

Origin of the α -Effect in Detoxification of Paraoxon and Parathion by Hydrogen Peroxide Anion

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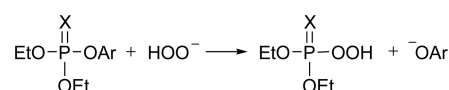
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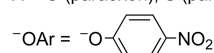
The term α -effect was given to the abnormally enhanced reactivity shown by nucleophiles possessing one or more nonbonding electron pairs at the atom α to the reaction site.¹ Due to the high reactivity, the α -effect nucleophiles have often been used as an antidote for toxic organophosphorus compounds (OPs).²⁻⁴ Especially in the presence of a cationic surfactant such as cetyltrimethylammonium bromide (CTAB), the use of α -effect nucleophiles (*e.g.*, HOO^- , oximates, hydroxamates, *o*-iodosylbenzoate anions) has been reported to be highly effective in destruction of various OPs under mild conditions.⁵⁻⁹

Numerous studies have been carried out to investigate origins of the α -effect.^{3,4,10-22} Some important theories suggested as the origin of the α -effect include destabilization of the ground state (GS) due to the electronic repulsion between the nonbonding electron pairs, stabilization of transition state (TS), thermodynamic stabilization of reaction products, and solvent effects.^{3,4,10-22} However, none of these theories alone can fully explain the α -effect phenomenon. Particularly, solvent effects on the α -effect remain controversial.¹⁰⁻²² It has been reported that HOO^- and OH^- ions show a similar reactivity in gas-phase reaction of methyl formate (*i.e.*, absence of the α -effect in the gas-phase reaction).¹⁹ In contrast, recent gas-phase studies have shown that HOO^- exhibits lower activation energies than isobasic $\text{CH}_3\text{CH}_2\text{O}^-$ for the gas-phase reactions of dimethyl methylphosphonate and alkyl halides (*i.e.*, an intrinsic α -effect).²⁰⁻²² Thus, absence of the α -effect in the gas-phase reaction has been attributed to the fact that HOO^- is less basic than OH^- in the gas-phase.²⁰⁻²²

We have reported that solvent effect on the α -effect is significant for nucleophilic substitution reactions of various esters (*e.g.*, $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{P}=\text{O}$, $\text{P}=\text{S}$ and SO_2 centered esters) with butane-2,3-dione monoximate (Ox^-) and 4-chlorophenoxide (4-ClPhO^-) in DMSO- H_2O mixtures of varying compositions.¹²⁻¹⁸ We have shown that the magnitude of the α -effect (*i.e.*, the $k_{\text{Ox}}/k_{4\text{-ClPhO}}$ ratio) increases as the mol % DMSO in the medium increases up to *ca.* 50 mol % DMSO and then decreases thereafter.¹²⁻¹⁸ Dissection of the activation parameters has revealed that desolvation of the GS is responsible for the increasing α -effect up to 50 mol % DMSO while differential stabilization of the TS results in the decreasing α -effect beyond 50 mol % DMSO.¹²⁻¹⁸



X = O (paraoxon), S (parathion)



Scheme 1

Our study has been extended to detoxification reactions of 4-nitrophenyl diethyl phosphate (paraoxon) and 4-nitrophenyl diethyl phosphorothioate (parathion) with HOO^- in various concentrations of CTAB to investigate the origin of the α -effect as well as the effect of CTAB on reactivity (Scheme 1). We wish to report origins of the enhanced reactivity of HOO^- toward these toxic $\text{P}=\text{O}$ and $\text{P}=\text{S}$ centered insecticides.

Results and Discussion

The current reactions proceeded with quantitative liberation of 4-nitrophenoxide ion and obeyed pseudo-first-order kinetics in the presence of a large excess of HOO^- . Pseudo-first-order rate constants (k_{obsd}) were determined from the equation $\ln(A_\infty - A_t) = -k_{\text{obsd}}t + c$. The plots of $\ln(A_\infty - A_t)$ vs. t were linear over 90% of the total reaction. The correlation coefficient for the linear regression was always higher than 0.9995. The uncertainty in the k_{obsd} values is estimated to be less than $\pm 3\%$ from replicate runs. The kinetic conditions and results for the reactions of paraoxon and parathion with HOO^- are summarized in Table 1.

Effects of CTAB on Reactivity of HOO^- . As shown in Table 1, the pseudo-first-order rate constant (k_{obsd}) increases as the concentration of CTAB in the medium increases, *e.g.*, the k_{obsd} value for the reaction of paraoxon with 1.11×10^{-3} M of HOO^- is $6.03 \times 10^{-4} \text{ s}^{-1}$ when $[\text{CTAB}] = 0$ mM in the reaction medium and it increases up to $1.26 \times 10^{-2} \text{ s}^{-1}$ when $[\text{CTAB}] = 4.71$ mM, where the maximum k_{obsd} is observed. A similar result is shown for the corresponding reaction of parathion, although parathion is 2-3 times less reactive than paraoxon, *i.e.*, $k_{\text{obsd}} = 2.24 \times 10^{-4} \text{ s}^{-1}$ when $[\text{CTAB}] = 0$ mM and $k_{\text{obsd}} = 5.83 \times 10^{-3} \text{ s}^{-1}$ when $[\text{CTAB}] = 1.96$ mM. The k_{obsd} values for the reactions of paraoxon and parathion increase over 20 times upon addition of the surfactant up to a

Table 1. Summary of Kinetic Results for the Reactions of Paraoxon and Parathion with HOO^- (and OH^- in parenthesis) in Various Concentrations of CTAB at $25.0 \pm 0.1^\circ\text{C}$

[CTAB]/mM	$10^4 k_{\text{obsd}}/\text{s}^{-1}$	
	paraoxon	parathion
0	6.03 (0.109) ^a	2.24 (0.00773) ^a
0.784	21.5	14.2
1.18	42.4	37.8
1.57	63.5	53.9
1.96	90.1	58.3
2.35	105	56.5
2.74	114	55.2
3.92	123	50.2
4.71	126	46.3
6.28	121	39.7
7.07	118	37.2

^aThe k_{obsd} values for the reactions with OH^- when $[\text{OH}^-] = 1.11 \times 10^{-3} \text{ M}$, $[\text{paraoxon}] = [\text{parathion}] = 1.0 \times 10^{-5} \text{ M}$; $[\text{HOO}^-] = 1.11 \times 10^{-3} \text{ M}$.

certain concentration, indicating that the effect of CTAB on reactivity is significant.

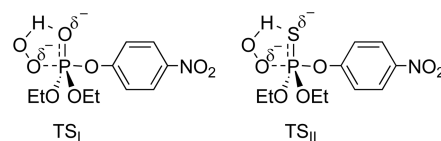
The effects of added CTAB on the reactivity of HOO^- toward paraoxon and parathion are illustrated in Figure 1. It is seen that the k_{obsd} for the reaction of paraoxon increases as the concentration of CTAB increases up to *ca.* 5 mM of CTAB and then decreases thereafter, although the decrease in k_{obsd} is modest. A similar result is shown for the reaction of parathion. However, the k_{obsd} value for the reaction of parathion increases more steeply up to *ca.* 2 mM of CTAB than that for the reaction of paraoxon and then decreases more rapidly beyond that point. This demonstrates convincingly that the effect of CTAB on reactivity is strongly dependent on the nature of the electrophilic centers (*i.e.*, $\text{P}=\text{O}$ vs. $\text{P}=\text{S}$), and that addition of a proper amount of CTAB is necessary to maximize the effect of CTAB on reactivity.

Significant rate enhancements have often been reported for reactions of esters with anionic nucleophiles upon addition of cationic surfactants in the reaction medium, *e.g.*, for nucleophilic substitution reactions of 4-nitrophenyl di-

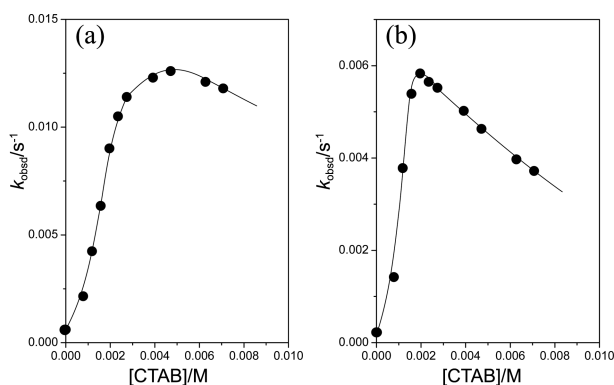
phenylphosphinate with butane-2,3-dione monoximate,^{7a} for decompositions of various organophosphonate and phosphate esters by using *o*-iodosylbenzoate and HOO^- anions,^{5,6} and for acyl-group transfer reactions of 4-nitrophenyl acetate with aryloxides and hydroxamates.^{7b} The enhanced nucleophilicity of anionic nucleophiles in cationic micellar solutions has been attributed to an increase in the concentration of reactants at the micellar interface rather than an increase in the intrinsic reactivity.^{9,10} In fact, the second-order rate constants have often been reported to be smaller at the micellar interface than the one measured in the absence of surfactants.^{9,10}

The concentration of reactants at the micellar interface would be affected by the ionic and hydrophobic interactions between the micellar aggregates and reactants. Since HOO^- is a common nucleophile used in the reactions of paraoxon and parathion, the ionic interaction between the cationic micellar aggregates and HOO^- ion would be constant. Accordingly, one can suggest that the contrasting CTAB effects shown in Figure 1 are not due to any difference in the ionic interaction but are caused by the difference in the hydrophobic interactions between the micellar aggregates and substrates (*i.e.*, paraoxon and parathion). Since the $\text{P}=\text{S}$ bond in parathion is considered to be more hydrophobic than the $\text{P}=\text{O}$ bond in paraoxon, parathion would exert a stronger hydrophobic interaction with the micellar aggregates than paraoxon. This idea can be supported by the fact that H_2S is little soluble in water. Besides, H_2S is a gas at room temperature while H_2O is liquid. Thus, one might expect that the effect of CTAB on reactivity would be more significant for the reaction of parathion than for that of paraoxon. In fact, as shown in Figure 1, k_{obsd} increases more steeply for the reaction of parathion than for that of paraoxon upon addition of CTAB to the reaction medium up to a certain concentration, and then decreases more rapidly upon further addition of CTAB.

Origin of the α -Effect shown by HOO^- . Stabilization of the TS through an intramolecular H-bonding interaction as modeled by TS_I has previously been suggested to be responsible for the α -effect shown by HOO^- , since such five-membered cyclic TS is not possible for the reaction with OH^- .²³ One might suggest a similar cyclic TS for the reaction of parathion with HOO^- (*e.g.*, TS_II). However, the H-bonding interaction depicted in TS_II would not be as strong as that in TS_I . This is because negatively charged sulfur atoms do not form a strong H-bonding with H_2O molecules (*e.g.*, HS^- is not very soluble in H_2O).



Thus, HOO^- would exhibit a smaller α -effect for the reaction of parathion than for that of paraoxon, if the reaction of parathion with HOO^- proceeds through TS_II . However, the α -effect is much larger for the reaction of parathion than for

**Figure 1.** Effects of CTAB on k_{obsd} for the reactions of paraoxon (a) and parathion (b) with HOO^- in H_2O at $25.0 \pm 0.1^\circ\text{C}$. $[\text{paraoxon}] = [\text{parathion}] = 1.0 \times 10^{-5} \text{ M}$; $[\text{HOO}^-] = 1.11 \times 10^{-3} \text{ M}$.

that of paraoxon, *e.g.*, $k_{\text{HOO}^-}/k_{\text{OH}^-} = 55$ and 290 for the reactions of paraoxon and parathion, respectively (Table 1). Since this is contrary to the expectation, TS stabilization through TS_{II} appears to be irresponsible for the α -effect observed in the reaction of parathion with HOO^- .

DePuy *et al.* have reported that HOO^- and OH^- show a similar reactivity in gas-phase reaction of methyl formate (*i.e.*, absence of the α -effect).^{19a} Recent computational studies have also shown that HOO^- does not exhibit lower activation energies than OH^- in the gas-phase reactions of alkyl halides.²⁰⁻²² The absence of the α -effect in the gas-phase reactions has been attributed to the fact that OH^- is more basic than HOO^- .²⁰⁻²² In contrast, HOO^- in this study is 55 and 290 times more reactive than OH^- toward paraoxon and parathion, respectively (*i.e.*, presence of the α -effect), although the former is *ca.* 4 pK_a units less basic than the latter in H_2O . Since HOO^- was reported to be 12 kcal/mol less strongly solvated than OH^- in H_2O ,²⁴ one might suggest that the solvent effect is responsible for the α -effect shown by HOO^- in the reactions of paraoxon and parathion at least to a certain degree.

It has often been reported that phosphorus esters possessing a P=S bond are *ca.* 50-60 times less reactive than those bearing a P=O bond, *e.g.*, for the reactions of paraoxon and parathion with ethoxide ion in ethanol.²⁵ Thus, the term thio-effect was given to the reactivity ratio of P=O and P=S centered compounds (*i.e.*, the rate constant ratio for the reactions of P=O and P=S compounds).²⁶ As shown in Table 1, the thio-effect (*i.e.*, $k_{\text{obsd}}^{\text{P=O}}/k_{\text{obsd}}^{\text{P=S}}$) for the reactions of paraoxon and parathion with HOO^- is only 2-3 in the absence or presence of CTAB. This is much smaller than the thio-effect of 14.1 for the corresponding reactions with OH^- (Table 1).

One might suggest that the small thio-effect found for the reactions of paraoxon and parathion with HOO^- is in accord with the hard-soft acids and bases (HSAB) principle. This is because HOO^- is known to be a soft base, although it is an oxygen-centered base, and the P=S bond in parathion is highly polarizable and a soft electrophilic center. Accordingly, one might expect that HOO^- exhibits a more enhanced reactivity toward the polarizable parathion than toward the less polarizable paraoxon on the basis of the HSAB principle. In contrast, OH^- would not show an enhanced reactivity toward the polarizable parathion, since it is a hard base. Thus, one can suggest that the high polarizability of HOO^- and parathion is responsible for the kinetic result that the α -effect is much larger for the reaction of parathion than for that of paraoxon.

Conclusions

(1) The k_{obsd} values for the reactions of paraoxon and parathion with HOO^- increase upon addition of CTAB up to a certain concentration and then decrease thereafter. (2) The k_{obsd} value for the reaction of parathion is more sensitive to the concentration of CTAB than that for the reaction of paraoxon. (3) Solvent effect is responsible at least to a

certain degree for the α -effect observed in the reactions of paraoxon and parathion with HOO^- . (4) The large α -effect observed in the reaction of parathion is not due to the stabilization of the TS through the H-bonding interaction depicted in TS_{II}. (5) The high polarizability of HOO^- is responsible for the larger α -effect observed for the reaction of more polarizable parathion.

Experimental Section

Materials. Paraoxon and parathion are commercially available and were used without further purification. CTAB, H_2O_2 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 equipped with a constant temperature circulating bath. The reactions were followed by monitoring the appearance of the leaving 4-nitrophenoxide ion. Since HOO^- is unstable in basic solution, HOO^- was prepared in situ by dissolving 10 equiv. of H_2O_2 and 1 equiv. of standardized NaOH solution in the reaction cell. All the solutions were transferred by gas-tight syringes. 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.

Product Analysis. 4-Nitrophenoxide was liberated quantitatively and identified as one of the products by comparison of the UV-Vis spectra after completion of the reaction with the authentic sample under the same reaction conditions.

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