Stability Constants of Mixed Ligand Complexes of Cu(II) and Ni(II) with Some Amino Acids and Phosphates

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Abstract: The binary and ternary metal complexes of Cu(II) & Ni(II) with some amino acids (leucine, isoleucine & serine) as primary ligand and pyrophosphate (PP), adenosine-5'-triphosphate (ATP), as secondary ligand have been studied potentiometrically at 35 °C and a constant ionic strength (1.0 mol dm⁻³ KNO₃). The formation of various binary and ternary complexes has been inferred from the corresponding titration curves. The Irving & Rossotti titration technique has been applied to determine the formation constants corresponding to various complexation equilibria.

Keywords: Amino acids, Adenosine -5'-triphosphate and Pyrophosphate

Introduction

The coordination chemistry of nucleotides, pyrophosphate (PP), adenosine-5'-triphosphate (ATP) has biochemical significance because they play a central role in the metabolism of living cells¹⁻⁴ and they serve as substrate for the enzyme-catalysed transfers of nucleotidyl or phosphoryl groups, which depends on the presence of metal ions⁵⁻⁶.

Amino acids are also well known potential ligands with numerous applications and play an important role in biological systems⁷. The present work concerns the formation of binary and ternary complexes of Cu(II) & Ni(II) with leucine (Leu), isoleucine (Ileu) and serine (Ser) as primary ligands and PP, ATP as secondary ligands.

The work aims to establish various equilibria existing in solution and to determine the dissociation constants of the free ligand and formation constants of binary and ternary complexes by using Calvin-Bjerrum⁸⁻⁹ titration technique as used by Irving & Rossotti¹⁰⁻¹¹.

Experimental

Adenosine-5'-triphosphate acid disodium salt (Na₂ATP.3H₂O) and pyrophosphate were provided by Fluka and used without further purification. A fresh sample was weighed and a solution was prepared for each titration to exclude loss by hydrolysis.

The metal salts and other reagents were provided by BDH. Stock solutions of the metal salts, HNO_3 and KOH were prepared in double-distilled water, and the metal concentration was obtained by standard analytical methods¹².

Apparatus

Potentiometric pH-measurements were performed on solutions in a double walled glass vessel at 35 °C using an Elico model digital pH-meter. The electrode solution was calibrated in terms of hydrogen ion concentration instead of activities and by periodic titration of HNO_3 (or KOH) solutions (1.0 M KNO_3) with standard KOH (or HNO_3) solution.

Procedure

The following solutions were prepared (total volume 50 mL) and titrated potentiometrically against standard CO_2 -free KOH (0.1 mol dm^{-3}) solution at constant temperature 35 °C and at a constant ionic strength ($I = 1.0 \text{ mol dm}^{-3} \text{ KNO}_3$).

- HNO_3 (0.001 mol dm^{-3}) + KNO_3 (1.0 mol dm^{-3}) solution
- solution 'a' + AA (0.001 mol dm^{-3})
- solution 'a' + ATP/PP (0.001 mol dm^{-3}) solution
- solution 'b' + Metal ion (0.001 mol dm^{-3}), binary MA system
- solution 'c' + Metal ion (0.001 mol dm^{-3}), binary ML system
- solution 'a' + AA (0.001 mol dm^{-3}) + Metal ion (0.001 mol dm^{-3}) + ATP/PP (0.001 mol dm^{-3}), ternary MAL system

Each of above solutions was left to stand for about 15 min. before titration. Multiple titrations have been performed for each system. The pH-metric readings were corrected by the method of Van Uitert and Hass¹³.

Results and Discussion

Figure 1 & 2 represents a set of constructed titration curve for the free and complexed ligand according to the sequence described in the experimental section for Cu(II)-Leu-ATP & Cu(II)-Leu-PP .

Figure 1. Titration curves for Cu(II)-Leu-ATP (35 °C, $I = 0.1 \text{ M KNO}_3$) (A) Free acid (B) Leu (C) ATP (D) Cu(II)-Leu (E) Cu(II)-ATP (F) Cu(II)-Leu-ATP

Figure 2. Titration curves for Cu(II)-Leu-PP (35°C, $I = 0.1 \text{ M KNO}_3$) (A) Free acid (B) Leu (C) PP (D) Cu(II)-Leu (E) Cu(II)-PP (F) Cu(II)-Leu-PP

In all the ternary systems the amino acids (HA) are regarded as primary ligand and ATP, PP (HL) as secondary ligand. The protonation constants have been determined from titration curves 'a' and 'b' for amino acids and curves 'a' and 'c' for ATP, PP and the values are listed in Table-1. Examination of the different titration curves 'd' obtained for binary MA (metal - amino acid) solutions reveals that the complexation equilibria involved occur in a stepwise manner.

Generally, MA binary complexes begin to form at pH value lower than that of free ligand. At higher volumes of alkali added, the relatively large drop in pH in metal titrations (curve 'd' & 'e') with respect to the ligand titration curve, confirm the formation of metal complex.

This is attained from the divergence of each of the 1:1 binary MA titration curve 'd' from that of the corresponding free ligand solution, curve 'b'. It is worth mentioning that there is no precipitation during the titration, ruling out the possibility of hydrolysis of the studied metal ions in the presence of excess ligand. This suggests that the amino acids have high tendency to form stable metal complexes in solution.

The titration curves 'e' obtained for binary ML (metal - secondary ligand) solution (1:1 molar ratio) displays that ML complexes are begin to form at $\text{pH} = 3.2\text{--}6.7$ and show a single inflection at two moles of base.

There are two sites in ATP at which chelation can take place, thus ATP acts primarily as a bidentate ligand with metal(II) and it is sterically difficult for the third phosphate group to bend around and bind the third position. So, the formation of M(II)-ATP can be represented in the Scheme 1.

Scheme 1

Table 1. Protonation constants of the free ligand and formation constants of binary systems (T = 35°C, I = 1.0 M KNO₃)

Ligands	Protonation Constants		Binary Formation Constants	
	pK _{a1}	pK _{a2}	Cu(II)	Ni(II)
Leu	2.38	9.59	8.15	5.87
Ileu	2.37	9.58	8.12	5.78
Ser	2.28	9.16	7.79	5.45
ATP	4.11	6.54	6.13	5.02
PP	5.93	8.24	8.37	5.57

Table 2. Formation constants of ternary MAL systems at 35°C, I = 1.0 M KNO₃.

Metal ion	logβ _{MAL} ^M	logK _{MAL} ^{MA}	Δlog K
M(II)-Leu-ATP			
Cu(II)	13.62	5.47	-0.65
Ni(II)	10.61	4.74	-0.27
M(II)-Leu-PP			
Cu(II)	15.53	7.41	-0.96
Ni(II)	11.32	5.45	-0.45
M(II)-Ileu-ATP			
Cu(II)	13.51	5.39	-0.73
Ni(II)	10.46	4.67	-0.34
M(II)-Leu-PP			
Cu(II)	15.27	7.16	-1.21
Ni(II)	10.99	5.36	-0.51
M(II)-Ser-ATP			
Cu(II)	13.12	5.32	-0.80
Ni(II)	9.96	4.50	-0.51
M(II)-Ser-PP			
Cu(II)	14.86	7.06	-1.30
Ni(II)	10.66	5.20	-0.67

The formation constants for the binary complexes formed are calculated by using standard procedures based on the calculation of the average number of ligands bound per metal ion ($\bar{n}$) and the free ligand exponent (pL), from the titration curve 'b', 'c', 'd' and 'e'. The formation constants values for binary systems are given in Table 1.

Analysis of the titration curve 'f' obtained for ternary MAL(metal-amino acid-ATP/PP) systems reveals that these curve deviate from curves for binary systems (MA) after the addition of about one mole of alkali. A comparison of the titration curve 'f' with the curve for free ATP & PP and the binary MA system, indicates the formation of a mixed ligand complex in acidic region of pH.

Titration curve 'f' show on inflection at four moles of base in the pH region 4.0 to 5.0 for Cu(II) complexes and around pH 5.0 to 6.0 unit for Ni(II) complexes. These observation suggests the formation of ternary complex through the initial formation of binary complex (MA). The complexation equilibria may be represented as-

$$K_{M(AA)(ATP)}^{M(AA)} = \frac{[M(AA)(ATP)]}{[M(AA)][(ATP)]} \quad (3)$$

The formation constants for the ternary complexes were calculated using a modified Irving-Rossotti titration technique¹⁴ and results are given in Table-2. The values of formation constants obtained for ternary systems follow on order Leu > Ileu > Ser, which in general is in accordance with the decreasing basicity of amino acids and also in fair agreement with the Irving and Williams order¹⁵.

The relative stability of mixed ligand complexes as compared to that of the corresponding binary systems involving secondary ligand can be quantitatively expressed¹⁶ in terms of $\Delta \log K$.

$$\Delta \log K = \log K_{MAL}^{MA} - \log K_{ML}^M$$

The negative values of $\Delta \log K$ indicate that the formation of ternary complexes is less favoured than the corresponding binary complexes. This can be due to the statistical factors¹⁷. By comparing the values of $\log K_{MAL}^{MA}$ for the complexes of pyrophosphate and ATP having a common amino acid, it can be summarized that the stability decreases in the order of their basicity.

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