Nucleophilic reactivity towards electrophilic fluorinating agents: reaction with *N*-fluorobenzenesulfonimide ($(PhSO_2)_2NF$)

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Second-order rate constants for the reaction of *N*-fluorobenzenesulfonimide (FBS) with nucleophilic reagents, k_{Nu} (M^{-1} s^{-1}), have been measured in aqueous solution at 25 °C. Analysis of the reaction products shows that *soft* polarizable nucleophiles (I^-, SCN^-, Br^-) react at fluorine, whereas *hard* nucleophiles (oxygen and nitrogen nucleophiles) react at sulfur. The ambident behaviour of this electrophile seems to be related to the relative contribution of electrostatic and orbital interactions in reaching the transition state. The preferential reaction of *soft* nucleophiles at fluorine and the correlation of k_{Nu} values with the one-electron oxidation potentials of the nucleophiles in water suggest that nucleophilic reactivity at fluorine is largely determined by the ease of one-electron transfer from the nucleophile to the electrophile. Nucleophilic addition to fluorine is far more sensitive to the nature of the attacking nucleophile than the corresponding reactions at both saturated (*n* scale) and unsaturated carbon (N_+ scale). Comparison of the rate constants for the reaction of nucleophiles at the sulfonyl group with those for reaction of the same nucleophiles with 2,4-dinitrophenyl acetate reveals a similar reactivity pattern for sulfonyl sulfur and carbonyl carbon as electrophilic centres.

Introduction

It is known that the presence of fluorine substituents in biologically active molecules may have an important effect on their physicochemical properties. Such fluorinated compounds are of interest in many areas, including biological and medicinal chemistry.[1–3] Consequently, much effort has been made to develop new synthetic methods for the selective fluorination of organic molecules.

In recent years, a variety of *N*-fluoro compounds have been introduced as useful selective sources of electrophilic fluorine ($F^{\delta+}$). These reagents have been successfully employed in the fluorination of aromatics, carbanions and olefins.[4] However, the mechanism by which these molecules transfer a positive fluorine atom to nucleophiles is not fully understood and has been the topic of recent investigations. Current discussions involve two possible mechanisms. An electron transfer pathway has been postulated by Umemoto *et al.*[5] to explain the reactivity of different *N*-fluoropyridinium salts as fluorinating agents in organic solvents. DesMarteau *et al.*[6] have proposed a similar mechanism for the electrophilic fluorination of olefins by *N*-fluorobis[(trifluoromethyl)sulfonyl]imide. On the other hand, Differding *et al.*[7,8] have found evidence to show that electrophilic fluorination reactions take place by an S_N2 mechanism involving nucleophilic attack at fluorine.

Although these *N*-fluoro compounds have become very popular in organic synthesis there seems to be no information on their reactivity towards nucleophiles in aqueous solution. This paper reports a kinetic study of the reaction of *N*-fluorobenzenesulfonimide (FBS) with primary, secondary and tertiary amines, azide ion, HO^-, $(CF_3)_2CHO^-$, SCN^- and halide ions in water. It also includes some results for the very fast reaction of nucleophiles with *N*-chlorobenzenesulfonimide (CBS). FBS is an ambident electrophile with two potential sites for reactions with nucleophiles. Nucleophilic attack at the fluorine atom is analogous to the S_N2 nucleophilic substitution on carbon. The main objective of this work is to analyse the factors that influence the addition of nucleophiles at fluorine and, in general, addition reactions at halogen centres.

Experimental

N-Fluorobenzenesulfonimide (FBS), benzenesulfonimide and the sodium salt of benzenesulfonic acid were purchased from Aldrich and used without further purification. *N*-Chlorobenzenesulfonimide (CBS) was synthesised by reaction of benzenesulfonimide with *tert*-butylhypochlorite[9] in methanol.[10] Inorganic salts and all other organic chemicals were obtained from commercial sources and were used as received.

Reactions of FBS with amines and amino acids were studied in buffer solutions of the nucleophile itself to control the pH. Reactions with thiocyanate and azide ion were carried out in the presence of a 0.05 M potassium phosphate buffer at pH 6.5. With iodide and bromide ion as nucleophiles, the reactions were studied in acid solutions of $HClO_4$ or HCl. pH values were always measured at the end of the reaction using a Radiometer pHM82 pH-meter with a pHC4006-9 combined glass electrode. Analysis of reaction products was carried out by ^1H NMR on a Bruker 500 MHz instrument. The products were identified by comparison of their NMR spectra with those of authentic samples.

All kinetic experiments were carried out at 25 °C and a constant ionic strength (*I*) of 1.0,† maintained with KCl, unless noted otherwise. The isolation method was used in all cases, with a great excess of the nucleophile over the substrate. The fast reactions of FBS with most of the nucleophiles were followed by monitoring the disappearance of the substrate at 240 nm using an Applied Photophysics DX.17MV sequential stopped-flow spectrofluorimeter. An aqueous solution containing the nucleophile and a solution of the substrate in acetonitrile were placed into the mixing syringes. These solutions were mixed in a ratio 25:1 to give a reaction mixture containing 1×10^{-4} M FBS and 4% acetonitrile. The reaction between FBS and azide ion did not show clean first-order absorbance–time plots at 240 nm due to the instability of the products. Rate constants for this reaction were therefore determined in the presence of a fixed concentration of iodide ion by

† Ionic strength is given in M throughout this paper.

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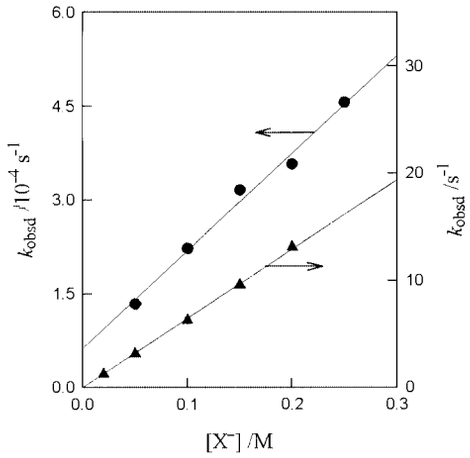


Fig. 1 Influence of the concentration of halide ion on k_{obsd} for reaction with FBS at 25 °C and $I = 0.3$ ($NaClO_4$); $[H^+] = 1 \times 10^{-3}$ M. (▲) Iodide ion. (●) Bromide ion. Left-hand *y*-axis, k_{obsd} for addition of Br^- to FBS. Right-hand *y*-axis, k_{obsd} for addition of I^- to FBS.

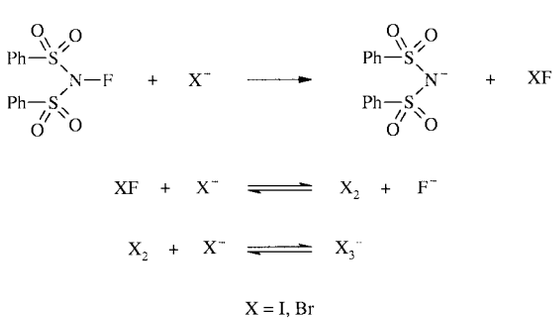
monitoring the increase in absorbance at 350 nm due to formation of I_3^-. The reaction with iodide ion was studied at a constant ionic strength of 0.3, maintained with $NaClO_4$. The concentration of substrate in the reaction mixture was 3×10^{-5} M and kinetics were followed at 350 nm by monitoring the appearance of I_3^-.

Reactions of FBS with bromide ion were initiated by making a 100-fold dilution of a solution of FBS in acetonitrile into the reaction mixture to give a final substrate concentration of 3×10^{-5} M. Rate constants for this reaction were determined spectrophotometrically by following the appearance of Br_3^- at 265 nm using a Kontron Uvikon 930 spectrophotometer equipped with a thermostatted multiple cell carrier.

First-order rate constants, k_{obsd} (s^{-1}), were determined by fitting the absorbance–time data to the first-order integrated equation. The values of k_{obsd} were reproducible to ±5%.

Results

The reaction between iodide ion and FBS led to the formation of I_3^- in quantitative yield (>97%), as shown by the UV-Vis spectrum of the final reaction mixture ($\lambda_{max} = 351$ nm, $\varepsilon = 27000$ M^{-1} cm^{-1}).[11] Additionally, ^1H NMR analysis of the reaction products in 20:80 (v/v) CD_3CN–D_2O ($[I^-] = 0.02$ M, $[FBS] = 5 \times 10^{-4}$ M and $[D^+] = 1 \times 10^{-3}$ M) showed the complete conversion of FBS to benzenesulfonimide. Similarly, the final product of the reaction of bromide ion with FBS was identified as tribromide by UV-Vis spectroscopy ($\lambda_{max} = 266$ nm, $\varepsilon = 40900 \pm 400$ M^{-1} cm^{-1}).[12] The observed products are therefore consistent with the reaction involving the attack of the halide ion on the FBS fluorine atom, according to Scheme 1.



Scheme 1

Fig. 1 shows the dependence of the observed rate constant, k_{obsd} (s^{-1}), on the concentration of the nucleophile for the disappearance of FBS in acidic solutions ($[H^+] = 1 \times 10^{-3}$ M) containing iodide or bromide at 25 °C and $I = 0.3$ ($NaClO_4$).

Table 1 Influence of $[H^+]$ upon k_{obsd} for the reaction of FBS with halide ions at 25 °C and $I = 0.3$ ($NaClO_4$)

I^- [a]		Br^- [b]	
$[H^+]$/M	k_{obsd}/s^{-1}	$[H^+]$/M	k_{obsd}/s^{-1}
1×10^{-3}	1.20	1×10^{-3}	2.09×10^{-4}
5×10^{-3}	1.21	5×10^{-3}	2.21×10^{-4}
1×10^{-2}	1.20	1×10^{-2}	2.34×10^{-4}
5×10^{-2}	1.21	1.5×10^{-2}	2.27×10^{-4}
0.1	1.19	2×10^{-2}	2.28×10^{-4}
0.2	1.19		

[a] $[I^-] = 0.02$ M. [b] $[Br^-] = 0.1$ M.

The data in Table 1 show that increasing the acid concentration had no effect on k_{obsd} for reactions at 0.02 M I^- and 0.1 M Br^-. Second-order rate constants, k_{Nu} (M^{-1} s^{-1}), for these reactions were determined as the slopes of the linear plots shown in Fig. 1, and are listed in Table 2. The reaction with bromide ion was also studied at $I = 1.0$ (KCl), and the value of k_{Br^-}, determined under these experimental conditions, differed by ~30% from that measured at $I = 0.3$ ($NaClO_4$). The small but significant intercept in the linear plot of k_{obsd} against $[Br^-]$ (see Fig. 1) corresponds to an uncatalysed process that probably involves the reaction of the substrate with water as the nucleophile.

The reaction of FBS with thiocyanate, in the presence of 0.05 M phosphate buffer at pH = 6.5, 25 °C and $I = 1.0$ (KCl), was found to be first-order with respect to the nucleophile (data not shown). The value of the bimolecular rate constant is given in Table 2. Attack on the fluorine atom was confirmed by ^1H NMR analysis of the products of the reaction of FBS (5×10^{-4} M) with SCN^- (0.1 M) in 20:80 (v/v) CD_3CN–D_2O at pD = 7.0 (0.05 M potassium phosphate), which showed quantitative formation of benzenesulfonimide.

The products of the nucleophilic addition of HO^- to FBS were characterised by ^1H NMR analysis of a sample containing 5×10^{-4} M FBS and 0.05 M KOD in 20:80 (v/v) CD_3CN–D_2O at 25 °C and $I = 1.0$ (KCl). The final spectrum showed the formation of benzenesulfonate anion, one of the expected products of the reaction of HO^- at one of the FBS sulfonyl groups. The absence of significant amounts of benzenesulfonimide in the reaction mixture confirmed that sulfonyl sulfur is the only electrophilic centre involved. The aromatic region of the spectrum also showed the signals of a second product, which was apparently *N*-fluorobenzenesulfonamide. However, this compound was unstable under the reaction conditions and slowly decomposed to give a final product that was not identified. Pseudo-first-order rate constants for the disappearance of FBS in basic aqueous solutions show a linear dependence on the concentration of HO^- and the slope of a plot of k_{obsd} against $[HO^-]$ gives $k_{HO^-} = 117$ M^{-1} s^{-1} as the bimolecular rate constant for the reaction of hydroxide ion with FBS.

Similarly, $(CF_3)_2CHO^-$ reacts at one of the SO_2 groups of FBS, as shown by the signals in the NMR spectrum of a reaction mixture in 20:80 (v/v) CD_3CN–D_2O ($[FBS] = 5 \times 10^{-4}$ M, $[(CF_3)_2CHOD]_t$ (total concentration) = 0.05 M, pD = 9.9). The reaction was found to be first-order with respect to the nucleophile, with a second-order rate constant of 11.2 M^{-1} s^{-1} (Table 2).

First-order rate constants for the reactions of methylamine, 2-methoxyethylamine, glycine ethyl ester, piperazine-H^+, morpholine, piperidine, 3-quinuclidinol and hydroxylamine with FBS at 25 °C and $I = 1.0$ (KCl) were plotted against the total concentration of the nucleophile (see Fig. 2 for representative examples). Observed second-order rate constants, $(k_{Nu})_{obsd}$, were determined as the slopes of these linear plots and values of k_{Nu} (Table 2) were obtained as $(k_{Nu})_{obsd}/f_{Nu}$ where f_{Nu} is the fraction of the nucleophile in the basic form. Pseudo-first-order rate constants for the reaction of FBS with azide ion were

Table 2 Values of the bimolecular rate constant, k_{Nu}, for the reaction of FBS with nucleophiles at 25 °C

Number	Nucleophile	pK_a [a]	Electrophilic site	k_{Nu}/M^{-1} s^{-1} [b]
1	HO^-	15.7	S	117 ± 2
2	$(CF_3)_2CHO^-$	9.2	S	11.2 ± 0.2
3	Glycine ethyl ester	7.9	S	1.76 ± 0.01
4	2-Methoxyethylamine	9.7	S	17.3 ± 0.1
5	Methylamine	11.0	S	210 ± 1
6	Piperazine-H^+	6.1	S	1.5 ± 0.1
7	Morpholine	8.9	S	63 ± 1
8	Piperidine	11.5	S	880 ± 7
9	3-Quinuclidinol	10.1	S	158 ± 2
10	Hydroxylamine	6.1	S	15.8 ± 0.4
11	N_3^-	4.6	S	0.345 ± 0.006
12	I^-	—	F	66 ± 1 [c]
13	Br^-	—	F	(2.1 ± 0.1) × 10^{-3} (1.6 ± 0.1) × 10^{-3} [c]
14	SCN^-	—	F	1.89 ± 0.06

[a] The pK_a of the conjugate acid of the nucleophile at 25 °C and I = 1.0 (KCl) was determined from the pH of partially neutralised solutions. [b] I = 1.0 (KCl). [c] I = 0.3 ($NaClO_4$).

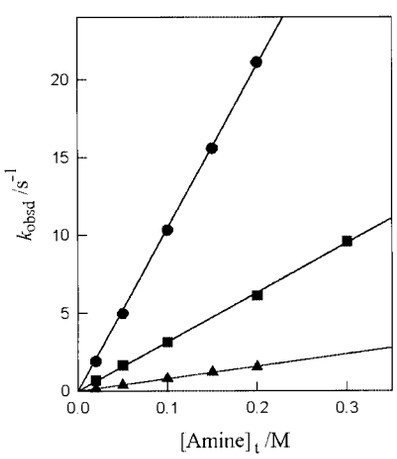


Fig. 2 Influence of the total amine concentration on k_{obsd} for reaction with FBS at 25 °C and I = 1.0 (KCl). (●) Methylamine, pH = 9.91. (■) Morpholine, pH = 8.86. (▲) Hydroxylamine, pH = 6.06.

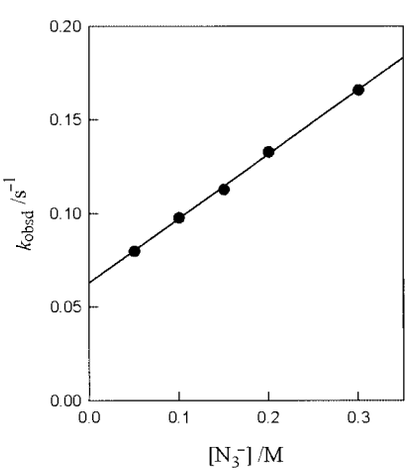


Fig. 3 Influence of the concentration of azide ion on k_{obsd} for reaction with FBS at 25 °C and I = 1.0 (KCl); [I^-] = 9.6 × 10^{-4} M; [phosphate]$_t$ = 0.05 M; pH = 6.5.

determined in the presence of 9.6 × 10^{-4} M I^- at pH = 6.5 (0.05 M phosphate buffer, 25 °C, I = 1.0 (KCl)). The linear dependence of k_{obsd} on the concentration of added N_3^- is shown in Fig. 3. The slope of this plot gives $k_{N_3^-}$ = 0.345 M^{-1} s^{-1} as the bimolecular rate constant for the reaction of the substrate with azide ion. A value of k_{I^-} = 65.4 M^{-1} s^{-1} for the nucleophilic attack of I^- on FBS at 25 °C and I = 1.0 (KCl) was calculated from the intercept and agrees reasonably well with that determined at I = 0.3 ($NaClO_4$) (see Table 2).

The products of the reaction between methylamine and FBS were analysed by ^{1}H NMR ([FBS] = 5 × 10^{-4} M, [CH_3ND_2]$_t$ = 0.05 M, pD = 11.5, 20:80 (v/v) CD_3CN–D_2O, 25 °C, I = 1.0 (KCl)) and are consistent with nucleophilic attack of the amine at the sulfonyl group. Similar results were obtained for the addition of N_3^- to FBS.

The disappearance of CBS in an aqueous solution containing bromide ion ([Br^-] = 0.2 M, [H^+] = 2 × 10^{-3} M, 25 °C, I = 1.0 (KCl)) led to an increase in absorbance at 265 nm due to the formation of Br_3^-. However, the reaction was too fast to be followed using a stopped-flow device. A value of $k_{obsd} \geq 400$ s^{-1} was estimated for the reaction of CBS in the presence of 10^{-3} M Br^- and this allowed the calculation of $k_{Br^-} \geq 4 \times 10^5$ M^{-1} s^{-1} as a lower limit for the value of the bimolecular rate constant for the addition of Br^- to CBS. Kinetic studies on the reactions of this substrate with other nucleophilic reagents, such as HO^-, I^-, SCN^- and methylamine, could not be carried out since they were too fast even at low concentrations of the nucleophiles.

The products of the reactions of CBS with nucleophiles were identified by ^{1}H NMR analysis of samples containing 2 × 10^{-3} M CBS in 15:85 (v/v) CD_3CN–D_2O at 25 °C and I = 1.0 (KCl). The results show the complete conversion of CBS to benzenesulfonimide for reactions in the presence of: (a) 0.05 M DO^-; (b) 0.05 M methylamine at pD = 11.5; (c) 0.05 M SCN^- at pD = 7.0 (0.1 M phosphate buffer); (d) 0.05 M hexafluoropropan-2-ol at pD = 9.9; (e) 0.05 M I^- at pD = 7.0 (0.1 M phosphate buffer).

Discussion

The results of the work reported here on the reactivity of FBS towards a wide range of nucleophiles show that this molecule has two different electrophilic sites. Oxygen and nitrogen nucleophiles react at the sulfonyl group whereas sulfur nucleophiles and halide ions attack the fluorine atom of FBS. This reactivity pattern can be rationalized in terms of Pearson's principle of hard and soft acids and bases.[13] According to Pearson's classification, HO^-, alkoxides and amines are *hard* nucleophiles in which the donor atom is of low polarizability and has a high charge density. Their preferential reaction at the SO_2 group shows that this is the *hardest* electrophilic centre of the molecule. However, the reaction of *soft* polarizable nucleophiles, such as I^- and SCN^-, with FBS involves nucleophilic substitution at fluorine.

A better understanding of ambident reactivity can be achieved by means of the classical concepts of charge- and orbital-controlled reactions developed by Klopman.[14] The change in energy due to the interaction between a nucleophile and an electrophile is given by eqn. (1). The first term, in which

$$\Delta E = -\frac{q_n q_e}{\varepsilon R_{ne}} + \frac{2c_n^2 c_e^2 \beta_{ne}^2}{E_{HOMO} - E_{LUMO}} \quad (1)$$

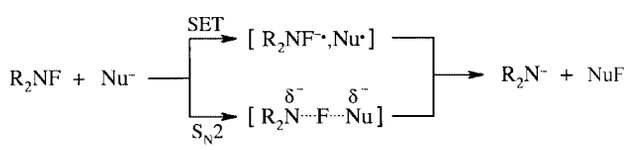
q_n and q_e are the charges on the reactive centres of the nucleophile and the electrophile, R_{ne} is the distance between them and ε is the relative permittivity of the medium, is a measure of the electrostatic interaction. The second term represents the orbital interaction and E_{HOMO} and E_{LUMO} are the energies of the frontier orbitals, c_n and c_e are the coefficients of the HOMO and LUMO at the interacting sites and β_{ne} is the bonding integral.

The high reactivity of non-polarizable nucleophiles towards electrophilic centres possessing a high positive charge suggests that the reaction between *hard* species is determined by a large electrostatic interaction. Therefore, nucleophilic attack at the sulfonyl group may be considered a charge-controlled process.

Fluorinating reagents of the N–F class are generally considered as sources of electrophilic fluorine ($F^{\delta+}$). However, whether there is real involvement of a positive fluorine in their reaction with nucleophiles has been the subject of some discussion.[15,16] The high ionisation potential of a fluorine atom argues against the unusual polarity of the N–F bond ($N^{\delta-}\leftarrow F^{\delta+}$) proposed to account for the ability of these compounds to transfer the fluorine to electron rich centres. We have carried out semiempirical AM1 calculations with complete geometry optimisation for two relevant conformations of FBS and these optimised molecular geometries were used for *ab initio* single-point calculations with the STO-3G basis set. The results of these calculations show that sulfur is, as expected, the most electron deficient centre in the molecule whereas the charge on the fluorine atom is close to zero. Therefore, the addition of nucleophiles to this electrophilic site appears to be controlled by frontier orbital interactions rather than by charge distribution.

Reaction of nucleophiles at the FBS fluorine atom

The few studies on the mechanism of fluorination with *N*-fluoro reagents that are available[4] have been focused on establishing whether the reaction takes place by a single-electron transfer (SET) or by direct nucleophilic addition to fluorine (S_N2) (see Scheme 2). Differding *et al.*[8] have used Marcus theory



Scheme 2

to estimate rate constants for the hypothetical electron transfer from nucleophiles to *N*-fluorosaccharin sultam. A comparison between the predicted and the experimental values of the rate constant strongly suggests that the reaction takes place by an S_N2 mechanism at fluorine. Additionally, a SET mechanism would involve the formation of a highly unstable radical anion, which would likely generate fluoride ion and therefore would not lead to fluorinated products.[17]

Several authors have suggested that S_N2 and SET mechanisms are extremes of a mechanistic spectrum for substitution reactions.[18–21] A comparison of the two pathways using the valence bond configuration mixing model developed by Pross and Shaik suggests that both nucleophilic and SET processes involve a single electron shift from the nucleophile to the electrophile and the only difference between the two pathways is whether or not the electron shift is concerted with bond breaking and bond formation.[19,20] The preferential reaction of nucleophiles with low oxidation potential (*soft* nucleophiles) at fluorine suggests that the transition state for nucleophilic addition to this electrophilic centre has at least some electron transfer character. Hoz has suggested that if the electrophile has a low energy LUMO, as seems to be the case for reactions at fluorine, the transition state for its reaction with nucleophiles has certain diradical character due to an important electron transfer component.[22] Additionally, there is a good correlation between the increasing values of k_{Nu} along the series Br^-, SCN^-, I^- and the one-electron oxidation potentials of the nucleophiles in water, $E^\circ_{Br} > E^\circ_{SCN} > E^\circ_{I}$,[23] suggesting that the relative reactivity of nucleophiles at fluorine is governed by the ease of one-electron transfer from the nucleophile to the electrophile.

Nucleophilic substitutions at halogen atoms are less familiar than the corresponding substitutions at carbon and quantitative data on nucleophilicity towards halogen centres are scarce. Although Differding *et al.* have recently reported that *N*-fluorobenzenesulfonimide is a useful reagent for the fluorination of carbanions in organic solvents,[24,25] as far as we know there have been no kinetic studies on the relative reactivity of this electrophile towards nucleophiles.

We have obtained values of the second-order rate constants, k_{Nu}, for the addition of I^-, Br^-, and SCN^- to the fluorine atom of FBS in aqueous solution at 25 °C (see Table 2). The observed order of reactivity, $I^- > SCN^- > Br^-$, is that predicted by the Swain–Scott nucleophilicity scale (n).[26–28] However, the selectivity of FBS towards these anions is greater than that of alkyl halides, as shown by the slope of $s \sim 4.5$ of a linear plot (not shown) of log k_{Nu} against the n value of the nucleophile.[28] Richard *et al.*[29] have recently shown that there is a good correlation between the values of Ritchie nucleophilicity parameter N_+ and n for both neutral and anionic nucleophiles, although azide ion and α-effect nucleophiles show significant positive deviations that are not well understood. The observation that the products of the reaction of azide ion with FBS are consistent with essentially quantitative attack of this nucleophile at sulfur shows that its reaction at fluorine is at least 20-fold slower than the former. Therefore, the rate constants for reaction at fluorine follow the order $I^- > SCN^- > N_3^-$, which is the same as that of the n scale but opposite to that predicted by the N_+ scale.[30] We can conclude that nucleophilic displacements at fluorine show a reactivity pattern similar to that of alkyl halides but are far more sensitive to changes in the nucleophilic strength of the attacking group than nucleophilic additions to both saturated and unsaturated carbon. This behaviour is similar to that found for the very fast addition of nucleophiles to electrophilic chlorine, for which a slope of $s = 4.7 \pm 0.1$ has been reported.[31] The rate constants for the reaction of nucleophiles at chlorine are much larger than those for their reaction at fluorine, but show a similar dependence on nucleophile reactivity. This constant selectivity is inconsistent with the predictions of the reactivity–selectivity principle.[32,33]

The difference in the Swain–Scott nucleophilic selectivities for substitution at fluorine ($s = 4.5$) and carbon ($s = 1.0$) reflects a larger extent of bond formation to the nucleophile at the transition state for addition to electrophilic fluorine compared with carbon. The increased transition state bonding to fluorine serves to minimise the build-up of positive charge at this strongly electronegative atom. The situation may be illustrated with a More O'Ferrall–Jencks diagram[34,35] (Fig. 4), in which the horizontal and vertical axes describe the extent of N–F bond cleavage and F–Nu bond formation, respectively. The dotted diagonal line represents a balanced concerted mechanism where the extents of bond fission and formation are equally advanced in the transition state. The high electronegativity of fluorine will result in a large barrier to the stepwise reaction through the F^+ intermediate in the lower right corner and will favour a stepwise addition–elimination reaction through the anionic hypervalent structure in the upper left corner of the diagram. As a result the reaction seems to follow a concerted mechanism through an imbalanced transition state in which N–F bond breaking lags behind F–Nu bond formation (solid line in Fig. 4). The fact that the value of the Swain–Scott selectivity parameter for the

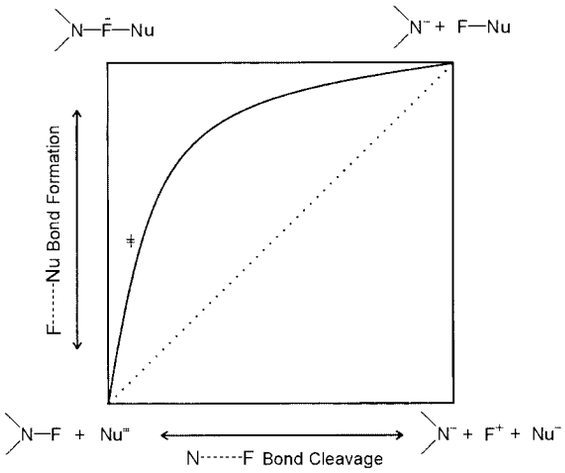


Fig. 4 Reaction coordinate diagram for nucleophilic substitution at electrophilic fluorine. The vertical axis is taken to be a measure of F–Nu bond formation and the horizontal axis a measure of N–F bond cleavage. The dotted line describes a synchronous reaction coordinate.

reaction of nucleophiles at fluorine is twice as large as for the addition of nucleophiles to a resonance-stabilised carbocation[29] is consistent with about twice the amount of partial bond formation to the nucleophile at the transition state. Following the suggestion of one of the referees we have calculated a value of 0.44 for the difference in the activation barriers for addition of *soft* nucleophiles to fluorine as a fraction of the difference in free energies for the one-electron oxidation of the nucleophiles.[23] This value is more than double the one obtained by Ritchie[36] for the reaction of nucleophiles with pyronin cation in aqueous solution and can be considered a measure of the extent of bond formation to fluorine at the transition state.

Reaction of nucleophiles at the FBS sulfonyl group

The products of the reaction of FBS with HO^-, $(CF_3)_2CHO^-$, amines and N_3^- are consistent with nucleophilic attack at sulfur rather than general base catalysis of the addition of water to the sulfonyl group.

Sulfonyl group transfer to a nucleophile may proceed by different mechanisms[37] including a stepwise or a concerted addition–elimination process. The stepwise route involves the formation of a trigonal bipyramidal intermediate. The fact that all the nucleophiles studied in this work are more basic than the leaving nitranion‡ suggests that if the intermediate is formed it will preferentially go on to products, so that the addition of the nucleophile should be rate determining. If an associative concerted mechanism is followed, the attack of the nucleophile at sulfur will be coupled with the departure of the leaving group in the transition state.

Fig. 5 shows a Brønsted-type correlation for the reaction of nucleophilic nitrogen compounds with *N*-fluorobenzenesulfonimide. The slopes of the lines in this plot are 0.66 for primary amines and 0.50 for secondary and tertiary amines. Primary amines react an order of magnitude slower than secondary and tertiary amines of comparable basicity and show a larger dependence of log k_{Nu} on the pK_a of the nucleophile, β_{nuc}. This structure–reactivity behaviour is similar to that found for other nucleophilic reactions at sulfonyl centres.[38,39] A straightforward interpretation of the Brønsted β_{nuc} value is not possible since a

‡ The pK_a of the conjugate acids of *N*-chloramines and *N*-bromamines is 8 to 10 units lower than that of the corresponding amine (J. M. Antelo, F. Arce, J. Crugeiras, E. T. Gray and P. Yebra, *J. Chem. Soc., Perkin Trans. 2*, 1999, 651). A value of p$K_a \leq 0$ for $PhSO_2NHF$ was estimated, assuming that the introduction of a fluorine atom lowers the pK_a of the parent sulfonamide ($PhSO_2NH_2$, pK_a = 10.1 (G. Dauphin and A. Kergomard, *Bull. Soc. Chim. Fr.*, 1961, **5**, 486)) by at least 10 units.

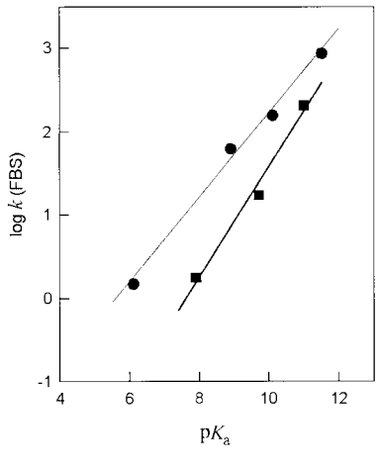


Fig. 5 Brønsted-type plot for the reaction of FBS with nitrogen nucleophiles in water at 25 °C and I = 1.0 (KCl). (■) Primary amines. (●) Secondary and tertiary amines.

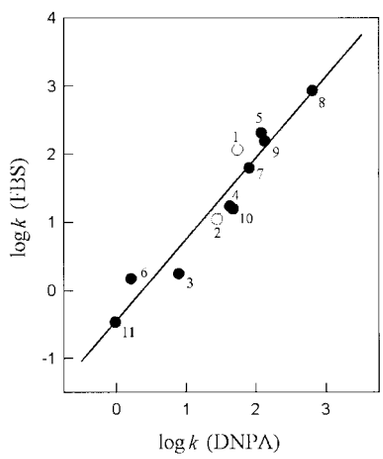


Fig. 6 Plot of log k for the reaction of (○) oxygen and (●) nitrogen nucleophiles with FBS *vs.* log k for their reactions with DNPA. The numbers refer to the nucleophiles listed in Table 2.

β_{eq} value for this reaction can not be easily obtained. However, the value of 0.50–0.66 suggests a substantial positive charge on the nitrogen in the transition state, consistent with a significant amount of N–S bond formation.

Comparison of the rate constants for the reaction of nucleophiles with FBS with those for the reaction of the same nucleophiles with 2,4-dinitrophenyl acetate (DNPA)[40] (Fig. 6) shows a good correlation line with a slope of 1.2. This suggests that the transition state for the reaction at sulfonyl sulfur resembles that for reaction at carbonyl carbon. Our results do not provide conclusive evidence as to whether an addition intermediate is formed in the reaction path but the rate-determining transition state represents either the formation of such an intermediate or a concerted process with properties similar to those expected for rate-determining nucleophilic attack.

Comparison of the reactivity of nucleophiles towards FBS and CBS

FBS and CBS are both ambident substrates with two potential electrophilic centres for reaction with nucleophiles. We have found that nucleophilic displacement at fluorine involves relatively polarizable nucleophiles, whereas non-polarizable nucleophiles do preferentially react at sulfur. However, the analysis of products for the reaction of CBS with *soft* and *hard* nucleophiles shows that the chlorine atom is the only electrophilic centre involved. These experimental observations might be explained by the following: (1) Fluorine is a better electron-withdrawing substituent than chlorine and therefore, nucleophilic attack at sulfur should be faster for FBS than for CBS.

(2) We have estimated a value of $k_{Br} \geq 4 \times 10^5$ M^{-1} s^{-1} for the addition of Br^- to the chlorine atom in CBS. Comparison of this rate constant with that for reaction of bromide ion at fluorine, $k_{Br}(CBS)/k_{Br}(FBS) \geq 2 \times 10^8$, shows that chlorine is a much better electrophile than fluorine. As a result of this extremely large difference in reactivity the reaction of nucleophiles with CBS occurs exclusively at chlorine.

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