Acylation. Part XXXVI.[1] The Kinetics and Mechanism of the Alkaline Hydrolysis and the n-Butaminolysis of Ethyl Thiolbenzoate in Aqueous Solution

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The hydrolysis of ethyl thiolbenzoate in aqueous solution between pH 9·80 and 10·75 obeys the rate equation $-d[Ester]/dt = k_{OH^-}[OH^-][Ester]$, with $k_{OH^-} = 1·6 \pm 0·1$ l mol^{-1} s^{-1} at 56 °C. The activation energy is 21·0 ± 0·2 kcal mol^{-1}. The n-butaminolysis of the same ester at 33·4 °C is general base-catalysed. Its rate displays dependencies upon [OH$^-$] and [amine] which point to the involvement of a carbonyl addition intermediate in the reaction, the breakdown of this intermediate to products being the only step catalysed by bases present. The rate constant for formation of the intermediate has a value (8·1 ± 0·2) × 10^{-3} l mol^{-1} s^{-1}. The relationships between the rate constants for the remaining steps of the mechanism have been evaluated. The other types of intermediate mechanism, and synchronous mechanism, normally considered in ester aminolysis appear to be excluded in the present instance.

PREVIOUS [2] kinetic studies of the alkaline hydrolysis of thiolesters, and of their aminolysis, have compared the reactivity of such esters with those of their *O*-analogues, and have also demonstrated that the same general kinetic form holds for both *O*- and *S*-esters in these reactions. In particular thiolester aminolysis in aqueous solutions has been shown to obey (at least approximately) the general rate equation $-d[Ester]/dt = \{k_2[Amine] + k_3[Amine]^2 + k_4[Amine][OH^-] + k_5[Amine][AmineH^+]\}[Ester]$. However, the terms in k_4 and k_5 are not always observed, and their presence, or absence, is not (yet) obviously related to ester structure. Acid-catalysed terms (k_5) would normally be expected to be small for thiol derivatives [3] since these have moderately good leaving groups, and the apparent importance of such terms in some cases is therefore surprising. Owing to their superior leaving groups, thiolesters are relatively more susceptible to aminolysis than to hydrolysis, compared with their *O*-analogues.[4] In principle this effect can be rationalised in terms of mechanisms involving tetrahedral addition intermediates or in terms of synchronous mechanisms.[3] This ambiguity of mechanism occurs throughout acylation and has only been resolved in relatively few cases.[3] Of the

[1] Part XXXV, B. Boopsingh and D. P. N. Satchell, *J.C.S Perkin II*, 1972, 1288.

[2] See T. C. Bruice and S. J. Benkovic, ' Bio-organic Mechanisms,' Benjamin, New York, vol. 1, 1966, for review up to 1965.

[3] D. P. N. Satchell and R. S. Satchell in ' The Chemistry of Carboxylic Acids and Esters,' ed. S. Patai, Wiley, New York, 1969.

[4] K. A. Connors and M. L. Bender, *J. Org. Chem.*, 1961, **20**, 2498.

different classes of acylating agent, esters are one of the likeliest to exhibit mechanisms involving intermediates, and it is for them that most of the kinetic evidence pointing to intermediates has accrued.[2,3,5] Recently, however, the American School,[6,7] which hitherto had postulated intermediates almost everywhere, has begun to take up the position for ester aminolysis that we have long advocated[3,8,9] for acylation generally, namely that in a great many cases the postulation of intermediates is unnecessary and that the reactions can well proceed with synchronous bond-formation and bond-breaking. There remain examples, however, where certain unusual effects of pH on the rate can best be interpreted in terms of kinetically important intermediate formation.[2,3,5] And one such example involves an intermolecular aminolysis of thiolesters; the reaction of thiolacetates and thiolactones with hydroxylamine or *O*-methylhydroxylamine.[10] Here the dependence of the apparent second- and third-order rate constants (k_2 and k_3 above) on pH suggested a scheme containing an addition intermediate which can coexist in three different states of protonation, and which enjoys general base-catalysed formation and general acid-catalysed decomposition to both starting materials and to products. A somewhat similar mechanism has recently been proposed for the aminolysis of methyl formate.[11] We report now on the alkaline hydrolysis, and particularly upon the n-butaminolysis, of ethyl thiolbenzoate.

EXPERIMENTAL

Materials.—Ethyl thiolbenzoate was a previous sample.[12] n-Butylamine was purified by distillation from potassium hydroxide under nitrogen. It had b.p. 77·3° and was stored under nitrogen. Benzoic acid was a recrystallised sample, m.p. 122°. Ethanethiol was purified by distillation under nitrogen. It had b.p. 34·5°. Deoxygenated distilled water was used for making up all solutions. Other reagents were of AnalaR or Reagent grade. Carbonate and n-butylamine–hydrogen chloride buffers were prepared by standard procedures. The aminolysis product, *N*-n-butylbenzamide, was prepared by mixing an ethereal solution of benzoyl chloride with a slightly more than equivalent quantity of n-butylamine in ether. After the mixture had stood at room temperature for 0·5 h it was washed with dilute hydrochloric acid, then with water, and dried (Na_2SO_4). The ether was removed in a rotary evaporator and the oily residue distilled. The product was a clear oil,[13] b.p. 152° at 0·9 mmHg.

Kinetic Arrangements.—All the kinetic measurements refer to essentially aqueous solutions. However, ethyl thiolbenzoate is very poorly soluble in pure water; all the mixtures therefore contained 3% v/v of ethanol to permit preparation of ester solutions of the required strength.

(i) *Alkaline hydrolysis.* The rate of hydrolysis was determined using carbonate buffers covering the pH range *ca.* 9·80—10·75. The ionic strength was maintained at 0·1M with potassium chloride. Reaction was initiated by addition to the thermostatted solvent, contained in a stoppered flask, of a suitable aliquot portion of a concentrated solution of ester in pure ethanol. The initial ester concentration in a reaction mixture was always *ca.* 10^{-4}M. Portions of reaction mixture were withdrawn at appropriate intervals and analysed spectrophotometrically. The disappearance of ester was followed by noting the decrease in absorption at 280 nm. Every hydrolysis was followed for more than two half-lives and infinity readings taken after *ca.* 10 half-lives. The observed loss of ester was always an accurately first-order process. Duplicate runs were performed at each pH value used. The observed first-order rate constants, k_{obs}, were reproducible to within ±3%. Measurements were made at three temperatures. Our results are in Table 1.

TABLE 1

Alkaline hydrolysis of ethyl thiolbenzoate in water containing 3% v/v ethanol

$[PhCO{\cdot}SEt]_{initial} \sim 10^{-4}$M; k_{obs} = observed first-order rate constants (min^{-1}); ionic strength = 0·10M; pH maintained by carbonate buffers, prepared as described in R. G. Bates and V. E. Powers, *Analyt Chem.*, 1956, **28**, 1322. The total buffer concetration varied from 0·033 to 0·045M.

(i) Temp. = 56 °C

pH	9·85	10·00	10·10	10·25	10·32
10^2k_{obs}	0·68	1·07	1·25	1·75	2·07
$10^6k_{obs}/[OH^-]$	0·97	1·07	0·99	0·99	0·99
pH	10·35	10·40	10·45	10·75	
10^2k_{obs}	2·20	2·45	2·58	5·20	
$10^6k_{obs}/[OH^-]$	0·98	0·98	0·91	0·91	

(ii) Temp. = 45 °C

pH	10·45	10·75
10^2k_{obs}	0·90	1·90
$10^6k_{obs}/[OH^-]$	0·32	0·33

(iii) Temp. = 34 °C

pH	10·45	10·75
10^2k_{obs}	0·27	0·58
$10^6k_{obs}/[OH^-]$	0·095	0·103

(ii) *n-Butaminolysis.* Butaminolysis was examined at a series of total buffer concentrations at three pH values at 33·4 °C, using n-butylamine–hydrogen chloride buffers and an ionic strength of 0·3M. Our general concentration conditions were similar to those of Connors and Bender [4] in their analogous study of ethyl *p*-nitrothiolbenzoate, except we used a wider range of butylamine concentrations. Loss of ester was again observed spectrophotometrically at 280 nm. Reaction mixtures were made up, at the required temperature, in 50 ml graduated flasks and a sample then transferred to a thermostatted spectrophotometer cell (1 cm path, quartz, ground-glass stoppered) for monitoring. Reactions were followed for 2—3 half-lives and infinity readings taken after *ca.* 10 half-lives. The observed loss of ester was always an accurately first-order process (k_{obs}). Duplicate runs were performed at most buffer concentrations and their reproducibility was similar to that for the hydrolysis. Our results are in Table 2.

In both (i) and (ii) the pH of mixtures was measured (with a Radiometer pH meter) at the start and end of each run.

[5] W. P. Jencks, 'Catalysis in Chemistry and Enzymology,' McGraw-Hill, New York, 1969.

[6] (*a*) W. P. Jencks and M. Gilchrist, *J. Amer. Chem. Soc.*, 1968, **90**, 2622; (*b*) A. R. Fersht and W. P. Jencks, *ibid.*, 1970, **92**, 5442.

[7] T. C. Bruice, A. F. Hegarty, S. M. Felton, A. Donzel, and N. G. Kundu, *J. Amer. Chem. Soc.*, 1970, **92**, 1370.

[8] D. P. N. Satchell, *Quart. Rev.*, 1963, **17**, 160.

[9] J. Hipkin and D. P. N. Satchell, *J. Chem. Soc.* (*B*), 1966, 345.

[10] T. C. Bruice and L. R. Fedor, *J. Amer. Chem. Soc.*, 1964, **86**, 4886.

[11] G. M. Blackburn and W. P. Jencks, *J. Amer. Chem. Soc.*, 1968, **90**, 2638.

[12] D. P. N. Satchell and I. I. Secemski, *J. Chem. Soc.* (*B*), 1970, 1306.

[13] G. H. Coleman and H. P. Howells, *J. Amer. Chem. Soc.*, 1923, **45**, 3088.

In every case a negligible change in pH occurred during a run. All spectrophotometric measurements were made with a Unicam SP 500 instrument.

TABLE 2

n-Butaminolysis of ethyl thiolbenzoate in water containing 3% v/v ethanol at 33·4 °C

$[PhCO{\cdot}SEt]_{initial} \sim 10^{-4}$M; k_{obs} = observed first-order rate constant for loss of ester (min^{-1}); ionic strength = 0·30M; n-butylamine–HCl buffers

(i) pH = 10·50					
$10[n\text{-}BuNH_2]_{free}$	0·28	0·57	0·85	1·14	1·42
10^2k_{obs}	0·70	1·19	2·02	3·02	4·02
$10[n\text{-}BuNH_2]_{free}$	1·71	2·00	2·28	2·56	
10^2k_{obs}	4·95	6·01	7·26	8·26	
(ii) pH = 10·75					
$10[n\text{-}BuNH_2]_{free}$	0·67	1·01	1·34	1·68	1·85
10^2k_{obs}	1·96	2·98	4·11	5·45	6·04
$10[n\text{-}BuNH_2]_{free}$	2·02	2·19	2·36	2·52	2·69
10^2k_{obs}	6·77	7·28	8·15	8·64	9·54
$10[n\text{-}BuNH_2]_{free}$	2·85	3·03			
10^2k_{obs}	10·08	10·74			
(iii) pH = 10·90					
$10[n\text{-}BuNH_2]_{free}$	0·40	0·80	1·20	1·60	2·00
10^2k_{obs}	1·42	2·61	4·10	5·70	7·21
$10[n\text{-}BuNH_2]_{free}$	2·40	2·80	3·20	3·60	
10^2k_{obs}	8·75	10·24	11·93	13·30	

Reaction Products.—The reaction of ethyl thiolbenzoate in carbonate buffers at pH >10 is clearly likely to follow the overall hydrolysis (1). In butylamine buffers con-

$$\begin{array}{ccccc} PhCO{\cdot}SEt & + & OH^- & \longrightarrow & PhCO_2H \quad + \quad EtS^- \\ & & & & \uparrow H_2O \qquad \downarrow H_3O^+ \\ & & & & PhCO_2^- \quad + \quad H_3O^+ \quad EtSH \quad + \quad H_2O \end{array} \qquad (1)$$

current butaminolysis (2) is expected, the percentage of butaminolysis depending on the pH and on the buffer concentration. Owing to the poor solubility of the thiol

$$\begin{array}{ccccc} PhCO{\cdot}SEt & + & BuNH_2 & \longrightarrow & PhCO{\cdot}NHBu \quad + \quad EtSH \\ & & & & \uparrow\downarrow H_2O \\ & & & & EtS^- + H_3O^+ \end{array} \qquad (2)$$

ester in aqueous solution it is inconvenient to demonstrate the expected products by direct preparative methods using the same conditions as in the kinetic runs. However,[4] comparison of the u.v. spectra of mixtures taken after more than 10 half-lives with the spectra of artificially prepared product mixtures appropriate to the various pH values and buffer concentrations, led in every case to excellent agreement. At most of the butylamine concentrations used the hydrolysis contributes relatively little to the overall reaction (see Table 2). The product, *N*-n-butylbenzamide, is stable in the solutions used.

RESULTS AND DISCUSSION

(i) *Alkaline Hydrolysis of Ethyl Thiolbenzoate in Carbonate Buffers.*—As can be seen from Table 1 the hydrolysis obeys the rate equation (3). In the pH region involved a term like $k_{H_2O}[H_2O][Ester]$ makes a negligible contribution to the rate. The values of k_{OH^-} at the different temperatures and pH values lead to a

$$-d[Ester]/dt = k_{obs}[Ester] = k_{OH^-}[OH^-][Ester] \qquad (3)$$

value of 21·0 ± 0·2 kcal mol^{-1} for the activation energy of reaction (1). At 25·6 °C k_{OH^-} will have a value *ca.* 0·05 l mol^{-1} s^{-1}. Connors and Bender's value [4] of k_{OH^-} for ethyl *p*-nitrothiolbenzoate at this temperature is 0·52 l mol^{-1} s^{-1}. As expected the nitro-ester is the more susceptible to attack by OH^-.

(ii) *n-Butaminolysis of Ethyl Thiolbenzoate.*—Values of k_{obs} determined at pH 10·50 and 10·90 for a series of butylamine buffer concentrations are plotted in Figure 1. An analogous curve was obtained at pH = 10·75

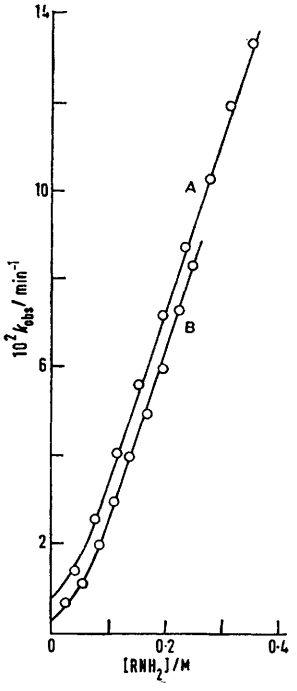


FIGURE 1 Plots of k_{obs} against $[RNH_2]$
A, pH = 10·90; B, pH = 10·50

(Table 2). A rather similar pattern of results was observed by Connors and Bender [4] with ethyl *p*-nitrothiolbenzoate. These authors analysed their results in terms of equation (4) in which the terms in k_2—k_6

$$\begin{aligned} -d[Ester]/dt = k_{obs}[Ester] = \{&k_{OH^-}[OH^-] + \\ &k_2[Amine] + k_3[Amine]^2 + k_4[Amine][OH^-] + \\ &k_5[Amine][AmineH^+] + k_6[AmineH^+]\}[Ester] \end{aligned} \qquad (4)$$

represent the rates of possible spontaneous, base-catalysed, and acid-catalysed routes to butaminolysis. Equation (4) is equivalent to (5) where $K_a = [H^+][Amine]/[AmineH^+]$. By plotting $(k_{obs} - k_{OH^-}[OH^-])/[Amine]$ against [Amine] at various pH values, Connors

$$\frac{(k_{obs} - k_{OH^-}[OH^-])}{[Amine]} = \left(k_3 + k_5\frac{[H^+]}{K_a}\right)[Amine] + \left(k_2 + k_4[OH^-] + k_6\frac{[H^+]}{K_a}\right) \qquad (5)$$

and Bender [4] obtained a series of approximately straight and approximately parallel lines from whose slopes and intercepts they deduced the values of the various rate constants. They showed that, at 25·6 °C and ionic strength 0·5M, $k_5 = k_6 \sim 0$ and that $k_2 = 0{\cdot}0151\ \text{l mol}^{-1}\ \text{s}^{-1}$, $k_3 = 0{\cdot}27\ \text{l}^2\ \text{mol}^{-2}\ \text{s}^{-1}$ and $k_4 = 13{\cdot}6\ \text{l}^2\ \text{mol}^{-2}\ \text{s}^{-1}$.

Similar plots of our results for ethyl thiolbenzoate are shown in Figure 2. The curvature evident in Connors and Bender's plots (and admitted by them [4]) is much more pronounced in ours. This is due to our use of a wider range of total buffer concentrations. An analysis of the initial (low [Amine]) regions of our plots, along the lines of Connors and Bender, leads to the values $k_5 = k_6 \sim 0$ and $k_2 = 8{\cdot}0 \times 10^{-4}$ l mol^{-1} s^{-1}, $k_3 = 2{\cdot}5 \times 10^{-2}$ l^2 mol^{-2} s^{-1}, and $k_4 = 1{\cdot}6$ l^2 mol^{-2} s^{-1}, at 33·4 °C and an ionic strength of 0·3M. These values

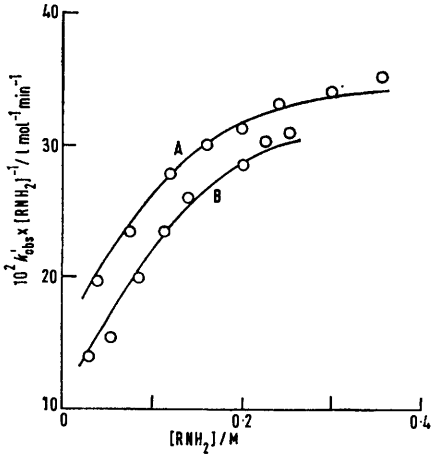
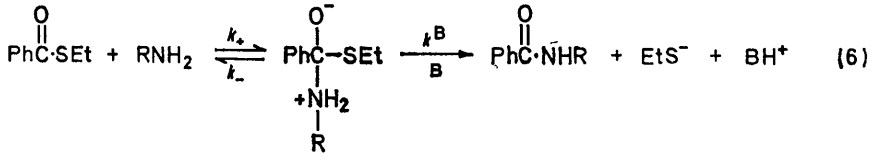


FIGURE 2 Plots of $k'_{obs}/[RNH_2]$ against $[RNH_2]$
A, pH = 10·90; B, pH = 10·50. $k'_{obs} = (k_{obs} - k_{OH^-}[OH^-])$

all bear sensible relationships to those found for the nitro-substituted compound, and, as for the latter, there is no evidence for an important acid-catalysed term (k_5). The particularly interesting feature of our results is, however, the evident curvature of the plots in Figure 2. Clearly equation (5) is not obeyed at high amine concentrations. Were it obeyed the term in k_3 would dominate the rate equation at high amine concentrations and plots like Figure 1 would continue to curve upwards parabolically. There is no doubt, however, from our results, that at high amine concentrations k_{obs} becomes rectilinearly related to [Amine] at each pH studied and does not continue to rise fast enough to satisfy equation (5). Although this result partially undermines Connors and Bender's kinetic analysis,[4] it can, paradoxically, only be explained readily by an outline mechanism for the aminolysis which these authors favour,[4] a mechanism involving an intermediate. We suggest scheme (6) in which the intermediate's breakdown to products is catalysed by a second molecule of base (B). Application of the steady state treatment to this scheme, assuming that H_2O, OH^-, and RNH_2 can all function as B, leads to equation (7), in which $k'_{obs} = (k_{obs} - k_{OH^-}[OH^-])$. This equation predicts behaviour like that observed. Thus when $(k^{RNH_2}[RNH_2] + k^{OH^-}[OH^-] + k^{H_2O}[H_2O]) \gg$



(6)

k_- we have equation (8) and rectilinear dependence of k'_{obs} on $[RNH_2]$. This is the approximate situation at

$$-\frac{1}{[\text{Ester}]}\frac{d}{dt}[\text{Ester}] = k'_{obs} = \frac{k_+[RNH_2](k^{RNH_2}[RNH_2] + k^{OH^-}[OH^-] + k^{H_2O}[H_2O])}{k_- + (k^{RNH_2}[RNH_2] + k^{OH^-}[OH^-] + k^{H_2O}[H_2O])} \quad (7)$$

high amine concentration in our experiments. Equation (8) predicts that the straight region of plots like those in

$$k'_{obs} = k_+[RNH_2] \quad (8)$$

Figure 1 will have a constant slope, k_+, independent of pH. This is found to be so. Our average value for k_+ is $(8{\cdot}1 \pm 0{\cdot}2) \times 10^{-3}$ l mol^{-1} s^{-1}.

Equation (7) can, under certain conditions, be written in the form of equation (4), *i.e.* as a sum of terms like equation (9), and plotted as in Figure 2. If we assume temporarily that this is valid at the lowest amine concentrations used by us, then the values of k_2, k_3, and k_4

$$k'_{obs} = k_2[RNH_2][H_2O] + k_3[RNH_2]^2 + k_4[RNH_2][OH^-] \quad (9)$$

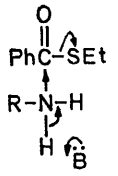
obtained from our initial slope analysis of Figure 2 suggest * that $k^{RNH_2}[RNH_2] \sim k^{OH^-}[OH^-] \sim k^{H_2O}[H_2O]$

* $k_2 = k_+k^{H_2O}/\{k_- + (k^{RNH_2}[RNH_2] + k^{OH^-}[OH^-] + k^{H_2O}[H_2O])\}$, *etc.*

when $[RNH_2] \sim 0{\cdot}03$M and pH = 10·50. If, in keeping with these results, we take $k_+ = 8{\cdot}1 \times 10^{-3}$ and $k^{RNH_2}[RNH_2] : k^{OH^-}[OH^-] : k^{H_2O}[H_2O] : k_-$ as 1 : 1 : 1 : 7 when $[RNH_2] = 0{\cdot}03$M and pH = 10·5, then equation (7) accurately reproduces the experimental plots in Figures 1 and 2, the full lines in these Figures being the theoretical curves. Equation (7) can only be written as (9) if the contribution of $k^{RNH_2}[RNH_2]$ to the denominator is not too great for the variation of $[RNH_2]$, at constant pH, to leave the denominator little changed. Our values suggest that an equation like (9) is only likely to be a reasonable approximation at $[RNH_2] \lesssim 0{\cdot}1$M. As we have seen from Figure 2, this is so. In obtaining their values for k_2, k_3, and k_4 from plots like those in Figure 2, Connors and Bender [4] largely ignored the curvature present; their values would

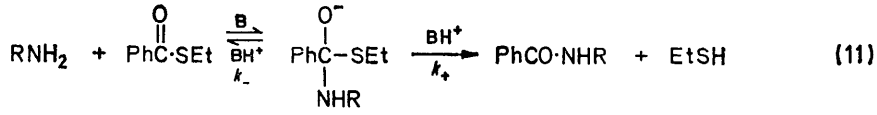
therefore be improved by taking initial slopes, although the difference involved will not be great.

With regard to the relevance of our results to ester aminolysis generally there are two main conclusions: first, synchronous mechanisms like (10) are excluded since the appropriate rate equation will, under all circumstances, be just a sum of terms like (9); secondly, mechanisms like (11) in which the base catalysis assists



(10)

the addition step [11] are also probably excluded. Mechanism (11) leads to the rate equation (12), which



(11)

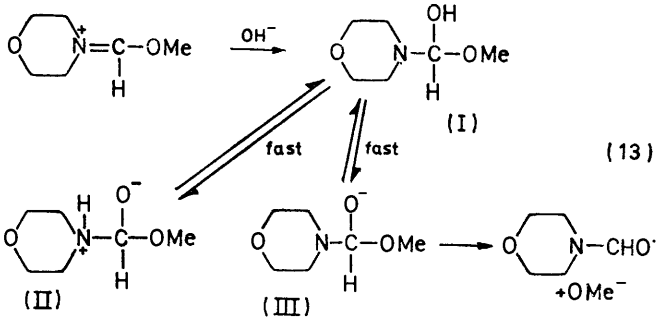
can, for appropriate values of the various terms, mirror kinetic behaviour somewhat similar to, although distinct

$$\frac{k'_{obs}}{[RNH_2]} = \frac{k^{H_2O}[H_2O] + k^{RNH_2}[RNH_2] + k^{OH^-}[OH^-]}{1 + \dfrac{k_-^{H_3O^+}[H_3O^+] + k_-^{RNH_3^+}[RNH_3^+] + k_-^{H_2O}[H_2O]}{k_+^{H_3O^+}[H_3O^+] + k_+^{RNH_3^+}[RNH_3^+] + k_+^{H_2O}[H_2O]}} \quad (12)$$

from, that found by Connors and Bender and ourselves. This has been demonstrated by Blackburn and Jencks [11] who, for the aminolysis of methyl formate, also found that plots of $k'_{obs}/[RNH_2]$ against $[RNH_2]$ led to curves. These authors identified small, or negligible, terms in k^{OH^-}, but sizeable terms in k^{RNH_2} and $k^{H_3O^+}$. The initial slopes and intercepts of their plots are both functions of pH, and this is satisfactorily accounted for by equation (12) even if k^{OH^-} is negligible, provided that $k_-^{H_3O^+}$ is finite. When, however, $k^{H_2O}[H_2O]$ and $k^{OH^-}[OH^-]$ are both important and of comparable magnitude (as in our experiments) then because, by the principle of microscopic reversibility, $k_-^{H_3O^+}$ must still contribute importantly, equation (12) does not easily permit the initial slopes of Figure 2 to be independent of pH and, at the same time, reproduce the observed effects of increases in $[RNH_2]$.

It is possible, as Blackburn and Jencks hint,[11] that their results could be represented by a mechanism like (6) with the addition of appropriate terms representing acid catalysis of leaving group departure. They prefer mechanism (11) on the grounds that the direction of decomposition of the intermediate (I) formed by addition of OH^- to the *N*-(methoxymethylene)morpholinium cation *always* leads to amide and alcohol at high pH (13), since this implies that, under these conditions, in the corresponding aminolysis of methyl formate by morpholine, which involves the 'same' intermediate [*i.e.* (II) or (III)], loss of OMe cannot be even partially rate-determining as it will be if mechanism (6) is correct. This argument depends, however, as Blackburn and Jencks realise,[11] on the assumption that proton transfers among the various intermediates are rapid compared with the breakdown of intermediates to reactants or products. And this is not necessarily the case.[14] If it is not, and if the intermediate formed in the aminolysis has, as we suggest in equation (6), a structure like (II) rather than like (III) as implied by equation (11), then it is very likely that loss of amine will be preferred to loss of OMe^-, and hence that the latter will affect the rate.

We find it strange that in one paper [6a] Jencks can conclude that in aminolysis there is no evidence that the term in k_2 (p. 1 *et seq.*) represents base catalysis by water and that the transition state for this path is formally neutral [*e.g.* like (II)], yet in the following paper [11] can include a mechanism, (11), whose adequacy is critically dependent on the existence of such catalysis. It is



(13)

particularly strange when it is realised that Jencks believes that the two types of ester involved in these contradictory conclusions fall in fact into the *same* (supposed) sub-category of mechanism.[6b] Our results support the conclusions of the first [6a] of these two papers and suggest (to our own considerable surprise [3]) that the mechanism of ester aminolysis originally proposed by Bunnett and Davies [15] operates in the present system. In a recent paper [14] on intramolecular thiolester aminolysis Jencks himself reaches a somewhat similar conclusion for that particular reaction (although he does not comment on it). We suggest that all aminolyses which give kinetic evidence of intermediates, involve a scheme based on (6), when necessary with additional routes employing acid catalysis of leaving group departure.

[2/342 *Received*, 15*th February*, 1972]

[14] R. E. Barnett and W. P. Jencks, *J. Amer. Chem. Soc.*, 1969, **91**, 2358.

[15] J. F. Bunnett and G. T. Davies, *J. Amer. Chem. Soc.*, 1960, **82**, 665.