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Kinetic Study on Aminolysis of Y-Substituted-Phenyl X-Substituted-Benzoates: Effects of Substituents X and Y on Reactivity and Reaction Mechanism

Seong Hoon Jeon,[†] Hyun Soo Kim,[†] Young Joon Han,[†] Min-Young Kim, and Ik-Hwan Um[*]

Department of Chemistry and Nano Science, Ewha Womans University, Seoul 120-750, Korea. [*]E-mail: ihum@ewha.ac.kr
[†]Sejong Science High School, Seoul 152-881, Korea
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A kinetic study on aminolysis of 2-chloro-4-nitrophenyl X-substituted-benzoates (**2a-k**) in 80 mol % H_2O/20 mol % DMSO at 25.0 °C is reported. The Brønsted-type plot for the reactions of 2-chloro-4-nitrophenyl benzoate (**2g**) with a series of cyclic secondary amines curves downward (*e.g.*, $\beta_1 = 0.25$, $\beta_2 = 0.85$ and $pK_a^o = 10.3$), which is typical of reactions reported to proceed through a stepwise mechanism with a change in rate-determining step (RDS). The Hammett plot for the reactions of **2a-k** with piperidine consists of two intersecting straight lines, while the corresponding Yukawa-Tsuno plot exhibits an excellent linear correlation with $\rho_X = 1.15$ and $r = 0.59$. Thus, it has been concluded that the nonlinear Hammett plot is not due to a change in RDS but is caused by stabilization of substrates through resonance interactions between the electron-donating substituent and the C=O bond. Substrates possessing a substituent at the 2-position of the leaving aryloxide deviate negatively from the curved Brønsted-type plot for the reactions of Y-substituted-phenyl benzoates (**3a-i**), implying that the steric hindrance exerted by the substituent at the 2-position is an important factor which governs the reactivity of Y-substituted-phenyl benzoates.

Key Words : Brønsted-type plot, Hammett plot, Yukawa-Tsuno plot, Nucleofugality, Steric hindrance

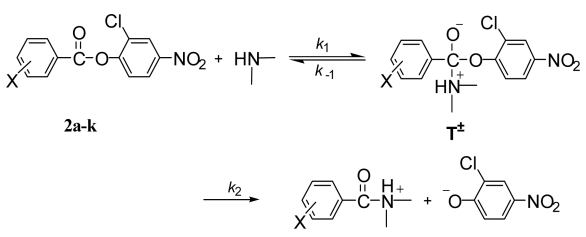
Introduction

Due to the importance in biological processes and synthetic applications, aminolysis of esters has intensively been investigated.[1-11] Many factors have been suggested to affect reactivity and reaction mechanism (*e.g.*, the nature of electrophilic center, reaction medium, substituents, amine basicity, *etc.*).[2-11] Aminolysis of P=O and P=S centered esters (*e.g.*, 4-nitrophenyl diphenylphosphinate and diphenylphosphinothioate) has been reported to proceed through a concerted mechanism on the basis of a linear Brønsted-type plot with $\beta_{nuc} = 0.5 \pm 0.1$.[6,7] In contrast, aminolysis of C=O centered esters has generally been reported to proceed through a stepwise mechanism, in which the rate-determining step (RDS) is dependent on the basicity of the incoming amine and the leaving-group.[2-11] It is now firmly understood that RDS changes from breakdown of a zwitterionic tetrahedral intermediate ($T^{\pm}$) to its formation as the incoming amine becomes more basic than the leaving group (or the leaving group is less basic than the amine) by 4-5 pK_a units.[2-11]

Reactions of 2,4-dinitrophenyl benzoate with a series of cyclic secondary amines in 80 mol % H_2O/20 mol % DMSO have been reported to proceed through a stepwise mechanism with a change in RDS on the basis of a curved Brønsted-type plot.[8a] However, the corresponding reactions in MeCN have been suggested to proceed through a concerted mechanism on the basis of a linear Brønsted-type plot with $\beta_{nuc} = 0.40$,[9a] indicating that the nature of the reaction medium is an important factor which governs the reaction mechanism.

In contrast, aminolysis of 4-pyridyl X-substituted-benzoates in MeCN has been reported to proceed through a stepwise mechanism with one or two intermediates (*i.e.*, $T^{\pm}$ and its deprotonated form T^{-}) depending on the electronic nature of the substituent X.[10] We have shown that the reaction proceeds through a stepwise mechanism with two intermediates $T^{\pm}$ and T^{-} when X is a strong electron-withdrawing group (EWG) but the deprotonation process to yield T^{-} from $T^{\pm}$ is absent when X is a weak EWG or an electron-donating group (EDG).[10] This demonstrates convincingly that the nature of the leaving group and substituent X in the nonleaving group affects the reaction mechanism.

We have recently reported that reactions of 4-chloro-2-nitrophenyl X-substituted-benzoates (**1a-k**) with a series of cyclic secondary amine in 80 mol % H_2O/20 mol % DMSO proceed through a stepwise mechanism with a change in RDS, *e.g.*, from breakdown of $T^{\pm}$ to its formation as the pK_a of the conjugate acid of the incoming amine exceeds 10.5.[11] Our study has now been extended to the corresponding reac-



X = 3,5-$(NO_2)_2$ (**2a**), 4-Cl-3-NO_2 (**2b**), 4-NO_2 (**2c**), 3-NO_2 (**2d**), 4-CN (**2e**), 3-Cl (**2f**), H(**2g**), 3-CH_3 (**2h**), 4-CH_3 (**2i**), 4-OCH_3 (**2j**), 4-$N(CH_3)_2$ (**2k**)

HN = HN–Z ; R = H or CH_3 ; Z = CH_2, NH, NCH_2CH_2OH, O, NH_2^+

Scheme 1

tions of 2-chloro-4-nitrophenyl X-substituted-benzoates (**2a-k**) to obtain further information on the effects of substituent X on reactivity and reaction mechanism. The kinetic data in this study have also been compared with those reported previously for the corresponding reactions of Y-substituted-phenyl benzoates (**3a-i**) to explore the effect of leaving-group substituent on reactivity and reaction mechanism.

Result and Discussion

The reactions of **2a-k** with all of the amines in this study obeyed pseudo-first-order kinetics. Pseudo-first-order rate constants (k_{obsd}) were calculated from the equation, ln ($A_\infty - A_t$) = $-k_{obsd}t + C$. The plots of k_{obsd} *vs*. [amine] were linear and passed through the origin, indicating that general base catalysis by a second amine molecule is absent and the contribution of H_2O and/or OH^- from hydrolysis of amine to k_{obsd} is negligible. Accordingly, the second-order rate constants (k_N) were calculated from the slope of the linear plots of k_{obsd} *vs*. [amine]. The correlation coefficient for the linear regression was always higher than 0.9995. The uncertainty in the k_N values is estimated to be less than ± 3% from replicate runs. The second-order rate constants (k_N) are summarized in Tables 1-4 for the reactions of **2a-k** and their related substrates.

Effect of Amine Basicity on Reactivity and Reaction Mechanism. As shown in Table 1, the k_N decreases as the incoming amine becomes less basic, *e.g*., the k_N value for the reactions of 2-chloro-4-nitrophenyl benzoate (**2g**) decreases from 30.0 $M^{-1}s^{-1}$ to 2.97 and 0.0124 $M^{-1}s^{-1}$ as the pK_a of the conjugate acid of the amine decreases from 11.02 to 9.38 and 5.95, in turn. A similar result is shown for the corresponding reaction of 4-chloro-2-nitrophenyl benzoate (**1g**). However, **2g** is 5-6 times more reactive than **1g** regardless of the amine basicity.

The effect of amine basicity on k_N is illustrated in Figure 1. The statistically corrected Brønsted-type plots[12] for the reactions of **1g** and **2g** exhibit downward curvature. Such nonlinear Brønsted-type plots are typical of reactions reported previously to proceed through a stepwise mechanism with a change in RDS.[2,8] In fact, the reactions of **1g** have been reported to proceed through a stepwise mechanism, in which the RDS changes from breakdown of $T^{\pm}$ to its formation as the pK_a of the conjugate acid of the incoming amine exceeds 10.5.[11] Thus, one can suggest that the reactions of **2g** in this study proceed also through a stepwise mechanism with a change in RDS on the basis of the nonlinear Brønsted-type plot.

Table 1. Summary of Second-order Rate Constants (k_N) for Aminolysis of 4-Chloro-2-Nitrophenyl Benzoate (**1g**) and 2-Chloro-4-Nitrophenyl Benzoate (**2g**) in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C

	amines	pK_a	$k_N/M^{-1}s^{-1}$	
			1g[a]	**2g**
1	piperidine	11.02	5.91	30.0
2	3-methylpiperidine	10.80	5.17	25.3
3	piperazine	9.85	2.16	12.3
4	1-(2-hydroxyethyl)piperazine	9.38	0.579	2.97
5	morpholine	8.65	0.305	1.81
6	piperazinium ion	5.95	0.00215	0.0124

[a]The kinetic data for the reactions of **1g** were taken from ref. 11.

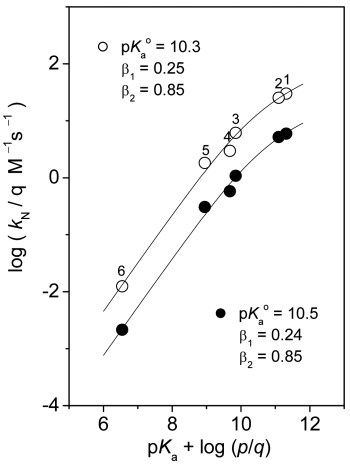


Figure 1. Brønsted-type plots for the aminolysis of 4-chloro-2-nitrophenyl benzoate (**1g**, ●) and 2-chloro-4-nitrophenyl benzoate (**2g**, ○) in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 1. The pK_a and k_N values in the plots were statistically corrected using p and q (*i.e*., q = 1 except q = 2 for piperazine while p = 2 except p = 4 for piperazinium ion).[12]

Dissection of k_N into Microscopic Rate Constants k_1 and k_2/k_{-1}. As shown in Table 1 and Figure 1, **2g** is more reactive than **1g** toward all the amines studied. One can suggest that the reactivity of **1g** and **2g** toward a given amine would be governed by the magnitude of k_1 and k_2. One might expect that **2g** would result in a larger k_2 than **1g**, since the less basic 2-chloro-4-nitrophenoxide (pK_a = 5.45) is a better nucleofuge than the more basic 4-chloro-2-nitrophenoxide (pK_a = 6.46).

To examine the above idea, the k_N values have been dissected into the microscopic rate constants (*e.g*., k_1 and k_2/k_{-1} ratio). One can analyze the nonlinear Brønsted-type plot for the reactions of **2g** using a semiempirical equation, Eq. (1), in which β_1 and β_2 represent the slope of the nonlinear Brønsted-type plot for the strongly basic and weakly basic amines, respectively, while k_N^o refers to the k_N value at pK_a^o, defined as the pK_a at the center of the Brønsted curvature.[13] The β_1, β_2, and pK_a^o calculated for the reactions of **2g** are 0.25, 0.85, and 10.3, respectively. The β_1 and β_2, values for the reactions of **2g** are almost identical to those reported for the corresponding reactions of **1g**.

$$\log (k_N/k_N^o) = \beta_2(pK_a - pK_a^o) - \log [(1 + \alpha)/2]$$
$$\text{where } \log \alpha = (\beta_2 - \beta_1)(pK_a - pK_a^o) \quad (1)$$

The k_N values for the reactions of **2g** have been dissected into the microscopic rate constants using the following equations. Eq. (2) can be simplified to Eqs. (3) and (4). Then, β_1 and β_2 can be expressed as Eqs. (5) and (6), respectively.

Table 2. Summary of Microscopic Rate Constants Associated with Aminolysis of 4-Chloro-2-Nitrophenyl Benzoate (**1g**)[a] and 2-Chloro-4-Nitrophenyl Benzoate (**2g**) in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C

	amines	pK_a	k_2/k_{-1}		$k_1/M^{-1}s^{-1}$	
			1g	**2g**	**1g**	**2g**
1	piperidine	11.02	3.16	4.09	7.78	37.3
2	3-methylpiperidine	10.80	2.32	3.02	7.40	33.7
3	piperazine	9.85	0.401	0.537	7.54	35.2
4	1-(2-hydroxyethyl)piperazine	9.38	0.316	0.425	2.41	9.96
5	morpholine	8.65	0.113	0.155	3.00	13.5
6	piperazinium ion	5.95	0.00390	0.00562	0.554	2.22

[a]The kinetic data for the reactions of **1g** were taken from ref. 11.

$$k_N = k_1k_2/(k_{-1} + k_2) = k_1/(k_{-1}/k_2 + 1) \quad (2)$$

$$k_N = k_1k_2/k_{-1}, \text{ when } k_2 << k_{-1} \quad (3)$$

$$k_N = k_1, \text{ when } k_2 >> k_{-1} \quad (4)$$

$$\beta_1 = d(\log k_1)/d(pK_a) \quad (5)$$

$$\beta_2 = d(\log k_1k_2/k_{-1})/d(pK_a) = \beta_1 + d(\log k_2/k_{-1})/d(pK_a) \quad (6)$$

Eq. (6) can be rearranged as Eq. (7). Integral of Eq. (7) from pK_a^o results in Eq. (8). Since $k_2 = k_{-1}$ at pK_a^o, the term $(\log k_2/k_{-1})_{pKa}^o$ is zero. Therefore, one can calculate the k_2/k_{-1} ratio for the reactions of **2g** from Eq. (8) using $\beta_1 = 0.25$, $\beta_2 = 0.85$ and $pK_a^o = 10.3$. The k_1 values have been calculated from Eq. (2) using the k_N values in Table 1 and the k_2/k_{-1} ratios calculated above.

$$\beta_2 - \beta_1 = d(\log k_2/k_{-1})/d(pK_a) \quad (7)$$

$$(\log k_2/k_{-1})_{pKa} = (\beta_2 - \beta_1)(pK_a - pK_a^o) \quad (8)$$

The k_1 and k_2/k_{-1} ratios calculated for the reactions of **2g** are summarized in Table 2 together with those reported for the corresponding reactions of **1g** for comparison. As shown in Table 2, the k_2/k_{-1} ratio for the reactions of **2g** is only slightly larger than that for the corresponding reaction of **1g**. In contrast, the k_1 value for the reaction of **2g** is 4-5 times larger than that for the corresponding reaction of **1g**. Thus, one can suggest that the reactivity of **1g** and **2g** in this study is governed mainly by k_1 but not by the k_2/k_{-1} ratio. This is quiet an unexpected result, since **2g**, which possesses a better nucleofuge than **1g**, is expected to result in a larger k_2 value.

Table 2 shows that the k_1 value for the reactions of **2g** decreases as the amine basicity decreases, *e.g.*, it decreases from 37.3 $M^{-1}s^{-1}$ to 9.96 and 2.22 $M^{-1}s^{-1}$ as the pK_a of the conjugate acid of the amine decreases from 11.02 to 9.38 and 5.95, in turn. The k_2/k_{-1} ratio also decreases as the amine basicity decreases, although it decreases more rapidly than k_1. The effects of amine basicity on the microscopic rate constants are illustrated in Figure 2. The Brønsted-type plots for the reactions of **1g** and **2g** are linear with a slope of 0.60 ± 0.01 and 0.25 ± 0.01 for k_2/k_{-1} and k_1, respectively. It is also noted that the k_2/k_{-1} ratio for the reactions of **1g** and **2g** is similar. In contrast, k_1 is much larger for the reaction of **2g** than for that of **1g** regardless of the amine basicity. This indicates that modification of the leaving group from 4-chloro-2-nitrophenoxide to 2-chloro-4-nitrophenoxide results in an increase in reactivity by increasing k_1 but not by increasing the k_2/k_{-1} ratio.

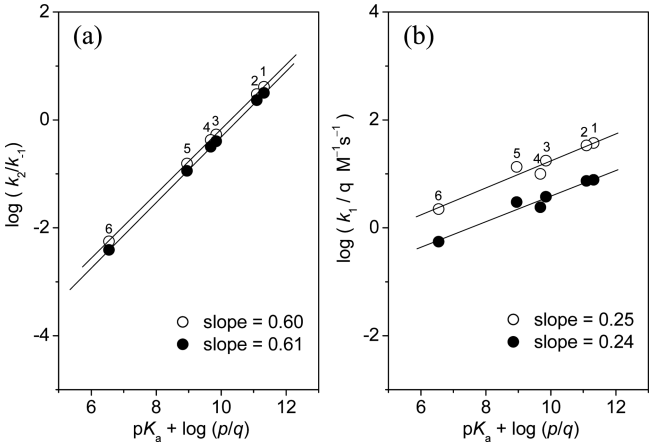


Figure 2. Correlations of log k_2/k_{-1} with pK_a (a) and log k_1 with pK_a (b) for the aminolysis of 4-chloro-2-nitrophenyl benzoate (**1g**, ●) and 2-chloro-4-nitrophenyl benzoate (**2g**, ○) in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 2.

Effect of Substituent X on Reactivity and Reaction Mechanism. To investigate the effect of nonleaving-group substituent X on reactivity and reaction mechanism, the second-order rate constants for the reactions of 2-chloro-4-nitrophenyl X-substituted-benzoates (**2a-k**) have been measured. The k_N values for the reactions of **2a-k** are summarized in Table 3. As shown in Table 3, the k_N for the reactions of **2a-k** decreases as the substituent X changes from a strong EWG to a strong EDG, *e.g.*, it decreases from 1230 $M^{-1}s^{-1}$ to 30 and 1.37 $M^{-1}s^{-1}$, as the substituent X changes from 3,5-$(NO_2)_2$ to H and 4-$N(CH_3)_2$, in turn.

The effect of substituent X on reactivity is illustrated in Figure 3 for the reactions of **2a-k** with piperidine. It is shown that the Hammett plot consists of two intersecting straight lines (*i.e.*, the slope decreases from a large ρ_X to a small one as the substituent X changes from EDGs to EWGs). Such nonlinear Hammett plot has traditionally been interpreted as a change in RDS.[14] Thus, one might suggest

Table 3. Summary of Second-Order Rate Constants (k_N) for the Reactions of 2-Chloro-4-Nitrophenyl X-Substituted-Benzoates (**2a-k**) with Piperidine in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C

	X	$k_N/M^{-1}s^{-1}$
2a	3,5-$(NO_2)_2$	1230
2b	4-Cl-3-NO_2	362
2c	4-NO_2	275
2d	3-NO_2	243
2e	4-CN	177
2f	3-Cl	100
2g	H	30.0
2h	3-CH_3	25.7
2i	4-CH_3	17.1
2j	4-OCH_3	9.03
2k	4-$N(CH_3)_2$	1.37

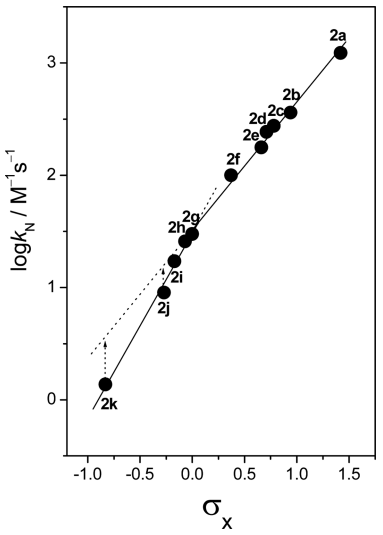
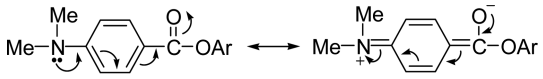


Figure 3. Hammett plots for the reactions of 2-chloro-4-nitrophenyl X-substituted-benzoates (**2a-k**) with piperidine in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 3.

that the RDS changes from formation of $T^{\pm}$ (*i.e.*, the k_1 step) to its breakdown (*i.e.*, the k_2 step) as the substituent X changes from EDGs to EWGs. This idea appears to be reasonable since an EDG in the benzoyl moiety of the substrate would decrease k_1 but increase k_2 by increasing the electron density of the reaction center. On the contrary, an EWG would accelerate the k_1 process but retard the k_2 step.

However, we propose that the nonlinear Hammett plot is not due to a change in RDS. This is because RDS is not determined by the magnitude of k_1 and k_2 values. Furthermore, k_1 and k_2 cannot be compared directly due to the difference in their units, since k_1 is a second-order rate constant with a unit of $M^{-1}s^{-1}$ while k_2 is a first-order rate constant with a unit of s^{-1}. It is apparent that the RDS should be determined by the k_2/k_{-1} ratio (*e.g.*, RDS = the k_1 step when $k_2/k_{-1} > 1$ while RDS = the k_2 step when $k_2/k_{-1} < 1$).

We propose that the nonlinear Hammett plot is caused by stabilization of substrates through resonance interactions between the electron-donating substituent X and the C=O bond as illustrated by the resonance structures I and II. Such resonance interactions would stabilize the ground state (GS) of the substrate and cause a decrease in reactivity. This idea is supported by the fact that substrates possessing an EDG in the benzoyl moiety deviate negatively from the linear line composed with substrates possessing an EWG. Moreover, the negative deviation is more significant for the substrate bearing a stronger EDG.



I **II**

To examine the above argument, the Yukawa-Tsuno equation, Eq. (9), is employed. The r value in Eq. (9) represents the resonance demand of the reaction center or the extent of resonance contribution, while the term $(\sigma_X^+ - \sigma_X^o)$ is the resonance substituent constant that measures the capacity for π-delocalization of the π-electron donor substituent.[15,16] Eq. (9) was originally derived to account for the kinetic data obtained from solvolysis of benzylic systems in which a positive charge develops partially in TS.[15] However, we have shown that Eq. (9) is highly effective in elucidation of ambiguities in the reaction mechanism for reactions of esters with various nucleophiles (*e.g.*, amines and anionic nucleophiles such as OH^-, CN^-, N_3^- and $CH_3CH_2O^-$).[17]

$$\log k^X/k^H = \rho_X[\sigma_X^o + r(\sigma_X^+ - \sigma_X^o)] \quad (9)$$

Thus, the Yukawa-Tsuno plot for the reactions of **2a-k** has been constructed. As shown in Figure 4, the Yukawa-Tsuno plot exhibits an excellent linear correlation with $\rho_X = 1.15$ and $r = 0.59$. Such good linear Yukawa-Tsuno plot indicates that the nonlinear Hammett shown in Figure 3 is not due to a change in the RDS but is caused by stabilization of sub-

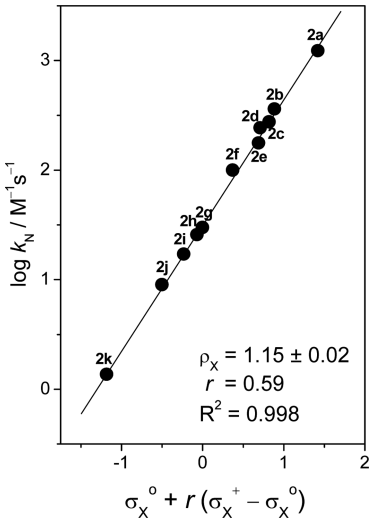


Figure 4. Yukawa-Tsuno plot for the reactions of 2-chloro-4-nitrophenyl X-substituted-benzoates (**2a-k**) with piperidine in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 3.

Table 4. Summary of Second-order Rate Constants (k_N/$M^{-1}s^{-1}$) for the Reactions of Y-Substituted-Phenyl Benzoates (**3a-i**) with Piperidine in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C

	Y	pK_a	k_N/$M^{-1}s^{-1}$
3a	3-COMe	9.19	0.00650[a]
3b	3-Cl	9.02	0.0159[a]
3c	4-COMe	8.05	0.236[a]
3d	4-CHO	7.66	0.852[a]
3e	4-NO_2	7.14	5.94[a]
3f	4-Cl-2-NO_2	6.46	5.91
3g	2-Cl-4-NO_2	5.45	30.0
3h	3,4-$(NO_2)_2$	5.42	191[a]
3i	2,4-$(NO_2)_2$	4.11	174[b]

[a]The data were taken from ref. 9b. [b]The k_N was taken from ref. 8a.

strates possessing an EDG through resonance interactions. Besides, the *r* value of 0.59 implies that the resonance interactions are significant.

Effect of Leaving-Group Basicity on Reactivity. It is generally known that the reactivity of esters increases as the leaving-group becomes less basic, since nucleofugality of leaving groups would increase as the leaving-group basicity decreases. To investigate the effect of leaving-group basicity on reactivity and reaction mechanism, the second-order rate constants for the reactions of Y-substituted-phenyl benzoates (**3a-i**) with piperidine are summarized in Table 4. It is shown that the k_N value increases as the pK_a of the conjugate acid of the leaving group decreases except substrates possessing a substituent at the 2-position of the leaving aryloxide (*e.g.*, **3f**, **3g** and **3i**).

The effect of leaving-group basicity on reactivity is demonstrated graphically in Figure 5. The Brønsted-type plot curves downward when substrates **3f**, **3g** and **3i** are excluded from the curved plot. The nonlinear Brønsted-type plot has previously been taken as evidence for a change in RDS.[9b] In the preceding section, the reaction of **3g** with piperidine is discussed to proceed through a stepwise mechanism with

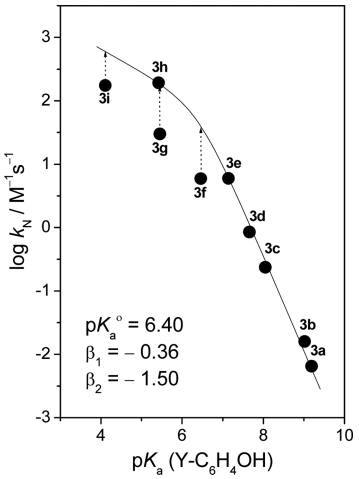


Figure 5. Brønsted-type plot for the reactions of Y-substituted-phenyl benzoates (**3a-i**) with piperidine in 80 mol % H_2O/20 mol % DMSO at 25.0 ± 0.1 °C. The identity of points is given in Table 4.

formation of $T^{\pm}$ being the RDS. The reactions of **3f** and **3i** with piperidine have also been reported to proceed through a stepwise mechanism, in which formation of $T^{\pm}$ is the RDS. Thus, one can suggest that the negative deviation (shown by substrates **3f**, **3g** and **3i**) from the curved Brønsted-type plot is not due to a difference in the reaction mechanism.

A common feature of substrates **3f**, **3g** and **3i**, which deviate negatively from the curved Brønsted-type plot, is possession of a bulky substituent at the 2-position of the leaving aryloxide. It is apparent that the bulky substituent at the 2-position would exert steric hindrance. Thus, one can attribute the negative deviation shown by substrates **3f**, **3g** and **3i** to the steric hindrance exerted by the substituent at the 2-position of the leaving group.

Conclusions

The current study has allowed us to conclude the following: (1) The Brønsted-type plot for the aminolysis of **2g** curves downward (*e.g.*, β_1 = 0.25, β_2 = 0.85 and pK_a^o = 10.3), indicating that the reaction proceeds through a stepwise mechanism with a change in RDS at pK_a = 10.3. (2) Dissection of k_N into the microscopic rate constants has revealed that the more reactive **2g** results in a larger k_1 value than the less reactive **1g**, while the k_2/k_{-1} ratios for the reactions of **1g** and **2g** are similar. (3) The Hammett plot for the reactions of **2a-k** with piperidine consists of two intersecting straight lines while the Yukawa-Tsuno plot exhibits an excellent linear correlation with ρ_X = 1.15 and *r* = 0.59, indicating that the nonlinear Hammett plot is not due to a change in the RDS but is caused by stabilization of substrates possessing an EDG through resonance interactions. (4) Substrates bearing a substituent at the 2-position of the leaving aryloxide deviate negatively from the curved Brønsted-type plot for the reactions of **3a-i**. (5) Steric hindrance exerted by the substituent at the 2-position of the leaving group is an important factor which affects the reactivity of Y-substituted-phenyl benzoates.

Experimental Section

Materials. 2-Chloro-4-nitrophenyl X-substituted-benzoates (**2a-k**) were readily prepared from the reaction of the respective benzoyl chloride with 2-chloro-4-nitrophenol in anhydrous ether under the presence of triethylamine as reported previously.[11] The crude products were purified by column chromatography and their purity was checked by their melting points and spectral data such as ^1H and ^{13}C NMR spectra. DMSO and other chemicals were of the highest quality available. Doubly glass distilled water was further boiled and cooled under nitrogen just before use. Due to low solubility of the substrates in pure water, aqueous DMSO (80 mol % H_2O/20 ml % DMSO) was used as the reaction medium.

Kinetics. The kinetic study was performed using a UV-Vis spectrophotometer for slow reactions (*e.g.*, $t_{1/2}$ 10 s) or a stopped-flow spectrophotometer for fast reactions (*e.g.*, $t_{1/2}$ < 10 s) equipped with a constant temperature circulating bath

to maintain the reaction mixture at 25.0 ± 0.1 °C. The reactions were followed by monitoring the appearance of 2-chloro-4-nitrophenoxide ion. All of the reactions in this study were carried out under pseudo-first-order conditions, in which the concentration of the amine was kept in excess over that of the substrate.

Typically, the reaction was initiated by adding 5 μL of a 0.02 M solution of the substrate 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 amine stock solution, which was prepared by adding 2 equiv. of amine and 1 equiv. of standardized HCl solution to make a self-buffered solution. All solutions were transferred by gas-tight syringes. Generally, the amine concentration in the reaction mixtures was varied over the range $(2 – 50) \times 10^{-3}$ M, while the substrate concentration was *ca*. 4×10^{-5} M. Pseudo-first-order rate constants (k_{obsd}) were calculated from the equation, $\ln (A_\infty – A_t) = – k_{obsd}t + C$. The plots of $\ln (A_\infty – A_t)$ *vs*. time were linear over 90% of the total reaction. Usually, five different amine concentrations were employed to obtain the second-order rate constants (k_N) from the slope of linear plots of k_{obsd} *vs*. amine concentrations.

Products Analysis. 2-Chloro-4-nitrophenoxide ion was liberated quantitatively and identified as one of the products by comparison of the UV-Vis spectrum after completion of the reaction with that of authentic sample under the same reaction condition.

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