

efficient, and calculated¹⁵ from the equation

$$pK_A = pH - \log \frac{A - A_1}{A_2 - A} \quad (18)$$

In eq. 18, A = absorbance of the buffered solution, A_1 = absorbance of the hydrochloric acid solution, A_2 = absorbance of the sodium hydroxide solution, and pH refers to the pH of the buffered solution. All pK_A values re-

(15) H. F. Walton, "Principles and Methods of Chemical Analysis," Prentice-Hall, Inc., New York, N. Y., 1952, p. 271.

ported in Table I are uncorrected for the activity of the anion and hence are apparent rather than thermodynamic (see Table I, Ref. a).

Acknowledgments.—This study was supported in part by a research grant from the Robert A. Welch Foundation. The statistical calculations were performed by the Data Processing Center, Texas Engineering Experiment Station, College Station, Texas, on an IBM-650 computer.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CORNELL UNIVERSITY, ITHACA, N. Y.]

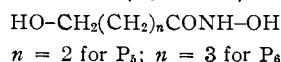
The Mechanism of the Reaction of Hydroxylamine with γ -Butyro- and δ -Valerolactones. Examples of Reactions Kinetically both Third and Fourth Order

BY THOMAS C. BRUCE AND JOHN J. BRUNO¹

RECEIVED APRIL 10, 1961

The reaction of hydroxylamine with γ -butyro- and δ -valerolactones in aqueous solution afforded the hydroxamic acids of γ -hydroxybutyric and δ -hydroxyvaleric acids *via* the rate expression $d \text{ product} / dt = k_1(\text{NH}_2\text{OH})^2(\text{OH}^-)(\text{lactone}) + k_3(\text{NH}_2\text{OH})^2(\text{lactone})$. The deuterium kinetic solvent isotope effects (k^H/k^D) were, for k_1 1.2, and for k_3 2.5. When the hydroxylaminolysis reaction was carried out in the presence of the general base imidazole ($\text{C}_3\text{H}_4\text{N}_2$) the rate expression for the formation of hydroxamic acid was determined to be $d \text{ product} / dt = k_4(\text{NH}_2\text{OH})^2(\text{OH}^-)(\text{lactone}) + k_3(\text{NH}_2\text{OH})^2(\text{lactone}) + k_{1M}(\text{NH}_2\text{OH})(\text{C}_3\text{H}_4\text{N}_2)(\text{lactone})$. On the basis of both the solvent deuterium isotope effect and the experiments with imidazole, the general kinetic expression for the hydroxylaminolysis of the lactones is established to involve a mechanism of general base catalysis and a mechanism involving both specific base and general base catalysis.

In aqueous solution at 30° hydroxylamine was found to react with γ -butyro- and δ -valerolactones (L_5 and L_6) to give, in a quantitative yield, the derived hydroxamic acids (P_5 and P_6)



Under the conditions of excess hydroxylamine and at pH values between 6.5 and 8.0 the hydrolysis of L_5 and L_6 was kinetically imperceptible and the rate of hydroxamic acid production and lactone disappearance was found to accurately follow the expression²

$$-\frac{dL}{dt} = \frac{dP}{dt} = \left[k_3(L) + \frac{k_4 K_W}{a_H} (L) \right] \left[\frac{(N_T) K_A}{K_A + a_H} \right]^2 \quad (1)$$

or

$$dP/dt = k_3(N_F)^2(L) + k_4(N_F)^2(\text{OH}^-)(L) \quad (2)$$

The kinetic expressions for the hydroxylaminolysis of L_5 and L_6 are most unusual in that they contain terms both third and fourth order. In this paper the procedures leading to the establishment of eq. 1-2 and to plausible mechanisms of the reactions are described.

Results and Discussion

When hydroxylamine is employed in a large excess over L_5 and L_6 and the pH is constant, the production of P_5 and P_6 is pseudo first order.

$$dP/dt = k_{obs}(L) \quad (3)$$

If the pH is kept constant and the value of N_T varied, then plots of k_{obs} *vs.* N_F exhibit decidedly up-

(1) Postdoctoral Fellow, Department of Chemistry, Cornell University.

(2) N_T equals total stoichiometric concentration of hydroxylamine, $N_F = \text{NH}_2\text{OH}$, IM_F = free imidazole base, IM_T total stoichiometric concentration of imidazole, K_W = autoprotolysis constant of water, $K_A = K_1$ = first dissociation constant of hydroxylamine, K_2 = second dissociation constant of hydroxylamine, and a_H is the hydrogen ion activity as measured by the glass electrode.

ward curvatures. The hydroxylaminolysis reaction with L_5 and L_6 then involves hydroxylamine to more than the first power. The reaction was found to be bimolecular in N_F by the establishment of a linear relationship between N_F^2 and k_{obs} at constant pH . When reactions were carried out at other constant pH values, linear plots of N_F^2 *vs.* k_{obs} were invariably obtained, but the pseudo-third-order rate constant (k_3'), as obtained from the slopes, were found to vary with pH (Fig. 1).

$$k_3' = k_{obs}/N_F^2 \quad (4)$$

Plots of the values of k_3' *vs.* K_W/a_H were linear for both L_5 and L_6 and established the rate expressions 1 and 2 (Fig. 2).

The slopes of the plot of Fig. 2 equal the values of k_4 and the intercepts at $K_W/a_H = 0$, equal k_3 . The values so obtained are recorded in Table I.

The question of the mechanistic interpretation of the rate expressions next arose. The fact that the terms of k_3 and k_4 both involve the second power of the hydroxylamine strongly suggested general base-catalyzed mechanisms. If this were so, then, in the presence of the general base imidazole³ we could have:

Case I: General base catalysis only in the k_3 term. Then at any constant pH

$$v = k_{obs}(L)$$

$$v = k_4(\text{OH}^-)(N_F)^2(L) + k_3(N_F)^2(L) + k_{1M}(N_F)(\text{IM}_F)(L)$$

$$\frac{k_{obs}}{N_F^2} = k_4(\text{OH}^-) + k_3 + \frac{k_{1M}}{N_F}(\text{IM}_F) \quad (5)$$

and a plot of k_{obs}/N_F^2 *vs.* IM_F/N_F should be linear with slope k_{1M} and intercept $k_4(\text{OH}^-) + k_3$ (*i.e.*, pH dependent intercept and pH independent slopes).

Case II: The second hydroxylamine molecule in both k_3 and k_4 terms is involved as a general base

(3) Imidazole was chosen as the general base because its pK_a' of 7.1 made it about the most effective general base available in the pH ranges employed in this study.

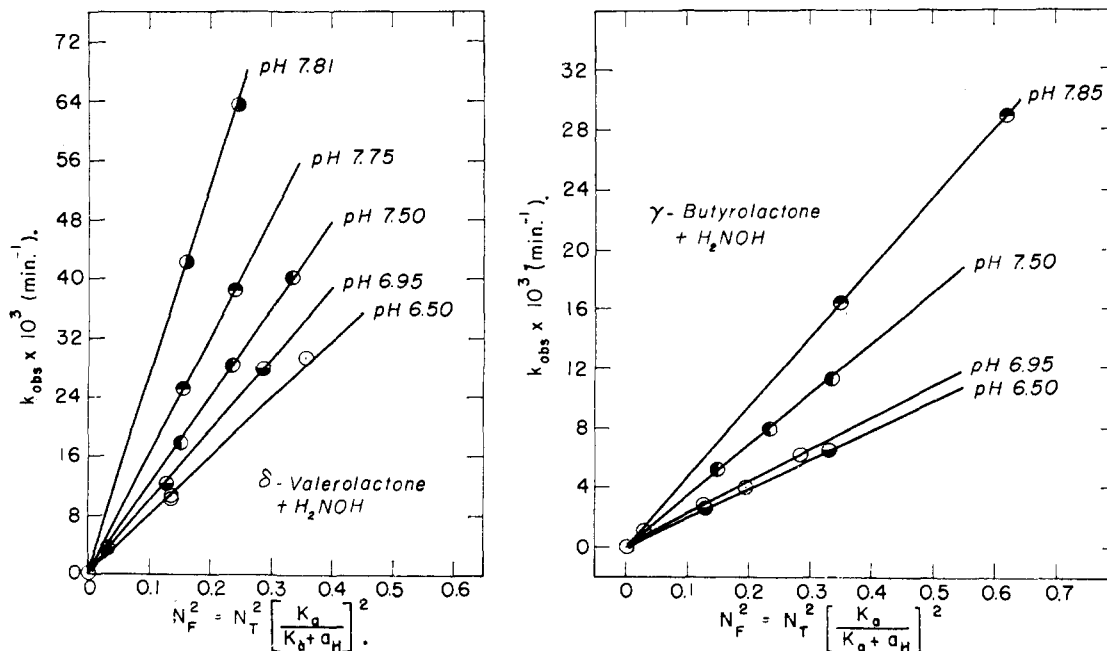


Fig. 1.—Plots of the square of the concentration of NH_2OH (i.e., N_F^2) vs. the determined *pseudo* first order rate constants (k_{obs}) of hydroxylaminolysis as a function of pH. ($T = 30^\circ$, solvent H_2O ; $\mu = 1.0M$.)

catalyst. Then at any constant pH

$$\frac{k_{\text{obs}}}{N_F^2} = k_4(\text{OH}^-) + k_3 + \frac{k_{1M}IM_F + k_{1M}'(IM_F)(\text{OH}^-)}{N_F} \quad (6)$$

Plots of k_{obs}/N_F^2 vs. IM_F/N_F would have as intercepts the values $k_4(\text{OH}^-) + k_3$ and as slopes the pH variable $k_{1M} + k_{1M}'(\text{OH}^-)$.

TABLE I

A TABULATION OF KINETIC AND EQUILIBRIUM CONSTANTS DETERMINED IN THIS STUDY

| Lactone constants for hydroxylaminolysis | γ -Butyro- | δ -Valero- |
|------------------------------------------------------|----------------------|----------------------|
| k_3 , $1.2 \text{ mole}^{-2} \text{ min.}^{-1}$ | 1.8×10^{-2} | 7.7×10^{-2} |
| k_4 , $1.3 \text{ mole}^{-3} \text{ min.}^{-1}$ | 2.9×10^4 | 9.9×10^4 |
| k_{1M} , $1.2 \text{ mole}^{-2} \text{ min.}^{-1}$ | 8.7×10^{-3} | |
| k_3^D , $1.2 \text{ mole}^{-2} \text{ min.}^{-1}$ | | 3.1×10^{-2} |
| $k_3^{H/D}$ | | 2.5 |
| k_4^D , $1.3 \text{ mole}^{-3} \text{ min.}^{-1}$ | | 8.2×10^4 |
| k_4^H/k_4^D | | 1.2 |

Second-order constants for reaction of imidazole with lactones (78°), $1. \text{ mole}^{-1} \text{ min.}^{-1}$ 1.2×10^{-3} 23.6×10^{-3}

Second-order constants for reaction of OH^- with lactones (78°), $1. \text{ mole}^{-1} \text{ min.}^{-1}$ 1.2×10^3 7.9×10^3

pK_1^H (Hydroxylamine) 6.04^a
 pK_1^D (Hydroxylamine) 6.49^a
 pK_1 (Imidazole) 7.10^a

^a Determined in H_2O or D_2O at 30° , $\mu = 1.0 M$.

Case III: Only in k_4 is one of the hydroxylamine molecules involved as a general base catalyst. Then at constant pH

$$\frac{k_{\text{obs}}}{N_F^2} = k_4(\text{OH}^-) + k_3 + \frac{k_{1M}(\text{OH}^-)(IM_F)}{N_F} \quad (7)$$

For this case the plots of k_{obs}/N_F^2 vs. IM_F/N_F would have the variable intercept $k_4(\text{OH}^-) + k_3$ and the pH variable slope $k_{1M}(\text{OH}^-)$.

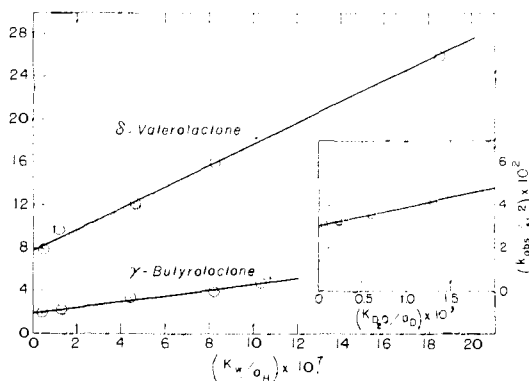


Fig. 2.—Plots of the *pseudo* third order rates of hydroxylaminolysis ($k_3' = k_{\text{obs}}/N_F^2$) vs. hydroxide ion concentration. In the inset k_3' for hydroxylaminolysis of δ -valerolactone has been plotted against the concentration of OD^\ominus .

Case IV: In the k_3 term, one of the hydroxylamine molecules is involved as a general base and in the k_4 term a hydroxylamine anion is involved as a general base. The plot of k_{obs}/N_F^2 vs. IM_F/N_F^2 would be of the same form as for Case I. The plots of k_{obs}/N_F^2 vs. IM_F/N_F for the four possible cases of general base catalysis would then possess as intercepts $k_4(\text{OH}^-) + k_3$ but uncommon and easily distinguishable functions determining slopes.

Because imidazole is capable of acting as a nucleophilic catalyst for the hydrolysis of the ester bond^{4,5} it could not be employed as the general base in this study prior to the establishment of its inability to catalyze the hydrolysis of L_5 and L_8 under the conditions employed for the hydroxylaminolysis reactions. It was found that at 30° , imidazole

(4) T. C. Bruice and co-workers, *J. Am. Chem. Soc.*, **79**, 1663 (1957); **80**, 148 (1958); **80**, 1173 (1958); **80**, 2265 (1958); **81**, 2860 (1959); **81**, 5444 (1959); **82**, 3386 (1960).

(5) M. L. Bender and B. W. Turnquest, *ibid.*, **79**, 1652 (1957).

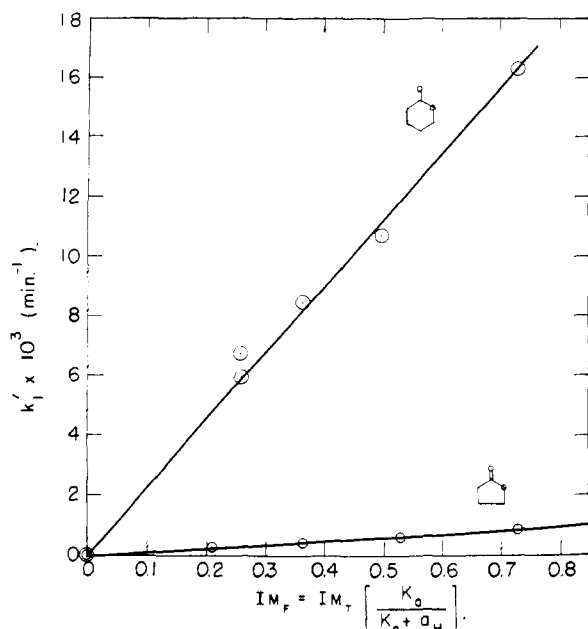


Fig. 3.—Dependence of the hydrolytic constants of δ -valero and γ -butyrolactones on the concentration of neutral imidazole base (IM_F). The values of k'_1 represent the observed *pseudo* first order rates of hydrolysis (k_{obs}) corrected for hydrolysis by lyate species (k_w); i.e., $k_{obs} - k_w = k'_1$ ($T = 78^\circ$; solvent water; $\mu = 1.0M$).

catalysis of the hydrolysis of the lactones did not occur at rates that would at all invalidate its use as the general base. However, at 78° imidazole was found to be a very effective catalyst of lactone hydrolysis (Fig. 3). The values of the second-order catalytic coefficients for the hydrolysis of L_5 and L_6 are recorded in Table I. In the course of determining the rate constants for imidazole catalysis of the hydrolysis of L_5 and L_6 , it was essential to determine also the second-order rate constants for hydroxide ion catalysis of the hydrolysis of the lactones (k_{OH}) at 78° . These values were determined from *pH*-rate profiles (Fig. 4) and are recorded in Table I.

In Fig. 5 there is presented a plot of k_{obs}/N_F^2 vs. IM_F/N_F for the hydroxylaminolysis of L_6 at various *pH* values. For each linear plot we have employed values of k_{obs} determined with varying concentrations of both N_F and IM_T . The variable intercepts and constant slopes of Fig. 5 are only in accord with Case I or Case IV. The kinetic term associated with k_3 is then the usual general base-catalyzed reaction common to the nucleophilic attack of all but tertiary nitrogen bases at the ester bond.^{6-8,12}

In order to gain additional insight into the mechanism for k_4 , the hydroxylaminolysis of L_6 was studied in D_2O . In the inset of Fig. 2 there is plotted the value of k_{obs}/N_F^2 vs. K_{D_2O}/a_D . The slope of the plot affords k_4^D and the intercept k_3^D . These values are recorded in Table I. The deuterium solvent isotope effects are then $k_3^H/k_3^D =$

(6) J. F. Bunnett and G. T. Davis, *J. Am. Chem. Soc.*, **82**, 865 (1960).

(7) W. P. Jencks and J. Carriolo, *ibid.*, **82**, 675, 1778 (1960).

(8) T. C. Bruce and M. F. Hayahi, *ibid.*, **82**, 3067 (1960).

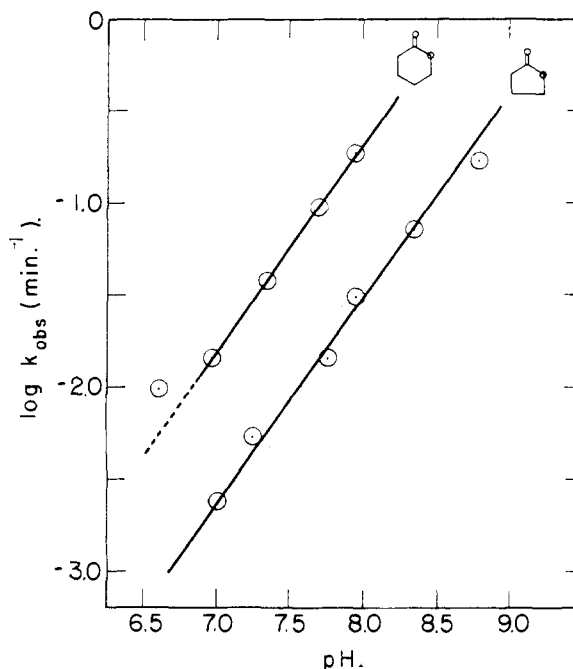


Fig. 4.—Partial *pH*-rate profiles for the hydrolysis of δ -valero and γ -butyrolactones at 78° (solvent H_2O ; $\mu = 1.0M$).

2.5 and $k_4^H/k_4^D = 1.2$. An isotope ratio of 2.5 for k_3 is in complete accord⁷ with the established fact that this term represents general base catalysis. An isotope ratio of 1.2 for k_4 would be in accord with the complete lack of either general base or specific base catalysis or the involvement of both specific and general base catalysis in the associated mech-

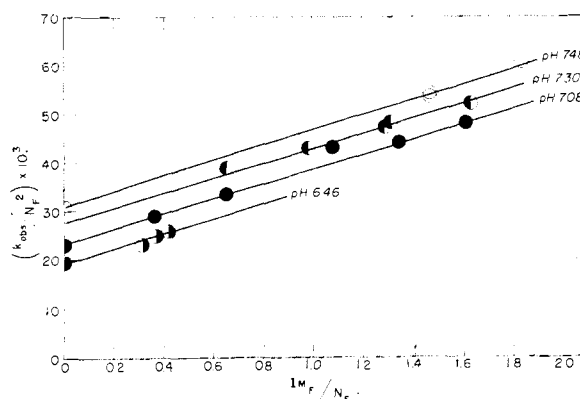
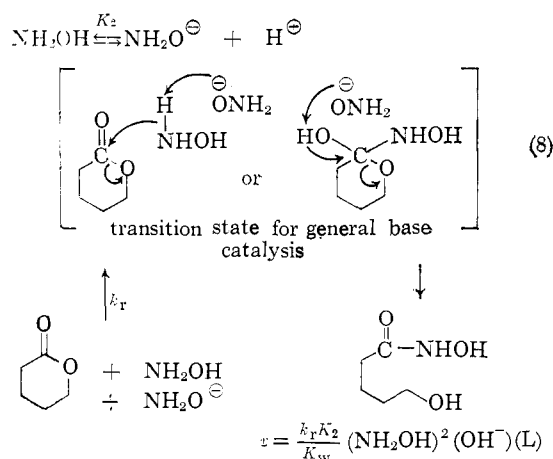
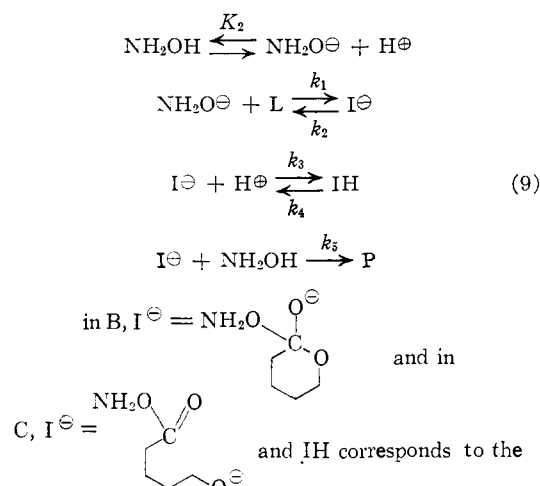


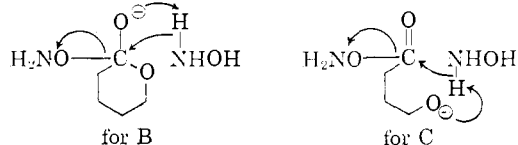
Fig. 5.—The parallel and linear dependence of the *pseudo* third order rates of hydroxylaminolysis (k_{obs}/N_F^2) of γ -butyrolactone on the ratio of free imidazole base to free hydroxylamine base (IM_F/N_F).

anism. For the former it would be essential to construct a transition state or a series of reactions involving simultaneous or stepwise nucleophilic displacement by three base species. This appears impossible so that we are left with the requirement of involving in a mechanism both specific and general base catalysis. The possibilities are:

Mechanism A: The hydroxylamine anion acts as a general base in the formation of hydroxamic acid from lactone and hydroxylamine.

**Mechanisms B and C:**

corresponding neutral conjugate acids. The transition states involving general base catalysis would then be



Assuming a steady state in I^- and IH

$$v = \frac{k_1(\text{NH}_2\text{OH})(\text{NH}_2\text{O}^-)(\text{L})}{(\text{NH}_2\text{OH}) + (k_2/k_5)} \quad (10)$$

Since in B and C, $k_2 \gg k_5$

$$v = \frac{k_1 k_2 K_2}{k_2 K_w} (\text{NH}_2\text{OH})^2 (\text{OH}^-) (\text{L}) \quad (11)$$

In theory it should be possible to equate the value of $k_4^{\text{H}}/k_4^{\text{D}}$ to the ratio of the rate expression calculated from the mechanisms A to C.

Thus for B and C

$$\frac{k_4^{\text{H}}}{k_4^{\text{D}}} = 1.2 = \frac{k_1^{\text{H}} k_2^{\text{H}} K_2^{\text{H}}}{k_1^{\text{D}} k_2^{\text{D}} K_2^{\text{D}}} \cdot \frac{k_2^{\text{D}} K_{\text{L}_2\text{O}}}{k_1^{\text{D}} k_3^{\text{D}} K_2^{\text{D}}} \quad (12)$$

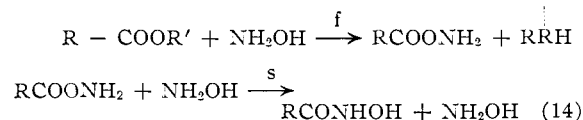
If we assume that the change of solvent from H_2O to D_2O alters only those constants associated with a proton or deuteron transfer step,^{9,10} then

(9) This, of course, may well be an oversimplification since there are deuterium solvent effects on reaction steps not involving a proton transfer (see, for example, P. Ballinger and F. A. Long, *J. Am. Chem.*

$$\left(\frac{K_2^{\text{H}}}{K_2^{\text{D}}}\right) \left(\frac{K_{\text{D}_2\text{O}}}{K_w}\right) \left(\frac{k_2^{\text{H}}}{k_2^{\text{D}}}\right) = (4.5)(0.15)(2) = 1.3^{10} \quad (13)$$

An expression analogous to 13 would of course also be valid for mechanism A.

It is not possible at this time to assign with certainty mechanism A, B or C. Thus, if NH_2O^- plays the part of a general base (mechanism A), then one might have expected detectable catalysis by imidazole anion as well. Though it has been observed that some esters react with hydroxylamine to yield an O-acyl intermediate^{11,12}



the hydroxylamine anion has never been shown to be the nucleophile in the formation of the O-acyl intermediate (mechanism B and C). Also, an $\text{S}_{\text{N}}2$ displacement on the high energy tetrahedral intermediate (mechanism B) is not common but has been proposed in several instances.¹³

While there is no precedent for mechanism C, nevertheless the ready reversibility of formation of O-acyl hydroxylamine can be accommodated by the fact that with the lactones, but not with ordinary esters, the ejected alkoxide ion remains a part of the molecule and therefore is in a position for return to regenerate lactone and hydroxylamine. Thus, in mechanism C we have a means of relating the previously unobserved fourth-order reaction to the special lactone structure. In order to ascertain the plausibility of C vs. A, B, we have initiated a study of the hydroxylaminolysis of other cyclic acyl systems in which the displaced group is a strong nucleophile and possesses a lower pK_a' than the alkoxide group of species I (*i.e.*, $-\text{N}-$, $\text{S}-$ in lactams and thiolactones).

Experimental

Apparatus.—All spectrophotometric studies were made with a model PMQII Zeiss spectrophotometer. A model 22 Radiometer pH meter was employed for pH determination. The rates of lactone hydrolysis at $78^\circ (\pm 0.1^\circ)$ were studied by means of a pH-Stat assembly based on the Radiometer TTT1a autotitrator.¹⁴ The study of the imidazole-catalyzed lactone hydrolysis (78°) was carried out in a Blue M Magni-Whirl constant temperature bath ($\pm 0.2^\circ$). All weighings were carried out to ± 0.05 mg. on a Sartorius SMR balance.

Materials.— γ -Butyrolactone (Eastman Kodak Co. white label) and δ -valerolactone (Union Carbide Chemicals Co.) were purified by distillation *in vacuo* and stored at -4° until used. The hydroxylamine hydrochloride (Allied Chemical Co.) was recrystallized slowly from methanol-water and stored *in vacuo* and the imidazole (Eastman Kodak Co. white label) was dried in a vacuum desiccator before use. The D_2O employed (du Pont Chemical Co., Savannah River Plant) was 99.7% pure.

Stock Solutions.—For the development of the hydroxamate ferric ion complex, the stock hydrochloric acid solution

Soc., **81**, 2347 (1959) and not all reactions characterized by a proton step actually do exhibit a solvent deuterium isotope effect (see, for example, the data of ref. 7).

(10) For estimation of the effect of deuterium solvent isotope effects on rates and dissociation constants see R. P. Bell "General Acid Base Catalysis," Oxford University Press, New York, N. Y., 1940, and "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y. 1959, p. 188, as well as ref. 18 and 19.

(11) A. W. Scott and B. L. Wood, *J. Org. Chem.*, **7**, 508 (1942).

(12) W. P. Jencks, *J. Am. Chem. Soc.*, **80**, 4581 and 5485 (1958).

(13) E. R. Garrett, *ibid.*, **79**, 3401 (1957).

(14) T. C. Bruice and T. H. Fife, *J. Am. Chem. Soc.*, **83**, 1124 (1961).

was 3 *N* and the ferric chloride solution was 5% ferric chloride in 0.1 *N* hydrochloric acid. The aqueous stock hydroxylamine solution was prepared by neutralizing a 28% hydroxylamine solution (w./v.) with an equal volume of 14% sodium hydroxide solution (w./v.). This solution was buffered with an equal volume of a solution made by mixing 4 parts of 0.1 *M* sodium acetate solution and 1 part of 0.1 *M* acetic acid. The resulting stock hydroxylamine solution was usable for over a week if kept under refrigeration.

Kinetic Measurements.—All experiments were carried out in aqueous solutions adjusted to a calculated ionic strength of 1.0 *M* with KCl. The hydroxylamine and imidazole served as their own buffers in the pH range employed. The buffering capacity of all solutions was great enough to assure against pH drift during the studies. The concentration of hydroxylamine was sufficiently large, as compared to lactone, so that pseudo-first-order kinetics were always obtained. The pH of each kinetic run was routinely determined at 0 and ∞ time.

Imidazole Catalyzed Lactone Hydrolysis at 78°.—The hydrolysis of approximately 0.02 *M* solutions of lactone were followed at two pH's (6.45 and 6.83) and at two imidazole concentrations (0.5 *M* and 1.0 *M*) at each pH. The kinetic procedure employed was a modification of that of Lippmann and Tuttle.¹⁵ One-ml. aliquots of the aqueous lactone-imidazole solution were pipetted into 15 × 135 mm. screw-cap (neoprene lined) Pyrex vials. The tightly capped vials were thermostated at 78°. To determine lactone concentration at the desired time intervals, tubes were periodically removed from the 78° bath and quenched in an ice-bath. Two ml. of the buffered hydroxylamine stock-solution was introduced and the tube heated at 100° for 1 hour (to prevent evaporation of the water solvent the tubes were capped with marbles). The hydroxamic acid ferric ion complex was then developed by introducing to the cooled solution 1 ml. each of the stock hydrochloric acid and ferric chloride solutions. The absorbance was measured at 540 m μ . The reactions were followed to 50% of completion with a minimum of ten points (tubes). The pseudo-first-order constants (k_{obs}) were obtained from the slope of the plot of $\log [O.D._t/O.D._\infty]$ against time. The catalytic constants for imidazole were obtained by plotting $k_{obs}-k_w$ (where k_w is the solvolytic constant in the absence of imidazole) against $IM_T (K_a/(K_a + a_H))$.

Hydroxylaminolysis of Lactones.—One-ml. aliquots of the aqueous lactone (0.01–0.02 *M*) hydroxylamine solution were pipetted into screw-cap vials (*vide supra*) which were thermostated at 30° ($\pm 0.01^\circ$). For the general base catalysis studies the imidazole (0.20–1.20 *M*) was included in the hydroxylamine (0.40–0.80 *M*) solution. Tubes were withdrawn from the water bath at appropriate time inter-

(15) F. Lippmann and I. C. Tuttle, *J. Biol. Chem.*, **159**, 21 (1945).

vals and quenched by the addition of 2 ml. of 3 *N* HCl. The hydroxamate ferric ion complex color developed instantly on addition of 2 ml. of the stock ferric chloride solution and the absorbance was determined spectrophotometrically as before. The hydroxylaminolysis reactions were followed to 75% completion employing 12–13 readings (tubes) plus final readings in duplicate. The pseudo-first-order rate constants (k_{obs}) were obtained by plotting $\log [O.D._\infty/O.D._t - O.D._t]$ vs. time. Precise first-order plots were invariably obtained.

D₂O Solvent Kinetic Isotope Effect.—The rates of hydroxylaminolysis of δ -valerolactone were determined in D₂O by the same procedure followed above, taking care that all solutions remained anhydrous. In the determination of a_D the glass electrode correction formula of Fife and Bruce¹⁶ was employed. The ion product of deuterium oxide at 30° was calculated to be 0.224×10^{-14} from the values $K_{D_2O} = 0.154 \times 10^{-14}$ (25°),¹⁷ $K_w = 1.47 \times 10^{-14}$ (30°)¹⁸ and $K_w = 1.008 \times 10^{-14}$ (25°)¹⁸ by assuming that the change in K_{D_2O} from 25 to 30° is proportional to the change in K_w from 25 to 30°.

pK Determinations.—The pK's of hydroxylamine and imidazole were determined by the method of half-neutralization and serial dilution maintaining a calculated ionic strength of 1.0 *M* (KCl) at 30°. The apparent pK_a' values did not change on dilution. Using the determined values of pK_a' it was possible to calculate accurately (± 0.02 pH unit) the desired composition of all reaction solutions. Thus, final adjustment of reaction solutions to the desired pH was not necessary. The pK_a' of hydroxylamine in D₂O agreed with the value predicted from the equation of Li¹⁹ within 0.05 pK unit; see Table I for the determined dissociation constants.

While the pK₂' values for H₂NOH in H₂O and D₂O are too large to be determined with any accuracy by the half-neutralization technique,²⁰ they were shown to be far beyond the range of pH employed in this study. Thus, the species H₂NO⁺ could only be present in trace amounts.

Acknowledgments.—This work was supported by grants from the National Science Foundation and the National Institutes of Health. We wish to thank Professor F. A. Long for stimulating discussions.

(16) T. H. Fife and T. C. Bruce, *J. Phys. Chem.*, **65**, 1079 (1961).

(17) R. W. Kingerley and V. K. LaMer, *J. Am. Chem. Soc.*, **63**, 3276 (1941).

(18) H. S. Harned and R. A. Robinson, *Trans. Faraday Soc.*, **36**, 973 (1940).

(19) N. C. Li, Abstract of paper presented to the A. C. S. Meeting in St. Louis, Mo., March 21–30, 1961, Division of Phys. Chem., Paper 14.

(20) P. Ballinger and F. A. Long, *J. Am. Chem. Soc.*, **81**, 1050 (1959).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE GEORGE WASHINGTON UNIVERSITY, N.W. WASHINGTON, D. C.]

The Interrelation of Reaction and Substituent Constants and the Role of Electronegativity in Linear Free Energy or Enthalpy Relationships

BY W. F. SAGER AND CALVIN D. RITCHIE

RECEIVED SEPTEMBER 14, 1960

An equation is derived relating the reaction constant ρ with the substituent constants of the groups involved in reactions which are not complicated by variable resonance or steric interactions. The relationship between electronegativity and substituent constants is discussed. Application of the equation is made to the linear free energy relationships of Grunwald and Winstein and of Swain and Scott, as well as to reactions involving ambident groups.

In recent years, increasing progress has been made toward solving the troublesome problem of separating the interlocking factors which govern reaction rates and equilibria. The Hammett equation, which allows the separation of steric and other factors within aromatic series, has had a major influence on the development of structure-reactivity correlations.¹ Extended insight has been gained from the

work of Taft, who, by separation of polar and steric factors, was able to show the existence of linear free energy relationships in the aliphatic series.²

(1) L. P. Hammett, *Chem. Revs.*, **17**, 125 (1935); H. H. Jaffé, *ibid.*, **53**, 191 (1953).

(2) For a recent review of the development and applicability of the Taft equation, see R. W. Taft, Jr., in M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1959, p. 556 ff.