Nucleophilic Substitution Reactions of Phenacyl Benzenesulphonates with Anilines in Methanol–Acetonitrile Mixtures[1]

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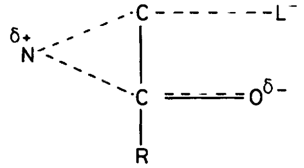
The nucleophilic substitution reactions of phenacyl benzenesulphonates with anilines in methanol–acetonitrile have been studied. A stronger nucleophile was found to cause less bond cleavage, while a better leaving group led to less bond formation, in complete agreement with predictions by the potential energy surface model. The reactions were also found to adhere to the Bell–Evans–Polanyi principle as well as the reactivity–selectivity principle, and hence constituted a good example of a thermodynamically controlled reaction series. Cross interaction constants, ρ_{ij}, for the reaction series were used to characterize the transition state structure. The α-carbonyl group was shown to provide a 'shunt' in the resonance in the transition state, which resulted in a remarkable decrease in the cross interaction between substituents in the nucleophile and those in the substrate. The magnitudes of ρ_{ij} indicated that in the transition state bond breaking had progressed very little but bond formation was substantial. Consideration of cross interaction constants led us to conclude that the involvement of a bridged transition state is unlikely.

The nucleophilic substitution reactions of α-carbonyl derivatives have attracted the attention of both theoretical[2] and experimental[3] organic chemists; however, many aspects of the reaction mechanism remain controversial and not well understood. A particular source of disagreement was the presence of a bridged transition state (TS) structure (**1**).

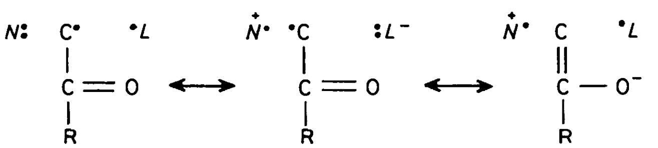


(**1**)

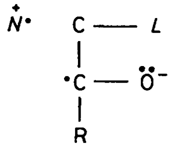
Although there appears to be a consensus of opinion as to the rate-enhancing effect of the α-carbonyl group, especially for strong, anionic nucleophiles, the reason behind it is poorly understood. Recently McLennan and Pross[4] applied the valence-bond configuration mixing (VBCM) model to explain the mechanism by which the rate-enhancing effect of the carbonyl group is transmitted to the reaction centre. As Dewar[5] had suggested, the α-carbonyl group was shown to stabilize the TS through resonance delocalization involving an enolate ion (**4**). McLennan and Pross argued that three configurations [reactant (**2**), product (**3**), and the enolate form of the carbanion (**4**)] suffice to express the TS structure for the S_N2 reactions of α-carbonyl compounds. However, the carbanion configuration can also accommodate a valence-bond structure (**5**), which would lead to bridging in the TS (**1**), as Winstein[6] suggested. Recently we have introduced mechanistic criteria based on the inverse distance dependence of the cross-interaction constant ρ_{ij} between substituents i and j [equation (i)].[7] The criteria have

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

been successfully applied to the rationalization of the various mechanistic details involved in nucleophilic substitution,[7a] elimination,[7b] identity reaction,[7b] and retentive displacement.[7c] We report here the results of our kinetic investigations of the nucleophilic substitution reactions of phenacyl benzenesulphonates with anilines in methanol–acetonitrile mixtures (Scheme).



(**2**) (**3**) (**4**)



(**5**)

$$2XC_6H_4NH_2 + YC_6H_4COCH_2OSO_2C_6H_4Z \xrightarrow[45.0\ °C]{MeOH-MeCN}$$

$$YC_6H_4COCH_2NHC_6H_4X + {}^-OSO_2C_6H_4Z + XC_6H_4NH_3^+$$

X = *p*-OMe, *p*-Me, H, or *p*-Cl

Y = H, *p*-Cl, or *p*-NO_2

Z = *p*-Me, H, *p*-Cl, or *m*-NO_2

Scheme.

With the use of cross-interaction constants determined in this work, we propose that a 'resonance shunt' phenomenon occurs in the TS of the nucleophilic substitution reactions of α-carbonyl derivatives.

Results and Discussion

Substituent Effects.—The second-order rate constants, k_2, for the reaction of phenacyl benzenesulphonates with anilines in methanol–acetonitrile at 45.0 °C (Scheme) are given in Table 1. The reaction is more than twice as fast as similar reactions of the

Table 1. Second-order rate constants (10^4k_2/l mol^{-1} s^{-1}) for the reactions of substituted phenacyl benzenesulphonates with substituted anilines in MeOH–MeCN at 45.0 °C[a]

% MeOH (v/v)		Y = *p*-H				Y = *p*-Cl				Y = *p*-NO$_2$			
		Z = *p*-Me	H	*p*-Cl	*m*-NO$_2$	*p*-Me	H	*p*-Cl	*m*-NO$_2$	*p*-Me	H	*p*-Cl	*m*-NO$_2$
100	*p*-OMe	14.5	22.4	42.3	147	19.9	29.2	50.1	158	101	116	148	234
	p-Me	8.73	13.2	25.9	95.5	12.6	18.5	32.7	100	66.8	77.6	98.9	159
	H	3.81	6.16	12.2	46.7	5.60	9.23	15.5	52.5	31.6	38.0	49.0	81.3
	p-Cl	1.32	2.22	4.45	18.8	1.95	3.07	5.75	20.9	11.5	14.1	18.6	33.9
80	*p*-OMe	9.86	15.3	27.5	97.5	14.1	20.4	34.8	105	69.2	79.4	97.7	151
	p-Me	5.75	9.23	17.3	63.1	8.71	13.2	21.9	69.2	44.7	52.5	64.6	105
	H	2.58	4.27	7.93	30.8	3.89	6.14	10.5	34.0	20.4	25.1	31.6	51.3
	p-Cl	0.871	1.45	2.82	11.2	1.35	2.09	3.83	12.6	7.24	9.12	11.7	20.0
50	*p*-OMe	6.76	10.5	18.8	63.1	9.44	13.8	23.0	67.6	46.8	52.5	63.8	95.5
	p-Me	4.07	6.61	12.2	41.7	5.89	8.51	14.8	45.7	28.8	34.7	42.2	64.5
	H	1.78	2.92	5.64	20.4	2.57	3.99	6.93	21.9	13.5	16.2	20.4	32.4
	p-Cl	0.603	0.976	1.91	7.16	0.851	1.36	2.45	7.94	4.79	5.75	7.33	12.0

[a] Correlation coefficients for second-order plots [equation (vi)]; $r > 0.998$.

Table 2. Hammett and Brønsted coefficients, ρ_X and β_N, for the reactions of substituted phenacyl benzenesulphonates with substituted anilines in MeOH–MeCN at 45.0 °C[a]

% MeOH (v/v)	Y	Z = *p*-Me		H		*p*-Cl		*m*-NO$_2$	
		ρ_X	β_N	ρ_X	β_N	ρ_X	β_N	ρ_X	β_N
100	H	−2.08	0.75	−1.99	0.72	−1.95	0.70	−1.78	0.65
	p-Cl	−2.01	0.73	−1.95	0.70	−1.88	0.68	−1.74	0.63
	p-NO$_2$	−1.89	0.68	−1.81	0.66	−1.80	0.65	−1.68	0.61
80	H	−2.09	0.76	−2.04	0.74	−1.98	0.71	−1.88	0.68
	p-Cl	−2.04	0.74	−1.98	0.72	−1.91	0.69	−1.84	0.67
	p-NO$_2$	−1.97	0.71	−1.88	0.68	−1.84	0.67	−1.77	0.64
50	H	−2.10	0.76	−2.06	0.75	−1.99	0.72	−1.89	0.68
	p-Cl	−2.09	0.76	−2.00	0.72	−1.95	0.70	−1.87	0.68
	p-NO$_2$	−1.97	0.71	−1.93	0.70	−1.88	0.68	−1.80	0.65

[a] Correlation coefficients for ρ_X and β_N were in all cases greater than 0.998, with confidence limits of 99%.

alkyl analogues, 2-phenylethyl benzenesulpnonates.* Table 1 reveals that there is an enhancement in the rate of nucleophilic substitution for a given substrate when nucleophile or nucleofuge becomes stronger, *e.g.* X = *p*-MeO or Z = *m*-NO$_2$. The rate is also seen to increase with a more electron-withdrawing substituent in the substrate, *e.g.* Y = *p*-NO$_2$, indicating that negative charge developed in the TS at the reaction centre, C_α, is stabilized; this also suggests that formation of the N–C_α bond is more advanced than bond rupture of the C_α-leaving group (C_α–LG) bond in the TS.

Hammett and Brønsted plots generally yielded excellent linear correlations, with correlation coefficients (r) better than 0.998. The ρ_X[9] and β_N[10] values for substituent variations in the nucleophile are summarized in Table 2. The relatively large magnitudes of these parameters are indicative of substantial bond formation in the TS. Trends of changes in the magnitudes of ρ_X and β_N are similar for variations in nucleophile and leaving group; the magnitudes of both ρ_X and β_N, and hence the extent of bond formation, decrease with a better leaving group (Z = *m*-NO$_2$) and with a more electron-withdrawing substituent in the substrate (Y = *p*-NO$_2$). These trends are in contrast with those found in the rate variation. Thus the rate increases observed with a stronger nucleofuge and with a more electron-withdrawing substituent in the substrate are accompanied by less charge transfer and hence less N–C_α bond formation in the TS.

The ρ_Z and β_{lg}[11] values obtained for substituent changes in the leaving group are summarized in Table 3. The magnitudes of both ρ_Z and β_{lg} are considerably smaller than those of ρ_X and β_N, which suggests much less bond cleavage than bond formation in the TS of the reaction. Here again the trends of changes in the magnitudes of ρ_Z and β_{lg} contrast with those of the rate variation; the rate increases observed with a stronger nucleophile (X = *p*-MeO) and with a more electron-withdrawing substituent in the substrate (Y = *p*-NO$_2$) are accompanied by less bond cleavage.

Since a stronger nucleophile or nucleofuge leads to an increased exothermicity within a series of analogous reactions, the faster rate (lower activation barrier) with the earlier TS, *i.e.* less bond formation and bond cleavage, exhibited by a stronger nucleophile or nucleofuge demonstrates adherence to the Bell–Evans–Polanyi (BEP) principle.[12]

Hammett ρ_Y values obtained with three substituents (Y) in the substrate are given in Table 4. The ρ_Y values are positive and decrease with a stronger nucleophile or nucleofuge; the ρ_Y value is the smallest with X = *p*-MeO and Z = *m*-NO$_2$.

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* Unpublished results (I. Lee, Y. H. Choi, and H. W. Lee) show that $k_2 \simeq 10^{-4}$ l mol^{-1} s^{-1} at 65 °C for the reactions of 2-phenylethyl benzenesulphonates with anilines in methanol. The rate constant k_1 for methanolysis of 2-phenylethyl benzenesulphonates was found to be 4×10^{-6} s^{-1} at 55 °C.[8]

Table 3. Hammett and Brønsted coefficients, ρ_Z and β_{lg}, for the reactions of substituted phenacyl benzenesulphonates with substituted anilines in MeOH–MeCN at 45.0 °C[a]

% MeOH (v/v)	Y	X = *p*-OMe		*p*-Me		H		*p*-Cl	
		ρ_Z	β_{lg}	ρ_Z	β_{lg}	ρ_Z	β_{lg}	ρ_Z	β_{lg}
100	H	1.14	−0.38	1.19	−0.40	1.24	−0.41	1.31	−0.44
	p-Cl	1.03	−0.34	1.03	−0.34	1.09	−0.36	1.15	−0.39
	p-NO_2	0.42	−0.14	0.43	−0.14	0.47	−0.16	0.53	−0.18
80	H	1.13	−0.38	1.18	−0.39	1.22	−0.41	1.26	−0.42
	p-Cl	0.99	−0.33	1.02	−0.34	1.06	−0.36	1.10	−0.37
	p-NO_2	0.39	−0.13	0.42	−0.14	0.45	−0.15	0.50	−0.16
50	H	1.10	−0.37	1.14	−0.38	1.20	−0.40	1.22	−0.41
	p-Cl	0.97	−0.32	1.02	−0.34	1.05	−0.35	1.10	−0.37
	p-NO_2	0.36	−0.12	0.39	−0.13	0.43	−0.14	0.45	−0.15

[a] Correlation coefficients for ρ_Z and β_{lg} were in all cases greater than 0.998, with confidence limits of 99%.

Transition State Structure.—The parameter ρ_Y can be regarded as a balance of charge gained from the nucleophile in N–C_α bond formation ($\rho_{form} > 0$) and charge lost to the leaving group in C_α–LG bond breaking ($\rho_{break} < 0$),[13] *i.e.* equation (ii).

$$\rho_Y = \rho_{form} + \rho_{break} > 0 \qquad \text{(ii)}$$

Since ρ_Y is positive, the magnitude of ρ_{form} is greater than that of ρ_{break} as can be seen in Tables 2 and 3. Now let us assume that $\rho_{break} = a\rho_Z$ and $\rho_{form} = b\rho_X$ where a and b are positive constants which are in general unequal.[14] We can then express equation (ii) as (iii). Thus a greater degree of bond formation

$$\rho_Y = |b\rho_X| - |a\rho_Z| \qquad \text{(iii)}$$

(larger $|\rho_X|$) with a weaker nucleofuge (Z = *p*-Me) gives a larger ρ_Y in Table 4. Similarly we should expect a greater ρ_Y for a stronger nucleophile (X = *p*-MeO), which has a smaller $|\rho_Z|$ and hence $|a\rho_Z|$. On the contrary, however, we find in Table 4 that the ρ_Y value is actually smaller for a stronger nucleophile. This shows that the assumption $\rho_{break} = a\rho_Z$ does not hold; a is not constant within the series of substituents σ_X and charge transfer to the leaving group in the TS is not only a function of ρ_Z but also a function of σ_X, *i.e.* $\rho_{break} = f(\rho_Z,\sigma_X)$. This analysis demonstrates the limitations of the simple Hammett ρ values as a measure of TS structure.[7e,15] The extent of charge transfer, and hence the degree of bond tightness in the TS, cannot be assessed correctly with simple Hammett ρ values. We are thus led to re-examine our conclusion based on the simple Hammett ρ values regarding the TS structure.

In this context, a more useful measure of the TS structure is provided by the cross-interaction constants ρ_{ij}[7] in equation (i). It can be shown that the magnitude of ρ_{ij} is inversely proportional to the distance between the two substituents *i* and *j*, and represents a measure of the bond length involved in bond making and/or bond breaking in the TS.[7] A definition of ρ_{ij} is given from equation (i) as (iv). This shows that ρ_{ij} is a function of both ρ_j and σ_i, or of ρ_i and σ_j [equation (v)]. We can see from

$$\rho_{ij} = \left(\frac{\partial^2 \log k_{ij}}{\partial\sigma_i \partial\sigma_j}\right) = \left(\frac{\partial\rho_j}{\partial\sigma_i}\right) = \left(\frac{\partial\rho_i}{\partial\sigma_j}\right) \qquad \text{(iv)}$$

$$\rho_{ij} = f(\rho_j,\sigma_i) = f(\rho_i,\sigma_j) \qquad \text{(v)}$$

the expressions for ρ^{break} and ρ_{ij} that the correct measure of charge transfer, and hence bond tightness in the TS, should reflect dependence on both ρ_i and σ_j for a bond involving simultaneous variations of substituents *i* and *j*. The ρ_{ij} values determined by multiple linear regression analysis[16] of the second-order rate constants, k_2, for substituents *i* and *j*, by using equation (i), are summarized in Table 5.

We note that the magnitude of ρ_{YZ} is relatively large as compared with those for methanolysis ($\rho_{YZ} = -0.07$ at 45 °C)[8] and *E*lcB-like elimination ($\rho_{YZ} = -0.57$ at 40 °C)[7b] of the alkyl analogues, 2-phenylethyl benzenesulphonates. This indicates that bond breaking has progressed very little in the TS of the reaction. The size of ρ_{XZ} is also relatively large,* implying again a small degree of bond cleavage. The decrease in ρ_{XZ} values with a more electron-withdrawing substituent in the substrate (Y = *p*-NO_2) simply shows that the decrease in bond formation is greater than the decrease in bond breaking with an increase in the electron-withdrawing power of the substituent Y in the substrate. Two anomalies are recognized in the size of ρ_{ij} in Table 5: (i) $|\rho_{XY}|$ is unusually small, and (ii) $|\rho_{YZ}|$ increases in parallel with ρ_Y and ρ_Z. The magnitudes of ρ_{XY} for other S_N2 reactions were found to range from 0.60 to 1.20,† and hence the ρ_{XY} values of 0.05—0.14 in Table 5 should be considered abnormally small. This can, however, be rationalized in terms of a 'shunt' or 'leak' provided by the α-CO group in the resonance between the reaction centre, C_β, and the substituent Y, as in (**4**). This constitutes a counterpart of the 'resonance saturation' phenomena[21] observed in reactions with a cationic centre in the TS. Since charge transfer to the reaction centre from the nucleophile is greater than that from the reaction centre to the leaving group, the reaction centre is negatively charged in the TS as suggested by positive ρ_Y values in Table 5. Thus delocalization of negative charge into the α-carbonyl group [as in (**4**)] decreases the electron supply to the Y-substituted benzene ring so that the interaction between substituents X and Y, and hence $|\rho_{XY}|$, is decreased. Although bond formation proceeds substantially, as the relatively large ρ_{XZ} value[17] indicates, the interaction between X and Y is weakened markedly, not because of the large distance involved, but as a

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* The ρ_{XZ} value for reactions of X-substituted *N,N*-dimethylanilines with benzyl arenesulphonates (Z-substituted) in acetone at 35 °C was calculated[17] to be −0.15.

† X-Substituted anilines reacting with various substrates (with substituents Y) gave the following ρ_{XY} values:

$YC_6H_4CH_2SO_2Cl \xrightarrow[35.0\,°C]{MeOH} \rho_{XY} = -0.69$ (ref. 18)

$YC_6H_4SO_2Cl \xrightarrow[35.0\,°C]{MeOH} \rho_{XY} = -0.70$ (ref. 19)

$YC_6H_4CH_2Cl \xrightarrow[50\,°C]{EtOH} \rho_{XY} = -0.77$ (ref. 20)

$YC_6H_4CH_2OSO_2Ph \xrightarrow[35.0\,°C]{MeOH} \rho_{XY} = -0.62$ (ref. 7*a*)

$YC_6H_4CH_2SO_2F \xrightarrow[45.0\,°C]{MeOH} \rho_{XY} = -1.24$ (ref. 7*d*) result of a 'shunt' or a 'leak' in the resonance provided by the α-carbonyl group. This interpretation is supported by the second anomaly already noted: the parallel increase in the $|\rho_{YZ}|$ value with ρ_Y and ρ_Z. The size of the ρ_Y and ρ_Z values in Table 5 indicates that charge transfer from the nucleophile to the reaction centre (ρ_Y) as well as that from the reaction centre to the leaving group (ρ_Z) increases as the substituent in the nucleophile becomes more electron-withdrawing, *e.g.* X = *p*-Cl. The increase in the ρ_Z value within a series of reactions can be taken normally as the increase in bond cleavage; bond breaking increases with a more electron-withdrawing substituent in the nucleophile, which should result in a decrease, in contrast with the increase observed, in the $|\rho_{YZ}|$ values. This can be rationalized in terms of the enhanced contribution of the resonance 'shunt' by the α-carbonyl group charge transfer increases; this has a shortening effect on the C_α–C_β bond due to the double bond character in structure (**4**); the greater degree of charge transfer (the larger ρ_Y) will result in a greater contribution from the resonance shunt, which in turn will give a shorter C_α–C_β bond. The shorter C_α–C_β bond will naturally mean a larger $|\rho_{YZ}|$ value, as observed; hence the parallel increase in ρ_{YZ} with ρ_Y and ρ_Z can be accommodated.

In structure (**5**) there is an unpaired electron on C_α; the substituent Y can therefore interact with C_α, which in turn implies interaction between X and Y; here there is no decrease in the interaction (and hence in ρ_{XY}) between X and Y. Thus our results clearly support the involvement of structure (**4**) rather than (**5**) in the TS. We conclude that the involvement of the bridged TS structure is tenuous, in the light of our results with cross interaction constants.

Table 4. Hammett ρ_Y values for the reactions of substituted phenacyl benzenesulphonates with substituted anilines in MeOH–MeCN at 45.0 °C[a]

% MeOH (v/v)	Z	X = *p*-OMe	*p*-Me	H	*p*-Cl
100	*p*-Me	0.67	0.70	0.72	0.74
	H	0.57	0.60	0.61	0.63
	p-Cl	0.44	0.46	0.48	0.49
	m-NO_2	0.16	0.18	0.19	0.20
80	*p*-Me	0.67	0.69	0.70	0.72
	H	0.56	0.59	0.60	0.62
	p-Cl	0.43	0.45	0.47	0.48
	m-NO_2	0.15	0.16	0.17	0.20
50	*p*-Me	0.66	0.67	0.69	0.71
	H	0.55	0.57	0.59	0.60
	p-Cl	0.42	0.43	0.44	0.46
	m-NO_2	0.14	0.15	0.16	0.18

[a] Correlation coefficients for ρ_Y were in all cases greater than 0.998, with confidence limits of 95%.

Applicability of the Potential Energy Surface versus *the Quantum Mechanical Model.*—The magnitudes of ρ_X and ρ_{XY} indicate that bond formation decreases with a more electron-withdrawing substituent in the leaving group. This is consistent with the prediction of the potential energy surface (PES) model;[22] the PES diagram[22] in Figure 1 shows that an electron-withdrawing substituent in the leaving group will stabilize the upper corners, D and P, so that the TS will shift to F, which is obtained as a sum of the two vectors, $\overrightarrow{OE}$ and $\overrightarrow{OG}$, in accord with the Hammond[23] and anti-Hammond (or Thornton) rules.[23] Thus bond formation is predicted to decrease, as we

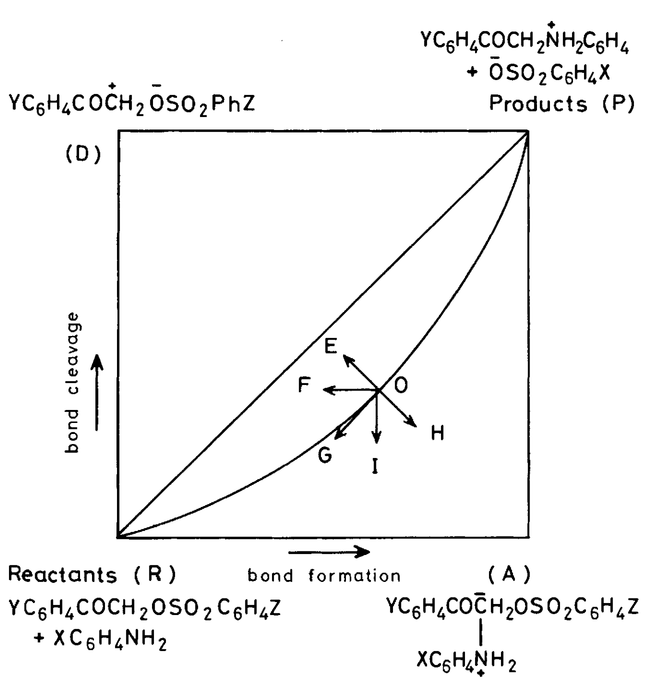

Figure 1. Potential energy surface diagram showing TS variations with substituent changes in the nucleophile and the leaving group

Table 5. Multiple Hammett correlations for the reactions of substituted phenacyl benzenesulphonates with substituted anilines in MeOH–MeCN (r = multiple correlation coefficient)[7a] at 45.0 °C

% MeOH (v/v)		ρ_X	ρ_Y	ρ_{XY}	r^a		ρ_Y	ρ_Z	ρ_{YZ}	r^a		ρ_X	ρ_Z	ρ_{XZ}	r^a
100	Z = *p*-Me	−2.06	0.71	0.14	0.999	X = *p*-OMe	0.60	1.14	−0.63	0.997	Y = H	−2.01	1.24	0.32	0.999
	H	−1.97	0.61	0.11	0.999	*p*-Me	0.64	1.17	−0.65	0.998	*p*-Cl	−1.96	1.09	0.31	0.999
	p-Cl	−1.92	0.47	0.10	0.999	H	0.66	1.23	−0.66	0.998	*p*-NO_2	−1.85	0.48	0.23	0.999
	m-NO_2	−1.77	0.18	0.07	0.999	*p*-Cl	0.67	1.30	−0.67	0.998					
80	*p*-Me	−2.07	0.70	0.09	0.999	*p*-OMe	0.60	1.12	−0.64	0.997	H	−2.04	1.21	0.24	0.999
	H	−2.00	0.60	0.09	0.999	*p*-Me	0.63	1.16	−0.65	0.997	*p*-Cl	−1.98	1.06	0.22	0.999
	p-Cl	−1.94	0.46	0.08	0.999	H	0.64	1.25	−0.66	0.998	*p*-NO_2	−1.91	0.45	0.21	0.999
	m-NO_2	−1.86	0.18	0.08	0.999	*p*-Cl	0.66	1.21	−0.66	0.998					
50	*p*-Me	−2.08	0.69	0.08	0.999	*p*-OMe	0.59	1.09	−0.64	0.997	H	−2.06	1.18	0.24	0.999
	H	−2.03	0.58	0.09	0.999	*p*-Me	0.61	1.14	−0.65	0.998	*p*-Cl	−2.02	1.05	0.24	0.999
	p-Cl	−1.96	0.44	0.06	0.999	H	0.63	1.19	−0.66	0.998	*p*-NO_2	−1.93	0.42	0.19	0.999
	m-NO_2	−1.87	0.16	0.05	0.999	*p*-Cl	0.64	1.22	−0.67	0.998					

[a] 99% Confidence limits.

found experimentally. On the other hand the magnitudes of ρ_Z and β_{lg} indicate that bond breaking decreases with a stronger nucleophile (X = *p*-MeO), which is also consistent with the prediction of the TS variation by the PES diagram in Figure 1: a strong nucleophile will stabilize the right-hand corners, P and A, so that the TS is expected to shift to I, *i.e.* towards less bond breaking. These effects of substituents is the nucleophile and the leaving group on the TS variation are in complete agreement with what we would expect thermodynamically; a stronger nucleophile and a better leaving group will give thermodynamically more stable products so that the reaction will become more exothermic. An increase in exothermicity will lead to an earlier TS, *i.e.* less bond formation and/or less bond breaking according to the BEP principle,[12] which is based on thermodynamic stabilities of reactants and products. We therefore conclude that the reaction in the Scheme constitutes a typical thermodynamically controlled series.

However, these TS variations are quite opposite to what we would expect from the quantum mechanical (QM) model,[24,25] which predicts a later TS for a stronger nucleophile or a better leaving group. It has been shown that nucleophilic substitutions of benzyl and 1-phenylethyl benzenesulphonates with anilines[7c,25] are compatible with the TS variations predicted by the QM model. Thus we can identify two distinct categories of reaction series:[26] one that follows the TS variations as predicted by the PES model, which is thermodynamically controlled, and the other that is consistent with the TS variations predicted by the QM model, which is intrinsically controlled.[26] In the former category, bond formation precedes bond cleavage in the TS and reactivity trends respond to the nucleophilicity of nucleophiles, whereas in the latter category bond breaking precedes bond cleavage and reactivity trends follow leaving group ability. The enhancement of rate found for the α-carbonyl derivatives is thus a result of enhanced bond formation due to an increased resonance (shunt) contribution of structure (4). We have shown here that a stronger nucleophile as well as a stronger nucleofuge leads to a greater rate with smaller selectivity parameters, $|\rho_Z|$ and $|\rho_X|$; thus the reactivity–selectivity principle (RSP)[27] holds for the reaction.

Solvent Effects.—The rate constant k_2 increases with the methanol content of the solvent mixtures, indicating the importance of electrophilic assistance by hydrogen bonding of methanol to the leaving group. This interpretation is supported by the increase in bond cleavage, as exhibited by greater ρ_Z and β_{lg} values with increase in methanol content. In contrast, bond formation decreases with increasing methanol content as shown by the smaller $|\rho_X|$ and β_N values in Table 2. These two contrasting effects of increasing methanol content on the TS structure are, however, quite small and may be insignificant. A net increase in the magnitude of ρ_{XZ} (Table 5), indicating a decrease in the distance between the substituents X and Z with increasing methanol content, might result from the greater ability of methanol to solvate the highly polar TS.

Experimental

Materials.—Reagent grade methanol and acetonitrile were used without further purification. Anilines were purified as described previously.[13b]

Silver Benzenesulphonates.—Benzenesulphonic acid monohydrate and Ag_2O in acetonitrile were refluxed with constant stirring at 50 °C. The white crystalline silver benzenesulphonates were obtained upon evaporation of solvent under reduced pressure, after removal of unchanged Ag_2O by filtration. After drying, the products were recrystallized from absolute ethanol.

Table 6. Identification of Y-phenacyl Z-benzenesulphonates

Substituent					
Y	Z	Colour	Yield (%)	M.p. (°C)	T.l.c. R_F
H	H	White	44.3	83	0.47
H	*p*-Me	White	50.1	99	0.47
H	*p*-Cl	White	42.6	97	0.48
H	*m*-NO_2	White	39.4	87	0.43
p-Cl	H	White	52.5	78	0.47
p-Cl	*p*-Me	White	47.2	124	0.47
p-Cl	*p*-Cl	Pale yellow	49.3	137	0.48
p-Cl	*m*-NO_2	White	31.3	107	0.45
p-NO_2	H	Pale yellow	43.2	96	0.47
p-NO_2	*p*-Me	White	47.8	140	0.47
p-NO_2	*p*-Cl	Pale yellow	43.0	93	0.48
p-NO_2	*m*-NO_2	Pale yellow	32.0	95	0.50

Substituted Phenacyl Benzenesulphonates.—Y-Substituted phenacyl bromide and Z-substituted silver benzenesulphonate were dissolved in anhydrous acetonitrile, and refluxed with constant stirring at 50 °C for 15 h. Precipitated AgBr was filtered off, and the solvent evaporated off under reduced pressure. The residue was extracted with anhydrous ether. White crystalline products were recrystallized from propan-2-ol. Each product showed a single spot on t.l.c. (silica gel plate; eluant 10% ethyl acetate–benzene). M.p.s and R_F values are summarized in Table 6.

Phenacyl benzenesulphonate showed $\nu_{max.}$(KBr) 1 701 (C=O sym. str.), 1 447 (CH_2 sym. str.), 1 379 (SO_2 asym. str.), 1 191 (SO_2 sym. str.), and 1 060 cm^{-1} (S–O sym. str.); δ_H(60 MHz; $CDCl_3$) 5.3 (2 H, s, CH_2), 7.51—7.83 (5 H, d, *J* 5.0 Hz, C_6H_5), and 7.84—8.09 (5 H, d, *J* 5.0 Hz, $C_6H_5SO_3$) (Found; C, 60.0; H, 4.3. $C_{14}H_{12}O_4S$ requires C, 60.9; H, 4.4%).

Phenacyl tosylate showed $\nu_{max.}$(KBr) 1 713 (C=O sym. str.), 1 450 (CH_2 sym. str.), 1 376 (CH_3 sym. str.), 1 358 (SO_2 asym. str.), 1 193 (SO_2 sym. str.), and 1 054 cm^{-1} (S–O sym. str.); δ_H(60 MHz; $CDCl_3$) 5.3 (2 H, s, CH_2), 2.4 (3 H, s, 4-CH_3), 7.16—7.47 (5 H, d, *J* 4.5 Hz, C_6H_5), and 7.70—8.00 (4 H, d, *J* 4.4 Hz, 4-$CH_3C_6H_4SO_3$) (Found: C, 61.8, 5.0. $C_{15}H_{14}O_4S$ requires C, 62.05; H, 4.9%).

Phenacyl p-*chlorobenzenesulphonate* showed $\nu_{max.}$(KBr) 1 711 (C=O sym. str.), 1 451 (CH_2 sym. str.), 1 368 (SO_2 asym. str.), 1 188 (SO_2 sym. str.), and 1 054 cm^{-1} (S–O sym. str.); δ_H(60 MHz; $CDCl_3$) 5.4 (2 H, s, CH_2), 7.49—7.82 (5 H, d, *J* 4.5 Hz, C_6H_5), and 7.83—8.33 (4 H, t, *J* 6.8 Hz, 4-$ClC_6H_4SO_3$) (Found: C, 54.3; H, 3.4. $C_{14}H_{11}ClO_4$ requires C, 54.1; H, 3.6%).

Phenacyl m-*nitrobenzenesulphonate* showed $\nu_{max.}$(KBr) 1 711 (C=O sym. str.), 1 451 (CH_2 sym. str.), 1 354 (SO_2 asym. str.), 1 189 (SO_2 sym. str.), and 1 045 cm^{-1} (S–O sym. str.); δ_H(60 MHz; $CDCl_3$) 5.2 (2 H, s, CH_2), 7.36—7.71 (5 H, d, *J* 4.6 Hz, C_6H_5), and 7.73—8.19 (4 H, t, *J* 6.7 Hz, 3-$NO_2C_6H_4SO_3$) (Found: C, 52.7; H, 3.2. $C_{14}H_{11}NO_6S$ requires C, 52.3; H, 3.45%).

p-*Chlorophenacyl benzenesulphonate* showed $\nu_{max.}$(KBr) 1 706 (C=O sym. str.), 1 448 (CH_2 sym. str.), 1 358 (SO_2 asym. str.), 1 189 (SO_2 sym. str.), and 1 050 cm^{-1} (S–O sym. str.); δ_H(60 MHz; $CDCl_3$) 5.3 (2 H, s, CH_2), 7.39—7.81 (4 H, t, *J* 6.7 Hz, 4-ClC_6H_4), and 7.80—8.02 (5 H, d, *J* 4.5 Hz, $C_6H_5SO_3$) (Found: C, 54.4; H, 3.5. $C_{14}H_{11}ClO_4$ requires C, 54.1; H, 3.6%).

p-*Chlorophenacyl tosylate* showed $\nu_{max.}$(KBr) 1 703 (C=O sym. str.), 1 430 (CH_2 sym. str.), 1 400 (CH_3 sym. str.), 1 361 (SO_2 asym. str.), 1 175 (SO_2 sym. str.), and 1 060 cm^{-1} (S–O sym. str.); δ_H(60 MHz; $CDCl_3$) 5.3 (2 H, s, CH_2), 2.4 (3 H, s, 4-CH_3), 7.29—7.71 (4 H, t, *J* 6.8 Hz, 4-ClC_6H_4), and 7.70—8.09 (4 H, d, *J* 4.3 Hz, 4-$CH_3C_6H_2SO_3$) (Found: C, 55.6; H, 4.1. $C_{15}H_{13}ClO_4S$ requires C, 55.5; H, 4.0%).

p-*Chlorophenacyl* p-*chlorobenzenesulphonate* showed $\nu_{max.}$-

(KBr) 1 703 (C=O sym. str.), 1 433 (CH_2 sym. str.), 1 365 (SO_2 asym. str.), 1 175 (SO_2 sym. str.), and 1 055 (S–O sym. str.); δ_H(60 MHz; $CDCl_3$) 5.3 (2 H, s, CH_2), 7.18—7.58 (4 H, t, *J* 6.5 Hz, 4-ClC_6H_4), and 7.57—8.01 (4 H, t, *J* 6.6 Hz, 4-$CH_3C_6H_4SO_3$) (Found: C, 49.0; H, 3.4. $C_{14}H_{10}Cl_2O_4S$ requires C, 48.7; H, 3.5%).

p-*Chlorophenacyl* m-*nitrobenzenesulphonate* showed $\nu_{max.}$(KBr) 1 697 (C=O sym. str.), 1 425 (CH_2 sym. str.), 1 355 (SO_2 asym. str.), 1 194 (SO_2 sym. str.), and 1 060 cm^{-1} (S–O sym. str.); δ_H(60 MHz; $CDCl_3$) 5.4 (2 H, s, CH_2), 7.38—7.75 (4 H, t, *J* 6.8 Hz, 4-ClC_6H_4), and 7.78—8.20 (4 H, t, *J* 6.7 Hz, 3-$NO_2C_6H_4SO_3$) (Found: C, 47.4; H, 2.7. $C_{14}H_{10}ClNO_6S$ requires C, 47.3; H, 2.8%).

p-*Nitrophenacyl benzenesulphonate* showed $\nu_{max.}$(KBr) 1 700 (C=O sym. str.), 1 400 (CH_2 sym. str.), 1 345 (SO_2 asym. str.), 1 190 (SO_2 sym. str.), and 1 078 cm^{-1} (S–O sym. str.); δ_H(60 MHz; $CDCl_3$) 5.3 (2 H, s, CH_2) and 7.38—8.03 (9 H, m, C_6H_5) (Found: C, 52.6; H, 3.3. $C_{14}H_{11}NO_6S$ requires C, 52.3; H, 3.45%).

p-*Nitrophenacyl tosylate* showed $\nu_{max.}$(KBr) 1 708 (C=O sym. str.), 1 410 (CH_2 sym. str.), 1 380 (CH_3 sym. str.), 1 345 (SO_2 asym. str.), 1 190 (SO_2 sym. str.), and 1 063 cm^{-1} (S–O sym. str.); δ_H(60 MHz; $CDCl_3$) 5.4 (2 H, s, CH_2), 2.4 (3 H, s, CH_3), and 6.9—7.6 (8 H, m, C_6H_5) (Found: C, 54.1; H, 3.8. $C_{15}H_{13}NO_6S$ requires C, 53.7; H, 3.9%).

p-*Nitrophenacyl* p-*chlorobenzenesulphonate* showed $\nu_{max.}$(KBr) 1 704 (C=O sym. str.), 1 401 (CH_2 sym. str.), 1 343 (SO_2 asym. str.), 1 192 (SO_2 sym. str.), and 1 065 cm^{-1} (S–O sym. str.); δ_H(60 MHz; $CDCl_3$) 5.3 (2 H, s, CH_2) and 7.4—8.0 (8 H, m, C_6H_5) (Found: C, 47.6; H, 2.65. $C_{14}H_{10}ClNO_6S$ requires C, 47.3; H, 2.8%).

p-*Nitrophenacyl* m-*nitrobenzenesulphonate* showed $\nu_{max.}$(KBr) 1 700 (C=O sym. str.), 1 401 (CH_2 sym. str.), 1 340 (SO_2 asym. str.), 1 189 (SO_2 sym. str.), and 1 050 cm^{-1} (S–O sym. str.); δ_H(60 MHz; $CDCl_3$) 5.4 (2 H, s, CH_2) and 7.6—8.2 (8 H, m, C_6H_5) (Found: C, 46.1; H, 2.6. $C_{14}H_{10}N_2O_8S$ requires C, 45.9; H, 2.75%).

Rate Constants.—Rates were measured conductimetrically at 45.0 (±0.1) °C. A calibration curve (Figure 2) shows that conductivity varies linearly with concentration of product solution, prepared using independently synthesized anilides.[28] Pseudo-first-order rate constants, k_1^{obs}, were determined by the Guggenheim method with anilines in large excess, and second-order rate constants, k_2, were obtained from the slopes of plots of k_1^{obs} *vs.* [aniline] [equation (vi), where k_1 is the rate constant

$$k_1^{obs} = k_1 + k_2[\text{aniline}] \qquad \text{(vi)}$$

for methanolysis; this found to be negligibly small as compared with the second-order term as evidenced by zero intercepts (k_1 = 0) in all cases].

Product Analysis.—The identify of products was confirmed by t.l.c. and i.r. analyses. T.l.c. analysis of reaction mixtures showed three spots, corresponding to two reactants, aniline and $YC_6H_4COCH_2OSO_2C_6H_4Z$, and one product, $YC_6H_4COCH_2NHC_6H_4X$.[28] The three R_F values agreed with those determined independently. Products were also identified by i.r., n.m.r., and elemental analysis.

N-*Phenacyl*-p-*methylaniline* showed R_F(silica gel plate; solvent 10% ethyl acetate–benzene) 0.44 (*cf.* 0.29 for aniline and 0.47 for starting sulphonate); $\nu_{max.}$(KBr) 3 370 (NH sym. str.), 1 688 (C=O sym. str.), 1 510 (C–N sym. str.), 1 450 (CH_2 sym. str.), 1 360 (CH_3 sym. str.), and 1 270 cm^{-1} (Ph–N sym. str.); δ_H(60 MHz; $CDCl_3$) 6.5 (2 H, s, CH_2), 3.5 (3 H, s, CH_3), 7.32—7.78 (5 H, d, *J* 4.6 Hz, C_6H_5), and 7.77—8.23 (4 H, d, *J* 4.4 Hz, 4-$CH_3C_6H_4SO_3$) (Found: C, 80.3; H, 6.6. $C_{15}H_{15}NO$ requires C, 80.0; H, 6.7%).

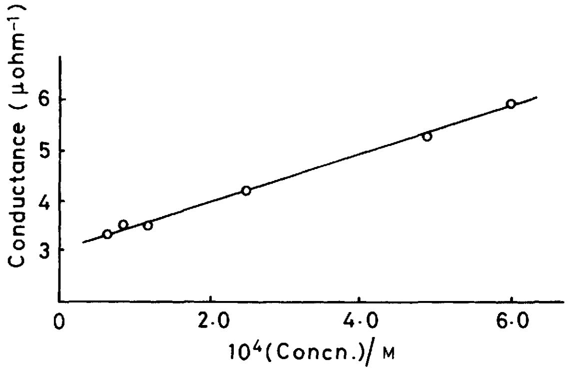

Figure 2. Calibration curve of concentration *vs.* conductance for phenacylanilinium benzenesulphonate in methanol at 45.0 °C

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