Nucleophilic Substitution Reactions of Trimethylsilylmethyl Arenesulfonates with Anilines and Benzylamines in Acetonitrile

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The results of kinetic studies on the reactions of trimethylsilylmethyl arenesulfonates, **1** ($Me_3SiCH_2OSO_2C_6H_4Z$), with anilines and benzylamines in acetonitrile at 65.0 °C are reported. The relatively large positive value of the cross-interaction constant between substituents in the nucleophile (X) and leaving group (Z), ρ_{XZ}, indicates that the reaction proceeds by a S_N2 process with a relatively tight transition state. The enhanced rate of **1** compared with the rates for other corresponding carbon analogues leads us to conclude that the destabilizing effect of the α-silyl group on the ground state of **1** due to geminal interaction is important not only for S_N1 but also for S_N2 reactivities.

The effect of the α-silyl group on the reactivity of nucleophilic substitution reactions has recently attracted considerable attention of physical organic chemists. The solvolysis of neopentyl-like silylmethyl sulfonates, **1** [$(CH_3)_3SiCH_2OSO_2C_6H_4Z$)], in aqueous ethanol mixtures is reported to proceed by a concerted bimolecular (S_N2) mechanism,[1] in contrast to the well known S_N1 solvolysis of the carbon analogues, neopentyl derivatives [$(CH_3)_3CCH_2OSO_2C_6H_4Z$]. On the other hand, the α-silyl group has been shown to destabilize the ground state electronically relative to that of the corresponding α-methyl group and enhance the solvolytic reactivity when the leaving group (LG) in a cleaving C–LG bond is benzoate or sulfonate. This geminal effect is small for LG = Br or Cl.[2]

In view of this recent interest in the α-silyl effect, we have carried out kinetic studies on the nucleophilic substitution reactions of **1** with anilines and benzylamines. Our primary purpose in this work is to determine the tightness of the transition state (TS) using the magnitude of cross-interaction constants ρ_{XZ}, eqn. (1).[3] In a series of studies involving the

$$\log\left(\frac{k_{XZ}}{k_{HH}}\right) = \rho_X\sigma_X + \rho_Z\sigma_Z + \rho_{XZ}\sigma_X\sigma_Z \qquad (1)$$

application of cross-interaction constants to organic reaction mechanism in solution, we have shown that the size of ρ_{XZ} reflects the tightness of the TS; a tight TS involved in an associative S_N2 process shows relatively large magnitude of ρ_{XZ}, whereas the ρ_{XZ} value is small for a loose 'exploded' S_N2 TS, decreasing down to zero for an S_N1 TS.[3,4] The results of this work show that the TS for the nucleophilic substitution reaction of the α-silyl system, **1**, is indeed quite tight as expected from an associative S_N2 process but the rate is also higher than that normally predicted by the polar substituent effect.

Results and Discussion

The second order rate constants, k_2, for the reactions of trimethylsilylmethyl arenesulfonates, **1**, with anilines and benzylamines in methanol and acetonitrile at 65.0 °C are summarized in Table 1. The rate is faster with a stronger nucleophile and with a better leaving group. The rate is also faster in methanol than in acetonitrile. The rate ratio, k_{MeOH}/k_{MeCN}, increases as the rate becomes slower, which is consistent with the reactivity–selectivity principle (RSP);[5] the k_{MeOH}/k_{MeCN} value rises from 2.7 to 5.7 as the rate drops from that for reactants with X = p-CH_3O and Z = p-NO_2 to that for reactants with X = p-Cl and Z = p-CH_3. Methanolysis is somewhat slower than the aminolysis.

Table 1 Second order rate constants, $10^{-4}\ k_2/dm^3\ mol^{-1}\ s^{-1}$, for reactions of Z-substituted trimethylsilylmethyl arenesulfonates with X-substituted anilines and benzylamines in MeCN and MeOH at 65.0 °C

		Z			
Nucleophile	X	p-CH_3	H	p-Cl	p-NO_2
Aniline[a]	p-CH_3O	3.84	6.63	13.8	58.6
	p-CH_3	2.14	3.85	7.74	34.6
	H	0.958	1.69	3.59	16.2
	p-Cl	0.312	0.574	1.32	6.83
Aniline[b]	(MeOH)[c]	(4.46)	(6.53)	(11.3)	(43.3)
	p-CH_3O	13.8	20.7	40.1	157
	p-CH_3	8.48	13.0	26.2	110
	H	4.32	7.08	14.6	64.7
	p-Cl	1.78	3.02	6.27	29.3
Benzylamine[a]	p-CH_3O	66.0	106	193	839
	p-CH_3	55.6	86.3	169	727
	H	43.6	70.2	133	584
	p-Cl	30.4	49.4	97.0	436

[a] In MeCN. [b] In MeOH. [c] Methanolysis rate constants, $10^{-5}\ k_1/s^{-1}$, are given in parentheses at 65.0 °C.

The Hammett ρ_X and ρ_Z and the corresponding Brönsted β_X and β_Z values for the substituent variations in the nucleophile (X) and leaving group (Z) respectively are collected in Table 2. The ρ_Z value for methanolysis is slightly lower (ρ_Z = 1.05, r = 0.999) than the ρ values of the aminolysis. The rate constants, k_2, in Table 1 are subjected to multiple regression analysis using eqn. (1), and the cross-interaction constants, ρ_{XZ}, between the two substituents in the nucleophile (X) and leaving group (Z) determined are shown in Table 3. Reference to Tables 2 and 3 reveals that the ρ_{XZ} (β_{XZ}) values are all positive, and in agreement with the positive ρ_{XZ}, the magnitude of ρ_Z (β_Z) decreases with a stronger nucleophile and that of ρ_X (β_X) decreases with a better leaving group;[3] a stronger nucleophile and/or a better leaving group lead to an earlier TS. This means that the TS variation is in accord with that predicted by the More O'Ferrall–Jencks diagram.[6] For the reactions with benzylamine in acetonitrile the magnitude of ρ_{XZ} is *ca.* one quarter of that for the reactions with aniline, in contrast to the magnitude of β_{XZ} which is smaller approximately by one half.

Table 2 Hammett (ρ_X and ρ_Z) and Bronsted (β_X and β_Z) coefficients for reactions of Z-substituted trimethylsilylmethyl arenesulfonates with X-substituted anilines and benzylamines

Nucleophile	Z	ρ_X[c]	β_X[a]	X	ρ_Z[c]	β_Z[d]
Aniline[a]	*p*-CH_3	−2.18	0.78	*p*-CH_3O	1.24	−0.34
	H	−2.13	0.77	*p*-CH_3	1.26	−0.34
	p-Cl	−2.03	0.73	H	1.29	−0.35
	p-NO_2	−1.87	0.67	*p*-Cl	1.41	−0.38
Aniline[b]	*p*-CH_3	−1.78	0.64	*p*-CH_3O	1.12	−0.30
	H	−1.66	0.60	*p*-CH_3	1.18	−0.32
	p-Cl	−1.61	0.58	H	1.24	−0.34
	p-NO_2	−1.46	0.53	*p*-Cl	1.28	−0.35
Benzylamine[a]	*p*-CH_3	−0.67	0.65	*p*-CH_3O	1.16	−0.39
	H	−0.65	0.61	*p*-CH_3	1.18	−0.39
	p-Cl	−0.60	0.60	H	1.19	−0.40
	p-NO_2	−0.59	0.55	*p*-Cl	1.22	−0.41

[a] In MeCN. [b] In MeOH. [c] The σ values were taken from ref. 8. The correlation coefficients were better than 0.995 in all cases. [d] The pK_a values were taken from ref. 8. Table 8 for anilines, and from R. V. Hoffman and J. M. Shankweiler, *J. Am. Chem. Soc.*, 1986, **108**, 5536 for arenesulfonates involving methyl transfers. The correlation coefficients were better than 0.994 in all cases.

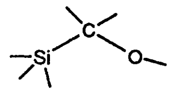
This difference is of course partly due to an intervening CH_2 group between the substituent X and the reaction centre N in benzylamine, which causes ρ values to fall-off by half but does not affect β values.[3] Even after allowing for this fall-off, the magnitudes of cross-interaction constants, ρ_{XZ} and β_{XZ}, are distinctly smaller for benzylamine, a stronger nucleophile, than for aniline, a weaker nucleophile. The smaller magnitude of β_{XZ} (ρ_{XZ}) suggests that the TS structure is much looser for the reactions with benzylamine. This is also reflected in the smaller β_X values (a lesser degree of bond making) and the greater magnitude of β_Z values (a greater degree of bond breaking) for benzylamine compared with those corresponding values for aniline in Table 2. Comparisons of the magnitudes of ρ_{XZ} and β_{XZ} values in Table 3 show that the values for the reactions of **1** are quite similar to those for the associative S_N2 reactions of methyl and ethyl arenesulfonates under the same reaction conditions.[3] This clearly indicates that the reactions of **1** with anilines (and benzylamines) proceed by the S_N2 mechanism with a relatively tight TS.[3] We note in Table 3 that the ρ_{XZ} value is zero for an S_N1 reaction (entry 4) and is quite small for an open, loose type of S_N2 TS (entries 3 and 5).

We have compared the rate, k_2, for the reaction of **1** with those of other corresponding reactions in Table 4. Examination of Table 4 reveals that the rate increases with an increase in the electron withdrawing power of the group Y (R = CH_2Y) in $ROSO_2C_6H_5$ in general, with the exception of the trimethylsilyl group [Y = $(CH_3)_3Si$]. The rate for the benzenesulfonate with a $(CH_3)_3Si$ group is faster only by 2.5 times of the corresponding compound with a methyl group when reacting with aniline but it is greatly enhanced to 47 times when reacting with benzylamine. The $(CH_3)_3Si$ group exhibits a strong positive deviation from the Taft plot, eqn. (2);[7,8] for the five compounds

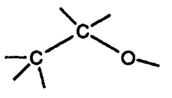
$$\log(k_X/k_H) = \rho^*\sigma^* \qquad (2)$$

in Table 4,† the straight line plot is fair with $\rho^* = 3.7$ (r = 0.951), and the experimental k_2 value for the $(CH_3)_3Si$ group is far above the straight line plot, deviating positively by ~ 10^3 times the k_2 value expected from the plot.†

Apeloig *et al.*,[1] have shown that silylmethyl [$(CH_3)_3SiCH_2$–] sulfonates solvolyze slower *via* the S_N1 mechanism, but faster *via* the S_N2 mechanism than their neopentyl [$(CH_3)_3CCH_2$–] analogues. Estimation of the bimolecular rate constant, k_2, with aniline under similar reaction conditions using the Taft σ^* value[8] of −0.30 for the *tert*-butyl group in eqn. (2) leads us to $k_2[(CH_3)_3Si]/k_2[(CH_3)_3C] \cong 40$ in agreement with their results of enhanced S_N2 rates for α-silyl substitution, albeit the rate enhancement is smaller than that for the solvolysis results. The rate enhancements of α-silyl substituted sulfonates (and benzoates) was attributed[2] to electronic geminal interactions; the geminal interactions between the C–O and C–Si bonds destabilize the ground state (GS) of α-silyl compounds,



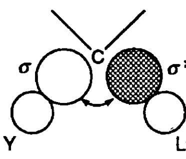
II



III

II, relative to that of the corresponding sulfonates (or benzoates), **III**. This effect disappears when the leaving group is chloride or bromide (or iodide). Similar geminal effects are also reported by Richard *et al.*;[9] electronic geminal interactions are strongly stabilizing in methoxymethyl fluoride and methoxymethyl methyl ether toward hydrolysis in comparison with methoxymethyl chloride which has a much weaker stabilizing geminal interaction.

Geminal interactions between two σ bonds are known to be destabilizing since the delocalization is σ–σ* antibonding, in contrast to the well-known π–π* bonding delocalization in π-conjugated systems.[10] Destabilizing geminal interactions are found to be especially strong between a bond with a strong donor (Y) (*e.g.* Me_3Si) and that with a strong acceptor (LG) (*e.g.* F, $OCOC_6H_4$ or $OSO_2C_6H_4$), **IV**.[2] This combination of a



IV

strong donor Y with a strong acceptor LG affords a strongest destabilizing geminal pair due to a strongest antibonding geminal interaction or overlap between strongly polarized bonding orbital $\sigma_{(C-Y)}$ and strongly polarized antibonding orbital $\sigma^*_{(C-LG)}$ toward C;[11] these strong polarizations lead to a large sp^3 hybridized bond-orbital size at the carbon end of both the C–Y and C–LG bonds,[11] which in turn lead to a large overlap ($S_{\sigma\sigma^*}$) with efficient charge transfer from σ_{C-Y} toward σ^*_{C-LG}, weakening the σ^*_{C-LG} bond. The charge transfer energy, E_{CT}, is proportional to a square of overlap integral $(S_{\sigma\sigma^*})^2$, and inversely proportional to the energy gap, $\Delta\varepsilon = \varepsilon_{\sigma^*} - \varepsilon_{\sigma}$, eqn. (3).[12] Since an electron donor elevates the σ level

$$E_{CT} \cong \frac{H_{\sigma\sigma^*}^{\;2}}{\Delta\varepsilon}; \text{ where } H_{\sigma\sigma^*} \propto S_{\sigma\sigma^*} \qquad (3)$$

and an electron acceptor depresses the σ* level, the above combination of a strong donor Y with a strong acceptor LG leads not only to the largest $S_{\sigma\sigma^*}$ value but also to the smallest $\Delta\varepsilon$ value, resulting in the most efficient charge transfer. This antibonding geminal delocalization will destabilize the ground state and facilitate bond cleavage of the C–LG bond in the TS. Other types of donor–acceptor combination for Y and LG

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† One of the referees raised doubt about using the σ^* values taken from ref. 8, especially the use of $\sigma^* = -0.81$ for $(CH_3)_3Si$. It was suggested that $\sigma^* \cong -0.4$ might be more appropriate for the group. However the use of this value leads only to a lowering of rate enhancement to 10^2 instead of 10^3. The linearity of the Taft plot does not change since the $(CH_3)_3Si$ group is not included in the plot.

Table 3 Cross-interaction constants, ρ_{XZ} and β_{XZ}, for some nucleophilic substitution reactions

Reaction	Solvent	T/°C	ρ_{XZ}	β_{XZ}
1. $XC_6H_4NH_2 + CH_3OSO_2C_6H_4Z$[3]	MeOH	65	0.30	0.18
	MeCN	65	0.32	0.20
2. $XC_6H_4NH_2 + CH_3CH_2OSO_2C_6H_4Z$[3]	MeOH	65	0.33	0.19
	MeCN	65	0.34	0.21
3. $XC_6H_4NH_2 + (CH_3)_2CHOSO_2C_6H_4Z$[4]	MeCN	65	0.10	0.06
4. $XC_6H_4NH_2 + C(CH_3)_3CHC_6H_5OSO_2C_6H_4Z$[a]	MeOH	35	0.0	0.0
5. $XC_6H_4NH_2 + C_6H_5CH_2OSO_2C_6H_4Z$[3]	MeOH	30	−0.10	−0.06
6. $XC_6H_4NH_2 + (CH_3)_3SiCH_2OSO_2C_6H_4Z$[b]	MeOH	65	0.31 (0.999)[c]	0.18 (0.993)[c]
	MeCN	65	0.33 (0.999)	0.20 (0.991)
$XC_6H_4CH_2NH_2 + (CH_3)_3SiCH_2OSO_2C_6H_4Z$[b]	MeCN	65	0.08 (0.999)	0.12 (0.999)

[a] I. Lee, M. S. Choi and H. W. Lee, to be published. [b] This work. [c] The values in parentheses are the correlation coefficients at 99% confidence level.

Table 4 The k_2 (10^4 dm^3 mol^{-1} s^{-1}) values for the reactions of $ROSO_2C_6H_5$ with aniline (AN) and benzylamine (BA) at 65.0 °C in MeCN ($R = CH_2Y$)

R	(Y)	k_2 (AN)	k_2 (BA)	$\sigma^*_{(Y)}$[a]
CH_3[3]	H	7.47	47.3	0.49
CH_3CH_2[3]	CH_3	0.676	1.48	0.0
$(CH_3)_2CH$[4]	$[(CH_3)_2]$	0.411	1.82	(0.0)
$(CH_3)_3SiCH_2$[b]	$(CH_3)_3Si$	1.69	70.2	−0.81
$C_6H_5CH_2$	C_6H_5	137[c]		0.60
CH_2CHCH_2	CH_2CH	(100)[d]		0.56

[a] Taft's polar substituent constant for Y (ref. 8). [b] This work. [c] Extrapolated from k_2 values at 35.0, 45.0 and 55.0 °C in MeCN; J. H. Lee, Ph.D. Thesis, Hanyang Univ., 1992. [d] Estimated value from k_2 at 45.0 °C, H. K. Oh, H. J. Koh and I. Lee, *J. Chem. Soc., Perkin Trans. 2*, 1991, 1981.

invariably lead to a more stabilized or less destabilized GS relative to that of the strong donor Y–strong acceptor LG combination. Thus when both Y and LG are strong acceptors, *e.g.* methoxymethyl fluoride, the GS of the compound is stabilized due to inefficient σ–σ* geminal antibonding delocalization (or overlap) relative to the compound with a strong donor Y and a strong acceptor LG of a cleaving C–LG bond.

If the enhanced rate for the reactant with a trimethylsilyl group were due to such a ground state destabilization arising from antibonding geminal interactions, the relative rates in Table 4 should indicate that the effect of α-silyl substitution on the precursor, GS, is destabilizing (and hence the rate is faster) relative to methyl ($Y = CH_3$ in $R = CH_2Y$) whereas it is stabilizing (and hence the rate is slower) relative to hydrogen ($Y = H$ in $R = CH_2Y$). This is in agreement with the conclusion reached by Apeloig *et al.*,[2b] on the effect of α-silyl substitution from the (S_N1) solvolysis studies of 2-trimethylsilyl-2-adamantyl *p*-nitrobenzoate. Thus the ground state destabilization effect due to geminal interaction is important not only for S_N1 but also for S_N2 reactivities and due care must be exercised in evaluating and interpreting substituent effects on S_N1 as well as on S_N2 reactivities. In contrast to the reactions with aniline and also to the results reported on the effect of stability at a carbenium ion centre the relative rates in Table 4 reveal that α-silyl substitution is destabilizing and the rate is enhanced relative to both hydrogen ($R = CH_3$, $Y = H$) and methyl ($R = CH_3CH_2$, $Y = CH_3$). This could be ascribed to the strong nucleophilicity of benzylamine affecting TS structure, which is an additional effect on the reactivity not related to the ground state stability of the reactant.

We conclude that the reactions of trimethylsilylmethylene arenesulfonates, **1**, with anilines and benzylamines proceed *via* the S_N2 mechanism with a relatively tight TS, and the ground state destabilization effect of the α-silyl group due to geminal interactions [between C–Si(Me)$_3$ and C–O] causes rate enhancement similar to the rate enhancement reported for S_N1 reactions.

Experimental

Materials.—Merck GR acetonitrile was used after three distillations. Merck GR methanol was used without further purification. Substrates, trimethylsilylmethyl arenesulfonates, were prepared by reacting Aldrich GR trimethylsilylmethanol with benzenesulfonyl chlorides.[13] The NMR (Bruker AC-100) spectroscopic data are as follows (*J*-values in Hz). Trimethylsilylmethyl benzenesulfonate (liquid) δ 0.03 [9 H, s, $Si(CH_3)_3$], 3.63 (2 H, s, CH_2) and 7.51–7.91 (5 H, m, Ar); trimethylsilylmethyl toluene-*p*-sulfonate (liquid) δ 0.05 [9 H, s, $Si(CH_3)_3$], 2.45 (3 H, s, CH_3), 3.62 (2 H, s, CH_2), 7.34 (2 H, d, *J* 8.2, *m*) and 7.78 (2 H, d, *J* 8.1, *o*); trimethylsilylmethyl chlorobenzene-*p*-sulfonate (m.p. 53–54 °C) δ 0.07 [9 H, s, $Si(CH_3)_3$], 3.65 (2 H, s, CH_2), 7.53 (2 H, d, *J* 8.8, *m*) and 8.84 (2 H, s, *J* 8.6, *o*); trimethylsilylmethyl *p*-nitrobenzene-*p*-sulfonate (m.p. 107–108 °C) δ 0.09 [9 H, s, $Si(CH_3)_3$], 3.73 (2 H, s, CH_2), 8.09 (2 H, d, *J* 9.8, *m*) and 8.42 (2 H, d, *J* 8.9, *o*).

Kinetics.—Rates were measured conductometrically and k_2 values were determined with at least four nucleophile concentrations using the procedure described previously.[4,14] The k_2 values were reproducible to within 3%.

Product Analysis.—The analysis of final products was difficult due to partial decomposition during product separation and purification. We therefore analysed the reaction mixture by NMR (JEOL 400 MHz) at appropriate intervals under exactly the same reaction conditions as the kinetic measurements in CD_3CN at 65.0 °C. Initially we found a peak for CH_2 in the reactant, $Me_3SiCH_2OSO_2C_6H_4$-*p*-NO_2, at 3.76 ppm, which was gradually reduced, and a new peak for CH_2 in the product, $Me_3SiCH_2NHC_6H_5$, grew at 2.55 ppm as the reaction proceeded. No other peaks or complications were found during the reaction except the two peak height changes indicating that the reaction proceeds with no other side reactions. The reactions with benzylamine had two corresponding peaks at 3.64 and 2.06 ppm.

Acknowledgements

We thank the Korea Science and Engineering Foundation and the Ministry of Education for support of this work.

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Paper 3/02784H
Received 17*th May* 1993
Accepted 17*th August* 1993