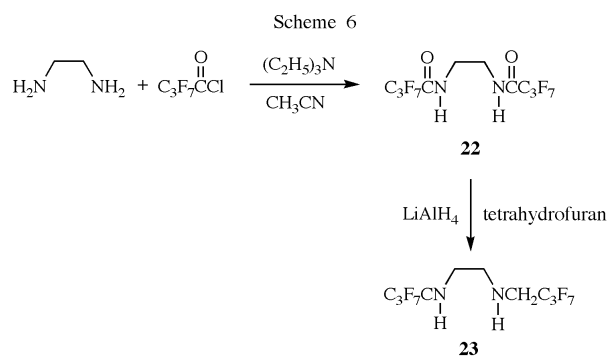
duced *sym*-(mesyloxy)dicyclohexano-16-crown-5 (**19**) in 91% yield. Synthesis of new lariat ethers **20** and **21** with a pentafluorophenoxy side arm by reaction of mesylates **16** and **19**, respectively, with pentafluorophenoxide ion was performed as shown in Scheme 5. Reaction of the lariat ether mesylates **16** and **19** with pentafluorophenol and cesium carbonate in dimethylformamide gave the desired products **20** and **21** in 67 and 57% yields, respectively. No elimination product **18** was detected. Presumably the electron-withdrawing fluorine atoms make the oxygen of pentafluorophenoxide less basic so the substitution reaction predominated. In previous work, we found that macrocycles containing pentafluorobenzyl groups exhibited good extraction efficiencies for alkali metal cations [16].

Macrobicyclic polyethers or bis(crown ethers) exhibit somewhat different cation-complexing properties than the corresponding monocyclic analogues. Bis(crown ethers) can form intramolecular sandwich complexes in which adjacent crown ether units cooperate in metal ion binding

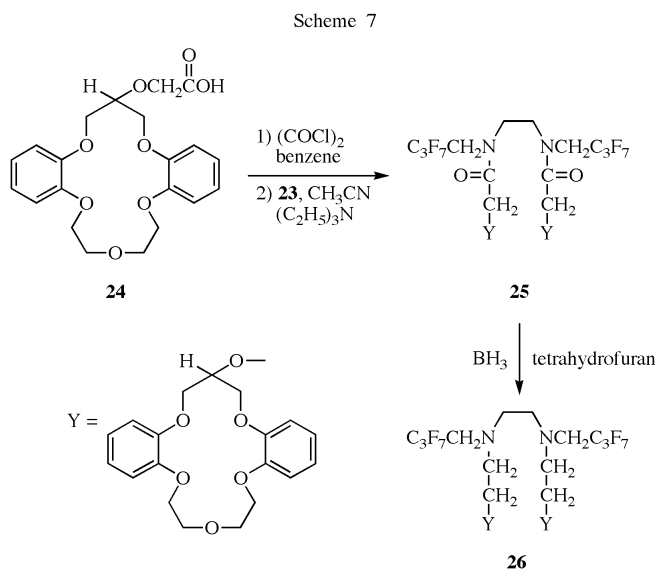


[24–30]. As a result of sandwich complex formation, they may exhibit remarkable selectivity toward some metal ions in crown ether-based, ion-selective electrodes [26]. We have prepared several bis(crown ethers) that contain *sym*-dibenzo-16-crown-5 units, including one in which the bridge contains an ethylene diamide group [19b].

The final synthetic strategy was to prepare a bis(crown ether) diamide and the corresponding diamine. Preparation of ethylenediamine substituted with a fluorine-containing group, on each nitrogen, is shown in Scheme 6. Reaction of perfluorobutanoyl chloride with ethylenediamine and triethylamine in acetonitrile gave diamide **22** in 94% yield. Reduction of **22** with lithium aluminum hydride in tetrahydrofuran gave an 85% yield of the corresponding diamine **23**.



In the next step, lariat ether carboxylic acid **24** was treated with oxalyl chloride to give the corresponding acid chloride that was coupled with diamine **23** in acetonitrile in the presence of triethylamine to produce the bis(crown ether) diamide **25** in 73% yield (Scheme 7). Reduction of macrobicyclic diamide **25** with borane-tetrahydrofuran



complex in tetrahydrofuran gave a 75% yield of the corresponding bis(crown ether) diamine **26**.

Structures of the new, partially fluorinated macrocyclic and macrobicyclic compounds were confirmed by ir spectroscopy, ^1H and ^{19}F nmr spectroscopy, and by combustion analyses.

Our preliminary investigations indicate that the partially fluorinated lariat ether **12** with 1,2-cyclohexano substituents on the macroring exhibit greater extraction efficiency for alkali metal picrates than do the analogues with 1,2-benzo substituents. The selectivity order for **13** is: $\text{Na}^+ > \text{Li}^+ > \text{K}^+ > \text{Rb}^+ > \text{Cs}^+$. Further studies concerning the extraction efficiency and selectivity of these macrocyclic and macrobicyclic ligands are ongoing in our laboratory and the results will be reported independently.

EXPERIMENTAL

Reagents and solvents were purchased from commercial suppliers and used without purification unless otherwise noted. Tetrahydrofuran was dried and purified by distillation from sodium under nitrogen with benzophenone ketyl as indicator. Benzene was dried over sodium. Acetonitrile was dried over and distilled from calcium hydride. Starting materials *sym*-(hydroxy)dibenzo-16-crown-5 [31], **5** [19a], **6** [19b], **13** [32], **16** [19a] and **24** [32] were prepared by reported procedures. Infrared (ir) spectra were recorded with a Perkin Elmer Model 1600 FT-ir spectrophotometer. Proton nuclear magnetic resonance (^1H nmr) spectra were measured with Bruker AF-200 (200 MHz) or AF-300 (300 MHz) spectrometers with tetramethylsilane as the internal standard. Fluorine nuclear magnetic resonance (^{19}F nmr) were recorded with a Bruker AF-300 (282.4 MHz) spectrometer with trichlorofluoromethane as the internal standard. Elemental analyses were performed by Desert Analytics Laboratory of Tucson, AZ. In some cases, the presence of water was indicated by the combustion analysis results and confirmed in the ^1H nmr spectrum.

Preparation of *sym*-(Hydroxy)dicyclohexano-16-crown-5 (**1**) [19].

A mixture of of *sym*-(hydroxy)dibenzo-16-crown-5 (5.00 g, 14.4 mmole), 5% rhodium on alumina (1.00 g), and acetic acid (1.00 g) in 500 ml of 1-butanol was subjected to hydrogen (500–600 psi) at 80° for 20 hours. The reaction mixture was passed through filter paper and then through a Teflon filter (0.22 μm). The solvent was evaporated *in vacuo* to give 4.70 g (91% of a colorless oil; ir (neat): ν 3462 (OH), 1107 (CO) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.21–1.87 (m, 16H), 3.23–3.26 (d, 1H, $J = 6$ Hz), 3.43–3.79 (m, 16H), 3.90 (m, 1H).

Preparation of *sym*-Dicyclohexano-16-crown-5-oxyacetic acid (**2**).

Tetrahydrofuran (40 ml) was added to dry sodium hydride (3.60 g, 150 mmole) under nitrogen and the mixture was stirred for 30 minutes at room temperature. Alcohol **1** (5.30 g, 15 mmole) in 40 ml of tetrahydrofuran was added dropwise over a 1-hour period and the mixture was stirred at room temperature for 1 hour, followed by dropwise addition of a solution of bromoacetic acid (4.17 g, 30 mmole) in 30 ml of tetrahydrofuran over a 2-hour period. The reaction mixture was stirred at room temperature for 24 hours. Careful addition of water to destroy the excess sodium hydride was followed by evaporation of the tetrahydrofuran *in vacuo*. To the

residue, 50 ml of water was added and the mixture was extracted with diethyl ether to remove the unreacted alcohol. The aqueous layer was acidified with 6 *N* hydrochloric acid and extracted with dichloromethane. The combined organic layers were washed with water, dried over magnesium sulfate, and evaporated *in vacuo* to give 4.60 g (74%) of an oily product, ir (neat): ν 3420 (COOH), 1707 (C=O), 1205, 1115 (CO) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.21-1.88 (m, 16H), 3.27-3.85 (m, 16H), 4.14-4.34 (m, 3H), 9.81 (br s, 1H).

Anal. Calcd. for $\text{C}_{21}\text{H}_{36}\text{O}_8 \cdot 0.4\text{H}_2\text{O}$: C, 59.53; H, 8.75. Found: C, 59.46; H, 9.05.

Preparation of *sym*-Dicyclohexano-16-crown-5-oxyacetamide (**3**).

Carboxylic acid **2** (4.24 g, 10.2 mmole) was added to 20 ml of dry benzene under nitrogen. After cooling to 0°, oxalyl chloride (4.0 ml) was added dropwise and the mixture was stirred at room temperature for 1 hour and then warmed to 60° for 1 hour. The benzene was evaporated *in vacuo* and the resultant acid chloride was used directly in the next step.

Anhydrous ammonia was introduced into a cooled acetonitrile solution of the lariat ether acid chloride. The mixture was allowed to warm to room temperature, stirred for 12 hours, and evaporated *in vacuo*. The residue was dissolved in ethyl acetate and the solution was washed with 0.6 *N* hydrochloric acid, water, 0.6 *M* aqueous sodium bicarbonate, and water again. The solution was dried over magnesium sulfate and evaporated *in vacuo* to give amide **3** as an oil in 77% yield; ir (neat): ν 3394 (NH₂), 1687 (C=O), 1206, 1106 (CO) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.22-1.84 (m, 16H) 3.46-3.78 (m, 16H), 4.09-4.14 (m, 3H), 5.75 (br s, 2H). Although macrocyclic amide **3** was not submitted for elemental analysis, satisfactory combustion analysis results were obtained for macrocycle **4** that was prepared by its reduction.

Preparation of 2-(*sym*-Dicyclohexano-16-crown-5-oxy)ethylamine (**4**).

A solution of **3** (2.23 g, 5.36 mmole) in 30 ml of dry tetrahydrofuran was cooled at 0° under nitrogen and 30 ml of borane-tetrahydrofuran complex (1.0 *M* solution in tetrahydrofuran) was added dropwise over a period of 15 minutes. The cooling bath was removed and the reaction mixture was kept at room temperature for 30 minutes and then refluxed for 6-8 hours. The solution was cooled to 0° and the excess borane was destroyed by addition of water. The white solid was collected by filtration and dissolved in concentrated hydrochloric acid-water-methanol (2:3:10). The solution was refluxed for 5 hours and evaporated *in vacuo*. The residue was treated with a strongly alkaline aqueous solution and extracted with dichloromethane. The combined organic extracts were dried over sodium sulfate and evaporated *in vacuo*. The crude product was purified by chromatography on silica gel with dichloromethane-methanol (9:1) as eluent to give a colorless oil in 86% yield; ir (neat): ν 3372 (NH₂), 1207, 1105 (CO) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.27-1.89 (m, 16H), 2.43 (br s, 2H), 2.82-2.87 (t, 2H, J = 5 Hz), 3.44-3.91 (m, 19H).

Anal. Calcd. for $\text{C}_{21}\text{H}_{39}\text{NO}_6$: C, 62.81; H, 9.79, N, 3.49. Found: C, 62.70; H, 10.04, N, 3.32.

General Procedure for Preparation of Partially Fluorinated Lariat Ether Amides **7-9**.

The lariat ether amine (2.00 mmole) was dissolved or suspended in 10 ml of dry acetonitrile, followed by triethylamine (2.00 mmole). The mixture was cooled to 0° and an acetonitrile

solution of perfluorooctanoyl chloride (2.00 mmole) was added dropwise. The mixture was allowed to warm to room temperature, stirred for 12 hours, and evaporated *in vacuo*. The residue was dissolved in ethyl acetate, and the solution was washed with 0.6 *M* hydrochloric acid, water, 0.6 *N* aqueous sodium bicarbonate, and water again. The solution was dried over anhydrous magnesium sulfate and evaporated *in vacuo* to provide the lariat ether amide. Combustion analyses were not performed for the lariat ether amides, but satisfactory elementary analysis results were obtained for each of the subsequent lariat ether amine compounds.

N-(*sym*-Dibenzo-16-crown-5-) Perfluorooctanoyl Amide (**7**).

Recrystallization from hexanes gave 92% of a white solid with mp 65-65°; ir (deposit from dichloromethane solution on a sodium chloride plate): ν 3322 (NH), 1714 (C=O), 1209, 1148 (CO) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 3.95-4.35 (m, 13H), 6.83-7.01 (m, 8H), 9.95 (br s, 1H), ^{19}F nmr (deuteriochloroform): δ -81.16 (t, 3F, J = 9 Hz), -119.03 to -119.14 (m, 2F), -122.38 to -122.48 (m, 4F), -123.23 to -123.41 (m, 2F), -123.51 (s, 2F), -126.48 to -126.63 (m, 2F).

N-[(2-*sym*-Dibenzo-16-crown-5-oxy)ethyl] Perfluorooctanoyl Amide (**8**).

Recrystallization from hexanes provided a 90% yield of a white solid with mp 78-79°; ir (deposit from dichloromethane solution on a sodium chloride plate): ν 3328 (NH), 1711 (C=O), 1207, 1142 (CO) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 3.91-4.30 (m, 17H), 6.85-7.04 (m, 8H), 9.98 (br s, 1H); ^{19}F nmr (deuteriochloroform): δ -81.16 (t, 3F, J = 9 Hz), -120.20 (t, 2F, J = 13 Hz), -122.13 (s, 2F), -122.49 (s, 2F), -122.90 (d, 2F, J = 14 Hz), -123.18 (s, 2F), -126.50 to -126.62 (m, 2F).

N-(2-*sym*-Dicyclohexano-16-crown-5-oxy)ethyl] Perfluorooctanoyl Amide (**10**).

This compound was obtained in 90% yield as an oil; ir (neat): ν 3219 (NH), 1696 (C=O), 1206, 1147 (CO) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.22-1.96 (m, 16H), 3.26-3.98 (m, 21H), 9.78 (br s, 1H); ^{19}F nmr (deuteriochloroform): δ -80.82 to -81.02 (m, 3F), -117.20 (t, 2F, J = 13 Hz), -119.36 to -119.65 (m, 2F), -121.90 to -121.97 (m, 2F), -122.62 to -122.69 (m, 2F), -122.98 (s, 2F), -126.33 to -126.45 (m, 2F).

General Procedure for the Preparation of Partially Fluorinated Lariat Ether Amines **10-12**.

A solution of the lariat ether amide (2.0 mmole) in 20 ml of dry tetrahydrofuran was cooled at 0° under nitrogen and 20 ml of borane-tetrahydrofuran complex (1.0 *M* solution in tetrahydrofuran) was added dropwise over a period of 15 minutes. Reaction conditions and the work-up procedure were the same as described for the preparation of lariat ether amine **4**.

N-(1*H*,1*H*-Perfluorooctyl) *sym*-(Amino)dibenzo-16-crown-5 (**10**).

Chromatography on silica gel with dichloromethane-methanol (9:1) as eluent and recrystallization from methanol gave a 61% yield of white solid with mp 111-113°; ir (deposit from dichloromethane solution on a sodium chloride plate): ν 3337 (NH), 1207, 1144 (CO) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.27 (br s, 1H), 3.57-3.68 (t, 2H, J = 16 Hz), 3.87-3.97 (m, 5H), 4.11-4.23 (m, 8H), 6.79-6.98 (m, 8H); ^{19}F nmr (deuteriochloroform): δ -81.19 (t, 3F, J = 9 Hz), -119.05 (t, 2F, J = 17 Hz), -122.35 to -122.45 (m, 4F), -123.20 to -123.44 (m, 2F), -123.48 (s, 2F), -126.52 to -126.66 (m, 2F).

Anal. Calcd. for $C_{27}H_{24}F_{15}NO_5$: C, 44.58; H, 3.38; N, 1.93. Found: C, 44.30; H, 3.04; N, 1.86.

N-(1*H*,1*H*-Perfluorooctyl) *sym*-(2-Aminoethyl)dibenzo-16-crown-5 (**11**).

Chromatography on silica gel with dichloromethane-methanol (9:1) as eluent and recrystallization from methanol provided a 70% yield of white solid with mp 81–83°; ir (deposit from dichloromethane on a sodium chloride plate): ν 3353 (NH), 1208, (CO) cm^{-1} ; 1H nmr (deuteriochloroform): δ 1.92 (br s, 1H), 2.96–3.01 (t, 2H, $J = 5$ Hz), 3.24–3.41 (t, 2H, $J = 16$ Hz), 3.86–4.01 (m, 6H), 4.15–4.27 (m, 7H), 4.29–4.34 (m, 2H), 6.81–7.00 (m, 8H); ^{19}F nmr (deuteriochloroform): δ -81.19 (t, 3F, $J = 11$ Hz), -118.31 to -118.53 (m, 2F), -122.28 to -122.52 (m, 4F), -123.19 (s, 2F), -123.84 (s, 2F), -126.53 to -126.63 (m, 2F).

Anal. Calcd. for $C_{29}H_{28}F_{15}NO_6$: C, 45.15; H, 3.66; N, 1.82. Found: C, 45.32; H, 3.72; N, 1.80.

N-(1*H*,1*H*-Perfluorooctyl) *sym*-(2-Aminoethyl)dicyclohexano-16-crown-5 (**12**).

Chromatography on silica gel with dichloromethane-methanol (9:1) as eluent gave 94% of a colorless oil; ir (neat): ν 3342 (NH), 1209, 1144 (CO) cm^{-1} ; 1H nmr (deuteriochloroform): δ 1.22–1.96 (m, 17H), 2.87–2.91 (t, 2H, $J = 5$ Hz), 3.20–3.37 (m, 2H, $J = 16$ Hz), 3.47–3.75 (m, 19H); ^{19}F nmr (deuteriochloroform): δ -80.74 (t, 3F, $J = 9$ Hz), -118.07 to -118.18 (m, 2F), -121.88 to -122.11 (m, 4F), -122.79 (s, 2F), -123.47 (s, 2F), -126.10 to -126.22 (m, 2F).

Anal. Calcd. for $C_{29}H_{40}F_{15}NO_6$: C, 44.45; H, 5.14; N, 1.79. Found: C, 44.72; H, 5.38; N, 1.78.

General Procedure for Preparation of Partially Fluorinated Lariat Ethers **14** and **15**.

To a mixture of *sym*-(allyloxy)dibenzo-16-crown-5 (**13**) (1.16 g, 3.00 mmole), zinc powder (0.20 g), and propionic acid (0.22 g, 3.0 mmole) in 25 ml of dichloromethane, 3.0 mmole of perfluorobutyl iodide or perfluorooctyl iodide was added dropwise at 25°. Stirring was continued for 2–3 hours after completion of the addition. The resultant colorless solution was washed with 10% hydrochloric acid and water, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was purified by chromatography on silica gel with dichloromethane as eluent, followed by recrystallization from methanol.

sym-(2*H*,2*H*,3*H*,4*H*,4*H*-3-Iodo-1-oxaperfluoroheptyl)dibenzo-16-crown-5 (**14**).

A white solid with mp 52–54° was realized in 69% yield; ir (deposit from dichloromethane solution on a sodium chloride plate): ν 1205, 1141 (CO) cm^{-1} ; 1H nmr (deuteriochloroform): δ 2.64–2.86 (m, 1H), 3.12–3.32 (m, 1H), 3.88–4.06 (m, 5H), 4.14–4.28 (m, 8H), 4.29–4.43 (m, 3H), 6.84–7.01 (m, 8H); ^{19}F nmr (deuteriochloroform): δ -81.41 to -81.49 (m, 3F), -114.18 to -114.40 (m, 2F), -124.94 to -124.97 (t, 2F, $J = 4$ Hz), -126.32 to -126.43 (m, 2F).

Anal. Calcd. for $C_{26}H_{26}F_9IO_6$: C, 42.64; H, 3.58. Found: C, 42.73; H, 3.59.

sym-(2*H*,2*H*,3*H*,4*H*,4*H*-3-Iodo-1-oxaperfluoroundecyl)dibenzo-16-crown-5 (**15**).

A white solid with mp 84–86° was obtained in 24% yield; ir (deposit from dichloromethane solution on a sodium chloride

plate): ν 1206, 1142 (CO) cm^{-1} ; 1H nmr (deuteriochloroform): δ 2.63–2.76 (m, 1H), 3.22–3.31 (m, 1H), 3.89–4.07 (m, 5H), 4.14–4.22 (m, 8H), 4.31–4.36 (m, 3H), 6.84–7.00 (m, 8H); ^{19}F nmr (deuteriochloroform): δ -81.18 (t, 3F, $J = 10$ Hz), -114.06 (t, 2F, $J = 16$ Hz), -122.04 (s, 2F), -122.37 (s, 4F), -123.16 (s, 2F), -124.00 (s, 2F), -126.57 to -126.61 (m, 2F).

Anal. Calcd. for $C_{30}H_{26}F_{17}IO_6 \cdot 0.5H_2O$: C, 38.27; H, 2.89. Found: C, 38.14; H, 2.77.

Preparation of *sym*-(Phenoxy)dibenzo-16-crown-5 (**17**).

A mixture of **16** (1.00 g, 2.4 mmole), phenol (0.27 g, 2.9 mmole), and cesium carbonate (0.93 g, 2.9 mmole) in 50 ml of dry dimethylformamide was stirred at 90° for 48 hours. The dimethylformamide was evaporated *in vacuo* and the residue was dissolved in 50 ml of dichloromethane. The solution was washed with water (3 x 30 ml), dried over magnesium sulfate, and evaporated *in vacuo*. Chromatography on silica gel with dichloromethane, then dichloromethane-ethyl acetate (20:1) as eluents gave 0.36 g (36%) of **17** with mp 96–97° and 0.21 g (27%) of **18** with mp 81–82°; **17**: ir (deposit from dichloromethane solution on a sodium chloride plate): ν 1258, 1222, and 1124 (CO) cm^{-1} ; 1H nmr (deuteriochloroform): δ 3.88–3.98 (m, 4H), 4.16–4.19 (m, 4H), 4.28–4.36 (dd, 2H, $J = 4$ Hz), 4.46–4.53 (dd, 2H, $J = 4$ Hz), 4.97–5.05 (p, 1H), 6.82–6.99 (m, 8H), 7.07–7.34 (m, 5H).

Anal. Calcd. for $C_{25}H_{26}O_6$: C, 71.06; H, 6.20. Found: C, 70.84; H, 6.14.

Compound **18** has ir (deposit from dichloromethane solution on a sodium chloride plate): ν 1666 (C=C), 1257 and 1126 (CO) cm^{-1} ; 1H nmr (deuteriochloroform): δ 3.91–3.99 (m, 4H), 4.12–4.22 (m, 4H), 4.85–4.89 (d, 2H, $J = 8$ Hz), 5.09–5.19 (m, 1H), 6.49–6.52 (d, 1H, $J = 6$ Hz), 6.85–7.06 (m, 8H).

Anal. Calcd. for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.10; H, 6.03.

Preparation of *sym*-(Methanesulfonyl)dicyclohexano-16-crown-5 (**19**).

To a solution of **1** (2.50 g, 6.97 mmole) and triethylamine (0.85 g, 8.4 mmole) in dichloromethane (200 ml) was added methanesulfonyl chloride (0.88 g, 7.7 mmole) at 0°. The reaction mixture was stirred at room temperature for 2 hours, washed with 2 *N* hydrochloric acid (100 ml), water (100 ml), saturated aqueous sodium bicarbonate (2 x 100 ml), and then brine (100 ml). The dichloromethane layer was dried over magnesium sulfate and evaporated *in vacuo*. Chromatography of the residue on silica gel with ethyl acetate-dichloromethane (1:5), followed by ethyl acetate as eluents gave 2.76 g (91%) of a semi-solid; ir (deposit from dichloromethane solution on a sodium chloride plate): ν 1357 and 1175 (S=O), 1108 (CO) cm^{-1} ; 1H nmr (deuteriochloroform): δ 1.22–1.81 (m, 16H), 3.09–3.11 (m, 3H), 3.44–3.96 (m, 16H), 4.80–4.90 (m, 1H).

Anal. Calcd. for $C_{20}H_{36}O_8S$: C, 55.15; H, 8.31. Found: C, 55.07; H, 8.17.

General Procedure for the Synthesis of Pentafluorophenoxy Lariat Ethers **20** and **21**.

A mixture of the lariat ether mesylate (14.1 mmole), cesium carbonate (6.90 g, 2.12 mmole), and pentafluorophenol (3.90 g, 21.2 mmole) in 250 ml of dry dimethylformamide was stirred at 105° for 2 days. The dimethylformamide was evaporated *in vacuo* and the residue was dissolved in dichloromethane

(100 ml), washed with water (2 x 100 ml) and brine (100 ml), dried over magnesium sulfate, and evaporated *in vacuo*.

sym-(Pentafluorophenoxy)dibenzo-16-crown-5 (**20**).

Chromatography on silica gel with dichloromethane-hexanes (2:1) as eluent gave 67% of a white solid with mp 135°; ir (deposit from dichloromethane solution on a sodium chloride plate): ν 1257 and 1120 (C-O), 1224 (C-F) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 3.36-3.94 (m, 4H), 4.09-4.20 (m, 4H), 4.37-4.45 (dd, 2H, $J = 4$ Hz), 4.50-4.58 (dd, 2H, $J = 4$ Hz), 4.85-4.93 (p, 1H), 6.82-6.99 (m, 8H); ^{19}F nmr (deuteriochloroform): δ -164.15 (t, 2F, $J = 20.9$ Hz), -163.72 (t, 1F, $J = 21.7$ Hz), -155.67 (t, 2F, $J = 20.9$ Hz).

Anal. Calcd. for $\text{C}_{25}\text{H}_{21}\text{F}_5\text{O}_6$: C, 58.60; H, 4.13. Found: C, 58.83; H, 4.07.

sym-(Pentafluorophenoxy)dicyclohexano-16-crown-5 (**21**).

Chromatography on silica gel with ethyl acetate-hexanes (1:2) as eluent provided 67% of a pale yellow oil; ir (neat): ν 1246 (CF), 1109 (CO) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.15-1.81 (m, 16H), 3.49-4.63 (m, 17H).

Anal. Calcd. for $\text{C}_{25}\text{H}_{33}\text{F}_5\text{O}_6$: C, 57.25; H, 6.34. Found: C, 57.39; H, 6.52.

Preparation of *N,N'*-Di(heptafluorobutyl) Ethylenediamide (**22**).

Ethylenediamine (0.90 g, 15 mmole) was dissolved in 40 ml of dry acetonitrile and 30 mmole of triethylamine was added. The mixture was cooled to 0° and heptafluorobutyl chloride (30 mmole) was added dropwise. Reaction conditions and the work-up procedure were the same as described for the preparation of lariat ether amides **7-9**. A white solid with mp 150-152° was obtained in 94% yield; ir (potassium bromide): ν 3325 (NH), 1710 (C=O) cm^{-1} ; ^1H nmr (dimethylsulfoxide- d_6): δ 3.38 (s, 4H), 9.53 (br s, 2H); ^{19}F nmr (acetone d_6): δ -76.84 (t, 6F, $J = 10$ Hz), -116.35 to -116.46 (m, 4F), -123.08 (d, 4F, $J = 4$ Hz).

Anal. Calcd. for $\text{C}_{10}\text{H}_6\text{F}_{14}\text{N}_2\text{O}_2$: C, 26.56; H, 1.34; N, 6.19. Found: C, 26.54; H, 1.25; N, 6.14.

Preparation of *N,N'*-Bis(1*H*,1*H*-perfluorobutyl) Ethylenediamine (**23**).

Diamide **22** (6.30 g, 14.0 mmole) dissolved in 75 ml of tetrahydrofuran was added dropwise into a stirred mixture of 75 ml of tetrahydrofuran and 2.50 g of lithium aluminum hydride at 0-10°. The mixture was refluxed for 48 hours and cooled. Aqueous 5% sodium hydroxide (15 ml) was added to the mixture at 0-10°. After stirring for 2 hours, the mixture was filtered and the residue was washed several times with 40-ml portions of hot tetrahydrofuran. The filtrate was evaporated *in vacuo* and the residue was dissolved in ethyl acetate. The solution was washed with water, dried over sodium sulfate, and evaporated *in vacuo* to give an oil in 85% yield; ir (neat): ν 3368 (NH) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.54 (br s, 2H), 2.80 (s, 4H), 3.14-3.30 (t, 4H, $J = 16$ Hz).

Anal. Calcd. for $\text{C}_{10}\text{H}_{10}\text{F}_{14}\text{N}_2$: C, 28.32; H, 2.38; N, 6.60. Found: C, 28.45; H, 2.52; N, 6.70.

Preparation of Partially Fluorinated Bis(crown ether)diamide **25**.

Carboxylic acid **24** (4.0 mmole) was added to 10 ml of dry benzene under nitrogen. After cooling to 0°, oxalyl chloride

(16.0 mmole) was added dropwise and the mixture was stirred at room temperature for 1 hour and then warmed to 60° for 1 hour. The mixture was evaporated *in vacuo* and the resultant acid chloride was used directly in the next step.

Diamine **23** (0.85 g, 2.0 mmole) was dissolved in 15 ml of dry acetonitrile and 4.0 mmole of triethylamine was added. The mixture was cooled to 0° and an acetonitrile solution of lariat ether acid chloride was added dropwise. Reaction conditions and the work-up procedure were the same as described for the preparation of lariat ether amides **7-9**. A white solid with mp 150-152° was obtained in 73% yield; ir (potassium bromide): ν 1674 (C=O), 1225, 1118 (CO) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 3.20 (s, 4H), 3.50-3.67 (t, 4H, $J = 16$ Hz), 3.87-4.32 (m, 30H), 6.80-6.98 (m, 16H). Although bis(crown ether)diamide **25** was not submitted for combustion analysis, satisfactory elemental analysis results were obtained for bis(crown ether)diamine **26** that was prepared by reduction of this precursor.

Preparation of Partially Fluorinated Bis(crown ether)diamine **26**.

A solution of **25** (2.0 mmole) in 20 ml of dry tetrahydrofuran was cooled at 0° under nitrogen and 25 ml of borane-tetrahydrofuran complex (1.0 *M* solution in tetrahydrofuran) was added dropwise over a period of 15 minutes. Reaction conditions and the workup procedure were the same as described for the preparation of lariat ether amine **4**. The crude product was purified by chromatography on silica gel with dichloromethane-methanol as eluent to provide an oil in 75% yield; ir (neat): ν 1224, 1115 (CO) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.90 (s, 4H), 3.15 (s, 4H), 3.31-3.48 (t, 4H, $J = 17$ Hz), 3.84-3.94 (m, 12H), 4.01-4.11 (m, 14H), 4.17-4.31 (m, 4H), 6.82-7.33 (m, 16H); ^{19}F nmr (deuteriochloroform): δ -84.17 (t, 6F, $J = 9$ Hz), -121.64 to -121.67 (m, 4F), -131.12 to -131.27 (m, 4F).

Anal. Calcd. for $\text{C}_{52}\text{H}_{58}\text{F}_{14}\text{N}_2\text{O}_{12}$: C, 53.43; H, 5.00; N, 2.39. Found: C, 53.18; H, 4.96; N, 2.70.

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