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NUCLEOPHILIC SUBSTITUTION REACTIONS OF ISOPROPYL BENZENESULPHONATES WITH ANILINES AND BENZYLAMINES

HYUCK KEUN OH AND YOUNG BONG KWON
Department of Chemistry, Chonbuk National University, Chonju, 560-756, Korea
AND
IKCHOON LEE*
Department of Chemistry, Inha University, Inchon 402-751, Korea

The nucleophilic substitution reactions of isopropyl arenesulphonates with anilines and benzylamines in acetonitrile at 65·0 °C were investigated. The cross-interaction constants ρ_{XZ} (and β_{XZ}) between substituents in the nucleophile (X) and leaving group (Z) are positive and relatively small. The transition state (TS) variation is consistent with that predicted by the More O'Ferrall–Jencks diagram, as expected from the positive ρ_{XZ}. The small magnitude of ρ_{XZ} correctly reflects a relatively loose TS structure, in contrast to the tight TS for ethyl (or methyl) derivatives under similar reaction conditions.

INTRODUCTION

It is well known that the hydrolyses of the α-methylated series of alkyl halides, i.e. methyl, ethyl, isopropyl and *tert*-butyl, show a rate change from a gradual reduction for the first three to a sudden dramatic increase for the last due to a change in mechanism from S_N2 to S_N1. The isopropyl derivative in this series tends to have some S_N1 character within a spectrum of S_N1–S_N2 mechanisms.[1] It has been shown that the isopropyl derivatives solvolyse by S_N1 through a carbocation intermediate or by S_N2 through nucleophilic solvent assistance, depending on the solvent.[1c–e]

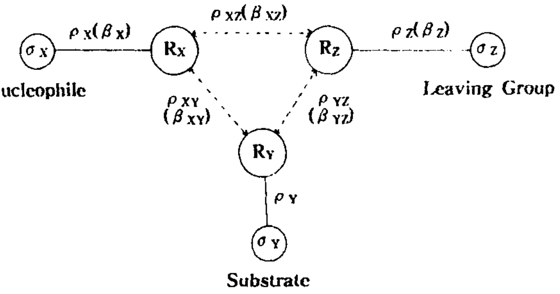
We have reported the application of cross-interaction constants, ρ_{ij}:

$$\log(k_{ij}/k_{HH}) = \rho_i\sigma_i + \rho_j\sigma_j + \rho_{ij}\sigma_i\sigma_j \qquad (1)$$

where i and j denote the substituents in the nucleophile (X), substrate (Y) and leaving group (Z), $i, j =$ X, Y or Z, to the investigation of the mechanisms of organic reactions in solution.[2] We have shown that the intensity of interaction between substituents X and Z in the transition state (TS), indicated by the magnitude of the cross-interaction constants $|\rho_{XZ}|$, varies inversely with the distance between the two reaction centres in the nucleophile and leaving group, r_{XZ} (Scheme 1). In addition, if the sign of ρ_{XZ}, defined by

$$\rho_{XZ} = \frac{\partial^2 \log k_{XZ}}{\partial\sigma_X\sigma_Z} = \frac{\partial\rho_Z}{\partial\sigma_X} = \frac{\partial\rho_X}{\partial\sigma_Z} \qquad (2)$$

is positive a stronger nucleophile ($\delta\sigma_X < 0$) and a better leaving group ($\delta\sigma_Z > 0$) lead to an earlier TS with a lower degree of bond formation ($\delta\rho_X > 0$) and breaking ($\delta\rho_Z < 0$). Conversely if ρ_{XZ} is negative, a stronger nucleophile and a better leaving group lead to a later TS.



Scheme 1

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* Author for correspondence.

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In this paper, we report the results of kinetic studies on the nucleophilic substitution reactions of isopropyl arenesulphonates (IPA) with anilines (AN) and benzylamines (BA) in acetonitrile at 65·0 °C:

$$2XRNH_2 + (CH_3)_2CHOSO_2C_6H_4Z \xrightarrow[65\cdot0\,^{\circ}C]{MeCN} (CH_3)_2CHNHRX + XRNH_3^+ + {}^-OSO_2C_6H_4Z \quad (3)$$

$R = C_6H_4$ or $C_6H_4CH_2$
$X = p\text{-}CH_3O$, $p\text{-}CH_3$, H or $p\text{-}Cl$
$Z = p\text{-}CH_3$, H, $p\text{-}Cl$ or $p\text{-}NO_2$

We discuss the TS structures based on the sign and magnitude of the cross-interaction constants ρ_{XZ}.

RESULTS AND DISCUSSION

The second-order rate constants, k_2, for the reactions of isopropyl arenesulphonates with anilines and benzylamines are summarized in Table 1. The rate sequence of methyl > ethyl > isopropyl is followed for aniline nucleophiles, which is consistent with direct displacement reactions (S_N2) of the simple alkyl systems.[3]

For the benzylamine nucleophile, the rates for ethyl

Table 1. Second-order rate constants, k_2 ($10^4\,l\,mol^{-1}\,s^{-1}$), for reactions of Z-substituted isopropyl benzenesulphonates with X-substituted anilines and benzylamines in acetonitrile at 65·0 °C

		Z			
Nucleophile	X	p-CH$_3$	H	p-Cl	p-NO$_2$
Aniline	p-CH$_3$O	0·802	1·13	2·51	9·88
	p-CH$_3$	0·494	0·728	1·60	6·39
	H	0·269	0·411 (7·47, 0·676)[a]	0·902	3·54
	p-Cl	0·136	0·208	0·469	1·92
Benzylamine	p-CH$_3$O	2·71	3·80	7·82	27·8
	p-CH$_3$	1·88	2·74	5·56	20·5
	H	1·24	1·82 (47·3, 1·48)[a]	3·76	13·7
	p-Cl	0·758	1·11	2·28	8·45

[a] The pairs in parentheses are for methyl and ethyl benzenesulphonates, respectively, under the same reaction conditions.

Table 2. Hammett (ρ_X and ρ_Z)[a] and Brønsted (β_X[b] and β_Z[c]) coefficients

Nucleophile	Z	ρ_X	β_X	X	ρ_Z	β_Z
Aniline	p-CH$_3$	−1·53 (0·995)[d]	0·56 (0·994)	p-CH$_3$O	1·17 (0·997)	−0·32 (0·999)
	H	−1·46 (0·997)	0·53 (0·996)	p-CH$_3$	1·19 (0·998)	−0·32 (0·998)
	p-Cl	−1·45 (0·996)	0·52 (0·995)	H	1·19 (0·998)	−0·33 (0·997)
	p-NO$_2$	−1·42 (0·995)	0·51 (0·994)	p-Cl	1·22 (0·998)	−0·33 (0·997)
Benzylamine	p-CH$_3$	−1·09 (0·994)	0·98 (0·998)	p-CH$_3$O	1·08 (0·998)	−0·28 (0·999)
	H	−1·06 (0·996)	0·97 (0·998)	p-CH$_3$	1·10 (0·999)	−0·29 (0·999)
	p-Cl	−1·05 (0·996	0·96 (0·999)	H	1·11 (0·998)	−0·29 (0·999)
	p-NO$_2$	−1·03 (0·997)	0·96 (0·998)	p-Cl	1·12 (0·998)	−0·29 (0·999)

[a] The σ values were taken from Ref. 5.
[b] The pK_a values were taken from Refs 6–8.
[c] The pK_a values are for methyl transfer.[9]
[d] Correlation coefficients.

and isopropyl are similar, the latter being slightly greater. This could be an indication that the reaction of the isopropyl derivative with benzylamine proceeds with some S_N1 character. The rates are accelerated by a stronger nucleophile ($X = p$-CH_3O) and by a better leaving group ($Z = p$-NO_2), as expected from a normal S_N2 reaction.[1a,b]

The Hammett (ρ_X and ρ_Z) and Brønsted coefficients (β_X and β_Z) are given in Table 2 and the cross-interaction constants (ρ_{XZ}) (and β_{XZ}) in Table 3. It is noted that ρ_{XZ} and β_{XZ} are positive so that a stronger nucleophile ($X = p$-CH_3O) and a better leaving group ($Z = p$-NO_2) lead to an earlier TS, i.e. both ρ_Z and $|\rho_X|$ are smaller with a stronger nucleophile and a better leaving group, respectively; this is consistent with those predicted with a More O'Ferrall–Jencks diagram[10] (Figure 1).

Table 3 gives some ρ_{XZ} and β_{XZ} values for comparison. The magnitude of ρ_{XZ} and β_{XZ} for the isopropyl [equation (3)] derivatives is similar to that of the corresponding reactions of benzyl benzenesulphonates (first entry). This indicates that the reactions of both isopropyl and benzyl derivatives proceed via an S_N2 mechanism with a loose TS in which bond breaking has progressed to a much greater extent compared with the relatively early stage of bond making.[11] Application of the modified Grunwald–Winstein equation:[12]

$$\log(k/k_0) = mY + lN \qquad (4)$$

to the solvolysis of isopropyl systems led Schadt *et al.*[1c] to l values of 0·38–0·49,[1c] which is significantly greater than value of 0·0 expected for S_N1 reactions,[13] so that the solvolysis is considered to proceed by the S_N2 pathway. Since benzylamine is more basic, and hence is a stronger nucleophile, than aniline and ρ_{XZ} and β_{XZ} are positive, we should expect a lesser degree of bond breaking with benzylamine, leading to a tighter TS with a greater β_{XZ}. This TS variation is also consistent with that predicted with a More O'Ferrall–Jencks diagram[10] (Fig. 1).

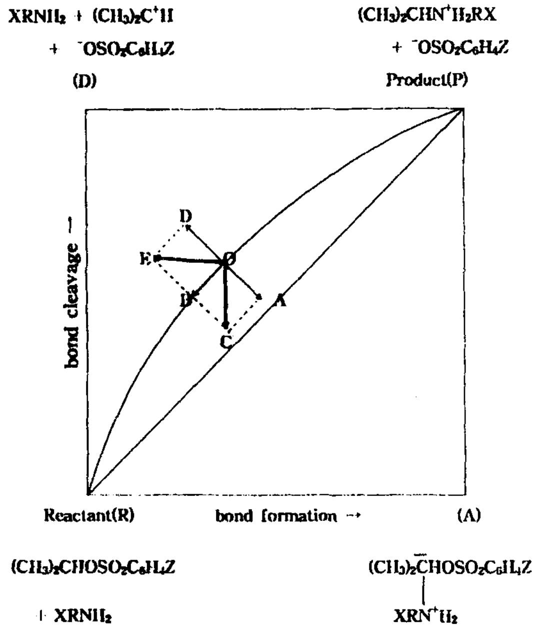

Figure 1. More O'Ferrall–Jencks diagram showing TS variations with substituent changes ($R = C_6H_4$ or $C_6H_4CH_2$). A stronger nucleophile (O → B and O → A) and a better leaving group (O → B and O → D) lead to decreases in bond cleavage (O → C) and bond formation (O → E), respectively

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

Reaction	Solvent	Temperature (°C)	ρ_{XZ}[a]	β_{XZ}[b]
$XC_6H_4NH_2 + YC_6H_4CH_2OSO_2C_6H_4Z$	MeOH	30·0	−0·10	−0·06
$XC_6H_4NH_2 + CH_3OSO_2C_6H_4Z$	MeOH	65·0	0·30 (0·32)[c]	0·18 (0·20)[c]
$XC_6H_4NH_2 + C_2H_5OSO_2C_6H_4Z$	MeOH	65·0	0·33 (0·34)[c]	0·19 (0·21)[c]
$XC_6H_4CH_2NH_2 + CH_3OSO_2C_6H_4Z$	MeCN	65·0	0·18	0·26
$XC_6H_4CH_2NH_2 + C_2H_5OSO_2C_6H_4Z$	MeCN	65·0	0·19	0·28
$XC_6H_4NH_2 + CH_2{=}CHCH_2OSO_2C_6H_4Z$	MeCN	45·0	0·37[d]	0·21[d]
$XC_6H_4NH_2 + CH_2{=}C(CH_3)CH_2OSO_2C_6H_4Z$	MeCN	45·0	0·40[d]	0·24[d]
$XC_5H_4NH_2 + (CH_3)_2CHOSO_2C_6H_4Z$	MeCN	65·0	0·10[e]	0·06[e]
$XC_6H_4CH_2NH_2 + (CH_3)_2CHOSO_2C_6H_4Z$	MeCN	65·0	0·06[e]	0·04[e]

[a] The σ values were taken from Ref. 5.

[b] The pK_a values of BAs were taken from Ref. 6.

[c] The values in parentheses are those in acetonitrile.

[d] Ref. 16.

[e] This work.

The smaller ρ_{XZ} value observed for benzylamines in Table 3 is due to a fall-off factor of *ca* 1/2 by an extra intervening CH_2 group[14] in the nucleophile, benzylamine, which is absent in β_{XZ}. The magnitude of ρ_{XZ} and β_{XZ} in Table 2 is about one third of those for the S_N2 reactions with a tight TS (entries 2 and 3 in Table 3), so that in the reaction of isopropyl derivatives the TS has a loose structure with significant S_N1 character within the spectrum of S_N1–S_N2 variation. This conclusion, based on the magnitude of ρ_{XZ} and β_{XZ}, is consistent with the generally accepted S_N mechanism for isopropyl derivatives.

EXPERIMENTAL

Materials. Analytical-reagent grade chemicals were used throughout; the substrates were prepared by the well known method[15] with Aldrich isopropyl alcohol and benzenesulphonates. The nucleophiles, aniline and benzylamines, were purchased from Tokyo Kasei and redistilled or recrystallized before use. Acetonitrile from Merck was purified by three distillations.

The NMR spectral data for the synthesized substrates were as follows: isopropyl benzenesulphonate, liquid, δ 1·25 (6H, d, $J = 6{\cdot}3$ Hz, $2CH_3$), 4·75 (1H, m, $J = 6{\cdot}3$ Hz, CH), 7·43–7·99 (5H, m, aromatic); isopropyl tosylate, liquid, δ 1·23 (6H, d, $J = 6{\cdot}3$ Hz, $2CH_3$), 2·41 (3H, t, $PhCH_3$), 4·70 (1H, m, $J = 6{\cdot}3$ Hz, CH), 7·27–7·81 (4H, m, aromatic); isopropyl *p*-chlorobenzenesulphonate, liquid, δ 1·23 (6H, d, $J = 6{\cdot}3$ Hz, $2CH_3$), 4·71 (1H, m, $J = 6{\cdot}3$ Hz, CH), 7·43–7·84 (4H, m, aromatic); and isopropyl *p*-nitrobenezenesulphonate, m.p. 40–41 °C, δ 1·33 (6H, d, $J = 6{\cdot}3$ Hz, $2CH_3$), 4·89 (1H, m, $J = 6{\cdot}3$ Hz, CH), 8·06–8·52 (4H, m, aromatic).

Product analysis. $(CH_3)_2CHOSO_2C_6H_4CH_3$ (0·05 mol) was reacted with aniline (0·5 mol) and with benzylamine (0·5 mol) under the same reaction conditions as used in the kinetic measurements. The reaction products were left for more than 2 days, after which the solvent was removed under low pressure. The salts were washed with diethyl ether and water and the anilides were separated by column chromatography. The analytical data were as follows: $C_6H_5NHCH(CH_3)_2$ liquid, $R_F = 0{\cdot}42$, δ 1·21 (6H, d, $J = 6{\cdot}3$ Hz, $2CH_3$), 3·18 (1H, broad, NH), 3·64 (1H, m, $J = 6{\cdot}3$ Hz, CH), 6·56–7·33 (5H, m, aromatic); $C_6H_5CH_2NHCH(CH_3)_2$, liquid, $R_F = 0{\cdot}43$, δ 1·25 (6H, d, $J = 6{\cdot}3$ Hz, $2CH_3$), 2·17 (2H, s, CH_2), 4·03 (1H, broad, NH), 4·61 (1H, m, $J = 6{\cdot}3$ Hz, CH), 6·89–7·63 (5H, m, aromatic); $C_6H_5NH_3^{+}\,{}^{-}OSO_2\ C_6H_4CH_3$, m.p. 226–228 °C, $R_F = 0{\cdot}01$, δ 2·26 (3H, s, CH_3), 4·92 (3H, broad, NH_3^+), 6·93–7·56 (9H, m, aromatic). and $C_6H_5CH_2NH_3^{+}\,{}^{-}OSO_2C_6H_4CH_3$, m.p. 202–204 °C, $R_F = 0{\cdot}02$, δ 2·37 (3H, s, CH_3), 3·45 (3H, broad, NH_3^+), 4·35 (2H, s, CH_2), 7·01–7·45 (9H, m, aromatic).

Kinetic procedures. Reaction rates were followed by a conductimetric method and the rate constants were determined as described previously.[16]

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