Solution Equilibria of Binary and Ternary Systems Involving Transition Metal Ions, Adenosine 5′-Triphosphate, and Amino Acids

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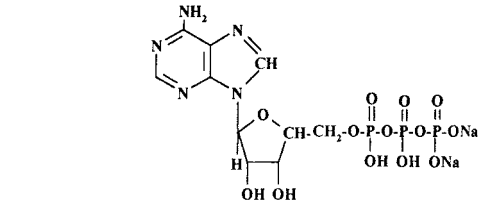
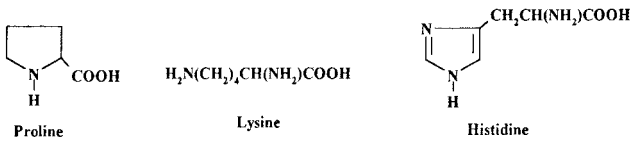
Solution equilibria of the binary and ternary systems involving M^{n+} ion, adenosine 5′-triphosphate, and some mono- and dicarboxylic amino acids ($M^{n+} = Cu^{II}$, Ni^{II}, Co^{II}, La^{III}, and Ce^{III}) have been investigated potentiometrically at (25 ± 0.1) °C and $I = 0.10$ mol dm^{-3} (KNO_3). The formation of the different binary and ternary complexes is inferred from the corresponding titration curves. The stability constants of the various complexes formed were determined and discussed in terms of the nature of both the metal ion and the ligand. Moreover, the stability of the mixed ligand complexes is discussed in relation to that of the corresponding binary complexes of amino acids.

Introduction

Adenosine 5′-triphosphate (ATP) is considered to be one of the biologically important ligands. It is generally recognized that numerous metal ions form ATP adducts which could be involved in many enzymatic processes (Crisponi et al., 1984). Thus, considerable interest has focused on the study of the binary metal complexes formed with ATP. Ternary complexes of some transition metal ions with ATP and some secondary ligands have been studied using several techniques (Azab et al., 1993a,b, 1994; Verma et al., 1993; Sun and Gong, 1995; Cini and Bozzi, 1996). However, few studies have been made on the mixed ligand complexes containing the biologically important ligands ATP and amino acids (Mahmoud et al., 1989a,b; Venkataiah et al., 1994; Molodkin et al., 1996). Moreover, no studies appear to have been made on the ternary systems of the trivalent transition metal ions containing ATP and amino acid ligands. Continuing our studies on the mixed ligand complexes (Ahmed et al., 1996, 1997, 1998), this paper represents a systematic potentiometric study on the complex formation between some transition metal ions (Cu^{II}, Ni^{II}, Co^{II}, La^{III}, and Ce^{III}) and adenosine 5′-triphosphate, in the form of the disodium salt $(H_2L)^{2-}$, as a primary ligand and some monocarboxylic as well as dicarboxylic amino acids (proline, lysine, histidine, asparagine, glutamine, aspartic acid, and glutamic acid) as secondary ligands in aqueous media at (25 ± 0.1) °C. The structures of the ligands used in this study are



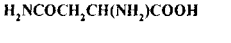
Adenosine-5′-triphosphate disodium salt (ATP)



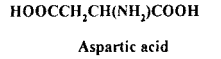
Proline

Lysine

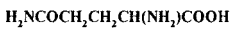
Histidine



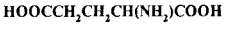
Asparagine



Aspartic acid



Glutamine



Glutamic acid

The study adopts the Irving and Rossotti technique (Irving and Rossotti, 1953, 1954) for the determination of the stability constants of the different binary and mixed ligand complexes in such systems. Formation, structure, and stability of the different binary and mixed ligand complexes have been discussed in terms of the nature of both the structure and the basicity of the ligand as well as the nature of the metal ion used. Moreover, the stability of the ternary complexes has been compared to that of the corresponding binary complexes of the amino acids.

Experimental Section

Materials and Solution. Adenosine 5′-triphosphate tetrahydrate (ATP) in the form of the disodium salt and the amino acids used were analytical grade (BDH) products

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with high purity. All other chemicals employed were of A.R. grade. Due to the possible hydrolysis of ATP, a stock solution could not be prepared and kept for a period of time. Thus, the desired concentration was prepared by dissolving an accurate mass of the ligand in the appropriate volume of CO_2-free doubly distilled water before each titration. During the course of the experimental work the ATP was frequently checked for purity (and for hydrolysis) by potentiometric titration. A stock solution of each amino acid was also prepared in a similar way. Solutions of Cu^{II}, Ni^{II}, Co^{II}, La^{III}, and Ce^{III} were prepared from their nitrate salts and were standardized as recommended (Vogel, 1975). Carbonate-free KOH was prepared and standardized by a standard solution of potassium hydrogen phthalate. A solution of HNO_3 was prepared and used after standardization. A stock solution of KNO_3 was also prepared by dissolving the required mass in the appropriate volume of doubly distilled water.

pH Metric Titration. A solution made from metal ion, primary ligand ATP, and/or secondary ligand amino acid (proline, lysine, histidine, asparagine, glutamine, aspartic, or glutamic acid) in a molar ratio of 1:1:1 or 1:2:1 was titrated with a relatively concentrated standard CO_2-free KOH solution at (25 ± 0.1) °C. Precipitation was observed on using the molar ratio 1:1 for the binary metal complex solution of ATP with each trivalent metal ion (La^{III} or Ce^{III}) due to hydrolysis of the complexes leading to the formation of hydroxo complex species. Thus, a 1:2:1 molar ratio was used for such cases. Generally, a constant ionic strength was maintained with 0.10 mol dm^{-3} KNO_3, and the total volume of 25 cm^3 was used for each titration. The pH measurements were carried out with an Orion 701A digital pH meter accurate to ±0.005 pH unit with a glass−calomel electrode assembly. The accuracy of the pH meter was checked using standard buffer solutions with pH values of 4.01 and 9.18 at (25 ± 0.1) °C. The temperature was adjusted by making use of a Fisher Scientific isotemp refrigerated circulator model 9000 water thermostat accurate to ±0.1 °C. The various solutions titrated were as follow: (a) (0.0015−0.00327) mol dm^{-3} HNO_3; (b) solution a + 0.001 mol dm^{-3} of an amino acid; (c) solution b + 0.001 mol dm^{-3} M^{n+}; (d) solution a + 0.001 mol dm^{-3} ATP; (e) solution d + 0.001 mol dm^{-3} M^{II}; (f) solution e + 0.001 mol dm^{-3} of an amino acid. A concentration of 0.002 mol dm^{-3} ATP was used for the titrated solutions d−f for a 1:2:1 molar ratio in the case of the trivalent metal ion La^{III} and Ce^{III}. However, the titration of the solutions containing ATP was completed in the shortest time to avoid the possibility of hydrolysis of ATP. The equations used for various calculations were programmed using an IBM computer.

Results and Discussion

A typical set of experimental titration curves obtained according to the sequence described in the Experimental Section for the different M^{n+} + ATP + amino acids systems are displayed in Figures 1 and 2. The titration curve d corresponding to the solution of the disodium salt of ATP [$(H_2L)^{2-}$] exhibits a moderate inflection at 1 mol of base followed by another steep inflection at 2 mol of base per 1 mol of ATP. A buffer region indicating the release of two protons in the two distinct steps separates these two inflections. The calculated two acid dissociation constant values pK_{a1} and pK_{a2} for ATP are 4.08 and 6.57 which are in a fairly good agreement with the literature values under the same conditions (4.06 and 6.53, respectively) (Mahmoud et al., 1989a,b; Khan and Martell, 1966).

In general, the various titration curves e obtained for the different 1:1 and 1:2 binary (M^{n+} + ATP) solutions

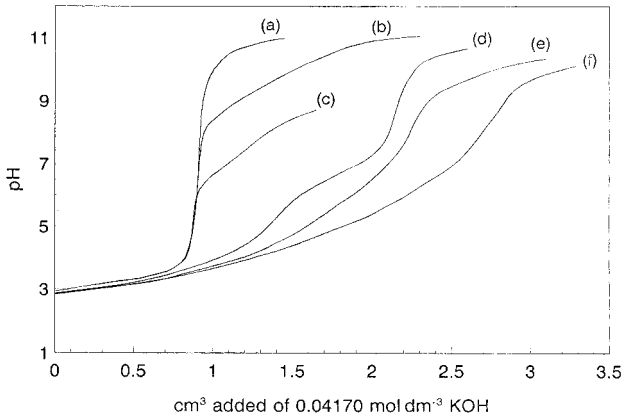

Figure 1. pH metric titration curves for the Ni^{II} + ATP + lysine system at (25 ± 0.1) °C and an ionic strength I = 0.10 mol dm^{-3} (KNO_3): (a) 0.0015 mol dm^{-3} HNO_3; (b) solution a + 0.001 mol dm^{-3} lysine; (c) solution b + 0.001 mol dm^{-3} Ni^{II}; (d) solution a + 0.001 mol dm^{-3} ATP; (e) solution d + 0.001 mol dm^{-3} Ni^{II}; (f) solution e + 0.001 mol dm^{-3} lysine.

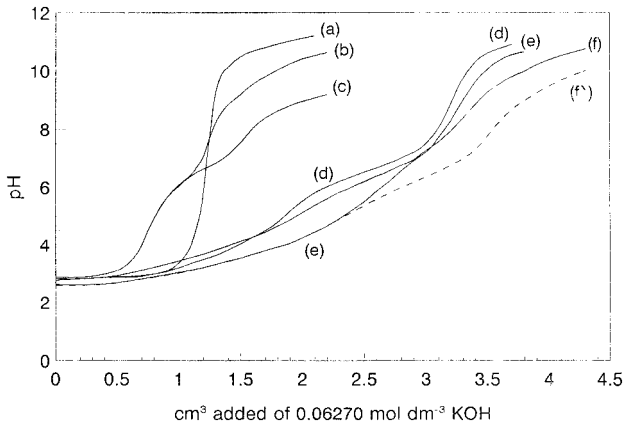

Figure 2. pH metric titration curves for the Ce^{III} + $(ATP)_2$ + histidine system at (25 ± 0.1) °C and an ionic strength I = 0.10 mol dm^{-3} (KNO_3): (a) 0.003 07 mol dm^{-3} HNO_3; (b) solution a + 0.001 mol dm^{-3} histidine; (c) solution b + 0.001 mol dm^{-3} Ce^{III}; (d) solution a + 0.002 mol dm^{-3} ATP; (e) solution d + 0.001 mol dm^{-3} Ce^{III}; (f) solution e + 0.001 mol dm^{-3} histidine; (f′) solution f + volume of KOH equivalent to the concentration (0.001 mol dm^{-3}) of histidine base in the solution.

diverge from that corresponding to the free ligand solution (curve d) at a lower pH value (~3.20), indicating the formation of the binary (M^{n+} + ATP) complex. However, the titration curves corresponding to the 1:1 binary (M^{II} + ATP) complex solutions show an inflection after the addition of 2 mol of base per 1 mol of ATP, indicating a simultaneous dissociation of two protons from ATP. This could be interpreted on the basis of the high acidity of the ATP ligand which leads to the formation of a protonated 1:1 binary metal complex $[MHL]^{1-}$ at the addition of 1 mol of base per 1 mol of ATP. Accordingly, the formed protonated binary complexes act as strong acids that dissociate readily to form the unprotonated 1:1 binary metal complexes $[ML]^{2-}$. This is supported by the absence of an inflection point in the titration curves of these binary complex solutions corresponding to the addition of 1 mol of base per 1 mol of ATP. The titration curves for the 1:2 binary M^{III} + $(ATP)_2$ metal complexes displayed two moderate inflections at the addition of 2 and 4 mol of base, respectively, revealing the stepwise formation of the 1:1 $[ML]^{1-}$ and 1:2 $[ML_2]^{5-}$ binary metal complexes. The different 1:1 and 1:2 binary (M^{n+} + ATP) complexes are quite stable up to high pH values, i.e., have no tendency

to form hydroxo complex species.

The titration curves of the 1:1 binary (M^{n+} + amino acid) complex solutions indicate that the complexes begin to form at pH ranges of 3.20−4.80, 4.20−6.80, and 4.80−7.60 for Cu^{II}, Ni^{II}, and Co^{II}, respectively. With respect to the titration curves of the 1:1 binary complexes of Ce^{III} and La^{III}, these complexes begin to form in the pH ranges of 5.60−6.50 and 6.30−7.00, respectively. This is attained from the appeared divergence of each titration curve c of the 1:1 binary complex solution from that of the corresponding free amino acid (curve b). Generally, the titration curves reveal that the 1:1 binary metal complexes of dicarboxylic amino acids (aspartic or glutamic) are formed at lower pH values compared with those of monocarboxylic amino acids studied. Moreover, no inflection point was observed in the titration curves of the different 1:1 binary (M^{n+} + amino acid) complexes denoting the formation of normal complexes. Further, all the 1:1 binary M^{n+} + amino acid titration curves do not show any precipitate in the pH range of complex formation, pointing out that hydrolysis reactions do not interfere in the determination of the stability constants of these binary complexes. Except in the case of the dicarboxylic amino acids, the binary complex solutions of Cu^{II}, Ni^{II}, and Co^{II} show precipitates at pH ranges of 5.50−7.00, 6.00−9.00, and 6.80−9.40, respectively. For the 1:1 binary Ce^{III} and La^{III} amino acid complex solutions precipitation occurred at relatively high pH values of 7.90−10.60 and 8.40−10.40, respectively. This is due to the formation of hydroxo complex species resulting from the possible hydrolysis of these complexes. Thus, further studies beyond the precipitation point were not possible for such complexes.

Titration curve f obtained for the different ternary complex solutions of molar ratios 1:1:1 (M^{II} + ATP + amino acid) and 1:2:1 (M^{III} + $(ATP)_2$ + amino acid) are strongly overlapped with the corresponding titration curve of 1:1 or 1:2 binary metal complex solutions of M^{n+} + ATP at lower pH values where the binary metal complex is formed, indicating that the amino acid (aa) ligands do not bind with the metal ion in this pH range. In the case of histidine as a secondary ligand a constant volume of KOH equivalent to the concentration of histidine in the ternary complex solution was added to the different volumes of KOH at each pH value (curve f′). Generally, at a high pH value, which is largely dependent upon the nature of the metal ion as well as the nature of the secondary ligand aa used, the ternary titration curve (f or f′) is diverged from that of the 1:1 or 1:2 binary metal complex {$[M(ATP)]^{2-}$ or $[M(ATP)_2]^{5-}$} of ATP. For the 1:1:1 ternary complexes, the ternary titration curve diverges from the corresponding 1:1 binary (M^{II} + ATP) titration curve (e) after pH ranges of 3.40−7.40, 3.20−7.00, and 3.20−4.80 for Co^{II}, Ni^{II}, and Cu^{II}, respectively. The divergence of the 1:2:1 ternary complexes titration curve from the corresponding binary titration curve of the [M^{III} + $(ATP)_2$] complex starts at pH ranges of 3.80−8.00 and 3.40−8.50 for La^{III} and Ce^{III}, respectively. This behavior clearly indicates that the coordination of an amino acid as a secondary ligand to the binary metal complex of ATP, which is first formed, leading to the formation of the ternary complex takes place in a stepwise manner. Generally, the reaction of the complex formation can be represented by the following equations:

$$M^{n+} + k(ATP) \rightleftharpoons [M(ATP)_k]^{(n-4k)} + 2kH^+$$

$$[M(ATP)_k]^{(n-4k)} + (aa)^{m-} \rightleftharpoons [M(ATP)_k(aa)]^{(n-4k-m)}$$

where M = Co^{II}, Ni^{II}, Cu^{II}, La^{III}, and Ce^{III}; ATP = disodium salt of adenosine 5′-triphosphate $(H_2L)^{2-}$; k is the number of ATP molecules (k = 1 and 2 for divalent and trivalent metal ion complexes, respectively); m = 1 for monocarboxylic amino acids (proline, lysine, asparagine, glutamine, and histidine), and m = 2 for the dicarboxylic amino acids (aspartic and glutamic acid).

The binary $[M(ATP)_k]^{(n-4k)}$ complexes are stable up to the pH ranges where the attachment of the secondary ligand aa takes place, affording the ternary mixed ligand complexes. Accordingly, it can be considered that the secondary ligand amino acid would combine with the binary complex species $[M(ATP)_k]^{(n-4k)}$ in the ternary system as it does with $[M^{n+}(H_2O)_6]^{n+}$ in a binary system. On the other hand, except in case of Co^{II} + ATP + proline, the ternary metal complex solutions under investigation do not show any precipitation up to the pH value corresponding to the complete complex formation. This designates that the different 1:1:1 and 1:2:1 mixed ligand complexes studied have no tendency to form hydroxo complex species. However, the titration curves of the ternary Co^{II} + ATP + proline complex solution show a precipitate at low pH value. This is attributable to the formation of hydroxo complex species resulting from the possible hydrolysis of this complex. Moreover, no divergence is observed for the titration curve f corresponding to the ternary Ce^{III} + $(ATP)_2$ + lysine complex solution from that of the binary Ce^{III} + $(ATP)_2$ complex solution, indicating no ternary complex is formed. However, a small divergence is observed for the ternary La^{III} + $(ATP)_2$ + lysine complex titration curve f, characterizing a very weak complex formation. In general, studies could not be possible for these complexes.

The horizontal distance between curves e and f (or f′ in the case of histidine) was measured and used for calculation of $\bar{n}_{mix}$ (number of the secondary ligand amino acid anions attached to one binary $[M(ATP)_k]^{(n-4k)}$ complex molecule). The equation used for the calculation of $\bar{n}_{mix}$ was the same as that reported in the original papers (Irving and Rossotti, 1953, 1954).

$$\bar{n}_{mix} = [(V_f \text{ or } V_{f'} - V_e)][C_b + C_a + C_L(y - \bar{n}_H)]/[(V_o + V_e)]\bar{n}_H C_M$$

Here C_M is the concentration of $[M(ATP)_k]^{(n-4k)}$ which is equal to the concentration of M^{n+} used, C_L is the concentration of the secondary ligand, y = the number of dissociable protons of the secondary ligand (y = 1 in the case of monocarboxylic amino acids except histidine and y = 2 for the dicarboxylic amino acids and histidine), and V_o is the original volume (25 cm^3). V_f or $V_{f'}$ and V_e are the volumes of alkali (KOH) consumed to reach the same pH values in curves f or f′ and e, respectively. C_a and C_b are the concentrations of HNO_3 and KOH, respectively. $\bar{n}_H$ values (the average number of protons associated with the ligand) for secondary ligand amino acids at different pH values were available from the determination of their proton−ligand dissociation constants. The $\bar{n}_{mix}$ do not exceed unity, indicating that only one secondary ligand molecule combines with the complex $[M(ATP)_k]^{(n-4k)}$. The free secondary ligand exponent, pL_{mix}, was calculated from the obtained values of $\bar{n}_{mix}$ using the equation (Irving and Rossotti, 1953, 1954):

$$pL_{mix} = \log\left\{\left[\sum_{y=0}^{y=1\text{or}2} \beta_y^H \left(\frac{1}{10^B}\right)/C_L - \bar{n}_{mix}C_M\right][V_o + (V_f \text{ or } V_{f'})/V_o]\right\}$$

Table 1. Acid Dissociation Constants of the Ligands Used and the Stability Constants of 1:1 and 1:2 M^{n+} + ATP[a] as Well as 1:1 M^{n+} + aa[a] Binary Complexes Formed at (25 ± 0.1) °C and an Ionic Strength I = 0.1 mol dm^{-3} (KNO_3)

			log $K^{M}_{M(ATP)}$ or log $K^{M}_{M(ATP)_2}$ or log $K^{M}_{M(aa)}$				
ligand	pK_{a2}	pK_{a2}	Co^{II}	Ni^{II}	Cu^{II}	Ce^{III}	La^{III}
ATP[b]			4.40 ± 0.08 (4.26)[c]	4.93 ± 0.06 (5.05)[d]	6.00 ± 0.08 (6.13)[d]	4.16 ± 0.05 (4.22)[c]	4.03 ± 0.07 (4.15)[c]
histidine	6.05 ± 0.04	9.20 ± 0.03	7.06 ± 0.03	8.70 ± 0.09	10.11 ± 0.05 (10.10)[e]	6.30 ± 0.04	5.40 ± 0.05
proline	10.69 ± 0.02		5.13 ± 0.06	6.60 ± 0.07	8.60 ± 0.03	5.90 ± 0.05	5.26 ± 0.06
lysine	9.45 ± 0.02		4.80 ± 0.07	5.80 ± 0.06	8.13 ± 0.04	5.33 ± 0.06	4.80 ± 0.07
asparagine	8.82 ± 0.03		4.37 ± 0.08 (4.38)[f]	5.61 ± 0.06 (5.57)[f]	8.05 ± 0.05 (8.05)[f]	5.14 ± 0.07 (5.14)[f]	4.44 ± 0.06
glutamine	9.06 ± 0.02		4.06 ± 0.06 (4.05)[d]	5.05 ± 0.09 (5.17)[d]	7.76 ± 0.07 (7.74)[d]	4.77 ± 0.06	3.88 ± 0.07
aspartic acid	3.92 ± 0.06	9.96 ± 0.03	6.14 ± 0.04 (6.30)[c]	7.20 ± 0.04 (7.15)[c]	8.83 ± 0.04 (8.85)[f]	8.46 ± 0.03	7.10 ± 0.04
glutamic acid	4.38 ± 0.05	9.66 ± 0.02	4.50 ± 0.07 (4.56)[d]	5.95 ± 0.07 (5.90)[c]	8.50 ± 0.06 (8.34)[d]	6.90 ± 0.05	6.52 ± 0.06

[a] aa = an amino acid, and ATP = adenosine 5′-triphosphate. [b] The pKa1 and pKa2 of ATP are 4.08 and 6.57, respectively. [c] Mahmoud et al., 1989. [d] Martell and Sillen, 1971. [e] Krishna and Ram, 1991. [f] Ahmed et al., 1996.

Table 2. Stability Constants of the Various 1:1:1 and 1:2:1 M^{n+} + ATP + aa[a] Mixed Ligand Ternary Complexes Formed at (25 ± 0.1) °C and an Ionic Strength I = 0.1 mol dm^{-3} (KNO_3) Along with the Values of Δ log K

	histidine		proline		lysine		asparagine		glutamine		aspartic acid		glutamic acid	
metal ion	log K	Δ log K	log K	Δ log K	log K	Δ log K	log K	Δ log K	log K	Δ log K	log K	Δ log K	log K	Δ log K
							log $K^{M}_{M(aa)}$							
Co^{II}	6.90 ± 0.06	−0.16	ppt		4.47 ± 0.11	−0.33	4.09 ± 0.12	−0.28	3.96 ± 0.12	−0.10	8.68 ± 0.08 (8.50)[b]	+2.54	7.62 ± 0.11 (7.30)[b]	+3.12
Ni^{II}	8.23 ± 0.08	−0.47	5.95 ± 0.11	−0.65	5.43	−0.37	4.66 ± 0.09	−0.95	4.36 ± 0.11	−0.69	8.95 ± 0.11 (8.90)[b]	+1.75	7.90 ± 0.10 (7.53)[b]	+1.95
Cu^{II}	9.2 ± 0.05	−1.09	7.61 ± 0.09	−0.99	6.84 ± 0.12	−1.29	6.62 ± 0.08	−1.43	6.43 ± 0.08	−1.33	9.43 ± 0.07	+0.60	8.89 ± 0.08	+0.39
							log $K^{M}_{M(ATP)_2(aa)}$							
Ce^{III}	6.10 ± 0.10	−0.20	4.82 ± 0.08	−1.08	no complex is formed		4.18 ± 0.09	−0.96	3.73 ± 0.12	−1.04	8.58 ± 0.09	+0.12	7.48 ± 0.09	+0.58
La^{III}	4.98 ± 0.12	−0.42	4.13 ± 0.11	−1.13	very weak complex		3.68 ± 0.10	−0.76	3.25 ± 0.13	−0.63	7.95 ± 0.10	+0.85	6.84 ± 0.11	+0.32

[a] aa = an amino acid, and ATP = adenosine 5′-triphosphate. [b] Mahmoud et al., 1989.

where β^{H}_{y} are the proton−ligand dissociation constant values of the applying amino acids and B is the pH value. All other terms have the same meaning as defined above.

The second acid dissociation constant values of all secondary ligand amino acids as well as the third acid dissociation constants of the dicarboxylic amino acids (aspartic and glutamic) and of histidine were determined from the titration curves a and b, making use of the Irving and Rossotti formulation (Irving and Rossotti, 1953, 1954). In this respect, it is worth reporting that titration curve b for lysine (Figure 1) shows only one inflection, indicating one dissociation step corresponds to the release of one proton. However, the first acid dissociation constant values of all amino acids studied are very low (∼2.00) (Weast, 1973; Martell and Sillen, 1971), occurring only in strongly acidic solutions; therefore, they were not used in the calculations. Generally, the acid dissociation constant values obtained are in good agreement with the corresponding literature values determined under the same condition (Weast, 1973; Martell and Sillen, 1971). The formation constant (log K) values of the different 1:1 and 1:2 binary complexes (Table 1) were determined by applying the original equations of Irving and Rossotti to the binary complex solution systems (curves b, c and d, e for $[M(aa)]^{(n-m)}$ and $[M(ATP)_k]^{(n-4k)}$, respectively. Some of the log K values are in good agreement with those found in the literature (Mahmoud et al., 1989a,b; Ahmed et al., 1996; Krishna and Ram, 1991; Martell and Sillen, 1971).

The mean log K values for the different binary and ternary complexes obtained from the corresponding titration curves using the average value and straight line methods along with the error as estimated by applying the least-squares fits are given in Tables 1 and 2. The results obtained clearly indicate that the stability of the 1:1 binary and 1:1:1 ternary complexes, of the same metal ion, containing the dicarboxylic amino acids (aspartic and glutamic) is higher than that of the complexes containing the monocarboxylic amino acids. This can be mainly ascribed to the behavior that the dicarboxylic amino acids are more prone to complex formation than the monocarboxylic amino acids. This is due, in addition to the effective high basicity of the dicarboxylic amino acids (i.e., good σ-donor), to the tendency of the dicarboxylic amino acids to act as tridentate ligands (OON donor).

On the other hand, in terms of the effect of the secondary ligand monocarboxylic amino acid on the stability constant, the data cited in Tables 1 and 2 show that the stability of the binary and ternary complexes of the same metal ion follow the order histidine (pK_{a2} = 6.00, pK_{a3} = 9.20) > proline (pK_{a2} = 10.69) > lysine (pK_{a2} = 9.45, this work) > asparagine (pK_{a2} = 8.82) > glutamine (pK_{a2} = 9.06) (Weast, 1973; Martell and Sillen, 1971). This behavior can be interpreted on the basis of the effective basicity of the conjugate base of these ligands as well as the steric effect. Generally, increasing the length of the ligand chain would result in more strain on its bending, i.e., relatively low stability. The observed high stability of the binary or ternary complex containing aspartate anion (pK_{a2} = 3.86, pK_{a3} = 9.80) (Weast, 1973; Martell and Sillen, 1971) relative to that containing glutamate anion (pK_{a2} = 4.31, pK_{a3} = 9.47) (Weast, 1973; Martell and Sillen, 1971) can be considered convincing evidence for this explanation. Though the two ligands act as an OON tridentate ligand, two metal chelate rings are formed, five- and six-membered metal chelate rings in the case of aspartate anion and six- and seven-membered metal chelate rings in the case of glutamate anion.

The data cited in Table 2 indicate that the stability of the 1:1:1 mixed ligand complexes of the same ligand is higher than that of the corresponding 1:2:1 ternary complexes. This behavior can be ascribed to the fewer coordination sites available in the case of 1:2:1 relative to that in the 1:1:1 molar ratio. Further, in addition to the possible steric effect that exists in the 1:2:1 ternary complexes, there is a higher Coulombic repulsion in 1:2:1 mixed ligand complexes compared with 1:1:1 mixed ligand complexes. This could be substantiated by the observation that the divergence of the ternary titration curve f or f′ from curve e in the case of the 1:1:1 molar ratio of M^{II} + ATP + aa occurred at a lower pH value relative to that for the 1:2:1 molar ratio of M^{III} + $(ATP)_2$ + aa. Moreover, the stability of the mixed ligand complex on being compared to that of the corresponding 1:1 binary amino acid complex is expressed in terms of $\Delta \log K$. Examination of Tables 1 and 2 reveals that the stability of the ternary complex containing a monocarboxylic amino acid ligand is lower than that of the corresponding 1:1 binary M^{n+} + aa complex (i.e., $\Delta \log K$ is negative). This behavior can be explained on the basis that there are fewer sites available for binding an amino acid ligand on the $[M(ATP)_k]^{(n-4k)}$ complex than on $[M(H_2O)_6]^{n+}$. Moreover, there is a Coulombic repulsion in the mixed ligand complex formation between the negative charges carried by the binary $[M(ATP)_k]^{(n-4k)}$ complex and the mononegative charge on the secondary ligand monocarboxylic amino acid moiety. On the other hand, there is a Coulombic attraction in the binary M^{n+} + aa complex between the positive charges carried by the aquatic M^{n+} ion and the mononegative charge on the amino acid moiety. These two effects would result in a lower stability for the mixed ligand $[M(ATP)_k(aa)]^{(n-4k-m)}$ complex relative to that for the 1:1 binary M^{n+} + aa complex. However, the stability of the mixed ligand complexes containing the dicarboxylic amino acids (aspartic and glutamic) is higher than that of the corresponding 1:1 binary M^{n+} + aa complex (i.e., $\Delta \log K$ is positive). This can mainly be ascribed to the higher effective basicity of these amino acids relative to that of the monocarboxylic ones studied as well as the tendency of the dicarboxylic amino acids to act as an OON tridentate ligand yielding two metal chelate rings (as discussed above). However, the stability constants of the 1:1:1 Co^{II} + ATP + proline and the 1:2:1 M^{III} + $(ATP)_2$ + lysine ternary complexes could not be determined due either to the precipitation or to no ternary complex being formed (as discussed above).

Therefore, on the basis of the above discussion, one can deduce that the basicity of the secondary ligand as well as the structure of the complex formed and the electrostatic attraction play a significant role in determining the stability of the complexes studied.

Further, in terms of the nature of the metal ion used, the results obtained reveal that the stability of the different binary or mixed ligand complexes in the systems under investigation follow the order Cu > Ni > Co for the divalent metal ions and Ce > La for the trivalent metal ions. This order is in good accordance with the usual order of stability of such metal ion complexes (Irving and Williams, 1953; Grinberg and Yatsimerski, 1952; Cotton and Wilkenson, 1972).

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