

The Effect of Medium on the α -Effect: Nucleophilic Substitution Reaction of *p*-Nitrophenyl Diphenyl Phosphinate with Butane-2,3-dione Monoximate and Substituted Phenoxides in Cationic Micelles[†]

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Pseudo-first-order rate constants (k_{obs}) have been determined for the nucleophilic substitution reactions of *p*-nitrophenyl diphenyl phosphinate (PNPDPP) with substituted phenoxides ($\text{XC}_6\text{H}_4\text{O}^-$) and butane-2,3-dione monoximate (Ox^-) in 0.1 M borate buffer (pH = 10.0) at 25.0 ± 0.1 °C. The k_{obs} value increases sharply upon addition of cetyltrimethylammonium bromide (CTAB) to the reaction medium up to near 7×10^{-4} M CTAB and then decreases smoothly upon further addition of CTAB. The rate enhancement upon the addition of CTAB is most significant for the reaction with $^- \text{O}_2\text{CC}_6\text{H}_4\text{O}^-$ and least significant for the one with $\text{C}_6\text{H}_5\text{O}^-$, indicating that the reactivity of these aryloxides in the presence of CTAB cannot be determined by the basicity alone. The strength of the interaction of these anionic aryloxides with the positively charged micellar aggregates has been suggested to be an important factor to determine the reactivity in the presence of CTAB. The k_{obs} value for the reaction with Ox^- increases also upon the addition of CTAB. However, the increase in the k_{obs} value is much more significant for the reaction with Ox^- than for the one with $\text{ClC}_6\text{H}_4\text{O}^-$, indicating that Ox^- is less strongly solvated than $\text{ClC}_6\text{H}_4\text{O}^-$ in H_2O . The α -effect shown by Ox^- in H_2O has been attributed to the ground-state solvation difference between Ox^- and $\text{ClC}_6\text{H}_4\text{O}^-$.

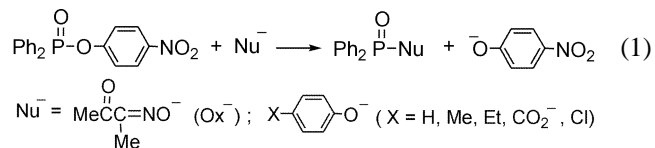
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Introduction

Abnormally enhanced nucleophilic reactivity has often been reported for reactions with a certain type of nucleophiles.^{1,2} A common feature of these nucleophiles is the possession of one or more nonbonding electron pairs on the atom at the α -position from the nucleophilic atom. Therefore, the term α -effect was given to the enhanced nucleophilic reactivity of these nucleophiles compared with an isobasic reference nucleophile.^{1,2} The nucleophiles exhibiting the α -effect are oximates ($\text{R}_2\text{C}=\text{NO}^-$), hydroxamates ($\text{RC}(\text{O})\text{NHO}^-$), peroxide anions (ROO^-), hydrazines (RNH-NH_2), hydroxylamine (HONH_2), etc.^{1,2} Numerous studies have been performed to investigate the cause of the α -effect.²⁻⁹ Some suggested origins of the α -effect are destabilization of the ground-state, stabilization of the transition-state and the reaction product, and solvent effect.²⁻⁹

We have performed systematic studies to investigate the effect of medium on the α -effect for the nucleophilic substitution reaction of *p*-nitrophenyl acetate (PNPA) with butane-2,3-dione monoximate (Ox^-) and with *p*-chlorophenoxide ($\text{ClC}_6\text{H}_4\text{O}^-$) as an α -nucleophile and a corresponding normal-nucleophile, respectively, in dimethylsulfoxide (DMSO)- H_2O mixtures of varying compositions.⁷ The magnitude of the α -effect ($k^{\text{Ox}^-}/k^{\text{ClC}_6\text{H}_4\text{O}^-}$) has been found to

increase with increasing the DMSO content up to near 50 mole % DMSO followed by a gradual decrease upon further addition of DMSO to the reaction medium, resulting in a bell-shaped α -effect profile.⁷ However, the corresponding reaction run in $\text{CH}_3\text{CN-H}_2\text{O}$ mixtures has shown an increasing α -effect profile as the CH_3CN content in the medium increases.⁸ The effect of medium on the α -effect has also been investigated for the reaction of PNPA with Ox^- and $\text{ClC}_6\text{H}_4\text{O}^-$ in the presence of a cationic surfactant, cetyltrimethyl ammonium bromide (CTAB).⁹ We have found that the reactivity of these nucleophiles increases with increasing the concentration of CTAB in the reaction medium up to ca. 4×10^{-3} M. However, the α -nucleophile Ox^- has exhibited much larger rate enhancement than the normal nucleophile $\text{ClC}_6\text{H}_4\text{O}^-$ upon the addition of CTAB.⁹



In order to obtain further information, we have extended our study to the reaction of *p*-nitrophenyl diphenyl phosphinate (PNPDPP) with Ox^- and a series of X-substituted phenoxides including $\text{ClC}_6\text{H}_4\text{O}^-$ in the presence and absence of CTAB, eq (1).

Experimental Section

Materials. *p*-Nitrophenyl diphenyl phosphinate (PNPDPP) was easily prepared from the reaction of diphenyl phos-

[†]This paper is dedicated to Professor Sang Chul Shim for his distinguished achievement in organic photochemistry and his outstanding contributions to the chemistry community in Korea.

phenyl chloride with *p*-nitrophenol in the presence of triethylamine as a catalyst in dry ether. The phenols, butane-2,3-dione monoxime, and CTAB were recrystallized before use. Other chemicals used were of the highest quality available from Aldrich. Doubly glass distilled water was boiled and cooled under nitrogen.

Kinetics. The kinetic study was performed with a Scinco S-2100 Photodiode Array UV-vis spectrophotometer for slow reactions ($t_{1/2} \geq 10$ s) or with an Applied Photophysics SX-17 MV stopped-flow spectrophotometer for fast reactions ($t_{1/2} < 10$ s) equipped with a Leslab RTE-110 constant temperature circulating bath to keep the temperature in the reaction cell at 25.0 ± 0.1 °C. The reaction was followed by monitoring the appearance of the leaving *p*-nitrophenoxide at 400 nm. Pseudo-first-order rate constants (k_{obs}) were determined from the well-known equation, $\ln(A_{\infty} - A_t) = -k_{\text{obs}} \cdot t + c$. The concentration of the reactants was diluted to 1.0×10^{-5} M and 2.00×10^{-4} M for the substrate and the anionic nucleophiles, respectively in order to minimize perturbation of micellar structures. All the solutions were prepared just before use under nitrogen and were transferred by Hamilton gas-tight syringes. Other detailed kinetic procedures were reported previously.^{7,8}

Results and Discussion

Pseudo-first-order rate constants (k_{obs}) are summarized in Table 1 for the nucleophilic substitution reactions of PNPDP with a series of substituted phenoxides ($\text{XC}_6\text{H}_4\text{O}^-$) and butane-2,3-dione monoximate (Ox^-) in 0.1 M borate buffer solution (pH = 10.0). As shown in Table 1, the k_{obs} value is similar for all the reactions with the aryloxides in the absence of CTAB. However, the reactivity of the aryloxides is strongly dependent on the nature of the substituent X in the presence of CTAB. The effect of CTAB on the k_{obs} value is illustrated in Figure 1. It is shown that the k_{obs} value for the reaction with the aryloxides increases sharply with increasing the concentration of CTAB in the reaction medium up to

ca. 7×10^{-4} M and then decreases smoothly upon further addition of CTAB.

Significant rate enhancements have often been observed for nucleophilic substitution reaction with anionic nucleophiles upon addition of various cationic surfactants.¹⁰⁻¹³ Iglesias has recently shown that the k_{obs} value for hydrolysis of ethyl cyclohexanone-2-carboxylate passes through a maximum with increasing surfactant concentration followed by a gradual but steady decrease in the rate as the surfactant concentration increases further.¹¹ Similarly, Toullec¹² and Moss *et al.*¹³ have found that the decontamination of toxic phosphonates and phosphates (*e.g.*, pesticides or chemical warfare agents) are highly effective in aqueous micellar solution. Such a rate enhancement in aqueous micellar solutions has been attributed to an increase in the concentration of reactants at the interface of micellar aggregates but not to an increase in the intrinsic reactivity.¹⁰⁻¹³ In fact, the second-order rate constants have often been found to be smaller at the micellar interface than the one measured in water.¹⁰⁻¹³

The ionic interaction between the positive micellar aggregates and the anionic nucleophiles is considered to be an important factor which influences the concentration of the reactants at the interface of micellar aggregates. As shown in Figure 1, the rate enhancement upon the addition of CTAB to the reaction medium is most significant for the reaction with $\text{O}_2\text{CC}_6\text{H}_4\text{O}^-$. Therefore, one can suggest that $\text{O}_2\text{C}-\text{C}_6\text{H}_4\text{O}^-$ exerts the strongest ionic interaction with the positive micellar aggregates among the anionic aryloxides. This argument can be easily acceptable since there are two negative charges on $\text{O}_2\text{CC}_6\text{H}_4\text{O}^-$. It is also shown that $\text{ClC}_6\text{H}_4\text{O}^-$ is more reactive than $\text{C}_6\text{H}_5\text{O}^-$ in the presence of CTAB, although the former is less basic than the latter, indicating that $\text{ClC}_6\text{H}_4\text{O}^-$ exerts a stronger interaction with the micelles of CTAB than $\text{C}_6\text{H}_5\text{O}^-$ does. Therefore, one can suggest that the reactivity of these anionic nucleophiles cannot be determined by the basicity alone in the presence of CTAB. This argument can be further supported by the fact that the k_{obs} value at 7×10^{-4} M CTAB, in which the

Table 1. Summary of kinetic data for the reaction of PNPDP with butane-2,3-dione monoximate (Ox^-) and X-substituted phenoxides (*p*-X- $\text{C}_6\text{H}_4\text{O}^-$) in 0.1 M borate buffer (pH = 10.0) containing various concentrations of CTABr at 25.0 ± 0.1 °C^a

[CTABr] × 10 ⁴ , M	$k_{\text{obs}} \times 10^2, \text{s}^{-1}$						
	buffer	X = Ox ⁻	X = Cl	X = CO ₂ ⁻	X = H	X = CH ₃	X = C ₂ H ₅
0	0.450	0.562	0.483	0.483	0.485	0.485	0.490
1	0.483	1.90	0.640	0.550	0.500	0.533	0.683
2	0.967	6.42	5.42	7.67	1.32	1.97	4.48
3	3.28	27.0	8.52	12.9	5.27	7.17	8.87
4	5.17	55.8	10.2	15.6	7.42	9.55	12.0
5	6.42	76.9	10.9	17.1	8.52	10.9	13.6
6	6.48	88.0	11.1	17.7	8.93	12.1	13.9
7	6.55	94.4	11.3	19.3	9.32	12.5	14.4
10	7.23	101	11.2	19.0	9.45	12.0	13.6
16	6.87	98.0	9.60	17.6	9.03	11.4	12.0
28	6.17	82.7	7.97	15.1	7.95	9.18	9.55
40	5.72	70.8	7.13	11.7	7.08	8.15	8.18

^a[PNPDP] = 1.0×10^{-5} M, [Nu⁻] = 2.00×10^{-4} M, where Nu⁻ = Ox⁻ or XC₆H₄O⁻

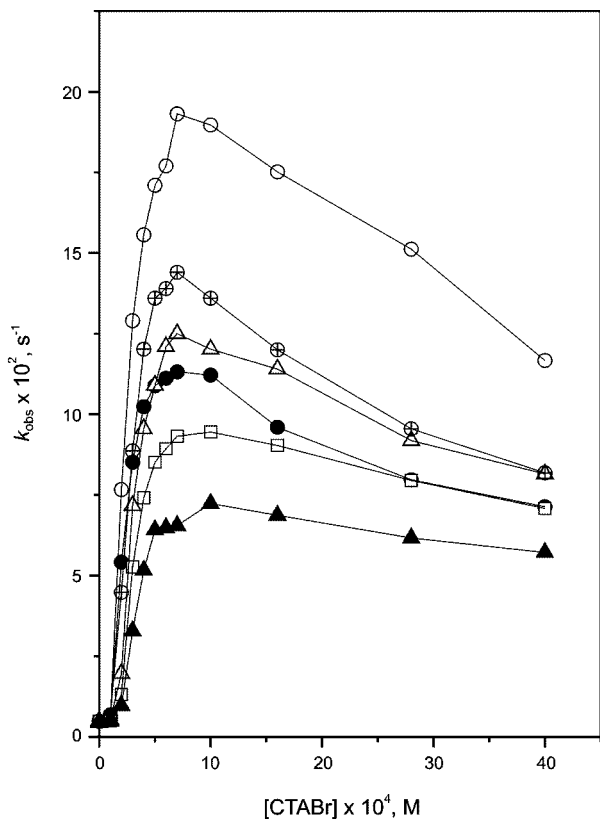


Figure 1. Plots of observed rate constants vs concentration of CTAB for the reaction of PNPDP with substituted phenoxides (p -X-C₆H₄O⁻) in 0.1 M borate buffer (pH = 10.0) at 25.0 ± 0.1 °C. (X = Cl (●), CO₂⁻ (○), H (□), CH₃ (△), C₂H₅ (⊕), buffer alone (▲)).

maximum k_{obs} value is observed, is in the order C₆H₅O⁻ < MeC₆H₄O⁻ < EtC₆H₄O⁻ although the basicity of these aryloxides is similar each other (See Table 1 and Figure 1).

It has been reported that the association constant (K_{ass}) between the micelle of CTAB and the aryloxides is in the order EtC₆H₄O⁻ > MeC₆H₄O⁻ > C₆H₅O⁻,¹⁴ which is the same as the k_{obs} value for the reaction of PNPDP with the three aryloxides. Therefore, one can suggest that the reactivity of these anionic nucleophiles would be governed by two factors as shown in eq (2), where a and b represent the sensitivity parameter for K_{ass} and K_{b} (= basicity of aryloxides), respectively. Eq (2) would resemble the Brønsted equation when the first term of eq (2) becomes zero. On the other hand, the reactivity of nucleophiles would be determined by the strength of the interaction between the micelle and the anionic nucleophile when the basicity of the nucleophiles is similar.

$$\log k_{\text{obs}} = a \log K_{\text{ass}} + b \log K_{\text{b}} \quad (2)$$

Some years ago, we performed nucleophilic substitution reactions of p -nitrophenyl acetate (PNPA) with a series of aryloxides in the presence of CTAB.⁹ The k_{obs} value was found to increase with increasing the concentration of CTAB up to ca. 4×10^{-3} M and then remained nearly constant upon further addition of CTAB to the medium.⁹ However, the rate

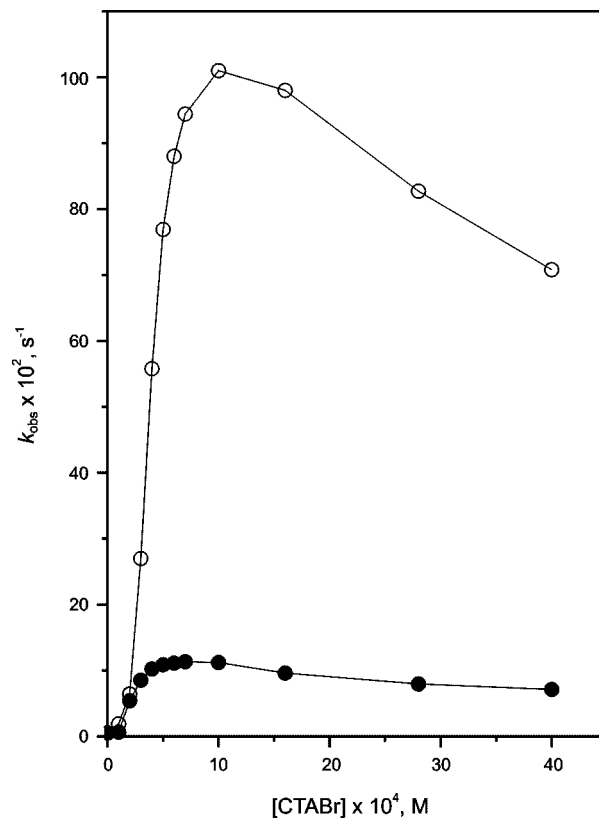


Figure 2. Plots of observed rate constants vs concentration of CTAB for the reaction of PNPDP with p -chlorophenoxide (●) and butane-2,3-dione monoximate (○) in 0.1 M borate buffer (pH = 10.0) at 25.0 ± 0.1 °C.

enhancement upon addition of CTAB for the reaction of PNPA was calculated to be only about 10, which is much smaller than the corresponding rate enhancement for the reaction of PNPDP under the same reaction condition (*e.g.*, the rate enhancement of about 20–40, see Table 1). Thus, one can suggest that the effect of micelle on rate is also dependent of the nature of the substrate for given nucleophiles. The difference in the hydrophobicity between PNPDP and PNPA is considered to be responsible for the difference in the micellar effect on rate and the position of the maximum k_{obs} value appeared (*e.g.*, PNPDP being more hydrophobic than PNPA).

Table 1 shows that Ox⁻ is more reactive than ClC₆H₄O⁻ in the presence and absence of CTAB although the basicity of Ox⁻ and ClC₆H₄O⁻ is similar each other. The α -effect nucleophile (Ox⁻) has often exhibited higher reactivity than the corresponding normal nucleophile (ClC₆H₄O⁻) toward a variety of substrates (*e.g.*, the α -effect).^{7,8} We have recently performed nucleophilic substitution reactions of S - p -nitrophenyl thioacetate (PNPTA) with Ox⁻ and ClC₆H₄O⁻ in DMSO-H₂O mixtures of varying compositions.¹⁵ The nucleophilic reactivity was found to increase significantly with increasing the concentration of DMSO in the reaction medium. However, the rate enhancement upon additions of DMSO was found to be more remarkable for the reaction with Ox⁻ than for the one with ClC₆H₄O⁻ up to ca. 50 mole % DMSO.¹⁵

The difference in the ground-state solvation of Ox^- and $\text{ClC}_6\text{H}_4\text{O}^-$ was suggested to be responsible for the differential medium effect on rate.¹⁵ A similar result has been observed for the reactions of PNPA,⁷ PNPDP and *p*-nitrophenyl benzenesulfonate (PNPBS)¹⁶ under the same reaction condition, although the magnitude of the α -effect was found to be dependent on the substrates.

Figure 2 illustrates the effect of CTAB on the reactivity of Ox^- and $\text{ClC}_6\text{H}_4\text{O}^-$ toward PNPDP. One can see that the k_{obs} value increases upon addition of CTAB to the reaction medium up to *ca.* $7 \cdot 10 \times 10^{-4}$ M CTAB. However, the increase in the k_{obs} value is much more remarkable for the reaction with Ox^- than with $\text{ClC}_6\text{H}_4\text{O}^-$. Since the basicity of the two nucleophiles is similar each other,⁷ the differential micellar effect would be mainly due to the difference in the interaction between the micelle and the nucleophile. The ionic interaction of the positive micelles with Ox^- and with $\text{ClC}_6\text{H}_4\text{O}^-$ would be similar since both of the nucleophiles have a negative charge. Therefore, a difference in the ground-state solvation between Ox^- and $\text{ClC}_6\text{H}_4\text{O}^-$ would be responsible for the differential micellar effect on rate shown in Figure 2. The fact that the rate enhancement upon the addition of CTAB is more significant for the reaction with Ox^- indicates that Ox^- is less strongly solvated than $\text{ClC}_6\text{H}_4\text{O}^-$ in H_2O . This argument is consistent with our recent calorimetric study, *i.e.*, Ox^- is about 4 kcal/mole less solvated than $\text{ClC}_6\text{H}_4\text{O}^-$ in H_2O at 25.0 °C.^{7b} Therefore, the present result suggests that differential ground-state solvation (Ox^- vs $\text{ClC}_6\text{H}_4\text{O}^-$) is responsible for the enhanced nucleophilic reactivity of Ox^- in the reaction with various substrates.

Conclusion

The k_{obs} value for the reaction of PNPDP with $\text{XC}_6\text{H}_4\text{O}^-$ and Ox^- increases sharply with increasing the concentration of CTAB in the reaction medium up to *ca.* 7×10^{-4} M and then decreases gradually upon further addition of CTAB. The fact that micellar effect on rate is much more significant for the reaction with Ox^- than for the one with $\text{ClC}_6\text{H}_4\text{O}^-$ suggests that Ox^- is less strongly solvated than $\text{ClC}_6\text{H}_4\text{O}^-$ in

H_2O . Therefore, the α -effect shown by Ox^- in H_2O is attributed to the ground-state solvation difference between Ox^- and $\text{ClC}_6\text{H}_4\text{O}^-$ in H_2O .

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