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CROSS-INTERACTION CONSTANTS AS A MEASURE OF THE TRANSITION STATE STRUCTURE (PART V).* THE TRANSISTION STATE STRUCTURE FOR REACTIONS OF PHENACYL BENZENESULPHONATES WITH BENZYLAMINES IN METHANOL

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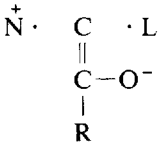
ABSTRACT

The kinetics of reactions of phenacyl benzenesulphonates with benzylamines were investigated in methanol at 45·0 °C and the cross-interaction constants λ_{XY}, λ_{YZ} and β_{XZ} were determined in order to elucidate the transition-state structure. The unusually small magnitude of λ_{XY} can only be accounted for by the resonance 'shunt' effect of the α-CO group of the phenacyl system. Large $|\lambda_{YZ}|$ values indicate a small degree of bond breaking whereas relatively large $|\beta_{XZ}|$ values compared with those for the dissociative S_N2 reaction indicate a relatively tight transition state for the reactions. Further, the similar magnitudes of β_{XZ} values compared with those of the corresponding aniline nucleophile series suggest a similar transition-state structure for the two aromatic amine nucleophile series

In our previous studies we have shown that the α-CO group of the phenacyl derivatives participates in S_N2-type reactions as an enolate form (I),



$$\overset{+}{N}\cdot\ \begin{array}{c} C \\ \| \\ C-O^- \\ | \\ R \end{array}\ \cdot L$$

I

lending extra stabilization to the transition state (TS);[1] this, however, does not lead to an interaction between substituents X in the nucleophile N and Y in the substrate R, but causes the electronic charges on the reaction centre carbon due to the charge transmission in the TS leaking to the α-CO group with no cross-interaction between the two substituents.[1] This remarkable electronic 'shunt' phenomenon was found to be reflected in the unusually small

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* For Part IV, see ref. 3.

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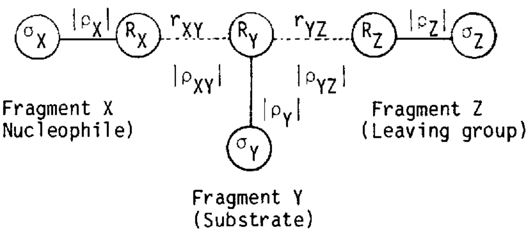

Scheme 1. Typical S_N2 transition state

Hammett-type cross-interaction constants $|\rho_{XY}|$, $i, j = X, Y$ in the equation[1]

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

The Hammett-type cross-interaction parameters, ρ_{ij} in general, are used as a measure of indirect interactions between substituents i and j through reaction centres R_i and R_j[1,2] (Scheme 1), whereas the Brønsted-type-cross-interaction constants, β_{ij} in equation (2), represent a more direct measure of interactions between reaction centres R_i and R_j and hence a direct measure of the distance r_{ij} in the TS.[3]

$$\log(k_{ij}/k_{HH}) = \beta_i\,\Delta pK_i + \beta_j\,\Delta pK_j + \beta_{ij}\,\Delta pK_i\,\Delta pK_j \tag{2}$$

The mixed Hammett–Brønsted-type parameters, λ_{ij} in the equation,

$$\begin{aligned}\log(k_{ij}/k_{HH}) &= \rho_i\sigma_i + \beta_j\,\Delta pK_j + \lambda_{ij}^{(j)}\sigma_i\,\Delta pK_j \\ &= \beta_i\,\Delta pK_i + \rho_j\sigma_j + \lambda_{ij}^{(i)}\,\Delta pK_i\sigma_j\end{aligned} \tag{3}$$

can also be used as a measure of the TS structure for reactions involving substituent changes in one fragment only,[3] e.g. in the substrate.

In this paper, we report the results of a kinetic investigation of the nucleophilic substitution reaction of phenacyl benzenesulphonates with benzylamines (BA) in methanol:

$$\begin{aligned}2XC_6H_4CH_2NH_2 + YC_6H_4COCH_2OSO_2C_6H_4Z \xrightarrow[45\cdot0\,^{\circ}C]{MeOH} &YC_6H_4COCH_2NHCH_2C_6H_4X \\ &+ XC_6H_4CH_2NH_3^+ + {}^-OSO_2C_6H_4Z\end{aligned} \tag{4}$$

$X = p\text{-}CH_3O,\ p\text{-}CH_3,\ H,\ p\text{-}Cl$

$Y = H,\ p\text{-}Cl,\ p\text{-}NO_2$

$Z = p\text{-}CH_3,\ H,\ p\text{-}Cl,\ m\text{-}NO_2$

Our main interest is to elucidate the TS structure in light of the magnitudes of various cross-interaction constants, with special emphasis on the electronic 'shunt' phenomenon in the phenacyl system involving the enolate form I.[1] A comparison of the cross-interaction parameters is made with those for the reactions of phenacyl benzenesulphonates and anilines (AN)[1c] in order to examine the effect of nucleophilicity on the TS structure.

RESULTS AND DISCUSSION

The second-order constants, k_2, for the reactions of phenacyl benzenesulphonates with BA in methanol at 45·0 °C are summarized in Table 1. The rates are ca 20 times faster than those for the corresponding reactions with AN[1c] owing to the increase in the nucleophilicity. Other

Table 1. Second-order rate constants, k_2 ($\times 10^3 \, \mathrm{l\,mol^{-1}\,s^{-1}}$), for the reactions of phenacyl benzenesulphonates with benzylamines in methanol at 45·0 °C

		X			
Y	Z	p-CH$_3$O	p-CH$_3$	H	p-Cl
H	p-CH$_3$	13·0	10·5	7·81	5·22
	H	18·2	15·1	11·2	7·60
	p-Cl	31·2	26·0	19·1	13·2
	m-NO$_2$	95·5	80·0	60·3	43·5
p-Cl	p-CH$_3$	17·6	14·3	10·7	7·20
	H	24·0	20·0	15·1	10·2
	p-Cl	37·2	32·0	24·0	17·1
	m-NO$_2$	110	92·9	70·5	50·7
p-NO$_2$	p-CH$_3$	72·4	61·2	46·0	31·7
	H	85·1	70·8	54·3	37·6
	P-Cl	106	89·9	67·6	48·4
	m-NO$_2$	166	141	108	78·5

Table 2. Hammett and Brønsted coefficients, ρ_X and β_X ($=\beta_N$), for the reactions of phenacyl benzenesulphonates with benzylamines in methanol at 45·0 °C[a,b]

	Z							
	p-CH$_3$		H		p-Cl		m-NO$_2$	
Y	ρ_X	β_X	ρ_X	β_X	ρ_X	β_X	ρ_X	β_X
H	−0·79	0·76	−0·76	0·74	−0·75	0·73	−0·68	0·66
	(−2·08)	(0·75)	(−1·99)	(0·72)	(−1·95)	(0·70)	(−1·78)	(0·65)
p-Cl	−0·77	0·74	−0·74	0·73	−0·70	0·68	−0·67	0·65
	(−2·01)	(0·73)	(−1·95)	(0·70)	(−1·88)	(0·68)	(−1·74)	(0·63)
p-NO$_2$	−0·72	0·71	−0·70	0·69	−0·68	0·67	−0·65	0·63
	(−1·89)	(0·68)	(−1·81)	(0·66)	(−1·80)	(0·65)	(−1·68)	(0·61)

[a] For all reaction series the correlation coefficients were better than 0·998.

[b] Values in parentheses[1c] are those for the reactions with anilines in methanol at 45·0 °C.

reactivity trends are similar for the two nucleophile series; the rate increases with a more electron-withdrawing substituent both in the leaving group, e.g. Z = m-NO$_2$, and in the substrate, e.g. Y = p-NO$_2$, and with a more electron-donating substituent in the nucleophile, e.g. X = p-CH$_3$O, for reactions with both BA and AN.

Simple Hammett and Brønsted coefficients, ρ_X and β_X($=\beta_N$), are given in Table 2. As we have pointed out,[3] the magnitudes of ρ_X for BA are less than half of those for the AN series owing to an extra non-conjugating CH$_2$ group between the ring and the reaction centre R$_X$, i.e. the N atom in BA, which is, in general, known to reduce the intensity of interaction between a substituent, X, and the reaction centre, R$_X$, by more than a factor of two. In contrast, however, the magnitudes of β_X are remarkably similar for the two nucleophile series of BA and AN, indicating that the degree of bond formation in the TS is, in reality, very similar. These behaviours of the magnitudes of ρ_X and β_X are consistent with the interrelationships in equation

(5a):

$$\rho_i = \rho_e^i \beta_i \tag{5a}$$

$$\rho_{ij} = \rho_e^i \rho_e^j \beta_{ij} \tag{5b}$$

where $i = \mathrm{X}$ and $\rho_e^i = \Delta \mathrm{p}K_i/\sigma_i$. For the approximately same β_X, i.e. $\beta_\mathrm{X}(\mathrm{AN}) \approx \beta_\mathrm{X}(\mathrm{BA})$, the ρ_X values for the AN series should be ca 2·6 times greater than those of the BA series (Table 2), since the use of equation (5a) gives

$$\frac{\rho_\mathrm{X}(\mathrm{AN})}{\rho_\mathrm{X}(\mathrm{BA})} = \frac{\rho_e^\mathrm{X}\beta_\mathrm{X}(\mathrm{AN})}{\rho_e^\mathrm{X}\beta_\mathrm{X}(\mathrm{BA})} \approx \frac{\rho_e^\mathrm{X}(\mathrm{AN})}{\rho_e^\mathrm{X}(\mathrm{BA})} = \frac{-2{\cdot}77}{-1{\cdot}06} \approx 2{\cdot}6$$

We note that the sign of $\beta_\mathrm{X}(>0)$ is opposite to that of $\rho_\mathrm{x}(<0)$, since ρ_e^X is negative,* in equation (5a).

The Hammett and Brønsted coefficients for leaving group changes, ρ_Z and $\beta_\mathrm{Z}(=\beta_{\mathrm{lg}})$, for reaction (4) are summarized in Table 3. In the determination of β_Z, we used the methyl transfer p*K* values, $\mathrm{p}K^{\mathrm{CH_3}}$,[6] for both the BA and the AN series. Here again the signs of ρ_Z and β_Z differ owing to the negative ρ_e^Z value $(-2{\cdot}99)$ in equation (5a), where $i = \mathrm{Z}$. The magnitude of β_Z is approximately one third of $|\rho_\mathrm{Z}|$ since $\rho_e^\mathrm{Z} \approx -3$.[6] In striking contrast to the large difference in $|\rho_\mathrm{X}|$ between the BA and the AN series in Table 2, both the $|\rho_\mathrm{Z}|$ and $|\beta_\mathrm{Z}|$ values are similar between the two nucleophile series, since the leaving groups are the same ($^-\mathrm{OSO_2C_6H_4Z}$) and apparently a nearly equal degree of bond breaking is involved in the TS for the two nucleophile series (BA and AN).

The Hammett ρ_Y values are given in Table 4. The sign of ρ_Y is positive, indicating a greater degree of bond formation than bond breaking in the TS for the reaction series (4).[7] The magnitude of ρ_Y values differs very little between the BA and AN series. This is an indication that in both series a similar degree of bond formation and of bond breaking has been achieved with the former being more advanced than the latter.[7]

Multiple linear regression analysis of the rate constants k_2[7] using equations (1)–(3) gave the

Table 3. Hammett and Brønsted coefficients, ρ_Z and β_Z $(=\beta_{\mathrm{lg}})$, for the reactions of phenacyl benzenesulphonates with benzylamines in methanol at 45·0 °C[a,b]

	X							
	p-CH₃O		*p*-CH₃		H		*p*-Cl	
Y	ρ_Z	β_Z[c]	ρ_Z	β_Z	ρ_Z	β_Z	ρ_Z	β_Z
H	0·99	−0·33	1·01	−0·34	1·02	−0·34	1·10	−0·35
	(1·14)	(−0·38)	(1·19)	(−0·40)	(1·24)	(−0·41)	(1·31)	(−0·44)
p-Cl	0·91	−0·30	0·93	−0·31	0·93	−0·31	0·97	−0·32
	(1·03)	(−0·34)	(1·03)	(−0·34)	(1·09)	(−0·36)	(1·15)	(−0·39)
p-NO₂	0·41	−0·14	0·42	−0·14	0·42	−0·16	0·46	−0·18
	(0·42)	(−0·14)	(0·43)	(−0·14)	(0·47)	(−0·16)	(0·53)	(−0·18)

[a] For all reaction series the correlation coefficients were better than 0·998.

[b] Values in parentheses[1c] are those for the reactions with anilines in methanol at 45·0 °C.

[c] The p*K* values used in the determination of β_Z were those of methyl transfer reactions, i.e. $\mathrm{p}K^{\mathrm{CH_3}}$.[6]

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* The plot of $\Delta \mathrm{p}K_\mathrm{a} = \rho_e^\mathrm{X}\sigma_\mathrm{X}$ for aniline gave $\rho_e^\mathrm{X} = -2{\cdot}77$[4] and $\rho_e^\mathrm{X} = -1{\cdot}06$[5] for benzylamine. The pK_a values in these determinations were obtained from ref. 4.

Table 4. Hammett ρ_Y values for the reactions of phenacyl benzenesulphonates with benzylamines in methanol at 45·0 °C[a,b]

Z	X			
	p-CH_3O	*p*-CH_3	H	*p*-Cl
p-CH_3	0·59 (0·67)	0·60 (0·70)	0·61 (0·72)	0·62 (0·74)
H	0·53 (0·57)	0·53 (0·60)	0·54 (0·61)	0·55 (0·63)
p-Cl	0·42 (0·44)	0·43 (0·46)	0·43 (0·48)	0·44 (0·49)
m-NO_2	0·18 (0·16)	0·19 (0·18)	0·19 (0·19)	0·20 (0·20)

[a] Correlation coefficients >0·998.

[b] Values in parentheses[1c] are those for the reactions with anilines in methanol at 45·0 °C.[1c]

Table 5. Cross-interaction constants for the reactions of phenacylbenzenesul phonates with benzylamines in methanol at 45·0 °C[a,b]

Z	ρ_{XY}	λ_{XY}	X	ρ_{YZ}	λ_{YZ}[c]	Y	ρ_{XZ}	β_{XZ}[c]
p-CH_3	0·04 (0·14)	−0·03 (−0·05)	*p*-CH_3O	−0·51 (−0·63)	1·08 (0·99)	H	0·12 (0·32)	0·20 (0·20)
H	0·03 (0·11)	−0·04 (−0·04)	*p*-CH_3	−0·52 (−0·65)	0·82 (1·02)	*p*-Cl	0·11 (0·31)	0·18 (0·19)
p-Cl	0·02 (0·10)	−0·04 (−0·04)	H	−0·52 (−0·66)	0·82 (1·04)	*p*-NO_2	0·09 (0·23)	0·15 (0·14)
m-NO_2	0·02 (0·07)	−0·02 (−0·03)	*p*-Cl	−0·52 (−0·67)	0·83 (1·05)			

[a] Correlation coefficients >0·997.

[b] In the calculations of λ_{YZ} and β_{XZ}, the pK_a values for the leaving group (benzenesulphonates) used were the proton acidity, pK^{H^+}, values.[6]

three types of cross-interaction constants, ρ_{XY}, ρ_{YZ} and ρ_{XZ} and λ_{XY}, λ_{YZ} and β_{XZ}, as shown in Table 5. Here again we find large differences in $|\rho_{XY}|$ and $|\rho_{XZ}|$ but no difference in $|\rho_{YZ}|$ between the BA and AN series due to the intervening CH_2 group in BA. We note that signs of ρ_{XY} and λ_{XY} and of ρ_{YZ} and λ_{YZ} are opposite but those of ρ_{XZ} and β_{XZ} are the same, as expected from the correlation (5b), where *i*, *j* = X, Y or Z, since ρ_e^X and ρ_e^Z are both negative.

In contrast to the large difference in $|\rho_{XY}|$ and $|\rho_{XZ}|$ values between BA and AN series, we obtain similar values of $|\rho_{YZ}|$ for the two series (BA and AN). This shows that as long as the nucleophiles (*i* = X) are not involved in the correlation, the cross-interaction constants do not vary significantly between the two nucleophile series; hence the TS for the two series are very similar in reality, and it is only the intervening CH_2 group in BA that makes a large difference in the magnitude of Hammett-type cross-interaction constants ρ_{ij} from the corresponding values for the AN series. The values of $|\lambda_{XY}|$, $|\lambda_{YZ}|$ and $|\beta_{XZ}|$ are all similar for the two nucleophile series (BA and AN), indicating that these cross-interaction parameters are a more direct measure of the interactions between reaction centres R_X, R_Y and R_Z and hence a more direct measure of the TS structure.[3] The very small magnitude of λ_{XY} values (0·03–0·04) in Table 5 compared with those for the normal S_N2 reactions ($\lambda_{XY} \approx 0{\cdot}20$–$0{\cdot}27$)[3] may be partly due to the intervening C=O group in the phenacyl system, which should account for a decrease in $|\lambda_{XY}|$ of slightly more than a factor of two.[2h] There is a decrease in $|\lambda_{XY}|$ of a further factor of two, which can only be accounted for by the resonance 'shunt' phenomenon of the α-CO group.[1b,c] This phenomenon occurs in the phenacyl system, and hence the change of nucleophile from AN to BA should have little effect on the intensity of the 'shunt' as we find nearly the same $|\lambda_{XY}|$ values for BA and AN series in Table 5. The relatively large $|\rho_{YZ}|$ values (0·82–1·08) indicate that the degree of bond breaking is small compared with the normal S_N2 reactions, for which the $|\rho_{YZ}|$ values were 0·18–0·26.[3] The size of β_{XZ}, a measure of tightness (or looseness) of the TS, is nearly the same for the two nucleophile series, indicating very similar TS structures. The TS structure does seem to become loose with a more electron-withdrawing substituent in the substrate (e.g. Y = p-NO_2); the magnitudes of both β_X (Table 2) and β_Z (Table 3) tend to decrease with a more electron-withdrawing substituent in the substrate, but a net effect of looser TS (a smaller $|\beta_{XZ}|$) implies that the decrease in bond formation ($|\beta_X|$) is slightly greater than the decrease in bond breaking ($|\beta_Z|$).

EXPERIMENTAL

Materials

Anilines were purified by distillation or recrystallization,[2h] and benzylamines were purified by distillation.[2h] Phenacyl benzenesulphonates were prepared and purified as described.[1c] Reagent-grade methanol was used without further purification.

Rate constants

Rates were measured conductimetrically at 45·0 ± 0·1 °C. The conductivity was found to vary linearly with the concentration of the product solution, which was prepared using independently synthesized amides. Pseudo-first-order rate constant, k_1^{obs}, were determined by the Guggenheim method with a large excess of benzylamines and second-order rate constants, k_2, were obtained from the slope of a plot of k_1^{obs} vs [BA]:

$$k_1^{obs} = k_1 + k_2[BA]$$

where k_1 is the rate constant for methanolysis, which was found to be negligibly small compared with the second-order term, as evidenced by zero intercepts ($k_1 = 0$) in all cases.

Product analysis

Products were confirmed with TLC and IR analyses. Two reactants and one product gave three TLC spots. The three R_F values were found to agree with those determined independently (R_F values with a silica gel plate and 10% cyclohexane–dichloromethane as eluent were BA 0·67, p-$ClC_6H_4COCH_2OSO_2C_6H_5$ 0·63 and anilide 0·18).

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