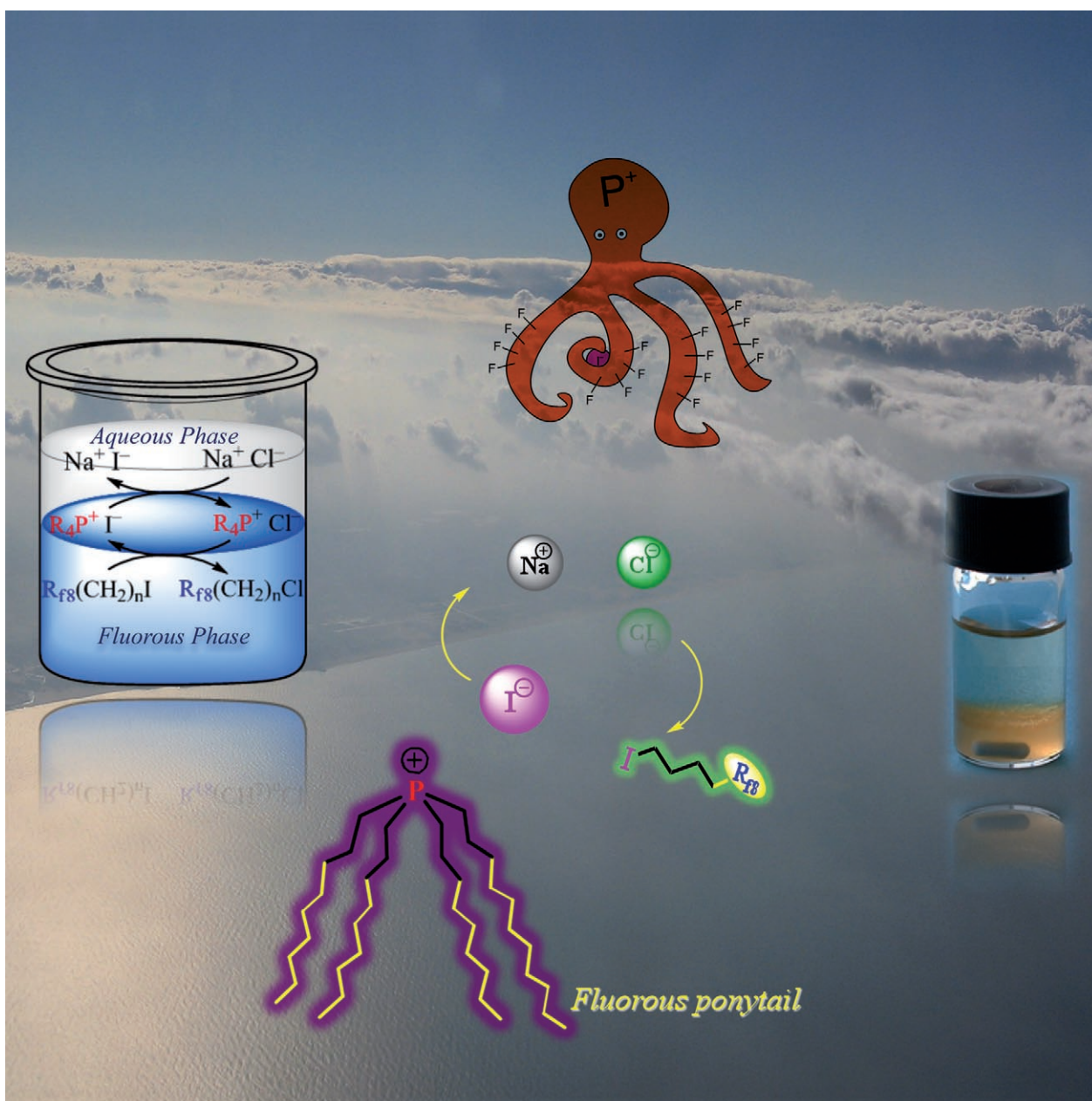


# Ionic Transformations in Extremely Nonpolar Fluorous Media: Easily Recoverable Phase-Transfer Catalysts for Halide-Substitution Reactions

Debaprasad Mandal, Markus Jurisch, Crestina S. Consorti, and John A. Gladysz\*<sup>[a]</sup>

*Dedicated to the Noguchi Institute (Tokyo) and its Directors*



**Abstract:** Solutions of the fluororous alkyl halides  $R_{18}(CH_2)_mX$  ( $R_{18} = (CF_2)_{n-1}CF_3$ ;  $m = 2, 3$ ;  $X = Cl, Br, I$ ) in perfluoromethylcyclohexane or perfluoromethyldecalin are inert towards solid or aqueous NaCl, NaBr, KI, KCN, and NaOAc. However, halide substitution occurs in the presence of fluororous phosphonium salts ( $R_{18}(CH_2)_2$ ) ( $R_{16}(CH_2)_2$ ) $_3P^+X^-$  ( $X = I$  (**1**), Br (**3**)) and ( $R_{18}(CH_2)_2$ ) $_4P^+I^-$  (10 mol %), which are soluble in the fluororous solvents under the reaction conditions (76–100 °C). Stoichiometric reactions of

a) **1** with  $R_{18}(CH_2)_2Br$  and b) **3** with  $R_{18}(CH_2)_2I$  were conducted under homogenous conditions in perfluoromethyldecalin at 100 °C and yielded the same  $R_{18}(CH_2)_2I/R_{18}(CH_2)_2Br$  equilibrium ratio ( $\approx 60:40$ ). This shows that ionic displacements can take place in extremely nonpolar fluororous phases

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and suggests a classical phase-transfer mechanism for the catalyzed reactions. Interestingly, the nonfluororous salt  $(CH_3(CH_2)_{11})(CH_3(CH_2)_7)_3P^+I^-$  (**4**) also catalyzes halide substitutions, but under triphasic conditions with **4** suspended between the lower fluororous and upper aqueous layers. NMR experiments established very low solubilities in both phases, which suggests interfacial catalysis. Catalyst **1** is easily recycled, optimally by simple precipitation onto teflon tape.

## Introduction

Much of the excitement associated with fluororous chemistry over the last 15 years has involved reactions conducted in organic or mixed organic/fluororous solvents.<sup>[1]</sup> Owing in part to the incompatibility of many organic reactants with fluororous phases,<sup>[2]</sup> there have been far fewer investigations of homogeneous reactions in fluororous solvents,<sup>[3]</sup> which are typically perfluoroalkanes or perfluoroethers and are much less polar than organic solvents.<sup>[4]</sup> However, scenarios are easily envisaged whereby it would be desirable to carry out a range or sequence of reactions in fluororous phases. For example, toxic compounds or nuclear waste could be rendered fluorophilic with suitable phase tags, and then further processed or remediated in situ.

Phase-transfer catalysis is potentially applicable to any process in which two reactants are localized in orthogonal phases, and is therefore an obvious means for expanding the vocabulary of reactions that can be conducted in fluororous

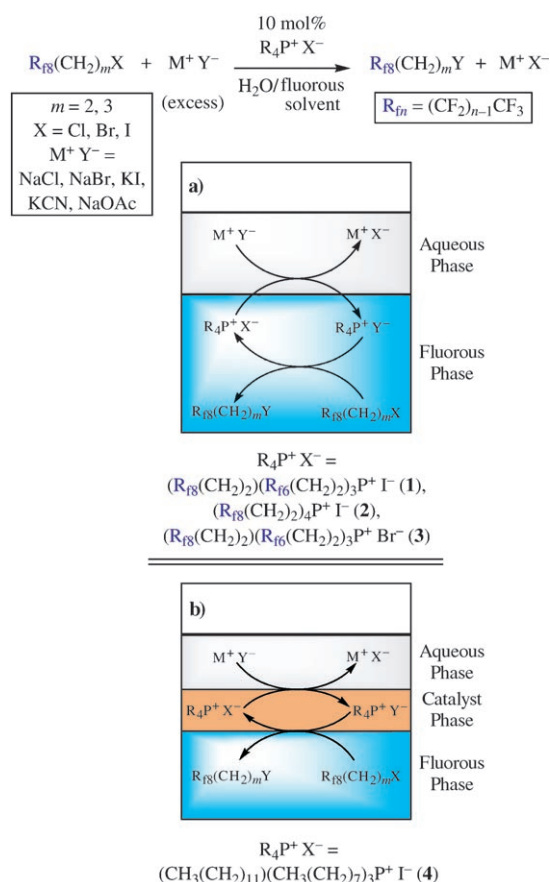
phases. There is extensive literature about processes that involve one reactant with high solubility in an organic phase and another with high solubility in an aqueous phase.<sup>[5,6]</sup> Catalysts are usually employed to bring the water-soluble reactant, typically an inorganic salt, into the organic phase.<sup>[5]</sup> However, protocols have also been devised to effect reactions in the aqueous phase.<sup>[6]</sup>

Given the immense utility of ionic displacement reactions, we were curious about whether reactions that involve ions might be possible in highly nonpolar fluororous solvents. When such reactions are conducted under phase-transfer conditions in organic solvents, ammonium and phosphonium salts with long *n*-alkyl substituents are typically used as catalysts.<sup>[5]</sup> We, Stuart and co-workers, Horváth and co-workers, and others have prepared a number of fluororous aliphatic phosphonium salts with “ponytails” of the formula  $CF_3(CF_2)_{n-1}(CH_2)_m$  (abbreviated  $R_{18}(CH_2)_m$ ).<sup>[7–9]</sup> Despite their charged nature, these salts often exhibit appreciable solubilities in fluororous solvents, especially at elevated temperatures.

In this paper, we report an investigation of Finkelstein type ionic displacement reactions<sup>[10]</sup> of simple fluororous electrophiles  $R_{18}(CH_2)_mX$  ( $X = Cl, Br, I$ ;  $m = 2, 3$ ) in fluororous solvents by using catalytic quantities of the fluororous and nonfluororous phosphonium iodide and bromide salts ( $R_{18}(CH_2)_2$ )( $R_{16}(CH_2)_2$ ) $_3P^+I^-$  (**1**),<sup>[7]</sup> ( $R_{18}(CH_2)_2$ ) $_4P^+I^-$  (**2**),<sup>[7]</sup> ( $R_{18}(CH_2)_2$ )( $R_{16}(CH_2)_2$ ) $_3P^+Br^-$  (**3**), and  $(CH_3(CH_2)_{11})(CH_3(CH_2)_7)_3P^+I^-$  (**4**), all of which are depicted in Scheme 1. Interestingly, substitutions occur readily at moderate temperatures. A number of experiments pertaining to the scope, mechanism, and phase in which substitution takes place are also presented. A portion of this work has been communicated,<sup>[11]</sup> and additional details can be found elsewhere.<sup>[12]</sup>

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Scheme 1. Phase-transfer catalysis of halide-substitution reactions in fluororous media.

## Results

### Basic Reactions

The fluororous alkyl chlorides, bromides, and iodides summarized in Table 1 were treated with NaCl, NaBr, KI, KCN, and NaOAc under various conditions as shown in the general Scheme 1 a.

For an initial series of experiments, 0.68 M solutions of  $R_{18}(CH_2)_3I$  in the common fluororous solvent perfluoromethylcyclohexane ( $CF_3C_6F_{11}$ ) were prepared. These were treated with nearly saturated 5.13 M aqueous solutions of NaCl to give samples with  $R_{18}(CH_2)_3I/NaCl$  molar ratios of 12:88. Next, 10 mol % of the phosphonium salts **1**, **2**, or **3** were added. These phosphonium salts are insoluble in water, sparingly soluble in most fluo-

rous solvents at room temperature, and highly soluble in fluororous solvents at elevated temperatures.<sup>[7]</sup> The samples were vigorously stirred for 72 h at 76 °C. As summarized in Table 1, entries 1–3, the  $^1H$  NMR spectra showed 90–93 % conversion into the fluororous alkyl chloride  $R_{18}(CH_2)_3Cl$ . With Table 1, entry 3, no further conversion was noted after 3 weeks.

Workup of Table 1, entry 1 gave a 93:7  $R_{18}(CH_2)_3Cl/R_{18}(CH_2)_3I$  mixture in 92 % yield, as assayed by  $^1H$  NMR spectroscopy. As illustrated below, the  $CH_2X$  signals (t) for all fluororous substrates and products were well-separated. No conversion was observed in experiments without **1–3**. As the boiling point of  $CF_3C_6F_{11}$  (76 °C) limits the temperature of these reactions, Table 1, entry 1 was repeated with perfluoromethyldecalin ( $CF_3C_{10}F_{17}$ ; b.p.: 160 °C) at 100 °C. The reaction was now complete within 24 h (Table 1, entry 4 and Figure 1 a), and this solvent was adopted as the standard for subsequent experiments. In many cases, the phosphonium salt did not precipitate upon cooling; after the reaction, the leaving group and the excess nucleophile can also serve as counteranions.

Additional nucleophiles were then tested. An analogous reaction with KCN (Table 1, entry 5) afforded the corresponding fluororous nitrile  $R_{18}(CH_2)_3CN$ , but at a much lower rate. As shown in Figure 2, the conversion was 17 % after 24 h and 88 % after 240 h. This new compound was independently synthesized by treating a suspension of the fluororous tosylate  $R_{18}(CH_2)_3OTs$ <sup>[13]</sup> in acetone with KCN at 68 °C (63 % after chromatography; see Experimental Section). The analogous reaction of  $R_{18}(CH_2)_3I$  with NaOAc (Table 1,

Table 1. Data for halide-substitution reactions catalyzed by fluororous phosphonium salts under the conditions of Scheme 1 a.<sup>[a]</sup>

Entry <sup>[b]</sup>	Substrate	$M^+Y^-$	$R_4P^+X^-$	Product	$T$ [°C]	$t$ [h]	Conv. [%]
1	$R_{18}(CH_2)_3I$	NaCl	<b>1</b>	$R_{18}(CH_2)_3Cl$	76	72	93
2		NaCl	<b>2</b>		76	72	90
3		NaCl	<b>3</b>		76	72	91
4 <sup>[c]</sup>	$R_{18}(CH_2)_3I$	NaCl	<b>1</b>	$R_{18}(CH_2)_3Cl$	100	24	95
5 <sup>[d]</sup>	$R_{18}(CH_2)_3I$	KCN	<b>1</b>	$R_{18}(CH_2)_3CN$	100	24	17
						72	29
						240	88
6	$R_{18}(CH_2)_3I$	NaOAc	<b>1</b>	$R_{18}(CH_2)_3OAc$	100	24	56
						48	58
7	$R_{18}(CH_2)_3Cl$	KI	<b>1</b>	$R_{18}(CH_2)_3I$	100	24	36
						48	61
						120	87
8	$R_{18}(CH_2)_2I$	NaCl	<b>1</b>	$R_{18}(CH_2)_2Cl$	100	24	26
						48	37
						120	71
9	$R_{18}(CH_2)_2I$	NaBr	<b>1</b>	$R_{18}(CH_2)_2Br$	100	24	42
						48	53
						120	79
10	$R_{18}(CH_2)_2Br$	KI	<b>1</b>	$R_{18}(CH_2)_2I$	100	24	43
						48	77
						120	92
11 <sup>[e]</sup>	$R_{18}(CH_2)_2Br$	NaCl	<b>1</b>	$R_{18}(CH_2)_2Cl$	100	120	67

[a] Conditions:  $R_{18}(CH_2)_mX$  (0.34 mmol),  $M^+Y^-$  (2.56 mmol), fluororous solvent (0.5 mL), water (0.5 mL),  $R_4P^+X^-$  (0.034 mmol, 10 mol %). [b] The reactions in entries 1–3 were conducted in  $CF_3C_6F_{11}$ . All others were conducted in perfluoromethyldecalin ( $CF_3C_{10}F_{17}$ ). [c] For the rate profile of a duplicate run, see Figure 6. [d] For the rate profile, see Figure 2. [e] For the rate profile, see Figure 3.

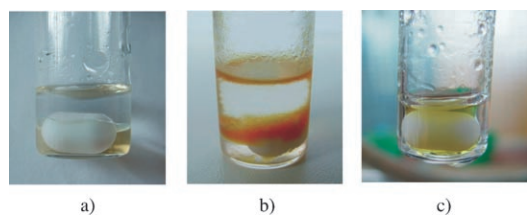


Figure 1. Representative reactions of  $R_{18}(\text{CH}_2)_3\text{I}$  and  $\text{NaCl}$ . a) Biphasic conditions of Table 1, entry 4 (catalyst **1**), photographed at room temperature. b) Triphasic conditions of Table 3, entry 1, but with excess **4** to visualize the catalyst phase better, photographed at  $100^\circ\text{C}$ . c) A reaction analogous to that in b), but without fluorosolvent and with the normal 10 mol% loading of **4**, photographed at  $100^\circ\text{C}$  (biphasic due to the solubility of **4** in  $R_{18}(\text{CH}_2)_3\text{I}$ ).

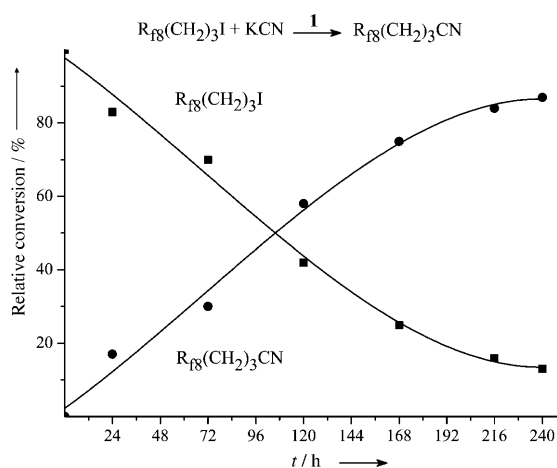


Figure 2. Rate profile for the reaction of  $R_{18}(\text{CH}_2)_3\text{I}$  and  $\text{KCN}$  catalyzed by **1** in perfluoromethyldecalin/water at  $100^\circ\text{C}$  (Table 1, entry 5).

entry 6) was faster (56% conversion after 24 h), but stopped at 58% conversion, which suggests the attainment of equilibrium. The product,  $R_{18}(\text{CH}_2)_3\text{OAc}$ , is also a new compound, so an authentic sample was prepared by acylation of the fluoros alcohol  $R_{18}(\text{CH}_2)_3\text{OH}$  in the absence of solvent (92% after distillation).

The reverse reaction of that in Table 1, entry 4 was investigated. As shown in Table 1, entry 7, a solution of  $R_{18}(\text{CH}_2)_3\text{Cl}$  in perfluoromethyldecalin, excess aqueous  $\text{KI}$  (12:88 molar ratio), and **1** were similarly combined at  $100^\circ\text{C}$ . Substitution occurred, but at a much lower rate (conversion after 24 h: 36%; after 120 h: 87%). As the data below indicate that the order of nucleophilicity is  $\text{I}^- > \text{Cl}^-$ , the poorer leaving-group ability of chloride (or equivalently, the diminished electrophilicity of the alkyl chloride) probably plays a key role in the reaction.

A reaction analogous to that in Table 1, entry 4 was conducted with the “two-methylene-spacer” fluoros alkyl iodide  $R_{18}(\text{CH}_2)_2\text{I}$ . As shown in Table 1, entry 8, substitution was much slower, with 26% conversion into  $R_{18}(\text{CH}_2)_2\text{Cl}$  after 24 h and 71% after 120 h. All fluoros electrophiles  $R_{18}(\text{CH}_2)_m\text{X}$  become less reactive towards nucleophiles as the length of the methylene spacer decreases.<sup>[14]</sup> An analogous reaction with  $\text{NaBr}$  (Table 1, entry 9) was somewhat

faster, with 42% conversion into  $R_{18}(\text{CH}_2)_2\text{Br}$  after 24 h and 79% after 120 h.

As shown in Table 1, entry 10, reaction of the two-spacer fluoros alkyl bromide  $R_{18}(\text{CH}_2)_2\text{Br}$  with  $\text{KI}$  gave, as expected,  $R_{18}(\text{CH}_2)_2\text{I}$  with 43 and 92% conversion after 24 and 120 h, respectively. This substitution was slightly faster than that with  $R_{18}(\text{CH}_2)_2\text{I}$  and  $\text{NaBr}$  (Table 1, entry 9). Thus, it can be extrapolated that the (degenerate) reaction of  $R_{18}(\text{CH}_2)_2\text{I}$  (a stronger electrophile than that in Table 1, entry 10) and  $\text{KI}$  would be faster still. Given the still slower reaction of  $R_{18}(\text{CH}_2)_2\text{I}$  and  $\text{NaCl}$  (Table 1, entry 8), the order of halide anion nucleophilicity under the conditions of Scheme 1a must be  $\text{I}^- > \text{Br}^- > \text{Cl}^-$ . Table 1, entries 4–6 in turn establish the nucleophilicity order  $\text{Cl}^- > \text{AcO}^- > \text{CN}^-$ .

Finally, an analogous reaction of  $R_{18}(\text{CH}_2)_2\text{Br}$  with  $\text{NaCl}$  afforded  $R_{18}(\text{CH}_2)_2\text{Cl}$  (Table 1, entry 11). Including the iodide anion from the catalyst (10 mol%), three halide anions participate in this transformation, in contrast to all of the other examples in Table 1, except entry 3. As shown in the rate profile in Figure 3 and the NMR spectra in

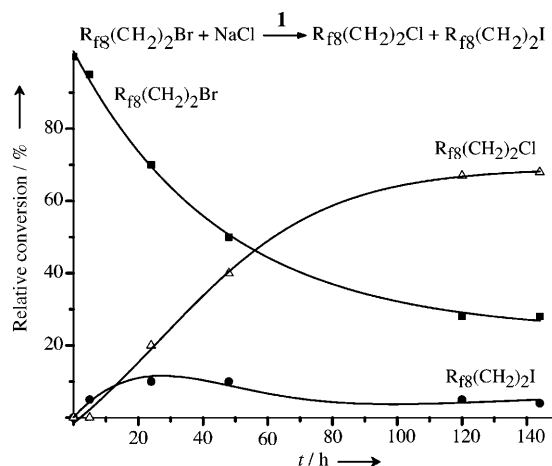


Figure 3. Rate profile for the reaction of  $R_{18}(\text{CH}_2)_2\text{Br}$  and  $\text{NaCl}$  catalyzed by **1** in perfluoromethyldecalin/water at  $100^\circ\text{C}$  (Table 1, entry 11).

Figure 4, some of the iodide  $R_{18}(\text{CH}_2)_2\text{I}$  was also detected. As the  $R_{18}(\text{CH}_2)_2\text{I}/R_{18}(\text{CH}_2)_2\text{Cl}$  ratios at low conversions are much greater than the iodide/chloride anion ratios (1:75), the iodide anion must have the greater nucleophilicity.

### Phase Requirements

The preceding data pose a variety of phase-based questions. One is whether aqueous solutions of nucleophiles are required. When Table 1, entries 1–3 were repeated with solid  $\text{NaCl}$ , no reaction or apparent dissolution occurred. Thus, liquid/solid phase-transfer catalysis does not take place.

The reciprocal question is whether a fluoros solvent is necessary. In an experiment comparable to Table 1, entry 4,  $R_{18}(\text{CH}_2)_3\text{I}$  was directly combined with catalyst **1** and 5.13 M aqueous  $\text{NaCl}$  (molar ratio of  $R_{18}(\text{CH}_2)_3\text{I}/\text{NaCl}$  = 12:88). After 24 h at  $100^\circ\text{C}$ , 87% conversion into  $R_{18}(\text{CH}_2)_3\text{Cl}$  had

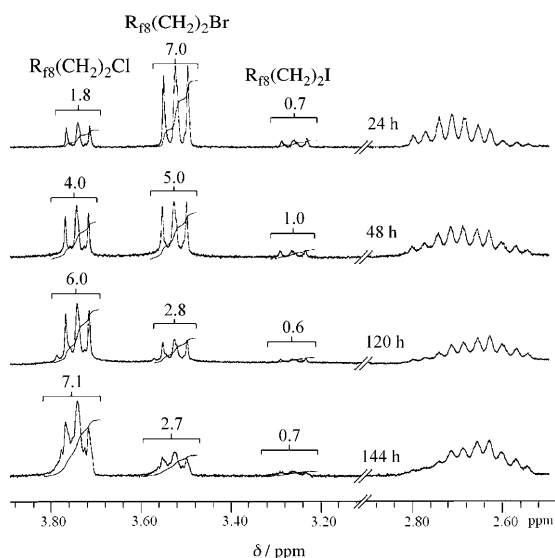


Figure 4.  $^1\text{H}$  NMR spectra recorded during the reaction in Figure 3 (Table 1, entry 11).

occurred. Hence, the fluoros substrate can serve as its own phase.

Although  $\text{CF}_3\text{C}_6\text{H}_5$  is not a fluoros solvent, it can be viewed as a hybrid medium,<sup>[4,15]</sup> as it commonly dissolves appreciable quantities of both fluoros and nonfluoros solutes. The phosphonium salt **1** was previously noted to have good solubility in  $\text{CF}_3\text{C}_6\text{H}_5$  at elevated temperatures.<sup>[7]</sup> Thus, a solution of  $\text{R}_{18}(\text{CH}_2)_3\text{I}$  in  $\text{CF}_3\text{C}_6\text{H}_5$  was combined with **1** and aqueous  $\text{NaCl}$  at  $100^\circ\text{C}$  in a manner analogous to Table 1, entry 4. Owing to the lower boiling point of  $\text{CF}_3\text{C}_6\text{H}_5$  ( $102^\circ\text{C}$ ), the vial was tightly capped.  $^1\text{H}$  NMR spectra of aliquots showed a somewhat slower reaction than in perfluoromethyldecalin, with 49 and 72% conversion after 24 and 72 h, respectively.<sup>[16]</sup> Nonetheless,  $\text{CF}_3\text{C}_6\text{H}_5$  is a less expensive solvent, and a similar protocol was used for the gram-scale preparation of  $\text{R}_{18}(\text{CH}_2)_2\text{Br}$  from  $\text{R}_{18}(\text{CH}_2)_2\text{OTf}$  and  $\text{LiBr}$  (70% after chromatography; see Experimental Section).

Given the feasibility of substitution under  $\text{CF}_3\text{C}_6\text{H}_5$ /aqueous biphasic conditions, we sought to check whether reactions might occur in organic/aqueous solvent systems. Thus, toluene or dibutyl ether solutions of the nonfluoros alkyl iodide  $\text{CH}_3(\text{CH}_2)_{11}\text{I}$  were combined with aqueous  $\text{NaCl}$  (12:88 molar ratio) and **1** (10 mol%). Samples were kept at  $100^\circ\text{C}$ , under which conditions only a small portion of **1** dissolved. Only trace levels of conversion were observed after extended periods.

Another immediate question concerns the loci of the reactions in Scheme 1a. All the above data are consistent with substitution occurring in the fluoros phase by a classical phase-transfer-catalysis mechanism. However, interfacial phenomena could also play a role. Hence, we sought to confirm that stoichiometric analogues of the preceding reactions could be realized solely in the fluoros phase.

Selected reactions with equimolar amounts of fluoros alkyl halides and phosphonium salts were conducted under

Table 2. Data for reactions of fluoros alkyl halides with equimolar amounts of fluoros phosphonium salts in perfluoromethyldecalin at  $100^\circ\text{C}$ .<sup>[a]</sup>

Entry	Substrate	$\text{R}_4\text{P}^+\text{X}^-$	Product	$t$ [h]	Conv. [%]
1	$\text{R}_{18}(\text{CH}_2)_2\text{Br}$	<b>1</b>	$\text{R}_{18}(\text{CH}_2)_2\text{I}$	1	23
				4	58
2	$\text{R}_{18}(\text{CH}_2)_2\text{I}$	<b>3</b>	$\text{R}_{18}(\text{CH}_2)_2\text{Br}$	1	15
				5	37
3	$\text{R}_{18}(\text{CH}_2)_3\text{Cl}$	<b>1</b>	$\text{R}_{18}(\text{CH}_2)_3\text{I}$	4	20
				24	20

[a] Conditions:  $\text{R}_{18}(\text{CH}_2)_m\text{X}$  (0.17 mmol), perfluoromethyldecalin (0.25 mL),  $\text{R}_4\text{P}^+\text{X}^-$  (0.17 mmol),  $100^\circ\text{C}$ .

homogeneous conditions in perfluoromethyldecalin at  $100^\circ\text{C}$ . As summarized in Table 2, substitutions occurred readily, and two informative rate profiles are depicted in Figure 5. As shown in Table 2, entry 1, reaction of the two-spacer fluoros alkyl bromide  $\text{R}_{18}(\text{CH}_2)_2\text{Br}$  and the phosphonium iodide **1** afforded the fluoros alkyl iodide  $\text{R}_{18}(\text{CH}_2)_2\text{I}$ . Over the course of 4 h, 58% conversion was reached, but no

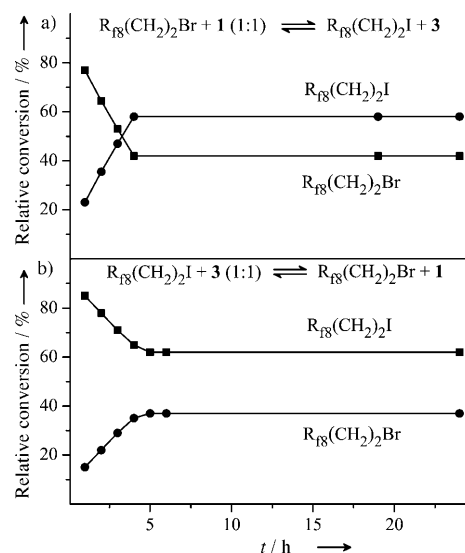


Figure 5. Rate profiles for the reactions of equimolar amounts of a)  $\text{R}_{18}(\text{CH}_2)_2\text{Br}$  and **1** (Table 2, entry 1) and b)  $\text{R}_{18}(\text{CH}_2)_2\text{I}$  and **3** (Table 2, entry 2) in perfluoromethyldecalin at  $100^\circ\text{C}$ .

further conversion occurred after a total of 24 h (Figure 5). The reverse reaction was carried out with the fluoros alkyl iodide  $\text{R}_{18}(\text{CH}_2)_2\text{I}$  and the phosphonium bromide **3** (Table 2, entry 2). Over the course of 5 h, 37% conversion was reached. This level remained constant after a total of 24 h. Hence, equilibrium ( $\approx 60:40$ ) can be approached from either direction.

Interestingly, reaction of the three-spacer fluoros alkyl chloride  $\text{R}_{18}(\text{CH}_2)_3\text{Cl}$  and the phosphonium iodide **1** gave only 20% conversion (Table 2, entry 3), perhaps due to the stronger carbon-halogen bond of the electrophile. Qualitatively similar results were reported in our original communication.<sup>[11]</sup> The data in Table 2 represent optimized values.

**Catalyst Requirements: Nonfluorous Phosphonium Salts and Neutral Molecules**

For obvious reasons, we sought to test a comparable nonfluorous phosphonium salt for catalytic activity. Thus, the iodide  $(\text{CH}_3(\text{CH}_2)_{11})(\text{CH}_3(\text{CH}_2)_7)_3\text{P}^+\text{I}^-$  (**4**), the carbon skeleton of which is similar to that in **1**, was synthesized by the alkylation of commercial  $(\text{CH}_3(\text{CH}_2)_7)_3\text{P}$  with  $\text{CH}_3(\text{CH}_2)_{11}\text{I}$  in  $\text{CF}_3\text{C}_6\text{H}_5$  at  $105^\circ\text{C}$  (71% after workup; see Experimental Section).

Table 1, entry 4 was repeated by using both **1** and **4**. Surprisingly, as shown by the data in Table 3 and the rate profiles in Figure 6, **4** proved to be the superior catalyst. As

Table 3. Data for halide-substitution reactions catalyzed by the nonfluorous phosphonium salt **4** at  $100^\circ\text{C}$  under the conditions of Scheme 1 b.<sup>[a]</sup>

Entry	Substrate	$\text{M}^+\text{Y}^-$	Product	$t$ [h]	Conv. [%]
1 <sup>[b]</sup>	$\text{R}_{18}(\text{CH}_2)_3\text{I}$	NaCl	$\text{R}_{18}(\text{CH}_2)_3\text{Cl}$	1	43
				24	93
2		KCN	$\text{R}_{18}(\text{CH}_2)_3\text{CN}$	1	17
				24	80
3		NaOAc	$\text{R}_{18}(\text{CH}_2)_3\text{OAc}$	1	22
				24	65

[a] Conditions:  $\text{R}_{18}(\text{CH}_2)_3\text{I}$  (0.10 mmol),  $\text{M}^+\text{Y}^-$  (0.80 mmol), perfluoromethyldecalin (0.5 mL), water (0.5 mL), **4** (0.01 mmol),  $100^\circ\text{C}$ . [b] For the rate profile, see Figure 6.

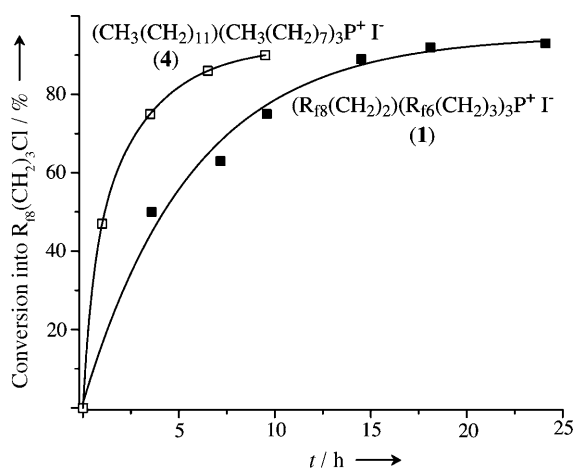


Figure 6. Rate profiles for the reactions of  $\text{R}_{18}(\text{CH}_2)_3\text{I}$  and NaCl catalyzed by **1** (■; duplicate of Table 1, entry 4) and **4** (□; Table 3, entry 1) in perfluoromethyldecalin/water at  $100^\circ\text{C}$ .

shown in Figure 1 b, the conditions were triphasic. The solid phosphonium salt occupied the interface between the fluorous and aqueous phases at lower temperatures, but melted by the reaction temperature to give a liquid/liquid/liquid system as generalized in Scheme 1 b. As shown by Table 3 and the rate profiles in Figure 7, **4** also catalyzed faster the reactions of  $\text{R}_{18}(\text{CH}_2)_3\text{I}$  with KCN and NaOAc. Interestingly, their nucleophilicities appeared much more comparable than with **1**.

NMR experiments with internal standards (see Experimental Section) revealed that **4** has a very low solubility in

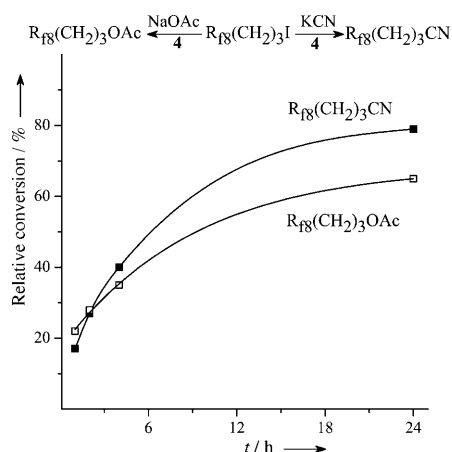


Figure 7. Rate profiles for the reactions of  $\text{R}_{18}(\text{CH}_2)_3\text{I}$  with KCN (■; Table 3, entry 2) and NaOAc (□; Table 3, entry 3) catalyzed by **4** in perfluoromethyldecalin/water at  $100^\circ\text{C}$ .

perfluoromethyldecalin at room temperature. Upper limits of  $0.0014\text{--}0.0016\text{M}$  ( $<0.001\text{ g mL}^{-1}$ ) were set at room temperature and  $100^\circ\text{C}$ . There was no detectable solubility in water at room temperature ( $<0.0006\text{M}$ ), but some solubility was found at  $100^\circ\text{C}$  ( $\approx 0.0039\text{M}$ ). Out of curiosity, equimolar amounts of **4** and the fluorous alkyl bromide  $\text{R}_{18}(\text{CH}_2)_2\text{Br}$  were combined in perfluoromethyldecalin at  $100^\circ\text{C}$ . This represents a heterogeneous analogue of the homogeneous experiments in Table 2. Within 1 h, 25% conversion into the iodide  $\text{R}_{18}(\text{CH}_2)_2\text{I}$  had occurred. This remained unchanged over the course of 24 h, which indicates the rapid establishment of a liquid/solid biphasic equilibrium.

Interestingly, when the fluorous solvent was omitted from the reaction with **4** in Figure 6, the conversion was still faster. Identical quantities of  $\text{R}_{18}(\text{CH}_2)_3\text{I}$  and **4** were combined in the absence of aqueous NaCl and heated to  $100^\circ\text{C}$ . The salt dissolved in the fluorous alkyl iodide, presumably owing to the greater polarity versus perfluoromethyldecalin. Hence, the fluorous-solvent-free reaction is biphasic (Figure 1 c). Salt **4** also catalyzed the reaction of the nonfluorous alkyl iodide  $\text{CH}_3(\text{CH}_2)_{11}\text{I}$  and NaCl (12:88 molar ratio) in a) nitrobenzene/water and b) dibutyl ether/water mixtures at  $100^\circ\text{C}$ . Under these biphasic conditions, conversions into the chloride  $\text{CH}_3(\text{CH}_2)_{11}\text{Cl}$  were a) 56 and 67% after 24 and 96 h, respectively, and b) 73% after 24 h. In the absence of **4**, no appreciable background reaction was observed ( $<2\%$ , 24 h).

An entirely different class of compounds was briefly investigated as phase-transfer catalysts. Metrangolo, Resnati, and co-workers showed that perfluoroalkyl iodides ( $\text{R}_{\text{FI}}\text{I}$ ) are superb halide anion acceptors and form adducts through "halogen bonds".<sup>[17]</sup> Furthermore, small quantities can enhance the solubilities of certain halide salts in fluorous media.<sup>[18]</sup> However, when Table 1, entry 4 was repeated with 10 mol% of  $\text{R}_{10}\text{I}$  in place of **1**, no conversion was observed over the course of 22 h.

In summary, the data with **4** suggest yet another dimension of possibilities for the catalysis of multiphase ionic dis-

placement reactions involving fluoruous solvents. However, most appear to be of secondary relevance to Scheme 1a, which is the main focus of the present work. Hence, further investigation of the many intriguing questions raised will be pursued in a separate study.

### Catalyst Recycling

The recycling of the fluoruous phosphonium salts after catalysis was investigated. Notably, the dominant rest state would be expected to contain the halide anion employed as the nucleophile, which is used in excess. Thus, hexane was added to the fluoruous phase after a reaction analogous to that in Table 1, entry 4, in which the iodide salt **1** was the original catalyst. The resulting precipitate, which should largely be the chloride salt  $(R_{18}(CH_2)_2)(R_{16}(CH_2)_2)_3P^+Cl^-$ , was washed with hexanes and water and used for a second cycle.

As summarized in Table 4, five cycles were conducted, involving two different substrate/nucleophile combinations.

Table 4. Recovery and reuse of fluoruous phosphonium salt **1** under the conditions of Scheme 1a.<sup>[a]</sup>

Cycle	Substrate	$M^+Y^-$	Product	$t$ [h]	Conv. [%]
1	$R_{18}(CH_2)_3I$	NaCl	$R_{18}(CH_2)_3Cl$	24	95
2	$R_{18}(CH_2)_3Cl$	KI	$R_{18}(CH_2)_3I$	120	85
3	$R_{18}(CH_2)_3I$	NaCl	$R_{18}(CH_2)_3Cl$	24	91
4	$R_{18}(CH_2)_3I$	NaCl	$R_{18}(CH_2)_3Cl$	24	81
5	$R_{18}(CH_2)_3I$	NaCl	$R_{18}(CH_2)_3Cl$	24	66

[a] Conditions:  $R_{18}(CH_2)_3X$  (0.34 mmol),  $M^+Y^-$  (2.56 mmol), perfluoromethyldecalin (0.5 mL), water (0.5 mL), **1** (0.034 mmol), 100 °C. Recovery involved hexane-assisted precipitation as described in the text.

After the fifth, for which the conversion was noticeably lower, 38% of the original catalyst mass remained. The  $^{31}P$  NMR spectrum exhibited only a single catalyst signal, which suggests little if any degradation. Separate analyses showed that the dominant mode of catalyst loss was incomplete precipitation.

We previously found that the recovery of fluoruous catalysts by precipitation is often enhanced by the presence of a fluoropolymer support, such as teflon shavings or tape.<sup>[19,20]</sup>

Thus, the adhesion of fluoruous phosphonium salts was tested. A suspension of **1** (0.010 mmol) in the hybrid solvent  $CF_3C_6H_5$  (1 mL) was heated to 90 °C to give a homogeneous solution. A  $30 \times 12 \times 0.0075$ -mm<sup>3</sup> strip of teflon tape was then immersed in the solution. The sample was allowed to cool; it first became turbid and then clear as **1** adsorbed onto the tape. The sample was kept briefly at 10 °C, and then the tape was removed, washed with hexane, and air-dried. Light-yellow patches were discernable upon close visual inspection of the tape.

As shown in Figure 8, the catalyst-coated tape was used in reactions analogous to that in Table 1, entry 4, but with  $CF_3C_6H_5$  as the non-aqueous solvent owing to the lower solubility of **1**. After 72 h, the mixture was cooled to room temperature.<sup>[21]</sup> The tape was removed, washed with water and hexane, and used in a subsequent reaction cycle. As summarized in Figure 8b, five cycles were conducted. Also, rate profiles were measured by  $^1H$  NMR spectroscopy for the first three cycles of an identical series of experiments (1', 2', 3'). This involved interrupting the reaction for a roughly 1-h cooling sequence for every data point. The conversion and rate data indicate an impressive retention of activity. Furthermore, in the rate experiments, the weights of the recovered tape were nearly constant.<sup>[22]</sup> Hence, there was minimal catalyst degradation or leaching by incomplete precipitation.

## Discussion

### Mechanism

The stoichiometric reactions of fluoruous phosphonium salts and fluoruous alkyl halides in Table 2 and Figure 5 unambiguously establish that ionic displacement reactions can occur at moderate temperatures in extremely nonpolar fluoruous media. The much lower polarity of fluoruous solvents relative to aliphatic hydrocarbons can be quantified by a variety of measures, as reviewed elsewhere.<sup>[4]</sup>

None of the fluoruous alkyl halides or fluoruous phosphonium salts **1–3** exhibited detectable solubilities in water. For reference, the  $CF_3C_6F_{11}$ /toluene partition coefficient for  $R_{18}(CH_2)_3I$  is 50.7:49.3;<sup>[23]</sup> other alkyl halides with fewer meth-

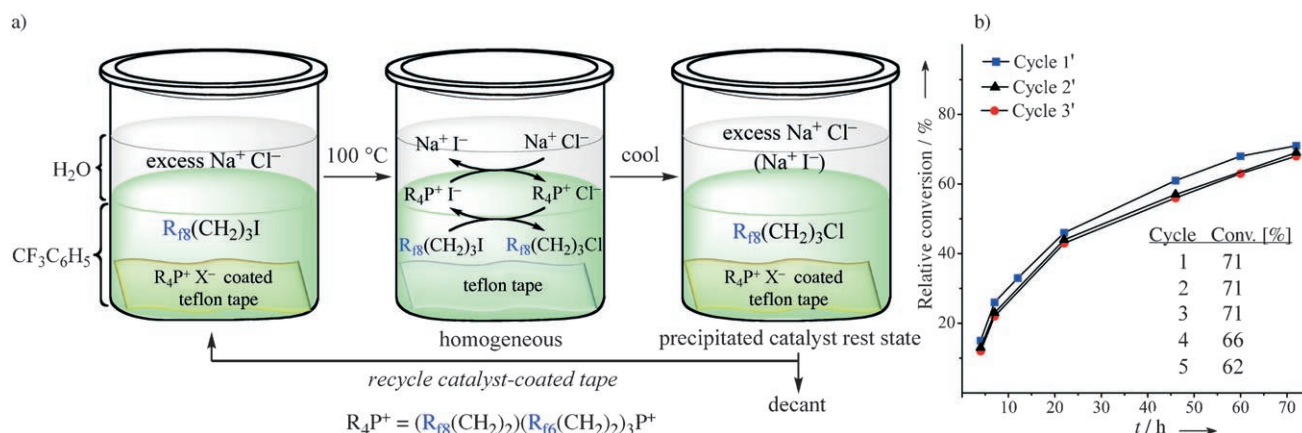


Figure 8. a) Recovery and reuse of fluoruous phosphonium salt **1** with teflon tape. b) Conversions and rate profiles as a function of cycle.

ylene groups or less-polarizable halides should be more fluorophilic. Therefore, we believe it highly probable that the biphasic reactions in Table 1 and Scheme 1a occur exclusively in the fluorous phase, or with at most very minor contributions from reactions in water.

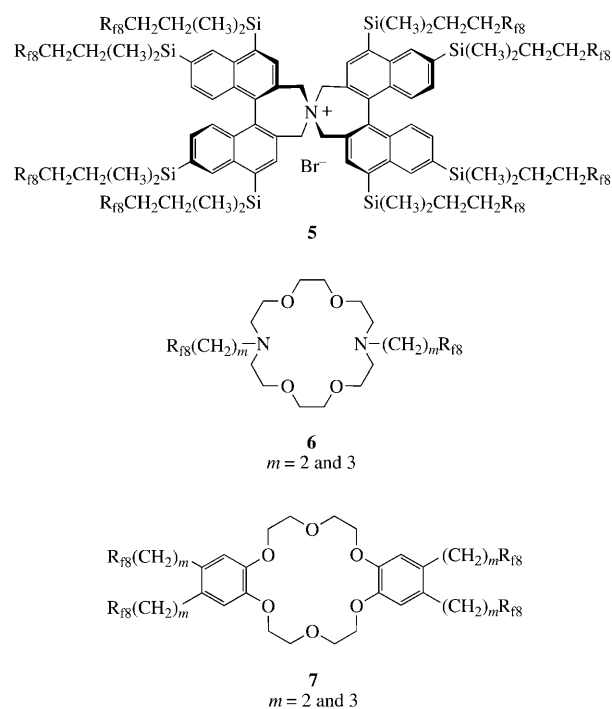
However, interfacial catalysis remains difficult to exclude. The viability of such a pathway is strongly suggested by the results with the nonfluorous phosphonium salt **4** (Table 3 and Figures 6 and 7), which exhibited only trace solubility levels in fluorous and aqueous solvents under the reaction conditions and occupied an interface as illustrated in Scheme 1b and Figure 1b. As noted above, a detailed investigation of this process is beyond the scope of the present study. Nonetheless, we believe it very probable that the dominant mechanism of catalysis is different from that with **1–3**. If so, the question as to why **4** effects a faster reaction with NaCl (Figure 6) or an altered  $\text{AcO}^-/\text{CN}^-$  nucleophilicity ratio (Figure 7) amounts to an apples/oranges comparison with no simple answer.

With regard to the long-term goal of sequestering and remediating toxic waste as fluorous derivatives in fluorous media noted in the Introduction, interfacial catalysts represent an important conceptual refinement. In principle, this removes the necessity of dissolving a catalyst in the fluorous phase, thus simplifying in situ processing and minimizing the generation of additional waste. The net effect is reminiscent of a membrane-based ion channel, with the attendant potential for new selectivities.

During the course of our extensive studies of fluorous molecules over the last 14 years, we occasionally encountered other fluorous salts that are soluble in fluorous solvents.<sup>[24]</sup> Deelman, van Koten, and co-workers described a series of fluorous anions, the  $\text{BAr}_f^-$  analogues  $\text{B}(4\text{-C}_6\text{H}_4\text{R}_{f6})_4^-$ ,  $\text{B}(3,5\text{-C}_6\text{H}_3(\text{R}_{f6})_2)_4^-$ , and  $\text{B}(4\text{-C}_6\text{H}_4\text{Si}(\text{CH}_3)_2(\text{CH}_2)_2\text{R}_{f6})_4^-$ , that give many such salts.<sup>[25]</sup> Maruoka and co-workers reported the ammonium salt **5** in Scheme 2.<sup>[26]</sup> There is the immediate question of how such species and the phosphonium salts **1–3** are solvated in fluorous media.

It has been suggested that the halide ions of quaternary ammonium and phosphonium salts penetrate deeply within the web of alkyl substituents in nonpolar solvents.<sup>[27]</sup> This maximizes attractive coulombic ion–dipole and van der Waals interactions. However, there is also much evidence for facile cavitation in fluorous solvents, consistent with the very low intermolecular enthalpic interactions.<sup>[4]</sup> The resulting free volumes are particularly accommodating of small neutral solutes and might similarly take up halide anions. Furthermore, “hydration shells” that consist of several water molecules are commonly associated with phosphonium salts used for phase-transfer catalysis in organic media.<sup>[28]</sup> Hence, water may participate when an aqueous phase is present.

As noted above, the data in Table 1 establish the operational nucleophilicity order  $\text{I}^- > \text{Br}^- > \text{Cl}^- > \text{OAc}^- > \text{CN}^-$  for catalyst **1** in perfluoromethyldecalin. Relative anion nucleophilicities have been extensively analyzed and depend strongly on the medium.<sup>[29]</sup> In organic/aqueous phase-transfer catalysis, nucleophilicities are commonly dependent on



Scheme 2. Other fluorous phase-transfer catalysts.

stirring speeds up to a certain threshold.<sup>[28]</sup> When phase transfer is no longer rate-determining, the cyanide anion is usually found to be a stronger nucleophile than halide anions.<sup>[28]</sup> Thus, phase-transfer catalysis involving fluorous media promises intriguing new selectivities, but further studies are required to interpret these trends fully.

### Catalyst Recovery: Other Fluorous Phase-Transfer Catalysts

The fluorous phosphonium salts **1–3** have, like many other fluorous substances,<sup>[30]</sup> highly temperature-dependent solubilities. This thermomorphism forms the basis for the recycling protocols in Table 4 and Figure 8, in which the catalyst was recovered by precipitation. Reactions that take place significantly above room temperature are particularly suitable, as the catalyst/solvent combination can be optimized for the lowest possible residual room-temperature solubility and leaching. In hindsight, the perfluoromethyldecalin selected for Table 4 was not optimal, as upon cooling the phosphonium salt did not fully precipitate, perhaps arising in part to the mixture of counteranions present as noted above. A cosolvent, hexane, was needed to enhance recovery.

However, the hybrid solvent  $\text{CF}_3\text{C}_6\text{H}_5$  employed in Figure 8 proved ideal. The additional use of teflon tape in these recycling experiments is significant in several regards. First, the fluorous support distinctly improves the recovery and retention of activity of **1**. There is no need for a cosolvent. Second, these results significantly extend the scope of this method, which was initially developed with the fluorous rhodium catalyst  $[\text{ClRh}\{\text{P}(\text{CH}_2\text{CH}_2\text{R}_{f6})_3\}_3]$  for hydrosilylations conducted in dibutyl ether at  $55^\circ\text{C}$ .<sup>[20,31]</sup> Third, the



coated tape is also used for initial catalyst delivery. In principle, instead of weighing out a small quantity of catalyst by mass, a suitable length of coated tape could be added to the reaction mixture. However, as noted above, **1** does not appear to coat uniformly on teflon tape, at least with the procedures we have examined to date.

Several efforts involving fluororous phase-transfer catalysts in other laboratories deserve emphasis. First, Maruoka and co-workers developed a family of chiral fluororous ammonium salts, as exemplified by **5** in Scheme 2.<sup>[26]</sup> However, they were designed for use in organic/aqueous phase-transfer reactions and subsequent catalyst recovery. The salts were applied to the enantioselective alkylation of glycine derivatives and recycled by extracting the reaction mixtures with fluororous solvents. Interestingly, **5** is also soluble in CH<sub>2</sub>Cl<sub>2</sub>, CHCl<sub>3</sub>, and diethyl ether.

Second, Stuart and Vidal synthesized two fluororous diaza derivatives of 18-crown-6 (**6**; Scheme 2).<sup>[32]</sup> These were shown to extract picrate from aqueous to organic solutions and to catalyze the reaction of C<sub>8</sub>H<sub>17</sub>Br and KI under liquid/solid biphasic conditions by using the hybrid solvent CF<sub>3</sub>C<sub>6</sub>H<sub>5</sub>. When aqueous solutions of KI were employed, yields were considerably lower. The fluororous crown ethers could be recovered by solid-phase extraction (filtration through fluororous silica gel). The synthesis of other types of fluororous crown ethers (**7**; Scheme 2) and their ability to catalyze ionic displacement reactions in fluororous media have also been described at conferences.<sup>[33]</sup>

## Conclusions

This study has opened up unexpected new vistas for both phase-transfer catalysis and fluororous chemistry. Ionic displacement reactions are easily conducted in extremely nonpolar fluororous media at 76–100 °C with either stoichiometric or catalytic quantities of fluororous phosphonium halide salts. This constitutes an important conceptual step in the realization of processing strategies for materials immobilized in fluororous phases. Nonfluororous phosphonium salts are even better catalysts, but appear to function interfacially. Owing to the highly temperature-dependent solubilities of the fluororous phosphonium salts, they can be easily recovered by precipitation onto teflon tape. In recent work, we found that analogous fluororous and nonfluororous ammonium salts are also effective phase-transfer catalysts for such reactions, and these even more active systems will be described in subsequent reports.<sup>[34]</sup> Important future contributions to these research themes from other laboratories can also be anticipated.<sup>[18,26,32,33]</sup>

## Experimental Section

### General

Reactions were conducted in air unless otherwise noted. Chemicals were treated as follows: hexanes, CHCl<sub>3</sub>, diethyl ether, acetone, ethyl acetate,

acetonitrile, CF<sub>3</sub>C<sub>6</sub>H<sub>5</sub> (ABCR, 99%), and CF<sub>3</sub>C<sub>6</sub>F<sub>11</sub> (ABCR, 90%); simple distillation; CF<sub>3</sub>C<sub>6</sub>F<sub>5</sub> (ABCR, 98%); passed through neutral alumina and stored over molecular sieves; CH<sub>2</sub>Cl<sub>2</sub>: distilled from CaH<sub>2</sub>; *N,N*-dimethylformamide (DMF): distilled from CaH<sub>2</sub> and freeze/pump/thaw degassed; perfluoromethyldecalin (ABCR, 85%), R<sub>18</sub>(CH<sub>2</sub>)<sub>3</sub>I (Lancaster, 97%), R<sub>18</sub>(CH<sub>2</sub>)<sub>3</sub>OH (Apollo), NaCl (Acros, 99.5%), LiCl (anhydrous, Fluka, ≥99%), KCN (Acros, 97%), LiBr (Fluka, ≥98%), KI (Acros, 99%), PBr<sub>5</sub> (Merck, >98%), acetyl chloride (Acros, 99+%), CH<sub>3</sub>(CH<sub>2</sub>)<sub>11</sub>I (TCI, >96%), (CH<sub>3</sub>(CH<sub>2</sub>)<sub>7</sub>)<sub>3</sub>P (Alfa, 90%), and resorcinol (Acros, 98%): used as received. For substitution reactions, educts and authentic samples of products were either purchased (above) or prepared by new procedures (below) or literature procedures (R<sub>18</sub>(CH<sub>2</sub>)<sub>3</sub>I,<sup>[35]</sup> R<sub>18</sub>(CH<sub>2</sub>)<sub>3</sub>Br,<sup>[36]</sup> R<sub>18</sub>(CH<sub>2</sub>)<sub>2</sub>Br<sup>[7]</sup>). Phosphonium salts not given below were prepared as described earlier.<sup>[7]</sup>

NMR spectra were recorded on Bruker 300- or 400-MHz spectrometers at ambient probe temperatures and referenced as follows: <sup>1</sup>H: residual internal CHCl<sub>3</sub> or [D<sub>3</sub>]acetone (δ = 7.24 or 2.04 ppm); <sup>13</sup>C: internal CDCl<sub>3</sub> or [D<sub>6</sub>]acetone (δ = 77.0 or 29.8 ppm); <sup>31</sup>P: internal H<sub>3</sub>PO<sub>4</sub> capillary (δ = 0.00 ppm). The highly coupled <sup>13</sup>C NMR signals of the fluorinated carbon atoms are not listed below. IR and mass spectra were recorded on ASI React-IR and Micromass Zabspec instruments. Elemental analysis was conducted on a Carlo Erba EA1110 instrument.

### Syntheses

R<sub>18</sub>(CH<sub>2</sub>)<sub>3</sub>Cl: A flask was charged with R<sub>18</sub>(CH<sub>2</sub>)<sub>3</sub>OTf<sup>[13]</sup> (1.700 g, 2.69 mmol; Ts = *p*-toluenesulfonyl), LiCl (3.400 g, 81.0 mmol), and acetone (7 mL) and fitted with a condenser. The suspension was kept at 68 °C for 19 h, cooled, and directly subjected to chromatography (silica-gel column, 40–60 °C petroleum ether/ethyl acetate = 19:1 v/v). The solvent was removed from the product containing fractions (R<sub>f</sub> (TLC) = 0.95) by rotary evaporation to give R<sub>18</sub>(CH<sub>2</sub>)<sub>3</sub>Cl as a colorless liquid (0.975 g, 1.97 mmol, 73%). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 3.59 (t, <sup>3</sup>J<sub>H,H</sub> = 6 Hz, 2H, CH<sub>2</sub>Cl), 2.32–2.19 (m, 2H, CF<sub>2</sub>CH<sub>2</sub>), 2.11–2.04 ppm (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>): δ = 43.4 (s, CH<sub>2</sub>Cl), 28.6 (t, <sup>2</sup>J<sub>C,F</sub> = 22 Hz, CF<sub>2</sub>CH<sub>2</sub>), 23.7 ppm (s, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); elemental analysis: calcd (%) for C<sub>11</sub>H<sub>2</sub>ClF<sub>17</sub>: C 26.61, H 1.21; found: C 26.45, H 1.47.

R<sub>18</sub>(CH<sub>2</sub>)<sub>3</sub>CN: A flask was charged with R<sub>18</sub>(CH<sub>2</sub>)<sub>3</sub>OTf<sup>[13]</sup> (0.1900 g, 0.301 mmol), KCN (0.040 g, 0.60 mmol), and acetone (7 mL) and fitted with a condenser. The suspension was kept at 68 °C for 48 h, cooled, and directly subjected to chromatography (silica-gel column, 40–60 °C petroleum ether/ethyl acetate = 19:1 v/v). The solvent was removed from the product containing fractions (R<sub>f</sub> (TLC) = 0.90) by rotary evaporation to give R<sub>18</sub>(CH<sub>2</sub>)<sub>3</sub>CN as a white solid (0.092 g, 0.189 mmol, 63%). M.p.: 46 °C; IR (powdered film):  $\tilde{\nu}_{\text{CN}}$  = 2250 cm<sup>-1</sup> (w); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 2.49 (t, <sup>3</sup>J<sub>H,H</sub> = 7 Hz, 2H, CH<sub>2</sub>CN), 2.19–2.32 (m, 2H, CF<sub>2</sub>CH<sub>2</sub>), 2.04–1.97 ppm (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>): δ = 118.2 (s, CN), 29.7 (t, <sup>2</sup>J<sub>C,F</sub> = 21 Hz, CF<sub>2</sub>CH<sub>2</sub>), 16.9 (s, CH<sub>2</sub>CN), 16.8 ppm (s, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); MS (3-nitrobenzyl alcohol (3-NBA), FAB+): *m/z* (%) = 488 [M]<sup>+</sup> (100); elemental analysis: calcd (%) for C<sub>12</sub>H<sub>4</sub>F<sub>17</sub>N: C 29.59, H 1.24, N 2.88; found: C 28.45, H 1.31, N 2.99.

R<sub>18</sub>(CH<sub>2</sub>)<sub>3</sub>OAc: A flask was charged with R<sub>18</sub>(CH<sub>2</sub>)<sub>3</sub>OH (5.00 g, 10.5 mmol) and acetyl chloride (5.00 g, 4.55 mL, 64.1 mmol). The mixture was stirred for 48 h, and water was added (80 mL). The mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (100 mL). The organic phase was washed with aqueous NaHCO<sub>3</sub> (0.1 M, 50 mL) and dried (Na<sub>2</sub>SO<sub>4</sub>). Distillation (64 °C, 1.0 × 10<sup>-2</sup> mbar) gave R<sub>18</sub>(CH<sub>2</sub>)<sub>3</sub>OAc as a clear liquid (5.019 g, 9.65 mmol, 92%). IR (KBr):  $\tilde{\nu}$  = 2972 (w), 1749 (s), 1370 (s), 1200 (s), 1146 (m), 1031 cm<sup>-1</sup> (m); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 4.48–4.15 (m, 2H, CH<sub>2</sub>O), 2.62–1.83 ppm (m, 7H, overlapping CF<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, CH<sub>3</sub>); <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>): 171.1 (C=O), 62.9 (s, CH<sub>2</sub>O) 27.9 (t, <sup>2</sup>J<sub>C,F</sub> = 22 Hz, CF<sub>2</sub>CH<sub>2</sub>), 20.7, 19.8 ppm (2 × s, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); elemental analysis: calcd (%) for C<sub>13</sub>H<sub>9</sub>F<sub>17</sub>O<sub>2</sub>: C 30.00, H 1.73; found: C 30.12, H 2.02.

R<sub>18</sub>(CH<sub>2</sub>)<sub>2</sub>Cl: A flask was charged with R<sub>18</sub>(CH<sub>2</sub>)<sub>2</sub>OTf<sup>[37]</sup> (4.91 g, 8.24 mmol), NaCl (5.80 g, 100 mmol), and acetonitrile (32 mL) and fitted with a condenser. The suspension was heated under reflux. After 16 h, the solvent was removed by rotary evaporation. Water (100 mL) and diethyl ether (100 mL) were added. The organic phase was separated and dried (MgSO<sub>4</sub>). The solvent was removed by rotary evaporation, and the

residue was distilled (28 °C,  $3.4 \times 10^{-2}$  mbar) to give  $R_{18}(CH_2)_2Cl$  as a clear liquid (1.167 g, 2.42 mmol, 29%). IR (thin film):  $\tilde{\nu}=2347$  (m), 1459 (w), 1370 (w), 1239 (s), 1200 (s), 1146 (s), 1116 (m), 976  $cm^{-1}$  (m);  $^1H$  NMR ( $CDCl_3$ ):  $\delta=3.73$ – $3.69$  (m, 2H,  $CH_2Cl$ ), 2.64–2.47 ppm (m, 2H,  $CF_2CH_2$ );  $^{13}C\{^1H\}$  NMR ( $CDCl_3$ ):  $\delta=34.6$  ppm (s with overlapping t,  $CF_2CH_2CH_2Cl$ ); elemental analysis: calcd (%) for  $C_{10}H_4ClF_{17}$ : C 24.90, H 0.83; found: C 24.11, H 0.67.

$R_{18}(CH_2)_2Br$ :<sup>[7,38]</sup> A flask was charged with  $PBr_5$  (1.295 g, 3.01 mmol) and  $CH_2Cl_2$  (10 mL) and cooled to 0 °C. A solution of  $R_{18}(CH_2)_2OH$  (2.959 g, 4.80 mmol) in  $CH_2Cl_2$  (10 mL) was added dropwise with vigorous stirring under  $N_2$  atmosphere. After 1 h, the cold bath was removed. After 16 h, the sample was cooled to 0 °C, and water (10 mL) was added. The mixture was extracted with diethyl ether ( $2 \times 10$  mL). The solvent was removed from the extract by rotary evaporation. The residue was subjected to chromatography (silica-gel column, hexane/ $CH_2Cl_2=9:1$  v/v). The solvent was removed from the product containing fractions ( $R_f$  (TLC)=0.80) by rotary evaporation to give  $R_{18}(CH_2)_2Br$  as a colorless liquid (1.682 g, 3.108 mmol, 65%).

$(R_{18}(CH_2)_2)(R_{16}(CH_2)_2)_3P^+Br^-$  (**3**): A flask was charged with  $R_{18}(CH_2)_2Br$  (0.900 g, 1.71 mmol),  $(R_{16}(CH_2)_2)_3P^{391}$  (1.830 g, 1.71 mmol), and DMF (2 mL) under  $N_2$  atmosphere. The mixture was stirred at 120 °C for 3 days. The volatiles were removed at 120 °C and  $3 \times 10^{-2}$  mbar. The residue was washed with toluene ( $1 \times 4$  mL), methanol ( $3 \times 4$  mL), and diethyl ether ( $7 \times 4$  mL) and dried by oil-pump vacuum to give **3** as a yellow solid (1.552 g, 0.971 mmol, 57%). M.p.: 54–54.5 °C; IR (powder film): 2887 (w), 1231 (s), 1189 (s), 1143  $cm^{-1}$  (s);  $^1H$  NMR ( $CF_3C_6F_5+2$  drops [ $D_6$ ]acetone; external lock  $CDCl_3$ ):  $\delta=3.46$ – $3.38$  (m, 8H,  $CH_2P$ ), 2.84–2.70 ppm (m, 8H,  $CF_2CH_2$ );  $^{13}C\{^1H\}$  NMR ( $CF_3C_6F_5+2$  drops [ $D_6$ ]acetone; external lock  $CDCl_3$ ):  $\delta=24.0$  (t,  $^2J_{CF}=22$  Hz,  $CF_2CH_2$ ), 11.9 ppm (d,  $^1J_{CP}=52$  Hz,  $CH_2P$ );  $^{31}P\{^1H\}$  NMR ( $CF_3C_6F_5/CDCl_3$ ):  $\delta=41.5$  ppm (s); MS (3-NBA, FAB+):  $m/z$  (%) = 1519 [ $(R_{18}(CH_2)_2)(R_{16}(CH_2)_2)_3P^+$ ] (100); elemental analysis: calcd (%) for  $C_{34}H_{16}BrF_{56}P$ : C 25.53, H 1.01; found: C 25.35, H 1.00.

$(CH_3(CH_2)_{11})(CH_3(CH_2)_7)_3P^+I^-$  (**4**): A flask was charged with  $CH_3(CH_2)_{11}I$  (1.900 g, 6.42 mmol),  $(CH_3(CH_2)_7)_3P$  (1.334 g, 3.61 mmol), and  $CF_3C_6H_5$  (5 mL) under  $N_2$  atmosphere. The mixture was stirred at 105 °C for 18 h. The volatiles were removed at 120 °C and  $3 \times 10^{-2}$  mbar. The residue was washed with cold hexane ( $2 \times 5$  mL) and dried by oil-pump vacuum to give **4** as a white solid (1.696 g, 2.54 mmol, 71%). M.p.: 53 °C;  $^1H$  NMR ( $CDCl_3$ ):  $\delta=2.45$ – $2.30$  (m, 8H), 1.59–1.45 (m, 16H), 1.30–1.25 (br m, 40H), 0.87 ppm (t,  $^3J_{HH}=6$  Hz, 12H, 4 $CH_3$ );  $^1H$  NMR ( $[D_6]$ acetone):  $\delta=2.59$ – $2.53$  (m, 8H), 1.78–1.68 (m, 8H), 1.55–1.49 (m, 8H), 1.48–1.30 (br m, 40H), 0.89 ppm (brs, 12H, 4 $CH_3$ );  $^{13}C\{^1H\}$  NMR ( $[D_6]$ acetone):  $\delta=32.5$ , 32.4 ( $2 \times s$ ,  $\approx 1:3$ ,  $CH_2$ ), 31.3 (d,  $^3J_{CP}=15$  Hz,  $CH_2CH_2CH_2P$ ), 30.4–29.1 (several signals obscured by [ $D_6$ ]acetone), 23.2 ( $2 \times s$ ,  $\approx 1:3$ ,  $CH_2$ ), 21.1 (d,  $^2J_{CP}=4$  Hz  $CH_2CH_2P$ ), 19.5 (d,  $^1J_{CP}=47$  Hz,  $CH_2P$ ), 14.2 ppm (s,  $CH_3$ );  $^{31}P\{^1H\}$  NMR ( $[D_6]$ acetone):  $\delta=33.3$  (s); MS (3-NBA, FAB+):  $m/z$  (%) = 540 [ $(CH_3(CH_2)_{11})(CH_3(CH_2)_7)_3P^+$ ] (100); elemental analysis: calcd (%) for  $C_{36}H_{76}P$ : C 64.84, H 11.49; found: C 64.83, H 11.53.

### Catalysis

Representative substitution reactions and recycling without support (Scheme 1a, Table 1, entry 4, and Table 4): A 4-mL vial was charged with  $R_{18}(CH_2)_2I$  (0.200 g, 0.341 mmol), **1** (0.055 g, 0.034 mmol), perfluoromethyldecalin (0.5 mL), NaCl (0.150 g, 2.56 mmol), and water (0.5 mL). The vial was tightly sealed, and the mixture was vigorously stirred at 100 °C for 24 h. The  $^1H$  NMR spectrum of an aliquot from the fluorous phase showed that more than 90% of the iodide was consumed. Hexane was added to precipitate the phosphonium salt from the biphasic supernatant (water below a combined fluorous/hexane layer). The upper phase was separated and dried ( $MgSO_4$ ). The solvents were removed by oil-pump vacuum to give  $R_{18}(CH_2)_2Cl$  as a colorless oil (0.154 g, 0.31 mmol, 92%) that contained about 7% of  $R_{18}(CH_2)_2I$ . The phosphonium salt was washed twice with distilled water (1 mL) and reused for the next reaction.  $R_{18}(CH_2)_2Cl$ :  $^1H$  NMR ( $CDCl_3$ ):  $\delta=3.60$  (t,  $J_{HH}=6.8$  Hz, 2H,  $CH_2Cl$ ), 2.36–2.04 ppm (2 m, 4H,  $CF_2(CH_2)_2$ );  $^{13}C\{^1H\}$  NMR ( $CDCl_3$ ):

$\delta=43.5$  (s,  $CH_2Cl$ ), 28.5 (t,  $^2J_{CF}=21$  Hz,  $CF_2CH_2$ ), 23.6 ppm (t,  $^3J_{CF}=6$  Hz,  $CH_2CH_2Cl$ ).

Phase requirements: A (reaction without fluorous solvent): A 4-mL vial was charged with  $R_{18}(CH_2)_2I$  (0.200 g, 0.341 mmol), **1** (0.055 g, 0.034 mmol), NaCl (0.150 g, 2.56 mmol), and water (0.5 mL). The vial was tightly sealed, and the mixture was vigorously stirred at 100 °C for 24 h. The sample was cooled, and  $CDCl_3$  was added. The  $^1H$  NMR spectrum of the  $CDCl_3$  layer showed 87% conversion into  $R_{18}(CH_2)_2Cl$ .

B ( $CF_3C_6H_5$  solvent): A 4-mL vial was charged with  $R_{18}(CH_2)_2I$  (0.200 g, 0.341 mmol), **1** (0.055 g, 0.034 mmol),  $CF_3C_6H_5$  (0.5 mL), NaCl (0.150 g, 2.56 mmol), and water (0.5 mL). The vial was tightly sealed, and the mixture was vigorously stirred at 100 °C. The  $^1H$  NMR spectrum of an aliquot from the fluorous phase showed 49% conversion after 24 h and 72% after 72 h.

C ( $CF_3C_6H_5$  solvent, preparative scale): A vial was charged with  $R_{18}(CH_2)_2OTf^{[13]}$  (1.850 g, 2.99 mmol), LiBr (1.040 g, 11.97 mmol), **3** (0.474 g, 0.296 mmol),  $CF_3C_6H_5$  (5 mL), and water (5 mL). The vial was tightly sealed, and the mixture was vigorously stirred at 98–100 °C for 180 h. The sample was cooled and extracted with hexane ( $2 \times 10$  mL). The solvent was removed from the extract by rotary evaporation. The residue was subjected to chromatography (silica-gel column, hexane/ $CH_2Cl_2=12:1$  v/v). The solvent was removed from the product containing fractions ( $R_f$  (TLC)=0.75) by rotary evaporation to give  $R_{18}(CH_2)_2Br$  as a colorless liquid (1.127 g, 2.08 mmol, 70%; see additional syntheses above).

D (representative reaction from Table 2 (entry 1)): A 4-mL vial was charged with  $R_{18}(CH_2)_2Br$  (0.092 g, 0.17 mmol), **1** (0.276 g, 0.17 mmol), and perfluoromethyldecalin (0.25 mL). The vial was tightly sealed, and the homogeneous sample was vigorously stirred at 100 °C. A  $^1H$  NMR spectrum of an aliquot was recorded hourly (Figure 5).

Representative reaction with nonfluorous catalyst (Table 3, entry 1): A 4-mL vial was charged with  $R_{18}(CH_2)_2I$  (0.200 g, 0.341 mmol), **4** (0.023 g, 0.034 mmol), perfluoromethyldecalin (0.5 mL), NaCl (0.150 g, 2.56 mmol), and water (0.5 mL). The vial was tightly sealed, and the mixture was vigorously stirred at 100 °C for 24 h. The  $^1H$  NMR spectrum of an aliquot from the fluorous phase showed 43% conversion after 1 h and 93% after 24 h.

Solubility data: A: A flask was charged with **4** (0.067 g, 0.10 mmol), resorcinol standard (0.330 g, 3.00 mmol), and  $D_2O$  (5.00 mL). The sample was vigorously stirred at 24 °C. Stirring was halted, and after the undissolved **4** had settled, an aliquot of the supernatant was removed and diluted with [ $D_6$ ]acetone. The sample was stirred at 100 °C. An aliquot of the supernatant was similarly removed and diluted with [ $D_6$ ]acetone.  $^1H$  NMR spectra of both aliquots were recorded, and the methyl signals of **4** (0.89 ppm, 12H) were integrated against the CH signals of resorcinol ( $\delta=6.94$ – $6.90$  and  $6.30$ – $6.27$  ppm, 4H). Data: see text. No signal was detected for **4** at 24 °C, so the limit was assigned by using a noise peak.

B: A flask was charged with **4** (0.0307 g, 0.046 mmol),  $R_{18}(CH_2)_2I$  (0.0162 g, 0.028 mmol), and perfluoromethyldecalin (1.00 mL). The sample was vigorously stirred at 23 °C. Stirring was halted, and after the undissolved **4** had settled, an aliquot of the supernatant was removed and diluted with  $CDCl_3$ . The sample was stirred at 100 °C. An aliquot of the supernatant was similarly removed and diluted with  $CDCl_3$ .  $^1H$  NMR spectra of both aliquots were recorded, and the  $CH_2I$  signals of  $R_{18}(CH_2)_2I$  ( $\delta=3.24$  ppm, 2H) were integrated against a multiplet of **4** ( $\delta=1.25$ – $1.30$  ppm, 40H), which overlapped with impurity signals that were magnified owing to the low solubility. This afforded the upper solubility limits noted in the text.

Catalyst-coated teflon tape: A suspension of **1** (0.019 g, 0.010 mmol) in  $CF_3C_6H_5$  (1 mL) was heated to 90 °C to give a homogeneous solution. A  $30 \times 12 \times 0.0075$ -mm<sup>3</sup> strip of teflon tape was then immersed in the solution, which was allowed to cool to room temperature (becoming turbid then clear) with occasional shaking. The sample was kept at 10 °C for 10 min. The white tape, which exhibited light-yellow patches, was then removed, washed with hexane (0.5 mL), and then air-dried.

Recycling with support: A (table in Figure 8b): A 4-mL vial was charged with  $R_{18}(CH_2)_2I$  (0.0588 g, 0.101 mmol),  $CF_3C_6H_5$  (0.5 mL), water (0.5 mL), and the teflon tape coated with **1** from the previous experi-

ment. The vial was tightly sealed, and the mixture was vigorously stirred at 98–100°C for 72 h. The  $^1\text{H}$  NMR spectrum of an aliquot of the  $\text{CF}_3\text{C}_6\text{H}_5$  phase showed 71% conversion. The heating bath was replaced by a cold tap-water bath, and the sample was stirred for a further hour.<sup>[21]</sup> The coated tape was removed, washed with distilled water ( $2 \times 2$  mL) and hexane, and reused for the next cycle.

B (rate profile in Figure 8b): The preceding experiment was repeated, but was periodically cooled. Small aliquots of the  $\text{CF}_3\text{C}_6\text{H}_5$  phase were then removed and diluted with  $\text{CDCl}_3$ , and  $^1\text{H}$  NMR spectra were recorded (typical interruption of reaction time: 1 h).<sup>[22]</sup>

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