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Hydrolysis of Benzohydroxamic Acid

Robert L. Fuller

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HYDROLYSIS OF BENZOHYDROXAMIC ACID

by
Robert L. Fuller

A thesis presented to the Faculty of the School
of Graduate Studies in partial fulfillment
of the
Degree of Master of Arts

Western Michigan University
Kalamazoo, Michigan
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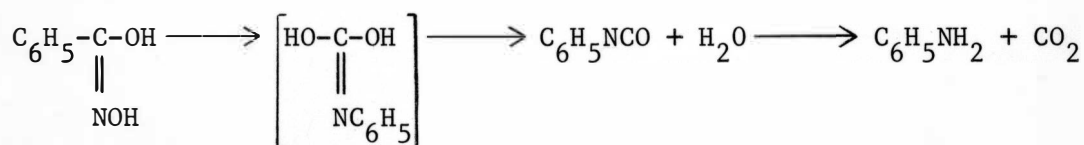
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INTRODUCTION

The hydroxamic acids were discovered in 1869 by H. Lossen¹. The nomenclature, structure, and chemistry of these compounds have been summarized in an excellent review article by Yale². Hydroxamic acids are carboxylic acid derivatives having the structures $R - \overset{\overset{O}{\parallel}}{C} - \overset{\overset{H}{\mid}}{N} - OH$ and $R - \overset{\overset{OH}{\mid}}{C} = N - OH$. These compounds are not known as separate substances, and hydroxamic acids would be expected to react as if they had either structure. Hydroxamic acids are solids; chemically they are weak acids. Both the aliphatic and aromatic compounds are fairly soluble in water. The decomposition of hydroxamic acids, their salts, and esters is accompanied by a rearrangement, usually called the Lossen rearrangement, in which the group attached to the carbon migrates to the nitrogen atom. Benzohydroxamic acid, on heating, gives a mixture of carbon dioxide, phenyl isocyanate, and aniline. A possible sequence is³



The preparation of hydroxamic acids is accomplished by the reaction of hydroxylamine with an ester, acid anhydride, or an amide³. It had long been noted that many metal ions form colored complexes with hydroxamic acids, but their use in analytical chemistry is only recent. Their uses as precipitating agents for uranium, cadmium, tantalum, and other metals, and for the colorimetric determinations of iron, vanadium, titanium, molybdenum, tungsten, and others are summarized by Brandt⁴.

The kinetics of ester hydrolysis has been extensively studied and the mechanisms well established⁵. The hydrolyses of other carboxylic acid derivatives have not been studied to the same extent. Meloche and Laidler⁶ have reported kinetic data for the acid and base catalyzed hydrolysis of benzamide and four substituted benzamides. Biechler and Taft⁷ and Mader⁸ have studied the alkaline hydrolysis of trifluoroacetanilide, and Morawetz and Otaki⁹ have studied alkaline hydrolysis of aliphatic amides. Similarly, hydrolyses of acid anhydrides, nitriles, and acid halides have been investigated to some extent. However, the hydroxamic acids have been neglected. It was the purpose of this research to investigate the alkaline and acid catalyzed hydrolysis of benzohydroxamic acid and to suggest reasonable mechanisms for the reactions.

EXPERIMENTAL

Preparation of Benzohydroxamic Acid

Benzohydroxamic acid was prepared according to the method of C. R. Hauser and W. B. Renfrow, Jr.¹⁰ Separate solutions of 46.7 g. (0.67 mole) of hydroxylamine hydrochloride in 240 ml. of methyl alcohol and 56.1 g. (1 mole) of C.P. potassium hydroxide in 140 ml. of methyl alcohol were prepared at the boiling point of the solvent. Both solutions were cooled to 30°C. and the alkali solution added with shaking to the hydroxylamine hydrochloride solution with occasional cooling in an ice bath. The mixture was allowed to cool in an ice bath for five minutes to insure complete precipitation of potassium chloride. Fifty grams (0.33 mole) of ethyl benzoate was added with thorough shaking and the mixture filtered immediately using suction. The filtrate was placed in a closed flask and allowed to stand forty-eight hours at room temperature. Crystals of potassium benzohydroxamate began to form within the first thirty minutes. The crystals were filtered and washed with ethyl alcohol and air dried. Two such batches were prepared and combined, the total yield being 82.5 g.

The potassium salt was added to 377 ml. of 1.25 N acetic acid and heated on a water bath until a clear solution was obtained. The solution was allowed to cool to room temperature and finally cooled in an ice bath. Benzohydroxamic acid separated as white crystals. The crystals were filtered and air dried with a yield of 61.1 g., m.p. 117-125°C.

The crude crystals were dissolved in 305 ml. of ethyl acetate by warming on a steam bath, filtered from a small amount of solids, and the filtrate

allowed to cool to room temperature. The crystals of benzohydroxamic acid which separated were filtered and air dried. This was repeated two more times using ethyl acetate in an amount of 4.5 times the weight of the crystals. The final yield was about 30 g., m.p. 128-129°C. The infrared spectrum was identical to Sadtler's reference number 8125, benzohydroxamic acid. (Toluene and benzene were also tried as crystallization solvents, but were not satisfactory because of the low solubility of benzohydroxamic acid in these solvents.)

Ferric Chloride Solution

A solution was prepared by dissolving 40 g. of ferric chloride hexahydrate in 4 l. of distilled water. A sufficient amount of concentrated hydrochloric acid was added to prevent formation of ferric hydroxide and to render acidic a mixture of 10 ml. of the ferric chloride solution and 1 ml. of the sodium hydroxide solution to be used in the hydrolysis rate measurements.

Sodium Hydroxide Solutions

Sodium hydroxide solutions of known concentrations were prepared by dissolving sodium hydroxide, A.R., in boiled and cooled compression distilled water. Each solution was prepared and standardized by titration against dried potassium acid phthalate just prior to its use. The following solutions were prepared:

2.179 M	0.985 M
1.757 M	0.609 M
1.578 M	0.119 M

The ionic strengths of the solutions were adjusted with dried potassium chloride to be 2.179 M.

Hydrochloric Acid Solutions

The hydrochloric acid solutions were prepared by dissolving concentrated hydrochloric acid, A.R., in boiled and cooled compression distilled water. Each solution was prepared and standardized with standard sodium hydroxide solution just prior to its use. The following solutions were prepared:

0.577 M	0.341 M
0.485 M	0.109 M
0.369 M	

The ionic strengths of the solutions were adjusted with dried potassium chloride to be 0.577 M.

Colorimeter

A Klett-Summerson Photoelectric Colorimeter using the number 54 filter (principle spectrum line 540 $m\mu$, range 500 - 560 $m\mu$) was used. Matching Klett tubes were used for analyses.

Constant Temperature Bath

The constant temperature bath consisted of a mineral oil bath fitted with two heating coils controlled by "Powerstats", one being regulated by a Sargent Laboratory Relay. The temperature of the bath was adjusted to exactly 88.6° or 78.6°C., using the Jumo MS temperature regulating device.

Reaction Vessels

For acidic hydrolysis pyrex glass tubes, 21.5 cm. long by 2 cm. diameter, fitted with sintered glass stoppers were used. It was found that the strong alkali attacked the glass; therefore polypropylene plastic tubes, 10 1/2 cm. long by 3 cm. diameter, fitted with polypropylene plastic caps were used for alkaline hydrolysis.

Test of Assay Procedure

At low pH iron (III) forms a characteristic violet color in the presence of benzohydroxamic acid. The color is produced by a complex ion in which the iron (III) - hydroxamate ratio is 1-1. The maximum absorption is at 520 $m\mu$ with a molar absorptivity¹¹ of 1450 liters per mole-cm. Benzohydroxamic acid, 3.1×10^{-4} moles (43 mg.), was added to 25.0 ml. of boiled distilled water and the solution placed in the bath at 88.6°C. After the temperature of the solution had reached equilibrium, two 1.0 ml. aliquots were taken. Each was added to 10.0 ml. of ferric chloride solution and diluted, one to 25.0 ml. (I) and one to 50.0 ml. (II). The absorption of I was twice that of II.

Determination of Hydrolysis Rates

Using 43 mg. of benzohydroxamic acid in 25.0 ml. of either standard sodium hydroxide or hydrochloric acid solution with constant ionic strength, the rate of disappearance of benzohydroxamic acid was followed by means of the assay described above. Exactly 1.0 ml. of solution at 88.6°C. was added to 10.0 ml. of ferric chloride solution and diluted to 25.0 ml. with distilled water. The same ferric chloride solution was used throughout one run. The formation of the complex ion at the lower temperature effectively quenched the reaction. The absorbance of each aliquot was measured at evenly spaced intervals (hourly, or even multiples or fractions of hours) to minimize errors in plotting.

Hydrolysis in pure boiled water at 88.6°C. was also attempted, but the samples showed no measurable hydrolysis after twenty-four hours.

Using the same procedure as above, the rate of hydrolysis in three of the acidic solutions was also determined at 78.6°C.

Isolation of Products in Alkaline Hydrolysis

It was observed that during alkaline hydrolysis the solutions turned from colorless to a yellowish color with the color deepening as the reaction proceeded. The remainder of three solutions used in the alkaline hydrolysis rate measurements were pooled and the hydrolysis allowed to go to completion. The pooled solutions, while still alkaline, were extracted with ether and the ether evaporated. The dried product was an amorphous, yellow substance whose infrared spectrum was not definitive. Hydroxylamine is rapidly decomposed by hot water to ammonia, water, nitrogen, and nitrous oxide in the presence of platinum as a catalyst^{12, 13}. In alkaline solution hydroxylamine slowly decomposes into nitrogen, ammonia, and, to some extent, nitrous oxide¹⁴. It is presumed that the yellow substance is a product of hydroxylamine decomposition. The solution remaining after the first extraction was acidified and extracted with ether; an infrared spectrum obtained of the dried residue was identical to that of Sadtler's reference number 779, benzoic acid.

Isolation of Products in Acidic Hydrolysis

The remainder of six of the solutions used in the acidic hydrolysis rate measurements were pooled and the hydrolysis allowed to go to completion. The pooled solutions were extracted with ether, the ether removed, and an infrared spectrum obtained of the dried residue. The spectrum was identical to that of Sadtler's reference number 779, benzoic acid.

RESULTS

Since the concentration of benzohydroxamic acid is relatively low as compared to that of the alkali or acid, a pseudo first-order reaction rate will be obtained. First-order plots of \log_{10} concentration versus time result in a straight line, with the slope equal to $-\frac{k}{2.303}$. Since the concentration of benzohydroxamic acid is directly proportional to the observed absorbance, the plot of \log_{10} absorbance versus time is the equivalent.

Tables I and II, page 9 and 11, give representative data for the hydrolysis of benzohydroxamic acid in alkali and acid at 88.6°C.; and Figures I and II, page 10 and 12, show the plot of \log_{10} absorbance versus time for the data given. The best straight line by inspection of the points is drawn. The observed rate constant is calculated from the slope according to the formula above.

Table III, page 13, shows the observed rate constants for all samples of alkaline hydrolysis at 88.6°C. Half-life time is obtained from the standard relation of first-order reactions, $t_{1/2} = \frac{0.693}{k}$. Figure III, page 14, indicates the relationship when the concentration of the catalyst is plotted against the observed rate constant.

Tables IV and V, page 15 and 17, and Figures IV and V, page 16 and 18, show the corresponding data for acid catalyzed hydrolysis at 88.6°C. and 78.6°C., respectively.

TABLE I

Hydrolysis of Benzohydroxamic Acid in 1.578 M NaOH^a

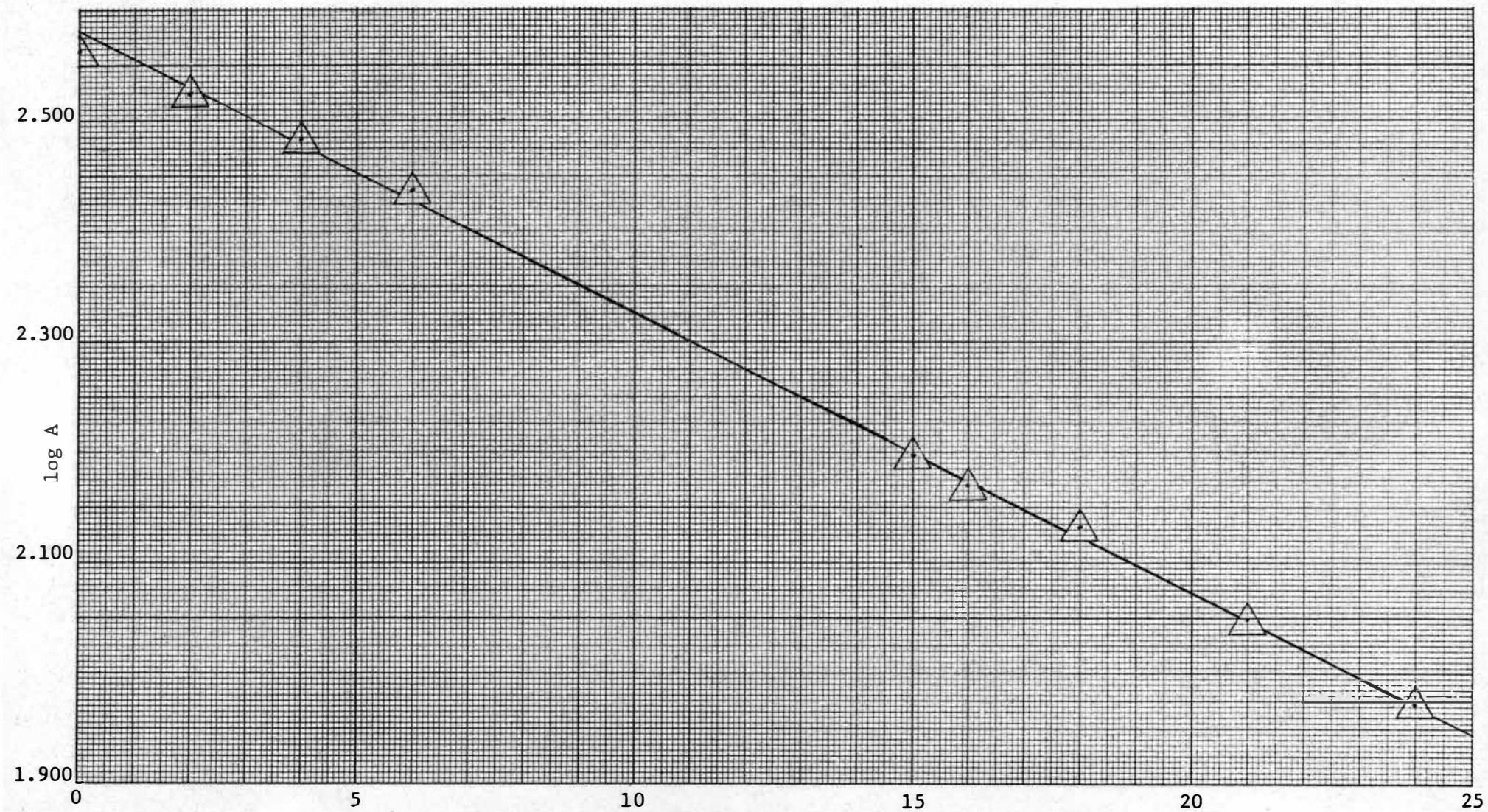
Time (Hours)	Relative Absorbance, A	Log ₁₀ A ^b
0	365	2.56229
2	335	2.52504
4	305	2.48430
6	270	2.43136
15	157	2.19590
16	148	2.17026
18	136	2.13354
21	112	2.04922
24	94	1.97313

^aThe amount of benzohydroxamic acid at the beginning (time equals zero) was 3.1×10^{-4} moles. The temperature was 88.6°C. The ionic strength was adjusted to 2.179 M with potassium chloride.

^bTaken from five place logarithm tables and do not necessarily represent significant figures.

FIGURE I

Plot of $\log_{10} A$ versus Time for Hydrolysis in 1.578 M NaOH



Time - Hours

Temperature 88.6°C.

TABLE II

Hydrolysis of Benzohydroxamic Acid in 0.109 M HCl^a

Time (Hours)	Relative Absorbance, A	Log ₁₀ A ^b
0	380	2.57978
0.5	345	2.53782
2	258	2.41162
3	210	2.32222
5	145	2.16137
7	99	1.99564
9	68	1.83251

^aThe amount of benzohydroxamic acid at the beginning (time equals zero) was 3.1×10^{-4} moles. The temperature was 88.6°C. The ionic strength was adjusted to 0.577 M with potassium chloride.

^bTaken from five place logarithm tables and do not necessarily represent significant figures.

FIGURE II

Plot of $\log_{10} A$ versus Time for Hydrolysis in 0.109 M HCl

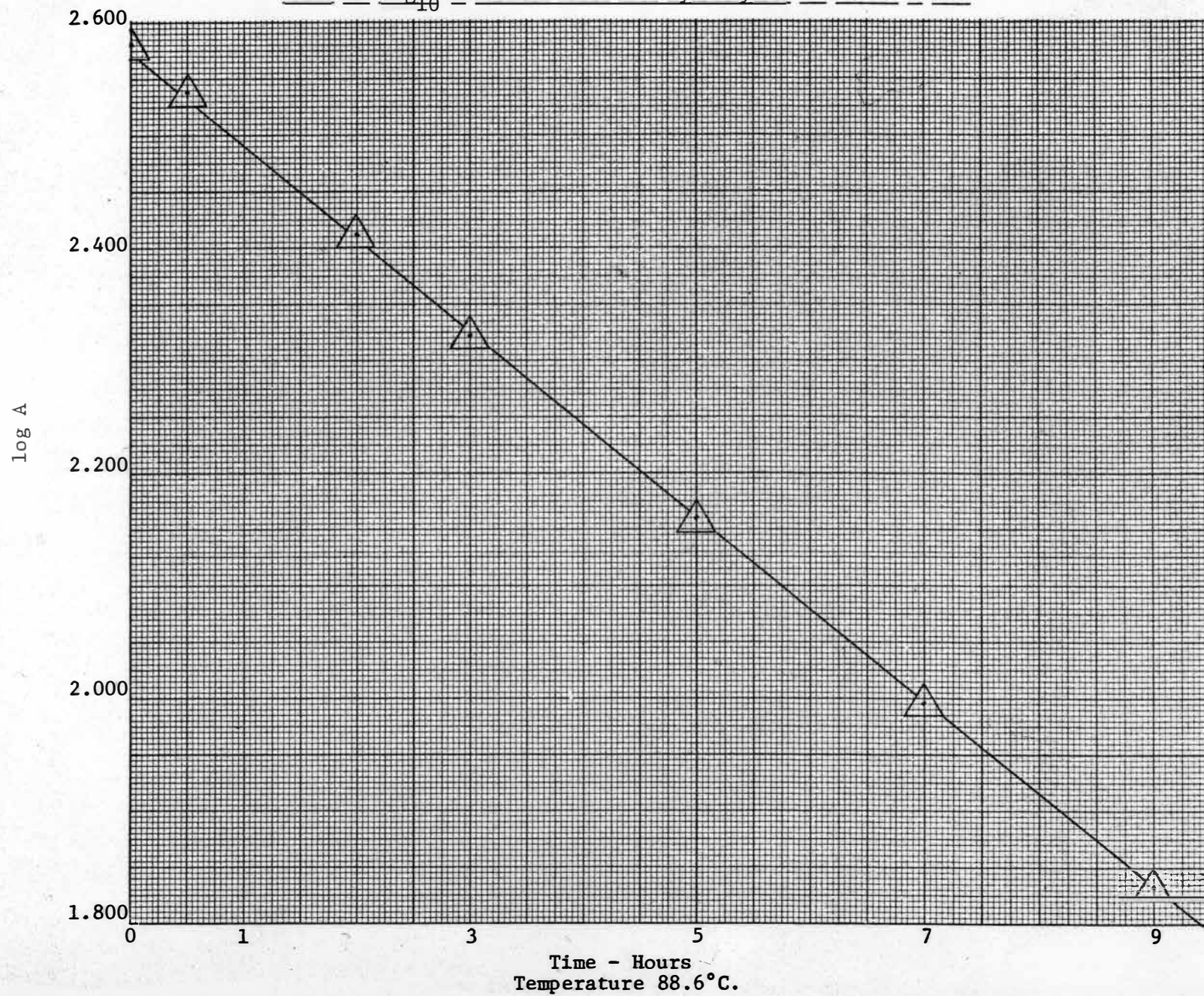


TABLE III

Summary of Alkaline Hydrolysis at 88.6°C.

Conc. NaOH moles/l.	Run No.	Rate Constant hr. ⁻¹	Ave. Rate Constant hr. ⁻¹	Deviation from Ave. %	t _{1/2} hr.	<u>Rate Const. - .0404</u> [OH ⁻]
2.179	1	0.0673	0.0678	-0.74	10.2	0.0126
	2	0.0682		+0.59		
1.757	1	0.0610	0.0630	-3.17	11.0	0.0129
	2	0.0635		+0.79		
	3	0.0648		+2.86		
	4	0.0627		-0.48		
1.578	1	0.0586	0.0592	-1.01	11.7	0.0119
	2	0.0608		+2.70		
	3	0.0591		-0.17		
	4	0.0583		-1.52		
0.985	1	0.0503	0.0533	-5.63	13.0	0.0131
	2	0.0541		+1.50		
	3	0.0556		+4.32		
0.609	1	0.0487	0.0476	+2.31	14.6	0.0118
	2	0.0463		-2.73		
	3	0.0466		-2.10		
	4	0.0487		+2.31		
0.119	1	0.0403	0.0421	-4.28	16.5	0.0143
	2	0.0442		+4.99		
	3	0.0418		-0.71		

Plot of Concentration NaOH versus Observed Rate Constant at 88.6°C.

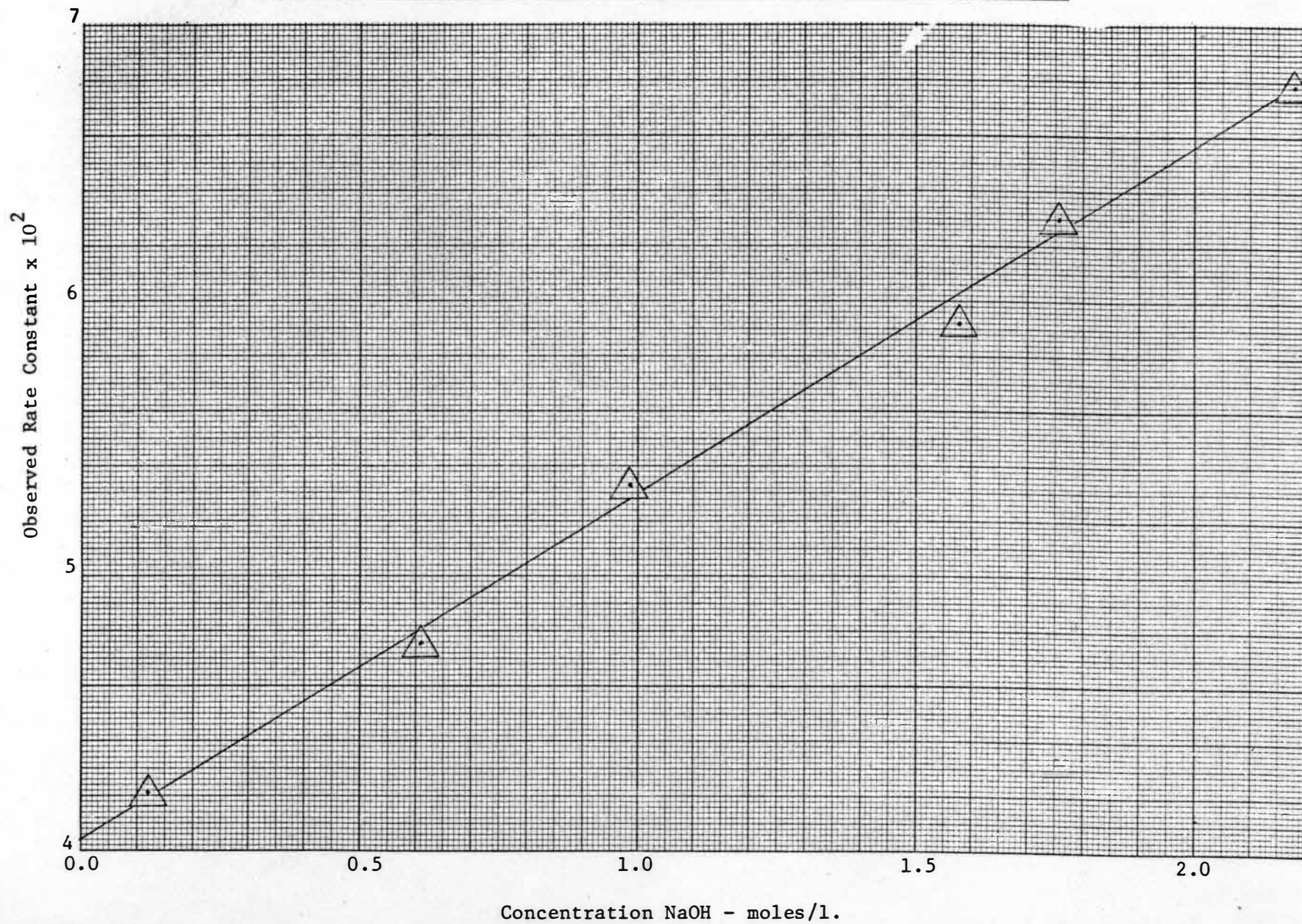


TABLE IV

Summary of Acidic Hydrolysis at 88.6°C.

Conc. HCl moles/l.	Run No.	Rate Constant hr. ⁻¹	Ave. Rate Constant hr. ⁻¹	Deviation from Ave. %	t _{1/2} hr.	<u>Rate Constant</u> [H ₃ O ⁺]
0.577	1	1.069	1.089	-1.84	0.64	1.89
	2	1.137		+4.41		
	3	1.060		-2.66		
0.485	1	0.920	0.928	-0.86	0.75	1.91
	2	0.921		-0.75		
	3	0.942		+1.51		
0.369	1	0.709	0.689	+2.90	1.01	1.87
	2	0.691		+0.29		
	3	0.667		-3.19		
0.341	1	0.641	0.643	-0.31	1.08	1.89
	2	0.652		+1.40		
	3	0.635		-1.24		
0.109	1	0.184	0.187	-1.60	3.71	1.72
	2	0.189		+1.07		

FIGURE IV

Plot of Concentration HCl versus Observed Rate Constant at 88.6°C.

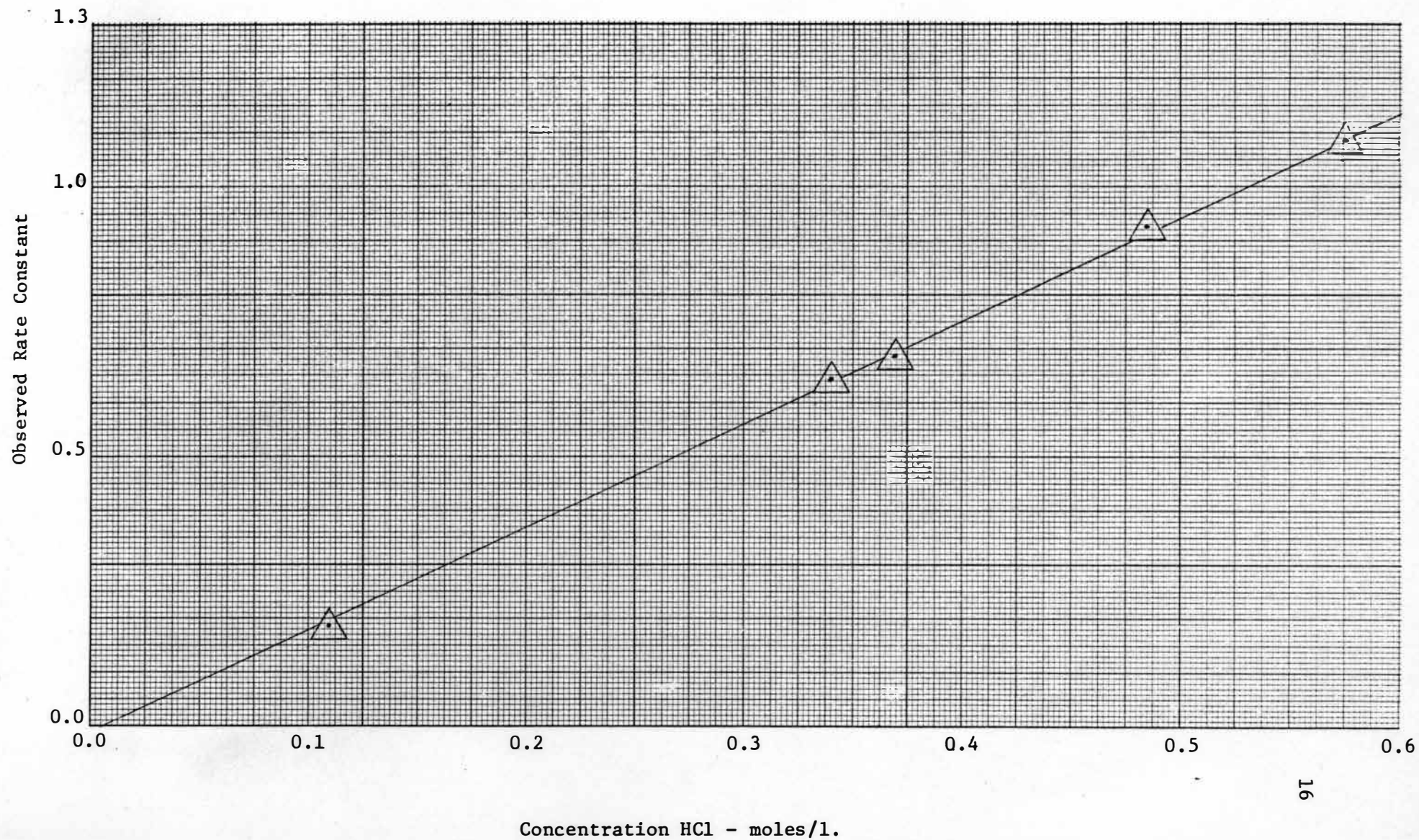


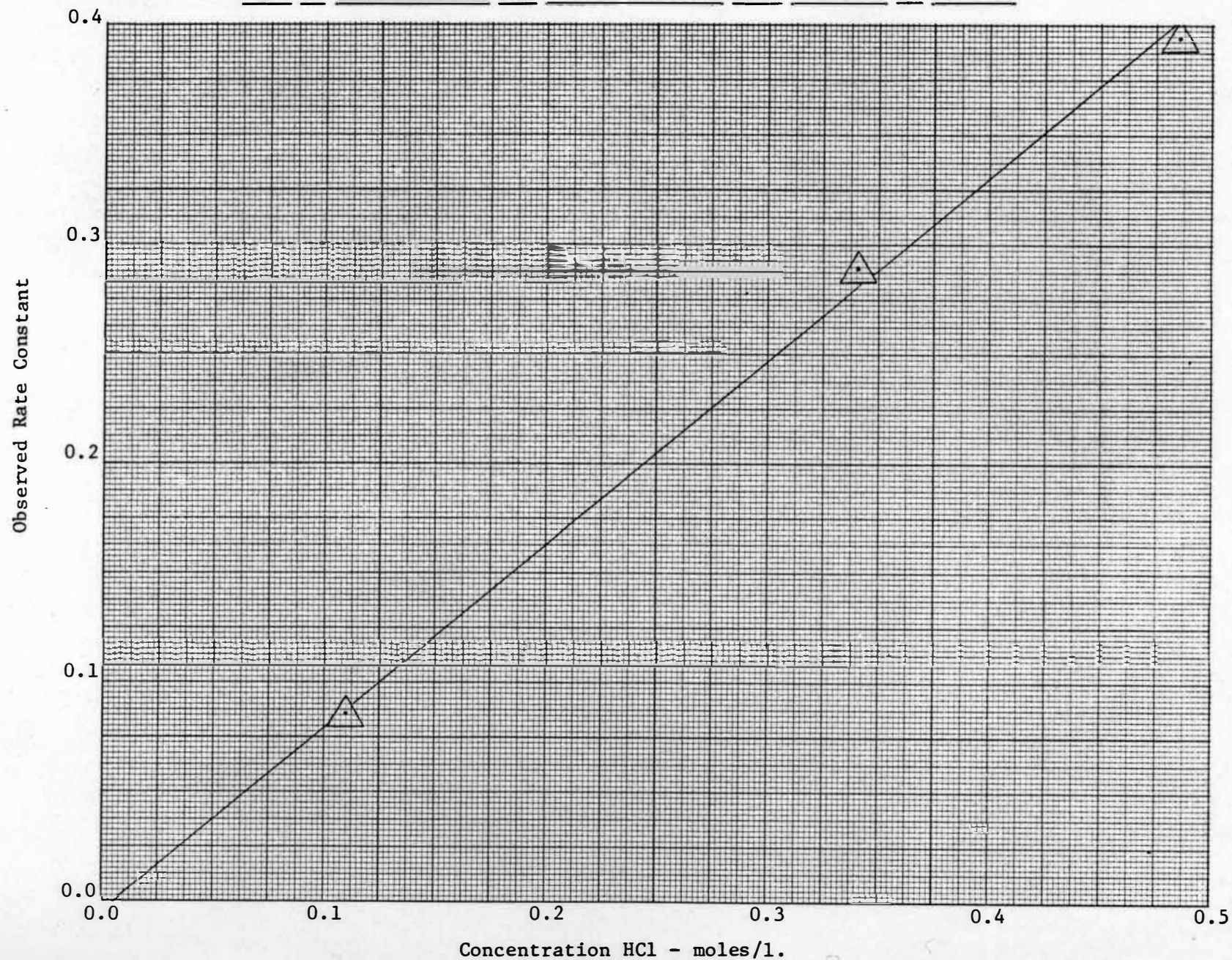
TABLE V

Summary of Acidic Hydrolysis at 78.6°C.

Conc. HCl moles/l.	Run No.	Rate Constant hr. ⁻¹	Ave. Rate Constant hr. ⁻¹	Deviation from Ave. %	t _{1/2} hr.	<u>Rate Constant</u> [H ₃ O ⁺]
0.485	1	0.394	0.394	0.00	1.76	0.812
	2	0.394		0.00		
0.341	1	0.282	0.290	-2.76	2.40	0.850
	2	0.290		0.00		
	3	0.298		+2.76		
0.109	1	0.0840	0.0861	-2.44	8.05	0.790
	2	0.0872		+1.28		
	3	0.0870		+1.05		

FIGURE V

Plot of Concentration HCl versus Observed Rate Constant at 78.6°C.



Energy of Activation

If the rate constant is known for two different temperatures, it is possible to calculate the energy of activation using the formula

$$E_a = \frac{2.303RT_1T_2}{T_2 - T_1} \log_{10} \frac{k_2}{k_1}$$

In this experiment rate constants were obtained at 88.6°C. and 78.6°C. for acid catalyzed hydrolysis for three different concentrations of hydrochloric acid. The average of the calculated second-order rate constants at 88.6°C. equals 1.84 liter mole⁻¹ hr.⁻¹; at 78.6°C. it equals 0.817 liter mole⁻¹ hr.⁻¹

Substituting these values into the above equation we find for E_a ,

$$E_a = \frac{(2.303)(1.987)(351)(361)}{361 - 351} \log_{10} \frac{1.84}{0.817}$$

$$E_a = 2.04 \times 10^4 \text{ cal.}$$

Frequency Factor

According to the Arrhenius equation for the effect of temperature on reaction rate,

$$k = Ae^{-E_a/RT}$$

The term A is a constant that can be divided into two terms: the collision number Z or the number of collisions per second per cc.; and the steric or probability factor P which is included to account for deviation from the simple theory. Thus:

$$\log k = \log PZ - \frac{E_a}{2.303RT}$$

The rate constant for acidic hydrolysis at 88.6°C. is 1.84 liter mole⁻¹ hr.⁻¹ which is equivalent to 5.11×10^{-4} liter mole⁻¹ sec.⁻¹

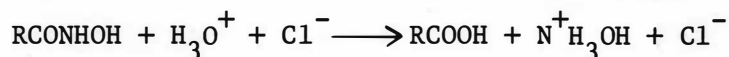
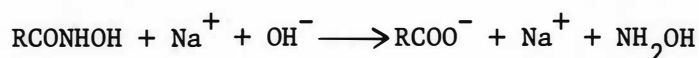
Substituting these values into the above formula:

$$\log_{10} 5.11 \times 10^{-4} = \log_{10} PZ - \frac{20,400}{(2.303)(1.987)(361)}$$

$$PZ = 1.14 \times 10^9 \text{ liter mole}^{-1} \text{ sec.}^{-1}$$

DISCUSSION

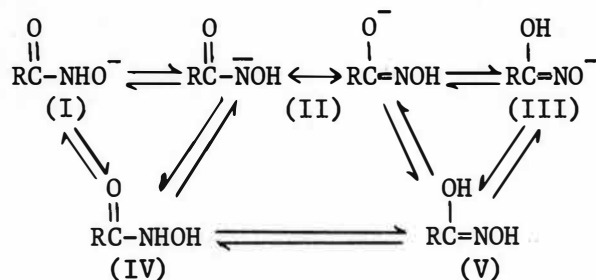
Benzohydroxamic acid does not hydrolyze easily. It does not react with pure water to a measurable extent, and both alkaline and acid catalyzed hydrolyses are slow; the reaction in acid is much faster. The molar concentration of sodium hydroxide or hydrochloric acid was ten or more times that of the concentration of benzohydroxamic acid, except for the lowest concentration of hydrochloric acid which was eight times the concentration of benzohydroxamic acid. In the presence of excess catalyst the stoichiometric equations for the hydrolyses are:



In this study it was found that the rate of hydrolysis is directly proportional to the concentration of either catalyst. Complete elucidation of the reaction mechanisms is not possible with the facts at hand. However, the following is consistent with the data so far obtained.

Mechanism of Alkaline Hydrolysis

According to Steinberg and Swidler¹⁵, in aqueous solution the benzo-hydroxamate anion can potentially exist in three forms in equilibrium with two neutral forms according to the scheme:



Forms I and II exist in approximately equal proportions, but Form III, if it exists at all, is 10^{-3} to 10^{-4} times the concentration of I or II.

In the system where:

A represents RCONHOH

B represents RCONHO^-

C represents RCONOH^-

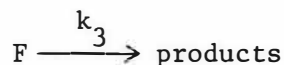
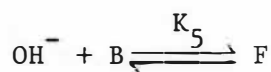
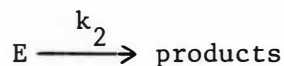
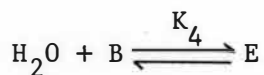
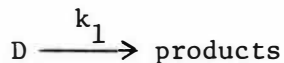
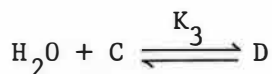
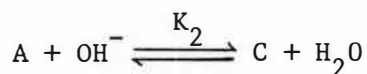
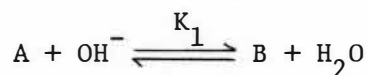
S represents stoichiometric amount of
benzohydroxamic acid at time t

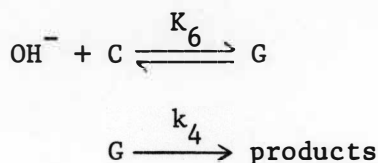
K represents equilibrium constant

k represents rate constant

D, E, F, and G represent other intermediates and where

$[\text{H}_2\text{O}]$ should appear in rate or equilibria, it is included in k or K because it is constant; then





$$S = A + B + C + D + E + F + G \quad (1)$$

The species D, E, F, and G are tetrahedral intermediates similar to those postulated for ester and amide hydrolyses^{5, 8, 16}. These intermediates (except for a few special cases¹⁶) are unstable and exist in only very small amounts in these solutions. In fact, they can be treated kinetically by the steady state approximation^{5, 16, 17, 18} which requires that these intermediates be reactive and present in only very small amounts. Therefore, equation (1) can be simplified to:

$$S = A + B + C \quad (2)$$

(For convenience the brackets indicating concentration in the equations are omitted except for OH^- .)

$$S = A + K_1 A[\text{OH}^-] + K_2 A[\text{OH}^-] \quad (3)$$

Factor A:

$$S = A(1 + K_1[\text{OH}^-] + K_2[\text{OH}^-]) \quad (4)$$

For the above mechanism the rate will be:

$$-\frac{dS}{dt} = k_{\text{obs.}} S = k_1 D + k_2 E + k_3 F + k_4 G \quad (5)$$

$$= k_1 K_2 K_3 A[\text{OH}^-] + k_2 K_4 K_1 A[\text{OH}^-] + k_3 K_5 K_1 A[\text{OH}^-]^2 + k_4 K_6 K_2 A[\text{OH}^-]^2 \quad (5a)$$

$$= A[\text{OH}^-] (k_1 K_2 K_3 + k_2 K_4 K_1 + k_3 K_5 K_1 [\text{OH}^-] + k_4 K_6 K_2 [\text{OH}^-]) \quad (5b)$$

To relate $k_{\text{obs.}}$ with hydroxide ion concentration, put A in terms of S from (4):

$$k_{\text{obs.}} S = \frac{S[\text{OH}^-] (k_1 K_2 K_3 + k_2 K_4 K_1 + k_3 K_5 K_1 [\text{OH}^-] + k_4 K_6 K_2 [\text{OH}^-])}{1 + K_1 [\text{OH}^-] + K_2 [\text{OH}^-]} \quad (6)$$

Cancel S and divide numerator and denominator by $[\text{OH}^-]$:

$$k_{\text{obs.}} = \frac{k_1 K_2 K_3 + k_2 K_4 K_1 + k_3 K_5 K_1 [\text{OH}^-] + k_4 K_6 K_2 [\text{OH}^-]}{\frac{1}{[\text{OH}^-]} + K_1 + K_2} \quad (7)$$

The largest value that can be assigned to $\frac{1}{[\text{OH}^-]}$ is about 10. Since K_1 and K_2 are much larger (for estimation of K_1 and K_2 , see below) than

$\frac{1}{[\text{OH}^-]}$, the denominator is essentially K_1 plus K_2 . Therefore:

$$k_{\text{obs.}} = \frac{k_1 K_2 K_3 + k_2 K_4 K_1 + [\text{OH}^-] (k_3 K_5 K_1 + k_4 K_6 K_2)}{K_1 + K_2} \quad (8)$$

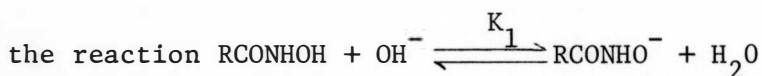
$$k_{\text{obs.}} = \frac{k_1 K_2 K_3 + k_2 K_4 K_1}{K_1 + K_2} + \frac{[\text{OH}^-] (k_3 K_5 K_1 + k_4 K_6 K_2)}{K_1 + K_2} \quad (9)$$

A plot of $k_{\text{obs.}}$ versus $[\text{OH}^-]$ should give a straight line with the y

intercept equal to $\frac{k_1 K_2 K_3 + k_2 K_4 K_1}{K_1 + K_2}$ and a slope of $\frac{k_3 K_5 K_1 + k_4 K_6 K_2}{K_1 + K_2}$.

Figure III, page 14, shows that $k_{\text{obs.}}$ is indeed linear with $[\text{OH}^-]$.

Equilibrium constants K_1 and K_2 may be estimated as follows. In



$$K_1 \text{ equil.} = \frac{[\text{RCONHO}^-]}{[\text{RCONHOH}][\text{OH}^-]}$$

Since water is in great excess relative to the concentration of RCONHO^- ,

RCONHOH , and OH^- , it is considered constant and $[\text{HOH}]$ is combined with K_1 .

According to Steinberg and Swidler¹⁵, the ionization constant of the

reaction $\text{RCONHOH} \rightleftharpoons \text{RCONHO}^- + \text{H}^+$ equals $10^{-8.6}$ (estimated). The

ionization equilibrium may be represented as

$$\frac{[\text{RCONHO}^-][\text{H}^+]}{[\text{RCONHOH}]} = K_{\text{ion}}$$

(H^+ represents H_3O^+)

The ionization constant for water at 90°C. equals¹⁹ 35.5×10^{-14} and may be represented as $K_w = [H^+][OH^-]$. Therefore:

$$\frac{K_{ion}}{K_w} = \frac{[RCONHO^-][H^+]}{[RCONHOH][H^+][OH^-]}$$

$$\frac{K_{ion}}{K_w} = \frac{[RCONHO^-]}{[RCONHOH][OH^-]} = K_1 \text{ equil.}$$

and $K_1 \text{ equil.} = \frac{K_{ion}}{K_w} = \frac{1 \times 10^{-8.6}}{35.5 \times 10^{-14}} = 3 \times 10^{3.4}$

In a manner similar to the above reasoning, $K_2 \text{ equil.}$ can be estimated. The ionization constant for the reaction $RCONHOH \rightleftharpoons RCONO^- + H^+$ is estimated¹⁵ as $10^{-8.9}$.

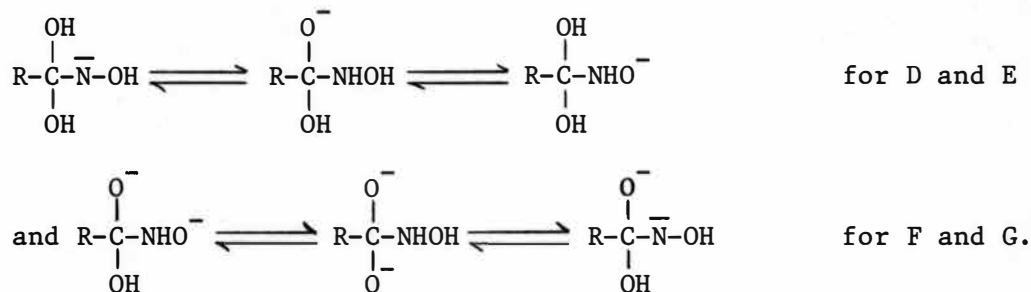
$$K_2 \text{ equil.} = \frac{K_{ion}}{K_w} = \frac{1 \times 10^{-8.9}}{35.5 \times 10^{-14}} = 3 \times 10^{3.1}$$

These values can be regarded as only approximate. The ionization values were estimated from data at 30°C.; however, it can be seen that K_1 and K_2 in equation (7) are large as compared to $\frac{1}{[OH^-]}$.

The order of reaction is complex. Examination of the rate equation (6), page 23, indicates two terms that are first-order in total benzo-hydroxamic acid and first-order in hydroxide ion plus two other terms that are first-order in total benzohydroxamic acid and second-order in hydroxide ion. This is comparable to the alkaline hydrolysis of various anilides^{7, 8, 20} in which terms involving one and two hydroxide ions occur in the rate equations.

Tetrahedral structures for the intermediates involved in the complex alkaline hydrolysis of these anilides have been proposed. The analogous

structures proposed for the tetrahedral intermediates involved in the alkaline hydrolysis of benzohydroxamic acid are shown below:



It may be presumed that attack by the more nucleophilic hydroxide ion on B or C, pages 22 and 23, would predominate. However, B, C, and hydroxide ion all carry a negative charge, and attack by the less nucleophilic, but neutral, water molecule may take precedence over the ionic attack. The values of the constants in equation (9) cannot be evaluated from the present data. However,

$$\frac{\text{slope}}{\text{intercept}} = \frac{k_3 K_5 K_1 + k_4 K_6 K_2}{k_1 K_2 K_3 + k_2 K_4 K_1}$$

which when multiplied by $[\text{OH}^-]$ gives the relative amount of reaction proceeding through F and G compared to D and E. When $[\text{OH}^-]$ equals one molar, the value $\approx \frac{0.013}{0.040}$. Thus, when $[\text{OH}^-]$ equals one, about 1/3 as much of the material reacts via the pathway involving two hydroxide ions as via the pathway with one hydroxide ion. Which of the various intermediates undergoes carbon-nitrogen bond cleavage cannot be predicted from present data. Bender and Ginger²¹ have observed in the alkaline hydrolysis of benzamide- O^{18} that the rate of oxygen exchange between benzamide- O^{18} and water was five times as fast as hydrolysis. This indicates that tetrahedral intermediates exist but does not strictly prove that the same intermediates are involved in the hydrolysis. Oxygen¹⁸ exchange

requires symmetrical intermediates, such as $\begin{array}{c} \text{OH} \\ | \\ -\text{C}- \\ | \\ \text{OH} \end{array}$ or $\begin{array}{c} \text{O}^- \\ | \\ -\text{C}- \\ | \\ \text{O}^- \end{array}$,

or unsymmetrical intermediates in rapid equilibrium,

such as $\begin{array}{c} \text{O}^- \\ | \\ -\text{C}- \\ | \\ \text{OH} \end{array} \rightleftharpoons \begin{array}{c} \text{OH} \\ | \\ -\text{C}- \\ | \\ \text{O}^- \end{array}$. It would be informative to study oxygen exchange

with benzohydroxamic acid- O^{18} and water to substantiate the presence of such intermediates.

In the preceding discussion it has been assumed that decomposition of the intermediates was the rate determining steps. If formation of the tetrahedral intermediates is rate determining (as it often is in reactions of carboxylic acid derivatives¹⁶), then equation (5) will be:

$$-\frac{dS}{dt} = k_{\text{obs.}} S = k_1' C + k_2' B + k_3' [\text{OH}^-] B + k_4' [\text{OH}^-] C \quad (10)$$

$$= k_1' K_2 A [\text{OH}^-] + k_2' K_1 A [\text{OH}^-] + k_3' K_1 A [\text{OH}^-]^2 + k_4' K_2 A [\text{OH}^-]^2 \quad (10a)$$

and in equations (5b) through (9) the following substitutions must be made:

$$k_1' K_2 \text{ for } k_1 K_2 K_3$$

$$k_2' K_1 \text{ for } k_2 K_4 K_1$$

$$k_3' K_1 \text{ for } k_3 K_5 K_1$$

$$k_4' K_2 \text{ for } k_4 K_6 K_2$$

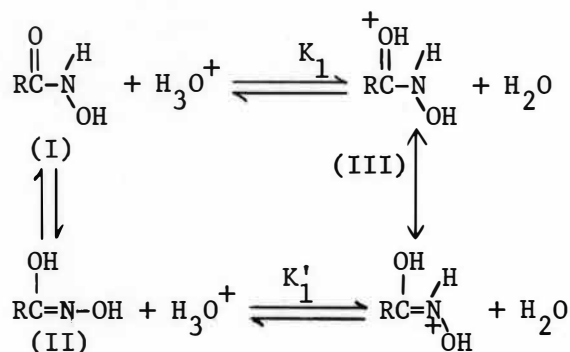
Although the numerical value of the constants may be different, the form of the equations is the same as that of equations (5b) through (9).

Consequently, the kinetic data cannot distinguish between these possibilities. Furthermore, the formation of some of the tetrahedral intermediates may be rate determining while for others the rate determining step may be their decomposition. A step, $A + \text{H}_2\text{O} \longrightarrow \text{products}$, has not been included

in the mechanism on page 22 since it was observed that benzohydroxamic acid in pure water at 88.6°C. showed no detectable reaction after 24 hours; whereas the half-life in 0.119 M basic solution is 16.5 hours.

Mechanism of Acidic Hydrolysis

The mechanism of acidic hydrolysis is much simpler than that of alkaline hydrolysis. In acidic solution benzohydroxamic acid can be protonated according to the following:



Fraenkel and Niemann²² and Katritzky and Jones²³ offer evidence that protonation of amides occurs at the oxygen atom. Protonation of benzohydroxamic acid also probably occurs predominantly at the carbonyl oxygen atom. However, if protonation at the nitrogen atom does occur, the result is the same.

In the system where:

A represents RCONHOH

B represents RCOH^+NHOH

C represents an intermediate

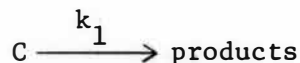
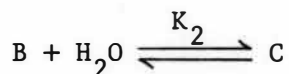
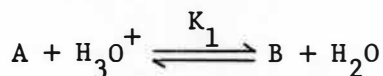
S represents stoichiometric amount of
benzohydroxamic acid at time t

K represents equilibrium constant

k represents rate constant

and where $[\text{H}_2\text{O}]$ should appear in rate or equilibria, it is included in

k or K because it is constant; then



$S = A + B \approx A$ since benzohydroxamic acid, $pK_a = 8.8^{15}$, is a weak acid.

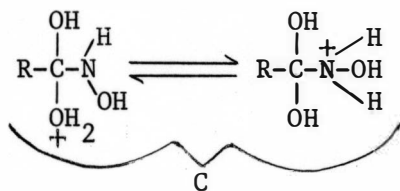
(For convenience the brackets indicating concentration in the equations are omitted except for H_3O^+ .)

$$-\frac{dS}{dt} = k_{\text{obs.}} S \approx k_{\text{obs.}} A = k_1 C = k_1 K_2 B = k_1 K_2 K_1 A [H_3O^+]$$

Therefore, $k_{\text{obs.}} = k_1 K_2 K_1 [H_3O^+]$. Consequently, a plot of $k_{\text{obs.}}$ versus $[H_3O^+]$ gives a straight line with intercept theoretically zero and slope $k_1 K_1 K_2$. Comparison with Figures IV and V, pages 16 and 18, shows that $k_{\text{obs.}}$ is linear with $[H_3O^+]$ and that the intercept is very nearly zero.

The reaction is first-order with respect to benzohydroxamic acid and first-order with respect to hydronium ion. This corresponds to the acidic hydrolysis of benzamide and substituted benzamides as determined by Meloche and Laidler⁶. (Benzene sulfonic acid was used instead of hydrochloric acid to avoid esterification of alcohol which was present as a solvent⁶.)

In the development of the rate equation it was assumed that the intermediate C is a single substance although there probably are more than one in equilibrium with one another. Postulated structures for C are shown below:



If the formation of C is rate determining rather than the decomposition of C, then

$$\frac{-dS}{dt} = k_{\text{obs.}} S \approx k_{\text{obs.}} A = k_1' K_1 A [H_3O^+]$$

$$k_{\text{obs.}} = k_1' K_1 [H_3O^+]$$

The same equation, $k_{\text{obs.}} = k_1' K_1 [H_3O^+]$, results if B reacts with water directly to give products. This equation has the same form as the equation if decomposition of C is rate determining. Thus, the kinetic data does not distinguish between these various possibilities. A step, $A + H_2O \longrightarrow \text{products}$, has not been included in the mechanism on page 29 since it was observed that benzohydroxamic acid in pure water at 88.6°C. showed no detectable reaction after 24 hours; whereas the half-life in 0.109 M acidic solution is 3.71 hours.

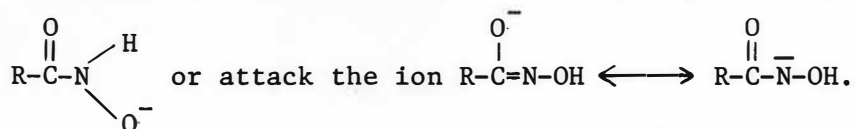
Comparison with Hydrolysis of Benzamide

Meloche and Laidler⁶ have observed that benzamide is hydrolyzed slightly faster in alkaline solution than in acidic solution and that both obey accurately the second-order rate law. The rates as compared to benzohydroxamic acid are shown below:

	$k \times 10^6 \text{ liter mole}^{-1} \text{ sec.}^{-1}$				
	100.1°C.	80.3°C.	99.6°C.	79.5°C.	88.6°C.
^a Benzamide in alkali	338	76.4			
^a Benzamide in acid			195	43.6	
Benzohydroxamic acid in acid					511

^aThe solvent used for the benzamide reactions was a 60-40 ethyl alcohol-water mixture.

Hydrolysis of benzohydroxamic acid in alkaline solution is not included in the table because it does not conform to second-order rate laws. It is, however, very much slower than alkaline or acidic hydrolysis of benzamide and much more complex. It can easily be seen why acid catalyzed hydrolysis is faster with benzohydroxamic acid than with benzamides. The replacement of one hydrogen with the electron withdrawing -OH group increases the vulnerability of the carbonyl group to nucleophilic attack. Alkaline hydrolysis of benzohydroxamic acid would be slower than alkaline hydrolysis of benzamide since the hydroxide ion or water must pass close to the negatively charged oxygen atom in



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APPROVAL OF EXAMINING COMMITTEE

(chairman)

date