by the usual methods before use. Pentamethylnitrobenzene was prepared by nitration of pentamethylbenzene with nitronium tetrafluoroborate.[12] Nafion-H was prepared by treatment of the commercial DuPont Nafion-K resin with dilute nitric acid, as described previously.[1]

General Procedure for Transfer Nitration. A solution of 9-nitroanthracene or pentamethylnitrobenzene (1 g) in the aromatic hydrocarbon (15 mL) was mixed with the acid catalyst (1 g) in a Teflon-lined, stainless steel bomb. The reaction mixture was heated to 180-190 °C for 6 h. The bomb was subsequently allowed to cool to room temperature and opened, and the products were worked up.

When Nafion-H was used as a catalyst, the reaction mixture was filtered, and the solid catalyst washed with chloroform (3 × 10 mL). The filtrate was concentrated and the products were analyzed by gas chromatography.

When $HF:SbF_5$ and $HF:TaF_5$ were used as catalysts, the reaction mixture was quenched with 10% aqueous sodium bicarbonate and extracted with chloroform (100 mL). The chloroform extract was dried over anhydrous sodium sulfate, concentrated, and analyzed by gas chromatography.

Protolytic Denitration of 9-Nitroanthracene with $HF:TaF_5$ in the Presence of *n*-Butyl Sulfide. A mixture of 9-nitroanthracene (5 mL), *n*-butyl sulfide (15 mL), and $HF:TaF_5$ (10 mL) was heated in a stainless steel bomb at 160° for 16 h. The reaction mixture was cooled to room temperature, extracted with benzene, and washed with 10% aqueous sodium bicarbonate solution and brine. The extract was dried over anhydrous sodium sulfate and evaporated to dryness. The residue was sublimed to give 250 mg (28%) of anthracene.

Analysis of Products. All reaction products were analyzed by gas-liquid chromatography, using a Varian Model 3700 gas chromatograph equipped with hydrogen flame ionization detector and using a 9 ft × 1/8 in. stainless steel column packed with 1.75% butanediol succinate on Chromosorb W (80-100 mesh). Nitro compounds were identified by comparison of retention times with those of authentic samples on the same column.

Determination of Kinetic Hydrogen Isotope Effects. Competitive Nitration of Benzene/Benzene-d_6, Naphthalene/Naphthalene-d_8, and Anthracene/Anthracene-d_{10}. A mixture of benzene (or naphthalene) (20 mmol) and benzene-d_6 (or naphthalene-d_8) (20 mmol) was dissolved in nitromethane (75 mL), and a solution of nitronium hexafluorophosphate (0.96 g, 5 mmol) in nitromethane (10 mL) was added with vigorous stirring, while maintaining the reaction mixture at 25 °C. In the case of anthracene/anthracene-d_{10}, 2.5 mmol of each was dissolved in nitromethane (200 mL), and nitrated with nitronium hexafluorophosphate (0.29 g, 1.5 mmol) dissolved in nitromethane (10 mL).

After 30 min, the reaction mixture was quenched with 10% aqueous sodium bicarbonate and extracted with ether (100 mL). The ethereal extract was washed with brine and dried over anhydrous sodium sulfate. The dried extract was concentrated and the product ratios were determined by GLC-mass spectrometry on a DuPont 21-094 mass spectrometer coupled to a Varian Associates Aerograph Model 2700 gas chromatograph.

Acknowledgment. Support of our work by the U.S. Army Office of Research is gratefully acknowledged.

References and Notes

(1) Aromatic Substitution. 44. For part 43, see: G. A. Olah, R. Malhotra, and S. C. Narang, *J. Org. Chem.*, **43**, 4628 (1978).

(2) (a) C. K. Ingold, "Structure and Mechanism in Organic Chemistry", 2nd ed., Cornell University Press, Ithaca, N.Y., 1969. (b) G. A. Olah and S. J. Kuhn, "Friedel-Crafts and Related Reactions", G. A. Olah, Ed., Interscience, New York, 1964, Vol. 3, p 1393.

(3) J. G. Hoggett, R. B. Moodie, J. R. Penton, and K. Schofield, "Nitration and Aromatic Reactivity", Cambridge University Press, London, 1971.

(4) On the other hand, some isomerization of the nitroarenium ion intermediates has been observed; see P. C. Myhre, *J. Am. Chem. Soc.*, **94**, 7921 (1972).

(5) W. N. White and J. R. Klink, *J. Org. Chem.*, **35**, 965 (1970).

(6) G. A. Olah, H. C. Lin, and Y. K. Mo, *J. Am. Chem. Soc.*, **94**, 3667 (1972).

(7) V. I. Mamatyuk, B. G. Derendyaev, A. N. Destina, and V. A. Koptyug, *Zh. Org. Khim.*, **10**, 2506 (1974).

(8) P. H. Gore, *J. Chem. Soc.*, 1437 (1957).

(9) H. Cerfontain and A. Telder, *Recl. Trav. Chim. Pays-Bas*, **86**, 371 (1967).

(10) Nafion is a registered trademark of the DuPont Company, whom we thank for samples of the potassium salt of Nafion 501 resin.

(11) P. C. Myhre and M. Beug, *J. Am. Chem. Soc.*, **88**, 1569 (1966).

(12) G. A. Olah, S. J. Kuhn, and S. H. Flood, *J. Am. Chem. Soc.*, **83**, 4571 (1961).

Effect of Acid Concentration on the Partitioning of the Tetrahedral Intermediate in the Hydrolysis of Thioacetanilide[1]

John T. Edward* and Sin Cheong Wong*

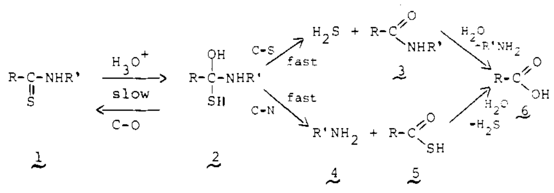
Contribution from the Department of Chemistry, McGill University, Montreal, Quebec, Canada H3A 2K6. *Received August 11, 1978*

Abstract: In dilute sulfuric acid, the hydrolysis of thioacetanilide to acetic acid, hydrogen sulfide, and aniline takes place chiefly by C-S cleavage of the tetrahedral intermediate to give hydrogen sulfide and acetanilide as intermediates. As the concentration of sulfuric acid is raised from 1.1 to 36%, hydrolysis via C-N cleavage to give aniline and thioacetic acid as intermediates becomes progressively more important, and is the exclusive pathway in 48% acid. The results may be explained by postulating that C-S cleavage involves the neutral, and C-N cleavage the amino-protonated, tetrahedral intermediate.

Introduction

The acid-catalyzed hydrolysis of a thioamide (e.g., **1**) most probably involves the rate-determining formation of a tetrahedral intermediate **2**,[2,3] which can then undergo fast C-O cleavage to give starting material, C-S cleavage to give hydrogen sulfide and amide (**3**), or C-N cleavage to give ammonia or amine (**4**) and thio acid (**5**),[2,4] as shown in Scheme I. The amide and the thio acid are then hydrolyzed to car-

Scheme I

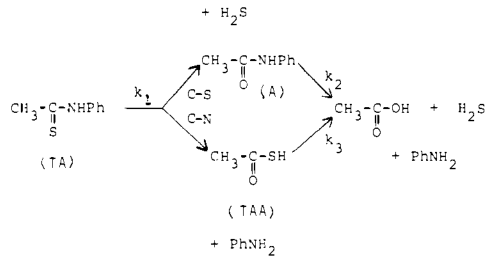


0002-7863/79/1501-1807$01.00/0

Table I. Activation Parameters for the Hydrolysis of Thioacetanilide and Acetanilide in Various Concentrations of Sulfuric Acid

	thioacetanilide		acetanilide	
% H_2SO_4	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu
3.2	18	−25	16	−32
6.3	18	−22	17	−28
12	18	−21	17	−26
24	17	−22	17	−25
36	15	−27	18	−24
48	16	−25	18	−25

Scheme II



boxylic acid **6** in subsequent steps. Our previous studies have focused on the effect of changing acid concentration on the rate-determining step **1** → **2** (R = CH_3, R′ = p-$NO_2C_6H_4$) and the information this sheds on the nature of the transition state for this step.[3] In dilute sulfuric acid this reaction is inconveniently slow, and so it was studied only in 22–96% sulfuric acid; over this range of acid concentration hydrolysis took place exclusively by the C–N pathway to give thio acid. It seemed likely that the C–S pathway would be favored in more dilute acid,[3] and in this paper we consider the effect of acid concentration on the partitioning of the intermediate **2** (R = CH_3; R′ = Ph) from the hydrolysis of thioacetanilide (**1**, R = CH_3; R′ = Ph), which hydrolyzes at a convenient rate even in dilute acid.

Results and Discussion

Rate Profile and Mechanism. The pseudo-first-order rate constants k_ψ for the hydrolysis of both acetanilide and thioacetanilide in aqueous sulfuric acid at 25 °C increase initially with acid concentration, reach a maximum (at ~25% acid concentration for acetanilide and ~36% for thioacetanilide), and then drop with further increase in acid concentration. Such rate profiles are characteristic of the A-2 hydrolysis of amides,[5,6] esters,[7] thio acids,[8] and other carboxylic acid derivatives. The A-2 mechanism is also supported by the large negative $\Delta S^{\ddagger}$ values[9] of the reactions (Table I), and by the variation with acid concentration of the transition-state activity coefficients $f_{S^{\ddagger}}{}^{*E}$ [3,10,11] (calculated from the kinetic and substrate activity coefficient data of this work and from the protonation equilibria,[12] hydrogen ion activity,[11] and water activity data[16] in the literature). The $f_{S^{\ddagger}}{}^{*E}$ values (Table II) are very similar to those found previously for the corresponding 4-nitro substituted compounds,[3] and indicate a well-advanced transition state for the amide hydrolysis and an early transition state for the thioamide hydrolysis.

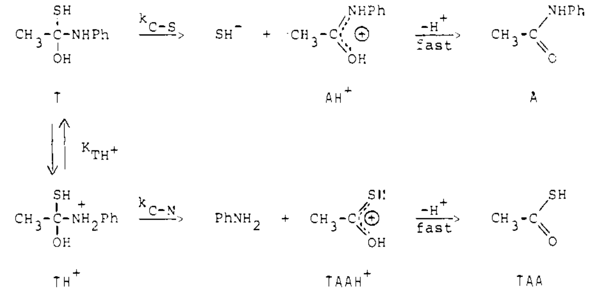
Product Distribution. Determination of the product distribution (Scheme II; cf. ref 4) is complicated by the further hydrolyses of both acetanilide and thioacetic acid to acetic acid. Fortunately, the different species of Scheme II have quite distinct UV spectra: in 6.1% H_2SO_4, for instance, thioacetanilide has λ_{max} 276 nm (ϵ_{max} 8090), λ_{min} 243 nm (ϵ_{min} 2480), while acetanilide has λ_{max} 240 nm (ϵ_{max} 8650), and all other species are either transparent or weakly absorbing above 230 nm. Consequently, the concentrations of the various compounds of Scheme II may be obtained by a spectrophotometric study at ~240 nm, as shown by the following analysis.

Table II. Comparison of Transition-State Activity Coefficients log $f_{S^{\ddagger}}{}^{*E}$ in Varying Concentrations of Sulfuric Acid

% H_2SO_4	p-nitrothioacetanilide[a]	thioacetanilide	p-nitroacetanilide[a]	acetanilide
10	0.4	0.4	0.7	0.6
15		0.7		0.9
20	0.9	0.9	1.4	1.3
25		1.2		1.8
30	1.4	1.6	2.2	2.2
35	1.7	1.9	2.6	2.7
40	2.0	2.3	3.1	3.2
45	2.3	2.7	3.6	3.8
50	2.7	3.1	4.2	4.3

[a] Data of ref 3.

Scheme III



Let the initial thioacetanilide concentration be C_0, and the fraction hydrolyzing by the C–S pathway be x. The rate of disappearance of thioacetanilide (TA) and the rates of formation of acetanilide (A) and thioacetic acid (TAA) are given by

$$-\frac{dC_{TA}}{dt} = k_1C_{TA} \tag{1}$$

$$\frac{dC_A}{dt} = xk_1C_{TA} - k_2C_A \tag{2}$$

$$\frac{dC_{TAA}}{dt} = (1 - x)k_1C_{TA} - k_3C_{TAA} \tag{3}$$

Solving these equations, we get

$$C_{TA} = C_0e^{-k_1t} \tag{4}$$

$$C_A = \frac{C_0xk_1}{k_2 - k_1}(e^{-k_1t} - e^{-k_2t}) \tag{5}$$

$$C_{TAA} = \frac{C_0(1 - x)k_1}{k_3 - k_1}(e^{-k_1t} - e^{-k_3t}) \tag{6}$$

$$C_{PhNH_2} = C_0 - C_{TA} - C_A \tag{7}$$

We have determined separately the rate constants k_1, k_2, and k_3 and the extinction coefficients for TA, A, TAA, and $PhNH_2$ in various sulfuric acid concentrations at various temperatures. A computer program was then designed to calculate, for hypothetical x values, the variation in the overall absorbance (the sum of the above concentrations, each multiplied by their respective extinction coefficients) with time.

Values of x were then determined (to the nearest 5% in more dilute acids, and 2% in more concentrated acids) by comparing the experimental and computed absorbance values over a period of 2 half-lives; an example is shown in Figure 1. Results, tabulated in Table III, show that, as expected,[3] C–S cleavage is preferred in dilute acid and C–N cleavage in more concentrated acid. The change occurs gradually from 1–48% sulfuric acid, and may be explained (following Hall and Satchell[2]) by postulating an equilibrium between the tetrahedral intermediate T and its N-protonated conjugate acid TH^+ (Scheme III), C–S cleavage occurring exclusively from T, SH^- being

Table III. Product Distribution in the Hydrolysis of Thioacetanilide

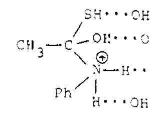
% H_2SO_4	temp, °C	C–N cleavage, %	
		exptl	calcd
1.1	70	20	
	80	5	
3.2	60	50	
	70	40	
	80	25	
6.1	50	55	
	60	55	50
	70	45	
12	50	65	
	60	65	67
	70	65	
18	50	80	
	60	75	78
24	40	88	
	50	88	
	60	88	88
36	40	98	
	50	98	
	60	96	96
48	40	100	
	50	100	
	60	100	99

superior to $PhNH^-$ as a leaving group, and C–N cleavage exclusively from TH^+, $PhNH_2$ (resonance stabilized, but not in TH^+) being superior to SH^- as a leaving group. The ratio of C–N to C–S cleavage products will then be given by

$$\frac{\text{C–N}}{\text{C–S}} = \frac{h_0^{m}}{k_{C\text{-}S}K_{TH^+}/k_{C\text{-}N}} \qquad (8)$$

if the protonation of T in acid concentrations above ~1 M follows h_0^{m}.[17] A plot of log ([C–N]/[C–S]) against $-H_0$ at 60 °C[19] gives a straight line of slope $m = 0.7$ and intercept log $(k_{C\text{-}S}K_{TH^+}/k_{C\text{-}N}) = 0$. The percentage of C–N cleavage in different acid concentrations at 60 °C using eq 8 with these parameters is given in Table III. The agreement with experimental values is satisfactory, and confirms the essential validity of the mechanism shown in Scheme III.

The relatively low value of m is surprising, since one would expect it to be ~1 for a secondary amine.[20] It may be explained by extensive hydration of the hydroxyl and sulfhydryl groups of TH^+ because of their enhanced acidities brought about by



TH^+

the inductive effect of the charged ammonium group.[21] If, as seems likely,[22] $pK_{TH^+} \simeq 0$, then $k_{C\text{-}S} \simeq k_{C\text{-}N}$.

The C–S path seems to be favored by higher temperatures (see Table III), the chief reason probably being a greater $\Delta H^{\ddagger}$ for C–S than for C–N cleavage.

Experimental Section

Materials. Thioacetanilide, acetanilide, and thioacetic acid were all commercial products. Sulfuric acid solutions were prepared and standardized as before.[3]

Kinetic Measurements. Rates of hydrolysis of thioacetanilide and acetanilide were followed by a Unicam SP 800 spectrophotometer thermostated at 25.0 ± 0.1 °C. Their rates and that of thioacetic acid were also followed at various temperatures from 40.0 to 80.0 °C (±0.3 °C). Pseudo-first-order rate constants k_ψ were calculated from the change in optical density using a least-squares computer program. Results are given in Tables IV and V of the supplementary material.

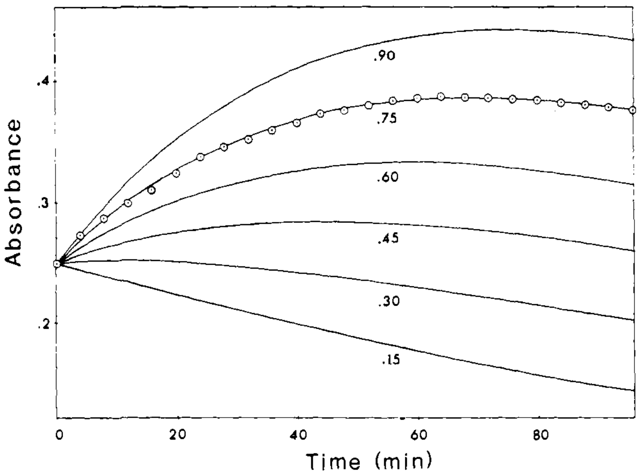


Figure 1. Hydrolysis of thioacetanilide in 3.2% sulfuric acid at 80 °C. Variation of UV absorbance of 10^{-4} M solution with time: curves computed using x values shown; experimental results shown as points.

Activity Coefficient Measurements. Activity coefficients f_S of thioacetanilide and acetanilide in sulfuric acid were determined at 25.0 ± 0.1 °C by the distribution method using methylene chloride as the inert solvent.[21] Compensation was made for changes due to hydrolysis and protonation. Results are given in Table VI of the supplementary material.

Acknowledgment. We are grateful to Professor R. A. McClelland for helpful correspondence.

Supplementary Material Available: Tables IV (pseudo-first-order rate constants at 25 °C), V (pseudo-first-order rate constants at various temperatures), VI (activity coefficients f_S), and VII (transition-state activity coefficients $f_S{}^{\ddagger *E}$ and $f_S{}^{\ddagger *E}/k_2$) (3 pages). Ordering information is given on any current masthead page.

References and Notes

(1) Research supported by the National Research Council of Canada.
(2) A. J. Hall and D. P. N. Satchell, *J. Chem. Soc., Perkin Trans. 2*, 1077 (1974).
(3) J. T. Edward, G. D. Derdall, and S. C. Wong, *J. Am. Chem. Soc.*, **106**, 7023 (1978).
(4) O. M. Peeters and C. J. de Ranter, *J. Chem. Soc., Perkin Trans. 2*, 1832 (1974).
(5) J. T. Edward and S. C. R. Meacock, *J. Chem. Soc.*, 2000 (1957).
(6) C. R. Smith and K. Yates, *J. Am. Chem. Soc.*, **93**, 6578 (1971).
(7) K. Yates and R. A. McClelland, *J. Am. Chem. Soc.*, **89**, 2686 (1967); C. A. Lane, M. F. Cheung, and G. F. Dorsey, *ibid.*, **90**, 6492 (1968).
(8) J. Hipkin and D. P. N. Stachell, *Tetrahedron*, **21**, 835 (1965); J. T. Edward, G. Welch, and S. C. Wong, *Can. J. Chem.*, **56**, 935 (1978).
(9) L. L. Schaleger and F. A. Long, *Adv. Phys. Org. Chem.*, **1**, 1 (1963).
(10) J. T. Edward and S. C. Wong, *J. Am. Chem. Soc.*, **99**, 7224 (1977).
(11) T. A. Modro, K. Yates, and J. Janata, *J. Am. Chem. Soc.*, **97**, 1492 (1975); R. A. McClelland, T. A. Modro, M. F. Goldman, and K. Yates, *ibid.*, **97**, 5223 (1975).
(12) Acetanilide has a pK_{SH^+} value of −1.25,[13] according to the revised h_A scale;[14] thioacetanilide follows the h_T acidity function and has a pK_{SH^+} value of −3.12.[15]
(13) C. J. Giffney and C. J. O'Connor, *J. Chem. Soc., Perkin Trans. 2*, 1357 (1975).
(14) J. T. Edward and S. C. Wong, *Can. J. Chem.*, **55**, 2492 (1977).
(15) J. T. Edward and M. J. Williamson, unpublished results.
(16) W. F. Giauque, E. W. Hornung, J. E. Kunzler, and T. R. Rubin, *J. Am. Chem. Soc.*, **82**, 62 (1960).
(17) The relation log $[SH^+]/[S] = mH_0 + pK_{SH^+}$ seems to work adequately at sulfuric acid concentrations above about 1 M,[7] in spite of theoretical objections.[16] At lower acid concentrations, when all acidity functions become identical with pH, it must be replaced by the relation log $[SH^+]/[S] = -\mathrm{pH} + pK_{SH^+}$. In a region of sulfuric acid concentrations about 1 M, only the relation employing the correct acidity function H_S will be valid; for this reason we have omitted results in 1.1 and 3.2% acid from our analysis.
(18) G. C. Greig and C. D. Johnson, *J. Am. Chem. Soc.*, **90**, 6453 (1968).
(19) C. D. Johnson, A. R. Katritzky, and S. A. Shapiro, *J. Am. Chem. Soc.*, **91**, 6654 (1969).
(20) J. M. Carpentier and P. Lemetais, *Can. J. Chem.*, **56**, 954 (1978).
(21) K. Yates and R. A. McClelland, *Prog. Phys. Org. Chem.*, **2**, 323 (1974); A. Levi, G. Modena, and G. Scorrano, *J. Am. Chem. Soc.*, **96**, 6505 (1974).
(22) R. A. McClelland, *J. Am. Chem. Soc.*, **100**, 1844 (1978); private communication.