to the mechanism presented, complicating reverse reactions occur through the un-ionized acid (see eq. 2 for example). Since no significant concentration of un-ionized thiocyanic acid is present in the solutions studied, the rate of thiocyanate production is independent of hydrogen ion concentration over a $10^9$-fold change in this variable.

A more detailed theoretical account of the effect of methyl substitution on the rate of decomposition will be presented in the last paper of this series when additional data on other methylated thioureas has accumulated.

**Acknowledgment.**—The authors gratefully acknowledge the generous grant from Research Corporation of New York that made this study possible. It is also a pleasure to express our thanks to the Humble Oil & Refining Company for the fellowship awarded to D.G.W. this past year.

AUSTIN, TEXAS

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

# A Study of the Mechanism and Kinetics of the Thioacetamide Hydrolysis Reaction[1]

BY DONALD ROSENTHAL[2] AND T. IVAN TAYLOR

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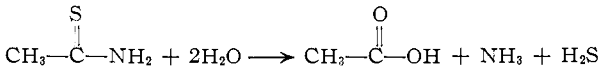
The hydrolysis of thioacetamide to acetic acid, ammonia and hydrogen sulfide is catalyzed by both acids and bases. The base-catalyzed reaction was found to be the more rapid. Thioacetic acid was detected as an intermediate in both reactions. The relative importance of thioacetic acid and acetamide as intermediates is not known. A spectrophotometric investigation of the hydrolysis showed the rate of disappearance of thioacetamide to be first order with respect to thioacetamide concentration. The acid-catalyzed reaction was investigated in HCl and $HClO_4$ solutions at concentrations from 0.3 to 6 $M$ at 35°. A maximum was observed in the first-order thioacetamide rate constant at an HCl concentration of about 4.5 $M$, and at an $HClO_4$ concentration of about 4 $M$. A mechanism involving the rapid and reversible addition of a proton followed by the rate-determining addition of water is consistent with the observed kinetics. The presence of a protonated thioacetamide ion in acid solution was detected spectrophotometrically. The observed first-order rate constants were not significantly different from those calculated using a rate expression $\log k = \log k_2K_1 + \log [H_3O^+] - \log(1 + K_1h_0) + BC$ derivable from the proposed detailed mechanism. In the above equation $k$ is the first-order thioacetamide rate constant, $h_0$ is the antilog of minus the acidity function, $C$ is the molar concentration of electrolyte, and $K_1$ and $k_2$ are simple or complex constants depending upon the detailed nature of the reaction. The $BC$ term is presumably equal to the logarithm of an activity coefficients quotient. The maximum and observed rate constants for acetamide hydrolysis at 50° can also be explained in terms of a similar mechanism and rate expression.

Thioacetamide has been found useful in qualitative analysis[3] as a substitute for hydrogen sulfide gas.

The stoichiometric equation for the complete hydrolysis of thioacetamide is[4]



$$CH_3-\overset{\overset{\textstyle S}{\|}}{C}-NH_2 + 2H_2O \longrightarrow CH_3-\overset{\overset{\textstyle O}{\|}}{C}-OH + NH_3 + H_2S$$

When this study was begun, no detailed information was available concerning the mechanism and kinetics of this reaction. The experiments described in this paper were initiated to obtain such information. Recently, Swift and Butler[5] have published some of their findings on the acid-catalyzed reaction at low acid concentrations and elevated temperatures.

**Intermediates in the Hydrolysis Reactions.**—In the course of the hydrolysis reaction two chemical bonds must be broken, *viz.*, the carbon-nitrogen and carbon-sulfur bonds. Depending upon which bond is first broken, there are two possible intermediates in the reaction, thioacetic acid and acetamide. In both the base- and acid-catalyzed reactions thioacetic acid was found to be an intermediate. In the base-catalyzed reaction there was a gradual shift in the absorption maximum with time toward the wave length at which the thioacetate ion absorbs, 2450 Å. (see Fig. 1). In the acid-catalyzed reaction a substance was extracted which gave an identical spectrum to that of thioacetic acid when treated in the same manner (see Fig. 2). Acetamide has no characteristic absorption maximum above 2150 Å. and consequently could not be detected by these measurements.

The fact that thioacetic acid is an intermediate does not preclude the possibility that acetamide is also an intermediate, and that two competitive reactions are occurring. Indeed, Swift and Butler[5] were able to explain the observed change in $p$H upon the hydrolysis of thioacetamide at low acid concentrations and elevated temperatures by postulating acetamide as an intermediate. From the available evidence, it is not possible to evaluate the relative importance of acetamide and thioacetic acid as intermediates in the hydrolysis under the conditions of the experiments described herein.

## Kinetics and Mechanism

**Dependence of Rate upon Thioacetamide Concentration.**—Preliminary experiments indicated that thioacetamide conforms to Beer's law for the range of concentration employed in these experiments, *ca.* 2 × $10^{-4}$ to $10^{-6}$ $M$, the absorption maximum at 2615 Å. being employed.

A plot of log absorbancy at 2615 A. *versus* time revealed the rate of the acid- and base-catalyzed

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[1] Taken in part from a dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science of Columbia University. Presented at the meeting of the American Chemical Society, Minneapolis, Minnesota, September 16, 1955.

[2] Department of Chemistry, The University of Chicago, Chicago, Illinois.

[3] H. H. Barber and T. I. Taylor, "Semimicro Qualitative Analysis," Harper and Bros., New York, N. Y., 1953.

[4] A. W. Hofmann, *Ber.*, **11**, 340 (1878); C. V. Jorgensen, *J. prakt. Chem.*, **66**, 33 (1902).

[5] E. H. Swift and E. A. Butler, *Anal. Chem.*, **28**, 146 (1956).

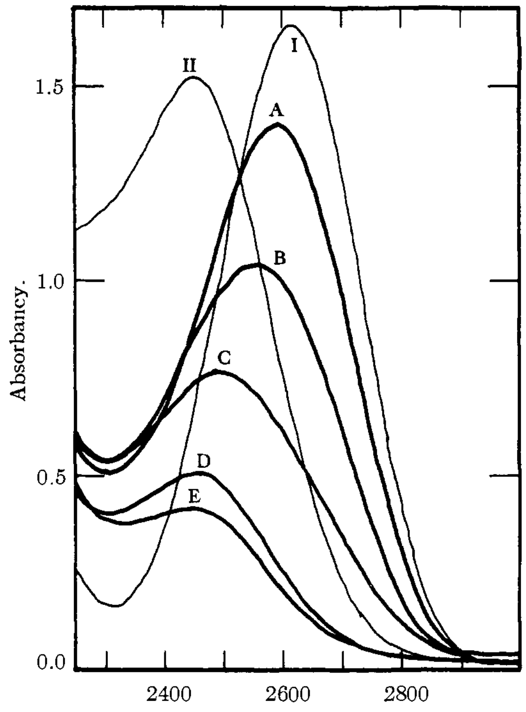

Fig. 1.—Identification of the intermediate in the base-catalyzed hydrolysis of thioacetamide; thioacetamide in 0.10 *N* NaOH: A, after 2.2 minutes; B, after 111 minutes; C, after 273 minutes; D, after 1521 minutes; E, after 7520 minutes; I, thioacetamide in water; II, thioacetic acid in water.

reactions to be first order with respect to thioacetamide concentration, *i.e.*

$$-d[T]/dt = k[T] \qquad (1)$$

where $T = CH_3\text{-}\overset{\overset{S}{\|}}{C}\text{-}NH_2$ (see Fig. 3).

The base-catalyzed reaction is much more rapid than the acid-catalyzed reaction (at 25° in 0.11 *M* NaOH $k$ is $7 \times 10^{-5}$ sec.$^{-1}$, in 0.1 *M* HCl $k$ is $7 \times 10^{-7}$ sec.$^{-1}$, and in distilled water $k < 4 \times 10^{-8}$ sec.$^{-1}$).

**Dependence of Rate upon Hydrogen Ion Concentration.**—A detailed investigation of the acid-catalyzed reaction at 35° revealed a non-linear increase of rate with increasing hydrogen ion concentration to a maximum at about 4.5 *M* HCl, or about 4 *M* $HClO_4$, and a subsequent decrease in rate (Tables I and III, column 2). Similar maxima have been found in the hydrolysis of amides[6] and in other cases.[7]

The cause and explanation of the amide maxima are not well understood.[6,8] Initially, the dependence of rate upon acid concentration at rates up to but not beyond the maximum will be considered. The maximum will be discussed in a later section of the paper.

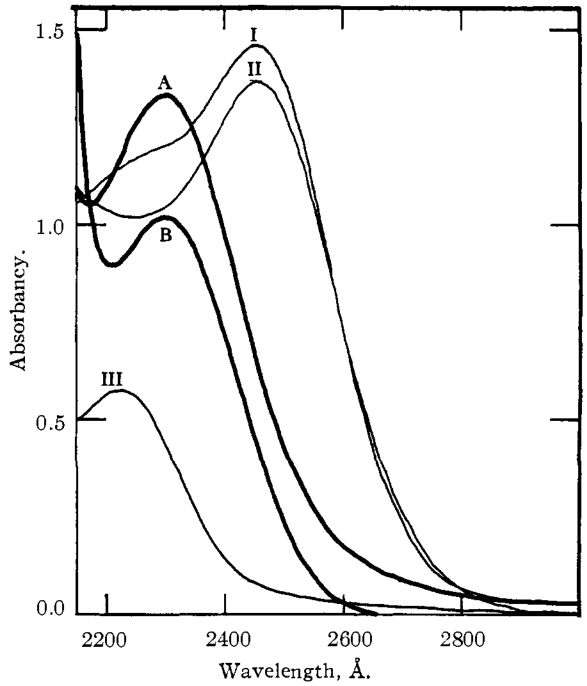

Fig. 2.—Identification of the intermediate in the acid-catalyzed hydrolysis of thioacetamide: A, extracted intermediate in 0.01 *N* NaOH; B, thioacetic acid extract in 0.04 *N* NaOH; I, thioacetic acid in water; II, thioacetic acid in 0.0001 *N* NaOH; III, thioacetic acid in 1.3 *N* HCl.

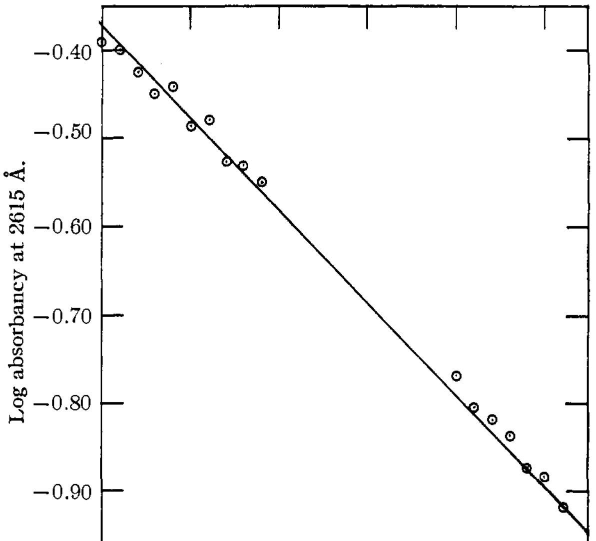

Fig. 3.—First-order plot of thioacetamide hydrolysis in 4.50 *M* HCl at 35°; initial thioacetamide concentration $1.43 \times 10^{-5}$ *M*; $k = 23.9 \times 10^{-5}$ sec.$^{-1}$, S.D.$_k = 0.35 \times 10^{-5}$ sec.$^{-1}$

If the rate-determining step in the hydrolysis were the initial reaction between thioacetamide (T) and $H_3O^+$, the reaction could be represented as

$$T + H_3O^+ \rightleftarrows (M^*) \xrightarrow{k_2} TH^+ + H_2O \quad \text{(slow)} \quad \text{(I)}$$
$$TH^+ + H_2O \longrightarrow \text{products} \quad \text{(fast)}$$

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[6] V. K. Krieble and K. A. Holst, THIS JOURNAL, **60**, 2976 (1938).

[7] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, chapter XI.

[8] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 786–787.

where M* is the critical complex in the Brønsted sense or a transition state in the absolute reaction rate theory. The rate is

$$-\frac{d[T]}{dt} = k_2[T][H_3O^+]\frac{f_T f_{H_3O^+}}{f_{M^*}} \qquad (2)$$

where $f$ refers to the molar concentration activity coefficients of the substance of the subscript. The thioacetamide rate constant is then

$$k = -\frac{1}{T}\frac{d[T]}{dt} = k_2[H_3O^+]\frac{f_T f_{H_3O^+}}{f_{M^*}} \qquad (3)$$

from which

$$\log k = \log k_2 + \log [H_3O^+] + \log \frac{f_T f_{H_3O^+}}{f_{M^*}} \qquad (4)$$

A plot of log $k$ *versus* log $[H_3O^+]$ reveals that no simple linear relationship exists for the HCl or the $HClO_4$ catalyzed reaction (Fig. 4). That the last term is of importance was demonstrated by the significant increase in the rate of hydrolysis upon addition of NaCl to an HCl solution of thioacetamide ($k$ was $6.79 \times 10^{-5}$ sec.$^{-1}$ for a 1.45 *M* HCl–1.45 *M* NaCl solution at 35° compared to $4.29 \times 10^{-5}$ sec.$^{-1}$ for a 1.50 *M* HCl solution). For acid concentrations below the maximum, the data could be represented reasonably well by eq. 4 by assuming the activity coefficients ratio to vary as a constant times the concentration of the acid as will be described later for another assumed mechanism.

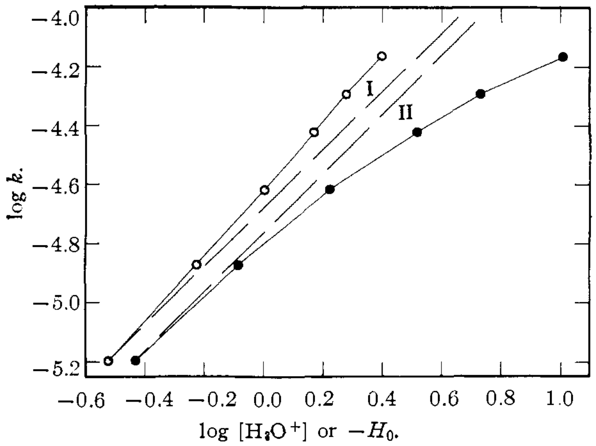

Fig. 4.—Plot of log $k$ *vs.* log $[H_3O^+]$ and $-H_0$ for $HClO_4$ at 35°: ○, log $k$ *vs.* log $[H_3O^+]$; ●, plot of log $k$ *vs.* $-H_0$; I, plot of log $k$ = log $[H_3O^+]$ + constant; II, plot of log $k = -H_0$ + constant. The experimental points are connected by straight lines.

A mechanism involving pre-equilibrium between thioacetamide and $H_3O^+$ followed by a unimolecular rate–determining step could be formulated as

$$\begin{array}{lll} T + H_3O^+ \overset{K_1}{\rightleftarrows} TH^+ + H_2O & \text{(fast)} & \\ TH^+ \rightleftarrows (M^*) \xrightarrow{k_2} X^+ & \text{(slow)} & \text{(II)} \\ X^+ + H_2O \longrightarrow \text{products} & \text{(fast)} & \end{array}$$

The rate is

$$\frac{d(\text{products})}{dt} = -\frac{d([T] + [TH^+])}{dt} = k_2[TH^+]\frac{f_{TH^+}}{f_{M^*}} \qquad (5)$$

$$= k_2K_1[T][H_3O^+]\frac{f_T f_{H_3O^+}}{f_{M^*}a_{H_2O}} = k_2K_1[T]h_0 \qquad (6)$$

where $h_0$ is the antilog of minus Hammett's acidity function[9] applicable to cases in which M* differs from T by a proton. The rate constant $k$ for the decrease in total concentration of thioacetamide, $[T] + [TH^+]$, is

$$k = \frac{1}{[T] + [TH^+]}\frac{d([T] + [TH^+])}{dt} = \frac{k_2K_1[T]h_0}{[T] + [TH^+]} \qquad (7)$$

Since $[TH^+] = K_1[T][H_3O^+]f_T f_{H_3O^+}/f_{TH^+}a_{H_2O} = K_1[T]h_0$

$$k = k_2K_1h_0\left(\frac{1}{1 + K_1h_0}\right) \qquad (8)$$

In our experiments the decrease in the concentration of the species T (thioacetamide) was measured. Substitution of $[T]K_1h_0$ for $[TH^+]$ in eq. 5 gives

$$-\frac{d([T] + [T]K_1h_0)}{dt} = -\frac{d[T](1 + K_1h_0)}{dt} = k_2K_1[T]h_0 \qquad (9)$$

and

$$k = -\frac{1}{[T]}\frac{d[T]}{dt} = k_2K_1h_0\left(\frac{1}{1 + K_1h_0}\right) \qquad (10)$$

or

$$\log k = \log k_2K_1 + \log h_0 - \log (1 + K_1h_0) \qquad (11)$$

Thus, the same constant applies to both the decrease in [T] and to the decrease in total concentration, $[T] + [TH^+]$. No simple linear relationship was found between log $k$ and log $h_0$, *i.e.*, $-H_0$ (see Fig. 4). If $K_1$ is sufficiently large, the inclusion of the last term in eq. 11 would result in a better fit than is obtained in Fig. 4, but this expression could only result in a limiting value of $k$ equal to $k_2$ at large values of $h_0$ and would not explain the observed maximum.

Perhaps a more reasonable mechanism is one similar to that for the hydrolysis of the amides[10] in which the slow step is a bimolecular reaction between the protonated thioacetamide and water

$$\begin{array}{lll} T + H_3O^+ \overset{K_1}{\rightleftarrows} TH^+ + H_2O & \text{(fast)} & \\ TH^+ + H_2O \rightleftarrows (M^*) \xrightarrow{k_2} \text{products} & \text{(slow)} & \text{(III)} \end{array}$$

In this formulation, the transition state is one which differs from T, not only by a proton, but also by a water molecule. The rate is

$$\frac{d(\text{products})}{dt} = -\frac{d([T] + [TH^+])}{dt} = k_2[TH^+]\frac{a_{H_2O}f_{TH^+}}{f_{M^*}}$$

$$= k_2K_1[T][H_3O^+]\frac{f_T f_{H_3O^+}}{f_{M^*}} \qquad (12)$$

and

$$-\frac{d[T]}{dt} = \frac{k_2K_1[T][H_3O^+]}{(1 + K_1h_0)}\frac{f_T f_{H_3O^+}}{f_{M^*}} \qquad (13)$$

As shown previously, the rate constant determined from the decrease in total thioacetamide concentration ($[T] + [TH^+]$) or from the decrease in thioacetamide concentration is

$$k = k_2K_1[H_3O^+]\frac{1}{(1 + K_1h_0)} \times \frac{f_T f_{H_3O^+}}{f_{M^*}} \qquad (14)$$

or

$$\log k = \log k_2K_1 + \log[H_3O^+] - \log (1 + K_1h_0) + BC \qquad (15)$$

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(9) L. P. Hammett and A. J. Deyrup, THIS JOURNAL, **54**, 2721 (1932).

(10) C. K. Ingold, ref. 8, pp. 784–787.

In eq. 15, $BC = \log f_T f_{H_3O^+}/f_{M^*}$, where $B$ is a constant depending upon the nature of the non-electrolyte (thioacetamide) and the electrolyte (acid) present, and $C$ is the "molar ionic strength" (acid concentration in moles/l.). This expression results from the fact that $\log f_T = B'C$ and $\log f_{H_3O^+}/f_{M^*}$ is relatively smaller in magnitude than the non-electrolyte term and can be written approximately equal to $B''C$ so that $B = B' + B''$.[11]

A plot of log $k/[H_3O^+]$ *versus* $C$ for the HCl and $HClO_4$ catalyzed reactions is presented in Fig. 5 for acid concentrations below the maxima in the rate of hydrolysis. In this plot, the data for each acid can be represented adequately by a straight line given by

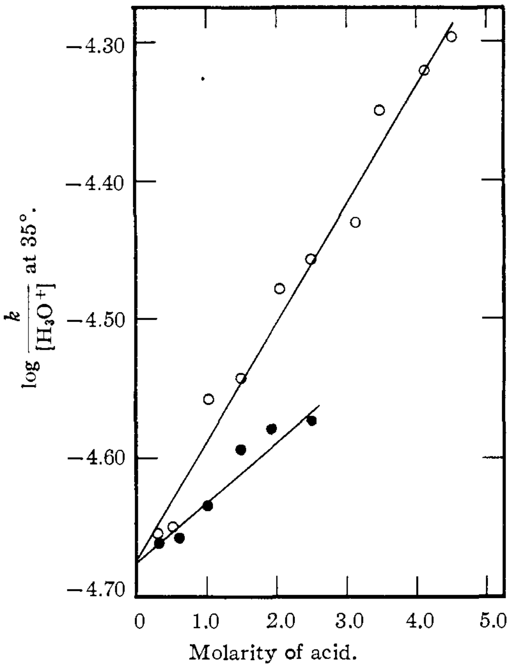

Fig. 5.—Plot of log $k/[H_3O^+]$ *vs.* molarity of acid at 35°: $k$ is the first-order thioacetamide rate constant in sec.$^{-1}$; ○, HCl; ●, $HClO_4$.

$$\log k = \log k_2K_1 + \log[H_3O^+] + BC \qquad (16)$$

which is similar to eq. 4 except for the pre-equilibrium constant. The least squares values of the constants in eq. 16 were calculated and are given in the last columns of Tables II and IV. The experimental rate constants did not differ significantly from the values calculated using the least squares constants and eq. 16 as shown by the values in the next to the last columns in Tables I and III.

The least squares values of log $k_2K_1$ are not significantly different for the HCl and $HClO_4$ data, while the $B$ values are significantly different. This is expected since $k_2$ and $K_1$ should be independent of the acid used while the values of $f_T$ and $f_{H_3O^+}/f_{M^*}$ may be different for acids with different anions. As the concentration of the acid approaches that for the maximum in the rate, this simplified eq. 16 does not satisfactorily represent the results.

**Consideration of the Maximum.**—Mechanism (III), usually referred to as A-2,[10] involves a pre-equilibrium in which $TH^+$ is in equilibrium with T (thioacetamide). Some evidence for the existence of the species $TH^+$ is presented in Fig. 6. In concentrated HCl solution a new absorption maximum appears at 2370 Å., presumably due to protonated thioacetamide (spectrum II, Fig. 6). Spectra III and IV demonstrate that this maximum is due to a species in equilibrium with thioacetamide and not to an irreversible intermediate in the reaction. A $pK_1$ of −1.76 was determined at room temperature (see Experimental section for details and assumptions involved in the calculations).

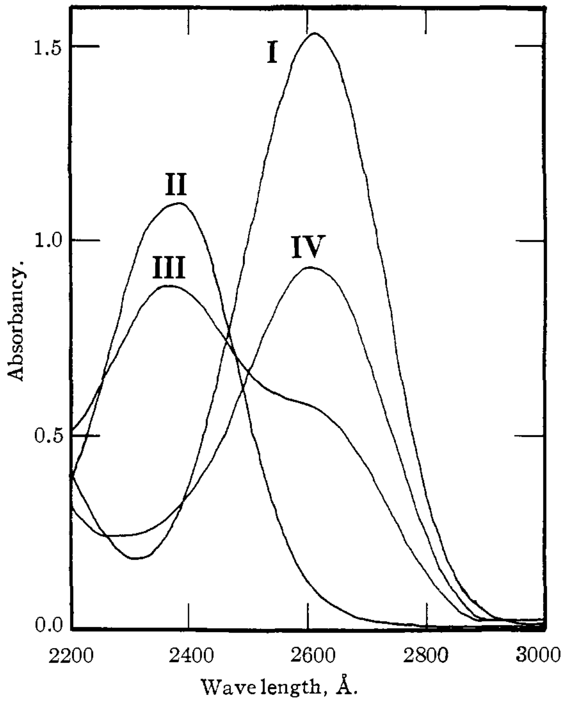

Fig. 6.—Spectrophotometric evidence for the existence of protonated thioacetamide: I, spectrum of *ca.* 6.4 × $10^{-5}$ $M$ thioacetamide in water (2 cm. absorption cell); II, spectrum of *ca.* 6.4 × $10^{-5}$ $M$ thioacetamide in 11.9 $M$ HCl; III, spectrum of 1.6 × $10^{-4}$ $M$ thioacetamide in 6 $M$ HCl about 5 minutes after mixing (10 cm. absorption cell); IV, solution in III, diluted about one-half with water and run 16 minutes after original mixing.

The more complete expression for the rate constant for this mechanism (III) is given by eq. 15. Since $h_0$ increases more rapidly than $[H_3O^+]$ at the higher acid concentrations, the term $\log(1 + K_1h_0)$ becomes increasingly larger causing a decrease in $k$ thus accounting for the observed maxima. The least squares values of the constants in eq. 15 were calculated for the $HClO_4$ data, including the data beyond the maximum. There are no significant differences between the experimental and the calculated rates employing the least squares values of the constants (Table I, column 3). The fact that the least squares value of $K_1$ of 0.028 is of the same relative order of magnitude as the value obtained at room temperature, 0.017, further supports the validity of the postulated rate eq. 15.

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(11) F. A. Long, F. B. Dunkel and W. F. McDevit, *J. Phys. Colloid Chem.*, **55**, 834 (1951).

TABLE I

COMPARISON OF THE OBSERVED AND CALCULATED RATES FOR THE $HClO_4$ CATALYZED HYDROLYSIS OF THIOACETAMIDE AT 35°

| Concn. $HClO_4$, moles/l. | Expt. $k \times 10^{-5}$ sec.$^{-1}$ | Least squares calcd. $k \times 10^{-5}$, sec.$^{-1}$ Eq. 15 | Eq. 15 + log $a_{H_2O}$ | Eq. 15 log $(1 + K_1h_0) = 0$ | $h_0$ |
|---|---|---|---|---|---|
| 0.301 | 0.66 | 0.64 | 0.65 | 0.65 | 0.37 |
| 0.600 | 1.32 | 1.34 | 1.37 | 1.35 | .83 |
| 1.008 | 2.34 | 2.41 | 2.49 | 2.36 | 1.68 |
| 1.486 | 3.79 | 3.80 | 3.95 | 3.67 | 3.31 |
| 1.908 | 5.04 | 5.09 | 5.31 | 4.92 | 5.41 |
| 2.500 | 6.68 | 6.83 | 7.09 | *6.87* | 10.2 |
| 2.936 | 8.55 | 7.85 | 8.10 | (8.45) | 16.1 |
| 2.958 | 7.63 | 7.89 | 8.12 | (8.53) | 16.5 |
| 3.983 | 8.16 | 7.97 | 7.97 | (12.81) | 52.0 |
| 5.007 | 5.30 | 5.44 | 5.31 | (17.95) | 168 |

Another possible mechanism for the reaction is one in which the rate-determining step involves concerted attack upon protonated thioacetamide by two water molecules.[12] In this case, the transition state differs from thioacetamide by a proton and two molecules of water. Assuming $f_T f_{H_3O^+}/_{M^*} = BC$ the rate constant expression differs from eq. 15 by + log $a_{H_2O}$. The results of least squares calculations for this new expression are shown in Table I, column 4 and in Table II. Comparison of the sum of the squares of the deviations for the bimolecular and termolecular expressions gives a ratio of 4.4 to 1. Assuming an F test can be applied to the results, it can be stated with 95% certainty that the bimolecular expression is significantly better than the termolecular expression in accounting for the observed results (F at the 95% level is 3.8).

TABLE II

RESULTS OF LEAST SQUARES CALCULATIONS FOR THE $HClO_4$ CATALYZED THIOACETAMIDE HYDROLYSIS AT 35°

| | Eq. 15 | Eq. 15 + log $a_{H_2O}$ | Eq. 15 assuming log $(1 + K_1h_0) = 0$ |
|---|---|---|---|
| log $k_2K_1$ | −4.7006 | −4.697 | −4.676 |
| S.D.$_{\log k_2K_1}$ | <0.0058 | <0.012 | 0.004 |
| $B$ | .0987 | .1283 | .0461 |
| S.D.$_B$ | < .0041 | < .0086 | .0053 |
| $K_1$ | .0281 | .0335 | .... |
| Sum of squares | .00238 | .0105 | .... |

Equation 15 is identical with eq. 16 when $K_1h_0 << 1$; *i.e.*, when the concentration of protonated thioacetamide is negligible compared to the concentration of thioacetamide. This was the assumption which was implicitly made in some of the earlier calculations. Comparison of the constants in Table II, columns 1 and 3 reveals that significantly different values of the least squares constants are obtained. Thus, despite the fact that the rates calculated assuming $K_1h_0 << 1$ are in good agreement with the experimental rates at hydrogen ion concentrations up to but not beyond the maximum, the constants so calculated are not in good agreement with the constants obtained from the more complete equation 15, nor is the assumption that $K_1h_0 << 1$ apparently valid.

Tables III and IV present the results of the least squares calculations for the HCl-catalyzed hydrolysis.

TABLE III

COMPARISON OF THE OBSERVED AND CALCULATED RATES FOR THE HCl-CATALYZED HYDROLYSIS OF THIOACETAMIDE AT 35°

| Concn. HCl, moles/l. | Expt. $k \times 10^{-5}$, sec.$^{-1}$ | Least squares calcd. $k \times 10^{-5}$, sec.$^{-1}$ Eq. 15 | Eq. 15 + log $a_{H_2O}$ | Eq. 15 log $(1 + K_1h_0) = 0$ | $h_0$ |
|---|---|---|---|---|---|
| 0.299 | 0.66 | 0.70 | 0.68 | 0.68 | 0.37 |
| .506 | 1.13 | 1.24 | 1.22 | 1.19 | 0.68 |
| 1.032 | 2.86 | 2.88 | 2.87 | 2.69 | 1.65 |
| 1.497 | 4.29 | 4.63 | 4.64 | 4.28 | 2.87 |
| 2.05 | 6.82 | 6.99 | 7.03 | 6.52 | 5.10 |
| 2.49 | 8.69 | 9.09 | 9.18 | 8.63 | 7.31 |
| 3.12 | 11.6 | 12.0 | 12.2 | 12.2 | 12.2 |
| 3.49 | 15.6 | 13.5 | 13.7 | 14.7 | 16.6 |
| 4.11 | 19.6 | 15.3 | 15.4 | *19.6* | 27.5 |
| 4.50 | 22.7 | 15.8 | 15.8 | (23.1) | 37.8 |
| 5.25 | 14.9 | 15.5 | 15.3 | (31.2) | 69.8 |
| 6.24 | 8.69 | 13.1 | 12.8 | (45.0) | 157 |

TABLE IV

RESULTS OF LEAST SQUARES CALCULATIONS FOR THE HCl-CATALYZED THIOACETAMIDE HYDROLYSIS AT 35°

| | Eq. 15 | Eq. 15 + log $a_{H_2O}$ | Eq. 15 assuming log $(1 + K_1h_0) = 0$ |
|---|---|---|---|
| log $k_2K_1$ | −4.669 | −4.680 | −4.671 |
| S.D.$_{\log k_2K_1}$ | <0.027 | <0.025 | 0.0056 |
| $B$ | .139 | .164 | .0849 |
| S.D.$_B$ | < .014 | < .013 | .0038 |
| $K_1$ | .042 | .041 | .... |
| Sum of squares | .0756 | .0703 | .... |

The differences between the calculated and experimental rates at the higher acid concentrations are much larger than the experimental error of the rate constants. However, the error in $h_0$ may be sufficiently large to account for the differences,[13,14] so that the discrepancy is not necessarily attributable to the inadequacy of eq. 15. Comparison of the results of the least squares calculations reveals no significant difference between the results obtained assuming the bimolecular or termolecular expressions (ratio of sum of squares 1.1, F at 95% level is 3.2). While there was no significant difference between the log $k_2K_1$ calculated using eq. 15 and 16, there was, as in the $HClO_4$ calculations, a significant difference between the $B$ values calculated from these two equations.

Summarizing the results for the $HClO_4$ and HCl hydrolysis reactions, the observed rates are consistent with the rates calculated assuming the mechanism (III) and rate expression 15. Further, the values of log $k_2K_1$ calculated from the $HClO_4$ and HCl catalyzed reactions are identical within experimental error; and the value of $B$ for HCl is significantly different from the value for $HClO_4$. These results are what would be anticipated for the detailed reaction postulated. The values of $K_1$ calculated for the HCl and $HClO_4$ reactions are probably not significantly different, although it is difficult to obtain a good estimate of S.D.$_{K_1}$; and the values of $K_1$ are relatively of the same order of magnitude as the value calculated at room temperature.

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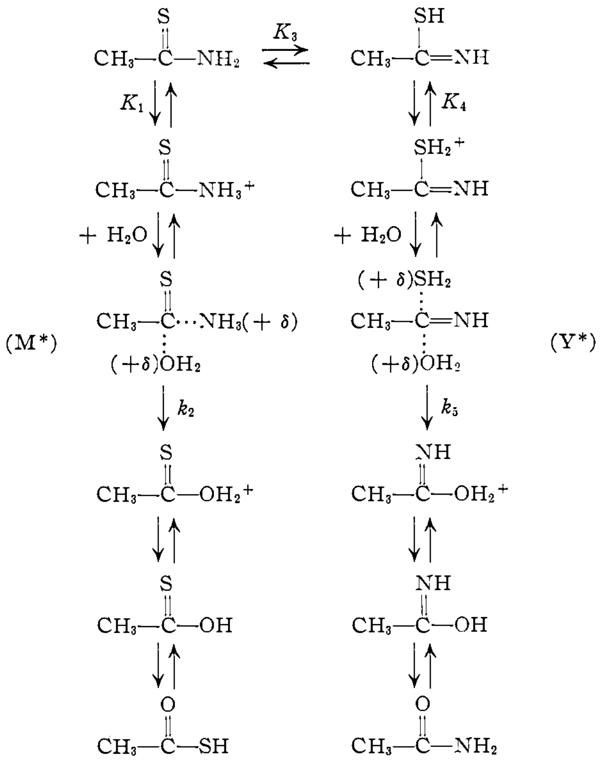
(12) C. G. Swain, THIS JOURNAL, **72**, 4578 (1950).

(13) M. A. Paul and F. A. Long, "$H_0$ and Related Indicator Acidity Functions," to be published in *Chem. Revs.*

(14) E. A. Braude, *J. Chem. Soc.*, 1871 (1948).

**Consideration of Tautomerism, the Detailed Mechanism of Thioacetamide Hydrolysis.**—One complication, which was neglected in the previous kinetic treatment, is that thioacetamide can be written in two tautomeric forms. The available evidence[15] seems to indicate that both forms are actually present in aqueous solution. Reaction *via* either form is possible, thus



It is assumed that species such as $CH_3\text{-}\overset{\overset{SH}{|}}{C}(OH)NH_2$ are present in negligibly small concentrations and do not affect the rate expression.

In terms of this mechanism the following rate expression (17) can be obtained

$$-\frac{dc}{dt} = k_2K_1\,[T][H_3O^+]\,\frac{f_Tf_{H_3O^+}}{f_{M^*}} + k_5K_3K_4\,[T][H_3O^+]\,\frac{f_Tf_{H_3O^+}}{f_{Y^*}} \qquad (17)$$

where $c$ is the sum of the concentrations of the two protonated and the two unprotonated species. Thus

$$c = [T] + K_3[T]\frac{f_T}{f_{TSH}} + K_1[T]h_0 + K_3K_4[T]h_0$$

where TSH is the thiolimido form of thioacetamide. Assuming the two activity quotients are equal, the expression is obtained

$$-\frac{d[T]}{dt} = \frac{(k_2K_1 + k_5K_3K_4)[T][H_3O^+]}{1 + K_3\dfrac{f_T}{f_{TSH}} + (K_1 + K_3K_4)h_0}\,\frac{f_Tf_{H_3O^+}}{f_{M^*}} \qquad (18)$$

Equation 18 is similar to eq. 13 except that the constants are now sums of products of more constants and the second term in the denominator is new. This expression can be written in a form identical with eq. 13, if $1 + K_3f_T/f_{TSH}$ is relatively constant under the conditions of the experiments, either because $K_3f_T/f_{TSH} << 1$ or because $f_T/f_{TSH}$ is relatively constant. Further study is necessary before any detailed conclusions concerning eq. 17 and 18 can be drawn.

The detailed mechanism postulated leads to thioacetic acid as an intermediate product when reaction occurs *via* the thionamide form, and to acetamide as an intermediate product when reaction occurs *via* the thiolimido form. The relative importance of reaction *via* these two routes is not known and thus the relative importance of thioacetic acid and acetamide as intermediate products in the hydrolysis cannot be evaluated.

If the reaction proceeds predominantly by one route, or if the equilibria between the protonated thionamide and thiolimido forms is very much in one direction, the constants in eq. 18 can be simplified somewhat.

**Consideration of the Hydrolysis of Amides.**—In the hydrolysis of several different amides the existence of a maximum has been reported.[6] The interpretation of most of the kinetic data is complicated by the fact that the concentrations of amide employed were comparable to the concentrations of acid, and the actual hydrogen ion concentrations can be appreciably affected if very much protonated amide is formed. There are some data available[16,17] for the hydrolysis of acetamide in which the acetamide concentration is rather small and therefore the hydrogen ion concentration is approximately equal to the concentration of HCl added.

Kinetic data for the HCl-catalyzed hydrolysis of acetamide at 50° are presented in Table V, column 2. The rates above the maximum at 4 and 5 $M$ HCl were calculated by extrapolating available data[17] to the appropriate temperature, assuming a simple Arrhenius type function was applicable. The results of least squares calculations are summarized in Tables V and VI.

TABLE V

COMPARISON OF THE OBSERVED AND CALCULATED RATES FOR THE HCl-CATALYZED HYDROLYSIS OF ACETAMIDE AT 50°

| Concn. HCl, moles/l. | Expt. $k \times 10^{-5}$, sec.$^{-1}$ | Least squares calcd. $k \times 10^{-5}$, sec.$^{-1}$ Eq. 15 | Eq. 15 + log $a_{H_2O}$ | Eq. 15 log $(1 + K_1h_0) = 0$ | $h_0$ |
|---|---|---|---|---|---|
| 0.100 | 1.13 | 1.06 | 1.05 | 1.07 | 0.11 |
| .200 | 2.07 | 2.06 | 2.06 | 2.08 | .24 |
| .300 | 3.00 | 3.01 | 3.01 | 3.03 | .37 |
| .600 | 5.14 | 5.59 | 5.60 | 5.57 | .83 |
| 1.00 | 8.19 | 8.41 | 8.43 | 8.31 | 1.58 |
| 1.50 | 11.3 | 11.0 | 11.1 | 10.9 | 2.88 |
| 2.00 | 12.9 | 12.8 | 12.8 | 12.6 | 4.79 |
| 2.60 | 13.9 | 13.9 | 13.9 | 13.9 | 8.00 |
| 3.12 | 14.2 | 14.0 | 14.0 | 14.4 | 12.2 |
| 4.00 | 12.7[a] | 12.7 | 12.6 | (14.5) | 25.1 |
| 5.00 | 9.30[a] | 9.35 | 9.35 | (13.7) | 57.5 |

[a] Rate calculated from the data[17] assuming an Arrhenius type function.

The experimental rates and the rates calculated using the least squares values of the constants in

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[15] A. Hantzsch, *Ber.*, **64B**, 664 (1931).

[16] H. v. Euler and A. Olander, *Z. physik. Chem.*, **131**, 111 (1928).

[17] T. W. J. Taylor, *J. Chem. Soc.*, 2743 (1930).

TABLE VI

RESULTS OF LEAST SQUARES CALCULATIONS FOR THE HCl-CATALYZED ACETAMIDE HYDROLYSIS AT 50°

| | Eq. 15 | Eq. 15 + log $a_{H_2O}$ | Eq. 15 assuming log $(1 + K_1h_0) = 0$ |
|---|---|---|---|
| log $k_2K_1$ | −3.966 | −3.967 | −3.960 |
| S.D.$_{\log k_2K_1}$ | <0.017 | <0.005 | 0.006 |
| $B$ | − .0994 | − .0832 | − .1206 |
| S.D.$_B$ | < .0034 | < .0034 | .0059 |
| $K_1$ | .0147 | .0121 | .... |
| Sum of squares | .00250 | .00254 | .... |

eq. 15 are in good agreement with each other (Table V, columns 2 and 3). The results assuming the bimolecular expression are not significantly better than those assuming the termolecular expression (ratio of sum of squares in Table VI is 1.02, F at the 95% level is 3.4). The $B$ values calculated from eq. 16 using data only up to the maximum and from eq. 15 are significantly different from each other, but there is no significant difference between the log $k_2K_1$ values. Here, as before, the assumption which is implicitly made in using eq. 16 to describe the rate data up to the maximum, *i.e.*, $K_1h_0 << 1$, is not valid. The importance of looking for the presence of a maximum and considering the concentration of protonated species which may be present, whenever a mechanism such as (III) is proposed, is readily apparent from the present studies. Such considerations may be useful in distinguishing between mechanisms (I), (II) and (III). The presence of a maximum is not consistent with mechanism (II) and is only consistent with (I) if $B$ is negative. A careful consideration of eq. 15 and 4 may be necessary to distinguish between mechanisms (I) and (III) unless the protonated species can be detected in substantial concentration.

## Experimental Details and Calculations

**Reagents.**—Eastman Kodak Co. white label brand thioacetamide was purified by recrystallization from benzene. The resulting material was white in color and had a melting point range of 109.8 to 111.9°.

Reagent grade HCl and $HClO_4$ were employed.

**Rate Measurements.**—The following general procedure was employed in all the rate determinations at 35° with only minor modifications in specific instances. The reaction was initiated by bringing both reactants to 35° in a thermostated water-bath, mixing them together and then transferring the reaction mixture to a 10-cm. quartz cell in a specially designed thermistor controlled thermostated Beckman spectrophotometer compartment (to be described elsewhere). The temperature in this compartment was controlled at 35 ± 0.1°. Sufficient time (*ca.* 45 minutes) was allowed for the reaction solution to return to 35° before readings were taken.

The initial concentration of thioacetamide employed in these experiments was about $1 \times 10^{-5}$ $M$. Absorbancy readings at 2615 Å. were taken five at a time, 200 seconds apart, at selected time intervals during the course of the reaction with a Beckman D.U. spectrophotometer. The time intervals were selected so that readings could be taken over a time period of several half-lives.

Upon completion of the experiment, a known volume of the reaction mixture was titrated with a standardized solution of sodium hydroxide to a methyl red-brom cresol green end-point, and the concentration of acid computed.

In some instances the absorbancy readings were corrected by determining the correction due to solvent or cell differences between the reaction and reference cells. In other instances the Guggenheim method[18] was employed to eliminate this source of error. The first-order rate constants were determined in each case by the method of least squares. At two different acid concentrations both the cell correction and Guggenheim method were employed. The rate constants obtained by the two techniques were not significantly different.

Generally, two rate determinations were performed at each acid concentration. The standard percentage deviation of the individual determination was 2.9%. The average values of these experimental rates are reported in Tables I and III.

***pK* of Thioacetamide.**—The stoichiometric equation for the equilibrium between thioacetamide and protonated thioacetamide is

$$T + H_3O^+ \overset{K_1}{\rightleftarrows} TH^+ + H_2O \text{ and } K_1 = [TH^+]/[T]h_0$$

where $h_0 = f_T a_{H_3O^+}/f_{TH^+}a_{H_2O} = [a_{H^+}(f_T/f_{TH^+})]$ and $h_0$ is the antilog of minus the acidity function.

The absorption maximum at 2615 Å. is due to unprotonated thioacetamide, and the absorption maximum at 2370 Å. presumably is due to protonated thioacetamide. The rate of hydrolysis in water and in concentrated HCl solution was found to be very slow. Assuming the thioacetamide exists exclusively in the unprotonated form in water, and in the protonated form in concentrated HCl solution, the absorptivities for thioacetamide and protonated thioacetamide at 2615 and 2370 Å. were determined. The isosbestic point was found to be 2470 Å. (Absorptivities in liters mole$^{-1}$ cm.$^{-1}$: thioacetamide, 2615 Å., $1.17 \times 10^4$; 2370 Å., $0.22 \times 10^4$; 2470 Å., $0.62 \times 10^4$; protonated thioacetamide, 2615 Å., $0.080 \times 10^4$; 2370 Å., $0.88 \times 10^4$; 2470 Å., $0.62 \times 10^4$.)

The absorbancy was measured at each of the three wave lengths for solutions of known HCl concentration where both maxima were in evidence. It was assumed that the decrease in absorbancy at the isosbestic point was due entirely to hydrolysis and not in any way due to tautomeric species which may have been present. If this assumption is not valid, the calculated equilibrium constants could be seriously in error. The absorbancies in each solution were multiplied by the appropriate factors to correct for hydrolysis. In 4.30 $M$ HCl log $[TH^+]/[T]$ was −0.49 (2615 Å.), −0.25 (2370 Å.); log $K_1$ was −2.00 and −1.76, respectively. In 5.52 $M$ HCl log $[TH^+]/[T]$ was 0.15 and 0.438; log $K_1$ was −1.79 and −1.50. $\overline{\log K_1} = -1.76$ and S.D.$_{\overline{\log K_1}} = 0.10$.

**Calculation of the Least Squares Constants for Equation 15.**—Since eq. 15 contains the non-linear term log $(1 + K_1h_0)$, simple linear regression methods cannot be employed. What was done was to assume a value for $K_1$, to evaluate log $(1 + K_1h_0)$ and then to calculate the least squares value of $B$ and log $k_2K_1$ for the linear expression

$$(\log k + \log (1 + K_1h_0) - \log [H_3O^+]) = \log k_2K_1 + BC$$

The sum of the squares of the deviations of the experimental log $k$ minus the calculated log $k$ was computed. This operation was repeated for various values of $K_1$ and in this way those values of the constants $K_1$, $B$ and log $k_2K_1$ for which the sum of the squares of the deviations was a minimum were computed. An estimate of S.D. of log $k_2K_1$ and $B$ was calculated from the linear expression, in which it is assumed there is no error in $K_1$. The "true" S.D. is presumably less than these estimated values.

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[18] E. A. Guggenheim, *Phil. Mag.*, [7] **2**, 538 (1926).