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THE BEHAVIOUR OF SOME COBALT, NICKEL AND COPPER AMINO ACID COMPLEXES AT DIFFERENT TEMPERATURES

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ABSTRACT

The behaviour of cobalt(II), nickel(II) and copper(II) complexes with cystine, cysteine and methionine ligands was investigated in the range 25–40 °C. The thermodynamic parameters were evaluated. The effect of the transition metal ion on the mode of ionization of the ligands was discussed. The scope of the study was realized, based on the pH-metric technique.

INTRODUCTION

Most of the transition metal–amino acid complexes are biologically active and possess many applications. Some show antiviral activities against the tobacco mosaic virus in host plants [1]. Others have been tested for anti-tumour activity [2] and as transfer agents of biological alkylating compounds [3]. The amino acids generally increase the diffusibility of the metal complexes and consequently their biological activity inside the cell [4]. However, some of the complexes can be absorbed readily through the skin [5].

In this paper, we present a study of the thermodynamic parameters of Co(II), Ni(II) and Cu(II) complexes with cystine, cysteine and methionine ligands using pH-metric methods. This elucidates the mechanism of ionization of the ligands with these metals at different temperatures (25–40 °C).

EXPERIMENTAL

All chemicals used were of high purity. The ligands (cystine, cysteine and methionine) were obtained from BDH, Poole, England. The Co(II), Ni(II)

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and Cu(II) chlorides were of A.R. quality. Solutions used were prepared in doubly-distilled water. The pH measurements were carried out using a Pye Unicam pH-meter model 291 MK_2. The electrode system was calibrated before and after each series of pH measurements, under the same conditions, using standard buffers of pH 4.0 and 9.0 [6]. A stream of purified nitrogen gas was passed through the solution to eliminate CO_2 dissolved in the medium throughout the course of the titrations. The titration procedure was carried out in aqueous medium to evaluate the dissociation constants of the free ligands at different temperatures (25–40 °C) and to calculate the thermodynamic parameters for these ligands. The same titration experiments were applied to study the complex equilibria at 25–40 °C. In these experiments the complex solutions (5 ml of 10^{-3} M metal + 25 ml of 10^{-3} M ligand + 5 ml of 0.5 M KCl as a supporting electrolyte) were titrated against standard KOH at the desired temperature which was attained using a thermostatic device (Ultra Thermostate U-10, G.D.R.). The thermodynamic quantities for the formation of Co(II), Ni(II) and Cu(II) complexes with cystine, cysteine and methionine are discussed with respect to those of the free ligands.

RESULTS AND DISCUSSION

Thermodynamic parameters of the ionization of the amino acids in aqueous medium

The dissociation constants for the ionization of the amino acids cystine, cysteine and methionine were determined in the range 25–40 °C in aqueous media in the presence of 0.5 M KCl as ionic background. The ΔH_2 values (kcal mol^{-1}) for the ionization of the three above-mentioned amino acids were determined. By plotting the pK values vs. $1/T$, straight lines were obtained with a slope equal to $\Delta H/2.3RT$; $\Delta G = 2.3RT$ pK and $\Delta G = \Delta H - T\Delta S$.

A formation curve was constructed by plotting $\bar{n}_A$ (the number of protons attached to the ligand) against the pH of the solution corresponding to each addition of alkali (based on the approach of Irving and Rossotti [7]).

The following conclusions could be drawn.

(1) The acid strengthening effect introduced by raising temperature is demonstrated as the pK values of the ligands decreased conclusively with increasing temperature (see Table 1).

(2) The great similarity in the enthalpy of ionization ΔH_a (which represents a difference between the enthalpy involved in breaking the carboxylate bond and the enthalpy of solvation of the H^+(aq) and acid anion) denotes the same mode of ionization. This indicates that the entropy term (ΔS) contributes significantly to the free energy changes (ΔG) for the amino acid

TABLE 1

Values of pK in the range 25–40 °C and thermodynamic parameters of ionization of sulphur-containing amino acids at 25 °C

Amino acid	pK				ΔG (kcal mol^{-1})	ΔH (kcal mol^{-1})	$-\Delta S$ (e.u.)
	25 °C	30 °C	35 °C	40 °C			
Cystine	11.05	10.94	11.84	10.73	15.15	4.60	35.39
Cysteine	8.35	8.25	8.15	8.05	11.44	4.60	22.95
	(10.35)	(10.10)	(9.90)	(9.65)	(14.18)	(5.11)	(30.45)
Methionine	9.15	9.00	8.90	8.80	12.54	4.18	28.05
	(10.50)	(10.38)	(10.20)	(10.10)	(14.39)	(5.75)	(29.00)

Values in parentheses are pK_2.

dissociation. The relatively large ΔS value for the first ionization of cysteine (-22.95 e.u.) at 25 °C showed that there should be less ordering of the solvent molecules upon dissociation leading to greater association [8]. Furthermore, the negative sign of the ΔS values is parallel to that reported for ligands containing sulphur [9] via intermolecular hydrogen bonding [10].

Formation constants and thermodynamic parameters for Co(II), Ni(II) and Cu(II) sulphur-containing amino acid complexes

For the reaction

$$M + nL \rightleftharpoons ML_n$$

(The symbols have the usual meaning and the charges are omitted for simplicity), it was assumed that: (i) the concentration of the metal ion was sufficiently low so that the formation of polynuclear complexes could be neglected under the experimental conditions; (ii) the metal ion did not participate in side reactions; and (iii) the formation of ion pairs between the anionic species and the positive part of the strong electrolyte could be neglected by taking a high and constant value of the ionic strength of the solution [11], where the activity coefficients of all species were constant, so concentration terms could be used.

The overall stability constant of the complex can be given as follows

$$\beta_n = [ML_n]/[M][L]^n = K_1, K_2, \ldots, K_n$$

Generally, this equation may be represented as follows

$$\beta_n = A\frac{a^n}{n}$$

where a and A are constants, or

$$\sum_{n=0}^{n=N} (\bar{n} - n)[L]^n \beta_n = 0$$

The pH measurements during titration with alkali of a solution of chelating agent in the presence and absence of metal ions could be used to calculate the free ligand concentration pL, the metal–ligand formation $\bar{n}$ and hence the stability constant of the complex present [12]. The formation curves were constructed by plotting $\bar{n}$ against pL. Maximum $\bar{n}$ values were found to be 1.0 and 2.0 indicating that 1 : 1 and 1 : 2 complexes were traced (see Table 2).

Focusing attention on the data collected in Table 2, the following observations can be made.

(1) The formation constants of the 1 : 1 metal–cystine and 1 : 1 metal–methionine complexes steadily increase with increasing temperature. The opposite trend was apparent in the 1 : 2 complexes and the Co(II) and Ni(II) cysteine 1 : 1 complexes.

(2) The order of stability of the amino acid complexes is Co > Ni < Cu. Therefore, the order of Irving and Williams [13] did not hold completely. This could be rationalized from the fact that the sulphur-containing amino acids involve two distinct types of potential donor centres available for chelation (S or $-NH_2$ and COO^-) [14]. Thus, it is proposed that N and O atoms are the coordination sites in Co(II) and Cu(II) [15] complexes, while in the Ni(II) complexes N and S atoms act as donor centres. In fact, Cu(II) readily oxidizes cysteine to cystine.

(3) In all complexes the $\log_{10} K_1$ values are higher than $\log_{10} K_2$. This is best explained in terms of the charge effects on the complex ion formed [16], where coulombic repulsions between the negative donor atoms in the 1 : 2 complexes tend to lower stability [17].

(4) The ΔH values for the formation of the 1 : 2 cystine complexes (Ni, Co and Cu) and the 1 : 2 Co–methionine complex are positive and have the values 5.75, 5.52, 4.18 and 8.36 kcal mol^{-1}, respectively. So, more energy is needed for the formation of the less stable nickel complexes than for the cobalt complexes. This accounts for the entropy term, where the larger ΔS value (-4.87 e.u.) is given for the Ni–$(cystine)_2$ complex.

(5) The 1 : 1 cystine complexes have $-\Delta H$ values of 2.30, 3.07 and 6.27 kcal mol^{-1} for Ni(II), Co(II) and Cu(II), respectively. Again the larger ΔS value (-32.11 e.u.) corresponds to the nickel–cystine system. The same trend holds for Ni(II) and Co(II) methionine complexes where the $-\Delta H$ values are 8.36 and 19.71 kcal mol^{-1} corresponding to ΔS values of -62.79 and -93.72 (e.u.), respectively. The unique exception is exhibited by the 1 : 1 M–cysteine complexes where Δ values are positive and amount to 8.36 and 11.50 kcal mol^{-1} for Ni(II) and Co(II), respectively.

(6) The $\log_{10} K$ (and consequently ΔG values) of the cystine ligand are strongly affected through transition metal complexation.

(7) The ΔH_a values for the first and second dissociation of the cysteine ligand (4.60 and 5.11 kcal mol^{-1}) are increased on complexation to give 8.36 and 11.50 for Ni(II) and Co(II) complexes, respectively. This corresponds to

TABLE 2

Formation constants in the range 25–40 °C and thermodynamic parameters for the Co(II), Ni(II) and Cu(II) sulphur-containing amino acid complexes at 25 °C

Complexes	$\log_{10} K_1$, 1:1 complexes				$\log_{10} K_2$, 1:2 complexes				1:1 complexes			1:2 complexes		
	25 °C	30 °C	35 °C	40 °C	25 °C	30 °C	35 °C	40 °C	ΔG	ΔH	ΔS	ΔG	ΔH	ΔS
Co–cystine	5.18	5.34	5.52	6.11	5.14	5.08	5.02	4.95	7.10	−3.07	−34.13	7.46	5.25	−6.51
Ni–cystine	5.30	5.30	5.42	5.85	5.25	5.18	5.12	5.05	7.27	−2.30	−32.11	7.20	5.75	−4.87
Cu–cystine	7.20	7.20	7.22	7.35	6.83	6.80	6.77	6.70	9.87	−6.27	−54.16	9.36	4.18	−17.38
Co–cysteine	11.20	11.10	11.00	10.80	–	–	–	–	15.35	11.50	−12.92	–	–	–
Ni–cysteine	9.75	9.20	9.10	9.00	–	–	–	–	13.37	8.36	−16.81	–	–	–
Co–methionine	6.00	6.10	6.45	6.60	4.56	4.50	4.40	4.30	8.22	−19.71	−93.72	6.25	8.36	−7.08
Ni–methionine	7.55	7.65	7.75	7.85	–	–	–	–	10.35	−8.36	−62.79	–	–	–
Cu–methionine	11.60	9.90	9.80	11.40	–	–	–	–	–	–	–	15.90	–	–

ΔH and ΔG in kcal mol^{-1}; ΔS in e.u.

a free energy change of 13.37 and 15.37 (kcal mol^{-1}) respectively. The thermodynamic quantities for the Cu(II)–cysteine complex could not be determined owing to its redox reaction.

(8) Regarding the copper–methionine system, no regular trend for the effect of temperature on $\log_{10} K$ values could be observed. This makes the computation of ΔH and ΔS difficult. However, we can mention that ΔG for methionine (12.54 and 14.39 kcal mol^{-1} for the first and second dissociation respectively) is increased on complexation with Cu(II) to give 15.90 kcal mol^{-1}.

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