

Studies on Mixed Ligand Complexes of Bivalent Metal Ions with 4,6-Diamino-2-Mercapto Pyrimidine

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Abstract: Interaction of Bivalent ions Mg(II),Ca(II), Sr(II), Ba(II), Co (II), Ni (II), Cu (II), Zn (II), Cd(II), Th(II), UO₂(II) with 4,6 – Diamino-2– MercaptoPyrimidine (DAMP) in presence of other ligands such as Oxalic acid (Ox), Succinic acid (Sua), Malonic acid (Mal), O-Phenylenediamine (OPDA), 2,2-Bipyridyl (Bipy), 1, 10-Phenanthroline (Phen) and Ethylenediamine (En) has been investigated by potentiometric studies. The ternary complexes are formed in stepwise manner in which DAMP behaves as primary ligand. The stability constants of ternary complexes have been reported at 35⁰ C and at $\mu=0.1\text{M KNO}_3$ in aqueous solution. The stability constants reveals that the order in terms of ligand (L) prefers O-O > N-N and the sequence is supported by the argument that M (II) \rightarrow Bipy/Phen π - interaction makes ternary complexes more stable.

Key Words: Substituted Pyrimidines: 4,6-Diamino-2 Mercapto Pyrimidines, Alkaline Earth Metals, Transition Metal ions, Rare Earth Metals, Secondary ligands Oxalic, Succinic, Malonic acid, O-Phenylenediamine (OPDA), 2,2 – Bipyridyl (Bipy), 1, 10 – Phenanthroline (Phen) and Ethylenediamine (En).

Introduction

Purines and pyrimidine molecules are very important in biological systems and are essential components of the nucleic acids. Metal ions are also required for the incorporation of purine and pyrimidine nucleosides in the DNA and RNA molecules. The presence of Ca(II),Mg(II) and Fe(III)¹⁻². Enhances the stability of double helix of DNA where as Cu(II) destabilises the double helix of DNA by forming cross links between the strands of unwound DNA and facilitates the separation of strands from each other. Therefore, to aid in the understanding of these important biological systems, much work has been concentrated as the study of metal ion interaction with isolated nucleic bases, nucleosides and nucleotides⁽³⁻⁷⁾. Substituted purines and pyrimidines are also proved biologically active. The divalent ions forms binary system with purines and pyrimidines⁹ in which purines mostly act as bidentate ligands and pyrimidines act as monodentate ligands in co-ordinating to a metal ion. Purines coordinate to metal ion through N₍₃₎ and N₍₉₎ positions forming chelated complexes, where as pyrimidines coordinate to the metal ion through N₍₃₎ position. The proton dissociation and its release is an important factor in determining the extent and nature of the metal ligand interaction in a metal nucleoside complex and its process of dissociation is investigated⁽¹¹⁻¹²⁾ in some cases. It is of great interest to study the metal ligand interaction in a metal nucleoside complex since metal ions plays important role in several biological reactions¹³. It is evident from the literature that most of the earlier investigations have been confined to spectroscopic methods on metal nucleoside complexes and less work has been reported an effect of the stability of the systems in solutions and also observed that the data are ternary complexes, which act as good models for metalloenzyme reactions is remarkably absent with respect to the physicochemical properties such as stability of the complexes with metal ions. Literature reveals that the metal- ligand stability constants of some diketones, substituted pyrazolines, isoxalline and some other substituted pyrimidines have been reported recently¹⁴. No reports have appeared for the interaction of 4,6-diamino-2-mercaptopyrimidine and some selected ligands with transition metal ions. Hence, it was considered an important to study in detail the

formation and stability of mixed ligand complexes of 4,6-diamino-2-mercaptopyrimidine with Mg(II),Ca(II), Sr(II), Ba(II), Co (II), Ni (II), Cu (II), Zn (II), Cd(II), Th(II), UO₂(II). The stability constants of the above complexes are addressed in this paper.

Experimental

Materials:

The 4,6-diamino-2-mercaptopyrimidine was purchased from sigma chemical company. 2,2- bipyridyl (bipy), 1,10-phenanthroline (phen), orthophenyldiamine (OPDA), oxalic acid (Ox), malonic acid (MAL), and succinic acid (SUA), were obtained from E. Merck, Darmstads. Alkaline Earth Metals Ca(II), Mg(II), Sr(II), Ba(II) and Transition metal nitrate of, Co(II), Ni(II), Cd(II), Cu(II), and Zn(II) used are of BDH/Analar grade. Rare earth metal nitrates Th(II), UO₂(II) (Actinides) have been obtained from Indian Rare-earth Ltd, Udyogamandal, Kerala. Sodium hydroxide, Potassium nitrate, Nitric acid and EDTA are of BDH/Analar grade. Deionised water used distilled twice.

Measurements

All measurements were carried out at $35 \pm 1^{\circ}\text{C}$ Digisun made digital p^H meter model D I – 707 with Toshiniwal combination glass electrode has been used to record p^H values. The electrode system has been calibrated using p^H 4.0, 7.0 and 9.2 buffers. The solution has been examined from time to time throughout the course of each titration to confirm that no precipitation occurred in the system. The metal ion solutions have been prepared using double distilled water and the concentrations is estimated by complexometric titrations using standard EDTA solutions as suggested by Flaskha¹⁶. The Rare Earth Metal ion solutions also prepared in double distilled water and standardised by EDTA titrations according to Schwarzenbach¹⁷. All the dissociation and the complex formation were determined using the BEST program.

Method

The potentiometric titrations have been carried out by taking 50ml of the reaction mixture into a double walled glass titration cell provided with an inlet and outlet for the circulation of water constant temp from the thermostat. Each ligand was titrated with standard sodium hydroxide solution in the absence and presence of metal ion. For binary systems of 1:1 metal to ligand molar ratio and for ternary system 1:1:1 metal, primary ligand and secondary ligand and concentration of metal ion was 0.0004M and the ionic strength of the solution was maintained at 0.1M KNO₃. The temperature was maintained at $35 \pm 0.1^{\circ}\text{C}$, pre-saturated Nitrogen was passed through the solution throughout the course of the titration. The experimental procedure involved the titration of the following sets of solutions against standard alkali (NaOH).

1. Mineral acid (HNO₃)(0.04M) ----- Acid titration
2. Mineral acid + Ligand (0.0002M) ----- Ligand titration
3. Mineral acid + Ligand + Metal ion (0.0004M) ----- Metal titration

Data Processing

Protonation constants of free ligand, formation constants of protonated metal complexes, monobinary complexes, bis binary complexes were calculated by P.C PB-410 and ternary metal complexes were calculated by BEST according to Martell & Motekaitis^{19,20}. The distributions and concentration of various species present as a function of pH were also computed from known constants in the form of pH species distribution profiles by using the computer programme BEST²¹.

Results And Discussion

Binary Systems

The relative basicities of ligand have been measured in terms of their acid dissociation constants. Acid dissociation constant of the DAMP also a prerequisite for evaluation of the metal – ligand stability constants, acid dissociation of DAMP. Potentiometric titration of the ligand 4,6-diamino-2 –mercaptopyrimidine(DAMP)

suggests the protonation of $N_{(1)}$ or $N_{(3)}$ of DAMP. The acid dissociation equilibrium of this ligand is represented by the following equations.



The pH was noted in aqueous medium each time after the addition of small amounts of alkali from a calibrated microburette set. Titration curves are obtained by plotting pH against the volume of alkali added.

From the acid and ligand pH titration curve, the value of n_H (average no. of proton bound to the ligand molecules), at each pH value have been calculated using Eq-1 according to Irving & Rosotti¹⁸. Similarly the values of \bar{n} (average no. of ligands bound to the metal ion) and pL (free ligand exponent) have been evaluated from the ligand and metal titration curves, using eqns -2&3 respectively.

$$\bar{n} = (V_1 - V_2) \{N + E^0 + T_L^0 (Y - \bar{n}_H)\} / (V^0 + V_2) / \bar{n}_H T_M^0 \text{ ----- (1)}$$

$$pL = \log \left[\sum_{j=0}^{j=j} \frac{\beta_j^H (1/\text{antilog pH})^j}{T_L^0 - \bar{n} T_M^0} \times \frac{(V^0 + V_3)}{V^0} \right] \text{ ----- (2)}$$

Where \bar{n}_H = average number of protons bound to the ligand molecule at each pH

E^0 = Total initial conc. Of mineral acid (HNO_3)

N = Normality of base (NaOH)

V^0 = Total initial Volume (50.0ml)

V_1, V_2 & V_3 = Volumes of the base consumed to reach a given pH value on titration curves of acid, ligand and metal respectively.

T_L^0 = Total initial conc. of ligand

T_M^0 = Total initial conc. of metal

Y = The no. of displaceable protons in the ligand

β_j^H = Successive overall proton ligand formation constants.

The \bar{n}_H , \bar{n} and pL values obtained at a given pH values are calculate the proton ligand as well as metal ligand stability constants.

It is evident from the equations that the first proton dissociation is from $N_{(3)}$ proved with its p^{Ka} value 3.33, the second proton dissociation is from $C_2 - S$ and the third proton from $^+NH_3$ group. (Scheme-1)

From the acid and ligand p^H titration curves, the values of \bar{n}_H (average number of protons bound to the ligand molecule) at each p^H value have been calculated using Irving and Rossotti given below .

$$\bar{n}_H = Y + \frac{(V_1 - V_2) (N + E^0)}{(V_0 + V_1) T_L^0} \text{ (3)}$$

Where Y denotes the displaceable protons in the ligand, N is the normality of base (NaOH), V_0 is the total initial volume, V_1 is the volume of base consumed to reach a given p^H value of titration curve of acid and base respectively, E^0 is the total initial concentration of mineral acid (HNO_3) and T_L^0 is the total initial concentration of ligand.

The ligand dissociation constant has been determined at 25^o, 35^o and 45^oC and thermodynamic parameters ΔG , ΔH and ΔS for the dissociation equilibrium are presented in Table I.

The positive free energy change (ΔG) reveals the nonspontaneous nature of the ionization reaction in the solution and positive enthalpy suggests the endothermic nature of the dissociation process. The negative entropy change illustrates that it is the major controlling factor in the acid dissociation reaction of these ligands. The acid – base equilibria are sensitive to change in the dielectric constants and the basicity of the medium. Lowering the dielectric constant increases the electrostatic attractive forces between ions and hence it facilitates the formation of neutral molecular species. The distribution diagrams for DAMP (Fig-1) suggest that at pH 3.0, H_3L^{2+} present to the extent of 70% and H_2L^+ present to 30%. H_3L^{2+} has come down to 50% at pH 3.30 where H_2L^+ is increased to 50% at the same pH, which corresponds to the pk_1 value of this ligand. At pH 5.3 pk_2 , the species H_2L^+ & HL are to the extent of 50% each. At higher pH, the predominant species is HL. At pH 10.06 pk_3 , the species HL and L^- are to the extent of 50% each. At higher pH, the predominant species is L^- .

Metal – Ligand Stability Constants

In the present investigation, the interaction of various bivalent metal ions Mg(II), Ca(II), Sr(II), Ba(II), Co (II), Ni (II), Cu (II), Zn (II), Cd(II), Th(II), UO₂(II) with the DAMP was followed using Irving Rossotti p^H titration technique . All the titrations were in aqueous media at 35^oC and at an ionic strength of 0.1M KNO₃. The metal to ligand ratio in all these systems has been maintained at ratio 1:5 in order to saturate the coordination number of the metal ion. Further, the low concentration of metal ion used are likely to prevent the formation of polynuclear species. The formation constants (Table – II) of bivalent metal ions with DAMP is in the following order Cu (II) > Zn (II) > Ni (II) > Co (II). The above order is in conformity with the Irving - William nature order of stability. The order of stability constants of bivalent transition metal ions can be explained in terms of crystal field stabilization energy for Cu (II) is lesser than Ni (II), the complex stability order is Cu (II) > Zn (II) . This may be attributed to the orbital stabilization due to John – Teller distortion added with maximum ability to have π - interactions with these ligands. The energies included in complexation reactions is studies based on variation of temperature. The formation constants at different temperatures (25^o, 35^o& 45^oC) are formed to increase with increase in temperature suggesting the endothermic nature of chelation. The negative values of free energy metal ion and ligand. All the metal complexes are accompanied by relatively large positive enthalpy. In these figures it is observed that metal-ligand curves lies below the proton-ligand curve indicating the complexation reaction. For this ligand different metal ions, the n values ranges between a=0.1 to 2.8 for Mg(II), Ca(II), Sr(II), Ba(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Th(II),UO₂(II),. The 1:2 complexes are not formed with Ca(II), Sr(II) and Ba(II). The stability constant of Alkaline earth metals ions with DAMP The Stability constant for alkaline earth metal are in the following order Mg(II) > Ca(II) > Sr(II) > Ba(II). The stabilities are decreasing with increasing ionic radii. The formation constant of Bivalent metal ions are determined with DAMP by taking UO₂ (II) and Th(II) ions. It is observed that thorium ions forms fairly high stable complexes with DAMP.

Ternary Systems

The potentiometric titration curves for ternary systems containing DAMP bivalent ions Co(II), Ni(II), Cu(II), Zn(II) and the ligands with O⁻--O⁻ donor like oxalic acid (OX), malonic acid (MAL), and succinic acid(SUA) and N—N donors like ethylenediamine (En), O-phenylenediamine (OPDA), 2, 2-bipyridyl(Bipy) and 1,10 – phenanthroline (Phen) in 1 : 1 : 1 molar ratio.

The stability constant of complexes of Cu(II) with DHMP as primary ligand and a variety of other secondary ligands are compiled in (Table – III). The ligand forms relatively more stable complexes in presence of O-O donors, than in N-N donors. The ternary systems containing DAMP, bivalent ions and bidentate ligands involve O-O donors exhibit inflection at m=3 followed by another inflection at m=5 meanwhile the same system containing N-N donors in place of O-O donors exhibit feeble inflection at m=3 followed by another inflection at m=4 which are represented in the following Fig (2).

It has been noted that the ligand DAMP form more relatively stable complexes in presence of O-O donor than in presence of N-N donors. The relative stabilities of the ternary complexes compared to the corresponding binary complexes can be quantitatively expressed in many different ways we have expressed the relative stabilities in terms of $\Delta \log K$ which can be defined as the difference in the stabilities of ternary and the corresponding binary and expressed as

$$\Delta \log K = \log K_{MLA}^M - (\log K_{MA}^M + \log K_{ML}^M) \quad (3)$$

The ternary formation constant $\log K_{MLA}^M$ along with the $\Delta \log K$ and % RS values stabilization energy values are listed in (Table – III). The $\Delta \log K$ and % RS values are negative for all the ternary systems investigated.

The effect of N - N donor atoms bound to the metal ion M(II) on the binding DAMP was investigated by studying the ternary systems and the data shows that $\Delta \log K$ values and % RS values reveal the following order.

1. The $\Delta \log K$ values and % RS values are more as if the coordination, in the secondary ligand is from the two nitrogen atoms
2. It is the least when, the secondary ligand has two oxygen atoms.

The perusal of the stability constants reveals that the DAMP is bond to the metal ions by sigma and π bonds in complex. The $\partial\pi - p\pi$ interactions do not allow the concentration of electrons and the metal ion. Hence, less repulsion between metal ion electrons and ligand ion pair electrons are observed. In the formation of binary complexes, there is electron repulsion between the metal ion $\partial\pi$ electron and a lone pair of electron present on the coordinating atom of the sigma bonding ligand L. However, in the ternary complex, there is back – donation of electrons through π - bonding between the metal ion and the DAMP and hence the electron density on binary complex (M – DAMP) are reduced. This reduces the repulsion between metal $\partial\pi$ electrons and the additional lone pair of electrons over the secondary ligand in ternary complex. Hence, with this the ligand stability order with respect to secondary is found to be: Ox > Mal > Bipy > Phen > en. The order with respect to metals is in conformity with Irving – Williams order.

Conclusion

This study offers a investigation and mechanistic details associated with formation of binary and ternary complexes with various bivalent ions with DAMP as a primary ligand and (L) represent a wide range of secondary ligands. The stability of binary and ternary complexes explained in view of their $\log \Delta K$ values.

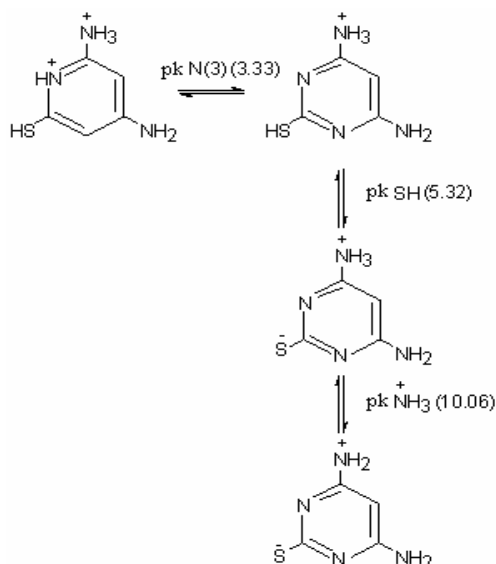


Table: I. Ligand Dissociation constant and Thermodynamic parameters for the dissociation equilibrium

Temperature	Dissociation Constants (DAMP)		Thermodynamic Parameters (KJ Mole ⁻¹)		
			ΔG	ΔH	ΔS
305 ^o K	pk ₁	3.33	19.63	9.38	-33.31
	pk ₂	5.32	31.37	15.00	-53.15
	pk ₃	10.06	59.32	7.50	-168.25

Table: II Formation constants (log K) and Thermodynamic Parameters of 1:1 M(II) – DAMP complexes at different temperatures. $\mu = 0.1M KNO_3$

Metalion	Formation Constants (logK ₁) of 1:1 M-II - DAMP Complexes			Thermodynamic Parameters				
	298 ^o K	308 ^o K	318 ^o K	-ΔG K.J. Mole ⁻¹			ΔH K.J. Mole ⁻¹ between 308 ^o -318 ^o K	ΔS deg ⁻¹ Mole ⁻¹ at 308 ^o K
				298 ^o K	308 ^o K	318 ^o K		
Mg(II)	4.53	4.64	4.67	26.13	27.36	28.44	5.62	107.08
Ca(II)	3.40	3.43	3.48	19.40	20.23	21.19	9.38	96.14
Sr(II)	3.10	3.12	3.15	17.69	18.39	19.18	5.63	77.99
Ba(II)	3.00	3.04	3.07	17.11	17.93	18.69	5.62	76.46
Co(II)	4.10	4.13	4.15	23.39	24.35	25.27	3.75	91.23
Ni(II)	4.82	4.84	4.86	27.50	28.54	29.59	3.75	104.84
Cu(II)	10.44	10.47	10.50	59.57	61.74	63.93	5.62	218.70
Zn(II)	4.80	4.83	4.90	27.38	28.48	29.84	13.13	135.09
Cd(II)	5.50	5.54	5.58	31.38	32.67	33.98	7.50	130.42
UO ₂ (II)	7.65	7.69	7.71	43.65	45.35	46.95	3.75	159.42
Th(II)	9.62	9.64	9.68	54.89	56.85	58.94	7.50	208.93

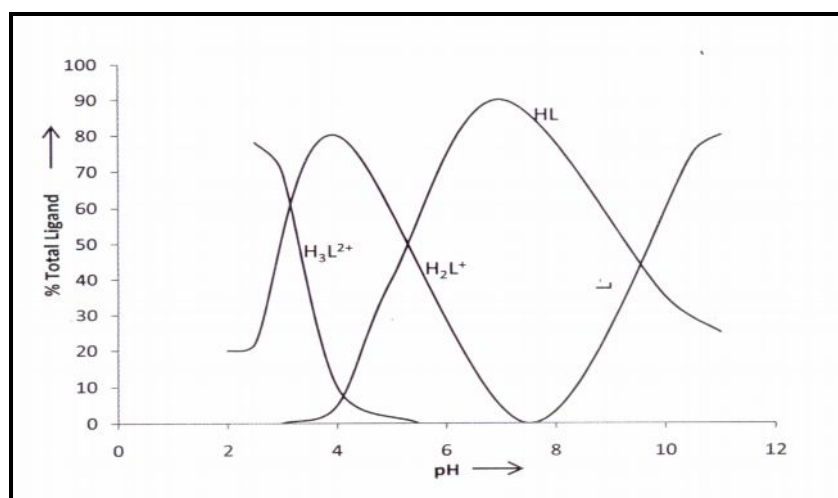
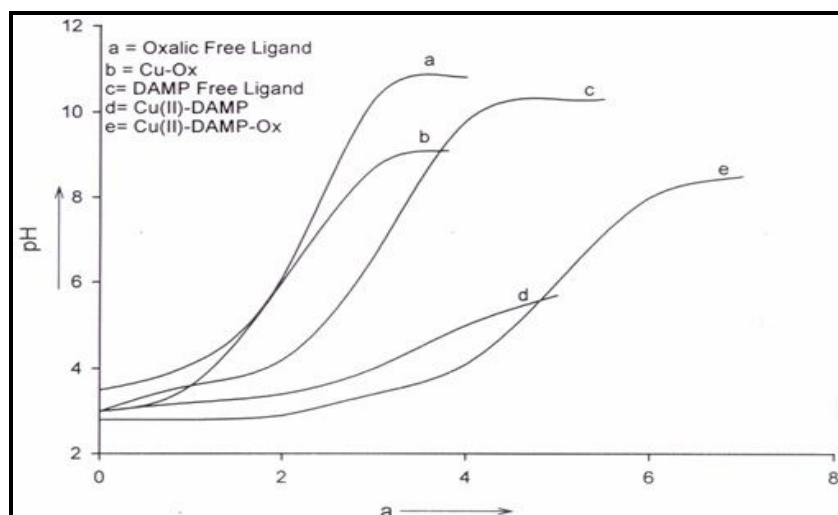
**Figure1. Species Distribution Curves for the ligand DAMP at 35°C****Fig.2. Potentiometric Titration curves of Cu(II) Ternary Complex involving DAMP-Ox at 35°C and $\mu=0.1M(KNO_3)$ Med=aq.**

Table: III Formation Constants of Ternary Bivalent Metal ions [M-II-DAMP] L= x/Mal/OPDA/Bipy/En Temp = 35⁰C, μ= -0.1M KNO₃, Aqueous Medium

Ligand	Bivalent Metal ion															
	Co II				Ni II				Cu II				Zn II			
	Log K ^{M-} _{MA/L}	logK ^{M-} _{MAL}	ΔlogK	%RS	Log K ^{M-} _{MA/L}	logK ^{M-} _{MAL}	ΔlogK	%RS	Log K ^{M-} _{MA/L}	logK ^{M-} _{MAL}	ΔlogK	%RS	Log K ^{M-} _{MA/L}	logK ^{M-} _{M-MA L}	ΔlogK	%RS
OX		7.15	-0.72	-17.43		8.35	-0.51	-10.54		14.44	-0.72	-6.88		7.79	-0.83	-17.18
Mal		6.41	-0.68	-16.46		7.34	-0.73	-15.04		15.11	-0.61	-6.09		7.29	-1.61	-33.33
Sua		5.56	-0.83	-20.09		7.15	-0.67	-13.84		13.66	-0.75	-7.16		7.27	-0.74	-15.32
OPDA		5.55	-0.63	-15.25		7.04	-0.43	-8.88		14.10	-1.11	-10.60		6.74	-0.85	-17.59
Bipy		8.14	-0.97	-23.49		10.73	-0.88	-18.18		17.57	-0.98	-9.36		8.76	-1.21	-25.05
Phen		9.05	-1.01	-24.46		11.48	-1.03	-21.28		17.82	-1.81	-17.29		10.95	-1.09	-22.57
En		8.44	-1.37	-33.17		10.23	-1.42	-29.34		19.75	-1.22	-11.65		8.81	-1.28	-26.50

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