

Notes

The Origin of the α -Effect : Reactions of *p*-Nitrophenyl X-Substituted Benzenesulfonates with Butane-2,3-dione Monoximate and *p*-Chlorophenoxide

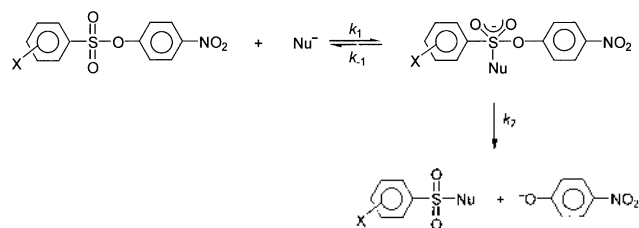
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A certain group of nucleophiles has been reported to show abnormally higher nucleophilicity than would be expected from their respective basicity.¹ A common feature of these nucleophiles is the possession of one or more nonbonding electron pairs at the position α to the nucleophilic center. Therefore, the abnormally enhanced nucleophilicity has been termed the α -effect.¹ The suggested origins of the α -effect are: (1) Ground state destabilization of the nucleophile, (2) Stabilization of the transition state, (3) Enhanced thermodynamic stability of reaction products, and (4) Differential solvent effect.² Many factors have been suggested to influence the magnitude of the α -effect, e.g., reaction medium,^{3,4} basicity of α -effect nucleophiles,⁵ hybridization type of the electrophilic center,^{6,7} magnitude of β_{nuc} value,⁸ etc.² Recently, the magnitude of the α -effect has been reported to be dependent on the electronic nature of the acyl substituent X for the reaction of *p*-nitrophenyl X-substituted benzoates with hydrazine and glycylglycine.⁹

We now expand our study to the reactions of *p*-nitrophenyl X-substituted benzenesulfonates with anionic nucleophiles as shown in Scheme 1 in order to investigate the origin of the α -effect. The present study is also expected to allow us to examine whether the dependence of the α -effect on the acyl substituent is a general or a limited result for the aminolysis reaction of the carboxylic esters.

Experimental Section

Materials. *p*-Nitrophenyl X-substituted benzenesulfonates in the present study were easily prepared from the reaction of *p*-nitrophenol and X-substituted benzenesulfonyl

X : *p*-MeO, *p*-Cl, H, *p*-Cl, *m*-NO₂, *p*-NO₂Nu⁻ : *p*-ClPhO⁻ (ClPhO⁻), a normal nucleophileMeC(O)C(Me)NO⁻ (Ox⁻), an α -effect nucleophile

Scheme 1

chlorides in the presence of triethylamine in anhydrous ether. Their purity was checked by means of their melting point and spectral data such as IR and ¹H NMR characteristics. Other chemicals were of the highest quality available from Aldrich. DMSO was distilled over CaH₂ under a reduced pressure (64–66 °C at 7–8 mmHg). Doubly glass distilled water was boiled and cooled under a nitrogen atmosphere just before use. All the solutions were prepared under a nitrogen atmosphere, and transferred by means of Hamilton gas-tight syringes. Only freshly made solutions were used.

Kinetics. The kinetic study was performed with a Hitachi U-2000 UV-vis spectrophotometer for slow reactions ($t_{1/2} \geq 10$ sec) or an Applied photophysics SX 17MV stopped-flow spectrophotometer for fast reactions ($t_{1/2} < 10$ sec) equipped with a Neslab RTE-110 constant temperature circulator to keep the temperature of the reaction mixture at 25.0 ± 0.1 °C. The reactions were followed by monitoring the appearance of *p*-nitrophenoxide (the leaving group) at 410 nm. The solvent employed was H₂O containing 30 mole % DMSO in order to eliminate the solubility problem. All the reactions were carried out under pseudo-first-order conditions in which the concentration of nucleophile was at least 20 times greater than that of the substrate.

Results and Discussion

All the reactions in the present study obeyed excellent pseudo-first-order kinetics over 90% of the total reaction. Pseudo-first-order rate constants (k_{obs}) were calculated from the well known equation, $\ln(A_{\infty} - A_t) = -k_{\text{obs}} \cdot t - C$. Correlation coefficients of the linear regressions were usually higher than 0.9995. In Table 1 are summarized the ranges of nucleophile concentration and pseudo-first-order rate constants. Generally five different concentrations of nucleophile solutions were used to obtain second-order rate constants (k_{Nu}) from the slope of the plot of k_{obs} versus nucleophile concentration. In Figure 1 are demonstrated typical plots of k_{obs} versus nucleophile concentration.

In Figure 2 is demonstrated the dependence of k_{Nu} on the electronic nature of the substituent X for the reactions of *p*-nitrophenyl X-substituted benzenesulfonate with *p*-chlorophenoxide (ClPhO⁻) and butane-2,3-dione monoximate (Ox⁻), as a normal nucleophile and a corresponding α -effect

Table 1. Experimental conditions and pseudo-first-order rate constants (k_{obs}) for the reactions of *p*-nitrophenyl X-substituted benzenesulfonate with Ox^- and *p*-ClPhO $^-$ in H_2O containing 30 mole% DMSO at 25.0 ± 0.1 °C.

| X | $[\text{Ox}^-]/10^{-3}$, M | $k_{\text{obs}}/10^{-3}$, s^{-1} | $[\text{p-ClPhO}^-]/10^{-3}$, M | $k_{\text{obs}}/10^{-6}$, s^{-1} |
|---------------------------|--------------------------------|---|-------------------------------------|---|
| <i>p</i> -MeO | 6.11-9.99 | 0.316-0.515 | 17.9-56.1 | 8.66-20.7 |
| <i>p</i> -CH ₃ | 6.11-9.99 | 0.634-0.947 | 17.9-56.1 | 14.0-33.1 |
| H | 2.08-9.99 | 0.479-2.33 | 17.9-39.4 | 34.0-66.1 |
| <i>p</i> -Cl | 0.984-8.51 | 0.657-6.85 | 14.5-32.5 | 84.7-167 |
| <i>m</i> -NO ₂ | 0.984-4.82 | 9.22-52.7 | 3.83-17.7 | 399-1460 |
| <i>p</i> -NO ₂ | 1.04-5.11 | 11.7-60.4 | 3.83-17.7 | 425-1760 |

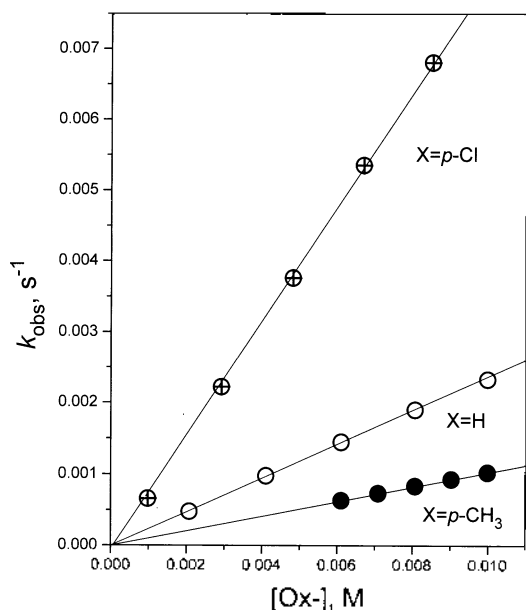


Figure 1. Plots showing dependence of k_{obs} on the concentration of nucleophiles for the reaction of *p*-nitrophenyl X-substituted benzenesulfonate with Ox^- in H_2O containing 30 mole% DMSO at 25.0 ± 0.1 °C.

nucleophile, respectively. It is shown that the k_{Nu} value increases with increasing electron withdrawing ability of the sulfonyl substituent X, resulting in good linear Hammett plots for both Ox^- and ClPhO^- systems. The magnitude of ρ_x values has been calculated to be *ca.* 2.3. Generally, the ρ_x value for ester aminolysis has been reported to be 0.7-1.6.⁹⁻¹² Therefore, the ρ_x value of 2.3 in the present system is quite large.

The magnitude of ρ_x value has been suggested to represent the degree of charge transfer from a nucleophile to an electrophile.⁹⁻¹² Since more charge transfer is expected for the reactions with anionic nucleophiles than for the ones with neutral amines, one might attribute the large ρ_x value obtained in the present study to a difference in charge type between anionic and neutral nucleophiles. However, the nature of reaction mechanism has been suggested to be more responsible for the large ρ_x value than the charge type of nucleophiles.^{10,13}

Unlike reactions of esters with neutral amines, reactions with anionic nucleophiles have not been completely under-

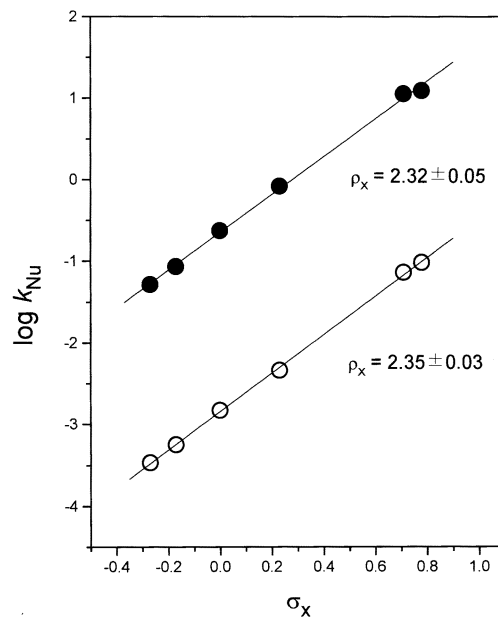


Figure 2. Hammett plots for the reaction of *p*-nitrophenyl X-substituted benzenesulfonates with Ox^- (●) and ClPhO^- (○) at 25.0 ± 0.1 °C.

stood and their reaction mechanism is controversial, *i.e.*, a concerted mechanism versus a stepwise mechanism.¹³⁻¹⁶ However, the effect of substituent on reaction rates would be similar for both reactions with amines and anionic nucleophiles, *i.e.*, an electron withdrawing substituent would accelerate the nucleophilic attack to the substrate (the k_1 step) but retard the leaving group departure (the k_2 step), while an electron donating substituent would retard the k_1 step but accelerate the k_2 step. Therefore, one would expect a small ρ_x value for the reaction whose rate determining step (RDS) is the k_2 step due to the opposite substituent effect. However, a large ρ_x value would be expected for a reaction whose RDS is the k_1 step since the reaction rate is governed only by the k_1 step in this case. This argument can be supported by our recent report that the magnitude of ρ_x value increases from 0.7 to 1.6 as the RDS changes from the k_2 step to the k_1 step for the reactions of 2,4-dinitrophenyl X-substituted benzoates with a series of secondary alicyclic amines.¹⁰ Since the ρ_x value of 2.3 for the present system is quite large, one can suggest that the RDS for the present reaction is the k_1 step. This argument is also consistent with our recent proposal that σ_x constants give better Hammett correlation for reactions whose RDS is the k_1 step and σ_x^- constants result in better correlation for reactions whose RDS is the k_2 step.¹⁰ As shown in Figure 2, excellent Hammett correlations are obtained when σ_x constants are used, indicating that the k_1 step is the RDS for the present system. Therefore, the nature of the reaction mechanism is also considered to be responsible for the large ρ_x value obtained in the present system.

Figure 2 demonstrates that Ox^- is more reactive than ClPhO^- toward all the substrates studied. The higher reactivity shown by Ox^- is clearly the α -effect. Figure 3 shows the effect of sulfonyl substituent X on the magnitude of the α -effect for the reaction of *p*-nitrophenyl X-substituted benze-

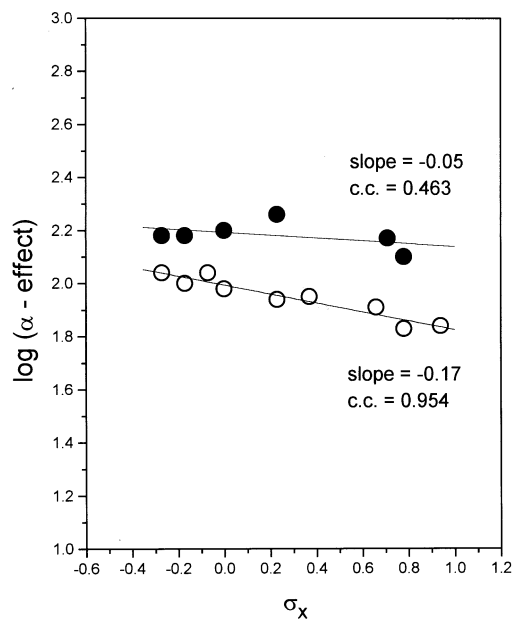


Figure 3. The effect of substituent X on the magnitude of the α -effect for the reaction of *p*-nitrophenyl X-substituted benzenesulfonates with Ox^- and ClPhO^- (●) and the reaction of *p*-nitrophenyl X-substituted benzoates with hydrazine and glycyglycine (○) at 25.0 ± 0.1 °C. The data for the benzoate system were taken from ref. 9.

nesulfonates with Ox^- and ClPhO^- , together with the corresponding data for the reactions of *p*-nitrophenyl X-substituted benzoates with hydrazine and glycyglycine for a comparison purpose. Interestingly, the magnitude of the α -effect for the Ox^- system exhibits no dependence on the electronic nature of the sulfonyl substituent X, while the one for the hydrazine system shows an increasing trend upon changing the substituent X from an electron withdrawing substituent to an electron donating one.

It is clear that a decrease in the free energy gap between the ground state (GS) and transition state (TS) of the reaction should be responsible for the enhanced nucleophilic reactivity shown by the α -effect nucleophiles. Therefore, among the theories suggested to explain the origin of the α -effect, two factors (GS destabilization and TS stabilization) will be considered. The GS of the α -effect nucleophiles can be destabilized either by desolvation, repulsion by the non-bonding electrons, or others. However, the difference in the GS energy between Ox^- and ClPhO^- (or between hydrazine and glycyglycine) is constant for a given solvent system. Therefore, the magnitude of the α -effect should be constant upon changing the substituent X if the difference in the GS energy between Ox^- and ClPhO^- is mainly responsible for the α -effect shown by Ox^- in the present system. As shown in Figure 3, the magnitude of the α -effect for the Ox^- system is nearly constant, while the one for hydrazine system increases with increasing electron donating ability of the substituent X. Therefore, one can suggest that the GS energy difference is responsible for the α -effect observed in the Ox^- system, while the TS stabilization but not GS destabilization is important for the cause of the α -effect shown by hydra-

zine.

The present result clearly suggests that the origin of the α -effect for the reactions with anionic nucleophiles is different from the one for the reactions with neutral amines. The difference in the reaction mechanism between the two systems is considered to be responsible for the difference in the origin of the α -effect.

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