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Evidence for a Catalytic Six-Membered Cyclic Transition State in Aminolysis of 4-Nitrophenyl 3,5-Dinitrobenzoate in Acetonitrile: Comparative Brønsted-Type Plot, Entropy of Activation, and Deuterium Kinetic Isotope Effects

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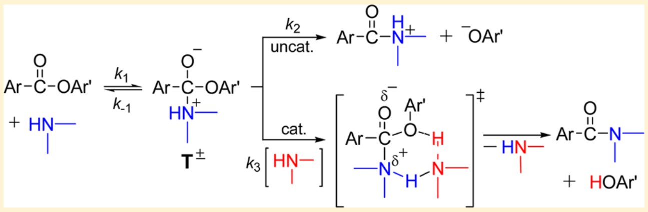
S Supporting Information



ABSTRACT: A kinetic study for reactions of 4-nitrophenyl 3,5-dinitrobenzoate (**1a**) with a series of cyclic secondary amines in acetonitrile is reported. Plots of the pseudo-first-order rate constant (k_{obsd}) vs [amine] curve upward, while those of k_{obsd} /[amine] vs [amine] exhibit excellent linear correlations with positive intercepts, indicating that the reaction proceeds through both uncatalyzed and catalyzed routes. Brønsted-type plots for uncatalyzed and catalyzed reactions are linear with β_{nuc} = 1.03 and 0.69, respectively. The $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values measured for the catalytic reaction with morpholine are −0.80 kcal/mol and −61.7 cal/(mol K), respectively. The negative $\Delta H^{\ddagger}$ with a large negative $\Delta S^{\ddagger}$ suggests that the reaction proceeds through a highly ordered transition state (i.e., a six-membered cyclic transition state, which includes a second amine molecule that accepts a proton from the aminium moiety of the zwitterionic tetrahedral intermediate and simultaneously donates a proton to the aryloxyl oxygen of the nucleofuge with concomitant C−OAr bond scission). This proposal is consistent with the smaller β_{nuc} value for the catalyzed reaction as compared to the uncatalyzed reaction. An inverse deuterium kinetic isotope effect (DKIE) value of 0.93 and a contrasting normal primary DKIE value of 3.23 for the uncatalyzed and catalyzed routes, respectively, also support the proposed cyclic transition state.

■ INTRODUCTION

Nucleophilic substitution reactions of esters with amines have been the subject of extensive experimental and theoretical studies, not least due to their importance in biological processes (e.g., enzyme action and peptide biosynthesis) but also in synthetic applications.[1−10] Experimental studies based on linear free energy relationships (LFERs) have reported that aminolysis of carboxylic esters proceeds through a concerted mechanism or via a stepwise pathway depending on the reaction conditions (e.g., the nature of the reaction medium and electrophilic center, the basicity of the incoming amine and leaving group, etc.).[2−5] A curved or biphasic Brønsted-type plot, often observed in aminolysis of esters possessing a weakly basic leaving group (e.g., 2,4-dinitrophenoxide), has been taken as evidence for a stepwise mechanism with a change in the rate-determining step (RDS).[2−5] Recent theoretical studies have advanced three different mechanistic regimes: (1) a concerted mechanism, (2) a stepwise mechanism with a neutral tetrahedral intermediate, and (3) a stepwise mechanism with a zwitterionic tetrahedral intermediate ($T^{\pm}$).[6−10] However, the existence of $T^{\pm}$ in the gas phase or in aprotic solvents has been questioned; e.g., Ilieva et al. failed to identify $T^{\pm}$ for the reaction of methyl formate with ammonia,[8a] while Sung et al. reported that at least five explicit water molecules are required to stabilize $T^{\pm}$ in the reaction of phenyl acetate with ammonia.[10a]

Our kinetic study has also shown that the nature of the reaction medium is a crucial factor that governs the reaction mechanism.[4] The reaction of 2,4-dinitrophenyl benzoate with a series of cyclic secondary amines has been proposed to proceed through a stepwise mechanism with a change in the RDS in H_2O on the basis of a curved Brønsted-type plot (i.e., β_2 = 0.74 and β_1 = 0.34),[4a] but via a concerted pathway in MeCN on the basis of a linear Brønsted-type plot with β_{nuc} = 0.40.[4b] We have previously proposed that instability of $T^{\pm}$ in the aprotic solvent forces the reaction to proceed through a concerted mechanism,[4b] because MeCN is a poor solvent for the ionic species.[11]

Our present study comprises an extension to the reaction of 4-nitrophenyl 3,5-dinitrobenzoate (**1a**) with a series of cyclic secondary amines in MeCN to further elucidate the reaction mechanism. We report that the aminolysis of **1a** in the aprotic

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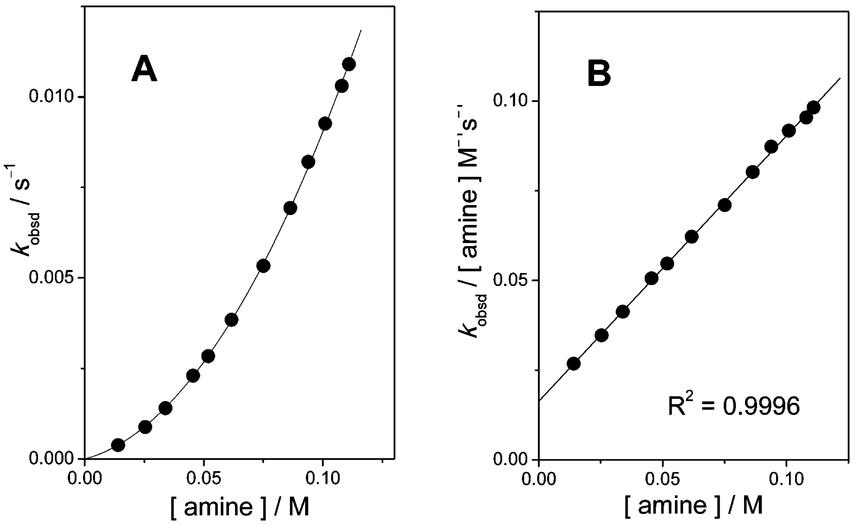


Figure 1. k_{obsd} vs [amine] (A) and k_{obsd}/[amine] vs [amine] (B) for the reaction of **1a** with morpholine in MeCN at 25.0 ± 0.1 °C.

solvent proceeds through a stepwise mechanism with $T^{\pm}$, which decomposes to the products in the RDS via uncatalytic and catalytic routes. We present conclusive evidence that the catalytic reaction proceeds through a six-membered cyclic transition state (TS), e.g., a comparative Brønsted-type plot, a negative enthalpy of activation with a large negative entropy of activation, and deuterium kinetic isotope effects (DKIEs) for the uncatalyzed as contrasted with the catalyzed routes.

Addition−elimination nucleophilic reactions at carbonyl electrophilic sites bear significant similarities to the addition−eliminition reaction of nucleophiles at electrophilic carbon in electron-deficient aromatic compounds, the S_NAr mechanism.[12] For both, the nucleophile attacks at the electrophilic sp^2-hybridized carbon that bears a good leaving group (or a leaving group that becomes more nucleofugic subsequently) which rehybridizes to an sp^3 center. A major difference is that in the S_NAr mechanism nucleophilic attack results in loss of aromaticity, and rearomatization occurs upon expulsion of the leaving group from the reaction site. We have previously exploited this similarity to apply the Brønsted analysis to S_NAr displacements[13a,b] and, most recently, have applied the full range of physical organic tools to probe the reaction of a series of 1-(Y-substituted phenoxy)-2,4-dinitrobenzenes with cyclic secondary amines in MeCN.[13c] This recent kinetic study revealed a concerted pathway from the initially formed zwitterionic Meisenheimer complex, comparable to $T^{\pm}$ in the present work, involving a six-membered TS. The present study, therefore, also explores the similarities in the addition−elimination processes in aminolysis at C═O with S_NAr displacement.

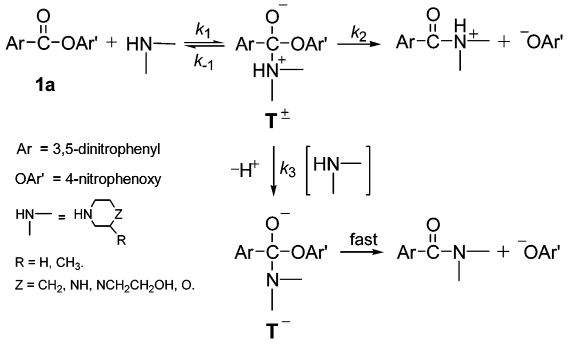
The current kinetic study is analyzed using a comparative Brønsted-type plot, activation parameters, particularly various entropies of activation, and hydrogen−deuterium kinetic isotope effects.

■ RESULTS AND DISCUSSION

The kinetic study was carried out spectrophotometrically by monitoring the appearance of the leaving 4-nitrophenoxide under pseudo-first-order conditions with the amine nucleophile in excess. All reactions in this study obeyed pseudo-first-order kinetics, and pseudo-first-order rate constants (k_{obsd}) were calculated from the slope of plots of $\ln(A_\infty - A_t)$ vs t, which were linear over 90% of the total reaction ($R^2 > 0.9995$). The uncertainty in the k_{obsd} values is estimated to be less than 3% as determined from replicate runs. The plot of k_{obsd} vs amine concentration curves upward for the reaction of **1a** with morpholine as shown in the representative Figure 1A. Similarly curved plots are illustrated in Figures S1A−S8A in the Supporting Information for the reactions of **1a** with the other amines used in this study.

Traditionally, such upward curvature has been understood as evidence for reactions reported previously to proceed through a stepwise mechanism with $T^{\pm}$, which decomposes to the products in the RDS via competitive uncatalyzed and catalyzed routes.[2−5] Thus, one might suggest that the current aminolysis of **1a** proceeds through a stepwise mechanism with two intermediates (i.e., $T^{\pm}$ and its deprotonated form T^-) as shown in Scheme 1. However, this is in contrast to the report that the catalyzed process is absent for the corresponding reactions of 4-nitrophenyl X-substituted benzoates when X = H, 2-MeO, and 4-MeO.[4b,5c] This demonstrates convincingly that the electronic nature of the substituent X in the benzoyl moiety governs the reaction mechanism.

Scheme 1



Dissection of k_{obsd} into Kk_2 and Kk_3. The k_{obsd} for the aminolysis of **1a** can be expressed as eq 1 on the basis of the kinetic results and the reaction mechanism proposed in Scheme 1. Equation 1 can be simplified to eq 2 under the assumption $k_{-1} \gg k_2 + k_3[\text{amine}]$. Accordingly, the plot of k_{obsd}/[amine] vs [amine] would be linear if the above assumption is valid. In fact, as shown in Figure 1B, the plot of k_{obsd}/[amine] vs [amine] exhibits an excellent linear correlation with a positive intercept. The corresponding plots for the reactions with the other amines are also linear as shown in Figures S1B−S8B in the Supporting Information, indicating that the assumption $k_{-1} \gg k_2 + k_3[\text{amine}]$ is valid regardless of the amine basicity. Thus, the Kk_2 and Kk_3 values were calculated from the intercept and slope of the linear plots, respectively, and are summarized in Table 1.

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

$$k_{obsd}/[\text{amine}] = Kk_2 + Kk_3[\text{amine}] \quad \text{where} \quad K = k_1/k_{-1} \quad (2)$$

Table 1. Summary of Rate Constants for the Aminolysis of 1a in MeCN at 25.0 ± 0.1 °C

	amine	pK_a^{a}	Kk_2, M^{-1} s^{-1}	Kk_3, M^{-2} s^{-1}	k_3/k_2, M^{-1}
1	morpholine	16.6	0.0163	0.741	45.5
2	1-(2-hydroxyethyl) piperazine	17.6	0.169	4.2	25.3
3	piperazine	18.5	1.32	38.3	29.0
4	3-methylpiperidine	18.6	2.02	21.3	10.5
5	piperidine	18.8	2.88 (3.10)^b	22.4 (6.94)^b	7.78

^{a}The pK_a values in MeCN were taken from ref 14. ^{b}Rate constant measured for the reaction with deuterated piperidine.

As shown in Table 1, the Kk_2 value increases as the amine basicity increases (e.g., it increases from 0.0163 to 0.169 and 2.88 M^{-1} s^{-1} as the pK_a of the conjugate acid of the amine increases from 16.6 to 17.6 and 18.8 in turn). A similar result is shown for Kk_3, except piperazine, which possesses two basic sites, although the rate constant for the catalyzed route (Kk_3) is much larger than that for the uncatalyzed process (Kk_2) regardless of the basicity of the incoming amine. It is notable that *the catalytic effect exerted by a second amine molecule (i.e., the k_3/k_2 ratio) decreases linearly as the amine basicity increases* (see also Figure 2). The dependence of the catalytic effect on amine basicity will be discussed in detail subsequently.

Brønsted-Type Analysis of Kk_2 and Kk_3. The effect of amine basicity on Kk_2 and Kk_3 values is illustrated in Figure 3. The Brønsted-type plots exhibit excellent linear correlations ($R^2 \geq 0.996$) with $\beta_{nuc} = 1.03$ for Kk_2 and $\beta_{nuc} = 0.69$ for Kk_3 when the rate constants and pK_a values are statistically corrected using p and q (i.e., $p = 2$, while $q = 1$, except $q = 2$ for piperazine).[15] It is important to note that the slope of the Brønsted-type plots is much larger for Kk_2 than for Kk_3, indicating that k_2 is more sensitive to the amine basicity than k_3. This is consistent with our recent report that β_{nuc} is much larger for Kk_2 than for Kk_3 for aminolysis of 4-pyridyl 3,5-dinitrobenzoate (i.e., $\beta_{nuc} = 0.98$ for Kk_2 and $\beta_{nuc} = 0.79$ for Kk_3)[5b] and for S_NAr reactions of 1-(Y-substituted phenoxy)-2,4-dinitrobenzenes with the amines used in this study in MeCN (i.e., $\beta_{nuc} = 1.10$ for Kk_2 and $\beta_{nuc} = 0.85$ for Kk_3).[13c]

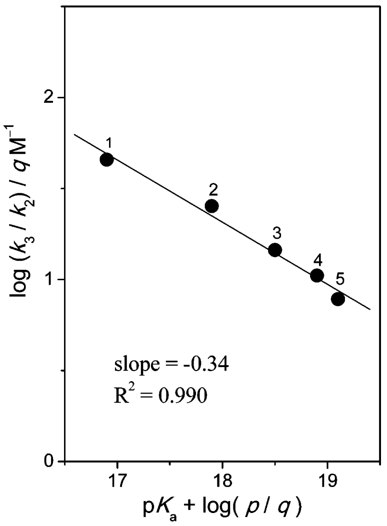


Figure 2. Comparative Brønsted-type plot for the reactions of **1a** with a series of cyclic secondary amines in MeCN at 25.0 ± 0.1 °C. The identity of the points is given in Table 1.

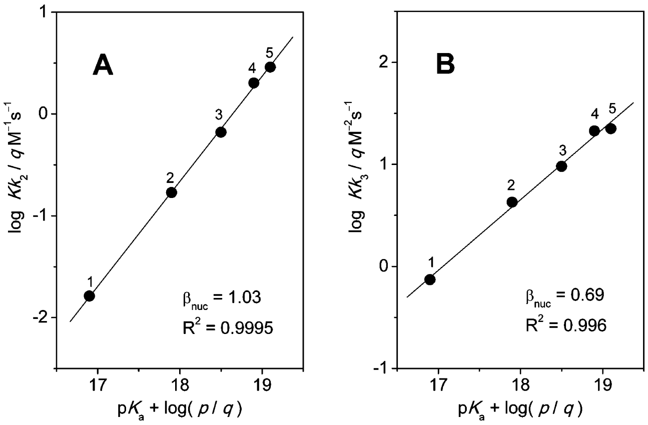


Figure 3. Brønsted-type plots for the reactions of **1a** with cyclic secondary amines in MeCN at 25.0 ± 0.1 °C: (A) Kk_2, (B) Kk_3. The identity of the points is given in Table 1.

Gresser and Jencks have concluded that amine basicity does not affect the k_2 value in quinuclidinolysis of aryl 2,4-dinitrophenyl carbonates, because there is little or no electron donation from the aminium moiety of $T^{\pm}$ to push out the leaving group.[3b] Castro et al. have drawn a similar conclusion for aminolyses of various thionocarbonates (e.g., ethyl phenyl thionocarbonate,[16a] methyl 4-nitrophenyl thionocarbonate,[16b] 4-methyl 4-nitrophenyl thionocarbonate,[16c] and 3-methoxyphenyl 4-nitrophenyl thionocarbonate[16d]). It is also expected that amine basicity would not influence the k_3 value, because a more basic amine would tend to deprotonate more rapidly from the aminium moiety of $T^{\pm}$ while the aminium ion would hold the proton more strongly as amine basicity increases. Accordingly, one might expect that both k_2 and k_3 would be independent of amine basicity, if the current reaction proceeds as shown in Scheme 1. However, in fact, the Brønsted-type plot using Kk_2 results in a much larger β_{nuc} value than that involving Kk_3 (Figure 3), a clear indication that k_2 is more sensitive to amine basicity than k_3. This is contrary to expectations if the reactions proceed as proposed in Scheme 1. Thus, one might suggest that the catalyzed reaction may not proceed as shown in Scheme 1.

Analysis of Activation Parameters. To obtain further information on the TS structure, activation parameters ($\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$) have been calculated from the rate constants measured at five different temperatures for the reactions of **1a** with morpholine in MeCN. The plots of k_{obsd} vs [amine] curve upward, while the plots of k_{obsd}/[amine] vs [amine]

Table 2. Summary of Kinetic Data for the Reactions of **1a** with Morpholine and Piperidine Carried Out at Five Different Temperatures in MeCN

	morpholine		piperidine	
	Kk_2, M^{-1} s^{-1}	Kk_3, M^{-2} s^{-1}	Kk_2, M^{-1} s^{-1}	Kk_3, M^{-2} s^{-1}
15.0 °C	0.0109	0.751	2.16	23.7
20.0 °C	0.0139	0.748	2.53	22.8
25.0 °C	0.0163	0.741	2.88	22.4
30.0 °C	0.0211	0.739	3.40	21.5
35.0 °C	0.0253	0.734	3.84	21.3
$\Delta H^\ddagger$, kcal mol^{-1}	6.82 ± 0.28	−0.80 ± 0.02	4.51 ± 0.12	−1.55 ± 0.09
$\Delta S^\ddagger$, cal mol^{-1} K^{-1}	−43.7 ± 1.0	−61.7 ± 0.1	−41.2 ± 0.4	−57.5 ± 0.3

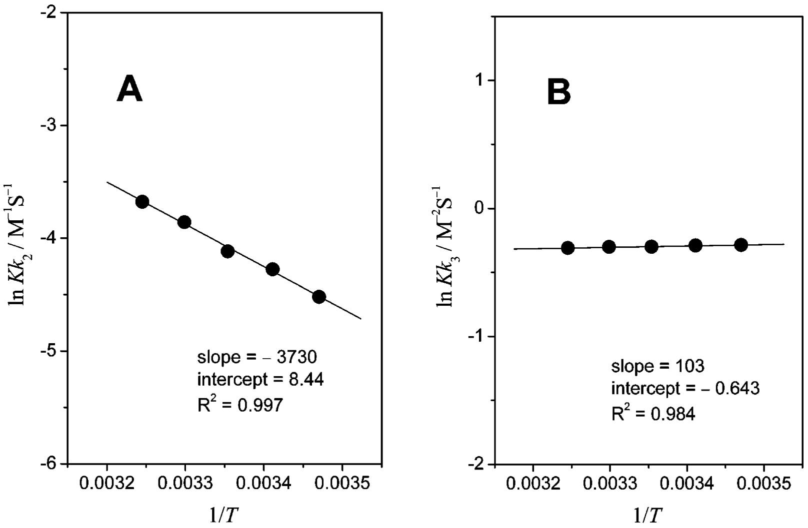


Figure 4. Arrhenius plots for the reactions of **1a** with morpholine at five different temperatures in MeCN: (A) Kk_2, (B) Kk_3.

exhibit excellent linear correlations with positive intercepts in all cases (see Figures S5A and S5B in the Supporting Information). Thus, Kk_2 and Kk_3 values were calculated from the intercept and slope of the linear plots, respectively, and are summarized in Table 2.

As shown in Table 2, Kk_2 increases as the reaction temperature increases. Interestingly, the Kk_2 term is not highly susceptible to modification of the reaction temperature; e.g., the Kk_2 value for the reaction of **1a** with morpholine increases from 0.0109 to 0.0163 and 0.0253 M^{-1} s^{-1} as the reaction temperature increases from 15.0 to 25.0 and 35.0 °C in turn. More interestingly, Kk_3 *decreases as the* reaction *temperature increases*, although the decrease in Kk_3 is not large (i.e., the Kk_3 value for the reaction of **1a** with morpholine decreases from 0.751 to 0.741 and 0.734 M^{-2} s^{-1} as the reaction temperature increases from 15.0 to 25.0 and 35.0 °C in turn).

The activation parameters ($\Delta H^\ddagger$ and $\Delta S^\ddagger$) were calculated from the Arrhenius eq 3. As shown in Figure 4, the Arrhenius plots for the reaction of **1a** with morpholine performed at five different temperatures resulted in good linear correlations for both the uncatalyzed and catalyzed reactions. The slope of the linear plots ln Kk_2 (or Kk_3) vs $1/T$ is equal to $-E_a/R$. The enthalpy of activation ($\Delta H^\ddagger$) was calculated using eq 4. The entropy of activation ($\Delta S^\ddagger$) was calculated from eq 5. The $\Delta H^\ddagger$ and $\Delta S^\ddagger$ values calculated in this way are summarized in Table 2.

$$k = Ae^{-E_a/RT} \quad \text{or} \quad \ln k = -E_a/RT + \ln A \tag{3}$$

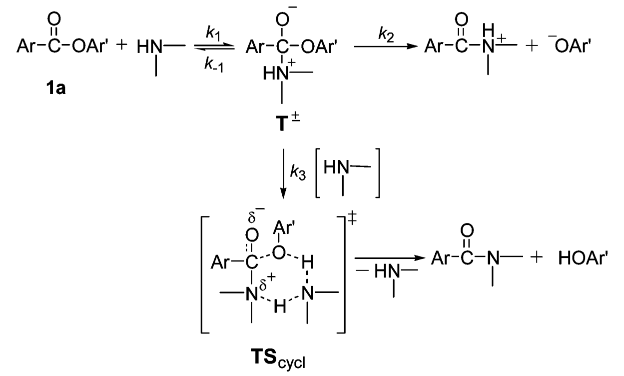
$$\Delta H^\ddagger = E_a - RT \tag{4}$$

$$\Delta S^\ddagger = \ln A - \ln T - \ln K_B/h - 1 \tag{5}$$

As shown in Table 2, the $\Delta H^\ddagger$ values for the uncatalyzed reactions are 6.82 and 4.51 kcal/mol for the reactions with morpholine and piperidine, respectively. However, surprisingly, the $\Delta H^\ddagger$ values for the catalyzed reactions are −0.80 and −1.55 kcal/mol for the reactions with morpholine and piperidine, respectively. Such negative activation enthalpies are quite unusual[17,18] but are in accord with the fact that the Kk_3 values decrease as the reaction temperature increases (Table 2). More importantly, the entropy of activation for the catalyzed reaction (Kk_3) is highly negative (i.e., $\Delta S^\ddagger$ = −61.7 and −57.5 cal/(mol K) for the reactions with morpholine and piperidine, respectively). Such a large negative entropy of activation would not arise through solvation of $T^\pm$ in MeCN, because the zwitterionic $T^\pm$, in which the negative charge is exposed on the O atom while the positive charge is buried in the middle of $T^\pm$, would not be strongly solvated in the aprotic solvent. In fact, electronic repulsion between the negative dipole end of MeCN and the negatively charged oxygen atom of $T^\pm$ should predominate.[19]

Deduction of the Reaction Mechanism. We thus propose that the catalyzed reaction proceeds through a concerted mechanism with a six-membered cyclic TS structure as modeled by TS_{cycl} in Scheme 2 rather than via the alternative stepwise pathway with an anionic intermediate T^- in Scheme 1. This cyclic TS includes a second molecule of the amine that

Scheme 2



accepts a proton from the aminium moiety of T± and in concerted fashion donates a proton to the aryloxyl oxygen of the leaving group with concomitant C−OAr bond scission. Such a six-membered cyclic TS can account for the large negative $\Delta S^{\ddagger}$ value since the rotational and vibrational degrees of freedom in the cyclic TS are restricted. Furthermore, TS_{cycl}, in which the charges are dispersed, would be more favorable than the anionic T^- in the aprotic solvent because the electronic repulsion would be less significant for the charge-dispersed cyclic TS than T^-.

The cyclic TS proposed for the catalyzed process (i.e., TS_{cycl} in Scheme 2) can be further supported by the fact the β_{nuc} value is much smaller for the catalyzed reaction than for the uncatalyzed reaction (Figure 3) and by the result that the k_3/k_2 ratio decreases linearly as the amine basicity increases (Figure 2). As mentioned in the preceding section, the k_2 and k_3 values would be independent of amine basicity if the reaction proceeds through T± and T^- as shown in Scheme 1. However, if the catalyzed reaction proceeds via the cyclic TS (i.e., TS_{cycl} in Scheme 2), amine basicity should affect k_3, because the proton donation by the second amine molecule to the O atom of the leaving group would be retarded as a function of increasing amine basicity. Accordingly, *the catalytic effect would decrease as the amine basicity increases.* This argument is consistent with the fact that the catalytic effect (i.e., the k_3/k_2 ratio) decreases linearly as the amine basicity increases (Table 1 and Figure 2) and the catalyzed reaction results in a smaller β_{nuc} value than the uncatalyzed reactions (Figure 3).

Deuterium Kinetic Isotope Effect. The proposed reaction mechanism in Scheme 2 is further supported by DKIEs. As shown in Table 1 (also in Figure S8 in the Supporting Information), the Kk_2 value for the reaction with deuterated piperidine is larger than that for the reaction with piperidine. Consequently, an inverse DKIE is obtained (i.e., Kk_2^H/Kk_2^D = 2.88/3.10 = 0.93). One can attribute the inverse DKIE for the uncatalyzed reaction, where the deprotonation process from the aminium moiety of T± is absent, as a consequence of reduced steric hindrance, because the amplitude of the stretching vibration of a N−D bond is smaller than that of a N−H bond. In contrast, the Kk_3 value for the reaction with deuterated piperidine is much smaller than that for the reaction with piperidine (i.e., Kk_3^H/Kk_3^D = 22.4/6.94 = 3.23). The normal primary DKIE for the catalyzed reaction is consistent with the proposed cyclic TS (i.e., TS_{cycl}), in which the deprotonation and the donation of a proton by a second amine molecule occur in the RDS. That DKIE (3.23) is smaller than the theoretical value (ca. 7) indicates that the TS is not symmetrical and proton transfer does not occur in a linear fashion.[20] Concerted but not synchronous proton transfer occurs.

TS_{cycl} (Scheme 2) is reminiscent of the transition state that we have recently proposed for the catalyzed route in S_NAr displacement of aryl oxides by cyclic secondary amines in acetonitrile.[13c] The fundamental similarity between the two types of addition−elimination reactions, namely, nucleophilic displacement at carbonyl and at an electron-deficient aromatic carbon, is, thus, emphasized.

■ CONCLUSIONS

Traditionally, the upward curvature in the plots of k_{obsd} vs [amine] for the current aminolysis of **1a** has been taken as evidence for a stepwise mechanism with two intermediates (T± and T^-). However, we have concluded that the catalyzed reaction (i.e., breakdown of T± to the products) proceeds through a concerted mechanism with a six-membered cyclic TS (i.e., TS_{cycl} in Scheme 2) rather than via the alternative stepwise pathway with an anionic intermediate T^- in Scheme 1. This proposal is based on the following data: (1) The catalytic effect decreases with increasing basicity of the incoming amine (a comparative Brønsted-type plot). This is possible only when a second amine molecule relays protons from the aminium moiety of T± to the aryloxy leaving group. (2) A large negative entropy of activation is caused by restriction of the rotational and vibrational degrees of freedom in the cyclic TS. (3) An inverse DKIE is observed for the uncatalyzed reaction (i.e., Kk_2^H/Kk_2^D = 2.88/3.10 = 0.93), but a normal primary DKIE is obtained for the catalyzed process, in which the deprotonation and the donation of a proton by a second amine molecule occur in the RDS (i.e., Kk_3^H/Kk_3^D = 22.4/6.94 = 3.23). The proposed TS for the catalyzed route, TS_{cyc}, also bears a strong similarity to that previously advanced in the S_NAr reaction of 1-(Y-substituted phehnoxy)-2,4-dinitrobenzenes with cyclic secondary amines in the same reaction medium (i.e., acetonitrile).

■ EXPERIMENTAL SECTION

Materials. **1a** was readily prepared from the reaction of 3,5-dinitrobenzoyl chloride with 4-nitrophenol in anhydrous ether in the presence of equimolar triethylamine.[21] The crude product was purified by column chromatography, and the purity was checked by the melting point and ^1H NMR spectrum (500 MHz, $CDCl_3$), e.g., δ 9.354−9.339 (m, 3H), δ 8.415−8.397 (d, J = 9.0 Hz, 2H), δ 7.515−7.497 (d, J = 9.0 Hz, 2H). MeCN was distilled over P_2O_5 and stored under nitrogen. Other chemicals, including the amines, were of the highest quality available.

Kinetics. The kinetic study was carried out using a UV−vis spectrophotometer for slow reactions (e.g., $t_{1/2} \geq 10$ 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 temperature. The reactions were followed by monitoring the appearance of 4-nitrophenoxide. 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. All solutions were transferred by gastight syringes. Generally, the amine concentration in the reaction mixtures was varied over the range $(5-150) \times 10^{-3}$ 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 t were linear over 90% of the total reaction.

Product Analysis. 4-Nitrophenoxide ion (and/or its conjugate acid) 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 an authentic sample under the same reaction conditions.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

k_{obsd} vs [amine], k_{obsd}/[amine] vs [amine], and kinetic results for reactions of **1a** in various conditions and ^{1}H NMR spectrum of substrate **1a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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