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Catalysis of the Hydrolysis of Ethyl Glycinate by Divalent Transition Metal Ions

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The rate of hydrolysis of ethyl glycinate in the presence of cobalt(II), nickel(II), and zinc(II) was determined in 1.0 M sodium perchlorate at 30° in the pH region of 6–7. Stability constants for all major complexes were calculated. The rate law observed is: rate $= k_{OH}[ME][OH^-] + k_{HOH}[ME][HOH]$, where [ME] represents the concentration of the 1:1 metal:ester complex and k_{OH} and k_{HOH} represent the rate constants for hydrolysis by hydroxide ion and water, respectively. No complexes of the form M(OH)E were detected and none of this type is required to explain the observed rate data. The magnitude of k_{OH} is observed to be of about 10^9 that of k_{HOH}.

The metal ion catalysis of the hydrolysis of ethyl glycinate has already been examined most thoroughly for the case of catalysis by copper(II). The present work was undertaken to provide more precise data on the catalysis of this reaction by other divalent first-row transition ions. The information collected includes the stability constants for the complexes of nickel(II), zinc(II), and cobalt(II) with ethyl glycinate, rate measurements on the catalyzed hydrolysis in the presence of these ions, and the manner in which these rates vary with pH. The basic problems whose solutions were sought involve the nature of the attacking species in the hydrolysis reaction (*i.e.*, H_2O or OH^-), the relationship between the stability constants and the rates, and the relative importance of the various complexes as routes for the catalytic reaction.

Some of the previous literature on this type of reaction has been summarized.[1,2] The principal factor which we have sought to evaluate is the relative importance of partially hydrolyzed metal ions, that is, species such as $M(OH)^+$, as catalysts, which have been utilized previously in mechanisms of the copper(II) catalysis of this reaction.[1]

Experimental Section

Reagents.—The metal perchlorates used were obtained from G. Frederick Smith Chemical Co. as the hexahydrates. Qualitative analysis by paper chromatography[3] showed less than 1% contamination by other metal ions; therefore, the salts were used without further purification. The ethyl glycinate was obtained as the hydrochloride from Nutritional Biochemicals Corp. All other reagents as well as solvents were of ACS reagent grade. All solutions of these reagents were standardized by analysis.

Preparation of Ethyl Glycinate Solution.—Ethyl glycinate hydrochloride was slurried in chloroform cooled by an ice bath. Anhydrous sodium sulfate powder was added to absorb water. Approximately 95% of the calculated equivalent of 50% sodium hydroxide was then slowly added to the slurry to liberate the ethyl glycinate. An excess of base was avoided in order to prevent base-catalyzed hydrolysis or polymerization of the ester. The water–salt residue which formed was filtered from the chloroform solution. The ethyl glycinate was then extracted from the chloroform into a slight excess of 2.0 M perchloric acid; the solution was adjusted to pH 3.5–4.0 and then diluted to the desired concentration with distilled water and standardized by titration with base. No free halide could be detected in this solution by addition of silver nitrate. This solution was stored under refrigeration and observed to maintain its titer for over 1 month. The pK_a of ethyl glycinate in 1.00 M sodium perchlorate was found to be 7.657 ± 0.010 from the titration curve.

Instrumentation and Procedures.—A Radiometer titrator with scale expander was used as a pH meter for obtaining the stability constant data. The potentiometric method of Bjerrum[4] was used to determine the stability constants of the various metal–ester complexes. For these titrations 5.00 ml of 0.100 M metal perchlorate and 10.00 ml of 0.428 M ethyl glycinate solution were placed in 100.0 ml of 1.00 M sodium perchlorate in the reaction vessel. A solution pH of about 3.0 resulted. Standard sodium hydroxide was then added in increments, and the resulting pH curve was determined to about pH 6.5–7.0. In order that hydrolysis would be minimized, these titrations were carried out as rapidly as possible while still maintaining good technique.

The titrator with scale expander, titrigraph, and syringe buret unit was used as a pH stat for obtaining the hydrolysis rate data. The method of Connor[1] was used to determine the rate constants for hydrolysis in the metal–ester systems. Hydrolysis of the free ester was neglected since it is negligibly slow under the conditions of these experiments. The hydrolysis medium consisted of varied amounts (5.00–10.00 ml) of 0.100 M metal perchlorate and varied amounts (1.00–10.00 ml) of 0.884 M ethyl glycinate solution placed with 100.0 ml of 1.00 M sodium perchlorate in the reaction vessel. The pH was then adjusted to the desired value with 0.1 N sodium hydroxide. The titrigraph was then activated. As the ester hydrolyzed, ethanol and glycine were produced. In order to maintain a constant pH, the titrigraph automatically added 0.100 N base to neutralize the liberated acid while plotting the amount of base added *vs.* time on the recorder. Thus, plots of glycine produced, or equivalently ester hydrolyzed, were obtained which were used to obtain the kinetic data.

The pH region between 6 and 7 was found to be the most ideal for investigation. The hydrolyses became too slow to follow accurately by this method below about pH 6 while metal hydroxide precipitation limited investigation above pH 7.0.

All reactions were followed in a thermostated beaker maintained at 30.00 ± 0.02°.

Results

Calculations.—All experimental data were handled by an IBM computer. Stability constants were calculated by a nonlinear least-squares program written by the author.[5] Linear, quadratic, and cubic equations were fitted to the data to obtain theoretical stability constants assuming formation of, respectively, 1:1,

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[1] W. A. Connor, M. M. Jones, and D. L. Tuleen, *Inorg. Chem.*, **4**, 1129 (1965).

[2] H. L. Conley, Jr., and R. B. Martin, *J. Phys. Chem.*, **69**, 2914, 2923 (1965).

[3] S. V. Vaeck, *Anal. Chim. Acta*, **10**, 48 (1954).

[4] J. Bjerrum, "Metal Ammine Formation in Aqueous Solutions," P. Haase and Son, Copenhagen, 1940.

[5] Details available from J. E. H.

1:1, and 2:1 and 1:1, 2:1, and 3:1 ester to metal complexes. The statistical standard deviations (uncertainties) in all calculated constants were obtained by the method used by Baird.[6] A program was also written to calculate the analytical concentration of all species present in the hydrolysis media. From these calculations, the rate data were treated by standard graphical techniques to obtain rate constants.

Stability Constants of the Metal–Ethyl Glycinate Systems.—The concentration of free ester present in solution, [E], was calculated using

$$[\mathrm{E}] = K_a[\mathrm{HE}^+]/[\mathrm{H}^+] = K_a([\mathrm{E}]_\mathrm{T} - [\mathrm{B}])/[\mathrm{H}^+] \qquad (1)$$

where [HE$^+$], the concentration of protonated ester, is equal to the difference between the total ester present, $[\mathrm{E}]_\mathrm{T}$, and the amount of base added, [B]. The amount of base added is corrected for the excess amount of free acid present in the initial solution. Since the K_a of ethyl glycinate is less than 10^{-7}, all ester present in solution initially is protonated. The quantity [H$^+$] represents the hydrogen ion concentration corresponding to [B]. The ratio of the concentrations of coordinated ester, $[\mathrm{E}]_\mathrm{c}$, to total metal, $[\mathrm{M}]_\mathrm{T}$, defined by Bjerrum[4] as $\bar{n}$, was calculated from

$$\bar{n} = [\mathrm{E}]_\mathrm{c}/[\mathrm{M}]_\mathrm{T} = ([\mathrm{B}] - [\mathrm{E}])/[\mathrm{M}]_\mathrm{T} \qquad (2)$$

where $[\mathrm{E}]_\mathrm{c}$ is the difference between the amount of free ester produced by the added base, [B], and the free ester present in solution, [E], from eq 1. A sample run is summarized in Figures 1 and 2.

Owing to the protonic equilibrium of the ligand, the $\bar{n}$ values obtained in the calculations were never as large as 1.0 and rarely as high as 0.5. Although one could calculate stability constants for as many complexes as desired, the small maximum $\bar{n}$ values led to a large uncertainty in the calculated stability constants if more than two complexes are considered. Therefore, only the first two stability constants were calculated. A theoretical $\bar{n}$ curve calculated using the obtained constants is shown compared with the experimental $\bar{n}$ values in Figure 2. The stability constants are collected in Table I.

In the above calculations, metal hydroxide complexes were neglected since at the pH values involved less than 1% of the total metal ions is present as the hydroxide.[7]

The deviations indicated in Table I illustrate the reproducibility of the data and the degree with which the constants fit the experimental data. However, since hydrolysis is proceeding at a finite rate while the data are being collected, the actual uncertainty in the constants is somewhat greater. Thus, the fact that in the case of Zn(II) the calculated value of K_2 is greater than the calculated value of K_1 is not unreasonable but only indicates that both constants are of the same relative magnitude.

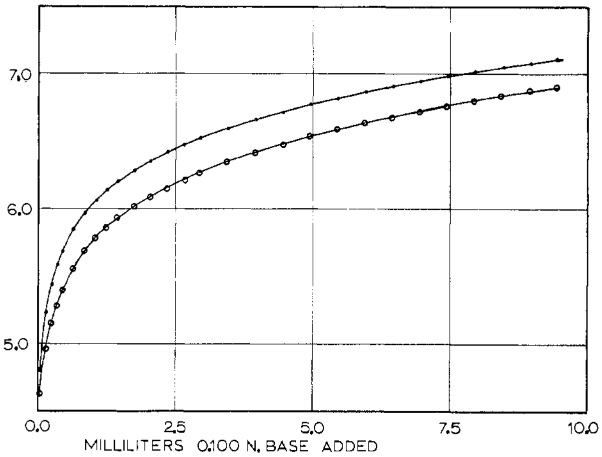

Figure 1.—Sample titration curves for ethyl glycinate with (○) and without (●) metal ions present. In this case nickel(II) was used. See text for species concentrations.

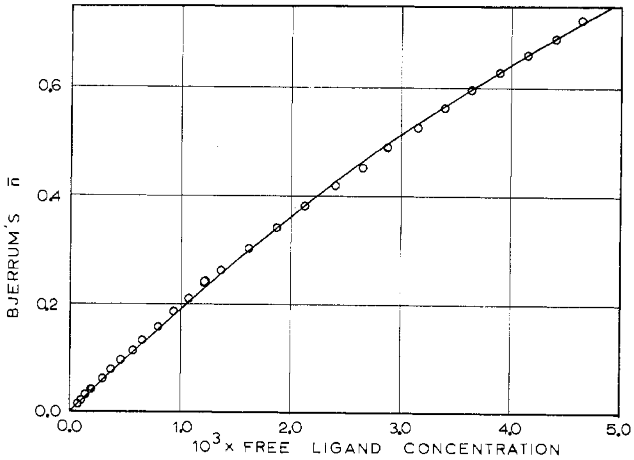

Figure 2.—Comparison between experimental values of Bjerrum's $\bar{n}$ (○) and the calculated values (line), using the equilibrium constants obtained for nickel(II) with ethyl glycinate. See text for species concentrations.

Table I

Stability Constants of Metal Complexes with Ethyl Glycinate 30° [a]

Metal	K_1, M^{-1}	K_2, M^{-1}
Ni^{2+}	198 ± 5	84 ± 5
Co^{2+}	26.8 ± 1.3	15 ± 4
Zn^{2+}	62.0 ± 2.5	79 ± 7

[a] Ionic strength = 1.0; $[\mathrm{M}^{2+}] = 5 \times 10^{-3}\ M$; $[\mathrm{E}]_\mathrm{T} = 4 \times 10^{-2}\ M$; pH region 4–6.5.

Rate Constants for the Metal-Catalyzed Hydrolysis.—The hydrolysis was followed to about 60% completion in most cases (slow reactions to about 30%). Beyond 1 half-life, the presence of glycine, which also complexes with the metal ions, complicates the calculations to a degree that the data become difficult to interpret. The hydrolysis of the ester is not only catalyzed by the presence of metal ions but is also catalyzed at a different rate by the metal complex with glycine.

As in the case of Connor,[1] the reaction was found to approximate pseudo first order in total ester, and the corresponding over-all rate constant was calculated from the first part of the hydrolysis curve using the

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[6] D. C. Baird, "Experimentation: An Introduction to Measurement Theory and Experiment Design," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1962, p 187.

[7] $K_{\mathrm{NiOH}^+} = 4 \times 10^4$, $K_{\mathrm{CoOH}^+} = 1.2 \times 10^6$, $K_{\mathrm{ZnOH}^+} = 2 \times 10^5$: S. Chaberek, Jr., R. C. Courtney, and A. E. Martell, *J. Am. Chem. Soc.*, **74**, 5057 (1952).

limiting slope. These constants k_{TE} are tabulated in Table II. A sample plot is illustrated in Figure 3.

TABLE II

PSEUDO-FIRST-ORDER RATE CONSTANTS WITH RESPECT TO TOTAL ESTER (k_{TE}) AND 1:1 METAL:ESTER COMPLEX (k_{ME}) AT 30° [a]

pH	$10^3[E]_T$, *M*	$10^3[M]_T$, *M*	$10^5 k_{TE}$, sec^{-1}	$10^4 k_{ME}$, sec^{-1}
		Nickel(II)		
7.10	7.96	9.01	15.5	7.02
7.00	7.96	9.01	11.3	5.72
6.80	7.96	9.01	6.44	4.20
6.60	7.96	9.01	4.51	4.01
6.20	7.96	9.01	0.612	2.97
5.40	7.96	9.01	0.0142	1.48
6.50	38.4	8.70	2.36	3.55
6.50	40.2	4.55	1.07	3.05
6.50	7.96	90.1	16.8	3.27
		Cobalt(II)		
7.00	7.96	9.01	5.90	14.8
6.90	7.96	9.01	4.13	12.4
6.80	7.96	9.01	3.04	11.0
6.60	7.96	9.01	1.36	7.26
5.50	7.96	9.01	0.0943	5.67
6.50	7.96	90.1	9.02	6.72
		Zinc(II)		
6.58	7.96	9.01	5.18	13.3
6.50	7.96	9.01	3.62	10.7
6.26	7.96	9.01	1.75	8.48
6.15	7.96	9.01	1.19	7.33
6.00	7.96	9.01	0.714	6.09
5.50	7.96	90.1	2.12	5.72

[a] $[E]_T$ = total ester concentration; $[M]_T$ = total metal concentration; ionic strength ≅ 1.00.

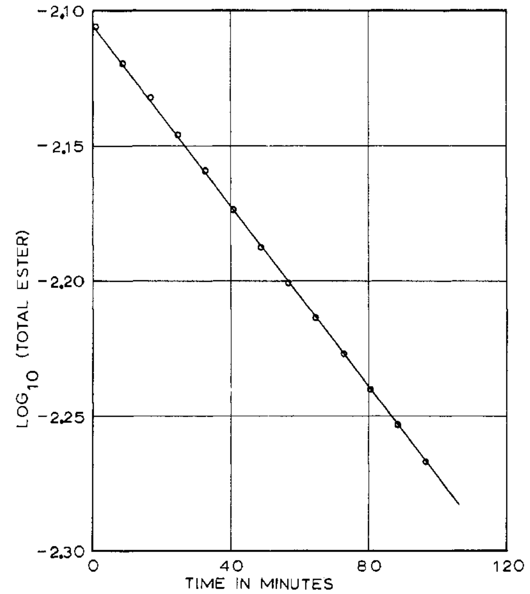

Figure 3.—Pseudo-first-order rate plot for the hydrolysis of ethyl glycinate in the presence of 0.00901 *M* nickel(II) at pH 6.80.

Discussion

At constant pH, the kinetic data are consistent with previously proposed mechanisms in which the principal catalytic route is through a complex which contains one metal ion and one ester.[1,2] First-order rate constants, k_{ME}, were calculated from the experimental over-all constants, k_{TE}, using the expressions

$$\text{rate} = k_{TE}[E]_T = k_{ME}[ME] \tag{3}$$

$$k_{ME} = k_{TE}[E]_T/[ME] \tag{4}$$

where $[E]_T$ represents the total ester concentration and [ME] represents the analytical concentration of the 1:1 metal:ester complex. In calculating the ratio $[E]_T/[ME]$ the following equilibria were considered

$$HE^+ \overset{K_a}{\rightleftarrows} H^+ + E \tag{5}$$

$$M^{2+} + E \overset{K_1}{\rightleftarrows} ME^{2+} \tag{6}$$

$$ME^{2+} + E \overset{K_2}{\rightleftarrows} ME_2^{2+} \tag{7}$$

$$M^{2+} + OH^- \overset{K_{MOH^+}}{\rightleftarrows} MOH^+ \tag{8}$$

$$M^{2+} + G^- \overset{K_{MG^+}}{\rightleftarrows} MG^+ \tag{9}$$

G^- represents free glycinate ion, present as a result of hydrolysis. K_{MOH^+} and K_{MG^+} were obtained from the literature.[7,8] The derived rate constants are listed in Table II.

The pH dependence of the reaction can only be explained by the mechanism of Conley[2] which corresponds to a competition between the two reactions

$$ME^{2+} + OH^- \xrightarrow{k_{OH^+}} MG^+ + HOC_2H_5$$

$$ME^{2+} + HOH \xrightarrow{k_{HOH}} MG^+ + HOC_2H_5 + H^+$$

Thus the rate expression followed is

$$\text{rate} = k_{OH}[ME^{2+}][OH^-] + k_{HOH}[Me^{2+}][HOH] \tag{10}$$

$$\text{rate} = k_{ME}[ME^{2+}] \tag{11}$$

where

$$k_{ME} = k_{OH}[OH^-] + k_{HOH}[HOH] \tag{12}$$

The specific rate constants k_{OH} and k_{HOH} were then obtained by plotting k_{ME} *vs.* hydroxide concentration, as in Figure 4, the slope being k_{OH} and the intercept being $k_{HOH}[HOH]$. These constants are listed in Table III.

No conclusions can be made concerning activity of the 1:2 metal:ester complexes toward hydrolysis since any such activity is masked by the 1:1 complexes present in much greater concentrations. It is strongly evident that the 1:1 complexes are much more susceptible to attack by hydroxide ion than by water. It does appear, however, that the catalytically active species present in the systems studied here are all the 1:1 metal:ester complexes, unlike the 1:1:1 metal:hydroxide:ester complex reported in the case of copper(II) by Connor and Jones.

In spite of the extensive evidence favoring the importance of complexes of the sort $Cu_2(OH)_2L_2$ in copper(II) systems at pH values above 5.5,[9] there is good reason for believing that such complexes are *not* important in any of the systems studied in the present paper.

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(8) $K_{NiG^+} = 5.9 \times 10^5$, $K_{CoG^+} = 4.1 \times 10^4$, $K_{ZnG^+} = 6.3 \times 10^4$: J. Bjerrum, G. Schwarzenbach, and L. G. Sillén, "Stability Constants," Special Publication No. 6, The Chemical Society, London, 1957.

(9) D. D. Perrin and V. S. Sharma, *J. Inorg. Nucl. Chem.*, **28**, 1271 (1966).

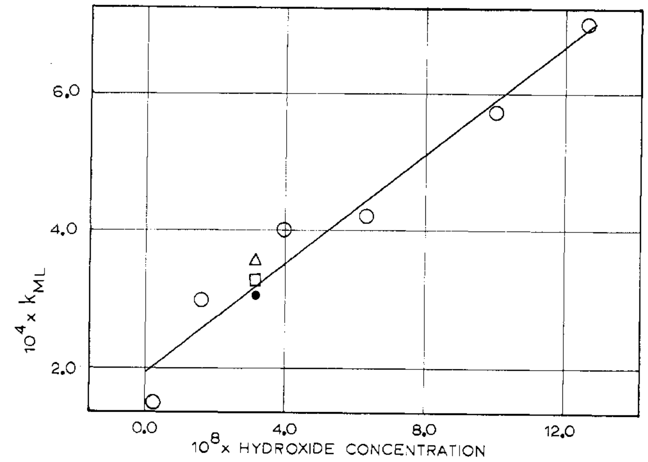

Figure 4.—Plot of pseudo-first-order rate constants with respect to the 1:1 nickel(II):ethyl glycinate complex as a function of hydroxide ion concentration (hydroxide calculated from pH and K_w for water). Initial concentrations of ester and nickel are, respectively: ○, 0.00796, 0.00901 *M;* △, 0.0384, 0.00870 *M;* ●, 0.0402, 0.00455 *M;* and □, 0.00796, 0.0901 *M.*

TABLE III

SPECIFIC RATE CONSTANTS FOR THE NICKEL(II)-, COBALT(II)-, AND ZINC(II)-CATALYZED HYDROLYSIS OF ETHYL GLYCINATE AT 30° (IONIC STRENGTH = 1.0)

Metal	$10^{-4}k_{OH}$, M^{-1} sec^{-1}	10^6k_{HOH}, M^{-1} sec^{-1}
Ni(II)	0.398 ± 0.013	3.5 ± 1.6
Co(II)	0.99 ± 0.11	8.3 ± 1.4
Zn(II)	2.33 ± 0.18	7.07 ± 0.83

The results obtained here are in agreement with the mechanism of Conley and Martin in that the 1:1 metal:ester complex is the principal species undergoing hydrolysis. No complex of the type $[Me(OH)L]_x$ is required to explain the data. Following a suggestion from Martin, the copper(II) data obtained previously in this laboratory was reevaluated and found to be consistent with the mechanism of Conley and Martin. The data obtained under most conditions, especially at low pH, may be explained more readily with this mechanism.

The kinetic constants reported by Conley and Martin[2] ($k_{OH} = 7.64 \times 10^4\ M^{-1}$ sec^{-1} and $k_{HOH} = 0.77 \times 10^{-6}\ M^{-1}$ sec^{-1} using $K_1 = 7400$ for CuE) are of the same order of magnitude as those found for the ions examined in the present work. The rate constants for metal–ester complex attack by hydroxide are of the order Cu(II) ≫ Zn(II) > Co(II) > Ni(II), which is the same order as that found for the stability constants of the 1:1 metal:hydroxide complexes.[7] The order indicates that the same basic factors may be implicated in the determination of both orders. The rate constants for attack by water (Co(II) > Zn(II) > Ni(II) ≫ Cu(II)) vary inversely with the stabilities of the 1:1 metal:ester complexes as determined in the present work.[10]

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[10] Material supplementary to this article has been deposited as Document No. 9045 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington, D. C. 20540 A copy may be secured by citing the document number and by remitting $1.25 for photoprints, or $1.25 for 35-mm microfilm. Advance payment is required. Make checks or money orders payable to: Chief, Photoduplication Service, Library of Congress.

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Rate and Equilibrium Constants for the Formation of the Monooxalate Complex of Iron(III) [1]

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The rate of formation of the monooxalate complex of iron(III) has been studied by the use of flow techniques. The first and second dissociation constants of oxalic acid determined by pH measurements are $8.4 \times 10^{-2}\ M$ and $2.79 \times 10^{-4}\ M$, respectively, at ionic strength 1.0 *M* and 25.0°; and $5.5 \times 10^{-2}\ M$ and $1.58 \times 10^{-4}\ M$, respectively, at ionic strength 3.0 *M* and 25.0°. From spectrophotometric measurements, the stability constant K_1 for the reaction $Fe^{3+} + Ox^{2-} \rightleftharpoons FeOx^+$ is $3.9 \times 10^7\ M^{-1}$ at ionic strength 1.0 *M* and 25.0°; and $5.5 \times 10^7\ M^{-1}$ at ionic strength 3.0 *M* and 25.0°. The results of the kinetic studies are interpreted in terms of the reactions $FeOH^{2+} + HOx^- \underset{k_{2d}}{\overset{k_{2f}}{\rightleftharpoons}} FeOx^+$ and $Fe^{3+} + HOx^- \underset{k_{3d}}{\overset{k_{3f}}{\rightleftharpoons}} FeOx^+ + H^+$. At 25.0° and ionic strength 1.0 *M*, $k_{2f} = 2.0 \times 10^4\ M^{-1}$ sec^{-1}, $k_{3f} = 8.6 \times 10^2\ M^{-1}$ sec^{-1}, $k_{2d} = 3.0 \times 10^{-3}$ sec^{-1}, and $k_{3d} = 7.8 \times 10^{-2}\ M^{-1}$ sec^{-1}. The results are discussed in terms of a model in which loss of the first water molecule coordinated to the iron(III) is the rate-determining step.

The kinetics of formation of complexes of iron(III) with monodentate ligands have been extensively studied.[2-4] These studies have shown that the rate of complex formation is primarily determined by the rate of loss of a water molecule coordinated to the iron(III).

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[1] Research performed under the auspices of the U. S. Atomic Energy Commission.

[2] D. Seewald and N. Sutin, *Inorg. Chem.*, **2**, 643 (1963).

[3] J. F. Below, Jr., R. E. Connick, and C. P. Coppel, *J. Am. Chem. Soc.*, **80**, 2961 (1958).

[4] R. E. Connick and C. P. Coppel, *ibid.*, **81**, 6389 (1959).