Pathways in Thioacetamide Hydrolysis in Aqueous Acid: Detection by Kinetic Analysis

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Kinetic studies of the acid-catalysed hydrolysis of thioacetamide have shown that both hydrolysis sequences (attack at sulphur followed by attack at nitrogen and *vice versa*) occur. The rate constants of the steps in the two competitive reactions have been determined in the temperature range 60—90° and the activation energies calculated. The relative importance of the two competitive reactions and the concentration of the intermediates are temperature-dependent. but are not influenced by variation in pH in the range 1·00—2·50.

THIOACETAMIDE (TAA), which on hydrolysis gives hydrogen sulphide, has been found useful in qualitative and quantitative analysis as a substitute for H_2S. The stoicheiometric equation (1) describes the complete hydrolysis reaction. In the course of the hydrolysis of

$$CH_3CSNH_2 + 2H_2O \longrightarrow CH_3CO_2H + H_2S + NH_3 \quad (1)$$

TAA two of its bonds must be broken, the carbon–nitrogen and the carbon–sulphur bonds.[1] Depending upon which bond is broken first, there are two possible intermediates in the reaction, acetamide (AA) and thioacetic acid (TA). These two distinct reaction paths are represented in the Scheme.

SCHEME
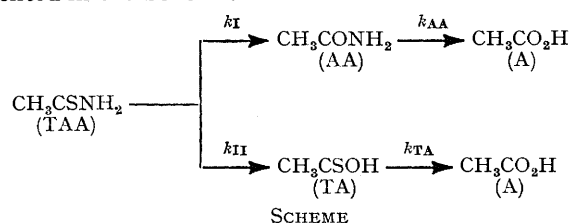
Swift and Butler,[2] from a study of the acid-catalysed hydrolysis of TAA at low acid concentrations and elevated temperatures, showed that the rate of hydrolysis to H_2S is first order in thioacetamide and in hydronium ion. Their findings have been confirmed by Butler *et al.*[3] on the basis of spectrophotometric measurements of the rate of disappearance of TAA. From this it was concluded that hydrolysis of the thione is predominant and that the rate of hydrolysis of the amino-group is too low to be measurable by the methods used. Rosenthal and Taylor,[1] investigated the hydrolysis of TAA at 35° in HCl solutions

at concentrations from 0·3 to 6M and demonstrated the presence of TA, formed as an intermediate.

From these experimental facts it seemed to us that the hydrolysis of TAA in acid solutions could occur by two parallel consecutive reaction mechanisms. The present study has confirmed this hypothesis. The individual reaction rates have been evaluated, as has the relative importance of the formation of AA and TA as intermediates. Rate constants have been determined in the temperature range of 60—90° and at pH 1·00—2·50.

EXPERIMENTAL

Reagents.—All chemicals were AnalaR grade. 0·1M-TAA and 0·1M-AA aqueous solutions were prepared by weight. Buffers were magnesium acetate–acetic acid (pH 6·4) and ammonia–ammonium chloride (pH 10). Other solutions were 0·1M-zinc sulphate and 0·1M-EDTA. HCl (364·8 mg ml^{-1}) solution was used to control the pH to a predetermined value. The glass electrode was calibrated against 0·05M-potassium tetroxalate buffer solution.

Apparatus.—The reaction vessel was similar to that of Swift and Butler.[2] In addition, a flat-bottomed flask (500 ml) was fitted with an Ingold HA 405 combined glass electrode, connected to a Tacussel U-5 titrimeter, and with a delivery tube from a Tacussel Electroburapot reagent supply unit. The pH was held constant within 0·01 unit by the titrimeter which controlled the Electroburapot electronically. A constant-temperature bath was used to keep the reaction mixture at the desired temperature. A Corning model 12 pH meter, provided with a Corning monovalent cation electrode and a double junction silver–silver chloride reference electrode, was used to measure the ammonia concentration.

A Shimadzu QV 50 spectrophotometer was used.

Procedure.—The experiments were performed at various temperatures ($\pm 0·5°$). The TAA solution was stirred

[1] D. Rosenthal and T. I. Taylor, *J. Amer. Chem. Soc.*, 1960, **82**, 4169.

[2] E. H. Swift and E. A. Butler, *Analyt. Chem.*, 1956, **28**, 146.

[3] E. A. Butler, D. G. Peters, and E. H. Swift, *Analyt. Chem.*, 1958, **30**, 1379.

magnetically and pure nitrogen gas was bubbled continuously through the solution to purge the H_2S formed in the hydrolysis reaction. Samples (6 ml) were taken at fixed intervals, transferred to test tubes, and placed in an ice-bath to quench the reaction. 1 ml of each sample was diluted and acidified by HCl to give a 10^{-4}—10^{-5}M solution of TAA of pH 1. The TAA concentration was measured spectrophotometrically at 261·5 nm.[1,3,4] 2 ml of each sample was diluted to 100 ml with the pH 6·4 buffer and the NH_4^+ concentration determined by the monovalent cation electrode. Hydrogen sulphide concentrations were obtained by collecting H_2S gas in pH 10 buffer (2 × 20 ml). Zinc sulphate was added and the precipitated zinc sulphide was centrifuged. The excess of zinc was back-titrated with EDTA and Eriochrome Black T as indicator. Mean concentration values were obtained from at least three independent measurements and in all cases the relative standard deviation was <2%.

RESULTS AND DISCUSSION

Hydrolysis of TAA at pH 1·00 and 80°.—As previously mentioned, Swift *et al.*[2,3] considered that the hydrogen sulphide evolved arose directly from the hydrolysis of TAA to AA and that the rate of hydrolysis of TAA to TA and ammonium ion was negligibly low. In fact the same result would be obtained if decomposition of TA took place much faster than its formation. Thus evaluation of the relative importance of the two reaction paths is useful in elucidating the reaction mechanism. Therefore the concentrations of AA and NH_3 formed were followed.

A series of experiments was performed at pH 1·00 and elevated temperature in order to give a reasonable rate of hydrolysis. A plot of the concentrations of TAA, AA, and NH_3 against time is shown in Figure 1. As no
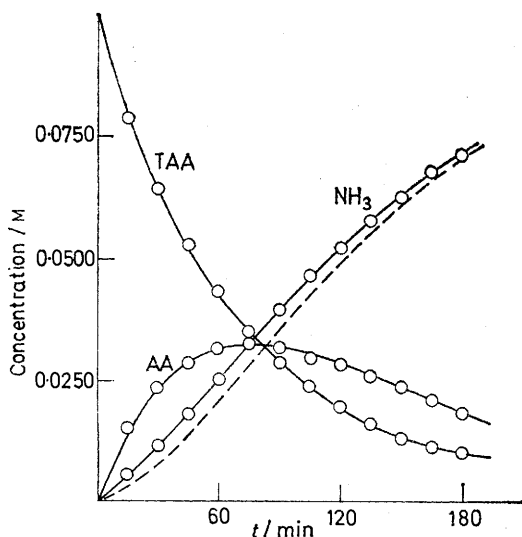
FIGURE 1 Change in concentration of the products in the hydrolysis of TAA at 80° and pH 1·00. The broken line represents a theoretical curve for the change in NH_3 concentration

method for accurate AA determination was available for the experimental conditions used, the concentration of AA formed was calculated from the observed TAA and

NH_3 concentrations by equation (2) where $[TAA]_0$ represents the initial concentration.

$$[AA]_t = [TAA]_0 - [TAA]_t - [NH_3]_t \qquad (2)$$

To describe theoretically the variation of the concentrations of AA and NH_3 the hydrolysis rate constants of TAA and AA (k_{TAA} and k_{AA}) are needed.

Determination of k_{TAA}. The results found by spectrophotometric determination of the concentrations of unhydrolysed TAA are shown in Figure 2A. The rate
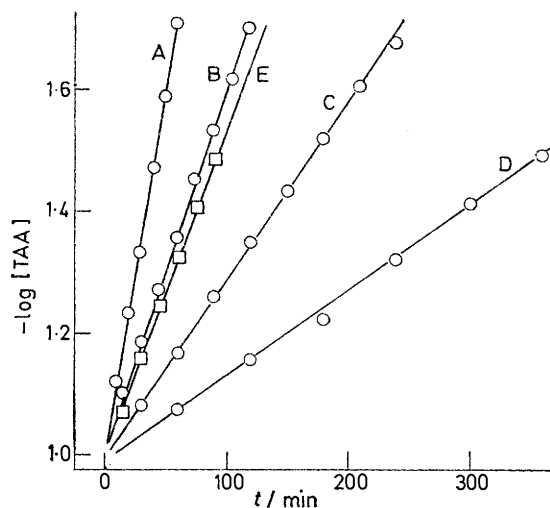
FIGURE 2 Hydrolysis of TAA at pH 1·00 and various temperatures: A, 90°; B and E, 80°; C, 70°; D, 60°. In A—D disappearance of TAA was followed; in E H_2S formation was measured

constant, obtained from the slope of the straight line (from least squares), is the mean of at least three independent experiments: $k_{TAA} = 13·5 \times 10^{-3}$ min^{-1} (standard deviation s $0·47 \times 10^{-3}$ min^{-1}).

Variation of the initial TAA concentration from 10^{-4} to 10^{-1}M showed that the hydrolysis is first order in TAA.[1-3] The mean value of the rate constant over this concentration range is $13·5 \times 10^{-3}$ min^{-1} (s $0·58 \times 10^{-3}$ min^{-1}). To exclude the possibility of loss of TAA because of bubbling N_2 through the solution to remove H_2S, similar experiments without gas bubbling were performed and no difference in rate constant was obtained.

Swift *et al.*[2,3] reported the same second-order rate constant for the decomposition of TAA and for the formation of H_2S at 90° (k_{TAA} 0·21 1 mol^{-1} min^{-1}, k_{H_2S} 0·21 ± 0·023 1 mol^{-1} min^{-1}), but at 80° we found a difference beteeen the two constants. This difference is greater than the sum of the standard deviations of the two values and might be an indication that only a part of the TAA which has disappeared has reacted to give H_2S. The measured H_2S concentrations are shown in Figure 2E and the calculated rate constant k_{H_2S} is $12·4 \times 10^{-3}$ min^{-1} (s $0·35 \times 10^{-3}$ min^{-1}).

Determination of k_{AA}. As the variation with time of the concentration of AA could not be followed directly,

[4] D. G. Peters and A. Salajegheg, *Analyt. Chem.*, 1966, **38**, 1824.

the concentration of the liberated NH_3 was measured. By applying equation (3) the concentrations of unchanged

$$[AA]_t = [AA]_0 - [NH_3]_t \qquad (3)$$

AA was calculated. From these data (Figure 3B) the rate constant is $12 \cdot 9 \times 10^{-3}$ min^{-1} (s $0 \cdot 10 \times 10^{-3}$ min^{-1}).
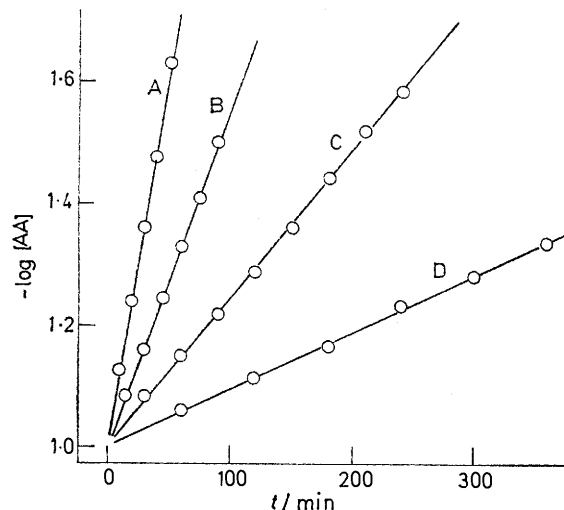

FIGURE 3   Hydrolysis of AA at pH $1 \cdot 00$ and various temperatures: A, 90°; B, 80°; C, 70°; D, 60°
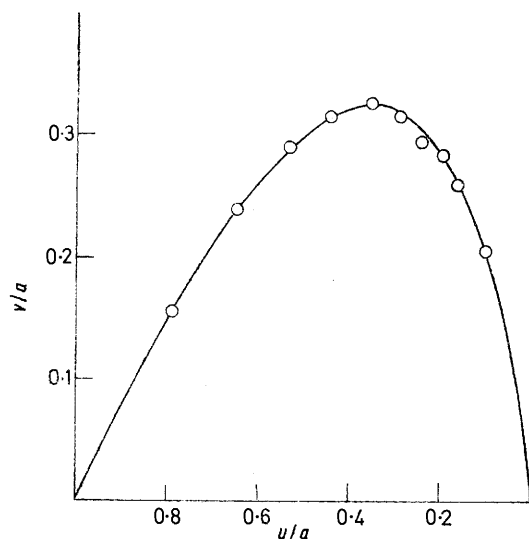

FIGURE 4   Hydrolysis of TAA at 80° and pH $1 \cdot 00$ AA concentration as a function of TAA concentration

The consecutive reaction TAA $\longrightarrow$ AA $\longrightarrow$ NH_3. Provided that amino-group hydrolysis of TAA is negligible compared with that of the thione, the concentration of ammonia formed by hydrolysis of the intermediate AA is given by equation (4)[5] where a is the initial

$$[NH_3] = a\left(1 - \frac{k_{AA}}{k_{AA} - k_{TAA}} \cdot e^{-k_{TAA}t} + \frac{k_{TAA}}{k_{AA} - k_{TAA}} \cdot e^{-k_{AA}t}\right) \qquad (4)$$

[5] A. A. Frost and R. G. Pearson, ' Kinetics and Mechanism,' Wiley, New York–London, 1961, p. 167.

TAA concentration and t the time. The results of this calculation are represented by the broken line in Figure 1. These values are lower than the experimental ones. Consequently the above assumption is wrong and the hydrolysis of the amino-group to give TA cannot be neglected.

The variation of the experimental [AA] : [TAA] ratios is represented by a concentration–concentration diagram (Figure 4 where the symbols v, a, and u denote the concentration of intermediate AA, the initial concentration of TAA, and the instantaneous concentration of TAA respectively). Jungers has shown[6] that at the maximum of the curve [AA]/[TAA] $= k_I/k_{AA}$ so that a first estimate of the value of k_I can be made.

As the two competitive reactions, (I) and (II), were found to be pseudo-first-order $k_{TAA} = k_I + k_{II}$, and an approximate value of k_{II} can also be obtained.

Equation (5)[6] gives the change of AA concentration as

$$\frac{v}{a} = \frac{k_I}{k_{AA} - (k_I + k_{II})} \left[\left(\frac{u}{a}\right) - \left(\frac{u}{a}\right)^{\frac{k_{AA}}{k_I + k_{II}}}\right] \qquad (5)$$

a function of the instantaneous TAA concentration. By application of the provisional values of k_I and k_{II} equation (5) has been solved iteratively to give the best agreement with the experimental points (Figure 4). The resulting rate constants are k_1 $10 \cdot 9 \times 10^{-3}$ (s $0 \cdot 32 \times 10^{-3}$) and k_{II} $2 \cdot 6 \times 10^{-3}$ min^{-1} (s $0 \cdot 57 \times 10^{-3}$ min^{-1}). The [AA] : [TAA] ratio ($k_I : k_{AA}$) at the maximum of the curve is $0 \cdot 84$ at 80°.

The consecutive reaction TAA $\longrightarrow$ TA $\longrightarrow$ H_2S. The change in TA concentration can be plotted against the TAA concentration as for AA formation. The [TA] : [TAA] ratio can then be calculated by using the appropriate constants. The value of k_{TA} at 80° was obtained by extrapolating the results of Hipkin and Satchell.[7] The [TA] : [TAA] ($k_{II} : k_{TA}$) ratio at the maximum of the curve is $0 \cdot 033$. This very low value explains the small difference between the rate constants k_{TAA} and k_{H_2S}.

As the two competitive reactions are isomorphous (see later) the selectivity, *i.e.* the ratio of the intermediates formed, is given by[8] $S = k_I : k_{II}$. In the case of the TAA hydrolysis $S = 4 \cdot 2$, which means that 81% of the reacting TAA disappears along reaction path (I) and that only 19% hydrolyses to TA.

Effect of Temperature on the Hydrolysis at pH $1 \cdot 00$.— *Hydrolysis of TAA and AA.* The hydrolyses were carried out from 60 to 90° and from a plot of $-\log k$ against T^{-1} the energies of activation were calculated. The results at the different temperatures are shown in Figures 2 and 3, and the calculated rate constants are given in Tables 1 and 2. The activation energy for the overall TAA hydrolysis is $17 \cdot 6$ (s $0 \cdot 21$); for AA hydrolysis it is $20 \cdot 6$ kcal mol^{-1} (s $0 \cdot 20$ kcal mol^{-1}).

The consecutive reaction TAA $\longrightarrow$ AA $\longrightarrow$ NH_3.

[6] J. C. Jungers and L. Sajus, ' L'analyse cinétique de la transformation chimique,' Editions Technip, Paris, 1967, tome I, p. 524.

[7] J. Hipkin and D. P. N. Satchell, *Tetrahedron*, 1965, **21**, 835.

[8] Ref. 6, p. 337.

The concentrations of AA at the different temperatures were estimated by use of equation (2). The concentration–concentration plots show that at the maximum of the curve the ratio [AA] : [TAA] decreases, while the AA concentration increases with rising temperature. It will be seen later that this increase of AA concentration is a consequence of selectivity effects.

The decrease of the [AA] : [TAA] ratio is closely related to the k_I : k_{AA} ratio as discussed previously. The values

TABLE 1

Effect of temperature on the first-order rate constants
for hydrolysis of TAA

T/°C	10^3k_{TAA}/min^{-1}	10^3s/min^{-1}	10^3k_I/min^{-1}	10^3s/min^{-1}	10^3k_{II}/min^{-1}	10^3s/min^{-1}
60	3·0	0·14	2·1	0·11	0·9	0·18
70	6·6	0·14	5·0	0·15	1·6	0·20
80	13·5	0·47	10·9	0·32	2·6	0·57
90	26·9	0·75	22·9	0·69	4·0	1·02

TABLE 2

Effect of temperature on the rate constants k_{AA} and k_{TA}
and on the k_I : k_{AA}, k_{II} : k_{TA}, and k_I : k_{II} ratios

T/°C	10^3k_{AA}/min^{-1}	10^3s/min^{-1}	10^3k_{TA}/min^{-1}	k_I : k_{AA}	k_{II} : k_{TA}	k_I : k_{II}
60	2·2	0·08	13·0	0·95	0·069	2·3
70	5·6	0·10	30·6	0·89	0·052	3·1
80	12·9	0·10	79·2	0·84	0·033	4·2
90	27·8	0·31	184	0·82	0·022	5·7

of k_I and k_{II} at each temperature were obtained by applying equation (5) iteratively and the results are summarized in Table 1. The activation energy is 19·2 (s 0·22) for path (I) and 11·9 kcal mol^{-1} (s 1·18 kcal mol^{-1}) for path (II).

The consecutive reaction $TAA \longrightarrow TA \longrightarrow H_2S$. The values of k_{TA} at the different temperatures were obtained from the data of Hipkin and Satchell.[7] TA Concentration is a maximum when [TA]/[TAA] $= k_{II}/k_{TA}$ and the results are summarized in Table 2. Here also it can be concluded that the higher the temperature the faster the intermediate TA will hydrolyse to H_2S and the more difficult it will become to determine the TA formed.

As the activation energies of the two paths (I) and (II) are quite different, the relative importance of AA and TA as intermediates will also change at elevated temperatures. From the values of k_I : k_{II} in Table 2 it can be seen that the preference for AA over TA increases considerably with temperature. This explains why systematically higher AA concentrations were observed at the maxima of the concentration–concentration curves.

These temperature effects on the different rate constants are the reason why Butler et al.,[3] working at 90°, found no difference between k_{TAA} and k_{H_2S} within the

limits of the experimental error and why Rosenthal and Taylor [1] could report TA as an intermediate at 35°.

Effects of pH on Hydrolysis at 80°.—The hydrolysis of TAA and AA was studied in the pH range 1·00—2·50 and the rate constants are given in Table 3. A plot of
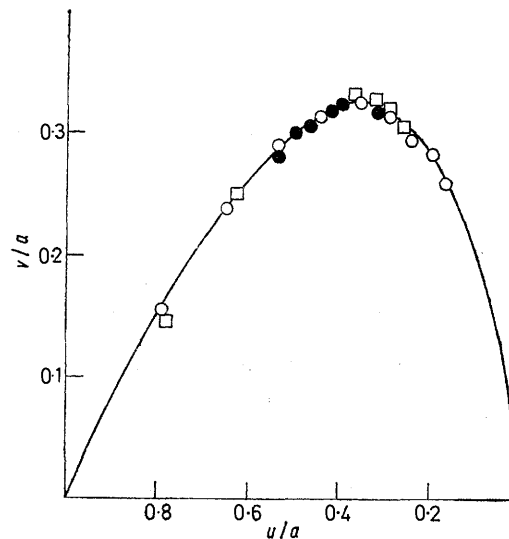

FIGURE 5 Effect of the pH on AA concentration at 80° as a function of TAA concentration: ○ pH 1·00; □ pH 1·50; ● pH 2·00

TABLE 3

Effect of pH on the first-order rate constants for
hydrolysis of TAA and AA

pH	10^3k_{TAA}/min^{-1}	10^3k_{AA}/min^{-1}
1·00	13·5	12·9
1·50	4·30	4·10
2·00	1·24	1·21
2·50	0·436	0·374

$-\log k$ *versus* pH revealed that a linear relationship exists between k and $a_{H_3O^+}$ and that both reactions are first order with respect to hydronium ion activity.

Figure 5 shows that the experimental values of AA concentration as a function of TAA concentration at pH 1·00, 1·50, and 2·00, fit the calculated concentration curve very well. It is thus clear that the pH does not influence either the selectivity of the two competitive reactions or the [AA] : [TAA] ratio at the maximum of the curve.

From this and from the first-order dependence of the hydrolysis reactions of TAA, AA, and TA [7] on hydronium ion activity it can be concluded that the subsequent steps in each of the two reaction paths are first order in hydronium ion activity and thus that both reactions are isomorphous.