Articles

The α-Effect in Nucleophilic Substitution Reactions of Y-Substituted-Phenyl Diphenylphosphinates with HOO⁻ and OH⁻

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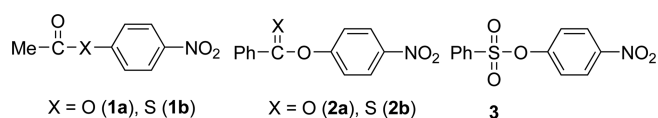*[†]Department of Chemistry, Duksung Women's University, Seoul 132-714, Korea*

Second-order rate constants (k_{HOO^-}) for the nucleophilic substitution reactions of Y-substituted-phenyl diphenylphosphinates (**4a-4i**) with HOO⁻ in H_2O have been measured spectrophotometrically. The α-nucleophile HOO⁻ is 10-70 times more reactive than the reference nucleophile OH⁻ although the former is *ca.* 4 pK_a units less basic than the latter, indicating the α-effect is operative. The Brønsted-type plot for the reactions of **4a-4i** with HOO⁻ is linear with $\beta_{lg} = -0.51$, a typical β_{lg} value for reactions which were reported to proceed through a concerted mechanism. The Yukawa-Tsuno plot is also linear with $\rho = 1.40$ and $r = 0.47$, indicating that a negative charge develops partially on the O atom of the leaving group, which can be delocalized to the substituent Y through resonance interactions. Thus, the reactions have been proposed to proceed through a concerted mechanism. The magnitude of the α-effect (*i.e.*, the k_{HOO^-}/k_{HO^-} ratio) decreases linearly as the leaving-group basicity increases. It has been concluded that solvation effect is not solely responsible for the α-effect found in this study but the transition-state stabilization through an intramolecular H-bonding interaction is also responsible for the α-effect.

Key Words : The α-effect, Ground state, Transition state, Solvation effect, H-bonding interaction

Introduction

The term α-effect was given to the abnormally enhanced reactivity shown by the nucleophiles possessing an atom with one or more nonbonding electron pairs α to the reaction center.[1] Numerous studies have been carried out to investigate the origin of the α-effect.[2-18] Some important theories suggested to account for the α-effect are: (1) destabilization of the ground state (GS) due to the repulsion of the nonbonding electron pairs, (2) stabilization of the transition state (TS), (3) thermodynamic stabilization of products, (4) solvent effects.[2-18]
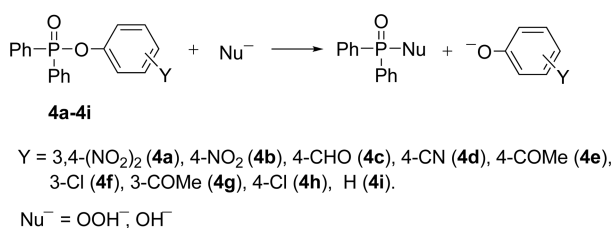
However, the origin of the α-effect has not been completely understood. Particularly, solvent effects on the α-effect remains controversial.[2-7,16-18] DePuy *et al.* performed reactions of methyl formate with HOO⁻ and OH⁻ in gas phase and found that HOO⁻ does not exhibit the α-effect.[3] Thus, solvation effect has been suggested to be responsible for the α-effect shown by HOO⁻ in aqueous reactions,[3] since HOO⁻ was reported to be 12 kcal/mol less strongly solvated than OH⁻ in water.[4] In contrast, recent development of mass spectrometric techniques and computational methods has shown that the α-effect is present in gas phase reactions of alkyl halides with HOO⁻ and EtO⁻.[5] It has been also reported that HOO⁻ reacts with a lower activation energy than MeO⁻ from a study of dimethyl methylphosphonate in a modified quadrupole ion trap mass spectrometer combined with a

DFT calculation study.[6,7] Thus, solvent effects on the α-effect have been suggested to be insignificant.[5-7]

We have reported that the α-effect is strongly dependent on the solvent compositions for the reactions of 4-nitrophenyl acetate (**1a**),[16] *S*-4-nitrophenyl thioacetate (**1b**),[17a] 4-nitrophenyl benzoate (**2a**),[17b] *O*-4-nitrophenyl thionobenzoate (**2b**),[17c] and 4-nitrophenyl benzenesulfonate (**3**)[17d] with butane-2,3-dione monoxime (an α-nucleophile) and 4-chlorophenoxide (a reference nucleophile) in DMSO-H_2O mixtures of varying compositions. We have shown that the magnitude of the α-effect increases as the DMSO content in the reaction medium increases up to *ca.* 50 mol % and then decreases thereafter, *e.g.*, a bell-shaped α-effect profile.[16-18] Dissection of the α-effect into GS and TS contributions through combination of the kinetic data with our calorimetric data has led us to conclude that GS destabilization is mainly the cause of the increasing α-effect up to *ca.* 50 mol % DMSO, while differential TS stabilization contributes to the decreasing α-effect beyond 50 mol % DMSO.[16b]

Our study has now been extended to the reactions of Y-substituted-phenyl diphenylphosphinates (**4a-4i**) with HOO⁻ in H_2O (Scheme 1). The kinetic data have been compared

Scheme 1

Y = 3,4-(NO$_2$)$_2$ (**4a**), 4-NO$_2$ (**4b**), 4-CHO (**4c**), 4-CN (**4d**), 4-COMe (**4e**), 3-Cl (**4f**), 3-COMe (**4g**), 4-Cl (**4h**), H (**4i**).

Nu$^-$ = OOH$^-$, OH$^-$

with those reported previously[19] for the corresponding reactions with OH$^-$ to get further information on the origin of the α-effect.

Results and Discussion

The kinetic study was performed spectrophotometrically under pseudo-first-order conditions in which the concentration of HOO$^-$ was in large excess over that of **4a-4i**. All of the reactions in this study obeyed pseudo-first-order kinetics and proceeded with quantitative liberation of Y-substituted phenoxide anions. Pseudo-first-order rate constants (k_{obsd}) were calculated from the slope of linear plots of ln ($A_\infty - A_t$) *vs. t*. It is estimated from replicate runs that the uncertainty in the k_{obsd} values is less than ± 3%. The plots of k_{obsd} *vs.* [HOO$^-$] were linear and passed through the origin, indicating that the contribution of H$_2$O and/or OH$^-$ from hydrolysis of HOO$^-$ to k_{obsd} is negligible. Thus, the second-order rate constants (k_{HOO^-}) were calculated from the linear plots of k_{obsd} *vs.* [HOO$^-$] and are summarized in Table 1 together with those reported previously for the corresponding reactions with OH$^-$ (*i.e.*, k_{HO^-})[19] for comparison.

Effect of Substituent Y on Reactivity and the α-Effect. As shown in Table 1, k_{HOO^-} decreases as the leaving-group basicity increases, *e.g.*, it decreases from 6310 M^{-1}s^{-1} to 190 and 16.9 M^{-1}s^{-1}, as the pK_a of the conjugate acid of the leaving aryloxide increases from 5.42 to 8.05 and 9.95, in turn. A similar reactivity pattern is demonstrated for the corresponding reactions with OH$^-$. It is also noted that HOO$^-$ is more reactive than OH$^-$ although the former is *ca.* 4

Table 1. Summary of Second-Order Rate Constants for the Reactions of Y-Substituted-Phenyl Diphenylphosphinates (**4a-4i**) with HOO$^-$ and OH$^-$ in H$_2$O at 25.0 ± 0.1 °C[a]

Entry	Y	pK_a (Y-PhOH)[b]	k_{HOO^-}/ M^{-1}s^{-1}	k_{HO^-}/ M^{-1}s^{-1}	k_{HOO^-}/ k_{HO^-}
4a	3,4-(NO$_2$)$_2$	5.42	6310	89.7	70.3
4b	4-NO$_2$	7.14	449	22.1	20.3
4c	4-CHO	7.66	300	12.6	23.8
4d	4-CN	7.95	354	15.1	23.4
4e	4-COMe	8.05	190	8.84	21.5
4f	3-Cl	9.02	102	5.12	19.9
4g	3-COMe	9.19	81.7	5.44	15.0
4h	4-Cl	9.38	55.1	3.79	14.5
4i	H	9.95	16.9	1.61	10.5

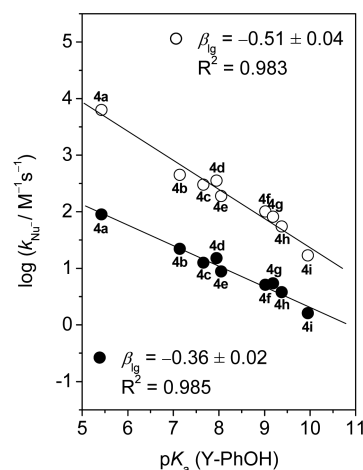[a]The data for the reactions with OH$^-$ were taken from ref 19. [b]The pK_a values were taken from ref 20.

Figure 1. Brønsted-type plots for the reactions of Y-substituted-phenyl diphenylphosphinates (**4a-4i**) with HOO$^-$ (○) and OH$^-$ (●) in H$_2$O at 25.0 ± 0.1 °C. The identity of points is given in Table 1.

pK_a units less basic than the latter. This demonstrates convincingly that HOO$^-$ exhibits the α-effect in the reactions of **4a-4i**.

The effect of the leaving-group basicity on reactivity is graphically illustrated in Figure 1 for the reactions of **4a-4i** with HOO$^-$ and OH$^-$. As shown in Figure 1, the Brønsted-type plots are linear with β$_{lg}$ = −0.51 and −0.36 for the reactions with HOO$^-$ and OH$^-$, respectively. Interestingly, the more reactive HOO$^-$ is more sensitive to the leaving-group basicity than the less reactive OH$^-$, indicating that the reactivity-selectivity principle (RSP) is not applicable to the current reactions of **4a-4i** with HOO$^-$ and OH$^-$.

We have recently reported that the α-effect in the reactions of Y-substituted-phenyl methanesulfonates with HOO$^-$ and OH$^-$ in H$_2$O (*i.e.*, the k_{HOO^-}/k_{HO^-} ratio) increases as the leaving-group basicity increases,[18a] which is opposite to the α-effect trend in this study (Table 1). However, we have suggested that the dependence of the α-effect in the reactions of Y-substituted-phenyl methanesulfonates on the leaving-group basicity has no significant meaning since their reaction mechanisms are different, *i.e.*, an S$_N$2 (S) mechanism for the reactions with HOO$^-$ and an E1cb reversible pathway for those with OH$^-$.[18a] Thus, it is necessary to investigate the reaction mechanism for the reactions of **4a-4i** to assess the validity of the α-effect found in this study.

Deduction of Reaction Mechanism. The reactions of **4a-4i** with OH$^-$ have been reported to proceed through a concerted mechanism, although the β$_{lg}$ value of −0.36 shown in Figure 1 could be taken as evidence for a stepwise mechanism with formation of an addition intermediate being the rate-determining step (RDS).[19] The β$_{lg}$ value of −0.51 found for the reactions with HOO$^-$ is typical of reactions reported previously to proceed through a concerted mechanism.[21-25] Thus, one can suggest that the reactions of **4a-4i** with HOO$^-$ also proceed through a concerted mechanism on the basis of the β$_{lg}$ value of −0.51.

However, more conclusive evidence is necessary to examine the above argument. It is apparent that a partial
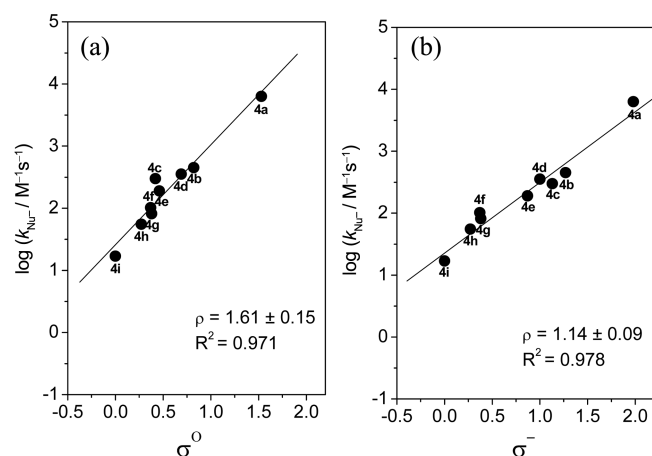
Figure 2. Hammett plots correlated with σ^o (a) and σ^- constants (b) for the reactions of Y-substituted-phenyl diphenylphosphinates (**4a-4i**) with HOO⁻ in H_2O at 25.0 ± 0.1 °C. The identity of points is given in Table 1.

negative charge would develop on the O atom of the leaving aryloxide, if the reactions proceed through a concerted mechanism. Since such a negative charge can be delocalized to the substituent Y through resonance interactions, one might expect σ^- constants would result in a better Hammett correlation than σ^o constants. In contrast, if the reactions proceed through stepwise mechanism, the departure of the leaving group should occur after the RDS. This is because HOO⁻ is more basic and a poorer nucleofuge than the leaving Y-substituted phenoxides. Accordingly, if the reactions with HOO⁻ proceed through a stepwise mechanism, no negative charge would develop on the O atom of the leaving group. In this case, σ^o constants should result in a better Hammett correlation than σ^- constants.

To examine the above argument, Hammett plots have been constructed using σ^o and σ^- constants. As shown in Figure 2, both Hammett plots are linear but exhibit many scattered points. (*i.e.*, $R^2 = 0.971 - 0.978$). Thus, one cannot obtain
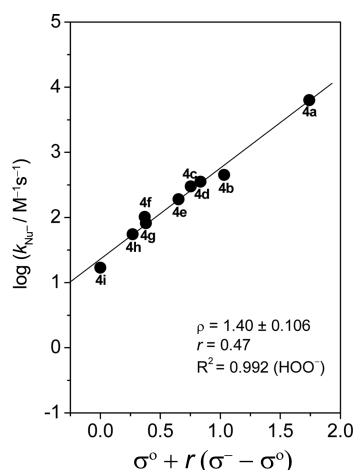
any conclusive information on the reaction mechanism from these Hammett plots.

We have shown that the Yukawa-Tsuno Eq. (1) is highly effective to elucidate ambiguities in reaction mechanisms for aminolyses of various esters (*e.g.*, C=O, C=S, P=O, P=S and SO$_2$ centered esters), alkaline ethanolyses of P=O, P=S and SO$_2$ centered esters, and Michael-type reactions of activated acetylenes with amines.[25a-h] Thus, Yukawa-Tsuno plot has been constructed in Figure 3. The Yukawa-Tsuno plot exhibits an excellent linear correlation ($R^2 = 0.992$) with $\rho = 1.40$ and $r = 0.47$.

$$\log k^Y/k^H = \rho[\sigma^o + r(\sigma^- - \sigma^o)] \qquad (1)$$

The r value in Eq. (1) represents the resonance demand of the reaction center or the extent of resonance contributions.[26,27] Thus, the r value of 0.47 obtained from the reactions with HOO⁻ indicates that a negative charge develops partially on the oxygen atom of the leaving aryloxide, which can be delocalized to the substituent Y through resonance interactions. This is possible only for reactions in which breakdown of the P–OAr bond occurs in the RDS. Thus, the linear Yukawa-Tsuno plot with $r = 0.47$ supports the preceding argument that the reactions of **4a-4i** with HOO⁻ proceed through a concerted mechanism.

Origin of the α-Effect. In the preceding section, the reactions of **4a-4i** with HOO⁻ and OH⁻ have been concluded to proceed through the same mechanism (*i.e.*, a concerted mechanism). Thus, the dependence of the α-effect on the substituent Y involves important information on the origin of the α-effect. It is apparent that the reactivity is governed by the GS and TS energies. Thus, our discussion will focus on the GS and TS effects.

It has often been reported that OH⁻ is less reactive than expected from its basicity and exhibits negative deviation from Brønsted-type plots.[2] It is well known that OH⁻ is strongly solvated in H_2O. Thus, solvation effect has been suggested to be responsible for the decreased reactivity of OH⁻.[3,4] It is noted that HOO⁻ and OH⁻ are used as an α-
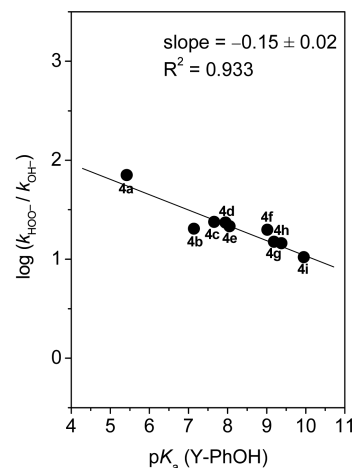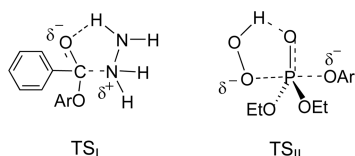

Figure 3. Yukawa-Tsuno plot for the reactions of Y-substituted-phenyl diphenylphosphinates (**4a-4i**) with HOO⁻ in H_2O at 25.0 ± 0.1 °C.

Figure 4. Plot of log (k_{HOO^-}/k_{HO^-}) *vs.* pK_a of Y-PhOH for the reactions of Y-substituted-phenyl diphenylphosphinates (**4a-4i**) with HOO⁻ and OH⁻ in H_2O at 25.0 ± 0.1 °C.

nucleophile and the reference nucleophile, respectively, throughout the reactions of **4a-4i**. This implies that the GS energy difference between the two nucleophiles is constant throughout the whole reactions. Accordingly, if the α-effect observed in this study is due to solvation effect (*i.e.*, GS effect), one might expect that the magnitude of the α-effect (*i.e.*, the k_{HOO^-}/k_{HO^-} ratio) should be nearly constant. However, in fact, Table 1 shows that the α-effect decreases as the substituent Y becomes a weaker EWG. Thus, the GS effect cannot be solely responsible for the α-effect in this study.

As shown in Figure 4, the α-effect decreases as the leaving-group basicity increases. This is in contrast to our previous report that the α-effect increases as the leaving-group basicity increases for the reactions of Y-substituted-phenyl benzoates with hydrazine and glycylglycine, which have been suggested to proceed through a stepwise mechanism with breakdown of the intermediate being the RDS.[28] The α-effect shown by hydrazine has been suggested to be TS stabilization through an intramolecular H-bonding interaction as modeled by TS_I since such a five-membered cyclic TS is not possible for the reactions with glycylglycine.[28] A similar intramolecular H-bonding interaction has been suggested for the reaction with HOO⁻ (*i.e.*, TS_{II}). Thus, one can suggest that TS stabilization through TS_{II} is also responsible for the α-effect observed in this study. The contrasting α-effect trends exhibited by hydrazine and HOO⁻ might be due to the different reaction mechanisms, *i.e.*, a stepwise mechanism for the reactions of aryl benzoates with NH₂NH₂ *vs.* a concerted mechanism for the reactions of **4a-4i** with HOO⁻.

$$TS_I \qquad TS_{II}$$

Conclusions

The current study has allowed us to conclude the following: (1) HOO⁻ is 10-70 times more reactive than OH⁻ although the former is *ca.* 4 pK_a units less basic than the latter, indicating the α-effect is operative in the reactions of **4a-4i**. (2) The linear Brønsted-type plot with $\beta_{lg} = -0.51$ and Yukawa-Tsuno plot with $\rho = 1.40$ and $r = 0.47$ indicate that the reactions proceed through a concerted mechanism. (3) Solvation effect is not solely responsible for the α-effect observed in this study. TS stabilization through an intramolecular H-bonding interaction is also responsible, in part, for the substituent dependent α-effect.

Experimental Section

Materials. Y-Substituted-phenyl diphenylphosphinates (**4a-4i**) were readily prepared from the reaction of diphenylphosphinyl chloride with Y-substituted phenol in anhydrous ether under the presence of triethylamine as reported previously.[29] H₂O₂ and other chemicals were of the highest

quality available. Doubly glass distilled water was further boiled and cooled under nitrogen just before use.

Kinetics. The kinetic study was performed using a UV-Vis-spectrophotometer for slow reactions (*e.g.*, $t_{1/2} > 10$ s) or a stopped-flow spectrophotometer for fast reactions (*e.g.*, $t_{1/2} \leq 10$ s) equipped with a constant temperature circulating bath to maintain the reaction mixture at 25.0 ± 0.1 °C. The reactions were followed by monitoring the appearance of Y-substituted phenoxide ion. The reactions were carried out under pseudo-first-order conditions. All solutions were transferred by gas-tight syringes. The stock solution of HOO⁻ was prepared by adding 10 equiv. of H₂O₂ and 1 equiv. of NaOH solution to make a self-buffered solution. Generally, the HOO⁻ concentration was varied over the range $(5-100) \times 10^{-3}$ M, while the substrate concentration was *ca.* 2×10^{-5} M. Pseudo-first-order rate constants (k_{obsd}) were calculated from the equation, $\ln (A_\infty - A_t) = -k_{obsd}t + C$. The plots of $\ln (A_\infty - A_t)$ *vs.* time were linear over 90% of the total reaction. Usually, five different HOO⁻ concentrations were employed and replicate values of k_{obsd} were determined to obtain the second-order rate constants (k_{HOO^-}) from the slope of linear plots of k_{obsd} *vs.* HOO⁻ concentrations.

Products Analysis. Y-Substituted-phenoxide was liberated quantitatively and identified as one of the products in the reaction of **4a-4i** by comparison of the UV-Vis spectrum after completion of the reaction with that of authentic sample under the same reaction condition.

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