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The Copper(II)-Catalyzed Hydrolysis of Ethyl Glycinate¹

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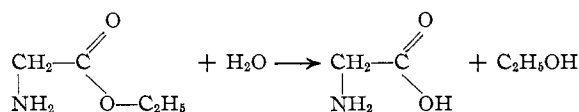
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The rate of hydrolysis of ethyl glycinate was measured in the presence of varying amounts of copper(II) over a pH range of 1 to 6.5 and at temperatures from 20 to 30°. The determination of the stability constants of the copper complexes of ethyl glycinate, carried out over the same range, showed that the principal reactive species was a copper complex containing one ethyl glycinate per copper. The pH dependence of the rate of the catalytic reaction shows a nominal second-order dependence on the hydroxide ion concentration. Combination of the rate and equilibrium data leads to a rate equation of the form

$$\text{rate} = [k_{\text{H}^+}(\text{H}^+)^2 + k_{\text{OH}^-}(\text{OH}^-) + k_{\text{Cu}(\text{OH})\text{E}} K'_{1\text{B}} K_1 (\text{Cu}^{2+})(\text{OH}^-)^2](\text{E})$$

where (E) represents the ethyl glycinate concentration and the subscripts on k refer to the paths whose rates of hydrolysis are described by the respective rate constants. $K'_{1\text{B}} K_1$ is the over-all stability constant of the complex $\text{Cu}(\text{OH})\text{E}$. Evaluation of the temperature variation of the rate constants showed that the reaction path through the basic complex, $\text{Cu}(\text{OH})\text{E}$, has a larger activation energy but also a much larger frequency factor than either the acid- or the base-catalyzed reaction.

The fact that the hydrolysis of ethyl glycinate is accelerated by the addition of copper(II) salts was first established by Kroll.² This type of reaction was subsequently studied by a number of investigators from various points of view.³⁻⁷ The purpose of the present work was to investigate some factors not studied in detail by these earlier investigators, specifically (a) the rates of hydrolysis of the various complexed forms of the ester, (b) the effect of temperature on the rate of hydrolysis, and (c) the relative velocities of hydrolysis rates catalyzed by added copper(II), acid, or base. The reaction examined here is



Prior to this work no investigation of the rate of the acid- or base-catalyzed hydrolysis involving variation of temperature or pH has been carried out. In addition, it was hoped that some of the conflicting points of view on the mechanism of this process could be reconciled.

Experimental

Materials.—The ethyl glycinate used was obtained from the Sigma Chemical Co. The copper(II) nitrate, sodium nitrate, and other inorganic reagents used were all of A.C.S. reagent grade, and the solutions prepared from them were standardized by analysis. The titrations and the rate data were obtained by the use of a recording pH-Stat (Radiometer, Inc., Copenhagen). The syringe of this pH-Stat was calibrated in terms of the weight of distilled water it delivered at 25°. The reaction vessel used was a jacketed beaker of about 200-ml. capacity which was

held at the desired temperature by means of water from a constant-temperature bath.

pK_a Values.—The pK_a values for the ethyl glycinate cation were determined using the pH-Stat as a recording titrator. A known weight of purified ethyl glycinate hydrochloride was dissolved in a known volume of thermostated distilled water. This solution was then titrated with 1.000 N sodium hydroxide solution. At the half-way point to the end point, the relationship pH = pK_a was used to obtain the pK_a value.

Results

The results obtained fall into several categories. These include the dissociation constant of ethyl glycinate cation at various temperatures and its rate of hydrolysis in acidic and basic media, the equilibria involving copper(II) and its complexes with ethyl glycinate as well as the hydrolysis of copper(II) under the conditions of the rate studies, and the rates of hydrolysis of ethyl glycinate in the presence of copper(II). These will be considered in that order.

Properties of Ethyl Glycinate.—The acid dissociation constant of ethyl glycinate cation was determined over the temperature range 20 to 45° by the titrimetric method using the Radiometer pH-Stat. Each of the values given is the average of three or more separate determinations, and the variation of the pK_a value at a given temperature was always 0.05 or less. The values obtained are

T, °C.	20	25	30	35	40	45
pK _a	7.84	7.75	7.65	7.56	7.48	7.38

From a plot of log K_a vs. 1/T, ΔH° for this reaction was found to be 7.60 kcal./mole and at 25° ΔF° = 10.57 kcal./mole and ΔS° = -9.96 e.u.

The rate of hydrolysis of ethyl glycinate in the presence of both acid and base was determined by a method essentially the same as that described by Bell.⁸ The reaction is first order in gross ester or ester cation in each case as was found by earlier workers. The determination of the pseudo-first-order rate constants as a function of pH was carried out with the results shown in Table I. The ionic strength in these, as well

(1) This research was supported by the U. S. Public Health Service through Grant No. GM-10972. Derived from a thesis submitted by William Anthony Connor in partial fulfillment of the requirements for the Ph.D. degree, Sept. 1964. This thesis, available from University Microfilms, Ann Arbor, Mich., contains detailed information on aspects of this work which has been omitted from this paper for the sake of brevity.

(2) H. Kroll, *J. Am. Chem. Soc.*, **74**, 2036 (1952).

(3) N. C. Li and R. A. Manning, *ibid.*, **77**, 5225 (1955).

(4) J. M. White, R. A. Manning, and N. C. Li, *ibid.*, **78**, 2367 (1956).

(5) M. L. Bender and B. W. Turnquest, *ibid.*, **79**, 1889 (1957).

(6) N. C. Li, Br. E. Doody, and J. M. White, *ibid.*, **79**, 1889 (1957).

(7) R. Mathur and N. C. Li, *ibid.*, **86**, 1289 (1964).

(8) R. P. Bell, *Trans. Faraday Soc.*, **60**, 1087 (1964).

TABLE I
PSEUDO-FIRST-ORDER RATE CONSTANTS FOR THE
HYDROLYSIS OF ETHYL GLYCINATE

(Ionic Strength = 0.1)					
pH	T, °C.	Rate constant, sec. ⁻¹	pH	T, °C.	Rate constant, sec. ⁻¹
0.90	30	3.40×10^{-3}	9.50	4.4	1.26×10^{-6}
1.10	30	2.14×10^{-3}	9.50	25.0	3.89×10^{-5}
1.30	30	1.35×10^{-3}	9.50	35.0	2.14×10^{-4}
1.90	30	3.40×10^{-4}	2.0	20.30	1.19×10^{-4}
9.50	30	8.36×10^{-6}	2.0	26.35	2.19×10^{-4}
10.10	30	3.33×10^{-4}	2.0	31.70	3.00×10^{-4}
10.56	30	9.60×10^{-4}	2.0	45.30	9.22×10^{-4}

as all subsequent studies, was 0.1. From a plot of the logarithm of this rate constant as a function of pH it can be shown that there is a first-order dependence of the acid-catalyzed reaction on the hydrogen ion concentration and a first-order dependence of the base-catalyzed reaction on the hydroxyl ion concentration. When no metal ion is present, the over-all rate can be expressed as

$$\text{rate} = k_{\text{H}^+}(\text{H}^+)(\text{HE}^+) + k_{\text{OH}^-}(\text{OH}^-)(\text{E})$$

From the values of the rate constants obtained for the over-all reaction and from studies at other temperatures, the following values in Table II were obtained for k_{H^+} and k_{OH^-} at various temperatures. These results represent the first systematic study of the temperature dependence of either of these reactions. From the temperature dependence of k_{H^+} and k_{OH^-} the activation energies and entropies were determined for these processes. These were $E = 15.2$ kcal./mole and $\Delta S^* = +20.1$ e.u. for the acid-catalyzed reaction and $E = 18$ kcal./mole and $\Delta S^* = -2.3$ e.u. for the base-catalyzed reaction.

TABLE II

T, °C.	k_{H^+} , l. mole ⁻¹ sec. ⁻¹	T, °C.	k_{OH^-} , l. mole ⁻¹ sec. ⁻¹
20.30	1.19×10^{-2}	4.40	0.23
26.35	2.19×10^{-2}	25.00	1.23
31.70	3.00×10^{-2}	30.00	1.80
45.30	9.22×10^{-2}	35.00	3.24

Stability Constants of the Copper(II)-Ethyl Glycinate Complexes.—The stability constants of these complexes were determined by the titrimetric method of Bjerrum.⁹ The reaction vessel contained 200 ml. of 0.1 M sodium nitrate, 10.0 ml. of 0.05004 M copper nitrate solution, and 2.0 ml. of 0.1 M hydrochloric acid. The titrant used was a solution of standardized ethyl glycinate, 2.993 M. The results of such a run at 30° are summarized in Table III. From the \bar{n} , (E) data, the successive stability constants were obtained using an IBM computer and a program obtained from the Share General Program Library, No. 1428 DPE 2135(PA). The results of these calculations are summarized in Table IV. It is probable that K_1 is accurate to about 0.1 log unit. It must be emphasized that the ligand hydrolysis reaction occurs throughout the titrations

(9) J. Bjerrum, "Metal Ammine Formation in Aqueous Solution," P. Haase and Son, Copenhagen, 1940.

TABLE III
 \bar{n} AND (E) DATA AT 30° OBTAINED BY DIRECT TITRATION
 $C_{\text{H}} = 0.2000$ mequiv.; $(\text{M})_t = 0.5004$ mequiv.

pH	ml. of ligand	(E) _t , mequiv.	\bar{n}	(E), M
5.15	0.0915	0.2739	0.15	2.9×10^{-6}
5.25	0.1036	0.3101	0.22	3.7×10^{-6}
5.35	0.1286	0.3847	0.37	4.7×10^{-6}
5.45	0.1513	0.4526	0.50	5.9×10^{-6}
5.55	0.2118	0.6337	0.86	7.4×10^{-6}
5.65	0.2791	0.8351	1.27	9.3×10^{-6}
5.75	0.3328	0.9958	1.59	11.7×10^{-6}

TABLE IV

LOG K_n VALUES FOR THE SYSTEM Cu(II)-ETHYL
GLYCINATE AT VARIOUS TEMPERATURES

T, °C.	log K_1	log K_2	log K_3
20	4.14	3.29	4.38
25	4.04	3.89	4.80
30	3.99	4.97	4.24
35	3.85	4.31	4.21
40	4.15	4.18	4.01
45	4.78	3.53	4.36

used to determine the stability constants. This reaction makes K_2 and K_3 successively more inaccurate.

The hydrolysis of copper(II) has been studied carefully by Berecki-Biedermann,¹⁰ who found that the entire course of the reaction could be accounted for if the only product of hydrolysis contained Cu^{2+} and OH^- in a 1:1 ratio and had the composition $\text{Cu}_2(\text{OH})_2^{2+}$. We have accordingly assumed that no species with a lower $\text{Cu}^{2+}:\text{OH}^-$ ratio are formed under the conditions used in these studies. The percentage of the total copper(II) which is tied up in this form during the kinetic studies is rather small. At a pH of 4 it can be estimated to be much less than 1% by the use of the equilibrium constants of Berecki-Biedermann, even if one assumes that the ethyl glycinate does not form any complex.

Rate Constants for the Hydrolysis.—The rate constants were determined in a medium containing 200 ml. of 0.1 M sodium nitrate, 25 ml. of 0.100 M ethyl glycinate, and, for most of the runs, 25 ml. of 0.0500 M copper(II) nitrate. The pH was adjusted to the desired value by the addition of 1.000 M sodium hydroxide. The volume of base corresponding to the complete hydrolysis of the ethyl glycinate added is 2.65 ml. A typical run is summarized in Table V. The data for the initial part of the reaction give a straight line when plotted as a first-order reaction. A point by point calculation of the first-order rate constant showed a variation of about 4% over the first 50% of the reaction. From such runs at various pH values, the variation of the copper-catalyzed reaction with pH was determined. The data obtained at 30° are shown in Table VI. The rate constant given here, k_1' , gives the measured rate when multiplied by the total ester concentrations, $[\text{E}]_t$.

The results obtained at different values of the pH and temperature are shown in Table VII.

The slope of a plot of $\log k_1'$ (the pseudo-first-order

(10) C. Berecki-Biedermann, *Arkiv Kemi*, **9**, 175 (1956).

TABLE V
 TYPICAL KINETIC RUN DATA

Time, min.	40°, pH 5.5, 1.000 M NaOH used as titrant																		
	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36
Hydrolysis, %	...	3.3	7.6	11.8	15.8	19.9	23.4	26.9	30.1	33.1	35.9	38.8	41.2	43.4	45.6	47.7	49.7	51.7	53.4

TABLE VI

 VARIATION OF RATE CONSTANT WITH pH AT 30°
 (Metal present in all cases)

pH	4.0	5.0	5.2	5.4	5.6	5.8
Rate constant, sec. ⁻¹ × 10 ⁶	0.60	8.1	16	66	110	270

rate constant) vs. the pH was determined at these temperatures and is approximately 2, with a range from 2.3 at 20° to 1.6 at 45°.

Here G stands for glycine, the product of the hydrolysis. The catalytically active species is the complex, Cu(OH)E⁺, which is attacked by hydroxide ion.

Employing these equations, the rate of hydrolysis may be expressed

$$\text{rate} = k_{\text{Cu(OH)E}}[\text{Cu(OH)E}^+][\text{OH}^-] \quad (5)$$

OR

$$\text{rate} = k_{\text{Cu(OH)E}}K_{1B}K_1[\text{Cu}^{2+}][\text{E}][\text{OH}^-]^2 \quad (6)$$

TABLE VII

 k_1' VALUES AS A FUNCTION OF TEMPERATURE AT CONSTANT pH^a

T, °C.	k_1' values, sec. ⁻¹				
	4.0	4.5	5.0	5.5	6.0
20	1.56×10^{-10}	6.36×10^{-9}	2.61×10^{-7}	1.07×10^{-5}	4.39×10^{-4}
25	4.63×10^{-8}	4.69×10^{-7}	4.91×10^{-6}	5.06×10^{-5}	5.21×10^{-4}
30	1.32×10^{-7}	1.06×10^{-6}	8.46×10^{-6}	6.80×10^{-5}	5.45×10^{-4}
35	1.24×10^{-6}	6.23×10^{-6}	3.13×10^{-5}	1.08×10^{-4}	7.93×10^{-4}
38	5.90×10^{-7}	3.61×10^{-6}	2.21×10^{-5}	1.36×10^{-4}	8.31×10^{-4}
40	2.70×10^{-6}	1.33×10^{-6}	6.63×10^{-5}	3.58×10^{-4}	1.63×10^{-3}
45	4.26×10^{-6}	2.61×10^{-5}	1.62×10^{-4}	9.95×10^{-4}	6.30×10^{-3}

^a Initial solution conditions: 200.0 ml. of 0.1 M sodium nitrate solution, 25.0 ml. of 0.05004 M metal solution, 25.0 ml. of 0.1007 M ester solution; titrant = 0.100 M sodium hydroxide.

In addition, the variation of the pseudo-first-order rate constants with varying metal ion concentrations was determined at three different pH values. These are listed in Table VIII.

TABLE VIII

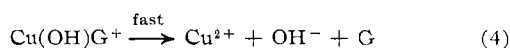
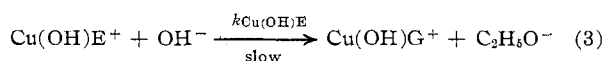
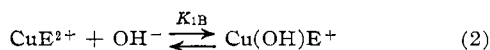
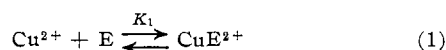
RATE CONSTANTS FOR VARYING METAL CONCENTRATIONS AT 30°

 $(\text{E})_t = 1.007 \times 10^{-2} M$

(M) _t × 10 ³ M	10 ⁶ k_1' , sec. ⁻¹		
	pH 5.00	pH 5.25	pH 5.50
1.988	0.387	1.92	9.48
3.975	0.790	5.18	13.9
5.963	1.82	8.15	25.8
7.950	2.03	10.7	31.0
9.375	2.88	13.2	35.7
11.925	3.32	15.4	42.5

Discussion

A careful consideration of the results compiled in Table VIII, together with the variations in concentration of catalytically active species with temperature, indicate that the gross rate of the copper(II)-catalyzed hydrolysis exhibits a second-order dependence on hydroxide ion concentration. The data are reasonably explained by a mechanistic scheme involving eq. 1-4, in which eq. 3 represents the rate-determining step.



as, from eq. 2 and 1

$$[\text{Cu(OH)E}^+] = K_{1B}[\text{CuE}^{2+}][\text{OH}^-] \quad (7)$$

and

$$[\text{CuE}^{2+}] = K_1[\text{Cu}^{2+}][\text{E}] \quad (8)$$

As a test of this mechanism, one can initially equate the over-all rate to a series of terms which involve the possible reaction with CuE²⁺ as well as the acid- and base-catalyzed reactions of the free ligand and the reaction of Cu(OH)E⁺

$$\text{rate} = k_{\text{H}^+}[\text{H}^+][\text{HE}^+] + k_{\text{OH}^-}[\text{OH}^-][\text{E}] + k_{\text{CuE}}[\text{CuE}^{2+}][\text{OH}^-] + k_{\text{Cu(OH)E}}[\text{Cu(OH)E}^+][\text{OH}^-] \quad (9)$$

From a knowledge of the first two terms of eq. 9, it is possible to subtract out their contribution to the total rate in a given reaction mixture. If the portion of the rate which is due only to the metal-catalyzed processes is designated as $k'_{1\text{cor}}[\text{E}]_t$ where $[\text{E}]_t$ is the total ester concentration, then

$$k'_{1\text{cor}} = \frac{k'_{1[\text{E}]_t} - k_{\text{H}^+}[\text{H}^+][\text{HE}^+] - k_{\text{OH}^-}[\text{OH}^-][\text{E}]}{[\text{E}]_t} \quad (10)$$

Also

$$k'_{1\text{bor}}[\text{E}]_t = k_{\text{CuE}}[\text{CuE}^{2+}][\text{OH}^-] + k_{\text{Cu(OH)E}}K_{1B}[\text{CuE}^{2+}][\text{OH}^-]^2 \quad (11)$$

$$k'_{1\text{cor}}[\text{E}]_t = [\text{CuE}^{2+}]\{k_{\text{CuE}}[\text{OH}^-] + k_{\text{Cu(OH)E}}K_{1B}[\text{OH}^-]^2\} \quad (12)$$

If both sides are divided by $[\text{OH}^-]$, the resultant equation is

$$\frac{k'_1 \text{ cor } [\text{E}]_t}{[\text{OH}^-]} = [\text{CuE}] \{ k_{\text{CuE}} + k_{\text{Cu(OH)E}} K_{1B} [\text{OH}^-] \} \quad (13)$$

Since all the terms on the left-hand side are known, and $[\text{CuE}]$ can be calculated from the measured stability constants, a plot of the left-hand side as ordinate and $[\text{CuE}]$ as abscissa should be a straight line of slope $\{ k_{\text{CuE}} + k_{\text{Cu(OH)E}} K_{1B} [\text{OH}^-] \}$ and intercept zero. A plot of this sort gives a reasonably straight line of very small or zero intercept. From plots of this sort at three different values of the pH, the slopes obtained are

pH	5.00	5.25	5.50
Slope	1.92×10^5	4.93×10^5	5.79×10^5

We can then proceed to plot this slope as ordinate and the hydroxide ion concentration as abscissa. If our analysis is correct, this should give a straight line with zero as intercept and $k_{\text{Cu(OH)E}} K_{1B}$ as slope. From such a plot the factor $k_{\text{Cu(OH)E}} K_{1B}$ is found to be 1.24×10^{-14} . From data on a wide variety of very closely related systems, K_{1B} was estimated to be 1.62×10^6 at 30° .¹

The important points which can be deduced from such plots are: (1) CuE^{2+} has little or no catalytic activity as shown by the intercept of plots of the first type and (2) Cu(OH)E^+ is the catalytically active complex in the copper(II)-catalyzed hydrolysis of ethyl glycinate under the conditions utilized. The rate constants for these species are obtained from these plots as $k_{\text{Cu(OH)E}} = 7.41 \times 10^7 \text{ l. mole}^{-1} \text{ sec.}^{-1}$ and $k_{\text{CuE}} \approx 0$. The slope of a plot of $k_{\text{Cu(OH)E}}$ vs. pH is found to be 1.05. This is what would be expected for a reaction in which a hydroxide ion attacked the basic complex, Cu(OH)E , in the rate-determining step. The variation of the over-all rates with temperature, given earlier, was then broken down making use of the rate expression

$$\text{rate} = k_{\text{H}^+}(\text{H}^+)(\text{H}^+\text{E}) + k_{\text{OH}^-}(\text{OH}^-)(\text{E}) + k_{\text{Cu(OH)E}}[(\text{Cu(OH)E})(\text{OH}^-)] \quad (14)$$

and the variation in $k_{\text{Cu(OH)E}}$ with temperature was obtained. Two sets of temperature-dependent rate constants were obtained, that of the over-all rate constant k'_1 and that of $k_{\text{Cu(OH)E}}$. From the variation of k'_1 with temperature an apparent activation energy of 21 kcal./mole and an entropy of activation of -10.8 e.u. were obtained. The value of $k_{\text{Cu(OH)E}}$ could be obtained only when some additional assumptions were invoked. Over the pH range of 4.0 to 6.0, the over-all rate has only negligible contributions from either the acid- or the base-catalyzed reactions. Under such circumstances

$$k'_1(\text{E})_t \approx k_{\text{Cu(OH)E}} [\text{Cu(OH)E}] [\text{OH}^-] \quad (15)$$

so

$$k'_1 \approx k_{\text{Cu(OH)E}} K_{1B} \left[\frac{[\text{CuE}][\text{OH}^-]^2}{[\text{E}]_t} \right] \quad (16)$$

$$\approx A e^{-E_a/RT} e^{-\Delta F^\circ/RT} \left[\frac{[\text{CuE}][\text{OH}^-]^2}{[\text{E}]_t} \right] \quad (17)$$

so

$$\log k'_1 = \log A - \left[\frac{E_a + \Delta F^\circ}{2.303RT} \right] + \log \left[\frac{[\text{CuE}][\text{OH}^-]^2}{[\text{E}]_t} \right] \quad (18)$$

From these equations

$$A' \approx A \left[\frac{[\text{CuE}][\text{OH}^-]^2}{[\text{E}]_t} \right] \quad (19)$$

and

$$E' \cong E_a + \Delta F^\circ \quad (20)$$

For $\Delta F^\circ = -8.61$ kcal./mole, $[\text{E}]_t = 8.33 \times 10^{-3} M$, $[\text{CuE}] = 1.334 \times 10^{-3} M$, and $[\text{OH}^-] = 1.472 \times 10^{-9} M$, one finds $\Delta S^* = 70$ e.u. and $E_a = 29.6$ kcal./mole. These values are certainly both too large and lead to the thought that if k_{CuE} were quite small, but not zero, there might be a significant contribution from such a term. The principal objection to such an argument is that it does not allow the pH dependence of the reaction to be explained. The second-order dependence on hydroxide ion concentration is simply not compatible with such a process. The effectiveness of the copper(II) in promoting this reaction can thus be ascribed to its ability to furnish a complex intermediate which is formed with an extremely favorable entropy change. The rate law reveals only the fact that the transition state has the composition CuE(OH)_2 . It seems very likely that the value of ΔS^* obtained here is much too high.¹¹ The basic problem involved here is the difficulty of obtaining reliable estimates of the stability constants of a complex which is concurrently undergoing a rather rapid reaction. Thus, attempts to detect the presence of complexes of the type $\text{Cu}_2\text{E}_2(\text{OH})_2$ were unsuccessful because the ligand was hydrolyzed completely before the titration could be completed. This prevented an evaluation of a mechanism proceeding through a complex such as $\text{Cu}_2\text{E}_2(\text{OH})_2$, which would also have the required dependence on $[\text{OH}^-]$. Such a mechanism would not have the required dependence on $[\text{E}]$, however, unless the hydrolysis rates of the two coordinated esters were different.

The mechanism for the copper(II)-catalyzed hydrolysis of ethyl glycinate which seems most consistent with the data is depicted in path B of Figure 1. The interaction of the carbonyl oxygen with the copper is a transient one.¹² This route clearly should exhibit a second-order dependence on hydroxide ion concentration, whether addition of OH^- or loss of $\text{C}_2\text{H}_5\text{O}^-$ is rate determining. Both of the potential hydrolysis routes of Figure 1 are similar in many respects to those

(11) L. L. Schaleger and F. A. Long, *Advan. Phys. Org. Chem.*, **1**, 23 (1963).

(12) M. P. Springer and C. Curran, *Inorg. Chem.*, **2**, 1270 (1963).

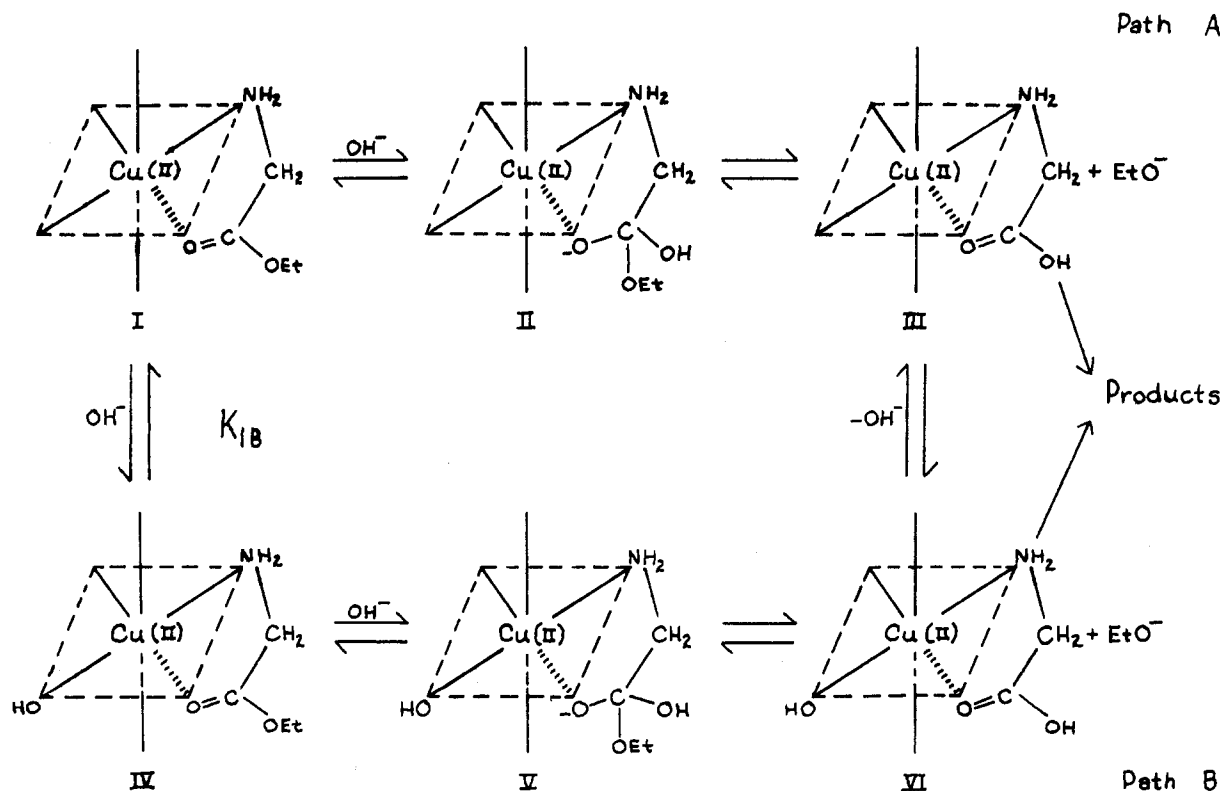


Figure 1.—Mechanism proposed for the copper(II)-catalyzed hydrolysis of ethyl glycinate near pH 5.

of Bender and Turnquest,⁵ but involve hydroxide ion as the principal attacking species rather than water. Path A of Figure 1 represents the extremely unimportant portion of the hydrolysis of ethyl glycinate which exhibits a first-order dependence on hydroxide ion concentration.

The preponderance of path B over path A in the hydrolysis may reflect the relative ease of departure of

the leaving group, ethoxide ion, from the intermediate structures II and V. Loss of ethoxide ion from II should be much less facile than from V. In II, the complex copper has an effective positive charge of two, whereas in V the charge has been reduced to one by the hydroxide ion ligand. This rationale suggests, but does not demand, that loss of ethoxide ion is the rate-determining step in both paths of hydrolysis.

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Nuclear Magnetic Resonance Spectra of Titanocene Sandwich Compounds^{1a}

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Proton chemical shifts of cyclopentadienyl ring protons in a series of substituted bis(cyclopentadienyl)titanium compounds have been correlated with electronegativities of the ligands on titanium. A similar correlation of ring proton shifts with ligand electronegativities was found for a series of methyl-substituted titanocene halides and titanocene dihalides, and a reverse trend was noted when the chemical shift of the methyl protons was considered in the methyl-substituted series. In a series of substituted diaryltitanocenes the average chemical shift of *ortho* and *meta* protons relative to the chemical shift of a reference (bis(cyclopentadienyl)diphenyltitanium) as well as the chemical shifts of the cyclopentadienyl ring protons give a linear correlation with Taft's inductive and resonance parameters and a satisfactory Hammett line.

Introduction

Nuclear magnetic resonance data are of much value in studies of structure elucidation and molecular electronic

configurations of metallocene compounds as in many other chemical systems. Since very little n.m.r. data has been published on cyclopentadienyl compounds of titanium, and no references were found concerning the n.m.r. spectra of diaryltitanocene derivatives, n.m.r.

(1) (a) Supported by a grant from The National Lead Company; (b) taken from the Ph.D. Thesis of S.A.B., June 1965.