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Perfluorocarbon Soluble Crown Ethers as Phase Transfer Catalysts

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Abstract: Fluorous derivatives of dibenzo-18-crown-6 ether were readily prepared by means of metal-catalyzed cross-coupling reactions, and then successfully applied as catalysts in representative solid-liquid phase transfer catalysis (PTC) reactions, which were performed in standard organic solvents, such as chlorobenzene and toluene, and also in fluorous solvents, such as perfluoro-1,3-dimethylcyclohexane (PFDMC). It was clearly shown that properly designed fluoroponytailed crown ethers can promote the disintegration of the crystal lattice of alkali salts and transfer anions from the solid surface into an apolar, non-coordinating perfluorocarbon phase. Far from being a simple chemical curiosity, this unprecedented observation has relevant implications in the design of PTC scenarios of wide applicability. This new paradigm represents an advance in crown ether chemistry, and their use as recyclable phase transfer catalysts.

Keywords: crown compounds; fluoroponytails; Heck reaction; nucleophilic substitution; oxidation; phase-transfer catalysis

Introduction

Crown ethers (CE) have played a very significant role in many aspects of organic chemistry, and especially in phase transfer catalysis (PTC), where their ability to form specific complexes with metal cations, M^+, leads to the formation of organophilic ion pairs $[CE\text{-}M]^+X^-$ and to the consequent activation and transfer of anions X^- from a solid, or less frequently aqueous phase, to a liquid organic phase.[1] The term PTC encompasses several different techniques for accelerating reactions between two or more reactants present in two or more phases, all characterized by operational simplicity, mild conditions, high reaction rates, high selectivity, and the utilization of inexpensive reagents.[2] These techniques, that offer significant advantages over conventional procedures, have been widely applied in industry for the synthesis of pharmaceuticals, perfumes, flavorants, dyes, agricultural chemicals, monomers, polymers, and for many other applications.[3] PTC processes still have great potential for waste reduction and catalyst reuse. Indeed, removal of traditional phase-transfer (PT) catalysts from the reaction mixture can be achieved by solvent extraction, distillation, adsorption, or simply by washing the organic phase with copious amounts of water. In most cases, such PT catalysts have not been recovered from the effluents, or, once recovered, they have not been pure enough, and have been disposed of as waste, thus increasing the process costs and reducing the otherwise remarkable environmental benefits of the PTC approach. CE have shown higher chemical stability in comparison to other popular PT catalysts, such as ammonium and phosphonium (onium) salts, but are also more expensive and present potential health risks.[1] Therefore, their efficient separation and recovery from reaction mixtures, and, if possible, their recycle are greatly desirable.

Heterogeneous PT catalysts, bound to either an insoluble polymer or an insoluble inorganic support, have been developed in order to overcome these problems.[4] They can be easily separated from reaction products by simple filtration and then reused; but unfortunately, their broad application has been limited by the fact that most PTC reactions are much slower with insoluble catalysts owing to mass transfer limitations. More importantly, most solid-bound catalysts have not been found to be mechanically robust

enough to survive repeated reaction/separation cycles. As an alternative, immobilization of PT catalysts on soluble polymers, such as poly(ethylene glycol)s (PEGs), has been proposed.[5] Reactions were performed under standard PTC conditions, after which selective precipitation of the supported catalyst was induced by thorough dilution of the organic phase with an additional solvent, showing little affinity for the polymer matrix (e.g., Et_2O in the case of PEGs). This method showed some limitations as well, in particular, large amounts of extra solvent were required in the precipitation step, and also for the efficient washing of the crude precipitate. In addition, its applicability to catalysts other than simple ammonium salts has been not demonstrated as yet.

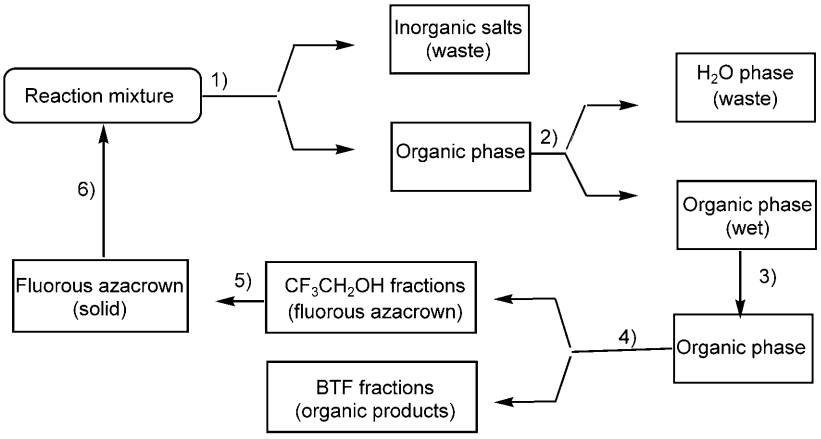
Fluorous biphasic catalysis, with its many variants,[6] has been shown to be important for the separation of catalysts and products, and it could have a beneficial impact on PTC techniques, as demonstrated by a few recent studies describing the use of fluorous PT in typical PTC reactions.[7] In a first example, an enantiopure C_2-symmetric fluorous ammonium bromide developed by Maruoka and co-workers was applied to the asymmetric synthesis of both natural and unnatural α-amino acids through enantioselective liquid-liquid PTC alkylation of a protected glycine derivative.[8] Reactions were conducted at 0 °C in a 50% aqueous KOH/toluene liquid-liquid biphasic system, where the fluorous PT catalysts formed a third solid phase. At the end of the reaction, the fluorous salt was separated from the organic products by extraction of the reaction mixture with perfluorohexane, and it could be reused at least two more times without any loss of activity and selectivity. However, the efficiency and enantioselectivity of this catalyst were clearly inferior to those exhibited by similar non-fluorous onium salts under analogous conditions. Stuart, Gladysz and co-workers synthesized a series of symmetrically and unsymmetrically substituted phosphonium salts by quaternarization of tertiary fluorous phosphines with primary fluorous and non-fluorous alkylating agents.[9] Their viability as catalysts in liquid-liquid PTC halide exchange (Finkelstein) reactions between fluorous substrates $C_8F_{17}(CH_2)_nX$, (n = 2 or 3, X = I, Br or Cl) dissolved in either octafluorotoluene or perfluoromethyldecalin, and aqueous MY (KI, NaCl, or NaBr) was demonstrated. Recovery of such fluorous onium salts by their selective, although incomplete, precipitation from the fluorous phase upon addition of hexane was also feasible, with regard to the superior solubility of the $C_8F_{17}(CH_2)_nY$ products in the mixture hexane/perfluorocarbon.[9b]

The only literature report dealing with fluorous PT catalysts other than onium salts was made by Stuart and Vidal, and it was focussed on perfluoroalkylated 4,13-diaza-18-crown-6 ethers.[10] Common organic solvents, such as halocarbons, toluene, Et_2O, and EtOAc were good solvents for these compounds, and their partition coefficients between perfluoro-1,3-dimethylcyclohexane (PFDMC) and organic solvents were somewhat biased towards the organic phase. Only in the case of extremely polar, fluorophobic organic solvents like CH_3CN, was there a bias towards the fluorous phase. Due to this behaviour, typical of light fluorous compounds, perfluoroalkylated 4,13-diaza-18-crown-6 ethers could only be tested as catalysts under standard solid-liquid PTC conditions. Two substitution reactions were studied: namely, the halide exchange reaction between 1-bromooctane and solid KI (organic solvent = trifluoromethylbenzene, BTF), and the aromatic nucleophilic substitution of an activated chlorobenzene derivative with solid KF (organic solvent = CH_3CN). The fluorinated macrocycles could be recovered from the organic phase using a multistep procedure based on fluorous solid-phase extraction with BTF and CF_3CH_2OH as the organophilic and fluorophilic solvents, respectively (Scheme 1), and one of them could be reused six times in the Finkelstein reaction. At the end of the recycling experiments, 70% of the original catalyst quantity was recovered.

What was extremely surprising was that, despite the potential advantages associated with the use of an additional fluorous liquid phase in the reaction step, PTC involving organic substrates and fluorous PT catalysts dissolved in perfluorocarbons has been largely ignored, since no examples have been published, to the best of our knowledge. Therefore, we wish to report on the synthesis of the first perfluorocarbon soluble CE derivatives of dibenzo-18-crown-6 ether, their solubilization of potassium anion salts, such as KI, KCN, KOMe, and KOH in the fluorous phase, and their subsequent reactivity in PTC nucleophilic substitution and oxidation reactions with aliphatic and aromatic halogen substrates, and a aromatic substituted hydrocarbon, respectively.

Results and Discussion

Perfluorocarbon-soluble CE derivatives were designed on the basis of the experience gained from our previous investigations on fluorous macrocylic ligands.[11] It was thus realized that, besides a relatively high fluorine loading, the presence of more than two fluoroponytails was crucial for ensuring a suitable degree of fluorophilicity to the CE derivatives. To this end, dibenzo-18-crown-6 ether (**DB18-C-6**) was an ideal scaffold, due to the ease of controlled functionalization of its aromatic moieties, and to their possible shielding effect towards the electron-withdrawing effect of perfluoroalkyl substituents, which could significantly reduce the Lewis basicity of the oxygen binding sites, and thus the utility of the resulting fluoroponytailed CE as a PT catalyst. We found that up



1) Filtration; 2) aqueous washing; 3) drying; 4) fluorous solid-phase extraction (BTF washing followed by CF_3CH_2OH washing); 5) evaporation of CF_3CH_2OH; 6) addition of the catalyst and solid inorganic reagent to a fresh BTF solution of organic reagent and new reaction cycle.

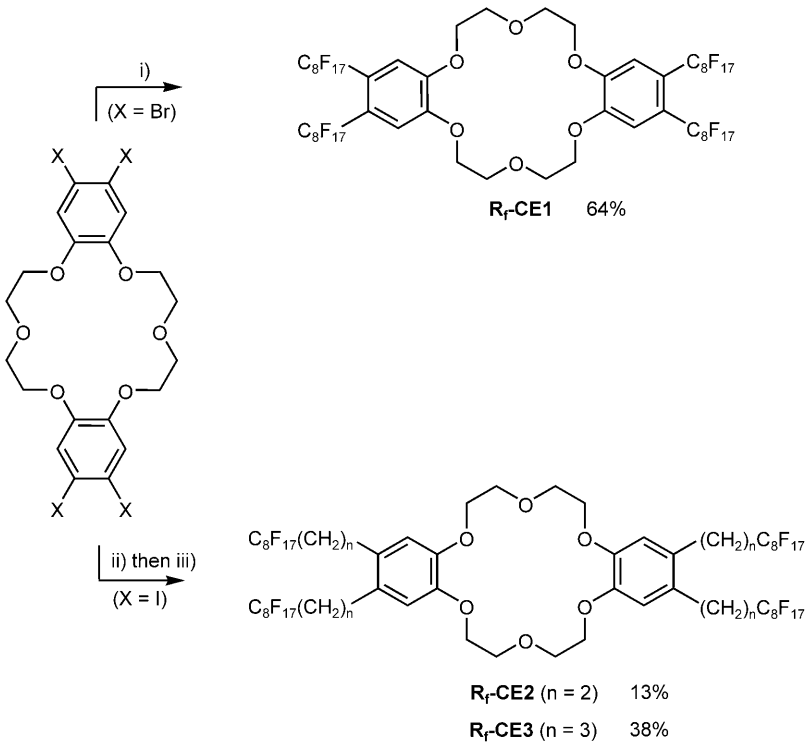
Scheme 1. Separation and reuse of light fluorous azacrowns used as PT catalysts under standard solid-liquid PTC conditions.[10]

to four fluoroponytails, C_8F_{17}, could be directly introduced into the aromatic subunits of **DB18-C-6** by means of metal-catalyzed cross-coupling reactions, as exemplified by the synthetic pathways shown in Scheme 2.

***R*$_f$-CE1** (% F = 63.6%), a derivative of **DB18-C-6** bearing fluoroalkyl-ponytailed C_8F_{17} substituents directly attached to the aromatic subunits, was readily prepared in 64% yield by copper-catalyzed perfluoroalkylation of 4,4′,5,5′-tetrabromodibenzo-18-crown-6 with $C_8F_{17}I$.[12] Both ***R*$_f$-CE2** (% F = 60.2) and ***R*$_f$-CE3** (% F = 58.7) were prepared by Heck vinylation of 4,4′,5,5′-tetraiododibenzo-18-crown-6 with an appropriate perfluoroalkene under Jeffery's conditions,[13,14] and this was followed by hydrogenation of the perfluoroalkenyl-substituted intermediates. Overall yields were 13% and 38% in the case of ***R*$_f$-CE2** and ***R*$_f$-CE3**, respectively.

In contrast to previously reported perfluoroalkylated 4,13-diaza-18-crown-6 ethers,[10] the three fluoroponytailed **DB18-C-6** derivatives were found to be almost insoluble in common organic solvents at room temperature, with the exception of CH_2Cl_2 and $CHCl_3$, but totally soluble in BTF, and also in perfluorocarbons at temperatures slightly above 40 °C, with partial precipitation of ***R*$_f$-CE2** and ***R*$_f$-CE3** from their 10^{-2} M solutions, after standing at room temperature for a few hours. The significant fluorophilicity exhibited by the three CE was confirmed by partition coefficient measurements between PFDMC and organic solvents, including low polar ones (Table 1). Values ranged from > 98/2 to 70/30 in the cases of ***R*$_f$-CE1** and ***R*$_f$-CE3** (organic solvent = CH_2Cl_2), respectively.

The complexation ability of the new macrocyclic ligands towards alkali metal cations was evaluated by studying the extraction of the corresponding picrate salts from aqueous solutions into selected solvents, and the results are summarized in Table 2. **DB18-C-6** has been known to bind K^+ ions preferentially over other alkali metal cations, on the basis of the match between the cavity and the cation size. This property was maintained by its fluorous CE derivatives, ***R*$_f$-CE1–3**, as shown by the comparison of potassium and sodium picrate extraction performed in CH_2Cl_2 (entries 1–4). Furthermore, it was also demonstrated that the two, and the better three methylene spacers with the fluoroponytails, was necessary for efficient K^+ binding, since the powerful electron-withdrawing effect of a C_8F_{17} group directly bonded to the aromatic ring, inhibited cation binding to the CE oxygen array. This behaviour was similar to the well-known inverse relationship between the cumulative electron-withdrawing power of the substituents, and the complexation ability of dibenzo-18-crown-6 ether derivatives towards potassium and sodium salts.[15] The presence of three methylene spacer units in ***R*$_f$-CE3** ensured a picrate extraction ability very close to that of the classical PT catalyst, **DB18-C-6**, both in a typical organic solvent (CH_2Cl_2, entry 1 *vs.* 4), and in the partially fluorinated BTF (entry 5 *vs.* 8). As previously observed in related experiments with fluorous phosphonium salts or perfluoroalkylated 4,13-diaza-18-crown-6 ethers,[9a,10] the nature of the non-aqueous solvent



i) $C_8F_{17}I$, Cu, DMF, T = 120 °C

ii) $C_8F_{17}(CH_2)_{n-2}CH{=}CH_2$, $Pd(OAc)_2$, Bu_4NHSO_4, $NaHCO_3$, DMF/BTF, T = 90 °C.

iii) H_2 (1 atm), Pd/C, MeOH/BTF

Scheme 2. Synthesis of perfluorocarbon soluble CE derivatives.

Table 1. Partition coefficients *P* of fluorous CE between PFDMC and organic solvents.[a]

Organic Solvent	P [R_f-CE]$_{PDMC}$/[R_f-CE]$_{Org.\ Solv.}$		
	R_f-CE1	R_f-CE2	R_f-CE3
Toluene	>98/2	96.9/3.1	86.5/13.5
CH_2Cl_2	>98/2	89.4/10.6	69.7/30.3
CH_3CN	>98/2	97.0/3.0	96.4/3.6

[a] Determined gravimetrically at $T=20$ °C (see Experimental Section). PFDMC = perfluoro-1,3-dimethylcyclohexane. Fluorous CE structures are defined in Scheme 2.

had a great influence on the level of potassium picrate extraction by fluorous CE (entries 2 *vs.* 6 and 9, 3 *vs.* 7, and 10, 4 *vs.* 8 and 11), and extractions in BTF proved to be far less efficient than those performed in CH_2Cl_2. Quite interestingly, the extraction ability of **DB18-C-6** was affected likewise by this change of solvent (entry 1 *vs.* 5), thus suggesting BTF may be a less efficient medium for PTC reactions. However, the most outstanding feature of these experiments was the clear demonstration that ***R*$_f$-CE3**, and ***R*$_f$-CE2** to a much lesser extent, retained their potassium ion complexing abilities even in an apolar, non-coordinating perfluorocarbon such as PFDMC (entries 10 and 11). This unprecedented behaviour considerably increased the chances that fluorous CE could act as PT catalysts in perfluorocarbons.

Table 2. Picrate extraction experiments.[a]

Entry	CE	Picrate extracted [%]		
		Solvent	Na^+	K^+
1	**DB18-C-6**	CH_2Cl_2	2.5	35.2
2	***R*$_f$-CE1**	CH_2Cl_2	<1	2.5
3	***R*$_f$-CE2**	CH_2Cl_2	1.2	20.9
4	***R*$_f$-CE3**	CH_2Cl_2	2.3	37.3
5	**DB18-C-6**	BTF[b]	–	12.3
6	***R*$_f$-CE1**	BTF	–	n.d.[c]
7	***R*$_f$-CE2**	BTF	–	3.2
8	***R*$_f$-CE3**	BTF	–	10.8
9	***R*$_f$-CE1**	PFDMC	–	n.d.
10	***R*$_f$-CE2**	PFDMC	–	1.1
11	***R*$_f$-CE3**	PFDMC	–	30.7

[a] Equal volumes of a 10^{-4} M aqueous solution of alkali metal picrate and a 10^{-4} M organic or fluorous solution of CE at $T=25$ °C (see Experimental Section).
[b] BTF = Trifluoromethylbenzene
[c] n. d. = not detected.

Lipophilic CE able to form complexes with alkali metal cations have been shown to be the catalysts of choice in many solid-liquid PTC reactions;[1b] namely, in reactions where a solid ionic reagent was suspended in an anhydrous organic solution containing the substrate and the PT catalyst. The latter interacts with the surface of the solid salt, thus promoting the collapse of the crystal lattice and the subsequent transfer of the anion, as a reactive ion pair, from the surface of the solid into the liquid organic phase. This option offers specific advantages over liquid-liquid PTC, in particular, it avoids the presence of water, which may cause the reduction of the rate of the main process, lead to undesired side reactions, and complicate the isolation of the products.[2a] To get an insight into the impact of the residual electron-withdrawing effect of the fluoroponytails and the nature of the solvent system on the efficiency of the solid-liquid PTC process, the catalytic activities of ***R*$_f$-CE1–3** were first investigated in the classical Finkelstein reaction between 1-bromooctane and KI [Eq. (1)] and compared to that of **DB18-C-6**.

$$C_8H_{17}\text{—Br} + KI \xrightarrow[\text{solvent/90 or 110 °C}]{\textbf{CE} \text{ (2 mol\%)}} C_8H_{17}\text{—I} \qquad (1)$$

BTF has been shown to be a credible solvent both for fluorous and purely organic molecules, while it was completely miscible with most organic solvents. Such amphiphilic behaviour was clearly incompatible with the requirements of the fluorous biphasic reaction systems. However, BTF has been widely used in reactions where fluorous reagents and/or catalysts showing limited solubility in perfluorocarbons were involved, including the halide exchange between 1-bromooctane and KI under solid-liquid PTC conditions.[10] This model reaction was thus initially performed in the presence of 2 mol% of ***R*$_f$-CE1–3** or **DB18-C-6** in BTF at 90 and 110 °C, and the results are shown in Table 3 and Figure 1. Independent of the

Table 3. Finkelstein reaction [Eq. (1)] in BTF under PTC conditions.[a]

Entry	CE	T [°C]	t [h]	Yield [%]	TON[b]	TOF[c]
1	–	90	24	3	–	–
2	**DB18-C-6**	90	24	89	45	1.88
3	***R*$_f$-CE1**	90	24	20	10	0.41
4[d]	***R*$_f$-CE1**	90	24	17	9	0.36
5	***R*$_f$-CE2**	90	24	90	45	1.88
6	***R*$_f$-CE3**	90	15	91	45	3.03
7	–	110	24	3	–	–
8	**DB18-C-6**	110	15	94	47	3.14
9	***R*$_f$-CE1**	110	24	21	11	0.45
10	***R*$_f$-CE2**	110	15	92	46	3.08
11	***R*$_f$-CE3**	110	12	95	47	3.94

[a] Solid/liquid PTC. *Reaction conditions:* substrate = 1 mmol, KI = 5 mmol, CE = 2 mol%, BTF = 4 mL. Selectivity for $C_8H_{17}I > 98\%$.
[b] TON = mmol converted substrate/mmol catalyst.
[c] TOF = mmol converted substrate/(mmol catalyst × hour).
[d] Liquid/liquid PTC. *Reaction conditions:* substrate = 1 mmol, KI = 5 mmol, CE = 2 mol%, BTF = 2 mL, H_2O = 0.6 mL.

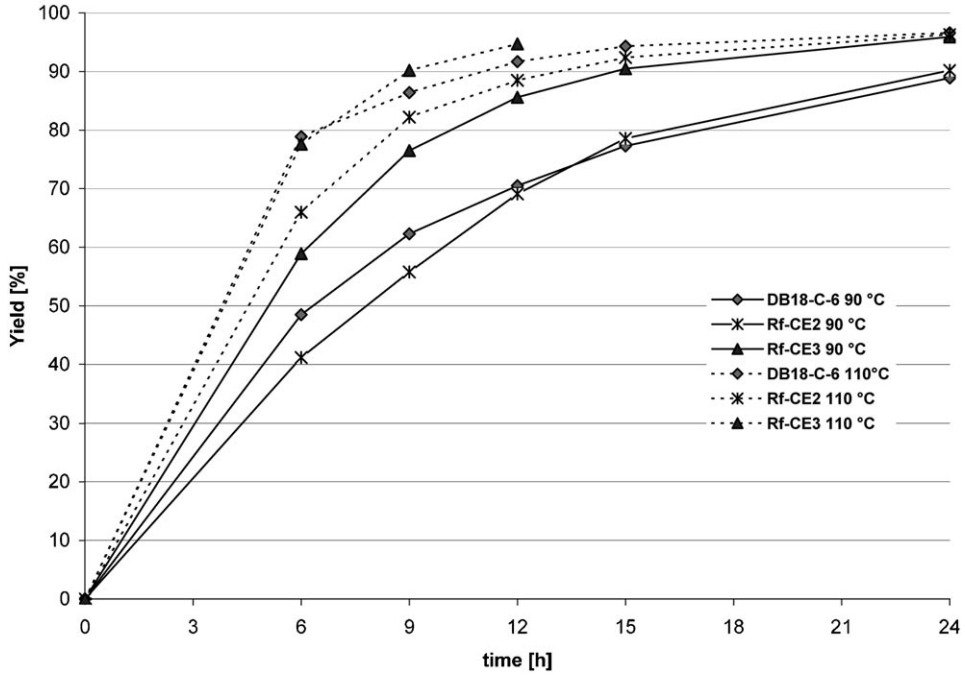


Figure 1. Rates of formation of 1-iodooctane in solid-liquid PTC reactions run in BTF.

temperature, the halide exchange occurred to a very limited extent in the absence of a PT catalyst (Table 3, entries 1 and 7), while the addition of R_f-**CE2** (entries 5, 10), R_f-**CE3** (entries 6, 11), or **DB18-C-6** (entries 2, 8) catalyzed the formation of 1-iodooctane in high yields, with reaction rates following the order: R_f-**CE3** > **DB18-C-6** > R_f-**CE2**, both at 90 and 110 °C, although as shown in Figure 1, the catalytic activities of R_f-**CE3** and **DB18-C-6** became closer as the reaction temperature was increased. Alternatively, R_f-**CE1** proved to be a poor PT catalyst, both under solid-liquid (entries 3 and 9) and liquid-liquid (entry 4) PTC conditions, in agreement with the results obtained in the picrate extraction tests.

Further experiments performed in chlorobenzene (Table 4 and Figure 2) demonstrated the central role of the solvent in determining the PTC activity of fluorous CE. Indeed, chlorobenzene was known to be an excellent medium for anion-promoted reactions catalyzed by standard PT catalysts,[16] and in this solvent the best results were obtained with **DB18-C-6** (Table 4, entries 2 and 7). Both reaction yields and rates (Figure 2) were superior to those observed in BTF with the same catalysts, and also with R_f-**CE3**. The behaviour of the latter (entries 5 and 10) was not improved by the change of solvent, while the catalytic activities of R_f-**CE1** (entries 3 and 8) and R_f-**CE2** (entries 4 and 9) were drastically reduced. This effect was more pronounced for reactions run at 90 °C where, in the case of R_f-**CE2**, the low solubility of the fluorous CE in chlorobenzene also provided a negative effect. Nevertheless, R_f-**CE2** gave comparatively poorer results in chlorobenzene than in BTF, even at 110 °C. At that temperature, the fluorous CE was completely soluble in the reaction environment, thus highlighting the inherent influence exerted by the solvent nature on the outcome of the PTC process.

Table 4. Finkelstein reaction [Eq. (1)] in chlorobenzene under PTC conditions.[a]

Entry	CE	T [°C]	t [h]	Yield [%]	TON[b]	TOF[c]
1	–	90	24	1	–	–
2	**DB18-C-6**	90	15	97	49	3.24
3	R_f-**CE1**	90	24	7	4	0.15
4	R_f-**CE2**	90	24	32	16	0.68
5	R_f-**CE3**	90	15	92	46	3.05
6	–	110	24	3	–	–
7	**DB18-C-6**	110	9	96	48	5.32
8	R_f-**CE1**	110	24	21	11	0.44
9	R_f-**CE2**	110	24	94	47	1.96
10	R_f-**CE3**	110	12	95	47	3.95

[a] Solid/liquid PTC. *Reaction conditions:* substrate = 1 mmol, KI = 5 mmol, CE = 2 mol%, chlorobenzene = 4 mL. Selectivity for $C_8H_{17}I$ > 98%.
[b] TON = mmol converted substrate/mmol catalyst.
[c] TOF = mmol converted substrate/(mmol catalyst × hour).

Based on these results, we were intrigued by the possibility of using both a perfluorocarbon and the more promising fluorous CE compounds, R_f-**CE2** and R_f-**CE3**, in PTC nucleophilic substitution reactions, with KI, KCN, and KOMe, along with aromatic and aliphatic halogen substrates. In fact, the achievement of reactivity and selectivity comparable or even supe-

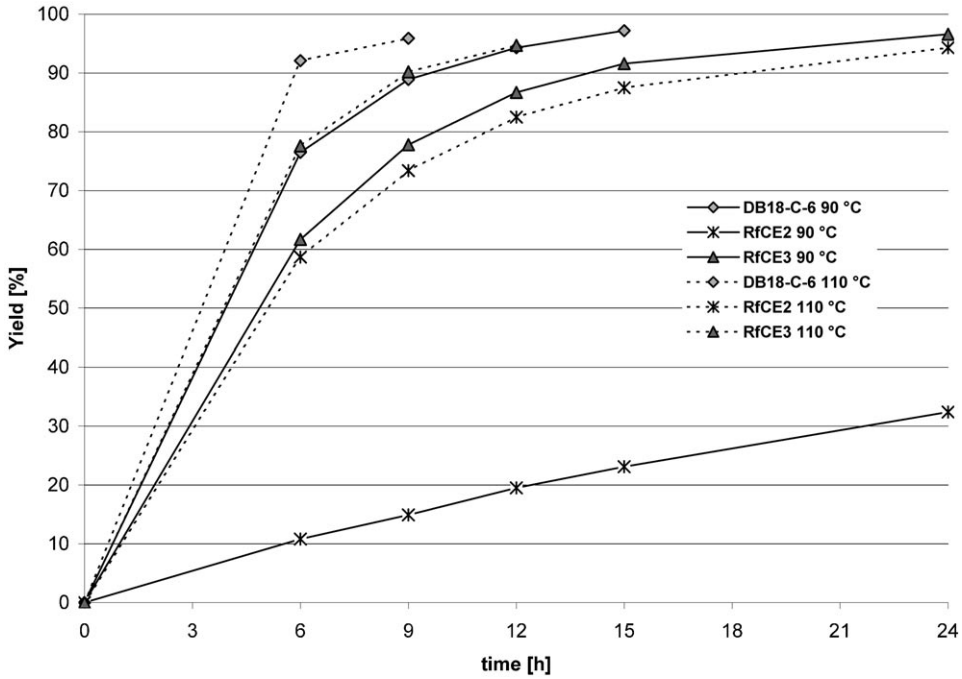
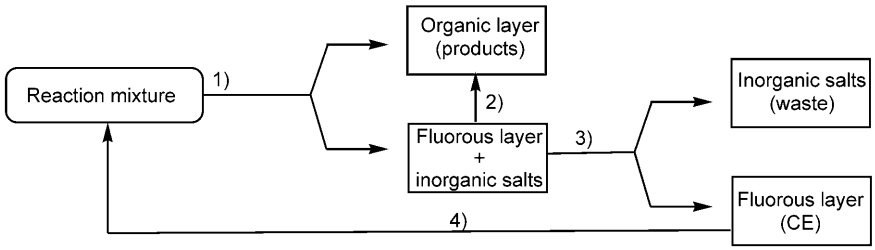


Figure 2. Rates of formation of 1-iodooctane in solid-liquid PTC reactions run in chlorobenzene.

rior to those observed with classical PT agents, without compromising the ease of recovery and the recycling efficiency, was a primary goal of our research on fluorous PT catalysts. These goals could not be attained without the systematic search for optimal reaction conditions and PTC techniques in association with these particular CE compounds. Thus far, simple liquid-liquid and solid-liquid PTC systems have been explored, but fluorous PT catalysts would also offer the opportunity to consider alternative approaches; for example, the use of a triphasic system consisting of a fluorous, organic, and an inorganic phase. We expected that, in analogy to other multiphase PTC systems,[17] at the end of the reaction, the immiscible fluorous phase containing ***R*$_f$-CE2** and ***R*$_f$-CE3** could be easily recovered and reused without resorting to any specific treatment, such as fluorous solvent or solid-phase extraction techniques (Scheme 3).

The benchmark PTC experiment with PFDMC was obviously the same Finkelstein reaction as already performed under standard solid-liquid conditions. This time, the KI was in the bottom solid phase, the ***R*$_f$-CE2** and ***R*$_f$-CE3** compounds in the PFDMC layer, while 1-bromooctane was the top layer (photographic illustrations are shown in the Supporting Information). Results are summarized in Table 5.

Clearly, ***R*$_f$-CE2** and ***R*$_f$-CE3** were necessary for the PTC reaction to occur, while entries 4–6 define recycle of the CE, which was accomplished by simple phase separation as shown in Scheme 2, as a facile process that circumvents the necessity of any cumbersome, waste-producing, post-reaction manipulations, including the use of fluorous solid-phase materials (see Scheme 1). Interestingly, a ^{1}H NMR spectrum of the recovered solid during evaporation of the PFDMC layer, after four recycles, showed downfield



1) Phase separation; 2) organic washing; 3) filtration; 4) addition of fresh reagents to the fluorous layer and new reaction cycle.

Scheme 3. Separation and reuse of perfluorocarbon soluble CE.

Table 5. Finkelstein reaction [Eq. (1)] in PFDMC under PTC conditions.[a]

Entry	CE	*T* [°C]	*t* [h]	Yield [%]	TON[b]	TOF[c]
1	–	90	24	9	–	–
2	***R*$_f$-CE2**	90	24	64	32	1.33
3 (Run 1)	***R*$_f$-CE3**	90	8 (15)	69 (95)	34 (48)	4.31 (3.16)
4 (Run 2)[d]		90	8 (15)	68 (93)	34 (47)	4.31 (3.10)
5 (Run 3)[d]		90	8 (15)	66 (93)	33 (47)	4.25 (3.10)
6 (Run 4)[d]		90	8 (15)	68 (90)	34 (45)	4.31 (3.01)
7	–	110	24	17	–	–
8	***R*$_f$-CE2**	110	24	87	44	1.81
9	***R*$_f$-CE3**	110	12	96	48	4.01
10 (Run 1)[e]	***R*$_f$-CE3**	90	24	78	39	1.63
11 (Run 2)[e,f]		90	24	73	37	1.52
12 (Run 3)[e,f]		90	24	69	35	1.45

[a] Solid/liquid PTC. *Reaction conditions:* substrate = 1 mmol, KI = 5 mmol, CE = 2 mol%, PFDMC = 4 mL. Selectivity for $C_8H_{17}I > 98\%$.

[b] TON = mmol converted substrate/mmol catalyst.

[c] TOF = mmol converted substrate/(mmol catalyst × hour).

[d] Recycling experiment: the fluorous layer was recovered at room temperature from the preceding reaction, and reused in subsequent reaction cycles.

[e] Solvent = toluene.

[f] Recycling experiment: the solid catalyst was recovered at 0 °C from the preceding reaction, and reused; the inorganic salts were first centrifuged from the hot mixture.

shifts of the -OCH_2CH_2O- resonances from 4.00 and 4.15 ppm to 4.25 and 4.17 ppm, while the aromatic resonance were shifted upfield from 6.65 to 6.61 ppm. This was similar to the literature values for the inclusion complexes of several K^+X^- in **DB18-C-6**,[18] and clearly defines the formation of **[(R_f-CE3)K]$^+$I$^-$** in a fluorous solvent. Moreover, we independently synthesized the **[(R_f-CE3K]$^+$I$^-$** complex, which corroborated the above-mentioned NMR results (see Supporting Information). Furthermore, entries 10–12 in Table 5 allowed a pertinent example of the thermomorphic property of **R_f-CE3**,[19] with this catalyst being insoluble in toluene at 0 °C, while at 90 °C it was fully soluble (see Supporting Information); recycle was *via* filtration of the ice-cold suspension, after removal of the inorganics from the hot reaction mixture (Experimental Section). This latter thermomorphic property of **R_f-CE3** added a new dimension to the PTC process, and furthermore, was accomplished without the perfluorocarbon solvent.

The nucleophilic displacement reaction of *n*-octyl methanesulfonate with solid KCN in PFDMC to provide *n*-octyl cyanide in >98% selectivity was then studied. The control experiment (Table 6, entry 1)

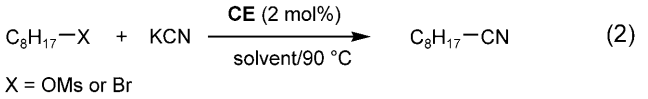
Table 6. Nucleophilic substitution reactions with KCN under PTC conditions [Eq. (2)].[a]

Entry	CE	X	Solvent	Yield [%]
1	–	OMs	PFDMC	35
2	**R_f-CE3**	OMs	PFDMC	71
3	–	Br	PFDMC	<1
4	**R_f-CE3**	Br	PFDMC	7
5	**DB18-C-6**	Br	toluene	9
6[b]	–	Br	PFDMC/H_2O	<1
7[b]	**R_f-CE3**	Br	PFDMC/H_2O	93

[a] Solid/liquid PTC. *Reaction conditions:* substrate = 0.5 mmol, KCN = 2.5 mmol, CE = 2 mol%, solvent = 2 mL, time = 24 h. Selectivity for $C_8H_{17}CN$ >98%.

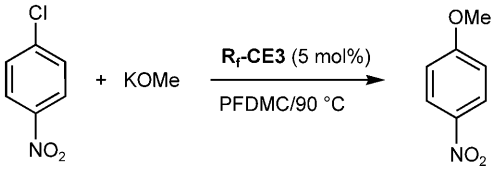
[b] Thin-layer PTC. *Reaction conditions:* substrate = 0.5 mmol, KCN = 2.5 mmol, CE = 2 mol%, PFDMC = 2 mL, H_2O = 0.16 mL, time = 24 h. Selectivity for $C_8H_{17}CN$ >98%.

clearly afforded less of the product in comparison to the addition of **R_f-CE3** (entry 2). The less reactive 1-bromooctane [Eq. (2), X = Br] was also used as a substrate in order to demonstrate the catalytic effect of **R_f-CE3**. Thus, traces of *n*-octyl cyanide were formed in the absence of a catalyst (entry 3), but also solid-liquid PTC reactions run in the presence of either 2 mol% of **R_f-CE3** (entry 4) or **DB18-C-6** (entry 5) gave product yields of ~10%. Moreover, the rate of the PTC cyanide displacement reaction of 1-bromooctane in organic solvents was previously found to be a function of the amount of added water.[20] We observed similar behaviour for reactions in PFDMC, while the catalytic effect of **R_f-CE3** was clearly evident using thin-layer PTC conditions (entries 6 and 7),[21] where the addition of a small amount of water generates a third liquid phase coating on the surface of the solid.[22]



(2)

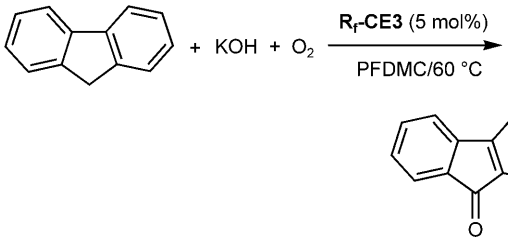
The PTC of anion solubility in PFDMC was further extended to KOMe, and its nucleophilic aromatic substitution reaction (S_NAr) with 4-nitrochlorobenzene [Eq. (3)]. Pertinently, these S_NAr reactions were known to be challenging under standard conditions,[23] while other competitive reactions were also known to interfere in the absence of a CE.[23b] What was so important, as epitomized in the model reaction, was the three-fold increase in yield of product, from 24%, in the absence of a CE, to 70%, afforded by **R_f-CE3** (5 mol%). As observed in common organic solvents, the addition of the fluorous CE selectively increased the rate of the S_NAr process, and therefore, it was highly beneficial with respect to the product selectivity.



(3)

It has been previously shown that carbanions of organic compounds with acidic C–H bonds can be generated in the presence of inorganic bases under liquid-liquid or solid-liquid PTC conditions, and then oxidized with molecular oxygen.[24] The substrate most studied for the above-mentioned reaction was fluorene, which undergoes a PTC aerobic oxidation to yield fluorenone. Therefore, analogously to organic CE and cryptates, **R_f-CE3** was able to catalyze that model reaction when solid KOH was used as the base [Eq. (4)]. In a blank reaction performed at 60 °C in PFDMC, conversion of the substrate was as low as 30%, and fluorenone was obtained in 26% yield, while conversion reached 99%, with a yield in fluorenone of 93%, when **R_f-CE3** (5 mol%) was added to the reaction mixture.

Having finally established the feasibility and convenience of PTC involving organic substrates and fluorous PT catalysts dissolved in perfluorocarbons, specific studies addressing the manifold of mechanistic issues of this process ,e.g., the way anions could be transported from the solid to the liquid phase, the



(4)

nature of the reactive ion pairs formed by the fluorous PT catalysts, and the solvent phase where the final interaction with the organic substrates takes place, can be now pursued. This can be expected to be a long-term project, as in the case of conventional PTC.[3,22]

Conclusions

Polyfluorinated onium salts and macrocylic ligands with typical fluorous characteristics, and yet retaining the ability to transfer reactive anionic species from water or from a solid surface into a second liquid phase, have recently emerged on the PTC scene. Therefore, their true potential in PTC reactions has still to be discerned, and the field will be expected to continue to grow in the near future. In these present studies, we have demonstrated, for the first time, that properly designed fluorous CE, such as ***R*$_f$-CE2** and ***R*$_f$-CE3**, are excellent phase-transfer catalysts that allow solubilization of potassium salts in a non-coordinating, apolar perfluorocarbon solvent, leading to their reactivity in nucleophilic substitution and oxidation reactions. Recycle was shown to be facile by simply reusing the fluorous phase for each catalytic run. Moreover, ***R*$_f$-CE3** was found to be thermomorphic in toluene, and fully extends the PTC paradigm for catalyst recycle.

At this stage, the remarkable PTC activity of ***R*$_f$-CE3** in PFDMC can be reasonably ascribed to a poorly solvated anion effect in a hydrophobic solvent environment that provides a driving force for nucleophilic substitution at the solvent/substrate interface, and to a minor extent, the fluorous phase. Further mechanistic investigations will lead to a better understanding of the numerous facets of PTC in a perfluoro-carbon environment.

Experimental Section

General Remarks

Solvents were purified by standard methods, except perfluoro-1,3-dimethylcyclohexane (PFDMC, CAS [335–27–3], Apollo Scientific Ltd.) that was used as received. *n*-Perfluoro-octyl iodide (Fluka), 1*H*,1*H*,2*H*-heptadecafluoro-1-decene (Aldrich) and all commercially available reagents were used as received. 4,4′,5,5′-Tetrabromodibenzo-18-crown-6 ether,[12] 4,4′,5,5′-tetraiododibenzo-18-crown-6 ether,[14a] and 1*H*,1*H*,2*H*,3*H*,3*H*-heptadecafluoro-1-undecene[14b] are known compounds and were prepared as described in the literature. Reactions were monitored by TLC on silica gel 60 F_{254}. Column chromatography was carried out on silica gel SI 60 (Merck, Germany), 0.063–0.200 mm (normal) or 0.040–0.063 mm (flash). Melting points (uncorrected) were determined with a capillary melting point apparatus Büchi SMP-20. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on Bruker AC 300 and Bruker Avance 400 spectrometers. UV-Vis measurements were performed on a Nicolet Evolution 500 spectrophotometer. GC analyses were performed on an Agilent 6850 instrument (column: HP-1 100% dimethylpolysiloxane 30 m × 320 μm × 0.25 μm). Carrier gas = He (constant flow); mode = split (split ratio = 80:1); injector T = 250 °C; detector (FID) T = 280 °C. Elemental analyses: Departmental Service of Microanalysis (University of Milano).

4,4′,5,5′-Tetra(*n*-heptadecafluorooctyl)dibenzo-18-crown-6 Ether (*R*$_f$-CE1)

Copper powder (3.15 g, 49.6 mmol) was added to a solution of 4,4′,5,5′-tetrabromodibenzo-18-crown-6 ether (0.676 g, 1.00 mmol) in dry, degassed DMF (15 mL) in a flame-dried Schlenk flask. The mixture was warmed to 120 °C and *n*-perfluorooctyl iodide (5.46 g, 10.0 mmol) was added dropwise to the stirred suspension over 15 min. After 16 h the reaction mixture was cooled to room temperature, treated with H_2O (30 mL) and Et_2O (80 mL) and filtered through a celite plug. The solid residue was further washed with AcOEt (5 × 30 mL). The aqueous layer was separated and extracted with Et_2O (2 × 10 mL) and the combined organic layers were washed with H_2O (40 mL) and dried over $MgSO_4$. The volatiles were evaporated at reduced pressure affording a green paste that was purified by column chromatography (silica gel, hexane/AcOEt, 3/2) affording the title compound as a white solid; yield: 1.30 g (64%); mp 109–110 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 315 K): δ = 3.97 (m, 8H), 4.24 (m, 8H), 7.13 (s, 4H); ^{13}C NMR (75.4 MHz, $CDCl_3$, 315 K): δ = 69.2, 70.1, 105.0–121.4 (m, R_F), 115.0, 150.9 (the signals for the *ipso* carbon atoms, designated with reference to the R_F substituents, were not detected); ^{19}F NMR (282 MHz, $CDCl_3$, 315 K): δ = −81.2 (t, $J_{F,F}$ = 10.0 Hz, 12 F), −103.3 (br s, 8 F), −118.7 (br s, 8 F), −122.2 (br s, 24 F), −123.2 (br s, 8 F), −126.6 (m, 8 F); anal. calcd. for $C_{52}H_{20}F_{68}O_6$ (2032.60): C 30.73, H 0.99; found: C 30.83, H 0.97%.

4,4′,5,5′-Tetra(1*H*,1*H*,2*H*,2*H*-heptadecafluorodecyl)-dibenzo-18-crown-6 Ether (*R*$_f$-CE2)

4,4′,5,5′-Tetraiododibenzo-18-crown-6 ether (0.864 g, 1.00 mmol), $Pd(OAc)_2$ (0.0404 g, 0.180 mmol), $NaHCO_3$ (0.840 g, 10.0 mmol), Bu_4NHSO_4 (1.36 g, 4.00 mmol) and crushed 4 Å molecular sieves (1.60 g) were transferred under nitrogen into a flame-dried Schlenk flask.[13] Dry DMF (8 mL) and $CF_3C_6H_5$ (known as BTF, 2 mL) were added and the resulting suspension was carefully degassed (vacuum/nitrogen × 3). A degassed solution of 1*H*,1*H*,2*H*-

heptadecafluoro-1-decene (3.57 g, 8.00 mmol) in BTF (2 mL) was added and the mixture was stirred for 20 h under nitrogen at 90 °C. The reaction mixture was then cooled to room temperature and the volatiles removed under reduced pressure. The brown residue was taken up in Et_2O (100 mL), washed with H_2O (3×20 mL) and dried over $MgSO_4$. The solvent was evaporated at reduced pressure affording a sticky dark-brown solid that was purified by column chromatography (silica gel, AcOEt) affording 4,4′,5,5′-tetra(1*H*,2*H*-heptadecafluorodecen-1-yl)dibenzo-18-crown-6 ether that was pure enough for further reactions; yield: 0.364 g (17%, mostly the all-*trans* C=C isomer). ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.02 (m, 8H), 4.23 (m, 8H), 5.92 (dt, $J_{H,H}$=16.3 Hz, $J_{H,F}$=12.5 Hz, 4H), 6.90 (s, 4H), 7.29 (dt, $J_{H,H}$=16.3 Hz, $J_{H,F}$=2.5 Hz, 4H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ=69.2, 70.2, 112.2, 105.1–120.9 (m, R_F), 117.5 (t, $J_{C,F}$=23.1 Hz), 127.1, 136.9 (t, $J_{C,F}$=9.2 Hz), 150.6; ^{19}F NMR (282 MHz, $CDCl_3$): δ=−81.2 (t, $J_{F,F}$= 9.8 Hz, 12 F), −111.4 (m, 8 F), −121.8 (br s, 8 F), −122.4 (br s, 16 F), −123.2 (br s, 8 F), −123.6 (br s, 8 F), −126.6 (m, 8 F).

To a solution of 4,4′,5,5′-tetra(1*H*,2*H*-heptadecafluoro-1-decenyl)dibenzo-18-crown-6 ether (0.215 g, 0.100 mmol) in BTF/MeOH (30 mL/5 mL) 5% Pd/C (0.212 g) was added. The mixture was stirred for 6 h under atmospheric pressure of H_2, then it was filtered through a celite plug. The clear filtrate was evaporated under reduced pressure affording a pale yellow solid that was purified by column chromatography (silica gel, AcOEt) followed by washing with ice-cold Et_2O (5 mL). The title compound was obtained as an off-white solid; yield: 0.161 g (75%); mp 124–125 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.25 (m, 8H), 2.81 (m, 8H), 3.99 (m, 8H), 4.15 (m, 8H), 6.67 (s, 4H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ=22.9, 33.0 (t, $J_{C,F}$=23.1 Hz), 69.3, 70.0, 115.4, 105.0–118.5 (m, R_F), 129.6, 148.0; ^{19}F NMR (282 MHz, $CDCl_3$,): δ=−81.3 (t, $J_{F,F}$=9.8 Hz, 12 F), −115.0 (m, 8 F), −122.2 (m, 24 F), −123.2 (br s, 8 F), −123.9 (br s, 8 F), −126.6 (m, 8 F); anal. calcd. for $C_{60}H_{36}F_{68}O_6$ (2144.82): C 33.60, H 1.69; found: C 33.43, H 1.81%.

4,4′,5,5′-Tetra(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-heptadecafluoroundecyl)dibenzo-18-crown-6 Ether (R_f-CE3)

4,4′,5,5′-Tetraiododibenzo-18-crown-6 ether (0.433 g, 0.501 mmol), $Pd(OAc)_2$ (0.0402 g, 0.180 mmol), $NaHCO_3$ (0.422 g, 5.02 mmol), Bu_4NHSO_4 (0.679 g, 2.00 mmol) and crushed 4 Å molecular sieves (1.62 g) were transferred under nitrogen into a flame-dried Schlenk flask. Dry DMF (12 mL) and BTF (4 mL) were added and the resulting suspension was carefully degassed (vacuum/nitrogen×3). A degassed solution of 1*H*,1*H*,2*H*,3*H*,3*H*-heptadecafluoro-1-undecene (3.68 g, 8.00 mmol) in BTF (4 mL) was added and the mixture was stirred for 24 h under nitrogen at 105 °C. The reaction mixture was then cooled to room temperature and diluted with BTF (50 mL). The mixture was filtered through a celite plug and the solid residue was washed with BTF (3×15 mL). The combined liquid layers were washed with H_2O (3×20 mL). The solid formed was discarded and the clear liquid phase was dried over $MgSO_4$ and evaporated under reduced pressure to give a sticky brown residue (1.04 g) that was dissolved in CH_2Cl_2 (10 mL). The solution was extracted with PFDMC (3×15 mL). The combined fluorous layers were evaporated under reduced pressure affording a brown paste (0.463 g) containing 4,4′,5,5′-tetra(1*H*,2*H*,3*H*,3*H*-heptadecafluoroundecen-1-yl)dibenzo-18-crown-6 ether [all-*trans* C=C isomer, ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.01 (m, 8H), 4.02 (m, 8H), 4.19 (m, 8H), 5.83 (dt, $J_{H,H}$=15.8 Hz, $J_{H,H}$=7.2 Hz, 4H), 6.75 (d, $J_{H,H}$=15.8 Hz, 4H), 6.86 (s, 4H)] contaminated by fluorinated by-products.

To this crude compound dissolved in BTF/MeOH (30 mL/5 mL), 10% Pd/C (0.232 g) was added. The mixture was stirred for 3 h under atmospheric pressure of H_2, then it was filtered through a celite plug. The clear filtrate was evaporated under reduced pressure affording a pale brown solid that was purified by column chromatography (silica gel, CH_2Cl_2/MeOH, 95/5) followed by crystallization from isooctane (10 mL). The title compound was obtained as an off-white solid; overall yield: 0.424 g (38%); mp 94–96 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.84 (m, 8H), 2.07 (m, 8H), 2.60 (t, $J_{H,H}$=8.1 Hz, 8H), 4.00 (m, 8H), 4.15 (m, 8H), 6.65 (s, 4H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ=22.3, 30.9 (t, $J_{C,F}$=23.4 Hz), 31.8, 69.7, 70.4, 105.0–118.5 (m, R_F), 115.8, 131.7, 147.8; ^{19}F NMR (282 MHz, $CDCl_3$,): δ=−81.2 (t, $J_{F,F}$=9.3 Hz, 12 F), −114.4 (m, 8 F), −122.3 (m, 24 F), −123.1 (br s, 8 F), −123.8 (br s, 8 F), −126.5 (m, 8 F); anal. calcd. for $C_{64}H_{44}F_{68}O_6$ (2200.92): C 34.93, H 2.02; found: C 34.82, H 2.21%.

Determination of Partition Coefficients *P*

A 10-mL vial equipped with a magnetic stirrer was charged with the fluorous-crown R_f-CE (45 mg), PFDMC (2.0 mL) and the organic solvent (2.0 mL). The mixture was thermostated at 30 °C, vigorously stirred for 0.5 h and then cooled to room temperature and allowed to stand for 15 min for the phases to separate. A 1.0-mL sample was taken out of each phase, evaporated to dryness under vacuum and weighed on an analytical balance. The partition coefficient *P* was determined as the ratio between the weight of the fluorous phase residue and the weight of the organic phase residue.

Alkali Metal Picrate Extraction

The classical Frensdorff's procedure, as modified by Kikuchi and Sakamoto, was adapted.[25] Aqueous solutions were prepared that contained the alkali metal picrate (1.0×10^{-4} M) and the corresponding alkali metal chloride (1.0×10^{-1} M). Into a stoppered test tube was placed 3.0 mL of the aqueous metal picrate solution and 3.0 mL of a 1.0×10^{-4} M solution of CE in the proper solvent. The biphasic mixture was stirred for 0.5 h at 25 °C. The sample was allowed to stand for 2 h at the same temperature to allow complete phase separation. The absorbance of the picrate in the aqueous phase was measured at 356 nm with a UV-Visible spectrophotometer. The percentage of picrate extracted into the non-aqueous phase was calculated by: % Extraction = $100\times(Abs_0-Abs)/Abs_0$ where Abs_0 is the absorbance of a sample of the unextracted metal picrate aqueous solution and Abs is the absorbance of aqueous layer after extraction. Three independent extractions were performed for each combination of metal picrate and crown ether, and the results were averaged.

Typical Procedure for Finkelstein Reactions in Organic Solvents

A 20-mL Pyrex tube fitted with a magnetic stirring bar was charged with 4.0 mL of a 0.25 M solution of 1-bromooctane in the appropriate solvent containing *n*-dodecane (0.25 M) as internal standard for GC, solid KI (5.0 mmol) and and the phase-transfer catalyst (0.020 mmol) if required. The tube was sealed with a Teflon-lined screw-cap, placed in an oil bath maintained at the desired temperature and the reaction mixture was vigorously stirred. Samples of the liquid phase (0.1 mL) were taken at regular time intervals, diluted with the reaction solvent (0.5 mL) and analyzed by GC.

In the case of recycling experiments run in toluene (Table 5, entries 10–12) the reaction mixture was centrifuged while still hot, and the clear, yellowish liquid phase was separated from the inorganic solid residue, which was then washed with hot toluene (0.5 mL). The combined toluene layers were transferred into a 20-mL Pyrex tube and cooled to 0 °C. The upper liquid phase was removed, the tube containing the solid precipitate was refilled with fresh 1-bromooctane solution (4.0 mL, 0.25 M) and solid KI (5.0 mmol) and the whole process was repeated. After the third run, 35 mg of yellowish solid (80% of the initial CE mass) were recovered.

Typical Procedure for Finkelstein Reactions in PFDMC and Catalyst Recycling

A 20-mL Pyrex tube fitted with a magnetic stirring bar was charged with 1-bromooctane (1.0 mmol), KI (5.0 mmol), the phase-transfer catalyst (0.020 mmol) if required and PFDMC (4.0 mL). The tube was sealed with a silicone-lined screw-cap, placed in an oil bath maintained at the desired temperature and the reaction mixture was vigorously stirred for the time indicated in Table 5. After cooling to room temperature, the mixture was extracted with cold toluene (2× 1.0 mL). The upper colourless organic layer (see Figure 1, Supporting Information) was removed and a sample (0.2 mL) was transferred into a vial containing 1.0 mL of a 1.0 M solution of *n*-dodecane in toluene and analyzed by GC (70 °C for 7 min followed by: a) 7 °C min^{-1} ramp to 90 °C; b) 20 °C min^{-1} ramp to 280 °C, held for 10 min. Retention times: 1-bromooctane = 10.72 min; *n*-dodecane 12.04 min, 1-iodooctane 12.21 min).

In the case of recycling experiments (Table 5, entries 3–6), extraction with toluene and separation of the organic phase was followed by centrifugation of the remaining mixture. The clear, yellowish fluorous phase was separated from the the inorganic solid residue, which was further washed with CH_2Cl_2 (0.5 mL) and centrifuged again. The fluorous phase and CH_2Cl_2 washings were combined and gently warmed at 50 °C in an open 20-mL Pyrex tube. Once the upper organic solvent was evaporated and just enough PFDMC was added to restore the initial volume, fresh 1-bromooctane (1.0 mmol) and KI (5.0 mmol) were added to the fluorous phase and the whole process was repeated. After the fourth run, the combined clear fluorous phase and CH_2Cl_2 washings were evaporated to dryness under reduced pressure, affording 40 mg of yellowish solid (91% of the initial CE mass).

Cyanide Displacement Reactions on *n*-Octyl Methanesulfonate

Reactions were performed according to the procedure described for halogen exchange reactions in PFDMC. Reaction conditions and the amount of reagents and catalyst are summarized in Table 6 (entries 1 and 2). GC conditions: 70 °C for 7 min followed by: a) 7 °C min^{-1} ramp to 90 °C; b) 20 °C min^{-1} ramp to 280 °C, held for 10 min. Retention times: nonanitrile = 11.21 min; *n*-dodecane 12.04 min, *n*-octyl methanesulfonate 14.67 min.

Cyanide Displacement Reactions on 1-Bromooctane

A 10-mL Pyrex tube fitted with a magnetic stirring bar was charged with 1-bromooctane (0.50 mmol), KCN (2.5 mmol), ***R_f*-CE3** (0.010 mmol) if required, H_2O (0.16 mL) and PFDMC (2.0 mL). The tube was sealed with a silicone-lined screw-cap, placed in an oil bath maintained at 90 °C and the reaction mixture was vigorously stirred for 24 h (Table 6, entries 6 and 7). After cooling to room temperature, 4.0 mL of a 0.13 M solution of *n*-dodecane in *n*-hexane were added. A homogeneous organic phase was thus obtained that was analyzed by GC (70 °C for 7 min followed by: a) 7 °C min^{-1} ramp to 90 °C; b) 20 °C min^{-1} ramp to 280 °C, held for 10 min. Retention times: 1-bromooctane = 10.72 min; nonanitrile = 11.21 min; *n*-dodecane 12.04 min).

Chloride Displacement Reaction on 4-Chloronitrobenzene

A 10-mL Pyrex tube fitted with a magnetic stirring bar was charged with 4-chloronitrobenzene (0.25 mmol), KOMe (0.50 mmol), ***R_f*-CE3** (0.0050 mmol) and PFDMC (1.0 mL). The tube was sealed, placed in an oil bath maintained at 90 °C and the reaction mixture was vigorously stirred. After cooling to room temperature, 2.0 mL of a 0.13 M solution of *n*-dodecane in hexane was added. The homogeneous liquid phase thus obtained was analyzed by GC (70 °C for 7 min followed by: a) 7 °C min^{-1} ramp to 90 °C; b) 20 °C min^{-1} ramp to 280 °C, held for 10 min. Retention times: 4-chloronitrobenzene = 11.85 min; *n*-dodecane 12.04 min; 4-nitroanisole = 13.58 min). Nitroanisole was obtained in 70% yield after 4 h, whereas a blank reaction run under otherwise identical conditions afforded the S_NAr product in 24% yield after the same time.

Oxidation of Fluorene to Fluorenone

A 10-mL Schlenk tube fitted with a magnetic stirring bar was charged with fluorene (0.125 mmol), powdered KOH (1.00 mmol), ***R_f*-CE3** (0.00625 mmol) if required and PFDMC (1.0 mL). The tube was placed in an oil bath maintained at 60 °C, attached to a gas burette filled with oxygen and the reaction mixture was vigorously stirred for 1 h. After cooling to room temperature, 4.0 mL of a 0.032 M solution of *n*-dodecane in hexane were added. The homogeneous liquid phase thus obtained was analyzed by GC (90 °C for 5 min followed by: a) 10 °C min^{-1} ramp to 150 °C; b) 15 °C min^{-1} ramp to 180 °C; c) 25 °C min^{-1} ramp to 280 °C, held for 7 min. Retention times: *n*-dodecane 7.71 min; fluorene = 12.80 min; fluorenone = 14.03 min).

Supporting Information

Preparation of **[(R_f-CE3K]$^+$I$^-$**, comparison of the ^{1}H NMR spectra of **R_f-CE1–3** and **[(R_f-CE3K]$^+$I$^-$**, photographs showing the phase behaviour of **R_f-CE3** in PFDMC and toluene, experimental procedures for the evaluation of the influence of *T* on the solubility of 1-bromooctane and 4-chloronitrobenzene in PFDMC are available in the Supporting Information.

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