JOURNAL OF PHYSICAL ORGANIC CHEMISTRY. VOL. 2, 35–42 (1989)

CROSS INTERACTION CONSTANTS AS A MEASURE OF THE TRANSITION STATE STRUCTURE (PART III). MECHANISM OF REACTIONS BETWEEN 1-PHENYLETHYL BENZENESULFONATES WITH N,N-DIMETHYLANILINES

IKCHOON LEE, HYUNG YOON KIM, HAI WHANG LEE AND IN CHUL KIM
Department of Chemistry, Inha University, Inchon, 402–751, Korea

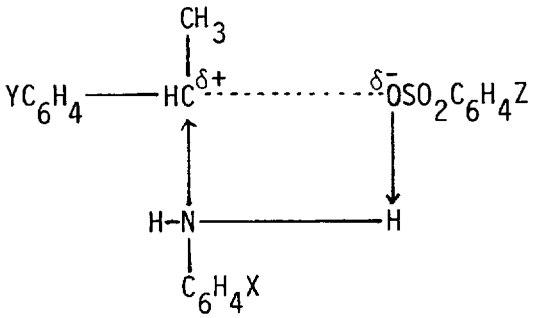
ABSTRACT

The kinetics and mechanisms of the reactions between 1-phenylethyl benzenesulfonates (1-PEB) with N,N-dimethylanilines are investigated in methanol at 35·0°C. Reactivity and selectivity trends were found to be similar to those for the reactions of 1-PEB with anilines, but the magnitudes of cross interaction constants, ρ_{XZ}, between substituents X in the nucleophile and Z in the leaving group were substantially smaller indicating no hydrogen-bond bypass bridge formation in the transition state. However, the magnitude of ρ_{XZ} suggested a direct electrostatic interaction between the reaction centers in the nucleophile and leaving group in the frontside nucleophilic attack with a loose transition state structure.

In a previous report[1] we interpreted the unusually large magnitudes of cross interaction constants ρ_{XZ}, equation (1),[2] between substituents X in the nucleophile and Z and in the substrate for the nucleophilic substitution reactions of 1-phenylethyl benzenesulfonates (1-PEB) with anilines in methanol–acetonitrile mixtures, equation (2), as evidence in support of the intermolecular S_Ni mechanism[3] involving a four-center transition state (TS), (I).

$$\log(k_{XZ}/_{HH}) = \rho_X\sigma_X + \rho_Z\sigma_Z + \rho_{XZ}\sigma_X\sigma_Z \qquad (1)$$

$$2XC_6H_4NH_2 + YC_6H_4CHCH_3OSO_2C_6H_4Z \rightleftarrows YC_6H_4CHCH_3NHC_6H_4X + XC_6H_4NH_3^+ + {}^-OSO_2C_6H_4Z \qquad (2)$$



(I)

0894–3230/89/010035–08$05.00
© 1989 by John Wiley & Sons, Ltd.

Received 25 January 1988
Revised 11 March 1988

A similar TS has originally been proposed by Okamoto *et al.*,[4] in their phenolysis studies of various 1-phenylethyl derivatives, to account for the net retention of the product configuration. In this type of TS, the approach of the nucleophile is restricted to frontside so that the product configuration is retained and the nucleophile provides a hydrogen atom which can hydrogen-bond to the leaving group (LG) forming a bypass bridge. In the structure, (I), the two substitutents X and Z can interact via two routes through —N—C—O— and —N—H—O—; an additional interaction route provided by the hydrogen-bond bridge enhances the intensity of interaction between the two substituents and leads to a remarkably large magnitude of cross interaction constant ρ_{XZ}.

One way of confirming the involvment of this four-center TS, (I), in reaction (2) is to compare the magnitude of ρ_{XZ} with those for the reactions having no hydrogen atom for the bridge formation in the nucleophile.

In this work we report the results of our kinetic studies on the reactions of 1-PEB with N,N-dimethylanilines (DMA),[5] reaction (3), in which no such hydrogen-bond bridge formation is possible. We have discussed the structure of the TS in detail using various selectivity parameters, especially the cross interaction constants.

$$XC_6H_4N(CH_3)_2 + YC_6H_4CHCH_3OSO_2C_6H_4Z \rightleftarrows YC_6H_4CHCH_3{}^+N(CH_3)_2C_6H_4X + {}^-OSO_2C_6H_4Z \qquad (3)$$

$X = p\text{-}OCH_3,\ p\text{-}CH_3,\ H,\ p\text{-}Cl$

$Y = p\text{-}OCH_3,\ p\text{-}CH_3,\ H,\ p\text{-}Cl$

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

RESULTS AND DISCUSSION

Second order rate constants k_2 for the reactions of 1-PEB with DMA, (3), are summarized in Table 1. Reference to Table 1 reveals that the rate increases with a stronger nucleophile ($X = p\text{-}OCH_3$) and with a better LG ($Z = p\text{-}NO_2$). The rate decreases, however, with a more electron-withdrawing substituent in the substrate ($Y = p\text{-}Cl$). All these reactivity trends are similar to those for the reactions of 1-PEB with anilines.[1]

The Hammett ρ_X[6a] values obtained by varying substituent X in the nucleophile are presented in Table 2. The magnitudes of ρ_X values ($\rho_X < 0$) are relatively large[6b] but somewhat smaller than those for reaction (2);[1] the size of ρ_X increases with a better LG and with a more electron-withdrawing substituent in the substrate suggesting a greater degree of bond formation.

The ρ_Z values for substituent (Z) variations in the LG are given in Table 3. The magnitude of ρ_Z with a more electron-donating substituent in the nucleophile and with a more electron-withdrawing substituent in the substrate, implying a greater degree of bond breaking. Thus a stronger nucleophile ($\rho_X < 0$) is accompanied by a greater degree of bond breaking, i.e. $\Delta r_{YZ} > 0$, and a better LG ($\rho_Z > 0$) leads to tighter bond formation, i.e. $\Delta r_{XY} < 0$. Here r_{ij} denotes the distance between reaction centers R_i and R_j in (II), where we have schematically shown the TS structure for normal S_N1 or S_N2 reactions with backside nucleophilic attack (inversion) comprising three fragments, the nucleophilic with substituent X (σ_X) and reaction center R_X, the substrate with Y (σ_Y) and R_Y, and the LG with Z (σ_Z). These

Table 1. Second order rate constants ($k_2 \times 10^2$ M^{-1} sec^{-1}) for reactions of 1-phenylethyl benzenesulfonates with N,N-dimethylanilines, (3), in MeOH at 35·0 °C

Y	X Z	*p*-CH$_3$	H	*p*-Cl	*p*-NO$_2$
p-OCH$_3$	*p*-OCH$_3$	5·06	9·69	15·9	76·2
	p-CH$_3$	3·53	6·68	10·8	50·4
	H	1·84	3·41	5·54	25·1
	p-Cl	0·723	1·36	2·08	8·69
p-CH$_3$	*p*-OCH$_3$	4·68	9·04	15·0	72·9
	p-CH$_3$	3·22	6·14	10·0	47·3
	H	1·65	3·10	5·18	23·2
	p-Cl	0·664	1·18	1·88	7·91
H	*p*-OCH$_3$	4·12	8·07	13·6	67·5
	p-CH$_3$	2·75	5·33	8·89	42·5
	H	1·38	2·64	4·13	20·4
	p-Cl	0·541	0·998	1·59	6·76
p-Cl	*p*-OCH$_3$	3·44	6·90	11·9	60·3
	p-CH$_3$	2·23	4·42	7·58	36·8
	H	1·08	2·13	3·41	17·1
	p-Cl	0·413	0·711	1·27	5·45

Table 2. The Hammett ρ_X values[a] for reaction (3)

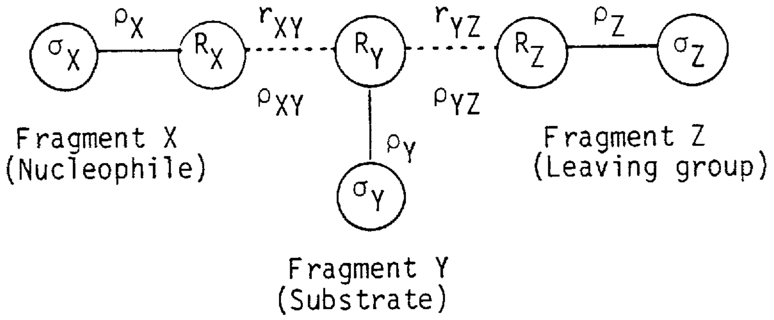
Y Z	*p*-CH$_3$	H	*p*-Cl	*p*-NO$_2$
p-OCH$_3$	−1·69	−1·70 (−2·13)[b]	−1·76	−1·84
p-CH$_3$	−1·71	−1·77 (−2·15)	−1·81	−1·97
H	−1·77	−1·80 (−2·19)	−1·87	−1·95
p-Cl	−1·88	−1·92 (−2·24)	−1·99	−2·08

[a] Correlation coefficients > 0·998.
[b] Values in parentheses are those for reaction (2).

Table 3. The Hammett ρ_Z values[a] for reaction (3)

X Y	*p*-OCH$_3$	*p*-CH$_3$	H	*p*-Cl
p-OCH$_3$	1·21	1·23	1·25	1·28
p-CH$_3$	1·19	1·20	1·22	1·25
H	1·17 (0·95)[b]	1·18 (0·95)	1·20 (0·97)	1·23 (1·00)
p-Cl	1·10	1·11	1·13	1·17

[a] Correlation coefficients > 0·997.
[b] Values in parentheses are those for reaction (2).



(II)

substituent effects on the TS variation are consistent with those for an intrinsic controlled reaction series,[7] for which the following relations are shown to hold.[8]

$$\Delta r_{XY} = \lambda\, \sigma_Z$$

$$\Delta r_{YZ} = \lambda'\, \sigma_X \qquad (4)$$

where λ and λ' are negative constants.

The variation of substitutent in the substrate from Y = *p*-OCH$_3$ to Y = *p*-Cl seems to cause a smaller increase in ρ_Z compared to that in ρ_X, indicating that bond formation is enhanced more than bond breaking by a more electron-withdrawing substitutent in the substrate. This is reasonable since bond breaking has already progressed much further than bond formation in the TS, so that further increase in bond breaking will be small. This is supported by a smaller $|\rho_Y|$, in Table 4, for a better LG due to a greater increase in bond formation than bond cleavage with an increase in the LG ability. Log (k_Y/k_H) vs σ_Y was better correlated with normal Hammett substituent constants rather than with σ_Y^+, albeit the TS will be shown to have a very loose structure (*vide infra*).[1]

The cross interaction constants for the reactions of 1-PEB with DMA are determined by multiple regression analysis[9] of the k_2 values in Table 1 using equation (1) and its analogs.

The results of the multiple regression analysis are summarized in Table 5.Comparison of ρ_X, ρ_Y and ρ_Z values in Table 5 with the corresponding values obtained by simple linear Hammett plots in Tables 2–4 shows very good agreement between the two. Table 5a shows that the

Table 4. The Hammett ρ_Y values[a] for reaction (3)

X Z	*p*-CH$_3$	H	*p*-Cl	*p*-NO$_2$
p-OCH$_3$	−0·33	−0·29	−0·25	−0·20
p-CH$_3$	−0·40	−0·36	−0·31	−0·27
H	−0·46	−0·41	−0·44	−0·33
	(−0·39)[b]	(−0·41)	(−0·36)	(−0·32)
p-Cl	−0·49	−0·50	−0·43	−0·40

[a] Correlation coefficients > 0.994.

[b] Values in parentheses are those for reaction (2).

Table 5. The cross interaction constants, ρ_{ij}, for reaction (3)

a

Z	ρ_X	ρ_Y	ρ_{XY}	Corr coeff*
p-CH_3	−1·76	−0·45	−0·35 (−0·22)†	1·00
H	−1·81	−0·40	−0·36 (−0·21)	0·999
p-Cl	−1·87	−0·38	−0·37 (−0·23)	1·00
p-NO_2	−1·99	−0·32	−0·39 (−0·25)	1·00

b

X	ρ_Y	ρ_Z	ρ_{YZ}	C.C.
p-OCH_3	−0·30	1·25	0·13 (0·10)†	0·998
p-CH_3	−0·36	1·22	0·13 (0·11)	0·998
H	−0·42	1·20	1·13 (0·13)	0·998
p-Cl	−0·50	1·13	0·13 (0·14)	0·998

c

Y	ρ_X	ρ_Z	ρ_{XZ}	C.C.
p-OCH_3	−1·71	1·15	−0·23 (−0·55)†	0·999
p-CH_3	−1·74	1·16	−0·24 (−0·55)	0·999
H	−1·80	1·19	−0·24 (−0·56)	0·999
p-Cl	−1·88	1·21	−0.25 (−0·56)	0·999

*A test for statistical significance indicated a confidence level of 99% in all cases: S. Wold and M. Sjöström, *Correlation Analysis in Chemistry*, ed. by N. B. Chapman, and J. Shorter, Plenum, New York, 1978, Chapter 1.

†Values in parentheses are those for reaction (2).

magnitudeof ρ_{XY} is relatively small, $|\rho_{XY}| \cong 0{\cdot}35$, which is approximately half the value for the normal S_N2 type reaction series ($|\rho_{XY}| \cong 0{\cdot}70$).[10] This suggests that bond formation in the TS is much less for the reactions of 1-PEB with DMA than in the S_N2 type reactions. The size of ρ_{XY} is, however, somewhat greater than that for the reactions of 1-PEB with anilines, [11] implying some increase in the degree of bond formation. The magnitude of ρ_{XY}, and hence the degree of bond formation in the TS, r_{XY}, is greater for a better LG ($\sigma_Z > 0$), which is in accord with our conclusion based on the magnitudes of ρ_X and ρ_Z; thus the correlation (5) holds for the reaction series (3).

$$\log|\rho_{XY}| = k\,\sigma_Z \qquad (5)$$

where k is a positive constant.[8] This is in line with equation (4), which has been shown to hold for an intrinsic controlled reaction series.

The magnitudes of ρ_{YZ} values in Table 5b are the smallest among the three cross interaction constants, $|\rho_{XY}|$, $|\rho_{YZ}|$ and $|\rho_{XZ}|$, and comparable to those for the dissociative S_N2 reactions of benzyl benzenesulfonates with anilines (0·11)[11] and for the reactions of 1-PEB with anilines

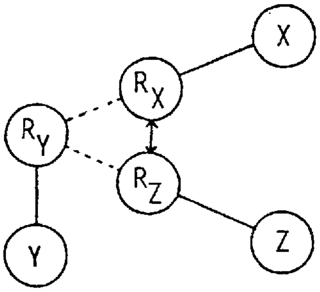
(0·13),[1] indicating the grossly dissociative nature of this reaction. Relatively little bond formation (small $|\rho_{XY}|$) and large bond cleavage (small $|\rho_{YZ}|$) therefore suggest an open 'exploded' TS structure that closely resembles that of an S_N1 type reaction.[12] The $|\rho_{YZ}|$ values are, however, nearly constant with respect to the substituent (X) variations in the nucleophile.

Since the polar and resonance effects of the substituents are transmitted through reaction centers R_X, R_Y and R_Z, the magnitude of cross interaction will be inversely proportional to the distances between the reaction centers,[2a,13] the lengths of carbon chains connecting substituents to the reaction centers remaining practically constant in the activation process.[13] Thus the size of ρ_{XZ} should be the smallest since the distance between R_X and R_Z is the longest, which is indeed true for the reactions of benzyl benzenesulfonate with anilines.[11]

On the contrary to the smallest $|\rho_{XZ}|$ expected for an S_N2 reaction, the ρ_{XZ} values for the reaction of 1-PEB with anilines were the greatest.[1] This remarkable enhancement of the cross interaction between X and Z was rationalized by a four-center TS, (I), involved in the intermolecular S_Ni mechanism.[3]

With the use of DMA as a nucleophile in this work, there will be no such enhancement of the cross interaction between X and Z in the four-center TS, (I), and the smaller $|\rho_{XZ}|$ values corresponding to those for a dissociative S_N2 reaction series (~0·11)[11] are expected. This expectation is indeed borne out in the low $|\rho_{XZ}|$ values of Table 5c; the size of $|\rho_{XZ}|$ is however still substantially greater than those for the normal S_N1 or dissociative S_N2 reactions with the backside nucleophilic attack,[11](II).

Steric hindrance by the methyl group of 1-PEB should be enhanced with DMA as the nucleophile as compared to the aniline, since two methyl groups surrounding the reaction center nitrogen will be more bulky, This implies that with the DMA the frontside approach of the nucleophile is even more likely to be enforced in the TS and the reaction will proceed with retention of the product configuration. The only difference between structure (I) and that of the TS with the DMA reaction (III) will be the absence of the H-bonded bypass bridge in the DMA reaction series. In the type of retentive S_N2 TS structure, however, there is a possibility of a direct electrostatic interaction[2i] between R_X and R_Z since the distance between them is now diminished substantially unlike in the case of (II); the cross interaction between X and Z should be enhanced somewhat, and hence a little greater $|\rho_{XZ}|$ will be obtained, as we find in Table 5c for this reaction series.



(III)

EXPERIMENTAL

Materials were as described in the previous report.[1] N,N-Dimethylanilines were prepared from anilines using dimethylsulfate by the known method.[14] The melting points and boiling points are summarized below.

Table 6

	$XC_6H_4N(CH_3)_2$			
	X = *p*-OCH_3	*p*-CH_3	H	*p*Cl
m.p. or B. (°C)	48–49	93–94/15 mm	79/13 mm	33
(lit)[15]	49	211/760 mm	194/760 mm	33·5
color	white	pale yellow	pale yellow	white

Rate constants. Rates were measured conductometrically at 35·0 °C. Pseudo-first order rate constants, k_1^{obs}, were determined by the Guggenheim method[16] with a large excess of aniline and second order rate constants, k_2, were obtained from the slope of a plot of k_1^{obs} vs [aniline], equation (6).

$$k_1^{obs} = k_1 + k_2[\text{aniline}] \qquad (6)$$

k_1 is the rate constant for methanolysis, which was found to be negligibly small compared to the second order term as evidenced by zero intercepts ($k_1 = 0$) in all cases. Good second order kinetics with linear correlation coefficients of better than 0·999 for the plots of equation (6) indicated that the reaction is free from an ionic strength effect or from the base catalysis by aniline.

ACKNOWLEDGEMENTS

We thank the Ministry of Education and the Korea Center for Theoretical Physics and Chemistry for support of this work.

REFERENCES

1. I. Lee, H. K. Kang and H. W. Lee, *J. Org. Chem.*, In press.
2. (a) I. Lee and S. C. Sohn, *J. Chem. Soc. Chem. Commun.*, 1055 (1986); (b) I. Lee and H. K. Kang, *Tetrahedron Lett.*, **28**, 1183 (1987); (c) I. Lee, H. Y. Kim and H. K. Kang, *J. Chem. Soc. Chem. Commun.*, 1216 (1987); (d) I. Lee, *Bull. Korean Chem. Soc.*, **8**, 200 (1987); (e) I. Lee, *Bull. Korean Chem. Soc.*, **8**, 426 (1987); (f) I. Lee, H. K. Kang and H. W. Lee, *J. Am. Chem. Soc.*, **109**, 7472 (1987); (g) I. Lee, C. S. Shim, S. Y. Chung and H. W. Lee, *J. Chem. Soc., Perkin 2*, In press; (h) I. Lee, Y. H. Choi and H. W. Lee, *J. Chem. Soc., Perkin 2*, In press; (i) W. P. Jenks, *Chem. Rev.*, **85**, 511 (1985); (j) M-F. Ruasse, A. Argile and J-E. Dubois, *J. Am. Chem. Soc.*, **106**, 4840 (1984).
3. E. S. Gould, *Mechanism and Structure in Organic Chemistry*, Holt, Rinehart and Winston, New York, 1959, p. 294.
4. K. Okamoto, K. Takeuchi and T. Inoue, *J. Chem. Soc., Perkin 2*, 842 (1980), and previous papers cited therein.
5. (a) T. Ando, H. Tanabe and H. Yamataka, *J. Am. Chem. Soc.*, **106**, 2084 (1984); (b) S-D. Yoh, *J. Korean Chem. Soc.*, **6**, 116 (1975).
6. (a) The σ values taken from: J. A. Dean, *Handbook of Organic Chemistry*, McGraw-Hill, New York, 1987, Section 7; (b) C. D. Johnson, *The Hammett Equation*, Cambridge Univ. Press, Cambridge, 1973, Chapt. 1.
7. I. Lee and H. S. Seo. *Bull. Korean Chem. Soc.*, **7**, 448 (1986).
8. I. Lee, Submitted for publication.
9. J. Short, *Correlation Analysis of Organic Reactivity*, Research Studies Press, Chichester, 1982, Chapt. 2.

10. I. Lee, C. S. Shim, S. Y. Chung, H. Y. Kim and H. W. Lee, *J. Chem. Soc. Perkin 2*, In press.
11. (a) I. Lee, H. W. Lee, S. C. Sohn and C. S. Kim, *Tetrahedron*, **41**, 2635 (1985); (b) I. Lee, S. C. Sohn, C. H. Kang and Y. J. Oh, *J. Chem. Soc., Perkin 2*, 1631 (1986); (c) I. Lee, S. C. Sohn, Y. J. Oh and B. C. Lee, *Tetrahedron*, **42**, 4713 (1986).
12. J. P. Richard and W. P. Jenks, *J. Am Chem. Soc.*, **106**, 1383 (1984).
13. I. Lee, Submitted for publication.
14. F. G. Bordwell and P. J. Boutan, *J. Am. Chem. Soc.*, **78**, 87 (1956).
15. R. C. Weast, M. J. Astle and W. H. Beyer, *CRC Handbook of Chemistry and Physics*, 65th ed., 1985, p. c-94–95.
16. E. A. Guggenheim, *Phil. Mag.*, **2**, 538 (1926).