in the immediate vicinity of the ion. This proposal merits further consideration and it will be particularly interesting to make direct comparisons between VO^{2+} and Ni^{2+} in a variety of solvents as soon as more data are available. Unfortunately, the solvent-exchange data for the VO^{2+}–ligand systems are insufficient to allow meaningful comparisons to be made.

From the rate of formation of $VOHGly^{2+}$ and the equilibrium constant for the reaction it is possible to calculate the rate of dissociation of $VOHGly^{2+}$. Calculated values of k_{-1} at various temperatures are given in Table II. Angerman and Jordan[6a,14a,16] suggested that the activation parameters for the k_{-1} process are indicative of an S_N1 type dissociative mechanism. The agreement between the activation parameters for this dissociative process (k_{-1}) and that for the water-exchange reaction strongly suggests similar processes.

Line-broadening techniques allow for calculation of exchange rates at various temperatures and for calculation of the corresponding activation parameters. It has been shown that the exchange rate of glycine on $VOHGly^{2+}$ is independent of the concentration of glycine. This suggests that the rate-determining step in the exchange process must be the loss of the monodentate glycine from the complex. We conclude that the activation parameters for the dissociation of $VOHGly^{2+}$ as calculated from the stopped-flow experiments and the nmr results on the exchange of glycine with VO-

$HGly^{2+}$ are not distinguishable experimentally [*i.e.*, $\Delta H^{\ddagger}$(stopped flow) $= 13.1 \pm 1.5$ kcal/mol, $\Delta H^{\ddagger}$(nmr) $= 12 \pm 1$ kcal/mol, $\Delta S^{\ddagger}$(stopped flow) $= -2.4 \pm 2.0$ eu, $\Delta S^{\ddagger}$(nmr) $= -3 \pm 1$ eu]. If this is true, the rate of exchange and the rate of dissociation should be identical and the activation parameters of these two processes would necessarily be the same.

The rate of glycine exchange on $VO(Gly)_2$ in aqueous solution at pH 6.8 was found to be 360 sec^{-1} with substantially different activation parameters from that observed with the $VOHGly^{2+}$ exchange reaction. The values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are comparable with those for the exchange of CH_3CN and DMF on VO^{2+} in the respective anhydrous solvents.[6a,14a] Angerman and Jordan[14a,16] suggested that these two latter exchange processes could be associated with an S_N2 type mechanism in which the formation of a bond with a solvent molecule outside the first coordination sphere is important. If this is the case and if, on the basis of similar activation parameters, similar mechanisms can be inferred, we suggest that the rate of exchange of glycine with $VO(Gly)_2$ is limited by an associative step.

Thermodynamics of Ion Association. XXIV. The Formation of Mixed Complexes of Copper with Glycine, Alanine, Serine, and Valine

BY TING PO I* AND GEORGE H. NANCOLLAS

The formation of mixed complexes of copper(II) with pairs of ligands chosen from the series of similar amino acids glycine, α-alanine, serine, and valine has been studied by potentiometric and calorimetric methods at 25° and at an ionic strength of 0.10 ± 0.01 M maintained with potassium nitrate. In addition to determining the thermodynamic data for the simple complexes of copper with these amino acids, the following mixed complexes have been characterized: Cu(gly)(ala), Cu-(gly)(val), Cu(gly)(ser), Cu(ala)(val), Cu(ala)(ser), and Cu(val)(ser). The data show that the mixed complexes are more stable than the parent binary complexes and that this stabilization is almost entirely due to the statistical effects. Temperature-dependent and temperature-independent components of the thermodynamic properties are calculated and these are discussed in terms of the important factors involved in mixed-complex formation.

Introduction

In mixed-ligand complexes, two or more different ligands, other than the solvent molecule, bond simultaneously to the central metal ion. They are frequently formed in solutions containing metal ions and more than one kind of suitable ligand and are thus of considerable importance as components in natural waters and various biological fluids.

Sarkar and Kruck have reported the isolation of a mixed complex Cu^{II}(histidine)(threonine) from normal human serum[1] and the detection of mixed complexes Cu(histidine)(glutamine) and Cu(histidine)(serine) in

solutions prepared at physiological pH.[2] In many instances enzymes are known to be activated by certain metal ions with the formation of a mixed complex among an enzyme, metal ion, and the substrate.[3] The first unequivocal demonstrations of the mediating action of metal ions in the binding of small molecules to proteins were provided by Klotz and Ming[4] and by Gurd.[5] Recently Mildvan and Cohn[6] in their kinetic studies of the pyruvate kinase reaction have made further important contributions to our understanding of the mode

(1) B. Sarkar and T. Kruck in "Biochemistry of Copper," J. Peisach, P. Aisen, and W. E. Blumberg, Ed., Academic Press, New York, N. Y., 1966, p 183.

(2) B. Sarkar and T. P. A. Kruck, *Can. J. Biochem.*, **45**, 2046 (1967).

(3) B. G. Malmstrom and A. Rosenberg, *Advan. Enzymol. Relat. Subj. Biochem.*, **21**, 131 (1959).

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(5) F. R. N. Gurd in "Ion Transport Across Membranes," H. T. Clarke, Ed., Academic Press, New York, N. Y., 1954, p 246.

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of interaction between enzyme-bound metal and the substrate, *i.e.*, the formation of the enzyme–metal–substrate bridge structure. Besides the activation action, the inactivation of many enzymes has been shown to occur through the removal of the active metalloenzyme by the formation of an ezymatically inactive mixed complex between the metalloenzyme and the inhibitor.[7]

Mixed complexes may be involved in many analytical methods based on complex formation. Nomura has proposed a volumetric titration method to determine cyanide (thiocyanide and iodide) ions using mercury-(II)–EDTA as titrant and using mercury(II)–cresolphthalein complexon–cyanide (thiocyanide and iodide) ion or mercury(II)–Methylthymol Blue–cyanide (thiocyanide and iodide) ion mixed complexes as indicators.[8] The tendencies of different unsaturated binary complexes to take up one or two further ligands to form mixed complexes are widely different. The formation of a mixed complex may result in marked changes in the physical properties of the original complex and hence may contribute considerably to the selectivity of certain analytically important reactions. Based on the above principle, Burger and Ruff[9] have developed a novel specific method for the spectrophotometric determination of minute amounts of cobalt. The discrimination of these analytical procedures depends on the stability or other physical properties of the mixed complex formed.

Mixed complexes play important roles as intermediates in ligand displacement reactions[10-12] and in ligand-catalyzed complex formation reactions.[13,14] In some redox reactions the catalytic effect of metal ions can be explained by the simultaneous coordination of both reactants, and in these cases the metal ion promotes the electron transfer from the reductant to the oxidant.[15]

We can distinguish between two types of mixed-complex formation according to the affinity of two ligands (A represents a "primary" ligand and B represents a "secondary" ligand) for the metal ion (M). In the first type, one of the complexes, MA, is considerably more stable than MB, and ligand exchange does not occur between MA and the secondary ligand B. The mixed complex is formed in two distinct steps; the combination with the primary ligand is completed before reaction with the secondary ligand takes place. The uptake of a second ligand by a metal–aminopolycarboxylic acid is one example in which the number of donor groups of a primary multidentate ligand is less than the coordination number of the central metal ion.[16] The remaining coordination site(s) may be occupied by the secondary ligand. The composition of a mixed complex of this type is usually simple, in most cases only one secondary ligand being taken up by the aminopolycarboxylate complex and various methods

such as pH titrimetry,[17-19] spectrophotometry,[20] and polarography[21] have been used for their investigation.

In the second type of mixed-complex formation, two ligands have comparable affinity for the metal ion so that each of the ligands is capable of competing with the other for the metal ion. Thus two ligands may combine simultaneously in a single step or one ligand may gradually replace the other in several overlapping steps to form the mixed complexes.

Newman and coworkers,[22-24] in their studies of mixed-metal complexes MA_iB_j of halides, were able to limit the species present to those of constant n, where $n = i + j < N$. Concentrations of free ligands as well as complexes of lower and higher order were rendered negligible by suitable choice of T_A/T_B. Where the basicities of the ligands are very different, pH measurements can be used to characterize the mixed complexes.[25-27] Because of this large basicity difference the mixed complexes formed predominantly under conditions of pH where the less basic ligand is almost completely dissociated and the more basic ligand is ionized only to a very slight extent. Thus only the proton association of the more basic ligand had to be considered. In the present work involving amino acids of similar basicity, the proton association equilibria of both ligands have to be taken into account and the mixed complexes are formed under conditions where appreciable concentrations of undissociated amino acids are present. Since it is not possible to derive an explicit functional relationship among measured pH, the measured titrant value, and the total concentrations of metal and ligands, the conventional computational methods[28] cannot be used.

Two mathematical approaches have been used to calculate the stability constants of mixed complexes. In the search method of Sillén[29-32] and Leussing[33] the stability constants are refined by minimizing the error sum of squares. In the second method Sayce[34] has used the Gauss nonlinear least-squares approach, in which the fitting of nonlinear functions is achieved by iterations involving a series of linear approximations. Our laboratory has also developed a general computer program which uses a modified Gauss method for this purpose.[35] In solutions containing copper(II) ion and a mixture of two different bidentate ligands, only one mixed complex, CuAB, would be expected. Thus the calculations are greatly simplified, and the use of the much more complicated and time-consuming general computer program can be avoided. Perrin, Sayce, and

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(8) T. Nomura, *Bull. Chem. Soc. Jap.*, **43**, 104 (1970).

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Sharma[36] have employed a general computer program (SCOSUS) to study systems comprising copper(II) ion with each of six possible pairs of ligands: histamine, ethylenediamine, serine monoanion, and salicylate dianion. Näsänen, et al.,[37,38] and Lim[39] have developed a method which uses algebraic manipulation to reduce the mass balance equations into one equation cubic in the concentration of either undissociated or free ligands. In the present work, we have employed a modified Newton–Ralphson algorithm[40] to solve simultaneous nonlinear mass balance equations.

Previous mixed-complex studies of copper(II)–amino acid systems[36,41–45] have been confined to the determination of the stability constants. No data are available for the enthalpy and entropy of the formation which yield information regarding the nature of the statistical effect repulsion between unlike ligands, geometric factors, dipole interactions with the solvent, the number and type of bonds formed, and the effect of chelation.[46] The simpler amino acids were chosen in the present study so as to minimize steric-hindrance effects and to eliminate the changes in both number and type of bonds formed and in the chelating effect.

Experimental Procedure

Materials.—Grade A glassware and reagent grade chemicals were used, and solutions were prepared with doubly distilled water. Carbon dioxide was excluded by bubbling with nitrogen. Copper nitrate solutions were analyzed by titration with standard EDTA and also by exchanging the cations for hydrogen ions on a Dowex 50 ion-exchange resin column and titrating the liberated nitric acid with standard carbonate-free potassium hydroxide solution. Potassium nitrate solution was analyzed by the ion-exchanger method. L-Alanine, L-glycine, serine, and valine were obtained as free bases (zwitterion) from Nutritional Biochemical Corp. and used without further purification after drying at 110° for 1 hr. Their purity was estimated to be greater than 99.5% from potentiometric titration.

Potentiometric Experiments.—Emf measurements were made at $25 \pm 0.02°$ with cells of the type

glass electrode|soln under study|satd KCl, Hg₂Cl₂, Hg
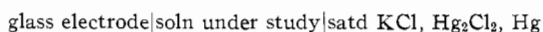
using Beckman glass (Types 39099-E3 and 40471) and reference (Type 39071) electrodes and a Leeds and Northrup K3 potentiometer in conjunction with a Victoreen picometer (Model 474) as null detector. Readings, reproducible to ±0.1 mV, were made with a pair of glass electrodes so that any irregularity in the response of one of them was immediately apparent. Titrations were made in a 150-ml jacketed titration cell, the inner compartment of which was maintained at a constant temperature by circulating water from a constant-temperature bath, and nitrogen, saturated by bubbling through a thermostated 0.1 M potassium nitrate solution, was passed slowly through the cell during experiments.

The electrode systems were standardized over the entire pH range of interest before and after each experiment with NBS standard buffer solutions freshly prepared according to Bates:[47] 0.05 M potassium tetraoxalate, pH 1.65; 0.05 M potassium

hydrogen phthalate, pH 4.008; 0.025 M potassium dihydrogen phosphate plus 0.025 M disodium hydrogen phosphate, pH 6.865; 0.01 M borax, pH 9.180. pH ($= -\log a_{H^+}$) values were converted to hydrogen ion concentration by using an f_{H^+} activity coefficient value (0.7815) calculated from the Davies equation.[48]

Successive protonation equilibrium constants K_B and K_A were evaluated from separate titrations performed at high and low pH, employing potassium hydroxide and nitric acid, respectively. Formation constants for simple copper(II) complexes were determined by adding standard potassium hydroxide solution to solutions containing 1:1 and 2:1 mole ratios of amino acid to copper nitrate. Titrations with potassium hydroxide of mixed systems were carried out on solutions containing copper(II) nitrate and amino acid A and amino acid B in a 1:1:1 ratio. Sufficient potassium nitrate was added in each run to maintain an ionic strength to within 1% of 0.1 M over the entire titration. The total concentration of copper(II) was 5×10^{-3} M and the concentrations of amino acids ranged from 5×10^{-3} to 10×10^{-3} M.

Calorimetric Experiments.—The calorimeter and experimental technique previously described[49] were modified slightly for this work. A single calorimeter vessel with a working volume of 150 ml was used and temperatures were measured with a quartz thermometer (Hewlett-Packard, Model 2801A) which had a temperature resolution of $\pm 10^{-4}°$, requiring a 10-sec integration interval between temperature readouts. The output of the quartz thermometer was fed to a digital-analog converter (Hewlett-Packard, Model 580A). The converter output drove a strip-chart recorder (Varian Association, Model 400) requiring 100 mV for full-scale deflection. The heating coil of resistance 73.5086 ohms was constructed of enameled 36-gauge manganin wire wound on a thin 1×1.5 cm mica plate cemented to a tube. Instead of measuring the pH potentiometrically during the titration, we employed the computer program EQUIL[40] to calculate the equilibrium concentrations of all the species at any point in the titration. The removal of the electrodes from the calorimeter substantially reduced the heat capacity of the calorimeter. The heats of protonation for the amino acids were determined by the addition of nitric acid to the almost completely deprotonated form of the amino acid. At least two independent enthalpy titrations were performed for each amino acid. The constant ionic strength of 0.1 M was maintained with potassium nitrate in all the titrations.

For the determination of the heat of complex formation, the amino acid was weighed into the calorimeter dewar vessel together with copper(II) nitrate solution to give a ligand to metal ratio of approximately 2:1 and sufficient potassium hydroxide to attain the desired pH. The ionic strength was also adjusted to 0.1 M. The titrant used was nitric acid (~0.1 M). ΔH values for the mixed copper(II) complex formation were measured by means of similar titrations of nitric acid into solutions containing copper(II) nitrate, amino acid A, and amino acid B in a 1:1:1 ratio and the appropriate amount of potassium hydroxide.

Results and Discussion

The following protonation equilibria must be considered

$$L^- + H^+ \rightleftharpoons HL^{\pm} \qquad K_B \quad (1)$$

$$HL^{\pm} + H^+ \rightleftharpoons H_2L^+ \qquad K_A \quad (2)$$
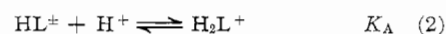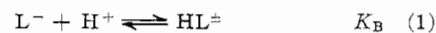
Where L^- represents the anion of the amino acids. Concentrations of ionic species in the acid and base titrations were calculated in the usual manner from mass balance and electroneutrality expressions,[46] and the values of the protonation constants K_B ($= [HL^{\pm}]/[L^-][H^+]$) and K_A ($= [H_2L^+]/[HL^{\pm}][H^+]$) at 25° and 0.1 M ionic strength are given in Table I. Each value is the mean of three titrations comprising about 30 points on each titration curve. The standard deviations are also given in Table I together with available literature values.

In a solution containing a metal ion M and a ligand

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(39) M. C. Lim, Ph.D. Thesis, The State University of New York at Buffalo, Buffalo, N. Y., 1970.

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(42) R. P. Martin and R. A. Paris, *ibid.*, **257**, 3932 (1963).

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(49) A. P. Brunetti, M. C. Lim, and G. H. Nancollas, *J. Amer. Chem. Soc.*, **90**, 5120 (1968).

TABLE I
PROTON ASSOCIATION CONSTANTS FOR AMINO ACIDS IN
AQUEOUS SOLUTION AT 25°

Ligands	[Medium], M	Log K_B	Log K_A
Glycine	0.1 (NaClO$_4$)	9.56	2.39[b]
α-Alanine	0.1 (KNO$_3$)	9.70 ± 0.01	2.55 ± 0.02[a]
	0.1 (NaClO$_4$)	9.59	2.53[c]
	0.2 (KCl)	9.77	2.40[d]
	0.1	9.75	2.40[e]
Valine	0.1 (KNO$_3$)	9.50 ± 0.01	2.28 ± 0.03[a]
	0.5 (NaClO$_4$)	9.62	2.35[f]
	~0.01	9.62	2.32[g]
Serine	0.1 (KNO$_3$)	9.15 ± 0.01	2.55 ± 0.02[a]
		9.15	2.21[h]
	0.2 (KNO$_3$)	9.12	2.29

[a] This study. [b] Reference 39. [c] M. Matsukawa, M. Ohta, S. Takata, and R. Tsuchiga, *Bull. Chem. Soc. Jap.*, **38**, 1235 (1965). [d] V. S. Sharma, H. B. Mathur, and P. S. Kulkarni, *Indian J. Chem.*, **3**, 146, 475 (1965). [e] A. Bonmiol and P. Vieles, *J. Chim. Phys. Physicochim. Biol.*, **65**, 414 (1968). [f] M. M. Ramel and M. R. Paris, *Bull. Soc. Chim. Fr.*, 1359 (1967). [g] L. E. Maley and P. P. Mellor, *Aust. J. Sci. Res., Ser. A*, 579 (1949). [h] S. Pelletier, Ph.D. Thesis, University of Paris, 1960.

L, a series of mononuclear complexes ML$_j$ ($1 \le j \le N$) exists in equilibrium with the metal ion and the ligand. Applying the law of mass action to the equilibria

$$ML_{j-1} + L \rightleftharpoons ML_j \qquad K_j \quad (3)$$

$$M + jL \rightleftharpoons ML_j \qquad \beta_j \quad (4)$$
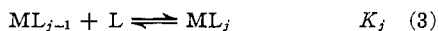
we obtain

$$K_j = [ML_j]/[ML_{j-1}][L] \qquad (5)$$

and an overall stability constant

$$\beta_j = [ML_j]/[M][L]^j = \prod_1^j K_j \qquad (6)$$

The extent of complex formation can be characterized by the complex formation function or the ligand number introduced by Bjerrum[50]

$$\bar{n} = (T_L - [L])/T_M = f(\beta_1, \ldots, \beta_j, \ldots, \beta_n, [L]) =$$
$$\sum_{j=1}^N j\beta_j[L]^j/(1 + \sum \beta_j[L]^j) \quad (7)$$

In the present investigation the Calvin–Bjerrum method[51] was used in which the pH was measured as a function of the concentration of base added at effectively constant metal ion and ligand concentrations. The experimental data were the tetrads: C_B, the base concentration; T_M, the total metal concentration; T_L, the total ligand concentration; and [H$^+$], the equilibrium hydrogen ion concentration. The errors in each of these quantities were estimated and used for the computation of the variances. Values of $\bar{n}$ and [L$^-$] can be calculated from the equations[28]

$$[L^-] = (T_L - \theta)/\gamma \qquad (8)$$

$$\bar{n} = (T_L - \alpha[L^-])/T_M \qquad (9)$$

where

$$\alpha = 1 + K_B[H^+] + K_A K_B[H^+]^2 \qquad (10)$$

$$\theta = C_B + [H^+] - [OH^-] \qquad (11)$$

$$\gamma = K_B[H^+] + 2K_A K_B[H^+]^2 \qquad (12)$$

When a set of numerical values of $\bar{n}$ and [L$^-$] has

(50) J. Bjerrum, "Metal Ammine Formation in Aqueous Solution," P. Haase and Son, Copenhagen, 1941.
(51) M. Calvin and K. W. Wilson, *J. Amer. Chem. Soc.*, **67**, 2003 (1945).

been obtained, the overall stability constants in eq 6 can be refined by the weighted least-squares procedure using our modified Gaussian method.[35] In the computer program a set of trial values of the stability constants is inserted, and the residuals between the observed and computed values of the dependent variable $\bar{n}_i$

$$R_i = \bar{n}_i - \left[\sum_{j=1}^N j\beta_j[L^-]^j/(1 + \sum_{j=1}^N \beta_j[L^-]^j) \right]_i \quad (13)$$

are obtained. The initial trial values can be estimated from available data for similar systems.

The weighted least-squares adjustment requires that β's be so refined that the sum of squares of the weighted residuals

$$S(\beta_1, \beta_2, \ldots, \beta_N) = \sum_{i=1}^{NP} W_i R_i^2 \qquad (14)$$

shall be a minimum, where NP is the number of titration points. Because of the nonlinear functional relationship existing between R_i and the experimental variables, the same small errors in the measured quantities at separate points may correspond to different residuals. The variance of R_i at the ith experimental point is $\sigma_{R_i}^2$; hence the weighting factor W_i ($= 1/\sigma_{R_i}^2$) can be calculated according to the variance propagation theory by the formula[35]

$$\sigma_R^2 = \sigma_{C_B}^2 \left(\frac{\partial R}{\partial C_B}\right)^2 + \sigma_{T_L}^2 \left(\frac{\partial R}{\partial T_L}\right)^2 +$$
$$\sigma_{T_M}^2 \left(\frac{\partial R}{\partial T_M}\right)^2 + \sigma_E^2 \left(\frac{\partial R}{\partial E}\right)^2 \quad (15)$$

where σ_{C_B}, σ_{T_L}, σ_{T_M}, and σ_E are errors asocciated with the quantities of C_B, T_L, T_M, and the emf of the cells, assigned according to the precision of the various measurements. The partial derivatives can be calculated from the functional relationships (8), (9), and (13). A copper(II)–amino acid system is a special case of the above-mentioned procedure in which $N = 2$. The values for the stability constants obtained in this investigation together with the available literature values are given in Table II.

TABLE II
STABILITY CONSTANTS OF SIMPLE COPPER(II) COMPLEXES IN
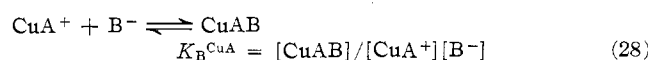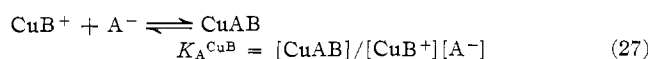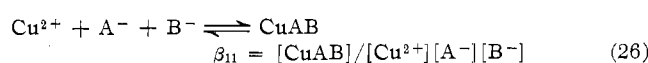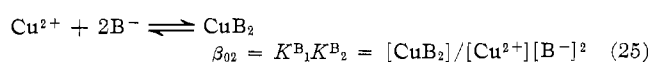AQUEOUS SOLUTION AT 25°

Ligands	[Medium], M	Log K_1	Log K_2	Log β_2
Glycine	0.1 (NaClO$_4$)	8.22	6.80	15.02[a]
α-Alanine	0.1 (KNO$_3$)	8.15 ± 0.01	6.67 ± 0.01	14.82[b]
	0.01	8.18	6.65	14.83[c,d]
	0.1 (NaClO$_4$)	8.19	6.75	14.94[b]
	0.16 (KNO$_3$)	7.84	6.64	14.48[e]
Valine	0.1 (KNO$_3$)	8.11 ± 0.01	6.68 ± 0.01	14.79[b]
	0.16 (KNO$_3$)	7.80	6.70	14.50[e]
	0.5	7.98	6.73	14.71[f]
Serine	0.1 (KNO$_3$)	7.92 ± 0.01	6.65 ± 0.01	14.57[b]
	0.16 (KNO$_3$)	7.85	6.65	14.50[g]
	0.2 (KNO$_3$)	7.89	6.51	14.40[h]

[a] Reference 39. [b] This study. [c] L. E. Maley and P. P. Mellor, *Aust. J. Sci. Res., Ser. A*, 579 (1949). [d] L. E. Maley and D. P. Mellor, *Nature (London)*, **165**, 453 (1950). [e] J. L. Meyer and J. E. Bauman, Jr., *J. Chem. Eng. Data*, **15**, 404 (1970). [f] M. M. Ramel and M. R. Paris, *Bull. Soc. Chim. Fr.*, 1359 (1967). [g] J. E. Letter, Jr., and J. E. Bauman, Jr., *J. Amer. Chem. Soc.*, **92**, 437 (1970). [h] E. V. Ragu and M. B. Mathur, *J. Inorg. Nucl. Chem.*, **30**, 2181 (1968).

Stability Constant for CuAB.—In a solution containing a mixture of copper(II) nitrate and two different amino acids in 1:1:1 ratio the following species would be expected to be present in significant amounts: A^-, B^-, Cu^{2+}, H^+, OH^-, $HA^{\pm}$, H_2A^+, $HB^{\pm}$, H_2B^+, CuA^+, CuA_2, CuB^+, CuB_2, and $CuAB$. The following equilibria must be considered

$$A^- + H^+ \rightleftharpoons HA^{\pm}$$
$$K^A_B = [HA^{\pm}]/[A^-][H^+] \quad (16)$$

$$HA^{\pm} + H^+ \rightleftharpoons H_2A^+$$
$$K^A_A = [H_2A^+]/[HA^{\pm}][H^+] \quad (17)$$

$$B^- + H^+ \rightleftharpoons HB^{\pm}$$
$$K^B_B = [HB^{\pm}]/[B^-][H^+] \quad (18)$$

$$HB^{\pm} + H^+ \rightleftharpoons H_2B^+$$
$$K^B_A = [H_2B^+]/[HB^{\pm}][H^+] \quad (19)$$

$$Cu^{2+} + A^- \rightleftharpoons CuA^+$$
$$K^A_1 = \beta_{10} = [CuA^+]/[Cu^{2+}][A^-] \quad (20)$$

$$CuA^+ + A^- \rightleftharpoons CuA_2$$
$$K^A_2 = [CuA_2]/[CuA^+][A^-] \quad (21)$$

$$Cu^{2+} + 2A^- \rightleftharpoons CuA_2$$
$$\beta_{20} = K^A_1K^A_2 = [CuA_2]/[Cu^{2+}][A^-]^2 \quad (22)$$

$$Cu^{2+} + B^- \rightleftharpoons CuB^+$$
$$K^B_1 = \beta_{01} = [CuB^+]/[Cu^{2+}][B^-] \quad (23)$$

$$CuB^+ + B^- \rightleftharpoons CuB_2$$
$$K^B_2 = [CuB_2]/[CuB^+][B^-] \quad (24)$$

$$Cu^{2+} + 2B^- \rightleftharpoons CuB_2$$
$$\beta_{02} = K^B_1K^B_2 = [CuB_2]/[Cu^{2+}][B^-]^2 \quad (25)$$

$$Cu^{2+} + A^- + B^- \rightleftharpoons CuAB$$
$$\beta_{11} = [CuAB]/[Cu^{2+}][A^-][B^-] \quad (26)$$

$$CuB^+ + A^- \rightleftharpoons CuAB$$
$$K_A^{CuB} = [CuAB]/[CuB^+][A^-] \quad (27)$$

$$CuA^+ + B^- \rightleftharpoons CuAB$$
$$K_B^{CuA} = [CuAB]/[CuA^+][B^-] \quad (28)$$
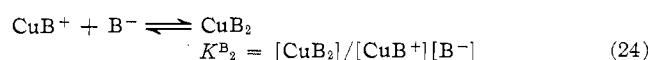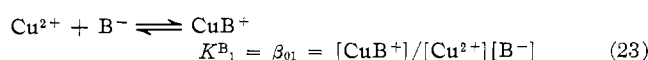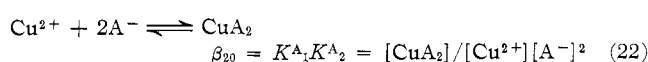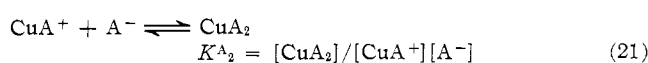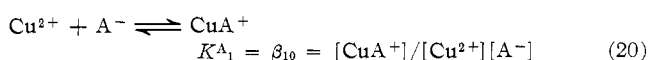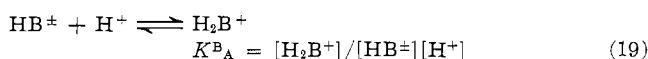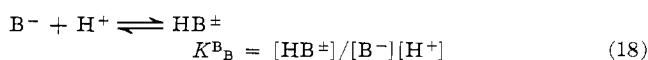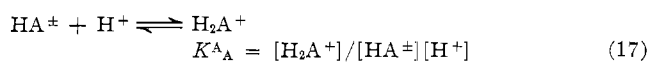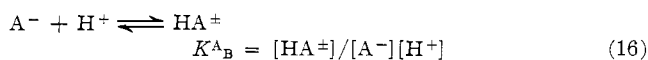
Mass conservation leads to the set of equations

$$T_M = [Cu^{2+}] + [CuA^+] + [CuA_2] + [CuB^+] + [CuB_2] + [CuAB] \quad (29)$$

$$T_A = [A^-] + [HA^{\pm}] + [H_2A^+] + [CuA^+] + 2[CuA_2] + [CuAB] \quad (30)$$

$$T_B = [B^-] + [HB^{\pm}] + [H_2B^+] + [CuB^+] + 2[CuB_2] + [CuAB] \quad (31)$$

$$T_H = T_A + T_B - C_B = [H^+] - [OH^-] + 2[H_2A^+] + 2[H_2B^+] + [HA^+] + [HB^+] \quad (32)$$

where the quantities on the left-hand side are the known concentrations of copper(II) ion, ligand A, ligand B, and replaceable hydrogen ions.

Substituting equilibrium constant expressions into the above mole balance relationships gives

$$F_1 = m + \beta_{10}ma + \beta_{20}ma^2 + \beta_{01}mb + \beta_{02}mb^2 + \beta_{11}mab - T_M = 0 \quad (33)$$

$$F_2 = a + K^A_AK^A_Bh^2a + K^A_Bha + \beta_{10}ma + 2\beta_{20}ma^2 + \beta_{11}mab - T_A = 0 \quad (34)$$

$$F_3 = b + K^B_AK^B_Bh^2b + K^B_Bhb + \beta_{01}mb + 2\beta_{02}mb^2 + \beta_{11}mab - T_B = 0 \quad (35)$$

$$F_4 = h - (K_w/f_1^2)h^{-1} + 2K^A_AK^A_Bh^2a + K^A_Bha + 2K^B_AK^B_Bh^2b + K^B_Bhb - T_H = 0 \quad (36)$$

where m, a, b, and h are the concentrations of free copper(II) ion, free ligand A, free ligand B, and hydrogen ion. At each titration point, m, a, b, and β_{11} must be obtained from the four nonlinear simultaneous equations (33)–(36).

Näsänen, et al.,[37,38] and Lim[39] have demonstrated that it is possible to reduce the above calculation to the problem of finding the appropriate root of a high-order polynomial in one variable. The solution of the resulting polynomial can be effected by the Newton–Raphson method. This method is usually beset with severe numerical problems. Wilkinson[52] pointed out that the roots of the polynomial can be extremely sensitive to relatively small errors in the polynomial coefficients and, in fact, the computed roots may bear no relationship to the actual roots. This is compounded by the fact that in order to determine m, a, b, and β_{11}, it is necessary to find the appropriate root (positive real root) among the many false roots that have been introduced while effecting the reduction to polynomial form. This consideration has led us to employ a modified Newton–Raphson iterative algorithm[40] directly to the set of nonlinear simultaneous equations.

Expanding eq 33–36 about an approximate set of values of m, a, b, and β_{11} into a Taylor series and neglecting higher order terms we have four linear equations in four fractional shifts, $\delta m/m$, $\delta a/a$, $\delta b/b$, and $\delta\beta_{11}/\beta_{11}$, written in the matrix form

$$\mathbf{CX} = \mathbf{B} \quad (37)$$

where $\mathbf{C}$ is a 4×4 matrix; see Matrix I. $\mathbf{X}$ is a four-dimensional unknown vector

$$\mathbf{X} = \{\delta m/m, \delta a/a, \delta b/b, \delta\beta_{11}/\beta_{11}\} \quad (38)$$

and $\mathbf{B}$ is a four-dimensional constant vector

$$\mathbf{B} = \{-F_1, -F_2, -F_3, -F_4\} \quad (39)$$

The numerical procedures such as the matrix scaling, eigenvalue analysis, matrix inversion, iterative formula, convergence criterion, and techniques to satisfy the constraints of the solution have been described in a separate report.[40] NP values of β_{11}, $(\beta_{11})_i$

$$i = 1, 2, \ldots, NP \quad (40)$$

are obtained for an experiment with NP titration points. The best value of β_{11} can be obtained from

$$\bar{\beta} \text{ (best value of } \beta_{11}) = \sum_1^{NP} W_i(\beta_{11})_i / \sum_1^{NP} W_i \quad (41)$$

If we assume the error lies entirely in the measured value of emf, then the variance of hydrogen ion concentration, σ_h^2, can be calculated from the error associated with the measurement of emf, according to the variance propagation principle. Following the same rule, the variance σ_i^2 of β_{11} can be calculated by

$$\sigma_i^2 = (\partial\beta_{11}/\partial h)^2\sigma_h^2 \quad (42)$$

Since there is no explicit functional relationship between β_{11} and the free hydrogen ion concentration, h, the partial derivative $\partial\beta_{11}/\partial h$ must be calculated by numerical differentiation

(52) J. H. Wilkinson, "The Algebraic Eigenvalue Problem," Clarendon Press, Oxford, 1965.

MATRIX I

$$C = \begin{bmatrix} m + \beta_{10}ma + \beta_{20}ma^2 + \\ \beta_{01}mb + \beta_{02}mb^2 + \beta_{11}mab & \beta_{10}ma + 2\beta_{20}ma^2 + \beta_{11}mab & \beta_{01}mb + 2\beta_{02}mb^2 + \beta_{11}mab & \beta_{11}mab \\[2ex] \beta_{10}ma + 2\beta_{20}ma^2 + \beta_{11}mab & \begin{array}{l} a + \beta_{10}ma + 4\beta_{20}ma^2 + \\ K^A{}_A K^A{}_B h^2 a + K^A{}_B ha + \\ \beta_{11}mab \end{array} & \beta_{11}mab & \beta_{11}mab \\[2ex] \beta_{01}mb + 2\beta_{02}mb^2 + \beta_{11}mab & \beta_{11}mab & \begin{array}{l} b + \beta_{01}mb + 4\beta_{02}mb^2 + \\ K^B{}_A K^B{}_B h^2 b + K^B{}_B hb + \\ \beta_{11}mab \end{array} & \beta_{11}mab \\[2ex] 0 & 2K^A{}_A K^A{}_B h^2 a + K^A{}_B ha & 2K^B{}_A K^B{}_B h^2 b + K^B{}_B hb & 0 \end{bmatrix}$$

TABLE III

REPRESENTATIVE pH TITRATION DATA FOR SOLUTIONS CONTAINING COPPER(II), α-ALANINE, AND VALINE AT 25°[a]

Titer V_B, ml	pH_A	pH_B	pH	$10^3 T_A$, M	$10^3 T_B$, M	$10^3 T_M$, M	$10^3 [Cu^{2+}]$, M	$10^8 [ala^-]$, M	$10^8 [val^-]$, M	$10^{-15}\beta_{11}$[b]
2.7500	4.091	4.092	4.092	5.173	5.066	5.102	1.570	0.663	0.890	1.41571
3.0000	4.190	4.191	4.190	5.164	5.058	5.094	1.359	0.803	1.066	1.43688
3.2500	4.294	4.295	4.294	5.156	5.050	5.086	1.157	0.979	1.287	1.46350
3.5000	4.402	4.403	4.403	5.148	5.042	5.077	9.689	1.201	1.563	1.49692
3.7500	4.515	4.515	4.515	5.139	5.033	5.069	7.982	1.481	1.906	1.53205
4.0000	4.630	4.631	4.631	5.131	5.025	5.061	6.474	1.832	2.333	1.56477
4.2500	4.750	4.751	4.750	5.123	5.017	5.053	5.172	2.274	2.862	1.58779
4.5000	4.872	4.874	4.873	5.114	5.009	5.044	4.073	2.827	3.517	1.60130
4.7500	4.999	5.000	4.999	5.106	5.001	5.036	3.159	3.526	4.334	1.59801
5.0001	5.128	5.130	5.128	5.098	4.993	5.028	2.420	4.396	5.337	1.59313
5.2500	5.241	5.242	5.241	5.090	4.985	5.020	1.905	5.231	6.284	1.74667
5.5000	5.380	5.382	5.381	5.081	4.977	5.012	1.412	6.574	7.793	1.70976
5.7500	5.529	5.529	5.529	5.073	4.969	5.004	1.024	8.330	9.737	1.66151
6.0000	5.688	5.690	5.689	5.065	4.961	4.996	7.196	10.706	12.333	1.59418
6.2501	5.864	5.866	5.865	5.057	4.953	4.988	4.862	14.027	15.916	1.50824
6.5000	5.064	6.065	6.064	5.049	4.945	4.980	3.105	18.957	21.177	1.39040

[a] The ionic strength $I = 0.1$ M (KNO$_3$), the concentration of titrant $C_B = 0.1977$ M, initial total volume $T^0{}_V = 150$ ml, initial total concentration of alanine $T^0{}_A = 5.268 \times 10^{-3}$ M, initial total concentration of valine $T^0{}_B = 5.159 \times 10^{-3}$ M, and initial total concentration of copper ion $T^0{}_M = 5.196 \times 10^{-3}$ M. [b] $\beta = (1.58 \pm 0.03) \times 10^{15}$.

$$\frac{\partial \beta_{11}}{\partial h} = \frac{\beta_{11}(h + h\Delta) - \beta_{11}(h)}{h\Delta} \quad (43)$$

where $\Delta = 10^{-5}$.

The estimated standard error of β_{11}, σ_{ext}^2, can be calculated from the formula

$$\sigma_{ext}^2 = \frac{\sum_1^{NP} W_i[(\beta_{11})_i - \bar{\beta}]^2}{(NP - 1)\sum_1^{NP} W_i} \quad (44)$$

Representative titration data for solutions containing copper(II) ion, α-alanine, and valine are summarized in Table III. Stability constants for the resulting mixed complexes are given in Table IV. In these calculations, only those titration points within a pH range of 4.5–6.5 were used. Within this pH region the concentrations of the mixed complex formed were more than 5% of the total copper(II) ion concentration and the ligands were not more than 90% neutralized.

In the present study we have employed the computer program EQUIL[40] to calculate the equilibrium composition of various species present at each stage in a calorimetric titration experiment. Since relatively small volumes of titrant of ionic strength, 0.1 M, were added, corrections for heats of dilution were negligible. The observed heat change, Q_{exptl}, therefore resulted from the protonation, complexation, and water formation reactions taking place in the calorimeter. In the protonation experiments, the amino acids were present either as the zwitterion or the anion;

the concentration of the protonated form was negligible within the pH range studied.

In addition to reaction 1 (enthalpy change ΔH_B), equilibrium 45 must be considered.

$$OH^- + H^+ \rightleftharpoons H_2O \qquad \Delta H_{H_2O} \quad (45)$$
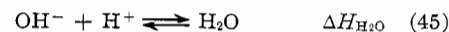
Thus, for each protonation titration step

$$Q_{exptl} = Q_{HL^{\pm}} + Q_{H_2O} \quad (46)$$

The heat of formation of water was calculated from eq 47 using the enthalpy of the neutralization, ΔH_{H_2O}, valid at 0.1 M ionic strength of -13.49 kcal/mol (calculated from $\Delta H_{H_2O} = -13.34$ kcal/mol at infinite dilution)[46]

$$Q_{H_2O} = \Delta H_{H_2O}(-D[OH^-]) \quad (47)$$

where $D[OH^-]$ is the change in moles of hydroxyl ion for each titrant addition.

The enthalpy of protonation ΔH_B was evaluated using eq 48

$$\Delta H_B = \frac{Q_{exptl} - Q_{H_2O}}{D[HL]} \quad (48)$$

where $D[HL]$ is defined similarly to $D[OH^-]$. The results are summarized in Table V along with available literature values.

In the stepwise formation of mononuclear complexes CuL^+ and CuL_2, the additional reactions (49) and (50) must be taken into account.

TABLE IV
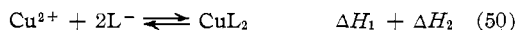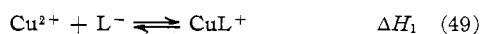#### STABILITY CONSTANTS FOR MIXED-LIGAND COPPER(II) COMPLEXES IN AQUEOUS SOLUTION AT 25°

Ligand A	Ligand B	[Medium], M	Log β_{11}	Log $K_A{}^{CuB}$	log $K_B{}^{CuA}$
Glycine	α-Alanine	0.1 (KNO₃)	15.05 ± 0.02	6.90 ± 0.02	6.84 ± 0.02[a]
		0.1 (NaClO₄)	15.24	7.06	7.03[b]
		0.15 (NaClO₄)	15.17[c]		
Glycine	Valine	0.1 (KNO₃)	15.06 ± 0.01	6.95 ± 0.01	6.84 ± 0.01[a]
		0.1 (NaClO₄)	15.40	7.17	7.08[b]
		0.5 (NaClO₄)	15.75[d]		
Glycine	Serine	0.1 (KNO₃)	14.66 ± 0.02	6.74 ± 0.02	6.44 ± 0.02[a]
α-Alanine	Valine	0.1 (KNO₃)	15.20 ± 0.01	7.09 ± 0.01	7.05 ± 0.01[a]
α-Alanine	Serine	0.1 (KNO₃)	14.91 ± 0.01	6.99 ± 0.01	6.76 ± 0.01[a]
Valine	Serine	0.1 (KNO₃)	14.84 ± 0.01	6.92 ± 0.01	6.73 ± 0.01[a]

[a] This study. [b] Reference 39. [c] Reference 41. [d] M. M. Ramel-Petit and M. R. Paris, *Bull. Soc. Chem. Fr.*, 2791 (1968).

TABLE V
THERMODYNAMIC PROPERTIES FOR THE PROTONATION OF AMINO ACIDS H⁺ + L⁻ ⇌ HL± IN AQUEOUS SOLUTION AT 25°

Ligands	[Medium], M	pK_B	ΔG_B, kcal mol⁻¹	ΔH_B, kcal mol⁻¹	ΔS_B, cal deg⁻¹ mol⁻¹
Glycine	0.1 (NaClO₄)	9.56	−13.04	−10.2 (c)	9.5
α-Alanine	0.1 (KNO₃)	9.70 ± 0.01	−13.23 ± 0.01	−10.85 ± 0.1 (c)	8.0 ± 0.5[a]
	0.1 (NaClO₄)	9.67	−13.19	−10.60 (c)	8.7[b]
	0.16 (KNO₃)	9.60		−10.62 (c)	8.3[c]
	∼0.0	9.87		−10.91 (c)	8.6[d]
Valine	0.1 (KNO₃)	9.50 ± 0.01	−12.96	−10.99 (c)	6.61 ± 0.5[a]
	0.16 (KNO₃)	9.44		−10.97 (c)	6.4[c]
	∼0.0	9.719		−10.73 (c)	8.5[e]
Serine	0.1 (KNO₃)	9.14 ± 0.01	−12.48 ± 0.01	−10.46 ± 0.01 (c)	6.3 ± 0.5[a]
	0	9.208		−10.41 (t)	7.2[f]
	0.16 (KNO₃)	9.18	−12.52	−10.05 (c)	8.3[g]

[a] This study. [b] Reference 39. [c] J. L. Meyer and J. E. Bauman, Jr., *J. Chem. Eng. Data*, **15**, 404 (1970). [d] J. A. Partridge, J. J. Christensen, and R. M. Izatt, *J. Amer. Chem. Soc.*, **88**, 1649 (1966). [e] J. J. Christensen, R. M. Izatt, P. P. Wrathall, and D. H. Hansen, *J. Chem. Soc. A*, 1212 (1969). [f] P. K. Smith, A. T. Gorham, and E. R. B. Smith, *J. Biol. Chem.*,, **144**, 737 (1942). [g] J. E. Letter, Jr., and J. E. Bauman, Jr., *J. Amer. Chem. Soc.*, **92**, 437 (1970).

$$Cu^{2+} + L^- \rightleftharpoons CuL^+ \qquad \Delta H_1 \quad (49)$$

$$Cu^{2+} + 2L^- \rightleftharpoons CuL_2 \qquad \Delta H_1 + \Delta H_2 \quad (50)$$

The measured heat change of the system, Q_{exptl}, is given by

$$Q_{exptl} = Q_{H_2O} + Q_{HL} + Q_{H_2L} + Q_{CuL} + Q_{CuL_2} \quad (51)$$

where

$$Q_{HL} = \Delta H_B D[HL]$$

$$Q_{H_2L} = (\Delta H_A + \Delta H_B)D[H_2L]$$

$$Q_{CuL} = \Delta H_1 D[CuL]$$

$$Q_{CuL_2} = (\Delta H_1 + \Delta H_2)D[CuL_2]$$

Thus the heat contributions due to the formation of CuL and CuL₂, $Q_{CuL} + Q_{CuL_2}$, are given by

$$Q_{CuL} + Q_{CuL_2} = Q_{exptl} + \Delta H_{H_2O}D[OH^-] -$$
$$\Delta H_B\{D[HL] + D[H_2L]\} - \Delta H_A D[H_2L] =$$
$$\Delta H_1\{D[CuL] + D[CuL_2]\} + \Delta H_2 D[CuL_2] \quad (52)$$

from which eq 53 can be derived.

$$\frac{Q_{CuL} + Q_{CuL_2}}{D[CuL_2]} = \frac{D[CuL] + D[CuL_2]}{D[CuL_2]} \Delta H_1 + \Delta H_2 \quad (53)$$

A typical plot of $(Q_{CuL} + Q_{CuL_2})/D[CuL_2]$ vs. $(D[CuL] + D[CuL_2])/D[CuL_2]$ for the copper(II)–valine complex is shown in Figure 1; a least-squares analysis was performed to provide ΔH_1 and ΔH_2. The thermodynamic parameters for the mononuclear copper(II) complexes are listed in Table VI, where the values available in the literature are compared.
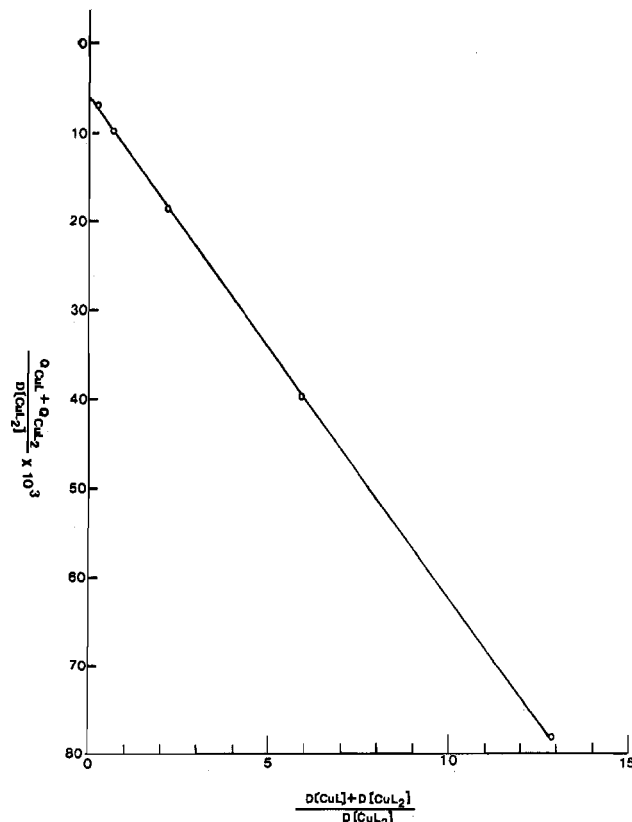

Figure 1.—Plot of $(Q_{CuL} + Q_{CuL_2})/D[CuL_2]$ against $(D[CuL] + D[CuL_2])/D[CuL_2]$ for copper–valine complex formation at 25°.

In the presence of two ligand molecules, the equilibria involved are (16)–(20), (22), (23), (25), (26), and (45). Following the same argument we have

TABLE VI
THERMODYNAMIC PROPERTIES FOR COPPER(II)–AMINO ACID COMPLEXES IN AQUEOUS SOLUTION AT 25°

Ligands	[Medium], M	Log K_1	ΔG_1, kcal mol^{-1}	ΔH_1, kcal mol^{-1}	ΔS_1, cal deg^{-1} mol^{-1}
			$Cu^{2+} + L^- \rightleftharpoons CuL^+$		
Glycine	0.1 (NaClO$_4$)	9.56	-11.21	-6.0 (c)	17.5[a]
α-Alanine	0.1 (KNO$_3$)	8.15 ± 0.01	-11.12 ± 0.01	-5.6 ± 0.15 (c)	18.5 ± 0.5[b]
	0.1 (NaClO$_4$)		-11.17	-6.3 (c)	16.3[a]
	0.16 (KNO$_3$)	7.84		-5.62 (c)	17.0[c]
Valine	0.1 (KNO$_3$)	8.11 ± 0.01	-11.07 ± 0.01	-5.56 ± 0.15 (c)	18.5 ± 0.5[b]
	0.16 (KNO$_3$)	7.80		-5.46 (c)	17.4[c]
	0.1 (KNO$_3$)	7.92 ± 0.01	-10.8 ± 0.01	-5.5 ± 0.15 (c)	17.8 ± 0.5[b]
	0.16 (KNO$_3$)	7.85	-10.71	-5.51 (c)	17.5[d]
			$CuL^+ + L^- \rightleftharpoons CuL_2$		
Glycine	0.1 (NaClO$_4$)	6.80	-9.27	-6.6 (c)	8.9
α-Alanine	0.1 (KNO$_3$)	6.67 ± 0.01	-9.10 ± 0.01	-6.15 ± 0.08 (c)	9.9 ± 0.3[b]
	0.1 (NaClO$_4$)	6.75	-9.21	-5.4 (c)	12.8[a]
	0.16 (KNO$_3$)	6.64		-6.00 (c)	10.3[c]
Valine	0.1 (KNO$_3$)	6.68 ± 0.01	-9.11 ± 0.01	-6.22 ± 0.08 (c)	9.7 ± 0.3[b]
	0.16 (KNO$_3$)	6.70		-5.84 (c)	11.1[c]
Serine	0.1 (KNO$_3$)	6.65 ± 0.01	-9.07 ± 0.01	-6.1 ± 0.1 (c)	10.0 ± 0.3[b]
	0.16 (KNO$_3$)	6.65	-9.07	-6.13 (c)	9.9[d]

[a] Reference 39. [b] This work. [c] S. Pelletier, Ph.D. Thesis, University of Paris, 1960. [d] J. E. Letter, Jr., and J. E. Bauman, Jr., *J. Amer. Chem. Soc.*, **92**, 437 (1970).

TABLE VII
THERMODYNAMIC PROPERTIES FOR MIXED-COMPLEX FORMATION REACTIONS Cu + A + B → CuAB IN
AN AQUEOUS SOLUTION OF 0.1 M KNO$_3$ AT 25°

Ligand A	Ligand B	Log β_{11}	$\Delta G_{\beta_{11}}$, kcal mol^{-1}	$\Delta H_{\beta_{11}}$, kcal mol^{-1}	$\Delta S_{\beta_{11}}$, cal deg^{-1} mol^{-1}
Glycine	α-Alanine	15.05 ± 0.02	-20.53 ± 0.03	-11.75 ± 0.3	29.4 ± 1.0
Glycine	Valine	15.06 ± 0.01	-20.55 ± 0.01	-11.84 ± 0.3	29.2 ± 1.0
Glycine	Serine	14.66 ± 0.02	-20.00 ± 0.03	-11.7 ± 0.3	27.8 ± 1.0
α-Alanine	Valine	15.20 ± 0.01	-20.74 ± 0.01	-11.78 ± 0.3	30.0 ± 1.0
α-Alanine	Serine	14.91 ± 0.01	-20.34 ± 0.01	-11.7 ± 0.3	29.0 ± 1.0
Valine	Serine	14.84 ± 0.01	-20.24 ± 0.01	-11.65 ± 0.3	28.8 ± 1.0

$$Q_{CuAB} = Q_{exptl} - (Q_{HA} + Q_{H_2A} + Q_{HB} + Q_{H_2B} +$$
$$Q_{CuA} + Q_{CuA_2} + Q_{CuB} + Q_{CuB_2} - Q_{H_2O}) = Q_{exptl} +$$
$$\Delta H_{H_2O}D[OH^-] - \{\Delta H^A{}_B(D[HA] + D[H_2A]) +$$
$$\Delta H^A{}_A D[H_2A] + \Delta H^B{}_B(D[HB] + D[H_2B]) +$$
$$\Delta H^B{}_A D[H_2B] + \Delta H^A{}_1(D[CuA] + D[Cu_2A]) +$$
$$\Delta H^A{}_2 D[CuA_2] + \Delta H^B{}_1(D[CuB] + D[CuB_2]) +$$
$$\Delta H^B{}_2 D[CuB_2]\} = \Delta H_{CuAB}D[CuAB] \quad (54)$$

The enthalpy of mixed-complex formation ΔH_{CuAB} may be evaluated from

$$\Delta H_{CuAB} = Q_{CuAB}/D[CuAB] \quad (55)$$

and the results are collected in Table VII.

Figure 2 shows a distribution diagram for the Cu(II)–alanine–valine system; diagrams for all other systems showed the same qualitative features. In solution of equimolar concentrations of copper(II) ion, amino acid A, and amino acid B, within the pH range of 3.5–6.5, all the species Cu^{2+}, CuA$^+$, CuB$^+$, CuA$_2$, CuB$_2$, and CuAB are present in significant amounts and the mixed complexes are seen to be more stable than either of the bis complexes.

In order to make a more detailed discussion of the thermodynamic quantities, it is convenient to separate them into temperature-dependent and temperature-independent components.[53] The former represents the long-range electrostatic contributions which depend upon the environment, and the latter, the short-range covalent contributions which are insensitive to the environment. The electrostatic components ΔG_e and ΔH_e may be calculated from[53]

(53) G. Degischer and G. H. Nancollas, *J. Chem. Soc. A*, 1125 (1970).

$$\Delta G_e = \nu(\Delta S + \Delta nR \ln 55.5) \quad (56)$$
$$\Delta H_e = (T - \nu)(\Delta S + \Delta nR \ln 55.5) \quad (57)$$

Where Δn is the decrease in the number of solute particles in the ion association reaction and ν is a temperature characteristic of the solvent (219°K for water). The temperature-independent part of the enthalpy, $\Delta H_c = \Delta H - \Delta H_e$, and values are given in Table VIII.

The protonation thermodynamic data in Table V are similar to those for most primary amines[54] and they do not show the linear relationship between ΔG and ΔS predicted by Bjerrum's electrostatic theory.[55] The ΔH and ΔS values for protonation decrease in a regular manner as methylene groups are substituted in the hydrocarbon chain in going from glycine through α-alanine to valine. These compensating changes in ΔH and $T\Delta S$ maintain ΔG and hence the amino proton association constant, pK_B, practically constant. Christensen, *et al.*,[54] have proposed a "hydrocarbon chain stiffening" phenomenon in which the presence of charge causes the hydrocarbon chain to lose both rotational enthalpy and entropy in order to explain the compensating changes in ΔH and $T\Delta S$. The protonation enthalpy change for serine is lower than that of α-alanine. Because of the electron-withdrawing properties of the OH group in the β position, the electron density associated with the nitrogen atom of serine is decreased relative to that of alanine, hence weakening the N–H bond.

(54) J. J. Christensen, R. M. Izatt, D. P. Wrathall, and L. D. Hansen, *ibid.*, 1212 (1969).
(55) E. J. King in "Acid-Base Equilibria," R. A. Robinson, Ed., Macmillan, New York, N. Y., 1965; "International Encyclopedia of Physical Chemistry and Chemical Physics," Vol. 4, Topic 15, p 153.
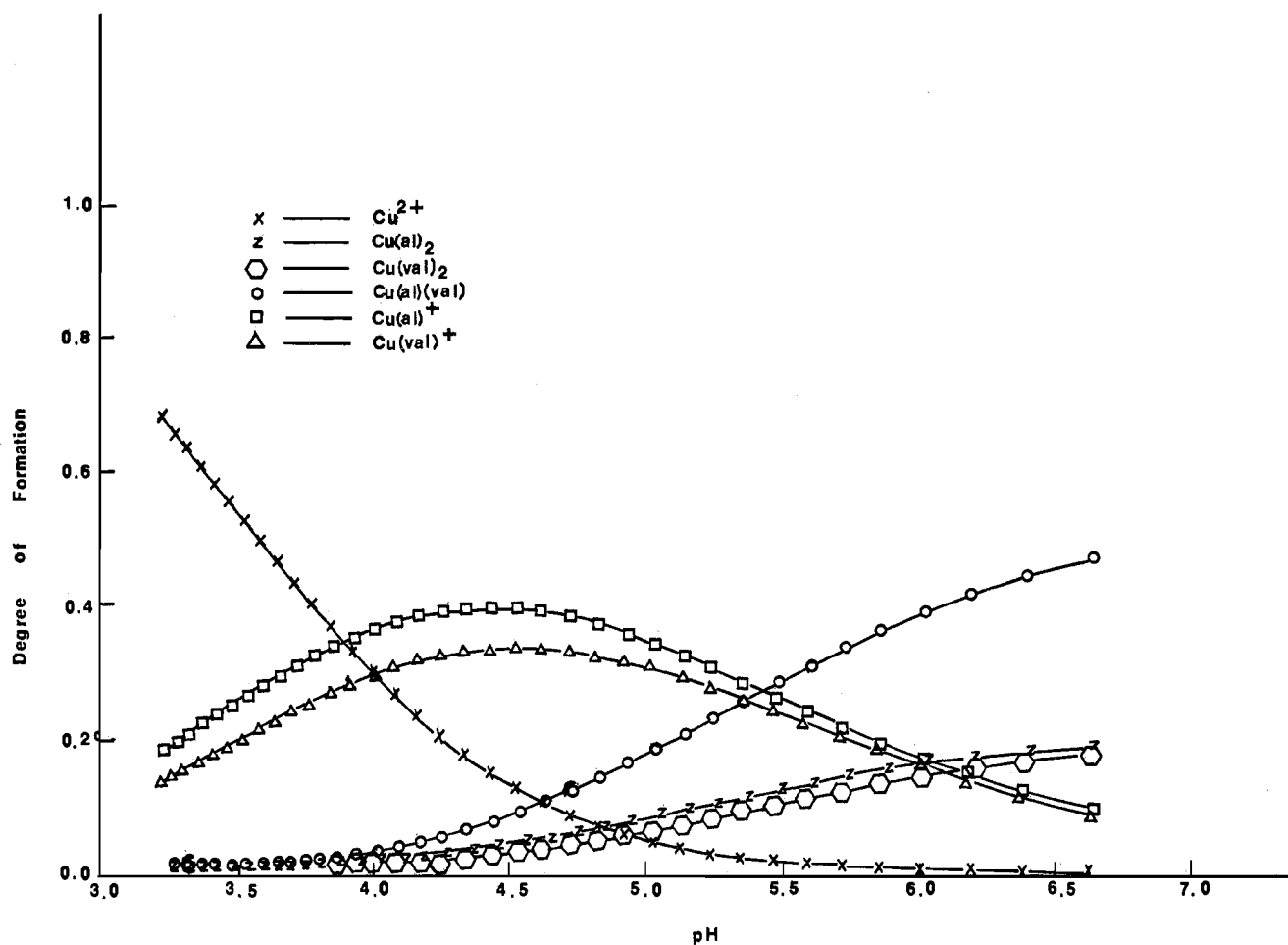
Figure 2.—Distribution of complex species in the Cu(II)–α-alanine–valine system as a function of pH.

TABLE VIII

THERMODYNAMIC PROPERTIES FOR SIMPLE AND MIXED COPPER(II)–AMINO ACID COMPLEXES IN
AQUEOUS SOLUTION OF 0.1 M KNO$_3$ AT 25°

Reactions	pK	$-\Delta G$, kcal mol^{-1}	$-\Delta H$, kcal mol^{-1}	ΔS, cal deg^{-1} mol^{-1}	ΔH_e, kcal mol^{-1}	$-\Delta H_c$, kcal mol^{-1}
Cu^{2+} + 2gly$^-$ ⇌ Cu(gly)$_2$	15.02	20.47	12.6	26.4	3.3	15.9
Cu^{2+} + 2α-ala$^-$ ⇌ Cu(α-ala)$_2$	14.82 ± 0.01	20.22 ± 0.02	11.75 ± 0.17	28.4 ± 0.6	3.5	15.1
Cu^{2+} + 2 val$^-$ ⇌ Cu(val)$_2$	14.79 ± 0.01	20.18 ± 0.02	11.78 ± 0.17	28.2 ± 0.6	3.5	15.3
Cu^{2+} + 2 ser$^-$ ⇌ Cu(ser)$_2$	14.57 ± 0 01	19.87 ± 0.02	11.6 ± 0.17	27.8 ± 0.6	3.4	15.0
Cu^{2+} + gly$^-$ + α-ala$^-$ ⇌ Cu(gly)(α-ala)	15.05 ± 0.02	20.53 ± 0.03	11.75 ± 0.3	29.4 ± 1.0	3.6	15.3
Cu^{2+} + gly$^-$ + val$^-$ ⇌ Cu(gly)(val)	15.06 ± 0.01	20.55 ± 0.01	11.84 ± 0.3	29.2 ± 1.0	3.6	15.4
Cu^{2+} + gly$^-$ + ser$^-$ ⇌ Cu(gly)(ser)	14.66 ± 0.02	20.00 ± 0.03	11.7 ± 0.3	27.8 ± 1.0	3.4	15.2
Cu^{2+} + α-ala$^-$ + val$^-$ ⇌ Cu(α-ala)(val)	15.20 ± 0.01	20.74 ± 0.01	11.78 ± 0.3	30.0 ± 1.0	3.6	15.4
Cu^{2+} + α-ala$^-$ + ser$^-$ ⇌ Cu(α-ala)(ser)	14.91 ± 0.01	20.34 ± 0.01	11.7 ± 0.3	29.0 ± 1.0	3.6	15.2
Cu^{2+} + val$^-$ + ser$^-$ ⇌ Cu(val)(ser)	14.84 ± 0.01	20.24 ± 0.01	11.65 ± 0.3	28.8 ± 1.0	3.5	15.1
Cu^{2+} + gly$^-$ ⇌ Cu(gly)$^+$	8.22	11.2	6.0	17.5	2.0	8.0
Cu(gly)$^+$ + gly$^-$ ⇌ Cu(gly)$_2$	6.80	9.27	6.6	8.9	1.3	7.9
Cu^{2+} + α-ala$^-$ ⇌ Cu(α-ala)$^+$	8.15 ± 0.01	11.12 ± 0.01	5.6 ± 0.15	18.5 ± 0.5	2.1	7.7
Cu(α-ala)$^+$ + α-ala$^-$ ⇌ Cu(α-ala)$_2$	6.67 ± 0.01	9.10 ± 0.01	6.15 ± 0.08	9.9 ± 0.3	1.4	7.6
Cu^{2+} + val$^-$ ⇌ Cu(val)$^+$	8.11 ± 0.01	11.07 ± 0.01	5.56 ± 0.15	18.5 ± 0.5	2.1	7.6
Cu(val)$^+$ + val$^-$ ⇌ Cu(val)$_2$	6.68 ± 0.01	9.11 ± 0.01	6.22 ± 0.08	9.7 ± 0.3	1.4	7.6
Cu^{2+} + ser$^-$ ⇌ Cu(ser)$^+$	7.92 ± 0.01	10.80 ± 0.01	5.5 ± 0.15	17.8 ± 0.5	2.0	7.5
Cu(ser)$^+$ + ser$^-$ ⇌ Cu(ser)$_2$	6.65 ± 0.01	9.07 ± 0.01	6.1 ± 0.1	10.0 ± 0.3	1.4	7.5
Cu(gly)$^+$ + α-ala$^-$ ⇌ Cu(gly)(α-ala)	6.83 ± 0.01	9.33 ± 0.01	5.75 ± 0.3	12.0 ± 1.0	1.6	7.3
Cu(gly)$^+$ + val$^-$ ⇌ (Cu(gly)(val)	6.84 ± 0.01	9.35 ± 0.01	5.84 ± 0.3	11.8 ± 1.0	1.6	7.4
Cu(gly)$^+$ + ser$^-$ ⇌ Cu(gly)(ser)	6.44 ± 0.01	8.80 ± 0.01	5.7 ± 0.3	10.4 ± 1.0	1.4	7.2
Cu(α-ala)$^+$ + gly$^-$ ⇌ Cu(α-ala)(gly)	6.90 ± 0.01	9.41 ± 0.01	6.15 ± 0.3	11.0 ± 1.0	1.5	7.6
Cu(α-ala)$^+$ + val$^-$ ⇌ Cu(α-ala)(val)	7.05 ± 0.01	9.62 ± 0.01	6.18 ± 0.3	11.5 ± 1.0	1.5	7.7
Cu(α-ala)$^+$ + ser$^-$ ⇌ Cu(α-ala)(ser)	6.76 ± 0.01	9.22 ± 0.01	6.1 ± 0.3	10.5 ± 1.0	1.5	7.6
Cu(val)$^+$ + gly$^-$ ⇌ Cu(val)(gly)	6.95 ± 0.01	9.48 ± 0.01	6.28 ± 0.3	10.7 ± 1.0	1.5	7.8
Cu(val)$^+$ + α-ala$^-$ ⇌ Cu(val)(α-ala)	7.09 ± 0.01	9.76 ± 0.01	6.22 ± 0.3	11.6 ± 1.0	1.5	7.8
Cu(val)$^+$ + ser$^-$ ⇌ Cu(val)(ser)	6.73 ± 0.01	9.17 ± 0.01	6.09 ± 0.3	10.3 ± 1.0	1.4	7.5
Cu(ser)$^+$ + gly$^-$ ⇌ Cu(ser)(gly)	6.74 ± 0.01	9.20 ± 0.01	6.2 ± 0.3	10.1 ± 1.0	1.4	7.6
Cu(ser)$^+$ + α-ala$^-$ ⇌ Cu(ser)(α-ala)	6.99 ± 0.01	9.54 ± 0.01	6.2 ± 0.3	11.2 ± 1.0	1.5	7.7
Cu(ser)$^+$ + val$^-$ ⇌ Cu(ser)(val)	6.92 ± 0.01	9.44 ± 0.01	6.15 ± 0.3	11.0 ± 1.0	1.5	7.6

<div align="center">

TABLE IX

THERMODYNAMIC PROPERTIES FOR THE REACTION

$$Cu^{2+} + CuL_2 \overset{K_r}{\rightleftharpoons} 2CuL^+$$

IN AQUEOUS SOLUTION AT 25°

</div>

Ligand	Log K_r	ΔG_r, kcal mol^{-1}	ΔH_r, kcal mol^{-1}	ΔS_r, cal deg^{-1} mol^{-1}	$\Delta G_{r,t}$,[a] kcal mol^{-1}	$\Delta S_{r,t}$,[b] cal deg^{-1} mol^{-1}	$\Delta G_{r,e}$, kcal mol^{-1}	$\Delta G_{r,c}$, kcal mol^{-1}	$\Delta H_{r,e}$, kcal mol^{-1}	$\Delta H_{r,c}$, kcal mol^{-1}
Glycine	1.42	−1.93	0.6	8.6	−0.70	4.5	−0.98	+0.28	+0.36	+0.24
α-Alanine	1.48	−2.02	0.55	8.6	−0.79	4.5	−0.98	+0.19	+0.36	+0.19
Valine	1.43	−1.96	0.66	8.8	−0.73	4.7	−1.03	+0.30	+0.37	+0.29
Serine	1.27	−1.73	0.6	7.8	−0.50	3.7	−0.81	+0.31	+0.29	+0.31

[a] $\Delta G_{r,t} = \Delta G_r + RT \ln 8$.   [b] $\Delta S_{r,t} = \Delta S_r - R \ln 8$.

A mixed oxygen–nitrogen donor such as an amino acid with its hard oxygen and relatively soft nitrogen donors will be able to form strong complexes with the copper(II) ion which lies in the border region between a hard and a soft acceptor.[56] Both the enthalpy and entropy terms contribute to the stability of the complexes ML as shown by the data presented in Table VIII. Since the temperature-independent part of the enthalpy, ΔH_c, reflects both the covalent interactions and the structural changes, the very similar values for all the stepwise complex formation reactions, including the mixed-complex formation, indicate that the same number and type of copper(II)–ligand bonds are formed in each case. Furthermore, a comparison of the ΔH_c changes associated with the complex formation by copper(II) ion and amino acid with corresponding changes associated with ammonia and acetate ion[53] strongly suggests that in the copper(II) complexes of amino acids the coordination occurs through the amino nitrogen and the carboxyl oxygen; most of the enthalpy changes arise from the covalent interaction between copper(II) ion and the soft nitrogen donor atom. The hydroxyl group in the β position of serine therefore probably does not take part in the binding to copper(II) ion. The entropy changes are due to the displacement of water dipoles from the hydration shells of the interacting ions accompanying the essentially electrostatic interaction between Cu(II) and COO$^-$.[46,57]

It is seen from Table VIII that, of the two stepwise complexes formed between copper(II) and the amino acid anion, the mono complex is energetically more favored as shown by the greater negative ΔG_1 values compared to ΔG_2. This is essentially an entropy effect, the greater ΔS_1 compared with ΔS_2 overcoming the opposing trend in ΔH ($\Delta H_2 < \Delta H_1$). These observations can best be interpreted by considering reaction 58 in which the cratic part of the free energy has been

$$Cu^{2+} + CuL_2 \overset{K_r}{\rightleftharpoons} 2CuL^+ \qquad (58)$$
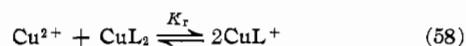
removed. The thermodynamic parameters for the above equation are obtained from the expressions

$$K_r = K_1/K_2 \qquad (59)$$

$$\Delta G_r = \Delta G_1 - \Delta G_2 \qquad (60)$$

$$\Delta H_r = \Delta H_1 - \Delta H_2 \qquad (61)$$

$$\Delta S_r = \Delta S_1 - \Delta S_2 \qquad (62)$$

Bjerrum[50] has made a careful study of the factors which influence consecutive complex formation by

dividing them into a "statistical effect" and a "ligand effect." The latter was further subdivided into an "electrostatic effect" and the "rest effect." We can therefore write

$$\Delta G_r = RT \ln K_{stat} + \Delta G_{r,e} + \Delta G_{r,c} \qquad (63)$$

where the first term on the right-hand side represents the free energy contribution attributable to purely statistical causes and K_{stat} is the value of K_r if reaction 58 proceeded statistically; $\Delta G_{r,e}$ and $\Delta G_{r,c}$ are the electrostatic and covalent components of the free energy change ΔG_r. K_{stat} can be assessed from the considerations of the different reaction paths available at each step. For a bidentate ligand binding to a copper(II) ion, $K_{stat} = 8$, and so $\Delta G_{stat} = RT \ln K_{stat} = 1.23$ kcal mol^{-1} and $\Delta S_{stat} = R \ln K_{stat} = 4.1$ kcal deg^{-1}. The electrostatic components $\Delta G_{r,e}$ and $\Delta H_{r,e}$ may be calculated using

$$\Delta G_{r,e} = -\nu(\Delta S_r - R \ln K_{stat}) \qquad (64)$$

$$\Delta H_{r,e} = (T - \nu)(\Delta S_r - R \ln K_{stat}) \qquad (65)$$

The temperature-independent part of the enthalpy, $\Delta H_{r,c}$, is given by the difference shown in

$$\Delta H_{r,c} = \Delta G_{r,c} = \Delta H_r - (T - \nu)(\Delta S_r - R \ln K_{stat}) \qquad (66)$$

The various values for all the amino acids calculated from eq 59–66 are listed in Table IX.

The overall entropy change ΔS_r of reaction 58 is given by

$$\Delta S_r = \Delta S_g + 2\Delta S_{hyd}(CuL^+) - \Delta S_{hyd}(Cu^{2+}) - \Delta S_{hyd}(CuL_2) \qquad (67)$$

where ΔS_{hyd} is the hydration entropy of the species contained in the parentheses and ΔS_g is the entropy change for the hypothetical gas-phase reaction.[58] ΔS_g does not change appreciably during a series of related reactions and can be approximately equated to ΔS_{stat} leading to eq 68

$$\Delta S_r = \Delta S_{stat} + 2\Delta S_{hyd}(CuL^+) - \Delta S_{hyd}(Cu^{2+}) - \Delta S_{hyd}(CuL_2) \qquad (68)$$

Thus the values of $\Delta S_{r,t} = \Delta S_r - \Delta S_{stat}$ in Table IX represent the entropy contributions due to differences in the solvation of various species which participate in reaction 58.

For the reactions of copper(II) ion with a series of ligands, $\Delta S_{r,t}$ will be a linear function of $\Delta S_{hyd}(CuL^+)$ if $\Delta S_{hyd}(CuL_2)$ is constant (or negligible in comparison with $\Delta S_{hyd}(Cu^{2+})$). All the $\Delta S_{r,t}$ values, with the

(56) S. Ahrland in "Structure and Chemical Bonding," Vol. 1, C. K. Jørgensen, J. B. Neilands, R. S. Nyholm, D. Reinen, and R. J. P. Williams, Ed., Springer-Verlag, Heidelberg, 1966, p 207.

(57) V. S. Sharma and H. B. Mathur, *Indian J. Chem.*, **3**, 475 (1965).

(58) G. H. Nancollas and A. C. Park, *Inorg. Chem.*, **7**, 58 (1968).
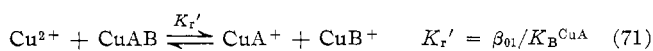
TABLE X

THERMODYNAMIC PROPERTIES FOR THE REACTION

$$Cu^{2+} + CuAB \overset{K_r'}{\rightleftharpoons} CuA^+ + CuB^+$$

IN AQUEOUS SOLUTION AT 25°

Ligands	Log K_r'	ΔG_r, kcal mol⁻¹	ΔH_r, kcal mol⁻¹	ΔS_r, cal deg⁻¹ mol⁻¹	$\Delta G_{r,t}$,[a] kcal mol⁻¹	$\Delta S_{r,t}$,[b] cal deg⁻¹ mol⁻¹	$\Delta G_{r,e}$, kcal mol⁻¹	$\Delta G_{r,c}$, kcal mol⁻¹	$\Delta H_{r,e}$, kcal mol⁻¹	$\Delta H_{r,c}$, kcal mol⁻¹
Glycine + α-alanine	1.32	−1.79	0.15	6.6	−0.97	3.8	−0.83	−0.14	+0.30	−0.15
Glycine + valine	1.27	−1.72	0.24	6.8	−0.90	4.0	−0.88	−0.02	+0.32	−0.08
Glycine + serine	1.48	−2.02	0.20	7.5	−1.20	4.7	−1.03	−0.17	+0.37	−0.17
α-Alanine + valine	1.06	−1.45	0.62	7.0	−0.63	4.2	−0.92	+0.29	+0.33	+0.29
α-Alanine + serine	1.16	−1.58	0.6	7.3	−0.76	4.5	−0.98	+0.22	+0.36	+0.24
Valine + serine	1.19	−1.63	0.59	7.5	−0.81	4.7	−1.03	+0.22	+0.37	+0.23

[a] $\Delta G_{r,t} = \Delta G_r + RT \ln 4$. [b] $\Delta S_{r,t} = \Delta S_r - R \ln 4$.

exception of those involving serine, are very similar, reflecting the same extent of solvation for all mono complexes CuL^+. The lower value of $\Delta S_{r,t}$ for serine can be attributed to the electron-withdrawing property of the hydroxyl group in the β position which renders the net positive charge on the $Cu(ser)^+$ higher than for the other mono(amino acid)complexes. Interaction with solvent will therefore be stronger in the case of $Cu(ser)^+$ resulting in a lower $\Delta S_{r,t}$.

The negative value of $\Delta G_{r,e}$ for reaction 58 indicates that the mutual electrostatic repulsion between ligands in a bis complex reduces its stability and hence favors the mono-complex formation. The $\Delta H_{r,c}$ (or $\Delta G_{r,c}$) reflects the covalent interactions and the mutual influence of the ligands and it is seen that the values favor the bis-complex formation. This may reflect the greater energy required to remove coordinated water molecules from the free copper(II) ion as compared with the mono complex. The coordination of the first amino acid by the copper(II) ion may facilitate the breaking of the remaining copper–water bonds in the complex.[58] Since all the ligands studied are simple amino acids, the $\Delta H_{r,c}$ values would be expected to be similar.

For the mixed complexes, eq 69–71 can be written

$$Cu^{2+} + B^- \rightleftharpoons CuB^+ \qquad \beta_{01} \qquad (69)$$

$$CuA^+ + B^- \rightleftharpoons CuAB \qquad K_B^{CuA} = \beta_{11}/\beta_{10} \quad (70)$$

$$Cu^{2+} + CuAB \overset{K_r'}{\rightleftharpoons} CuA^+ + CuB^+ \qquad K_r' = \beta_{01}/K_B^{CuA} \quad (71)$$

and $\log K_r'$ can be calculated from the stability constants of the binary and ternary complexes, *i.e.*

$$\log K_r' = \log \beta_{01} - \log K_B^{CuA} = \log \beta_{10} - \log K_A^{CuB} =$$
$$\log \beta_{01} + \log \beta_{10} - \log \beta_{11} \quad (72)$$

Equation 72 demonstrates that the influence of both ligands in the mixed complex is mutual and of the same size; they are either stabilized or destabilized in their coordination to the same metal ion. In the present case $K_{stat} = 4$, $\Delta S_{stat} = R \ln 4 = 2.8$ kcal deg⁻¹ mol⁻¹, $\Delta G_{stat} = RT \ln 4 = -0.82$ kcal mol⁻¹, and the corresponding values for the mixed-complex system are collected in Table X. Comparing the corresponding terms in Table X with those in Table IX, we see that, with the exception of Cu(gly)(ser), the $\log K_r'$ for the mixed-complex systems are smaller, indicating that compared with the binary species, mixed complex formation is more appreciable. After correction for the statistical effect, the values $\Delta G_{r,t}$ ($= \Delta G_r - \Delta G_{stat}$) are more negative for the ternary complexes as compared with binary complexes. This indicates that the

statistical factor is the sole effect which enhances the mixed-complex formation. In Table X the values of $\Delta H_{r,c}$ are all rather small and, although differences between the values for the various systems are quite close to the estimated error in ΔH, it can be seen that they change in the same general direction as the values of ΔG_r. This suggests that the mutual ligand interaction is responsible for the destabilization of the mixed complexes as compared to the parent mono complexes.

Another way of describing mixed-complex formation is to use the "mixing" constant,[59] K_M, which is the equilibrium constant for the reaction of the form

$$\tfrac{1}{2}CuA_2 + \tfrac{1}{2}CuB_2 \overset{K_M}{\rightleftharpoons} CuAB \qquad (73)$$
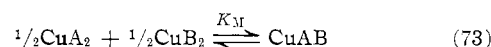
The "mixing" constant, K_M, reflects the relative stability of the mixed complex in solution as compared to the parent binary complexes. The "mixing" constant can be obtained from the stability constants of the binary complexes by the expression

$$K_M = \beta_{11}/\sqrt{\beta_{10}\beta_{01}} \qquad (74)$$

A major contribution to K_M will arise from statistical effects alone. If formation of a mixed complex, CuAB, proceeds only statistically, the value of K_{stat} would be 2. It is therefore convenient to define a stabilization constant, K_s, which for ligands of equal denticity will be given by

$$\log K_s = \log K_M - \log K_{stat} \qquad (75)$$

Thermodynamic functions for reaction 73 can thus be evaluated from

$$\Delta G_M = RT \ln K_M \qquad (76)$$

$$\Delta H_M = \Delta H_{CuAB} - \tfrac{1}{2}\Delta H_{CuA_2} - \tfrac{1}{2}\Delta H_{CuB_2} \quad (77)$$

$$\Delta S_M = \Delta S_{CuAB} - \tfrac{1}{2}\Delta S_{CuA_2} - \tfrac{1}{2}\Delta S_{CuB_2} = \Delta S_g +$$
$$\Delta S_{hyd}(CuAB) - \tfrac{1}{2}[\Delta S_{hyd}(CuA_2) +$$
$$\Delta S_{hyd}(CuB_2)] = \Delta S_{stat} + \Delta S_{hyd}(CuAB) -$$
$$\tfrac{1}{2}[\Delta S_{hyd}(CuA_2) + \Delta S_{hyd}(CuB_2)] \quad (78)$$

The results obtained from calculations using eq 76–78 are given in Table XI.

With the exception of the copper(II)–glycine–serine system, all $\log K_M > 0$. In addition, $\log K_s < 0$ except for copper(II)–alanine–valine, indicating that after correction for the statistical effect, the mixed complex is destabilized as compared to the parent binary complexes. This destabilization is due to two effects: (i) unfavorable ligand–ligand interactions, as can be

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TABLE XI

THERMODYNAMIC PROPERTIES FOR THE MIXED-COMPLEX FORMATION REACTION

$$\tfrac{1}{2}CuA_2 + \tfrac{1}{2}CuB_2 \overset{K_M}{\rightleftharpoons} CuAB$$

IN AQUEOUS SOLUTION AT 25°

Systems	Log K_M	$-\Delta G_M$, kcal mol^{-1}	ΔH_M, kcal mol^{-1}	ΔS_M, cal deg^{-1} mol^{-1}	$-$Log K_s	ΔG_s,[a] kcal mol^{-1}	ΔS_s,[b] cal deg^{-1} mol^{-1}	$\Delta G_{M,e}$, kcal mol^{-1}	$\Delta H_{M,e}$, kcal mol^{-1}	$\Delta G_{M,c}$, kcal mol^{-1}	$\Delta H_{M,c}$, kcal mol^{-1}
Cu + gly + α-ala	0.13	0.19	0.42	2.0	0.17	0.22	0.6	−0.13	0.05	0.35	0.37
Cu + gly + val	0.16	0.22	0.35	1.9	0.14	0.19	0.5	−0.11	0.04	0.30	0.31
Cu + gly + ser	−0.14	−0.17	0.40	0.8	0.44	0.58	−0.6	+0.15	−0.05	0.45	0.45
Cu + α-ala + val	0.40	0.54	−0.02	1.7	−0.10	−0.13	0.3	−0.07	0.02	−0.06	−0.04
Cu + α-ala + ser	0.22	0.29	−0.03	0.9	0.08	0.12	−0.5	0.11	−0.04	0.01	0.01
Cu + val + ser	0.17	0.23	−0.04	0.6	0.13	0.18	−0.8	0.17	−0.06	0.01	0.02

[a] $\Delta G_s = \Delta G_M + R \ln 2$. [b] $\Delta S_s = \Delta S_M - R \ln 2$.

seen from the positive $\Delta H_{M,c}$ (or $\Delta G_{M,c}$) values, and (ii) the differences in the degree of solvation between the more polar mixed complex and the symmetrical binary complexes. It can be seen in Table XI that when serine is one of the competing ligands, ΔS_s ($= \Delta S_M - R \ln K_{stat}$) values are negative for the mixed-complex formation. Serine has an electron-withdrawing hydroxyl group which effectively reduces its σ-donor properties. When a covalent mixed complex is formed between serine and glycine, α-alanine, or valine, there is an increase in the strength of the bond formed by the ligand with greater σ-donor properties. At the same time, the bond formed by the weaker σ donor, serine, becomes progressively less strong

relative to the strength of the same bond in the nonmixed complex. The resulting redistribution of the electron density leads to a change in the polarity of the individual bonds.

In competition with a stronger σ donor such as glycine, α-alanine, or valine, the resulting mixed complex involving serine is more polar than either of the nonmixed binary complexes. This is reflected in a greater degree of solvation of the complex and a lower entropy change.

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Out-of-Plane Bonding in the α and β Forms of Bis(8-hydroxyquinolinato)copper(II)

BY GUY W. INMAN, JR., WILLIAM E. HATFIELD,* AND ROBERT F. DRAKE

The magnetic susceptibilities of the α and β forms of bis(8-hydroxyquinolinato)copper(II) have been measured from 4.2 to 62°K for the α form and 3.2 to 77°K for the β form. The magnetic data indicate that there is little spin–spin coupling between the copper(II) ions in either the chain structure (α form) or the dimeric structure (β form). The results suggest that out-of-plane copper–oxygen distances of 2.8 Å or greater are too long to transmit significant spin–spin interactions.

Introduction

Suito and Sekido[1] first prepared two forms of Cu(8-OQuin)$_2 \cdot$2H$_2$O by reacting cupric sulfate with 8-hydroxyquinoline (8-OQuin) in water at various temperatures and concentrations. Fanning and Jonassen[2] prepared the anhydrous complexes and studied their room temperature magnetic properties and infrared spectra. Frazer, *et al.*,[3] measured the magnetic susceptibilities as a function of temperature for both forms down to 88°K. The crystal structure of the α form was determined by Hoy and Morriss[4] and the structure of the β form by Palenik.[5] The structure of the α form, depicted in Figure 1, consists of a chain of essentially planar Cu(8-

OQuin)$_2$ molecules. Each copper atom is six-coordinate and is weakly coordinated in the apical positions by oxygen atoms from neighboring molecules; the copper–oxygen out-of-plane distance being 3.32 Å. The in-plane copper–oxygen distance is 1.94 Å. The β form exists as a dimer-like unit (see Figure 2) in which copper is five-coordinate and the copper–oxygen out-of-plane distance is 2.83 Å. The copper–oxygen in-plane distance of 1.93 Å is almost identical with that observed for the α form.

Since it has been shown previously[6,7] that out-of-plane interactions in similar complexes can be important, we have undertaken a study of the low-temperature magnetic and spectral properties of both the α and β forms of Cu(8-OQuin)$_2$. This was done as a part of

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