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Syntheses of fluorous quaternary ammonium salts and their application as phase transfer catalysts for halide substitution reactions in extremely nonpolar fluorous solvents

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Perfluoromethyldecalin solutions of the fluorous alkyl halides $R_{f8}(CH_2)_mX$ (m=2, 3; X=Cl, I) are inert toward aqueous NaCl, KI, KCN, and NaOAc. However, substitution occurs at 100 °C in the presence of 10 mol % of the fluorous ammonium salts $(R_{f8}(CH_2)_2)(R_{f8}(CH_2)_5)_3N^+\ I^-$ (**1**) or $(R_{f8}(CH_2)_3)_4N^+\ Br^-$ (**2**) (10 mol %), which are fully or partially soluble in perfluoromethyldecalin under these conditions. Stoichiometric reactions of (a) **1** and $R_{f8}(CH_2)_3Br$, and (b) **2** and $R_{f8}(CH_2)_2I$ are conducted in perfluoromethyldecalin at 100 °C, and yield the same $R_{f8}(CH_2)_mI/R_{f8}(CH_2)_mBr$ equilibrium ratio (60–65:40–35). This shows that ionic displacements can take place in extremely nonpolar fluorous phases, and suggests a classical phase transfer mechanism for the catalyzed reactions. Interestingly, the non-fluorous ammonium salt mixture $CH_3(CH_3(CH_2)_m)_3N^+\ Cl^-$ (**3**, Aliquat® 336; m=2:1 7/9) also catalyzes halide substitutions, but under triphasic conditions with **3** suspended between the lower fluorous and upper aqueous layers. NMR experiments establish very low solubilities in both phases, suggesting interfacial catalysis.

1. Introduction

Fluorous liquid phases such as perfluoroalkanes are, by a variety of measures, the least polar known.[1,2] They are rivaled only by the noble gases, which are liquid over much narrower temperature ranges. Hence, it is not surprising that common inorganic salts and other ionic compounds are insoluble in such media. However, there is a growing recognition that some fluorous salts can dissolve in fluorous liquids, either at room temperature or upon heating, which often dramatically enhances the solubilities of fluorous solutes.[3] Some examples are collected in Figure 1, in which R_{fn} denotes a perfluoroalkyl group $(CF_2)_{n-1}CF_3$.

Deelman and van Koten have synthesized a series of fluorous BAr_f^- ('Barf') type anions, $B(4\text{-}C_6H_4R_{f6})_4^-$, $B(4\text{-}C_6H_4Si(CH_3)_2(CH_2)_2R_{f6})_4^-$, and $B(3,5\text{-}C_6H_3(R_{f6})_2)_4^-$.[4] These have been employed to solubilize several cations. For example, the ammonium salt $n\text{-}Bu_4N^+\ B(4\text{-}C_6H_4\text{-}Si(CH_3)_2(CH_2)_2R_{f6})_4^-$ (**I**, Fig. 1) exhibits a solubility of 0.000052 M at room temperature in FC-72,[4b] a medium that consists mainly of perfluorohexane. Note that due to the high molecular weights commonly associated with fluorous molecules, molar solubilities that appear modest translate to mass-based solubilities that are more substantial (0.113 g/L for **I**).

The related rhodium salt $[Rh(dppe)_2]^+\ B(4\text{-}C_6H_4R_{f6})_4^-$ is insoluble in FC-72 (<0.000006 M), but $[Rh(dppe)_2]^+\ B(3,5\text{-}C_6H_3(R_{f6})_2)_4^-$ (**IIa**), which features four additional perfluorohexyl groups in the anion, partitions nearly equally between toluene and perfluoromethylcyclohexane. Bühlmann has reported that the analogous sodium salt **IIb** is quite soluble in perfluorodecalin (0.0011 M), perfluoroperhydrophenanthrene (0.0014 M), and a perfluoroether (0.00091 M).[5] Not unsurprisingly, distinctly higher solubilities are realized when the cations are also fluorous, as in the rhodium salts **IIIb**,**c**. In partitioning experiments, these showed much greater affinities for perfluoromethylcyclohexane than toluene.[4a]

In unpublished work from some time ago, we prepared the fluorous primary ammonium (anilinium) salt $(3,5\text{-}C_6H_3((CH_2)_2\text{-}R_{f8})_2)NH_3^+\ Cl^-$ (**IV**, Fig. 1) and noted a solubility of ca. 10 g/L (0.01 M) in perfluoromethylcyclohexane at room temperature.[6] Pozzi and coworkers have reported that the related fluorous anilinium triflates **V** and **VI**, as well as the fluorous aliphatic secondary ammonium salt **VII**, exhibit appreciable (and temperature dependent) solubilities in perfluoro-1,3-dimethylcyclohexane.[7]

Neumann and Fish synthesized the fluorous quaternary ammonium salt $(CH_3)(R_{f8}(CH_2)_3)_3N^+\ CH_3SO_3^-$, and used the cation to render the dodecaanion in **VIII** 'freely soluble in perfluorohydrocarbons'.[8] Bühlmann combined the same cation with a fluorous BAr_f^- anion to give **IX**, which exhibited solubilities of 0.010 M in FC-72 and perfluoroperhydrophenanthrene.[5] Maruoka has utilized the chiral fluorous ammonium salt **X** as a phase transfer catalyst for enantioselective

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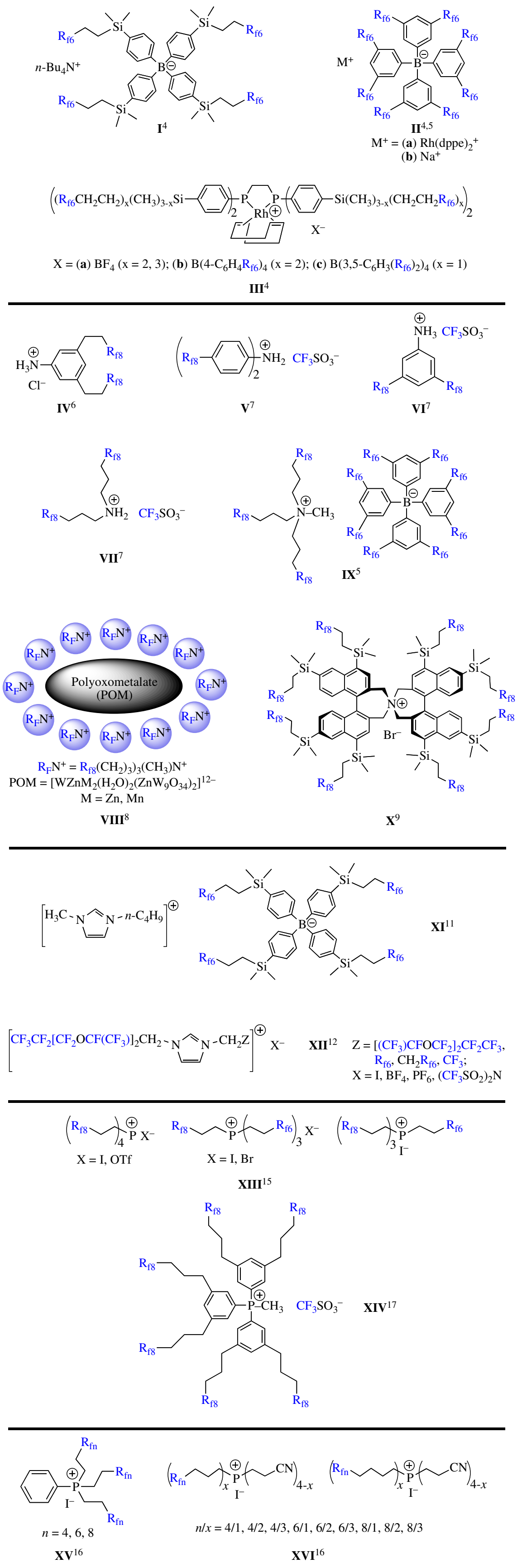


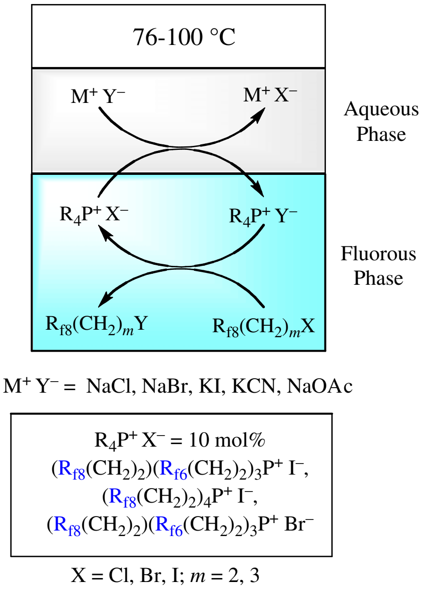
Figure 1. Fluorous salts that have documented solubilities in fluorous liquid phases (**I-XIV**), and related species (**XV-XVI**) (R_{fn}=$(CF_2)_{n-1}CF_3$).

alkylations in *organic* media, with subsequent recovery by extraction with FC-72.[9] Ammonium salts with fewer perfluoroalkyl groups per nitrogen atom have also been described, but no data regarding solubilities in fluorous solvents (which should be lower) are yet available.[10]

The ammonium or imidazolium salt **XI**, which features a nonfluorous cation and a fluorous BAr$_f^-$ anion, exhibits a solubility of 0.37 g/L (0.00018 M) in FC-72, and is a room temperature ionic liquid.[11] More recently, Kvíčalová has described a large family of liquid salts with fluorous imidazolium cations (**XII**).[12] These are highly soluble in perfluoromethylcyclohexane, exceeding 50 g/L in the best cases, and show much greater affinities for this solvent than toluene. Other fluorous ionic liquids have been described, but solubility data in fluorous solvents have not to our knowledge been reported.[13]

Yasuda, Sakakura, Stuart, Horváth, Bühlmann, and ourselves have prepared a number of fluorous quaternary aliphatic phosphonium halides and triflates (**XIII-XVI**).[14–17] Those grouped in **XIII** have been shown to be highly soluble in perfluoromethylcyclohexane at elevated temperatures.[15] With the triarylphosphonium salt **XIV**, solubilities exceed 0.014 M in FC-72, perfluoromethylcyclohexane, and perfluoroperhydrophenanthrene at room temperature. Presumably many of **XV-XVI** would also exhibit significant solubilities. Phosphonium salts with a single perfluoroalkyl moiety have also been reported.[18] The manner in which the preceding salts are solvated in fluorous media is an intriguing question that remains to be addressed.

The growing portfolio of fluorous salts that are soluble in fluorous liquid phases offers increased options for introducing polar ions that may interact or react with fluorous solutes. One obvious application would be phase transfer catalysis,[19] whereby an ion of a salt that is insoluble in a fluorous solvent is transported across a phase barrier by a fluorous counter-ion with an appreciable fluorous phase affinity. Indeed, we recently established that fluorous quaternary aliphatic phosphonium salts such as $(R_{f8}(CH_2)_2)(R_{f6}(CH_2)_2)_3P^+\ X^-$ (X=I, Br) and $(R_{f8}(CH_2)_2)_4P^+\ I^-$ catalyze Finkelstein-type[20] substitution reactions of fluorous alkyl halides $R_{f8}(CH_2)_mX$ (m=2, 3; X=Cl, Br, I) in perfluoromethylcyclohexane ($CF_3C_6F_{11}$) or perfluoromethyldecalin ($CF_3C_{10}F_{17}$) by aqueous NaCl, NaBr, KI, KCN, and NaOAc at 76–100 °C.[21] These transformations are illustrated in Scheme 1. Other creative approaches to interfacing fluorous chemistry with phase transfer catalysis have also been described.[9,22–24]



Scheme 1. Phase transfer catalysis of halide substitution reactions in fluorous media using fluorous phosphonium salts.