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STRUCTURE–REACTIVITY RELATIONSHIP OF BENZYL BENZENESULFONATES. PART 3. PREDICTION OF REACTION MECHANISM BY THE USE OF CORRELATION INTERACTION COEFFICIENTS

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Nucleophilic substitution reactions of (Z)-benzyl (X)-benzene sulfonates with (Y)-pyridines were investigated in acetone at 35 °C. The magnitudes of the Hammett reaction constants ρ_X, ρ_Y and ρ_Z indicate that a stronger nucleophile leads a lesser degree of bond breaking and a better leaving group is accompanied by a lesser degree of bond formation. The magnitude of interaction term, ρ_{ij}, can be used to determine the structure of the transition state (TS) for the S_N reaction. In particular, the comparison of ρ_{XZ} with ρ_{YZ} and the sign of ρ_Z can predict that this reaction series proceed via dissociative S_N2 process. This result also accords with the treatment of the MOFJ diagram. The sign of the product $\rho_{XZ}\rho_{YZ}$ can predict the movement of the TS.

INTRODUCTION

Linear free energy relationships (LFER),[1-3] notably the Hammett and Brønsted types, have been used as an empirical means of characterizing transition-state (TS) structures. The Hammett and Brønsted coefficients, ρ and β, are first derivatives of log k, as shown in equations (1) and (2), respectively, and reflect TS structures involved in a series of reactions with structural changes affecting the reaction center.

$$\rho = \partial \log k/\partial \sigma \tag{1}$$

$$\beta = \partial \log k/\partial \mathrm{p}K \tag{2}$$

The magnitudes of the ρ and β values in the nucleophile and leaving group can estimate the degree of bond formation and bond dissociation. However, it has occasionally been suggested that the ρ and β values cannot be used as a measure of TS structure, since the efficiency of charge transmission for different reactions series may differ.[4,5]

In previous work,[6-8] we proposed that the TS structure in nucleophilic substitution (S_N) reactions can be predicted by the sign and absolute values of ρ_Z and comparison of the relative value of the correlation interaction coefficient ρ_{XZ} with ρ_{YZ}.

In this work, we show practical aspects of the correlation interaction terms and their application to characterizing TS structures.

$$\text{(Z)-}C_6H_4CH_2OSO_2C_6H_4\text{-(X)} + \text{(Y)-}C_5H_4N \longrightarrow$$

$$\text{(Z)-}C_6H_4CH_2\text{-}N^+C_5H_4\text{-}N^+C_5H_4\text{-(Y)}\ {}^-OSO_2C_6H_4\text{-(X)}$$

$X = 3\text{-}NO_2, H, 4\text{-}CH_3$

$Y = H, 3,4\text{-}(CH_3)_2, 4\text{-}NH_3$

$Z = 4\text{-}NO_2, 4\text{-}Cl, H, 4\text{-}CH_3$

RESULTS AND DISCUSSION

Kinetic studies

The reaction rates were determined by monitoring the changes in conductance on formation of the salt[9] from the reaction of substituted (Z)-benzyl (X)-benzenesulfonates with substituted (Y)-pyridines in acetone. The reactions, carried out with a large excess of substituted (Y)-pyridines, follow pseudo-first-order kinetic to at least 85% completion.

The rate constants, k_{obs}, are linearly correlated with the nucleophile concentration, indicating that the reaction is second order overall and first order with respect to each reagent, according to the simple rate law

$$k_{obs} = k_2[\mathrm{Nu}] \tag{3}$$

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The second-order rate constants, k_2, for this reaction are summarized in Table 1. The data reveal that the rates increase with a stronger nucleophile and with a better leaving group. However, the rates decrease with more electron-withdrawing substituents in the substrate. The Hammett plots are generally good linear correlations and the ρ values are summarized in Tables 2–4.

The Hammett ρ_Y value obtained on changing the substituent in the nucleophile can be used to estimate the length of the Nu—C_α bond and are presented in Table 2. A large ρ_Y value indicates that the charge on the nucleophile has changed markedly on going to the TS. This means that a large proportion of the electron density on the nucleophile has been used to form the Nu—C_α bond. The Hammett ρ_X value obtained by changing the substituent in the leaving group can be used to estimate the degree of dissociation of the C_α—L bond in the TS. The ρ_X values for variation of substituent X in the leaving group are given in Table 3; a large ρ_X value indicates that a large proportion of the electron density is on the leaving moiety, i.e. the C_α—L bond must be longer in the TS. The Hammett ρ_Z values are given in Table 4. The sign of ρ_Z gives information on the charge distribution of the reaction center of the substrate, a negative sign of ρ_Z indicates that the reaction center of the substrate has positive charge.

Table 1. Second-order rate constants, 10^4 k_2 (l mol^{-1} s^{-1}), for the reactions of (Z)-benzyl (X)-arenesulfonates with (Y)-pyridines in acetone at 35 °C

		X		
Z	Y	3-NO_2	H	4-CH_3
4-NO_2	H	61·4	3·48	1·33
	3,4-$(CH_3)_2$	179	11·0	5·02
	4-NH_2	833	112	60·6
4-Cl	H	138	6·83	3·33
	3,4-$(CH_3)_2$	340	20·9	11·80
	4-NH_2	981	160	105
H	H	164	10·6	5·02
	3,4-$(CH_3)_2$	431	27·8	15·5
	4-NH_2	1050	190	135
4-CH_3	H	227	14·4	8·37
	3,4-$(CH_3)_2$	504	33·8	20·6
	4-NH_2	1340	227	150

Table 2. Reaction constants (ρ_Y[a]) and correlation interaction terms (ρ_{ij}) for the reactions of (Z)-benzyl (X)-benzenesulfonates with substituted (Y)-pyridines in acetone at 35 °C

	ρ_Y			
Z	X = m-NO_2	X = H	X = p-CH_3	ρ_{XY}
p-NO_2	−1·79	−2·43	−2·66	0·96
p-Cl	−1·33	−2·19	−2·39	1·21
H	−1·24	−2·02	−2·29	1·17
p-CH_3	−1·21	−1·94	−2·03	0·97
ρ_{YZ}	−0·64	−0·52	−0·61	

[a] The σ_Y values [H 0; 3,4-$(CH_3)_2$ −0·189; 4-NH_3 −0·617] were taken from Ref. 10 and the correlation coefficients were ≥0·995.

Table 3. Reaction constants (ρ_X[a]) and correlation interaction terms (ρ_{ij}) for the reactions of (Z)-benzyl (X)-benzenesulfonates with substituted (Y)-pyridines in acetone at 35 °C

	ρ_X			
Z	Y = H	Y = 3,4-$(CH_3)_2$	Y = 4-NH_2	ρ_{XY}
p-NO_2	1·85	1·75	1·27	0·96
p-Cl	1·84	1·67	1·11	1·21
H	1·71	1·65	1·02	1·18
p-CH_3	1·65	1·60	1·08	0·97
ρ_{ZX}	0·21	0·15	0·24	

[a] Correlation coefficients ≥0·998.

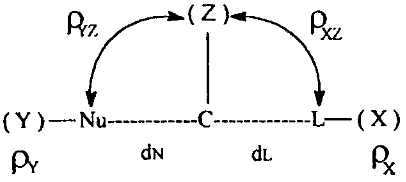
Table 4. Reaction constants (ρ_Z[a]) and correlation interaction terms (ρ_{ij}) for the reactions of (Z)-benzyl (X)-benzenesulfonates with substituted (Y)-pyridines in acetone at 35 °C

	ρ_Z			
X	Y = H	Y = 3,4-$(CH_3)_2$	Y = 4-NH_2	ρ_{YZ}
m-NO_2	−0·59	−0·48	(−0·19)	−0·64
H	−0·64	−0·51	−0·32	−0·52
p-CH_3	−0·81	−0·64	−0·42	−0·61
ρ_{ZX}	0·21	0·17	0·24	

[a] Correlation coefficients ≥0·993.

Development of the model

The principle of the present approach can be illustrated by a hypothetical nucleophilic substitution (S_N) reaction between nucleophile (Nu) and a leaving group (L) proceeding through a single bridging substrate molecule, C_α—R, for a Menschutkin-type reaction. The TS may be represented as shown in Scheme 1, where d_N (or d_L) is the distance between Nu (or L) and C_α.



Scheme 1

In previous papers,[7,8] we have shown that the correlation interaction term ρ_{ij} derived from Taylor series expansion is $\log(k_{ij}/k_{00}) = \rho_i\sigma_i + \rho_i\sigma_j + \rho_{ij}\sigma_i\sigma_j$, and therefore ρ_{XZ} (ρ_{ZX}) and ρ_{YZ} (ρ_{ZY}) are represented by the equations

$$\log(k_{XZ}/k_{00}) = \rho_X\sigma_X + \rho_Z\sigma_Z + \rho_{XZ}\sigma_X\sigma_Z \qquad (4)$$

$$\log(k_{YZ}/k_{00}) = \rho_Y\sigma_Y + \rho_Z\sigma_Z + \rho_{YZ}\sigma_Y\sigma_Z \qquad (5)$$

where X, Y and Z are the substituents of the leaving group, nucleophile and substrate, respectively.

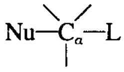
ρ_{ij} (ρ_{XZ} or ρ_{YZ}) is dependent on the change in distance between the reaction centers of *i* and *j*, which can express the sensitivity of $\rho_i\sigma_j$ (or $\rho_j\sigma_i$) *i.e.*, ρ_{XZ} and ρ_{YZ} indicate the degree of C_α—L bond fission and Nu—C_α bond formation, respectively.

In Table 5, the signs of ρ_Y are negative and the magnitudes of the ρ_Y values are fairly large, with the nucleophilic nitrogen atom located in the aromatic ring. The size of ρ_Y increases with a lower leaving ability of the leaving group and with a more electron-withdrawing substituent in the substrate, suggesting a greater degree of bond formation. The variation of the substituent in the substrate from Z = *p*-CH_3 to Z = *p*-NO_2 seems to cause a smaller increase in ρ_X compared with that in $|\rho_Y|$.

The sign of ρ_Z is negative in Table 4, indicating that the reaction center of the substrate has developed a positive charge, and thus a greater degree of bond breaking than bond formation, on the TS for the reaction series.

The magnitudes of the ρ_X values decrease with more electron-donating substituents in the substrate and nucleophile, implying a lesser degree of bond breaking. Thus a stronger nucleophile is accompanied by a lesser degree of bond breaking and a better leaving group is accompanied by a lesser degree of bond formation, i.e. a stronger nucleophile and/or a better leaving group lead to the formation of an early TS. These results suggest that bond formation is enhanced more than bond breaking by a more electron-withdrawing substituent; in the substrate. This is reasonable, since bond breaking has already progressed much further than bond formation in the TS, so that further increases in bond breaking will be small. These results will affect the ρ_{ij} values; the magnitude of $|\rho_{YZ}|$ evaluated from the plot of ρ_Y against σ_Z is larger than that of $|\rho_{XZ}|$, since the length of the C_α—L bond in the TS stays the same or become slightly longer than that of the Nu—C_α bond when the substituent of the substrate is *p*-CH_3. As the substituent of the substrate is changed from Z = *p*-CH_3 to Z = *p*-NO_2, the formation of the Nu—C_α bond increases considerably, but the breaking of the C_α—L bond increases slightly in the TS. The magnitude of ρ_{XZ} is smaller than that of ρ_{YZ} with a change of substituent of the substrate, indicating that the leaving moiety is already away from the reaction center of the substrate, so the degree of variation of the distance from the reaction center is small, but large in the case of ρ_{YZ}. Thus, from the sign of ρ_Z and the comparison of $\rho_{ij}(|\rho_{ZY}| > |\rho_{XZ}|)$, this reaction can be ascribed to a dissociative S_N2 mechanism.

The recent method of predicting substituent effects was suggested by the More O'Ferrall–Jencks (MOFJ) diagrarm[11,12] in Figure 1. The MOFJ diagram can be predicted from the changes that occur in the structure of the TS when a substituent in the substrate, nucleophile or leaving group is changed. The energies of the reactants, products and the two possible intermediates, the carbonium ion and the pentavalent complex, are represented at the corner of the energy surface. The *x* and *y* axes represent changes in the bond length in the Nu—C_α bond and the C_α—L bond, respectively. The energy contour shows the lowest energy pathway, i.e. the reaction coordinate, through the energy surface. The TS is designated with an asterisk from the data in Table 5. The effect of changing a substituent in one of the reactants is determined by considering how this change would affect the energies of the reactants, the products and the two possible intermediates.



$Nu—C_\alpha—L$

Changing to a more electron-withdrawing substituent of Z on the substrate will lead to a higher energy of the top left corner or a lower energy of the bottom right corner of energy surface. This result will cause the TS to move to the bottom right, a perpendicular effect

Table 5. Influence of a change of substituent (Z) of the substrate on the TS of a diss-S_N2 reaction at 35 °C reaction at 35 °C in acetone

(Z)	ρ_Y	Relative Nu—C_α bond length	C_α	Relative C_α—L bond length	ρ_X
p-NO_2	−2·43	Nu················	C_α	·······················L	1·85
p-Cl	−2·19	Nu····················	C_α	······················L	1·84
H	−2·02	Nu························	C_α	··················L	1·71
p-CH_3	−1·94	Nu····························	C_α	···············L	1·65
	$\rho_{YZ} = -0{\cdot}5$		$\rho_Z < 0$		$\rho_{XZ} = 0{\cdot}2$

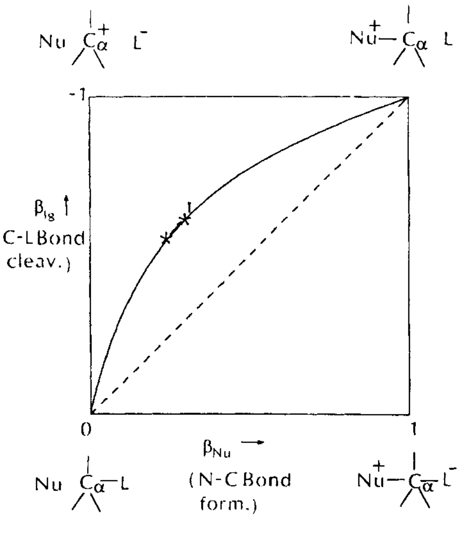


Figure 1. MOFJ diagram based on SR coefficient for the reaction of (Z)-benzyl (X)-arenesulfonates with (Y)-pyridines. The energy contours are not shown. The transition state * moves towards *′ with lowering of the energy of the intermediate when the substituent of the substrate changes from p-CH_3 to p-NO_2

(Thornton effect).[13] In the case of Thornton effect, the sign of the product $\rho_{XZ}\rho_{YZ}$ is expressed as positive.

$$\underset{\longleftarrow}{Nu^{\delta+}}\cdots\cdots Ca^{\delta+}\cdots\cdots \underset{\longrightarrow}{L^{\delta-}} \qquad \underset{\longleftarrow}{Nu^{\delta+}}\cdots\cdots \underset{\longrightarrow}{Ca^{\delta+}}\cdots\cdots \underset{\longleftarrow}{L^{\delta-}}$$

(perpendicular) (parallel)

For the parallel vibration, changing to a more electron-withdrawing substituent of the substrate will lead to a more product-like TS, i.e. with a shorter Nu—C_α and a longer C_α—L bond in the TS (Hammond effect).[14] In the case of the Hammond effect, the sign of the product $\rho_{XZ}\rho_{YZ}$ becomes negative.

The Brønsted β_{Nu} and β_{lg} values are summarized in Tables 6 and 7. From the comparison of β_{Nu} with β_{lg} on changing the substituent in the substrate from Z = p-CH_3 to Z = p-NO_2, the TS movement could be monitored on the MOFJ diagram. When the substituent of the substrate is changed from Z = p-CH_3 to Z = p-NO_2, the value of β_{Nu} showed a larger increase than that of β_{lg}. Hence the formation of the Nu—C_α bond increases more than the breaking of the C_α—L bond in the TS; both the degree of Nu—C_α bond formation and C_a—L bond fission increase in the TS when the substituent of Z in the substrate changes from Z = p-CH_3 to Z = p-NO_2, and therefore the TS moves to a more product-like (* → *′). This result indicates that the TS movement accords with the Hammond effect and the sign of the product $\rho_{XZ}\rho_{YZ}$ is negative.

Table 6. Brønsted β_{Nu} values for the reactions of substituted (Z)-benzyl (X)-benzenesulfonates with pK_as[a] of pyridines in aceton at 35 °C

	X		
Z	m-NO_2	H	p-CH_3
p-NO_2	0·23	0·32	0·35
p-Cl	0·17	0·29	0·31
H	0·16	0·26	0·30
p-CH_3	0·16	0·25	0·26

[a] pK_as were evaluated from 1·199pK_a(water) + 5·630 (r = 0·986) in MeCN.[15]

Table 7. Brønsted β_{lg}[a] values for the reactions of substituted (Z)-benzyl (X)-benzenesulfonates with substituted (Y)-pyridines in acetone at 35 °C

	Y		
Z	H	3,4-$(CH_3)_2$	4-NH_2
p-NO_2	−0·62	−0·58	−0·43
p-Cl	−0·62	−0·56	−0·37
H	−0·57	−0·55	−0·34
p-CH_3	−0·55	−0·54	−0·36

[a] pK_as of arenesulfonates were relative to benzenesulfonate in sulfolane at 55 °C.[16]

In conclusion, the Hammett ρ values of the nucleophile, leaving group and substrate can be estimated from the structure of the TS, but the effect of the reactivity of the reactants themselves upon ρ has received scant consideration.

The magnitude of ρ_{ij} can be used to determine the structure of TS in the S_N reaction. In particular, the comparison of ρ_{YZ} with ρ_{XZ} and the sign of ρ_Z can indicate the type of S_N reaction, i.e. the results $\rho_z < 0$ and $\rho_{YZ} > \rho_{XZ}$ indicate that this reaction series proceeds via a dissociative S_N2 process. This result also accords with the treatment of the MOFJ diagram, and also predicts the movement of TS from the sign of the product $\rho_{XZ}\rho_{YZ}$, i.e. if the sign of the product $\rho_{XZ}\rho_{YZ}$ is positive, the TS movement accords with the Thornton effect, but if it is negative, the TS movement obeys the Hammond effect. In the case of these reaction series, a negative sign of $\rho_{XZ}\rho_{YZ}$ would permit the TS to move according to the Hammond effect.

EXPERIMENTAL

Materials. Materials were purchased from Wako or Merck. Acetone, used as the reaction solvents was refluxed over $KMnO_4$ for 1 day until the violet colour persisted, distilled, dried with anhydrous Na_2CO_3 for 3 days and fractionated by using a Widmer column.[7,17] Liquid pyridines were distilled after drying with KOH and stored in brown ampoules. Solid pyridines were recrystallized before use.[18] The preparation of the substrate and the product analysis were as described previously.[9]

Kinetic measurements. Rates were measured conductimetrically as described previously.[9] The pseudo-first-order rate constants, k_{obs}, were determined by a least-squares computer program. The precision of the fit to pseudo-first-order kinetics was generally satisfactory, with correlation coefficients >0·9999 over three half-lives of the reaction. Second-order rate constants, k_2, were determined by dividing k_{obs} by the initial pyridine concentration.

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