Anal. Calcd. for $C_{12}H_{20}O_5NBr$: C, 42.64; H, 5.96; N, 4.14. Found: C, 43.01; H, 6.14; N, 4.15.

Potassium Cyanide-C^{14}.—Radioactive barium carbonate-C^{14} (0.1686 g., 11.11 mc.), obtained from Oak Ridge National Laboratories, was converted to potassium cyanide-C^{14} in 86.8% yield by the sodium azide method.[4] By the addition of non-radioactive potassium cyanide, 0.0541 g. of this radioactive potassium cyanide, representing 9.64 mc., was diluted to 3.25 g. (50 mmoles, 0.19 mc./mmole).

Ethyl α-Acetamido-α-carbethoxy-δ-cyano-C^{14}-valerate (III).—To a *solution* of 3.25 g. of *potassium* cyanide-C^{14} (50 mmoles, 0.19 mc./mmole) in 49.5 ml. of water and 165 ml. of absolute alcohol, was added 16.20 g. (50 mmoles) of ethyl α-acetamido-α-carbethoxy-δ-bromovalerate, and the mixture refluxed for 2.25 hours. The hydrogen cyanide evolved during refluxing and subsequent solvent distillation was absorbed in a trap containing 35 ml. of 1.5 *N* sodium hydroxide (carbonate free). The reaction flask was placed in a refrigerator overnight. The solvent was then completely removed by distillation under diminished pressure, and the residue extracted with several small portions of ether. The residual potassium bromide corresponded to the theoretical yield.

Evaporation of the dried extracts (Na_2SO_4) yielded a dark oil, presumably ethyl α-acetamido-α-carbethoxy-δ-cyano-C^{14}-valerate.

DL-Lysine-6-C^{14} Monohydrochloride.—The crude cyano compound was dissolved in 60 ml. of acetic anhydride, 0.3 g. of platinum oxide (Adams catalyst) was added and hydrogenation was carried out at 60 p.s.i. and 50° for 12 hours, then 0.2 g. of PtO_2 was added and the hydrogenation continued for an additional 24 hours. At the end of this time, 50 ml. of ice-water was added to hydrolyze the acetic anhydride, and the mixture allowed to stand for 1 hour. The catalyst was filtered off, $1^1/_2$ volumes of concentrated hydrochloric acid were added, and the mixture was then refluxed for 20 hours. The lysine dihydrochloride was isolated and converted to the monohydrochloride by the usual methods.[5] The yield of DL-lysine-6-C^{14} monohydrochloride was 1.90 g., which, after taking into account the recovery of 45% of the original radiocyanide, corresponds to 38% of theoretical.

DL-α-Aminoadipic Acid-6-C^{14}.—To a solution of 2 g. of ethyl α-acetamido-α-carbethoxy-δ-bromovalerate in 20 ml. of ethanol, was added 400 mg. of radioactive potassium cyanide in 5.4 ml. of water. An additional 2 ml. of water was used to rinse the last of the cyanide into the reaction flask. The mixture was refluxed for 2.5 hours, distilled to dryness *in vacuo*, and the residue extracted four times with ether. The residual potassium bromide weighed 0.73 g. (100%).

The ether extracts were evaporated and hydrolyzed for 5 hours with 30 ml. of concentrated hydrochloric acid. The resulting solution was distilled to dryness under diminished pressure. Addition of water and distillation to dryness was repeated twice, yielding a crystalline residue which was dissolved in a small amount of water and filtered. The volume was made up to about 12 ml. with water and 15 ml. of ethanol was added. The solution was treated with a slight excess of pyridine, stirred and placed in the refrigerator overnight. The white, crystalline DL-α-aminoadipic acid-6-C^{14} was filtered, washed with 50% ethanol until halogen free, and dried; yield 0.389 g. (41%). A paper chromatogram (phenol–water) showed one spot only, *Rf* = 0.33.

Benzoylation of material from a similar but non-radioactive preparation gave α-benzamidoadipic acid, m.p. 183.5–184.5° (lit.[6] m.p. 184–185°).

Acknowledgment.—The authors wish to thank Dr. R. W. Helmkamp for his helpful suggestions and Mr. John Morgenthau, Jr., for his technical assistance.

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[4] C. J. Claus, D. C. Camp, J. L. Morgenthau, Jr., P. Olynyk and R. W. Helmkamp, Abstracts of Meeting of Am. Chem. Soc., Buffalo, N. Y., March 1952, p. 51K.

[5] "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 375.

[6] R. Gaudry, *Can. J. Research*, **27B**, 21 (1949).

ROCHESTER, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

Studies on Model Compounds for Coenzyme A. A Kinetic Study of Aminolysis and Hydrolysis of Ethyl Thioacetate and β-Acetaminoethyl Thioacetate in Aqueous Solution

BY PETER J. HAWKINS AND D. STANLEY TARBELL

RECEIVED DECEMBER 4, 1952

A kinetic study of the reaction of *n*-butylamine with ethyl thioacetate (I) and with β-acetaminoethyl thioacetate (II) in aqueous solution showed the rate of hydrolysis of the thioesters in aqueous amine solution to be appreciable. The rate of disappearance of ester by aminolysis and hydrolysis was in agreement with the following rate equation: $-d([\text{Ester}]/dt) = k_4\,[\text{Ester}][\text{RNH}_2][\text{OH}^-] + k_5[\text{Ester}][\text{OH}^-]$. The rate of reaction of the ethyl thioacetate is similar to that of β-acetaminoethyl thioacetate, indicating little effect on the reaction rate of the amide group in the β-position. Bis-(β-acetaminoethyl) disulfide and N-*n*-butylacetamide have been isolated in high yield from the action of *n*-butylamine on β-acetaminoethyl thioacetate in aqueous solution.

The interest in this Laboratory in the general problem of the cleavage of the carbon–sulfur bond[1] has recently included kinetic studies of the alkaline and acid hydrolysis of thioesters.[2] The properties of this class of compound are at present of both biochemical and chemical significance, due to the discovery that Coenzyme A, which plays a key role in metabolism, is an N-acylated derivative of β-aminoethyl mercaptan.[3] The S-acylated Coenzyme A rapidly transfers its acyl group to other substrates (in the presence of the appropriate enzyme), and it was the purpose of the present work to relate, if possible, the high reactivity of the S-acylated Coenzyme A to structural features and thus explain its reactivity on purely chemical grounds.

The present paper describes kinetic studies of the aminolysis and hydrolysis of ethyl thioacetate (I) and β-acetaminoethyl thioacetate (II), using *n*-butylamine, to determine the effect on the reactivity of the thiolester of the amide group on the β-carbon.

$CH_3COSCH_2CH_3$ I

$CH_3COSCH_2CH_2NHCOCH_3$ II

The reactions were carried out in aqueous solution in order to approach biological conditions more

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[1] D. S. Tarbell and D. P. Harnish, *Chem. Revs.*, **49**, 1 (1951).

[2] (a) P. N. Rylander and D. S. Tarbell, THIS JOURNAL, **72**, 3021 (1950); (b) B. K. Morse and D. S. Tarbell, *ibid.*, **74**, 416 (1952).

[3] (a) J. D. Gregory and F. Lipmann, *ibid.*, **74**, 4017 (1952), and numerous earlier papers; (b) F. Lynen, E. Reichert and L. Rueff, *Ann.*, **574**, 1 (1952); (c) E. E. Snell, *et al.*, THIS JOURNAL, **72**, 5349 (1950); (d) J. Baddiley and E. M. Thain, *J. Chem. Soc.*, 3421 (1951).

closely and to define the kinetic conditions more exactly. The reaction of II with *n*-butylamine according to equation (1) was first measured by titration of the liberated thiol group with standard iodine.

$$RNH_2 + II = CH_3CONHR + HSCH_2CH_2NHCOCH_3 \qquad R = n\text{-}C_4H_9 \quad (1)$$

Previous studies of the aminolysis and ammonolysis of esters[4] have shown that the second-order rate constants obtained from equation (2) show a marked drift to lower values as the reaction proceeds. Similar effects were observed in the present case, but in this system the amine concentration is subject to the equilibria

$$RNH_2 + H_2O = RNH_3^+ + OH^- \qquad (3)$$

$$RNH_2 + R'SH = RNH_3^+ + R'S^- \qquad (4)$$

It was also shown in separate experiments that the hydrolysis of the ester, occurring at the *p*H of the amine solutions, could not be neglected as it could under the conditions employed by previous workers.[5]

To eliminate some of the uncertainties due to these factors, pseudo first-order rate constants (first order in ester) were obtained, using a suitable excess of amine. In order to retain a reasonable rate of reaction, the ester concentrations were necessarily small and beyond the limit of sensitivity of the iodine titration method. The results reported were therefore obtained by following the rate of disappearance of the thioester spectrophotometrically.[6]

Experimental

Preparation of Materials. β-Acetaminoethyl Thioacetate.—β-Phthalimidoethyl mercaptan[7] (70 g.) was hydrolyzed following Gabriel's procedure,[8] and the amine hydrochloride (28 g.) was converted to the free base by treatment with sodium methoxide in methanol. After removal of the sodium chloride the solvent was evaporated and the residue purified by sublimation in vacuum, giving 11.1 g. of β-aminoethyl mercaptan, m.p. 80–85°. This material (11.1 g.) was allowed to stand overnight in 150 cc. of pyridine with 38 cc. of acetic anhydride. Methanol (40 cc.) was then added, and after 1 hour the volatile material was removed at the water pump. The residue was fractionated twice *in vacuo*, and 16.3 g. of β-acetaminoethyl thioacetate obtained with the following properties[9]: b.p. 131–133° (1 mm.), $n^{27}D$ 1.5070, m.p. 28–30°. Analyses for carbon, hydrogen and nitrogen were satisfactory, and quantitative hydrolysis experiments used 98.5–99.6% of the theoretical quantity of alkali.

Ethyl thioacetate had the following properties: b.p. 114°, $n^{25}D$ 1.4564. The reported values[10] are b.p. 113.5°, $n^{20.4}D$ 1.4583.

***n*-Butylamine** (Eastman Kodak Co.) was fractionally distilled twice, b.p. 76–76.5°.[11] Titration with standard acid to a methyl red end-point showed it to be better than 98% pure.

Procedure.—The molar extinction coefficients at 233 mμ for ethyl thioacetate (I) and β-acetaminoethyl thioacetate (II) in 0.01 *N* HCl solution were determined to be 4.57 × 10^3 and 4.51 × 10^3, respectively. Ethyl mercaptan, butylacetamide and butylamine were shown to have negligible absorptions at 233 mμ, and as it was possible to follow the hydrolysis of the diacetylated compound to at least 96% reaction, the N-acetyl mercaptan cannot have an appreciable absorption.

A solution of ester in air and carbon dioxide-free water in a volumetric flask and a similar solution of sodium hydroxide or amine were allowed to reach thermal equilibrium in an ice-bath. A suitable aliquot of the amine or hydroxide solution was then rapidly transferred to the ester solution and the volume made up to the mark. The flask was rapidly shaken, replaced in the bath and allowed a further 5–10 min. to return to temperature. Aliquots were then withdrawn at suitable intervals and the reaction quenched in an appropriate amount of 0.01 *N* HCl. The optical densities at 233 mμ were determined using a Beckman spectrophotometer and the concentrations of the thiol esters were calculated.

Isolation of Products from Butylamine and β-Acetaminoethyl Thioacetate.—The diacetyl compound (5.4 g.) was allowed to stand with 10 g. of *n*-butylamine in 25 cc. of water for a day and air was bubbled through it for 3 hr. The solvent was removed *in vacuo*, and distillation of the residue yielded 3.20 g. of N-*n*-butylacetamide, b.p. 138–141° (23 mm.). Redistillation gave a material of b.p. 136° (22 mm.), $n^{23.8}D$ 1.4392. This material had a slightly low carbon content, possibly due to a trace of water, but its physical properties indicated its identity.[12]

Distillation of the column and pot residues gave 1.60 g., b.p. 84–91° (0.4 mm.); and 1.34 g., b.p. 92–95° (0.4 mm.). Titration of both fractions with standard iodine solution showed a content of N-acetyl-β-aminoethyl mercaptan (assuming this to be the mercaptan component, which is reasonable from the b.p.)[13] of 0.78 and 1.25 g., respectively; the balance is undoubtedly N-*n*-butylacetamide. The pot residue yielded 0.9 g. of solid, from which crystalline bis-(β-acetaminoethyl) disulfide, m.p. 92–93° (cor.), was obtained. Kuhn[9] reported this compound to melt at 87°. This sample gave no depression on mixed m.p. with a sample of this compound obtained in another run, which had been recrystallized from alcohol. The compound showed no nitroprusside test for mercaptan, and the analysis supported the expected structure.

Anal. Calcd. for $C_8H_{16}N_2O_2S_2$: C, 40.65; H, 6.82. Found: C, 40.63; H, 7.05.

The total yield of butylacetamide was 3.2 g. plus 0.8 g., or 4.0; the calculated yield was 3.86 g. The total yield of N-acetyl-β-aminoethyl mercaptan was 3.35 g.; the calculated yield was 3.99 g.

Discussion of the Results

The significant experimental results for the aminolysis, by *n*-butylamine, and the hydrolysis, of I and II, are given in Table I. Except for the cases noted in the table, the $k_{obs.}$ are the pseudo first-order constants for the rate of disappearance of the thioester, determined spectrophotometrically. The degree of constancy of $k_{obs.}$ during a run is indicated by the typical examples in Table II.

Since previous observations[4] indicated that aminolysis was second order, *i.e.*, rate = k[Amine][Ester], the data in Table I were examined to see if they agreed with the kinetic equation

$$\text{rate} = k[RNH_2][\text{Ester}] + k'[OH^-][\text{Ester}] \qquad (5)$$

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[4] (a) R. L. Betts and L. P. Hammett, THIS JOURNAL, **59**, 1569 (1937); (b) M. Gordon, J. G. Miller and A. R. Day, *ibid.*, **70**, 1946 (1948); (c) E. M. Arnett, J. G. Miller and A. R. Day, *ibid.*, **72**, 5635 (1950); (d) R. Baltzly, I. M. Berger and A. A. Rothstein, *ibid.*, **72**, 4149 (1950).

[5] The basic dissociation constant of *n*-butylamine at 25° is 4.1 × 10^{-4} (C. W. Hoerr, M. R. McCorkle and A. W. Ralston, *ibid.*, **65**, 328 (1943)).

[6] (a) Sjöberg, *Z. physik. Chem.*, **52**, 209 (1942); (b) L. Noda, Abstracts of Papers presented at the 121st Meeting of the A.C.S., p. 42C; (c) H. P. Koch, *J. Chem. Soc.*, 387 (1949).

[7] J. Baddiley and E. M. Thain, *ibid.*, 2258 (1951).

[8] S. Gabriel, *Ber.*, **22**, 1137 (1889); **24**, 1110 (1891).

[9] The reported values (R. Kuhn and K. Quadbeck, *Ber.*, **84**, 844 (1951)) are m.p. 29–30°, $n^{24}D$ 1.5069, b.p. 181–182° (15 mm.).

[10] J. R. Schaefgen, THIS JOURNAL, **70**, 1308 (1948).

[11] H. Schlundt, *J. Phys. Chem.*, **5**, 508 (1901), gives the b.p. as 76–77°.

[12] N-*n*-Butylacetamide boils at 229° (760 mm.) (H. O. Nicholas and J. L. E. Erickson, THIS JOURNAL, **48**, 2175 (1926)), and has $n^{25}D$ 1.4388: R. H. Wiley, O. H. Borum and L. L. Bennett, Jr., *ibid.*, **71**, 2899 (1949). N-*n*-Butylacetamide prepared by treating ethyl thioacetate with *n*-butylamine had identical physical properties.

[13] Kuhn (ref. 9) reported a b.p. of 138–140° (7 mm.) for N-acetyl-β-aminoethyl mercaptan.

TABLE I

HYDROLYSIS AND AMINOLYSIS

A. Ethyl thioacetate, $CH_3COSC_2H_5$: Hydrolysis

Run no.	[Ester], mole/l.	$[OH^-]$, mole/l.	$k_{obs.}$,[a] min.$^{-1}$	$k_{obs.}/[OH^-]$
13	0.000237	0.005215	0.00347	0.665
14	.000463	.005215		.660
16	.0003952	.01043	.00635	.626
			Mean	.650

Aminolysis by *n*-butylamine

Run no.	[Ester], mole/l.	Amine $[RNH_2]$ + $[RNH_3^+]$, mole/l.	$k_{obs.}$, min.$^{-1}$	$k_{obs.}/[RNH_2]^{1/2}$
5	0.000760	0.01660	0.0282	0.237
7	.000655	.01819	.0315	.252
8	.000339	.01039	.0134	.145
9	.000330	.01039	.0136	.147
10	.0001225	.00487	.00465	.0770
11	.0001225	.00487	.00452	.0748
12	.0001225	.00487	.00454	.0752

B. β-Acetaminoethyl thioacetate, $CH_3COSCH_2CH_2NHCOCH_3$: Hydrolysis

Run no.	[Ester], mole/l.	$[OH^-]$, mole/l.	$K_{obs.}$, min.$^{-1}$	$k_{obs.}/[OH^-]$
17	0.0006995	0.01043	0.0111	1.07
18	.0003497	.01043	.0116	1.11
19	.0001679	.005215	.00601	1.15
			Mean	1.11

Aminolysis by *n*-butylamine

Run no.	[Ester] mole/l.	Amine $[RNH_2]$ + $[RNH_3^+]$, mole/l.	$k_{obs.}$, min.$^{-1}$	$k_{obs.}/[RNH_2]^{1/2}$
20	0.0003497	0.006905	0.0131	0.178
21	.0006995	.01381	.0344	.319
22	.0001672	.005524	.00902	.139
23	.0002990	.01104	.0254	.266

[a] In runs 13 and 16, $k_{obs.}$ are first-order constants, OH^- in excess. In run 14, $k_{obs.}$ is a second-order constant where the base was not in excess.

which has an additional term for the hydrolysis reaction. In the calculations, it was necessary to use the actual free amine concentration $[RNH_2]$, making allowance for the amount existing as $[RNH_3^+]$, due to the basic ionization of the amine according to equation 3. $[RNH_2]$ was calculated by solving the two simultaneous equations

$$[RNH_2] + [RNH_3^+] = \text{Total amine concentration} \quad (6)$$

$$[RNH_3^+]^2 = [RNH_2]K_b \quad (7)$$

Equation 7, where K_b is the basic dissociation constant for the amine, is obtained from equation 3, by setting $[OH^-] = [RNH_3^+]$. The values for $[RNH_2]$ listed in Table I were calculated by the above procedure.

Equation 5 may be transformed as follows, using equation 7 and remembering that the observed (pseudo) first-order rate constant $k_{obs.}$ represents the total rate of disappearance of ester.

$$k_{obs.} = k_1 = k[RNH_2] + k'[OH^-] \quad (8)$$

$$k_{obs.} = k[RNH_2] + k'K_b^{1/2}[RNH_2]^{1/2} \quad (9)$$

A plot of $k_{obs.}/[RNH]^{1/2}$ *vs.* $[RNH_2]^{1/2}$ did not yield a satisfactory linear plot, however, and the intercept (which should be $k'K_b^{1/2}$) was negative, which was not in agreement with the experimental fact that the concurrent alkaline hydrolysis, whose constant is k', was actually appreciable.

TABLE II

REPRESENTATIVE RUNS

Hydrolysis of β-Acetaminoethyl Thioacetate, 0° C., run 18, $[OH^-]$, 0.01043 mole/l.

Time, min.	[Ester], mole/l. × 10^4	$k_{obs.} \times 10^2$, min.$^{-1}$
0	2.835	
16.85	2.348	1.12
25.55	2.093	1.19
34.80	1.883	1.18
46.10	1.672	1.14
59.65	1.417	1.16
74.25	1.207	1.15
90.55	1.008	1.14
110.25	0.7984	1.15
∞ 12 hours	.1288	

Aminolysis of ethyl thioacetate, run 12, $[RNH_2]$ + $[RNH_3^+]$, 0.004870 mole/l., 0.0°C.

Time, min.	[Ester], mole/l., × 10^4	$k_{obs.} \times 10^3$, min.$^{-1}$
0	1.053	
30.15	0.9175	4.58
45.55	.8523	4.64
60.50	.7981	4.58
80.80	.7438	4.31
104.25	.6678	4.38
166.95	.4886	4.60
221.95	.3691	4.72

The following equation did yield satisfactory linear plots, when $k_{obs.}/[RNH_2]^{1/2}$ was plotted against $[RNH_2]$, as shown in Figs. 1 and 2.

$$k_1 = k_{obs.} = k_2[RNH_2]^{3/2} + k_3[RNH_2]^{1/2} \quad (10)$$

$[RNH_2]$ again represents the actual free amine concentration calculated as shown above.

One interpretation of this equation (and in our view the most reasonable) is in terms of a hydroxyl ion catalyzed aminolysis (*cf.* Betts and Hammett[4a]) and the concurrent hydrolysis. Thus, equation 10 is equivalent to the following equation

$$\text{rate} = k_{obs.}[\text{Ester}] = k_4[RNH_2][\text{Ester}][OH^-] + k_5[\text{Ester}][OH^-] \quad (11)$$

by the appropriate substitutions of $K_b^{1/2}[RNH_2]^{1/2}$ for $[OH^-]$.

The validity of this interpretation is supported by the independent determination of k_5 in separate alkaline hydrolysis experiments.

$$\text{rate of hydrolysis} = k_5[\text{Ester}][OH^-] \quad (12)$$

The intercept of the plots of equation 10 (Figs. 1 and 2) is k_3, and this is related to k_5 by

$$k_3 = k_5K_b^{1/2} \quad (13)$$

Column A of Table III shows the alkaline hydrolysis rate constants obtained in separate hydrolysis experiments, and column B shows those derived from the aminolysis runs from the plots of equation 10 by the use of equation 13.

TABLE III

SECOND-ORDER ALKALINE HYDROLYSIS CONSTANTS AT 0°, L./MOLE/MIN.

	A	B
β-Acetaminoethyl thioacetate	1.11	1.77
Ethyl thioacetate	0.65	1.02

It must be remembered that such a derivation relies on a dissociation constant for *n*-butylamine determined at 25°,[5] whereas the kinetic data are at 0°. In view of this and the graphical methods involved, the agreement seems to us sufficient for the purpose.

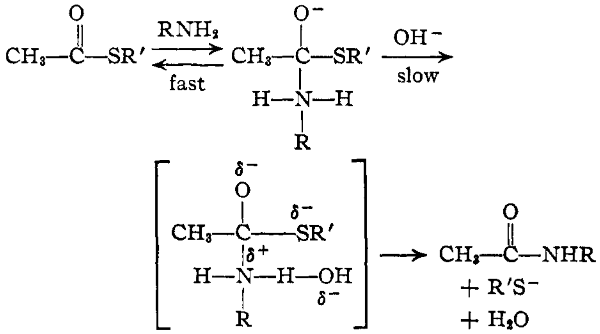
While equation 11 represents the aminolysis as a hydroxyl ion catalyzed reaction, the data are equally compatible with an ammonium ion catalyzed reaction according to the following equation.

$$\text{rate} = k_4[\text{Ester}][\text{RNH}_2][\text{RNH}_3^+] + k_5[\text{Ester}][\text{OH}^-] \qquad (14)$$

The values of the aminolysis rate constant k_4 in equation 11 or 14 for ethyl thioacetate and β-acetaminoethyl thioacetate were 753 and 1253, respectively.[14]

Support for the former interpretation may be found in the observations of Betts and Hammett[4a] on the ammonolysis of methyl phenylacetate. These authors demonstrated a strong methoxide ion catalysis of the ammonolysis which has since been utilized in synthetic methods.[15] It is also generally observed[2a] that acid catalyzed are much slower than the corresponding alkaline-catalyzed reactions and it is therefore likely that it is the latter type of catalysis which is being measured.

An acceptance of equation 11, involving the hydroxyl ion catalysis, leaves the exact mode of attack of the reagents to be decided. While little evidence is at present available, the following mechanism seems plausible, in which the hydroxyl ion removes a proton from the ammonium nitrogen with the simultaneous expulsion of the mercaptide ion.



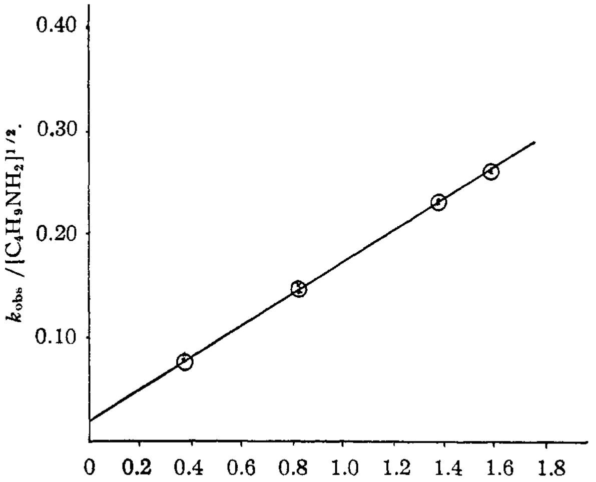


Fig. 1.—Plot of equation 10 for the aminolysis of ethyl thiolacetate.

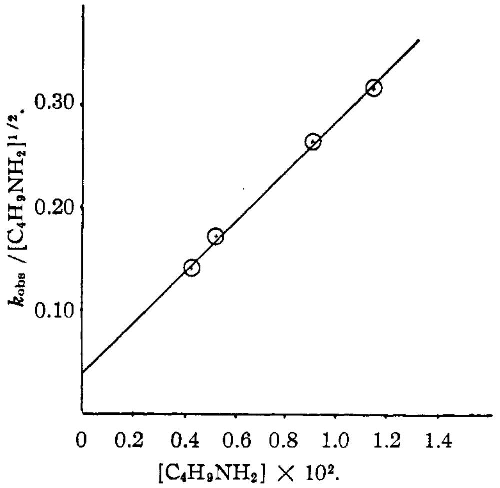


Fig. 2.—Plot of equation 10 for the aminolysis of β-acetaminoethyl thioacetate.

The similarity of the aminolysis and hydrolysis rate factors for the two esters indicates little or no effect on the rates of these reactions of a neighboring acetamino group. If the acetyl group of the acetyl Coenzyme A is, therefore, unusually reactive, the presence of the amide group on the β-carbon is evidently not the cause.

The mechanism of aminolysis suggested above is somewhat analogous to that proposed for the hydroxyl catalyzed cleavage of acetylacetone,[16] which is second-order in hydroxyl ion and first order in diketone.

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[14] ADDED IN PROOF.—Further work by (P. J. H.) and I. Piscalnikov, which will be reported later, indicates that another factor instead of the change in the value of K_b in going from 25 to 0° may explain the discrepancy between the value of the hydrolysis constant measured and that obtained from the aminolysis data. T. A. Koch, J. G. Miller and A. R. Day, THIS JOURNAL, **75**, 953 (1953), have recently reported a small catalytic effort of ammonium ion on aminolysis, and suggest that aminolysis requires both acid and basic attack.

[15] P. B. Russell, THIS JOURNAL, **72**, 1853 (1950).

[16] R. G. Pearson and E. A. Mayerle, *ibid.*, **73**, 926 (1951); *cf.* E. H. Cook and R. W. Taft, Jr., *ibid.*, **74**, 6103 (1952).