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Macrocyclic Ligands with Partially Fluorinated Sidearms: Synthesis and Metal Ion Complexation

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Abstract—Derivatives of aza-12-crown-4, aza-15-crown-5, aza-18-crown-6, 1,10-diaza-18-crown-6 and 1,4,8,12-tetraazacyclopentadecane with partially fluorinated substituents attached to nitrogen are prepared. Their efficiencies and selectivities in alkali metal and silver picrate extractions from aqueous solutions into chloroform are determined and compared with those of appropriate model compounds. Ionophores with longer spacers of $-CH_2OCH_2CH_2-$ and $-CH_2CH_2OCH_2CH_2-$ between the nitrogen atom(s) of the macroring and the perfluoroalkyl group(s) exhibit greater extraction efficiencies than do analogues with shorter spacers consisting of one or two methylene groups.

Introduction

Since Pedersen discovered that cyclic polyether compounds (crown ethers) possess unique complexation capabilities, there has been great interest in these compounds as complexing agents for a wide variety of metal ions.[1] Many different modifications have been made to probe the influence of ligand structure on the cation-complexing properties of crown ethers.[2] Although a wide variety of macrocyclic ligands with different donor atoms and other substituents have been prepared, only a very limited number of fluorine-containing macrocycles have appeared in the literature.

In the first report of perfluorocrown ethers by Lagow and coworkers, the compounds were synthesized by direct fluorination of the corresponding crown ethers.[3] Using the same approach, they later prepared several other perfluorinated macrocycles.[4] These compounds may have some medical applications as ^{19}F NMR imaging agents[5] and oxygen carriers.[4b] However, 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.[6]

Farnham and coworkers prepared partially fluorinated macrocyclic polyethers.[7] A remarkable property of such polyfluorinated crown ethers is their ability to complex anions, particularly fluoride ion.[7a] Kimura and coworkers synthesized a series of mono-, di- and tetrafluorinated tetraazacyclotetradecanes (cyclams) and demonstrated that these ligands form stable Cu(II) and Ni(II) complexes.[8] Plenio and Diodone showed that partially fluorinated crown ethers and cryptands prepared from small fluorine-containing building blocks form stable complexes with Group I metal ions.[9] Plenio has published an excellent review on the coordination chemistry of fluorine-containing ligands, including fluoro macrocycles.[10]

Shreeve and coworkers synthesized a series of 18-crown-6 derivatives which contain fluorinated side arms.[11] That such macrocycles are capable of forming stable complexes with lanthanum ion was demonstrated by an X-ray crystal structure.[11]

In a patent, Okahara and coworkers reported the preparation of fluorine-containing azacrown ethers by reaction of monoaza-15-crown-5, 2-(perfluorohexyl)ethyl tosylate and Na_2CO_3 in dioxane.[12] Although it was claimed that such compounds are useful in ion-selective transport of cations through liquid membranes, no data were provided. Using a similar approach, Quici and coworkers synthesized a cyclam derivative with highly fluorinated tails and found that its copper and cobalt complexes act as catalysts for hydrocarbon oxidation under fluorous biphasic (FB) conditions.[13]

Macrocyclic ligands with one or more fluorine-containing sidearms have potential applications in metal ion separations involving a fluorous phase[14] or supercritical carbon dioxide.[15]

We now report the preparation of a series of macrocyclic ligands **1**–**16** with partially fluorinated sidearms attached to

Keywords: ionophores; macrocycles; perfluoroalkyl compounds; complexation.

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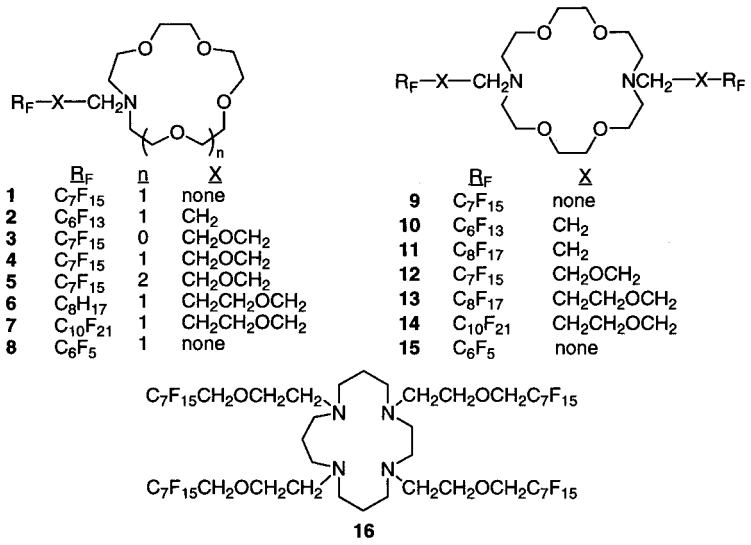
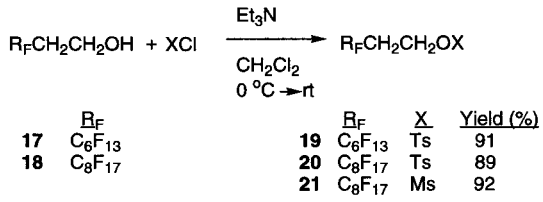


Figure 1. New macrocyclic ligands with partially fluorinated sidearms.

nitrogen (Fig. 1) and the evaluation of their metal ion complexation behavior. The objective of this research effort was the preparation of partially fluorinated macrocycles which will possess good solubility in nonpolar, partially fluorinated and chlorofluorinated hydrocarbon solvents or supercritical carbon dioxide, yet provide strong metal ion complexing ability. Aza-12-crown-4, aza-15-crown-5, aza-18-crown-6, and 1,10-diaza-18-crown-6 macrocycles were selected as starting materials in view of their potential for facile *N*-functionalization.[16] This strategy allows the introduction of fluorine-containing groups at specific sites in the macrocyclic ligands without forming a mixture of isomers.



Scheme 1. Synthesis of partially fluorinated tosylates and mesylate.

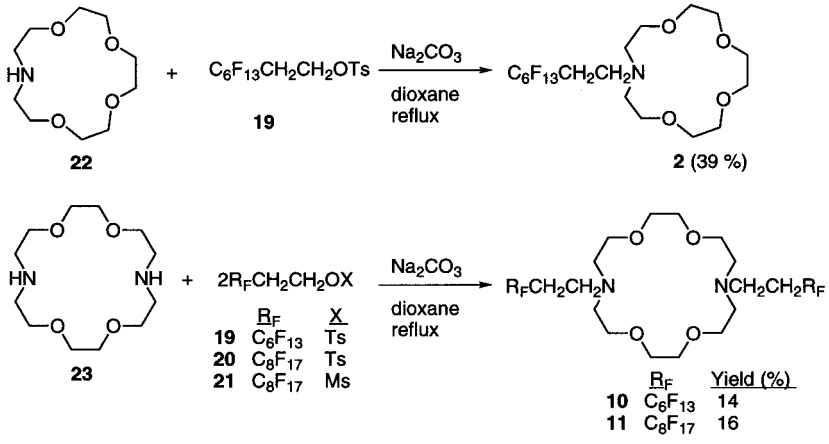
Also, macrocycles with mixed donor atoms form stable complexes with a wide variety of metal ions.[2c–f,17,18]

Results and Discussion

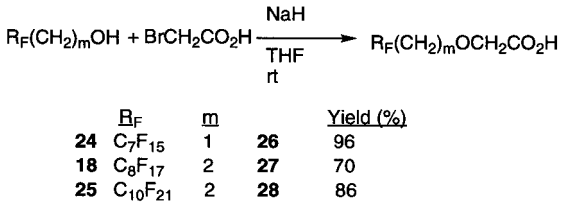
Synthesis of macrocycles with partially fluorinated sidearms

For the preparation of macrocyclic ligands with partially fluorinated sidearms, several synthetic approaches were explored.

The preparation of a fluorine-containing azacrown ether by reaction of aza-15-crown-5 and 2-(perfluorohexyl)ethyl tosylate was described in a patent.[12] To explore the scope of this reaction, 1H,1H,2H,2H-perfluoroalkyl tosylates **19** and **20** and mesylate **21** were synthesized in high yields by reaction of the corresponding alcohols **17** and **18** and *p*-toluenesulfonyl or methanesulfonyl chloride (Scheme 1). In the next step (Scheme 2), reaction of aza-15-crown-5 (**22**), partially fluorinated tosylate **19** and Na_2CO_3 in refluxing dioxane gave a 39% yield **2** (compared with a reported[12]

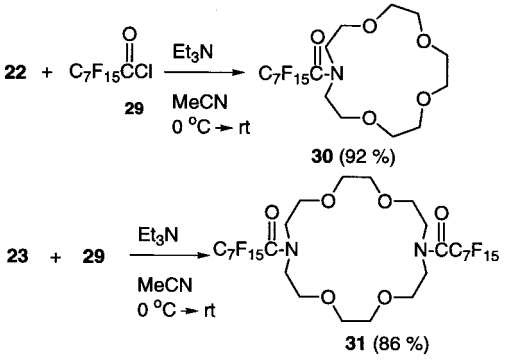


Scheme 2. Synthesis of mono- and diazacrown ethers with $R_FCH_2CH_2-$ sidearms.



	R_F	m		Yield (%)
24	C_7F_{15}	1	**26**	96
18	C_8F_{17}	2	**27**	70
25	$C_{10}F_{21}$	2	**28**	86

Scheme 3. Synthesis of partially fluorinated carboxylic acids.



Scheme 4. Reactions of mono- and diazacrown ethers with perfluorooctanoyl chloride.

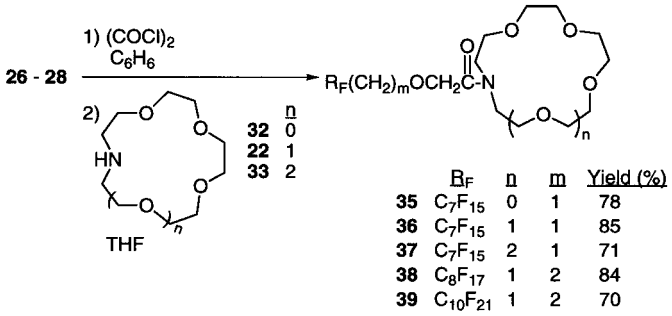
58% yield). Analogous reactions of two equivalents of partially fluorinated tosylates **19** and **20** with 1,10-diaza-18-crown-6 (**23**) gave only very low yields (14–16%) of the desired products **10** and **11**, respectively. Variation of the base from Na_2CO_3 to K_2CO_3 and changing the solvent from dioxane to MeCN did not increase the yield. Replacement of the partially fluorinated tosylate **20** with the corresponding mesylate **21** failed to enhance the yield of macrocycle **10**. From the reaction of commercially available 1-iodo-1H,1H,2H,2H-perfluorodecane with **23** and K_2CO_3 in refluxing MeCN, no **10** could be isolated.

The next synthetic strategy for the preparation of macrocycles with partially fluorinated sidearms involved coupling of a fluorine-containing acid chloride with an azacrown ether and subsequent reduction of the resultant amide to an amine. Only perfluorinated acid chlorides are commercially available. After reduction of the resultant partially fluorinated macrocyclic amide there would be only a single methylene group between the nitrogen of the macroring and the perfluoroalkyl group. Therefore the strongly electron-withdrawing effect of the perfluoroalkyl group might diminish the electron density of that potential donor atom. Interposition of a longer spacer unit between the nitrogen of the macroring and the perfluoroalkyl substituent should enhance metal ion binding. To this end, partially fluorinated carboxylic acids **26**–**28** with spacers of $-CH_2OCH_2-$ and $-CH_2CH_2OCH_2-$ between the perfluoroalkyl group and carboxylic acid functionality were prepared (Scheme 3). Thus, partially fluorinated alcohols **24**, **18** and **25** were reacted with NaH and bromoacetic acid in THF at room temperature to provide partially fluorinated carboxylic acids **26**–**28** in very good yields (70–96%).

Reactions of commercially available perfluorooctanoyl chloride (**29**) with aza-15-crown-5 (**22**) and 1,8-diaza-18-crown-6 (**23**) in the presence of Et_3N in MeCN gave high yields of the corresponding macrocyclic amides **30** and **31**, respectively (Scheme 4). Partially fluorinated carboxylic acids **26**–**28** were converted into the corresponding partially fluorinated acid chlorides by reaction with oxalyl chloride in benzene (Scheme 5). These acid chlorides were reacted with aza-12-crown-4 (**35**), aza-15-crown-5 (**22**), aza-18-crown-6 (**33**), 1,10-diaza-18-crown-6 (**23**) and 1,4,8,12-tetraazacyclopentadecane (**34**) in the presence of Et_3N in MeCN to produce 70–95% yields of the corresponding macrocyclic amides **35**–**39** (Scheme 5), diamides **40**–**42** and tetramide **43** (Scheme 6). Reduction of **30**, **31** and **35**–**43** with BH_3–THF complex in THF gave corresponding macrocyclic ligands **1**, **3**–**7**, **9**, **12**–**14** and **16** in high yields (70–90%). Thus, this approach is demonstrated to be convenient and quite general for the *N*-functionalization of different azamacrocycles with partially fluorinated substituents.

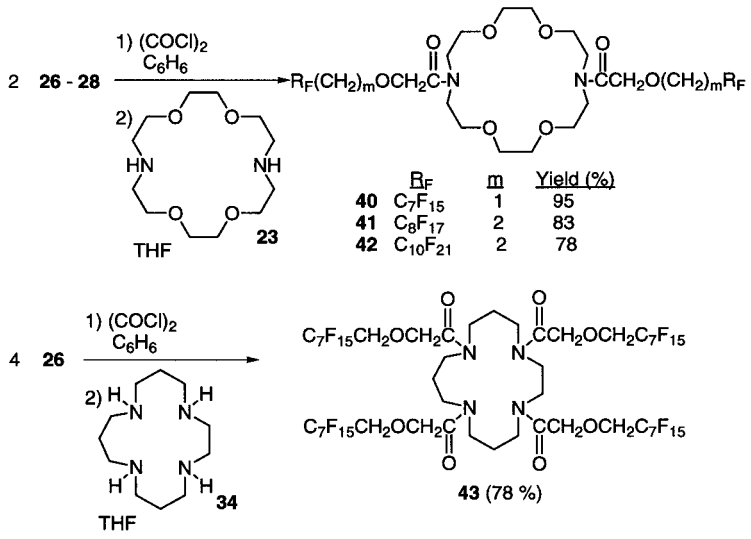
In addition to their use in the preparation of macrocyclic amides described above, partially fluorinated carboxylic acids **27** and **28** can be reduced with BH_3–THF in THF at room temperature to the corresponding partially fluorinated alcohols **44** and **45** as shown in Scheme 7. In view of the ease of isolation and purification of these alcohols, this approach is more convenient than one in which the alcohols **24** and **18** would be reacted with base and THP-protected 2-bromoethanol.

Pentafluorobenzyl derivatives of aza-15-crown-5 (**22**) and 1,10-diaza-18-crown-6 (**23**) were also prepared (Scheme 8). Reactions of these azacrown ethers with commercially available pentafluorobenzyl bromide and K_2CO_3 in MeCN at room temperature gave *N*-pentafluorobenzyl aza-15-crown-5 (**8**) and di-(*N*-pentafluorobenzyl) 1,10-diaza-18-crown-6 (**15**) in good yields (60–63%).

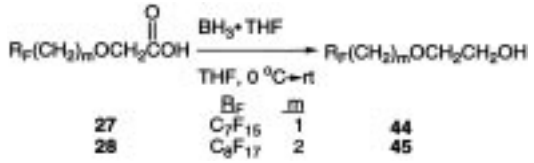


	R_F	n	m	Yield (%)
35	C_7F_{15}	0	1	78
36	C_7F_{15}	1	1	85
37	C_7F_{15}	2	1	71
38	C_8F_{17}	1	2	84
39	$C_{10}F_{21}$	1	2	70

Scheme 5. Synthesis of monoazacrown ether amides with partially fluorinated sidearms.



Scheme 6. Synthesis of diazacrown ether diamides and a tetraazamacrocycle tetraamide with partially fluorinated sidearms.



Scheme 7. Synthesis of partially fluorinated alcohols.

To provide model compounds for use in the metal ion complexation studies, aza-15-crown-5 (**22**) and 1,10-diaza-18-crown-6 (**23**) were *N*-alkylated by reaction with 1-bromodecane and K_2CO_3 in MeCN at reflux to give **46** and **47**, respectively, in high yields (88–93%, Scheme 9). Compound **47** has been prepared earlier by two other methods.[19]

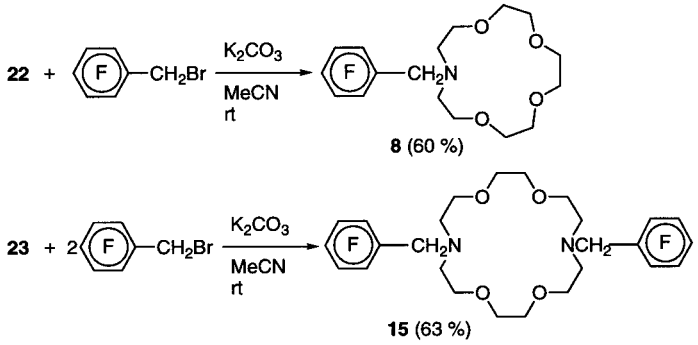
Identities of the new partially fluorinated macrocyclic ligands were confirmed by IR, ^1H and ^{19}F NMR spectroscopy and by combustion analyses.

Alkali metal and silver picrate extractions

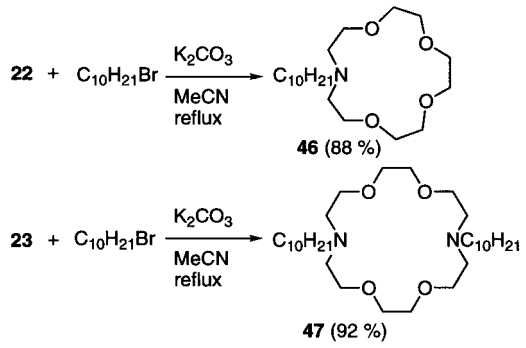
Having accomplished the synthesis of a variety of macrocycles with partially fluorinated sidearms, we next sought to investigate the various factors that affect their metal ion complexation characteristics. The following structural variations were probed: (i) the cavity size of the macrocycle; (ii) the number and type of donor atoms; (iii) the length of the spacer that separates the nitrogen atoms(s) of the macroring from the fluoroalkyl group(s); and (iv) the nature of the fluorine-containing group (partially fluorinated alkyl or aralkyl).

The metal cation complexing abilities of partially fluorinated aza-12-crown-4, aza-15-crown-5 and aza-18-crown-6 derivatives, partially fluorinated 1,10-diaza-18-crown-6 derivatives, and four model compounds (i.e. *N*-benzyl aza-15-crown-5,[20] *N*-decyl aza-15-crown-5, *N*,*N*′-dibenzyl 1,10-diaza-18-crown-6,[21] *N*,*N*′-didecyl 1,10-diaza-18-crown-6) were assessed by solvent extraction of alkali metal and silver picrates from aqueous solutions into chloroform.[22] The extraction results are presented in Tables 1–4.

Highest extraction of Na^+ normally would be anticipated for a 15-crown-5 ligand based on its ring size.[1,23] In agreement, the data in Table 1 show the following orders of alkali metal picrate extraction by the partially fluorinated aza-15-crown-5 derivatives: for **1**, $Na^+ > Li^+ > K^+ \approx Rb^+ \approx Cs^+$; for **2**, $Na^+ > K^+ \approx Li^+ \approx Rb^+ \approx Cs^+$; and for **4** and **6**–**8**, $Na^+ > K^+ > Rb^+ > Li^+ \approx Cs^+$. Similarly, preferred extraction of Na^+ is noted for two model compounds: for *N*-decyl aza-15-crown-5, $Na^+ > K^+$, $Li^+ \approx Rb^+ > Cs^+$; and for *N*-benzyl aza-15-crown-5: $Na^+ > K^+ > Li^+ \approx Rb^+ > Cs^+$.



Scheme 8. Reactions of mono- and diazacrown ethers with pentafluorobenzyl bromide.



Scheme 9. Synthesis of *N*-decyl mono- and diazacrown ether compounds.

For the partially fluorinated aza-15-crown-5 macrocycles, the Na^+ extraction efficiency is enhanced as the length of the spacer between the nitrogen atom of the macroring and the perfluoroalkyl unit is increased: **1**≪**2**<**4**<**6**, **7**. Extraction efficiencies for alkali metal picrates by the partially fluorinated macrocycles **4**, **6** and **7** are comparable with those for *N*-decyl aza-15-crown-5. Thus the $-CH_2OCH_2CH_2-$ and $-CH_2CH_2OCH_2CH_2-$ spacers between the macroring and perfluoroalkyl moieties are long enough to effectively attenuate the electron-withdrawing effects of the perfluoroalkyl groups. Macrocycle **8** that contains a pentafluorobenzyl group exhibits similar selectivity and efficiency for Na^+ extraction as do the non-fluorinated analog *N*-benzyl aza-15-crown-5 and partially fluorinated macrocycle **2**.

Based on the metal ion-macroring size compatibility concept, highest extraction of K^+ is anticipated for partially fluorinated 1,10-diaza-18-crown-6 derivatives and their nonfluorinated analogs.[1,23] In agreement, the data in Table 2 show the following alkali metal picrate extraction orders for partially fluorinated compounds **9** and **11**–**15**, as well as for *N*,*N*′-didecyl 1,10-diaza-18-crown-6 and *N*,*N*′-dibenzyl 1,10-diaza-18-crown-6: $K^+>Rb^+>Na^+>Cs^+>Li^+$.

Partially fluorinated macrocycles **12**–**14** which have longer spacer units between the macroring and the perfluoroalkyl group exhibit greater K^+ extraction efficiency than do ligands **9** and **11** which have shorter spacers. The K^+ extraction efficiencies of **12**–**14** are essentially the same as that for the *N*,*N*′-didecyl 1,10-diaza-18-crown-6. The K^+ extraction efficiency of *N*, *N*′-di(pentafluorobenzyl) 1,10-diaza-18-crown-6 (**15**) is slightly higher than that of *N*, *N*′-dibenzyl 1,10-diaza-18-crown-6.

The strong electron-withdrawing property of fluorine atoms in the sidearm is reflected in the amide carbonyl stretching frequencies, $\nu_{C=O}$, of 1681, 1659 and 1651 cm^{-1} for partially fluorinated aza-15-crown-5 compounds **30**, **36** and **38**, respectively, and of 1670, 1659 and 1650 cm^{-1} for partially fluorinated 1,10-diaza-18-crown-6 compounds **31**, **40** and **41**, respectively. For comparison with compounds in the latter series, $\nu_{C=O}$ for *N*,*N*′-didecanoyl 1,10-diaza-18-crown-6 is 1639 cm^{-1}.[19b]

The data presented in Table 3 illustrates the effect of the macrocycle ring size variation for partially fluorinated azacrown ether compounds **3**–**5** with a common ($-CH_2OCH_2CH_2C_7F_{15}$) sidearm. The selectivity order for these three partially fluorinated macrocycles are: for **3**, $Li^+>Rb^+>K^+\approx Cs^+>Na^+$; for **4**, $Na^+>K^+>Rb^+>''' Li^+>Cs^+$; and for **5**, $K^+>Rb^+>Na^+\approx Cs^+>Li^+$. Thus, for each ligand, the best extracted alkali metal cation is that which would be predicted based on the match between the cation and ligand cavity diameters.

Table 1. Alkali metal picrate extractions from aqueous solutions into chloroform by partially fluorinated aza-15-crown-5 derivatives **1**, **2**, **4** and **6**–**8** and by relevant model compounds

Ionophore	Picrate extracted (%)				
	$Li^{\pm}$	$Na^{\pm}$	$K^{\pm}$	$Rb^{\pm}$	$Cs^{\pm}$
1	1.2±0.4	10.7±0.5	0.4±0.7	0.3±0.5	0.0±0.5
2	3.3±0.3	37.7±0.0	4.0±0.4	3.1±0.9	2.7±0.4
4	5.8±0.5	48.8 ±1.0	25.6±0.3	11.5±0.9	4.6±0.5
6	7.2±0.6	52.6±0.3	25.0±0.4	11.7±0.2	4.8±0.3
7	1.8±0.7	56.8±0.5	30.7±0.7	11.9±0.7	4.3±0.3
8	1.5±0.5	42.5±0.5	5.6±0.5	3.8±0.5	1.0±0.7
N-decyl aza-15-crown-5	15.5±0.3	58.3±0.0	17.6±0.0	15.1±0.5	11.9±0.5
N-benzyl aza-5-crown-5	7.2±0.7	35.5±0.5	13.5±0.6	6.8±0.5	5.5±0.3

Table 2. Alkali metal picrate extractions from aqueous solutions into chloroform by partially fluorinated diaza-18-crown-6 derivatives **9** and **11**–**15** and by relevant model compounds

Ionophore	Picrate extracted (%)				
	$Li^{\pm}$	$Na^{\pm}$	$K^{\pm}$	$Rb^{\pm}$	$Cs^{\pm}$
9	0.6±0.0	2.4±0.6	29.5±0.5	3.9±0.2	0.2±0.6
11	2.9±0.5	6.1±0.6	46.8±0.5	15.3±0.2	3.7±0.6
12	5.8±0.7	15.2 ±0.5	69.9 ±0.2	51.2 ±0.5	12.2 ±0.4
13	8.1±0.5	22.1±0.5	73.3±0.6	52.8±0.0	13.6±0.5
14	6.6±0.6	22.6±0.5	72.1±0.3	56.4±0.6	14.1±0.7
15	1.7±0.6	10.4±0.5	58.9±0.3	31.4±0.3	3.4±0.4
N,*N*′-didecyl diaza-18-crown-6	15.4±0.5	31.9±0.5	69.8±0.2	11.6±0.9	16.2±0.8
N,*N*′-dibenzyl diaza-18-crown-6	6.8±0.3	10.4±0.7	45.7±0.5	27.6±0.4	7.2±0.2

Table 3. Alkali metal picrate extractions from aqueous solutions into chloroform by aza-12-crown-4, aza-15-crown-5 and aza-18-crown-6 compounds with a common, partially fluorinated *N*-substituent

Ionophore	Picrate extracted (%)				
	$Li^{\pm}$	$Na^{\pm}$	$K^{\pm}$	$Rb^{\pm}$	$Cs^{\pm}$
3	25.7±0.6	1.6±0.4	3.2±0.5	4.2±0.3	2.9±0.9
4	5.8±0.5	48.6±1.1	25.6±0.3	11.6±0.9	4.6±0.5
5	26.5±0.7	29.5±0.5	84.0±0.2	74.2±0.5	28.2±0.9

It is noted that *N*-1H,1H-3-oxaperfluoroundecyl aza-18-crown-6 (**5**, Table 3), exhibits a higher K^+ extraction efficiency than does its diaza-18-crown-6 analogue **12** (Table 2), while the extraction selectivity order remains the same. This is in good agreement with observations of Frensdorff that substitution of N or S for O in 18-crown-6 and dibenzo-18-crown-6 reduces the stability constant for K^+ complexation due a decrease in the negative charge on the heteroatom.[24]

Recently Tsukube and coworkers have reported that some lariat azacrown ether and multi-armed macrocyclic polyamine derivatives form strong complexes with Ag^+.[25] Therefore the affinity of partially fluorinated monoaza, diaza and tetraaza derivatives toward Ag^+ was investigated. The data in Table 4 shows that partially fluorinated 1,10-diaza-18-crown-6 compounds **11**–**13** exhibit very high extraction efficiency for Ag^+ that is comparable to that for *N*,*N*′-didecyl 1,10-diaza-18-crown-6. The greater Ag^+ extraction efficiencies of partially fluorinated diaza-18-crown-6 derivatives than for aza-18-crown-6 analogues is attributed to the presence of the second nitrogen donor atom in the former. The partially fluorinated tetraaza macrocycle **16** exhibited high Ag^+ extraction efficiency with formation of a silver mirror.

The fluorine effect on Ag^+ extraction efficiency by partially fluorinated macrocycles is best assessed for macrocycles **9**, **11** and **12** which have the same ring size and the same perfluoroalkyl group length, but different spacers between the macroring and the perfluoroalkyl moiety. Macrocycle **9** with a single methylene group as the spacer exhibits much lower Ag^+ extraction efficiency than does ligand **11**, which has two methylene groups in the spacer. Further elongation of the spacer to $-CH_2OCH_2CH_2-$ in ionophore **12** further enhances the Ag^+ extraction efficiency.

Table 4. Silver picrate extractions from aqueous solutions into chloroform by partially fluorinated monoaza, diaza and tetraaza macrocycles

Ionophore	Picrate extracted (%)
4	83.9±0.5
5	81.4±0.2
9	37.7±0.8
11	91.0±0.5
12	93.9±0.3
13	97.4±0.5
15	83.1±0.3
16	93.1±0.3[a]
N-decyl aza-15 crown-5	76.7±0.3
N,*N*′-didecyl 1,10-diaza-18-crown-6	95.1±1.3

[a] A silver mirror was formed.

Additional investigations of the complexing abilities of these new partially fluorinated macrocycles are ongoing in our laboratory and the results will be reported in due course.

Conclusions

A series of *N*-substituted aza-, diaza-, and tetraazacrown ethers with partially fluorinated substituents has been synthesized. Spacer units of $-(CH_2)_n-$, and $-(CH_2)_nO(CH_2)_m-$ separate the nitrogen atom(s) of the macroring from the perfluoroalkyl group(s). The metal ion complexation properties of several of these new macrocyclic ligands have been assessed by solvent extraction of alkali metal and silver picrates from aqueous solutions into chloroform. Macrocycles with longer spacers between the macroring and perfluoroalkyl group are found to exhibit greater extraction efficiencies than do analogues with shorter spacers.

Due to their high fluorine content and strong metal ion complexation abilities, these macrocyclic ligands are expected to have applications in metal ion separations involving a fluorous phase[14] or supercritical carbon dioxide.[15]

Experimental

General

Starting materials and solvents were purchased from commercial sources and used without further purification unless otherwise noted. Tetrahydrofuran (THF) was distilled from benzophenone ketyl under nitrogen. Melting points were determined with a MEL-TEMP™ capillary melting point apparatus and are uncorrected. Infrared spectra were recorded as films deposited from CH_2Cl_2 solutions onto NaCl plates. NMR spectra were recorded in $CDCl_3$ or CD_3OCD_3 with TMS as the internal standard for ^1H (200 or 300 MHz) or $CFCl_3$ as the internal standard for ^{19}F (282.4 MHz). Thin-layer chromatography was performed on silica gel 60 F_{254} plates from Analtech and visualized by UV irradation and/or iodine vapor. Elemental analyses were performed by Desert Analytics Laboratory of Tucson, AZ.

General procedure for the preparation of 1H,1H,2H,2H-perfluoroalkyl tosylates 19 and 20 and mesylates 21

To an ice-cold stirred solution of the perfluoro-alcohol **17** or **18** (12 mmol) and Et_3N (15 mmol) in CH_2Cl_2 (20 mL) was added dropwise a solution of *p*-toluenesulfonyl or methanesulfonyl chloride (12 mmol) in 20 mL of CH_2Cl_2. After addition was complete (30 min), the reaction mixture was allowed to come to room temperature and stirring was continued overnight. The CH_2Cl_2 solution was washed with water, dried over $MgSO_4$ and evaporated in vacuo to give a white solid which was recrystallized from MeOH.

1H,1H,2H,2H-Perfluorooctyl tosylate (19). 91% yield of white solid with mp 70–71°C. ^1H NMR ($CDCl_3$): δ 2.46 (s+m, 5H), 4.30 (t, 2H, J=6 Hz), 7.38 (d, 2H, J=8 Hz), 8.82 (d, 2H, J=8 Hz). ^{19}F NMR ($CDCl_3$): δ −81.2 (s, 3F),

−113.9 to −114.2 (m, 2F), −123.4 (s, 2F), −124.1 (s, 2F), 125.0 (s, 2F), −126.6 to −126.7 (m, 2F). Anal. calcd for $C_{15}H_{11}F_{13}O_3S$: C, 34.76; H, 2.14. Found: C, 34.44; H, 2.01.

1H,1H,2H,2H-Perfluorodecyl tosylate (20). 89% yield of white solid with mp 49–50°C. ^{1}H NMR ($CDCl_3$): δ 2.47 (s+m, 5H), 4.30 (t, 2H, J=6 Hz), 7.38 (d, 2H, J=8 Hz), 7.82 (d, 2H, J=8 Hz). ^{19}F NMR ($CDCl_3$): δ −81.2 (s, 3F), −114.0 (s, 2F), −122.2 to −122.4 (m, 6F), −123.2 (s, 2F), −124.0 (s, 2F), −126.5 to −126.6 (m, 2F). Anal. calcd for $C_{17}H_{11}F_{17}O_3S$: C, 33.02; H, 1.79. Found: C, 33.02; H, 1.94.

1H,1H,2H,2H-Perfluorodecyl mesylate (21). 92% yield of white solid with mp 72–73°C. ^{1}H NMR ($CDCl_3$): δ 2.53–2.70 (m, 2H), 3.07 (2, 3H), 4.53 (t, 2H, J=6 Hz). ^{19}F NMR ($CDCl_3$): δ −81.3 (s, 3F), −114.0 to −114.2 (m, 2F), −122.2 to −122.4 (m, 6F), −123.2 (s, 2F), −124.0 (s, 2F), −126.6 to −126.7 (m, 2F). Anal. calcd for $C_{11}H_7F_{17}O_3S$: C, 24.36; H, 1.30. Found: C, 23.95; H, 0.92.

General procedure for the preparation of partially fluorinated macrocycles 10 and 11

A mixture of 1.05 g (4.0 mmol) of 1,10-diaza-18-crown-6, 8.0 mmol of the perfluoroalkyl tosylate (**19** or **20**), Na_2CO_3 (0.85 g, 8.0 mmol) and 30 mL of dioxane was refluxed under nitrogen for 48 h. After cooling to room temperature, water was added and the dioxane evaporated in vacuo. The aqueous mixture was extracted with CH_2Cl_2. The CH_2Cl_2 extracts were combined, dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by column chromatography on silica gel with CH_2Cl_2 (to remove the unreacted perfluoroalkyl tosylate) and then with EtOAc as eluents. The EtOAc fractions were combined and evaporated in vacuo to give a white solid, which was recrystallized from MeOH.

***N,N′*-Bis(1H,1H,2H,2H-Perfluorooctyl 1,10-diaza-18-crown-6 (10).** 14% yield of fluffy white solid with mp 60–62°C. ^{1}H NMR ($CDCl_3$): δ 2.14–2.41 (m, 4H), 2.79 (t, 8H, J=6 Hz), 2.73 (t, 4H, J=8 Hz), 3.58–3.63 (m, 16H). ^{19}F NMR ($CDCl_3$): δ −81.3 (s, 6F), −114.4 to −114.6 (m, 4F), −122.4 (s, 4F), −123.4 (s, 4F), −124.0 (s, 4F), −126.6 to −126.7 (m, 4F). Anal. calcd for $C_{28}H_{32}F_{26}N_2O_4$: C, 35.23; H, 3.38; N, 2.93. Found: C, 35.23; H, 3.25, N, 2.93.

***N,N′*-Bis(1H,1H,2H,2H-Perfluorodecyl 1,10-diaza-18-crown-6 (11).** 16% yield of fluffy white solid with mp 60–62°C. ^{1}H NMR ($CDCl_3$): δ 2.15–2.43 (m, 4H), 2.79 (t, 8H, J=6 Hz), 2.89 (t, 4H, J=8 Hz), 3.57–3.62 (m, 16H). ^{19}F NMR ($CDCl_3$): δ −81.2 (s, 6F), −114.3 to −114.6 (m, 4F), −122.4 (s, 12F), −123.2 (s, 4F), −123.9 (s, 4F), −126.6 (s, 4F). Anal. calcd for $C_{32}H_{32}F_{34}N_2O_4$: C, 33.29; H, 2.79; N, 2.42. Found: C, 32.87; H, 2.84; N, 2.49.

General procedure for the preparation of partially fluorinated carboxylic acids 26–28

To a mixture of NaH (0.86 g, 36 mmol) and 30 mL of dry THF under nitrogen, a solution of 6.0 mmol of perfluoroalcohol **24**, **18** or **25** dissolved in 30 mL of dry THF was added dropwise over a 30 min period. The mixture was stirred for 1 h at room temperature and a solution of 12.0 mmol of bromoacetic acid dissolved in 30 mL of THF was added dropwise over a period of 1 h. The mixture was stirred for 24 h and then the excess NaH was destroyed by careful addition of water. The THF was evaporated in vacuo. To the residue, 50 mL of water was added and the aqueous mixture was acidified with aqueous 6 N HCl and extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with water, dried over Na_2SO_4 and evaporated in vacuo. The crude product was recrystallized from hexanes to give a white solid.

1H,1H-Perfluorooctyloxyacetic acid (26). 96% yield of white solid with mp 55–56°C. IR (NaCl plate): 3510–2855 (COOH), 1728 (C=O) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 4.13 (t, 2H, J=14 Hz), 4.32 (s, 2H). ^{19}F NMR ($CDCl_3$): δ −81.0 (s, 3F), −120.1 to −120.2 (m, 2F), −122.3 (s, 4F), −123.0 (s, 2F), −123.6 (s, 2F), −126.3 to −126.4 (m, 2F). Anal. calcd for $C_{10}H_5F_{15}O_3$: C, 26.22; H, 1.10. Found: C, 26.16; H, 0.97.

1H,1H,2H,2H-Perfluorodecyloxyacetic acid (27). 70% yield of white solid with mp 47–48°C. IR (NaCl plate): 3500–2850 (COOH), 1734 (C=O) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.66–2.05 (m, 2H), 3.34 (t, 2H, J=6 Hz), 3.65 (s, 2H). ^{19}F NMR ($CDCl_3$): δ −81.0 (s, 3F), −113.5 to −113.8 (m, 2F), −122.0 to −122.2 (m, 6F), −123.0 (s, 2F), −123.9 (s, 2F), −126.3 to −126.4 (m, 2F). Anal. calcd for $C_{12}H_7F_{17}O_3$: C, 27.60; H, 1.35. Found: C, 27.64; H, 1.37.

1H,1H,2H,2H-Perfluorododecyloxyacetic acid (28). 86% yield of white solid with mp 95–96°C. IR (NaCl plate): 3550–2835 (COOH), 1732 (C=O) cm^{-1}. ^{1}H NMR (acetone-d_6): δ 2.40–2.58 (m, 2H), 3.73 (t, 2H, J=8 Hz), 4.16 (s, 2H). ^{19}F NMR (acetone-d_6): δ −81.2 (s, 3F), −113.3 (s, 2F), −121.8 (s, 10F) −122.8 (s, 2F), −123.7 (s, 2F), −126.3 (s, 2F). Anal. calcd for $C_{14}H_7F_{21}O_3$: C, 27.02; H, 1.13. Found: C, 26.77; H, 0.92.

General procedure for the preparation of partially fluorinated macrocyclic amides 30, 31 and 35–43

To a solution of the partially fluorinated carboxylic acid **26**–**28** (6.0 mmol) in benzene (15 mL) at 0°C under nitrogen, oxalyl chloride (25 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 1 h, heated at 60°C for 1 h and evaporated in vacuo to give the corresponding acid chloride which was used immediately in the next step. (Perfluorooctanoyl chloride **29** is commercially available.)

The aza macrocycles (6.0 mmol for monoazacrown ethers, 3.0 mmol for diazacrown ethers, and 1.5 mmol for the tetraaza macrocycle) and Et_3N (6.0 mmol) were dissolved in MeCN (15 mL) and the solution was cooled to O°C. An MeCN solution of the acid chloride was added dropwise during a period of 30 min. The mixture was allowed to warm to room temperature and stirring was continued overnight. The mixture was evaporated in vacuo and the residue was dissolved in EtOAc. This solution was washed with 0.6 N HCl, water, 0.6 M aq $NaHCO_3$ and water, dried over Na_2SO_4 and evaporated in vacuo to produce the

partially fluorinated macrocyclic amide. (Although macrocyclic amides **30**, **31** and **35–43** were not submitted for combustion analysis, satisfactory combustion analysis results were obtained for each macrocycle that was prepared by the reduction of these precursors.)

***N*-Perfluorooctanoyl aza-15-crown-5 (30).** 92% yield of yellowish oil. IR (NaCl plate): 1681 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.63–3.71 (m, 20H). ^{19}F NMR ($CDCl_3$): δ −80.9 (s, 3F), −111.2 to −111.3 (m, 2F), −120.5 to −120.9 (m, 4F), −122.7 (s, 2F), −122.8 (s, 2F), −126.2 to −126.4 (m, 2F).

***N,N′*-Bis(Perfluorooctanoyl 1,10-diaza-18-crown-6 (31).** 86% yield of white solid with mp 72–74°C. IR (NaCl plate): 1670 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.56–3.76 (m, 24H). ^{19}F NMR ($CDCl_3$): δ −80.8 (s, 6F), −111.0 to −111.2 (m, 4F), −120.5 to −120.9 (m, 8F), −122.1 (s, 4F), −122.7 (s, 4F), −126.1 to −126.3 (m, 4F).

***N*-2H,2H,4H,4H-3-Oxaperfluoroundecanoyl aza-12-crown-4 (35).** 78% yield of yellowish oil. IR (NaCl plate): 1657 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.40 (t, 2H, J=6 Hz), 3.52 (t, 2H, J=6 Hz), 3.57–3.66 (m, 8H), 3.76 (t, 2H, J=6 Hz), 3.98 (t, 2H, J=6 Hz), 4.13 (t, 2H, J=15 Hz), 4.52 (s, 2H). ^{19}F NMR ($CDCl_3$): δ −81.3 (s, 3F), −120.4 to −120.6 (m, 2F), −122.6 (s, 4F), −123.3 (s, 2F), −123.9 (s, 2F), −126.7 (s, 2F).

***N*-2H,2H,4H,4H-3-Oxaperfluoroundecanoyl aza-15-crown-5 (36).** 85% yield of yellowish oil. IR (NaCl plate): 1659 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.46 (t, 2H, J=6 Hz), 3.56–3.72 (m, 16H), 3.81 (t, 2H, J=6 Hz), 4.15 (t, 2H, J=14 yHz), 4.43 (s, 2H). ^{19}F NMR ($CDCl_3$): −80.9 (s, 3F), −120.1 to −120.2 (m, 2F), −122.2 (s, 4F), −122.9 (s, 2F), −123.4 (s, 2F), −126.2 to −126.3 (m, 2F).

***N*-2H,2H,4H,4H-3-Oxaperfluoroundecanoyl aza-18-crown-6 (37).** 71% yield of colorless oil. IR (NaCl plate): 1659 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.56 (t, 2H, J=6 Hz), 3.62–3.68 (m, 20H), 3.74 (t, 2H, J=6 Hz), 4.10–4.15 (t, 2H, J=15 Hz), 4.47 (s, 2H). ^{19}F NMR ($CDCl_3$) δ −81.3 (s, 3F), −120.4 to −120.5 (m, 2F), −122.6 (s, 4F), −123.3 (s, 2F), −123.8 (s, 2F), −126.6 to −126.7 (m, 2F).

***N*-2H,2H,4H,4H,5H,5H-3-Oxaperfluorotridecanoyl aza-15-crown-5 (38).** 84% yield of yellowish oil. IR (NaCl plate): 1651 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.36–2.58 (m, 2H), 3.46 (t, 2H, J=6 Hz), 3.58–3.72 (m, 18H), 3.65 (t, 2H, J=6 Hz), 4.27 (s, 2H). ^{19}F NMR ($CDCl_3$): δ: −81.0 (s, 3F), −113.5 to −113.7 (m, 2F), −121.9 to −122.2 (m, 6F), −122.9 (s, 2F), −123.8 (s, 2F), −126.2 to −126.4 (m, 2F).

***N*-2H,2H,4H,4H,5H,5H-3-Oxaperfluoropentadecanoyl aza-15-crown-5 (39)**: 70% yield of an oil that solidifed on standing. IR (NaCl plate): 1650 (C=O) cm^{-1}. ^1H NMR (acetone-d_6): δ 2.47–2.64 (m, 2H), 3.46 (q, 4H, J=6 Hz), 3.54–3.65 (m, 14H), 3.75 (t, 2H, J=6 Hz), 4.28 (s, 2H). ^{19}F NMR (acetone-d_6): δ −81.4 (s, 3F), −113.5 (s, 2F), −122.1 (s, 10F), −123.0 (s, 2F), −123.9 (s, 2F), −126.5 (s, 2F).

***N,N′*-Bis(2H,2H,4H,4H-3-Oxaperfluoropentadecanoyl 1,10-diaza-18-crown-6 (40).** 95% yield of white solid with mp 76–77°C. IR (NaCl plate): 1659 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.45–3.64 (m, 24H), 4.13 (t, 4H, J=14 Hz), 4.40 (s, 4H). ^{19}F NMR ($CDCl_3$): δ −81.2 (s, 6F), −120.4 (s, 4F), −122.5 (s, 8F), −123.2 (s, 4F), −123.8 (s, 4F), −126.6 (s, 4F).

***N,N′*-Bis(2H,2H,4H,4H,5H,5H-3-Oxaperfluorotridecanoyl 1,10-diaza-18-crown-6 (41).** 83% yield of white solid with mp 63–65°C. IR (NaCl plate): 1650 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.21–2.54 (m, 4H), 3.36–3.45 (m, 24H), 3.65 (t, 4H, J=8 Hz), 4.05 (s, 4H). ^{19}F NMR ($CDCl_3$): δ −81.2 (s, 6F), −113.8 to −114.0 (m, 4F), −122.4 (s, 12F), −123.2 (s, 4F), −124.1 (s, 4F), −126.6 (s, 4F).

***N,N′*-Bis(2H,2H,4H,4H-3-Oxaperfluoropentadecanoyl 1,10-diaza-18-crown-6 (42).** 78% yield of white solid with mp 79–81°C. IR (NaCl plate): 1650 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.38–2.56 (m, 4H), 3.55–3.64 (m, 24H), 3.84 (t, 4H, J=8 Hz), 4.23 (s, 4H). ^{19}F NMR ($CDCl_3$): δ −81.3 (s, 6F), −113.9 (s, 4F), −122.3 (s, 20F), −123.2 (s, 4F), −124.1 (s, 4F), −126.6 (s, 4F).

***N,N′,N″,N‴*-Tetra-(2H,2H,4H,4H-3-Oxaperfluoroundecanoyl 1,4,8,12-tetraazacyclo-pentadecane (43).** 78% of white solid with mp 102–104°C. IR (NaCl plate): 1651 (C=O) cm^{-1}. ^1H NMR (acetone-d_6): δ 1.49–1.72 (m, 6H), 3.08–3.50 (m, 16H), 4.16–4.54 (m, 16H). ^{19}F NMR (acetone-d_6): δ −80.8 (s, 12F), −119.6 (s, 8F), −121.8 (s, 6F), −122.5 (s, 8F), −122.9 (s, 8F), −126.0 (s, 8F).

General procedure for the reduction of macrocyclic amides 30, 31 and 35–43 to form the corresponding macrocyclic amines 1, 3–7, 9, 12–14 and 16

A solution containing the macrocyclic amide (**30**, **31**, **35–43**) (4.0 mmol for the azacrown ether derivatives, 2.0 mmol for the diazacrown ether derivatives and 1.0 mmol for the tetraaza macrocycle derivative) in 30 mL of dry THF was cooled at 0°C under nitrogen and 30 mL of BH_3–THF (1.0 M solution in THF) was added dropwise over a period of 30 min. The cooling bath was removed and the reaction mixture was kept at room temperature for 30 min and then refluxed overnight. The solution was cooled to 0°C and excess borane was destroyed by the addition of water. The THF was evaporated in vacuo and the white solid obtained was dissolved in HCl–H_2O–MeOH (6:9:30 mL) and refluxed for 8 h. The mixture was evaporated in vacuo and the residue was treated with a strongly alkaline solution and extracted with CH_2Cl_2. The CH_2Cl_2 extracts were dried over Na_2SO_4 and evaporated in vacuo. The crude product was purified by column chromatography on silica gel with CH_2Cl_2 and then EtOAc as eluents for macrocycles **1**, **3–7**, **9** and **16** and by recrystallization from MeOH for ionophores **9** and **12–14**.

***N*-1H,1H-Perfluorooctyl aza-15-crown-5 (1).** 90% yield of yellowish oil. ^1H NMR ($CDCl_3$): δ 3.00 (t, 4H, J=6 Hz), 3.36 (t, 2H, J=15 Hz), 3.59–3.69 (m, 16H). ^{19}F NMR ($CDCl_3$): δ −81.4 (s, 3F), −117.5 (s, 2F), −122.4 to −122.7 (m, 4F), −123.4 (s, 2F), −124.1 (s, 2F), −126.7 to −126.8 (m, 2F). Anal. calcd for $C_{18}H_{22}F_{15}NO_4 \cdot 0.3CH_2Cl_2$:

C, 35.06; H, 3.63; N, 2.23. Found: C, 34.97; H, 3.45; N, 2.03.

***N*-1H,1H,2H,2H,4H,4H-3-Oxaperfluoroundecyl aza-12-crown-4 (3).** 85% yield of yellowish oil. ^{1}H NMR ($CDCl_3$): δ 2.73–2.79 (m, 6H), 3.62–3.78 (m, 14H), 4.01 (t, 4H, J=15 Hz). ^{19}F NMR ($CDCl_3$): δ −81.2 (s, 3F), −120.1 to −120.2 (m, 2F), −122.6 (s, 4F), −123.4 (s, 2F), −123.8 (s, 2F), −126.6 (s, 2F). Anal. calcd for $C_{18}H_{22}F_{15}NO_4$: C, 35.95; H, 3.68; N, 2.33. Found: C, 36.04; H, 3.62; N, 2.09.

***N*-1H,1H,2H,2H,4H,4H-Perfluoroundecyl aza-15-crown-5 (4).** 88% yield of yellowish oil. ^{1}H NMR ($CDCl_3$): δ 2.78–2.83 (m, 6H), 3.61–3.72 (m, 18H), 4.00 (t, 2H, J=15 Hz). ^{19}F NMR ($CDCl_3$): δ −80.9 (s, 3F), −119.7 to −119.9 (m, 2F), −122.2 (s, 4F), −122.9 (s, 2F), −123.5 (s, 2F), −126.2 (s, 2F). Anal. calcd for $C_{20}H_{26}F_{15}NO_5$: C, 37.22; H, 4.06; N, 2.17. Found: C, 37.67; H, 4.20; N, 2.09.

***N*-1H,1H,2H,2H,4H,4H-3-Oxaperfluoroundecyl aza-18-crown-6 (5).** 86% yield of yellowish oil. ^{1}H NMR ($CDCl_3$): δ 2.78–2.84 (m, 6H), 3.59–3.71 (m, 22H), 3.99 (t, 2H, J=15 Hz). ^{19}F NMR ($CDCl_3$): δ −81.2 (s, 3F), −120.0 to −120.1 (m, 2F), −122.5 (s, 4F), −123.2 (s, 2F), −123.8 (s, 2F), −126.5 to −126.6 (m, 2F). Anal. calcd for $C_{22}H_{30}F_{15}NO_6$: C, 38.32; H, 4.38; N, 2.03. Found: C, 38.09; H, 4.46; N, 2.04.

***N*-1H,1H,2H,2H,4H,4H,5H,5H-Perfluorotridecyl aza-15-crown-5 (6).** 81% yield of yellowish oil. ^{1}H NMR ($CDCl_3$): δ 2.27–2.52 (m, 2H), 2.75–2.84 (m, 6H), 3.55 (t, 2H, J=6 Hz), 3.62–3.69 (m, 16H), 3.72 (t, 2H, J=6 Hz). ^{19}F NMR ($CDCl_3$): δ −80.9 (s, 3F), −113.5 to −113.7 (m, 2F), −121.9 to −122.1 (m, 6F), −122.9 (s, 2F), −123.8 (s, 2F), −126.3 (s, 2F). Anal. calcd for $C_{22}H_{28}F_{17}NO_5$: C, 37.24; H, 3.97; N, 1.97. Found: C, 37.61; H, 4.02; N, 1.71.

***N*-1H,1H,2H,2H,4H,4H,5H,5H-Perfluorotricecyl aza-15-crown-5 (7).** 79% yield of yellowish oil. ^{1}H NMR ($CDCl_3$): δ 2.30–2.48 (m, 2H), 2.74–2.84 (m, 6H), 3.55 (t, 2H, J=6 Hz), 3.61–3.74 (m, 16H), 3.99 (t, 2H, J=6 Hz). ^{19}F NMR ($CDCl_3$): δ −81.2 (s, 3F), −114.0 (s, 2F), −122.2 (s, 10F), −123.2 (s, 2F), −124.1 (s, 2F), −126.6 (s, 2F). Anal. calcd for $C_{24}H_{28}F_{21}NO_5$: C, 33.21; H, 3.36; N, 1.53. Found: C, 33.02; H, 2.91; N, 1.13.

***N*,*N*′-Bis(1H,1H-Perfluorooctyl 1,10-diaza-18-crown-6 (9).** 80% yield of white solid with mp 52–53°C. ^{1}H NMR ($CDCl_3$): δ 2.99 (t, 8H, J=6 Hz), 3.43 (t, 4H, J=18 Hz), 3.58–3.64 (m, 16H). ^{19}F NMR ($CDCl_3$): δ −81.3 (s, 6F), −118.0 to −118.3 (m, 4F), −122.3 (s, 8F), −123.3 (s, 4F), −124.1 (s, 4F), −126.7 to −126.8 (m, 4F). Anal. calcd for $C_{28}H_{28}F_{30}N_2O_4$: C, 32.76; H, 2.75; N, 2.73. Found: C, 32.74; H, 2.71; N, 2.77.

***N*,*N*′-Bis(1H,1H,2H,2H,4H,4H-3-Oxaperfluoroundecyl 1,10-diaza-18-crown-6 (12).** 80% yield of yellowish oil. ^{1}H NMR ($CDCl_3$): δ 2.77–2.84 (m, 12H), 3.57–3.61 (m, 16H), 3.69 (t, 4H, J=6 Hz), 3.98 (t, 4H, J=15 Hz). ^{19}F NMR ($CDCl_3$): δ −81.2 (s, 6F), −120.0 to −120.2 (m, 4F), −122.6 (s, 8F), −123.2 (s, 4F), −123.8 (s, 4F), −126.5 to −126.7 (m, 4F). Anal. calcd for $C_{32}H_{36}F_{30}N_2O_6$: C, 34.48; H, 3.25; N, 2.51. Found: C, 34.56; H, 3.31; N, 2.47.

***N*,*N*′-Bis(1H,1H,2H,2H,4H,4H,5H,5H-3-Oxaperfluorotridecyl 1,10-diaza-18-crown-6 (13).** 81% of white solid with mp 49–50°C. ^{1}H NMR ($CDCl_3$): δ 2.32–2.45 (m, 4H), 2.76 (t, 4H, J=6 Hz), 2.84 (t, 8H, J=6 Hz), 3.51 (t, 4H, J=6 Hz), 3.56–3.62 (m, 16H), 3.72 (t, 4H, J=6 Hz). ^{19}F NMR ($CDCl_3$): δ −81.0 (s, 6F), −113.6 to −113.8 (m, 4F), −122.0 to −122.2 (m, 12F), −123.0 (s, 4F), −123.9 (s, 4F), −126.3 to −126.4 (m, 4F). Anal. calcd for $C_{36}H_{40}F_{34}N_2O_6$: C, 34.79; H, 3.24; N, 2.25. Found: C, 34.68; H, 3.24; N, 2.13.

***N*,*N*′-Bis(1H,1H,2H,2H,4H,4H,5H,5H-3-Oxaperfluoropentadecyl 1,10-diaza-18-crown-6 (14).** 70% of white solid with mp 75–76°C. ^{1}H NMR ($CDCl_3$): δ 2.30–2.47 (m, 4H), 2.76 (t, 4H, J=6 Hz), 2.84 (t, 8H, J=6 Hz), 3.54 (t, 4H, J=6 Hz), 3.58–3.62 (m, 16H), 3.71 (t, 4H, J=6 Hz). ^{19}F NMR ($CDCl_3$): δ −81.0 (s, 6F), −113.7 (s, 4F), −122.0 (s, 20F), −123.0 (s, 4F), −123.9 (s, 4F), −126.4 (s, 4F). Anal. calcd for $C_{40}H_{40}F_{42}N_2O_6$: C, 33.30; H, 2.79; N, 1.94. Found: C, 33.26; H, 2.85; N, 1.87.

***N*,*N*′,*N*″,*N*‴-Tetra(1H,1H,2H,2H,4H,4H-3-Oxaperfluoroundecyl 1,4,8,12-tetraaza-cyclopentadecane (16).** 76% yield of colorless oil. ^{1}H NMR ($CDCl_3$): δ 1.55 (q, 6H, J=6 Hz), 2.48–2.56 (m, 20H), 2.66 (q, 4H, J=6 Hz), 3.63–3.78 (m, 8H), 3.95 (t, 8H, J=16 Hz).). ^{19}F NMR ($CDCl_3$): δ −81.0 to −81.2 (m, 12F), −119.8 to −120.0 (m, 8F), −122.4 (s, 6F), −123.1 (s, 8F), −123.7 (s, 8F), −126.5 to −126.6 (m, 8F). Anal. calcd for $C_{51}H_{46}F_{60}N_4O_4{\cdot}0.6H_2O$: C, 31.74; H, 2.46; N, 2.90. Found: C, 31.36; H, 2.57 N, 2.96.

General procedure for the reduction of partially fluorinated carboxylic acids 27 and 28 to the corresponding alcohols 44 and 45

At 0°C under nitrogen, BH_3–THF (1.0 M solution in THF, 15 mL) was slowly added to a solution of 3.0 mmol of the carboxylic acid **27** or **28** in 15 mL of THF. The solution was stirred at room temperature overnight and the excess borane was destroyed by the addition of water. The aqueous phase was saturated with K_2CO_3. THF was evaporated in vacuo from the mixture and the aqueous residue was extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with water, dried over Na_2SO_4 and evaporated in vacuo.

1H,1H,2H,2H,4H,4H-3-Oxaperfluoroundecan-1-ol (44). The crude product was purified by column chromatography on silica gel with CH_2Cl_2 then EtOAc as eluents to give a colorless oil in 96% yield. IR (NaCl plate): 3373–2855 (OH) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.76–3.97 (m, 4H), 4.06 (t, 2H, J=10 Hz). ^{19}F NMR ($CDCl_3$): δ −81.0 (s, 3F), −119.8 to −119.9 (m, 2F), −122.2 to −122.3 (m, 4F), −122.9 (s, 4F), −123.5 (s, 4F), −126.3 to −126.4 (m, 2F). Anal. calcd for $C_{10}H_7F_{15}O_2$: C, 27.04; H, 1.59. Found: C, 27.08; H, 1.42.

1H,1H,2H,2H,4H,4H,5H,5H-3-Oxaperfluorotridecan-1-ol (45). Recrystallization from hexanes gave a white solid with mp 29–30°C in 79% yield. IR (NaCl plate): 3390 (OH)

cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.33–2.52 (m, 2H), 3.56–3.61 (m, 2H), 3.69–3.83 (m, 4H). ^{19}F NMR ($CDCl_3$): δ −81.3 to −81.6 (m, 3F), −113.9 to −114.1 (m, 2F), −122.3 to −122.5 (m, 6F), −123.3 (s, 2F), −124.2 (s, 4F), −126.7 to −126.8 (m, 2F). Anal. calcd for $C_{12}H_9F_{17}O_2$: C, 28.36; H, 1.78. Found: C, 28.29; H, 1.50.

General procedure for the preparation of partially fluorinated macrocycles 8 and 15 with pentafluorobenzyl groups

To a mixture of the aza macrocycle (5.0 mmol of **22** and 2.5 mmol of **23**), 0.69 g (5.0 mmol) of K_2CO_3 and 20 mL of MeCN, 1.33 g (5.0 mmol) of pentafluorobenzyl bromide was added dropwise over a period of 15 min. The reaction mixture was stirred at room temperature for 48 h. The mixture was filtered and the filtrate was evaporated in vacuo. The residue was dissolved in CH_2Cl_2. This solution was washed with water, dried over Na_2SO_4 and evaporated in vacuo to give the crude product.

***N*-Pentafluorobenzyl aza-15-crown-5 (8).** The crude product was purified by column chromatography on silica gel with CH_2Cl_2 then EtOAc as eluents to give a yellowish oil in 60% yield. ^{1}H NMR ($CDCl_3$): δ 2.78 (t, 4H, J=6 Hz), 3.63–3.68 (m, 16H), 3.86 (s, 2H). ^{19}F NMR ($CDCl_3$): δ −141.6 to −141.8 (m, 2F), −155.6 to −155.7 (t, 1F), −162.4 to −162.6 (m, 2F). Anal. calcd for $C_{17}H_{22}F_{15}NO_4$: C, 51.13; H, 5.55; N, 3.51. Found: C, 51.40; H, 5.58; N, 3.50.

***N*,*N*′-Bis(Pentafluorobenzyl) 1,10-diaza-18-crown-6 (15).** Recrystallization from MeOH gave a white solid with mp 74–75°C in 63% yield. ^{1}H NMR ($CDCl_3$): δ 2.78 (t, 8H, J=6 Hz), 3.60–3.66 (m, 16H), 3.85 (s, 4H). ^{19}F NMR ($CDCl_3$): δ −141.9 to −142.0 (m, 4F), −155.6 to −155.7 (t, 2F), −162.5 to −162.7 (m, 4F). Anal. calcd for $C_{26}H_{28}F_{10}N_2O_4$: C, 50.16; H, 4.53; N, 4.50. Found: C, 49.93; H, 4.50; N, 4.46.

General procedure for the preparation of macrocycles 46 and 47

A mixture of 4.0 mmol of **22** or 2.0 mmol of **23**, 0.88 g (4.0 mmol) of 1-bromodecane, 0.55 g, (4.0 mmol) of K_2CO_3 and 20 mL of MeCN was refluxed for 24 h. After cooling to room temperature, the solid was filtered and washed with MeCN. The filtrate and washings were combined and evaporated in vacuo. The residue was dissolved in CH_2Cl_2. The solution was washed with water, dried over Na_2SO_4 and evaporated in vacuo to give an oil.

***N*-Decyl aza-15-crown-5 (46).** The crude product was purified by column chromatography on silica gel with CH_2Cl_2 then CH_2Cl_2:MeOH (9:1) as eluents to give an oil in 88% yield. ^{1}H NMR ($CDCl_3$): δ 0.86 (t, 3H, J=6 Hz), 1.25 (s, 14H), 1.46 (m, 4H), 2.49–2.56 (m, 2H), 2.75–2.81 (m, 4H), 3.63–3.69 (m, 16H). Anal. calcd for $C_{20}H_{41}NO_4{\cdot}0.4H_20$: C, 65.44; H, 11.49; N, 3.82. Found: C, 65.57; H, 11.50; N, 3.90.

***N*,*N*′-Didecyl 1,10-diaza-18-crown-6 (47).** 92% yield of a colorless oil that solidified on standing, mp 34–35°C. ^{1}H NMR ($CDCl_3$): δ 0.86 (t, 6H, J=6 Hz), 1.25 (s, 28H), 1.42 (m, 4H), 2.46 (q, 4H, J=8 Hz), 2.76 (t, 8H, J=6 Hz), 3.57–3.63 (m, 16H). Anal. calcd for $C_{32}H_{66}N_2O_4$: C, 70.79; H, 12.25; N, 5.16. Found: C, 70.82; H, 12.46; N, 5.33.

Alkali metal picrate extraction

Aqueous solutions were prepared that contained the alkali metal picrate (5.0 mM) and the corresponding alkali metal chloride (55 mM). Into a capped, metal-free, plastic 15-mL centrifuge tube was placed 1.00 mL of the aqueous metal picrate solution and 1.00 mL of a 5.0 mM chloroform solution of the ionophore. The tube was shaken on a vortex mixer for 5 min for thorough mixing and then centrifuged for 5 min to promote complete phase separation. A sample (10 μL) of the aqueous phase was removed with a syringe and transferred to a 5.0 mL volumetric flask. The flask was filled to the mark with MeCN. The absorbance of the solution at 275 nm was measured with a Shimadzu UV-260 UV/vis spectrophotometer. The % extraction was calculated by:

$$\%\ \text{Extraction} = 100\ (\text{Abs}_{\text{before}} - \text{Abs}_{\text{after}})/\text{Abs}_{\text{before}}$$

where $\text{Abs}_{\text{before}}$ is the absorbance of a similarly diluted sample of the unextracted alkali metal picrate solution and $\text{Abs}_{\text{after}}$ is the absorbance of the alkali metal picrate soution after extraction. Three independent extractions were performed for each combination of alkali metal and ionophore. The results were averaged and the standard deviation was calculated.

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