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

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Pseudo-first-order rate constants (kobs) have been determined for the nucleophilic substitution reactions of p-nitrophenyl diphenyl phosphinate (PNPDPP) with substituted phenoxydes (XC6H4O-) and butane-2,3-dione monoximate (Ox-) in 0.1 M borate buffer (pH = 10.0) at 25.0 ± 0.1 °C. The kobs value increases sharply upon addition of cetyltrimethylammonium bromide (CTAB) to the reaction medium up to near 7 × 10−1 M CTAB and then decreases smoothly upon further addition of CTAB. The rate of enhancement upon the addition of CTAB is most significant for the reaction with O=C6H4H2O and least significant for the one with C6H4O-. 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 kobs value for the reaction with Ox increases also upon the addition of CTAB. However, the increase in the kobs value is much more significant for the reaction with Ox than for the one with C6H4H2O, indicating that Ox is less strongly solvated than C6H4H2O in H2O. The α-effect shown by Ox in H2O has been attributed to the ground-state salvation difference between Ox and C6H4H2O.

Key Words: The α-effect, Micellar effect, Basicity, Nucleophilicity, Brunsted equation

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 presence 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 oximes (R–C=NOH), hydroxamines (R(C)NH(OH)), peroxide anions (ROO-), hydrazines (RNNH2), hydroxylamine (HONH2), etc.1,3 Numerous studies have been performed to investigate the cause of the α-effect.2,4 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.5,6

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 (CIC6H4O-) as an α-nucleophile and a corresponding normal-nucleophile, respectively, in dimethylsulfoxide (DMSO)-H2O mixtures of varying compositions. The magnitude of the α-effect (kα/kα0) 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 CH2CN–H2O mixtures has shown an increasing α-effect profile as the CH2CN 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 CIC6H4O- in the presence of a cationic surfactant, cetyltrimethylammonium 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 × 10−2 M. However, the α-nucleophile Ox- has exhibited much larger rate enhancement than the normal nucleophile CIC6H4O- upon the addition of CTAB.9

\[
\text{Ph}_2\text{P}+\text{O} \quad \overset{\text{Nu}}{\xrightarrow{\text{Ph}_2\text{P} \cdot \text{Nu} + \text{O}} \quad \text{Ph}_2\text{P} \cdot \text{Nu} + \text{O}}
\]

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 phenoxydes including CIC6H4O- 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-
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 reagent stabilized before use. Other chemicals used were of the highest quality available from Aldrich. Doubly distilled water was boiled and cooled under nitrogen.

Kinetics. The kinetic study was performed with a Seineco S-2100 Photodiode Array UV–vis spectrophotometer for slow reactions (t≥10 s) or with an Applied Photophysics SX-17 MV stopped-flow spectrophotometer for fast reactions (t<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 groups-nitrophenoxide at 400 nm. Pseudo-first-order rate constants (kobs) were determined from the well-known equation: ln (A0–A)/A = –kobs t + c. The concentration of the reactants was diluted to 1.0 × 10⁻³ M and 2.00 × 10⁻¹ 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 repeated previously.7,8

Results and Discussion

Pseudo-first-order rate constants (kobs) are summarized in Table 1 for the nucleophilic substitution reactions of PNPDPP with a series of substituted phenoxides (X•C₆H₄(OH)) and butane-2,3-dione monoxime (OX) in 0.1 M borate buffer solution (pH = 10.0). As shown in Table 1, the kobs value is similar for all the reactions with the areoxides in the absence of CTAB. However, the reactivity of the areoxides is strongly dependent on the nature of the substituent X in the presence of CTAB. The effect of CTAB on the kobs value is illustrated in Figure 1. It is shown that the kobs value for the reaction with the areoxides increases sharply with increasing the concentration of CTAB in the reaction medium up to ca. 7 × 10⁻¹ 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 kobs 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, Toullou et al.12 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

Theionic 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 O•C₆H₄(CH₃)O⁻. Therefore, one can suggest that O•C₆H₄(CH₃)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 O•C₆H₄(CH₃)O⁻. It is also shown that CIC₆H₄(OH)⁻ is more reactive than C₆H₄(OH)⁻ in the presence of CTAB, although the former is less basic than the latter, indicating that CIC₆H₄(OH)⁻ exerts a stronger interaction with the micelles of CTAB than C₆H₄(OH)⁻ 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 kobs value at 7 × 10⁻¹ M CTAB, in which the

<table>
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<th>[CTAB] × 10⁻¹, M</th>
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<tr>
<td>butler</td>
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<td>28</td>
<td>6.17</td>
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[PNPDPP] = 1.0 × 10⁻³ M, [Na⁺] = 2.00 × 10⁻¹ M, where Na⁺ = OX⁻ or X•C₆H₄(OH)⁻
maximum $k_{obs}$ value is observed, is in the order $\text{C}_6\text{H}_5\text{O}^- < \text{MeC}_6\text{H}_5\text{O}^- < \text{EtC}_6\text{H}_5\text{O}^-$ 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 $\text{EtC}_6\text{H}_5\text{O}^- > \text{MeC}_6\text{H}_5\text{O}^- > \text{C}_6\text{H}_5\text{O}^-$, which is the same as the $k_{obs}$ value for the reaction of PNPDPP 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.

$$\log k_{obs} = a \log K_{ass} + b \log K_b$$

(2)

Some years ago, we performed nucleophilic substitution reactions of $p$-nitrophenyl acetate (PNPA) with a series of aryloxides in the presence of CTAB.7 The $k_{obs}$ value was found to increase with increasing the concentration of CTAB up to $ca. 4 \times 10^{-4} \text{M}$ and then remained nearly constant upon further addition of CTAB to the medium.7 However, the rate 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 PNPDPP 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 PNPDPP 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., PNPDPP being more hydrophobic than PNPA).

Table 1 shows that $\text{Ox}^-$ is more reactive than $\text{CIC}_6\text{H}_5\text{O}^-$ in the presence and absence of CTAB although the basicity of $\text{Ox}^-$ and $\text{CIC}_6\text{H}_5\text{O}^-$ is similar each other. The $\alpha$-effect nucleophile ($\text{Ox}^-$) has often exhibited higher reactivity than the corresponding normal nucleophile ($\text{CIC}_6\text{H}_5\text{O}^-$) toward a variety of substrates (e.g., the $\alpha$-effect).15 We have recently performed nucleophilic substitution reactions of $S$-$p$-nitrophenyl thiocarbonate (PNPTA) with $\text{Ox}^-$ and $\text{CIC}_6\text{H}_5\text{O}^-$ 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 addition of DMSO was found to be more remarkable for the reaction with $\text{Ox}^-$ than for the one with $\text{CIC}_6\text{H}_5\text{O}^-$ up to ca. 50 mole % DMSO.15

Figure 1. Plots of observed rate constants vs concentration of CTAB for the reaction of PNPDPP with substituted aryloxides ($p$-$\text{X-C}_6\text{H}_5\text{O}^-$) in 0.1 M borate buffer (pH = 10.0) at 25.0 ± 0.1 °C (X = Cl (●), $\text{CO}_2^-$ (○), $\text{H}$ (□), $\text{Cl}_4^-$ (■), $\text{Cl}_2\text{H}_5^-$ (▲), buffer alone (▼)).

Figure 2. Plots of observed rate constants vs concentration of CTAB for the reaction of PNPDPP with $p$-chlorophenoxide (●) and butano-2,3-dione monoximate (●) in 0.1 M borate buffer (pH = 10.0) at 25.0 ± 0.1°C.
The difference in the ground-state solvation of Ox⁻ and CIC₆H₄O⁻ was suggested to be responsible for the differential medium effect on rate. A similar result has been observed for the reactions of PNPA, PNPDPP and p-nitrophenyl benzensulfonate (PNPBS) 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 CIC₆H₄O⁻ toward PNPDPP. One can see that the \( k_{obs} \) value increases upon addition of CTAB to the reaction medium up to ca. \( 7 \times 10^{2} \) M CTAB. However, the increase in the \( k_{obs} \) value is much more remarkable for the reaction with Ox⁻ than with CIC₆H₄O⁻. Since the basicity of the two nucleophiles is similar each other, 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 CIC₆H₄O⁻ would be similar since both of the nucleophiles have a negative charge. Therefore, a difference in the ground-state solvation between Ox⁻ and CIC₆H₄O⁻ 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 CIC₆H₄O⁻ in H₂O. This argument is consistent with our recent calorimetric study, i.e., Ox⁻ is about 4 kcal/mole less solvated than CIC₆H₄O⁻ in H₂O at 25.0°C. Therefore, the present result suggests that differential ground-state solvation (Ox⁻ vs CIC₆H₄O⁻) is responsible for the enhanced nucleophilic reactivity of Ox⁻ in the reaction with various substrates.

Conclusion

The \( k_{obs} \) value for the reaction of PNPDPP with \( X \) or H₂O and Ox⁻ increases sharply with increasing the concentration of CTAB in the reaction medium up to ca. \( 7 \times 10^{-2} \) 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 CIC₆H₄O⁻ suggests that Ox⁻ is less strongly solvated than CIC₆H₄O⁻ in H₂O. Therefore, the α-effect shown by Ox⁻ in H₂O is attributed to the ground-state solvation difference between Ox⁻ and CIC₆H₄O⁻ in H₂O.

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References