greatest catalysis is observed in complexes of the ligands $C_2H_5OOC(CH_2)_nN(CH_2COOH)_2$, when $n = 1$. Increasing n to a value of 2 decreases the rate for the Cu(II) complex by a factor of 45 but only by a factor of 5.7 for Pb(II). For Sm(III) such a change decreases the rate only by a factor of 1.2, while the rate actually increases for Lu(III) by a factor of 1.3 in going from $n = 1$ to $n = 2$. While the relative catalytic abilities of different metal ions in the $n = 2$ series are not understood, the larger ions appear to be able to more effectively catalyze esters containing longer linkages between the N atom and the ester group. Extending the chain to $n = 3$ yields complexes of Cu(II), Sm(III), and Lu(III) which undergo no measurable hydrolysis up to pH 8. Models of these complexes show that it is very difficult for the ester carbonyl group to coordinate to the metal ion.

Acknowledgment. We again gratefully acknowledge support of this research by the U. S. Public Health Service through Grant No. GM-12626.

Equilibrium and Stereochemical Studies of the Interactions of Amino Acids and Their Esters with Divalent Metal Nitrilotriacetate Complexes

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Abstract: The formation constants of glycine (K_{fGly}) with a series of divalent metal nitrilotriacetates ($[M(NTA)]^-$) to form $[M(NTA)(Gly)]^{2-}$ follow the Irving-Williams order, Mn < Co < Ni < Cu > Zn. The formation constants of ethyl valinate (K_{fEtVal}), a representative α-amino acid ester which hydrolyzes negligibly during the potentiometric titrations, were also measured with the $[M(NTA)]^-$ complexes. The latter constants show a significantly different trend to that exhibited by the constants for glycine complexation. The parameter $K_{\mathrm{fGly}}/K_{\mathrm{fEtVal}}$ increases from about unity to 800 along the series $\mathrm{Mn} \lesssim \mathrm{Pb} \ll \mathrm{Co} < \mathrm{Zn} < \mathrm{Cu} < \mathrm{Ni}$, suggesting that extensive coordination to both the amino and ester groups occurs only in the complexes of manganese and lead; these metal ions are the best oxygen acceptors in the series. On the other hand, α-amino acid esters are probably monodentate in their complexes with copper and nickel nitrilotriacetates. The complexes of *l*-valine and its ethyl ester with $[Co(NTA)]^-$ exhibited Cotton effects which indicate a small extent of ester chelation, probably about 15%. This is consistent with the formation constant data. The absorption spectra of a series of $[Cu(NTA)]^-$ complexes with various ligands show that large tetragonal distortions only occur with chelating ligands such as α-amino acids or ethylenediamine. Monodentate ligands form complexes of approximate cubic symmetry. Histidine and its methyl ester have very similar donor properties toward $[Cu(NTA)]^-$. They act as monodentate ligands at low pH bonding through the imino nitrogen, then chelate at higher pH through the imino and amino nitrogen atoms. The formation constants of a series of bidentate α-amino acids, $NH_2CH(R)CO_2H$, or of their esters with $[Cu(NTA)]^-$ are relatively invariant.

Since the discovery of the metal-ion-catalyzed hydrolysis of amino acid esters in 1952,[1] these reactions have been studied by a number of research groups with hopes of elucidating the role of metal ions in biological systems.[2-4] The generally accepted mechanism of ester catalysis is one in which the carbonyl carbon atom is activated toward nucleophilic attack by the polarizing effect of the metal ion. This can occur by induction through the coordinated amino group or by interaction of the carbonyl oxygen atom with the metal. The former is proposed for the hydrolysis of copper(II) complexes of the potentially tridentate histidine esters in which carbonyl group interaction with the metal is less favorable.[5] The latter is postulated for the hydrolysis of metal complexes of potentially bidentate esters of α-amino acids such as glycine.[6] In this case transient coordination of the carbonyl oxygen prior to nucleophilic attack is postulated for labile metal ions such as copper(II). Such ester carbonyl coordination has not, however, been conclusively established for amino acid ester–metal complexes in aqueous solution,[7] although it is present in some complexes in the solid state.[8,9] In solution the extent of ester coordination is probably very small, but Alexander and Busch[10] have demonstrated that it is necessary for a large rate enhancement for ethyl glycinate hydrolysis in the complex $[Co(en)_2\text{-}EtGly]^{3+}$.

Current studies in this laboratory are concerned with the interaction of complexes of divalent metal ions and quadridentate ligands with amino acid esters. Re-

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[1] H. Kroll, *J. Am. Chem. Soc.*, 74, 2036 (1952).

[2] F. Basolo and R. G. Pearson, "Mechanisms of Inorganic Reactions," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1967, pp 625–632.

[3] M. M. Jones in "Mechanisms of Inorganic Chemistry," Advances in Chemistry Series, No. 49, American Chemical Society, Washington, D. C., 1965, pp 153–166.

[4] T. C. Bruice and S. Benkovic, "Bioorganic Mechanisms," Vol. 1, W. A. Benjamin, Inc., New York, N. Y., 1966, pp 110–118.

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

[6] H. L. Conley and R. B. Martin, *J. Phys. Chem.*, 69, 2194 (1965).

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

[9] R. W. Hay and L. J. Porter, *Australian J. Chem.*, 20, 675 (1967).

[10] M. D. Alexander and D. H. Busch, *J. Am. Chem. Soc.*, 88, 1130 (1966).

ported here are equilibrium and stereochemical studies of the reactions of amino acids and their esters with complexes of nitrilotriacetic acid (NTA) with the divalent ions of manganese, cobalt, nickel, copper, zinc, and lead. The formation constants of the $[M(NTA)]^-$ complexes were measured by Schwarzenbach, *et al.*,[11] and range from about 10^8 for manganese to 10^{13} for copper; hence 1:1 mole ratio mixtures of a divalent metal ion and NTA exist entirely as the $[M(NTA)]^-$ complex under the conditions used in this work. Kinetic studies of amino acid ester hydrolysis as catalyzed by $[Cu(NTA)]^-$ are reported in a subsequent paper.[12]

Experimental Section

Materials. Amino acids and methyl glycinate (MeGly), ethyl alaninate (EtAla), and ethyl leucinate (EtLeu) were supplied by Mann Research Laboratories. Eastman Organic Chemicals supplied ethyl and *n*-butyl glycinates (Et- and BuGly), and samples of ethyl valinate (EtVal), ethyl phenylalaninate (EtPhAla), ethyl β-alaninate (Etβ-Ala), and methyl histidinate (MeHist) were prepared by standard techniques.[13] *l*-Valine, from Aldrich Chemical Co., was used for Cotton effect experiments; otherwise, either the *l* or *dl* compounds were used. Some commercial esters contained traces of the parent amino acid and these were purified by standard methods.[13] The customary abbreviations for the names of amino acids are used in the paper and are given in parentheses above. The hydrochloride salts of the esters were used. Nitrilotriacetic acid (NTA) and *d*-amphetamine were supplied by Aldrich Chemical Co., and the chloride or nitrate salts of divalent metal ions were of analytical grade. The exact metal salts used are given in a previous paper.[14]

Potentiometric Apparatus. Potentiometric measurements were made by using the following Radiometer equipment: TTT1c titrator, PHA 630T scale expander, SBR2c titrigraph, and SBU1a syringe buret. The electrode system consisted of glass electrode G202B and calomel electrode K401. The pH meter was standardized by using five standard buffer solutions covering the pH range 4–10.

Equilibrium Measurements. pK_a values for the esters BuGly, EtAla, Etβ-Ala, and EtVal were determined by manual titration of

$$HE^+ \xrightleftharpoons{K_a} H^+ + E$$

an 8-ml aqueous solution containing 0.0067 M ester and 0.050 M KNO_3, with 0.206 M NaOH solution. The pH of the solution was measured, using the scale expander, after each addition of an aliquot of NaOH solution. The hydroxo complex, $[M(NTA)(OH)]^{2-}$, formation constants, and the formation constants for the interaction of $[M(NTA)]^-$ (M = Mn, Co, Ni, Cu, Zn, Pb) with EtVal, Etβ-Ala, MeHist, and the amino acids were determined in the same manner. The formation constants for the other esters with $[Cu(NTA)]^-$ were determined by relatively fast automatic titration (~10 min), three titrations per ester, to minimize errors due to ester hydrolysis. The concentrations of starting materials in the 8-ml aqueous solutions were 0.0067 M MCl_2 or $M(NO_3)_2$, 0.0067 M NTA, 0.0067 M amino acid or ester, and 0.05 M KNO_3. These solutions were titrated with 0.206 M NaOH. Corrections were made for volume increases during the titrations, all of which were carried out under 1 atm of nitrogen at 25.0°.

Activity Coefficients. The activity coefficients, $\gamma_\pm$, of hydrogen and hydroxide ions were estimated from Davies' equation[15]

$$-\log \gamma_\pm = 0.50 Z_1 Z_2 I^{1/2}/(1 + I^{1/2}) - 0.1I$$

This equation is in excellent agreement with experimental data up to $I = 0.1\ M$, regardless of the nature of the electrolyte. Hence hydrogen and hydroxide ion concentrations were calculated by using the following relationships

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

where K_w is the autoionization constant of water.

Negligible increases of ionic strength occur in the titrations of the esters, both in the presence and absence of $[M(NTA)]^-$ complexes. In cases where the ionic strength did change during the titration, the mean ionic strength, *i.e.*, that at the half-equivalence point of each titration, was used to estimate activity coefficients. Mean ionic strengths are given in Tables II and III. Even in titrations where the ionic strength changed, the change in activity coefficients had a negligible effect on the over-all equilibrium constant being determined.

Literature pK values for amino acids and esters were used when they were in agreement with the values we measured.

Spectrophotometric Measurements. Absorption spectra in the near-infrared and visible regions were measured with a Cary 14 recording spectrophotometer. Cotton effects were recorded with a Jasco Model ORD/UV-5 dichrograph modified by Drs. J. G. Foss and M. E. McCarville. All measurements were made on aqueous solutions of suitable concentration in 1-cm silica cells. The desired species were generated by adjusting the pH with NaOH solution.

Results

(A) Equilibrium Constants. (1) Ionization Constants of the Amino Acid Esters. These were calculated from the expression

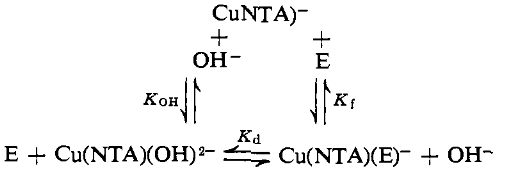
$$pK_a = pH + \log \gamma_\pm + \log \frac{[E]_{tot} - ([Na^+] + [H^+] - [OH^-])}{[Na^+] + [H^+] - [OH^-]}$$

This equation was derived from standard expressions for electroneutrality and total ester concentration ($[E]_{tot}$). The values of pK_a given in Table III are an average of ten determinations calculated over the range 20–80% of titration.

(2) Hydroxo-Complex Formation Constants. The complexes $[M(NTA)]^-$ (M = Cu, Zn) exhibit titration curves which show that only a monohydroxo complex $[M(NTA)(OH)]^{2-}$ is formed in the pH range below 12. Further substitution by hydroxide ions occurs above pH 12. On the other hand, the complexes of NTA with Mn, Co, Ni, and Pb appear not to form discrete monohydroxo complexes but also to form dihydroxo complexes in the pH region 10–13. Experimental limitation precluded accurate determination of hydroxo complex formation constants for these metal ions.

Ionization constants, $K_i = [MZOH^{2-}][H^+]/[MZ^-]$, where MZ = [M(NTA)], were computed for the Cu and Zn systems in the same way as those for the amino acid esters. The hydroxo complex formation constants, $K_{OH} = [MZOH^{2-}]/[MZ^-][OH^-]$, were derived from the K_i values and are given in Table II.

Potentiometric titrations of 1:1 mole ratios of $[Cu(NTA)]^-$ with Gly and with EtVal show that 2 equiv of NaOH is added in the pH range up to about pH 12. The addition of the second equivalent is postulated as due to formation of a Cu(II) hydroxo species. The data from these titrations show that hydroxo complex formation occurs only by displacement of the acid or ester, *i.e.*, that the following equilibria are involved



$$\begin{tikzcd} & \text{CuNTA)}^- & \\ & +\ \ OH^- \qquad +\ \ E & \\ E + Cu(NTA)(OH)^{2-} \arrow[rr, shift left, "K_d"] & & Cu(NTA)(E)^- + OH^- \arrow[ll, shift left] \end{tikzcd}$$

$$CuNTA)^- + OH^- \underset{}{\overset{K_{OH}}{\rightleftharpoons}} Cu(NTA)(OH)^{2-} \qquad CuNTA)^- + E \overset{K_f}{\rightleftharpoons} Cu(NTA)(E)^-$$

$$E + Cu(NTA)(OH)^{2-} \xrightleftharpoons{K_d} Cu(NTA)(E)^- + OH^-$$

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[11] G. Schwarzenbach, G. Anderegg, W. Schneider, and H. Senn, *Helv. Chim. Acta*, 38, 1147 (1955).

[12] R. J. Angelici and D. Hopgood, *J. Am. Chem. Soc.*, **90**, 2514 (1968).

[13] J. P. Greenstein and M. Winitz, "Chemistry of the Amino Acids," Vol. 2, John Wiley and Sons, Inc., New York, N. Y., 1961, pp 925–927.

[14] B. E. Leach and R. J. Angelici, *J. Am. Chem. Soc.*, **90**, 2504 (1968).

[15] C. W. Davies, *J. Chem. Soc.*, 2093 (1938).

where $K_d = [MZOH^{2-}][E]/[MZE^-][OH^-] = K_{OH}/K_f$, where K_f is the formation constant of the acid or ester with $[Cu(NTA)]^-$. The values of log K_d in Table I were calculated from the expression

Table I. Hydroxo Complex Formation in $[Cu(NTA)]^-$ Systems at 25.0°

MZ:L	$pH_{1.5\ equiv}$	Log K_d	Log K_f	Log K_{OH}
$[Cu(NTA)]^-$				4.39
$[Cu(NTA)]^-$-EtVal	9.99	1.22	2.88	4.10
$[Cu(NTA)]^-$-Gly	12.1	−0.7	5.46	4.8

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

where $pH_{1.5\ equiv}$ is the pH of the solution when 1.5 moles of NaOH has been added per mole of $[Cu(NTA)]^-$. Also given in Table I are values of log K_{OH} calculated from the expression $\log K_{OH} = \log K_d + \log K_f$, and these compare well with the value determined by titration of $[Cu(NTA)]^-$ alone.

(3) **Formation Constants of the Amino Acids and Esters with $[M(NTA)]^-$.** Formation constants were calculated, by using a digital computer,[16] at several points during the course of a potentiometric titration. The average formation constant and its standard deviation were computed for the range 20–80% titration. The average K_f value was used to calculate theoretical titration data which in all cases reproduced the experimental data well. The relationships used were derived by solving simultaneous equations for total acid or ester (L) concentration, total $[M(NTA)]^-$,MZ^-, concentration, and electroneutrality. K_{OH} was taken as zero except for the Cu and Zn systems.

(i) **Monobasic Esters.** NH_2CHRCO_2R' (L). The assumption was made that only a mono ester complex is formed under conditions of 1:1 mole ratios of $[M(NTA)]^-$ and ester. This assumption is supported for copper by the observation that only a mono ammine complex is formed with $[Cu(NTA)]^-$ even in the presence of a 50-fold excess of ammonia. For the other metals no deviations were observed which would indicate formation of a bis ester complex under the conditions used.

The following equilibrium constants were considered in evaluating the titration data: $K_f = [MZL^-]/[MZ^-][L]$, $K_{OH} = [MZOH^{2-}]/[MZ^-][OH^-]$, $K_a = [L][H^+]/[LH^+]$. From equations for electroneutrality, total ligand ($[L]_{tot}$), total metal ($[M]_{tot}$), and the relationship $[M]_{tot} = [L]_{tot}$, the following expression for K_f was derived

$$K_f = \frac{(\beta - \delta)[(\beta - \delta)[M]_{tot} - \alpha\gamma(1 + \delta)]}{(1 + \delta)} \qquad (1)$$

where $\alpha = 1 + [H^+]/K_a$, $\beta = [H^+]/K_a$, $\gamma = [OH^-] + [M]_{tot} + [Cl^-] - [Na^+] - [H^+]$, and $\delta = K_{OH}[OH^-]$. Calculated values of K_f for several amino acid esters with $[M(NTA)]^-$ are given in Tables II and III.

(ii) **Dibasic Amino Acids.** $^+NH_3CHRCO_2^-$ (LH). The equilibrium constants $K_f = [MZL^{2-}]/[MZ^-][L^-]$, $K_{OH} = [MZOH^{2-}]/[MZ^-][OH^-]$, $K_{a1} = [LH][H^+]/[LH_2^+]$, and $K_{a2} = [L^-][H^+]/[LH]$ were used in evaluating the titration data.

Table II. Formation Constants of $[M(NTA)]^-$ with Glycine and Ethyl Valinate at 25.0°

M^{2+}	Log K_{OH}[b]	Log K_{fEtVal}[c]	Log K_{fGly}[b]	R[a]
Mn		2.39 ± 0.02	2.24 ± 0.005	0.7
Co		1.88 ± 0.014	3.65 ± 0.014	59
Ni		2.03 ± 0.011	4.95 ± 0.011[d]	830
Cu	4.39 ± 0.01	2.88 ± 0.002	5.46 ± 0.008[d]	360
Zn	3.55 ± 0.05	1.58 ± 0.08	3.64 ± 0.007	110
Pb		1.55 ± 0.10	1.93 ± 0.009	2.4

[a] $R = K_{fGly}/K_{fEtVal}$. [b] $I = 0.073\ M$. [c] $I = 0.077\ M$. [d] Y. J. Israéli, *Can. J. Chem.*, **41**, 2710 (1963), reports values of 4.4 and 5.44 for Ni and Cu, respectively, at an unspecified temperature, and $I = 0.5\ M$; N. E. Jackobs and D. W. Margerum, *Inorg. Chem.*, **6**, 2038 (1967), report a value of 4.89 at 25.0° and $I = 0.50\ M$ for Ni.

Table III. Formation Constants of $[Cu(NTA)]^-$ with Amino Acids and Their Esters at 25.0° (log standard deviation <0.01)

Acid	pK_a[f]	Log K_f[a]	Ester	pK_a	Log K_f[d]
Gly	2.35		Me	7.62[g]	3.06
	9.78	5.44	Et	7.68	3.15
			n-Bu	7.78	3.33
Ala	2.34				
	9.87	5.42	Et	7.91	3.10
PhAla	1.83				
	9.13	4.99	Et	7.12[g]	2.77
Leu	2.36				
	9.60	5.35	Et	7.64[g]	2.79
Val	2.32				
	9.62	5.10	Et	7.75	2.88
β-Ala	3.55				
	10.35	4.56	Et	9.13	3.65
Hist	1.82	4.16[b,i]			3.98[e,i]
	6.04		Me	5.01[h]	
	9.12	5.73[c,j]		7.23	4.90[e,j]

[a] Ionic strength = 0.073 M except where noted. [b] $I = 0.083\ M$. [c] $I = 0.087\ M$. [d] $I = 0.077\ M$. $I = 0.083\ M$. [f] Reference 28. [g] R. W. Hay, L. J. Porter, and P. J. Morris, *Australian J. Chem.*, **19**, 1197 (1966). [h] Reference 5. [i] K_{f1} to form complex with monodentate I. [j] K_{f2} to form complex with bidentate structure II.

From equations for electroneutrality and total metal and ligand concentrations, and since $[M]_{tot} = [L]_{tot}$, the following computable relationship was derived

$$K_f = \frac{[\beta + (\beta - \alpha)\delta]\{[\beta + (\beta - \alpha)\delta][M]_{tot} - \alpha\gamma(1 + \delta)\}}{\alpha\gamma^2(1 + \delta)} \qquad (2)$$

where

$$\alpha = 1 + [H^+]/K_{a2} + [H^+]^2/K_{a1}K_{a2}$$

$$\beta = [H^+]/K_{a2} + 2[H^+]^2/K_{a1}K_{a2}$$

$$\gamma = 2[M]_{tot} + [Cl^-] + [OH^-] - [Na^+] - [H^+]$$

$$\delta = K_{OH}[OH^-]$$

Calculated K_f values are listed in Tables II and III.

(iii) **Histidine and Its Methyl Ester.** The systems of Hist and MeHist with $[Cu(NTA)]^-$ are more complicated as these ligands are potentially tridentate. Cu^{2+}–Hist systems contain mixtures of species in which Hist is bonded either as the anion or as the zwitterion with the amino group protonated.[17] Because of tetragonal dis-

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[16] The program was written in FORTRAN IV language and executed by an IBM System/360 Operating System at the Iowa State University Computation Center.

[17] D. D. Perrin and V. S. Sharma, *J. Chem. Soc., A*, 724 (1967), and references cited therein.

tortion, it seems likely that little carboxyl group interaction with the metal will occur in the former case,[17] although this point is still being debated.[18] Recent X-ray crystallographic studies[19] of Hist with zinc(II) show that the carboxyl group is weakly coordinated as shown by Zn-O distances of 2.8–2.9 Å. Chakravorty and Cotton[20] measured the formation constants of the divalent ions of nickel, copper, and zinc with a series of ligands related to Hist and came to the conclusion that Hist carboxyl group interactions with copper and nickel, if present at all, are very weak. The Hist zwitterion probably coordinates to copper(II) by chelation through the imino and carboxyl groups.[17,21]

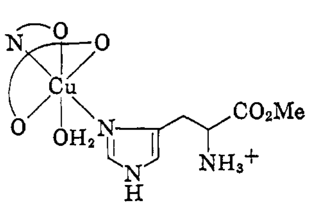
We will first consider titration data from the system $[Cu(NTA)]^-$-MeHist in which ester carbonyl oxygen interaction with the metal is very unlikely. The titration curve shows an inflection at its midpoint, and the data were precisely analyzed by assuming the formation of a one-ended complex (I) which subsequently chelated (II). The assumption was made that these processes

$$\text{pH 2.5-5}\quad MZ^- + LH^+ \xrightleftharpoons{K_{f1}} MZLH$$

$$\text{pH 5-8}\quad MZLH \xrightleftharpoons{K_i} MZL^- + H^+,\ \text{loss of amine proton}$$

do not overlap. Computed K_{f1} values, using eq 1, showed no deviation up to 60% of the loss of the first proton. pK_i values were determined as given before for pK_a values of the esters and were used to calculate the formation constant of the chelated species, $K_{f2} = [MZL^-]/[MZ^-][L]$, from the relationship

$$K_{f2} = K_{f1}K_i/K_{a2}$$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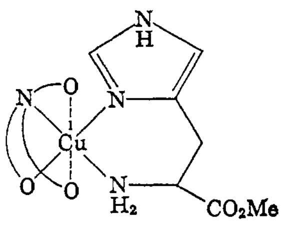
II

Similar procedures were used to analyze the data from the Hist system, and it appears that a one-ended complex analogous to I is first formed, rather than imino and carboxyl group chelation, as shown by the similarities of the K_{f1} values (Table III) and the absorption spectra (Table IV, Figure 1) of the MeHist and Hist systems.

The computed formation constants are given in Table III. The standard deviations are for 10 to 60% loss of the first proton for K_{f1}, and from 15 to 80% loss of the second proton for K_{f2}, except for MeHist where the limit was 50% because of deviations due to ester hydrolysis.

(B) Absorption Spectra of M(NTA)L Species of Copper(II) and Nickel(II). In 1955, Jørgensen proposed[22] that the ratio ν_{Cu}/ν_{Ni}, between the principal band of a copper(II) complex and the first band of the corresponding paramagnetic nickel(II) complex, is a qualitative measure of the degree of tetragonal distortion of the copper complex. This ratio is approximately 1 in complexes of cubic symmetry increasing to about 1.8 for extreme tetragonal distortion.

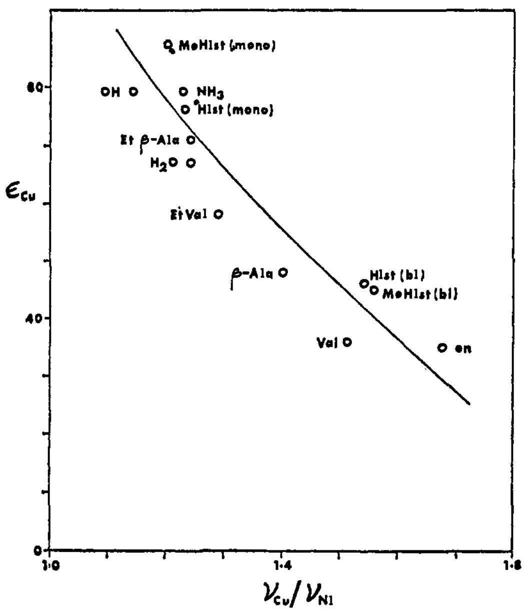

Figure 1. Electronic absorption spectral data for complexes of the type M(NTA)L (M = Ni(II), Cu(II)); see text.

Table IV. Visible Absorption Spectra of the Complexes M(NTA)L (M = Cu, Ni) at 25°

	$Cu(NTA)L^a$		$Ni(NTA)L^b$		
L	λ_{max}, mμ	ϵ_{max}, M^{-1} cm^{-1}	λ_{max}, mμ	ϵ_{max}, M^{-1} cm^{-1}	ν_{Cu}/ν_{Ni}
en	633	35	1060[c]	11.0	1.68
MeHist[f]	675	45	1057	14.0	1.56
Hist[f]	670	46	1037	11.3	1.54
Val	680	36	1025	9.8	1.51
β-Ala	723	48	1015	15.0	1.40
EtVal	805	58	1035	12.3	1.29
H_2O	845[d]	67	1050	15.5	1.24
Etβ-Ala	824	71	1032	14.1	1.24
Hist[e]	858	76			1.23
NH_3	850	79			1.23
MeHist[e]	870	87			1.21
OH	920	79			1.14
$(NH_3)_2$			1045[c]	11.0	

[a] Principal band. [b] First transition $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$. [c] Reference 23. [d] Spectrum given in ref 23 is of a mixture of $[(Cu(NTA)]^-$ and $[Cu(NTA)OH]^{2-}$. [e] Monodentate, structure I. [f] Bidentate, structure II.

We measured the absorption spectra of a series of complexes of $[M(NTA)]^-$ (M = Cu, Ni) with various ligands to estimate the stereochemistry of the complexes of $[Cu(NTA)]^-$ with amino acids and esters. The data are presented in Table IV. In some cases corresponding nickel complexes cannot be generated; for example, a discrete one-ended complex of Hist or its ester, and in these cases the value of ν_{Ni} was taken from a closely similar compound. However, the error introduced by these estimates is negligible because ν_{Ni} is insensitive to changes in ligand donor atoms, whereas ν_{Cu} is very sensitive to such changes. It is also noted that the

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(18) A. C. Andrews and D. M. Zebolsky, *J. Chem. Soc.*, 742 (1965).

(19) (a) M. M. Harding and S. J. Cole, *Acta Cryst.*, **16**, 643 (1963); (b) R. Kretzinger, F. A. Cotton, and E. F. Bryan, *ibid.*, **16**, 651 (1963).

(20) A. Chakravorty and F. A. Cotton, *J. Phys. Chem.*, **67**, 2878 (1963).

(21) R. H. Carlson and T. L. Brown, *Inorg. Chem.*, **5**, 268 (1966).

(22) C. K. Jørgensen, *Acta Chem. Scand.*, **9**, 1362 (1955).

(23) C. K. Jørgensen, *ibid.*, **10**, 887 (1956).

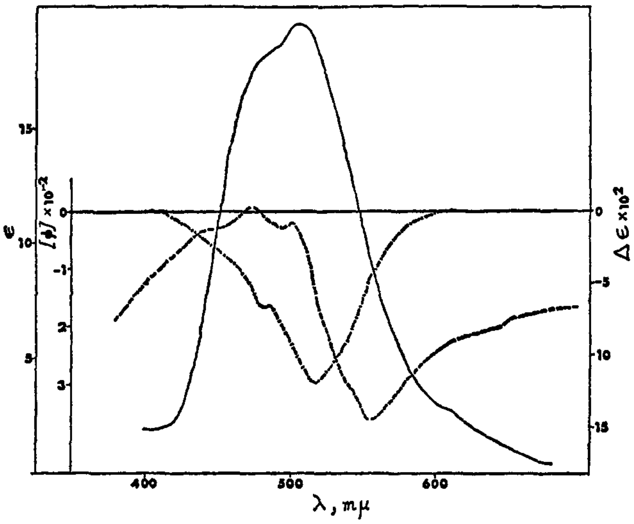


Figure 2. The electronic absorption spectrum (———), the CD curve (–·–·–·–·), and the ORD (- - - -) curve of [Co(NTA)(*l*-Val)]$^{2-}$.

molar extinction coefficients of the principal band of the copper complex lie on a smooth curve when plotted against the ν_{Cu}/ν_{Ni} ratios (Figure 1).

The spectra of a series of solutions of [Cu(NTA)]$^-$ in the presence of NH_4^+ of varying amounts were measured. Over a relative concentration range of [Cu(NTA)$^-$]:[NH_4^+] of 1:1 to 1:50, with from 1 to 3 equiv of base per mole of [Cu(NTA)]$^-$ added, identical absorption spectra were obtained showing that only a monoammine complex is formed. In contrast, [Ni(NTA)]$^-$ appears to form a bisammine complex.[23]

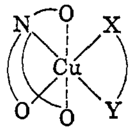
(C) Cotton Effects. Larsen and Olsen proposed[24] that an optically active ligand with an asymmetric center only exhibits Cotton effects if the ligand is *chelated* to a metal ion chromophore. In an attempt to determine whether amino acid esters were bonded through both the amino and ester groups or not, the ORD and CD spectra of their complexes were examined.[25] Hence by comparing Cotton effects exhibited by corresponding complexes of an optically active amino acid (which chelates) and its ester, one may be able to estimate the degree of chelation of the ester.

l-Val and its ethyl ester were suitable ligands as the amount of ester hydrolysis is negligible during the time necessary for measurement. Complexes of these ligands with [M(NTA)]$^-$ (M = Co, Ni, Cu) were examined as these complexes have suitable absorption spectra. Only the cobalt compounds exhibited measurable Cotton effects; the absorption spectrum, ORD, and CD curves of the [Co(NTA)(*l*-Val)]$^{2-}$ ion are depicted in Figure 2. Both of the overlapping absorption bands at 510 and 485 mμ are active, giving negative Cotton effects in the CD spectrum with extrema at 517 and 483 mμ, respectively.

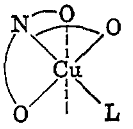
It is reported that metal ions catalyze the racemization of optically active amino acids.[26] However, no racemization of [Co(NTA)(*l*-Val)]$^{2-}$ was observed over the time intervals of our experiments. The absorption spectra and CD curve profiles of the acid and ester complexes are virtually identical, but the Δε values of the ester complex are only 15% of those of the acid complex. To determine whether Δε would be very small for a nonchelating optically active ligand, as suggested by Larsen and Olsen,[24] the CD spectrum of the *d*-amphetamine complex, [Co(NTA)($NH_2CH(CH_3)CH_2C_6H_5$)]$^-$, was examined and found not to give a measurable Cotton effect. Making the assumptions that Δε is zero for [Co(NTA)(*l*-EtVal)]$^-$ when *l*-EtVal is coordinated only through the nitrogen atom and that Δε would be the same as that for [Co(NTA)(*l*-Val)]$^{2-}$ if the ester were completely chelated with the metal, the observed Δε for [Co(NTA)(*l*-EtVal)]$^-$ suggests that roughly 15% of the ester is chelated.

Discussion

The absorption spectra of a series of copper(II) and nickel(II) complexes, M(NTA)L, are classified according to the Jørgensen criterion[22] in Table IV and Figure 1. These data show that large tetragonal distortions ($\nu_{Cu}/\nu_{Ni} > 1.5$) only occur in [Cu(NTA)]$^-$ complexes with chelating ligands such as α-amino acids, Hist and its esters, and ethylenediamine. This suggests that these chelating ligands are coordinated in the plane with two other strongly bound donor atoms (III and II).



III



IV

The six-membered ring systems exhibit lesser degrees of tetragonal distortion in comparison with analogous five-membered systems, *e.g.*, Hist(II) < en and β-Ala < Val. This is probably due to the lower stability of a six-membered ring in comparison to a five-membered ring. That ν_{Cu}/ν_{Ni} is roughly the same for Hist and Val is probably due to the better donor properties of nitrogen as compared with oxygen donor atoms.

All the monodentate ligands have ν_{Cu}/ν_{Ni} values of about 1.2 showing that the stereochemistry of these complexes is approximately cubic irrespective of whether the donor atom is nitrogen or oxygen. The ligands (L) presumably coordinate in the plane of the three NTA donor atoms (IV and I). There is little correlation between formation constants and ν_{Cu}/ν_{Ni} values.

The amine group basicities of β-Ala and its ester are considerably higher than those of the α-amino acids and their esters, respectively (Table III). This is reflected in their formation constants with [Cu(NTA)]$^-$; *e.g.*, $K_{fEt\beta\text{-}Ala}$ is greater than K_{fEtVal} by a factor of 6 but K_{fVal} is greater than $K_{f\beta\text{-}Ala}$ by a factor of 4. The relative stabilities of the five- and six-membered rings of the respective acids can be crudely estimated by using the parameter, $\log K_{f,acid} - \log K_{f,ester}$, where the acid is chelated and the ester is not. Values of 0.9 and 2.2 are obtained for β-Ala and Val, respectively, and these are consistent with their absorption spectra. The values for the α-amino acids are relatively invariant and lie in the range 2.2–2.5.

An examination of the pK_a values of the esters of α-amino acids and their formation constants with [Cu-

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(24) E. Larsen and I. Olsen, *Acta Chem. Scand.*, 18, 1025 (1964); S. Kirschner and K. H. Pearson, *Inorg. Chem.*, 5, 1614 (1966).

(25) We thank D. H. Busch for suggesting this approach.

(26) J. Olivard, D. E. Metzler, and E. E. Snell, *J. Biol. Chem.*, 199, 669 (1952).

$(NTA)]^-$ (Table III) shows that no regular relationship exists except for the series of Gly esters. These give a linear free-energy relationship whereby

$$\log K_f = 1.7pK_a - 9.7$$

The lack of a relationship in the series of esters, NH_2CHRCO_2Et, probably indicates that other factors, such as steric effects of R, are more important than the basicity of the amino nitrogen donor in determining the relative values of K_f.

Since the formation constant, K_f, and spectral data of the ester complexes, $[Cu(NTA)(E)]^-$, suggested that the ester carbonyl oxygen atom was not coordinated to the metal to an appreciable extent, it was of interest to determine whether there was any such interaction in $[M(NTA)(E)]^-$ complexes of other metals. For comparison, the formation constants, K_{fGly}, of $[M(NTA)(Gly)]^{2-}$ were first determined (Table II) and found to follow the Irving–Williams order:[27] Mn < Co < Ni < Cu > Zn. It is assumed that the Gly is chelated in all cases, and the trend for different metals is very similar to that for the second formation constants ($K_2 = [ML_2]/[ML][L]$) of Gly^- with M^{2+}.[28]

For the complexes of Mn, Co, Ni, and Zn, the K_2 values for Gly^- are remarkably close to K_{fGly} despite the fact that Gly^- is chelating with complexes having +1 and −1 charges, $[M(Gly)]^+$ and $[M(NTA)]^-$, respectively. For Cu(II) K_{fGly} is significantly smaller than K_2. The low value of K_{fGly} is probably a result of weak coordination to the sixth coordination position of Cu(II).

In contrast, the K_{fEtVal} values for coordination of EtVal to $[M(NTA)]^-$ show a radically different trend than observed for K_{fGly} or the K_2 values for Gly^-. If EtVal were bonding only through the amino group, the Irving–Williams order of stabilities would be expected. If, however, ester coordination did occur to some extent with the metals, K_{fEtVal} values would be higher than expected. Since it is unlikely[29] that the ester group of EtVal coordinates in $[Cu(NTA)(EtVal)]^-$ this complex can be used as a reference point. Relative to this complex, $[Cu(NTA)(Gly)]^{2-}$ is 360 times more stable as indicated by the ratio K_{fGly}/K_{fEtVal}. This ratio may be used to approximate the extent of ester coordination in complexes of the other metals; low ratios indicate a greater degree of EtVal chelation. This ratio varies from about unity for Mn to about 800 for Ni along the series Mn $\leq$ Pb $\ll$ Co < Zn < Cu < Ni (Table II). The values of about unity for the Mn and Pb complexes suggest that the extent of ester chelation is quite high. That Mn and Pb appear to bond with the ester oxygen atom to the greatest degree is consistent with the known tendency of these ions to bond strongly to oxygen donor atoms.[11] This result is in contrast to that observed for complexes of ethyl glycinate-N,N-diacetate where ester carbonyl coordination to Pb(II) was not considered likely.[29] The value of 59 for this ratio for Co is sufficiently low to suggest that some ester chelation occurs. The CD data for the complexes $[Co(NTA)(l\text{-}Val)]^{2-}$ and $[Co(NTA)(l\text{-}EtVal)]^-$ suggest that about 15% of the ester is coordinated to the metal, in qualitative agreement with the equilibrium results.

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(27) Reference 2, p 80.

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

(29) R. J. Angelici and B. E. Leach, *J. Am. Chem. Soc.*, **90**, 2499 (1968).