Comparison of the rate constants which we have obtained in hexane and decane with each other and with the value of Marshall and Davidson[3] for heptane indicates that there is no large effect of chain length on the rate constant over this range. A small effect may exist within the error limits of these determinations.

Calculation of the apparent activation energy from the rate constants in CCl_4 at 23 and 50° gives a value of 3.2 kcal./mole. This is in the range which would be expected for a diffusion controlled process such as this. The activation energy for the diffusion of iodine molecules in CCl_4 has been found to be 3.3 kcal./mole.[9]

The activation energy found for the gas phase recombination of iodine atoms in the presence of argon is −1.4 kcal./mole,[2e] the negative value being ascribed to the decreasing stability of the two-body complex which is believed to play a role in the "three body" recombination process. In solution "third body" solvent molecules are always present so the rate of diffusion rather than the stability of the two body complex is rate controlling.

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MADISON, WISCONSIN

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[9] E. W. Haycock, B. J. Alder and J. H. Hildebrand, *J. Chem. Phys.*, **21**, 1601 (1953).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

Kinetic Studies of Thiourea Derivatives. I. Methylthiourea

BY WILLIAM H. R. SHAW AND DAVID G. WALKER

RECEIVED DECEMBER 19, 1956

The decomposition of methylthiourea in aqueous media has been studied over a wide *p*H range. In acid solutions two parallel first-order reactions were observed and corresponding rate constants evaluated at several temperatures. Above *p*H 7 additional complicating reactions were encountered. The experimental results are compared with those previously reported for urea and thiourea. A possible mechanism is discussed.

Introduction

The isomerization of urea to ammonium cyanate has been investigated previously in this Laboratory.[1] Recently, analogous results were also reported for thiourea,[2] and the marked similarity of the two reaction systems noted. Since both reactions were found to be strictly first-order, presumably unimolecular, decompositions, it seemed desirable to obtain comparable data with related compounds. The present paper is the first in a series to be devoted to the kinetic study of urea and thiourea derivatives.

Although the fundamental organic chemistry of methylthiourea recently has been thoroughly discussed and reviewed by Sahasrabudhey and Singh,[3] no kinetic data on the decomposition of this compound could be found in the literature. Moreover, reasoning based on the mechanism previously postulated for the isomerization of thiourea indicated that the decomposition of the 1-methyl derivative should exhibit several novel features.

Experimental

Methylthiourea was prepared by the addition of ammonia to methyl isothiocyanate.[4] The crude product was recrystallized twice from water, m.p. 118.7–120.4° (lit.[4] m.p. 119–120.5°). Titration of weighed amounts of the purified material with standard mercuric nitrate[5] indicated that the compound was at least 99% pure.

Anal. Calcd. for $C_2H_6N_2S$: C, 26.60; H, 6.70; N, 31.07. Found: C, 26.65; H, 6.69; N, 30.82.

The apparatus and techniques utilized in this investigation were those employed in earlier work[1,2] except as noted below.

Reaction mixtures were analyzed for ammonia and methylamine by the following modification of the ion-exchange method previously described.[1,2,6] Samples of the reacted solutions were adjusted to *p*H 6–7 and passed through ion-exchange columns containing Dowex 50. After careful washing the adsorbed ammonium and methylammonium ions were eluted from the resin with dilute sodium hydroxide. After suitable *p*H adjustment separate aliquots were used to determine ammonia by nesslerization, and methylamine by a colorimetric analysis described in detail elsewhere.[7] The methylamine analysis was not affected by the amounts of ammonia present in the reaction mixtures. In the ammonia analysis, on the other hand, a moderate interference by methylamine was encountered. Suitable corrections could, however, be made by appropriate calibration of the Nessler reagent in the presence of the interfering substance. The average deviation of a set of 8 independent analyses of a 1.11 m*M* methylamine hydrochloride solution was 3.0%. Whereas the average deviation of a set of 8 analyses of 0.148 m*M* ammonium chloride that was also 0.286 m*M* in methylamine sulfate was found to be 4.4%.

Results

As in previous papers the reactions were studied by the method of initial rates. The equation

$$p_1/t = k_1\bar{u} \tag{1}$$

was used in the analysis of experimental data. In this equation $\bar{u}$ is the average methylthiourea concentration; p_1 denotes the concentration of a particular product, P_1, formed in the reaction time, t; and k_1 is an empirical rate constant based on the rate of formation of P_1. Since very little reactant was consumed during the reaction period, $\bar{u}$ differed from the initial reactant concentration by less than 2%. The rates of formation of three reaction prod-

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[1] W. H. R. Shaw and J. J. Bordeaux, THIS JOURNAL, **77**, 4729 (1955).

[2] W. H. R. Shaw and D. G. Walker, *ibid.*, **78**, 5769 (1956).

[3] R. H. Sahasrabudhey and R. Singh, *J. Indian Chem. Soc.*, **30**, 469 (1953).

[4] E. C. Horning, Ed., "Organic Syntheses," Vol. 3, John Wiley and Sons, Inc., New York, N. Y., 1955, pp. 617–618.

[5] R. H. Sahasrabudhey and R. Singh, *J. Indian Chem. Soc.*, **30**, 223 (1953).

[6] W. H. R. Shaw and J. J. Bordeaux, *Anal. Chem.*, **27**, 138 (1955).

[7] F. D. Snell and C. T. Snell, "Colorimetric Methods of Analysis," 3rd Edition, Vol. 4, D. Van Nostrand Co., Inc., New York, N. Y., 1954, pp. 34–35.

ucts: (1) thiocyanate ion, (2) ammonia and (3) methylamine were followed and corresponding empirical rate constants k_1, k_2 and k_3 were calculated by means of equation 1.

In acid solution all the k's were independent of reactant concentration and reaction time, establishing that the rates of formation of all products were first order with respect to methylthiourea. Measurements conducted with solutions varying in average methylthiourea ($\bar{u}$) from 44.5 to 444 mM, for reaction times from 11.8 to 24.8 hr. gave the following best values for the empirical first-order constants at 100.0 ±0.1°: $k_1 = 0.57 \pm 0.07 \times 10^{-7}$ sec.$^{-1}$, $k_2 = 1.84 \pm 0.15 \times 10^{-7}$ sec.$^{-1}$, $k_3 = 2.49 \pm 0.25 \times 10^{-7}$ sec.$^{-1}$. All of the experimental solutions used to obtain the above values were 0.01 M in H_2SO_4. The behavior of these constants with changing acidity of the media is displayed in Fig. 1. The constant based on the rate of thiocyanate production (k_1) was found to be independent of $\bar{u}$ and t in both acidic and basic solutions, nor was the magnitude of this parameter affected by pH changes over a very wide range. The behavior of the other two constants was considerably more complex. Above pH 7 these parameters were strongly dependent on pH, $\bar{u}$ and t. As indicated in the legend, the results plotted in Fig. 1 were obtained with a reactant concentration of 0.050 M and a reaction time of 36 hours.

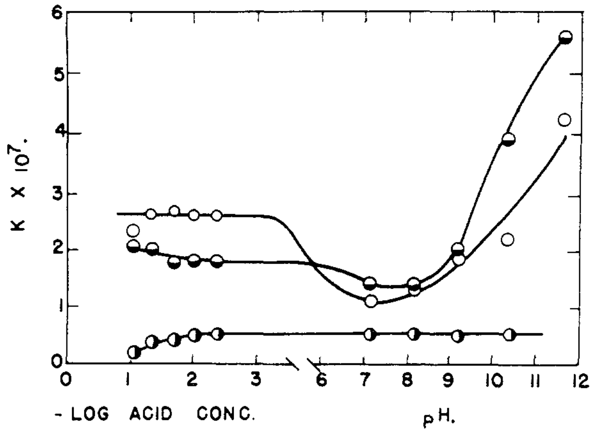


Fig. 1.—Empirical first-order rate constants as a function of acid concentration. The constants: k_1, k_2 and k_3 are based on the rate of formation of thiocyanate (◑), ammonia (◒), and methylamine (○), respectively. Runs above pH 7 were made in buffered 0.01 M borax solutions. Results recorded below pH 7 were based on data collected for HCl. All runs were made at 100.0 ± 0.1° at an initial methylthiourea concentration of 0.050 M and a reaction time of 36.0 hr.

The temperature dependencies of the constants based on thiocyanate production (k_1) and ammonia production (k_2) were also measured (Table I). These runs were made in acid media to eliminate the complexities mentioned in the preceding paragraph. The effect of ionic strength was likewise studied in media of low pH. Experiments were performed with solutions containing added sodium sulfate varying in concentration from 0.00 to 0.50 M at 100°. These solutions were also 0.01 M in H_2SO_4. A reaction time of 88.7 hr. was employed with an average methylthiourea concentration of 38 mM. No salt effects were observed.

As in the case of thiourea the reaction mixtures were subjected to a qualitative test for sulfide ion. Reacted samples obtained at all pH's studied were acidified (unless already acidic) and treated with mercuric nitrate solution. No precipitate was obtained with solutions that had reacted at pH's below 7, but those above pH 7 yielded a faint precipitate that became increasingly pronounced with increasing pH of reaction.

The rate constants recorded in Table I are reported to one more significant figure than is justified by the experimental data. The over-all average percentage deviations for k_1, k_2 and k_3 were approximately 10, 5 and 9%, respectively. Within a given run, however, much smaller deviations were encountered. In the extended reaction periods employed (as long as 89 hours) it was somewhat difficult to maintain precise temperature control, and, consequently, part of the lack of reproducibility from run to run could be attributed to this source of error. For these long reaction periods the temperature was controlled only to approximately ±0.1°.

TABLE I

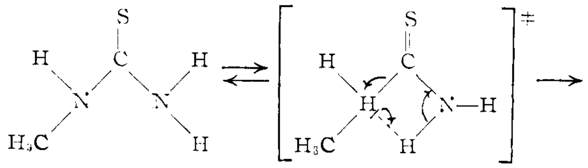
RATE CONSTANTS OBTAINED AT VARIOUS TEMPERATURES IN ACID SOLUTIONS

Temp., °C. ±0.1	$\bar{u}$[a]	t[b]	First-order rate constants,[c] sec.$^{-1}$ × 10^7 k_1	k_2
		A. Medium, 0.01 M HCl		
100.0	49.3	29.5	0.65[d]	2.09[d]
110.1	49.2	9.82	2.40	7.55
120.2	48.8	4.00	8.13	24.8
130.0	48.3	1.90	24.7	68.8
140.0	46.7	1.40	86.0	197
		B. Medium, 0.015 M HNO_3		
100.0	100	6.55	0.62[d]	1.93[d]
110.0	49.5	6.17	2.30	7.02
120.0	24.4	4.58	8.20	25.1
130.0	9.43	3.62	28.1	74.0
140.0	8.96	2.78	78.9	169

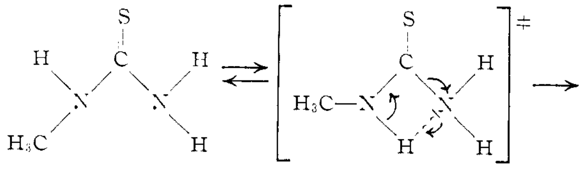
[a] $\bar{u}$ is the average concentration of methylthiourea (millimoles/liter). [b] t is reaction time in hours. [c] The constants k_1 and k_2 are based on the rate of production of thiocyanate and ammonia, respectively. [d] For the least squares arrhenius analysis a value of 0.57 was used for k_1 and 1.84 for k_2 at this temperature. These values represent the average of all experimental data obtained at 100° whereas the values presented in Table I are based on 4 runs.

Discussion

The mechanism previously postulated for the thiourea decomposition assumed intramolecular hydrogen transfer and dissociation of the activated complex to form ammonia and thiocyanic acid. In this case hydrogen transfers from N to N′ and from N′ to N cannot be distinguished experimentally since the reaction products formed by both processes are identical. This degeneracy should, however, be removed in the decomposition of methylthiourea and different reaction products should result from these two different modes of hydrogen transfer. A tentative reaction scheme might be formulated as



$CH_3NH_2 + HNCS$ (2)



$CH_3—NCS + NH_3$ (3)

Additional reaction by the products must also be considered.

$$HNCS \longrightarrow H^+ + NCS^- \qquad (4)$$

$$CH_3 - NCS + H_2O \longrightarrow CH_3NH_2 + COS\uparrow \qquad (5)$$

$$NH_3 + H^+ \rightleftharpoons NH_4^+ \qquad (6)$$

$$CH_3NH_2 + H^+ \rightleftharpoons CH_3NH_3^+ \qquad (7)$$

Since isothiocyanic acid is a strong acid,[8] equation 4 is written as an irreversible process. In acid, methyl isothiocyanate is converted[9] rapidly into methylamine and carbon oxysulfide (eq. 5). It follows, therefore, that the final products of reaction 2 in acid solution will be methylammonium ions and thiocyanate ions. From stoichiometric considerations the thiocyanate concentration produced by this reaction should be equal to the methylammonium ion simultaneously generated. Reaction 3 will yield ammonium and methylammonium ions in equimolar amounts. It becomes apparent, therefore, that the empirical first-order rate constant based on the production of thiocyanate, k_1, is the true rate constant for reaction 2. Similarly, k_2, based on ammonia production should be assigned to reaction 3. k_3, on the other hand, must be regarded as a composite constant; and, if the preceding reasoning is correct, it follows from the stoichiometry of reactions 2–7 that

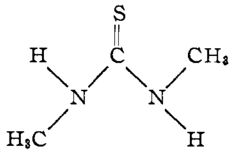
$$k_3 = k_1 + k_2 \qquad (8)$$

As previously mentioned (Results) the best values for the various constants at 100° are as follows: $k_1 = 0.57 \pm 0.07 \times 10^{-7}$ sec.$^{-1}$, $k_2 = 1.84 \pm 0.15 \times 10^{-7}$ sec.$^{-1}$, $k_3 = 2.49 \pm 0.25 \times 10^{-7}$ sec.$^{-1}$. It becomes apparent, therefore, that equation 8 correctly represents the experimental data. The decomposition of methylthiourea in acid solution must, consequently, be regarded as two parallel first-order reactions producing methylamine as a common product. The rate constant for these reactions can, however, be unambiguously assigned from experimental data on the rate of formation of other products (*e.g.*, SCN^- and NH_4^+).

A further examination of these results and those displayed in Table I reveals several points of interest. The rate constant (k_1) for reaction 2 is less than the constant (k_2) characterizing reaction 3. This generalization is true at all temperatures studied. Moreover, both of these constants differ significantly from the corresponding values reported for urea and thiourea particularly when statistical factors are also considered. In the most concentrated acid solutions studied (Fig. 1), k_1 falls off slightly and k_2 shows a corresponding increase. This same phenomenon was observed with thiourea and was attributed[2] to the conversion of thiocyanate to ammonium ion. With the addition of this known reaction, therefore, all the data obtained in acid solutions can be rationalized by the reaction scheme presented (equations 2–7). A least squares Arrhenius analysis of the data in Table I gave the following parameters describing the temperature dependence of k_1: $A = 9.87 \times 10^{14}$ sec.$^{-1}$, $E = 37.9$ kcal. Analogous parameters for k_2 are: $A = 3.37 \times 10^{13}$ sec.$^{-1}$, $E = 34.5$ kcal. The frequency factors and activation energies are reported to three figures solely for purposes of calculation of rate constants at various temperatures from the A and corresponding E. Because of the limited temperature range studied and experimental error (see Results) it is possible to select a wide variety of A's and corresponding E's that will give an adequate fit.

In solutions above pH 7 the empirical constants show a more complex behavior. As the hydrogen ion concentration is reduced, the equilibria described by eq. 6 and 7 will lie farther toward the left. The rate of conversion of methyl isothiocyanate to methylamine should also be diminished since this reaction is presumably acid catalyzed. Thus in media of slightly alkaline pH an increased ratio of methylamine to methylammonium ion should be encountered and methyl isothiocyanate should enjoy a longer lifetime than in solutions of greater acidity. Consequently, since the reverse of reaction 3 is a well known comparatively fast reaction, the decrease in k_2 and k_3 readily can be understood. The reaction

$CH_3NCS + CH_3NH_2 \rightleftharpoons$



(9)

is also most probably involved. Other evidence substantiates the existence of such complicating reactions. Thus, in alkaline media, the observed dependence of k_2 and k_3 on $\bar{u}$ and t can be interpreted on this same basis. In analogy to the thiourea case[2] the subsequent increase in these two empirical constants with increasing pH can be ascribed to the onset of a parallel base-catalyzed reaction that does not produce thiocyanate. The production of increasing amounts of sulfide precipitate (see Results) indicates, as before,[2] the onset of this reaction.

One rather striking aspect of the kinetic behavior of methylthiourea remains to be discussed—the remarkable pH independence of k_1. Since thiocyanic acid (unlike cyanic) is strong, the only species to be considered in water solutions in the pH range studies is the thiocyanate ion. However, according

[8] H. E. Williams, "Cyanogen Compounds," 2nd ed., Edward Arnold & Co., London, England, 1948, pp. 307–309.

[9] A. W. Hofmann, *Ber.*, **1**, 169 (1868).

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.

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AUSTIN, TEXAS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

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

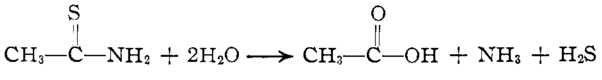
BY DONALD ROSENTHAL[2] AND T. IVAN TAYLOR

RECEIVED OCTOBER 3, 1956

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]



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

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).