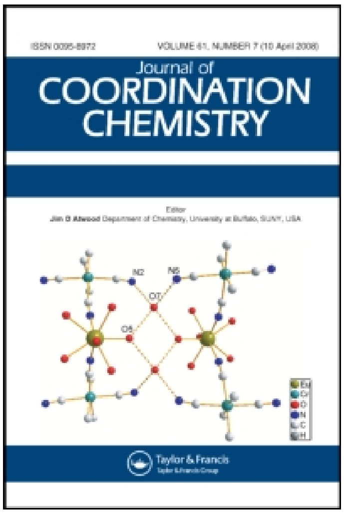

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TERNARY COMPLEXES OF TRANSITION METAL IONS WITH ADENOSINE-5′-TRIPHOSPHATE AND 1,10-PHENANTHROLINE

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Potentiometric studies show that in solutions containing a 1:1:1 molar ratio of adenosine-5′-triphosphate, 1,10-phenanthroline and a bivalent metal ion, stable ternary complexes are formed with transition metal ions (metal=Cu(II), Zn(II) and Mn(II)) but not with alkaline earth metal ions (metal=Ca(II) and Mg(II)). Potentiometric studies further show that the 1:1 adenosine-5′-triphosphate-metal chelates have very little or no tendency to further interact with another adenosine-5′-triphosphate molecule or a sulphosalicylic acid molecule. Stability constants for the various binary and ternary metal complexes are reported at 35.0° and $\mu = 0.1(KNO_3)$.

INTRODUCTION

In view of the participation of bivalent metal ions in the biological functions of adenosine-5′-triphosphate (ATP), a detailed study of the stability and the thermodynamic quantities associated with the formation of 1:1 chelates of ATP with a number of bivalent metal ions, has been carried out by Khan and Martell.[1] However, the in vivo activation of enzyme catalysed reactions of ATP by bivalent metal ions, implies the formation of mixed complexes involving the enzyme, ATP and the metal ion. Useful information regarding such biological mixed ligand complexes can be obtained by studying model ternary complexes formed by a metal ion with ATP and a secondary ligand. Studies of ternary systems would also reveal the nature and extent of statistical, steric and electrostatic restrictions imposed by a ligand already bound to a metal ion towards further complexation with other ligands. Sigel, *et al*,[2] have previously investigated the stabilities of ternary complexes in solutions containing ATP, $\alpha\alpha'$ dipyridyl and a few bivalent metal ions. Rajan[3,4] has studied the ternary complexes of Mg(II) and Fe(II) with ATP and a number of biogenic amines. In the present work complex formation in solutions containing a 1:2 molar ratio of metal ion and ATP, and in solutions containing a 1:1:1 molar ratio of metal ion, ATP and 1,10-phenanthroline (PHEN) or sulphosalicylic acid (SSA) has been investigated. The metal ions studied include Cu(II), Zn(II), Mn(II), Mg(II) and Ca(II).

EXPERIMENTAL

Materials Adenosine-5′-triphosphate disodium was obtained from Mann Research Laboratories, U.S.A.; 1-10-phenanthroline and 5-sulfosalicylic acid were obtained from Eastman Kodak Co. Ethylenediamine tetraacetic acid disodium salt (EDTA) and potassium acid phthalate were of the B.D.H. Analar grade. Carbonate free-sodium hydroxide was standardised by titration with potassium acid phthalate. Stock solutions of the metal salts (.02 M) were prepared and standardised by EDTA titration by the method of Schwarzenbach.[5] Standard stock solutions of SSA and PHEN (.02 M) in the diprotonated form were prepared. ATP was weighed directly into the reaction vessel in the solid form to avoid any possible hydrolysis. The purity of all ligands was further checked by potentiometric titrations.

Method Titrations were carried out in a 50 ml jacketed titration cell serviced by a constant temperature bath at 35.0° ± 0.1°. The cell was fitted with a

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rubber stopper which held nitrogen inlet and outlet tubes, delivery tube from a 5 ml microburette and electrodes. During titrations a magnetic stirrer was employed and a positive pressure of CO_2-free nitrogen, presaturated at 35.0°, was maintained in the reaction cell. In all titrations the ionic strength of the reaction solution was made initially to be 0.1 M, by suitable addition of KNO_3. The binary systems were investigated with a 1:1 molar ratio of metal ion and ligand while in the ternary systems a 1:1:1 molar ratio was employed. The concentration of the metal ion was 2.0×10^{-3} M. Multiple titrations were carried out for each system.

The changes in the pH of the solution during the titrations were determined with a Elico pH meter equipped with a Phillips combined electrode. The electrode system was calibrated by direct titration of acetic acid, the observed pH meter reading being compared with the actual hydrogen ion concentration calculated from data tabulated by Harned and Owen.[6] The pH regions below 3.5 and above 10.5 were calibrated by measurements in the HCl and NaOH solutions respectively.

Calculations The dissociation constants for the free ligands (K_a and K_{2a}) and the stability constants for the following equilibria were calculated from the

$$M^{2+} + HATP^{3-} \xrightleftharpoons{K^{M}_{MHA}} M(HATP)^{-} \qquad (1)$$

$$M^{2+} + ATP^{4-} \xrightleftharpoons{K^{M}_{MA}} M(ATP)^{2-} \qquad (2)$$

$$M^{2+} + PHEN \xrightleftharpoons{K^{M}_{ML}} M(PHEN)^{2+} \qquad (3)$$

$$M(PHEN)^{2+} + HATP^{3-} \xrightleftharpoons{K^{ML}_{MHLA}} M(PHEN)(HATP)^{-} \qquad (4)$$

$$M(PHEN)^{2+} + ATP^{4-} \xrightleftharpoons{K^{ML}_{MLA}} M(PHEN)(ATP)^{2-} \qquad (5)$$

titration data using a corrected version of the computer program SCOGS.[7]

RESULTS

1:1 metal–ligand systems To facilitate the interpretation of titration curves and data of the 1:2 metal-ligand and the 1:1:1 ternary systems, the stability constants of the 1:1 metal–ATP and metal–PHEN chelate species were redetermined at 35.0°

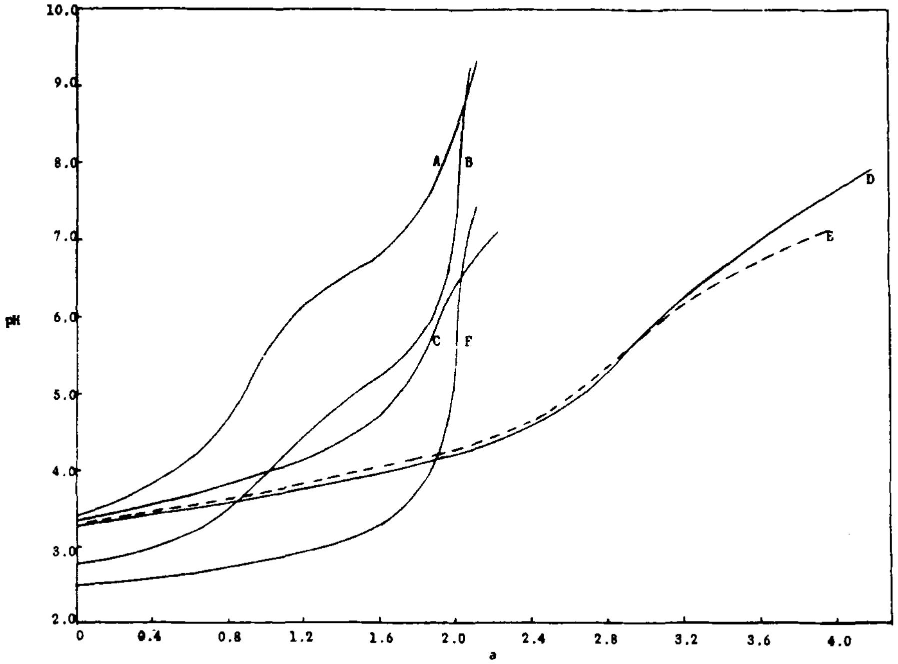

FIGURE 1 Titration curves for 1:1 and 1:2 metal–ATP and 1:1 metal–PHEN systems at 35.0° and $\mu = 0.1$ (KNO_3). A = ATP, B = PHEN, C = 1:1 Cu(II)–ATP curve, D = 1:2 Cu(II)–ATP experimental curve, E = 1:2 Cu(II)–ATP calculated curve, F = 1:1 Zn(II)–PHEN. Similar curves were obtained for other metal ions. a = moles of base added per mole of ligand. For curves D and E the abscissa represents m, the moles of base added per mole of metal ion.

TABLE I
Stability constants of the 1:1 metal chelates with ATP and PHEN. t = 35.0°, $\mu = 0.1$ (KNO_3)

	$\log K_a = 3.90 \pm .02$ ATP	$\log K_{2a} = 6.67 \pm .01$	$\log K_a = 2.13 \pm .04$ PHEN	$\log K_{2a} = 5.03 \pm .01$
Metal	$\log K^{M}_{MHA}$	$\log K^{M}_{MA}$	$\log K^{M}_{ML}$	
Cu(II)	3.59 ± .08	6.34 ± .03	7.49 ± .10	
Zn(II)	2.68 ± .06	5.25 ± .01	5.94 ± .02	
Mn(II)	3.11 ± .04	5.25 ± .02	4.23 ± .04	
Mg(II)	2.77 ± .02	4.50 ± .01	2.21 ± .02	
Ca(II)	2.16 ± .07	3.91 ± .01	2.20 ± .02	

and $\mu = 0.1(KNO_3)$. Titrations of solutions containing a 1:1 molar ratio of a metal ion and ATP or PHEN resulted in a steep inflexion at a = 2 for all the metal ions studied (Figure 1–C,F). In the titrations of PHEN with Mg(II) or Ca(II) the 1:1 curve overlaps with the free PHEN curve till a = 1, indicating that the first proton of the ligand is neutralised before complex formation. The stability constants of the protonated and normal metal–ATP chelates and the stability constants of the normal metal–PHEN chelates were calculated and are listed in Table I. These constants are in agreement with those reported earlier.[8]

1:2 metal–ATP systems The possibility of the formation of metal chelates involving the attachment of two ATP molecules to a single metal ion was investigated by potentiometric titration of solutions containing a 1:2 molar ratio of metal ion and ATP. In these titrations an inflexion was obtained at m = 3 (Figure 1–D), where m = moles of base per gram ion of metal. Attempts to calculate formation constants for 1:2 metal–ATP complexes proved unsuccessful. By addition of the abscissas of separate potentiometric curves for ATP and the 1:1 metal–ATP chelate, a calculated curve can be obtained for a system involving no interaction between the second mole of ATP and the 1:1 chelate. Figure 1–E shows that the calculated curve more or less overlaps the experimental curve indicating that 1:2 chelate compounds are not formed in significant amounts under the experimental conditions employed.

Ternary Systems

1:1:1 metal–ATP–SSA Potentiometric titration of solutions containing metal ion, ATP and SSA were carried out to investigate the possible formation of ternary complexes. As in the case of the 1:2 metal–ATP systems, an inflexion was obtained at m = 3 and the calculated curve obtained for a system involving no interaction between SSA and the 1:1 metal–ATP chelate is found to overlap with the experimental 1:1:1 curves, (Figure 2-A,B). Thus there seems to be no appreciable complexation of SSA with the 1:1 metal–ATP chelates.

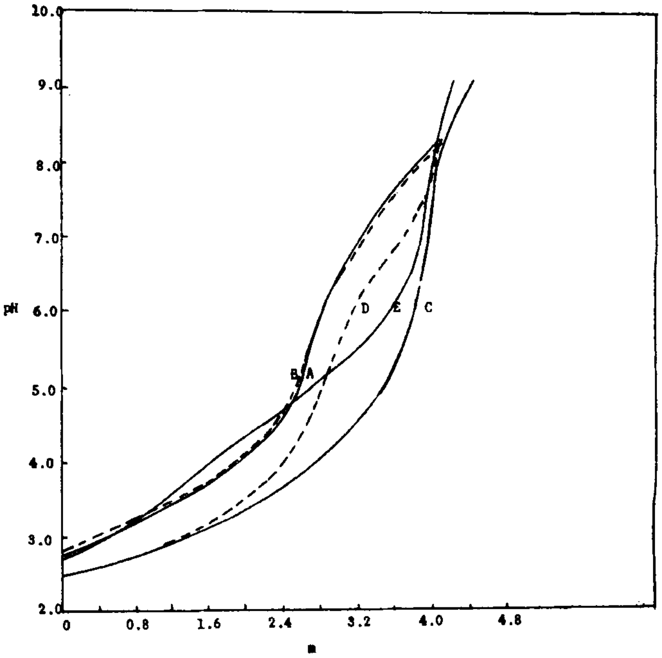

FIGURE 2 Titration curves for ternary systems involving metal ion, ATP and PHEN or SSA at 35.0° and $\mu = 0.1$ (KNO_3). A = 1:1:1 Cu(II)-ATP-SSA experimental curve, B = 1:1:1 Cu(II)-ATP-SSA calculated curve, C = 1:1:1 Zn(II)-ATP-PHEN experimental curve, D = 1:1:1 Zn(II)-ATP-PHEN calculated curve, E = 1:1:1 Mg(II)-ATP-PHEN experimental curve. Similar curves were obtained for other metal ions. m = moles of base added per mole of metal ion.

1:1:1 metal–ATP–PHEN Titration of solutions

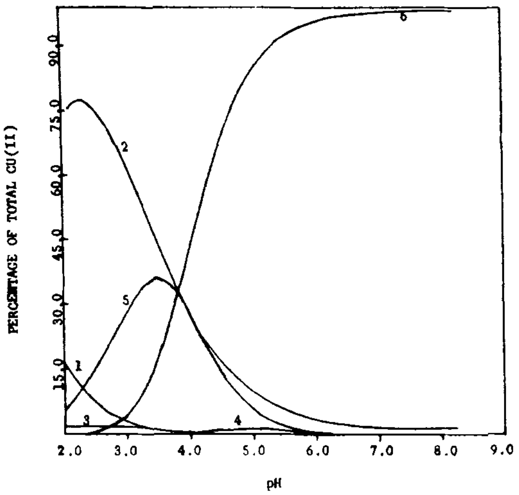

FIGURE 3 Variation with pH of the composition of a solution of copper(II) ions (0.002M), PHEN (0.002M) and ATP (0.002M). Curves 1–6 show the percentage of the total copper present as free metal ion, Cu:PHEN, Cu:HATP, Cu:ATP, Cu:HATP:PHEN and Cu:ATP:PHEN respectively, calculated from the constants in Tables I and II.

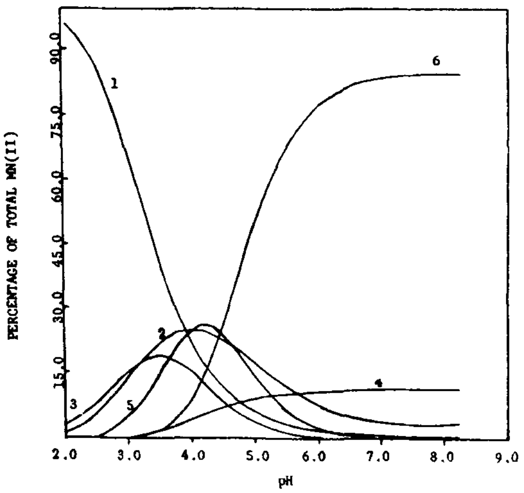

FIGURE 5 Variation with pH of the composition of a solution of manganese(II) ions (0.002M), PHEN (0.002M) and ATP (0.002M). Curves 1–6 show the percentage of the total manganese present as free metal ion, Mn:PHEN, Mn:HATP, Mn:ATP, Mn:HATP:PHEN and Mn:ATP:PHEN respectively, calculated from the constants listed in Tables I and II.

containing a 1:1:1 molar ratio of metal ion, ATP and PHEN resulted in a steep inflexion at m = 4 for all the metal ions studied (Figures 2–C,E). Computer analysis of the titration curves obtained for ternary systems involving Cu(II), Zn(II) or Mn(II) as the metal ion indicated the formation of both protonated and normal ternary complexes. The equilibrium constants for these complexes are given in Table II. Figures 3,4 and 5 represent diagrametrically the percentage distribution of the various metal complex species as a function of pH. Attempts to calculate the equilibrium constants of any ternary complexes formed in systems containing a 1:1:1 molar ratio of ATP, PHEN and either Ca(II) or Mg(II) as the metal ion proved unsuccessful, indicating that in these systems ternary complexes are not formed in significant amounts under the experimental conditions employed.

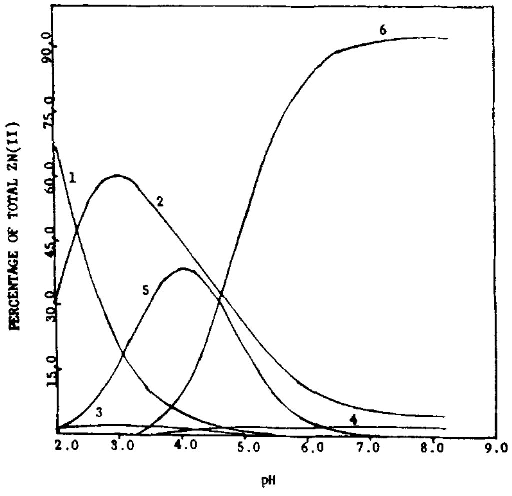

FIGURE 4 Variation with pH of the composition of a solution of zinc(II) ions (0.002M), PHEN (0.002M) and ATP (0.002M). Curves 1–6 show the percentage of the total zinc present as free metal ion, Zn:PHEN, Zn:HATP, Zn:ATP, Zn:HATP:PHEN and Zn:ATP:PHEN respectively, calculated from the constants in Tables I and II.

TABLE II
Stability constants of the ternary metal complexes involving PHEN and ATP. t = 35.0°, $\mu = 0.1$ (KNO_3)

Metal	$\log K_{MLHA}^{ML}$	$\log K_{MLA}^{ML}$	$\log K_{MLA}^{M}$ [a]
Cu(II)	3.51	6.38	13.87 ± .05
Zn(II)	3.21	5.29	11.23 ± .02
Mn(II)	3.29	5.51	9.73 ± .03
Mg(II)	–	–	–
Ca(II)	–	–	–

[a] Overall stability constants for the equilibrium $M + L + A \rightleftharpoons MLA$

DISCUSSION

Binary Complexes

The comparison of the stability constants of the 1:1 normal metal–ATP chelates with the corresponding PHEN chelates, Table I, shows that complexes of Mn(II), Mg(II), and Ca(II) with ATP are more stable than those formed with PHEN. The reverse order of stability is found in the Cu(II) and Zn(II) chelates. These results are in accordance with Pearsons HSAB principle[9] whereby hard acids like Mg(II), Ca(II) and Mn(II) prefer complexation with a hard base like phosphate ion, whereas Cu(II) and Zn(II) show greater interaction with the relatively softer nitrogen donors on PHEN.

The study of the 1:2 metal–ATP systems show that the 1:1 metal–ATP chelate has little or no affinity to further interact with a second ATP molecule. This is expected on the basis of statistical, steric and electrostatic considerations. Complex formation between the positively charged aquo metal ion and the anionic ATP molecule to form a 1:1 chelate is strongly favoured by electrostatic attraction between the two. However, the negative charges on the ATP moleucle in the 1:1 metal–ATP chelate will then strongly hinder further interaction with a second anionic ATP molecule, due to electrostatic repulsion. This is further substantiated by the lack of interaction between the 1:1 ATP metal chelates and SSA which is a less bulky anionic oxygen donor.

Ternary Complexes

The equilibrium constants of the ternary metal complexes listed in Table II and the species distribution plots in Figures 3,4 and 5 clearly show that stable ternary protonated and normal complexes are formed in systems containing ATP, PHEN and a transition metal ion. On a purely statistical basis $\log K^{ML}_{MHLA}$ and $\log K^{ML}_{MLA}$ are expected to be lower than $\log K^{M}_{MHA}$ and $\log K^{M}_{MA}$ respectively, by a factor of 0.6 for square planar complexes and 0.4 for octahedral complexes.[10] However, comparison of data in Table I and II show that the 1:1 complexes of PHEN with transition metal ions have equal to if not greater tendancy to interact with an ATP molecule, than the free aquo metal ion. This enhanced stability of the ternary complexes involving transition metal ions is obviously due to electrostatic[11] and π-bonding effects. Complexation of bivalent metal ions by PHEN through its two nitrogen atoms gives rise to positively charged metal complex species. Further complexation with an anionic ATP molecule according to the equilibria 4 and 5 is favoured both by coulombic attraction (enthalpy) and release of the oriented solvent molecules (entropy) resulting from the neutralization of charge. In complexes involving PHEN and a transition metal ion, in addition to the σ bonding, strong $M \rightarrow N\pi$ interaction involving back donation of electrons from the metal $d\pi$ orbitals to the vacant delocalised $p\pi$ orbitals over the PHEN molecule takes place.[12] Due to these $d\pi$–$p\pi$ interactions, the effective positive charge on the metal ion may remain more or less the same, as on the free aquo metal ion, thereby facilitating interaction with an anionic ATP molecule. NMR experiments[13,14] have shown that in the 1:1 metal complexes of ATP with Cu(II), Zn(II) and Mn(II), coordination takes place both through the phosphate and the adenine moieties. With four coordinate metal ions like Cu(II) and Zn(II), formation of stable ternary complexes implies that the bidentate PHEN displaces ATP from one of its coordinating sites on the metal ion. Sigel[2] by NMR experiments has shown that in ternary systems involving Cu(II), ATP and α, α' bipyridyl, the metal ion is no longer bound to the adenine ring of the ATP molecule. It is possible that this holds good for system involving ATP, PHEN and Cu(II) or Zn(II).

Evidence of appreciable ternary complex formation in systems involving PHEN, ATP and Mg(II) or Ca(II) could not be obtained potentiometrically, reflecting on the low stabilities of these complexes. Absence of π-bonding effects in the PHEN alkaline earth–metal complexes and statistical effects could be two reasons for this. Although numerous studies on the ternary complex formation involving transition metal ions have been carried out,[15] studies on systems involving the alkaline earth metal ions are very few. Experimental techniques more suited for determining the stability constants of weak complexes may be used to investigate ternary complexation involving the biologically important Mg(II) and Ca(II) ions.

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REFERENCES

1. M. M. Taqui Khan and A. E. Martell, *J. Amer. Chem. Soc.*, **88**, 668 (1966).
2. H. Sigel, K. Becker and D. B. McCormick, *Biochemica et Biophysica Acta.*, **148**, 655 (1967).

3. K. S. Rajan, *J. Neurochem.*, **18**, 345 (1971).
4. K. S. Rajan, *J. Neurochem.*, **19**, 1099 (1972).
5. G. Schwarzenbach, *Complexometric Titrations*, pp. 76–82, Interscience, New York (1957).
6. H. S. Harned and B. B. Owen, *Physical Chemistry of Electrolyte Solutions*, 3rd Edn., pp. 638, 752, Reinhold, New York (1958).
7. I. G. Sayce, *Talanta*, **15**, 1397 (1968).
8. R. M. Smith and A. E. Martell, Critical Stability Constants, Vol. 2, Plenum Press, New York (1975).
9. R. G. Pearson, *J. Chem. Educ.*, **45**, 581 and 643 (1963).
10. H. Sigel, *Angew. Chem. Internat. Edit.*, **14**, 394 (1975).
11. G. A. L'Heureux and A. E. Martell, *J. Inorg. Nucl. Chem.*, **28**, 481 (1966).
12. K. Nakamoto, *Infrared Spectra of Inorganic and Coordination Compounds*, John Wiley, New York, pp. 193 (1963).
13. H. Sternlicht, R. B. Shulman and E. W. Anderson, *J. Chem. Phys.*, **43**, 3123 (1965).
14. H. Sternlicht, R. B. Shulman and E. W. Anderson, *J. Chem. Phys.*, **43**, 3133 (1965).
15. H. Sigel, *Metal Ions in Biological Systems*, Vol. 2, pp. 63, Marcell Dekker, Inc., New York (1973).