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Aminolyses of Aryl Diphenylphosphinates and Diphenylphosphinothioates: Effect of Modification of Electrophilic Center from P═O to P═S

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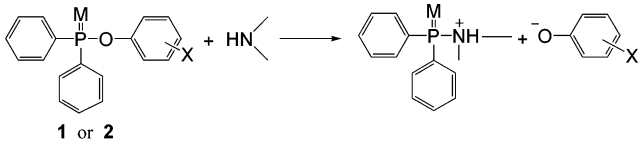

1 or **2**

M = O (**1**), S (**2**)

X = 2,4-$(NO_2)_2$ (**a**), 3,4-$(NO_2)_2$ (**b**), 4-NO_2 (**c**), 4-CHO (**d**), 4-CN (**e**), 4-COMe (**f**), 3-Cl (**g**), 3-COMe (**h**), 4-Cl (**i**)

HN = 7 different alicyclic secondary amines

A kinetic study is reported for aminolysis of aryl diphenylphosphinothioates (**2a**−**i**). The phosphinothioates **2a**−**i** are less reactive than aryl diphenylphosphinates (**1a**−**i**), the oxygen analogues of **2a**−**i**, regardless of the basicity of the leaving aryloxides or the attacking amines. The Yukawa−Tsuno plot for the reactions of **2b**−**i** with piperidine exhibits good linearity with a small *r* value ($r = 0.28$), indicating that the leaving group departs at the rate-determining step with a small degree of bond fission. Reactions of 2,4-dinitrophenyl diphenylphosphinothioate (**2a**) with alicyclic secondary amines result in a good linear Brønsted-type plot with $\beta_{nuc} = 0.52$, implying that the reactions proceed through a concerted mechanism. The β_{nuc} value determined for the reactions of **2a** is slightly larger than that reported for the corresponding reactions of 2,4-dinitrophenyl diphenylphosphinate (**1a**, i.e., $\beta_{nuc} = 0.38$), suggesting that reactions of **2a** proceed through a tighter transition state (TS) than that of **1a**. The reaction of **2a** with piperidine exhibits a ca. 0.4 kcal/mol more favorable enthalpy of activation ($\Delta H^{\ddagger}$) than that of **1a**. On the contrary, the entropy of activation at 25.0 °C ($T\Delta S^{\ddagger}$) is ca. 1.5 kcal/mol more unfavorable for the reaction of **2a** than for that of **1a**. This result supports the proposal that the reaction of **2a** proceeds through a tighter TS than that of **1a** and explains why **2a**−**i** are less reactive than **1a**−**i**.

Introduction

There is continuous interest in phosphoryl transfer and related reactions due to their importance in the environment as well as in biological processes.[1−12] The need for improved methods of environmental decontamination has provided the impetus for numerous studies aimed at enhancing the rate of decomposition of toxic organophosphorus compounds.[2−7] Accordingly, various methods have been developed. These include the use of highly reactive α-effect nucleophiles[2−4] or the use of various metal ions as Lewis acid catalysts.[5−7] The α-effect nucleophiles (e.g., oximates, *o*-iodosylbenzoate, and HOO^- anions) have been reported to exhibit significantly enhanced nucleophilic reactivity than would be predicted from their basicity, particularly in the presence of a cationic surfactant such as hexadecyltrimethylammonium ion.[2−4] Alkali metal ions[5] and divalent metal ions

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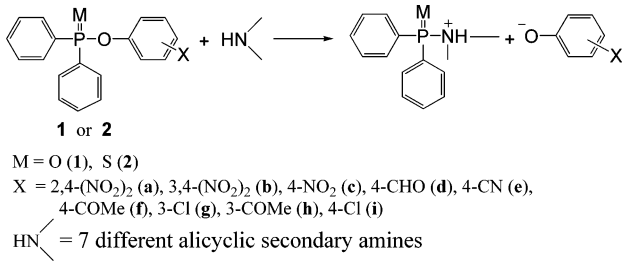
(e.g., Mg^{2+}, Ca^{2+}, Zn^{2+}, Cu^{2+}, Co^{2+}, and Mn^{2+})[6] have also exhibited significant catalytic effects in nucleophilic substitution reactions of aryl diphenylphosphinates and their analogues. Besides, the La^{3+} ion has been shown to be highly effective on alkaline methanolysis of phosphate di- and triesters.[7]

Kinetic studies have also been performed intensively to understand the reaction mechanisms of biological processes.[1−6,8−12] Linear free-energy relationships such as Hammett and Brønsted equations have most commonly been employed to investigate reaction mechanisms.[1−6,8−12] For example, alkaline ethanolysis of aryl dimethylphosphinates has been concluded to proceed through a pentacoordinate intermediate with its formation being the rate-determining step (RDS) on the basis of the fact that σ^o constants result in significantly better Hammett correlations than σ^- constants.[5a] A similar conclusion has been drawn for alkaline hydrolysis of aryl diphenylphosphinates[8a,8b] and imidazole catalyzed hydrolysis of aryl diphenylphosphinates.[9a]

SCHEME 1



On the contrary, nucleophilic substitution reactions of 4-nitrophenyl diphenylphosphinate with aryloxides have been concluded to proceed through a concerted mechanism.[9b] 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.[9b] A similar result has been obtained for reactions of aryl dimethylphosphinothioates with aryloxides (i.e., a linear Brønsted-type plot for the reactions of 4-nitrophenyl dimethylphosphinothioate with aryloxides having a wide pK_a range (i.e., pK_a = 5.53−10.2)).[1c] Besides, σ^- constants have resulted in much better Hammett correlations than σ^o constants for reactions of aryl dimethylphosphinothioates with phenoxide. Accordingly, Hengge and co-workers have concluded that the reactions proceed through a concerted mechanism.[1c] This conclusion has been further supported by the primary ^{18}O and secondary ^{15}N kinetic isotope effects.[1c]

Only a few reports are available for aminolysis of phosphoryl and related compounds.[10−12] Reactions with amines have been suggested to proceed either through a concerted or through a stepwise mechanism. From studies of leaving group effects, solvent effects, and activation parameters, Cook et al. have concluded that aminolysis of aryl diphenylphosphinates and related compounds in MeCN proceeds through a zwitterionic pentacoordinate intermediate with its breakdown being the RDS.[10] However, Lee et al. have proposed that pyridinolysis of phenyl-substituted phenyl chlorophosphates proceeds through a concerted mechanism on the basis of linear Brønsted-type plots with small β_{nuc} values (β_{nuc} = 0.16−0.18).[11]

We have recently performed aminolysis of aryl diphenylphosphinates (**1a**−**i**) and concluded that the reactions proceed through a concerted mechanism although σ^o constants result in a better Hammett correlation than σ^- constants.[12] This was because the Yukawa−Tsuno plot for the same reactions exhibits a significantly better linearity than the Hammett plot correlated with σ^o constants.[12] The concerted mechanism has been further supported from the linear Brønsted-type plot with β_{nuc} = 0.38 for the reactions of 2,4-dinitrophenyl diphenylphosphinate (**1a**) with a series of alicyclic secondary amines.[12]

We have extended our study to aminolysis of aryl diphenylphosphinothioates (**2a**−**i**), the thio analogues of **1a**−**i**, as shown in Scheme 1. Replacement of O by a polarizable S atom in the P═O bond of **1a**−**i** would be expected to provide insights into both the reactivity and the comparative reaction mechanism. We report the effect of modification of the electrophilic center from P═O to P═S on reactivity and reaction mechanisms. In addition to our Brønsted analysis, we have analyzed the substituent effects according to the dual-parameter Yukawa−

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TABLE 1. Summary of Second-Order Rate Constants (k_N, M^{-1} s^{-1}) for Reactions of X-Substituted Phenyl Diphenylphosphinates (1) and Diphenylphosphinothioates (2) with Piperidine in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C

	X	pK_a[a] (X-PhOH)	10^2 k_N (M^{-1} s^{-1}) **1**[b]	**2**	$k_N^{P=O}/k_N^{P=S}$
a	2,4-$(NO_2)_2$	4.11	419	74.7	5.6
b	3,4-$(NO_2)_2$	5.42	66.4	6.63	10.0
c	4-NO_2	7.14	3.06	0.230	13.3
d	4-CHO	7.66	0.720	0.0634	11.4
e	4-CN	7.95	1.57	0.147	10.7
f	4-COMe	8.05	0.587	0.0615	9.5
g	3-Cl	9.02	0.245	0.0213	11.5
h	3-COMe	9.19	0.211	0.0194	10.9
i	4-Cl	9.38	0.149	0.0166	9.0

[a] The pK_a data were taken from ref 36. [b] Data for the reactions of **1a**−**i** were taken from ref 12.

Tsuno equation (eq 1).[13,14] This combined approach has previously proven to be highly effective to elucidate ambiguities in reaction mechanisms of acyl transfer and related reactions.[12,15−18]

$$\log k^X/k^H = \rho_X[\sigma^o + r(\sigma^- - \sigma^o)] \quad (1)$$

Results and Discussion

All reactions in this study obeyed pseudo-first-order kinetics in the presence of a large excess of amine. Diphenylpiperidinophosphine sulfide was found quantitatively as one of the reaction products, indicating that the amine behaves as a nucleophile but not as a general base catalyst. Pseudo-first-order rate constants (k_{obsd}) were determined from the equation $\ln(A_\infty - A_t) = -k_{obsd}t + c$. The plots of k_{obsd} versus the amine concentration were linear, indicating that general base catalysis by the second amine molecule is absent. The second-order rate constants (k_N) were determined from the slope of the linear plots of k_{obsd} versus the amine concentration. The uncertainty in the k_N values is estimated to be less than 3% from replicate runs. The k_N values determined are summarized in Tables 1−3. The activation parameters ($\Delta H^‡$ and $\Delta S^‡$) were calculated from the Arrhenius equation.[19] The Arrhenius plots for the reactions of **1a** and **2a** with piperidine performed at five different temperatures resulted in good linear correlations ($R^2 = 0.9930$ and 0.9990 for the reactions of **1a** and **2a**, respectively; see Figure S1 in the Supporting Information).

TABLE 2. Summary of Second-Order Rate Constants (k_N, M^{-1} s^{-1}) for Reactions of 2,4-Dinitrophenyl Diphenylphosphinate (1a) and Diphenylphosphinothioate (2a) with Alicyclic Secondary Amines in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C

amines	pK_a[a]	10^2 k_N ($M^{-1}s^{-1}$) **1a**[b]	**2a**	$k_N^{P=O}/k_N^{P=S}$
piperidine	11.02	419	74.7	5.6
3-methyl piperidine	10.80	429	72.9	5.9
piperazine	9.85	234	39.6	5.9
1-(2-hydroxyethyl)-piperazine	9.38	93.9	9.64	9.7
morpholine	8.65	57.3	5.50	10.4
1-formyl piperazine	7.98	33.2	2.38	13.9
piperazinium ion	5.95	7.09	0.262	27.1

[a] pK_a data in 20 mol % DMSO were taken from ref 15. [b] Data for the reactions of **1a** were taken from ref 12.

Effect of Replacing P═O by P═S on Reactivity. Table 1 shows that the phosphinothioates **2a**−**i** are ca. 5−13 times less reactive than their oxygen analogues **1a**−**i**. The current result is consistent with the reports that replacing the O atom in the P═O bond of phosphoryl compounds by an S atom causes a decrease in reactivity.[1,2,20,21] The thio effect, defined as the ratio of rate constants $k^{P=O}/k^{P=S}$, has been reported to be 4−11 for reactions of the methyl 2,4-dinitrophenyl phosphate/phosphorothioate system with various nucleophiles[1c,20] and 12.4 for alkaline hydrolysis of the triethyl phosphate/phosphorothioate system.[21] Similar results have been reported for reactions that have been suggested to proceed through a concerted mechanism (i.e., $k^{P=O}/k^{P=S} = 2-5$ for alkaline hydrolysis of the aryl dimethylphosphinate/phosphinothioate system).[1c] Several proposals have been advanced to account for the decreased reactivity on replacing P═O by P═S (e.g., decreased electron donating ability of P−O$^-$ as compared to P−S$^-$,[22,23] greater electrophilicity of phosphorus in phosphoryl than in thiophosphoryl compounds,[24,25] and enhanced polarizability of the P═S bond).[26]

On the contrary, the 4-nitrophenyl phosphorothioate dianion has been reported to be more reactive than its oxygen analogue, 4-nitrophenyl phosphate dianion, under alkaline hydrolysis conditions (i.e., $k^{P=O}/k^{P=S} = 0.1-0.3$).[1e] The enhanced reactivity shown by the P═S compound has been attributed to the difference in the reaction mechanism (i.e., a stepwise dissociative mechanism (i.e., $D_N + A_N$) for the phosphorothioate vs a concerted mechanism for the phosphate).[1e]

Accordingly, the $k^{P=O}/k^{P=S}$ ratio has been used to predict mechanistic details of enzymatic phosphoryl transfer.[27,28] However, the magnitude of the thio effect alone cannot differentiate

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TABLE 3. Summary of Kinetics Results for Reactions of 2,4-Dinitrophenyl Diphenylphosphinate (1a) and Diphenylphosphinothioate (2a) with Piperidine in 80 mol % H_2O/20 mol % DMSO at 15.0, 20.0, 25.0, 35.0, and 45.0 ± 0.1 °C

	k_N (M^{-1} s^{-1})						
	15.0 °C	20.0 °C	25.0 °C	35.0 °C	45.0 °C	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (eu)
1a	3.09	3.85	4.19	7.71	12.0	7.73 (±0.56)	−29.3 (±1.8)
2a	0.489	0.584	0.747	1.16	1.79	7.34 (±0.02)	−34.3 (±0.6)

a concerted mechanism from a stepwise associative mechanism (i.e., $A_N + D_N$) since the $k^{P=O}/k^{P=S}$ ratio has also been reported to be ca. 10−25 for reactions that have been suggested to proceed through a stepwise $A_N + D_N$ mechanism (e.g., alkaline hydrolysis of the alkyl dialkylphosphinate/phosphinothioate system[29] and ethanolysis of the 4-nitrophenyl diethyl phosphate/phosphorothioate system).[5d] Thus, the $k^{P=O}/k^{P=S}$ ratio of 5−13 observed in the current system cannot provide conclusive information on the reaction mechanism. Clearly, further analysis of the kinetic data is required to elucidate the reaction mechanism.

Effect of Leaving Group on Reactivity. Table 1 shows that the second-order rate constant k_N increases as the basicity of the leaving group decreases for the reactions of **1a**−**i** and **2a**−**i** with piperidine. The effect of basicity of the leaving group on reactivity is illustrated in Figure 1. The Brønsted-type plot for the reactions of **2a**−**i** is linear with many scattered points. A similar Brønsted-type plot can be seen for the corresponding reactions of **1a**−**i**.

The linear Brønsted-type plots for the current system contrast to the curved Brønsted-type plot reported for the corresponding reactions of aryl benzoates. We have reported that the Brønsted slope (β_{lg}) changes from −1.50 to −0.36 as the basicity of the leaving aryloxide decreases.[30] Such a curved Brønsted-type plot is typical for reactions that proceed through a stepwise mechanism with a change in the RDS (i.e., from breakdown of the intermediate to its formation as the basicity of the leaving group decreases).[15−18] On the other hand, a linear Brønsted-type plot with a moderate β_{lg} value has often been reported for reactions that proceed through a concerted mechanism.[12,30−32] Although the Brønsted-type plot for the reactions of **2a**−**i** is linear with a moderate β_{lg} value, it exhibits many scattered points. Thus, one cannot obtain reliable information on the reaction mechanism from the current Brønsted plot.

Reaction Mechanism Determined from Hammett and Yukawa−Tsuno Plots. Hammett correlations have most frequently been used to investigate reaction mechanisms of aryl phosphinates.[1,5,8,33] It is generally accepted that σ^- constants result in a good correlation with rate constants for reactions in which departure of the leaving group occurs at the RDS whether the reaction proceeds through a concerted mechanism or through a stepwise manner. On the other hand, σ^o constants give a good correlation with rate constants for reactions that proceed through a stepwise mechanism with departure of the leaving group occurring after the RDS.

Hammett plots have been constructed for the reactions of **2b**−**i** with piperidine with the use of the σ^- and σ^o constants obtained from the literature.[34] As illustrated in Figure 2, the σ^- constants exhibit a poor correlation with rate constants (R^2 = 0.956). However, as shown in the inset of Figure 2, the σ^o constants result in a better correlation (R^2 = 0.987). The fact that the σ^o constants give a better correlation than the σ^- constants implies that direct resonance interactions between the substituent in the leaving group and the reaction center are not occurring in the TS.[35] Thus, one might conclude that the current reactions proceed through a pentacoordinate intermediate in which the departure of the leaving group is not advanced in the RDS. A similar conclusion has been drawn for nucleophilic substitution reactions of various phosphinates and phosphinothioates on the basis of the result that σ^o constants result in a better correlation than σ^- constants (e.g., reactions of aryl dimethylphosphinates with ethoxide,[5a] alkaline hydrolysis of aryl diphenylphosphinothioates[8a] and diphenylphosphinates,[8b] and imidazole catalyzed hydrolysis of aryl diphenylphosphinates).[9a]

We have recently reported that the determination of a reaction mechanism based just on Hammett correlations with σ^- or σ^o constants as the only mechanistic evidence can be misleading.[12] It has been shown that the dual-parameter Yukawa−Tsuno equation (eq 1) is highly effective to elucidate ambiguities in reaction mechanisms of phosphinyl transfer reactions.[12] Accordingly, Yukawa−Tsuno plots have been constructed for the current reactions. As shown in Figure 3, the Yukawa−Tsuno plot for the reactions of **2b**−**i** with piperidine results in a significantly improved correlation (R^2 = 0.998) with ρ_X = 1.91 and r = 0.28. A similar result is shown for the reactions of **1b**−**i** (i.e., ρ_X = 1.91 and r = 0.30). It is noted that the ρ_X and r values are practically identical for the reactions of **1b**−**i** and **2b**−**i**.

The magnitude of the r value in the Yukawa−Tsuno plot represents the resonance demand of the reaction center or the extent of resonance contribution.[13,14] The fact that r = 0.28 for the aminolysis of **2b**−**i** (or r = 0.30 for the reactions of **1b**−**i**) indicates that a partial negative charge develops on the O atom of the leaving aryloxides in the TS. Thus, one can conclude that the departure of the leaving group occurs at the RDS, although the degree of bond fission would not be significant on the basis of the small r value. However, the current result alone cannot discern whether the reactions proceed through a concerted mechanism or through a stepwise manner with departure of the leaving group being the RDS. To get further information on the reaction mechanism, the reactions of **2a** with a series of alicylic secondary amines have been performed.

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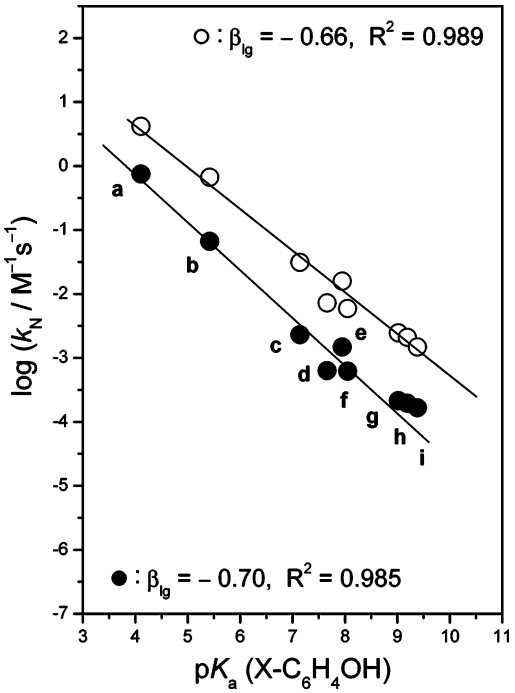

FIGURE 1. Brønsted-type plots for reactions of X-substituted phenyl diphenylphosphinates (**1a**−**i**, ○) and diphenylphosphinothioates (**2a**−**i**, ●) with piperidine in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 1.

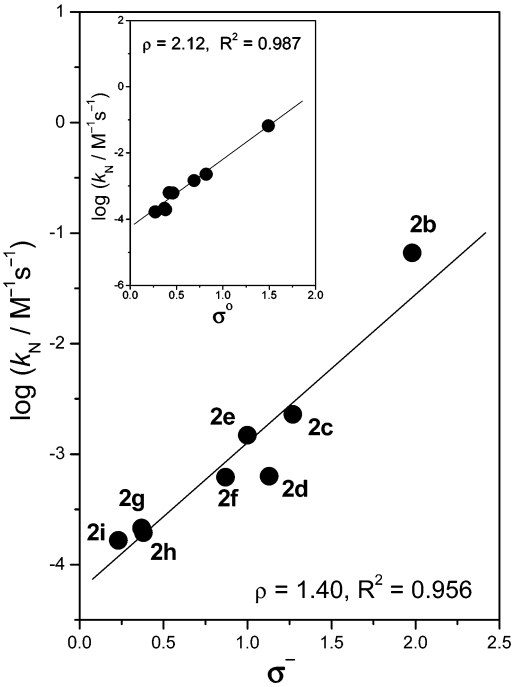

FIGURE 2. Plots of log k_N vs σ^- (or σ°, inset) for reactions of X-substituted phenyl diphenyl phosphinothioates (**2b**−**i**) with piperidine in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C. The identity of the points is given in Table 1.

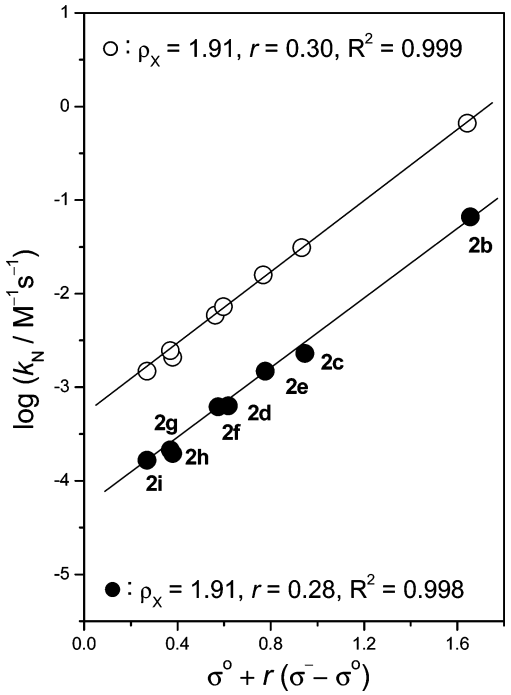

FIGURE 3. Yukawa−Tsuno plots for reactions of X-substituted phenyl diphenylphosphinates (**1b**−**i**, ○) and diphenylphosphinothioates (**2b**−**i**, ●) with piperidine in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C. The identity of the points is given in Table 1.

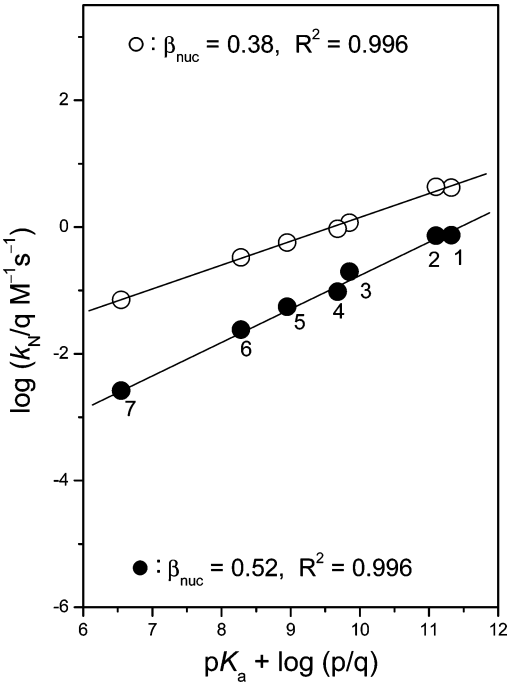

FIGURE 4. Brønsted-type plots for reactions of 2,4-dinitrophenyl diphenylphosphinate (**1a**, ○) and diphenylphosphinothioate (**2a**, ●) with alicyclic secondary amines in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 2.

Effect of Amine Basicity on Reactivity. Table 2 shows that k_N decreases as the basicity of amines decreases. It is also noted that **2a** is less reactive than **1a** regardless of the amine basicity. The effect of amine basicity on reactivity is illustrated in Figure 4. The Brønsted-type plots exhibit good linear correlations for the reactions of **1a** and **2a**. These linear Brønsted-type plots also contrast to the curved Brønsted-type plots reported for the corresponding reactions of 2,4-dinitrophenyl benzoate and related compounds that have been suggested to proceed through a stepwise mechanism with a change in the RDS.[16−18]

The β_{nuc} values are 0.38 and 0.52 for the reactions of **1a** and **2a**, respectively. The β_{nuc} value of 0.38 or 0.52 is too small for reactions that proceed through a stepwise mechanism with breakdown of the intermediate being the RDS but is typical for reactions that proceed through a concerted mechanism.[30−32] Thus, one can suggest that the aminolysis of **1a** and **2a** proceeds through a concerted mechanism. It is noted that the reactions of **2a** exhibit a larger β_{nuc} value than those of **1a**, indicating that the degree of bond formation between the amine and the electrophilic center at the RDS is slightly more advanced for the reactions of **2a**. On the other hand, the degree of the leaving group departure would be the same for the reactions of **1a**−**i** and **2a**−**i** on the basis of the fact that their ρ_X and r values are practically the same (Figure 3). Accordingly, one can propose that the aminolysis of **2a**−**i** proceeds through a tighter TS than the corresponding reactions of **1a**−**i** (i.e., the degree of bond formation is more advanced for the reactions of **2a** than for those of **1a**, while the leaving group departure is nearly identical in the TS of the RDS).

TS Structures and Activation Parameters. The reactions of **1a** and **2a** with piperidine have been performed at 15.0, 20.0, 25.0, 35.0, and 45.0 °C to determine the activation parameters ($\Delta H^{‡}$ and $\Delta S^{‡}$). As shown in Table 3, the enthalpies of activation ($\Delta H^{‡}$) are 7.73 and 7.34 kcal/mol for the reactions of **1a** and **2a**, respectively, indicating that the $\Delta H^{‡}$ term is ca. 0.4 kcal/mol more favorable for the reaction of **2a** than for that of **1a**. On the contrary, the reaction of **2a** is accompanied by a more negative entropy of activation ($\Delta S^{‡}$) than that of **1a** (i.e., −29.3 and −34.3 eu for the reactions of **1a** and **2a**, respectively). This result implies that $T\Delta S^{‡}$ at 25.0 °C is ca. 1.5 kcal/mol more unfavorable for the reaction of **2a** than for that of **1a**. Thus, one can suggest that the difference in $T\Delta S^{‡}$ between the two systems is a possible origin of the thio effect found in the current study. Furthermore, the fact that **2a** exhibits a more negative $\Delta S^{‡}$ value than **1a** indicates that the TS is more ordered for the reaction of **2a** than for that of **1a**. This argument clearly supports the preceding proposal that the reactions of **2a** proceed through a tighter TS than those of **1a**.

Conclusion

The present study has allowed us to conclude the following: (1) the phosphinothioates **2a**−**i** are less reactive than their oxygen analogues **1a**−**i**, regardless of the basicity of the leaving group or attacking amine. (2) The Yukawa−Tsuno plots exhibit good linear correlations with a small r value for the reactions of **1b**−**i** and **2b**−**i**, implying that departure of the leaving group occurs at the RDS but that the degree of bond fission is insignificant. (3) The Brønsted-type plots are linear for the reactions of **1a** and **2a** with β_{nuc} values of 0.38 and 0.52, respectively, suggesting that these reactions proceed through a concerted mechanism. (4) The aminolysis of **2a** exhibits ca. 0.4 kcal/mol more favorable $\Delta H^{‡}$ but ca. 1.5 kcal/mol more unfavorable $T\Delta S^{‡}$ than that of **1a**, indicating that the $T\Delta S^{‡}$ term is a possible origin of the thio effect found in this study. (5) The fact that **2a** exhibits a larger β_{nuc} and more negative $T\Delta S^{‡}$ suggests that the reaction of **2a** proceeds through a tighter TS than that of **1a**.

Experimental Section

Materials. Aryl diphenylphosphinothioates **2a**−**i** were prepared by modification of literature procedures:[10,22] Diphenylphosphinodithioic acid (2.5 g, 10 mmol), *N*,*N*′-dicyclohexylcarbodiimide (1.5 equiv), and 4-(dimethylamino) pyridine (0.2 equiv) were dissolved in methylene chloride (30 mL) and stirred for 3 h. X-Substituted phenol (10 mmol) dissolved in methylene chloride (20 mL) was added to the acid solution dropwise. The reaction mixture was stirred under nitrogen at room temperature. The progress of the reaction was monitored by TLC. When the reaction was completed, the reaction mixture was worked up as follows: *N*,*N*′-dicyclohexylthiourea was filtered off, and then the methylene chloride solution was concentrated under a reduced pressure. The crude product was purified by column chromatography (silica gel, methylene chloride/*n*-hexane 50:50). The purity was checked by their melting points for the known compounds, and the identity of unreported compounds **2a**, **2b**, **2d**, **2g**, and **2h** was checked by elemental analysis and ^{1}H NMR spectra (Supporting Information). All unreported compounds gave good elemental analyses except **2a**, which was shown to contain a small amount of 2,4-dinitrophenol. However, the phenol impurity was shown to have no effect on kinetic determination.

2,4-Dinitrophenyl Diphenylphosphinothioate (2a). mp 105−108 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.49−7.57 (m, 6H), 7.73−7.77 (dd, J_1 = 1.3 Hz, J_2 = 10 Hz, 1H), 7.96−8.05 (m, 4H), 8.28−8.33 (dd, J_1 = 2.8 Hz, J_2 = 10 Hz, 1H), 8.76−8.77 (d, J = 2.3 Hz, 1H), Anal. Calcd for $C_{18}H_{13}N_2O_5PS$: C, 54.00; H, 3.27. Found: C, 53.80; H, 3.37.

3,4-Dinitrophenyl Diphenylphosphinothioate (2b). mp 91−93 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.52−7.53 (d, J = 2.5 Hz, 1H), 7.54−7.58 (m, 7H), 7.90−8.00 (m, 5H), Anal. Calcd for $C_{18}H_{13}N_2O_5PS$: C, 54.00; H, 3.27. Found: C, 54.02; H, 3.29.

4-Formylphenyl Diphenylphosphinothioate (2d). mp 91−93 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.92−7.25 (dd, J_1 = 2.5 Hz, J_2 = 10 Hz, 2H), 7.50−7.55 (m, 6H), 7.78−7.82 (d, J = 10 Hz, 2H), 7.94−8.03 (m, 4H), 10.27 (s, 1H), Anal. Calcd for $C_{19}H_{15}O_2PS$: C, 67.44; H, 4.47. Found: C, 67.53; H, 4.39.

3-Chlorophenyl Diphenylphosphinothioate (2g). mp 85−87 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.08−7.12 (d, 10 Hz, 1H), 7.48−7.50 (m, 3H), 7.51−7.54 (m, 6H), 7.91−8.00 (m, 4H), Anal. Calcd for $C_{18}H_{14}ClOPS$: C, 62.70; H, 4.09. Found: C, 62.71; H, 4.10.

3-Acetylphenyl Diphenylphosphinothioate (2h). mp 61−62 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.50 (s, 3H), 7.25−7.49 (m, 2H), 7.50−7.53 (m, 7H), 7.54−7.57 (d, J = 7.5 Hz, 1H), 7.94−8.03 (m, 4H), Anal. Calcd for $C_{20}H_{17}O_2PS$: C, 68.17; H, 4.86. Found: C, 68.20; H, 4.84.

Amines and other chemicals were of the highest quality available. Doubly glass distilled water was further boiled and cooled under nitrogen just before use. Because of a low solubility of **2a**−**i** in pure water, aqueous DMSO (80 mol % H_2O/20 mol % DMSO) was used as the reaction medium.

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 aryloxide. All the reactions were carried out under pseudo-first-order conditions in which amine concentrations were at least 100 times greater than the substrate concentration. The amine stock solution of ca. 0.2 M was prepared by dissolving 2 equiv of free amine and 1 equiv of standardized HCl solution to make a self-buffered solution in a 25.0 mL volumetric flask.

Typically, the reaction was initiated by adding 5 μL of a 0.02 M solution of 2,4-dinitrophenyl diphenylphosphinothioate (**2a**) in acetonitrile to a 10 mm quartz UV cell containing 2.50 mL of the thermostated reaction mixture made up of solvent and an aliquot of the amine stock solution. All the solutions were transferred by gastight syringes. Generally, the amine concentration was varied over the range (5−200) × 10^{-3} M, while the substrate concentration was 2 × 10^{-5} M. Pseudo-first-order rate constants (k_{obsd}) were calculated from the equation, $\ln(A_\infty - A_t) = -k_{obsd}t + C$. The plots of $\ln(A_\infty - A_t)$ versus time were

linear over ca. 90% of the total reaction. Usually, five different amine concentrations were employed, and replicate values of k_{obsd} were determined to obtain the second-order rate constants (k_N) from the slope of linear plots of k_{obsd} versus amine concentrations.

Product Analysis. X-Substituted phenoxide was liberated quantitatively and identified as one of the products in the reaction of **2a**−**i** with piperidine by comparison of the UV−vis spectra after completion of the reaction with the authentic sample under the same reaction conditions. The other product from the reactions of **2a**−**i** with piperidine (i.e., diphenylpiperidinophosphine sulfide) was analyzed quantitatively by HPLC (R_t = 10.4 min, a reversed phase 250 mm × 4.6 mm i.d. column, CH_3CN/H_2O = 70:30 as a mobile phase, flow rate = 1.0 mL/min, detection at 229 nm).

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Supporting Information Available: ^{1}H NMR spectra for compounds **2a**, **2b**, **2d**, **2g**, and **2h**; Tables S1−S9 of the kinetic conditions and data for the reactions of **2a**−**i** with piperidine; Tables S10−S16 of the reactions of **2a** with seven different alicyclic secondary amines; and Tables S17−S20 of the reactions of **1a** and **2a** with piperidine at 15.0, 20.0, 35.0, and 45.0 °C. Figure S1 of Arrhenius plots for the reactions of **1a** and **2a** with piperidine at five different temperatures. This material is available free of charge via the Internet at http://pubs.acs.org.

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