

Decomposition of Paraoxon and Parathion by Amines, HOO^- and OH^- Ions: Reaction Mechanism and Origin of the α -Effect

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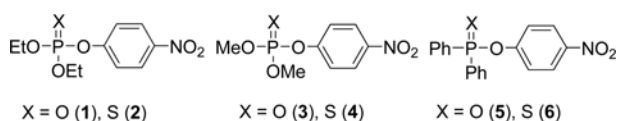
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The second-order rate constants have been measured spectrophotometrically for the reactions of paraoxon **1** and parathion **2** with a series of alicyclic secondary amines, OH^- and HOO^- ions in H_2O at 25.0 ± 0.1 °C. A linear Brønsted-type plot with $\beta_{\text{nuc}} = 0.40$ was obtained for the reactions of **1** with amines and OH^- . The reaction has been concluded to proceed through a concerted mechanism. HOO^- deviates positively from the linear Brønsted-type plot, implying that the α -effect is operative. The magnitude of the α -effect ($k_{\text{HOO}^-}/k_{\text{OH}^-}$) was found to be *ca.* 55 for the reaction of **1** and 290 for that of parathion **2**, indicating that HOO^- is highly effective in decomposition of the toxic phosphorus compounds although it is over 4 pK_a units less basic than OH^- . Among the theories suggested as origins of the α -effect (*e.g.*, TS stabilization through an intramolecular H-bonding interaction, solvent effect, and polarizability effect), polarizability effect appears to be the most important factor for the α -effect in this study, since the polarizable HOO^- exhibits a larger α -effect for the reaction of the more polarizable substrate **2**.

Key Words : Paraoxon, Parathion, Concerted mechanism, Solvent effect, Polarizability effect

Introduction

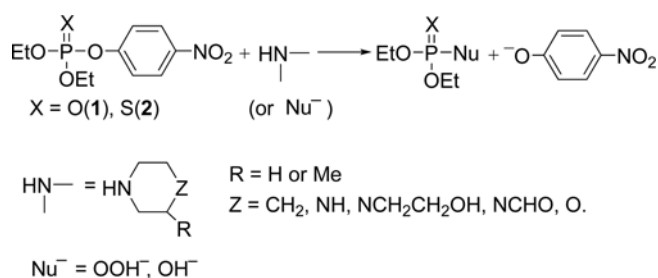
Organophosphorus esters such as paraoxon **1**, parathion **2**, and their methyl analogues (*i.e.*, methylparaoxon **3** and methylparathion **4**) have widely been used as insecticides. Accordingly, these organophosphorus compounds have often caused serious environmental pollution and unexpected accidents due to their high toxicity toward living organisms. Numerous studies have been performed to increase the rate of decomposition of toxic organophosphorus compounds under mild conditions.¹⁻⁷ Accordingly, various methods have been developed, *e.g.*, the use of highly reactive α -effect nucleophiles or the use of various metal ions as a Lewis acid catalyst.²⁻⁷ The α -effect nucleophiles (*e.g.*, oximates, *o*-iodosylbenzoate, and HOO^- anions) have been reported to be highly effective in decomposition of the toxic organophosphorus compounds.² Multivalent metal ions (*e.g.*, Mg^{2+} , Ca^{2+} , Zn^{2+} , Cu^{2+} , Co^{2+} , La^{3+}) as well as alkali metal ions have been reported to exhibit strong catalytic effects in nucleophilic substitution reactions of various organophosphorus compounds.³⁻⁷



Kinetic studies on the reactions of **5** and **6** have also been performed intensively to understand the reaction mechanisms.^{3-6,8-10} Alkaline ethanolysis of aryl dimethylphosphinates has been reported to proceed through a stepwise mechanism, in which expulsion of the leaving group occurs after the rate-determining step (RDS) on the basis of the

kinetic results that σ^o constants exhibit significantly better Hammett correlation than σ^- constants.^{3e} A similar conclusion has been drawn for alkaline hydrolysis of aryl diphenylphosphinates.⁸ On the contrary, nucleophilic substitution reactions of 4-nitrophenyl diphenylphosphinate **5** with a series of aryloxides have been reported to proceed through a concerted mechanism.⁹ The evidence provided for a concerted mechanism is a linear Brønsted-type plot for the reactions with a series of substituted phenoxides whose pK_a values straddle the basicity of the leaving 4-nitrophenoxide.⁹ We have also reported that reactions of 4-nitrophenyl diphenylphosphinate **5** and diphenylphosphinothioate **6** with a series of alicyclic secondary amines proceed through a concerted mechanism on the basis of linear Brønsted-type plots with $\beta_{\text{nuc}} = 0.38$ and 0.52 for the aminolyses of **5** and **6**, respectively.¹⁰ The concerted mechanism has been further supported from the linear Yukawa-Tsuno plots with $\rho = 1.91$ and $r = 0.30$ for the reactions of Y-substituted phenyl diphenylphosphinates including **5** while $\rho = 1.91$ and $r = 0.28$ for the reactions of Y-substituted phenyl diphenylphosphinothioates including **6**.¹⁰

However, kinetic studies on the reactions of **1-4** have much less been investigated. Castro *et al.* have recently performed the reaction of **1** with a series of alicyclic secondary amines in 44% aqueous ethanol and obtained a linear Brønsted-type plot with $\beta_{\text{nuc}} = 0.39$.¹¹ The reaction has been concluded to proceed through a concerted mechanism, since $\beta_{\text{nuc}} = 0.50 \pm 0.1$ is typical for reactions reported previously to proceed through a concerted mechanism. It has also been reported that the contribution of water and/or OH^- from hydrolysis of amines to the pseudo-first-order rate constant k_{obsd} is significant.¹¹ However, no further analysis of k_{obsd} has



been carried out. Thus, we have reinvestigated the reaction of **1** with a series of alicyclic secondary amines in pure H₂O to get further information on the reaction mechanism. We have also employed HOO⁻ and OH⁻ as an α-nucleophile and its corresponding normal-nucleophile, respectively in the reactions of **1** and **2** to investigate the α-effect.

Results and Discussion

All reactions in this study obeyed pseudo-first-order kinetics in the presence of a large excess of the amines or the anionic nucleophiles. Pseudo-first-order rate constants (k_{obsd}) were determined from the equation $\ln(A_{\infty} - A_t) = -k_{\text{obsd}}t + c$. As shown in Figure 1, the plot of k_{obsd} vs [piperidine] is linear with a large positive intercept. The plots for the reactions with the other amines exhibited also a good linear correlation with a large positive intercept (Figures not shown), indicating that the contribution of H₂O and/or OH⁻ from hydrolysis of amines to k_{obsd} is significant.

Thus, k_{obsd} can be expressed as Eq. (1), in which k_N and k_0 represent the second-order rate constants for the reactions with amines and the contribution of H₂O and/or OH⁻ from hydrolysis of amines to k_{obsd} , respectively, while $k_{\text{H}_2\text{O}}$ and k_{OH^-} represent the rate constant for the reaction with water and OH⁻, respectively. The k_N values were calculated from the slope of the linear plots of k_{obsd} vs [amine]. The uncertainty in the k_N values is estimated to be less than 3% from replicate runs. The k_N and k_0 values calculated in this way are summarized in Table 1. The second-order rate constants for the reactions of **1** and **2** with OH⁻ (*i.e.*, k_{OH^-})

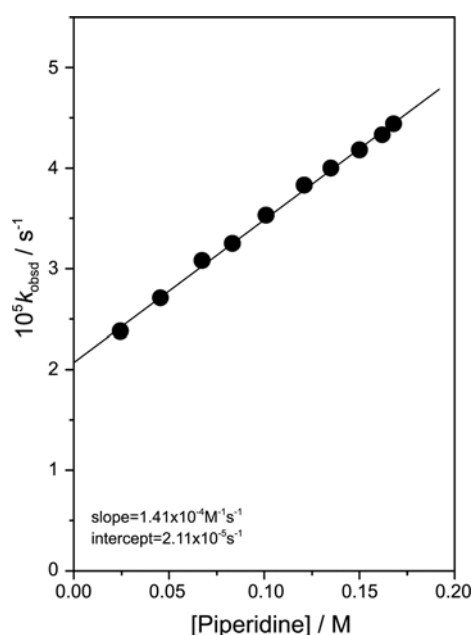


Figure 1. Plot of k_{obsd} vs [piperidine] for the reaction of paraoxon **1** with piperidine in H₂O at 25.0 °C.

and HOO⁻ (*i.e.*, k_{HOO^-}) are also presented in Table 1 and in its footnote, respectively.

$$k_{\text{obsd}} = k_N[\text{amine}] + k_0, \text{ where } k_0 = k_{\text{H}_2\text{O}} + (k_{\text{OH}^-} \times [\text{OH}^-]) \quad (1)$$

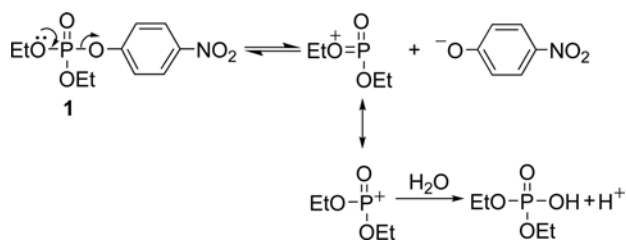
Dissection of k_0 into $k_{\text{H}_2\text{O}}$ and $(k_{\text{OH}^-} \times [\text{OH}^-])$. 4-Nitrophenoxide ion is stable in H₂O and a fairly good leaving group. Besides, EtO is a good electron-donating group through resonance interactions.¹² Accordingly, one cannot exclude a possibility that the reaction of **1** in H₂O would proceed through an S_N1 mechanism (Scheme 2) to a certain extent as well as through a nucleophilic substitution at the P=O center. This idea appears to account for the large positive intercept shown in Figure 1.

To examine the above argument, the reaction of **1** with OH⁻ has been performed. If the reaction proceeds through an S_N1 mechanism as shown in Scheme 2, formation of diethyl phosphoryl cation is the RDS. Thus, one might expect that

Table 1. Summary of second-order rate constants (k_N) for the reactions of paraoxon **1** with a series of alicyclic secondary amines, HOO⁻, and HO⁻ in H₂O at 25.0 ± 0.1 °C

| Amines | pK _a | 10 ⁵ k_N / M ⁻¹ s ⁻¹ | 10 ⁷ k_0 / s ⁻¹ | 10 ⁷ ($k_{\text{OH}^-} \times [\text{OH}^-]$) / s ⁻¹ | |
|--------|------------------------------|---|---|--|--------------------|
| 1 | 1-Formylpiperazine | 7.98 | 0.917 | 2.34 | 0.094 ^a |
| 2 | Morpholine | 8.36 | 1.94 | 2.51 | 0.24 ^a |
| 3 | 1-(2-Hydroxyethyl)piperazine | 9.38 | 2.56 | 5.52 | 2.35 ^a |
| 4 | Piperazine | 9.82 | 6.58 | 16.0 | 6.48 ^a |
| 5 | 3-Methylpiperidine | 11.07 | 17.2 | 162 | 118 ^a |
| 6 | Piperidine | 11.22 | 14.1 | 211 | 163 ^a |
| 7 | HOO ⁻ | 11.62 | 54300 | — | — |
| 8 | HO ⁻ | 15.74 | 981 | — | — |

^aCalculated values from the second-order rate constant k_{OH^-} and the concentration of OH⁻ in each reaction mixture as described in the text. The second-order rate constants for the reactions of **2** with HOO⁻ and HO⁻ have been measured to be 0.202 and $6.96 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$, respectively (see Figures S2 A and B in the Supporting information).



k_{obsd} should be independent of the hydroxide concentration if the reaction proceeds through an $\text{S}_{\text{N}}1$ mechanism. However, as shown in Figure S1A in the Supporting Information (SI), the plot of k_{obsd} vs $[\text{OH}^-]$ is linear with a large slope and passes through the origin. Clearly, this is not possible for reactions which proceed through an $\text{S}_{\text{N}}1$ mechanism. Thus, one can suggest that the large intercept shown in Figure 1 is not due to the nature of the reaction mechanism but due to the large contribution of H_2O and OH^- to the k_{obsd} value, *i.e.*, $k_{\text{o}} = k_{\text{H}_2\text{O}} + (k_{\text{OH}^-} \times [\text{OH}^-])$.

To dissect k_{o} into $k_{\text{H}_2\text{O}}$ and $(k_{\text{OH}^-} \times [\text{OH}^-])$, the second-order rate constant for the reaction of **1** with OH^- (*i.e.*, k_{OH^-}) and the concentration of OH^- in each reaction mixture are necessary. The k_{OH^-} value measured in this study for the reaction of **1** with OH^- is $9.81 \times 10^{-3} \text{ M}^{-1}\text{s}^{-1}$ (see also Figure S1 in the Supporting Information). The pH of the reaction mixtures can be calculated from the Henderson-Hasselbalch equation (2), where $[\text{NH}]$ and $[\text{NH}_2^+]$ represent the concentration of the amine and its conjugate acid, respectively. The pK_{a} values of the conjugate acids of all the amines studied are known.¹³ Besides, the buffer ratio $[\text{NH}]/[\text{NH}_2^+]$ was kept 1.0/1.0 throughout the whole reactions. Thus, the pH of each reaction mixture is the same as the pK_{a} of the conjugate acid of the amine used. The $(k_{\text{OH}^-} \times [\text{OH}^-])$ value can be calculated from the k_{OH^-} value determined above for the reaction of **1** with OH^- and the OH^- concentration calculated from the pH of the reaction mixture. Then, one can dissect the k_{o} values determined from the intercept of the linear plots of k_{obsd} vs [amine] into the $k_{\text{H}_2\text{O}}$ and $(k_{\text{OH}^-} \times [\text{OH}^-])$ values. The $k_{\text{H}_2\text{O}}$ value in the current reaction was estimated to be $2.24 \times 10^{-7} \text{ s}^{-1}$, which implies that the half-life of **1** is *ca.* 36 days in pure water at 25 °C.

$$\text{pK}_{\text{a}} = \text{pH} + \log [\text{NH}]/[\text{NH}_2^+] \quad (2)$$

The calculated $(k_{\text{OH}^-} \times [\text{OH}^-])$ values are summarized in Table 1 and illustrated graphically in Figure 2 as a function of the pH of the reaction mixtures. The plot is linear with a slope of 1.0. Furthermore, the $(k_{\text{OH}^-} \times [\text{OH}^-])$ and $(k_{\text{o}} - k_{\text{H}_2\text{O}})$ values are almost the same, indicating that the kinetic data including the $k_{\text{H}_2\text{O}}$ value of $2.24 \times 10^{-7} \text{ s}^{-1}$ are accurate.

Reaction Mechanism. Reactions of organophosphorus esters with amines have been suggested to proceed either through a concerted mechanism or through a stepwise pathway depending on reaction conditions.^{3-6,8-10} Cook *et al.* have concluded that aminolysis of aryl diphenylphosphinates (*e.g.*, **5** and its derivatives) in MeCN proceeds through a zwitterionic pentacoordinate intermediate with its break-

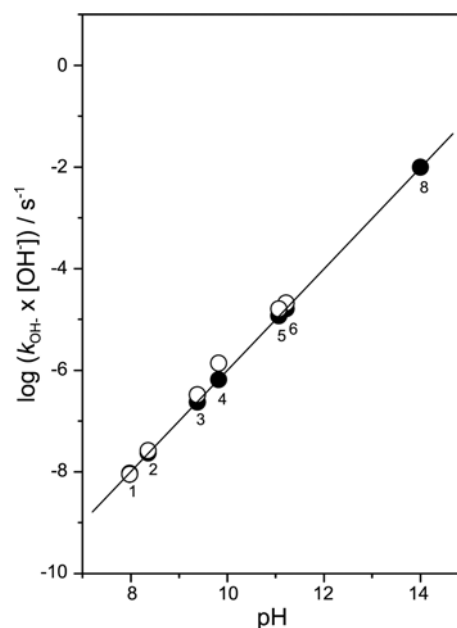


Figure 2. Plot of $\log(k_{\text{OH}^-} \times [\text{OH}^-])$ vs pH of the reaction mixture for the reactions of paraoxon **1** with alicyclic secondary amines and OH^- in H_2O at 25.0 ± 0.1 °C. The identity of the points is given in Table 1. The symbols ● and ○ in the linear plot represent the $(k_{\text{OH}^-} \times [\text{OH}^-])$ and $(k_{\text{o}} - k_{\text{H}_2\text{O}})$ values, respectively.

down being the RDS from studies of leaving group effects, solvent effects, and activation parameters.⁸ In contrast, we have reported that aminolysis of **5** and its derivatives in 80 mol % $\text{H}_2\text{O}/20$ mol % DMSO proceeds through a concerted

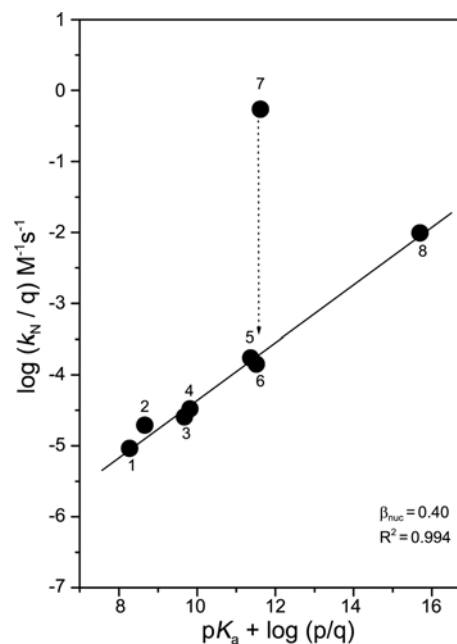


Figure 3. Brønsted-type plot for the reactions of paraoxon **1** with alicyclic secondary amines, OH^- and HOO^- in H_2O at 25.0 ± 0.1 °C. The identity of points is given in Table 1. The k_{N} and pK_{a} values for the reactions with the amines were statistically corrected using p and q , *i.e.*, $p = 2$ and $q = 1$ except $q = 2$ for piperazine (see ref 20).

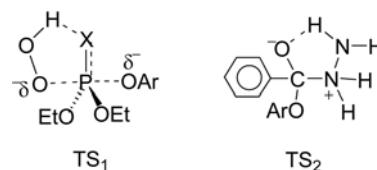
mechanism on the basis of the kinetic data that the Yukawa-Tsuno plot for the reactions of Y-substituted phenyl diphenylphosphinates including **5** exhibits an excellent linear correlation with $\rho = 1.91$ and $r = 0.30$.^{10a,c} The concerted mechanism has been further supported from the linear Brønsted-type plot with $\beta_{\text{nuc}} = 0.38$ for the reactions of 2,4-dinitrophenyl diphenylphosphinate with a series of alicyclic secondary amines.^{10a,c} A similar conclusion has been drawn for the corresponding reactions of aryl diphenylphosphinothioates although the thio compounds were much less reactive than their oxygen analogues.^{10b}

Linear free energy relationships such as Brønsted-type, Hammett and Yukawa-Tsuno equations are the most popular tool to investigate reaction mechanisms.¹⁴ Thus, a Brønsted-type plot has been constructed for the reactions of **1** with the alicyclic secondary amines together with the kinetic results for the reactions with HOO^- and OH^- .

As shown in Figure 3, the Brønsted-type plot exhibits a linear correlation with $\beta_{\text{nuc}} = 0.40$. Interestingly, the point for OH^- lies on the linear Brønsted-type plot composed of the amines. In contrast, the point for HOO^- deviates positively from the linearity. A β_{nuc} value of 0.5 ± 0.1 is typical for reactions reported previously to proceed through a concerted mechanism, e.g., $\beta_{\text{nuc}} = 0.38\text{--}0.52$ for reactions of 2,4-dinitrophenyl diphenylphosphinate and diphenylphosphinothioates with primary and secondary amines in 80 mol % $\text{H}_2\text{O}/20$ mol % DMSO.¹⁰ In fact, Castro *et al.* have recently concluded that reactions of **1** with a series of alicyclic secondary amines in 44% aqueous ethanol proceed through a concerted mechanism on the basis of a linear Brønsted-type plot with $\beta_{\text{nuc}} = 0.39$.¹¹ Thus, one can suggest that the current reactions of **1** with the amines in H_2O proceeds also through a concerted mechanism on the basis of the linear Brønsted-type plot with $\beta_{\text{nuc}} = 0.40$.

Origin of the α -Effect. Figure 3 shows that OH^- lies on the linear Brønsted-type plot composed of the amines 1-6, while HOO^- deviates positively from the linearity. As shown in Table 1 that HOO^- is *ca.* 55 times more reactive than OH^- toward **1**, although the former is over 4 $\text{p}K_{\text{a}}$ units less basic than the latter. This confirms that HOO^- is indeed an effective detoxifying agent for **1**.

HOO^- has often been reported to exhibit an unusually higher nucleophilic reactivity than would be predicted from its basicity (*i.e.*, the α -effect).^{2, 15-17} The suggested causes of the α -effect shown by HOO^- include intramolecular H-bonding interaction, solvent effect, and polarizability effect.^{2,16} It has previously been reported that HOO^- would form a cyclic TS through an intramolecular H-bonding interaction, e.g., TS_1 .¹⁶ A similar 5-membered cyclic TS has been suggested for the reaction of aryl benzoates with hydrazine, e.g., TS_2 , in which hydrazine exhibits the α -effect by stabilizing the TS (or intermediate) through an intramolecular H-bonding interaction.¹⁷ Since such 5-membered cyclic TS (e.g., TS_1) is not possible for the reaction with OH^- , stabilization of TS through an intramolecular H-bonding interaction has been suggested to be an origin of the α -effect shown by HOO^- .¹⁶



To examine the above argument, reactions of parathion **2** with OH^- and HOO^- have been performed. It is apparent that a partial negative charge would develop on the sulfur atom of **2** in the TS. However, a negatively charged S atom is not a good H-bonding acceptor. This idea is consistent with the fact that HS^- is not very soluble in H_2O , and H_2S is a gas at room temperature while H_2O is liquid. Since TS stabilization through TS_1 would be less effective for the reaction of **2** than for that of **1**, one might expect that the α -effect (*i.e.*, $k_{\text{HOO}^-}/k_{\text{OH}^-}$) would be smaller for the reaction of **2** than for that of **1** if the reactions of **1** and **2** proceed through TS_1 . As shown in the footnote of Table 1 and Figure S2 in the SI, $k_{\text{OH}^-} = 6.96 \times 10^{-4} \text{ M}^{-1}\text{s}^{-1}$ and $k_{\text{HOO}^-} = 0.202 \text{ M}^{-1}\text{s}^{-1}$. The $k_{\text{HOO}^-}/k_{\text{OH}^-}$ ratio for the reaction of **2** is *ca.* 290, which is much larger than that for the corresponding reaction of **1** (e.g., $k_{\text{HOO}^-}/k_{\text{OH}^-} = 55$ for the reaction of **1**). This is not possible if the reactions of **1** and **2** with HOO^- proceed through TS_1 . Thus, stabilization of TS through intramolecular H-bonding interactions cannot be an important origin of the α -effect for the reactions of **1** and **2**.

HOO^- was reported to be 12 kcal/mol less strongly solvated than OH^- in H_2O .¹⁸ Thus, solvent effect has often been suggested as a cause of the α -effect shown by HOO^- in H_2O .² If solvent effect is the main cause of the α -effect, one might expect that the magnitude of the α -effect would be similar for the reactions of **1** and **2**. This is because HOO^- and OH^- are the common nucleophiles employed for the reactions of **1** and **2**. Thus, the fact that the α -effect is much larger for the reaction of **2** suggests that solvent effect cannot be an important cause of the α -effect observed for the current reactions of **1** and **2**.

Jencks has attributed abnormally high reactivities of HOO^- and N_3^- to their high polarizability.¹⁹ It is apparent that the P=S bond in **2** is more polarizable than the P=O bond in **1**. Accordingly, one might expect that the α -effect is larger for the reaction of **2** than for that of **1** if enhanced polarizability of HOO^- is an important factor to determine the α -effect. In fact, the α -effect is much larger for the reaction of **2** with HOO^- than for the corresponding reaction of **1** (e.g., $k_{\text{HOO}^-}/k_{\text{OH}^-} = 290$ and 55 for the reactions of **2** and **1**, respectively). Thus, one can suggest that polarizability effect is responsible for the large α -effect found for the reactions of **2** with HOO^- .

Conclusions

The current study has allowed us to conclude the following: (1) The plot of k_{obsd} vs [amine] is linear with a large positive intercept, indicating that the contribution of H_2O and OH^- to k_{obsd} is significant. (2) The Brønsted-type plot is linear with $\beta_{\text{nuc}} = 0.40$ for the reactions of **1** with all the

amines studied and OH⁻, while HOO⁻ deviates positively from the linearity (*i.e.*, the α -effect). The β_{nuc} value of 0.40 is typical for reactions reported previously to proceed through a concerted mechanism. (3) Among the suggested origins of the α -effect, an intramolecular H-bonding interaction and solvent effect appear to be unimportant for the α -effect in the current study. (4) Polarizability effect is the main factor to affect the magnitude of the α -effect for the reactions of **1** and **2** with HOO⁻, since the magnitude of the α -effect (*i.e.*, $k_{\text{HOO}^-}/k_{\text{OH}^-}$) is larger for the reaction of **2** than for that of **1**. (5) HOO⁻ is highly effective in decomposition of the toxic organophosphorus esters in a moderately basic condition (*e.g.*, pH < 12).

Experimental Section

Materials. Paraoxon **1** and parathion **2** are commercially available and were used without further purification. Amines 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 with a UV-vis spectrophotometer equipped with a constant temperature circulating bath. The reactions were followed by monitoring the appearance of the leaving 4-nitrophenoxide ion. All the reactions were carried out under pseudo-first-order conditions in which nucleophile concentrations were at least 20 times greater than the substrate concentration. The amine stock solution of *ca.* 0.2 M was prepared by dissolving 2 equiv. of amine and 1 equiv. of standardized HCl solution to make a self-buffered solution (*i.e.*, [amine]/[amine-H⁺] = 1.0/1.0) in a 25.0 mL volumetric flask. In contrast, the buffer ratio of [HOO⁻]/[H₂O₂] was kept *ca.* 1.0/10 since H₂O₂ is unstable in a basic condition.

Typically, the reaction was initiated by adding 5 μ L of a 0.02 M solution of substrate **1** or **2** in acetonitrile to a 10-mm quartz UV cell containing 2.50 mL of the thermostated reaction mixture made up of solvent and aliquot of the nucleophile stock solution. All the solutions were transferred by gas-tight syringes. Generally, the nucleophile concentration was varied over the range $(5\text{--}100) \times 10^{-3}$ M, while the substrate concentration was 2×10^{-5} M. Pseudo-first-order rate constants (k_{obsd}) were calculated from the equation, $\ln(A_{\infty} - A_t) = -k_{\text{obsd}}t + C$. The plots of $\ln(A_{\infty} - A_t)$ vs time were linear over *ca.* 90% of the total reaction.

Products Analysis. 4-Nitrophenoxide was liberated quantitatively and identified as one of the products in the reactions of **1** and **2** by comparison of the UV-vis spectra after completion of the reactions with the authentic sample under the same reaction conditions.

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Supporting Information Available: Figures S1 and S2 for plots of k_{obsd} vs [nucleophile] for the reactions of paraoxon **1** and parathion **2** with OH⁻ (A) and with HOO⁻ (B) in H₂O at 25.0 \pm 0.1 $^{\circ}$ C.

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