

치환 2-Phenylethyl arenesulfonate 류와 치환 피리딘류의 Menschutkin 형 반응에 관한 치환기 효과

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Substituent Effects for the Menschutkin-Type Reaction of Substituted 2-Phenylethyl arenesulfonates with Substituted Pyridines

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요약. 치환 2-phenylethyl tosylate와 치환 피리딘을 아세토니트릴에서, 2-phenylethyl *m*-nitrobenzenesulfonate(2-PNS)와 치환 피리딘을 아세토니트릴과 메탄올 용매 중에서 각각 반응시켰다. 기질과 친핵체 다같이 전자를 미치는 치환기는 반응속도를 증가시켰다. 이들 결과는 전이상태 변화를 예측하는 More O'Ferrall 과 양자역학적인 모델에서 결합 파괴가 결합형성보다 더 진전된 S_N2 메커니즘으로 진행함을 보였다. 전이상태 변화는 양자 역학적인 모델의 예측이 실험치와 잘 일치하였고 이탈기에서는 More O'Ferrall 도시가 잘 맞지 않았다. 2-PNS와 피리딘류와의 반응에서는 아세토니트릴이 메탄올 용매보다 반응이 빨랐다.

ABSTRACT. The rates for the reaction of substituted 2-phenylethyl tosylates with substituted pyridines were measured in acetonitrile and that of 2-PNS with substituted pyridines were investigated in both acetonitrile and methanol. The substituent effect was accelerated by an electron-donating substituent on both substrate and nucleophile. Results showed that More O'Ferrall and quantum mechanical model of predicting transition state structure suggest the reaction proceeds via an S_N2 mechanism, in which bond-breaking is more advanced than bond-formation. Transition state variation predicted with the quantum mechanical model is consistent with the experimental results, whereas the predictions provided by the More O'Ferrall plots is found to be inconsistent in leaving group. In the reaction of 2-PNS, the rate constants in acetonitrile were larger than that in methanol.

INTRODUCTION

In previous papers,^{1,2} we reported on the Menschutkin-type S_N2 reaction for 2-phenylethyl arenesulfonates with pyridines in CH₃CN and solvent effect³ for the reaction of phenacyl bromide with substituted anilines in MeOH and DMF, respecti-

vely.

The substituent effect in substrate of 2-phenylethyl system was not so significant than expected, but still the electron-donating substituents showed the slight acceleration to give a small negative value and Hammett plot slight curvature on the acting substituents, even though it is not so re-

markable than that of benzyl system. These results represented a little bit favorable bond-breaking at the transition state by the electron-donating substituents. The effect of leaving group in arenesulfonates in which the rate constants were decreased by electron-donating substituents, while electron-withdrawing groups showed the reverse effects. On the other hand, in the nucleophile, electron-donating substituents accelerated the reaction rates. The rates of reaction for the phenacyl bromide with substituted anilines³ increased with electron-donating power of substituent and showed larger in DMF than in MeOH. The substituent effect of this reaction could be described as an S_N2 mechanism and bond-formation more proceeds in DMF relative to MeOH. In this paper we report the results of the relationship between substrate(Z), nucleophile(Y) and Brønsted β values to obtain more detailed information for Menschutkin-type S_N2 reactions of (Z)-substituted 2-phenylethyl (X)-substituted benzenesulfonated with (Y)-substituted pyridines. In addition we comment transition state variation in this reaction by the use of More O'Ferrall⁴, quantum mechanical model⁵, and solvent effects for the reaction of 2-PNS.

EXPERIMENTAL

All materials used throughout were commercial products (Wako, Japan). Acetonitrile and methanol were purified as described in a previous report¹. The rates were measured conductometrically using conductivity meter, Barnsted Model PM 70CB (U.S.A.), by the procedure previously reported and thermostatic bath as before.²

The reactions, carried out in a large excess of pyridine, follow a pseudo first-order kinetics,

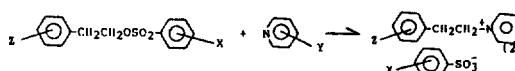
$$k_{\text{obs}} = k_2 \cdot (\text{pyridine}) \quad (1)$$

Second-order rate constants were calculated from

the slope of the plot of k_{obs} against pyridine concentration as eq. (1). 2-PNS and the pyridinium salt were prepared as before.⁶

RESULTS AND DISCUSSION

The reaction of (Z)-2-phenylethyl (X)-benzenesulfonates with (Y)-pyridines in acetonitrile yielded substituted 2-phenylethyl-pyridinium arenesulfonates quantitatively as equation (2)



Substituent and Solvent Effects. The rates show slight acceleration by electron donating substituents in substrate as shown in Table 1(a). In pyridines, rate constants increases by electron-donating substituents, while electron-withdrawing

Table 1. Kinetic data and activation parameters for the reaction of (X)-2-phenylethyl tosylates with (Y)-pyridines in acetonitrile

(a) $Z-\text{C}_6\text{H}_4-\text{CH}_2\text{CH}_2\text{OTs} + \text{N}(\text{C}_5\text{H}_4)$

Subs. (Z)	$k_2 \times 10^4 / \text{mol-min}$			ΔH^* (kcal/mol)	ΔS^* (e.u.)	ΔG^* (kcal/mol)
	50 °C	60 °C	70 °C			
<i>p</i> -CH ₃ O	15.6	35.2	74.1	16.7	20.6	23.6
H	10.3	21.8	49.2	16.8	20.4	23.6
<i>p</i> -Br	8.1	15.9	40.6	14.3	28.5	23.8
<i>p</i> -Cl	7.9	15.5	38.1	12.8	33.1	23.8
<i>p</i> -NO ₂	7.2	15.2	25.2	13.1	33.2	24.2

(b) $\text{C}_6\text{H}_5-\text{CH}_2\text{CH}_2\text{OTs} + \text{N}(\text{C}_5\text{H}_4\text{Y})$

Subs. (Y)	$k_2 \times 10^4 / \text{mol-min}$			E_a (kcal/mol)	$\Delta S^*(60^\circ\text{C})$ (e.u.)
	50 °C	60 °C	70 °C		
4-NH ₂	90.8	241.9	444.6	17.1	15.6
3,5-(CH ₃) ₂	16.5	47.7	106.1	18.1	17.0
3-CH ₃	15.2	24.3	51.1	16.9	22.0
H		22.0	48.9	18.1	18.8
3-CONH ₂		12.1	24.7	16.2	25.5
3-C ₆ H ₅ CO		8.3	20.4	20.6	13.4
3-Br		6.2	12.7	16.3	26.8
3-CN		5.7	11.5	15.9	27.9
4-CN		4.3	9.1	17.1	24.9

Table 2. Kinetic data for the reaction of 2-phenylethyl *m*-nitrobenzenesulfonate with pyridines in CH₃CN and MeOH (a) in CH₃CN

Subs. (Y)	$K_2 \times 10^5 (l/mol \cdot sec)$			ΔH^* (kcal/ mol)	ΔS^* (e.u.)	ΔG^* (kcal/ mol)
	40 °C	50 °C	60 °C			
Pyridine	4.42	10.6	22.8	16.35	26.21	24.82
3-Methyl pyridine	5.82	11.9	25.0	14.44	31.89	24.74
4-Methyl pyridine	7.98	14.2	26.5	11.78	39.77	24.63
3,5-Dimethyl pyridine	8.91	18.9	42.0	15.4	28.00	24.44
3,4-Dimethyl pyridine	16.7	20.3	49.0	10.74	42.28	24.40

(b) in MeOH

Pyridine	3.3	5.0	18.1	16.88	26.07	25.3
3-Methyl pyridine	4.20	9.03	22.2	16.58	25.82	24.92
4-Methyl pyridine	4.91	12.4	23.2	15.42	28.78	24.72
3,5-Dimethyl pyridine	6.92	16.4	41.2	17.81	20.83	24.54
3,4-Dimethyl pyridine	16.3	19.5	42.7	9.07	47.52	15.36

ents, while electron-withdrawing ones retard as a typical S_N2 reaction in Table 1(b).

In substrate, the resultant effects appear to be not so well correlate with linearity to give a small negative ρ values to cause slight curvature,² even though it is not so remarkable as that of benzyl system. These results represent a little favorable bond breakin by electron-donating (Z)-substituents, and the Hammett ρ value, which is variable but always negative, indicates the prevailing contribution of the bond breaking on the transition state, which is looser or tighter depending on the substituents.

In Table 2, although the rate constants in acetonitrile are larger than that in methanol, the changing tendencies of the rate constants in both solvents are same on the same substituents. The additivity of the Hammett equation is sometimes very good, provided interaction are absent, the additive principle² yield:

$$\log k/k = \rho(\sigma_A + \sigma_B) = \rho \Sigma \sigma \quad (3)$$

In this study, the σ values of 3,5- and 3,4-dimethyl pyridine were also used above additive principle. In case of methanolic, protic solvent, the rate con-

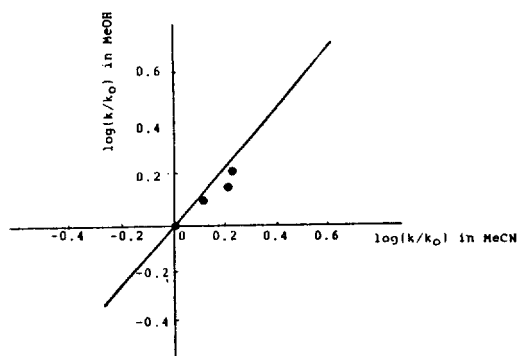


Fig. 1. Plot of the rate constants for the reaction of 2-phenyl ethyl *m*-nitrobenzenesulfonate with pyridines in MeCN and MeOH at 40 °C. The substituents included in this plot are H, 3-CH₃, 4-CH₃, 3,5-(CH₃)₂, and 3,4-(CH₃)₂.

stants are lower than that of dipolar aprotic acetonitrile solvent, it has been point out by Hughes and Ingold,⁷ that hydrogen bonding between the methanols and the pyridine, thus reducing the free energy of reactants. There does seem to be a consistent decrease in ΔH^* in the dipolar aprotic solvent. The decrease in ΔH^* can be attributed two possible cases. The first, and most common, explanation is that desolvation of nucleophile or base in the aprotic solvent relative to the protic solvent raises the energy of the reactants, thus diminishing

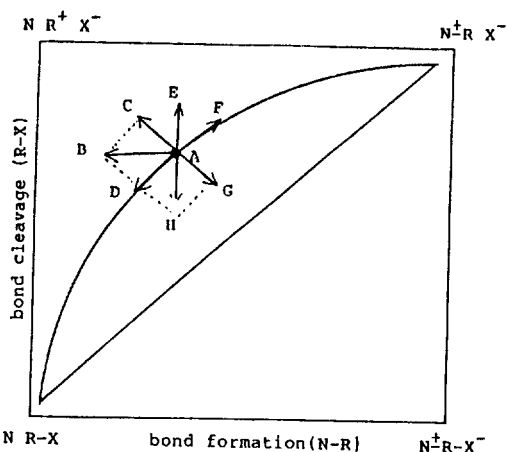


Fig. 2. A. More O'Ferrall plot for an S_N2 reaction of (Z)-2-phenylethyl-(X)-benzenesulfonates with (Y)-pyridines.

the energy gap between the reactants and the transition state, the second explanation is that the lowering of the activation energy is caused by increased solvation of the transition state in the dipolar aprotic solvent. These results are caused the large rate constants in acetonitrile.

The Hammett ρ value for the reaction of 2-PNS with (Y)-pyridines was large and negative, the reaction rate is very sensitive to substituents and increased with electron-donating power of substituted pyridines. The reaction, therefore, is a nucleophilic displacement of pyridine to 2-PNS and the following equation was obtained from the rate constants

$$\log k/k_0 = -2.44\sigma - 0.025 \text{ (in } \text{CH}_3\text{CN at } 40^\circ\text{C)}$$

$$\log k/k_0 = -2.95\sigma - 0.052 \text{ (in MeOH at } 40^\circ\text{C)}$$

Good linearity of Brønsted relationship has been reported⁹⁻¹² on quarternization of substituted N,N-dimethylanilines and pyridines.

$$\log k = 0.42p k_a - 6.58 \text{ (40}^\circ\text{C in } \text{CH}_3\text{CN)}$$

$$\log k = 0.50p k_a - 7.15 \text{ (40}^\circ\text{C in MeOH)}$$

On the other hand, $\log k/k_0$ plot for the reaction of 2-PNS with pyridines in MeOH and CH_3CN are good correlated with 0.812 of slope ($r = 0.997$;

Table 3. ρ_Z , ρ_Y , and β values for the reaction of substitute (Z)-2-phenylethyl *m*-nitrobenzenesulfonate with (Y)-pyridines in CH_3CN

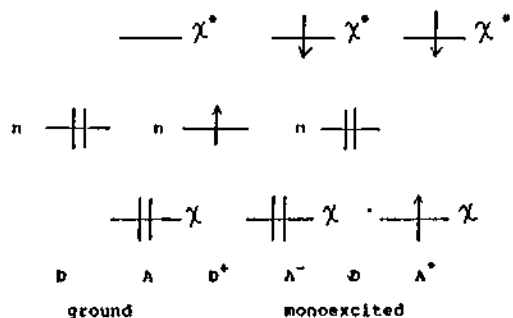
(a) ρ_Z values		
Y	ρ_Z	r
4-NH ₂	-0.008	0.923
4-Me	-0.060	0.930
H	-0.150	0.999
3-CONH ₂	-0.222	0.942

(b) ρ_Y and β values				
Z	<i>p</i> -MeO	H	<i>p</i> -Br	<i>p</i> -NO ₂
ρ_Z	-1.381	-1.638	-1.682	-1.740
	($r = 0.985$)	(0.993)	(0.992)	(0.998)
β	0.246	0.259	0.275	0.284
	($r = 0.987$)	(0.982)	(0.989)	(0.985)

Fig. 1). From good correlation, it was considered that the reaction mechanism has not different from both solvents.

Transition State Variation by Use of More O'Ferrall Plots and Quantum Mechanical Model. In this section, first, we apply the More O'Ferrall approach, quantum mechanical model, and examine the prediction of S_N2 transition state variations by the substituent effects of Z, Y, and X in eq.(2). The possible pathway for a nucleophilic substitution of 2-phenylethyl arenesulfonates with pyridine in acetonitrile are presented via dissociative S_N2 path², which will be located between S_N1 and S_N2 paths as presented in Fig. 2.

We examine the effect expected from increasing the electron-donating ability of substituent Z, eq.(2), thus stabilizing R^+X^- and lowering the upper left corner of Fig. 2. If transition state lies at the mid-way point A, then applying the Thornton's rule results in movement of the transition state to point C. In this case the transition state will be looser; involving more R-X bond cleavage, less N-R bond formation; more positive charge development on R, and negative charge development on X. Judging from the experimental results, the accelerating effects of electron-donating *p*-MeO (one of substituents Z) in Table 1(a) are therefore in line with the above prediction; this



Scheme 1. Ground and excited reactant configurations for the description of nucleophilic attacks*

*S. S. Shaik, *J. Am. Chem. Soc.*, **103**, 3692 (1981).

Table 4. Valence bond description of donor-acceptor configurations and their structural effect on the reaction complex^a

Configu- ration	Valence bond description		Structural effect on reaction complex	
	primary	secondary	N-R	R-X
DA	N:R·X	N:R+:X-	loose	tight
D+A-	N+:R:X-	N+R:·X	tight	loose
DA*	N:R+:X-	N:R·X	loose	loose

^aA. Pross and S. S. Shaik, *J. Am. Chem. Soc.*, **103**, 3702 (1981).

reaction proceeds via transition state in which there is significant positive charge development on carbon and such transition state result when R-X bond cleavage proceeds more rapidly than N-R bond formation. Other experimental results in Table 3(b) show that $|\rho_Y|$ and β values are decreased by electron-donating substituents on substrate.

This is consistent with the prediction of the More O'Ferrall model since the decrease in $|\rho_Y|$ and β values can be taken as the decrease in bond-formation. Substitution of above electron-donating groups on substrate will stabilize DA* configuration of quantum mechanical model as scheme 1 and Table 4, The loose structure of transition state will be expected.

The ρ_Z value of the experimental results in Table 3(a) is negative in which transition state is loose structure. Alternately, the right corners, and

the transition state A will now move to G and D. The new transition state will, therefore, lie at H. The resultant of these two vectors, and will be decreased in R-X cleavage, no change in N-R bond formation. Support for this prediction can be taken from the experimental data (in Table 3(a)). While, the substitution of electron-withdrawing groups in the pyridine would destabilized the right corners and move the transition state A to E, which is the result sum of vectors AC (Thornton's rule) and AF (Hammond's rule). The new transition state will have not change in bond-formation and increased bond-breaking, this is consistent with our experimental results, as Table 3(a). Next, we thought the substituent effect of leaving group in the sulfonate. An electron-withdrawing group on the leaving sulfonate, increase the rate in the order of $m\text{-NO}_2 > p\text{-CH}_3$. The More O'Ferrall model stabilize the upper corners and the transition state will move to point B. The variation of transition state expected from A to B is no change in bond-breaking and decreased bond-formation. The experimental results show that the $|\rho_Y|$ and β values are increased, while $|\rho_Z|$ values are decreased as previously reported^{1,2} going from $p\text{-CH}_3$ to $m\text{-NO}_2$ in the leaving group. This is not accord with the More O'Ferrall model. On the other hand, Pross *et al.*⁵ discussed the stabilized D+A- configuration in the leaving group will lead large effect in the transition state and expected that the more increasing the leaving ability, the more bond-formation will proceed. Experimental results show that an increasing of the leaving ability in sulfonate group is accompanied by the increasing of both $|\rho_Y|$ and β values, *i.e.* decreasing the $|\rho_Z|$ value means that the bond-formation of N-R is progressively proceeded in the transition state according to the sulfonate group. In view of the fact that the experimental results are in full accord with the prediction of quantum mechanical model but are only in partial accord with those of

the More O'Ferrall model.

We are thus lead to recognize the superior nature of the quantum mechanical model in the prediction of transition state variation for the reaction of substituted 2-phenylethyl arenesulfonates with substituted pyridines.

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