

Effect of Changing Electrophilic Center from Carbonyl to Sulfonyl Group on Electrophilicity

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Factors influencing nucleophilicity have intensively been investigated and many relationships have been established to correlate nucleophilicity with one or more properties of nucleophiles.¹⁻³ Among them, the basicity of nucleophiles has been most commonly used to correlate nucleophilicity, although nucleophiles possessing a heteroatom adjacent to the nucleophilic site have often been reported to exhibit abnormally enhanced nucleophilicity than would be predicted from their basicity.⁴⁻⁸ The enhanced nucleophilicity has been termed the α -effect and several theories have been suggested as the origin of the α -effect.⁴⁻⁸

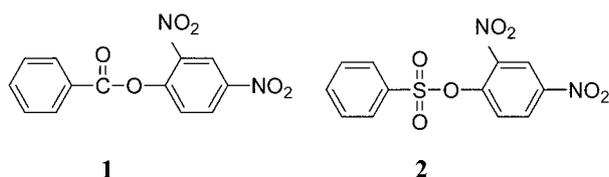
On the other hand, factors influencing electrophilicity have much less been investigated. Changing the electrophilic center from a carbonyl to a sulfonyl or phosphinyl group would exert significant effect on their electrophilicity. However, systematic studies on changing such electrophilic centers have been lacking. Only scattered information on the reactivity of carbonyl, sulfonyl, and phosphinyl esters of similar structures is available.⁹

reactions with 2,4-dinitrophenyl benzoate (**1**)¹⁰ and benzenesulfonate (**2**).¹¹ Besides, the mechanism for the reactions of **1** with three representative anionic nucleophiles such as OH^- , CN^- , and N_3^- has systematically been investigated.¹² We have extended our study to the reactions of **2** with these anionic nucleophiles to investigate the effect of changing the electrophilic center from a carbonyl to a sulfonyl group on the electrophilicity by comparing the data obtained in the present study with those obtained in our previous studies.^{10a,11a}

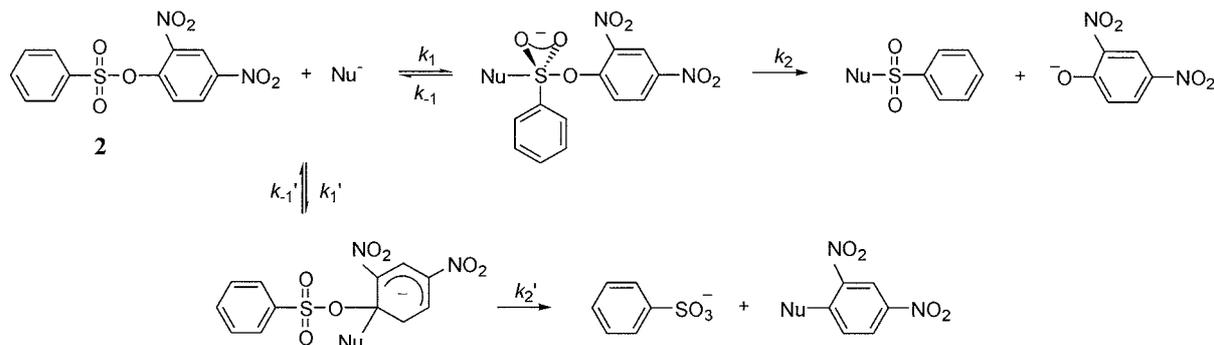
Results and Discussion

The reactions of **2** with the anionic nucleophiles obeyed pseudo-first-order kinetics in the presence of excess nucleophile. Pseudo-first-order rate constants (k_{obsd}) were determined from the equation, $\ln(A_\infty - A_t) = -k_{\text{obsd}}t + c$. Correlation coefficients of the linear regressions were higher than 0.9995 in all cases. The plots of k_{obsd} vs nucleophile concentration were linear passing through the origin. Generally five different nucleophile concentrations were used to determine the second-order rate constants (k_{N}) from the slope of the linear plots of k_{obsd} vs nucleophile concentration.

The reaction of **2** with strongly basic OH^- proceeded through the S–O bond fission exclusively, while those with CN^- and N_3^- proceeded through the S–O and C–O bond fissions competitively. Thus, the second-order rate constant



We have recently shown that secondary amines are more reactive than primary amines of similar basicity in the



$\text{Nu}^- = \text{OH}^-, \text{CN}^-, \text{N}_3^-$.

Scheme 1

Table 1. Summary of second-order rate constants for reactions of 2,4-dinitrophenyl benzoate (**1**) and benzenesulfonate (**2**) with OH⁻, CN⁻, and N₃⁻ in 20 mol % DMSO/80 mol % H₂O at 25.0 ± 0.1 °C

Nu ⁻	pK _a (NuH)	$k_N / M^{-1}s^{-1}$				$k_N^{C=O}/k_N^{SO_2}$
		k_N^{tot}	$k_N^{SO_2}$	k_N^{C-O}	$k_N^{C=O}$	
OH ⁻	15.7	8.02(1.00) ^a	8.02	—	85.9	10.7
CN ⁻	9.3	0.0531(0.90) ^a	0.0478	0.0053	1.22	25.5
N ₃ ⁻	4.0	0.0363(0.34) ^a	0.0123	0.0240	0.224	18.2

^aFigures in the parenthesis are the fractions of S–O bond fission.

determined above corresponds to the overall rate constant (k_N^{tot}).¹¹ The second-order rate constant for the S–O bond fission ($k_N^{SO_2}$) and the C–O bond fission (k_N^{C-O}) were calculated from the following relationships:

$$k_N^{SO_2} = k_N^{tot} \times \text{the fraction of S–O bond fission} \quad (1)$$

$$k_N^{C-O} = k_N^{tot} - k_N^{SO_2} \quad (2)$$

As shown in Table 1, the C–O bond fission occurs more predominantly as the nucleophile becomes a weaker base (*i.e.*, the fraction of C–O bond fission is 0.10 and 0.66 for the reaction with CN⁻ and N₃⁻, respectively), indicating that the basicity of nucleophiles is an important factor to determine the regioselectivity for the present reaction. A similar result has recently been reported for the reactions of **2** with a series of primary and secondary amines, *i.e.*, the S–O bond fission occurs exclusively for the reactions with strongly basic amines (*e.g.*, ethylamine and piperidine) while considerable C–O bond fission occurs for those with weakly basic amines (*e.g.*, trifluoroethylamine and piperazinium ion).¹¹

Table 1 also shows that **1** exhibits larger second-order rate

constants (k_N) than **2** irrespective of the nature of the nucleophilic atoms, *i.e.*, $k_N^{C=O}/k_N^{SO_2} = 10.7, 25.5,$ and 18.2 for the reaction with OH⁻, CN⁻, and N₃⁻, respectively. A similar result is demonstrated in Figure 1 for the reactions of **1** and **2** with a series of secondary amines, *i.e.*, **1** is more reactive than **2** regardless of the basicity of amines. Thus, one can suggest that the benzoate **1** is more reactive than the sulfonate **2** not only in the reactions with the anionic nucleophiles but also in the reactions with the neutral amines.

Aminolysis of esters has been suggested to proceed through an addition intermediate in which a change in the rate-determining step occurs from breakdown of the intermediate to its formation as the attacking amine becomes more basic than the leaving group by 4 to 5 pK_a units.^{10,13–16} On the basis of the nonlinear Brønsted-type plots shown in Figure 1, the reactions of **1** and **2** with the secondary amines have been suggested to proceed through an intermediate with a change in the rate-determining step at pK_a⁰, the center of the curvature of the curved Brønsted-type plots.^{10a,11a} Since the slope and pK_a⁰ values of the Brønsted-type plots

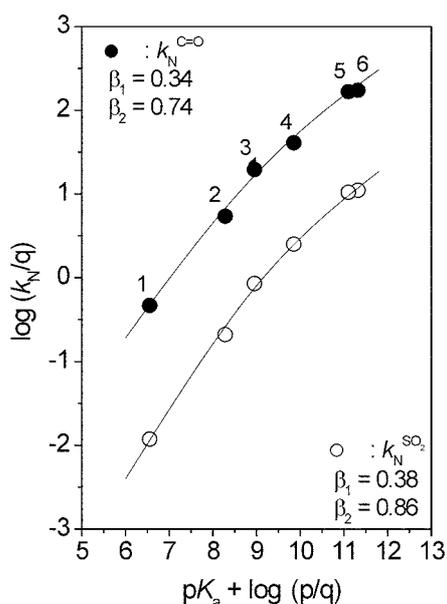


Figure 1. Brønsted-type plots for reactions of 2,4-dinitrophenyl benzoate (**1**, ●) and benzenesulfonate (**2**, ○) with a series of secondary alicyclic amines in 20 mol % DMSO/80 mol % H₂O at 25.0 ± 0.1 °C: (1) piperazinium ion; (2) 1-formylpiperazine; (3) morpholine; (4) piperazine; (5) 3-methylpiperidine; (6) piperidine. The kinetic data were taken from refs 10a and 11a.

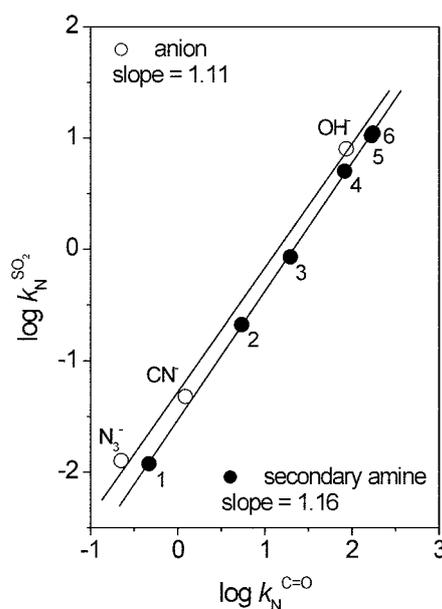


Figure 2. Plots of $\log k_N^{C=O}$ vs $\log k_N^{SO_2}$ for the reactions of **1** and **2** with amines (●) and anionic nucleophiles (○) in 20 mol % DMSO/80 mol % H₂O at 25.0 ± 0.1 °C. The kinetic data for the reactions of **1** and **2** with amines were taken from refs 10a and 11a, and those for the reactions of **1** with anionic nucleophiles were taken from ref 12.

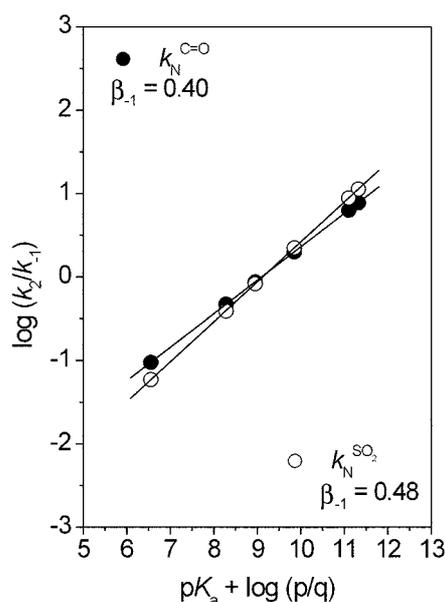


Figure 3. Brønsted-type plots for reactions of 2,4-dinitrophenyl benzoate (**1**, ●) and benzenesulfonate (**2**, ○) with a series of secondary alicyclic amines in 20 mol % DMSO/80 mol % H₂O at 25.0 ± 0.1 °C. The kinetic data (k_2/k_{-1} ratios) for the reactions of **1** and **2** with amines were taken from refs 10a and 11a.

are nearly the same for the aminolyses of **1** and **2**, these reactions are considered to proceed through the same mechanism.

The above argument can be further supported by the linear plot shown in Figure 2. The plot of $\log k_N^{\text{SO}_2}$ vs $\log k_N^{\text{C=O}}$ for the reactions with the secondary amines exhibits a good linearity with a slope close to unity, indicating the aminolyses of **1** and **2** proceed through the same mechanism. Accordingly, the higher reactivity shown by **1** compared to **2** is not due to any difference in their reaction mechanism. The same argument can be applied to the reactions of **1** and **2** with the anionic nucleophiles, since the corresponding plot of $\log k_N^{\text{SO}_2}$ vs $\log k_N^{\text{C=O}}$ shown in Figure 2 is also linear.

A larger k_N value can be obtained by increasing the k_1 value and/or the k_2/k_{-1} ratio since $k_N = k_1 k_2 / (k_{-1} + k_2)$ for the reaction proceeding through an intermediate as in the reactions of **1** and **2**. The microscopic rate constants (k_1 and k_2/k_{-1}) associated with the aminolyses of **1** and **2** have been determined.^{10a,11a} As shown in Figure 3, the k_2/k_{-1} ratio increases linearly with increasing amine basicity for both reactions of **1** and **2**. The benzoate **1** exhibits slightly larger k_2/k_{-1} ratio than the sulfonate **2** for the reactions with weakly basic amines while the reverse is true for the reactions with strongly basic amines. However, the difference in the k_2/k_{-1} ratio for the reactions of **1** and **2** is not significant, indicating that the k_2/k_{-1} ratio is little responsible for the larger k_N values for the aminolysis of **1** compared to **2**.

As shown in Figure 4, the k_1 value increases linearly with increasing the basicity of amines for the aminolyses of **1** and **2**. Interestingly, **1** exhibits much larger k_1 values than **2** for all the amines studied. Thus, one can suggest that the larger k_1 value for the aminolysis of **1** compared to **2** is mainly

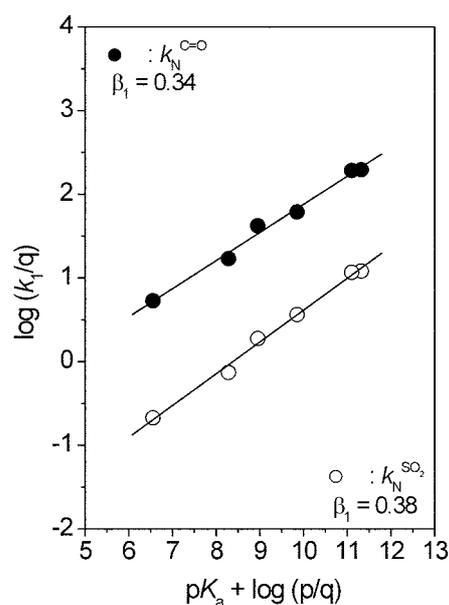


Figure 4. Brønsted-type plots for reactions of 2,4-dinitrophenyl benzoate (**1**, ●) and benzenesulfonate (**2**, ○) with a series of secondary alicyclic amines in 20 mol % DMSO/80 mol % H₂O at 25.0 ± 0.1 °C. The kinetic data (k_1 values) for the reactions of **1** and **2** with amines were taken from refs 10a and 11a.

responsible for its larger k_N value.

The reaction of **1** with anionic nucleophiles such as OH⁻, CN⁻, and N₃⁻ has been suggested to proceed through an addition intermediate in which the leaving group departure is little advanced at the rate-determining transition-state.¹² The mechanism for the reactions of **2** with these anionic nucleophiles would be the same as that for the reactions of **1** as mentioned above on the basis of the linear plot shown in Figure 2. In this case, the k_N value corresponds to the k_1 value for both reactions of **1** and **2** with the anionic nucleophiles. Thus, one can conclude the following: (1) The benzoate **1** is more electrophilic than the sulfonate **2** regardless of the nature of the nucleophiles such as the nucleophilic atom (*e.g.*, oxygen, carbon, and nitrogen), the charge type (*e.g.*, anionic or neutral nucleophiles), and the basicity of nucleophiles. (2) The larger k_1 value for the reaction with **1** compared to **2** is mainly responsible for its higher electrophilicity.

Experimental Section

Materials. 2,4-Dinitrophenyl benzenesulfonate (**2**) was prepared as reported previously.^{11,17} The reaction medium was H₂O containing 20 mol % DMSO to eliminate solubility problems. DMSO was distilled over calcium hydride at a reduced pressure and stored under nitrogen. Doubly glass distilled water was further boiled and cooled under nitrogen just before use. Other chemicals were of the highest quality available.

Kinetics. The kinetic studies were performed using a Scinco S-3100 UV-Vis spectrophotometer equipped with a constant temperature circulating bath. The reactions were

followed by monitoring the appearance of 2,4-dinitrophenoxide ion, an S–O bond fission product. Typically, the reaction was initiated by adding 5 μ L of a 0.02 M stock solution of **2** to a 10 mm UV cell containing 2.50 mL of the reaction medium and the nucleophile. All the transfers of solutions were carried out by means of gastight syringes.

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