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Perfluoroalkylated 4,13-Diaza-18-Crown-6 Ethers: Synthesis, Phase-Transfer Catalysis, and Recycling Studies

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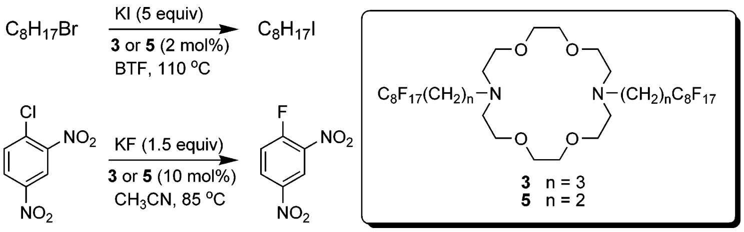

A series of *N*,*N*′-dialkyl-4,13-diaza-18-crown-6 lariat ethers possessing two C_8H_{17} (**2**), $(CH_2)_3C_8F_{17}$ (**3**), $(CH_2)_3C_{10}F_{21}$ (**4**), and $(CH_2)_2C_8F_{17}$ (**5**) side arms were synthesized in good yields by *N*-alkylation of 4,13-diaza-18-crown-6. Potassium picrate could be extracted from an aqueous solution into an organic phase by all of the perfluoroalkylated macrocycles demonstrating their potential to be used as phase-transfer catalysts, and preliminary studies on a classical nucleophilic substitution established that they each gave higher catalytic activities under solid−liquid than under liquid−liquid phase-transfer conditions. The light fluorous macrocycles gave similar, if not better, catalytic activity compared to the parent, non-fluorinated phase-transfer catalyst **2** under solid−liquid conditions in conventional organic solvents in both an aliphatic and an aromatic nucleophilic substitution. *N*,*N*′-Bis(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoroundecyl)-4,13-diaza-18-crown-6 (**3**) was recycled six times in the iodide displacement reaction of 1-bromooctane and four times in the fluoride displacement reaction of 2,4-dinitrochlorobenzene using fluorous solid-phase extraction without any loss in activity.

Introduction

Phase-transfer catalysis[1] is a powerful tool for promoting the reaction between reagents that are mutually immiscible and has been applied to over 600 industrial processes in a variety of industries covering a wide range of organic reactions. It is a popular technique because it increases the rate of reaction, product selectivity, and yield while lowering the energy requirements. The main disadvantage, however, is that the phase-transfer catalyst is not normally recovered and is disposed of as waste. This problem has been overcome by the use of insoluble phase-transfer catalysts that are bound to either an insoluble resin or an insoluble inorganic support. Although insoluble phase-transfer (PTC) catalysts offer easy separation of the PTC catalyst from the organic product and the potential to recycle the PTC catalyst, they are only used in an estimated 5−10% of industrial PTC reactions. The main reasons for this are that most reactions are much slower with insoluble PTC catalysts compared to using the analogous conventional soluble PTC catalyst, the cost of the resin-bound PTC catalyst is normally prohibitively expensive, and solid insoluble PTC catalysts are not normally robust enough to survive repeated long term use in industrial-scale reactors.

Recently, fluorous tetraalkyl phosphonium iodides were reported to catalyze the synthesis of propylene carbonate in supercritical carbon dioxide,[2] and a recyclable fluorous chiral ammonium salt[3] promoted the asymmetric alkylation of a protected glycine derivative in good yields and high enantioselectivities. The reactivity of the latter phase-transfer catalyst was reduced dramatically because the catalyst was heterogeneous as a result of its low solubility in toluene. At the end of the reaction, the fluorinated phase-transfer catalyst was recovered by extracting the reaction mixture with perfluorohexane three times, and good recycling results were obtained. We have also synthesized a series of fluorous quaternary aliphatic and aromatic phosphonium salts that contain either three or four fluorous

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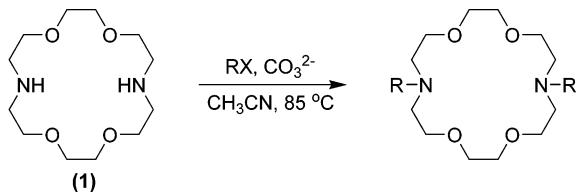
ponytails and have investigated their applications in phase-transfer catalysis.[4,5] The "heavy fluorous" phosphonium salt, $(R_{f8}(CH_2)_2)_3(R_{f6}(CH_2)_2)P^+ I^-$, promoted a nucleophilic aliphatic substitution in an aqueous/$CF_3C_6F_5$ biphase, but it was essential to use a perfluorinated solvent because of the high percentage of fluorine in the PTC catalyst. Fluorous separation techniques[6] have advanced significantly over the past decade and reagents/catalysts containing long perfluoroalkyl groups can now be recovered, recycled, and reused without the need to use expensive and environmentally persistent fluorous solvents.[7-10] Although Curran originally designed fluorous solid-phase extraction[9] for high throughput organic synthesis, our recent work has demonstrated that it can also be used to recycle conventional homogeneous catalysts as well as chiral ligands such as BINAP and BINOL.[10] Here, we describe the synthesis and applications of "light fluorous" 4,13-diaza-18-crown-6 ethers. The key characteristics of these new fluorous phase-transfer catalysts are their straightforward synthesis by *N*-functionalization of 4,13-diaza-18-crown-6, their solubility in conventional organic solvents that overcomes the mass-transfer problems associated with insoluble phase-transfer catalysts, their better chemical and thermal stability than ammonium and phosphonium salts that is essential for the development of a robust, reusable phase-transfer catalyst, and their efficient recycle using fluorous solid-phase extraction.

Results and Discussion

A series of novel 4,13-diaza-18-crown-6 ethers containing perfluoroalkylated sidearms were synthesized in good yields by refluxing 4,13-diaza-18-crown-6 (**1**) in acetonitrile with 2−3 equiv of the perfluoroalkyl iodide or triflate in the presence of base for 24−72 h (Table 1). Two types of spacer units, $(CH_2)_2$ and $(CH_2)_3$, were included to establish the effectiveness of the spacer units in insulating the nitrogen donor atoms from the electron-withdrawing effect of the perfluoroalkyl groups. The alkylated derivative **2** was also prepared to compare the activity of the fluorinated macrocycles **3**−**5** with the non-fluorinated analogue in phase-transfer catalyses. When 4,13-diaza-18-crown-6 was reacted with 1*H*,1*H*,2*H*,2*H*-perfluorodecyl iodide, only a 9% yield of macrocycle **5** was obtained, probably because the elimination of HI prevailed rather than alkylation[11] since the iodide is not insulated from the electron-withdrawing effect of the perfluoroalkyl group making it an extremely poor leaving group for nucleophilic substitution. Macrocycle **5** has been prepared previously in a low yield (16%) by refluxing 4,13-diaza-18-crown-6 with 1*H*,1*H*,2*H*,2*H*-perfluorodecyl tosylate (2 equiv) and sodium carbonate in dioxane for 48 h[12] and, here, we have improved the yield considerably (53%) by using 1*H*,1*H*,2*H*,2*H*-perfluorodecyl triflate (2.5 equiv) in ethyl acetate for 72 h.

TABLE 1. Synthesis of *N*,*N*′-Bis(alkyl)-4,13-diaza-18-crown-6 Ethers



PTC	R	X	time (h)	yield (%)
2	C_8H_{17}	Br	24	78
3	$(CH_2)_3C_8F_{17}$	I	24	53
4	$(CH_2)_3C_{10}F_{21}$	I	48	62
5	$(CH_2)_2C_8F_{17}$	OTf	72	53[a]

[a] EtOAc.

TABLE 2. Potassium Picrate Extractions

		picrate extracted (%)	
PTC	R	DCM	BTF
1	H	8.0	0.2
2	C_8H_{17}	47.7	52.9
3	$(CH_2)_3C_8F_{17}$	32.8	21.8
4	$(CH_2)_3C_{10}F_{21}$	26.2	17.4
5	$(CH_2)_2C_8F_{17}$	10.9	3.0

Macrocycles **2**, **3**, and **5** are soluble in most common organic solvents such as toluene, diethyl ether, dichloromethane, fluorobenzene, and ethyl acetate, as well as in hybrid (ambiphilic) solvents such as benzotrifluoride and trifluoroethanol. However, the perfluoroalkylated macrocycles are much less soluble in polar organic solvents, such as acetonitrile and methanol, compared to macrocycle **2**. Overall, the solubility of the macrocycle decreases as the alkyl group is replaced by perfluoroalkyl groups and as the length of the perfluoroalkyl group increases. For example, macrocycle **4** is only soluble in hot toluene, diethyl ether, hot dichloromethane, fluorobenzene, and hot ethyl acetate, as well as benzotrifluoride and trifluoroethanol. Although macrocycle **5** partitions preferentially into the organic phase of a toluene:perfluoro-1,3-dimethylcyclohexane biphase (59:41), by increasing the polarity of the organic phase, it becomes preferentially soluble in the fluorous phase of an acetonitrile:perfluoro-1,3-dimethylcyclohexane biphase (0.5:99.5) at room temperature.

The most important property of crown ethers is their ability to form stable complexes with metal ions, and this is essential for their applications as phase-transfer catalysts. Potassium picrate extraction studies[4,12-14] were performed to study the complexation ability of the new fluorinated macrocycles. In previous work, partially fluorinated 4,13-diaza-18-crown-6

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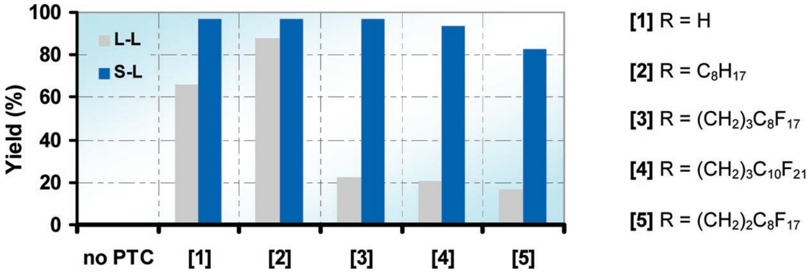

FIGURE 1. Iodination of 1-bromooctane under liquid−liquid and solid−liquid conditions after 24 h.

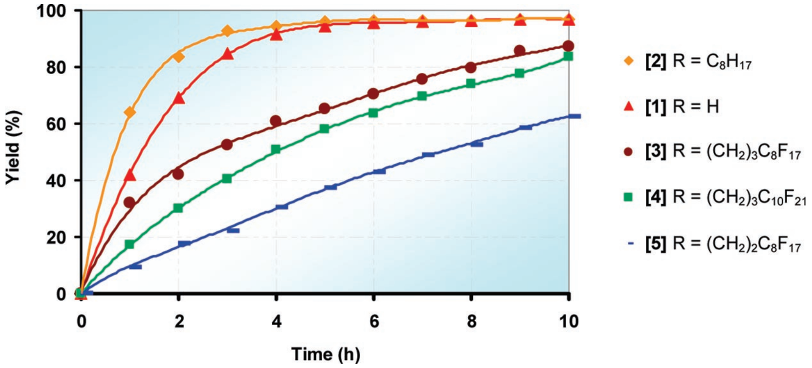

FIGURE 2. Rates of formation of 1-iodooctane under solid−liquid conditions.

TABLE 3. Recycling Results for Macrocycle 3

run	catalyst used (g)	recovered catalyst (g)	yield (%, GC)
1	0.257	0.248	88.0
2	0.248	0.239	86.8
3	0.239	0.225	86.6
4	0.225	0.202	86.0
5	0.202	0.191	85.8
6	0.191	0.179	85.6

derivatives exhibited greater selectivity for potassium, on the basis of the cavity size of the macrocycle, with the following alkali metal picrate extraction order: $K^+ > Rb^+ > Na^+ > Cs^+ > Li^+$.[12]

The extraction of potassium picrate from an aqueous solution into dichloromethane and benzotrifluoride was screened for macrocycles **1**−**5**, and the results are summarized in Table 2. Each macrocycle extracted a different amount of picrate into each solvent system, but the same general trend was observed in both sets of results. Macrocycle **2** containing the octyl groups exhibited the greatest potassium extraction efficiency and the partially fluorinated macrocycles **3** and **4**, which have longer spacer groups between the macrocycle and the electron-withdrawing perfluoroalkyl groups, were more efficient than macrocycle **5** which has only an ethyl spacer unit. The low extracting ability of 4,13-diaza-18-crown-6 was expected because its molecular conformation with the two NH bonds turned inward makes it more difficult for potassium to occupy the cavity.[14]

Having established that the fluorinated 4,13-diaza-18-crown-6 ethers retained their potassium ion complexing ability, all of the fluorinated macrocycles were evaluated as phase-transfer catalysts in a classical nucleophilic substitution: the conversion of 1-bromooctane into 1-iodooctane (eq 1).[15] The efficiency of the new phase-transfer catalysts was examined under both liquid−liquid conditions, which involves a heterogeneous reaction process between two liquid phases (benzotrifluoride/water biphase), and solid−liquid conditions, which involves the reaction of the solid ionic reagent, KI, with the reactant, 1-bromooctane, in benzotrifluoride. Figure 1 demonstrates clearly that the reaction did not proceed in the absence of a phase-transfer catalyst and that all of the derivatized 4,13-diaza-18-crown-6 ethers performed better under solid−liquid conditions. Under liquid−liquid conditions, however, there was a dramatic decrease in the activity of the fluorinated macrocycles **3**−**5** in comparison to that for the octyl derivative **2**. This may be due to the hydrophobic effect of the perfluoroalkyl groups making these macrocycles interact inadequately with the aqueous phase, causing the rate of anion transfer to slow down and essentially resulting in a transfer-limited process with restricted rates of anion transfer across the interface. A similar explanation could account for the dramatic reduction in the picrate extraction efficiency of the fluorinated macrocycles **3**−**5** compared to that for the octyl derivative **2** in benzotrifluoride (Table 2). This effect was more pronounced in benzotrifluoride and probably arises from a much lower solubility of benzotrifluoride in water ($S_w = 0.0031$ mol/L) compared to that for dichloromethane ($S_w = 0.23$ mol/L).[16]

$$C_8H_{17}Br \xrightarrow[\text{BTF, 110 °C, 24 h}]{\text{Rf-PTC (2 mol \%), KI (5 equiv)}} C_8H_{17}I \qquad (1)$$

The catalytic activities of the derivatized 4,13-diaza-18-crown-6 ethers **1**−**5** were compared under solid−liquid conditions by monitoring the aliphatic nucleophilic substitution (eq 1) every hour by gas chromatography (Figure 2). The reaction mixture contained an internal standard, biphenyl, and the individual response factors for 1-bromooctane and 1-iodooctane were used

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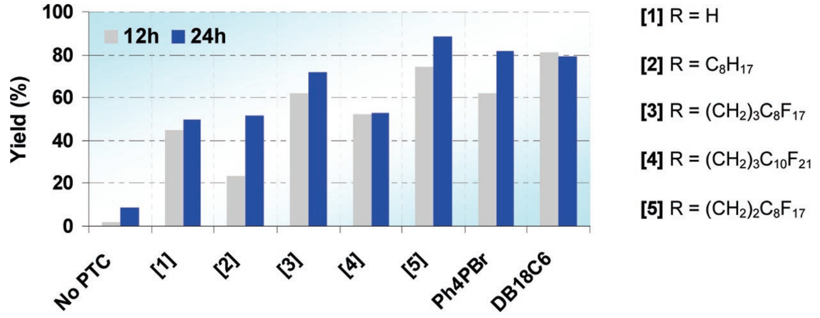


FIGURE 3. Fluorination of 2,4-dinitrochlorobenzene under solid−liquid conditions.

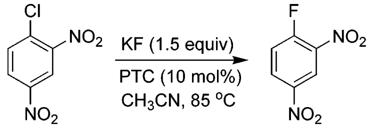
TABLE 4. Recycling Results of Macrocycle 3

run	catalyst used (g)	recovered catalyst (g)	yield (%, GC)
1	0.119	0.112	70.8
2	0.112	0.108	69.4
3	0.108	0.105	68.7
4	0.105	0.099	67.9

to ensure accurate monitoring of the reaction. The non-fluorinated macrocycles, **1** and **2,** were the most active PTC catalysts and the fluorinated macrocycles, **3** and **4**, with three methylene spacer groups exhibited higher activities than macrocycle **5** which contains two methylene spacer groups.

Attempts to recycle the non-fluorinated macrocycles, **1** and **2**, in the iodide displacement reaction were investigated using both conventional and fluorous solid-phase extraction. Although the organic products could be separated efficiently from both **1** and **2** by both methods, it was not possible to recover **1** or **2** from either a column of conventional silica gel or a column of fluorous reverse phase (FRP) silica gel. The separation and recovery of the most active fluorinated phase-transfer catalyst **3** was then investigated using fluorous solid-phase extraction. After 12 h, the organic phase was filtered and washed with water to eliminate the excess of potassium salts. After drying the organic phase over magnesium sulfate, the clear organic phase was passed through a short column of FRP silica gel (∼4 g), and the column was eluted with benzotrifluoride to obtain the organic products. The fluorinated PTC catalyst was then recovered quantitatively (90−96%) by eluting with trifluoroethanol. In this way, macrocycle **3** was reused in the aliphatic nucleophilic substitution six times (Table 3) using the same short column of FRP silica gel, and the slight drop in conversion can be accommodated for by the mechanical losses of **3** after each recycle. The aqueous wash in the recycling procedure was essential for removing the potassium that is coordinated in the macrocycle. Although macrocycle **3** could be recovered quantitatively (91−99%) without the aqueous wash, the conversions for the subsequent aliphatic nucleophilic substitutions were not consistent (see Supporting Information).

Iodide displacement reactions provide straightforward model reactions because of the relative ease of iodide transfer into organic phases combined with its strong nucleophilicity and neglible hydration. Consequently, we wanted to test our new fluorinated phase-transfer catalysts in a more demanding reaction such as fluoride displacements because the transfer of fluoride into organic solvents is difficult and fluoride is not a good nucleophile. Halogen exchange (halex) of chlorine by fluorine on an aromatic ring is the most widely used process for the synthesis of fluoroaromatics which are important intermediates for the pharmaceutical, agrochemical, and dye industries.[17] Potassium fluoride is normally used in expensive dipolar aprotic solvents but, since the solubility of the potassium fluoride is low, the reactions normally require high temperatures and long reaction times. Phase-transfer catalysts have been used to increase the solubility of fluoride in both dipolar and non-dipolar aprotic solvents. Here, the catalytic applications of macrocycles **1**−**5** were examined in the fluorination of the activated aromatic, 2,4-dinitrochlorobenzene, under solid−liquid conditions in acetonitrile at 85 °C with 1.5 equiv of spray-dried potassium fluoride (eq 2).[18] There was only 9% conversion to 2,4-dinitrofluorobenzene in 24 h in the absence of a phase-transfer catalyst because of the low solubility of fluoride in acetonitrile (Figure 3).[19] In contrast to the iodide displacements, the reactivity of macrocycles **1**−**5** was completely reversed. The fluorinated macrocycle **5** with the smallest spacer group (two methylene units) was more reactive than macrocycle **3**, which contained three methylene spacer groups, and they were both more reactive than the alkyl derivative **2** and 4,13-diaza-18-crown-6. The lower reactivity of macrocycle **4**, compared to macrocycle **3**, was expected because of its lower solubility in acetonitrile because of the longer perfluorodecyl groups. Surprisingly, *N*,*N*′-bis(1*H*,1*H*,2*H*,2*H*-perfluorodecyl)-4,13-diaza-18-crown-6 (**5**) proved to be an extremely effective phase-transfer catalyst for the halex reaction with higher reactivity than the conventional phase-transfer catalysts, tetraphenylphosphonium bromide (Ph_4PBr) and dibenzo-18-crown-6 (DB-18-C-6).



(2)

Using a similar protocol to that developed for the iodide displacement reaction, the perfluoroalkylated PTC catalyst **3** was recycled efficiently after the fluorination of 2,4-dinitrochlorobenzene by fluorous solid-phase extraction (Table 4). The clean organic products were eluted first from the short column of fluorous reverse phase silica using dichloromethane. By a

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TABLE 5. Recycling Results of Macrocycle 5

run	catalyst used (g)	recovered catalyst (g)	yield (%, GC)
1	0.116	0.100	89.9
2	0.100	0.084	82.6
3	0.084	0.062	68.8

simple solvent switch to trifluoroethanol, and then ethylacetate, the fluorinated PTC catalyst was recovered quantitatively (94−97%) and excellent recycling results were obtained over four cycles. The same protocol was also used for the recycling of the more active, fluorinated PTC catalyst **5** (Table 5) in the halex reaction. Unfortunately, only a low recovery of macrocycle **5** (74−86%) from the column of FRP silica gel resulted in a drop in conversion on recycling the catalyst in runs 2 and 3.

Conclusions

N,*N*′-Bis(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoroundecyl)-4,13-diaza-18-crown-6 (**3**) and *N*,*N*′-bis(1*H*,1*H*,2*H*,2*H*-perfluorodecyl)-4,-13-diaza-18-crown-6 (**5**) were synthesized in good yields by the *N*-alkylation of 4,13-diaza-18-crown-6. Under solid−liquid phase-transfer conditions, both of the fluorinated macrocycles give similar, if not better, phase-transfer catalytic activity compared to the non-fluorinated, parent macrocycles **1** and **2** in aliphatic and aromatic nucleophilic substitution reactions with iodide and fluoride, respectively. Although macrocycle **5** gave higher catalytic activity in the difficult aromatic chloride-to-fluoride exchange, only poor recycling results were obtained by fluorous solid-phase extraction. Macrocycle **3**, on the other hand, was recycled six times using fluorous solid-phase extraction in the conversion of 1-bromooctane into 1-iodooctane and four times in the conversion of 2,4-dinitrochlorobenzene into 2,4-dinitrofluorobenzene without any loss in activity. Work in our laboratory is now focused on further applications of this stable, recyclable phase-transfer catalyst as well as on the synthesis and applications of new fluorous analogues of conventional crown ethers that are more commonly used in phase-transfer catalysis.

Experimental Section

General Procedure for the Preparation of *N*,*N*′-Bis(perfluoroalkyl)-4,13-diaza-18-crown-6 Ethers. The procedure was adapted from ref 12. A solution of 4,13-diaza-18-crown-6 (200 mg, 0.76 mmol), K_2CO_3 (210 mg, 1.52 mmol), and the appropriate alkyl or perfluoroalkyl halide (1.52 mmol) in MeCN (20 mL) was refluxed for 24 h (Table 1). After cooling to room temperature, the solid was filtered and washed with hot acetonitrile. The filtrate and washings were combined and evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2 and the solution was washed with water, was dried over $MgSO_4$, and was evaporated under reduced pressure.

***N*,*N*′-Bis(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoroundecyl)-4,13-diaza-18-crown-6 (3).** The resultant solid was purified by recrystallization from methanol to give a white solid (479 mg, 53%). mp 66−68 °C; anal. calcd for $C_{34}H_{36}F_{34}N_2O_4$: C, 34.53; H, 3.07; N, 2.37%. Found: C, 34.61; H, 3.02; N, 2.32%; *m/z* (FAB) 1183 (M^+, 100%); δ_H ($CDCl_3$) 3.54 (16H, m), 2.69 (8H, t, $^3J_{HH}$ 5.7), 2.50 (4H, t, $^3J_{HH}$ 6.6), 2.06 (4H, m), 1.67 (4H, quintet, $^3J_{HH}$ 7.3); δ_F ($CDCl_3$) −80.74 (3F, t, $^4J_{FF}$ 9.5), −113.91 (2F, t, $^4J_{FF}$ 15.2), −121.86 (6F, m), −122.68 (2F, m), −123.35 (2F, m), −126.06 (2F, m); δ_C ($CDCl_3$) 70.8 (CH_2), 70.0 (CH_2), 54.5 (CH_2), 54.0 (CH_2), 28.6 (t, $^2J_{CF}$ 22.7, CH_2), 18.5 (CH_2).[20]

***N*,*N*′-Bis(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluorotridecyl)-4,13-diaza-18-crown-6 (4).** A solution of 4,13-diaza-18-crown-6 (1.00 g, 3.8 mmol), K_2CO_3 (1.50 g, 10 mmol), and 1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluorotridecyl iodide (7.84 g, 11.4 mmol) in MeCN (35 mL) was refluxed for 48 h. An identical workup to that for compound **3** gave **4** as a white solid (3.27 g, 62%) after recrystallization from methanol. mp 91−93 °C; anal. calcd for $C_{38}H_{36}F_{42}N_2O_4$: C, 33.01; H, 3.00; N, 2.24%; found: C, 32.92; H, 3.00; N, 2.37%; *m/z* (FAB) 1383 (M^+, 100%); δ_H ($CDCl_3$) 3.54 (16H, m), 2.68 (8H, t, $^3J_{HH}$ 6.9), 2.51 (4H, t, $^3J_{HH}$ 8.0), 2.10 (4H, m), 1.66 (4H, quintet, $^3J_{HH}$ 8.0); δ_F ($CDCl_3$) −80.80 (3F, t, $^4J_{FF}$ 9.8), −114.30 (2F, t, $^4J_{FF}$ 15.8), −121.77 (10F, m), −122.35 (2F, m), −123.39 (2F, m), −126.13 (2F, m); δ_C ($CDCl_3$) 70.8 (CH_2), 69.9 (CH_2), 54.4 (CH_2), 54.0 (CH_2), 28.6 (t, $^2J_{CF}$ 22.5, CH_2), 18.7 (CH_2).[20]

General Procedure for Iodide Displacement under Liquid−Liquid Conditions. A mixture of 1-bromooctane (200 mg, 1.0 mmol), potassium iodide (840 mg, 5.0 mmol), biphenyl (154 mg, 1.0 mmol), benzotrifluoride (4 mL), water (2 mL), and the appropriate dialkyl-4,13-diaza-18-crown-6 ether (0.02 mmol) was refluxed at 110 °C for 24 h. After cooling to room temperature, the organic phase was filtered through silica gel using benzotrifluoride as eluant. A sample of the collected solution was analyzed by gas chromatography to determine the yield of product using biphenyl as the internal standard (115 °C for 3 min followed by 45 °C min^{-1} ramp to 195 °C, held for 1 min. Injector: 300 °C, detector: 300 °C. R_t 2.13 min (1-bromooctane), 2.85 min (1-iodooctane), 4.05 min (biphenyl)).

General Procedure for Iodide Displacement under Solid−Liquid Conditions. A mixture of 1-bromooctane (200 mg, 1.0 mmol), potassium iodide (840 mg, 5.0 mmol), biphenyl (154 mg, 1.0 mmol), benzotrifluoride (4 mL), and the appropriate crown ether (0.02 mmol) was refluxed at 110 °C for 24 h. After cooling to room temperature, the organic phase was filtered through silica gel using benzotrifluoride as eluant. A sample of the collected solution was analyzed by gas chromatography to determine the yield of product using biphenyl as the internal standard.

The above reaction was also monitored by taking samples (25 μL) every hour for 10 h, and after diluting the sample with benzotrifluoride (2 mL), it was analyzed by GC.

General Procedure for the Separation and Recovery of Macrocycle 3 after Iodide Displacement Reaction. After 12 h, the reaction mixture was cooled to room temperature and was filtered to remove the excess potassium salts, which were extracted with benzotrifluoride (5 mL). The organic phase was then washed once with water (10 mL) before drying over magnesium sulfate. The clear organic phase was passed through a short column of fluorous reverse phase silica gel (∼4 g, 3 cm long, 1.5 cm diameter), and the column was eluted with benzotrifluoride (40 mL) to obtain the clean organic products. The fluorinated phase-transfer catalyst was then recovered (90−96%) by eluting with trifluoroethanol (70 mL). After removing the trifluoroethanol, the phase-transfer catalyst was dried in vacuo for 2 h at 60 °C before being reused in another aliphatic nucleophilic substitution.

General Procedure for Fluoride Displacement under Solid−Liquid Conditions. A mixture of 2,4-dinitrochlorobenzene (207 mg, 1.0 mmol), biphenyl (154 mg, 1.0 mmol), spray-dried potassium fluoride (87 mg, 1.5 mmol) which had been dried previously under oil pump vacuum at 170 °C for 8 h, acetonitrile (5 mL), and the appropriate phase-transfer catalyst (0.10 mmol) was refluxed at 85 °C under nitrogen. After cooling to room temperature, the organic phase was filtered through silica gel. A sample of the collected solution was analyzed by gas chromatography to determine the yield of product using biphenyl as the internal standard (115 °C for 1.2 min followed by 45 °C min^{-1} ramp to 195 °C, held for 1 min. Injector: 300 °C, detector: 300 °C. R_t 2.79 min (biphenyl), 2.92 min (2,4-dinitrofluorobenzene), 3.37 min (2,4-dinitrochlorobenzene)).

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(20) The highly coupled ^{13}C signals of the fluorinated carbons are not listed.

General Procedure for the Separation and Recovery of Macrocycles 3 and 5 after Fluoride Displacement Reaction. After 24 h, the reaction mixture was cooled to room temperature and was filtered to remove the excess potassium salts which were extracted with hot acetonitrile (5 mL). After adding water (15 mL), the organic phase was extracted with dichloromethane (5 mL) and was dried over magnesium sulfate. The organic phase was passed through a short column of fluorous reverse phase silica gel (∼3 g, 2.5 cm long, 1.5 cm diameter), and the column was eluted with dichloromethane (20 mL) to obtain the clean organic products. The fluorinated phase-transfer catalyst was then recovered (95−97%) by eluting with trifluoroethanol (20 mL) and ethyl acetate (20 mL). After removing the solvents, the phase-transfer catalyst was dried in vacuo for 2 h at 60 °C before being reused in another aromatic nucleophilic substitution.

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Supporting Information Available: General experimental information, experimental procedures and analytical data for the preparation of $C_{10}F_{21}(CH_2)_3OH$, macrocycles **2** and **5**, copies of NMR spectra, and the experimental procedures for the picrate extraction studies and partition coefficients. This material is available free of charge via the Internet at http://pubs.acs.org.

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