JOC Article

Aminolysis of *O*-Aryl Thionobenzoates: Amine Basicity Combines with Modulation of the Nature of Substituents in the Leaving Group and Thionobenzoate Moiety to Control the Reaction Mechanism

Ik-Hwan Um,*[†] So-Jeong Hwang, Sora Yoon, Sang-Eun Jeon,[‡] and Sun-Kun Bae[§]

Department of Chemistry and Nano Science, Ewha Womans University, Seoul 120-750, Korea

ihum@ewha.ac.kr

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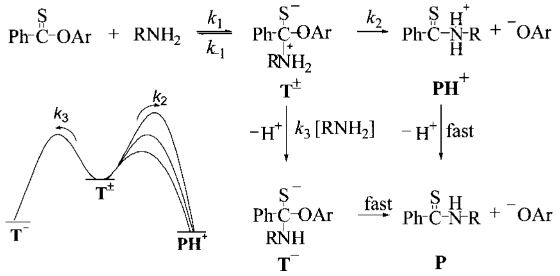

A kinetic study is reported for aminolysis of *O*-Y-substituted phenyl thionobenzoates (**1a−f**) and *O*-4-nitrophenyl X-substituted thionobenzoates (**2a−f**) in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C. The reaction proceeds through one or two intermediates (i.e., a zwitterionic tetrahedral intermediate $T^{\pm}$ and its deprotonated form T^{-}) depending on the basicity difference between the nucleophile and nucleofuge, that is, the reaction proceeds through $T^{\pm}$ when the leaving aryloxide is less basic than the attacking amine, but through $T^{\pm}$ and T^{-} when the leaving group is more basic than the amine. However, the reaction mechanism is not influenced by the electronic nature of the substituent X in the nonleaving group. The Hammett plot for the reactions of **2a−f** with benzylamine is consisted of two intersecting straight lines, which might be interpreted as a change in the rate-determining step (RDS). However, the Yukawa-Tsuno plot for the same reactions exhibits an excellent linear correlation, indicating that the nonlinear Hammett plot is not due to a change in the RDS but caused by stabilization of the ground-state of the substrate through resonance interaction between the electron-donating substituent X and the thionocarbonyl moiety.

Introduction

Reactions of carboxylic acid derivatives with amines have been intensively investigated due to their importance in biochemical pathways (e.g., enzyme action, peptide biosynthesis, etc.) as well as synthetic applications.[1−9] Aminolysis of carboxylic esters has generally been reported to proceed through a stepwise mechanism with a zwitterionic tetrahedral intermediate ($T^{\pm}$).[1−9] Curved Brønsted-type plots have often been reported for aminolysis of carboxylic esters that bear a good leaving group; such curvature is taken to be diagnostic of a change in the rate-determining step (RDS) of a stepwise mechanism.[1−6] Recent computational studies also favor a stepwise mechanism although some studies failed to identify the transition state and $T^{\pm}$ for aminolysis of carboxylic esters.[7−9]

In contrast, aminolysis of thiono (C=S) esters has been suggested to proceed through one or two intermediates, that is, $T^{\pm}$ and its deprotonated form T^{-}.[10−13] Factors proposed to influence the mechanism include: basicity of the attacking amines, the type of solvents (protic or aprotic) and the nature

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[†] Tel.: 82-2-3277-2349. Fax: 82-2-3277-2844.

[‡] Present Address: Environmental Research Complex, Incheon 404-708, Korea.

[§] Department of Chemistry, Kunsan National University, Kunsan 573-701, Korea.

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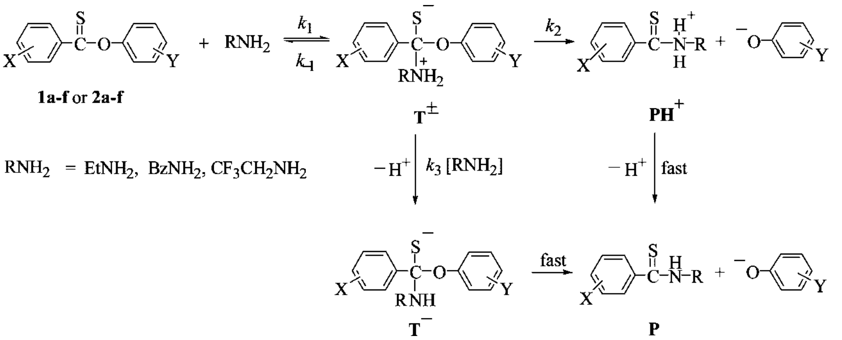
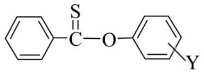
SCHEME 1



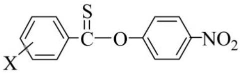
of amines (primary or secondary). Castro et al. have reported that reactions of thiono esters with weakly basic amines proceed through $T^{\pm}$ and T^{-} in aqueous solution, while the corresponding reactions with strongly basic amines proceed without the deprotonation process from $T^{\pm}$.[10] Thus, basicity of the attacking amine has been proposed to be a crucial factor that selects the mechanistic pathway.[10]On the other hand, Lee et al. have reported that reactions of aryl dithiobenzoates with a series of aniline and benzylamine derivatives proceed through $T^{\pm}$ in MeCN.[11d] They have found that the deprotonation process from $T^{\pm}$, which has often been observed for the reactions performed in H_2O, is absent in this aprotic solvent even for reactions with weakly basic anilines.[11d] Accordingly, the nature of the medium has been suggested to be a determinant of the presence/absence of the deprotonation process (i.e., $T^{\pm} \rightarrow T^{-}$).[11d]

However, we have shown that the reaction of *O*-4-nitrophenyl thionobenzoate (**1b**) with secondary amines (either cyclic or acyclic) proceeds via both $T^{\pm}$ and T^{-} in MeCN as well as in H_2O, while the corresponding reaction with primary amines proceeds only through $T^{\pm}$ *regardless of the basicity of amines*.[12] A similar confirmatory result has been found recently for aminolysis of 4-nitrophenyl phenyl thionocarbonate, that is, reactions with secondary amines proceed through $T^{\pm}$ and its conjugate base T^{-}, whereas the corresponding reactions with primary amines again proceed solely via $T^{\pm}$, indicating that the nature of amines is an important factor to determine reaction mechanism.[13]



1

Y = 3,4-$(NO_2)_2$ (**1a**), 4-NO_2 (**1b**), 4-COMe (**1c**)
3-COMe (**1d**), H (**1e**), 4-CH_3 (**1f**)



2

X = 4-NMe_2 (**2a**), 4-OCH_3 (**2b**), 4-CH_3 (**2c**)
H (**2d**), 3-OCH_3 (**2e**), 3-Cl (**2f**)

We have extended our study to aminolysis of a series of *O*-Y-substituted phenyl thionobenzoates (**1a**−**f**) and *O*-4-nitrophenyl X-substituted thionobenzoates (**2a**−**f**) to dissect the interplay of the factors determining the reaction mechanism. We have employed various substituents both in the leaving and nonleaving groups of the substrate. Moreover, three primary amines have been chosen as nucleophiles to probe the mechanistic behavior over an approximately 5 pK_a units, that is, strongly basic ethylamine ($EtNH_2$, $pK_a^{EtNH_3^+} = 10.67$), moderately basic benzylamine ($BzNH_2$, $pK_a^{BzNH_3^+} = 9.46$) and weakly basic trifluoroethylamine ($CF_3CH_2NH_2$, $pK_a^{CF_3}CH_2NH_3^+ = 5.70$). We have systematically investigated the effect of the basicity of attacking amines, but combined it with the electronic nature of the substituents X and Y, on reactivity and mechanism, as shown in Scheme 1.

Results and Discussion

The kinetic study was performed spectrophotometrically. All reactions proceeded with quantitative liberation of Y-substituted

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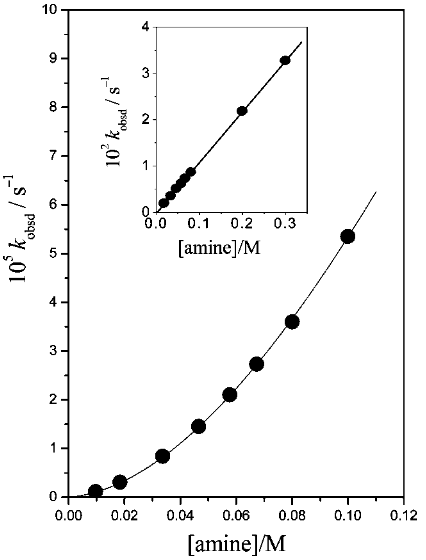

FIGURE 1. Plots of k_{obsd} vs [amine] for the reaction of trifluoroethylamine ($CF_3CH_2NH_2$) with **1f** and **1a** (inset) in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C.

phenoxide ion or its conjugate acid under pseudofirst-order conditions (i.e., the amine concentration in excess over the substrate concentration). The reactions obeyed first-order kinetics and pseudofirst-order rate constants (k_{obsd}) were determined from the equation, $\ln(A_\infty - A_t) = -k_{obsd}t + C$. Based on replicate runs, it is estimated that the uncertainty in the k_{obsd} values is less than ±3%. Plots of k_{obsd} versus [amine] were linear or curved upward depending on the basicity difference between the entering amine and the leaving aryloxide, namely, the plot was linear when the leaving aryloxide was less basic than the attacking amine but curved upward when the leaving group was more basic than the amine.

Reactions of 1a−f with $CF_3CH_2NH_2$ and $EtNH_2$: Effect of Amine Basicity. Reactions of *O*-Y-substituted phenyl thionobenzoates (**1a−f**) with weakly basic $CF_3CH_2NH_2$ and strongly basic $EtNH_2$ were performed to investigate the effect of amine basicity on mechanism. As shown in Figure 1, the plot of k_{obsd} versus [amine] for the reactions with weakly basic $CF_3CH_2NH_2$ exhibited an upward curvature except for the reaction of **1a**, implying that the aminolysis of **1b−f** proceeds through both $T^\pm$ and T^-. In contrast, the corresponding plots for the reactions of **1a−f** with strongly basic $EtNH_2$ were linear (passing through the origin), indicating that the deprotonation process from $T^\pm$ by the second amine molecule (i.e., the k_3 step in Scheme 1) is absent and the contribution of H_2O and OH^- from protonation of amine to the k_{obsd} value is negligible. Accordingly, one can suggest that the basicity of the attacking amine is an important determinant of presence/absence of the deprotonation process from $T^\pm$.

Reaction of 1a−f with $BzNH_2$: Effect of Leaving-Group Basicity. Reactions of **1a−f** with moderately basic $BzNH_2$ were performed to investigate the effect of leaving-group basicity on mechanism. Plots of k_{obsd} versus [amine] were linear for the reactions of **1a−d** but displayed upward curvature for those of **1e** and**1f**; here the reaction proceeds through $T^\pm$ without the deprotonation process when the substrate possesses a weakly basic leaving group (e.g., **1a−d**) but via the dual $T^\pm$ and T^- path when the leaving group is strongly basic (e.g., **1e** and **1f**).

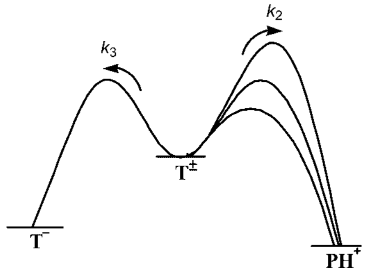

FIGURE 2. Qualitative energy profile for the process from $T^\pm$ to T^- and PH^+.

TABLE 1. Summary of Second-Order Rate Constants for Reactions of *O*-Y-Substituted Phenyl Thionobenzoates (1a−f) with Ethylamine ($EtNH_2$, pK_a = 10.67) and Benzylamine ($BzNH_2$, pK_a = 9.46)[a]

			k_N/$M^{-1}s^{-1}$	
entry	Y	pK_a	$EtNH_2$	$BzNH_2$
1a	3,4-$(NO_2)_2$	5.42	22.2	12.7
1b	4-NO_2	7.14	7.16	3.71
1c	4-COMe	8.05	4.37	2.14
1d	3-COMe	9.19	2.80	1.87
1e	H	9.95	2.12	(0.915)[b]
1f	4-Me	10.2	1.82	(0.871)[b]

[a] In 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C. [b] The k_1 values determined from eq 2.

Clearly, the current results show that the basicity of the leaving group is also an important factor to determine the reaction mechanism.

An important finding in the current study is that the basicity difference between the attacking amine and the leaving aryloxide (i.e., <130 > pK_a = p$K_a^{RNH_3^+}$ − pK_a^{ArOH}) governs the presence/absence of the deprotonation process (i.e., $T^\pm \rightarrow T^-$). For example, the reactions of **1a−f** with strongly basic $EtNH_2$ (i.e., p$K_a^{EtNH_3^+}$ = 10.67) proceed without this deprotonation process, where $\Delta pK_a > 0$ (i.e., $pK_a^{ArOH} \le 10.2$). On the contrary, the reactions of **1b−f** with weakly basic $CF_3CH_2NH_2$ (i.e., $pK_a^{CF_3}CH_2NH_3^+ = 5.70$) proceed through both $T^\pm$ and T^-, where $\Delta pK_a < 0$ (i.e., $CF_3CH_2NH_2$ is less basic than all the leaving groups of **1b−f**), while the reaction of **1a** proceeds without this deprotonation process, where $\Delta pK_a > 0$ (i.e., $CF_3CH_2NH_2$ is more basic than the leaving 3,4-dinitrophenoxide in **1a**). A similar result has been obtained for the reactions with moderately basic $BzNH_2$, that is, the deprotonation process from $T^\pm$ is absent for the reactions of **1a−d**, in which $\Delta pK_a > 0$, while the reactions of **1e** and**1f** proceed through $T^\pm$ and T^-, in which $\Delta pK_a < 0$.

A qualitative energy profile for the process from $T^\pm$ to T^- and PH^+ is illustrated in Figure 2, which accounts for our finding that ΔpK_a governs the presence/absence of the deprotonation process. The energy barrier for the k_2 step (i.e., departure of the leaving group from $T^\pm$ to give PH^+; Scheme 1) is expected to be strongly dependent on the basicity of the leaving aryloxide, that is, it would increase with increasing the basicity of the leaving group or vice versa. However, the energy barrier for the k_3 step (i.e., to form T^- from $T^\pm$) would be independent of amine basicity, because a stronger amine would deprotonate more rapidly from the aminium moiety of $T^\pm$ but the aminium ion would tend to hold the proton more strongly as the amine becomes more basic. Accordingly, amine basicity would not influence the energy barrier to form T^- from $T^\pm$.

TABLE 2. Summary of Microscopic Rate Constants for Reactions of *O*-Y-Substituted Phenyl Thionobenzoates (1a–f) with $CF_3CH_2NH_2$[a]

entry	Y	pK_a	k_N (M^{-1} s^{-1})	10^3 k_1 ($M^{-1}s^{-1}$)	10^2 k_2/k_{-1}	k_3/k_{-1} (M^{-1})	k_3/k_2 (M^{-1})
1a	3,4-$(NO_2)_2$	5.42	0.109[b]				
1b	4-NO_2	7.14		28.7	25.3	28.8	114
1c	4-COMe	8.05		13.5	13.3	15.8	119
1d	3-COMe	9.19		7.16	5.32	6.80	128
1e	H	9.95		2.74	3.14	4.28	136
1f	4-Me	10.2		1.97	2.46	3.47	141

[a] In 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C. [b] The k_N value determined from the slope of the linear plot of k_{obsd} vs [amine].

Figure 2 shows that reactions would proceed mainly through $T^{\pm}$ and T^- when the energy barrier for the k_2 step is higher than that for the k_3 process. On the contrary, reactions would proceed through $T^{\pm}$ (to PH^+) when the energy barrier to form PH^+ is lower than that to form T^- from $T^{\pm}$. Thus, Figure 2 accounts for the current results, that is, the reaction proceeds via both $T^{\pm}$ and T^- when the leaving aryloxide is more basic than the entering amine, but through $T^{\pm}$ without the deprotonation process when the leaving group becomes less basic than amine.

Determination of Rate Constants. The rate law is given by eq 1 for the reactions that resulted in linear plots of k_{obsd} versus [amine]. The second-order rate constants (k_N) have been determined from the slope of the linear plots of k_{obsd} versus [amine] for the reactions of **1a–f** with $EtNH_2$, **1a–d** with $BzNH_2$, and **1a** with $CF_3CH_2NH_2$. The k_N values determined in this way are summarized in Tables 1 and 2.

$$\text{rate} = k_{obsd}[\text{sub}],\ \text{where } k_{obsd} = k_N[\text{amine}] \qquad (1)$$

One can express k_{obsd} as eq 2 for the reactions that resulted in an upward curvature in the plot of k_{obsd} versus [amine]. Because the k_{-1} value is expected to be large for reactions with weakly basic $CF_3CH_2NH_2$, eq 2 simplifies to eq 3 under the assumption that $k_{-1} \gg k_2 + k_3$[amine]. In this case, the plot of k_{obsd}/[amine] vs [amine] is expected to be linear.

$$k_{obsd} = (k_1k_2[\text{amine}] + k_1k_3[\text{amine}]^2)/(k_{-1} + k_2 + k_3[\text{amine}]) \qquad (2)$$

$$k_{obsd}/[\text{amine}] = k_1k_2/k_{-1} + k_1k_3[\text{amine}]/k_{-1} \qquad (3)$$

As shown in Figure 3 for the reaction of **1f** with $CF_3CH_2NH_2$, the plot of k_{obsd}/[amine] versus [amine] shows good linearity. A similar result has been obtained for the corresponding reaction of **1e** (figure not shown).

In contrast, plots for the reactions of **1b–d** exhibit downward curvature as the amine concentration increases. Furthermore, the downward curvature becomes more significant as the leaving group becomes less basic (see the inset of Figure 3 for the reaction of **1b**). Thus, the assumption $k_{-1} \gg k_2 + k_3$[amine] is not valid for the reactions of **1b–d** in the region where the amine concentration is high. This is not an unexpected result because the k_2 value increases as the leaving group becomes less basic and the term k_3[amine] increases with an increase in the concentration of amine. Accordingly, only k_1k_2/k_{-1} values have been extracted from the intercept of the plot. More reliable k_1, k_2/k_{-1}, and k_3/k_{-1} values have been determined through the nonlinear least-squares fitting of eq 2 to the experimental data by using the k_1k_2/k_{-1} values obtained above as input values. The k_1, k_2/k_{-1} and k_3/k_{-1} values determined in this way are summarized in Table 2.

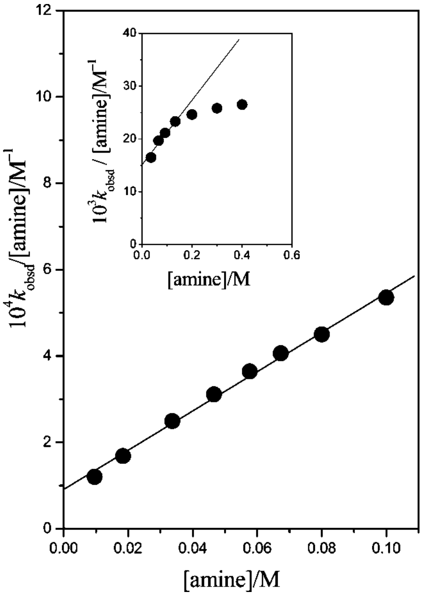

FIGURE 3. Plots of k_{obsd}/[amine] vs [amine] for the reactions of *O*-4-methylphenyl thionobenzoate (**1f**) and *O*-4-nitrophenyl thionobenzoate (**1b**; inset) with trifluoroethylamine ($CF_3CH_2NH_2$) in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C.

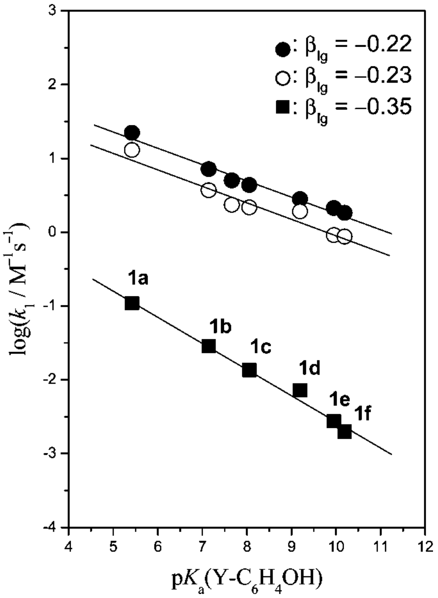

FIGURE 4. Brønsted-type plots for reactions of *O*-Y-substituted phenyl thionobenzoates (**1a–f**) with $EtNH_2$ (●), $BzNH_2$ (○), and $CF_3CH_2NH_2$ (■) in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C. The identity of points is given in Tables 1 and 2.

Table 2 shows that the microscopic rate constants for the reactions of **1b–f** with $CF_3CH_2NH_2$ are dependent on the basicity of the leaving group, that is, as the leaving aryloxide becomes more basic, k_1, k_2/k_{-1}, and k_3/k_{-1}ratios decrease while the k_3/k_2 ratio increases. It is noteworthy that $k_2/k_{-1} < 1$ for the reactions of **1b–f**, indicating that formation of $T^{\pm}$ occurs before the RDS. Further, the fact that $k_3/k_2 > 10^2$ implies that the k_3 process becomes dominant over the k_2 process when [amine] ≫ 0.01 M. Thus, the microscopic rate constants determined are consistent with the proposed mechanism.

The effect of leaving-group basicity on k_N and k_1 is illustrated in Figure 4 using the data in Tables 1 and 2. The Brønsted-type plot for the reactions of **1a–f** with $EtNH_2$ is linear with

TABLE 3. Summary of Second-Order Rate Constants (k_N) for the Reactions of *O*-4-Nitrophenyl X-Substituted Thionobenzoates (2a−f) with BzNH$_2$[a]

entry	X	k_N (M^{-1} s^{-1})
2a	4-NMe$_2$	0.0618
2b	4-OCH$_3$	0.939
2c	4-CH$_3$	1.96
2d	H	3.71
2e	3-OCH$_3$	5.62
2f	3-Cl	11.6

[a] In 80 mol % H$_2$O/20 mol % DMSO at 25.0 ± 0.1 °C.

$\beta_{lg} = -0.22$. Such a small β_{lg} value indicates that departure of the leaving group from $T^{\pm}$ is little advanced in the rate-determining transition state. Interestingly, the Brønsted-type plots for reactions of **1a−f** with BzNH$_2$ and CF$_3$CH$_2$NH$_2$ are also linear with $\beta_{lg} = -0.23$ and -0.35, respectively, although k_N and k_1 values are employed together to construct the plots. It follows that k_N is equivalent to k_1 for reactions of **1a−f** with EtNH$_2$, for those of **1a−d** with BzNH$_2$, and for nucleophilic reaction of **1a** with CF$_3$CH$_2$NH$_2$.

The argument may be extended as follows. The β_{lg} value of -0.3 ± 0.1 is typical of aminolyses that have been reported to proceed via rate-determining formation of $T^{\pm}$.[1−6,14] Moreover, one expects a small k_{-1} for the reactions with strongly basic EtNH$_2$ but a large k_2 for the reactions of substrates that possess a weakly basic leaving group. Consequently, it is reasonable to assume that $k_{-1} \ll k_2 + k_3$[amine] for reactions in where $\Delta pK_a > 0$ (i.e., when the entering amine is more basic than the leaving group). It follows, then, that eq 2 simplifies to eq 4. Comparison of eq 4 with eq 1 reveals that $k_N = k_1$, as noted above. This is consistent with the fact that the k_N values for reactions where $\Delta pK_a > 0$ were determined from the slope of their linear plots of k_{obsd} versus [amine].

$$k_{obsd}=k_1[\text{amine}] \qquad (4)$$

Reaction of 2a−f with BzNH$_2$: Effect of Nonleaving-Group Substituent. To investigate the effect of the nonleaving-group substituent on reactivity and potential change in mechanism, reactions of *O*-4-nitrophenyl X-substituted thionobenzoates (**2a−f**) with the moderately basic benzylamine (BzNH$_2$) were performed. Plots of k_{obsd} versus [amine] for reactions of **2a−f** with BzNH$_2$ were linear passing through the origin, indicating that the reaction proceeds through $T^{\pm}$ (to PH$^+$) and the deprotonation process from $T^{\pm}$ is absent *regardless of the electronic nature of the substituent X in the nonleaving group*. Note that BzNH$_2$ (pK_a = 9.46) is more basic than the leaving group, 4-nitrophenoxide (pK_a = 7.14). This result is in accord with the preceding argument that the deprotonation process from $T^{\pm}$ is absent for reactions in which $\Delta pK_a > 0$. Thus, the k_N values have been determined from the slope of the linear plots of k_{obsd} versus [amine] and summarized in Table 3. One can see that the k_N value is highly dependent on the nature of the substituent X, that is, it increases from 0.0618 M^{-1} s^{-1} to 11.6 M^{-1} s^{-1}, an approximately 190-fold increase, as the substituent X changes from 4-NMe$_2$ to 3-Cl.

The effect of the substituent X on reactivity is illustrated in Figure 5. The Hammett plot consists of two intersecting straight lines, that is, $\rho_X = 2.22$ when $\sigma_X < 0$ and $\rho_X = 1.33$ when $\sigma_X \geq 0$. Such a biphasic Hammett plot has traditionally been taken as evidence for change in RDS.[15,16] In fact, Jencks reported a nonlinear Hammett plot for the reactions of X-substituted benzaldehydes with semicarbazide in weakly acidic solution (pH = 3.9), that is, changeover from a large slope to a small one on changing the substituent X from EDGs to EWGs. A change in RDS was inferred by Jencks to be responsible for the nonlinear Hammett plot.[1a]

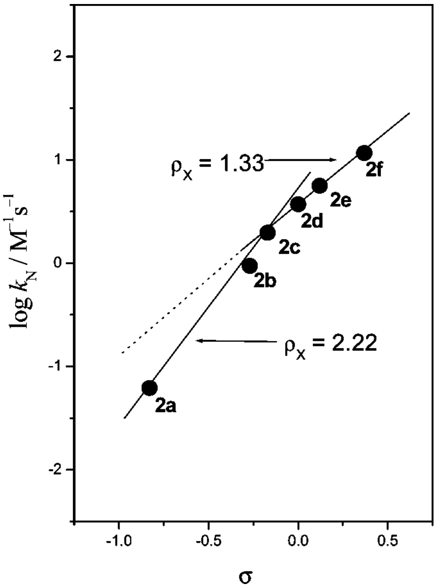

FIGURE 5. Hammett plot for reactions of *O*-4-nitrophenyl X-substituted thionobenzoates (2a-f) with benzylamine (BzNH$_2$) in 80 mol % H$_2$O/20 mol % DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 3.

In contrast to previous interpretations, we propose that the nonlinear Hammett plot (Figure 5) does not arise from a change in RDS. This follows from the idea that the k_2/k_{-1} ratio, which determines the RDS, would be independent of the electronic nature of the substituent X. Because the leaving aryloxide and amine depart from $T^{\pm}$ with the bonding-electron pair, an electron-withdrawing substituent X in the thionobenzoyl moiety would decrease both k_2 and k_{-1} values while an electron-donating substituent X would increase both. Accordingly, the k_2/k_{-1} ratio would not be influenced by the electronic nature of the substituent X. In fact, we have recently shown that the k_2/k_{-1} ratio remains nearly constant on changing X in the nonleaving group from strong EWG to strong EDG for aminolyses of aryl X-substituted benzoates and their related esters.[6,17]

Origin of Nonlinear Hammett Plot. We propose that stabilization of the ground state (GS) through resonance interaction, as illustrated by resonance structures I and II for the substrates, is responsible for the nonlinear Hammett plot shown (Figure 5). This idea can be supported by the fact that

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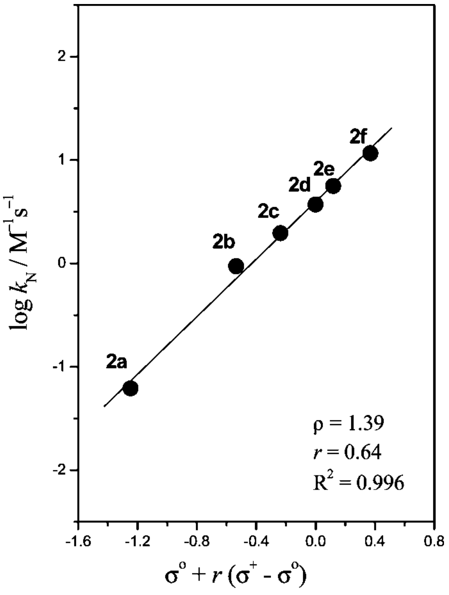
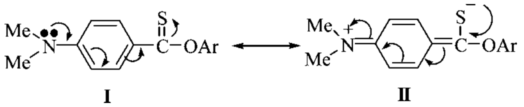


FIGURE 6. Yukawa-Tsuno plot for reactions of *O*-4-nitrophenyl X-substituted thionobenzoates (**2a−f**) with $BzNH_2$ in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 3.

the negative deviation from the Hammett plot is more significant as the substituent X in the nonleaving group becomes a stronger EDG.



I **II**

To further delineate this argument, the Yukawa-Tsuno equation (eq 5) has been employed. We have previously found application of eq 5 to be particularly useful in analyzing reaction mechanism.[6,17] The *r* value in the Yukawa-Tsuno equation represents the resonance demand of the reaction center or the extent of the resonance contribution, whereas the term $(\sigma^+ - \sigma^\circ)$ represents the resonance substituent constant that measures the capacity for π-delocalization of a given π-electron donor substituent.[18−20]

$$\log(k^X/k^H) = \rho_X[\sigma^\circ + r(\sigma^+ - \sigma^\circ)] \qquad (5)$$

The Yukawa-Tsuno plot (Figure 6) for the reactions of **2a−f** with $BzNH_2$ exhibits an excellent linear correlation ($R^2 = 0.996$) with $\rho_X = 1.39$ and $r = 0.64$, indicating that the nonlinear Hammett plot (Figure 5) results from GS stabilization through resonance interaction (e.g., I ↔ II) but, clearly, is not caused by a switch in RDS. Thus, deduction of reaction mechanism based just on linear or nonlinear Hammett plots can be misleading.

Conclusions

Our study has allowed us to conclude the following: (1) The current aminolysis of *O*-Y-substituted phenyl thionobenzoates (**1a−f**) proceeds either through $T^\pm$ or through $T^\pm$ and T^-, depending on the basicity difference between the entering amine and the leaving aryloxide. (2) The basicity of the amine nucleophile and the aryloxide leaving group has been shown to be an important determinant of presence/absence of the deprotonation process from $T^\pm$, that is, reactions proceed through $T^\pm$ (to PH^+ and, thence, to P) when amines are more basic than aryloxides but through both $T^\pm$ and T^- when amine becomes less basic than the leaving group. (3) The electronic nature of the substituent X in the nonleaving group does not influence the reaction mechanism. (4) The reactions of **2a−f** with $BzNH_2$ resulted in a biphasic Hammett plot but a linear Yukawa-Tsuno plot, indicating that the nonlinear Hammett plot is not due to a change in the RDS but is caused by stabilization of the GS of the substrate through resonance interaction between the electron-donating substituent and the thionocarbonyl moiety. (5) Deduction of reaction mechanism based solely on observation of a nonlinear Hammett plot can be misleading. In summary, amine basicity combines with modulation of the electronic nature (i.e., EDG vs EWG) of X and Y substituents to control the reaction mechanism.

Experimental Section

Materials. Compounds**1a−f** and **2b−f** were prepared as reported previously.[12,21,22] Compound **2a** was synthesized readily by reaction of 4-dimethylaminothionobenzoic acid with 4-nitrophenol under presence of *N*, *N*′-dicyclohexyl carbodiimide in anhydrous ether. The purity of **2a** was checked by means of the melting point (171−173 °C), ^1H NMR characteristics (250 MHz, $CDCl_3$) δ 8.34−8.31 (d, *J* = 7.5 Hz, 2H), 8.29−8.26 (d, *J* = 7.5 Hz, 2H), 7.31−7.28 (d, *J* = 7.5 Hz, 2H), 6.73−6.70 (d, *J* = 7.5 Hz, 2H), 3.05 (s, 6H) and elemental analysis (Calcd for $C_{15}H_{14}N_2O_3S$: C, 59.59; H, 4.67. Found: C, 59.48; H, 4.72). Other chemicals, including the amines used, were of the highest quality available. The reaction medium was H_2O containing 20 mol % DMSO due to low solubility of the substrates in pure H_2O. 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 for slow reactions ($t_{1/2} \geq 10$ s) or with a stopped-flow spectrophotometer for fast reactions ($t_{1/2} < 10$ s) equipped with a constant temperature circulating bath to maintain the temperature in the reaction cell at 25.0 ± 0.1 °C. The reaction was followed by monitoring the appearance of the leaving Y-substituted phenoxide ion or its conjugate acid. All the reactions were carried out under pseudofirst-order conditions in which amine concentrations were at least 30 times greater than the substrate concentration. The amine stock solution of about 0.2 M was prepared by dissolving 2 equiv of amine hydrochloride and 1 equiv of standardized NaOH solution to keep the pH constant in this self-buffered solution. All solutions were prepared freshly just before use under nitrogen and transferred by gastight syringes. Typically, the reaction was initiated by adding 5 μL of a 0.02 M solution of the substrate in CH_3CN by a 10 μL syringe to a 10 mm quartz UV cell containing 2.50 mL of the thermostatted reaction mixture made up of solvent and aliquot of the amine stock solution.

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Product Analysis. Y-Substituted phenoxide (and/or its conjugate acid) was liberated quantitatively and identified as one of the products by comparison of the UV−vis spectrum at the end of reaction with the authentic sample under the experimental condition.

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Supporting Information Available: Tables S1−S18 for the kinetic conditions and data for reactions of **1a−f** with $EtNH_2$, $BzNH_2$, and $CF_3CH_2NH_2$. Tables S19 − S23 for the kinetic data for reactions of **2a−f** with $BzNH_2$. This material is available free of charge via the Internet at http://pubs.acs.org.

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