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## The Thermodynamics of Formation of Metal Complexes and Ion-Pairs in Solution

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The problem of characterisation of species present at equilibrium in an electrolyte solution is discussed. Shortcomings of the free energy approach are shown due to inadmissible neglect of entropy changes in complex formation. It is shown that complexes formed with hard ligands are stabilised entirely by entropy changes. Soft or covalent interactions are always characterized by exothermic enthalpy changes.

An important problem in the chemistry of electrolyte solutions is the characterization of the species present. In the past, a great deal of work has been done in an attempt to obtain general relationships involving the free energy changes, calculated from the measured stability constants, and the properties of the ions taking part in the complex formation reactions. For closely similar series of complexes, such relationships have been used in an attempt to distinguish between covalent and ionic bonding<sup>1</sup> and to estimate the degree of such bonding.<sup>2</sup> Some information concerning the structures of the metal complexes in solution can also be inferred from a comparison of complexes of the same metal ion with two different ligands.<sup>3</sup> Although some patterns of behaviour manifest themselves, it is important to recognize that these relationships are of limited applicability since they are based solely upon considerations of the free energy changes accompanying the association reactions. It is clear that in many cases, these can mask important enthalpy and entropy changes.<sup>4</sup>

In recent years the determination, by direct calorimetric methods, of the enthalpy and entropy changes associated with metal complex and ion-pair formation in solution has enabled a much more detailed discussion to be made of the structures of the species present. Thus, in the case of transition metal complexes, the ligand field effects produce contributions most directly related to the enthalpy rather than the free energy changes, but the paucity of enthalpy data has led many workers to consider only changes in  $\Delta G$ . The use of  $\Delta G$  for comparison with ligand-field calculations for reactions of the metal ions with a given ligand presupposes that variations in the entropy changes can be ignored. This is clearly undesirable;<sup>5</sup> it is best to regard free energy changes as being a consequence of changes in enthalpy and entropy through the equation

$$\Delta G = \Delta H - T\Delta S.$$

$\Delta H$  is the property most directly related to the changes in the numbers and strengths of chemical bonds as the system passes from reactants to products

and in addition, the magnitude of  $\Delta H$  may reflect important steric effects especially if multidentate ligands are involved. The entropy change is a measure of the change of randomness, and the driving force in this process is the tendency of the system to go to the most probable, that is the most random, state. A knowledge of these thermodynamic functions provides information concerning the nature and type of bonding in the metal complexes, and the degree of hydration and steric properties of the ions and molecules taking part in the reactions.

Since there is no method by which unequivocal structures of aqueous complex species can be determined, it is important to use as many physical methods as possible for their characterization. Nuclear magnetic resonance offers attractive possibilities for the study of the structure of metal complexes in solution. The magnitudes of the chemical shifts of nuclear resonance in solution are determined by the electron distribution in the molecule or ion containing the nucleus and by the fields set up in the molecule by molecules or ions with which it interacts. Separate resonance bands are observed with magnetically distinct nuclei but a sufficiently rapid chemical exchange between them will result in a single resonance of some intermediate value of chemical shift. Proton magnetic resonance studies have been used extensively for studying protonation schemes in metal complexes with ligands such as the aminopolycarboxylates. Although these nonlabile protons are not bonded directly to the metal ions in the chelate, they may be sufficiently close to the potential coordination sites to act as effective monitors of the electronic environment in the vicinity of these sites.<sup>6,7</sup> The method has been particularly useful as a source of information for the identification of the ligand atoms to which the metal ions are bound in the complexes.<sup>8,9</sup>

In choosing the experimental conditions to be used for the study of a particular metal complexing system, the question arises as to whether to use a constant ionic strength by the addition of »neutral« electrolyte or whether to work at low ionic strengths in an attempt to compute the activity coefficients. Discussions of this question have been presented in some detail elsewhere.<sup>4</sup> The constant ionic medium is invaluable where a number of complicated equilibria are involved and different schools have tended to choose different ionic strengths for their studies of metal complex formation. The derived thermodynamic functions are, however, directly comparable for different systems only when obtained at the same ionic strength and for this reason, there continues to be an interest in the calculation of activity coefficients in order that thermodynamic equilibrium constants can be obtained. The derivation of the thermodynamic constants is made possible by a suitable choice of the concentrations of the reactants so that the number of complexes is limited to one or two. Where there is doubt as to the stoichiometry of the species present, these can usually be identified by making preliminary measurements at a constant ionic strength. This method was used to identify the complex species present in some bivalent metal succinate solutions in which it was known that either  $ML_2$  or  $MHL$  was present in addition to  $ML$ .<sup>10</sup> By making additional potentiometric measurements at low concentrations, it was then possible to calculate, by successive approximations, values for the activity coefficients and the thermodynamic association constants for the formation of  $ML$  and  $MHL$  found to be present under the particular experimental conditions.

Selection of the best values of the parameters  $a$  and  $C$  in a form of the Debye-Hückel equation such as

$$\log f_z = \frac{-Az^2 I^{1/2}}{1 + BaI^{1/2}} + CI, \quad (1)$$

may conveniently be made by carrying through the complete successive approximation procedures with various parameter values and choosing those which best fit the experimental data. Computations, with the aid of an electronic computer, have been made for a number of dicarboxylate and amino acid complexes.<sup>10-13</sup>

Complex formation in solutions of calcium phosphate has also been treated by this method<sup>14</sup>. The latter is of particular importance in biological systems especially for the interpretation of solubility data involving the various calcium phosphate phases. Thus a number of surface complexes have been invoked in an attempt to learn more about the reactions which take place at an hydroxyapatite solution interface. For the most part, however, there was considerable disagreement in the reported association constants. The relative insolubility of the calcium phosphate phases has contributed to the difficulty of studying ion association in the solutions since under such conditions, experimental errors are at their greatest. In addition, the liquid membrane-type specific ion calcium electrodes cannot be operated satisfactorily in solutions containing phosphate ions. By careful control of concentrations and experimental technique, however, it is possible to prepare solutions of calcium phosphate which are appreciably supersaturated and stable for at least one day.<sup>14</sup> It is thus possible to make potentiometric measurements over a much wider range of concentration than was previously thought possible.

A supersaturated solution of calcium phosphate may be prepared by the mixing of solutions of calcium chloride, phosphoric acid and sodium or potassium hydroxide (designated MOH). From the measured  $pH$  ( $-\log a_{H^+}$ ), and the known thermodynamic equilibrium constants:

$$k_{1a} = \frac{[H^+][H_2PO_4^-]f_1^2}{[H_3PO_4]} \quad (2)$$

$$k_{2a} = \frac{[H^+][HPO_4^{2-}]f_2}{[H_2PO_4^-]} \quad (3)$$

$$k_{3a} = \frac{[H^+][PO_4^{3-}]f_1f_3}{[HPO_4^{2-}]f_2} \quad (4)$$

$$K^+ = \frac{[CaH_2PO_4^+]}{[Ca^{2+}][H_2PO_4^-]f_2} \quad (5)$$

$$K^0 = \frac{[CaHPO_4]}{[Ca^{2+}][HPO_4^{2-}]f_2^2} \quad (6)$$

$$K^- = \frac{[CaPO_4^-]f_1}{[Ca^{2+}][PO_4^{3-}]f_2f_3} \quad (7)$$

and

$$K' = \frac{[\text{CaOH}^+]}{[\text{Ca}^{2+}][\text{OH}^-]} \frac{1}{f_2} \quad (8)$$

it is required to calculate the concentrations of the individual ionic species. The mass balance relationships may be written

$$T_{\text{Ca}} = [\text{Ca}^{2+}] + [\text{CaH}_2\text{PO}_4^+] + [\text{CaHPO}_4] + [\text{CaPO}_4^-] + [\text{CaOH}^+] \quad (9)$$

$$T_{\text{P}} = [\text{H}_3\text{PO}_4] + [\text{H}_2\text{PO}_4^-] + [\text{HPO}_4^{2-}] + [\text{PO}_4^{3-}] + [\text{CaH}_2\text{PO}_4^+] + [\text{CaHPO}_4] + [\text{CaPO}_4^-] \quad (10)$$

Combination of these equations results in the quadratic equation (11)

$$[\text{PO}_4^{3-}]^2 \left( \frac{\alpha\beta}{1 + K'[\text{OH}^-]f_2} \right) + [\text{PO}_4^{3-}] \left( \frac{\beta(T_{\text{Ca}} - T_{\text{P}})}{1 + K'[\text{OH}^-]f_2} + \alpha \right) - T_{\text{P}} = 0 \quad (11)$$

where

$$\alpha = \frac{[\text{H}^+]^3 f_1^3 f_3}{k_{1a} k_{2a} k_{3a}} + \frac{[\text{H}^+]^2 f_1 f_3}{k_{2a} k_{3a}} + \frac{[\text{H}^+] f_1 f_3}{k_{3a} f_2} + 1$$

and

$$\beta = \frac{K^+ [\text{H}^+]^2 f_1 f_2 f_3}{k_{2a} k_{3a}} + \frac{K^0 [\text{H}^+] f_1 f_2 f_3}{k_{3a}} + \frac{K^- f_2 f_3}{f_1}$$

from the measured pH ( $= -\log [\text{H}^+] f_1$ ) and the known equilibrium constants, the values of  $[\text{PO}_4^{3-}]$  may be calculated, using an electronic computer, by successive approximations for  $I$ , the ionic strength, from equation (11).  $I$  is given by

$$I = 0.5 \left[ \left\{ 4 + \frac{[\text{H}^+]^2 [\text{PO}_4^{3-}] f_1 f_2 f_3}{K^+ k_{2a} k_{3a}} + \frac{[\text{PO}_4^{3-}] f_2 f_3}{K^- f_1} + K' [\text{OH}^-] f_2 \right\} \right. \\ \left. \left\{ \frac{T_{\text{Ca}} - T_{\text{P}} + \alpha [\text{PO}_4^{3-}]}{1 + K' [\text{OH}^-] f_2} \right\} + [\text{PO}_4^{3-}] \left\{ \frac{[\text{H}^+]^2 f_1 f_3}{k_{2a} k_{3a}} + \right. \right. \\ \left. \left. + \frac{4 [\text{H}^+] f_1 f_3}{k_{3a} f_2} + 9 \right\} + [\text{H}^+] + [\text{M}^+] + [\text{OH}^-] + [\text{Cl}^-] \right] \quad (12)$$

and activity coefficients are calculated from equation (1) with  $a = 1$  and  $C = 0.3 \text{ Az}^2$ . The concentration of free calcium ion is given by

$$[\text{Ca}^{2+}] = \frac{T_{\text{Ca}} - T_{\text{P}} + \alpha [\text{PO}_4^{3-}]}{1 + K' [\text{OH}^-] f_2} \quad (13)$$

and the concentrations of all other ionic species can be readily obtained.

Enthalpy changes accompanying complex formation may be obtained from studies of the association constants as a function of temperature but the uncertainties in the  $\Delta H$  values derived from data over a small temperature range are considerable. When precise determinations of  $K$  values are made

over a wide range of temperature, the resulting enthalpy changes are much more reliable<sup>15</sup> and moreover can yield approximate values for the heat capacity changes. Under these circumstances, the agreement between the results of calorimetric and temperature coefficient methods is usually satisfactory<sup>16</sup> but in general, the former method is to be preferred. In a typical calorimetric experiment, measurements are made of the temperature changes on dilution of small volumes of a relatively concentrated solution of the ligand with (i) a larger volume of a solution containing the metal ion and (ii) a similar volume of the background electrolyte having the same ionic strength. When the ligand is an anion of a weak acid, it may be necessary to take into account heat changes accompanying the variation of the concentration of protonated species as well as that due to complex formation<sup>17,18</sup>. The method requires precise measurement of the pH values of the solutions in the calorimeter and it is possible to incorporate glass and reference electrodes in the differential calorimeters<sup>19</sup>.

Gurney was the first to propose, for proton ionization reactions, the separation of the thermodynamic functions into temperature dependent and temperature independent components. The method has now been extended to metal complex formation<sup>21</sup> for which  $W$ , the work required for the dissociation of a metal complex can be written

$$W = \frac{\Delta G}{N_0} - \Delta n k T \ln 55.5$$

In this equation,  $N_0$  is Avagadro's number and the term  $\Delta n k T \ln 55.5$ , representing the cratic part of the free energy, is characteristic of a reaction in solution in which the number of solute particles is decreased by  $\Delta n$ , 55.5 being the number of moles contained in 1000 g. of water. The temperature dependent component,  $W_e$ , representing long-range electrostatic forces and  $W_c$ , the temperature independent component, representing short-range covalent forces are given by

$$W = W_e + W_c$$

The corresponding free energies,  $\Delta G_e$  and  $\Delta G_c$ , may then be written in terms of the measured free energy change,  $\Delta G$ :

$$\Delta G = \Delta n R T \ln 55.5 + \Delta G_e + \Delta G_c \quad (14)$$

The electrostatic part of the free energy change will be inversely proportional to the dielectric constant,  $\epsilon$ , whose variation with temperature is given by

$$\epsilon = \gamma e^{-T/\nu}$$

where  $\gamma$  is a constant and  $\nu$  is a temperature characteristic of the solvent<sup>22</sup>. It follows that

$$\Delta G = \Delta n R T \ln 55.5 - \alpha e^{T/\nu} + \Delta G_c,$$

(where  $\alpha$  is a constant) and the corresponding entropy and enthalpy changes

$$\Delta S = \frac{-\delta(\Delta G)}{\delta T} = \frac{\alpha e^{T/\nu}}{\nu} - \Delta n R \ln 55.5 \quad (15)$$

and

$$\Delta H = \Delta G_c - \alpha e^{T/\nu} (1 - T/\nu) \quad (16)$$

From the experimentally measured thermodynamic functions, the electrostatic components may be calculated from the equations

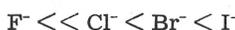
$$\Delta G_e = -\alpha eT/\nu = -\nu(\Delta S + \Delta nR \ln 55.5) \quad (17)$$

and

$$\Delta H_e = (T - \nu)(\Delta S + \Delta nR \ln 55.5) \quad (18)$$

For essentially electrostatic interactions between metal ions and charged ligands, appreciable positive entropy changes are observed which increase with charge<sup>21</sup>. These values reflect the release of bound solvent molecules from the hydrated ions when they interact and, when introduced into the above equation (18), yield the positive  $\Delta H_e$  values which are to be expected for electrostatic interactions<sup>4</sup>. It is of considerable interest to calculate the temperature independent part of the enthalpy,  $\Delta H_c$ , reflecting both the covalent interactions and structural changes. It is given by the difference,  $(\Delta H - \Delta H_e)$  and values have been calculated for a number of closely related complexes involving nitrogen and carboxylate oxygen ligand atoms<sup>22</sup> and for halide and pseudo halide complexes<sup>23</sup>. Metal-nitrogen coordination takes place with a considerably greater exothermic enthalpy change than that accompanying interaction with carboxylate oxygen atoms and the  $\Delta H_c$  values of a large number of such complexes can be correlated in terms of the number of nitrogen atoms coordinated to the metal ion<sup>22</sup>.

Metal complexes of halides and pseudo halides form a particularly suitable series for discussion since they are relatively simple and well characterized. As outlined above, the sensitivity of the electrostatic energy to changes of temperature, leads to the expectation of endothermic enthalpies formation in cases where such hard-hard<sup>24</sup> interactions take place. The driving force of these reactions will be the positive entropy change accompanying solvent release from the co-spheres of the ions. Increasingly covalent interactions between »soft« reactants will result in more exothermic enthalpies of formation. In the halide series, the ability for covalent bonding, or softness, increases in the inverse order of the electronegativities,



and some of the thermodynamic functions are given in Table I. The striking increase in exothermicity for the formation of 1:1 complexes as the ligand is changed from fluoride to iodide is immediately apparent. For the very hard fluoride ion, the complexes are stabilised entirely by the entropy changes accompanying the breakdown of the »iceberg« structure of coordinated solvent molecules around the ions. The concomitant endothermicity reflects both the electrostatic nature of the interactions and the energy required to break the ion-water bonds. For the alkaline earth monofluorides, the value of  $\Delta S$  ( $MgF^+$ ) is unusually close to that for  $CaF^+$  and the calculated  $\Delta S_h$  ( $MgF^+$ ) is therefore more negative than that for the other members. This may reflect the greater retention of the hydration co-sphere of the Mg(II) ion in  $MgF^+$  than is the case for the other alkaline earth monofluorides<sup>27</sup>. A similar suggestion was made for the acetate and formate complexes of magnesium, based upon thermodynamic functions derived from potentiometric studies<sup>28</sup>.

As the B-character or softness of the metal ion is increased, the enthalpy of formation of halide complexes becomes more favourable. It is seen in

TABLE I  
*Thermodynamic Functions for the Formation of Metal Halide and Pseudo-Halide Complexes at 25°*

Reaction	$-\Delta G$ k cal mole <sup>-1</sup>	$\Delta H$ k cal mole <sup>-1</sup>	$\Delta S$ cal deg <sup>-1</sup> mole <sup>-1</sup>	Ref.
Halides				
Cd <sup>2+</sup> + F <sup>-</sup>	0.63	1.23	6.2	25
Cd <sup>2+</sup> + Cl <sup>-</sup>	2.16	— 0.10	6.9	25
Cd <sup>2+</sup> + Br <sup>-</sup>	2.40	— 0.98	4.7	25
Cd <sup>2+</sup> + I <sup>-</sup>	2.84	— 2.26	2.0	25
Hg <sup>2+</sup> + Cl <sup>-</sup>	—	— 5.5	12.4	26
Hg <sup>2+</sup> + Br <sup>-</sup>	—	— 10.2	7.1	26
Hg <sup>2+</sup> + I <sup>-</sup>	—	— 18.0	— 1.5	26
Mg <sup>2+</sup> + F <sup>-</sup>	1.80	3.2	16.8	27
Ca <sup>2+</sup> + F <sup>-</sup>	0.86	3.5	15.0	27
Sr <sup>2+</sup> + F <sup>-</sup>	0.20	4	14	27
Ba <sup>2+</sup> + F <sup>-</sup>	— 0.3	0	0	27
Tl <sup>+</sup> + Cl <sup>-</sup>	0.93	— 1.43	1.7	25
Tl <sup>+</sup> + Br <sup>-</sup>	1.2	— 2.45	— 4.2	28
Tl <sup>3+</sup> + Cl <sup>-</sup>	9.74	— 5.45	14.5	29
Cyanides				
CH <sub>3</sub> Hg <sup>+</sup> + CN <sup>-</sup>	18.8	— 22.1	— 11.4	30
Cu <sup>+</sup> + 2 CN <sup>-</sup>	32.7	— 29.1	+ 12	31
Cu(CN) <sub>2</sub> <sup>-</sup> + CN <sup>-</sup>	7.23	— 11.1	— 13.4	31
Cyanides				
Ag <sup>+</sup> + 2 CN <sup>-</sup>	27.89	— 33.0	— 16	31
Ag(CN) <sub>2</sub> <sup>-</sup> + CN <sup>-</sup>	2.11	— 0.6	+ 5	31
Thiocyanates				
Mn <sup>2+</sup> + CNS <sup>-</sup>	1.68	— 0.9	2.5	32
Co <sup>2+</sup> + CNS <sup>-</sup>	2.35	— 1.6	2.2	32
Ni <sup>2+</sup> + CNS <sup>-</sup>	2.40	— 2.3	0.5	32
Cu <sup>2+</sup> + CNS <sup>-</sup>	3.18	— 3.0	0.6	32
Zn <sup>2+</sup> + CNS <sup>-</sup>	2.53	0.2	9	32
Cd <sup>2+</sup> + CNS <sup>-</sup>	3.42	— 0.7	9	32
Pb <sup>2+</sup> + CNS <sup>-</sup>	1.49	0.3	6	32

Table I that the enthalpies of formation of CdCl<sup>+</sup> and TlCl are negative indicating a greater covalency than for the monofluoride complexes. With the softer Hg(II) and Tl(III), the monochloride complexes are formed with appreciable exothermic enthalpy changes. The structure-breaking properties of the halide ions increase in the order Cl<sup>-</sup> < Br<sup>-</sup> < I<sup>-</sup> and it is seen that the values of the association entropies for all the monohalide complexes decrease along the series F<sup>-</sup> > Cl<sup>-</sup> > Br<sup>-</sup> > I<sup>-</sup> owing to the decreasing strength of interaction between ligand and solvent. In the case of the large iodide ion,

the  $\Delta S$  values is unfavourably negative in some instances (*e. g.*  $\text{HgI}^+$ ) reflecting the relative unimportance of solvent release from the interacting ions.

The behaviour of the cyanide ion as a very soft ligand is clearly seen from the thermodynamic data in Table I. Complexes with the B-character metal ions are appreciably stabilised almost without exception by the large exothermic enthalpy changes. Except for the formation of  $\text{Cu}(\text{CN})_2^-$  and  $\text{Ag}(\text{CN})_3^{2-}$  the entropy changes are all negative indicating only weak ligand-solvent interactions in addition to the expected loss of rotation entropy of the diatomic cyanide ion when it bonds to the metal ions. It can be seen that the enthalpy change for the formation of  $\text{M}(\text{CN})_3^{2-}$  from  $\text{M}(\text{CN})_2^-$  is much more exothermic for  $\text{M}^+ = \text{Cu}^+$  than is the case for  $\text{Ag}^+$ . Evidence from both Raman and Infrared intensity measurements indicates the additional influence of  $\pi$  bonding in  $\text{Cu}(\text{CN})_3^{2-}$  but not in  $\text{Ag}(\text{CN})_3^{2-}$ .<sup>34</sup> Such multiple bonding would account for the observed differences in the enthalpies of formation of these species.

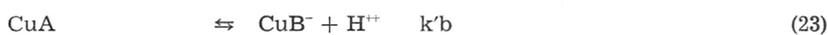
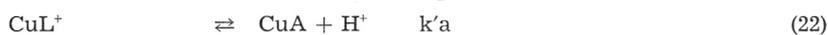
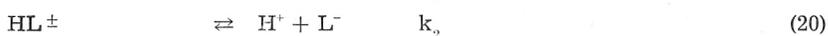
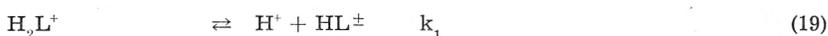
Thermodynamic functions for the formation of the rather weak monothiocyanate complexes are given in Table I. The entropy changes are small as would be expected for the formation of a charged complex which will retain some of its solvent-ordering properties. The abnormally endothermic enthalpy and large positive entropy changes for the formation of the zinc monothiocyanate complex may reflect the elimination of extra water molecules from the co-sphere of this small cation<sup>32</sup>. The thiocyanate ion exhibits linkage isomerism, bonding to the metal ion either through its sulphur or nitrogen atom. Coordination involving the sulphur atom, the most probable site of the negative charge would result in a more effective neutralization of charge in the formation of the complex and a more positive  $\Delta S$ . Metal ions of B-character such as Cd(II) and Pb(II) would be expected to show some bonding through the sulphur atom, and it is seen that their complexes are formed with abnormally large and positive entropy changes as compared with data for the other metal ions in Table I.

In the light of the arguments presented above, we are now in a position to make some general comments concerning the thermodynamic implications of hard and soft interactions. Complexes formed through the predominantly electrostatic interactions between hard ions are entropy stabilised; the enthalpy changes are usually small and endothermic reflecting the energy required for the removal of coordinated solvent molecules from the co-spheres of the ions. Soft or covalent interactions, on the other hand, are always characterised by exothermic enthalpy changes. The accompanying entropy terms become increasingly negative with increasing softness of the interacting acid-base species.

In recent years there has been considerable interest in the elucidation of the structures of the complex species formed in aqueous solutions of metal peptides because of their biological significance in enzyme reactions. The copper complexes of the polyglycines are of particular importance since dissociation of the peptide hydrogen atoms is facilitated in reactions which take place in the physiological range of pH. The structures of the complexes formed have been characterised in the solid state by x-ray methods<sup>35</sup>. In solution, however, there has been considerable disagreement as to the nature of the ligand atoms involved in coordination with the copper ion. There is

strong evidence, both from infra-red absorption studies and from the observation that the peptide hydrogen atoms in some of the metal complexes readily undergo ionization, that the peptide group is involved in the coordination with the metal ion. After the proton elimination, there is little doubt that the nitrogen atom of the peptide group is bound to the copper atom. In the cationic complexes,  $\text{CuL}^+$ , this situation is not as clear and both oxygen and nitrogen peptide coordinations in solution have been proposed. Rabin<sup>36</sup>, from a consideration of the effects of substituents in the peptide molecules suggested that prior to the proton ionization, the peptide oxygen rather than nitrogen atom was coordinated to the copper ion. Kim and Martell<sup>37</sup>, of the other hand, have assigned multichelated structures to the copper complexes of di-, tri- and tetraglycine with the peptide nitrogen atom coordinated. In order to account for the appreciably smaller stability of these complexes in solution as compared with that of the copper monoglycinate complex, it was assumed that the ligand atoms are only weakly coordinated to the metal ion.

Equilibria in the polyglycine solutions may be represented by the reactions



In these equations, the successively deprotonated species are derived from  $\text{L}^- = \text{GG}^- = \text{HA}^-$  for diglycine,  $\text{L}^- = \text{GGG}^- = \text{HA}^- = \text{H}_2\text{B}^-$  for triglycine and  $\text{L}^- = \text{GGGG}^- = \text{HA}^- = \text{H}_2\text{B}^- = \text{H}_3\text{C}^-$  for tetraglycine. Thermodynamic functions for these reactions, presented in Table II, exhibit a number of striking features. The substantial decrease in stability of the polyglycine complexes,  $\text{CuGG}^+$ ,  $\text{CuGGG}^+$  and  $\text{CuGGGG}^+$ , as compared with the monoglycinate,  $\text{CuG}^+$ , is seen to be entirely an entropy effect. The exothermic enthalpies of formation are remarkably constant for all four complexes indicating that di-, tri- and tetra-glycine are bound in bidentate structures similar to that for glycine itself and not in the multichelated structures proposed by Kim and Martell<sup>37</sup>. It is likely that the structures in solution resemble those in the solid state<sup>35</sup> with the copper bonded to the terminal  $-\text{NH}_2$  and the oxygen of the first peptide group in five-membered chelate ring structures<sup>38,39</sup>. The bond between the metal ion and the peptide oxygen atom will be essentially electrostatic in character leading to  $\Delta H$  values similar to that for  $\text{CuG}^+$  formation. Further evidence for copper-peptide oxygen bonding in equation  $\text{CuL}^+$  is based upon structural consideration. Thus binding of the nitrogen atom of the peptide group would require not only a considerable distortion of the polyglycine ligand molecule but would also be expected to result in more exothermic enthalpies of formation than those given in Table II. The planarity and resonance energy of the peptide group are not sacrificed if the copper atom is bound at the peptide oxygen.

TABLE II

*Thermodynamic Functions for the Association of Copper with Glycine and Polyglycines (25°, I = 0.01 M)*

Equation Number	Association Reactions	$\Delta G$ k cal mole <sup>-1</sup>	$\Delta H$ k cal mole <sup>-1</sup>	$\Delta S$ cal. deg <sup>-1</sup> mole <sup>-1</sup>
	$\text{Cu}^{2+} + \text{G}^- \rightleftharpoons \text{CuG}^+$	- 11.71	- 6.76	+ 16.6
	$\text{CuG}^+ + \text{G}^- \rightleftharpoons \text{CuG}_2$	- 9.47	- 6.89	+ 8.7
(21)	$\text{Cu}^{2+} + \text{GG}^- \rightleftharpoons \text{CuGG}^+$	- 7.58	- 6.1	+ 4.97
(21)	$\text{Cu}^{2+} + \text{GGG}^- \rightleftharpoons \text{CuGGG}^+$	- 6.87	- 6.3	+ 1.9
(21)	$\text{Cu}^{2+} + \text{GGGG}^- \rightleftharpoons \text{CuGGGG}^+$	- 7.00	- 6.0	+ 3.3

Equation Number	Dissociation Reactions	$\Delta G$ k cal mole <sup>-1</sup>	$\Delta H$ k cal mole <sup>-1</sup>	$\Delta S$ cal. deg <sup>-1</sup> mole <sup>-1</sup>
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## Diglycines

(19)	$\text{H}_2\text{GG}^+ \rightleftharpoons \text{HGG} + \text{H}^+$	+ 4.20	0.032	- 13.9
(20)	$\text{HGG} \rightleftharpoons \text{GG}^- + \text{H}^+$	+ 11.03	10.6	- 1.5
(22)	$\text{CuGG}^+ \rightleftharpoons \text{CuA} + \text{H}^+$	+ 5.54	6.9	+ 4.5

## Triglycines

(19)	$\text{H}_2\text{GGG}^+ \rightleftharpoons \text{HGGG} + \text{H}^+$	4.34	0.2	- 13.9
(20)	$\text{HGGG} \rightleftharpoons \text{GGG}^- + \text{H}^+$	10.73	10.1	- 2.1
(22)	$\text{CuGGG}^+ \rightleftharpoons \text{CuA} + \text{H}^+$	6.90	7.5	2.0
(23)	$\text{CuA} \rightleftharpoons \text{CuB}^- + \text{H}^+$	9.25	7.4	- 6.2

## Tetraglycines

(19)	$\text{H}_2\text{GGGG}^+ \rightleftharpoons \text{HGGGG} + \text{H}^+$	4.33	+ 0.18	- 13.9
(20)	$\text{HGGGG} \rightleftharpoons \text{GGGG}^- + \text{H}^+$	10.75	+ 10.40	- 1.2
(22)	$\text{CuGGGG}^+ \rightleftharpoons \text{CuA} + \text{H}^+$	7.38	+ 7.5	+ 0.4
(23)	$\text{CuA} \rightleftharpoons \text{CuB}^- + \text{H}^+$	9.28	+ 6.6	- 9.0
(24)	$\text{CuB}^- \rightleftharpoons \text{CuC}^{2-} + \text{H}^+$	12.49	+ 8.9	- 12.0

In the formation of a complex by the association of two oppositely charged ions, a moderately large and unfavourable negative entropy change would be expected, reflecting the disappearance of a particle in the system. In most cases of metal complex formation however, there is a favourable positive entropy change resulting from the breakdown of the «iceberg» structure of coordinated water molecules around the ions and decreased orientation of solvent molecules. This release of coordinated water molecules is the most important factor determining the entropy of association. In the structures proposed for the  $\text{CuL}^+$  species, the carboxyl groups are not bound to the copper ion and the resulting charge separation and retention of some solvent ordering will account for the small observed  $\Delta S$  values for their formation. In marked contrast, the larger positive  $\Delta S$  value for the formation of the monoglycinate complex reflects not only a more effective neutralization of charge through short bond formation in the xy plane of coordination but

also a greater degree of tetragonal distortion of the octahedral symmetry and freeing of the axial water molecules.

As the pH is raised above the range in which  $\text{CuL}^+$  species are formed, the proton dissociation reactions (22) (23) and (24) take place. The thermodynamic data in Table II clearly indicate that the labilization of the peptide hydrogenations is largely an enthalpy effect. Although there are no enthalpy data available for the dissociation of a hydrogen from an unbound peptide group, the values would be expected to be even more endothermic than the enthalpy changes accompanying the proton dissociation from the zwitterions  $\text{HL}^\pm$ . It is seen that the  $\Delta H$  values for reactions (22) and (23) are considerably less endothermic than those for reactions (20). Assuming multichelated structures for the  $\text{CuA}$  species, their enthalpies of formation reflect not only the proton dissociation but also the formation of bonds between the metal, the nitrogen atom of the peptide group and the carboxyl oxygen atoms.

In this paper, I have outlined a number of general arguments which, on the basis of experimental thermodynamic functions, can be used to discuss the details of metal complex formation reactions in aqueous solution. A large number of systems have now been studied and the results have thrown light on the nature and type of bonding between the metal ion and ligand molecule. The discussions are not exhaustive but the data, taken together with as many other physical chemical methods which can be brought to bear on the problem, provide much insight into the structures of the complex species. It is quite clear that, in the absence of any unequivocal method for the direct determination of these structures, it is important to regard the free energy changes as being a consequence of changes in enthalpy and entropy rather than attempting a correlation of the  $\Delta G$  values themselves.

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### IZVOD

#### Termodinamika stvaranja metalnih kompleksa i ionskih parova u otopinama

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Važan je problem kemije elektrolitskih otopina određivanje prisutnih vrsta. Velik dio napora uložen je u određivanje općih odnosa koji su uključivali promjene slobodne energije kod stvaranja kompleksa. Ti su odnosi bili donekle pogodni za određivanje odnosa ionskih i kovalentnih veza. Taj pristup je ipak ograničenog dometa, jer na primjer, u slučaju prijelaznih metala ligandno polje dovodi do energijskih promjena koje su mnogo više vezane s entalpijom sistema. Upotreba G vrijednosti za uspoređivanja s računima ligandnog polja za reakciju nekog metala s ligandom moguća je uz pretpostavku da su promjene entropije zanemarive.

U radu se diskutira metodologija mjerenja konstanti asocijacije i uspoređuju se rezultati dobiveni kalorimetrijskom metodom ili metodom temperaturnih koeficijenata. Prodiskutirani su podaci dobiveni za parove »tvrdih« ili »mekih« kationa i aniona, ili njihovih kombinacija. Opći je zaključak da su kompleksi, koji se stvaraju predominantno elektrostatskom interakcijom između tvrdih iona, entropijski stabilizirani; kod njih su promjene entalpije male i endotermičke uslijed utroška energije za uklanjanje koordinirane vode iz ko-sfera iona. Interakcije mekih iona su karakterizirane egzotermnim promjenama entalpije. Prateći iznosi promjene entropije su to negativniji što su mekši ioni koji ulaze u interakciju.

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