

real solution of the yellow residue was extracted with two portions of 5% sodium bicarbonate solution. The ether layer was dried and evaporated to dryness on a steam bath, affording a light yellow solid (0.478 g.), m.p. 90–119°. An infrared spectrum was identical with that of benzoylanthranil. The two portions of benzoylanthranil were combined (0.882 g., 80%) and crystallized twice from benzene-Skellysolve B, affording white needles, m.p. 123–124.5° (lit.²⁶ m.p. 124.5°). The mixture m.p. with an authentic sample, m.p. 122–123°, was 122–125°.

Acidification of the aqueous sodium bicarbonate extract produced crude N-benzoylanthranilic acid (0.201 g., 17%), m.p. 167–183°, identified by infrared analysis. One crystallization from benzene afforded the acid, m.p. 181.5–183°.

Benzoylanthranilic acid was subjected to the same conditions as were used in this reaction. The acid was recovered (m.p. 170–185°) on evaporation of the solvent on a rotary evaporator. Precautions were taken to exclude moisture. An infrared spectrum in chloroform exhibited very weak absorptions which appeared to be attributed to the presence of a small amount of benzoylanthranil.

Acid Hydrolysis of Benzoylanthranil.—A solution of benzoylanthranil (1.340 g., 6.01 mmoles) in 55 ml. of acetic acid, 0.91 M in sulfuric acid and 7.1 M in water, was heated at 82–85° (oil bath) for 20 min. The solution was quickly cooled in an ice bath and worked up in the same way as the blank extractions. Only resinous material was obtained in the neutral and basic fractions.

The acid fraction, m.p. 160–184°, was shown to be N-benzoylanthranilic acid (1.414 g., 98% corrected) by infrared analysis.

Basic Hydrolysis of *o*-Benzamido-N,N-dicyclohexylbenzamide (I).—A solution of *o*-benzamido-N,N-dicyclohexylbenzamide (0.923 g.) in 50 ml. of ethanol, 2.0 M in potassium hydroxide and 11 M in water (prepared by addition of 10 ml. of 10.0 M potassium hydroxide to 40 ml. of absolute ethanol), was heated at reflux (79–81°) for 5 hr. The solution was cooled to room temperature in an ice bath, adjusted to pH 6 with hydrochloric acid, and evaporated to dryness on a rotary evaporator. The residue was triturated with water to remove potassium chloride. The water-insoluble material was triturated with chloroform. Evaporation of the chloroform extract on a rotary evaporator afforded recovered starting material (0.406 g., 44%).

The chloroform-insoluble material, m.p. 182–186°, was shown to be *o*-amino-N,N-dicyclohexylbenzamide hydrochloride (0.352 g., 46%) by comparison of its infrared spectrum (Nujol mull) with an authentic sample (m.p. 175–185°). Attempts to recrystallize an authentic sample of the amine hydrochloride (prepared by treating an ethereal solution of the amine with ethereal hydrogen chloride) were unsuccessful. Ether extraction of a suspension in aqueous base of the amine hydrochloride obtained in this reaction afforded *o*-amino-N,N-dicyclohexylbenzamide, identified by its infrared spectrum. Recrystallizations from aqueous alcohol and Skellysolve B afforded the amine, m.p. 136–138°. The mixture m.p. with an authentic sample, m.p. 138–139°, was 137–139°.

[CONTRIBUTION NO. 320 FROM THE GRADUATE DEPARTMENT OF BIOCHEMISTRY, BRANDEIS UNIVERSITY, WALTHAM, MASSACHUSETTS 02154]

The Reaction of Hydroxylamine with Amides. Kinetic Evidence for the Existence of a Tetrahedral Addition Intermediate¹

BY WILLIAM P. JENCKS AND MARY GILCHRIST

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The rate of the reaction of hydroxylamine with simple amides passes through a maximum near pH 6 because of general acid catalysis of the reaction by hydroxylammonium ion. The reaction is also catalyzed by imidazole buffer. Plots of the apparent second-order rate constants at a given pH against catalyst concentration show a break because of a change in rate-determining step and, consequently, provide evidence for the existence of an intermediate in the reaction. The rate constants for the alkaline hydrolysis and hydroxylaminolysis of formamide are approximately $0.40 M^{-1} \text{ min.}^{-1}$ and $9 M^{-2} \text{ min.}^{-2}$, respectively.

It has recently become apparent that a number of simple substitution reactions at the carbonyl group display a complex dependence of the rate upon catalyst concentration, because of a change in the rate-determining step of the reaction with changing catalyst concentration. A positive deviation in a plot of rate against catalyst concentration demands only the addition of an extra term to the rate law, but a negative deviation (after correction for ionization or complexing of the reactants) is evidence for a change in rate-determining step and, consequently, for the existence of an intermediate of appreciable stability in reactions at the carbonyl group. Examples of such behavior have been reported for acid-catalyzed reactions² in which the deviation from linearity in the plot of rate

against hydrogen ion concentration often gives rise to bell-shaped pH-rate profiles, and for general acid-base catalyzed reactions, in which a plot of rate against catalyst concentration shows a decrease in slope as the rate-determining step of the reaction changes.³ In several cases the existence of an addition intermediate in these reactions has been confirmed by independent evidence.^{2b,g} The present report describes kinetic evidence for a change in rate-determining step and the existence of an addition intermediate in the reaction of hydroxylamine with amides to form hydroxamic acids.

Hydroxylamine is known to react with amides near neutrality and at alkaline pH. The reaction near neutrality is slow for most amides and is generally carried out at elevated temperatures for analytical purposes.^{4–8} The rate of this reaction shows a sharp maximum near pH 6 for a number of simple amides related to glutamine.⁶ The alkaline reaction is slower

(1) Supported by grants from the National Science Foundation and the National Institute of Child Health and Human Development of the National Institutes of Health (HD-01247).

(2) (a) A. V. Willi, *Helv. Chim. Acta*, **39**, 1193 (1956); (b) W. P. Jencks, *J. Am. Chem. Soc.*, **81**, 475 (1959); (c) E. H. Cordes and W. P. Jencks, *ibid.*, **84**, 832 (1962); (d) E. H. Cordes and W. P. Jencks, *ibid.*, **85**, 2843 (1963); (e) R. B. Martin, S. Lowey, E. L. Elson, and J. T. Edsall, *ibid.*, **81**, 5089 (1959); R. B. Martin and A. Parcell, *ibid.*, **83**, 4830 (1961); (f) B. Zerner and M. L. Bender, *ibid.*, **83**, 2267 (1961); (g) E. S. Hand and W. P. Jencks, *ibid.*, **84**, 3505 (1962); (h) R. B. Martin and R. I. Hedrick, *ibid.*, **84**, 106 (1962); (i) B. Hanson, *Acta Chem. Scand.*, **17**, 1307 (1963); (j) B. E. Dawson and T. Henshall, *J. Phys. Chem.*, **67**, 1187 (1963); (k) B. Capon and B. E. Connett, *Tetrahedron Letters*, **22**, 1395 (1964); (l) T. C. Bruice and L. R. Fedor, *J. Am. Chem. Soc.*, **86**, 738, 739 (1964).

(3) (a) E. H. Cordes and W. P. Jencks, *ibid.*, **84**, 4319 (1962); (b) R. B. Martin, A. Parcell, and R. I. Hedrick, *ibid.*, **86**, 2406 (1964).

(4) F. Lipmann and L. C. Tuttle, *J. Biol. Chem.*, **159**, 21 (1945).

(5) J. Katz, I. Lieberman, and H. A. Barker, *ibid.*, **200**, 417 (1953).

(6) A. Meister, L. Levintow, R. E. Greenfield, and P. A. Abendschein, *ibid.*, **215**, 441 (1955).

(7) C. Hoffman, *Ber.*, **22**, 2854 (1889).

(8) (a) G. Braunitzer, *Biochim. Biophys. Acta*, **19**, 574 (1956); (b) L. K. Ramachandran and K. Narita, *ibid.*, **30**, 616 (1958).

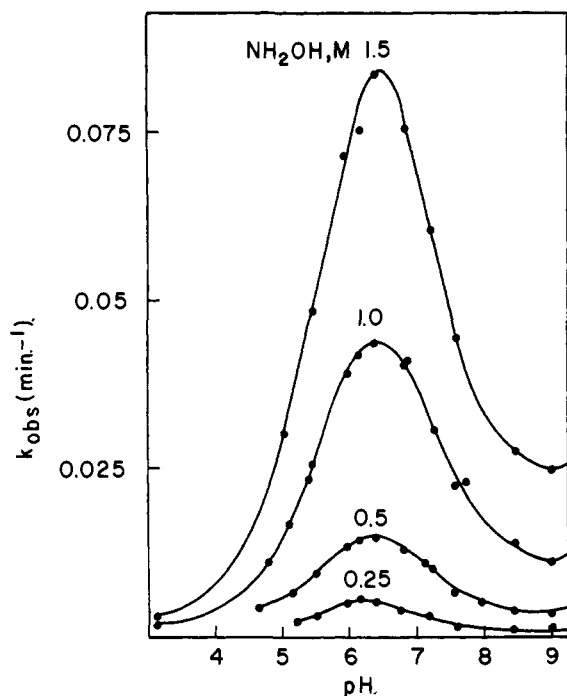


Fig. 1.—Dependence on pH of the rate of formohydroxamic acid formation from formamide at various concentrations of hydroxylamine at 39°, ionic strength 2.0. The experiments at pH 3.15 were carried out in 0.1 *M* 3-chloropyridine buffer and those at pH values over 8.0 were carried out in 0.2 *M* tris(hydroxymethyl)aminomethane buffer; the rate constants are not corrected for buffer catalysis.

than the alkaline reaction of esters, but occurs at a rate fast enough to follow conveniently to room temperature.⁹

Experimental

Reagent grade chemicals were redistilled or recrystallized before use. Glass-distilled water was used throughout.

The rate of formation of hydroxamic acid was determined⁴ by the addition of aliquots of the reaction mixture, usually 0.5 ml., to 4 ml. of 10% $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ in 0.3 *M* hydrochloric acid. The absorption was measured at 540 $\text{m}\mu$ after 3 to 5 min. against a reagent blank with a Zeiss PMQ II spectrophotometer. Reaction mixtures were incubated in a water bath at $39.0 \pm 0.1^\circ$. The ionic strength was maintained at 2.0 by the addition of potassium chloride. Unless otherwise noted, control of pH was maintained by the buffering action of hydroxylamine hydrochloride which was partially neutralized with potassium hydroxide. Measurements of pH were carried out at 25° with a Radiometer Model 4 pH meter. The pH of alkaline solutions of hydroxylamine, although constant during a kinetic run, changes with time because of hydroxylamine decomposition; the pH of such solutions was, therefore, measured immediately after completion of the rate determination.

The reactions with formamide were carried out under pseudo-first-order conditions with the concentration of hydroxylamine greatly in excess of the concentration of formamide (usually 0.005 *M*). The reactions followed pseudo-first-order kinetics and the rate constants were obtained from linear semilogarithmic plots of the extent of the reaction, $A_\infty - A_t$, against time and the relation $k = 0.693/t_{1/2}$. Ethylenediaminetetraacetic acid, 10^{-4} *M*, was added to some experiments which were carried out in alkaline solution.

The reactions with acetamide and substituted acetamides were followed by measurements of the initial rate of hydroxamic acid formation in solutions which were initially 0.15 *M* in respect to amide. The amounts of hydroxamic acid formed were determined by comparison with a standard solution of acetohydroxamic acid. Second-order rate constants were obtained by dividing the observed initial rates by the concentrations of amide and of hydroxylamine as the free base.

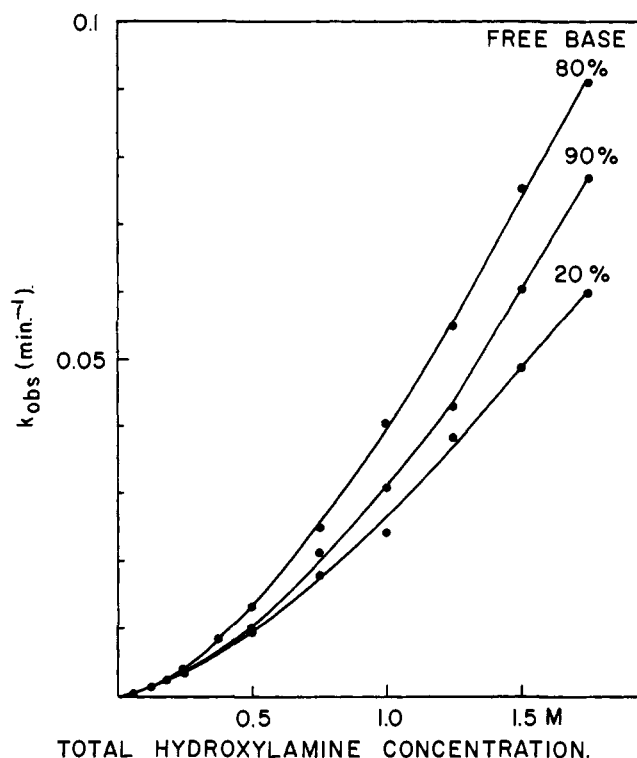


Fig. 2.—Dependence of the rate of formohydroxamic acid formation from formamide on the concentration of hydroxylamine at 20, 80, and 90% hydroxylamine free base at 39°, ionic strength 2.0.

Formamide concentration was measured by incubating 0.5-ml. samples with 0.5 ml. of a solution prepared from two volumes of 4 *M* hydroxylamine hydrochloride and one volume of 4 *M* potassium hydroxide for 1 hr. at 39°. The absorbance was measured at 540 $\text{m}\mu$ within 5 min. after the addition of 4.0 ml. of 10% $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ in 0.3 *M* hydrochloric acid.

If hydroxylamine or hydroxylammonium ion formed a hydrogen-bonded complex with amides, it would be expected that a change in pH would be observed if a concentrated solution of amide were added to a dilute solution of partially neutralized hydroxylamine hydrochloride. The pH of half-neutralized, 0.1 *M* hydroxylamine buffer was found to be unaltered immediately after the addition of 1 *M* formamide or acetamide, which provides no evidence for the formation of any such complex.

Results and Discussion

The rate of formohydroxamic acid formation from hydroxylamine and formamide exhibits a sharp pH-rate maximum in the range pH 6.2–6.5 (Fig. 1). Pseudo-first-order rate constants in the range pH 5 to 8 were determined in the presence of a large excess of hydroxylamine, which served as buffer; rate constants at higher and low pH values were determined in the presence of added buffer and are uncorrected for buffer catalysis.

The rate of formohydroxamic acid formation in a series of hydroxylamine buffers shows a greater than first-order dependence on the total concentration of hydroxylamine at a given hydroxylamine/hydroxylammonium ion ratio (Fig. 2). This fact and the pH dependence of the reaction (Fig. 1) suggest that hydroxylammonium ion acts as a catalyst for the reaction of hydroxylamine.

However, inspection of the data of Fig. 2 suggests that the upward curvature of the lines, reflecting the component of the reaction which is second order in respect to total hydroxylamine, becomes less significant as the hydroxylamine concentration is increased. That

(9) (a) F. Bergmann, *Anal. Chem.*, **24**, 1367 (1952); (b) V. Goldenberg and P. E. Spoerri, *ibid.*, **30**, 1327 (1958).

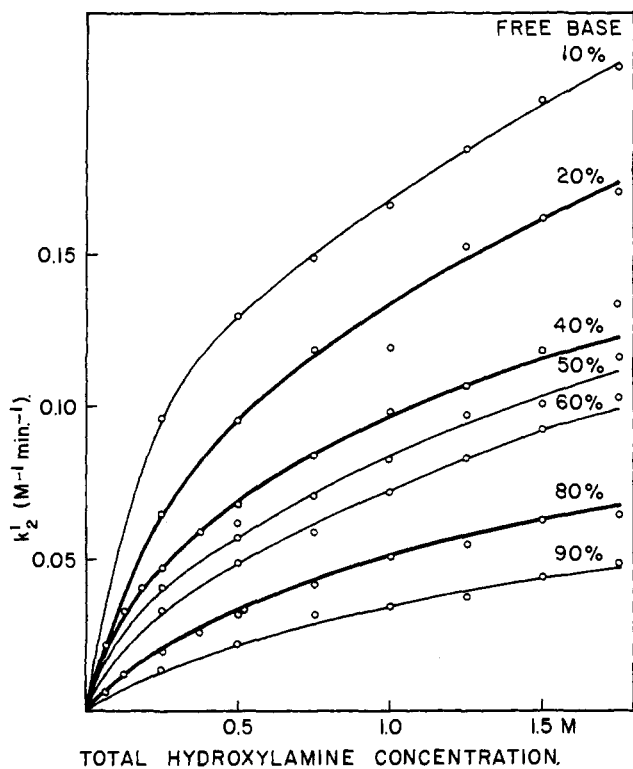


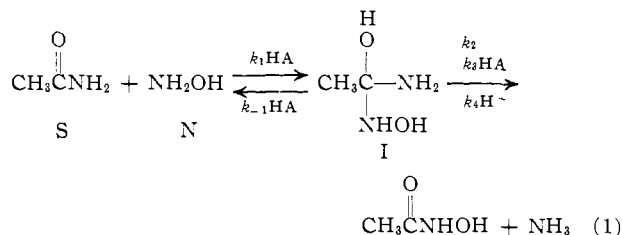
Fig. 3.—Dependence of the second-order rate constant for formhydroxamic acid formation ($k_2' = k_{\text{obsd}}/[\text{NH}_2\text{OH}]$) on hydroxylamine concentration at different fractions of hydroxylamine neutralization at 39°, ionic strength 2.0. The heavy lines were calculated from the steady-state rate equation (3).

this is the case is confirmed by plots of the apparent second-order rate constants for the reaction ($k_2' = k_{\text{obsd}}/[\text{NH}_2\text{OH}]$) against hydroxylamine concentration (Fig. 3). The slopes of the lines in this figure are the rate constants for catalysis of the reaction by hydroxylamine or hydroxylammonium ion. The lines extrapolate to a point near zero, which indicates that the uncatalyzed reaction of hydroxylamine makes only a minor contribution to the observed rates. The values of k_2' are larger in the more acidic solutions, which indicates that hydroxylammonium ion is a more effective catalyst than free hydroxylamine. The slopes of the lines, and hence the catalytic constants, are large at low hydroxylamine concentration and decrease at higher hydroxylamine concentration.

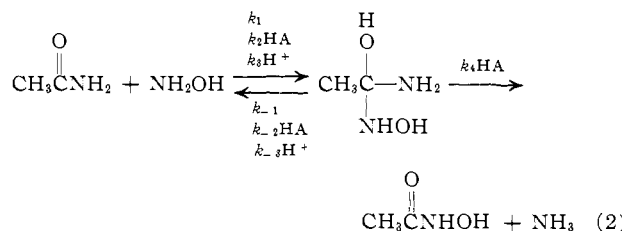
The decrease in the catalytic constant for hydroxylamine catalysis with increasing hydroxylamine concentration cannot be accounted for by a one-step reaction mechanism or rate law and is evidence for a change in the rate-determining step of the reaction with increasing hydroxylamine concentration. Hydroxylammonium ion catalysis is more important for that step of the reaction which is rate determining at low hydroxylamine concentration than for the step which becomes rate determining at high hydroxylamine concentration. The situation is analogous to that in propionic acid catalyzed semicarbazone formation from acetophenone at pH 4.10, in which the catalytic constant for propionic acid decreases with increasing catalyst concentration as the reaction undergoes a transition from predominantly rate-determining semicarbazide attack at low catalyst concentration, to rate-determining dehydration of the carbinolamine addition intermediate at high catalyst

concentration.^{3a} Martin and co-workers have very recently interpreted a nonlinearity in respect to borate buffer concentration of the cyclization of glutamine and glutamate esters in a similar manner.^{3b}

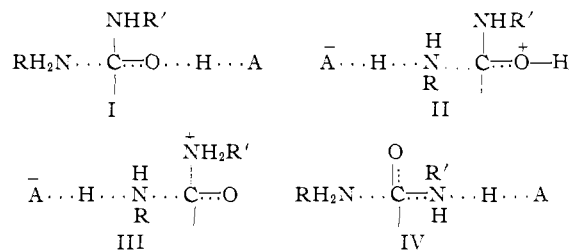
There are several possible mechanisms which would account for the data, but they are all similar in that they require a change in rate-determining step and, hence, an intermediate in the reaction. One such mechanism, in which the formation of a tetrahedral addition intermediate from the amide and hydroxylamine is subject to general acid catalysis, while the decomposition of the intermediate occurs by uncatalyzed and acid-catalyzed pathways, is shown in eq. 1. An alternative mechanism is shown in eq. 2. The



available data do not distinguish between these mech-



anisms; I, II, III, and IV in which R and R' are either H or OH are possible generalized transition states for the general acid catalyzed reactions. Attempts to



demonstrate the accumulation of an addition intermediate by infrared examination of the carbonyl group of formamide in deuterium oxide in the presence and absence of hydroxylamine gave negative results.¹⁰

The steady-state rate equation for the mechanism of eq. 1 is given in eq. 3. Values of $k_1 = 0.51 M^{-2} \text{min}^{-1}$, $k_2/k_{-1} = 0.18 M^2$, $k_3/k_{-1} = 0.09 M$, and k_4/k_{-1}

$$k_2' = \frac{dP}{dtNS} = \frac{k_1[\text{HA}](k_2 + k_3[\text{HA}] + k_4[\text{H}^+])}{k_2 + k_3[\text{HA}] + k_4[\text{H}^+] + k_{-1}[\text{HA}]} \quad (3)$$

$= 4 \times 10^4 M$ were obtained by successive approximations and were used to obtain the calculated rate constants shown as the heavy lines in Fig. 3. For hydroxylamine solutions between 20 and 80% free base the calculated rates provide a satisfactory fit to the

(10) J. Greenwald, unpublished experiments.

data. At extreme pH values the observed rate constants are less accurate and it is probable that additional terms become significant in the rate law. The alternative mechanism of eq. 2 gives the steady-state rate eq. 4 which is of the same form as eq. 3; mech-

$$k_2' = \frac{dP}{dtNS} = \frac{k_4[HA](k_1 + k_2[HA] + k_3[H^+])}{k_{-1} + k_{-2}[HA] + k_{-3}[H^+] + k_4[HA]} \quad (4)$$

anisms 1 and 2 are, therefore, kinetically indistinguishable.

The reaction is also catalyzed by imidazole buffers (Fig. 4). If the break in the curves for hydroxylamine catalysis is attributed to a change in rate-determining step, a similar break should be observed for imidazole catalysis. This is indeed the case. At a high hydroxylamine concentration, at which the reaction shows relatively little catalysis by hydroxylamine, there is only a small amount of catalysis by imidazole (Fig. 4, upper curve). As the hydroxylamine concentration is lowered, the catalytic constant for imidazole becomes larger at low imidazole concentration. As the concentration of catalyst increases, there is a decrease in the catalytic constant as the change in rate-determining step occurs (Fig. 4, lower curve).

Catalysis by pyridine, acetate, and carbonate buffers of the reaction of hydroxylamine with formamide or acetamide was also observed, but the kinetics of these catalyzed reactions were not investigated in detail.

The reaction exhibits a rate increase in the presence of concentrated potassium chloride and a rate decrease in the presence of 10% ethanol, but both effects are small (Table I). The reverse reaction, of formohy-

TABLE I
SALT AND SOLVENT EFFECTS ON THE REACTION OF
HYDROXYLAMINE WITH FORMAMIDE AT 39°^a

Conditions	Total hydroxylamine, M	$k_{\text{obsd}} \times 10^3$, min. ⁻¹
Control	0.25	3.6
+ KCl, 1.75 M	.25	4.2
+ Ethanol, 10% (v./v.)	.25	3.3
Control	1.0	35.9
+ KCl, 0.4 M	1.0	38.5
+ KCl, 1.0 M	1.0	40.8
+ Ethanol, 10% (v./v.)	1.0	33.8

^a Hydroxylamine hydrochloride neutralized 80% with potassium hydroxide.

droxamic acid with ammonia, was found not to proceed at a detectable rate in the presence of 1 M ammonium chloride at pH 7.2 and the reaction of formamide with hydroxylamine was found to proceed to completion in the presence of 1 M ammonium chloride at pH 6.8. Although activated acyl groups react with hydroxylamine to form O-acylhydroxylamines as well as hydroxamic acids,¹¹ O-acylhydroxylamine formation from amides is improbable on thermodynamic grounds in view of the much higher free energy of hydrolysis of esters than amides.¹² In any case, O-acylhydroxylamine is not the unstable intermediate in the reaction of hydroxylamine with amides, because O-acylhydroxyl-

(11) W. P. Jencks, *J. Am. Chem. Soc.*, **80**, 4581, 4585 (1958).

(12) See, for example, W. P. Jencks, S. Cordes, and J. Carriuolo, *J. Biol. Chem.*, **235**, 3608 (1960).

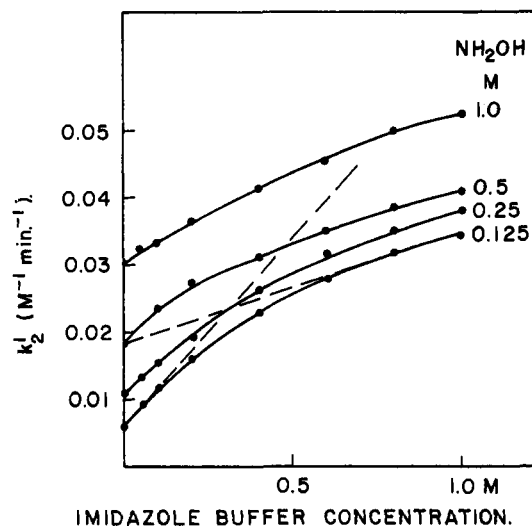


Fig. 4.—Catalysis by imidazole buffer (50% imidazole hydrochloride) of formohydroxamic acid formation from formamide in the presence of various concentrations of hydroxylamine at 39°, ionic strength 2.0.

amines are converted to hydroxamic acids at a rate which is much faster than either of the steps of hydroxamic acid formation from amides,¹¹ and the rate of the reaction is not affected by the ammonia released during the reaction or by added ammonia.

The rate of formohydroxamic acid formation could not be measured at pH values much below 3.0, because of the slow rate of the reaction and because of interfering hydrolysis of formohydroxamic acid. The rate constants for the hydrolysis of formohydroxamic acid were found to be 0.0037 and 0.0415 min.⁻¹ in 0.046 and 0.50 M hydrochloric acid, respectively, giving a second-order rate constant of 0.082 for the acid-catalyzed hydrolysis of formohydroxamic acid. This is significantly faster than the rate constant of 0.014 min.⁻¹ for the hydrolysis of formamide in 2 M hydrochloric acid.¹³

The reaction of hydroxylamine with acetamide occurs at about 4% of the rate of the corresponding reaction with formamide. The reaction is also catalyzed by hydroxylammonium ion and the catalytic constant shows a decrease with increasing hydroxylamine concentration, similar to that observed with formamide, which suggests a similar mechanism for the two reactions (Fig. 5). The reaction with N-methylacetamide is about one-fortieth as fast as that with acetamide, but shows similar evidence for a change in rate-determining step with increasing catalyst concentration (Fig. 5). The still slower reaction with N-dimethylacetamide, however, shows only a small curvature in the corresponding plot and it appears that the relative magnitudes of the various rate constants are different for this compound and that a change in rate-determining step does not occur within the range of hydroxylamine concentrations which were examined (Fig. 5).

Conant and Bartlett proposed that the bell-shaped pH-rate curve for oxime formation was caused by a requirement for hydroxylamine in the free base form for nucleophilic reaction and for hydroxylammonium ion for general acid catalysis,¹⁴ and Hammett showed

(13) V. K. Krieble and K. A. Holst, *J. Am. Chem. Soc.*, **60**, 2976 (1938).

(14) J. B. Conant and P. D. Bartlett, *ibid.*, **54**, 2881 (1932).

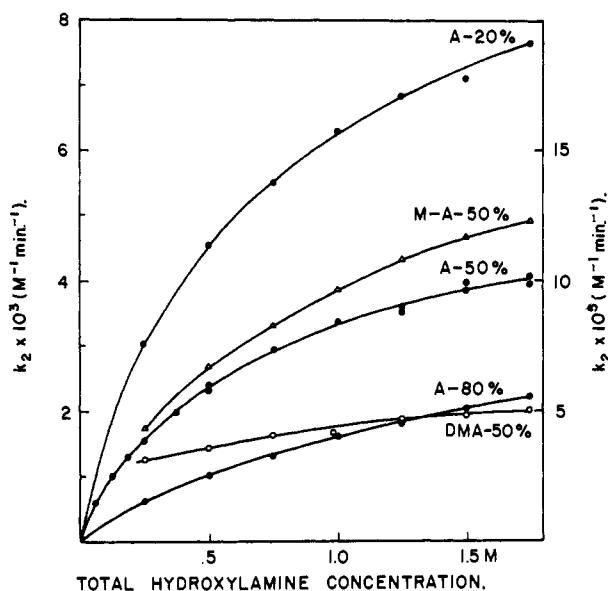


Fig. 5.—Dependence of the second-order rate constant for acetohydroxamic acid formation from acetamide (●, left ordinate), N-methylacetamide (Δ, right ordinate), and N-dimethylacetamide (○, right ordinate) on hydroxylamine concentration at different fractions of hydroxylamine as the free base at 39°, ionic strength 2.0.

quantitatively how a bell-shaped curve should result from such requirements.¹⁵ Although the pH-rate maximum in oxime formation is caused by a change in rate-determining step rather than by general acid catalysis,^{2b} the pH-rate profile of the reaction of hydroxylamine with amides is an example of a pH-rate maximum caused by general acid catalysis of the reaction. The change in rate-determining step in the reaction with amides occurs with increasing catalyst concentration, rather than with a change in pH. In contrast, the reaction of hydroxylamine with thiol esters has been described in a preliminary communication by Bruce and Fedor to be strictly second order in respect to total hydroxylamine concentration at a given acidity, but to show a break, indicative of a change in rate-determining step, in plots of rate against acidity.²¹

Alkaline Reaction.—Rate constants for the alkaline hydrolysis and hydroxylaminolysis of formamide are collected in Table II. The observed pseudo-first-

(15) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 331.

order rate constants for formohydroxamic acid appearance or formamide disappearance increase with increasing concentrations of both hydroxide ion and hydroxylamine. The third-order rate constants for base-catalyzed hydroxylaminolysis, according to the rate law of eq. 5 ($XH = NH_2OH$), decrease with in-

$$\text{rate} = k[\text{HCONH}_2][\text{XH}][\text{OH}^-] \quad (5)$$

creasing hydroxylamine concentration if the rates are based on the concentration of added base, but are approximately constant at $9 \text{ M}^{-2} \text{ min}^{-1}$ if the rate constants are based upon measured pH values. The difference probably is caused by a small amount of

TABLE II
ALKALINE REACTION OF HYDROXYLAMINE WITH FORMAMIDE
AT 39°, IONIC STRENGTH 2.0

[NH ₂ -OH], M	[OH ⁻], M	Ap- parent pH	k _{obsd} , min. ⁻¹	k ₃ , ^a M ⁻² min. ⁻¹	k ₃ , ^b M ⁻² min. ⁻¹	[RCONHOH]/ [RCONH ₂] ^c	Obsd	Calcd.
0.05	0.10	12.76	0.075	7.4	8.7	0.44	0.50	
.15	.10	12.78	.131	6.2	7.3	.71	.71	
.24	.05	12.33	.083	5.3	9.1	.80	.77	
.24	.10	12.62	.165	5.3	9.5	.80	.77	
.48	.05	12.22	.133	5.1	10.0	.90	.86	
.50	.10	12.58	.267	4.6	9.1	.91	.86	
					$k_{\text{OH}^-} =$ $k_{\text{obsd}}/[\text{OH}^-],$ M ⁻¹ min. ⁻¹			
0	0.05	12.42	0.018		0.36			
0	.10	12.83	.038		.38			
0	.20	13.16	.082		.41			

^a $k_3 = (k_{\text{obsd}} - k_{\text{hydrolysis}})/[\text{NH}_2\text{OH}][\text{OH}^-]$. ^b Same as k_3 , but based on observed pH, rather than added $[\text{OH}^-]$, taking $0.1 \text{ M } [\text{OH}^-] = \text{pH } 12.83$. ^c Fraction of initial formamide converted to formohydroxamic acid. Calculated value from $k_N/(k_N + k_H)$, where k_N and k_H are the pseudo-first-order rate constants for hydrolysis and hydroxylaminolysis, respectively.

base-catalyzed decomposition of hydroxylamine in the more alkaline solutions. The observed yields of hydroxamic acid at the end of the reaction agree satisfactorily with the yields calculated from the ratio of the rate constants for hydroxylaminolysis and hydrolysis. If the rate constant for the alkaline hydrolysis of formamide is also expressed according to eq. 5 ($XH = \text{H}_2\text{O}$) for comparison, the rate constant for the base-catalyzed hydroxylamine reaction is 1200 times larger than that for base-catalyzed hydrolysis.

Acknowledgment.—We are grateful to Miss E. Tarmy, Mr. B. Kitto, and Dr. L. Cuprak for carrying out preliminary experiments on this problem.