The effect of two Cu(I) preferring ligands,[35] chloride and cyanide ions, on the observed rate of H_2O_2 decomposition was investigated (Figure 6). In the concentration range $\approx 4 \times 10^{-4}$ *M*, chloride ion does not affect the observed rate of reaction. However, low concentrations of cyanide ion increased the rate, but when the concentration of cyanide was increased ($>4 \times 10^{-5}$ *M*), an inhibitory effect was observed. It might be surmised that at low concentrations of CN^-, 1:1 copper–cyanide species are formed which are presumably catalytically active. At high cyanide concentrations, the extremely stable dicyano-, tricyano-, and tetracyanocuprate complexes are formed. Because of strong M–C π bonding,[36] these species would be catalytically inactive as they should show little tendency to react with peroxide anion to form the intermediate, $(CN)_2CuOOH$.

(35) P. Hemmerich, in ref 29, pp 15–34.

(36) D. Cooper and R. A. Plane, *Inorg. Chem.*, **5**, 16 (1966).

Stereoselective Interaction of Optically Active Amino Acids and Esters with (L-Valine-N-monoacetato)copper(II)

Bruce E. Leach and Robert J. Angelici

Contribution from the Department of Chemistry, Iowa State University, Ames, Iowa 50010. *Received March 27, 1969*

Abstract: Equilibrium constants for the coordination of optically active amino acidates (A^-) and their esters (E) to (L-valine-N-monoacetato)copper(II), Cu(L-ValMA) + L- or D-$A^- \rightleftharpoons$ Cu(L-ValMA)(A^-), have been determined. For leucine, phenylalanine, alanine, and serine, the value of K_f is 3.3–6.5 times larger for the L than for the D isomer. For valine the K_f value for the D enantiomer is 2.5 times greater than that for the L. For the ester, ethyl leucinate, the L isomer gives a K_f which is 3.4 times larger than that for the D ester. It has also been determined that the rate of hydrolysis of methyl leucinate and methyl phenylalaninate in the complexes, Cu(L-ValMA)(E), is higher for the D-amino acid ester than for the L isomer. The mechanisms and the origins of the stereoselective effects are discussed.

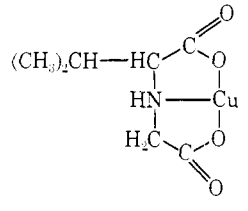
Like enzymes in general, metalloenzymes exhibit a high degree of specificity toward substrates of a particular structural type or optical configuration.[1] Since it is apparently the ligands surrounding the metal ion in these enzymes which are largely responsible for the over-all specificity of the enzyme, numerous attempts have been made to design simple metal complexes which also have some specificity. In this paper we shall be concerned with the specificity of labile metal complexes toward the two optical isomers of α-amino acids and their esters.[2] In some cases which have been studied, a metal complex which bears an optically active amino acidate, A^- ($NH_2CHRCO_2^-$), ligand shows no stereoselectivity in binding to a second L- or D-amino acidate. For example, the equilibrium constants for the reactions

$$\text{Cu(L-A)}^+ + \text{L-A}^- \rightleftharpoons \text{Cu(L-A)}_2$$

$$\text{Cu(L-A)}^+ + \text{D-A}^- \rightleftharpoons \text{Cu(L-A)(D-A)}$$

are identical for the amino acids alanine, phenylalanine, valine, and proline.[3] On the other hand, these equilibrium constants are reported to be different for asparagine.[4] Relative stabilities of analogous histidine complexes, M(L-Hist)$_2$ and M(L-Hist)(D-Hist), have been shown to be identical[5] when M is Ni^{2+} but different[6] when M is Co^{2+}. From these results it is not clear why stereoselectivity is observed in some cases but not in others.

In the present study, equilibrium constants for the coordination of optically active amino acids and esters to the complex (L-valine-N-monoacetato)copper(II), Cu-



(L-ValMA), have been determined. This complex does indeed form more stable complexes with one optical isomer than it does with the other enantiomer of most of the acids and esters examined. The Cu(L-ValMA) also exhibits some stereoselectivity in its catalysis of the hydrolysis of certain optically active amino acid esters.

Experimental Section

Materials. The amino acids, D- and L-valine (Val), D- and L-leucine (Leu), D- and L-serine (Ser), D- and L-alanine (Ala), and D- and L-phenylalanine (PhAla), were obtained from Mann Research Laboratories. The amino acid esters were prepared by the HCl-catalyzed reaction of the amino acid with the desired alcohol according to standard methods.[7] Proton nuclear magnetic resonance spectrometry was used to establish the identity of the isolated ester hydrochlorides. These spectra were measured on a

(1) A. E. Dennard and R. J. P. Williams in "Transition Metal Chemistry," Vol. 2, R. L. Carlin, Ed., Marcel Dekker, Inc., New York, N. Y., 1966, p 116.

(2) J. H. Dunlop and R. D. Gillard, *Advan. Inorg. Chem. Radiochem.*, **9**, 185 (1966).

(3) R. D. Gillard, H. M. Irving, R. M. Parkins, N. C. Payne, and L. D. Pettit, *J. Chem. Soc., A*, 1159 (1966); R. D. Gillard, H. M. Irving, and L. D. Pettit, *ibid.*, 673 (1968).

(4) W. E. Bennett, *J. Am. Chem. Soc.*, **81**, 246 (1959).

(5) J. E. Hix, Jr., and M. M. Jones, *ibid.*, **90**, 1723 (1968).

(6) C. C. MacDonald and W. D. Phillips, *ibid.*, **85**, 3736 (1963).

(7) J. P. Greenstein and M. Winitz, "Chemistry of the Amino Acids," Vol. 2, John Wiley and Sons, Inc., New York, N. Y., 1961, p 926.

Varian Associates Model A-60 spectrometer in D_2O solvent using sodium 2,2-dimethyl-2-silapentane-5-sulfonate as the internal standard (chemical shift, δ, is 0.0 ppm). Integration and splitting patterns allowed the following chemical shift assignments. As expected, spectra of optical isomers of the same ester were identical.

MeLeu, $NH_2CH(CH_2CH(CH_3)_2)CO_2CH_3$: α-CH, ~3.8; CH_2, ~3.8; γ-CH, ~1.8; $(CH_3)_2$, 0.95; CH_3, 3.8. MeAla, $NH_2CH(CH_3)CO_2CH_3$: CH, 4.25; β-CH_3, 1.58; CH_3, 3.85. MeSer, $NH_2CH(CH_2OH)CO_2CH_3$: CH, 4.25; CH_2, 4.03; CH_3, 3.87. MePhAla, $NH_2CH(CH_2C_6H_5)CO_2CH_3$: CH, 4.45; CH_2, 3.32; C_6H_5, ~7.4; CH_3, 3.87.

The L-ValMA, $HO_2CCH(CH(CH_3)_2)NH(CH_2CO_2H)$, was prepared according to a previously reported procedure.[8] Doubly distilled water was used in the preparation of all solutions. Solutions of $Cu(NO_3)_2$ were standardized by the method noted previously.[9] Amino acids were assayed for total titratable hydrogen.[10]

Equilibrium Measurements. The pK_E values for ionization of the protonated esters

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

and the log K_f values for reaction of Cu(L-ValMA) with the amino acidates (A^-) or their esters (E)

$$Cu(L\text{-ValMA}) + A^- \overset{K^f}{\rightleftharpoons} Cu(L\text{-ValMA})(A)^- \qquad (2)$$

$$Cu(L\text{-ValMA}) + E \overset{K_f}{\rightleftharpoons} Cu(L\text{-ValMA})(E) \qquad (3)$$

were determined with Radiometer pH equipment exactly as described previously.[8] Since the esters hydrolyzed during the titrations, it was possible to determine K_f values for only those esters which hydrolyzed very slowly under the conditions of the titrations. For this reason EtLeu was the most convenient; rapid titrations of MeSer and MePhAla gave somewhat less accurate results.

Kinetic Measurements. Rates of ester hydrolysis at 25.0° in the presence of Cu(L-ValMA) were determined by pH-Stat techniques used in earlier work.[8] Standard sodium hydroxide was added to maintain constant pH and also to provide a means of following the rate of hydrolysis. First-order plots[9] in total ester concentration were used to obtain pseudo-first-order rate constants, k_{obsd}.

Optical Rotatory Dispersion Measurements. A Jasco ORD/UV-5 spectrophotometer was used to show that Cu(L-ValMA) did not racemize during the equilibrium and kinetic studies.

Results

(1) Ionization Constants of Amino Acids and Their Esters. Ionization constants of the protonated esters, HE^+ (eq 1), were evaluated from the titration data as described in an earlier publication.[8] These results together with acid dissociation constants taken from the literature are given in Table I; these values were used in the evaluation of the formation constants of the amino acids and esters with Cu(L-ValMA).

(2) Formation Constants, K_f, for Coordination of the Optically Active Amino Acidates and Their Esters to Cu(L-ValMA). Values of K_f were calculated from the titration data in exactly the same manner as given previously[8] using equations reported in the literature.[11]

(3) Kinetics of Base Hydrolysis of Amino Acid Esters in the Presence of Cu(L-ValMA). The rates of hydrolysis of several optically active amino acid esters as catalyzed by Cu(L-ValMA) at several pH values are given in Table II. The pseudo-first-order rate constants given are functions of the pH and the Cu(L-ValMA) concentration and will be discussed in detail in the Discussion section.

Table I. Ionization Constants of Amino Acids and Their Esters at 25.0°

Acid	pK_a[a]	Optically active ester	pK_E[b]
Ala	2.34	L-Me	7.86
	9.87	D-Me	7.85
Ser	2.21	L-Me	7.04
	9.15	D-Me	7.04
Leu	2.36	L-Me	7.63[c]
	9.60	D-Me	7.63[c]
Val	2.32	L-Et	7.75[c]
	9.62		
PhAla	1.83	L-Me	7.00
	9.13	D-Me	7.00

[a] "Stability Constants," Special Publication No. 17, The Chemical Society, London, 1964. [b] Ionic strength is 0.050 M KNO_3 plus 0.0067 M HE^+Cl^-. [c] Reference 8.

Table II. Rates of Cu(L-ValMA)-Catalyzed Hydrolysis of D- and L-Amino Acid Esters at 25.0° [a]

pH	10^4k_{obsd}[a]	pH	10^4k_{obsd}[a]	pH	10^4k_{obsd}[a]
L-MeLeu		L-MePhAla		L-MeSer	
6.70	0.445	7.50	4.02	6.80	1.05
6.80	0.616	7.70	6.40	7.10	1.98
6.90	0.806			7.30	2.93
7.00	1.01	D-MePhAla		7.40	3.76
7.10	1.42	7.50	5.35	7.60	6.20
7.20	1.85	7.70	8.79	7.70	7.67
7.30	2.22			7.80	9.73
7.40	2.79	L-MeAla		7.90	12.2
7.50	3.48	7.20	3.35	8.00	15.1
7.60	4.55	7.30	5.15	8.10	18.5
7.90	9.36	7.40	8.18	8.20	24.5
		7.50	9.92		
D-MeLeu		7.60	12.3	D-MeSer	
6.80	0.333	7.70	15.0	7.60	7.14
6.90	0.519			7.70	8.55
7.00	0.795	D-MeAla		7.80	10.6
7.10	0.979	6.80	0.788	7.80	10.9
7.20	1.41	7.00	1.94		
7.20	2.54[b]	7.10	2.53		
7.20	4.10[c]	7.20	3.82		
7.20	5.27[d]	7.30	5.68		
7.20	5.42[e]	7.40	7.38		
7.30	2.02	7.50	10.2		
7.40	2.78	7.60	13.0		
7.50	4.25	7.70	16.1		
7.60	5.14	7.80	19.7		
7.70	6.14	7.90	24.4		
7.90	10.1	8.00	29.8		
8.20	20.3				

[a] Initial concentrations: [Cu(L-ValMA)] = 0.0033 M; [ester] = 0.00033 M; [KNO_3] = 0.05 M. [b] Initial concentrations same as in footnote *a* except [Cu(L-ValMA)] = 0.0067 M. [c] Initial concentrations same as in footnote *a* except [Cu(L-ValMA)] = 0.0100 M. [d] Initial concentrations same as in footnote *a* except [Cu(L-ValMA)] = 0.0133 M. [e] Initial concentrations same as in footnote *a* except [Cu(L-ValMA)] = 0.0200 M.

Discussion

Equilibria. The aminoacidates, A^-, given in Table III react with Cu(L-ValMA) to form the complex, $Cu(L\text{-ValMA})(A)^-$, according to eq 2. Except for valine, the L enantiomer of the amino acidate coordinates more strongly with Cu(L-ValMA) than does the D isomer. This stereoselectivity of the Cu(L-ValMA) complex for the L-enantiomer must almost certainly result from steric repulsion between the R group on the α-carbon atom of the amino acidate ligand and the $-CH(CH_3)_2$ group on the α-carbon atom of L-ValMA. One

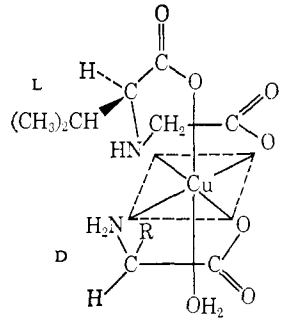
(8) B. E. Leach and R. J. Angelici, *Inorg. Chem.*, **8**, 907 (1969).
(9) R. J. Angelici and B. E. Leach, *J. Am. Chem. Soc.*, **89**, 4605 (1967).
(10) We thank Mrs. Juanita Allison, Iowa State University, for performing these analyses.
(11) D. Hopgood and R. J. Angelici, *J. Am. Chem. Soc.*, **90**, 2508 (1968).

Table III. Formation Constants, K_f, for the Reaction of Cu(L-ValMA) with Amino Acidates and Their Esters at 25.0°

Acidate	Log K_f[a,b]	Δ	Ester	Log K_f[a,b]
L-Leu	5.74	0.81	L-Et	3.73
D-Leu	4.93		D-Et	3.20
L-PhAla	5.52	0.58	L-Me	2.64
D-PhAla	4.92			
DL-PhAla	5.14			
L-Ala	5.29	0.55		
D-Ala	4.74			
L-Ser	5.55	0.52	L-Me	2.36
D-Ser	5.03			
L-Val	5.21	0.41		
D-Val	5.62			

[a] Standard deviations are approximately 0.1 log unit. [b] Ionic strength is 0.057 *M*. The solution contains 0.04 *M* KNO_3, 0.005 *M* $Cu(NO_3)_2$, 0.005 *M* L-ValMA, and 0.005 *M* amino acid or ester.

geometry which could account for the lower formation constants with the D isomers is shown in structure **1**. In this structure, there will be significant repulsion between these groups when the configuration of L-ValMA is L and that of the amino acidate is D. The structure is shown with nitrogen atoms of both ligands in a *cis* position. Models indicate that this is a requirement for maximum repulsion between the bulky groups. That the complex is likely to prefer *cis* N groups is not



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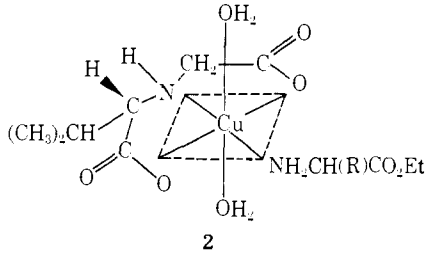
well established. The amino-acidate complex Cu(L-Ala)$_2$ is known[12] to exist in both *cis* and *trans* forms, and $Cu(Gly)_2 \cdot H_2O$ crystallizes in the *cis* form whereas $Cu(Gly)_2 \cdot 2H_2O$ has the geometry with the N atoms *trans*. From these observations and other studies,[13] it has been suggested[14] that the *cis* and *trans* isomers are of very similar stability and probably both exist in solution. Likewise, it has been suggested that complexes of Cr(III) and Co(III) with IMDA, $HN(CH_2CO_2^-)_2$, ligands have structures with both *cis* and *trans* N atoms. Thus $K[Cr(IMDA)_2] \cdot 2.5H_2O$[15] and $K[Co(IMDA)_2] \cdot 4H_2O$[16] have *cis* geometries, whereas $K[Co(IMDA)_2] \cdot 2H_2O$[17] and $Na[Cr(MIMDA)_2]$,[15] where MIMDA is the N-methyliminodiacetate ligand, contain *trans* N atoms.

(12) H. C. Freeman, *Advan. Protein Chem.*, 22, 257 (1967).
(13) T. Yasui and Y. Shimura, *Bull. Chem. Soc. Japan*, 39, 604 (1966); S. H. Laurie, *Aust. J. Chem.*, 20, 2609 (1967).
(14) K. Tomita, *Bull. Chem. Soc. Japan*, 34, 280 (1961).
(15) J. A. Weyh and R. E. Hamm, *Inorg. Chem.*, 7, 2431 (1968).
(16) M. Mori, M. Shibata, E. Kyuno, and F. Maryama, *Bull. Chem. Soc. Japan*, 35, 75 (1962).
(17) J. Hidaka, Y. Shimura, and R. Tsuchida, *ibid.*, 35, 567 (1962).

Perhaps in the present system the *cis* and *trans* isomers are in equilibrium and stereoselectivity only occurs because of the presence of the *cis* form. The only evidence to support the structure **1** are the differences in K_f for the different enantiomers of the amino-acidate ligands. Clearly more structural studies of labile metal complexes would be very useful.

The differences (Table III) between the K_f values for the L and D enantiomers of the various amino acidates decrease in the order: Leu > PhAla ~ Ala ~ Ser. Very roughly this is also the order of decreasing size of the R group on the α-carbon atom. In these instances K_f is largest for the L amino acidate. On the contrary, for the amino acidate with the bulkiest R group, Val, the D isomer forms the more stable complex with Cu(L-ValMA). The reason for this reversal in the case of Val is not obvious but must be related to a change in the structure from that proposed in **1**.

As expected, the K_f values (eq 3) for the complexation of the amino acid esters to Cu(L-ValMA) are much lower than observed for the corresponding amino acidates. This derives from at least two factors: (1) the basicity of the N atom is much lower in E than in A^-; (2) the A^- coordinates to the metal ion through both the $-NH_2$ and the $-CO_2^-$ groups, whereas the amino acid ester, E, almost certainly only binds through the $-NH_2$ donor group.[11,18] Because of the tendency of Cu(II) to coordinate to strong donor groups in a square plane, one might expect these complexes to have the geometry given in **2**. If indeed this is the configuration of the complex it is not clear why the L enantiomer of EtLeu forms a more stable complex than the D optical isomer. Models of structure **2** indicate that the asymmetric cen-



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ters are too far removed from each other to influence the relative stabilities of the complexes unless the $-CO_2Et$ group of the ester is either coordinated directly to the Cu(II) or is hydrogen bonded to an H_2O group which is coordinated to the Cu(II). In any case, structure **2** cannot account for the observed stereoselectivity.

To ensure that neither the amino acidates nor the Cu(L-ValMA) racemized during either the equilibrium or kinetic studies, the ORD curve of a solution of Cu(L-ValMA), prepared from $Cu(NO_3)_2$ and L-ValMA, was observed not to change over a period of several days at room temperature, and also no change was observed in 5 hr at pH 7.5.

Kinetics of Ester Hydrolysis. As discussed elsewhere[8,19] catalysis of amino acid ester hydrolysis depends upon coordination of E to the metal ion; this is followed by hydrolysis of coordinated E. The mechanism which will be used in this discussion assumes OH^- attack on the coordinated ester. It should be recognized, however, that a mechanism involving hy-

(18) R. J. Angelici and B. E. Leach, *J. Am. Chem. Soc.*, 90, 2499 (1968).
(19) R. J. Angelici and D. Hopgood, *ibid.*, 90, 2514 (1968).

droxo-complex formation also fits the rate data and has been discussed previously.[18] The general mechanism assumed here requires a rapid coordination equilibrium (eq 4), followed by a rate-determining attack of

$$\text{Cu(L-ValMA)} + \text{HE}^+ \overset{K_E K_f}{\rightleftharpoons} \text{Cu(L-ValMA)(E)} + \text{H}^+ \quad (4)$$

$$\text{Cu(L-ValMA)(E)} + \text{OH}^- \xrightarrow{k} \text{Cu(L-ValMA)(A)}^- + \text{alcohol} \quad (5)$$

OH^- on the ester in Cu(L-ValMA)(E). At low pH values equilibrium 4 is expected to lie far to the left, and the rate law for the over-all rate of HE^+ hydrolysis should be

$$\text{rate} = (kK_E K_f/K_w)[\text{HE}^+][\text{Cu(L-ValMA)}][\text{OH}^-]^2 \quad (6)$$

In the lowest pH region studied the reactions were in fact observed to exhibit a second-order dependence upon $[OH^-]$. In this region the rate constant, k, for the rate-determining step (eq 5) could be calculated from the experimental pseudo-first-order rate constant, k_{obsd}, using the known values of K_E, K_f, and K_w.

$$k_{obsd} = (kK_E K_f/K_w)[\text{Cu(L-ValMA)}][\text{OH}^-]^2 \quad (7)$$

More generally, however, the kinetic studies were carried out at sufficiently high pH values and high Cu(L-ValMA) concentrations that equilibrium 4 was shifted far to the right. Under these conditions, the rate law is simply

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

and the experimental rate constant, k_{obsd}, is

$$k_{obsd} = k[\text{OH}^-] \quad (9)$$

The values of k given in Table IV were usually calculated from expression 9.

Table IV. Rate Constants for Optically Active Amino Acid Ester Hydrolysis in Cu(L-ValMA)(E) According to Eq 5[a]

Ester	L isomer $10^{-3}k$, M^{-1} sec^{-1}	D isomer $10^{-3}k$, M^{-1} sec^{-1}
MeLeu	1.0	1.3
MePhAla	1.0	1.4
MeAla	2.5	2.5
MeSer	1.3	1.4

[a] At 25.0° with initial concentrations of [Cu(L-ValMA)] = 0.0033 M, [E] = 0.00033 M, and $[KNO_3]$ = 0.05 M.

As expected from eq 7 and 9, the pseudo-first-order rate constant, k_{obsd}, should depend on $[OH^-]$ to the second power at low pH and gradually become first order at high pH. This is the behavior that is observed, as shown by Figure 1 for the Cu(L-ValMA)-catalyzed hydrolysis of L-MeLeu and D-MeLeu.

The nonmetal-complex-catalyzed base hydrolysis of MeLeu[20] occurs with a rate constant of 0.455 M^{-1} sec^{-1} as compared to that for the base hydrolysis of the ester in Cu(L-ValMA)(L-MeLeu) for which the value is 1.0×10^3 M^{-1} sec^{-1}. The 2200-fold acceleration is presumed[18] to result from the direct interaction of the ester group with the metal. Thus the first step in the mechanism of reaction 5 is probably the chelation of the ester group to the metal. Whether the ester coordinates through the carbonyl or the ether oxygen is not known, but a recent X-ray study[8] suggests possible ether–oxygen coordination. Hydroxide attack at the activated ester carbon atom effects the hydrolysis. In terms of this mechanism, the calculated rate constant, k, is Kk_{OH}. Hence the difference (Table IV) in k values for, *e.g.*, Cu(L-ValMA)(L-MeLeu) and Cu(L-ValMA)(D-MeLeu), may be due to a change in K, k_{OH}, or in both. If the $(CH_3)_2CH$–group on L-ValMA and the R group on the ester were interacting in the chelated ester complex, K may differ for the two optical isomers of the ester. In the present study, it is possible to propose coordinated ester species in which the L ester would coordinate less strongly than the D ester because of repulsion between the ester R group and the $(CH_3)_2CH$– group on the L-ValMA. One is reluctant to make this suggestion because it has been shown earlier in this work that for the chelated amino acidates the L isomers coordinate *more* strongly than the D isomers—just the opposite of what must be proposed to account for the difference in rates of ester hydrolysis in Cu(L-ValMA)(NH_2CHRCO_2Me). The differences in k values (Table IV) for the different optical isomers could be due to differences in k_{OH} for the L and D isomers. The differences in k values must derive from the particular stereochemistry of Cu(L-ValMA)(NH_2CHRCO_2Me), but it is not clear from a study of models that the rate of OH^- attack should

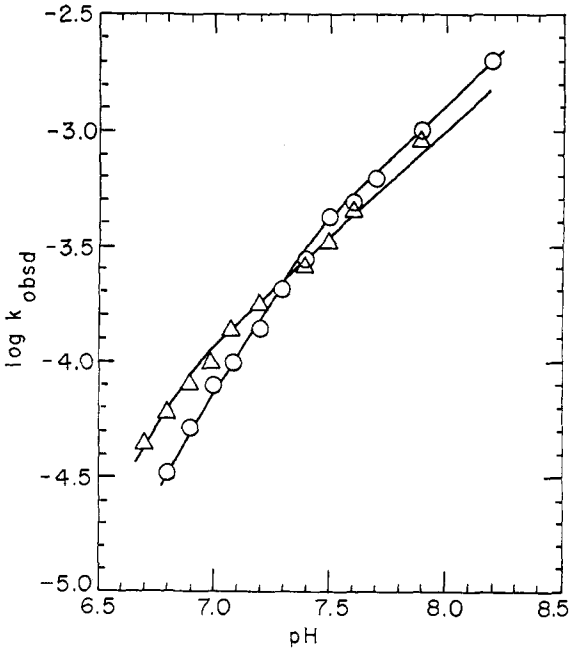
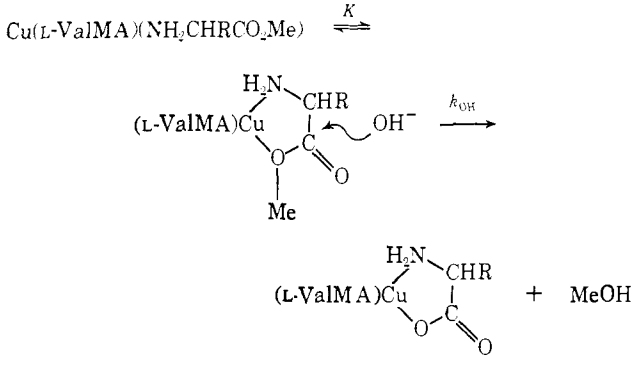


Figure 1. Rates of hydrolysis of L- (△) and D- (○) methyl leucinate in the presence of Cu(L-ValMA). Conditions are given in Table II.



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

differ for the two enantiomers. In the presence of a complex with no asymmetric center,[8] (N-cyclohexyliminodiacetato)copper(II), $C_6H_{11}N(CH_2CO_2)_2Cu$, L- and D-MeLeu hydrolyzed with values of k_{obsd} (1.17×10^{-3} and 1.13×10^{-3} sec^{-1}, respectively, at pH 6.80) which were the same.

Jones and Hix[5] have suggested that the difference in rates of hydrolysis of methyl histidinate in the histidinato(methyl histidinate)–nickel(II) complexes, Ni(L-Hist)(L-MeHist)$^+$ (17 M^{-1} sec^{-1}) and Ni(L-Hist)(D-MeHist)$^+$ (45 M^{-1} sec^{-1}), results from differences in the ester chelation equilibrium constants rather than differences in rates of OH^- attack on the coordinated ester. Hay and Morris[21] found no kinetic stereoselectivity in the analogous Cu(II) reactions. They suggested that the difference between the Cu(II) and Ni(II) systems originated in the preference of these metal ions for four and six coordination, respectively. Thus there is a greater possibility of ester group coordination to the metal in Ni(L-Hist)(L-MeHist) than in Cu(L-Hist)(L-MeHist) and therefore a greater degree of stereoselectivity in the ester coordination equilibrium.

Although the rates of hydrolysis of the enantiomers of MeLeu and of MePhAla are different in the Cu(L-ValMA)(NH_2CHRCO_2Me) complexes, there is no measurable difference (Table IV) for MeAla or MeSer. These latter esters have smaller R groups, and interaction with the $(CH_3)_2CH-$ group of the Cu(L-ValMA) is presumably not as great.

(21) R. W. Hay and P. J. Morris, *Chem. Commun.*, 18 (1969).

Attempts to determine accurate values of K_f for L- and D-MeLeu were hampered by the significant rate of hydrolysis of the ester during the equilibrium measurements. Instead K_f values for L- and D-EtLeu were determined (Table III); it was assumed that L- and D-MeLeu would have essentially the same K_f values. Taking advantage of the larger K_f value of L-MeLeu as compared to that for D-MeLeu, an attempt to maximize the difference (Figure 1) in the Cu(L-ValMA)-catalyzed rates (k_{obsd}) of hydrolysis of L- and D-MeLeu was carried out. Under conditions of pH 7.40, 0.00033 M L- or D-MeLeu, and 0.00066 M Cu(L-ValMA), the k_{obsd} values for L- and D-MeLeu were 1.80×10^{-4} and 1.04×10^{-4} sec^{-1}, respectively. Note that under these conditions, L-MeLeu is hydrolyzed *faster* than the D isomer; this is opposite to what is observed at higher pH and higher Cu(L-ValMA) concentration (Figure 1).

Stereoselective hydrolysis was attempted with one other complex,[8] (D-α-phenylglycine-N-monoacetato)-copper(II), $HN(CH_2CO_2)(CH(C_6H_5)CO_2)Cu$. At pH 6.30, L-MeLeu and D-MeLeu hydrolyzed in the presence of this complex with k_{obsd} values of 2.86×10^{-4} and 3.08×10^{-4} sec^{-1}, respectively. Although these reactions have not been studied in detail, it appears that this complex exhibits little, if any, stereoselectivity in catalyzing the hydrolysis of optically active amino acid esters.

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