Cambridge Isotope Laboratory and used without further purification. Cyclohexanone phenylimine and ^{15}N-labeled cyclohexanone phenylimine were prepared as described previously.[1] Analytically pure solvent-free lithiated cyclohexanone phenylimines $\mathbf{1}_{SF}$, [^{6}Li]-$\mathbf{1}_{SF}$, and [^{6}Li,^{15}N]-$\mathbf{1}_{SF}$ were prepared from ethyllithium or [^{6}Li]ethyllithium via the lithium tetramethylpiperidides as described previously.[1] Air- and moisture-sensitive materials were manipulated by standard glovebox and vacuum-line techniques with the aid of gas-tight syringes.

Molecular Weight Determinations. Molecular weights were measured by the freezing point depression technique in a modification of an apparatus described by Seebach[12] interfaced to a Commodore 64 or VIC 20 minicomputer. Samples were prepared in a glovebox, and measurements were made under Ar with standard inert-atmosphere techniques. Calibrations were performed with known concentrations of naphthalene in benzene. The linear least-squares fit in Figure 4 was anchored with a high statistical weight to the origin.

Nuclear Magnetic Resonance Studies. The following is a representative procedure for preparing samples for spectroscopic analysis. A stock solution was prepared in a glovebox by sequentially mixing [^{6}Li^{15}N]-$\mathbf{1}_{SF}$ (110 mg, 0.62 mmol), toluene-d_8 (600 μL), and THF (100 μL, 1.23 mmol). A 5-mm NMR tube was charged sequentially with the pale yellow stock solution (205 μL) and toluene-d_8 (395 μL), placed under septum, removed from the glovebox, and sealed with a flame under reduced pressures.

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Nucleophilic Substitution Reaction of Phenylmethanesulfonyl Halides with Anilines[1]

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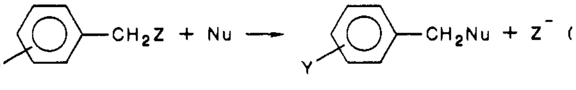
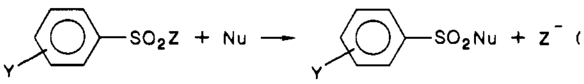
Abstract: Kinetic studies on the nucleophilic substitution reaction of Y-substituted phenylmethanesulfonyl halides with X-substituted anilines in methanol–acetonitrile have been carried out in order to elucidate the reaction mechanism. The phenylmethanesulfonyl fluorides (PSF) had markedly lower rates and smaller magnitudes of ρ_X and ρ_Y values compared with those for the chlorides (PSC). On the contrary, however, the magnitude of the cross-interaction constant $|\rho_{XY}|$ was greater for PSF than for PSC, so that the degree of bond making in the transition state is actually greater in the reaction of PSF as compared with that for PSC. We have thus demonstrated that extensive charge transfer from a nucleophile to a substrate does not necessarily mean a tight bond in the transition state. Moreover the nonzero ρ_{XY} values obtained for both PSC and PSF are taken as evidence in support of a common, associative S_N2 mechanism for the two halides.

Nucleophilic substitution reactions of substituted benzyl halides (eq 1) have been extensively studied.[2] In this reaction, halides


(1)

(Z) are displaced by a nucleophile (Nu) at the benzylic (C_α) carbon. On the other hand, nucleophilic substitution reactions of benzenesulfonyl halides (eq 2) have also attracted much interest;


(2)

terest;[3] in this case the displacement of halides (Z) occurs at the sulfonyl sulfur (S). There are similarities and differences in the mechanisms of these two nucleophilic reactions. The two reactions are notable examples of the S_N2 reaction with a borderline mechanism exhibiting U-shaped nonlinear Hammett plots;[2b,3a,e] with an uncharged neutral nucleophile (Nu), the former reaction (1) proceeds by a dissociative S_N2 mechanism in which the bond breaking is relatively more advanced than the bond formation,[2c] while the latter reaction (2) proceeds by an associative S_N2 mechanism with bond formation being more extensive than bond breaking in the transition state (TS).[3b,4] The main objective in this work is to gain insight into the mechanistic changes involved

Table I. Pseudo-First-Order Rate Constants ($k_1 \times 10^4$ s^{-1}) and Activation Parameters for the Methanolysis of Phenylmethanesulfonyl Chloride in MeOH–MeCN

	temp, °C		activation parameters	
MeOH (v/v), %	45.0	55.0	$\Delta H^{\ddagger\,a}$	$-\Delta S^{\ddagger\,b}$
100	0.527	1.21	16.6	26.0
90	0.489	1.16	17.3	24.0
80	0.430	1.00	16.9	25.6
70	0.351	0.814	16.8	26.2
50	0.190	0.421	15.9	30.4

[a] Kilocalories/mole. [b] Entropy units.

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(1) Nucleophilic Displacement at Sulfur Center. 22.

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Table II. Second-Order Rate Constants ($k_2 \times 10^2$ L mol^{-1} s^{-1}) for the Reaction of Y-Substituted Phenylmethanesulfonyl Chlorides with X-Anilines in MeOH–MeCN at 35.0, 45.0, and 55.0 °C[a]

		Y = *p*-OCH$_3$			Y = *p*-CH$_3$			Y = H			Y = *p*-Cl		
MeOH	X	35.0	45.0	55.0	35.0	45.0	55.0	35.0	45.0	55.0	35.0	45.0	55.0
100	*p*-OCH$_3$	3.16	5.32	8.95	7.33	10.9	15.2	23.0	27.4	32.2	66.1	92.0	120
	p-CH$_3$	1.35	2.54	4.12	2.48	4.60	7.08	7.89	11.0	15.5	25.1	34.0	51.4
	H	0.451	0.794	1.45	0.874	1.67	2.13	2.41	3.30	4.75	6.03	8.79	13.9
	p-Cl	0.0501	0.126	0.240	0.105	0.210	0.407	0.244	0.450	0.750	0.759	1.42	2.52
80	*p*-OCH$_3$	2.63	5.07	7.59	5.32	9.00	13.0	17.9	23.0	29.4	50.1	70.8	105
	p-CH$_3$	1.16	2.23	3.98	2.27	4.01	6.68	6.16	9.28	13.0	18.2	28.2	41.7
	H	0.283	0.661	1.10	0.543	1.01	1.82	1.57	2.60	3.90	4.79	7.63	12.4
	p-Cl	0.0403	0.101	0.200	0.0645	0.158	0.335	0.186	0.363	0.635	0.457	1.00	1.91
50	*p*-OCH$_3$	1.58	3.17	5.37	2.38	5.25	8.61	7.24	11.5	20.7	28.5	42.2	62.7
	p-CH$_3$	0.708	1.43	2.75	1.03	2.23	4.47	2.19	3.98	6.72	10.8	18.9	28.8
	H	0.132	0.325	0.676	0.206	0.466	1.05	0.481	1.00	2.20	2.00	3.98	6.68
	p-Cl	0.0200	0.0462	0.120	0.0282	0.0708	0.182	0.0661	0.130	0.359	0.249	0.451	1.00

[a] Correlation coefficients for second-order plots, eq 3; $r > 0.998$.

Table III. Second-Order Rate Constants ($k_2 \times 10^4$ L mol^{-1} s^{-1}) for the Reaction of Y-Substituted Phenylmethanesulfonyl Fluorides with X-Anilines in MeOH–MeCN at 45.0, 55.0, and 65.0 °C[a]

		Y = *p*-CH$_3$			Y = H			Y = *p*-Cl			Y = *p*-NO$_2$		
MeOH (v/v), %	X	45.0	55.0	65.0	45.0	55.0	65.0	45.0	55.0	65.0	45.0	55.0	65.0
100	*p*-OCH$_3$	3.02	5.89	10.1	4.52	9.15	18.5	10.5	20.4	43.8	49.9	98.7	219
	p-CH$_3$	2.51	5.01	8.91	3.87	7.33	14.0	7.38	16.9	27.3	29.0	68.1	134
	H	1.82	3.02	5.44	2.47	5.19	8.77	4.21	8.79	16.2	12.8	27.4	53.8
	p-Cl	1.15	1.04	2.75	1.50	2.38	4.37	1.98	3.53	6.30	5.01	10.1	18.1
80	*p*-OCH$_3$	2.88	6.30	11.2	5.08	9.47	17.7	10.9	20.4	39.2	45.5	95.0	191
	p-CH$_3$	2.37	4.79	9.05	3.72	7.58	14.8	6.42	14.8	31.6	27.8	61.6	130
	H	1.68	2.94	5.51	2.54	5.33	9.20	3.31	7.96	14.7	11.8	23.2	45.9
	p-Cl	0.982	1.58	2.65	1.50	2.42	3.95	1.90	3.08	5.27	4.34	7.52	13.9
50	*p*-OCH$_3$	2.09	4.12	7.74	3.16	5.56	10.8	6.66	12.6	25.2	21.9	51.6	97.1
	p-CH$_3$	1.58	2.98	5.08	2.31	4.69	8.71	4.76	8.74	15.2	13.8	30.7	53.6
	H	1.12	2.01	3.51	1.60	2.61	5.19	2.41	3.82	7.83	4.75	10.3	19.5
	p-Cl	0.603	0.987	1.41	0.729	1.08	1.91	0.912	1.45	2.43	1.97	3.58	5.90

[a] Correlation coefficients for second-order plots, eq 3; $n > 0.997$.

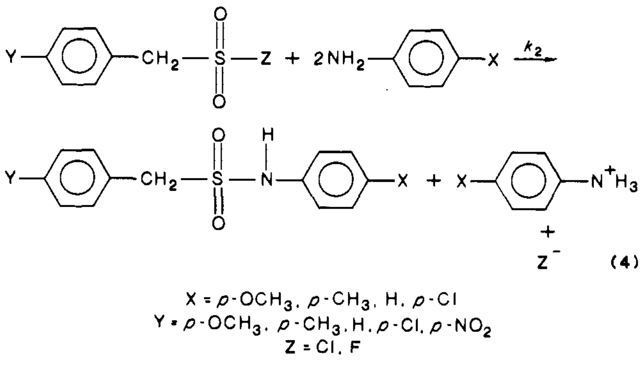
in the nucleophilic substitution reactions of sulfonyl fluorides, since Ciuffarin et al.[3c] suggested that the fluorides have bond breaking as the rate-determining step in contrast with the other halides, which react by rate-determining bond formation.

In this work we report results of our kinetic studies on the reaction of phenylmethanesulfonyl halides (chloride and fluoride) with substituted anilines in methanol–acetonitrile mixtures.

Results and Discussion

Rate constants for the methanolysis of phenylmethanesulfonyl chloride (PSC) in methanol–acetonitrile mixtures are reported in Table I together with the activation parameters. The rate is seen to increase with the methanol content of the solvent mixtures. Second-order rate constants k_2 obtained by eq 3 for the reaction of phenylmethanesulfonyl halides with substituted (X) anilines in methanol–acetonitrile (eq 4) are collected in Tables II and III.

$$k_1(\text{obsd}) = k_1 + k_2[\text{aniline}] \qquad (3)$$



(4)

Reference to Tables I–III reveals that k_1 is less by 10^2 times than k_2 for PSC and hence will be negligible compared with k_2 in eq 3; the assumption of $k_1(\text{obsd}) \simeq k_2[\text{aniline}]$ was therefore valid in the present work, as indicated by the zero intercept (k_1) of the plot. The second-order rate constant k_2 for phenylmethanesulfonyl fluoride (PSF) is found to be much smaller than that for PSC. This supports sulfonyl sulfur–halogen bond cleavage in the TS of reaction 4, since it has been shown that the leaving group ability of F$^-$ is very poor compared with Cl$^-$ and reactivity in general follows the leaving ability. Shaik and Pross[5] concluded in their analysis of reactivity factors for identity reactions of $X^- + CH_3X \rightarrow XCH_3 + X^-$ that the poor leaving group ability exhibited by F$^-$ is due to the poor electron acceptor ability of CH_3F, which in turn originates in the strong C–F bond. In this respect, the reactivity of sulfonyl fluoride is also expected to be very low; our MNDO calculations[6] on the isodesmic reaction 5 showed that the

$$\begin{gathered} CH_3SO_2F + Cl^- \rightleftharpoons CH_3SO_2Cl + F^- \\ \Delta E = 38.4 \text{ kcal/mol} \end{gathered} \qquad (5)$$

S–F bond is stronger by 38.4 kcal/mol than the S–Cl bond. The electron acceptor property of the S–F bond is also excepted to be poor on account of the large energy gap involved in the frontier MOs (FMO) of the reactants. The charge transfer from the highest occupied MO (HOMO) of the nucleophile to the substrate, and hence to the lowest unoccupied MO (LUMO) of the cleaving bond, which is σ antibonding (σ^*), is in general greater the smaller the energy gap between the FMOs.[2d,3e] Extended Hückel (EHT) calculations[7] on phenylmethanesulfonyl halides and aniline indeed gave a wider energy gap (6.6 kcal/mol) between the LUMO [σ^*(S–F) orbital] of PSF and the HOMO (nonbonding orbital of the nitrogen atom) of aniline compared with the corresponding energy gap (4.1 kcal/mol) for PSC.

Substituent Effect. Tables II and III show that the rate increases with an increase in the electron-donating ability of group (EDG) X in the nucleophile and with a more electron-withdrawing group (EWG) Y in the substrate, the increase being much greater for PSC than for PSF. These results suggest that bond making

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(6) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899, 4907.
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Table IV. Hammett and Brønsted Coefficients, ρ_x and β_x, for the Reaction of Y-Substituted Phenylmethanesulfonyl Chloride (PSC) and Fluoride (PSF) with X-Anilines in MeOH–MeCN at 55.0 °C.[a]

		PSC with Y substituent				PSF with Y substituent			
MeOH (v/v), %		p-OCH$_3$	p-CH$_3$	H	p-Cl	p-CH$_3$	H	p-Cl	p-NO$_2$
100	ρ_x	−3.10	−3.13	−3.25	−3.34	−1.09	−1.16	−1.56	−2.03
	β_x	1.12	1.13	1.18	1.21	0.39	0.42	0.57	0.73
80	ρ_x	−3.18	−3.20	−3.31	−3.43	−1.21	−1.18	−1.65	−2.23
	β_x	1.15	1.16	1.19	1.24	0.44	0.42	0.60	0.81
50	ρ_x	−3.34	−3.39	−3.42	−3.61	−1.22	−1.46	−1.91	−2.35
	β_x	1.21	1.23	1.24	1.31	0.44	0.53	0.69	0.85

[a] Correlation coefficient, $r = 0.993 \pm 0.007$.

Table V. Hammett ρ_Y values for the Reaction of Y-Substituted Phenylmethanesulfonyl Chloride (PSC) and Fluoride (PSF) with X-Anilines in MeOH–MeCN at 55.0 °C[a]

	PSC with X substituent				PSF with X substituent			
MeOH (v/v), %	p-OCH$_3$	p-CH$_3$	H	p-Cl	p-CH$_3$	H	p-Cl	p-NO$_2$
100	2.23	2.17	1.98	2.00	1.30	1.21	0.98	0.80
80	2.27	2.01	2.09	1.93	1.27	1.17	0.90	0.69
50	2.15	1.97	1.99	1.84	1.18	1.06	0.75	0.61

[a] Correlation coefficient, $r = 0.992 \pm 0.008$.

Table VI. Multiple Hammett Correlations for the Reaction of Y-Substituted Phenylmethanesulfonyl Chloride (PSC) and Fluoride (PSF) with X-Anilines in MeOH–MeCN (r = Multiple Correlation Coefficient)[13] at 55.0 °C

	PSC				PSF			
MeOH (v/v), %	ρ_X	ρ_Y	ρ_{XY}	r	ρ_X	ρ_Y	ρ_{XY}	r
100	−3.23	2.07	−0.50	0.999	−1.24	1.02	−1.02	0.998
80	−3.31	2.05	−0.52	1.000	−1.32	0.94	−1.17	0.998
50	−3.47	1.96	−0.52	0.999	−1.48	0.84	−1.18	0.998

is also important in the transition state (TS) of the reaction (4).

Hammett and Brønsted plots yielded generally good linear correlations. The ρ_X[8] and β_X[9] values for substituent changes in the nucelophile are summarized in Table IV. Trends of changes in ρ_X and β_X values are similar for the two substrates; the magnitudes of both parameters increase with a more EWG in the substrate. Thus the extent of charge transfer from a nucleophile to the substrate increases as the LUMO of the substrate is lowered by an EWG in the substrate (vide supra). The magnitude of the ρ_X and β_X values for PSC are comparable with those reported for other reactions of sulfonyl chloride[3b,g,10] but are much greater than those for PSF. A large difference in the magnitude of ρ_X or β_X, and hence in the extent of charge transfer in the TS, between PSC and PSF provides further support for the substantial difference in the acceptor ability of the two sulfonyl halides as discussed above.

Hammett coefficients ρ_Y for the substituent (Y) changes in the substrate are summarized in Table V. The positive ρ_Y values are seen to increase with a more EDG in the nucelophile, and here again the sizes are greater for PSC than for PSF; the negative charge at the reaction center S increases with the nucelophile strength in general and is greater for PSC. This is in keeping with the ease of charge transfer predicted based on the FMO theory, since a stronger nucelophile (X = p-OCH$_3$) has a higher HOMO so that it has a smaller FMO energy gap.

Transition-State Structure. The size of the Hammett reaction constant ρ is commonly believed to represent the extent of charge development at the atom of the reaction site directly involved in the bond-making and/or -breaking processes at the TS.[11] However, the ρ values are often not satisfactory as a measure of the TS structure, since the efficiency of charge transmission in different reaction series may differ.[11,12] Thus, in the discussions of ρ_X and ρ_Y values above, we were careful in interpreting the magnitudes of these Hammett constants and deliberately avoided linking them with the bond tightness in the TS. In a previous report[13] we showed that the magnitude of the cross-interaction constant ρ_{XY} between substituents X and Y (eq 6) is inversely

$$\log (k_{XY}/k_{HH}) = \rho_X\sigma_X + \rho_Y\sigma_Y + \rho_{XY}\sigma_X\sigma_Y \qquad (6)$$

proportional to the distance between X and Y when the two fragments with interacting substituents X and Y are the partners directly involved in bond-making and/or bond-breaking processes in the TS; thus in the nucelophilic substitution reaction between a nucleophile with substituent X and a substrate with Y, the degree of bond making will be greater the larger the $|\rho_{XY}|$, since the larger $|\rho_{XY}|$ is an indication of the closer distance between the nucleophile with X and the substrate with Y. This will be ture irrespective of the size of the individual ρ_X and/or ρ_Y values in eq 6.

Experimental second-order rate constants k_2 in Tables II and III were subjected to multiple linear regression analysis[14] using eq 6. The ρ_X, ρ_Y, and ρ_{XY} values determined are summarized in Table VI. The ρ_X and ρ_Y values in Table VI agree satisfactorily with those given in Tables IV and V for Y = H and X = H, respectively.[15] On the basis of the magnitudes of ρ_X and ρ_Y, one might be tempted to conclude that a much greater degree of bond making is achieved in the reaction of PSC at the TS. However, this conclusion is grossly misleading.

Reference to Table VI reveals that, in a striking contrast to the smaller $|\rho_X|$ and ρ_Y values for PSF, the absolute values of the cross-interaction constants $|\rho_{XY}|$ for PSF are actually greater than those for PSC. Hence, on the basis of the relative $|\rho_{XY}|$ values, we are led to conclude that bond making is more advanced for PSF as compared with that for PSC. Thus were it not for the cross-interaction constants, we might have reached the wrong

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[8] The pK_a values used in these plots were obtained from: Streitwieser, A., Jr.; Heathcock, C. H. *Organic Chemistry*, 2nd ed.; MacMillan: New York, 1976; p 737.

[9] The σ values used in these plots were obtained from: Gilliom, R. D. *Introduction to Physical Organic Chemistry*; Addison Wesley: Reading, 1970; p 147.

[10] Arcoria, A.; Ballistreri, F. P.; Musumarra, G.; Tomaselli, G. A. *J. Chem. Soc., Perkin Trans. 2* **1981**, 221.

[11] Johnson, C. D. *The Hammett Equation*; Cambridge University: Cambridge, 1973; p 7.

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[13] Lee, I.; Sohn, S. C. *J. Chem. Soc., Chem. Commun.* **1986**, 1055.

[14] Shorter, J. *Correlation Analysis of Organic Reactivity*; Research Studies: New York, 1982; Chapter 2.

[15] Equation 6 gives $\rho_X = \rho_{XH}$ and $\rho_Y = \rho_{HY}$, i.e., ρ values for Y = H and X = H cases, respectively.

Table VII. Rate Ratios k_{Cl}/k_F for the Reaction of Y-Substituted Phenylmethanesulfonyl Chloride and Fluoride with X-Anilines in MeOH–MeCN at 55.0 °C

		Y substituent		
MeOH (v/v), %	X	p-CH$_3$	H	p-Cl
100	p-OCH$_3$	258	352	588
	p-CH$_3$	141	211	304
	H	71	92	158
	p-Cl	39	32	71
50	p-OCH$_3$	209	372	498
	p-CH$_3$	150	143	330
	H	52	84	175
	p-Cl	18	33	69

conclusion as to the relative extent of bond making at the TS based simply on the relative magnitudes of ρ_X and ρ_Y values. The present results indicate that the extent of charge transfer is not an indication of bond tightness, i.e., considerable charge transfer does not necessarily mean a tight bond formation.[16] This is true especially in the case of widely varying structures[17] such as for PSC and PSF, which have leaving groups that are very much different in their leaving ability.

Theoretical[18] as well as experimental[19] studies have indeed shown that bond making is more complete at the TS for the substrate with the poor leaving group ability within a reaction series in which bond making is ahead of bond breaking.[20] It can be shown that the More-O'Ferrall–Jencks plots[21] also predict that the poor leaving group has a greater degree of bond formation, in agreement with our conclusion based on the $|\rho_{XY}|$ values.

Relative magnitudes of ρ values in Table VI clearly show that extensive charge transfer actually takes place at large intermolecular separation in the reactions of PSC. It is therefore dangerous to assess the degree of bond making at the TS by the magnitude of ρ_X and/or ρ_Y values alone.

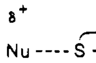
Relatively large positive ρ_Y values in Table V indicate that the reaction center S atom has substantial negative charge, owing to a greater degree of bond making compared with bond breaking at the TS for both substrates. This is in contrast with the contention of Ciuffarin et al.[3c,22] that sulfonyl fluoride reacts by a different mechanism from other sulfonyl halides. They argued that sulfonyl halides react by the addition–elimination (S$_A$N) mechanism involving an intermediate, and bond formation is rate limiting for sulfonyl halides except fluoride, for which bond breaking is rate limiting.

Moreover our mechanistic criteria based on the cross-interaction constants[12] clearly rule out the possibility of the rate-determining bond cleavage for sulfonyl fluoride; in contrast to the large $|\rho_{XY}|$ values obtained in this work, the rate-determining bond cleavage would require negligible values of $|\rho_{XY}|$ for PSF, since the two fragments, i.e., the nucleophile with X and the substrate with Y, are not the partners directly involved in the bond-breaking process in the TS.

The rate ratios k_{Cl}/k_F should provide a relative measure of charge transfer to the leaving group, and hence a relative measure of leaving group departure, in the TS.

The ratios summarized in Table VII correctly reflect the trends in the acceptor ability of the S–Z bonds; improving the acceptor ability either by lowering the LUMO of the substrate, i.e., σ^*(S–Z), with an EWG[23] or by elevating the HOMO of the nucleophile with an EDG[23] tends to increase the ratio, indicating the enhancement of charge transfer due to the FMO energy gap narrowing effect.[24]

Solvent Effects. Tables II and III show that the rate is faster in a solvent of higher ionizing power, i.e., higher MeOH content.[25] This could be ascribed to better solvation of the leaving halogen group by methanol providing electrophilic assistance to the leaving group by hydrogen bonds. This provides further support for the theoretical conclusion that the reactivity follows leaving group ability.[5] The magnitudes of ρ_X and β_X values in Table IV are found to increase as the polarity of solvent increases with the MeCN content.[25] Since the relative magnitude of the ρ_X and ρ_Y values within a series can be taken as a relative measure of the degree of the bond formation, this, together with a slight increase in the $|\rho_{XY}|$ values in Table VI, constitutes evidence in support of the TS structure with more advanced bond making in the more polar solvent. This can be accommodated with an associative S$_N$2 mechanism, since in an associative S$_N$2 TS bond formation is more advanced than bond breaking so that the nucelophile (Nu) bears considerable positive charge while the substrate (S) and the leaving group (L) share the equivalent amount of negative charge as in I. Thus increasing bond formation leads to a more polar TS, and hence the bond making is favored by a more polar solvent.



$$\overset{\delta^+}{\mathrm{Nu}}\text{----}\overset{\delta^-}{\overbrace{\mathrm{S}\text{----}\mathrm{L}}}$$

I

Solvent composition appears to have little effect on the leaving group ability as can be seen from the relative independence of the β_Z values in Table VII.

Activation Parameters. Enthalpies and entropies of activation for the reaction of PSC and PSF with anilines are summarized in Tables VIII and IX. Relatively small $\Delta H^{\ddagger}$ and large negative $\Delta S^{\ddagger}$ values are as expected for bimolecular reactions with polar transition states.[3b] An electron-donating substituent (X = p-OCH$_3$) in the aniline and more ionizing solvent (100% MeOH) decrease $\Delta H^{\ddagger}$ for PSC, while the reverse is true for PSF. Isokinetic plots[21] of $\Delta H^{\ddagger}$ vs $\Delta S^{\ddagger}$ (eq 7) for variations in both the substituent

$$\delta\Delta H^{\ddagger} = \beta\delta\Delta S^{\ddagger} \tag{7}$$

$$\delta\Delta G^{\ddagger} = (\beta - T)\delta\Delta S^{\ddagger} \tag{8}$$

(X) in anilines and solvent composition gave good linearities, and slopes of the plots β (isokinetic temperature) collected in Table X are seen to be greater for PSC, whereas they are smaller for PSF than the experimental temperature T_{exp}. This indicates according to eq 8 that the reactions of PSC are enthalpy controlled, while those of PSF are entropy controlled. Thus the enthalpy of activation shows a regular variation for PSC in that electron-donating substituent in the nucleophile and more ionizing solvent decrease $\Delta H^{\ddagger}$, reflecting correctly the energetics involved in the bond making and breaking. On the other hand, for PSF solute–solvent interactions seem to dominate the stability of the TS, fluoride being a strong hydrogen bond acceptor. We conclude that both phenylmethanesulfonyl chloride and fluoride react with anilines via a concerted S$_N$2 mechanism in which bond making is ahead of bond breaking at the TS, i.e., associated S$_N$2, and the fluoride has a tighter TS as compared with the chloride.

Experimental Section

Materials. Phenylmethanesulfonyl halides (PSC and PSF) were used after recrystallization of commercial (Tokyo-Kasei) products to constant melting points: chloride 91–93 °C;[26] fluoride 94 °C.[27] Anilines were purified as described previously.[28] G. R. grade solvents MeOH and

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Table VIII. Activation Parameters for the Reaction of Y-Substituted Phenylmethanesulfonyl Chlorides with X-Anilines in MeOH–MeCN at 45.0 °C[a]

		$\Delta H^\ddagger$, kcal·mol^{-1}, with Y substituent				$-\Delta S^\ddagger$, eu, with Y substituent			
MeOH (v/v), %	X	*p*-OCH$_3$	*p*-CH$_3$	H	*p*-Cl	*p*-OCH$_3$	*p*-CH$_3$	H	*p*-Cl
100	*p*-OCH$_3$	9.8	6.7	2.7	5.4	33.7	42.0	52.7	41.9
	p-CH$_3$	10.6	9.9	6.1	6.6	32.6	33.7	43.9	40.1
	H	11.1	8.4	6.2	7.7	33.4	40.4	46.0	39.3
	p-Cl	15.1	13.0	10.7	11.4	24.5	30.1	35.8	31.3
80	*p*-OCH$_3$	10.0	8.4	4.4	6.8	33.2	37.0	47.8	38.0
	p-CH$_3$	11.8	10.2	6.9	7.7	29.1	33.0	41.7	37.0
	H	13.0	11.5	8.5	8.9	27.8	31.6	39.2	35.8
	p-Cl	15.5	15.9	11.7	13.7	23.6	21.5	33.1	24.8
50	*p*-OCH$_3$	11.7	12.3	9.9	7.3	28.8	25.9	31.8	37.4
	p-CH$_3$	13.0	14.1	10.6	9.2	26.2	21.9	31.8	33.1
	H	15.8	15.7	14.6	11.5	20.4	20.0	21.9	28.9
	p-Cl	17.3	18.1	16.3	13.3	19.5	16.2	20.6	27.6

[a] Correlation coefficient, $r = 0.994 \pm 0.006$.

Table IX. Activation Parameters for the Reaction of Y-Substituted Phenylmethanesulfonyl Fluorides with X-Anilines in MeOH–MeCN at 55.0 °C[a]

		$\Delta H^\ddagger$, kcal·mol^{-1}, with Y substituent				$-\Delta S^\ddagger$, eu, with Y substituent			
MeOH (v/v), %	X	*p*-CH$_3$	H	*p*-Cl	*p*-NO$_2$	*p*-CH$_3$	H	*p*-Cl	*p*-NO$_2$
100	*p*-OCH$_3$	12.3	14.4	14.6	15.1	36.0	28.7	26.5	21.9
	p-CH$_3$	12.9	13.1	13.4	15.7	34.5	33.1	30.6	20.8
	H	11.0	12.9	13.7	14.7	41.3	34.4	31.0	25.6
	p-Cl	8.7	10.8	11.7	13.1	49.4	42.4	38.9	32.5
80	*p*-OCH$_3$	13.9	12.7	13.0	14.6	31.0	33.9	31.4	23.5
	p-CH$_3$	13.7	14.1	16.4	15.7	32.2	30.0	21.7	21.0
	H	12.0	13.1	15.3	13.9	38.3	33.8	26.3	28.4
	p-Cl	10.0	9.7	10.2	11.8	45.6	45.7	43.7	37.1
50	*p*-OCH$_3$	13.3	12.5	13.6	15.3	33.7	35.5	30.5	22.6
	p-CH$_3$	11.8	13.5	11.8	13.9	38.9	32.8	36.8	27.9
	H	11.6	11.9	12.0	14.6	40.3	38.9	37.8	27.9
	p-Cl	8.4	9.6	9.8	11.0	51.5	47.6	46.4	41.0

[a] Correlation coefficient, $r = 0.995 \pm 0.005$.

Table X. Isokinetic Temperatures (β) for the Reaction of Y-Substituted Phenylmethanesulfonyl Halides with X-Anilines in MeOH–MeCN[a]

	Y-PhCH$_2$SO$_2$Cl with X substituent				Y-PhCH$_2$SO$_2$F with X substituent			
MeOH (v/v), %	*p*-OCH$_3$	*p*-CH$_3$	H	*p*-Cl	*p*-CH$_3$	H	*p*-Cl	*p*-NO$_2$
100	369	416	382	404	203	209	237	260
80	369	408	423	360	275	217	247	230
50	453	420	482	434	204	216	246	244

[a] T_{exp} = 318 and 328 K for PSC and PSF, respectively.

Table XI. Identification of Para-Substituted Phenylmethanesulfonyl Halides

	Y-PhCH$_2$SO$_2$Cl with Y substituent				Y-PhCH$_2$SO$_2$F with Y substituent		
	p-OCH$_3$	*p*-CH$_3$	*p*-Cl	*p*-NO$_2$	*p*-CH$_3$	*p*-Cl	*p*-NO$_2$
color	pale yellow	white	white	yellow	white	white	pale yellow
cryst form	liquid	cryst	cryst	cryst	cryst	cryst	cryst
mp or bp,[a] °C	95–98	73–75	88–91	85–88	135–138	143–145	123–125
TLC, R_f	0.34	0.68	0.65	0.35	0.52	0.55	0.35

[a] At 760 mmHg.

MeCN were used without further purification.

Preparation of Para-Substituted Phenylmethanesulfonyl Halides.[29,30] Para-substituted benzyl alcohols were reacted with thiourea in 17.5% HCl solution under reflux with constant stirring at 100 °C for 5–7 days. White crystals (orange for *p*-NO$_2$) of *S*-alkylisothiourea hydrochloric acid salts were formed upon standing, which were washed once with 30% aqueous HCl and twice with ethanol. The dried salts were then dissolved in water, and solid products (oil layer for *p*-OCH$_3$) were obtained upon passage of Cl$_2$ gas through the aqueous solution. The products (PSCs) were recrystallized (or distilled) from chloroform.

PSCs were then reacted with KF (1:1 equiv) in dry acetonitrile with 5 mol % of 18-crown-6 ether for 3–5 days at the room temperature with constant stirring.[30] The precipitates, PSFs, were dried and recrystallized from chloroform.

Melting points and boiling points are summarized in Table XI together with the R_f values of TLC results.

For all compounds, purity was confirmed by the appearance of a single spot and peak in TLC and GC analyses, respectively. Spectral peaks[31,32] [Ir (ν_{max}) and ^{1}H NMR (δ)] were as follows.

(*p*-Methoxyphenyl)methanesulfonyl chloride: ν_{max}(neat) 2950, 2850, and 1105 (benzyl), 1267 (SO$_2$, asym, str), 1125 (SO$_2$, sym, str), 1325, and 1160 cm^{-1} (SO$_2$Cl); δ_H (60 MHz; CDCl$_3$) 3.9 (3 H, s, 4-CMe), 4.5 (2 H, s, benzylic), 6.9–7.5 (4 H, m, ring).

(*p*-Methylphenyl)methanesulfonyl chloride: ν_{max} (KBr) 3000, 2860, and 1110 (benzyl), 1319 (SO$_2$, asym, str), 1135 (SO$_2$, sym, str), 1349, and 1167 cm^{-1} (SO$_2$Cl); δ_H (60 MHz; CDCl$_3$) 2.4 (3 H, s, 4-Me), 4.9

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(2 H, s, benzylic), 7.4 (4 H, s, ring). Anal. Calcd for $C_8H_9SO_2Cl$: C, 46.95; H, 4.43. Found: C, 47.05; H, 4.26.

(*p*-Chlorophenyl)methanesulfonyl chloride: ν_{max} (KBr) 3000, 2950, and 1091 (benzyl), 1313 (SO_2, asym, str), 1151 (SO_2, sym, str), 1357, and 1168 (SO_2Cl); δ_H (60 MHz; $CDCl_3$), 4.9 (2 H, s, benzylic), 7.5 (4 H, s, ring). Anal. Calcd for $C_7H_6SO_2Cl_2$: C, 37.35; H, 2.69. Found: C, 37.47; H, 2.57.

(*p*-Nitrophenyl)methanesulfonyl chloride: ν_{max} (KBr) 3000, 2870, and 1110 (benzyl), 1319 (SO_2, asym, str), 1135 (SO_2, sym, str), 1349, and 1167 cm^{-1} (SO_2Cl); δ_H (60 MHz; $CDCl_3$) 5.1 (2 H, s, benzylic), 7.4–8.5 (4 H, m, ring). Anal. Calcd for $C_7H_6NSO_4Cl$: C, 35.68; H, 2.57. Found: C, 35.80; H, 2.45.

(*p*-Methylphenyl)methanesulfonyl fluoride: ν_{max} (KBr) 3050, 2920, and 1113 (benzyl), 1280 (SO_2, asym, str), 1150 (SO_2, sym, str), 1400, and 1210 cm^{-1} (SO_2F); δ_H (60 MHz; $CDCl_3$) 2.4 (3 H, s, 4-Me), 4.8 (2 H, s, benzylic), 7.4 (4 H, s, ring). Anal. Calcd for $C_8H_9SO_2F$: C, 51.05; H, 4.82. Found: C, 50.97; H, 4.97.

(*p*-Chlorophenyl)methanesulfonyl fluoride: ν_{max} (KBr) 3000, 2870, and 1110 (benzyl), 1305 (SO_2, asym, str), 1150 (SO_2, sym, str), 1400, and 1207 cm^{-1} (SO_2F); δ_H (60 MHz; $CDCl_3$) 5.2 (2 H, d, J = 5 Hz, benzylic), 7.4 (4 H, s, ring). Anal. Calcd for $C_7H_6SO_2FCl$: C, 40.30; H, 2.90. Found: C, 40.43; H, 2.98.

(*p*-Nitrophenyl)methanesulfonyl fluoride: ν_{max} (KBr) 3000, 2870, and 1100 (benzyl), 1305 (SO_2, asym, str), 1149 (SO_2, sym, str), 1398, and 1213 cm^{-1} (SO_2F); δ_H (60 MHz; $CDCl_3$) 5.0 (2 H, d, J = 4 Hz, benzylic), 7.9–8.0 (4 H, d, J = 8 Hz, ring), 8.5–8.7 (4 H, d, J = 8 Hz, ring). Anal. Calcd for $C_7H_6NSO_4F$: C, 38.36; H, 2.76. Found: C, 38.50; H, 2.88.

Rate Constants. Rates were measured conductometrically[28] at three temperatures for each substrate ranging from 35.0 to 65.0 (±0.1) °C. Pseudo-first-order rate constants k_1(obsd) were determined by the Guggenheim method with a large excess of anilines, and second-order rate constants k_2 were obtained from the slope of a plot of k_1(obsd) vs (aniline) according to eq 3, where k_1 is the rate constant for methanolysis, which was found to be negligibly small compared with k_2 (vide supra). More than four aniline concentrations were used in the plot of eq 3 in all cases. Duplicate kinetic runs showed that the rates are reproducible to within ±3%. The average error limits in the values of ΔH^* and ΔS^* are ±0.5 kcal $\cdot mol^{-1}$ and ±0.7 cal$\cdot mol^{-1}\cdot k^{-1}$, respectively.

Product Analysis. Products were identified by IR and TLC. The TLC results on the products from 1:1 phenylmethanesulfonyl halide–aniline reaction mixtures in *n*-hexane–ethyl acetate showed a distinct (single) spot (R_f 0.42) indicating no byproducts were involved. IR spectra[32] were taken on a Nicolet MX-1 FT-IR with KBr tablets; as the reaction proceeded, the pure characteristic peak of aniline at 1600–1650 cm^{-1} disappeared and the therminal –NH (sh) peak of aniline change to the intermediate –NH– (br) band at 3200–3500 cm^{-1}. Furthermore, the S–N bands (sh) were found to grow at 1350 cm^{-1}, confirming that the reaction proceeds as eq 4.

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Registry No. $4\text{-}MeOC_6H_4CH_2SO_2Cl$, 110661-59-1; $4\text{-}MeC_6H_4CH_2SO_2Cl$, 51419-59-1; $PhCH_2SO_2Cl$, 1939-99-7; $4\text{-}ClC_6H_4CH_2SO_2Cl$, 6966-45-6; $4\text{-}MeC_6H_4CH_2SO_2F$, 110661-60-4; $PhCH_2SO_2F$, 329-98-6; $4\text{-}ClC_6H_4CH_2SO_2F$, 1513-29-7; $4\text{-}O_2NC_6H_4CH_2SO_2F$, 110661-61-5; $4\text{-}MeOC_6H_4NH_2$, 104-94-9; $4\text{-}MeC_6H_4NH_2$, 106-49-0; $PhNH_2$, 62-53-3; $4\text{-}ClC_6H_4NH_2$, 106-47-8; $4\text{-}O_2NC_6H_4CH_2SO_2Cl$, 4025-75-6; $4\text{-}MeOC_6H_4CH_2OH$, 105-13-5; $4\text{-}MeC_6H_4CH_2OH$, 589-18-4; $4\text{-}ClC_6H_4CH_2OH$, 873-76-7; $4\text{-}O_2NC_6H_4CH_2OH$, 619-73-8; H_2NCSNH_2, 62-56-6.

Micellar Control of Organic Reactions: Propellane Substrates as Stereochemical Probes for Micellar Binding

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Abstract: Propellanediones and their reduction products have been used to demonstrate that micellar binding can control reaction diastereoselectivity. Borohydride reduction of the propellane carbonyl in an aqueous solution of a cationic surfactant provides clear evidence for this new kind of micellar perturbation of organic reactions. In addition to the expected rate enhancement that cationic micelles provide for the borohydride reduction, they direct the approach of the borohydride to one face of the reduction substrate. The source of this effect and its scope are explored. A correlation of micellar capabilities with substrate shape is presented. An explanation of these results is suggested. It is based on a particular model for the geometry of substrate–micelle binding and on micelle-directed attack of the prebound reagent.

The study of micellar effects on reaction stereochemistry has been an active area of investigation.[2] There have appeared in the literature a number of reports describing some limited success in attempts to use aqueous micelles and other aggregates to achieve optical induction.[2a] There is also ample precedent for the use of subtle changes in reaction stereochemistry as a diagnostic for particular capabilities of aqueous micelles to perturb a delicate balance among competing reaction pathways. Stereochemical probes of diazotate decomposition have provided insight into micellar influence on the partitioning of the carbocation–nitrogen–nucleofuge complex formed in that reaction[2b] and on the ability of the micelle to alter the balance among molecular rearrangement pathways.[2c] Changes in the stereochemistry of sulfonate solvolyses have revealed the enhanced nucleophilicity of surfactant sulfate head groups and their ability to compete with the nucleophilicity of water.[2d]

Our research program in the use of aqueous micelles to achieve synthetically useful perturbations of organic reactions has yielded successful control of olefin mercuration[3] and enone reduction.[4] We now report that in addition to such micelle-induced chemo-

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