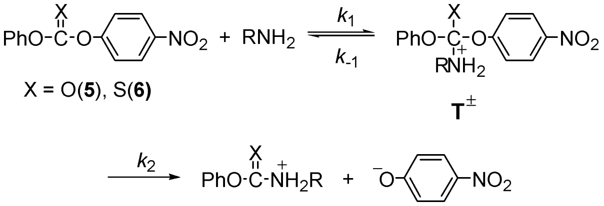
Aminolyses of 4-Nitrophenyl Phenyl Carbonate and Thionocarbonate: Effect of Modification of Electrophilic Center from C═O to C═S on Reactivity and Mechanism

Ik-Hwan Um,* Eun Young Kim, Hye-Ran Park, and Sang-Eun Jeon

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

ihum@mm.ewha.ac.kr

Received November 22, 2005



A kinetic study is reported for nucleophilic substitution reactions of 4-nitrophenyl phenyl carbonate (**5**) and 4-nitrophenyl phenyl thionocarbonate (**6**) with a series of primary amines. The thiono compound **6** is less reactive than its oxygen analogue **5** toward strongly basic amines but is more reactive toward weakly basic $CF_3CH_2NH_2$. The Brønsted-type plots obtained from the aminolyses of **5** and **6** are curved downwardly. The reactions are proposed to proceed through a stepwise mechanism with a change in the RDS on the basis of the curved Brønsted-type plots. The microscopic rate constants (k_1 and k_2/k_{-1} ratio) associated with the current aminolyses are consistent with the proposed reaction mechanism. The replacement of the C═O bond in **5** by a polarizable C═S group results in a decrease in the k_1 value but an increase in the k_2/k_{-1} ratio. Besides, such a modification of the electrophilic center causes a decrease in $pK_a°$, defined as the pK_a at the curvature center of curved Brønsted-type plots, but does not alter the reaction mechanism. The larger k_2/k_{-1} ratio for the reactions of **6** compared to those of **5** is proposed to be responsible for the decreased $pK_a°$ value.

Introduction

Nucleophilic substitution reactions of thionocarbonyl and thionophosphoryl compounds have received considerable attention due to their importance in biological processes as well as synthetic applications.[1−10] The first kinetic study on thionester has been performed by Campbell et al.[2] They have found that the reaction of *O*-4-nitrophenyl thionobenzoate (**2**) with a series of primary amines proceeds through a zwitterionic tetrahedral intermediate T$^{\pm}$, and **2** is up to 200 times more reactive than its oxygen analogue 4-nitrophenyl benzoate (**1**).[2] We have recently shown that the reaction of **2** with secondary amines proceeds through two intermediates, T$^{\pm}$ and its deprotonated

---

* To whom correspondence should be addressed. Fax: 822-3277-2844.

(1) (a) Castro, E. A. *Chem. Rev.* **1999**, *99*, 3505−3524. (b) Campodonico, P. R.; Fuentealba, P.; Castro, E. A.; Santos, J. G. *J. Org. Chem.* **2005**, *70*, 1754−1760. (c) Castro, E. A.; Cubillos, M.; Santos, J. G. *J. Org. Chem.* **2004**, *69*, 4802−4807.

(2) Campbell, P.; Lapinskas, B. A. *J. Am. Chem. Soc.* **1977**, *99*, 5378−5382.

(3) (a) Um, I. H.; Seok, J. A.; Kim, H. T.; Bae, S. K. *J. Org. Chem.* **2003**, *68*, 7742−7746. (b) Um, I. H.; Lee, S. E.; Kwon, H. J. *J. Org. Chem.* **2002**, *67*, 8999−9005. (c) Um, I. H.; Kwon, H. J.; Kwon, D. S.; Park, J. Y. *J. Chem. Res., Synop.* **1995**, 301.

(4) Um, I. H.; Jeon, S. E.; Baek, M. H.; Park, H. R. *Chem. Commun.* **2003**, 3016−3017.

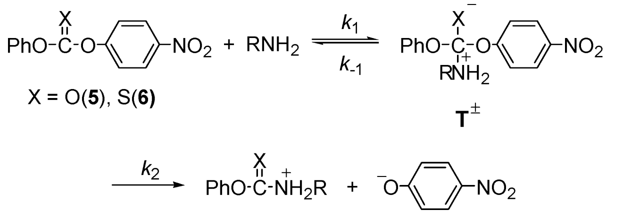
(5) (a) Balakrishnan, V.; Buncel, E.; VanLoon, G. W. *Environ. Sci. Technol*. **2005**, *39*, 5824−5830. (b) Onyido, I.; Albright, K.; Buncel, E. *Org. Biomol. Chem*. **2005**, *3*, 1468−1475. (c) Balakrishnan, V.; Han, X.; VanLoon, G. W.; Dust, J. M.; Toullec, J.; Buncel, E. *Langmuir*, **2004**, *20*, 6586−6593. (d) Buncel, E.; Albright, K.; Onyido, I. *Org. Biomol. Chem*. **2004**, *2*, 601−610. (e) Buncel, E.; Nagelkerke, R.; Thatcher, G. R. J. *Can. J. Chem*. **2003**, *81*, 53−63.

(6) (a) Thatcher, G. R. J.; Kluger, R. *Adv. Phys. Org. Chem*. **1989**, *25*, 99−265. (b) Moss, R. A.; Kanamathareddy, S.; Vijayaraghavan, S. *Langmuir* **2001**, *17*, 6108−6112. (c) Toullec, J.; Moukawim. M. *Chem. Commun.* **1996**, 221−222. (d) Lavey, B.; Janda, K. D. *J. Org. Chem*. **1996**, *61*, 7633−7636. (e) Kevill, D. N.; D'Souza, M. J. *Can. J. Chem*. **1999**, *77*, 1118−1122. (f) Kevill, D. N.; Carver, J. S. *Org. Biomol. Chem*. **2004**, *2*, 2040−2043.

(7) (a) Oh, H. K.; Oh, J. Y.; Sung, D. D.; Lee, I. *J. Org. Chem.* **2005**, *70*, 5624−5629. (b) Oh, H. K.; Oh, J. Y.; Sung, D. D.; Lee, I. *Collect. Czech. Chem. Commun*. **2004**, 69, 2174−2182. (c) Oh, H. K.; Park, J. E.; Sung, D. D.; Lee, I. *J. Org. Chem.* **2004**, *69*, 9285−9288. (d) Oh, H. K.; Ha, J. S.; Sung, D. D.; Lee, I. *J. Org. Chem.* **2004**, *69*, 8219−8223.

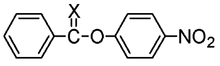
10.1021/jo052417z CCC: $33.50

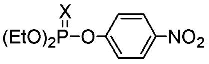
SCHEME 1

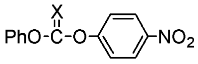


form T$^-$, whereas the corresponding reaction of **1** proceeds through T$^{\pm}$ only.[3]

Modification of the electrophilic center from a P═O to a P═S bond has also been reported to cause a remarkable effect on reactivity and reaction mechanism.[4−6] In the nucleophilic substitution reaction of diethyl 4-nitrophenyl phosphate (**3**) and its thiono analogue diethyl 4-nitrophenyl thionophosphate (**4**) with alkali metal ethoxides (EtO^-M^+) in anhydrous ethanol, we have shown that **3** is up to ca. 2×10^3 times more reactive than **4** and alkali metal ions catalyze the reactions with **3**, with the catalytic effect increasing in the order of $K^+ < Na^+ < Li^+$.[4] In contrast, alkali metal ions have been found to inhibit the reactions with **4**, and the inhibitory effect increases in the order of $K^+ < Na^+ < Li^+$.[4]


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


X = O(**3**), S(**4**)


X = O(**5**), S(**6**)

We have extended our study to aminolyses of 4-nitrophenyl phenyl carbonate (**5**) and 4-nitrophenyl phenyl thionocarbonate (**6**), a carbonate and its thiono analogue, respectively (Scheme 1). Although scattered information about the reactivity and mechanism for aminolysis of carbonate and thionocarbonate compounds is available,[1,7,8] the effect of such a modification of the electrophilic center (e.g., **5** → **6**) on reactivity and reaction mechanism has not been systematically investigated. In the current study, we have determined the apparent second-order rate constants (k_N) and the microscopic rate constants (k_1 and k_2/k_{-1} ratio) associated with the reactions of **5** and **6** with a series of primary amines and report the effect of replacing the oxygen by a polarizable sulfur in the C═O bond of **5** on reactivity and reaction mechanism.

Results and Discussion

Reactions of **5** and **6** with primary amines proceeded with quantitative liberation of 4-nitrophenoxide ion and/or its conjugate acid. The kinetic study was performed under pseudo-first-order conditions, i.e., the amine concentration in excess over the substrate concentration. All the reactions obeyed first-order kinetics over 90% of the reaction. Pseudo-first-order rate constants (k_{obsd}) were calculated from the equation $\ln(A_\infty - A_t) = -k_{obsd}t + C$. The k_{obsd} values obtained are summarized in Tables S1−S14 in Supporting Information. The plots of k_{obsd} vs nucleophile concentration are linear and pass through the origin, indicating that general base catalysis by a second amine molecule is absent and the contribution of OH^- and/or water to k_{obsd} is negligible. Thus, one can derive eqs 1 and 2, where [S] and [RNH_2] represent the concentration of the substrate and amines used, respectively. The apparent second-order rate constants (k_N) were determined from the slope of the linear plots of k_{obsd} vs amine concentration and are summarized in Table 1. It is estimated from replicate runs that the uncertainty in the rate constants is less than 3%.

TABLE 1. Summary of Apparent Second-Order Rate Constants (k_N, M^{-1} s^{-1}) for the Reaction of 4-Nitrophenyl Phenyl Carbonate (5) and Thionocarbonate (6) with Primary Amines, OH^-, and N_3^- in H_2O Containing 20 mol % DMSO at 25.0 ± 0.1 °C

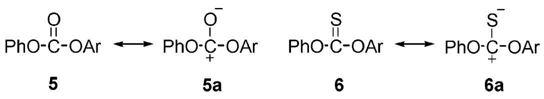
			k_N (M^{-1} s^{-1})	
entry	nucleophile	pK_a	**5**	**6**
1	trifluoroethylamine	5.70[a]	0.00495	0.0335
2	gylcine ethyl ester	7.68	0.620	0.576
3	glycylglycine	8.31	2.30	1.24
4	benzylamine	9.46	14.5	2.22
5	ethanolamine	9.67	18.8	2.98
6	ethylamine	10.67	63.9	4.45
7	propylamine	10.89	61.0	4.86
8	OH^-	15.7	160	5.14
9	N_3^-	4.0	0.258	6.78

[a] The pK_a data for amines in 20 mol % DMSO were taken from ref 3b.

$$\text{rate} = k_N[RNH_2][S] = k_{obsd}[S] \quad \text{where } k_{obsd} = k_N[RNH_2] \tag{1}$$

$$k_N = \frac{k_1k_2}{k_{-1} + k_2} \tag{2}$$

Effect of Replacing C═O by C═S on Reactivity: HSAB Principle. It is generally considered that a C═S bond is more polarizable than a C═O bond, since the overlap between 2p and 3p orbitals in a C═S bond is not as strong as that between 2p and 2p orbitals in a C═O bond. Thus, the contribution of **6a** is expected to be more significant than that of **5a**. This argument is consistent with the ^{13}C NMR spectra for **5** and **6** shown in Supporting Information. The chemical shifts for the carbon atoms of the C═O in **5** and the C═S bond in **6** are 150.7 and 193.4 ppm, respectively. Such a large downfield shift (42.7 ppm) suggests that the carbon atom of the C═S bond in **6** has a greater positive charge than that of the C═O bond in **5**, supporting the preceding argument that the contribution of **6a** outweighs that of **5a**. Thus, one might expect that **6** is more electrophilic and more reactive than **5**.



However, Table 1 shows that **6** is less reactive than **5** except for the reaction with the least basic $CF_3CH_2NH_2$. A similar reactivity trend has recently been reported, i.e., *O*-2,4-dinitrophenyl thionobenzoate is less reactive than its oxygen analogue, 2,4-dinitrophenyl benzoate, toward strongly basic pyridines but more reactive toward weakly basic pyridines.[9] Besides, **2** has been reported to be less reactive than its oxygen analogue **1** in the reactions with strongly basic hydroxide and ethoxide ions.[10] Castro et al. have also demonstrated that bis(4-nitrophenyl) thionocarbonate is less reactive than its oxygen analogue, bis-(4-nitrophenyl) carbonate, toward aryloxides.[8b] A common

---

[8] (a) Hill, S. V.; Thea, S.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1983**, 437−446. (b) Castro, E. A.; Angel, M.; Arellano, D.; Santos, J. G. *J. Org. Chem.* **2001**, *66*, 6571−6575. (c) Castro, E. A.; Pavez, P.; Santos, J. G. *J. Org. Chem.* **2003**, *68*, 3640−3645.

[9] Um, I. H.; Han, H. J.; Baek, M. H.; Bae, S. Y. *J. Org. Chem.* **2004**, *69*, 6365−6370.

[10] Kwon, D. S.; Park, H. S.; Um, I. H. *Bull. Korean Chem. Soc.* **1991**, *12*, 93−97.

feature for the reactivity of these compounds is that the thionocarbonyl compounds are less reactive than their oxygen analogues toward strongly basic amines or oxy anions.

The C═S bond in **6** is considered to be a soft electrophilic center due to the high poarizability of S, whereas the C═O bond in **5** is a hard electrophilic center. The primary amines used in this study have been classified as hard bases on the basis of their strong proton basicity.[11] Thus, the hard amine bases would not exhibit high reactivity toward the soft electrophile **6** on the basis of the hard−soft acids and bases (HSAB) principle. Since the hardness of amines increases with increase in their basicity, one might expect that the rate enhancement accompanied by increasing amine basicity is much less significant for the reactions of the soft electrophile **6** than for those of the hard electrophile **5**. This argument can be supported by the present kinetic results. Table 1 demonstrates that as the amine changes from the least basic $CF_3CH_2NH_2$ ($pK_a = 5.70$) to the most basic $C_3H_7NH_2$ ($pK_a = 10.89$), the k_N value increases from 4.95×10^{-3} to 61.0 M^{-1} s^{-1} for the reactions of **5** and from 3.35×10^{-2} to 4.86 M^{-1} s^{-1} for the reactions of **6**. The increase in the second-order rate constant ($k_N^{C_3H_7NH_2}/k_N^{CF_3CH_2NH_2}$) on increasing the amine basicity (e.g., from 5.70 to 10.89) is 1.2×10^4 for the reaction of **5** but only 1.3×10^2 for the reactions of **6**, i.e., ca. 2 orders of magnitude smaller.

To get further evidence for the preceding argument that **6** would not exhibit high reactivity toward hard nucleophiles, the second-order rate constants have been determined for the reactions of **5** and **6** with OH^- and N_3^- ions, a strongly hard base and a borderline one, respectively. As shown in Table 1, the second-order rate constants for the reactions of OH− ion with **5** and **6** are 160 and 5.14 M^{-1} s^{-1}, respectively, whereas those for the reactions of N_3^- ion with **5** and **6** are 0.258 and 6.78 M^{-1} s^{-1}, respectively. It is noted that **6** is ca. 30 times less reactive than **5** toward the hard base OH^- ion but ca. 25 times more reactive toward the borderline base N_3^- ion. More interestingly, N_3^- is more reactive than the strongly basic propylamine and OH^- in the reaction with **6**, although N_3^- is over 6 and 11 pK_a units less basic than propylamine and OH^-, respectively. It follows from the evidence presented here that the weak interaction between the soft electrophile and the hard amine nucleophiles might be a plausible cause for the current result that **6** exhibits lower reactivity than **5** in the reaction with highly basic amines.

Effect of Replacing C═O by C═S on Mechanism. The effect of amine basicity on the second-order rate constant k_N is illustrated in Figure 1. The Brønsted-type plot for the reaction of **5** exhibits a downward curvature, i.e., β_{nuc} decreases from 0.99 to 0.27 as the amine basicity increases. Such a nonlinear Brønsted-type plot is typical for aminolyses of esters with a good leaving group and has been interpreted as a change in the rate-determining step (RDS) of stepwise reactions, i.e., from breakdown of $T^\pm$ (the k_2 step) to its formation (the k_1 step) as the amine basicity increases.[1,12−14] Thus, one can suggest that the current aminolysis of **5** proceeds through $T^\pm$ with a change in the RDS.

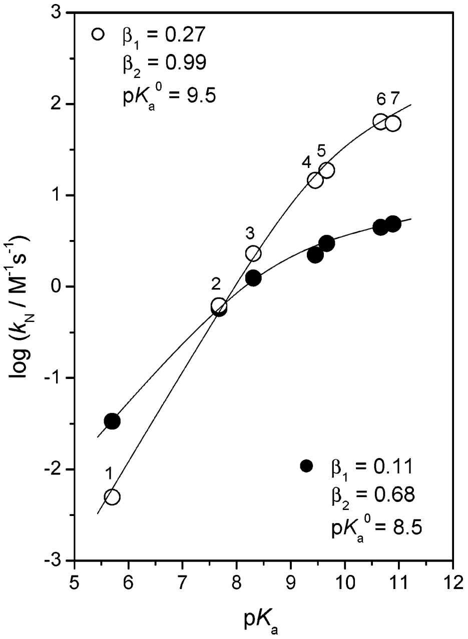


FIGURE 1. Brønsted-type plots for the reactions of **5** (○) and **6** (●) with primary amines in H_2O containing 20 mol % DMSO at 25.0 ± 0.1 °C. The numbers refer to the amines in Table 1. The solid line was calculated by eq 3.

As shown in Figure 1, the Brønsted-type plot for the reaction of **6** is also nonlinear, i.e., β_{nuc} decreases from 0.68 to 0.11 as the amine basicity increases. Since it has often been suggested that the β_{nuc} value should be larger than 0.8 for reactions that proceed through a stepwise mechanism,[15−17] one might insist that the aminolysis of **6** does not proceed through a stepwise mechanism, although the Brønsted-type plot is nonlinear. In fact, Jencks and Castro et al. have attributed such a nonlinear Brønsted-type plot to a normal Hammond effect for a concerted reaction with an earlier transition-state for a more reactive nucleophile.[15,16]

However, the above argument is inconsistent with the stability of the tetrahedral intermediate $T^\pm$. It has generally been reported that $T^\pm$ is less unstable for reactions of thionocarbonyl compounds than for those of carbonyl compounds. This has been attributed to the weaker ability of the C−S− moiety in $T^\pm$ to form a C═S bond and expel the nucleofuge, when compared to the C−O− moiety, due to a weaker π-bonding energy of the thionocarbonyl group relative to the carbonyl group.[8] This argument implies that the lifetime of the tetrahedral intermediate $T^\pm$ is longer for the reactions of **6** than for those of **5**. Thus, the curved Brønsted-type plot obtained for the aminolysis of **6** can be interpreted as a change in the RDS, although β_{nuc} is smaller than 0.8.

---

[11] (a) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed; Harper: New York, 1987; pp 318−320. (b) Pearson, R. G. *J. Am. Chem. Soc.* **1963**, *85*, 3533−3539.

[12] (a) Jencks, W. P. *Chem. Rev.* **1985**, *85*, 511−527. (b) Page, M. I.; Williams, A. *Organic and Bio-organic Mechanisms*; Longman: Harlow, U.K. 1997; Chapter 7.

[13] (a) Lee, I.; Sung, D. D. *Curr. Org. Chem.* **2004**, *8*, 557−567. (b) Oh, H. K.; Lee, J. M.; Sung, D. D.; Lee, I. *Bull. Korean Chem. Soc.* **2004**, *25*, 557−559.

[14] (a) Um, I. H.; Hong, J. Y.; Seok, J. A. *J. Org. Chem.* **2005**, *70*, 1438−1444. (b) Um, I. H.; Lee, J. Y.; Lee, H. W.; Nagano, Y.; Fujio, M.; Tsuno, Y. *J. Org. Chem.* **2005**, *70*, 4980−4987. (c) Um, I. H.; Kim, K. H.; Park, H. R.; Fujio, M.; Tsuno, Y. *J. Org. Chem.* **2004**, *69*, 3937−3942. (d) Um, I. H.; Chun, S. M.; Chae, O. M.; Fujio, M.; Tsuno, Y. *J. Org. Chem.* **2004**, *69*, 3166−3172. (e) Um, I. H.; Lee, J. Y.; Kim, H. T.; Bae, S. K. *J. Org. Chem.* **2004**, *69*, 2436−2441.

[15] Song, B. D.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 8479−8484. (b) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334−338.

[16] (a) Castro, E. A.; Aguayo, R.; Besselo, J.; Santos, J. G. *J. Org. Chem.* **2005**, *70*, 7788−7791. (b) Castro, E. A.; Santos, J. G.; Tellez, J.; Umana, M. I. *J. Org. Chem.* **1997**, *62*, 6568−6574.

[17] Oh, H. K.; Ku, M. H.; Lee, H. W.; Lee, I. *J. Org. Chem.* **2002**, *67*, 8995−8998.

To support the above argument that the aminolysis of **6** proceeds through $T^{\pm}$, we have performed the reaction of **6** with morpholine, an alicyclic secondary amine. As shown in Figure S1 in Supporting Information, the plot of k_{obsd} vs amine concentration exhibits an upward curvature. Such an upward curvature is definitive evidence for a reaction that proceeds through two intermediates, $T^{\pm}$ and its deprotonated form T^{-}.[3,18] It has been reported that the rate of amine expulsion from $T^{\pm}$ is slower for the reactions with primary amines than for those with isobasic secondary amines.[3b] Accordingly, one can expect that $T^{\pm}$ is more stable for the reaction of **6** with primary amines than for that with morpholine, being consistent with our preceding proposal that the reaction of **6** with primary amines proceeds through $T^{\pm}$ with a change in the RDS.

Microscopic Rate Constants. The nonlinear Brønsted-type plots shown in Figure 1 have been analyzed using a semiempirical equation (eq 3) in which β_1 and β_2 represent the slope of the Brønsted-type plot at the high and low pK_a region, respectively.[19] The curvature center of curved Brønsted-type plots has been defined as $pK_a°$, where $k_{-1} = k_2$.[19] The $k_N°$ refers the k_N value at $pK_a°$. The parameters determined from the fitting of eq 3 to the experimental points are $\beta_1 = 0.27$, $\beta_2 = 0.99$, and $pK_a° = 9.5$ for the reactions of **5**, whereas $\beta_1 = 0.11$, $\beta_2 = 0.68$, and $pK_a° = 8.5$ for the reactions of **6**.

$$\log\left(\frac{k_N}{k_N°}\right) = \beta_2(pK_a - pK_a°) - \log\left[\left(1 + \frac{a}{2}\right)\right]$$
$$\text{where } \log a = (\beta_2 - \beta_1)(pK_a - pK_a°) \quad (3)$$

To obtain more information about the reaction mechanism, the microscopic rate constants involved in the present system have been determined. As discussed above, the RDS of the reactions of **5** and **6** with RNH_2 is considered to change from the k_2 to the k_1 step as the basicity of RNH_2 increases. Therefore, eq 2 can be simplified to eq 4 or 5. Then, β_1 and β_2 can be expressed as eqs 6 and 7, respectively.

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

$$k_N = k_1, \quad \text{when } k_2 \gg k_{-1} \quad (5)$$

$$\beta_1 = \frac{d(\log k_1)}{d(pK_a)} \quad (6)$$

$$\beta_2 = \frac{d(\log k_1 k_2/k_{-1})}{d(pK_a)} = \beta_1 + \frac{d(\log k_2/k_{-1})}{d(pK_a)} \quad (7)$$

Equation 7 can be rearranged as eq 8. Integral of eq 8 from $pK_a°$ to pK_a results in eq 9. Since $k_2 = k_{-1}$ at $pK_a°$, the term $(\log k_2/k_{-1})_{pK_a°}$ is zero. Thus, one can calculate the k_2/k_{-1} ratio for the reactions of **5** and **6** with all the primary amines studied from eq 9 using $\beta_1 = 0.27$, $\beta_2 = 0.99$, and $pK_a° = 9.5$ for the reactions of **5**, and $\beta_1 = 0.11$, $\beta_2 = 0.68$, and $pK_a° = 8.5$ for the reactions of **6**.

TABLE 2. Summary of Microscopic Rate Constant (k_1, M^{-1} s^{-1}) Associated with Reaction of 4-Nitrophenyl Phenyl Carbonate (5) and Thionocarbonate (6) with Primary Amines in H_2O Containing 20 mol % DMSO at 25.0 ± 0.1 °C

			k_1 (M^{-1} s^{-1})	
entry	RNH_2	pK_a	**5**	**6**
1	trifluoroethylamine	5.70	2.70	1.35
2	gylcine ethyl ester	7.68	13.3	2.27
3	glycylglycine	8.31	18.8	2.83
4	benzylamine	9.46	30.0	2.85
5	ethanolamine	9.67	33.0	3.62
6	ethylamine	10.67	73.1	4.71
7	propylamine	10.89	67.1	5.07

TABLE 3. Summary of k_2/k_{-1} Ratios for Reaction of 4-Nitrophenyl Phenyl Carbonate (5) and Thionocarbonate (6) with Primary Amines in H_2O Containing 20 mol % DMSO at 25.0 ± 0.1 °C

			k_2/k_{-1}	
entry	RNH_2	pK_a	**5**	**6**
1	trifluoroethylamine	5.70	0.00184	0.0254
2	gylcine ethyl ester	7.68	0.0489	0.341
3	glycylglycine	8.31	0.139	0.779
4	benzylamine	9.46	0.936	3.53
5	ethanolamine	9.67	1.33	4.64
6	ethylamine	10.67	6.96	17.3
7	propylamine	10.89	10.0	23.0

$$\beta_2 - \beta_1 = \frac{d(\log k_2/k_{-1})}{d(pK_a)} \quad (8)$$

$$(\log k_2/k_{-1})_{pKa} = (\beta_2 - \beta_1)(pK_a - pK_a°) \quad (9)$$

$$k_1 = k_N\left(\frac{k_{-1}}{k_2} + 1\right) \quad (10)$$

Equation 2 can be rewritten as eq 10, which allows one to calculate the k_1 value using the k_N values in Table 1 and the k_2/k_{-1} ratios determined above. The k_1 values and the k_2/k_{-1} ratios calculated in this way are summarized in Tables 2 and 3, respectively.

Table 2 shows that k_1 values are smaller for the reactions of **6** than for those of **5**. This is consistent with the preceding argument that **6** would exhibit a weaker interaction than **5** toward the hard amine bases on the basis of the HSAB principle. As shown in Figure 2, the Brønsted-type plots for the k_1 values are linear. The slope of the linear plots (β_1) is smaller for the reactions of **6** than for those of **5**. This result is also in accord with the argument that the rate enhancement on increasing amine basicity would be much less significant for the reactions of **6** than for those of **5**.

Table 3 shows that the k_2/k_{-1} ratio increases with increasing the amine basicity, i.e., $k_2/k_{-1} < 1$ when $pK_a \leq 9.46$ but $k_2/k_{-1} > 1$ when $pK_a \geq 9.67$ for the reactions of **5**, whereas $k_2/k_{-1} < 1$ when $pK_a \leq 8.31$ but $k_2/k_{-1} > 1$ when $pK_a \geq 9.46$ for the reactions of **6**. Since a change in the RDS occurs at $pK_a°$ where $k_2/k_{-1} = 1$, the k_2/k_{-1} ratios shown in Table 3 are consistent with the proposed mechanism that the RDS of the aminolyses of **5** and **6** changes at pK_a 9.5 and 8.5, respectively.

---

[18] Castro, E. A.; Leandro, L.; Quesieh, N.; Santos, J. G. *J. Org. Chem.* **2001**, *66*, 6130−6135.

[19] (a) Castro, E. A.; Moodie, R. B. *J. Chem. Soc., Chem. Commun.* **1973**, 828−829. (b) Gresser, M. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 6963−6970.

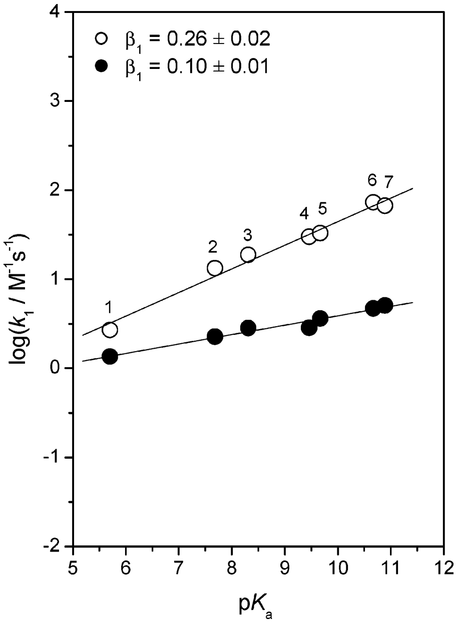


FIGURE 2. Brønsted-type plots for the reactions of **5** (○) and **6** (●) with primary amines in H_2O containing 20 mol % DMSO at 25.0 ± 0.1 °C. The numbers refer to the amines in Table 2.

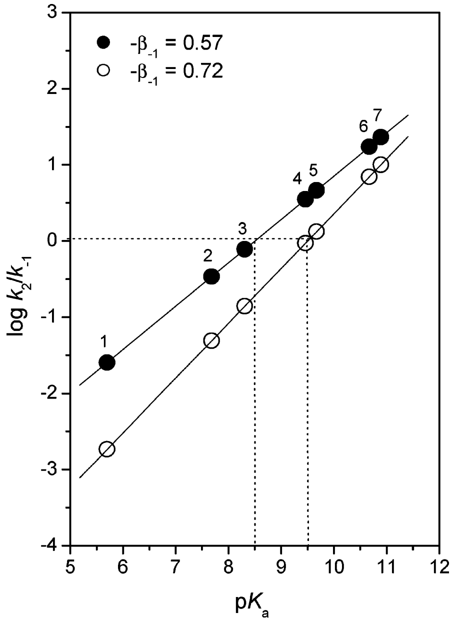


FIGURE 3. Plots of log k_2/k_{-1} vs pK_a of the conjugate acids of amines for the reactions of **5** (○) and **6** (●) with primary amines in H_2O containing 20 mol % DMSO at 25.0 ± 0.1 °C. The numbers refer to the amines in Table 3.

It is noted that the dotted lines in Figure 3 exhibit that the pK_a, where log $k_2/k_{-1} = 0$, is smaller by ca. 1 pK_a unit for the reactions of **6** than for those of **5**. Figure 3 also demonstrates that the k_2/k_{-1} ratio for a given amine is larger for the reaction of **6** than for that of **5**, which is responsible for the smaller pK_a° value determined for the aminolysis of **6** compared to that of **5**. Thus, one can suggest that the replacement of the C═O group in **5** by a C═S bond causes a decrease in pK_a° by increasing the k_2/k_{-1} ratio but does not alter the reaction mechanism.

Conclusions

The present study has allowed us to conclude the following: (1) The reactivity of **5** and **6** is greatly influenced by the basicity and hardness of nucleophiles, i.e., **6** is less reactive than **5** toward strongly basic primary amines and OH$^-$ ion but is more reactive toward the weakly basic trifluoroethylamine and N_3^- ion. (2) The curved Brønsted-type plots obtained from the aminolyses of **5** and **6** indicate that these reactions proceed through a stepwise mechanism with a change in the RDS. (3) The replacement of the C═O bond in **5** by a polarizable C═S group affects the reactivity by decreasing the k_1 value and increasing the k_2/k_{-1} ratio. (4) Such a modification of the electrophilic center does not alter the reaction mechanism but decreases the pK_a° value by increasing the k_2/k_{-1} ratio. (5) The larger k_2/k_{-1} ratio for the reactions of **6** than for those of **5** is responsible for the decreased pK_a° value.

Experimental Section

Materials. 4-Nitrophenyl phenyl carbonate (**5**) and thionocarbonate (**6**) were prepared as reported.[8b,16b,18] Their purity was checked by their melting points and NMR spectra. Amines and other chemicals were of the highest quality available. The reaction medium was H_2O containing 20 mol % dimethyl sulfoxide (DMSO) to eliminate solubility problems. DMSO was distilled over calcium hydride at a reduced pressure and was stored under nitrogen. 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 for slow reactions ($t_{1/2} > 10$ s) or a stopped-flow spectrophotometer for fast reactions ($t_{1/2} \leq 10$ s). The reactions were followed by monitoring the appearance of 4-nitrophenoxide ion at 405 nm. Typically, the reaction was initiated by adding 5 μL of a 0.02 M substrate stock solution in MeCN by a 10 μL syringe to a 10 mm UV cell containing 2.50 mL of the reaction medium and nucleophile. The amine stock solution of ca. 0.2 M was prepared in a 25.0 mL volumetric flask under nitrogen by adding 2 equiv of amine hydrochloride to 1 equiv of standardized NaOH solution to obtain a self-buffered solution. All transfers of solutions were carried out by means of gastight syringes. Concentrations and pseudo-first-order rate constants are summarized in Tables S1−S18 in Supporting Information.

Product Analysis. 4-Nitrophenoxide ion was liberated quantitatively and was identified as one of the products by comparison of the UV−vis spectra after completion of the reactions with those of the authentic sample under the same kinetic conditions.

Acknowledgment. This work was supported by a grant from KOSEF of Korea (R01-2004-000−10279−0).

Supporting Information Available: ^{13}C NMR spectra for **5** and **6**; kinetic data for reactions of **5** and **6** with seven primary amines and two anionic nucleophiles OH$^-$ and N_3^- ions (Table S1−S18); a plot of k_{obsd} vs amine concentration for the reaction of **6** with morpholine (Figure S1). This material is available free of charge via the Internet at http://pubs.acs.org.

JO052417Z