Structure-Reactivity Relationship of Benzyl Benzenesulfonates.
Part 4. Application of Correlation Interaction Coefficients

Soo-Dong Yoh*, Duk-Young Cheong, Jong-Hwan Park,
Sung-Hong Kim, and Kyu-Tak Howang[†]

Department of Chemistry Education, Kyungpook National University, Taegu 702-701, Korea
[†]*Department of Chemistry Education, Taegu University, Kyungsan 713-714, Korea*

The mechanism of nucleophilic displacement was studied by using three variable systems of ρ_X, ρ_Y, and ρ_Z obtained from the change of substituent X, Y, and Z for the reaction of (Z)-substituted benzyl (X)-benzensulfonates with (Y)-substituted thiobenzamides in acetone at 45 °C. The results $\rho_Z < 0$ and $\rho_{YZ} > \rho_{XZ}$ indicate that this reaction series proceeded *via* a dissociative S_N2 mechanism. The prediction of the movement of TS by using the sign of $\rho_{XZ} \cdot \rho_{YZ}$ accorded with the Hammond postulate.

Introduction

Nucleophilic displacement is promoted by facile bond formation with the nucleophile, facile bond breaking with the leaving group, and stabilization of the substrate moiety at the transition state (TS). In the detailed analysis of the mechanism, to establish the overall stabilization of the TS, it is important to evaluate contributions from three species as following; substrate, nucleophile, and leaving group.

In the previous works[1], we proposed the magnitude of the correlation interaction coefficient, ρ_{ij}, between substituents i and j, as expressed by

$$\log(k_{ij}/k_{00}) = \rho_i \sigma_i + \rho_j \sigma_j + \rho_{ij} \sigma_i \sigma_j$$

and therefore ρ_{XZ} (ρ_{ZX}) and ρ_{YZ} (ρ_{ZY}) are represented by the following equations,

$$\log(k_{XZ}/k_{00}) = \rho_X \sigma_X + \rho_Z \sigma_Z + \rho_{XZ} \sigma_X \sigma_Z \qquad (1)$$

$$\log(k_{YZ}/k_{00}) = \rho_Y \sigma_Y + \rho_Z \sigma_Z + \rho_{YZ} \sigma_Y \sigma_Z \qquad (2)$$

, 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 ρ_i with σ_j (or ρ_j with σ_i). That is, ρ_{XZ} and ρ_{YZ} mean the degree of C_α-L bond fission and Nu-C_α formation, respectively.

Recently, there has been considerable interest in multiple Hammett plots for benzylic and its related derivatives.[2] In the TS structure, the nucleophilic substitutions predicted by both the sign of ρ_Z and the comparison of the relative value of $|\rho_{XZ}|$ and $|\rho_{YZ}|$.[3]

In this paper, we report the results of kinetic investigation and the characterizing TS structures which can be predicted by the correlation interaction coefficient for the reaction of benzyl arenesulfonates with thiobenzamides, in relation to the previous successful applications for the substitution effect. The TS for an S_N reaction can be represented as being composed of three following fragments; nucleophile with Y, substrate with Z, and leaving moiety with X, which are attached to each reaction centre, as shown in Scheme 1, where dN (or dL) is the distance between Nu (or L) and C_α.
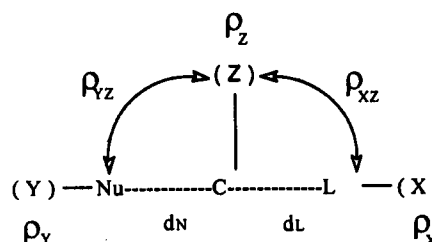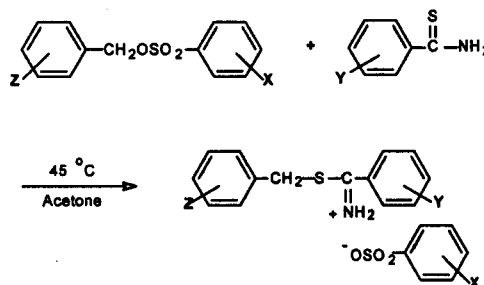
Scheme 1.

X = 4-CH₃, H, 3-NO₂
Y = 4-CH₃, H, 4-Cl
Z = H, 4-Cl, 4-NO₂

Scheme 2.

Results and Discussion

The kinetic scheme for the nucleophilic displacement to yield the salts of benzyl derivatives is depicted in Scheme 2.

The reaction rates were determined by monitoring the changes in the electrical conductance on formation of the salt from the reaction of substituted (Z)-benzyl (X)-benzenesulfonates with substituted (Y)-thiobenzamides in acetone, and the second-order rate constants, k_2, are summarized in Table 1.

The reaction rate is increased by electron-donating substituent in thiobenzamide, which indicates that the thiobenzamide plays a role of nucleophile. With increasing leaving ability of leaving moiety and electron-donating ability in

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Table 1. Second-order rate constants, $k_2 \times 10^4$ ($l \cdot mol^{-1} \cdot s^{-1}$), for the reactions of substituted (Z)-benzyl (X)-benzenesulfonates with (Y)-thiobenzamides in acetone at 45 °C

Z	X	Y		
		4-CH₃	H	4-Cl
4-NO₂	3-NO₂	103	70.8	48.2
	H	2.78	1.69	1.11
	4-CH₃	1.28	0.769	0.471
4-Cl	3-NO₂	270	200	144
	H	7.75	5.81	3.62
	4-CH₃	3.63	2.37	1.63
H	3-NO₂	296	244	198
	H	11.8	7.69	6.37
	4-CH₃	5.01	3.81	2.37

substrate, the reaction rate increases. The change of rate constants with variation of substituent is well linear and the results of Hammett plot, the ρ_X, ρ_Y, and ρ_Z values are listed in Table 2. The value of ρ_X is increased with the substituent of leaving moiety changes from electron-donating Y=4-CH₃ to electron withdrawing Y=4-Cl groups. In contrast, the $|\rho_Y|$ values are decreased as the σ value of the leaving group is increased when Z is constant. These results qualitatively suggest that the stronger (weaker) the nucleophilicity of nucleophiles is, the less (more) bond breaking between the benzylic α-carbon and the oxygen of the sulfonate in the TS is. The results are in harmony with the structure of the S_N2 transition state by Yoh *et al.*,[4(a)] Swain,[4(b)] Thornton,[4(c)] Harris, and Kurz.[4(d)] The sign of ρ_Z is negative, which indicates that the reaction center of the substrate has developed a positive charge, therefore the degree of bond breaking is more advanced than that of bond formation in the TS for the reaction series.

The magnitudes of ρ_X are larger than those of $|\rho_Y|$, and the sign of the ρ_X is positive and is increased with a more electron-withdrawing substituent in the nucleophile or the substrate. The sign of ρ_Y is negative and the magnitude of $|\rho_Y|$ is increased with a lower leaving ability of the leaving group and with a more electron withdrawing substituent in the substrate. When we compare the present reaction with the one between subsitiuted benzyl benzenesulfonates and pyridines, which obeyed with a dissociative S_N2 mechanism,[2(b)] the magenitudes of $|\rho_Y|$ are smaller and ρ_X are larger than the corresponding values for pyridine nucleophile. This result shows that bond formation is less advanced, but bond breaking is more enhanced than the case of pyridine. Therefore, the reaction between subsitiuted benzyl benzenesulfonates and thiobenzamides is more dissociative S_N2 path way than that of the reaction between subsitiuted benzyl benzenesulfonates and pyridines.

In Table 3, the variation of the substituents in the substrate from Z=H to p-NO₂ seems to be increased less in ρ_X than in $|\rho_Y|$. As mentioned above, this is reasonable to expect that bond breaking has already progressed much further than bond formation in the TS, so the increasing value in bond breaking will be small, but that in bond formation will be large. These results will affect the ρ_{ij} values, the magnitude of ρ_{XZ} is smaller than that of ρ_{YZ}, since the length of the C_α-L bond in the TS is the same or slightly

Table 2. Reaction constants (ρ_X, ρ_Y, and ρ_Z) and correlation interaction coefficient (ρ_{ij}) for the reactions of (Z)-benzyl (X)-benzenesulfonates with (Y)-thiobenzamides in acetone at 45 °C

Z	ρ_X			ρ_{XY}
	Y=4-CH₃	H	4-Cl	
4-NO₂	2.18	2.25	2.29	0.27
4-Cl	2.14	2.18	2.22	0.20
H	2.00	2.07	2.11	0.27
ρ_{XZ}	0.20	0.21	0.21	

Z	ρ_Y			ρ_{XY}
	X=3-NO₂	H	4-CH₃	
4-NO₂	−0.820	−0.981	−1.08	0.28
4-Cl	−0.676	−0.829	−0.862	0.21
H	−0.436	−0.652	−0.658	0.27
ρ_{YZ}	−0.45	−0.40	−0.52	

X	ρ_Z			ρ_{YZ}
	Y=4-CH₃	H	4-Cl	
3-NO₂	−0.619	−0.713	−0.801	−0.45
H	−0.806	−0.868	−0.963	−0.39
3-CH₃	−0.772	−0.891	−0.979	−0.51
ρ_{XZ}	0.20	0.21	0.21	

longer than that of the Nu-C_α bond when the substituents of the substrate change.[2(b)] So the degree of variation in the distance of dL (Scheme 1) from the reaction center is small, whereas the degree of variation in the distance of dN (Scheme 1) is large in the case of $|\rho_{YZ}|$. Thus, from both the sign of ρ_Z and the comparison of ρ_{ij} ($|\rho_{YZ}| > |\rho_{XZ}|$), this reaction can be described to be a dissociative S_N2 mechanism.

On the one hand, in Table 3, the TS movement can be predicted by the sign of product $\rho_{XZ} \cdot \rho_{YZ}$. With changing to a more electron withdrawing substituent of Z on the substrate, the values of $|\rho_Y|$ and ρ_X are increased, which means both of bond formation and bond cleavage are more enhanced. From this result, we can predict that the TS would move parallel vibration (Nu$^{\delta+}$ $\cdots \longrightarrow \cdots \cdots$ $C_\alpha^{\delta+}$ $\cdots \cdots \longrightarrow$ $\cdots L^{\delta-}$) and the sign of the product $\rho_{XZ} \cdot \rho_{YZ}$ would be reveal negative. The parallel vibration will lead that the TS movement accords with the Hammond effect. Therefore, we conclude that the sign of the product $\rho_{XZ} \cdot \rho_{YZ}$ is negative then the TS movement obeys the Hammond effect.

Table 3. The Influence of a Change of Substituent Z in the Substrate on the TS of an diss-S_N2 Reaction at 45 °C in Acetone

Z	ρ_Y (X=H)	Relative Nu-C_α bond length	C_α	Relative C_α-L	ρ_X
4-NO₂	−0.981	Nu········ C_α········L			2.25
4-Cl	−0.829	Nu········ C_α ······L			2.18
H	−0.652	Nu··········C_α·····L			2.11
	ρ_{YZ}=−0.40	ρ_Z < 0			ρ_{XZ}=0.21

Experimental

Materials. Materials were purchased from Wako or Merck. Acetone was refluxed over $KMnO_4$ for 1 day until the violet colour persists, distilled, dried with anhydrous Na_2CO_3 for 3 days, and fractionated by using Widmer column.[4,a),6] Thiobenzamides were used after recrystallization with ethanol.

M.p.s for $Y-C_6H_4C(S)NH_2$ were Y=p-CH_3, 167-168 °C (Lit.,[7] 168 °C); H, 115-116 °C (Lit.,[7] 115-116 °C); p-Cl, 129.5-130 °C (Lit.,[7] 130 °C).

Kinetic Measurements. Rates were measured conductimetrically as described before.[5] Pseudo-first-order rate constants, k_{obs}, were determined by the least-squares computer program. The precision of the fit to pseudo-first-order kinetics was generally satisfactory, with correlation coefficient $\geq$ 0.9999 over 3 half-lives of the reaction. Second-order rate constants, k_2, were determined by dividing k_{obs} by the initial thiobenzamide concentration.

Product analysis. Products of the reaction of substituted benzyl benzenesulfonates and substituted thiobenzamides were identified by IR, ^1H NMR, mass spectra.

Benzylthiobenzamidiniumsulfonate was prepared by a mixture of 0.015 mol benzyl- benzenesulfonate and 0.015 mol of thiobenzamide dissolved 100 mL acetone at 45 °C for 2 days. The product was collected by suction, and recrystallized from ethyl acetate. Yellowish-white solid were obtained with mp 149-150 °C. IR (KBr): 3170, 3160, 1640 (N-H), 1440, 1030, 160, and 130 (-S-), 1230, 1180, and 560 cm^{-1} (SO_2); ^1H NMR (300 MHz, $CDCl_3$) δ=11.4-12.6 (s, 2H, =NH_2), 7.6-7.9 (m, 5H, -S-C(=)-Φ), 7.2-7.5 (m, 10H, Φ-CH_2, O_3S-Φ), 4.8 (s, 2H, -CH_2-).

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A Novel Synthesis of Oligopyridines

Jae Gyu Park and Yurngdong Jahng*

College of Pharmacy, Yeungnam University, Kyongsan 712-749, Korea
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An efficient synthetic method applicable for the preparation of symmetrical as well as unsymmetrical terdentates, and 2-aryl-2,2'-bipyridines was developed, in which a Michael addition of enamine onto enaminone was employed as a key step.

Introduction

The terdentate, 2,2':6',2"-terpyridine has been attractive because of its potentials to form ML_2 metal complexes with various d_6 transition metals [especially Ru(II)] showing various intriguing properties.[1] Although a plenty of 2,2':6',2"-terpyridine derivatives as well as their Ru(II) complexes were prepared and studied, only a limited number of unsym-

metric terpyridines were reported presumably due to the lack of synthetic method with general applicability.[2] Because of low reactivity of pyridine nucleus, direct introduction of the substituent(s) on the pyridine nucleus is not an effective method to prepare the unsymmetric terpyridines. Among the limited number of synthetic methods for unsymmetric terpyridines, a coupling reaction[3] between 6-halo-2,2'-bipyridines and/or 2-halopyridines and the Krö