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Acid Dissociation Constant, Formation Constant, Enthalpy, and Entropy Values for Some Copper(II)–α-Amino Acid Systems in Aqueous Solution[1a,b]

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Equilibrium constants and calorimetrically determined enthalpy values are reported for the stepwise dissociation of protons from H_2L^+ (L = glycine, α-aminoisobutyric acid, threonine, or sarcosine) and for the stepwise interaction of L^- with Cu^{+2} in aqueous solution. Equilibrium constants are reported at 20 and 30°. Enthalpy values determined by a thermometric titration procedure are reported at 25°. $\Delta S°$ values for each reaction are calculated from corresponding $\Delta G°$ (interpolated from 20 and 30° $\Delta G°$ values) and $\Delta H°$ values.

Introduction

The present study is part of a program to obtain equilibrium constants and calorimetric $\Delta H°$ values as a function of temperature for a variety of metal–ligand systems in solutions of low ionic strength, μ.

Proton dissociation constants determined as a function of temperature have been reported for each of the amino acids, L, studied here, *e.g.*, glycine,[2,3] threonine,[4] sarcosine,[3] and α-aminoisobutyric acid.[5] Enthalpy values for stepwise proton dissociation, calculated from the pK data, are available for each protonated ligand,[2–5] and corresponding calorimetrically determined values have been reported for glycine.[6]

An over-all formation constant has been reported for the Cu^{+2}–threonine system[7] at 25°, and for the Cu^{+2}–glycine system as a function of temperature.[8] Consecutive formation constant data for the Cu^{+2}–glycine system also have been reported.[9–11]

ΔH and ΔS values for the reaction $Cu^{+2} + 2A^- = CuA_2$ (A = glycine) have been estimated by Li, *et al.*,[8] from equilibrium constants determined polarographically at 25, 30, and 35°. No formation constant data for the Cu^{+2}–sarcosine and –α-aminoisobutyric acid systems and no calorimetric ΔH data for any of the Cu^{+2}–L^- systems studied have been reported previously.

Equilibrium constants are reported in the present study at $\mu = 0$ for stepwise proton dissociation from each protonated amino acid, H_2L^+, and for the stepwise interaction of L^- with Cu^{+2} at 20 and 30°. Calorimetrically determined $\Delta H°$ values are reported for each of these reactions at 25° together with $\Delta S°$ values calculated for each reaction from the corresponding $\Delta G°$ (interpolated from the 20 and 30° $\Delta G°$ values) and $\Delta H°$ values.

Experimental

Materials.—A stock copper(II) perchlorate solution was prepared by dissolving electrolytic copper metal in concentrated HNO_3, precipitating the Cu^{+2} as $Cu(OH)_2$ with NaOH, washing the precipitate with water until the washings were free of NO_3^- and Na^+, and finally dissolving the wet $Cu(OH)_2$ in a measured excess of standard $HClO_4$. The solution was standardized with respect to Cu^{+2} by conventional means. Glycine (California Corp. for Biochemical Research, A grade), threonine (Nutritional Bio-chemicals Corp.), sarcosine (California Corp. for Biochemical Research, A grade), and α-aminoisobutyric acid (Sigma Chemical Co., Sigma grade) were used without further purification.

Calculations and Procedure.—The procedure used in the determination of the equilibrium constants from the experimental data has been described.[12] Molarity quotients and acid dissociation constants were determined at each of three μ values in the range μ = 0.001–0.008. At least two determinations were made at each μ value. The molarity quotients were corrected to $\mu = 0$ using a modified form of the Debye–Hückel equation.[12]

The thermometric titration procedure used in the calorimetric determinations has been described[13,14]; however, since the metal–amino acid systems studied here are considerably more complex than those previously described, an outline of the calculation procedure is given. A thermometric titration curve for a typical determination involving the titration of a Cu^{+2}–glycine mixture with $HClO_4$ is given in Fig. 1a. The time axis is proportional to moles of $HClO_4$ added during the titration. Further detail of the regions present in a thermometric titration determination is given in ref. 13. For each Cu^{+2}–amino acid system the species distribution throughout the thermometric titration is calculated by combination of the appropriate equilibrium constant, mass balance, and charge balance expressions. A species distribution plot is shown in Fig. 1b corresponding to the thermometric titration curve in Fig. 1a. The thermometric titration curve is a result of several competing reactions, as can be seen by comparing it to the species distribution plot over the range of reaction. These reactions are (1) combination of OH^- with H^+ to form H_2O, (2) the reaction of protons with the carboxyl

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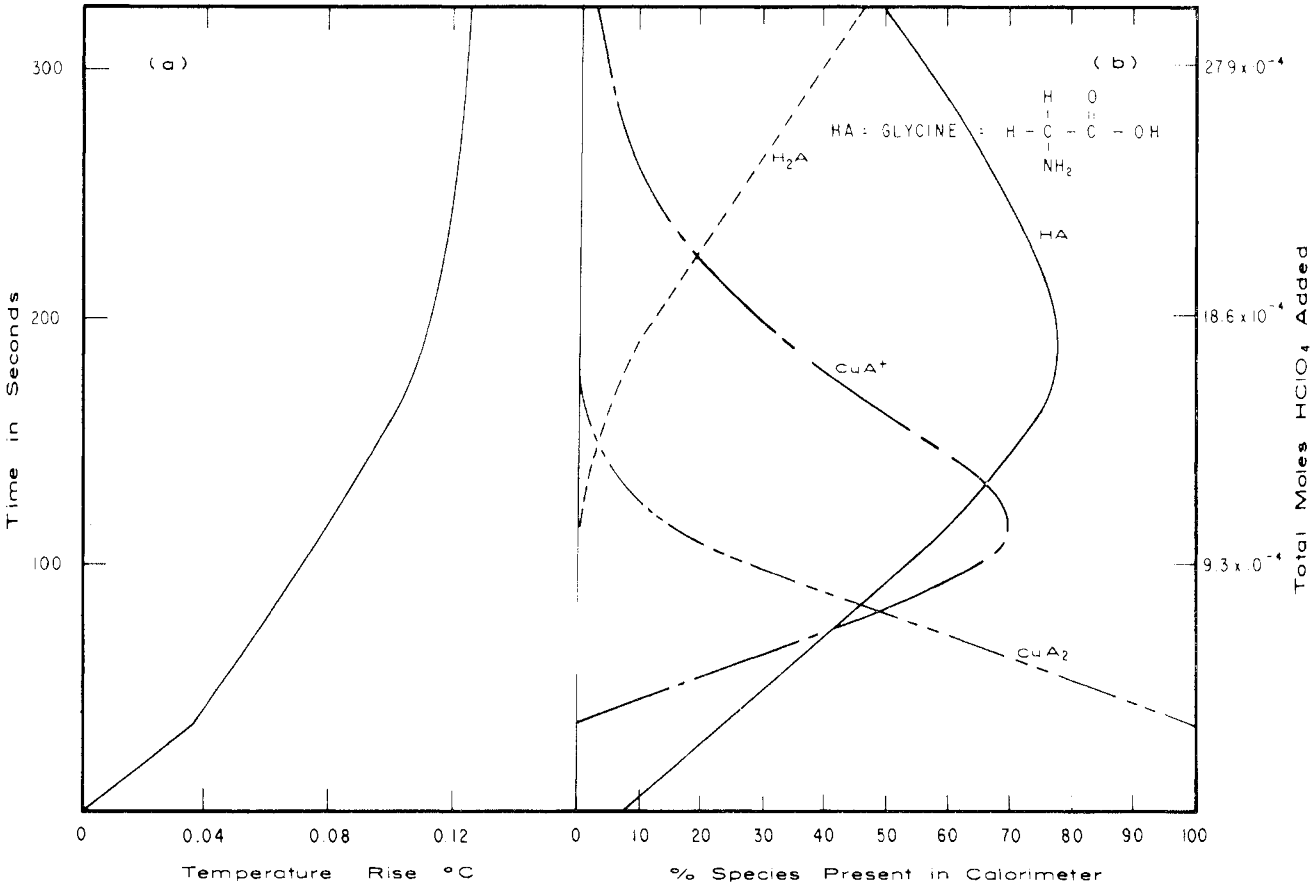

Fig. 1.—Correlation of temperature rise with per cent species present in calorimeter during the titration of CuA_2(aq.) with $HClO_4$.

group of glycine, (3) the reaction of protons with the amino group of glycine, (4) the dissociation of A^- from CuA_2 to form CuA^+, and (5) the dissociation of A^- from CuA^+ to form Cu^{+2}.

These reactions occur simultaneously, and this fact must be taken into account using the species distribution plot in subsequent calculation of the heats of reaction for (4) and (5). This is done by solving appropriate simultaneous equations in a manner similar to that described earlier for less complex systems.[13-15] All calculations were carried out on an IBM 7040 digital computer.

Results

Equilibrium constant values corrected to $\mu = 0$ for the systems studied here are given in Table I together with results obtained by others. The values given are averages of values obtained as described in the Experimental section. The precision in each case is estimated to be approximately ±0.03 log unit.

In Table II are given $\Delta H°$ values for the stepwise dissociation of protons from H_2L^+, and for the stepwise formation of CuL_2, together with corresponding $\Delta S°$ values calculated from the $\Delta G°$ (interpolated from the 20 and 30° $\Delta G°$ values) and $\Delta H°$ values. The experimental ΔH data did not show a significant trend with changing μ over the μ range 0.04—0.004; therefore all the data were used to calculate $\Delta H°$ values valid at $\mu = 0$ for the reactions given in Table II. The precision of the $\Delta H°$ values is estimated to be ±0.1 kcal./mole.

Table I

Equilibrium Constant Values (Corrected to $\mu = 0$) for Four Copper(II)–Amino Acid Systems

Each value is the average of two or more values determined at each of two μ values and subsequently corrected to $\mu = 0$

Temp., °C.	Proton dissociation		Cu^{+2}–L^- interaction	
	pK_1 (–COOH)	pK_2 ($-NH_3^+$)	log K_1	log K_2
Ligand, glycine				
20	2.34	9.73	8.59	7.24
	(2.37)^{a}	(9.92)^{a}	(8.12)^{b}	(6.91)^{b}
	(2.24)^{b}	(9.85)^{b}		
	(2.22)^{c}	(9.86)^{c}		
25	(2.35)^{a}	(9.78)^{a}	(8.62)^{d}	(6.97)^{d}
	(2.35)^{d}	(9.78)^{d}	(8.28)^{e}	(7.70)^{e}
		(9.78)^{f}		
30	2.33	9.65	8.47	7.04
	(2.34)^{a}	(9.65)^{a}		
Ligand, α-aminoisobutyric acid				
20	2.38	10.10	8.55	7.05
25	(2.36)^{g}	(10.21)^{g}		
30	2.35	10.08	8.53	7.04
Ligand, sarcosine				
20	2.12	10.19	8.16	6.89
25		(10.20)^{f}		
30	2.09	10.08	8.12	6.76
Ligand, threonine				
20	2.21	9.26	8.44	6.96
25	(2.09)^{h}	(9.10)^{h}		
30	2.14	9.01	8.41	6.91

[a] Ref. 2, $\mu = 0$. [b] Ref. 9, $\mu = 0.1$. [c] A. Albert, *et al.*, *Biochem. J.*, **47**, 531 (1950), $\mu = 0.1$. [d] Ref. 10, $\mu = 0$. [e] Ref. 11, $\mu = 0$. [f] Ref. 3, $\mu = 0$. [g] Ref. 5, $\mu = 0$. [h] Ref. 4, $\mu = 0$.

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TABLE II[a]

$\Delta H°$ AND $\Delta S°$ VALUES FOR PROTON DISSOCIATION AND Cu^{+2}–L^- INTERACTION FOR FOUR AMINO ACID SYSTEMS AT 25°

$\Delta H°$ values are in kcal./mole and $\Delta S°$ values are in e.u. Values in parentheses are from the literature.

	Proton dissociation				Cu^{+2}–L^- interaction			
	$H_2L^+ = HL^{\pm} + H^+$ (–COOH)		$HL^{\pm} = L^- + H^+$ (–NH_3^+)		$Cu^{+2} + L^- = CuL^+$		$CuL^+ + L^- = CuL_2$	
Ligand	$\Delta H°$	$\Delta S°$	$\Delta H°$	$\Delta S°$	$\Delta H°$	$\Delta S°$	$\Delta H°$	$\Delta S°$
Glycine	1.43	−6	10.6	−9	−6.0	19	−6.4	11
	(0.93)[6]		(10.6)[6]					
	(0.95)[2]	(−7.6)[2]	(10.55)[2]	(−9.4)[2]				
			(10.56)[3]	(−9.7)[3]				
α-Aminoisobutyric acid	1.41	−6	11.6	−7	−5.4	21	−5.7	13
	(0.56)[5]	(−8.9)[5]	(11.6)[5]	(−7.7)[5]				
Sarcosine	1.72	−4	9.75	−13	−4.6	22	−5.4	13
			(9.68)[3]	(−14.3)[3]				
Threonine	1.36	−5	10.04	−8	−5.3	21	−6.1	11
	(1.18)[4]	(−5.6)[4]	(9.96)[4]	(−8.2)[4]				

[a] All ΔH data in ref. 2–6 are valid at $\mu = 0$. The ΔH data in ref. 6 were determined calorimetrically; those in ref. 2–5 were determined from the temperature dependence of the equilibrium constant.

Discussion

The equilibrium constant and $\Delta H°$ values in Tables I and II agree well with previous data where these are available. The only ΔH value previously reported for interaction of any of the ligands studied here with Cu^{+2} is contained in a study of the Cu^{+2}–glycine system by Li, *et al.*[8] These workers determined the equilibrium constant by a polarographic procedure for the reaction $Cu^{+2} + 2A^- = CuA_2$ at 25, 30, and 35° in a medium of $\mu = 0.15$. From the temperature dependence of the equilibrium constant they report $\Delta H = -21.0$ kcal./mole and $\Delta S = -1.0$ e.u. This ΔH value differs considerably from that calculated using the data in Table II, −12.4 kcal./mole. Part of this difference can be attributed to the different media; however, the different procedures used in the two studies to obtain the ΔH values undoubtedly constitutes the major difference. We feel that the calorimetric results reported here are the more reliable. The importance of accurate ΔH values in subsequent calculation of ΔS values can be seen by comparison of ΔS calculated by Li, *et al.*, −1 e.u., with that calculated from the data in Table II, 30 e.u. The two values differ by 31 e.u. It is obvious that interpretation of ΔH and, particularly, of ΔS results based on the temperature dependence of equilibrium constant data is speculative unless very accurate equilibrium constant data are obtained at many temperatures in the region of interest.

The data in Table II show that the $\Delta H°$ values vary little among the substances studied for each step in the ionization of protons from H_2L^+, and in the formation of CuL_2. However, the $\Delta H°$ value for proton ionization from the –COOH group is much lower in each case than is that for proton ionization from the –NH_3^+ group, reflecting the differences in the proton donor atoms involved.

The $\Delta S°$ values for proton ionization from many neutral molecules range from −18 to −26 e.u.,[16] of which approximately −6 e.u. is associated with proton solvation. Any solvent ordering by the undissociated acid molecule should make the $\Delta S°$ value more positive. This effect has been observed by us in the case of HCN dissociation[14] where the $\Delta S°$ value is −7.4 e.u. Likewise, the relatively low $\Delta S°$ values in Table II for proton ionization from both H_2L^+ and $HL^{\pm}$ (except for the ionization of $HL^{\pm}$ in the case of sarcosine which is discussed below) suggest that the contributions to $\Delta S°$ of the charged amino acid species effectively cancel in each stepwise proton dissociation, leaving proton solvation as the main quantity determining the magnitude of $\Delta S°$. The considerably more negative $\Delta S°$ value for $HL^{\pm}$ ionization in the case of sarcosine can be understood by considering the effect of the N-methyl group upon the solvent ordering capacity of the $HL^{\pm}$ species. Because of the electron donor properties of the methyl group, the effectiveness of the positive charge associated with the –$NH_2CH_3^+$ in ordering the solvent is decreased relative to that of the –NH_3^+ group in the other amino acids.

The data presented here have been calculated on the assumption that stepwise formation of CuL_2 describes completely the reaction of L^- with Cu^{+2}. The equilibrium constant results obtained are consistent with this assuptmion for each amino acid studied.

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