Studies on mixed ligand complexes of bivalent metal ions with 4,6 - dihydroxy- 2 - mercapto pyrimidine

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ABSTRACT

Interaction of Bivalent ions Co (II), Ni (II), Cu (II) and Zn (II) reacts with 4,6 – dihydroxy – 2 – mercapto pyrimidine (DHMP) in presence of oxalic acid (Ox), malonic acid (Mal), o-phenylene diamine (OPDA), 2,2 – bipyridyl (Bipy), 1, 10 – phenanthroline (phen) and ethylene diamine (En) has been investigated by potentiometric studies. The tertiary complexes are formed in stepwise manner in which DHMP behaves as secondary ligand. The stability constants of tertiary complexes have been reported at 35^0 C and at µ=0.01 M KNO$_3$ in aqueous solution. The perusal of 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/Phentertiary- interaction makes the complexes more stable.
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INTRODUCTION

Purines and pyramidine 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 pyramidine 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 whereas Cu(II) destabilizes 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 understand 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 pyramidines are also proved biologically active. The divalent Ions forms binary system with purines and pyramidines[9] in which purines mostly act as bidentate ligands and pyramidines 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 pyramidines coordinate to the metal ion through N$_{(3)}$ position. The proton dissociation and its release is an important factor in determine the extent and nature of the metal ligand interaction in a metal nucleoside complex and its process of dissociation is an 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 an important role in several biological reactions[13.] 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 tertiary 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 pyrrazolines, isoxralline and some

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other substituted pyrimidines have been reported recently[14]. No reports have appeared for the interaction of 2,6-dihydroxy pyrimidine and some selected ligands with transition metal ions. Hence, it is considered an important to study the formation and stability of mixed ligand complexes of 4,6-dihydroxy-2-mercapto pyramidine with Cd(II),Co(II),Ni(II),Cu(II) and Zn(II). The stability constants of the above complexes are discussed in this paper.

MATERIALS AND METHODS

Materials:
The 4,6-dihydroxy-2-mercapto pyramidine was purchased from sigma chemicals 2,2-bipyridyl(bipy), 1,10 – phenonthroline (phen), orthophenyldiamine (OPDA), oxalic acid (Ox), malonic acid (MA), and succinic acid (SUA), were obtained from E. Merck, Darmstads. The transition metal nitrate of Cd(II), Co(II), Ni(II), Cu(II), andZn(II) used are of BDH/Analar grade. Sodium hydroxide, potassium nitrate, nitric acid, and EDTA are of BDH/Analar grade doubly dissolved deionized water is used.

Measurements:
All measurements were carried out at 35 $\pm 1^0$CDigisun made digital P^Hmeter model DI – 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.

Method:
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 0.001M and the ionic strength of the solution was maintained at 0.1M KNO_3. The temperature was maintained at 35 ± 0.1^0C, 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 NaOH.
1.   Mineral acid (HNO_3)(0.04M)-------Acid titration
2.   Mineral acid + Ligand(0.00002M)-----Ligand titration
3.   Mineral acid + Ligand + Metal ion (0.0004M) ----Metal titration

The P^H of solutions in aqueous ethanol mixtures were consumed according to the method suggested by the Van Uitert and Hase[15] using the following relationship.

$$P^H = B + \log U_H$$

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 DHMP also a prerequisite for evaluation of the metal – ligand stability constants, acid dissociation of DHMP.

Potentiometric titration of the ligand 4,6 – Dihydroxy - 2 –mercaptopyrimidine(DHMP) suggests the protonation of $N_{(!)}$ or $N_{(3)}$ of DHMP. The acid dissociation equilibrium of this ligand is represented by the following equations.

$$H_4L^+ \leftrightarrow H_3L + H^+ -----(1)$$
$$H_3L \leftrightarrow H_2L + H^+ -------(2)$$
$$H_2L \leftrightarrow HL^{2-}--------(3)$$
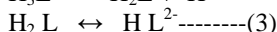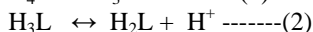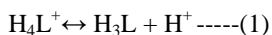
It is evident from the equations that the first proton dissociation is from $N_{(3)}$ proved with its P^{Ka} value   3.38, the second proton dissociation is from $C_2 – S$ and the third proton from OH group. (Scheme-1)

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

$$\bar{n}_H = Y + \frac{(V_1 - V_2)(N + E^O)}{(V_O + V_1)} / T^O_L$$

Where Y denotes the displacement of protons in the ligand, N is the normality of base (NaOH) , V_O is the total initial volume, V_1 is the volume of base consumed to reach a given PH value of titration curve of acid and base respectively, E^O is the total initial concentration of mineral acid (HNO_3) and T^O_L is the total initial concentration of ligand.

The ligand dissociation constant has been determined at 25^0 , 35^0 and 45^0C and thermodynamic parameters ΔG, ΔH and ΔS for the dissociation equilibrium are presented in (table1).

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 indicate,it is the major controlling factor in the acid dissociation reaction of these ligands. The acid – baseequilibriaindicates it is sensitive to change in the dielectric constants and the basicity of the medium and lowering dielectric constant increases the electrostatic attractive forces between ions, hence it facilitates the formation of neutral molecular species. The distribution diagrams for DHMP (Fig-I) suggest that at P^H 3.0, H_4L^+ present to the extent of 64% and H_3L present to 36%. At P^H 3.38 (P^{K1}) both the above species are present to the extent of 50% each with increase in P^H 5.7 H_3L reached to 100%. Further increase in P^H showed the presence of H_2L^{2-} .

Metal – Ligand Stability Constants:
In the present investigation, the interaction of various bivalent metal ions Co (II), Ni (II),Cu (II),and Zn (II) with the DHMP was followed using Irving RossottiP^H titration technique . All the titrations were made in aqueous media at 35^OC and at an ionic strength of 0.1 M KNO_3. In the reaction the metal to ligand ratio in all these systems has been maintained at ratio 1:5 inorder to saturate the co-ordination 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 2) of bivalent metalions with DHMP is in the following order.Cu (II) > Zn (II) > Ni (II) > Co (II). The above order confirms with the Irving-WilliamRossette nature order of stability. The order of stability constants of bivalent transition metal ions can be explained interms 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 tohave π- interactions with these ligands. The energies included in complexation reactions is studies based on variation of temperature. The formation constants of different complexes at different temperatures (25°, 35°& 45^OC) are found to increase with increase in temperature suggesting the endothermic nature ofchelation. The negative values of free energy change (ΔG) for all M(II) –DHMP systems indicate that thereaction involving the formation of metal

complexes were spontaneous. The relatively high values of ΔG obtained in these casesfurther suggest that the complexes formed are thermodynamically stable enough compared to the free metal ion and ligand. All the metal complexes are accompanies by large positive enthalpy relatively.

Ternary Systems
The potentiometric titration curves for ternary systems containing DHMP bivalent ions Co(II), Ni(II, Cu(II), Zn(II) and the ligands with O⁻--O⁻donar like oxalic acid (OX), malonic acid (MA), and succinic acid and N—N donors like ethylene diamine (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 given in (table – 2). The ligand forms relatively more stable complexes in presence of O-O donors, than in N-N donors.

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The ternary systems containing DHMP, bivalent ions and bidentate ligands involve ⁻O-O⁻donors exhibit inflection at m=4 meanwhile the same system containing N-N donors in place of O-O donors exhibit inflection at m=2 followed by another inflection at m=3 by Ni (II), Zn (II) , Co(II) & Cu(II) exit inflection at m=3 followed by another inflection at m=4.

It has been noted that the ligand DHMP 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 different ways we have expressed the relative stabilities inner most Δlog K which can be defined as the difference in the stabilities of ternary and the corresponding binary expressed as

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

The ternary formation constant log K_{ML}^{AM} along with the Δ log K and % RS values and stabilization energy values are listed in (table – 2). The Δ 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 DHMP was investigated by studying the ternary systems and the data shows that Δ log K values and % RS values reveal the following order.
1. The Δ log K values and % RS values are more as if the coordination, in the secondary ligand is formed in between the two nitrogen atoms
2. It is least when,the secondary ligand has two oxygen atoms.
The perusal of the stability constants reveals that the DHMP is bond to the metal ions by σ and πbonds in complex. The ∂π - pπ interactions do not allow the concentration of electrons and the metal ion. Hence, less repulsion takes place 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 ∂π 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 DHMP and hence the electron density on binary complex (M – DHMP) are reduced. This reduces the repulsion between metal ∂π electrons and the additional lone pair of electrons over the secondary ligand in ternary complexes Hence, the 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.

Table.1

Temperature	Dissociation Constants	Thermodynamic Parameters (KJ Mole⁻¹)		
		ΔG	Δ H	ΔS
305ᴼK	PK₁	19.93	7.5	40.36
	PK₂	45.02	9.37	-45.74
	PK₃	59.91	9.38	-164.00

Table: 2 Formation Constants of Ternary Bivalent Metal ions [M-II-DHMP]
L= Ox/Mal/OPDA/Bipy/En
Temp = 35ᴼC, μ= -0.10M KNO₃, Aqueous Medium

Ligand	Co II			Ni II			Cu II			Zn II		
	$\log K^M_{MAL}$	ΔlogK	%RS	$\log K^M_{MAL}$	ΔlogK	%RS	$\log K^M_{MAL}$	ΔlogK	%RS	$\log K^M_{MAL}$	ΔlogK	%RS
OX	7.36	-0.63	-14.8	8.44	-0.32	-6.75	11.25	-0.68	-9.36	8.81	-0.6	-11	-11
Mal	6.69	-0.52	-12.2	7.89	-0.08	-1.69	11.93	-0.56	-7.73	9.19	-0.5	-9.22	-9.22
Sua	5.81	-0.7	-16.5	7.02	-0.4	-14.8	10.45	-0.73	-10.1	8.05	-0.7	-12.9	-12.9
OPDA	5.49	-0.81	-19.1	6.59	-0.78	-16.5	11.07	-0.91	-12.6	7.52	-0.9	-15.4	-15.4
Bipy	8.27	-0.96	-22.6	10.57	-0.94	-19.8	14.32	-1	-13.8	9.85	-0.9	-16.5	-16.5
Phen	9.24	-0.94	-22.1	11.44	-0.97	-20.5	15.41	-0.99	-13.7	11.82	-1	-18.3	-18.3
En	8.7	-1.23	-28.9	10.45	-1.1	-23.2	16.32	-1.42	-19.7	8.61	-2.3	-40.6	-40.6

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Table: 3 Formation constants (log K) and Thermodynamic Parameters of 1:1 M(II) – DHMP complexes at different temperatures.
$\mu = 0.1$ M KNO_3

Metal ion	Formation Constants ($logK_1$) of 1:1 M-II - DHMP Complexes			Thermodynamic Parameters				
	298^OK	308^OK	318^OK	$-\Delta G$ K.J. Mole^{-1}			ΔH K.J. Mole^{-1} between 308°-318^OK	ΔS deg^{-1} Mole^{-1} at 308^OK
				298^OK	308^OK	318^OK		
Co (II)	4.16	4.25	4.33	23.73	25.06	26.37	15.00	130.06
Ni (II)	4.66	4.74	4.84	26.59	27.95	29.41	16.88	145.55
Cu (II)	7.18	7.24	7.30	40.97	42.69	44.45	11.25	175.13
Zn (II)	5.57	5.64	5.72	31.78	33.26	34.83	15.00	156.69

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