A Linear Brönsted-Type Behavior in the Aminolysis of Substituted Naphthyl Acetates

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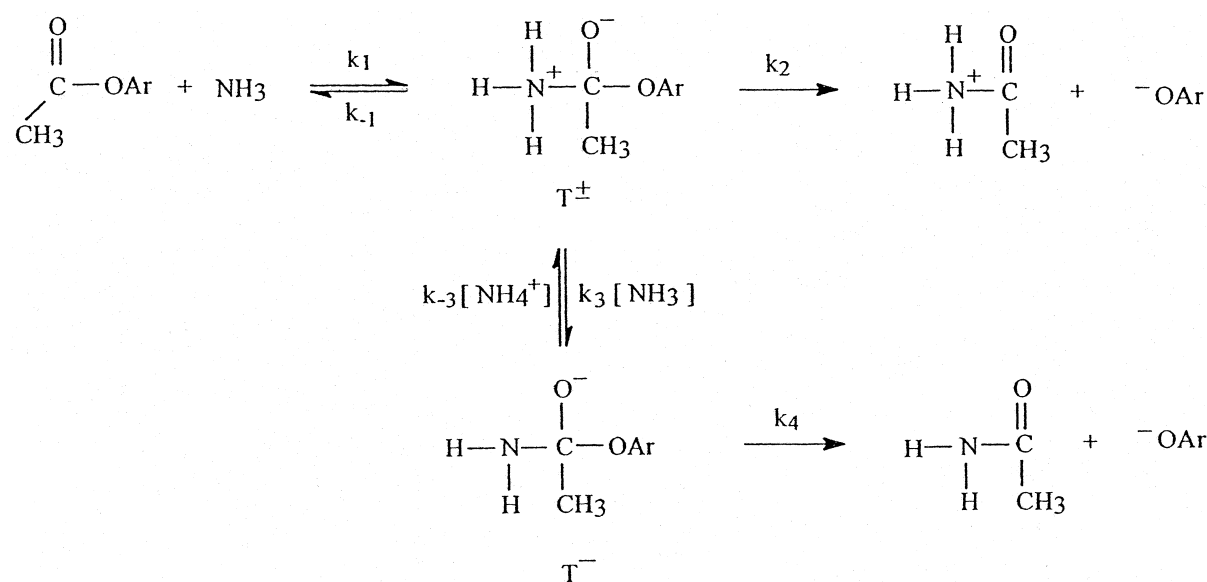[2]Department of Chemistry, Annamalai University, Tamilnadu, India 608002

ABSTRACT: The reactions of 4-acetyl-1-naphthyl acetate (**1**) and 6-acetyl-2-naphthyl acetate (**2**) with a series of amines of varying pK_a, viz. morpholine, ammonia, ethanolamine, glycine, n-butylamine, piperidine, hydrazine, imidazole, and hydroxylamine, are subjected to a kinetic investigation in aqueous medium, 30°C, ionic strength 0.1 M (KCl). Pseudo-first-order rate coefficients (k_{obs}) are found under amine excess. The plots of ($k_{obs} - k_H$) against free amine concentration are linear at constant pH. The macroscopic nucleophilic substitution rate coefficients (k_N) are obtained as the slopes of these plots and found to be pH-independent for all the amines employed. The Brönsted-type plots obtained (log k_N against amine pK_a) for the aminolysis of both esters **1** and **2** are linear with slope values of $\beta = 0.74$ and $\beta = 0.94$, respectively. From these values, the kinetic law and the analysis of products, it is deduced that for both esters aminolysis proceed through a zwitterionic tetrahedral addition intermediate ($T^\pm$) whereby its dissociation into products is rate-limiting (k_2 step). Comparison of k_N values among them shows that both esters follow an identical mechanistic pathway with **1** having higher reactivity than **2**, the reasons for which are discussed. © 2001 John Wiley & Sons, Inc. Int J Chem Kinet 33: 157–164, 2001

INTRODUCTION

The aminolysis of aryl acetates has been the subject of numerous kinetic studies. Specifically, extensive works on the aminolysis reactions of phenyl acetates [1–24] phenyl thiolacetates [25–28], and phenyl dithioacetates [29,30], in aqueous medium as well as in partly aqueous medium [31–33] have been made, and their mechanisms have been well established through structure-reactivity correlation. In spite of a great deal of information available on the aminolysis of phenyl acetates, less is known about the mechanism of similar reactions of naphthyl acetates [11,34–36].

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We have recently studied the kinetics and mechanism of aminolysis of several substituted naphthyl acetates in aqueous medium [37,38] and correlated the macroscopic nucleophilic substitution rate coefficients (k_N) to the nature of the leaving group. The reaction has been shown to occur through the pathways as shown in Scheme I. The results obtained therein showed that for the esters with better leaving group (good nucleofuges) ammonolysis proceeds through a zwitterionic tetrahedral addition intermediate ($T^\pm$), with its rate-determining formation (k_1 step) and assisted pathways of no kinetic significance. For the esters with poor leaving group (poor nucleofuges), $T^\pm$ is less unstable with $k_3[NH_3] \gg k_2$ and hence second-order rate coefficients in amine are found and the reaction proceeds through a general-base catalyzed path-

Scheme I

way with an anionic tetrahedral intermediate (T^-), whereby the k_3 step is rate-limiting. The pathway leading to cationic tetrahedral intermediate (T^+) through general-acid catalysis is discarded in view of the nondependence of the rate constants on pH of the medium. These results are consistent with earlier reported ones [4,14], and the work has brought some light on the influence of substituents on the relative nucleofugalities of naphthoxide ions.

In order to investigate further on the mechanism of the aminolysis of substituted naphthyl acetates and to assess the influence of amine basicity, we perform in the present work a kinetic study on the title reactions in aqueous medium. The Brönsted-type plots obtained in the study are compared among them and to those of similar ones of earlier reported works, and based on that, a plausible mechanism is deduced.

EXPERIMENTAL

Materials

The 4-acetyl-1-naphthyl acetate and 6-acetyl-2-naphthyl acetate were prepared from corresponding naphthols [39,40] by procedures from the literature [41]. Amines, with the exception of reagent-grade imidazole (Fluka) and glycine (BDH), were redistilled from KOH or recrystallized shortly before use. Ethanolamine was simply redistilled.

The amines were employed as buffers to maintain constant pH. The amine–amine hydrochloride buffers were prepared shortly before the kinetic run by the addition of calculated amounts of standardized hydrochloric acid or potassium hydroxide to the solutions of known concentrations of amine-free base or amine hydrochloride, as the case may be. At any fixed pH value, the concentration of free amine was evaluated using Eq. (1).

$$[N]_F = \frac{[N]_T \cdot K_a}{K_a + a_{H^+}} \qquad (1)$$

where $[N]_T$ is the total amine concentration, K_a is the dissociation constant of the conjugate acid of the amine, and a_{H^+} is the hydrogen ion activity. The pK_a of the conjugate acid of amines were determined from measurements of the pH of partially neutralized solutions under identical conditions to those of the kinetic experiments [2,11].

Kinetic Measurements

These were carried out in aqueous solution at $30.0 \pm 0.1°C$, ionic strength 0.1 M (KCl), by monitoring spectrophotometrically the release of the corresponding naphthoxy ions of the substrates **1** and **2** at 248 and 271 nm, respectively. The initial ester concentration was $(5-6) \times 10^{-5}$ M, and the amine concentration was kept at several times excess over the substrate.

Pseudo-first-order rate coefficients (k_{obs}) were found throughout, by means of the method of Guggenheim [42], employing the least-squares technique.

The experimental conditions of the reactions and the rate coefficients are given in Tables I and II.

In order to evaluate the results, the alkaline hydrolysis of esters was also followed spectrophotometrically using known concentrations of potassium hydroxide. Ionic strength was maintained at 0.1 M, and other experimental conditions were essentially the same as those maintained for aminolysis. Alkaline hydrolysis of esters followed second-order kinetics and the rate coefficients, k_{hyd} (where $k_{hyd} = k_{obs}/[OH^-]$), were unaffected when the hydroxide ion concentration was varied. (For **1**, $k_{hyd} = 6.52 \pm 0.09$ s^{-1} M^{-1}; and for **2**, $k_{hyd} = 3.19 \pm 0.04$ s^{-1} M^{-1}.)

Product Studies

The product studies was carried out according to the procedure already reported [37], based on the method of Katz et al. [43], which showed in all the cases at least 90% of the formation of amide product under the experimental conditions.

Table I Summary of Experimental Conditions and Rate Coefficients for the Aminolysis of 4-Acetyl-1-Naphthyl Acetate[a]

Amine	pH	10^3 $[N]_F$/M[b]	10^3 $(k_{obs} - k_H)$/s^{-1}	k_2'/s^{-1} M^{-1}
Morpholine	8.22	11.10–16.03	4.52–6.30	0.39 ± 0.03
	8.37	13.91–20.09	5.61–7.71	0.39 ± 0.02
	8.57	17.98–25.96	6.71–9.18	0.36 ± 0.02
	8.81	22.82–32.96	7.83–11.07	0.33 ± 0.01
Ammonia	9.21	1.51–1.87	1.57–1.92	0.92 ± 0.02
	9.38	1.83–2.31	1.77–2.22	0.84 ± 0.01
	9.55	2.10–2.65	2.16–2.62	0.85 ± 0.02
	9.73	2.36–2.87	2.60–3.04	0.86 ± 0.01
Ethanolamine	9.54	2.89–4.92	5.27–8.72	1.69 ± 0.03
	9.67	3.39–5.78	6.19–10.30	1.68 ± 0.02
	9.85	4.08–6.96	7.55–12.38	1.66 ± 0.02
	10.04	4.75–8.11	9.34–15.09	1.68 ± 0.03
Glycine	9.33	0.98–2.46	2.82–6.88	2.58 ± 0.11
	9.47	1.22–3.06	3.98–8.68	2.80 ± 0.16
	9.57	1.40–3.50	4.81–10.42	3.06 ± 0.20
	9.69	1.62–4.05	6.42–13.64	3.36 ± 0.19
n-Butylamine	9.94	0.24–0.45	2.66–8.03	10.81 ± 0.91
	10.15	0.34–0.66	3.13–9.65	8.60 ± 0.76
	10.30	0.43–0.84	4.30–12.09	8.41 ± 0.82
	10.51	0.58–1.12	5.73–15.78	7.47 ± 0.91
Piperidine	10.12	0.15–0.22	3.28–7.17	19.53 ± 0.88
	10.29	0.21–0.31	4.71–9.99	18.40 ± 0.71
	10.42	0.27–0.40	6.78–14.85	22.75 ± 0.93
	10.57	0.35–0.53	10.54–18.52	23.02 ± 0.81
Hydrazine	6.40	0.34–0.49	1.79–2.60	5.33 ± 0.01
	6.77	0.77–1.18	3.35–5.33	4.60 ± 0.07
	6.95	1.14–1.65	5.44–8.81	5.13 ± 0.09
	7.21	1.97–2.86	7.19–12.25	4.16 ± 0.09
Imidazole	7.12	1.51–2.60	3.22–5.59	2.14 ± 0.05
	7.29	1.80–3.10	4.06–6.95	2.24 ± 0.02
	7.43	2.00–3.51	4.93–8.39	2.39 ± 0.04
	7.55	2.21–3.78	5.73–9.63	2.59 ± 0.03
Hydroxylamine	6.04	0.91–1.57	3.20–5.20	3.53 ± 0.01
	6.21	1.09–1.76	3.94–6.18	3.54 ± 0.07
	6.44	1.31–2.10	4.63–7.26	3.47 ± 0.03
	6.68	1.47–2.39	5.36–8.59	3.57 ± 0.06

[a] In aqueous solution at 30.0 ± 0.1°C, ionic strength 0.1 M (KCl). At least five runs were carried out at each pH. The errors shown are standard deviations.
[b] Concentration of free amine.

Table II Summary of Experimental Conditions and Rate Coefficients for the Aminolysis of 6-Acetyl-2-Naphthyl Acetate[a]

Amine	pH	$10^3 [N]_F$/M[b]	$10^3 (k_{obs} - k_H)$/s^{-1}	k_2'/s^{-1} M^{-1}
Morpholine	8.23	157.90–278.20	3.61–6.02	0.023 ± 0.001
	8.37	194.70–343.10	4.12–6.86	0.021 ± 0.004
	8.57	251.70–443.40	4.85–8.20	0.020 ± 0.002
	8.79	314.10–553.40	5.48–9.11	0.017 ± 0.006
Ammonia	9.21	49.70–89.00	2.73–4.90	0.053 ± 0.001
	9.33	56.60–101.30	3.10–5.55	0.053 ± 0.003
	9.46	63.70–113.90	3.55–6.23	0.053 ± 0.003
	9.60	85.5–126.30	4.76–6.79	0.052 ± 0.004
Ethanolamine	9.39	19.00–32.77	3.19–5.48	0.16 ± 0.02
	9.52	22.88–39.46	3.80–6.36	0.16 ± 0.02
	9.67	27.60–47.60	4.47–7.50	0.15 ± 0.01
	9.84	32.93–56.80	5.21–8.67	0.15 ± 0.02
Glycine	9.32	14.91–18.54	3.46–4.18	0.22 ± 0.04
	9.45	18.21–22.65	4.23–5.19	0.22 ± 0.01
	9.57	21.49–26.73	5.11–6.31	0.22 ± 0.03
	9.69	24.94–31.02	6.42–7.96	0.24 ± 0.03
n-Butylamine	9.74	0.56–0.86	2.48–4.08	4.05 ± 0.12
	10.13	1.17–1.78	4.42–7.15	3.35 ± 0.15
	10.29	1.51–2.31	5.62–8.92	3.10 ± 0.17
	10.45	1.90–2.90	6.86–10.68	3.00 ± 0.27
Piperidine	10.12	0.35–0.56	2.84–4.76	6.21 ± 0.09
	10.28	0.48–0.78	3.83–6.36	6.20 ± 0.08
	10.42	0.63–1.03	5.14–8.20	6.00 ± 0.19
	10.55	0.81–1.31	6.03–9.93	5.61 ± 0.29
Hydrazine	6.42	0.97–2.92	0.98–2.27	0.85 ± 0.01
	6.76	2.08–6.24	1.60–4.82	0.75 ± 0.03
	6.94	3.09–9.28	2.21–6.73	0.74 ± 0.03
	7.23	5.68–17.04	3.11–9.42	0.56 ± 0.09
Imidazole	6.94	6.69–11.63	1.40–2.53	0.22 ± 0.01
	7.12	8.39–14.59	1.68–3.01	0.20 ± 0.01
	7.27	9.82–17.06	1.81–3.24	0.19 ± 0.04
	7.41	11.10–19.28	2.00–3.30	0.18 ± 0.04
Hydroxylamine	6.04	3.89–8.04	1.42–3.29	0.38 ± 0.03
	6.22	4.68–9.66	1.90–4.35	0.45 ± 0.02
	6.43	5.53–11.44	2.24–5.44	0.44 ± 0.04
	6.66	6.27–12.96	2.61–6.09	0.46 ± 0.03

[a] In aqueous solution at 30.0 ± 0.1°C, ionic strength 0.1 M (KCl). At least five runs were carried out at each pH. The errors shown are standard deviations.
[b] Concentration of free amine.

RESULTS AND DISCUSSION

The pseudo-first-order rate coefficients (k_{obs}) observed for the aminolysis of esters are converted to the apparent second-order rate coefficients, k_2', where $k_2' = (k_{obs} - k_H)/[N]_F$, where k_H is the product of k_{hyd}, the second-order rate coeffcient for the alkaline hydrolysis of esters and the concentration of hydroxide ion present in the system for aminolysis, calculated from a_{OH^-} and the activity coefficient of hydroxide ion [44]. In the aminolysis of esters, k_2' values calculated are almost constant within a given pH and are independent of free amine concentration. The values of k_2' are given in Tables I and II. Further, the plots of $\log(k_{obs} - k_H)$ against $\log[N]_F$ for all the amines are linear with unit slope (plots not shown). These indicate that aminolysis of these esters depends only upon the first power of the free amine concentration and the assistance by a second molecule of amine is absent. Hence the catalyzed pathway has no significance, and the reaction proceeds through a pathway whereby a simple unassisted attack of nucleophiles over esters prevails.

Table III Macroscopic Nucleophilic Substitution Rate Coefficients, $k_N/s^{-1} M^{-1}$, for the Aminolysis of 4-Acetyl-1-Naphthyl Acetate and 6-Acetyl-2-Naphthyl Acetate[a]

No.	Amine	pK_a	4-Acetyl-1-Naphthyl Acetate	6-Acetyl-2-Naphthyl Acetate
1.	Morpholine	8.48 ± 0.04	0.33 ± 0.04	0.022 ± 0.002
2.	Ammonia	9.21 ± 0.05	0.91 ± 0.02	0.053 ± 0.004
3.	Ethanolamine	9.50 ± 0.03	1.71 ± 0.01	0.15 ± 0.02
4.	Glycine	9.78 ± 0.04	2.82 ± 0.03	0.24 ± 0.05
5.	*n*-Butylamine	10.77 ± 0.03	19.55 ± 0.27	4.45 ± 0.09
6.	Piperidine	11.24 ± 0.05	46.88 ± 0.22	8.12 ± 0.15
7.	Hydrazine	7.97 ± 0.02	5.41 ± 0.04	0.67 ± 0.02
8.	Imidazole	6.95 ± 0.05	2.35 ± 0.02	0.19 ± 0.03
9.	Hydroxylamine	5.77 ± 0.03	3.72 ± 0.02	0.48 ± 0.01

[a] Values of both pK_a and k_N in aqueous solution, at 30.0 ± 0.1°C, ionic strength 0.1 M (KCl). The errors shown are standard deviations.

The reactions subjected to the present investigation can be kinetically described by Eqs. (2) and (3),

$$\frac{d[ArO^-]}{dt} = (k_{obs} - k_H)[Ester] \qquad (2)$$

$$(k_{obs} - k_H) = k_o + k_N F_N [N]_T \qquad (3)$$

where ArO^- is 4-acetyl-1-naphthoxide ion or 6-acetyl-2-naphthoxide ion, k_{obs} is the pseudo-first-order rate coefficient, k_o is the coefficient of assisted paths comprising general acid, general base, and specific base assisted attack of amines, k_N is the macroscopic nucleophilic substitution rate coefficient, F_N is the free-amine fraction and $[N]_T$ is the concentration of total amine (free-amine plus its conjugate acid). Since, $F_N = [N]_F/[N]_{tot}$, Eq. (3) becomes,

$$(k_{obs} - k_H) = k_o + k_N [N]_F \qquad (4)$$

The values of k_o and k_N were obtained as the intercept and slope, respectively, of plots of $(k_{obs} - k_H)$ against $[N]_F$ at constant pH, for at least four pH values. The values of k_N were found to be pH-independent over the pH range employed, and the mean k_N values are given in Table III. For all the reactions, the value of k_o was negligible compared to the aminolysis term (k_N) in Eq. (4).

The pK_a values of the amines employed and k_N values were statistically corrected [45–47] before plotting the Brönsted-type equation. For both esters, the plots are linear for the amines morpholine, ammonia, ethanolamine, glycine, *n*-butylamine, and piperidine, with slopes $\beta = 0.74$ ($r = 0.980$) and $\beta = 0.94$ ($r = 0.980$) for **1** and **2,** respectively. The plots are shown in Figures 1 and 2. The numbers given in the plots are

according to the order of amines given in Table III. Expectedly, hydrazine and hydroxylamine deviate from the plot owing to the 'α-effect' [48,49] and imidazole because of its reactivity towards the esters as a tertiary amine [1].

The values of the slopes are consistent with a stepwise mechanism, where a zwitterionic tetrahedral addition intermediate ($T^\pm$) is found on the reaction pathway and its breakdown to products is rate-determining.

Similar larger Brönsted slope values ($\beta = 0.8$–1.0) have been found in the aminolysis of phenyl acetates [50], 4-nitrophenyl acetate [4,17,48], 2,4-dinitrophenyl acetate [14], and 2-nitrophenyl acetate [24], where a stepwise mechanism has been invoked with the breakdown of $T^\pm$ to products being the rate-determining step. The slope values of the Brönsted plots above are also similar to those obtained in the ami-
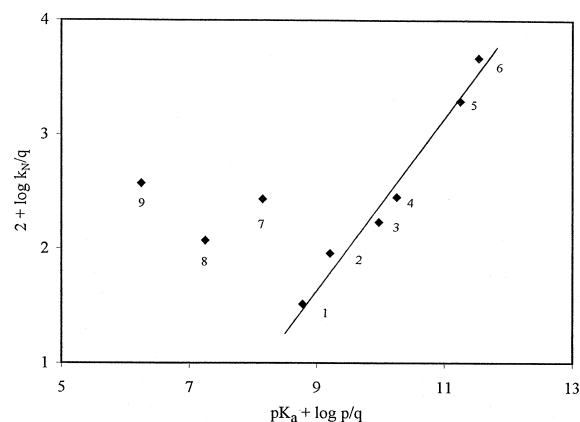

Figure 1 Brönsted-type plot (statistically corrected) obtained in the aminolysis of 4-acetyl-1-naphthyl acetate in aqueous mediums, 30°C, ionic strength 0.1 M (KCL).
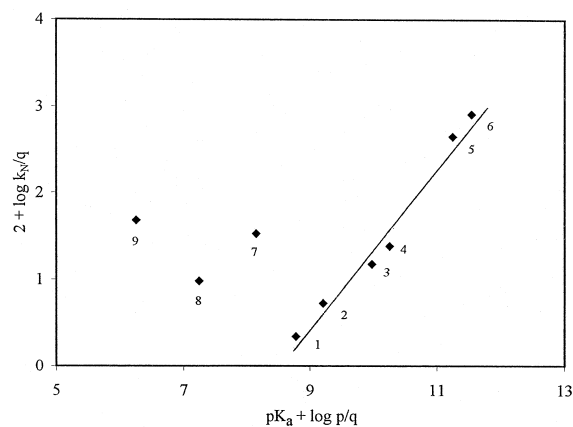
Figure 2 Brönsted-type plot (statistically corrected) obtained in the aminolysis of 6-acetyl-2-naphthyl acetate in aqueous medium, 30°C, ionic strength 0.1 M (KCl).
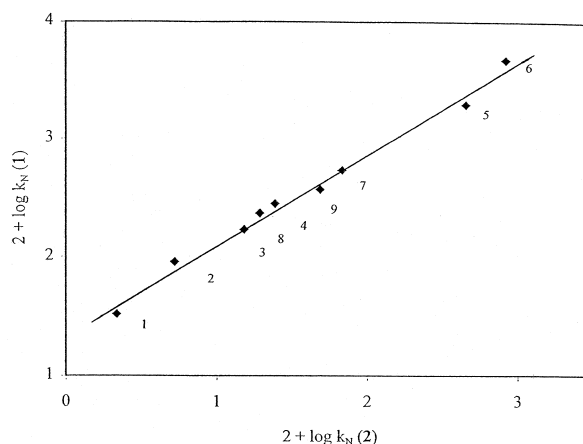

Figure 3 Comparative plot of k_N in the aminolysis of 4-acetyl-1-naphthyl acetate (**1**) and 6-acetyl-2-naphthyl acetate (**2**).

nolysis of phenyl thiolacetates in aqueous medium [26,27].

Larger Brönsted slope values have also been found in the aminolysis of 4-nitrophenyl benzoate [51,52], 2,4-dinitrophenyl 4-chlorobenzoate [53], 2,4-dinitrophenyl 4-nitrobenzoate [54], and other reactive carbonyl compounds [55–59], where a stepwise mechanism has been proposed with the breakdown of $T^\pm$ to products being the rate-determining step.

A smaller value of the Brönsted slope ($\beta = 0.1$–0.3) has been found in the aminolyses of these esters when the formation of a zwitterionic tetrahedral addition intermediate ($T^\pm$) is rate determining [4,26,27].

According to the results and rate law obtained, the analysis of products, and the Brönsted-type plots found for the reactions under investigation, the mechanism of these reactions can be described by Scheme II, where Ar is either of the naphthyl moiety of esters **1** and **2** and N represents the amine employed. In Scheme II, the k_2 step is rate limiting.

The macroscopic nucleophilic substitution rate coefficient k_N can be related to the microscopic rate coefficients of Scheme II through application of the steady-state approximation to the tetrahedral intermediate, as in Eq. (5).

$$k_N = \frac{k_1 k_2}{(k_{-1} + k_2)} \tag{5}$$

Since the large β values for the present reactions suggest that the second step of Scheme II is rate limiting, it follows that $k_{-1} \gg k_2$ and hence Eq. (5) takes the form,
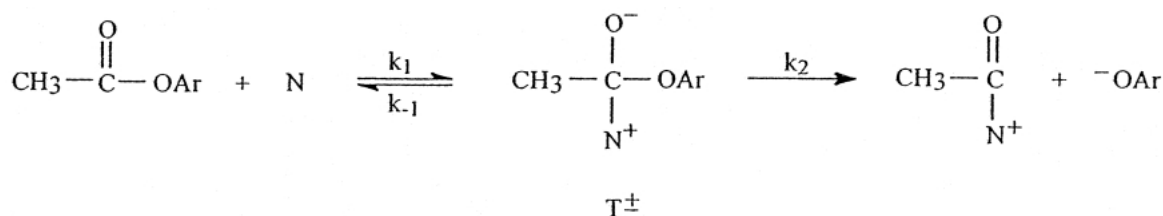
$$k_N = \frac{k_1 k_2}{k_{-1}} = K_1 k_2 \tag{6}$$

where K_1 is the equilibrium constant for the first step. The transition state for the aminolysis of these esters may exist as shown in Structure 1.
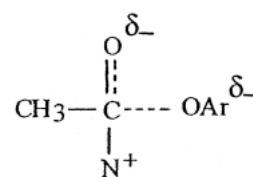
Structure 1

An analogous transition state and a similar rate equation with a pre-equilibrium step was proposed by Cas-

Scheme II

tro et al. [54] in the pyridinolysis of 2,4-dinitrophenyl 4-nitrobenzoate with a Brönsted slope of 0.9.

A comparative plot of esters **1** and **2** for k_N values, which is linear ($r = 0.990$), is shown in Figure 3. This indicates that for the aminolysis of these esters identical mechanism prevails irrespective of the position of substituent in the naphthalene ring. However, the reactivity of **1** is higher compared to **2** toward these amines (Table III), which is reflected in a smaller β value for **1,** which is consistent with the earlier reported works wherein smaller β values were obtained for more reactive esters [2,3,18]. Present observation conforms with the earlier reports, which suggest that the reactivity of 6-substituted naphthalene system is largely decided by the 3,4-benzo substituent (with larger σ values) rather than by the actual substituent present [60,61]. Thus, for **2** the electron-withdrawing effect of the acetyl group is less pronounced to reach the reaction center, which makes the naphthoxide ion act as a poor nucleofuge. Also, it makes the carbonyl carbon less positive for an effective amine attack. Therefore, it is probable that both K_1 and k_2 are smaller for the reactions of **2.**

BIBLIOGRAPHY

1. Jencks, W. P.; Carriuolo, J. J Am Chem Soc 1960, 82, 675, 1778.
2. Jencks, W. P.; Gilchrist, M. J Am Chem Soc 1968, 90, 2622.
3. Gravitz, N.; Jencks, W. P. J Am Chem Soc 1974, 96, 499, 507.
4. Satterthwait, A. C.; Jencks, W. P. J Am Chem Soc 1974, 96, 7018.
5. Cox, M. M.; Jencks, W. P. J Am Chem Soc 1978, 100, 5956.
6. Cox, M. M.; Jencks, W. P. J Am Chem Soc 1981, 103, 572, 580.
7. Fishbein, J. C.; Baum, H.; Cox, M. M.; Jencks, W. P. J Am Chem Soc 1987, 109, 5790.
8. Bruice, T. C.; Mayahi, M. F. J Am Chem Soc 1960, 82, 3067.
9. Bruice, T. C.; Benkovic, S. J. J Am Chem Soc 1964, 86, 418.
10. Bruice, T. C.; Willis, R. G. J Am Chem Soc 1965, 87, 531.
11. Bruice, T. C.; Donzel, A.; Huffman, R. W.; Butler, A. R. J Am Chem Soc 1967, 89, 2106.
12. Huffman, R. W.; Donzel, A.; Bruice, T. C. J Am Chem Soc 1967, 89, 1973.
13. Bruice, T. C.; Hegarty, A. F.; Felton, S. M.; Donzel, A.; Kundu, N. G. J Am Chem Soc 1970, 92, 1370.
14. Castro, E. A.; Freudenberg, M. J Org Chem 1980, 45, 906.
15. Castro, E. A.; Santander, C. L. J Org Chem 1985, 50, 3595.
16. Castro, E. A.; Ureta, C. J Org Chem 1990, 55, 1676.
17. Bond, P. M.; Castro, E. A.; Moodie, R. B. J Chem Soc, Perkin Trans 2 1976, 68.
18. Deady, L. W.; Finlayson, W. L. Aust J Chem 1980, 33, 2441.
19. Deady, L. W.; Finlayson, W. L. Aust J Chem 1983, 36, 1951.
20. Do Amaral, L.; Koehler, K.; Bartenbach, D.; Pletcher, T.; Cordes, E. H. J Am Chem Soc 1967, 89, 3537.
21. Kirsch, J. F.; Kline, A. J Am Chem Soc 1969, 91, 1841.
22. Kovach, I. M.; Belz, M.; Larson, M.; Rousy, S.; Schowen, R. L. J Am Chem Soc 1985, 107, 7360.
23. Knowlton, R. C.; Byers, L. D. J Org Chem 1988, 53, 3862.
24. Arcelli, A.; Concilio, C. J Org Chem 1996, 61, 1682.
25. Hupe, D. J.; Jencks, W. P. J Am Chem Soc 1977, 99, 451.
26. Castro, E. A.; Ureta, C. J Org Chem 1989, 54, 2153.
27. Castro, E. A.; Ureta, C. J Chem Soc, Perkin Trans 2 1991, 63.
28. Ananthakrishna Nadar, P.; Jeyakumar, T. Indian J Chem, Sect A 1994, 33A, 627.
29. Castro, E. A.; Ibanez, F.; Santos, J. G.; Ureta, C. J Chem Soc, Perkin Trans 2, 1991, 1919.
30. Castro, E. A.; Ibanez, F.; Santos, J. G.; Ureta, C. J Org Chem 1992, 57, 7024.
31. Castro, E. A.; Borquez, M. T.; Parada, P. M. J Org Chem 1986, 51, 5072.
32. Neuvonen, H. J Chem Soc, Perkin Trans 2 1987, 159.
33. Neuvonen, H. J Chem Soc, Perkin Trans 2 1995, 951.
34. Gordon, M.; Miller, J. G.; Day, A. R. J Am Chem Soc 1948, 70, 1946.
35. Gordon, M.; Miller, J. G.; Day, A. R. J Am Chem Soc 1949, 71, 1245.
36. Hawkins, P. J.; Piscalnikow, I. J Am Chem Soc 1955, 77, 2771.
37. Ananthakrishna Nadar, P.; Rajarathinam, D. Indian J Chem, Sect A 1997, 36A, 749.
38. Ananthakrishna Nadar, P.; Rajarathinam, D. Indian J Chem, Sect A 1998, 37A, 342.
39. Noller, C. R.; Adams, R. J Am Chem Soc 1924, 46, 1889.
40. Haworth, R. D.; Sheldrick, G. J Chem Soc 1934, 864.
41. Baliah, V.; Ganapathy, K. Trans Faraday Soc 1955, 77, 2771.
42. Frost, A. A.; Pearson, R. G. Kinetics and Mechanism, 2nd ed.; Wiley: New York, 1961; Chapter 3.
43. Katz, J.; Liebermann, I.; Barker, H. A. J Biol Chem 1953, 200, 417.
44. Kirsch, J. F.; Jencks, W. P. J Am Chem So*c* 1964, 86, 833.
45. Bell, R. P. The Proton in Chemistry, 2nd ed.; Chapman and Hall: London, 1973; Chapter 10.
46. Frost, A. A.; Pearson, R. G. Kinetics and Mechanism, 2nd ed.; Wiley: New York, 1961; Chapter 9.
47. Castro, E. A.; Moodie, R. B. J Chem Soc, Perkin Trans 2 1974, 658.

48. Edwards, J. O.; Pearson, R. G. J Am Chem Soc 1962, 84, 16.
49. Bruice, T. C.; Bruno, J. J.; Chou, W. S. J Am Chem Soc 1963, 85, 1659.
50. Johnson, S. L. Adv Phys Org Chem 1967, 5, 237.
51. Um, I. H.; Kwon, H. J.; Kwon, D. S.; Park, D. S. J Chem Res (S) 1995, 301(M), 1801.
52. Campbell, P.; Lapinskas, B. A. J Am Chem Soc 1977, 99, 5378.
53. Castro, E. A.; Valdivia, J. L. J Org Chem 1986, 51, 1668.
54. Castro, E. A.; Steinfort, G. B. J Chem Soc, Perkin Trans 2 1983, 453.
55. Gresser, M. J.; Jencks, W. P. J Am Chem Soc 1977, 99, 6963, 6970.
56. Castro, E. A.; Gil, F. J. J Am Chem Soc 1977, 99, 7611.
57. Palling, D. J.; Jencks, W. P. J Am Chem Soc 1984, 106, 4869.
58. Ferscht, A. R.; Jencks, W. P. J Am Chem Soc 1970, 92, 5442.
59. Hall, W. E.; Higuchi, T.; Pitman, I. H.; Uekama, K. J Am Chem Soc 1972, 94, 8153.
60. Fischer, A.; Packer, J.; Vaughan, J.; Wilson, A. F.; Wong, E. J Org Chem 1959, 24, 155.
61. Packer, J.; Vaughan, J.; Wong, E. J Org Chem 1958, 23, 1373.