Kinetics and mechanism of the aminolysis of ethyl aryl carbonates in acetonitrile

Han Joong Koh, Ji-Won Lee, Hai Whang Lee, and Ikchoon Lee

Abstract: The aminolysis reactions of ethyl aryl carbonates with benzylamines in acetonitrile at 25.0°C are investigated. The base-catalyzed path, k_2, disappears when strong nucleophiles (X = p-CH_3O and p-CH_3) react with a substrate activated by a strong nucleofuge (Z = p-NO_2). The large magnitude of ρ_x (–1.7 to –2.5), ρ_z (3.4 to 4.3), and ρ_{xz} (1.4) values, and relatively large k_H/k_D (1.6 to 1.8) found for the uncatalyzed path (k_1) can be accounted for in terms of a stepwise mechanism with rate-limiting expulsion of the phenoxide leaving group. The catalyzed process (k_2) is characterized by the much smaller magnitude of ρ_x (–1.0 to –1.7), ρ_z (0.4 to 0.7), and ρ_{xz} (0.2), the larger k_H/k_D (2.1 to 2.5) values, and the lower $\Delta H^\ddagger$ values (1.8–1.9 kcal mol^{-1}) than those of the uncatalyzed process (k_1) with large negative $\Delta S^\ddagger$ values (–65 to –67 cal K^{-1} mol^{-1}). These results are consistent with four- and six-centered transition states for the two processes, k_1 and k_2, respectively.

Key words: ethyl aryl carbonates, aminolysis mechanism, base catalysis, stepwise mechanism, cross-interaction constant.

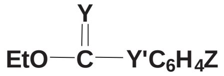
Résumé : On a étudié les réactions d'aminolyse des carbonates d'éthyle et d'aryle par les benzylamines, dans l'acétonitrile, à 25,0°C. La voie réactionnelle catalysée par les bases, k_2, disparaît lorsque des nucléophiles forts (X = p-CH_3O et p-CH_3) réagissent avec un substrat activé par un groupe fortement nucléofuge (Z = p-NO_2). Pour expliquer la grande amplitude des valeurs de ρ_x (de –1,7 à –2,5), ρ_z (3,4 à 4,3) et de ρ_{xz} (1,4) ainsi que de la valeur relativement importante observée pour k_H/k_D (1,6 à 1,8) observées pour la voie non catalysée, on peut imaginer un mécanisme par étapes impliquant une expulsion cinétiquement limitante du groupe phénolate partant. Le processus catalysé (k_2) est caractérisé par des amplitudes beaucoup plus faibles de ρ_x (de –1,0 à –1,7), ρ_z (0,4 à 0,7) et de ρ_{xz} (0,2), des valeurs beaucoup plus élevées de k_H/k_D (2,1 à 2,5) et des valeurs de $\Delta H^\ddagger$ (1,8 à 1,9 kcal mol^{-1}) beaucoup plus faibles que celles observées pour le processus non catalysé (k_1) avec des valeurs de $\Delta S^\ddagger$ très négatives (–65 à –67 cal K^{-1} mol^{-1}). Ces résultats sont en accord avec des états de transition à quatre et à six centres respectivement pour les deux processus k_1 et k_2.

Mots clés : carbonates d'éthyle et d'aryle, mécanisme d'aminolyse, catalyse par les bases, mécanisme par étape, constante d'interaction de croisement.

[Traduit par la rédaction]

Introduction

Aminolyses of sulfur analogs of ethyl aryl carbonates, **2**–**4** (1–4) have been shown to exhibit interesting mechanistic variations depending on sulfur substitution for oxygen and the reaction medium used. In the aminolysis of thiono compounds, **3** (3), a weaker π-bonding energy of the thio carbonyl (C=S) compared to the carbonyl (C=O) leads to the difficulty in forming the C=S bond to expel the nucleofuge, which results in a lowering of the nucleofugality (k_b in Scheme 1) of ArO^-. The change of O^- by S^- in $\mathbf{T}^\pm$ brings about therefore a mechanistic change in aqueous solution to a complex one in which the deprotonation step, k_d, can compete with k_{-a} and k_b (Scheme 1). The increased leaving ability (larger k_b) by introducing nitro groups (**3b**–**3d**) or suppressed proton transfer rate (smaller $k_d[RNH_2]$) by using an aprotic medium (5*a*) can, however, restore the mechanism to a simple rate-limiting breakdown (k_b) of the tetrahedral intermediate, $\mathbf{T}^\pm$, which is



$EtO{-}C({=}Y){-}Y'C_6H_4Z$

1 Y = Y′ = O (**a**) Z = H
2 Y = O, Y′ = S (**b**) Z = 4-NO_2
3 Y = S, Y′ = O (**c**) Z = 2,4-(NO_2)
4 Y = Y′ = S (**d**) Z = 2,4,6-$(NO_2)_3$

commonly observed in most of the aminolysis reactions of esters and carbonates (5). On the other hand, in the aminolysis of thiol compounds, **2** (2), the ethoxy group apparently destabilizes $\mathbf{T}^\pm$ and is known to enforce a concerted mechanism as a result of the enhanced leaving ability of 2,4-dinitro-, **2c**, and 2,4,6-trinitro-thiophenoxides, **2d** (relative to the corresponding phenoxides). This mechanistic change from a stepwise mechanism for oxyesters and oxycarbonates to a concerted mechanism for the thiol carbonate (**2**) has not been observed with acetates (EtO replaced by Me) (6), methyl aryl carbonates (EtO replaced by MeO) (3*b*), and benzoates (EtO replaced by Ph, in **1**–**4**) (7). The aminolyses of dithio (**4**) derivatives were

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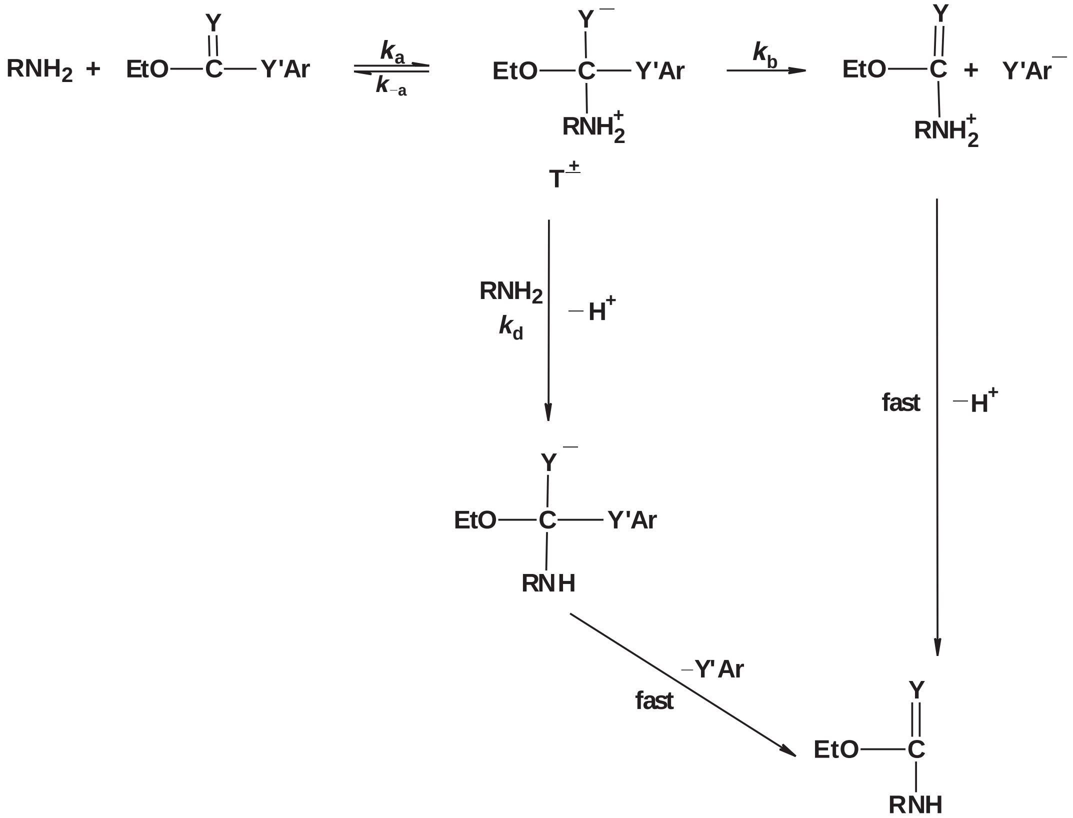
Scheme 1.



found, in general, to proceed by mechanisms similar to those for the thiono (**3**) series (4).

In this work, we carried out kinetic studies of the aminolysis of ethyl aryl carbonates, **1**, with benzylamines (BA, $XC_6H_4CH_2NH_2$) in acetonitrile at 25.0°C. We varied substituents X (X = p-CH_3O, p-CH_3, H, p-Cl, and m-Cl) in the nucleophile and Z (Z = m-NO_2, p-$COCH_3$, p-Cl + m-NO_2, p-CN, and p-NO_2) in the nucleofuge to probe the transition state (**TS**) structure through structure–reactivity correlation involving the cross-interaction constant, ρ_{XZ} in eqs. [1] (8). Our previous studies have shown that the sign and magnitude of ρ_{XZ} provide valuable mechanistic information (8).

$$[1a] \quad \log(k_{XZ}/k_{HH}) = \rho_X\sigma_X + \rho_Z\sigma_Z + \rho_{XZ}\sigma_X\sigma_Z$$

$$[1b] \quad \rho_{XZ} = \frac{\partial^2 \log k_{XZ}}{\partial \sigma_X \partial \sigma_Z} = \frac{\partial \rho_Z}{\partial \sigma_X} = \frac{\partial \rho_X}{\partial \sigma_Z}$$

In this work, we aim to test whether or not there is any mechanistic variation found in the aminolysis of thiono (**3**) and (or) thiol (**2**) derivatives, and to characterize the **TS** structure by determining the cross-interaction constant, ρ_{XZ}, and the secondary kinetic isotope effects (SKIEs) involving deuterated nucleophiles ($XC_6H_4CH_2ND_2$) (9).

Results and discussion

For all the carbonates investigated, solvolysis was not observed under the reaction conditions. The rates were measured with amine excesses, [BA] = 0.018–0.430 M and [Substrate] ≅ 1 × 10^{-4} M, and pseudo-first-order rate constants (k_{obs}) were obtained at more than 10 amine concentrations, Figs. 1 and 2. The plots of k_{obs} versus amine concentration, [BA], were linear, eq. [2], for the reactions of substrate with a strong electron acceptor, Z = p-NO_2, and nucleophile with a strong electron donor, X = p-CH_3O and p-CH_3, Fig. 1.

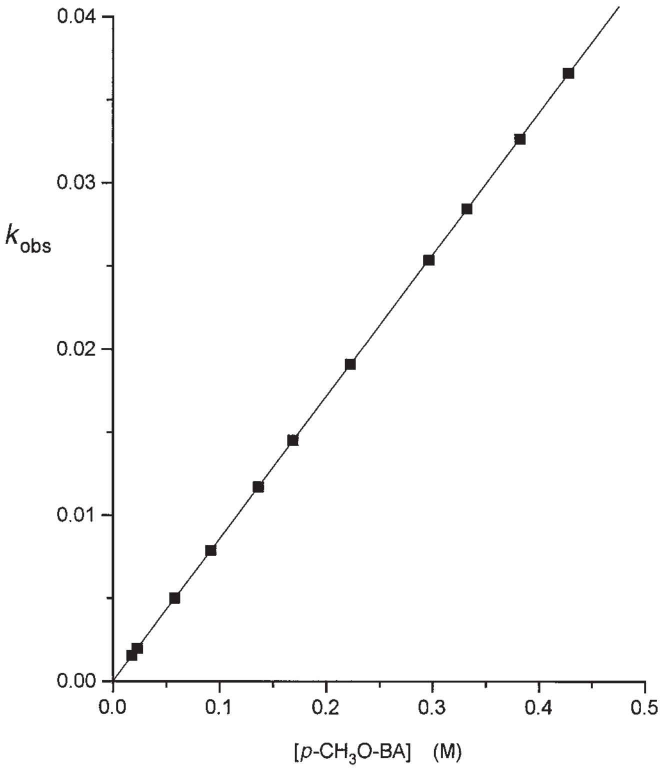
$$[2] \quad k_{obs} = k_1[BA]$$

For all other reactions, the plots were curvilinear, which can be fitted to a second-order equation in benzylamine concentration, eq. [3] and Fig. 2.

$$[3] \quad k_{obs} = k_1[BA] + k_2[BA]^2$$

Because of this second-order term, accurate determinations of the rate constants, k_1 and k_2, required more than 10 k_{obs} data with varied amine concentrations. Plots of k_{obs}/[BA] versus [BA] gave k_1 and k_2 as the intercepts and slopes of the straight line. The k_1 and k_2 values obtained are summarized in Tables 1 and 2. The catalytic rate constants, k_2, are ca. 2 (X = m-Cl, Z = p-NO_2) to 170 (X = m-Cl, Z = m-NO_2) times greater than the corresponding uncatalyzed rate constants, k_1; this comparison is unjustified since k_1 and k_2 have different units, but we are making only numerical comparisons with other similar results reported. Similar trends are reported for the reactions of p-Cl-phenyl acetates with pyrrolidine (10) and for the reactions of phenyl phenoxyacetates with benzylamines (5d) in acetonitrile at 25.0°C. For the aminolysis of p-nitrophenyl acetates the k_2 term was absent, but both k_1 and k_2 terms were observed for chloro- and dichloroacetates in acetonitrile (11). This should be an indication that a strong acceptor aryl moiety (the Taft σ^* values for CH_3, CH_2Cl, $CHCl_2$, $CH_2OC_6H_5$, and C_2H_5O are

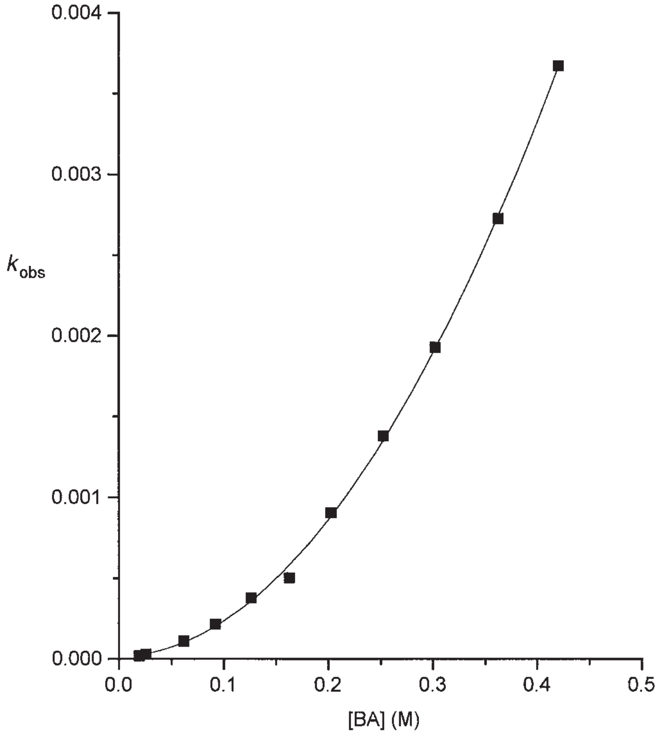
Fig. 1. The plot of k_{obs} vs. concentration of *p*-methoxybenzylamine for the reaction of ethyl *p*-nitrobenzyl carbonate in MeCN at 25.0°C.



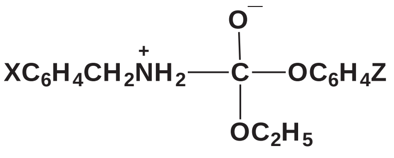
0.0, 1.05, 1.94, ca. 1.0, and 1.68, respectively) (5*d*, 12) requires general base catalysis, especially in aprotic solvents. Moreover, it has been well established that electron withdrawal from the acyl carbon favors amine expulsion relative to the negatively charged phenoxide expulsion from a tetrahedral intermediate, $\mathbf{T}^{\pm}$ (1*c*, 1*d*, 13). The results of the present work also show that the aminolysis of esters and carbonates can proceed without base catalysis even in aprotic solvents if the nucleophile and (or) nucleofuge are strong, i.e., for a strong donor X coupled with a strong acceptor Z. This is evident from the rate ratio (k_2/k_1) changes with the substituents X and Z. The k_2/k_1 ratio becomes smaller as the electron donor ability of X and acceptor power of Z increase: the k_2/k_1 values are 170, 32.4, 6.4, and 2.4 for X = *m*-Cl, Z = *m*-NO_2; X = *p*-Cl, Z = *p*-$COCH_3$; X = *p*-CH_3, Z = *p*-Cl + *m*-NO_2; and X = *p*-CH_3O, Z = *p*-CN, respectively, eventually reaching zero for X = *p*-CH_3O (and *p*-CH_3) with Z = *p*-NO_2. Thus when the aminolysis rate reaches a sufficiently large value by reacting a strong nucleophile with a strong nucleofuge, the base catalysis becomes redundant.

The Hammett ρ and Brönsted β values are listed in Tables 1 and 2. Examination of Table 1 reveals that magnitudes of ρ_X, ρ_Z, β_X, and β_Z values for the uncatalyzed path, k_1, are large and are much greater than the corresponding values for the catalyzed path (k_2). The large magnitudes of ρ_X (β_X) and ρ_Z (β_Z) are indicative of a stepwise mechanism with rate-limiting breakdown of a zwitterionic tetrahedral intermediate, $\mathbf{T}^{\pm}$ (1–5, 13). The importance of expulsion of the leaving group is reflected in the better Hammett correlations with σ_z^- than with σ_Z and in the large magnitude of ρ_Z, which suggests a strong negative charge development in the phenoxide leaving group.

Fig. 2. The plot of k_{obs} vs. concentration of benzylamine for the reaction of ethyl *m*-nitrobenzyl carbonate in MeCN at 25.0°C



For this mechanism, $k_1 = (k_a/k_{-a}) \times k_b = K\cdot k_b$. Such large ρ_z^- values reflect the importance of leaving group expulsion in the rate-determining step and are commonly found for the stepwise mechanism involving rate-limiting breakdown of $\mathbf{T}^{\pm}$. In acylation, when leaving group departure is kinetically important, substituent changes in leaving groups have a larger effect than do equivalent changes in the remaining group. Although β_X and β_Z values are also listed in Tables 1 and 2, they are less reliable since the pK_a values in water are used in the correlation instead of those in acetonitrile. However, the relative pK_a values ($\Delta pK_a = pK_{CH_3CN} - pK_{H_2O}$) remain constant for various conjugate acids of amines so that the solvent effect on β_X may be small (5*c*). The values of β_Z may be significantly smaller than those reported on the basis of aqueous acidities. We note that both ρ_X and ρ_Z are considerably greater in magnitude than the corresponding values for the reactions reported to proceed by rate-limiting breakdown of $\mathbf{T}^{\pm}$ (2*c*, 3*b*, 4*c*, 4*d*). Another strong support for the proposed mechanism comes from a large positive cross-interaction constant ρ_{XZ} (= 1.35): both the positive sign and the large magnitude of ρ_{XZ} have been shown to be the necessary conditions for the rate-limiting breakdown of $\mathbf{T}^{\pm}$ (8, 9, 13). Since an electron acceptor in the nucleophile, $\delta\sigma_X > 0$ (in the nucleofuge, $\delta\sigma_Z > 0$), leads to an increase in ρ_Z, $\delta\rho_Z >$



$$XC_6H_4CH_2\overset{+}{N}H_2\text{—}\underset{\underset{OC_2H_5}{|}}{\overset{\overset{O^-}{|}}{C}}\text{—}OC_6H_4Z$$

$\mathbf{T}^{\pm}$

Table 1. Second-order rate constants, k_1 ($\times 10^3$ dm^3 mol^{-1} s^{-1}), for the reactions of ethyl aryl carbonates with X-benzylamines in acetonitrile at 25.0°C.

	Z						
X	m-NO$_2$	p-OCH_3	p-Cl + m-NO$_2$	p-CN	p-NO$_2$	$\rho_Z{}^c$	$\beta_Z{}^d$
p-CH$_3$O	1.10 2.52^a 5.77^b	3.89	7.41	13.8	85.7	3.40	–1.22
p-CH$_3$	0.589	2.75	4.47	0.47	58.9	3.50	–1.58
H	0.17	0.813	1.58	2.24	24.5	3.81	–1.71
p-Cl	0.0575	0.275	0.525	0.933	11.8	4.12	–1.82
m-Cl	0.0295	0.138	0.269	0.477 1.02^a 2.34^b	7.24	4.26	–1.90
$\rho_X{}^e$	–2.47	–2.33	–2.27	–2.26	–1.69	$\rho_{XZ} = 1.35^g$	
$\beta_X{}^f$	2.38	2.37	2.25	2.09	1.66		

[a] At 35.0°C.

[b] At 45.0°C.

[c] The σ-values were taken from ref. 21. Correlation coefficients were better than 0.997 in all cases.

[d] The pK_a (H$_2$O, 25.0°C) values were taken from ref. 22. Correlation coefficients were better than 0.974 in all cases. Z = p-COCH$_3$ and p-Cl and m-NO$_2$ were excluded.

[e] The σ values were taken from ref. 23. Correlation coefficients were better than 0.993 in all cases.

[f] The pK_a (H$_2$O, 25.0°C) values were taken from ref. 24. Correlation coefficients were better than 0.992 in all cases. X = p-CH$_3$O was excluded from the Brönsted plot for β_X (benzylamine) due to unreliable pK_a value listed.

[g] Correlation coefficient was better than 0.997.

Table 2. Third-order rate constants, k_2 ($\times 10^2$ dm^6 mol^{-2} s^{-1}), for the reactions of ethyl aryl carbonates with X-benzylamines in acetonitrile at 25.0°C.

	Z					
X	m-NO$_2$	p- COCH$_3$	p-Cl + m-NO$_2$	p-CN	p-NO$_2$	$\rho_Z{}^c$
p-CH$_3$O	2.14 2.43^a 2.76^b	2.75	3.16	3.38	—	0.70
p-CH$_3$	1.91	2.51	2.88	3.16	—	0.77
H	1.22	1.50	1.66	1.76	7.93	0.56
p-Cl	0.708	0.891	1.02	1.13	3.61	0.69
m-Cl	0.501	0.575	0.631	0.664 0.757^a 0.863^b	1.76	0.44
$\rho_X{}^d$	–1.02	–1.08	–1.11	–1.11	–1.73	$\rho_{XZ} = 0.16^f$
$\beta_X{}^e$	1.08	1.16	1.18	1.19	1.71	

[a] At 35.0°C.

[b] At 45.0°C.

[c] The σ^- values were taken from ref. 21. Correlation coefficients were better than 0.995 in all cases.

[d] The σ values were taken from ref. 23. Correlation coefficients were better than 0.944 in all cases.

[e] The pK_a (H$_2$O, 25.0°C) values were taken from ref. 24. Correlation coefficients were better than 0.990 in all cases. X = p-CH$_3$O was excluded from the Brönsted plot for β_X (benzylamine) due to unreliable pK_a value listed.

[f] Correlation coefficient was better than 0.971.

0 ($\delta\rho_X > 0$), ρ_{XZ} is positive, eq. [1b]. Since the rate increase is invariably accompanied by a decrease in the magnitude of ρ (ρ_X or $\rho_z{}^-$), the reactivity–selectivity principle (RSP) holds (14). Adherence to the RSP is considered another criterion for the stepwise mechanism with rate-limiting expulsion of the leaving group (phenoxides) (14).

For the third-order process, k_2, the RSP is violated and the ρ_X, $\rho_z{}^-$, and ρ_{XZ} values are considerably smaller in magnitude than the corresponding values for the uncatalyzed path (k_1). These can be accommodated with a rate-limiting deprotonation mechanism, $k_2 = (k_a/k_{-a})\cdot k_d[\mathrm{RNH_2}]$ in Scheme 1. In this case, deprotonation of $\mathbf{T}^{\pm}$ leads to a decrease in the positive charge on the N atom (decrease in the magnitude of ρ_X) and also to a small increase in the negative charge on the O atom (small positive $\rho_z{}^-$) in the intermediate. Since the magnitudes of both ρ_X and $\rho_z{}^-$ are reduced to much smaller values, the cross-interaction constant ρ_{XZ} also decreases to a smaller value than that for the uncatalyzed process, k_1.

Secondary kinetic isotope effects involving deuterated benzylamine nucleophiles are summarized in Tables 3 and 4. The k_H/k_D values in Table 3 are all greater than 1.0. This is consistent with the stepwise mechanism proposed (5d, 7b, 15), k_1 =

Table 3. Kinetic isotope effects on the second-order rate constants (k_1) for the reactions of ethyl aryl carbonates with deuterated X-benzylamines ($XC_6H_4CH_2ND_2$) in acetonitrile at 25.0°C.

X	Z	k_H($\times 10^3$ dm^3 mol^{-1} s^{-1})	k_D($\times 10^3$ dm^3 mol^{-1} s^{-1})	k_H/k_D
p-CH_3O	m-NO_2	1.10±0.03[a]	0.705±0.006	1.56±0.04[a]
p-CH_3O	p-$COCH_3$	3.89±0.04	1.82±0.03	1.59±0.03
p-CH_3O	p-CN	13.8±0.3	8.52±0.06	1.62±0.04
p-CH_3O	p-NO_2	85.7±0.6	50.7±0.3	1.69±0.02
m-Cl	m-NO_2	0.0295±0.0004	0.0178±0.0006	1.66±0.05
m-Cl	p-$COCH_3$	0.138±0.003	0.0812±0.0004	1.70±0.04
m-Cl	p-CN	0.447±0.006	0.254±0.003	1.76±0.03
m-Cl	p-NO_2	7.24±0.06	4.07±0.04	1.78±0.02

[a] Standard deviation.

Table 4. Kinetic isotope effects on the second-order rate constants (k_2) for the reactions of ethyl aryl carbonates with deuterated X-benzylamines ($XC_6H_4CH_2ND_2$) in acetonitrile at 25.0°C.

X	Z	k_H($\times 10^2$ dm^6 mol^{-2} s^{-1})	k_D($\times 10^2$ dm^6 mol^{-2} s^{-1})	k_H/k_D
p-CH_3O	m-NO_2	2.14±0.03[a]	1.02±0.02	2.10±0.04[a]
p-CH_3O	p-$COCH_3$	2.75±0.03	1.97±0.03	1.97±0.04
p-CH_3O	p-CN	3.38±0.05	1.90±0.02	1.90±0.04
m-Cl	m-NO_2	0.501±0.004	0.197±0.003	2.54±0.05
m-Cl	p-$COCH_3$	0.575±0.005	0.246±0.006	2.40±0.07
m-Cl	p-CN	0.664±0.004	0.284±0.003	2.34±0.02
m-Cl	p-NO_2	1.76±0.07	0.782±0.006	2.25±0.09

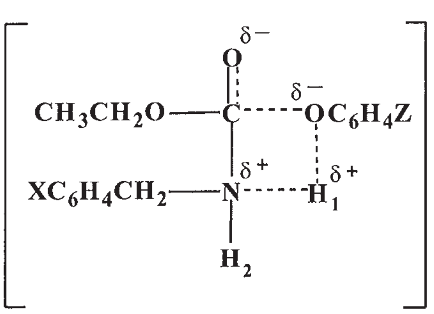
[a] Standard deviation.

Table 5. Activation parameters[a] for the reaction of ethyl aryl carbonates with X-benzylamines in acetonitrile at 25.0°C.

X	Z	Reaction path	$\Delta H^{\ddagger}$(kcal mol^{-1})	$-\Delta S^{\ddagger}$(cal mol^{-1} K^{-1})
p-CH_3O	m-NO_2	k_1	15.0±0.3	17±1
m-Cl	p-CN	k_1	14.4±0.7	21±2
p-CH_3O	m-NO_2	k_2	1.78±0.03	64.8±0.1
m-Cl	p-CN	k_2	1.85±0.04	66.9±0.1

[a] Calculated by the Eyring equation. Errors shown are standard deviations.

$(k_a/k_{-a})\cdot k_b = K\cdot k_b$. In this mechanism, the H-N-H moiety becomes sterically relieved in the rate-determining step of the leaving-group departure from $\mathbf{T}^{\pm}$. This will cause the decrease in the N–H vibration frequencies and the k_H/k_D values become greater than 1. In the equilibrium step, the effects of k_a and k_{-a} on the N–H vibrational frequencies approximately cancel out, leading to a k_H/k_D value of approximately 1.0 in the complex quantity of $k_1 = K\cdot k_b$ (5*d*, 7*b*, 15). We note, however, that the magnitude of the secondary kinetic isotope effects in Table 3 is somewhat larger with k_H/k_D = 1.6–1.8 than that found (k_H/k_D = 1.0–1.2) in most of the acyl transfer reactions (5*d*, 7*b*, 15) proceeding by a similar mechanism. We therefore suggest that there is weak deprotonation taking place through a four-center type **TS** (16), **5**. The cyclic proton transfer in **5** not only provides charge



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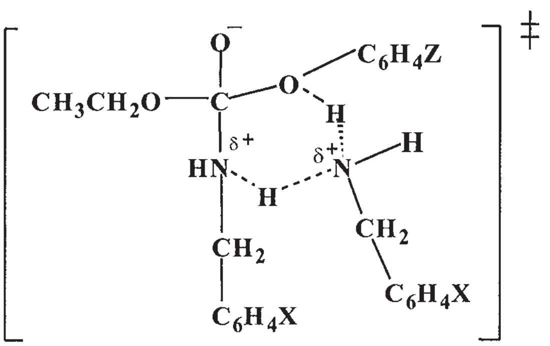

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dispersion, but it also assists leaving-group departure (17). This assistance is particularly important in the second-order path, k_1, when the (aprotic) solvent cannot assist by hydrogen bonding (17).

For the catalyzed path, the k_H/k_D values are further increased to 2.0–2.5, reflecting correctly the partial bond cleavage of the N—H(D) bond in the rate-determining step, $k_d[RNH_2]$ in Scheme 1. Among several conceivable **TS** structures for the catalyzed path, the cyclic hydrogen bonded structure, **6**, is considered to be the most likely candidate. The larger k_H/k_D and smaller ρ_z^-, ρ_X, and ρ_{XZ} values for **6** than for **5** can be explained as follows. Two hydrogen bonds are involved so that k_H/k_D should increase, but positive charge on N and negative charge on O should be partially offset by partial deprotonation from N and partial protonation on O. The decrease in the two ρ values, ρ_X and ρ_z^-, should result in a substantial decrease in the intensity of interaction leading to a large decrease in the ρ_{XZ} values (18). The trends of change in the magnitude of k_H/k_D in Tables 3 and 4 are also in line with our proposed **TS** structures, **5** and **6**. In structure **5**, the greater the leaving ability ($\delta\sigma_Z > 0$) of the phenoxide, the greater will be the extent of deprotonation and consequently the larger is the k_H/k_D value (Table 3). However, in **6**, the stronger the electron acceptor in the phenoxide ($\delta\sigma_Z > 0$), the less will be the negative charge on O due to the greater delocalization, and hence the weaker is the hydrogen bond between O and the catalyst amine nitrogen. Thus the k_H/k_D value will decrease as the electron-withdrawing power of Z increases (Table 4). In both structures, an electron acceptor X ($\delta\sigma_X > 0$) should increase the acidity of a substituted benzylammonium cation, i.e., deprotonation becomes more facile, so that k_H/k_D increases.

The proposed mechanism is also supported by the activation parameters (Table 5) determined from rate data at three temperatures, 25.0, 35.0, and 45.0°C. The relatively low positive $\Delta H^\ddagger$ and large negative $\Delta S^\ddagger$ values are in accord with the stepwise mechanism proposed (11, 19). For the catalyzed path, the $\Delta H^\ddagger$ values are lower than those for the uncatalyzed path and the $\Delta S^\ddagger$ values are large and negative. This is consistent with a simple proton transfer process involved in **TS 6**, where there is a two-proton bridge that is highly structured but very little energy will be required for the deprotonation.

In summary, the aminolysis of ethyl aryl carbonates in acetonitrile proceeds by a stepwise mechanism with rate-limiting expulsion of the phenoxide leaving group from the zwitterionic tetrahedral intermediate, $\mathbf{T}^\pm$. Two reaction pathways, catalyzed and uncatalyzed paths, compete in most of the reactions; base catalysis is not required for the reactions involving strong nucleophiles (X = p-CH_3O, p-CH_3) with a strong nucleofuge (Z = p-NO_2). The proposed mechanism is based on (*i*) the large magnitude of ρ_X and especially of ρ_z^-, (*ii*) the relatively large normal kinetic isotope effects ($k_H/k_D > 1.0$) involving a deuterated benzylamine nucleophile, (*iii*) the greater k_H/k_D values for the catalyzed path, and (*iv*) the low $\Delta H^\ddagger$ and $\Delta S^\ddagger$ values for both pathways, but with lower values for the base-catalyzed path than for the uncatalyzed reaction.

Experimental

Materials

Merck GR acetonitrile was used after three distillations. The benzylamine nucleophiles, Aldrich GR, were used without further purification. Preparation of deuterated benzylamines was as described previously (5). The analysis (NMR and GC mass spectroscopy) of the deuterated benzylamines showed more than 99% deuterium content, so that no corrections to kinetic isotope effects for incomplete deuteration were made. Ethyl aryl carbonates were prepared by reacting phenols with ethyl chloroformates. The substrates synthesized were confirmed by IR, NMR, and mass spectral analyses as follows.

$CH_3CH_2OC(O)OC_6H_4$–p-*CN*: mp 40–42°C. ν_{max}: 3100 (C-H), 3000 (C-H, aromatic), 2250 (C≡N), 1760 (C═O). $\delta_H(CDCl_3)$: 7.2–7.7 (C_6H_4, 4H, m), 4.3 (CH_2, 2H, q), 1.3 (CH_3, 3H, t). m/z = 119 (M^+).

$CH_3CH_2OC(O)OC_6H_4$–p-$COCH_3$: mp 44–45°C. ν_{max}: 3100 (C-H), 3000 (C-H, aromatic), 1750 (C═O), 1680 ($COCH_3$). $\delta_H(CDCl_3)$: 7.2–8.0 (C_6H_4, 4H, m), 4.3 (CH_2, 2H, q), 2.6 ($COCH_3$, 3H, s), 1.3 (CH_3, 3H, t). m/z = 208 (M^+).

$CH_3CH_2OC(O)OC_6H_4$–m-NO_2: mp 50–52°C. ν_{max}: 3100 (C-H), 3000 (C-H, aromatic), 1750 (C═O), 1680 ($COCH_3$). $\delta_H(CDCl_3)$: 7.3–8.1 (C_6H_4, 4H, m), 4.3 (CH_2, 2H, q), 1.2 (CH_3, 3H, t). m/z = 208(M^+).

$CH_3CH_2OC(O)OC_6H_3$–(p-*Cl*, m-NO_2): liquid. ν_{max}: 3100 (C-H), 3000 (C-H, aromatic), 1760 (C═O). $\delta_H(CDCl_3)$: 7.2–7.7 (C_6H_3, 3H, m), 4.2–4.4 (CH_2, 2H, q), 1.3 (CH_3, 3H, t). m/z = 245 (M^+).

$CH_3CH_2OC(O)OC_6H_4$–p-NO_2: mp 60–61°C. ν_{max}: 3100 (C-H), 3000 (C-H, aromatic), 1750 (C═O). $\delta_H(CDCl_3)$: 7.3–8.3 (C_6H_4, 4H, m), 4.2 (CH_2, 2H, q), 1.2 (CH_3, 3H, t). m/z = 211 (M^+).

Kinetic procedures

Rates were measured conductimetrically in acetonitrile. The conductivity bridge used in this work was a homemade computer-automatic A/D converter conductivity bridge. Pseudo-first-order rate constants, k_{obs}, were determined by the Guggenheim (20) method with a large excess of benzylamine. The k_1 and k_2 values were reproducible to ± 5%.

Product analysis

Ethyl *p*-nitrobenzyl carbonate was reacted with excess benzylamine with stirring for more than 15 half-lives at 25.0°C in acetonitrile, and the products were isolated by evaporating the solvent under reduced pressure. The product mixture was treated with column chromatography (silica gel, 20% ethyl acetate – n-hexane). Analysis of the product gave the following results.

$CH_3CH_2OC(O)NHCH_2C_6H_5$: Liquid. ν_{max}: 3300 (N-H), 3000 (C-H, aromatic), 1700 (C═O). $\delta_H(CDCl_3)$: 7.2–7.5 (C_6H_5, 5H, m), 5.2 (NH, 1H, s), 4.2 (CH_2, 2H, q), 4.4 (CH_2, 2H, s), 1.2 CH_3, 3H, t). m/z = 227 (M^+).

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