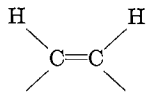
atoms. For example, recently King and Eggers[12] have shown that the ν(CO) infrared stretching frequencies in the (VPP)M(CO)$_4$ (M = Cr, Mo, W) complexes are slightly higher than in the corresponding dpe derivatives. These data indicate that VPP has a slightly higher π-acceptor character than does dpe. This effect may arise from the presence of empty antibonding orbitals in the C=C bond, but it may also be due to the more electronegative sp^2 carbon atoms. Furlani[13] pointed out that in a "regular" square pyramid the efficiency for π bonding is almost as good as in a square-planar complex. The d_{z^2} orbital becomes more fully σ^*, but d_{xy}, d_{xz}, and d_{yz} remain fully π in character for both in-plane and out-of-plane bonds. Similarly, if the metal is located in the basal plane of the square pyramid any interligand π conjugation would be most effective when the ligands are coplanar.

Another possible difference between the two diphosphines may be steric in origin. Molecular models indicate that the $-CH_2CH_2-$ linkage can allow the *o*-phenyl hydrogen atoms and/or the methylene hydrogens in the *gauche* conformation of the $-CH_2CH_2-$ chelate ring to block the coordination sites above and below the nickel atom. However, the planar



linkage of the VPP ligand leaves these sites open for coordination of an anion. The recent preparation of $[Ni(dpe)_{1.5}(CN)_2]_2$[7] would seem to fit this argument. The latter complex contains one chelating dpe ligand and one which bridges between the nickel atoms, thus facilitating attachment of the two cyano groups. However, it must also be remembered that cyano groups are particularly good at promoting five-coordination with nickel(II) and that the resulting complex is usually a trigonal bipyramid.[14]

Acknowledgments.—We are indebted to the National Science Foundation (Grant No. GP-8365) for financial support, to The Ohio State University for a postdoctoral fellowship to C. A. M., and to B. R. Cook for a supply of the ligand.

(12) R. B. King and C. A. Eggers, *Inorg. Chim. Acta*, **2**, 33 (1968).
(13) C. Furlani, *Coord. Chem. Rev.*, **3**, 141 (1968).
(14) A. Turco, personal communication; E. Alyea, D. W. Meek, J. Stalich, and J. A. Ibers, unpublished data, 1968.

CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY,
IOWA STATE UNIVERSITY, AMES, IOWA 50010

Equilibrium Studies of Copper(II) Complexes of Iminodiacetates with Amino Acid Esters and the Kinetics of Ester Hydrolysis

BY BRUCE E. LEACH AND ROBERT J. ANGELICI

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Formation constants for the interaction of various amino acids, HA, and amino acid esters, E, with a series of substituted iminodiacetate ($RN(CHR'CO_2)(CH_2CO_2)^{2-}$) complexes of Cu(II), Cu(RIMDA), indicate there are steric repulsions between bulky R groups of the substituted iminodiacetates and large groups on the esters. The amino acid esters in the complexes, Cu(IMDA)(E), hydrolyze with rates of hydrolysis decreasing in the order: MeGly > MeAla > EtSar > EtGly > BuGly > EtLeu. No hydrolysis is observed near pH 7 for esters such as ethylbetaine and N-benzoylglycine methyl ester which do not complex appreciably with Cu(IMDA). The equilibrium and kinetic data are consistent with the reactions

$$Cu(RIMDA) + HE^+ \rightleftarrows H^+ + Cu(RIMDA)(E) \xrightarrow[k]{OH^-\text{attack}} Cu(RIMDA)(A)^-$$

In the case of catalysis by Cu(IMDA), there is evidence that the last step also proceeds partially by H_2O attack. In both the OH^- and H_2O attack mechanisms it is assumed that the ester group is directly coordinated to the metal ion when the nucleophilic attack occurs. The rates of hydrolysis in Cu(RIMDA)(E) depend relatively little upon the nature of R except when R contains a coordinating group.

Introduction

Equilibrium and kinetic investigations of metal complexes of amino acid ester –N,N– diacetates, $MN(CH_2CO_2)_2(CHRCO_2C_2H_5)$ where the ester group is incorporated into the iminodiacetate ligand,[1-3] form the basis for extending our studies to the basic hydrolysis of amino acid esters (E) in the presence of metal ion complexes. The equilibria and kinetics of ester hydrolysis associated with the interaction of amino acid esters with the nitrilotriacetate (NTA) complex of copper(II)[4,5] have been published. The present

(1) R. J. Angelici and B. E. Leach, *J. Am. Chem. Soc.*, **89**, 4605 (1967).
(2) R. J. Angelici and B. E. Leach, *ibid.*, **90**, 2499 (1968).
(3) B. E. Leach and R. J. Angelici, *ibid.*, **90**, 2504 (1968).
(4) D. Hopgood and R. J. Angelici, *ibid.*, **90**, 2508 (1968).
(5) R. J. Angelici and D. Hopgood, *ibid.*, **90**, 2514 (1968).

study, using Cu(II) complexes of variously substituted iminodiacetates (RIMDA), was carried out under conditions which considerably simplified analysis of the kinetic results and in a pH region where the predominant species were Cu(RIMDA) and the amino acid ester complex Cu(RIMDA)(E). The purpose of this work was to examine the ability of the Cu(RIMDA) complexes to coordinate with amino acids and esters and then to determine the rates of hydrolysis of the esters in these complexes.

Experimental Section

With the exception of the iminodiacetates (see below) the preparation of the amino acid esters and the materials used were as given previously.[1-5] Iminodiacetic acid disodium salt (Na_2IMDA), methyliminodiacetic acid (MeIMDA), and D(−)-α-phenylglycine were obtained from Aldrich Chemical Co., Inc.; uramildiacetic acid (UrIMDA) was purchased from Eastman Organic Chemicals. Bromoacetic acid and the amines (cyclohexylamine, *t*-butylamine, furfurylamine, and aniline) used in the syntheses of the RIMDA ligands were reagent grade.

The customary abbreviations for organic groups and the names of amino acids are used, *e.g.*, glycine (Gly), alanine (Ala), leucine (Leu), valine (Val), sarcosine (Sar), β-alanine (β-Ala), ethyl (Et), methyl (Me), phenyl (Ph), and *t*-butyl (*t*-Bu). The esters are designated in the usual manner, *e.g.*, methyl glycinate as MeGly.

The nmr spectra were obtained on D_2O solutions with a Varian Associates Model A-60 spectrometer using sodium 2,2-dimethyl-2-silapentane-5-sulfonate as the internal reference compound (chemical shift, δ 0.0). Chemical shifts are reported in ppm downfield from the reference.

Preparation of Iminodiacetates.—*t*-Butyliminodiacetate (*t*-BuIMDA), phenyliminodiacetate (PhIMDA), cyclohexyliminodiacetate (CyIMDA), and furfuryliminodiacetate (FurIMDA) were prepared by first dissolving 38.9 g (0.28 mol) of bromoacetic acid in 15 ml of H_2O and chilling in an ice bath and then neutralizing slowly with 7 *N* KOH so as to maintain a temperature below 30°. After neutralization was complete, the remainder (of 80 ml total) of the base was added, and an aqueous solution containing about 20 ml of H_2O and 0.14 mol of the appropriate amine was added over a period of 30 min. The mixture was allowed to stir at room temperature for 2 hr to complete the reaction; then the substituted iminodiacetic acid was precipitated as the barium salt with $BaCl_2 \cdot 2H_2O$. The nmr spectra of the compounds were taken in D_2O solutions containing Zn(II) to improve the solubility of the IMDA derivatives. These spectra were consistent with the desired products.

Anal. Calcd for $(CH_3)_3CN(CH_2CO_2)_2Ba$: C, 29.60; H, 4.02; N, 4.32. Found: C, 29.52; H, 3.89; N, 4.34. Nmr: $(CH_3)_3$, 1.48; CH_2, 4.25. Calcd for $C_6H_5N(CH_2CO_2)_2Ba$: C, 34.88; H, 2.62; N, 4.07. Found: C, 35.29; H, 2.73; N, 4.32. Nmr: C_6H_5, 6.8–7.6; CH_2, 4.37. Calcd for $C_6H_{11}N(CH_2CO_2)_2Ba$: C, 34.15; H, 4.28; N, 4.00. Found: C, 34.22; H, 4.33; N, 3.73. Nmr: C_6H_{11}, 1.0–2.1; CH_2, 4.25. Calcd for FurIMDA, $\underline{OCH{=}CHCH{=}C}CH_2N(CH_2CO_2)_2Ba \cdot 0.5H_2O$: C, 30.25; H, 3.00; N, 3.92 Found: C, 30.13; H, 3.15; N, 4.23. Nmr: $(CH_2)_2$, 4.28; CH_2, 4.72; CH, 6.60; CH, 6.85; CH, 7.70.

The preparation of D(−)-α-phenylglycine-N-monoacetate (D-PhglyMA) and L-valine-N-monoacetate (L-ValMA) differed in that the neutralized bromoacetic acid was added dropwise to the neutralized phenylglycine or valine solution with addition of KOH to maintain a pH value of 11. The temperature of the solution was kept near 50°. The method of precipitation with $BaCl_2 \cdot 2H_2O$ was not successful, so, instead, the volume of the reaction solution was reduced under vacuum until a precipitate formed. The solution was acidified with HCl to pH 3, the precipitate filtered, and the solution volume reduced further. The initial precipitates were chiefly KBr and KCl; the final precipitate yielded the desired compounds.

Anal. Calcd for D-PhglyMA, $HO_2CCH(C_6H_5)N(H)(CH_2CO_2H) \cdot H_2O$: C, 53.00; H, 5.75; N, 6.16. Found: C, 54.06; H, 5.25; N, 5.64. Nmr: C_6H_5, 7.39; CH, 4.48; CH_2, 3.08 and 3.16. Calcd for L-ValMA, $HO_2CCH(CH(CH_3)_2)N(H)(CH_2CO_2H)$: C, 48.00; H, 7.43; N, 8.01. Found: C, 48.14; H, 7.60; N, 8.23. Nmr: $(CH_3)_2$, 1.10; CH, 2.3; CH, 4.0; CH_2, 4.0.

Kinetic Measurements.—Rates of reaction were determined with a Radiometer TT1c Titrator and SBR2C Titrigraph. The pH was maintained at the desired value by addition of 0.0187 *N* NaOH. Nitrogen was bubbled into the reaction vessel (10 ml volume) to exclude air. The reaction vessel was thermostated to 25.00 ± 0.05°. Details of the treatment of the kinetic data have been given previously.[1] Hydrogen ion activity measured by the pH meter has been converted into hydroxide ion concentration by using the expression: $\log [OH^-] = \log K_w + pH - \log \gamma_\pm$, where $\gamma_\pm$, the activity coefficient, has been estimated from Guggenheim's equation:[6] $\log \gamma_\pm = [AZ_1Z_2I^{1/2}/(1 + I^{1/2})] + BI$, where $A = 0.507$ and $B = 0.1$. The second-order rate constants were obtained by dividing the pseudo-first-order rate constants, k_{obsd}, by the hydroxide ion concentration. A general, nonlinear least-squares computer program[7] was used to calculate the second-order rate constant, k, and k'_{H_2O}, where such a term was observed (see Results).

Equilibrium Measurements.—The pK_E values for the esters

$$HE^+ \overset{K_E}{\rightleftharpoons} H^+ + E \qquad (1)$$

MeAla, L-MeLeu, D-MeLeu, and EtSar were determined by manual titration of a 10 ml aqueous solution containing 0.0067 *M* ester and 0.050 *M* KNO_3 with 0.206 *M* NaOH. The pH of the solution was recorded after additions of aliquots of NaOH solution. Formation constants of hydroxo species (see eq 2) of the Cu(RIMDA) complexes (0.0067 *M*) were also determined by pH titration. The formation constants of EtVal, EtLeu, BuGly,

$$Cu(RIMDA) + OH^- \overset{K_{f}^{OH}}{\rightleftharpoons} Cu(RIMDA)(OH)^- \qquad (2)$$

and Val with Cu(RIMDA) (see eq 3) were determined by

$$Cu(RIMDA) + NH_2CHRCOOR' \overset{K_f}{\rightleftharpoons} Cu(RIMDA)(NH_2CHRCOOR') \qquad (3)$$

manual titration of solutions prepared by mixing 3.0 ml of a solution containing 0.0167 *M* $Cu(NO_3)_2$ and 0.0167 *M* RIMDA, 3.0 ml of 0.0167 *M* amino acid or ester, 2.0 ml of 0.20 *M* KNO_3, and 2.0 ml of H_2O. These solutions were titrated with 0.206 *M* NaOH; pH readings were recorded after the addition of each aliquot of base. Corrections were made for volume increases during the titrations, all of which were carried out under an atmosphere of N_2 at 25.0°. The average formation constant, K_f, and its standard deviation were computed for 20–80% of titration. K_f was calculated from relationships derived by Hopgood and Angelici[4] using the appropriate equations for total metal concentration, total ligand concentration (amino acid or amino acid ester), and electroneutrality. The average formation constant, K_f, was used to calculate theoretical titration data which in all cases reproduced the experimental data well.

Results

The equilibria involving the Cu(RIMDA) complexes and amino acids and amino acid esters were extensively studied. The ionization constants of the amino acid

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(7) 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.

esters, K_E, were calculated using the equation

$$pK_E = pH + \log \gamma_{\pm} + \log \frac{E_{tot} - ([Na^+] + [H^+] - [OH^-])}{[Na^+] + [H^+] - [OH^-]} \quad (4)$$

which was derived[4] from expressions for total ester concentration, electroneutrality, and the ionization constant of HE^+. The values of pK_a and pK_E in Table I[4,8,9] are an average of 8–10 determinations calculated for 20–80% of titration of the ester hydrochloride with NaOH.

TABLE I

IONIZATION CONSTANTS OF AMINO ACIDS AND AMINO ACID ESTERS AT 25.0° AND 0.05 *M* KNO_3

Acid	pK_a[a]	Ester	pK_E
Gly	2.35	Me	7.62[c]
	9.78	Et	7.68[c]
		n-Bu	7.78[b]
Ala	2.34	Me	7.85
	9.87	Et	7.91[b]
Leu	2.36	L-Me	7.63
	9.60	D-Me	7.63
		Et	7.64[c]
Val	2.32	Et	7.75[b]
	9.62		
Sar	2.25	Et	8.10
	10.09		
β-Ala	3.55	Et	9.13[b]
	10.35		

[a] Reference 8. [b] Reference 4. [c] Reference 9.

Hydroxo complex formation constants, K_{fOH}, were considered in the determination of the formation constants, K_f. Because of the precipitation of $Cu(OH)_2$, the K_{fOH} values (Table II) are valid only over approximately the first 25% of the titration of Cu(RIMDA) with NaOH.

TABLE II

VALUES OF K_{fOH} FOR THE REACTION OF Cu(RIMDA) ACCORDING TO EQ 2 AT 25.0° AND 0.05 *M* KNO_3

Cu(RIMDA)	K_{fOH}	Cu(RIMDA)	K_{fOH}
Cu(PhIMDA)	2.5×10^6	Cu(FurIMDA)	1.15×10^5
Cu(IMDA)	1.8×10^6	Cu(L-ValMA)	6.2×10^4
Cu(MeIMDA)	6.4×10^5	Cu(D-PhglyMA)	5.0×10^4
Cu(CyIMDA)	6.0×10^5	$Cu(UrIMDA)^-$	3.8×10^4
Cu(*t*-BuIMDA)	1.9×10^5	$Cu(NTA)^-$	2.5×10^4[a]

[a] Reference 4.

Potentiometric titrations of 1:1 mole ratios of Cu(RIMDA) with EtVal·HCl showed that 2 equiv of NaOH was added up to about pH 10. The first equivalent corresponds to the deprotonation of the ester and its subsequent coordination to Cu(RIMDA); the second equivalent is postulated to be due to the displacement of the ester from the complex to form the hydroxo species $Cu(RIMDA)(OH)^-$

$$Cu(RIMDA)(E) + OH^- \overset{K_d}{\rightleftharpoons} Cu(RIMDA)(OH)^- + E$$

$$K_d = \frac{[Cu(RIMDA)(OH)^-][E]}{[Cu(RIMDA)(E)][OH^-]} = K_{fOH}/K_f \quad (5)$$

From the titration data, values of K_d may be calculated from the expression[4]

$$\log K_d = \log ([E]_{tot}/2) + pK_w - pH_{1.5\ equiv} + \log \gamma_{\pm} \quad (6)$$

Since the values of K_d are in reasonably good agreement with K_d calculated from expression 5 using independently determined values of K_{fOH} and K_f, it is assumed that E is displaced by OH^- according to the equilibrium expression given for K_d. For the interaction of Cu(IMDA) with EtVal, log K_d is 2.7 using eq 5 and 3.1 using eq 6.

TABLE III

FORMATION CONSTANTS, K_f, FOR THE REACTION OF Cu(RIMDA) WITH AMINO ACIDS AND ESTERS ACCORDING TO EQ 3 AT 25.0° AND 0.05 *M* KNO_3

Complex	Ligand	Log K_f
Cu(IMDA)	Gly	6.42 ± 0.06
	Ala	6.27 ± 0.06
	Leu	6.53 ± 0.04
	Val	6.17 ± 0.06
	EtVal	3.57 ± 0.06
	BuGly	3.69 ± 0.06
Cu(MeIMDA)	Val	6.19 ± 0.02
	BuGly	4.33 ± 0.07
	EtVal	3.19 ± 0.02
Cu(CyIMDA)	Val	6.58 ± 0.03
	EtLeu	3.21 ± 0.05
	BuGly	4.05 ± 0.04
Cu(*t*-BuIMDA)	Val	5.54 ± 0.07
	EtLeu	2.61 ± 0.02
	BuGly	3.50 ± 0.02
Cu(PhIMDA)	Val	6.77 ± 0.02
	EtLeu	2.60 ± 0.01
	BuGly	3.52 ± 0.01
Cu(FurIMDA)	Val	6.64 ± 0.03
	EtLeu	2.42 ± 0.01
	BuGly	3.88 ± 0.06
$Cu(UrIMDA)^-$	Val	4.57 ± 0.04
	EtLeu	3.05 ± 0.02
	BuGly	3.38 ± 0.02
Cu(L-ValMA)	L-Val	5.41 ± 0.01
	L-EtLeu	3.73 ± 0.06
Cu(D-PhglyMA)	L-Val	4.35 ± 0.04
	L-EtLeu	3.02 ± 0.03

Formation constants, K_f, were calculated by computer techniques for 20–25 experimental points in the 20–80% completion range of the potentiometric titration of solutions of Cu(RIMDA) and the amino acid or ester with NaOH. Average formation constants and their standard deviations are given in Table III. No deviations were observed which would indicate formation of a bis-ester complex under the conditions used.

(8) "Stability Constants," Special Publication No. 17, The Chemical Society, London, 1964.

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

TABLE IV

RATES OF ESTER HYDROLYSIS AS CATALYZED BY Cu(RIMDA) AT 25.0°

pH	10^4k_{obsd}, sec^{-1} [a]	pH	10^4k_{obsd}, sec^{-1} [a]	pH	10^4k_{obsd}, sec^{-1} [a]	pH	10^4k_{obsd}, sec^{-1} [a]
	Cu(IMDA)(MeGly)				Cu(MeIMDA)(MeGly)		
4.80	0.0650	6.10	2.84	5.60	0.125	6.40	0.905
5.00	0.0973	6.20	4.10	5.70	0.153	6.50	1.08
5.20	0.172	6.30	6.00	5.80	0.204	6.60	1.42
5.30	0.201	6.40	9.34	5.90	0.266	6.70	1.55
5.36	0 226	6.50	13.6	6.00	0.300	6.80	2.12
5.50	0.350	6.60	19.8	6.10	0.426	6.90	2.37
5.70	0.622	6.70	33.8	6.20	0.550	7.00	3.43
5.80	1.07	6.80	42.5	6.30	0.656		
6.00	1.68	6.90	71.0		Cu(*t*-BuIMDA)(MeGly)		
	Cu(IMDA)(EtGly)			6.10	1.05	6.50	2.62
5.70	0.200	6.30	2.00	6.20	1.40	6.60	3.31
5.90	0.342	6.40	3.27	6.30	1.74	6.70	4.17
6.00	0.512	6.50	4.92	6.40	2.20	6.80	5.30
6.10	0.769	6.60	7.92		Cu(CyIMDA)(MeGly)		
6.20	1.30	6.70	11.3	5.70	0.830	6.30	4.17
	Cu(IMDA)(BuGly)			5.80	1.06	6.40	5.18
6.10	0.708	6.40	2.80	5.90	1.45	6.50	6.36
6.20	0.927	6.50	4.05	6.00	1.75	6.60	8.10
6.30	1.74	6.60	5.72	6.10	2.32	6.70	9.79
	Cu(IMDA)(EtLeu)			6.20	3.16	6.80	12.1
6.10	0.428	6.50	1.45		Cu(FurIMDA)(MeGly)		
6.20	0.615	6.60	2.05	6.40	0.570	7.30	4.32
6.30	0.755	6.70	3.22	6.70	1.11	7.60	8.23
6.40	1.02	6.80	5.74	7.00	2.01		
	Cu(IMDA)(EtSar)				Cu(PhIMDA)(MeGly)		
6.10	0.680	6.40	1.76	6.30	2.55	6.90	11.3
6.20	0.859	6.50	2.65	6.60	5.50		
6.30	1.15	6.60	4.27		Cu(UrIMDA)$^-$		
	Cu(IMDA)(MeAla)			8.30	12.2	8.80	35.7
5.50	0.406	6.40	4.87	8.50	16.8		
5.70	0.581	6.50	8.54		Cu(D-PhglyMA)(MeGly)		
5.90	0.912	6.60	11.1	6.10	1.49	6.40	6.65
6.10	1.58	6.70	43.8	6.30	3.64	6.40	6.35
6.30	3.43			6.30	3.98		
					Cu(L-ValMA)(MeGly)		
				6.80	1.52	7.30	5.68
				7.00	2.13	7.40	7.64
				7.10	2.88	7.50	10.1
				7.20	3.98		

[a] Initial concentrations: [Cu(RIMDA)] = 0.0033 *M*; [E] = 0.00033 *M*; [KNO_3] = 0.050 *M*.

Pseudo-first-order rate constants, k_{obsd}, for the hydrolysis of various amino acid esters in the presence of Cu(RIMDA) at various pH values at 25.0° and 0.05 *M* KNO_3 are listed in Table IV. No hydrolysis due to uncoordinated ester was observed or expected at the relatively low pH values of this study[5,9]. The observed dependence on [OH^-] and the effect on the pseudo-first-order rate constant of doubling the concentration of Cu(RIMDA) are given in Table V.

Like other known cases of metal complex catalysis, the following reactions are probably involved and are consistent with the equilibrium and kinetic data

$$\text{Cu(RIMDA)} + \text{HE}^+ \overset{K_E K_f}{\rightleftharpoons} \text{H}^+ + \text{Cu(RIMDA)(E)} \xrightarrow[k]{\text{OH}^- \text{ attack}} \text{Cu(RIMDA)(A)} \quad (7)$$

where A is the resulting unprotonated amino acid. In the case of catalysis by Cu(IMDA), there is evidence that the last step proceeds partially by H_2O attack as well as by OH^- attack. Since the concentrations of Cu(RIMDA)$(OH)^-$ were very low in the pH range of the kinetic investigations, it was assumed that these species were not mechanistically involved in the hydrolysis. Although other studies[2] have suggested that hydroxo complexes are not important in the hydrolysis, this is still a debatable point.

If the first equilibrium in eq 7 is far to the right, the rate of ester hydrolysis should be given by the expression

$$\text{rate} = k[\text{Cu(RIMDA)(E)}][\text{OH}^-] \quad (8)$$

which exhibits a first-order OH^- dependence. Several

TABLE V

DEPENDENCE OF THE RATE OF HYDROLYSIS OF METHYL GLYCINATE ON [OH⁻] AND [Cu(RIMDA)]

RIMDA	pH	10^4k_{obsd}, sec⁻¹ [a]	10^4k_{obsd}, sec⁻¹ [b]	Kinetic orders in [OH⁻]
IMDA	6.3	6.00	12.00	First, second
MeIMDA	6.6	1.32	1.55	First
PhIMDA	6.3	2.55	2.68	First
t-BuIMDA	6.1	1.05	1.10	First
FurIMDA	6.4	0.570	0.555	First
CyIMDA	6.1	2.32	2.42	First
UrIMDA⁻	8.3	12.2	15.7	First
D-PhglyMA	6.3	3.98	7.90	Second
L-ValMA	7.4	7.64	8.24	First, second
	7.2	3.98	4.95	First, second
	7.0	2.13	3.42	First, second
	6.8	1.52	2.40	First, second

[a] Initial concentrations: [Cu(RIMDA)] = 0.0033 *M*; [E] = 0.00033 *M*; [KNO_3] = 0.050 *M*. [b] Initial concentrations: [Cu(RIMDA)] = 0.0067 *M*; [E] = 0.00033 *M*; [KNO_3] = 0.040 *M*.

complexes in Table V exhibit first-order OH^- dependence and as expected these rates are independent of the Cu(RIMDA) concentration. For these reactions, $k_{obsd} = k[OH^-]$.

If the equilibrium in eq 7 lies far to the left, the rate of reaction will increase with OH^- concentration not only because of the OH^- attack but also because the equilibrium will be shifted to give a higher concentration of Cu(RIMDA)(E). Therefore the rate of hydrolysis is second order in OH^- and first-order in Cu(RIMDA). That all of the reactions (Table V) which are second order in OH^- are also first-order in Cu(RIMDA) is consistent with the mechanism proposed in eq 7. Thus when the initial equilibrium is to the left, eq 8 becomes

$$\text{rate} = \frac{kK_EK_f}{K_w}[HE^+][Cu(RIMDA)][OH^-]^2 \quad (9)$$

where

$$k_{obsd} = \frac{kK_EK_f}{K_w}[Cu(RIMDA)][OH^-]^2 \quad (10)$$

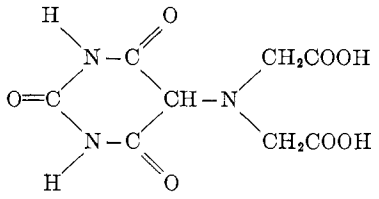
In these expressions K_E is the ionization constant of the ester (Table I), K_f is its formation constant with Cu(RIMDA) (Table III), and K_w is the autoionization constant of water. Values of k calculated from this expression are given in Table VI. For the hydrolysis of amino acid esters in the presence of Cu(IMDA), the rate law contained first- and second-order terms in $[OH^-]$, which suggested that both H_2O and OH^- attacks were important. If both types of attack are included, the rate law becomes

$$\text{rate} = \frac{kK_EK_f}{K_w}HE^+][Cu(RIMDA)][OH^-](k[OH^-] + k'_{H_2O}) \quad (11)$$

where $k'_{H_2O} = k_{H_2O}[H_2O]$. The ratio $k/k_{H_2O} \approx 10^{10}$ indicates the much greater nucleophilicity of OH^- as compared to H_2O. Similar differences in rate constants are observed for these nucleophiles toward simple organic esters[10,11] and ethyl glycinate.[12]

Discussion

Equilibrium Studies.—The substituted iminodiacetate (RIMDA) ligands coordinate strongly to Cu(II)[8,13–16] and formation constants for most of the RIMDA ligands with Cu(II) are known. Although the formation constants of uramildiacetic acid (UrIMDA)[14,15]



with several metal ions have been determined, they have not been measured with Cu(II). In the cases which have been studied UrIMDA is a tribasic acid, losing H^+ from the CH group which is bonded to the $N(CH_2CO_2H)_2$ portion of the ligand. It presumably acts as a tetradentate ligand, coordinating through the enol form of a carbonyl in the ring as well as through the three sites in the $N(CH_2CO_2H)_2$ group. Thus $Cu(UrIMDA)^-$ has a -1 charge and is more comparable to the $Cu[N(CH_2CO_2)_3]^-$ complex of the tetradentate ligand nitrilotriacetate (NTA) than to complexes Cu(RIMDA) where R does not contain a coordinating group.

The formation constants of furfuryliminodiacetate (FurIMDA) with Cu(II) were determined in this study by methods described previously.[2] The values of K_1 and K_2 at 25.0° in 0.05 *M* KNO_3 were 8×10^9 and 4×10^6, respectively. In comparison with formation constants of other substituted iminodiacetates,[13] it appears that FurIMDA is only a tridentate ligand with very little if any coordination of the furan oxygen to the Cu(II).

Solutions of the catalytic complexes Cu(RIMDA) were prepared by mixing 1:1 molar concentrations of Cu(II) and RIMDA. If a 10% molar excess of RIMDA over Cu(II) was added, the rates of ester hydrolysis decreased from those observed in the 1:1 solutions by approximately 10% indicating that probably some of the catalytically inactive $Cu(RIMDA)_2$ had formed. For this reason most equilibrium and kinetic studies were conducted with 1:1 molar concentrations of Cu(II) and RIMDA.

Formation constants, K_f, of the Cu(RIMDA) complexes with amino acids and amino acid esters (Table III) were determined in order to calculate the concentrations of $Cu(RIMDA)(NH_2CHRCOOR')$ and

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TABLE VI

RATE CONSTANTS k AND k_{H_2O} FOR THE HYDROLYSIS OF Cu(RIMDA)(E)[a] AT 25.0° AND 0.05 M KNO_3

Ester	Cu(RIMDA)	$10^{-4}k$, M^{-1} sec^{-1} [b]	$10^{6}k_{H_2O}$, M^{-1} sec^{-1}
MeGly	Cu(IMDA)	3.21	4.05
MeAla	Cu(IMDA)	2.62	6.42
EtSar	Cu(IMDA)	2.10	1.75
EtGly	Cu(IMDA)	1.85	2.70
BuGly	Cu(IMDA)	1.39	1.39
EtLeu	Cu(IMDA)	0.435	
$(CH_3)_3N^+CH_2CO_2Et$	Cu(IMDA)	No reaction	
$C_6H_5CONHCH_2CO_2Me$	Cu(IMDA)	No reaction	
MeGly	Cu(D-PhglyMA)	2.3	
MeGly	Cu(CyIMDA)	1.97	
MeGly	Cu(PhIMDA)	1.41	
MeGly	Cu(*t*-BuIMDA)	0.838	
MeGly	Cu(MeIMDA)	0.329	
MeGly	Cu(L-ValMA)	0.317	
MeGly	Cu(FurIMDA)	0.208	
MeGly	Cu(UrIMDA)$^-$	0.056	
MeGly	Cu(NTA)$^-$	0.046[c]	

[a] Initial concentrations: [Cu(RIMDA)] = 0.0033 M; [E] = 0.00033 M; [KNO_3] = 0.050 M. [b] Rate constants have standard deviations $\leq 10\%$. [c] Reference 5.

Cu(RIMDA)(NH_2CHRCO_2)$^-$ present under various concentration and pH conditions. In general, the amino acids coordinate much more strongly to Cu(RIMDA) than do the amino acid esters (K_f values are 100–1000 times larger for the acids). It is assumed that the amino acids are bidentate ligands as is usually observed,[4] whereas the esters are monodentate coordinating only through the amino group.[4,17,18] The formation constants for the complexation of different amino acids with Cu(IMDA) itself are similar indicating little if any specificity of Cu(IMDA) for certain amino acids. The formation constants for the complexation of EtVal and BuGly to Cu(IMDA) are the same within experimental error. However, if the iminodiacetate is substituted with a large bulky group, particularly on the nitrogen atom, then formation constants are as much as tenfold larger for complexation of the smaller BuGly than for EtLeu, *e.g.*, Cu(MeIMDA), Cu(PhIMDA), Cu(UrIMDA)$^-$, Cu(*t*-BuIMDA), Cu(FurIMDA), and Cu(CyIMDA). As noted above, UrIMDA is probably tetradentate in Cu(UrIMDA)$^-$.[14,15] The similarity between the formation constant of BuGly with Cu(UrIMDA)$^-$ and Cu[$N(CH_2CO_2)_3$]$^-$ (log K_f = 3.38 and 3.33,[4] respectively) is thus to be expected.

Kinetic Studies.—Under the conditions of the rate measurements, free HE^+ and E do not undergo measurable hydrolysis. For this reason, it is postulated that ester hydrolysis occurs in the complex Cu(RIMDA)(E) as shown in eq 7. Equilibrium studies have established the presence of these complexes, and, as noted in the discussion of the equilibria, it is believed that the ester in Cu(RIMDA)(E) is almost exclusively coordinated through the amino group, as has been suggested for other Cu–ester complexes.[2,4] For esters which do not coordinate strongly to Cu(RIMDA) and for which the first equilibrium in eq 7 lies to the left, the rate constant, k, for ester hydrolysis in Cu(RIMDA)(E) was calculated from eq 10 making use of appropriate K_f and K_E values. In the instances where the ester was MeGly, it was not possible to measure K_f because of concomitant ester hydrolysis during the K_f determination. The value of K_f used in these cases was that for BuGly. The assumption that K_f for MeGly is the same as that for BuGly has been shown[4] to be a fairly good one in similar systems. Where the ester was completely coordinated as Cu(RIMDA)(E) under the conditions of the rate studies, it was not necessary to use K_f in calculating k.

In earlier studies[2] of the Cu(II)-promoted hydrolysis of ethyl valinate-N,N-diacetate, the reaction was found to be catalyzed not only by OH^- but also by NO_2^-. That several nucleophiles catalyzed the hydrolysis was used as evidence to infer that the reaction proceeded by a mechanism (eq 12) in which the coordinated (either through the ether or carbonyl oxygen) ester group was attacked by the nucleophile. In the present study, it was established that NO_2^- also catalyzed the hydrolysis of the ester in Cu(IMDA)(MeGly). The value of k was determined to be 0.34 M^{-1} sec^{-1} at 25°. This compares with the value of 3.21×10^4 M^{-1} sec^{-1} for the OH^--catalyzed hydrolysis of Cu(IMDA)(MeGly). Although this interpretation is still open to debate, the observation that both OH^- and NO_2^- may act as nucleophiles in this system suggests that the last step of eq 7 may be represented in greater detail by the mechanism given in eq 12. In terms of this mechanism, the experimental rate constant, k, is Kk_{OH}. It has as yet not been possible to determine K or k_{OH}.

In other Cu–amino acid ester complexes[2,4] there is no evidence to indicate that the ester coordinates to

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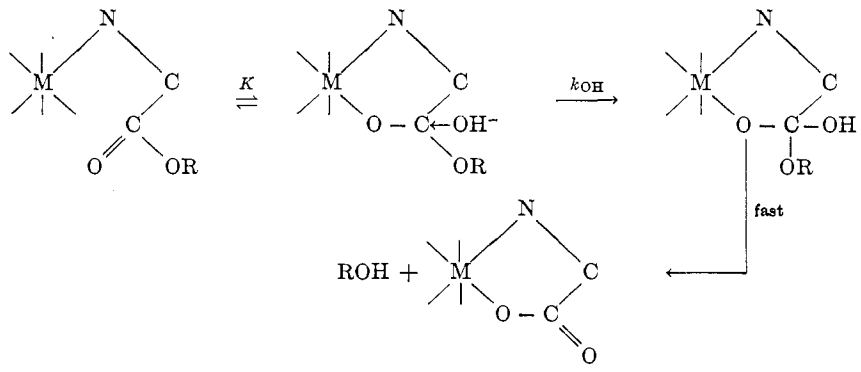

(12)

the Cu(II) in measurable concentrations. However, to account for the fact that the ester hydrolyzes about 10^4 times faster in Cu(RIMDA)(E) than as the free ester, it is assumed that an intermediate involving the coordinated ester group is important in the hydrolysis. Similar intermediates have been postulated in many other metal-catalyzed ester hydrolysis studies. In most instances, it was assumed that it was the carbonyl oxygen of the ester which coordinated to the metal. In a recent X-ray structural study[19] of an ester complex, $Cu[N(CH_2CO_2)_2(CH(CH(CH_3)_2)CO_2C_2H_5)] \cdot 2H_2O$, which we had studied earlier,[2] however, the ester group is coordinated to the Cu(II) at a very long distance (2.85 Å) along the tetragonal axis. Moreover it is the ether, rather than the carbonyl, oxygen which is directed toward the Cu(II). Although this is only a solid-state structure and coordination could be different in solution, it does raise the possibility that activation of the ester could occur by coordination of the ether oxygen to the Cu(II).

Only for the reactions of Cu(IMDA)(E) were both OH^- and H_2O attack terms observed. The second-order rate constant, k, for OH^- attack is about 10^{10} times greater than k_{H_2O} for water attack. This large difference in nucleophilicities between OH^- and H_2O is also observed in simple organic ester hydrolysis.[10-12] The values of k for both OH^- and H_2O attack are about 3×10^4 times larger when the ester is coordinated in Cu(RIMDA)(E) than when it is free in solution.

In the complexes Cu(IMDA)(E), where E is a glycine ester, the rate (Table VI) of hydrolysis of the ester decreases with the alcohol group as $CH_3 > C_2H_5 > n\text{-}C_4H_9$. This trend is normal for organic esters. The rates (Table VI) of hydrolysis of esters in Cu(IMDA)(E), where E is $NH_2CH(R)CO_2R'$, decrease with the nature of R in the order: $H > CH_3 > CH_2CH(CH_3)_2$. This is also the order observed for the base hydrolysis of the free amino acid esters.[5] The unreactivity of $(CH_3)_3N^+CH_2CO_2C_2H_5$ and $C_6H_5C(O)NHCH_2CO_2CH_3$ are undoubtedly due to the groups attached to the N atom which prevent (or severely diminish) coordination of the amino acid ester to Cu(IMDA).

The rate of hydrolysis of methyl glycinate in Cu(RIMDA)(MeGly) has been studied (Table VI) as a function of the nature of R in the iminodiacetate ligand. One conclusion appears valid: if R is an anionic coordinating group, as in $UrIMDA^{3-}$ and NTA^{3-}, the rate of hydrolysis of MeGly in, *e.g.*, $Cu(UrIMDA)(MeGly)^-$, is much slower than if R is a noncoordinating ligand. This low rate may be due to low values of K or k_{OH} in eq 12. Both of these constants are likely to be smaller if R coordinates to the Cu(II) since these coordinating groups will diminish the possibility of the ester group coordinating to the metal for both steric and electrostatic reasons. Moreover, once ester coordination has occurred, nucleophilic attack by OH^- is less favorable toward the negatively charged $Cu(UrIMDA)(MeGly)^-$ as compared to the neutral Cu(RIMDA)(MeGly).

In the series of complexes Cu(RIMDA)(MeGly), where R is a noncoordinating group, there is no obvious correlation between the rate of ester hydrolysis and the nature of R. Steric arguments may be used to rationalize partially the differences in rates, but at this time it does not appear fruitful to speculate on the origins of the rate variations.

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