

MIXED LIGAND COMPLEXES OF BIVALENT METAL IONS WITH 4,6-DIAMINO 2-HYDROXYPYRIMIDINE

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The interaction of Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) ions with 4,6-diamino 2-hydroxy pyrimidine in presence of biologically important ligands like oxalic acid, malonic acid, o-amino phenol, o-phenylenediamine, 2,2'-bipyridyl, 1,10-phenanthroline and ethylenediamine has been investigated by potentiometric studies. The proton dissociation constant of the substituted pyrimidine, stability constant of the binary complexes of 1:1 and ternary complexes of 1:1:1 molar ratios of the metal ion to ligands have been reported at 35°C and 0.1 M (KNO₃) ionic strength.

Key words: Mixed ligand complexes, Bivalent metal ion, 4,6-Diamino 2-hydroxypyrimidine, Stability constant.

Introduction

The interaction of various metal ions with nucleic acid constituents like purines, pyrimidines has attained much biological importance (Astwood *et al* 1945; Williams *et al* 1947; Gut *et al* 1959). It is evident from the literature that though much work has been reported on the binary complexes, comparatively less work has been reported on ternary complexes of nucleosides. Further the data on ternary complexes, which act as good models for many metalloenzyme reactions, is remarkably absent. So in continuation of our studies (Satyanarayan and Siddiram 1994 and 1995; Satyanarayan and Venkateshwar 1996) on the substituted pyrimidines, we report here in the study in detail the formation constants of mixed ligand complexes of 4,6-diamino 2-hydroxy pyrimidine (DAHP) with divalent metal ions Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) in presence of other biologically important ligands such as oxalic acid, malonic acid, o-amino phenol, o-phenylenediamine, bipyridyl, 1,10-phenanthroline and ethylenediamine in solution.

Experimental

The experimental method consisted of potentiometric titration of each ligand with standard sodium hydroxide solution in the absence and presence of the metal ions being investigated. The ionic strength of the solution was maintained constant in the course of the titration by 0.1 M (KNO₃) and in the determination of the dissociation constants of the free ligands the concentration of the ligand was 1.0 X 10⁻³ M. In the determination of formation constants of binary complexes a 1:1 metal-ligand ratio was employed and for ternary

complexes a 1:1:1 molar ratio of metal ion, primary ligand and secondary ligand was employed. The concentration of the metal ion was normally 1.0 X 10⁻³ M. The temperature was maintained at 35 ± 0.1 °C. Pre-saturated nitrogen was passed through the solution throughout the course of the titration. A Digisun pH meter with combination of glass and calomel electrodes was used to measure the hydrogen ion concentration. The electrode system was calibrated by direct titration with acetic acid and the observed pH-meter reading was compared with the actual hydrogen ion concentration as calculated from the data tabulated by Harned and Owen (Harned and Owen 1950). The pH regions below 3.5 and above 10.5 were calibrated by direct measurement of the hydrogen ion concentration in hydrochloric acid and sodium hydroxide solutions, respectively. The equilibrium constants reported in this investigation correspond to the reference state of infinitely dilute reaction species in a medium of 0.1 M (KNO₃) and thus all the determined equilibrium constants are very close to the thermodynamic constants.

Chromatographically pure sample of 4,6-diamino 2-hydroxy pyrimidine (DAHP) were purchased from Sigma Chemical Company (USA). The other ligands, viz. oxalic acid (Ox), malonic acid (Mal), o-aminophenol (OAP), o-phenylenediamine (OPDA), 2,2'-bipyridyl (Bipy), 1,10-phenanthroline (Phen), and ethylenediamine (En) were obtained from E. Merck, Darmstadt. All the metal ions Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) were of A.R. grade. Fresh solid ligand was weighed out for each titration to ensure no loss by hydrolysis or photochemical decomposition. The metal salt solutions were standardised by titration with the disodium salt of EDTA, as described by Schwarzenbach (1957). Carbon-

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ate-free sodium hydroxide was prepared by the method of Schwarzenbach and Biedermann (1948) and was standardised by titration with pure potassium acid phthalate.

The acid dissociation constants and all the binary stability constant were calculated by using ' computer programmes pKAS and BEST respectively (Motekaitis and Martell 1982). The equilibrium constants reported in this investigation correspond to the reference state of infinitely dilute reacting species in a medium of 0.1 M (KNO₃).

Results and Discussion

The free ligand titration curve of monoprotonated DAHP exhibits a single inflection at a = 1 indicating the release of a single proton. The acid dissociation constants of DAHP have been determined at three different temperatures (25, 35 and 45 °C) and at a constant ionic strength of 0.1 M (KNO₃) (Table 1). The thermodynamic parameters ΔG, ΔH and ΔS for the dissociation of DAHP have been evaluated and are presented in Table 2.

The positive free energy change (ΔG) that accompanies the acid dissociation process of the ligand, reveals the non-spontaneous nature of the ionization reaction in the solution.

Table 1
Formation constants (log K_f) of 1:1 M (II)-DAHP binary systems at different temperatures
μ = 0.10 M (KNO₃)

Metal ion	298° K	308° K	318° K
Mn (II)	1.09	1.17	1.23
Co (II)	1.22	1.28	1.33
Ni (II)	1.50	1.57	1.66
Cu (II)	3.64	3.73	3.80
Zn (II)	1.63	1.68	1.70
pKa of DAHP	6.23	6.30	6.35

The dissociation processes are endothermic in nature as revealed from the positive enthalpy change (ΔH). The negative entropy change illustrates that it is the major controlling factor in the acid dissociation reaction of the ligand DAHP.

The pKa values of DAHP have been determined at different compositions of aqueous-methanol mixture (Table 3). The pKa value increases with an increase in the methanol content of the solvent mixture. These trends are in conformity with the observations made on a number of nitrogenous bases.

Bivalent Metal Binary Systems: The potentiometric titration curves for the interaction of bivalent metal ion M (II) with DAHP in 1:1 molar ratio show a single inflection at m = 1 (m = moles of the base added per mole of the metal ion). The stability constants (Table 1) at different temperatures of the normal complexes (MA) are calculated in the buffer region m = 0 to 1 and are in the following order



All these systems are in conformity with the Irwing - William's natural order of stability. The order of stability constants can be explained in terms of crystal field stabilization energy (CFSE). There is a gradual rise in the CFSE values for Mn(II) to Ni(II) and a decrease in Cu(II) aquo complexes or complexes with weak field ligands. The stability order for Mn(II) to Ni(II) can therefore be attributed to the gradually increasing CFSE values. Though the CFSE for Cu(II) is lesser than Ni(II), the complex stability order is Cu(II) > Ni (II). This may be attributed to the orbital stabilisation due to John-Teller distortion added with maximum ability to have π-interactions with the ligand.

The formation constants (Table 1) of all M(II)-DAHP systems are found to increase with an increase in temperature suggesting the endothermic nature of chelation. The negative values of free energy (ΔG) values (Table 2) indicate that the reactions

Table 2
Thermodynamic parameters associated with the proton dissociation constant of DAHP and the formation of 1:1 M(II)-DAHP binary systems
μ = 0.10 M (KNO₃)

Metal ion	-ΔG kJ mole ⁻¹			ΔH kJ mole ⁻¹ between 308-318° K	ΔS J deg ⁻¹ mole ⁻¹ at 308° K
	298° K	308° K	318° K		
H ⁺	35.53	37.13	38.64	9.37	-90.13
Mn(II)	6.21	6.89	7.48	11.24	58.88
Co(II)	6.95	7.54	8.09	9.37	54.91
Ni(II)	8.55	9.25	10.10	16.87	84.80
Cu(II)	20.76	21.99	23.14	13.12	113.98
Zn(II)	9.29	9.90	10.46	7.49	56.50

Table 3

Proton dissociation constant (pKa) of DAHP and binary formation constants (log K_1) of 1:1 M(II)-DAHP in different proportions of methanol at 35°C.

$m = 0.10 \text{ M (KNO}_3\text{)}$

Metal ion	Mole fraction (X ₂) 100/D	0%	30%	40%	50%	60%	70%
			0.152	0.228	0.307	0.400	0.508
		1.541	1.658	1.778	1.951	2.162	
H+	6.30	6.35	6.38	6.42	6.45	6.47	
Ni(II)	1.57	1.65	1.70	1.74	1.78	1.81	
Cu(II)	3.73	3.78	3.82	3.87	3.91	3.96	

Table 4

Cumulative formation constants (log) K_{MLA}^M of [M(II)-DAHP-A] system.

Temp = 35°C	$\mu = 0.10 \text{ M (KNO}_3\text{)}$					Medium = aqueous
Ligand (A)	Mn(II)	Co(II)	Ni(II)	Cu(II)	Zn(II)	
Ox	2.50	2.89	3.56	7.33	4.22	
Mal	2.81	3.15	3.84	7.89	4.00	
OAP	6.05	6.81	7.63	10.15	7.90	
OPDA	0.17	1.82	1.73	6.07	1.93	
Bipy	2.50	4.77	5.90	9.43	4.63	
Phen	3.44	4.75	6.83	10.55	6.18	
En	3.28	4.53	6.00	11.94	5.53	

Table 5

The $\Delta \log K$ values of [M(II)-DAHP-A] systems.

Temp = 35°C	$\mu = 0.10 \text{ M (KNO}_3\text{)}$					Medium = aqueous
Ligand (A)	Mn(II)	Co(II)	Ni(II)	Cu(II)	Zn(II)	
Ox	-1.31 (-111.96)	-1.29 (-100.78)	-1.24 (-78.98)	-1.22 (-32.71)	-1.25 (-74.40)	
Mal	-1.21 (-103.34)	-1.19 (-92.96)	-1.14 (-72.61)	-1.09 (-29.22)	-1.15 (-68.45)	
OAP	-1.77 (-151.28)	-1.72 (-134.37)	-1.65 (-105.09)	-1.61 (-43.16)	-1.67 (-99.40)	
OPDA	-2.55 (-217.94)	-1.52 (-118.75)	-2.46 (-156.68)	-2.40 (-64.34)	-2.50 (-148.81)	
Bipy	-2.52 (-215.38)	-1.49 (-116.40)	-2.44 (-155.41)	-2.37 (-63.54)	-2.47 (-147.02)	
Phen	-2.49 (-212.82)	-2.46 (-192.18)	-2.41 (-153.50)	-2.35 (-63.00)	-2.43 (-144.64)	
En	-2.46 (-210.25)	-2.43 (-189.84)	-2.38 (-151.59)	-2.31 (-61.93)	-2.41 (-143.45)	

Percentages of relative stabilisation energies are in parentheses.

involving the formation of metal complexes are spontaneous. ΔG becomes more negative with an increase in temperature revealing the increase in the extent of complex formation at high temperature. All the metal complexes are accompanied by relatively large positive enthalpy (ΔH) values (Table 2). The entropy change (ΔS) for all the complexes (Table 2) is positive as expected.

The formation constants (Table 3) of Ni (II), Cu (II) and the ligand DAHP in 0%, 30%, 40%, 50%, 60% and 70% v/v methanol-water mixture increase with an increase in the amount of methanol. The observed increase in the stability of metal complexes in a medium of low dielectric constant can thus be accounted. The formation constants for 1:1 M(II)-Ox/MA/OAP/OPDA/Bipy/Phen/En have been remeasured and the values obtained are in close agreement with the values found in literature.

Bivalent metal ternary systems: A perusal of titration curves where ternary curve overlaps with the curve of 1:1 binary system ML upto $m=2$, later deviates reveals that DAHP is behaving as secondary ligand and other ligands (L) where L = Ox, Mal, OAP, OPDA, Bipy, Phen and En behaving as primary ligands. The ternary formation constants log K_{MLA}^M and the $\Delta \log k$ values along with % RS values are listed in Table 4 and 5 respectively.

The stability order of all the systems with respect to the metal ion is in conformity with Irving-William's natural order of stabilities:

Zn(II) < Cu(II) > Ni(II) > Co(II) > Mn(II).

The $\Delta \log K$ and % RS values are negative for all the ternary systems investigated.

To have a positive effect, one need not get a positive $\Delta \log K$ values, even less negative values also indicate the positive effect (Sigel 1975 and 1980). When compared, the negative values are less for the systems having malonic acid or oxalic acid, intermediate for OAP system and somewhat more for N-N donor systems.

In the case of malonic acid there are lone pairs of electrons over both carboxylate anionic groups and hence electronic repulsion in (M-Mal) formation is greater. The release of repulsion is, thus, more pronounced in the ternary complexes (M-Py-Mal), and this leads to less negative $\Delta \log K$ values.

There is no extra lone pair of electrons present on the σ -bonding nitrogen atoms in N-N donors, hence the favourable electron repulsive effect is not felt in the formation of (M-Py-(N-N)). In N-O-coordinating ligands, there is a lone pair of electrons only over the single oxygen atom. Due to the decrease of electrons repulsion in ternary complexes, $\Delta \log K$ is small negative quantity in (M-Py-(N-O-)) complex with N-O-donor atoms.

The special behaviour of Bipy, and Phen for less negative or positive values is explained by (Chidambaram and Bhattacharya 1970); (Griesser and Sigel 1970). The positive charge on the metal ion or its electronegativity in $[M(\text{Bipy})]^{2+}$ ion is almost the same as in $[M(\text{H}_2\text{O})_6]^{2+}$, and hence $K_{\text{M}(\text{Bipy})}^{\text{MBipy}}$ approximately equal to K_{ML}^{M} . The $K_{\text{M}(\text{Bipy-py})}^{\text{MBipy}}$ has much higher value than $K_{\text{M}(\text{py})_2}^{\text{Mpy}}$ as is expected from the difference in π -bonding, electrostatic repulsion in the formation of [M-Bipy-Py].

In the distribution diagram (Fig 1), various contributing species are indicated. The distribution reveals that 1:1 binary [Cu(II)-Ox] is the predominant species (80%) at around pH 4.6. A small amount of 1:1[Cu(II)-DAHP] (3%), 1:1:1 [Cu(II)-DAHP-Ox] (50%) and (Cu(II)-Ox) binary complex (47%) are present at pH 6. After pH 6, the major contributing species happens to be the [Cu(II)-OX-DAHP] complex.

The distribution diagram (Fig 2) shows the distribution of different species of ternary system [Cu(II)-DAHP-OAP] in a wide pH range from 3 to 9. The binary complex [Cu(II)-OAP] is the major contributing species upto pH 4.5. After the pH 4.5 the ternary species [Cu(II)-DAHP-OHP] increases its contribution and the maximum formation of ternary

species takes place around pH 7 onwards.

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