Metal Complex Catalysis of the Base Hydrolysis of Various Amino Acid Esters Coordinated to the Complex of Nitrilotriacetic Acid with Copper(II)

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Abstract: The rates of base hydrolysis of several amino acid esters coordinated to $[Cu(NTA)]^-$ are reported. A comparison of the rates of base hydrolysis of the ethyl esters of α-amino acids, $H_2NCHRCO_2Et$, with those exhibited by the esters coordinated to $[Cu(NTA)]^-$ shows that the steric effect of the group R is the main factor in determining the relative magnitude of the rate constants under both sets of conditions. The ratio of catalyzed to uncatalyzed rates is approximately constant at about 200, whereas the two sets of rate constants vary internally by a factor of 60. $[Cu(NTA)]^-$ catalyzes the hydrolysis of coordinated ethyl β-alaninate and methyl histidinate by factors of 30 and 7, respectively. In these cases interaction of the ester carbonyl group with the copper atom is less likely than with esters of α-amino acids. It is proposed that catalysis of esters of α-amino acids occurs by activation of the carbonyl carbon atom to intermolecular nucleophilic attack of OH^- by transient coordination of the carbonyl oxygen atom to the copper atom. Activation parameters for the base hydrolysis of the complex $[Cu(NTA)NH_2CH_2CO_2Et]^-$ are $\Delta H^* = 4.9$ kcal/mole and $\Delta S^* = -33$ eu. These show that catalysis is due to a substantial lowering of ΔH^*.

The previous part of this work[1] reports equilibrium and stereochemical studies of complexes of $[M(NTA)]^-$ (M = Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Pb(II); NTA = nitrilotriacetate ion) with amino acids and their esters. The present study, using $Cu(NTA)^-$ as catalyst, was done under conditions which considerably simplified analysis of the kinetic results. The hydrolysis reactions were carried out in a pH region where the predominant species was the mono amino acid ester complex of $Cu(NTA)^-$, $[Cu(NTA)(ester)]^-$.

Experimental Section

The materials used are as given previously.[1] The customary abbreviations for the names of amino acids are used in the paper and are given in parentheses as follows: glycine (Gly), α-alanine (Ala), phenylalanine (PhAla), leucine (Leu), valine (Val), β-alanine (β-Ala), and histidine (Hist). The esters of these acids are written as exemplified by the methyl, ethyl, and *n*-butyl esters of glycine (MeGly, EtGly, and BuGly, respectively).

Kinetic Measurements. Rates of reaction were determined with a Radiometer TTT1c titrator and SBR2c titrigraph. The titrigraph plotted per cent volume of an SBU1a syringe buret. The titrator was set for pH-Stat work, and the pH was maintained at the desired value by the addition of an NaOH solution of suitable concentration. The standard 10-ml Radiometer thermostated reaction vessel was maintained at ±0.05° of the desired temperature and nitrogen was bubbled through the 8-ml reaction solution. Radiometer electrodes and the standard stirrer were used.

Reaction solutions, under the following conditions of concentration, were placed in the vessel and thermostated for 15 min.

(1) Hydrolysis of esters: [ester] = 0.0067 *M*, $[KNO_3]$ = 0.05 *M*, and titrating base, [NaOH] = 0.206 *M;* except for the hydrolysis of EtVal in which [EtVal] = 0.067 *M*, $[KNO_3]$ = 0.05 *M*, and [NaOH] = 2.06 *M*.

(2) Hydrolysis of esters in the presence of $Cu(NTA)^-$: $[Cu(NTA)^-]$ = 0.0067 *M*, [ester] = 0.00067 *M*, $[KNO_3]$ = 0.05 *M*, and titrating base, [NaOH] = 0.0187 *M;* except for EtVal and MeHist where [ester] = 0.0067 *M* and [NaOH] = 0.206 *M*.

Ratios of $[Cu(NTA)^-]$:[ester] of 10:1 were generally used to maximize the amount of complexed ester. The pH was raised to the desired value and the reaction followed automatically by the addition of NaOH solution while maintaining the given pH. One obtains a plot of the per cent of the total syringe capacity of NaOH solution delivered *vs.* time. Since the per cent at the end of the reaction ($\%_\infty$) minus the per cent at any time t ($\%_t$) is proportional to the concentration of unreacted ester, the slope of first-order plots of ln ($\%_\infty - \%_t$) *vs.* time, which are linear to at least 90% completion of reaction, yielded pseudo-first-order rate constants, k_{obsd}. For all reactions the values of k_{obsd} are of the general form: $k_{obsd} = k_0 + k_1[OH^-]$. A general least-squares computer program[2] was used to calculate k_0 and k_1 from k_{obsd} and pH data.

Activity Coefficients. The activity coefficients of hydroxide ions were estimated from the Brønsted–Guggenheim equation[3]

$$\log \gamma_\pm = -A_\gamma Z_1 Z_2 I^{1/2}/(1 + I^{1/2}) + BI$$

where A_γ = 0.51, 0.52, and 0.53 at 25, 35, and 45°, respectively, and B = 0.1.[4] In cases in which the change in ionic strength is not negligible during the course of a reaction, then a mean ionic strength, *i.e.*, that at one half-life, is used. Thus hydroxide ion concentrations were calculated from the expression

$$\log [OH^-] = -pK_w + pH - \log \gamma_\pm$$

where pK_w = 14.00, 13.68, and 13.40[5] at 25, 35, 45°, respectively.

Results

(1) Rates of Base Hydrolysis of Some Amino Acid Esters. Most of the rates of base hydrolysis of the esters were taken from the work of Hay, *et al.*[6] In addition the rates of hydrolysis of BuGly, EtAla, Etβ-Ala, and EtVal were measured, and the results are given in Tables I and V. The base hydrolysis of an amino acid ester (E) obeys the rate equation

$$-d[E]/dt = d[H^+]/dt = k_1[E][OH^-] + k_2[EH^+][OH^-]$$

Thus the pseudo-first-order rate constants are of the form

$$k_{obsd} = k_0 + k_1[OH^-]$$

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(1) D. Hopgood and R. J. Angelici, *J. Am. Chem. Soc.*, **90**, 2508 (1968).

(2) R. H. Moore, based on a report from Los Alamos Scientific Laboratory, LA 2367, plus addenda. We thank Dr. J. P. Birk for modification of this program for use on the present problem and computer facilities.

(3) G. N. Lewis and M. Randall, "Thermodynamics," 2nd ed, revised by K. S. Pitzer and L. Brewer, McGraw-Hill Book Co., Inc., New York, N. Y., 1961, p 346.

(4) Reference 3, p 640.

(5) "Handbook of Chemistry and Physics," 44th ed, Chemical Rubber Publishing Co.,Cleveland, Ohio, 1963, p 1752.

(6) R. W. Hay, L. J. Porter, and P. J. Morris, *Australian J. Chem.*, **19**, 1197 (1966).

where $k_0 = k_2K_w/\gamma_{\pm}^2K_a$. The ester is almost entirely in the unprotonated form in the pH range used.

Table I. Rates of Hydrolysis of Some Amino Acid Esters at 25.0° and $I = 0.060\ M$[a,b]

Ester	pH	10^3k_{obsd}, sec^{-1}	Ester	pH	10^3k_{obsd}, sec^{-1}
BuGly	11.04	0.425	EtVal	12.33	0.317
	11.46	1.02		12.54	0.572
	11.66	1.83		12.76	0.640
	11.87	2.73		12.97	1.27
EtAla	11.04	0.499	Etβ-Ala	11.25	0.172
	11.25	0.695		11.46	0.309
	11.46	1.10		11.66	0.381
	11.66	1.62		11.87	0.604, 0.681

[a] Mean ionic strength. [b] Except for EtVal where $I \simeq 0.15\ M$.

Table II. Rate Constants for Amino Acid Ester Hydrolysis in the Presence of $Cu(NTA)^-$ at 25.0° and $I = 0.070\ M$[a]

pH	10^3k_{obsd}, sec^{-1}	pH	10^3k_{obsd}, sec^{-1}
$[Cu(NTA)(MeGly)]^-$		$[Cu(NTA)(EtAla)]^-$	
7.75	0.85	8.75	0.857
7.85	0.80	8.96	1.08
7.96	1.12	9.17	1.44
8.06	1.07	9.38	2.61
8.16	1.32	9.58	3.69, 3.50
8.27	1.64	$[Cu(NTA)(EtLeu)]^-$	
8.37	1.92	8.89	0.348
8.48	2.20	9.10	0.556
8.58	2.80	9.20	0.738
8.68	3.32	9.30	0.972
8.79	3.90	9.51	1.54
$[Cu(NTA)(EtGly)]^-$		$[Cu(NTA)(EtPhAla)]^-$	
7.95	0.216	8.96	0.564
8.57	0.503	9.17	0.786
8.99	1.23	9.38	1.01
9.10	1.33	9.48	1.46
9.20	1.92	9.58	1.61
9.30	2.44	$[Cu(NTA)(EtVal)]^-$	
9.51	3.20	9.05	0.037
8.40	1.02^{b}	9.37	0.061
8.60	1.44^{b}	9.69	0.095
8.70	1.47^{b}	$[Cu(NTA)(Et\beta\text{-}Ala)]^-$	
8.80	1.78^{b}	9.58	0.089
8.90	2.20^{b}	9.79	0.165
9.00	3.03^{b}	10.00	0.280, 0.305
7.80	1.03^{c}	$[Cu(NTA)(MeHist)]^-$	
8.00	1.07^{c}	9.79	0.410
8.20	1.46^{c}	10.00	0.710
8.30	1.88^{c}	10.21	0.850
8.50	2.65^{c}	10.42	1.42
$[Cu(NTA)(BuGly)]^-$		10.73	2.93
8.75	0.438		
8.96	0.585		
9.17	0.773		
9.38	1.31		
9.58	2.28		

[a] Except for EtVal and MeHist where the mean ionic strengths are 0.080 and 0.087 M, respectively. [b] At 34.8°. [c] At 44.5°.

(2) Rates of Base Hydrolysis of Some Amino Acid Esters Coordinated to $Cu(NTA)^-$. The over-all stoichiometry of the reaction[1] is

$$[Cu(NTA)NH_2(CHR)_nCO_2R']^- + OH^- \longrightarrow [Cu(NTA)NH_2(CHR)_nCOO]^{2-} + R'OH$$

The over-all observed rate law for the reaction is

$$-d[Cu(NTA)E^-]/dt = d[H^+]/dt = (k_0 + k_{1,cat}[OH^-])[Cu(NTA)E^-]$$

where $k_{obsd} = k_0 + k_{1,cat}[OH^-]$. The results are given in Tables II and V. The stereochemistry of the ester undergoing hydrolysis in the pH range used in these studies is as discussed previously.[1]

The rate dependence on $[Cu(NTA)^-]$ was determined with $[MeGly] = 0.00067\ M$ and $[KNO_3] = 0.05\ M$ at pH 8.48 and 25.0°. Ratios of $[Cu(NTA)^-]:[MeGly]$ of 10:1, 7.5:1, and 5:1 gave 10^3k_{obsd} values of 2.27, 2.43, and 2.36 sec^{-1}, respectively, showing that k_{obsd} is independent of $[Cu(NTA)^-]$ in the range of concentrations used and that all of the MeGly is present in solution as $[Cu(NTA)(MeGly)]^-$.

The effect of ionic strength was determined on the EtLeu and MeHist systems. The results given in Table III show that both reactions are independent of ionic strength.

Table III. Effect of Ionic Strength at 25.0°

$[KNO_3]$, M	I, M	10^4k_{obsd}, sec^{-1}	$k_{1,cat}$, M^{-1} sec^{-1}
$[Cu(NTA)(EtLeu)]^-$ at pH 9.20			
0.200	0.220	7.68	35.5
0.050	0.070		37.1 (av)[a]
0.017	0.037	6.52	34.7
...	0.020	6.38	35.2
$[Cu(NTA)(MeHist)]^-$ at pH 10.42			
0.200	0.237	14.9	4.04
0.050	0.087		4.10 (av)[a]
...	0.037	13.7	4.20

[a] Table V.

The temperature dependence of the $[Cu(NTA)(EtGly)]^-$ hydrolysis was determined over the temperature range 25–45°. Data for the reaction at 25.0, 34.8, and 44.5° are given in Tables II and V. Activation parameters for $k_{1,cat}$ of $\Delta H^* = 4.9 \pm 1.0$ kcal/mole and $\Delta S^* = -33 \pm 2$ eu were derived from these data.

Discussion

(1) Base Hydrolysis of Amino Acid Esters. Consideration of the rates of hydrolysis of a series of ethyl esters of α-amino acids, $H_2NCHRCO_2Et$, indicates that the steric effect of the R group is a major factor determining the relative rates. The data presented in Table IV show that the rates fall into an order predicted by Newman's "Rule of Six."[7] This rule states that those atoms which are effective in providing steric hindrance are separated from the attacking atom in the transition state by a chain of four atoms; *i.e.*, numbering the oxygen atom of the hydroxyl group attacking the carbonyl atom 1, then the greatest steric hindrance will result from atoms in position 6. Inductive effects explain second-order effects such as the low value of $k_2(EtAla)/k_2(EtGly) = 0.39$. In this case the carbonyl carbon is relatively deactivated by the $+I$ effect of the Me group in comparison with some other R group.

(2) Rates of Hydrolysis of Amino Acid Esters in the Presence of $Cu(NTA)^-$. The pH range over which the rate data were measured is centered on the relatively unbuffered region between the regions of formation of

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(7) M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p 206.

Table IV. Relative Rates of Base Hydrolysis of a Series of Ethyl Esters of α-amino Acids at 25°

Et ester	Gly[a]	Ala	PhAlA[a]	Leu[a]	Val
R	H	CH_3	CH_2Ph	$(CH_3)_2CHCH_2$–	$(CH_3)_2CH$–
k_1/k_1(EtGly)	1.0	0.39	0.37	0.29	0.016
No. of atoms in position 6	0	0	2	3	6

[a] Reference 6.

Table V. Rate Constants for Base Hydrolysis of Amino Acid Esters and Their Complexes with Cu(NTA)⁻ at 25°

Ester	No metal complex k_1, M^{-1} sec^{-1}	[Cu(NTA)(ester)]⁻ 10^4k_0, sec^{-1}	$k_{1,\text{cat}}$, M^{-1} sec^{-1}	$k_{1,\text{cat}}/k_1$
MeGly	1.32[a]	5.3 ± 0.7	460 ± 19	350
EtGly	0.635[a]	2.1 ± 1.2	78.2 ± 5.6	125
BuGly	0.305 ± 0.0008[d]	0	45.6 ± 3.3	150
EtAla	0.247 ± 0.0007[c]	3.1 ± 1.2	69.8 ± 3.8	285
EtPhAla	0.235[a]	2.1 ± 1.0	30.0 ± 3.1	130
EtLeu	0.187[a]	0	37.1 ± 0.7	200
EtVal	0.011 ± 0.001[d]	0.20 ± 0.09	1.86 ± 0.36	170
Etβ-Ala	0.078 ± 0.003[d]	0	2.25 ± 0.14	30
MeHist	0.620[b]	0.9 ± 0.6	4.10 ± 0.16	7

[a] Reference 6. [b] Reference 11. [c] $10^4k_0 = 1.80 \pm 0.35$ sec^{-1}. [d] $10^4k_0 = 0$. At 34.8°, $10^4k_0 = 3.0 \pm 1.7$ sec^{-1} and $k_{1,\text{cat}} = 96.6 \pm 9.8$ M^{-1} sec^{-1}; at 44.5°, $10^4k_0 = 4.8 \pm 1.0$ sec^{-1} and $k_{1,\text{cat}} = 134 \pm 11$ M sec^{-1}.

the [Cu(NTA)(E)]⁻ complex and of displacement of the ester ligand by a hydroxo group.[1]

$$\mathrm{Cu(NTA)^- + E \rightleftarrows [Cu(NTA)(E)]^-}$$

$$\mathrm{[Cu(NTA)(E)]^- + OH^- \rightleftarrows [Cu(NTA)(OH)]^{2-} + E}$$

For the purpose of kinetic analysis of the data, it was assumed that all the ester present in the systems was coordinated to Cu(NTA)⁻, and it transpired that deviations due to uncoordinated ester were less than experimental error in most systems. Rate laws of the form $d[H^+]/dt = k_{\text{obsd}}[\text{Cu(NTA)E}^-]$, where $k_{\text{obsd}} = k_0 + k_{1,\text{cat}}[OH^-]$, were observed. In systems which gave a nonzero value for k_0 this parameter can be due either to H_2O hydrolysis of the coordinated ester or to base hydrolysis of the protonated form of the free ester. In the latter case $k_0 = k_2K_w/\gamma_{\pm}^2K_a$ ($d[H^+]/dt = k_2 \cdot [EH^+][OH^-]$) and in the former $k_0 = k'[H_2O]$. The following k_0 values for base hydrolysis of the protonated forms of esters have been determined with k_2 values given in parentheses: MeGly, 4×10^{-5} sec^{-1} (58 M^{-1} sec^{-1});[6] EtGly, 2×10^{-5} sec^{-1} (24 M^{-1} sec^{-1});[8] EtAla, 1.8×10^{-4} sec^{-1} (340 M^{-1} sec^{-1}); and MeHist = 2×10^{-5} sec^{-1} (67 M^{-1} sec^{-1}).[6] The other esters have k_0 values which are within experimental error of zero. Thus the values of k_0 for Cu(NTA)⁻ catalysis are probably due to H_2O attack except for the EtAla and MeHist systems whose constants are within experimental error of their respective k_0 values for base hydrolysis of the protonated esters.

We may compare the relative nucleophilicities of OH⁻ and H_2O by taking [H_2O] as 55 M. This gives for most Cu(NTA)⁻ catalyzed systems $k_{1,\text{cat}}/k' \sim 10^7$. This value may be compared to the following literature values for hydrolysis of various ester systems: EtGlyH⁺ $\sim 10^{11}$,[8] CuEtGly^{2+} $\sim 10^{11}$,[8] and p-nitrophenyl acetate $\sim 10^9$.[9]

The k_0 values have large standard deviations (Table V); hence no correlations can be made between them and the nature of the Cu(NTA)(E)⁻ species. We are primarily concerned with the rates of base hydrolysis ($k_{1,\text{cat}}$) of esters coordinated to Cu(NTA)⁻ as compared with the uncatalyzed rates (k_1), and these values are given in Table V.

The catalysis constants, $C = k_{1,\text{cat}}/k_1$, for the series of ethyl esters of bidentate α-amino acids, NH_2CHRCO_2Et, are very approximately constant at about 200 in comparison with the wide range of either k_1 or $k_{1,\text{cat}}$. This suggests that the same factor, *i.e.*, the steric effect of R, controls the relative rates in both cases. These esters, with the exception of EtVal, also exhibit a linear free-energy relationship between $k_{1,\text{cat}}$ and their formation constants[1] (K_f). The Brønsted constants, using the relationship $k_{1,\text{cat}} = GK_f^{\gamma}$, are $\gamma \simeq 1.0$ and $G \simeq 0.056$.

We will now examine the factors which appear to determine the values of catalysis constants, C, for a series of copper(II) catalysts coordinated to the amino acid esters EtGly (representative α-amino acid ester), Etβ-Ala, and MeHist. Given in Table VI are the currently available data on copper(II) catalysis. Two significant trends are apparent. One is the increase in catalysis constants along the series MeHist, Etβ-Ala, and EtGly, which is the order of increasing steric possibility of ester carbonyl oxygen interaction with the copper atom.[1,10]

The [Cu(NTA)(MeHist)]⁻ system is a limiting case as ester interaction appears unlikely[1] and the low catalysis constant of 7 is probably due to activation by induction through the coordinated nitrogen atoms. Furthermore Hay, *et al.*,[11] considered that it was not necessary to invoke carbonyl–metal ion interaction to explain the degree of catalysis observed in the system CuMeHist^{2+}. Etβ-Ala is an intermediate case as interaction necessitates the formation of a six-membered ring which is less stable than the five-membered ring that an α-amino acid ester would form.[1]

The second trend is the expected increase in catalysis constants along the series of increasing positive charge on the catalysts, *i.e.*, Cu(NTA)⁻ < Cu(IMDA)⁰ < Cu^{2+}.

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(8) H. L. Conley and R. B. Martin, *J. Phys. Chem.*, **69**, 2914 (1965).

(9) W. P. Jencks and J. Carriuolo, *J. Am. Chem. Soc.*, **82**, 1778 (1960).

(10) R. J. Angelici and B. E. Leach, *ibid.*, **90**, 2499 (1968).

(11) R. W. Hay and P. J. Morris, *Chem. Commun.*, 23 (1967).

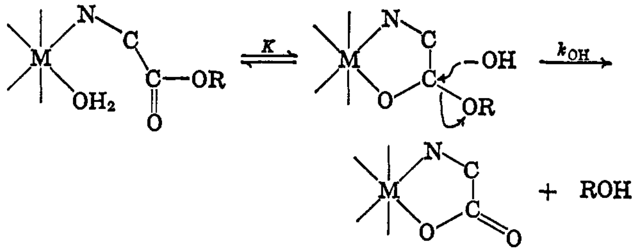
Table VI. Summary of Rate Data for the Catalysis of the Base Hydrolysis of Amino Acid Esters by Cu(II) Complexes at 25°

	$C = k_{1\text{cat}}/k_1$			
Catalyst	C_{EtGly}	$C_{\text{Et}\beta\text{-Ala}}$	C_{MeHist}	$C_{\text{EtGly}}/C_{\text{MeHist}}$
Cu^{2+}	1.2×10^{5} [a]		2.9×10^{2} [b]	400
Cu(IMDA)[e]	2.9×10^{4} [c]		1.9×10 [d]	150
$Cu(NTA)^-$	1.2×10^{2}	3.0×10	7	18
H^+	4.0×10 [a]		1.1×10^{2} [b]	

[a] Reference 8. [b] Reference 11. [c] B. E. Leach and R. J. Angelici, unpublished results. [d] D. Hopgood and R. J. Angelici, unpublished results. [e] IMDA = iminodiacetate ion.

The ratios $C_{\text{EtGly}}/C_{\text{MeHist}}$ also markedly increase along this series. This would not be expected if MeHist carbonyl oxygen interaction with the copper atom became important when free coordination sites, as in Cu(IMDA) and Cu^{2+}, are available. These results are in agreement with the conclusions of Hay, *et al.*[11] Also given in Table VI are *C* values of rate enhancement due to protonation of the ester amine group, and these support an activation by chelation mechanism for Gly as C_{Gly} increases along the series $H^+ < Cu(NTA)^- < Cu(IMDA)^0 < Cu^{2+}$, whereas the order of increasing C_{MeHist} is the order of increasing positive change on the catalysts. It is interesting that the *C* value for the ethyl glycinate-N,N-diacetate complex, Cu(EGDA), is 3.4×10^4, a value[12] which is virtually the same as that for Cu(IMDA)(EtGly). Both complexes have the same over-all charge but different numbers of ligand donor atoms.

Thus our data are in accord with the generally accepted catalysis mechanism for α-amino acid hydrolysis whereby transient coordination of the carbonyl group to the copper atom causes substantial activation toward nucleophilic attack by a hydroxide ion. In terms of the mechanism, the second-order rate constant for catalysis is $k_{1,\text{cat}} = Kk_{\text{OH}}$. However, this mechanism, which suffices for a description of the systems as given here, is in detail undoubtedly more complex as was demonstrated by the elegant O^{18} experiments of Bender and coworkers.[13,14] These experiments showed that the ratios of O^{18} exchange to hydrolysis rates of the tetrahedral intermediate are very similar for both the copper(II) and the nonmetal-ion-catalyzed hydrolyses.



An alternative mechanism is intramolecular attack by a hydroxo ligand. Since this mechanism has been found to be improbable in related Cu(II) systems[10,15] and species with both hydroxo and ester ligands are not measurably formed in the present system,[1] intramolecular OH^- attack is unlikely. The smooth increase in rates on going to more positively charged catalysts than $Cu(NTA)^-$ suggests that a change in mechanism does not occur.

The data in Table III show that the hydrolyses both of $[Cu(NTA)(MeHist)]^-$ and of $[Cu(NTA)(EtLeu)]^-$ are independent of ionic strength whereas both reactions have as a rate-determining step an anion–anion reaction, $Cu(NTA)E^- + OH^-$. No explanation for this anomalous behavior is apparent.

The activation parameters of $\Delta H^* = 4.9$ kcal/mole and $\Delta S^* = -33$ eu for $k_{1,\text{cat}}$ of $[Cu(NTA)(EtGly)]^-$ can be compared with those reported[16] for k_1 of EtGly of 10.3 kcal/mole and −22 eu, respectively. Thus rate enhancement is due to a large decrease in ΔH^* of about 5 kcal/mole. This decrease is probably associated with k_{OH}, the rate constant for hydroxide ion attack on the chelated ester.

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(12) R. J. Angelici and B. E. Leach, *J. Am. Chem. Soc.*, **89**, 4605 (1967).

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

(14) M. L. Bender and R. J. Thomas, *ibid.*, **83**, 4189 (1961).

(15) B. E. Leach and R. J. Angelici, *ibid.*, **90**, 2504 (1968).

(16) C. Gustaffson, *Ann. Acad. Sci. Fennicae*, 15 (1945); *Chem. Abstr.*, **41**, 903*h* (1947).