

pH Metric Studies of Interaction of Synthesized Ligands 2-amino-4-hydroxy-6-methylpyrimidine and 1-(4-hydroxy-6-methylpyrimidino)-3-phenylthiocarbamide with Cu(II), Cd(II), Cr(II), Cations At 0.1 M Ionic Strength

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Abstract

Guanidine was successfully interacted with acetoacetic ester to synthesize 2-amino-4-hydroxy-6-methylpyrimidine (L_1) which on further treatment with phenylisothiocyanate furnishes 1-(4-hydroxy-6-methylpyrimidino)-3-phenylthiocarbamide (L_2). The interactions of Cu(II), Cd(II), Cr(II) metal ions with L_1 and L_2 have been studied at 0.1 M ionic strength in 70 % Dioxane-water mixture by Bjerrum method as adopted by Calvin and Wilson. It is observed that Cu(II), Cd(II), Cr(II) metal ions form 1:1 and 1:2 complexes with ligands (L_1 and L_2). The data obtained were used to estimate and compare the values of proton-ligand stability constant (pK.) and metal-ligand stability constants (log k). The effect of substituents were studied from estimated data (pK & log k).

Keywords: Pyrimidines, Thiocarbamide, Acetoacetic ester, Ionic strength, pH metry

1. Introduction

Pyrimidino and thiocarbamido nucleus containing heterocycles possesses pharmaceutical, medicinal agricultural industrial and biotechnological significance (Barnes, D. M., 2002; Cyril V., 1977; Ghaigy, 1965; Bossinger, 1972; Seidal, 1964). Recently 2-amino-4-hydroxy-6-methylpyrimidine was successfully condensed with various isothiocyanates in acetone, ethanol, dioxane mediums to obtain 1-(4-hydroxy-6-methylpyrimidino)-3-substitutedthiocarbamides. (Patil, 2006) When above reaction mixture was condensed in acetone-ethanol medium in 1:1 molar praportion the yield and purity increases with decrease in time span.

The manifold research work has been done on the study of metal and nitrogen heterocyclic ligands containing complexes (Irving H, 1954; Martell, 1962). Many workers have reported their results on metal-ligand stability constants. With the view to understand the bio-inorganic chemistry of metal ions, Banarjee et al (1968) have synthesized a number of mixed-ligand alkaline earth metal complexes. The studies of metal-ligand complexes in solution having number of metal ions with ligands carboxylic acids, oximes, phenols etc. would be interesting which throw a light on the mode of storage and transport of metal ions in biological kingdom. Bejerrum's (1941) dissertation describes the initiative to develop this field. Metal complexation not only brings the reacting molecules together to give activated complexes (Irving H, 1953) but also polarized electrons from the ligands towards the metal. The relation between stability and basicity of the ligands is indicated by the formation constant and free energy change value. Bulkier group increases the basicity of ligands as well as stability. The stability of the complexes is determined by the nature of central metal atom and ligand. The stability of complexes is influenced by the most important characteristics degree of oxidation, radius and electronic structure. Irving and Williams had studied the order of stability of metal complexes of transition metal ions by comparing the ionic radius and second ionization potentials of metal ions, as it is valid for most nitrogen and oxygen donor ligands. Narwade et al (1985) have investigated metal-ligand stability constants of some lanthanides with some substituted sulphonic acids. Bodkhe et al (2003) have reported the metal-ligand stability constants of some β -diketones. Tekade et al (2005) have investigated stability constants of some substituted pyrazolines, isoxalline and diketone. Prasad et al (2005) have studied mixed ligand complexes of alkaline earth metals, Mg(II), Ca(II), Sr(II) and Ba(II) with 5-nitrosalicylaldehyde and β -diketones. Recently, Thakur et al (2010) studied the interaction between some lanthanide and radioactive metal ion with substituted Schiff's bases at 0.1 M ionic strength pH metrically and spectrophotometrically.

In present work an attempt has been made to study the interactions between Cu(II), Cd(II), Cr(II) and 1-(4-hydroxy-6-methylpyrimidino)-3-substitutedthiocarbamide (L_1 and L_2) at 0.1 M ionic strength pH metrically in 70% dioxane-water mixture.

2. Materials and Methods

All the chemicals used were analar grade (India make) alkyl/arylthiocyanates were prepared according to the literature, melting points of all synthesized compounds were determined in open capillary and uncorrected. IR spectra were recorded on Perkin-Elmer spectrophotometer in the range 4000-400 cm^{-1} in KBr pellets. PMR spectra were recorded with TMS as internal standard using CDCl_3 and DMSO. The purity of the compounds was checked on silica gel-G plates by TLC.

2.1 Synthesis of 2-amino-4-hydroxy-6-methyl pyrimidine [L_1]

The interaction of guanidine with acetoacetic ester had been carried out in acetone-ethanol (1:1) medium for eight hours in water bath. The precipitate was filtered. It was crystallized by precipitation method. (By precipitating it with acetic acid from its alkaline solution). Reaction yielded 79 %, m.p. was 168°C. Product was off-white solid, soluble in hot acetone, benzene, hot ethanol and dioxane and insoluble in water and chloroform. When hot aqueous solution of the product was treated with aqueous ferric chloride (5%) gave red colouration, indicating the presence of phenolic -OH group. Desulphuration was noticed when the product was warmed with alkaline plumbite solution. It formed picrate (m.p. 183°C). The reaction scheme was shown in Scheme-I. The spectral data for IR (Table 1), $^1\text{H-NMR}$ (Table 2) and CHNS-O analysis (Table 3) was reported.

2.2 Synthesis of 1-(4-hydroxy-6-methylpyrimidino)-3-phenylthiocarbamide [L_2]

The interaction of 2-amino-4-hydroxy-6-methylpyrimidine with phenylthiocyanates has been carried out in acetone-ethanol medium in 1:1 molar proportion in the boiling water bath for four hours, filter the reaction mixture to separate out 1-(4-hydroxy-6-methylpyrimidino)-3-phenylthiocarbamide [L_2], washed several times with 10 ml of water and crystallized with ethanol. Reaction yielded 62 %, m.p. was 132°C. Product was brown solid, soluble in hot acetone, benzene, ethanol and dioxane and insoluble in water and chloroform. When hot aqueous solution of the product was treated with aqueous ferric chloride (5%) it gave red colouration, indicating the presence of phenolic -OH group. Desulphuration was noticed when the product was warmed with alkaline plumbite solution. It formed picrate (m.p. 142°C). The reaction scheme was shown in Scheme-II. The spectral data for IR (Table 1), $^1\text{H-NMR}$ (Table 2) and CHNS-O analysis (Table 3) was reported.

3. pH metric analysis

Systronic microprocessor based instrument with accuracy in 0.01 unit with glass and saturated calomel electrode was used for the titrations. It was calibrated with the buffer solution of pH 7.00 and 9.20 at 28 ± 0.1 °C before titrations.

Titrations were carried out in an inert atmosphere by bubbling a constant flow of nitrogen gas.

The experimental procedure involved the titrations of

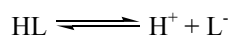
- i) Free acid HClO_4 (0.01 M)
- ii) Free acid HClO_4 (0.01 M) and ligand (20×10^{-4})
- iii) Free acid HClO_4 (0.01 M) and ligand (20×10^{-4}) and metal ion (4×10^{-4} M) with standard NaOH solution

The ionic strength of all the solution was maintained constant (0.1 M) by adding appropriate amount of NaClO_4 solution. All the titrations were carried out in 70 % dioxane-water mixture and the reading were recorded for each 0.1 ml addition. The graph of volume of alkali (NaOH) against pH were plotted (Fig. 1 to Fig. 6).

4. Results and Discussion

4.1 Proton-ligand stability constants:

The 1-(4-hydroxy-6-methylpyrimidino)-3-substitutedthiocarbamide was monobasic acids having only one dissociable H^+ ion from OH group. It can therefore, be represented as HL



The titration curves of the acid and ligand deviate at about 3.0 pH. The deviation between acid curves from ligand for all the systems showed the dissociation of H^+ ions from -OH groups of ligands.

The proton-ligand formation number ($\bar{n}_A$) were calculated by Irving and Rossotti expression.

$$\bar{n}_A = \gamma - \frac{(V_2 - V_1) \times (E^0 + N)}{(V^0 + V_1) T_L^0}$$

Where,

V^0 = Initial volume of solution (50 ml)

E^0 = Initial concentration of free acid (HClO_4)

T_L^0 = Concentration of ligand in 50 ml solution

γ = Number of dissociable protons from ligand

N = Avagadros Number

$(V_2 - V_1)$ = Volume of alkali (NaOH) consumed by acid and ligand on the same pH.

The pK values were calculated from the formation curves between pH Vs $\bar{n}_A$ noting the pH at which $\bar{n}_A = 0.5$ (half integral method) and point wise calculations which are represented in Table 4. It is observed that, the order of pK values of ligands is found to be as, $\text{pK } L_2 > \text{pK } L_1$. The reduction in pK values of L_1 is attributed to the presence of electron withdrawing -OH group.

4.2 Metal-Ligand Stability Constants

The stepwise formation constants of Cu(II), Cd(II), Cr(II) metal ions with ligands (L_1 and L_2) in 70% dioxane-water mixture were determined. The values of $\log K_1$ and $\log K_2$ were directly computed from the formation curve ($\bar{n}_A$ Vs pH) using half integral method. The most accurate values were calculated by point wise calculations which are presented in Table 5.

5. Conclusion

From the titration curves, it is observed that the departure between acid + ligand (A+L) curve and acid + ligand + metal (A+L+M) curve for all systems started from pH = 3.0. This indicated the commencement of complex formation. Also change in colour from yellow to red in the pH range from 3 to 11 during titration showed the complex formation between metal and ligand.

Observation of Table 5 and 6 shows that the less difference between $\log K_1$ and $\log K_2$ values indicates the complex formation between metal ion and ligand occurring simultaneously. The values of $\log K_1$ and $\log K_2$ (Table 4) the stability of complexes was decided. For 2-amino-4-hydroxy-6-methylpyrimidine (L_1) the difference between the values of $\log K_1$ and $\log K_2$ is higher with Cu(II) complex than Cd(II) and Cr(II). It indicates that Cu(II) forms

more stable complex with Ligand-1 (L_1) than Cd(II) and Cr(II). And for 1-(4-hydroxy-6-methylpyrimidino)-3-phenylthiocarbamide (L_2) the difference between the values of $\log K_1$ and $\log K_2$ is higher with Cd(II) complex than Cu(II) and Cr(II) complexes. Cd(II) forms more stable complex with ligand 2 than Cu(II) and Cr(II) metal ions.

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Table 1. IR spectra of synthesized compounds in (cm^{-1})

Compound	ν (N-H)	ν (C=N)	ν (N-C=N)	ν (>C-O)	ν (>C=S)
[3(L ₁)]	3180.9	1638.2	1579.6	1252.8	---
[5(L ₂)]	3170.3	1631.5	1562.3	1222.8	1162.2

Table 2. ¹H-NMR spectra of synthesized compounds in (ppm)

Compound	(Ar-OH)	(N-H)	(Ar-H)	(pyrimidino-H)	(-CH ₃)
[3(L ₁)]	10.80	9.76	6.20	7.74	2.19-2.59
[5(L ₂)]	10.55	9.56	6.92	7.31	2.58

Table 3. CHNS-O analysis of synthesized compounds in (ppm)

Compound	[3(L ₁)]		[5(L ₂)]	
	Calculated (%)	Found (%)	Calculated (%)	Found (%)
Carbon	48.00	47.33	56.47	56.14
Hydrogen	05.60	05.12	2.75	2.55
Nitrogen	33.06	32.92	21.96	21.66
Sulphur	---	---	12.55	12.12

Table 4.

Ligands	System	pK	
		Half internal method	Point wise method
L ₁	2-amino-4-hydroxy-6-methylpyrimidine	5.421	5.612
L ₂	1-(4-hydroxy-6-methylpyrimidino)-3-phenylthiocarbamide	6.751	7.332

Table 5. Metal-ligand stability constants (log K)

System	log K ₁	log K ₂
Cu(II) - ligand - 1	3.6970	2.5198
Cd(II) - ligand - 1	3.5969	2.5198
Cr(II) - ligand - 1	3.6969	2.3198
Cu(II) - ligand - 2	3.9968	2.8197
Cd(II) - ligand - 2	4.2969	2.3198
Cr(II) - ligand - 2	3.9969	2.8198

Table 6. Metal-ligand stability constants (log K)

System	log K ₁ - log K ₂	log K ₁ / log K ₂
Cu(II) - ligand -1	1.1772	1.4672
Cd(II) - ligand -1	1.0771	1.4275
Cr(II) - ligand -1	1.3771	1.5936
Cu(II) - ligand -1	1.1771	1.4175
Cd(II) - ligand -1	1.9771	1.8523
Cr(II) - ligand -1	1.1771	1.4174

Fig. 1
SYSTEM - Cu(II)-(L₁)

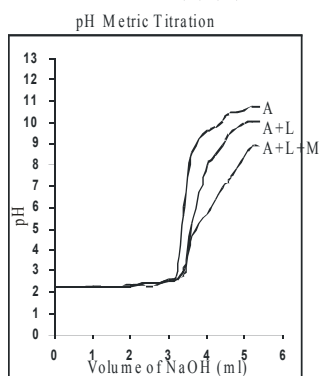


Fig. 2
SYSTEM - Cd(II)-(L₁)

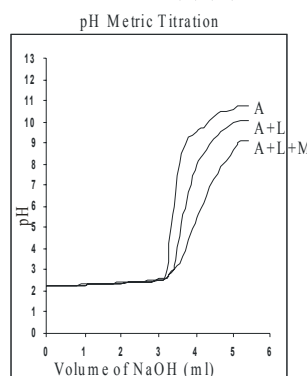


Fig. 3
SYSTEM - Cr(II)-(L₁)

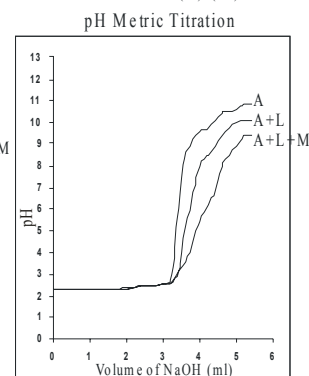


Fig. 4
SYSTEM - Cu(II)-(L₂)

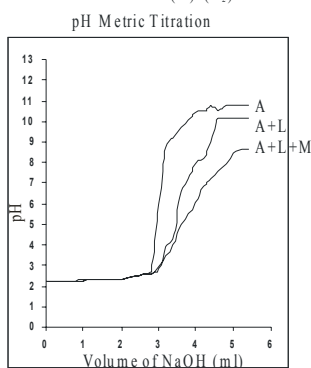


Fig. 5
SYSTEM - Cd(II)-(L₂)

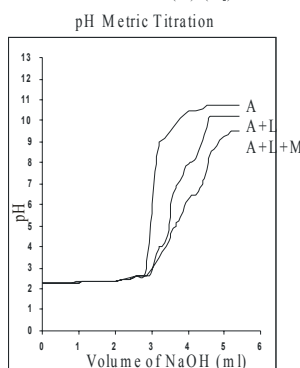
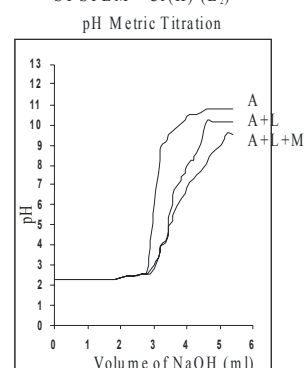
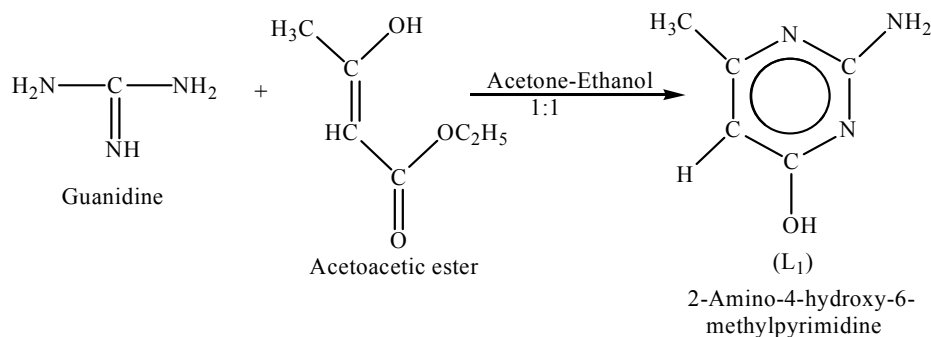


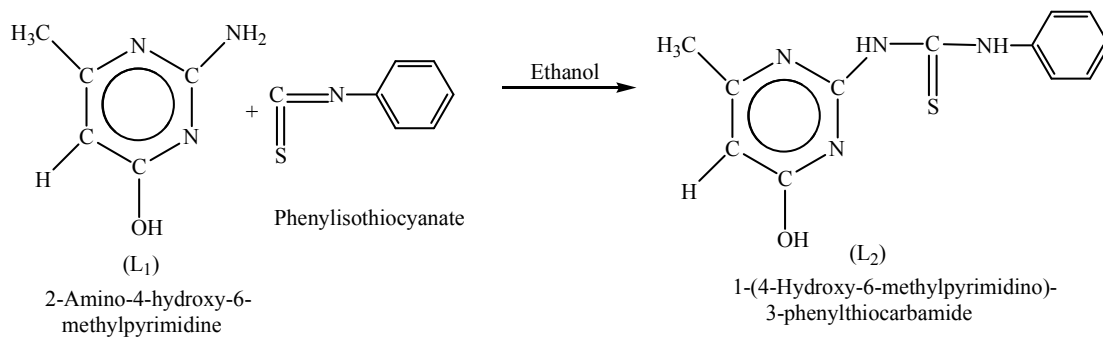
Fig. 6
SYSTEM - Cr(II)-(L₂)



Where, A - Acid, L - Ligand, M - Metal



SCHEME-I



SCHEME-II