Equilibrium studies on ternary Cu(II) complexes containing tripolyphosphate, pyrophophate or adenosine-5'-triphosphate and a series of secondary ligands

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Ternary metal complexes of the type MLA where M = Cu(II); L = tripolyphosphate (TPP), pyrophosphate (PP) or adenosine-5'-triphosphate (ATP) and A = alanine, serine, methionine, phenylalanine, tryptophan, histidine, aspartic acid, ethylenediamine, 2,2'-bipyridyl, 1,10-phenanthroline, malonic acid and pyrocatechol have been investigated potentiometrically at 35°C and $I = 0.2$ mol dm^{-3} (KNO₃). The stabilities of the ternary metal complexes have been quantitatively compared with the stabilities of the corresponding binary metal complexes (MA) determined under identical experimental conditions. Ternary complexes containing PP or ATP are found to be more stable than the corresponding complexes containing TPP. Various factors leading to differences in the relative stabilities of the ternary complexes are discussed.

Although the interaction of tripolyphosphate (TPP) and pyrophosphate (PP) with metal ions has been the subject of numerous studies[1], ternary metal complexes in which TPP or PP and a second ligand are simultaneously present in the coordination sphere of the metal ion have not been studied. Hence in the present investigation, we have carried out a detailed study of the formation and stability of ternary Cu(II) complexes (MLA) containing tripolyphosphate (TPP) or pyrophosphate (PP) as one ligand (L) and alanine (ala), serine (ser), methionine (met), phenylalanine (phe), tryptophan (try), histidine (his), ethylenediamine (en), 2,2'-bipyridyl (bipy), 1,10-Phenanthroline (phen), malonate (mal) or pyrocatechol (pyr), as the second ligand (A), by pH-metric method at 35°C and $I = 0.2$ mol dm^{-3} (KNO₃). The stabilities of these ternary complexes have been quantitatively compared with the corresponding binary metal complexes (MA) determined by us under identical experimental conditions[2-4]. The relative ability of TPP or PP and structurally analogous ligand adenosine-5'-triphosphate (ATP) in influencing the stability of ternary Cu(II) complexes has been compared.

Materials and Methods

Pentasodium tripolyphosphate, tetrasodium pyrophosphate, disodium adenosine 5'-triphosphate, ethylenediamine dihydrochloride and the various DL-amino acids were obtained from Sigma Chemical Co. USA. 2, 2'-Bipyridyl, 1, 10-phenantroline, malonic acid, pyrocatechol, potassium nitrate, Cu(II) nitrate trihydrate and sodium hydroxide were BDH reagents of AR grade. TPP was used in the triprotonated form whereas ATP, PP, En, Bipy, Phen, Mal, Pyr and His were used in diprotonated form and all other amino acids were used in the monoprotonated form. A stock solution of Cu(II) (0.02 mol dm^{-3}) was prepared and standardized by complexometric titration with EDTA[5]. Carbonate free NaOH was prepared and standardized by titrating with potassium hydrogen phthalate[6]. The experimental method consisted of potentiometric titration of solutions containing 1:2 molar ratio of Cu(II) and ligand (L) for binary systems and 1:1:1 molar ratio of ligand (L), metal ion and the secondary ligand (A) for ternary systems with standard carbonate free sodium hydroxide in a double walled titration cell at 35.0°C and $I = 0.2$ mol dm^{-3} (KNO₃). For each titration,

the requisite amount of fresh solid ligand was weighed out. In all titrations, the concentration of metal ion was 0.001 mol dm^{-3}. The titrations for each set of experiment were carried out thrice to check the reproducibility. Further details of experimental procedure are given in earlier papers[7-9].

The summary of experimental parameters for the systems investigated[10] are as follows:

Solution composition: T_L range 0.002 to 0.004 mol dm^{-3}; T_M range 0.002 mol dm^{-3}; Ionic strength, electrolyte: 0.20 mol dm^{-3}; KNO$_3$; pH range investigated: protonation 1.5 to 10.00; metal complexation 3.00 to 7.5; Experimental method: pH titration, calibrated by measurements in the HCl and NaOH solutions; temperature: 35°C; Method of calculation: SCOGS[11]; Species considered: For protonation H$_3$L, H$_2$L, HL, L, H$_2$A, HA and A; for M(II) binary system: H$_3$L, H$_2$L, HL, L, M, ML, ML$_2$ and H$_2$A, HA, A, M, MA and MA$_2$; for M(II) mixed ligand system: H$_3$L, H$_2$L, HL, L, H$_2$A, AHA, A, M, ML, ML$_2$, MA, MA$_2$ and MLA.

Computation of formation constants and pH-species distribution profiles

The protonation, binary and ternary constants were calculated from the potentiometric titration

Table 1 – Protonation constants of free ligands and formation constants of binary complexes in aqueous medium

[Temp. = 35°C; I = 0.2 mol dm^{-3} (KNO$_3$)]

System	p	q	r	s	logβ	System	p	q	r	s	logβ
Cu.PP	0	1	0	1	8.24(0.03)*	Cu.Phe	0	0	1	1	8.73(0.02)
	0	1	0	2	13.15(0.03)		0	0	1	2	10.85(0.03)
	1	1	0	1	13.58(0.02)		1	0	1	0	7.64(0.02)
	1	1	0	0	8.69(0.02)		1	0	2	0	14.33(0.04)
	1	2	0	0	13.72(0.03)	Cu.Try	0	0	1	1	8.94(0.02)
Cu.TPP	0	1	0	1	7.61(0.03)		0	0	1	2	11.16(0.02)
	0	1	0	2	13.13(0.02)		1	0	1	0	7.96(0.02)
	0	1	0	3	15.06(0.02)		1	0	2	0	15.00(0.03)
	1	1	0	1	12.63(0.04)	Cu.His	0	0	1	1	8.73(0.02)
	1	1	0	0	7.94(0.03)		0	0	1	2	14.59(0.02)
	1	2	0	0	10.98(0.02)		0	0	1	3	16.27(0.03)
Cu.ATP	0	1	0	1	6.58(0.02)		1	0	1	0	9.76(0.02)
	0	1	0	2	10.54(0.03)	Cu.En	0	0	1	1	9.73(0.02)
	1	1	0	1	9.36(0.02)		0	0	1	2	16.69(0.02)
	1	1	0	0	5.96(0.03)		1	0	1	0	10.32(0.02)
Cu.Ala	0	0	1	1	9.32(0.02)		1	0	2	0	19.12(0.03)
	0	0	1	2	11.60(0.03)	Cu.Bipy	0	0	1	1	4.34(0.04)
	1	0	1	0	7.94(0.02)	Cu.Phen	0	0	1	1	5.00(0.03)
	1	0	2	0	14.73(0.03)						
Cu.Ser	0	0	1	1	8.70(0.02)	Cu.Mal	0	0	1	1	5.14(0.02)
	0	0	1	2	10.90(0.02)		0	0	1	2	7.76(0.03)
	1	0	1	0	7.80(0.03)		1	0	1	0	4.78(0.03)
	1	0	2	0	14.54(0.05)						
Cu.Met	0	0	1	1	8.75(0.03)	Cu.Pyr	0	0	1	1	12.88(0.03)
	0	0	1	2	10.83(0.02)		0	0	1	2	22.00(0.03)
	1	0	1	0	7.70(0.03)		1	0	1	0	13.64(0.03)
	1	0	2	0	14.31(0.03)		1	0	2	0	24.08(0.04)

p,q,r,s corresponds to stoichiometric coefficients of metal ion, ligand L, ligand A and protons respectively.
*Values in parentheses indicates accuracy.

data using a corrected version of computer programme SCOGS[11] by takirg into consideration, the relevant species mentioned in the summary of the experimental parameters. The pH-species distribution profiles for various ternary systems were generated by using the Computer programme BEST[12] taking into consideration the relevant protonation, binary and ternary constants.

Results and Discussion

Protonation constants and stepwise formation constants for binary complexes are listed in Table 1 and formation constants for ternary complexes in Table 2. The relative stability of the ternary metal complexes (MLA) as compared to that of the corresponding binary complexe (MA) have been quantitatively expressed in terms of the parameter $\Delta\log K$, given by the expression[13]

$$\Delta \log K = \log K_{MLA}^{ML} - \log K_{MA}^{M} \qquad \ldots (1)$$

These values are listed in Table 2. In order to obtain accurate values of $\Delta\log K$, we have compared the ternary constants with the binary constants evaluated in the present study or reported by us earlier under identical experimental conditions[2-4]. The formation constants for the mono binary complexes of TPP, PP and ATP (Table 1) show that the stability decreases in the order PP > TPP > ATP. The higher stability of Cu(II) complexes containing PP relative to corresponding complexes containing TPP indicates that TPP although potentially tridentate, may be binding the metal ion in a bidentate fashion. The higher stability of the PP-Cu(II) relative to TPP complex can be attributed to the more basic nature of the PP which is reflected in the higher values for dissociation constants (pK_1 and pK_2) of PP relative to the dissociation constants of TPP (pK_2 and pK_3). The $\Delta\log K_b$ values (Eq. 2) for PP and TPP show that the bis binary complexes (ML$_2$) are considerably destabilized due to electrostatic repulsion between the negative charges on the two ligands in the coordination sphere of the metal ion

$$\Delta\log K_b = \log K_{ML_2}^{ML} - \log K_{ML}^{M} \qquad \ldots (2)$$

In ternary Cu(II) complexes, ATP^{4-} coordinates to Cu(II) using β and γ-phosphate oxygens[14]. In case of pyrophosphate (PP) complexes, PP binds to the metal through α and β phosphate oxygens whereas TPP can bind either through β and γ phosphate oxygens, or α and β phosphate oxygens. The statistically expected $\Delta\log K$ value for

Table 2 – The overall formation constants of ternary complexes and the corresponding $\Delta\log K$ values in aqueous medium [Temp. = 35°C; I = 0.2 mol dm^{-3} (KNO$_3$)]

System	p	q	r	s	$\log\beta$	$\Delta\log K$[†]
Cu.PP.Ala	1	1	1	0	15.45(0.03)*	− 1.18(0.05)
Cu.PP.Ser	1	1	1	0	15.32(0.03)	− 1.18(0.05)
Cu.PP.Met	1	1	1	0	15.33(0.02)	− 1.07(0.04)
Cu.PP.Phe	1	1	1	0	15.26(0.04)	− 1.08(0.05)
Cu.PP.Try	1	1	1	0	15.48(0.04)	− 1.18(0.06)
Cu.PP.His	1	1	1	0	16.67(0.04)	− 1.79(0.05)
Cu.PP.In	1	1	1	0	18.25(0.03)	− 0.77(0.04)
Cu.PP.Bipy	1	1	1	0	8.83(0.04)	+ 0.14(0.03)
Cu.PP.Phen	1	1	1	0	8.79(0.03)	+ 0.10(0.02)
Cu.PP.Mal	1	1	1	0	11.68(0.03)	− 1.80(0.04)
Cu.PP.Cat	1	1	1	0	19.81(0.03)	− 2.53(0.05)
Cu.TPP.Ala	1	1	1	0	14.34(0.02)	− 1.54(0.04)
Cu.TPP.Ser	1	1	1	0	14.25(0.03)	− 1.49(0.04)
Cu.TPP.Met	1	1	1	0	14.13(0.03)	− 1.51(0.05)
Cu.TPP.Phe	1	1	1	0	13.98(0.04)	− 1.60(0.06)
Cu.TPP.Try	1	1	1	0	14.43(0.03)	− 1.47(0.05)
Cu.TPP.His	1	1	1	0	15.57(0.04)	− 2.13(0.06)
Cu.TPP.En	1	1	1	0	17.13(0.03)	− 1.13(0.05)
Cu.TPP.Bipy	1	1	1	0	8.09(0.02)	+ 0.15(0.03)
Cu.TPP.Phen	1	1	1	0	8.26(0.02)	+ 0.32(0.04)
Cu.TPP.Mal	1	1	1	0	10.61(0.03)	− 2.11(0.05)
Cu.TPP.Cat	1	1	1	0	18.72(0.03)	− 2.86(0.05)
Cu.ATP.Ala	1	1	1	0	12.97(0.02)	− 0.93(0.03)
Cu.ATP.Met	1	1	1	0	12.57(0.02)	− 1.09(0.03)
Cu.ATP.Phe	1	1	1	0	12.92(0.02)	− 0.68(0.04)
Cu.ATP.Try	1	1	1	0	13.20(0.03)	− 0.72(0.04)
Cu.ATP.His	1	1	1	0	14.50(0.03)	− 1.22(0.04)
Cu.ATP.Bipy	1	1	1	0	6.38(0.02)	+ 0.42(0.03)
Cu.ATP.Phen	1	1	1	0	6.53(0.02)	+ 0.57(0.03)

*Values in parentheses indicate accuracy.
†$\log K$ is defined in Eq. 1.

the interaction of two different bidentate ligands with a square planar or distorted octahedral metal ion are − 0.6 or − 0.9 respectively[13]. The $\Delta\log K$ values for mixed ligand complexes containing Ala, Ser, Met, Phe, Try and His (Table 2) are more negative than expected on the statistical grounds due to electrostatic repulsion between the negatively charged oxygens of the amino acids and phosphate oxygens of TPP and PP. In all these systems, the higher negative charge on TPP^{5-} as compared to PP^{4-} results in greater destabilization of ternary complexes containing TPP. In con-
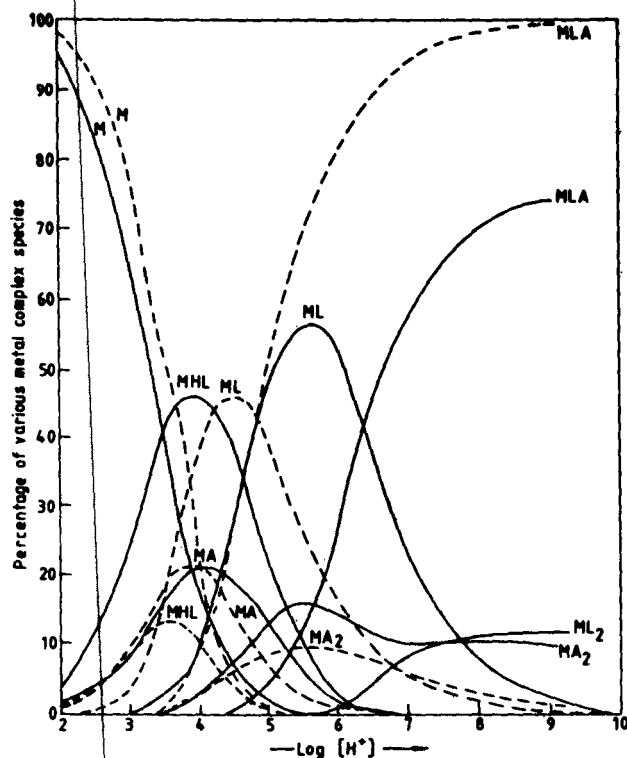
Fig. 1 — pH-Species distribution profile for the ternary 1:1:1 ATP: Cu(II):Phenylalanine (dotted lines) and for 1:1:1 TPP:Cu(II):Phenylalanine system (thick lines). Ordinate represents the percentage of a given metal complex species as a function of the total metal concentration L=ATP or TPP; M = Cu(II); A = phenylalanine M = L = A = 1 × 10^{-3}; Temp. = 35°C, I = 0.2 mol dm^{-3} (KNO$_3$)

trast to this, the corresponding ternary Cu(II) complexes containing ATP^{4-} and the amino acids Phe and Try are considerably more stable (Table 2) due to intramolecular metal ion mediated stacking interactions between aromatic moieties of the amino acids and the adenine ring of ATP[15-18]. The absence of such stacking interactions with TPP or PP leads to lower stability which is reflected in a representative pH-species distribution profile (Fig. 1). It is observed that in Cu(II) complexes containing ATP and Phe, the percentage of ternary complex at pH 7.4 is ≈97%, whereas the corresponding complex of TPP is present only to the extent of ≈64%.

It is observed that the ternary Cu(II) complexes containing Bipy or Phen and TPP, PP or ATP are characterised by positive $\Delta \log K$ values (Table 2). This can be attributed to the metal dπ → ligand pπ retro bonding which causes the metal ion to be more electropositive than in the aquo metal ion, thereby enhancing the binding of the negatively charged oxygen donor ligands[17-19]. Ternary Cu(II) complexes containing ATP and Bipy or

Phen are further stabilized by stacking interactions mentioned above. The calculations of the concentration of the ternary complex as a function of pH shows that at pH 7.4, the percentage of this species is ≈99% for all the ternary systems. Due to the absence of retrobonding effects, ternary complexes containing EN are characterized by negative $\Delta \log K$ values.

The $\Delta \log K$ values for ternary complexes containing Mal or Pyr (Table 2) are considerably negative reflecting the extensive destabilization of these complexes. In these systems, the stabilizing influences of stacking or retrobonding are not possible and hence the electrostatic repulsion between the negatively charged ligands L and A play a predominant role in destabilizing these complexes. At pH 7.4, the percentage of the ternary complexes containing TPP/PP and Pyr is only ≈70%. ·

The present investigation shows that for various ternary complexes (MLA) containing ligand A with an aromatic amine such as Bipy or Phen, the stability of the complexes with respect to the ligand L varies in the order ATP^{4-} > TPP^{5-} ≥ PP^{4-}, whereas in ternary complexes where A is an amino acid with an aromatic side chain such as Phe or Try, the order varies as ATP^{4-} > PP^{4-} > TPP^{5-}. Inspite of the fact that all the three ligands bind the metal ion in ternary complexes through phosphate oxygens, the presence of the purine ring in ATP enables it to stack with the aromatic moieties of the second ligand which may be biological significance.

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References

1 Smith R M, Martell A E, Critical stability constants, Vols 1-6 (Plenum, New York) 1974, 74, 76, 77, 1982, 1989.
2 Prasad K & Srinivas Mohan M, J coord Chem, 16 (1987) 1.
3 Prasad K, Koteshwar Rao A & Srinivas Mohan M, J coord Chem, 16 (1987) 251.
4 Prasad K, Srinivas Mohan M & Bhathina H B, J coord Chem, 17 (1988) 63.
5 Flashka H A, EDTA titrations (Pergamon Press, Oxford) 1964.
6 Schwarzenbach G & Biederman R, Helv chim Acta, 31 (1948) 337.
7 Srinivas Mohan M, Bancroft D & Abbott E H, Inorg Chem, 18 (1979) 175.
8 Srinivas Mohan M, Bancroft D & Abbott E H, Inorg Chem, 18 (1979) 344.
9 Srinivas Mohan M, Bancroft D & Abbott E H, Inorg Chem, 18 (1979) 2468.

10 Tuck D G, *Pure &Appl Chem*, 61 (1989) 1161.
11 Sayce I G, *Talanta*, 15 (1968) 1397.
12 Martell A E & Motekaities R J, *The determination and use of stability of constants* (Marcell Dekker, New York) 1988.
13 Sigel H, *Angew Chem Int Ed Engl*, 14 (1975) 194.
14 Tribolet R, Martin R B & Sigel H, *Inorg Chem*, 26 (1987) 638.

15 Koteshwar Rao A & Srinivas Mohan M, *Proc Indian Acad Sci (Chem Sci)*, 101 (1989) 1.
16 Sigel H & Naumann C F, *J Am chem Soc*, 98 (1976) 730.
17 Bhattacharya P K, *J scient Ind Res*, 40 (1981) 382.
18 Sigel H, *Metal ions in biological systems*, Vol. 2 (Marcell Dekker, New York) 1973.
19 Srinivas Mohan M, Bancroft D & Abbott E H, *Inorg Chem*, 18 (1979) 1527.