Dramatic Effect of the Specific Solvation on the Reactivity of Quaternary Ammonium Fluorides and Poly(hydrogen fluorides), $(HF)_n \bullet F^-$, in Media of Low Polarity

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A quantitative study of how the intrinsic reactivity (nucleophilicity and basicity) of the fluoride anion of $hexyl_4N^+F^-$ is affected in solvents of low polarity by the specific solvation of a limited number of water molecules has been performed. The nucleophilicity enhancement is extrapolated to be about 3 orders of magnitude by reducing the specific hydration n of the anion from 8.5 to 0. Such enhancement is much higher (~100 times) than that obtained, under the same conditions, by dehydrating the other halides. The nucleophilicity scale of anhydrous anions found, $F^- \gg Cl^- > Br^- > I^-$, reflects those well-known in dipolar aprotic solvents and in the gas phase. Comparison in the same hydration range shows that the basicity of the fluoride anion is much more affected by specific solvation than is its nucleophilicity. Extension of this study to quaternary ammonium poly(hydrogen fluorides) $Q^+(HF)n{\cdot}F^-$, where $n = 1, 2$, provides the following reactivity scale: $F^- \gg HF_2^- > H_2F_3^-$. The increasing stabilization of F^- anion, by interaction with hydrogen fluoride in the sequence $F^- \ll HF_2^- < H_2F_3^-$, accounts for the much lower reactivity observed in the case of poly(hydrogen fluorides) with respect to that of the hypothetical anhydrous fluoride ($F^-{:}HF_2^-{:}H_2F_3^- = 8.5 \times 10^5{:}1.2 \times 10^2{:}1$). This also explains the different sensitivity of these anions to the specific hydration which decreases in the same order: $F^- \gg HF_2^- > H_2F_3^-$.

The importance of ionic fluorides as sources of fluorine in the synthesis of organofluorine derivatives,[1] as proton abstractors in base-assisted reactions,[2] and as promotors of organosilyl compound reactions[3] is well documented. In particular, lipophilic quarternary onium fluorides are found to be reagents of choice for carrying out reactions in aprotic organic solvents even of low polarity.[1-3] In these media, bulky quaternary onium salts give rise to loose ion pairs in which the anions are unsolvated and hence highly reactive.[4,5]

However, their reactivity is noticeably reduced in the presence of a limited amount of protic material, such as water, which specifically solvates the anion. A particularly striking example is liquid-liquid phase-transfer catalysis where the anions are transferred in the organic phase with a few molecules of water.[4-6] The effect of this specific hydration on the anionic reactivity (nucleophilicity or basicity) is more relevant for anions with localized and/or less polarizable charge (Cl^-, CN^-, N_3^-)[5,7] and even dramatic for the highly hydrophilic OH^-.[8,9]

A great deal is known about the tendency of F^- anion to interact with protic solvents resulting in strong H bonds.[2,10] The effect of this interaction on the anion reactivity has been qualitatively reported,[2] and only very few kinetic data are available,[11-14] especially in solvents of low polarity.

Table I. Influence of the Specific Hydration of $Hexyl_4N^+F^- \bullet n\,H_2O$ on the Reaction Rate for Nucleophilic Substitution of Methanesulfonate by Fluoride Ion in *n*-Octyl Methanesulfonate in Chlorobenzene at 60 °C[a]

hydration state n of $hexyl_4N^+F^-{\cdot}nH_2O$[b]	10^3k,[c] $M^{-1}\ s^{-1}$	k_{rel}
8.5	2.3	1
6.0	2.4	1
4.0	4.3[d]	2
3.0	21[d]	9
2.6	46[d]	20
1.8	120[d]	52
1.5	220[d]	96
0.0	1890[e]	822

[a] [Substrate] = 2-4 × 10^{-2} M; $[Q^+F^-]$ = 3-4 × 10^{-2} M. [b] Average of at least four determinations. [c] Average of at least three runs. The error in these values is estimated to be 4%. [d] Initial rate constants. [e] Extrapolated value by plotting log k vs n.

Here we report a quantitative study of how the specific hydration affects both the nucleophilic reactivity and basicity of lipophilic quaternary ammonium fluorides in solvents of low polarity.

The reactivity of quaternary poly(hydrogen fluorides), $Q^+(HF)_n{\cdot}F^-$, where $n = 1, 2$, has also been measured and compared with that of F^- anion under the same conditions.

Results

Nucleophilic substitution reactions of the methanesulfonic group in n-octyl methanesulfonate by fluoride anion associated with tetrahexylammonium cation Q^+ (**2**) were carried out in chlorobenzene solution with comparable concentrations of substrate **1** (2-4 × 10^{-2} M) and quaternary fluoride **2a** (3-4 × 10^{-2} M) (reaction 1). The hydration state n of $Q^+F^-{\cdot}nH_2O$ used ranged from 1.5 to 8.5

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Table II. Effect of the Specific Hydration of Fluoride Ion on Its Basicity for the Elimination Reaction of Hexyl$_4$N$^+$F$^-$•n H$_2$O in Chlorobenzene at 60 °C[a]

hydration state n of hexyl$_4$N$^+$F$^-$·nH$_2$O[b]	10^5k,[c] s^{-1}	k_{rel}
6.0	*d*	–
4.6	0.005	1
3.2	0.035	7
2.4	1.7[e]	340
2.0	9.5[e]	1900
1.7	38[e]	7600
0	1.17×10^5[f]	2.34×10^7

[a] $[Q^+F^-] = 3\text{–}4 \times 10^{-2}$ M. [b] Average of at least four determinations. [c] Average of at least three runs. The error in these values is estimated to be 3%. [d] No elimination reaction occurred within 2 weeks. [e] Initial rate constants. [f] Extrapolated value by plotting log k vs n.

molar equiv, the latter being the highest value obtainable for F$^-$ anion in chlorobenzene (see Experimental Section) (Table I).

$$\underset{\mathbf{1}}{n\text{-}C_8H_{17}OSO_2Me} + \underset{\mathbf{2a}}{Q^+F^-} \rightarrow \underset{\mathbf{3}}{n\text{-}C_8H_{17}F} + \underset{\mathbf{2b}}{Q^+MeSO_3^-} \tag{1}$$

$$Q^+ = (C_6H_{13})_4N^+$$

$$\text{rate} = k[\text{substrate}][Q^+F^-] \tag{2}$$

The rates were measured by potentiometric titration of F$^-$ anion. Reaction 1 followed the second-order kinetic equation 2, up to at least 70% conversion only for hydration states $n \geqslant 6$. For lower n values ($n \leqslant 4$), second-order kinetics showed a downward curvature, progressively more pronounced by diminishing the hydration state, and in this case the initial rates were evaluated (Table I). This kinetic behavior is due to the progressive increase of the water-unreacted Q$^+$F$^-$ ratio, which slows down the rate during the reaction. This effect is negligible for the highest hydration numbers ($n \geqslant 6$) whereas it is particularly relevant at low n values (Table I).

It was impossible to carry out kinetic measurements of reaction 1 at $n < 1.5$, because all attempts of further dehydration led to extensive decomposition of the quaternary fluoride **2a** according to a Hofmann-like elimination (reaction 3).[15] For hydration values $n \geqslant 1.5$, the rate of reaction 3 is orders of magnitude lower than that of reaction 1 so that the decomposition of **2a** (eq 3) does not interfere in nucleophilicity determinations (see Tables I and II and Figure 1).

$$\underset{\mathbf{2a}}{2\text{hexyl}_4N^+F^-} \rightarrow \underset{\mathbf{4}}{\text{hex-1-ene}} + \underset{\mathbf{5}}{\text{hexyl}_3N} + \underset{\mathbf{2c}}{\text{hexyl}_4N^+HF_2^-} \tag{3}$$

$$\text{rate} = k[Q^+F^-] \tag{4}$$

Kinetic measurements of reaction 3 were carried out in chlorobenzene solution, at 60 °C, by changing the specific hydration n of quaternary fluoride **2a** from 1.7 to 6.0 molar equiv. For n values $\geqslant 6$, the quaternary salt **2a** was recovered unchanged after 2 weeks (Table II).

The stoichiometry of the elimination reaction 3 is due to the formation of hydrogen fluoride, which engages a second F$^-$ anion, giving the thermodynamically stable[15,16] and weakly basic[17] hydrogen difluoride ion, HF$_2^-$ (**2c**).

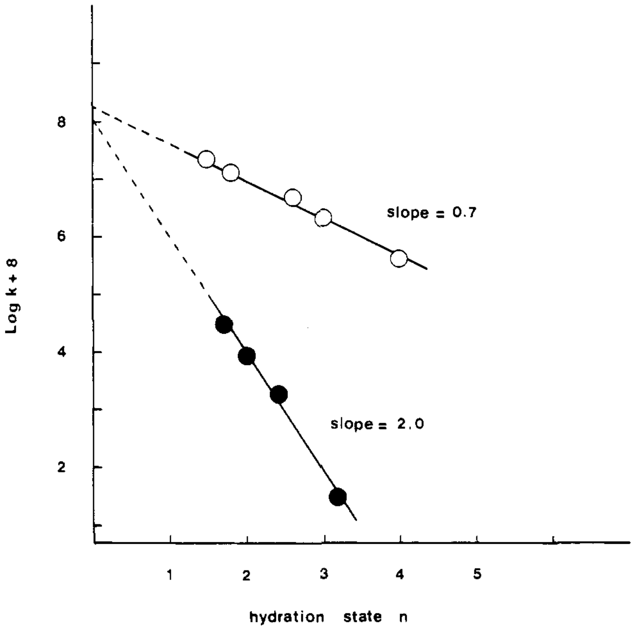

Figure 1. Correlation between log k and the hydration state n of quaternary onium fluoride Q$^+$F$^-$·nH$_2$O (**2a**) for the nucleophilic substitution (eq 1) (○) and the elimination reaction (eq 3) (●). For the reaction conditions, see footnotes *a* of Tables I and II.

Reaction 3 was measured by following the disappearance of quaternary cation **2**. It obeyed a regular first-order kinetic equation (4) up to at least 70% conversion only when the hydration state n of quaternary fluoride **2a** was $\geqslant 3.0$. For lower n values, an upward curvature of the first-order plot was observed and, hence, initial rates were also calculated in this case (Table II). Kinetic behavior can be explained in analogy with that discussed above for reaction 1.

The study of nucleophilic reactivity was extended to tetrahexylammonium hydrogen difluoride, hexyl$_4$N$^+$HF$_2^-$ (**2c**), and tetrahexylammonium dihydrogen trifluoride, hexyl$_4$N$^+$H$_2$F$_3^-$ (**2d**), with the same substrate **1** (reaction 5).

$$\underset{\mathbf{1}}{n\text{-}C_8H_{17}OSO_2Me} + \underset{\substack{\mathbf{2c},\ n\,=\,1\\ \mathbf{d},\ n\,=\,2}}{2Q^+(HF)_n{\cdot}F^-} \rightarrow \underset{\mathbf{3}}{n\text{-}C_8H_{17}F} + \underset{\mathbf{2b}}{Q^+MeSO_3^-} + \underset{\substack{\mathbf{2d},\ m\,=\,2\\ \mathbf{e},\ m\,=\,4}}{Q^+(HF)_m{\cdot}F^-} \tag{5}$$

$$\text{rate} = k[\text{substrate}][Q^+(HF)_n{\cdot}F^-] \tag{6}$$

Reactions were measured by GLC analysis following the disappearance of the substrate and/or the appearance of the fluorooctane in the presence of an internal standard. They were performed in benzene and/or *o*-dichlorobenzene instead of chlorobenzene because the latter interferes in the GLC analysis.

The stoichiometry of reaction 5 also requires a 2-fold excess of Q$^+$(HF)$_n$·F$^-$ (**2c,d**) with respect to the substrate because the HF resulting from the reaction engages a second (HF)$_n$·F$^-$ anion, giving the much less reactive (HF)$_m$·F$^-$, where $m = 2n$ (Table III). In all cases, a regular second-order kinetic equation (6) was found up to 70% conversion. Due to the very low nucleophilic reactivity of Q$^+$H$_2$F$_3^-$ (**2d**), reaction 5 with this anion was carried out at 90 °C. For a comparison of the rate constants at the same temperature, the extrapolated values at 90 °C for Q$^+$HF$_2^-$ (**2c**) and Q$^+$F$^-$ (**2a**) were obtained from kinetic measurements at 60, 70, 80 °C and 50, 60, 70 °C respectively (Table III).

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(17) A chlorobenzene solution of anhydrous **2c** was recovered unchanged after 2 weeks at 60 °C.

Table III. Reactivity of $Hexyl_4N^+F^-$ and $Hexyl_4N^+(HF)_n\bullet F^-$ (n = 1, 2) for the Nucleophilic Substitution of Methanesulfonate in *n*-Octyl Methanesulfonate by Fluoride Ion in *o*-Dichlorobenzene at Different Temperatures[a]

$hexyl_4N^+Y^-$	10^3k,[b] $M^{-1}\ s^{-1}$	T, °C	k_{rel}
2a $F^-\cdot 4H_2O$[c]	1.2	50	
	5.0	60	
	16.4	70	
	155 (6.5×10^4)[d]	90[e]	2000 (8.5×10^5)[d]
2c HF_2^-	0.7	60	
	1.7	70	
	4.2	80	122
	9.4	90[e]	
2d $H_2F_3^-$	0.077[f]	90	1

[a] [Substrate] = $2-4 \times 10^{-2}$ M; [$hexyl_4N^+Y^-$] = $4-5 \times 10^{-2}$ M. [b] Average of at least three runs. [c] Average of at least four determinations. The error in these values is estimated to be 6%. [d] Value corresponding to the hypothetical anhydrous quaternary fluoride **2a**.[31] [e] Extrapolated value by Arrhenius plot. [f] A similar value was obtained by using monohydrated $Q^+H_2F_3^-$ (**2d**).

Table IV. Influence of the Specific Hydration of $Hexyl_4N^+NF_2^-\bullet nH_2O$ on the Reaction Rate for Nucleophilic Substitution of Methanesulfonate in *n*-Octyl Methanesulfonate by Fluoride Ion in Benzene at 60 °C[a]

hydration state n of $hexyl_4N^+HF_2^-\cdot nH_2O$[b]	10^4k,[c] $M^{-1}\ s^{-1}$	k_{rel}
2.2	4.2	1
1.7	4.4	1.0
1.0	6.4	1.5
0.3	8.5	2.0
0.0	11.2	2.7

[a] [Substrate] = $2-3 \times 10^{-2}$ M; [$Q^+HF_2^-$] = $4-5 \times 10^{-2}$ M. [b] Average of at least four determinations. [c] Average of at least three runs. The error in these values is estimated to be 4%.

The effect of the specific hydration on the nucleophilic reactivity was examined also in the case of poly(hydrogen fluorides) HF_2^- (**2c**) (Table IV) and $H_2F_3^-$ (**2d**) (reaction 5) (Table III).

These salts are much less hygroscopic than the corresponding quaternary fluoride **2a**; indeed, they are easily prepared in the anhydrous state,[18] and the highest hydration numbers n, obtainable in solvents of low polarity (benzene, chlorobenzene, *o*-dichlorobenzene...), are 2 for $Q^+HF_2^-$ (**2c**) and only 1 in the case of $Q^+H_2F_3^-$ (**2d**) (see Experimental Section).

Discussion

Tables I and II clearly show the dramatic effect that a limited number of water molecules produces on the reactivity of F^- anion associated with a quaternary onium cation Q^+ in solvents of low polarity. Nucleophilicity and basicity enhancements found are not a linear function of the hydration state (n) but exponentially increase by diminishing n. In both cases, a good linear correlation (r = 0.992) was obtained in the range n = 1.5–3.0 when log k was plotted against n, as shown in Figure 1. By assuming that this correlation also works for $n < 1.5$ (where no direct measurements were possible), we extrapolated the rate constant values for reactions 1 and 3 corresponding to the hypothetical anhydrous quaternary fluoride **2a** (n = 0) (Tables I and II).

The nucleophilicity enhancement of $Q^+F^-\cdot nH_2O$ (**2a**) (reaction 1) is extrapolated to be about 3 orders of magnitude by reducing the anion hydration n from 8.5 to 0 (Table I). Such enhancement is much higher (~100 times) than that obtained in the same reaction by dehydrating the other halides (11, 2.5, and 1.5 times for Cl^-, Br^-, and I^-, respectively).[5,7,20,21] This behavior is in agreement with the increasing stabilization of these anions, due to the specific solvation, in the order $I^- < Br^- < Cl^- \ll F^-$, as expected from their hydration enthalpies ($-\Delta H_h°$): I^-, 294 kJ mol^{-1}; Br^-, 335 kJ mol^{-1}; Cl^-, 366 kJ mol^{-1}; F^-, 502 kJ mol^{-1}.[23]

It is interesting to point out that a similar trend has been found[24] in gas-phase determinations of hydration energies for a set of ($n - 1$, n) equilibria $X^-(H_2O)_{n-1} + H_2O = X^-(H_2O)_n$ where X^- = F^-, Cl^-, Br^-, I^- and n = 0–5. Indeed the enthalpy variations ($-\Delta H_{n-1,n}$) with n are constantly the highest in the case of fluoride anion, especially at low hydration values ($n \geqslant 3$).

The nucleophilicity order F^-:Cl^-:Br^-:I^- = 280:5:3:1 we found for reaction 1 under anhydrous conditions in chlorobenzene[21] reflects those previously reported in the gas phase by other authors.[25,26] Analogy underlines how dramatically the specific solvation by a limited number of water molecules can modify the intrinsic reactivity of small anions (i.e., F^-, OH^- [8]) associated with bulky quaternary cations in media of low polarity.[27]

The data of Table II show that the F^- basicity is even more affected than nucleophilicity by the specific hydration. Indeed, when the hydration sphere n of Q^+F^- (**2a**) is lowered from 4.6 to 0, the rate constant k of the elimination reaction (3) increases by more than 7 orders of magnitude. For higher n values ($n > 4.6$), differently from the nucleophilicity (Table I), the fluoride basicity becomes practically unimportant. In particular, in the range of hydration n = 3–0, the basicity variation is 10^4 times higher than that of nucleophilicity, as shown also by the different slopes of their plots log k vs n (i.e., 0.7 and 2.0 for nucleophilicity and basicity, respectively) (Figure 1). The absolute rates of the nucleophilic substitutions, however, are constantly higher than those of elimination reactions (Figure 1).

The great variation of F^- basicity with hydration accounts for the variable base strength of ionic fluorides observed in different solvents, for which only qualitative explanations were given.[2]

A similar effect was previously found also in the case of the highly hydrophilic OH^- for the Hofmann elimination of the $hexyl_4N^+OH^-\cdot nH_2O$ under the same conditions.[8]

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(18) Results from this laboratory accepted for publication in *Synthesis*. Similar behavior was also reported for $Ph_4P^+HF_2^-$ [16] and for $Bu_4N^+H_2F_3^-$.[19]

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(21) According to a recent classification of reactions of anions with neutral molecules,[22] nucleophilic substitutions by F^- may represent *solvactivated* reactions, while those by I^- and Br^- can be considered *autoactivated*, the reactions by Cl^- being a borderline case.

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(26) Indeed the absolute rates are still orders of magnitude lower than those found in the gas phase due to the ion pairing of the unsolvated anion with the quaternary cation.[25]

(27) In solid–liquid two-phase systems, e.g., CsF or KF adsorbed on CaF_2,[28] or solid KF/triethylbenzylammonium chloride,[29] the presence of a limited quantity of water was found[28,29] to increase the rate of fluorination. The apparent discrepancy with our results is due to the different role played by water in the two systems. In particular, under solid–liquid conditions a small amount of water favors the extraction of F^- anion in the organic phase and, hence, increases the fluorination rate, as authoritatively demonstrated by Sasson and Dermeik in a recent paper.[30]

Even if partially hydrated ($n = 4$), quaternary fluoride **2a** still has a nucleophilic reactivity substantially higher than that of the anhydrous hydrogen difluoride **2c** and dihydrogen trifluoride **2d** (17 and 2000 times, respectively) (Table III).[31] This behavior can be attributed to the higher stabilization of the fluoride in the HF_2^- anion with respect to that realized by the specific hydration in the $F^-{\cdot}nH_2O$, in agreement with the different values of hydrogen bond energies reported for these species: $HOH{\cdots}F^- = 23$ kcal mol^{-1} and $FH{\cdots}F^- = 38.6$ kcal mol^{-1}.[32,33] The H bond of F^- with HF in the highly symmetric HF_2^- is considered to be one of the strongest.[10,31]

On the other hand, the specific interaction of HF_2^- with a second hydrogen fluoride to form the chemically stable $H_2F_3^-$ species[18,19,34] must lead to a further anion deactivation and hence to a nucleophilicity decrease, as was found experimentally.

The dramatic deactivation of F^- anion by hydrogen fluoride is even more evident by comparing the reactivity of the poly(hydrogen fluorides) **2c** and **2d** with that of the hypothetical anhydrous **2a**[35] ($F^-:HF_2^-:H_2F_3^- = 8.5 \times 10^5:1.2 \times 10^2:1$ (Table III). This also explains the different sensitivities of these anions to the specific hydration, decreasing in the same order ($F^- \gg HF_2^- > H_2F_3^-$). In fact, when the hydration sphere n of HF_2^- is lowered from 2 to 0, the rate of reaction 5 increases less than 3 times (Table IV), and it is practically unchanged in the case of $H_2F_3^-$ (Table III).

By considering the obtained scale of nucleophilicity $F^- \gg F^-{\cdot}nH_2O > HF_2^- > H_2F_3^-$ (Table III), we can conclude that the partially hydrated quaternary fluoride $Q^+F^-{\cdot}nH_2O$, where $n = 3$–4, can always be considered the reagent of choice as fluorinating agent.[1d] In reactions where a rigorously anhydrous medium is needed, the slightly less reactive hydrogen difluoride HF_2^- can be alternatively used,[16,36] owing to the difficulties to synthesize anhydrous quaternary ammonium fluoride.[37,38] Indeed, our data concerning the F^- basicity clearly indicate the virtual impossibility to obtain perfectly "naked" tetraalkylammonium fluorides because they are not stable, neither as pure substances nor in solutions of anhydrous aprotic solvents.[15,18,37,38]

Experimental Section

Potentiometric titrations were performed with a Metrohm Titroprocessor E636 by using silver, fluoride or glass and calomel electrodes, the latter isolated with a potassium sulfate bridge. GLC data were carried out with a Varian 3700 gas chromatograph, equipped with a 50 cm × $^1/_8$ in. OV-101-5% on Chromosorb GHP 100–120-mesh column and were evaluated by an internal standard method. Proton NMR spectra (in δ) were recorded on a Varian EM-390 90-MHz spectrometer with Me_4Si as internal standard. ^{19}F NMR spectra (in δ) were performed with a Varian XL-300 spectrometer with fluorobenzene as internal standard.

Materials and Solvents. Inorganic salts were Analar grade commercial products, used without further purification. *n*-Octyl methanesulfonate, bp 112–114 °C (2 mm), $n^{20}{}_D$ 1.4398, was prepared according to the literature [lit.[39] bp 110–114 °C (2 mm), $n^{20}{}_D$ 1.4392]. Tetrahexylammonium fluoride (**2a**), hydrogen difluoride (**2c**), and dihydrogen trifluoride (**2d**) were prepared from the corresponding hydrogen sulfate **3d**[40] by exchange with the appropriate anion; experimental details will be reported elsewhere.[18] The fluoride **2a** was obtained as a trihydrate compound, whereas **2c** and **2d** were obtained as anhydrous oils.[18] Commercial benzene, chlorobenzene, and *o*-dichlorobenzene were carefully purified and dried by standard methods.[41] Karl Fischer analyses showed a water content ≤40 ppm.

Standardized Solutions of Quarternary Ammonium Fluoride 2a, Hydrogen Difluoride 2c, and Dihydrogen Trifluoride 2d and Their Hydration State. Tetrahexylammonium fluoride (**2a**) solutions were prepared by weighing out the quaternary salt **2a** as a trihydrate compound in a 100-mL volumetric flask, which was filled to the mark with the appropriate solvent (chlorobenzene, benzene, or *o*-dichlorobenzene) at the desired temperature. Less hydrated solutions of **2a** were obtained by adding molecular sieve beads, 4 Å (20 g/100 mL of solution). Aliquots (3–5 mL) of solution were withdrawn at intervals, and the water content was measured (Karl Fischer analysis). At the desired value of hydration, the onium salt solution was removed from the molecular sieves and used for kinetic runs. The ^{19}F NMR and ^1H NMR analyses showed that $Q^+F^-{\cdot}nH_2O$ ($n \leq 2.5$) was partially decomposed (5–20%), giving trihexylamine (**5**) and $hexyl_4N^+HF_2^-$ (**2c**).[15,38] A sample (6 mL) of organic solution was shaken with 2 mL of a saturated aqueous solution of NaBr together with 0.5 mL of 30% NaOH aqueous solution in order to neutralize HF and to completely convert Q^+F^- (**2a**) into the corresponding Q^+Br^-. The amounts of amine **5** and Q^+Br^- were independently measured by acid–base and argentometric titration (potentiometric titration), respectively. The Q^+F^- concentration was evaluated by subtracting the value of amine **5** from the Q^+Br^- concentration. Solutions of quaternary fluoride **2a** with hydration state $n = 4$, 6, and 8.5 were obtained by stirring, for 15 min, a volume of solution of $hexyl_4N^+F^-{\cdot}3H_2O$ (**2a**) (3–6×10^{-2} M) with a half-volume of an aqueous solution of KF, 10, 7, and 4 M, respectively. Stirring was stopped, and after 2 h, the water content of the organic phase was checked by Karl Fischer analysis. The concentration of quaternary salt in the organic layer was evaluated in parallel as described in the kinetic measurements (see below). The solutions of onium hydrogen difluoride **2c** and dihydrogen trifluoride **2d** were prepared by weighing out the anhydrous quaternary salts **2c** and **2d** in a polymethylenepentene volumetric flask, which was filled to the mark with the appropriate solvent (benzene or *o*-dichlorobenzene) at the desired temperature. The solutions of monohydrated onium salt **2d** were obtained by stirring a volume of the anhydrous solution with a half-volume of a saturated aqueous solution of KHF_2 for 15 min. Stirring was stopped, and after 2 h, the water content of the organic phase was measured by Karl Fischer analysis. The concentration of $hexyl_4N^+H_2F_3^-$ (**2d**) in the organic phase was checked as follows: the HF was measured by acid–base titration of a sample (2–3 mL); in parallel, another sample (5 mL) was shaken with 2 mL of a saturated aqueous solution of KBr in order to convert $Q^+H_2F_3^-$ into the corresponding Q^+Br^-, which was subjected to argentometric titration. The solution of dihydrated $hexyl_4N^+HF_2^-{\cdot}2H_2O$ (**2c**) was prepared by stirring an organic solution of $hexyl_4N^+F^-{\cdot}3H_2O$ with 1.1 molar equiv of KHF_2 dissolved in water (saturated solution). This treatment[18] affords the dihydrated **2c**, in agreement with ^{19}F NMR analysis, acid–base and argentometric titration (as far as **2d**), and Karl Fischer analysis. The solutions of **2c** with an intermediate hydration n ($n = 0.3$–1.7) were obtained

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by adding a calculated amount of water into the anhydrous solution of onium salt by means of a 250-μL syringe and checked by Karl Fischer analysis.

Kinetic Measurements of the Nucleophilic Substitutions. At zero time, a standardized chlorobenzene or *o*-dichlorobenzene solution (10 mL) of substrate 1 (10–20 × 10^{-2} M) was added to a standardized solution (40 mL) of hexyl$_4$N$^+$F$^-$ (**2a**) (4–5 × 10^{-2} M) in a 100-mL flask thermostated at the appropriate temperature. Samples (2–3 mL), periodically withdrawn, were diluted in 50 mL of 40% methanol in a water solution and analyzed by potentiometric titration of the fluoride anion with 0.01 N lanthanum nitrate.

From the equation $1/([B_0] - [A_0]) \ln [A_0][B_0 - x]/[B_0][A_0 - x] = kt$ where $[A_0]$ = [substrate] and $[B_0] = [Q^+F^-{\cdot}nH_2O]$ ($n \geqslant 6$) or vice versa, the second-order rate constants were calculated by using a least-squares computer program. All rates involved at least 10 samplings and gave correlation coefficients of 0.990 or better. For lower n values ($n \leq 4$), the second-order plot showed a downward curvature due to the increasing hydration of the unreacted quaternary fluoride **2a** during the reaction. The rate constants were graphically calculated by taking, for all the experiments, an initial variation of the reagent concentration corresponding to the 5% increase of the $[H_2O]/[Q^+F^-]$ ratio. In the case of hexyl$_4$N$^+$HF$_2^-$ (**2c**) and hexyl$_4$N$^+$H$_2$F$_3^-$ (**2d**), kinetic runs were performed in a Teflon-coated flask. At zero time, a standardized benzene or *o*-dichlorobenzene solution (10 mL) of substrate 1 (10–20 × 10^{-2} M) and of an appropriate GLC internal standard (8 × 10^{-2} M) was added to a standardized solution (40 mL) of quaternary salt (5–10 × 10^{-2} M). Samples (0.5–1 mL) of the organic phase were periodically withdrawn and quenched by adding, with stirring, a NaClO$_4$ aqueous solution (1 mL). This treatment eliminates the fluorinating agents from the organic phase, giving the corresponding Q$^+$ClO$_4^-$. Samples of the organic phase were analyzed by GLC (50 cm × $^1/_8$ in. OV-101-5% on Chromosorb GHP 100–120-mesh column, in a program temperature from 50 to 230 °C). The GLC internal standards used were decane and tetradecane in the runs performed in benzene and *o*-dichlorobenzene, respectively. The second-order rate constants were computer evaluated from the equation $1/([B_0] - [2A_0]) \ln [A_0][B_0 - 2x]/[B_0][A_0 - x] = kt$, where $[A_0]$ = [substrate] and $[B_0] = [Q^+(HF)_n{\cdot}F^-]$, which takes into account the particular stoichiometry of reactions 4 and 5. All rates involved at least 10 samplings and gave correlation coefficients $r = 0.995$ or better.

Kinetic Measurements of the Elimination Reaction. Kinetic runs were carried out in a Teflon-coated flask. In a typical procedure, the reaction flask[20] was thermostated at 60 °C and charged with 60 mL of a standardized chlorobenzene solution of quaternary salt hexyl$_4$N$^+$F$^-$ (**2a**) (3–4 × 10^{-2} M) and 40 mL of an aqueous KF solution (4–10 M) already thermostated. Stirring and timing were started. Samples (4–5 mL) of the organic phase were withdrawn at various times by stopping the stirrer for 40–60 s to allow adequate separation. They were then added to 5 mL of a NaBr aqueous solution. The heterogeneous mixture was stirred for 5 min in order to completely convert Q$^+$F$^-$ (**2a**) into the corresponding Q$^+$Br$^-$. Aliquots (2–3 mL) of the organic phase were potentiometrically titrated with 0.01 N silver nitrate. The kinetic runs of hexyl$_4$N$^+$F$^-$·nH$_2$O (**2a**), where $n < 3$, were carried out with wet chlorobenzene solutions of **2a** under homogeneous conditions as described for nucleophilic substitution reactions. From the equation $\ln ([A_0]/[A_0 - 2x]) = k_{obsd}t$ where $[A_0] = [Q^+F^-{\cdot}nH_2O]$ ($n \geqslant 3$), the first-order rate constants were calculated by using a least-squares computer program. All rates involved at least 10 samplings and gave correlation coefficients of 0.993 or better. For lower n values ($n < 3$), the first-order plot showed an upward curvature due to the increasing hydration of the unreacted quaternary fluoride during the reaction. Also in this case, the initial reaction rates were graphically evaluated as described above for nucleophilic substitution reactions. In reaction 3, $k_{elim} = k_{obsd}/2$, as only half of the converted substrate affords the elimination products (reaction 3). In the case of hexyl$_4$N$^+$HF$_2^-$ (**2c**), a standardized chlorobenzene solution (50 mL) of quaternary salt was kept in a reaction flask thermostated at 60 °C. Samples (4–5 mL) of the organic phase were periodically withdrawn and analyzed by potentiometric titration of Br$^-$ anion as described above. No elimination reaction was observed after 2 weeks.

Reaction Products. In a typical procedure, a 100-mL Teflon-coated vial was charged with 50 mL of a benzene solution of substrate 1 (1.0 M), of the appropriate quaternary onium salt (Q$^+$F$^-$·3H$_2$O (**2a**), 1.2 M; Q$^+$HF$_2^-$ (**2c**), 2.1 M; or Q$^+$H$_2$F$_3^-$ (**2d**) 2.1 M), and of decane (0.5 M) (as GLC internal standard). The reaction vial was closed and thermostated at 60 °C in the runs with Q$^+$F$^-$ (**2a**) and at 110 °C in those with Q$^+$(HF)$_n$·F$^-$ **2c** and **2d**. The progress of reaction was monitored by GLC analysis (50 cm × $^1/_8$ in. OV-101-5% on Chromosorb GHP 100–120-mesh column in a program temperature from 50 to 230 °C). The reactions of F$^-$ **2a** were complete in 24 h, whereas those of HF$_2^-$ **2c** and H$_2$F$_3^-$ **2d** reached a ⩾98% conversion in 48 and 92 h, respectively. The mass balance of the reaction mixture was 98% (by GLC analysis) in the expected fluorooctane **3**. In the reaction of Q$^+$HF$_2^-$ (**2c**), the ^{19}F NMR analysis of the crude product showed the presence of tetrahexylammonium dihydrogen trifluoride (**2d**) (^{19}F NMR δ −158).[18,19] The ^{19}F NMR spectrum of the crude product of the reaction of Q$^+$H$_2$F$_3^-$ showed the presence of a broad signal centered at δ −167, characteristic of a complex quaternary ammonium poly(hydrogen fluoride), Q$^+$(HF)$_n$F$^-$, where $n > 2$.[31] The reaction mixture was filtered over silica gel to eliminate quaternary onium salts, and the *n*-fluorooctane was obtained by fractional distillation: bp 142–144 °C (760 mm) [lit.[42] bp 144.4 °C (760 mm)]; ^{1}H NMR δ 0.97 (t, 3 H), 1.15–2.00 (m, 12 H), 4.42 (d, 2 H, $^2J_{HF}$ = 48.0 Hz); ^{19}F NMR δ −208 (br s).

In a typical procedure, the Teflon-coated flask, used for elimination reactions thermostated at 60 °C, was charged with 50 mL of a benzene solution of tetrahexylammonium fluoride dihydrate (**2a**) (1.0 M) and decane (0.5 M) (as GLC internal standard). The progress of the reaction was followed as described above for kinetic runs. At the end of the reaction (6 days), ^{1}H NMR, ^{19}F NMR, and GLC analyses of the crude products showed the presence of trihexylamine (**5**), hex-1-ene (**4**), and tetrahexylammonium hydrogen difluoride (**2c**) together with decane, in a ratio expected from the stoichiometry of the reaction (3), according to the literature.[15] The reaction mixture was filtered over silica gel to eliminate the onium salt (**2c**), and the trihexylamine (**5**) was obtained by fractional distillation: bp 158–160 °C (12 mm) [lit.[43] bp 165–170 °C (16 mm)]; ^{1}H NMR δ 0.92 (t, 9 H), 1.10–1.60 (m, 24 H), 2.4 (t, 6 H). Hex-1-ene (**4**) was not isolated.

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