

## THERMODYNAMIC BEHAVIOUR AND STABILITY CONSTANTS OF 5-ARYLAZO-2-METHYLTHIO-4-HYDROXY-6-METHYLPYRIMIDINE (AMHP) COMPLEXES

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(Received 4 September 1981)

### ABSTRACT

The thermodynamic behaviour and stability constants of 5-arylazo 2-methylthio-4-hydroxy-6-methylpyrimidine and its complexes with  $\text{Fe}^{3+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Fe}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{UO}_2^{2+}$ ,  $\text{Cd}^{2+}$ ,  $\text{Zn}^{2+}$ , and  $\text{Mn}^{2+}$  have been determined potentiometrically in 75% (v/v) methanol–water mixture at ionic strength 0.1 M  $\text{NaClO}_4$ . The stability constants have been determined by the Bjerrum–Calvin titration technique as modified by Irving and Rossotti at 25, 30 and 35  $\pm$  0.1°C. The order of stability is  $\text{Fe}^{3+} > \text{UO}_2^{2+} > \text{Cu}^{2+} > \text{Fe}^{2+} > \text{Ni}^{2+} > \text{Zn}^{2+} > \text{Co}^{2+} > \text{Cd}^{2+} > \text{Mn}^{2+}$ . Thermodynamic functions have been calculated and show that the stability of the complexes decreases with increase in temperature and the complex formation is an enthalpy directed process.

### INTRODUCTION

Pyrimidines in various guises are widely distributed in all living cells [1,2] in the form of several vitamins and co-enzymes, and play an important role in biological processes. Vitamin B<sub>1</sub>, a derivative of pyrimidine, has been reported as an antineuritic or antiberiberi [3,4] agent. A number of pyrimidines have found application as antibiotics [5]. Barbituric acid and its analogues have found extensive applications as anaesthetic agents [6,7]. As an arylazo group is of interest in promoting potential antineoplastic activity [8], the pyrimidine molecules having an arylazo group have been synthesized [9]. In the present communication the thermodynamic behaviour of proton ligand and metal ligand stability constants is determined potentiometrically using the Bjerrum–Calvin titration techniques as modified by Irving and Rossotti [10,11].

### EXPERIMENTAL

The ligand AMHP was prepared as described in the literature [9]. Metal salt solutions were prepared by dissolving them in doubly distilled water. An ECIL

expanded scale pH meter with glass and calomel electrode assembly and having an accuracy  $\pm 0.02$  pH units was employed. The pH-meter readings in 75% methanol-water mixture were corrected using the method of Van Uitert and Haas [12].

The titrations were carried out in an inert atmosphere by bubbling nitrogen through the solution. The ionic strength was kept constant at  $\mu = 0.1$  M using 1 M sodium perchlorate. The following set of solutions were titrated against 0.1 M sodium hydroxide at 25, 30 and  $35 \pm 0.1^\circ\text{C}$ .

(1) 4.0 ml of  $\text{HClO}_4$  (0.04 M) + 4 ml of  $\text{NaClO}_4$  (1.0 M) + 30 ml of methanol + 2.0 ml of water;

(2) 4.0 ml of  $\text{HClO}_4$  (0.04 M) + 4.0 ml of  $\text{NaClO}_4$  (1.0 M) + 10 ml of methanol + 20 ml of ligand (0.002 M) + 2.0 ml of water;

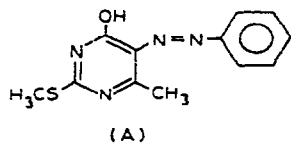
(3) 4.0 ml of  $\text{HClO}_4$  (0.04 M) + 4.0 ml of  $\text{NaClO}_4$  (1.0 M) + 10 ml of methanol + 20 ml of ligand (0.002 M) + 1.0 ml of (0.01 M) metal salt solution + 1.0 ml of water.

The ligand-to-metal ratio was maintained at 4:1 in all the titrations.

## RESULTS AND DISCUSSION

### *Proton ligand stability constant*

The average number of protons associated with the ligand ( $\bar{n}_H$ ) was determined from the acid ligand titration curves using the equation of Irving and Rossotti. It is seen from the structure of the ligand, A, that only one proton per ligand molecule is released on chelation. The maximum value of  $\bar{n}_H$  was found to be in all cases  $< 1$ . The protonation constant ( $\log K^H$ ) was calculated at half integral value from the plot of  $\bar{n}_H$  vs. pH. The proton ligand stability constants and their thermodynamic functions at different temperatures are given in Tables 1 and 2, respectively. It is seen from Table 1 that  $\log K^H$  decreases with increase in temperature.



### *Metal ligand stability constant*

The metal titration curves were well separated from the ligand titration curves. From the titration curves of solutions (II) and (III), the average number of ligand molecules attached per metal ion ( $\bar{n}$ ) and free ligand exponent pL were calculated. The  $\bar{n}$  values were plotted against the corresponding pL values to obtain formation curves of the complexes. In all cases the values of  $\bar{n}$  were found to be  $< 2$ , showing the formation of only two complexes, viz. 1:1 and 1:2 complexes. The values of  $\log K_1$  and  $\log K_2$  were calculated from the formation curves using the Bjerrum half  $\bar{n}$  method and least squares method. The values reported are the means of the two. The

TABLE 1

Stability constants of metal chelates of AMHP at different temperatures at  $\mu=0.1$  M NaClO<sub>4</sub>

Cation	Stability constant								
	25°C			30°C			35°C		
	log $K_1$	log $K_2$	log $\beta_2$	log $K_1$	log $K_2$	log $\beta_2$	log $K_1$	log $K_2$	log $\beta_2$
H <sup>+</sup>	7.20			7.00			6.90		
UO <sub>2</sub> <sup>2+</sup>	6.76	6.18	12.94	6.51	5.94	12.45	6.25	5.80	12.05
Cu <sup>2+</sup>	6.44	5.88	12.32	6.23	5.67	11.90	5.96	5.45	11.41
Fe <sup>3+</sup>	7.12	6.42	13.56	6.86	6.30	13.16	6.63	6.23	12.86
Fe <sup>2+</sup>	5.98	5.41	11.39	5.84	5.28	11.12	5.68	5.12	10.80
Ni <sup>2+</sup>	5.82	5.30	11.12	5.66	5.14	10.80	5.42	5.03	10.45
Zn <sup>2+</sup>	5.43	4.51	9.94	5.24	4.32	9.56	5.02	4.16	9.18
Co <sup>2+</sup>	5.16	4.54	9.70	4.97	4.35	9.32	4.73	4.24	8.97
Cd <sup>2+</sup>	4.62	4.20	8.82	4.48	4.00	8.48	4.26	3.82	8.08
Mn <sup>2+</sup>	4.16	3.46	7.62	3.98	3.23	7.21	3.72	3.16	6.88

metal ligand stability data log  $K_1$  ( $\pm 0.04$ ), log  $K_2$  ( $\pm 0.05$ ) and log  $\beta_2$  ( $\pm 0.09$ ) at various temperatures are reported in Table I. The order of stability for these complexes is found to be Fe<sup>3+</sup> > UO<sub>2</sub><sup>2+</sup> > Cu<sup>2+</sup> > Fe<sup>2+</sup> > Ni<sup>2+</sup> > Zn<sup>2+</sup> > Co<sup>2+</sup> > Cd<sup>2+</sup> > Mn<sup>2+</sup>. The stability order Cu<sup>2+</sup> > Ni<sup>2+</sup> > Zn<sup>2+</sup> > Co<sup>2+</sup> > Cd<sup>2+</sup> > Mn<sup>2+</sup> is in accordance with the Irving–Williams rule [13]. The order UO<sub>2</sub><sup>2+</sup> > Cu<sup>2+</sup> is in accordance with the greater affinity of UO<sub>2</sub><sup>2+</sup> for O<sup>-</sup>, O<sup>-</sup> donors than Cu<sup>2+</sup> [14]. The higher stability of the Fe<sup>2+</sup> complex has been observed in many cases.

TABLE 2

Thermodynamic functions of metal complexes at 30°C

Cation	$-\Delta G$ (kcal mole <sup>-1</sup> )			$-\Delta H$ (kcal mole <sup>-1</sup> )			$-\Delta S$ (cal mole <sup>-1</sup> )		
	$\Delta G_1$	$\Delta G_2$	$\Delta G^0$	$\Delta H_1$	$\Delta H_2$	$\Delta H^0$	$\Delta S_1$	$\Delta S_2$	$\Delta S^0$
H <sup>+</sup>			9.71			12.60			73.63
Fe <sup>3+</sup>	9.51	8.74	18.25	20.58	7.98	28.46	99.31	55.18	154.16
UO <sub>2</sub> <sup>2+</sup>	9.03	8.24	17.26	21.42	15.96	37.38	100.49	79.86	180.33
Cu <sup>2+</sup>	8.64	7.86	16.50	20.16	18.06	38.22	95.05	85.54	180.59
Fe <sup>2+</sup>	8.10	7.32	15.42	12.60	12.18	24.78	68.32	64.36	132.67
Ni <sup>2+</sup>	7.85	7.13	14.97	16.80	11.37	28.17	81.35	61.06	142.38
Zn <sup>2+</sup>	7.52	5.99	13.26	17.22	14.70	31.92	81.65	68.28	149.11
Co <sup>2+</sup>	6.89	6.03	12.92	18.06	12.60	30.66	82.34	61.48	143.82
Cd <sup>2+</sup>	6.21	5.55	11.76	15.12	15.96	31.08	70.39	70.99	141.38
Mn <sup>2+</sup>	5.52	4.48	9.99	20.16	12.60	32.76	84.75	56.37	141.09

particularly with aromatic ligands, e.g. riboflavin [15], folic acid [15], *ortho* phenanthroline [16], 1-(2,3 dihydroxy-4-pyridylazo) benzene-4-sulphonic acid [17], and may be attributed to the resonance stabilization energy of  $\text{Fe}^{2+}$  complexes of ligands having aromatic ring systems [16]. The higher stability of the  $\text{Fe(III)}$  complex as compared to that of divalent metal complexes is expected on the basis of charge and ionization potential of the metal ions. The separation factors between the first and second stability constants are well within the expected range and the absence of a high value implies there is no or little steric hindrance to the addition of a second chelate group. In the case of chelating agents, having bulky substituents near the donor atoms, such steric hindrance causes  $K_1/K_2$  to be unusually high. For an anionic ligand coulombic attraction is greater for  $\text{M}^{2+}$  compared to  $\text{MA}^+$ . As such,  $\log K_1 - \log K_2$  is usually positive. Table 1 shows that for all the systems studied here  $\log K_1 - \log K_2$  is positive [18]. The variation of the stability of the complexes of divalent metal ions may be represented by plotting  $\log \beta$  against the second ionization potential of the metal (Fig. 1). Such correlations were made by Calvin and Melchior [19] for the formation of metal chelates of 5-salicylaldehyde sulphonate. The lower stability constant of  $\text{Zn}^{2+}$  than that of  $\text{Cu}^{2+}$  may be explained on the basis of the following factors:

- (1) the  $d$ -orbital which is not taking part in homopolar bond formation;
- (2) ionic radii; and
- (3) higher charge density of electrons around the metal ion [20].

The free energy, enthalpy and entropy changes have been evaluated using standard relations. The values of  $\Delta H$  were obtained from the slope of  $\log K$  vs.  $1/T$  plots. Wherever a linear plot was not obtained, a tangent was drawn to obtain the

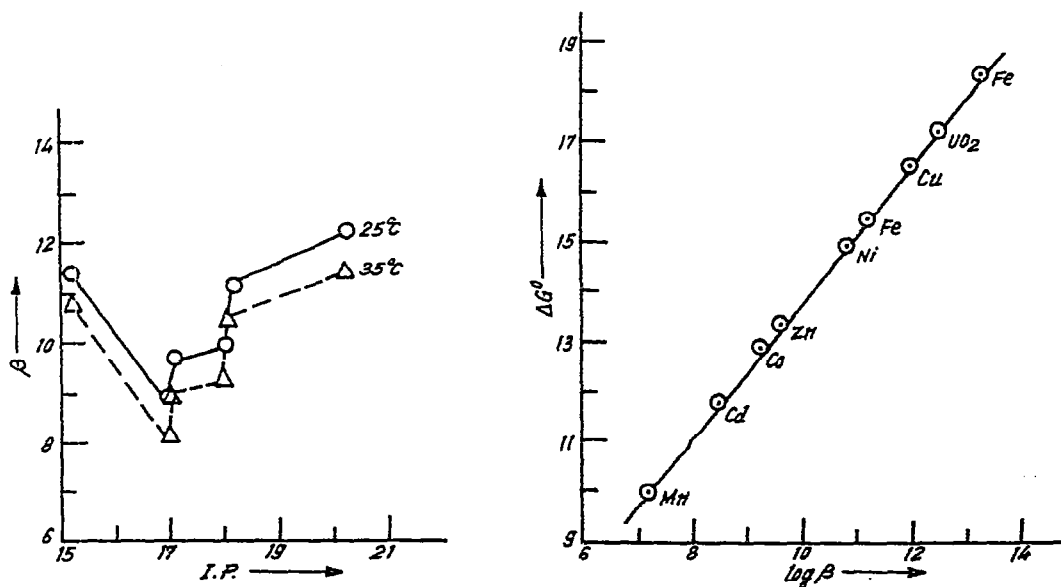
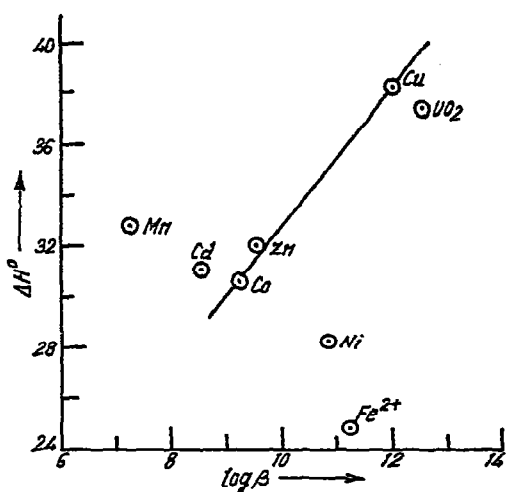
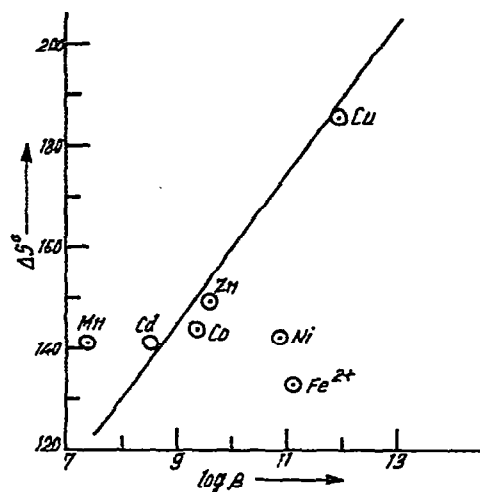


Fig. 1. Plots of  $\beta$  vs. second ionization potential with  $\text{M}^{2+}$  ions.

Fig. 2. Plot of  $\Delta G^0$  vs.  $\log \beta$ .

Fig. 3. Plot of  $\Delta H^0$  vs.  $\log \beta$ .Fig. 4. Plot of  $\Delta S^0$  vs.  $\log \beta$ .

slope which was taken equivalent to  $-\Delta H/4.57$ . These thermodynamic functions are summarized in Table 2. The negative  $\Delta G^0$  values and the decrease in stability constant with increase in temperature show (Table 1) that complex formation is spontaneous. The error in  $\Delta G^0$  and  $\Delta H^0$  values lies in the range  $0.4$ – $0.8$  kcal mole $^{-1}$  and that for  $\Delta S^0$  is  $0.8$  cal deg $^{-1}$  mole $^{-1}$ . It is evident from Table 2 that complex formation is exothermic and explains why the formation constants have higher values at lower temperature.

The net entropy changes associated with the metal–chelate formation can be attributed to a combination of (i) an increase in  $\Delta S^0$  values owing to the release of water of hydration; (ii) a decrease in entropy of translation on formation of one chelate from two species; and (iii) a decrease in configuration entropy of the ligand on complex formation. For reactions with charged donor groups, the entropy changes associated with (i) predominate because of neutralization of charge on the metal ion; this results in a greater release of water of hydration and hence greater disorder of the partially immobilized and oriented water dipoles. The negative values of both enthalpy and entropy encountered here suggest that the enthalpy term is favourable and entropy term unfavourable for chelate formation. This might be due to substitution of solvent molecules attached to the metal ion by the ligand, resulting in the release of these solvent molecules. It is of interest to compare the stability constant value with standard free energy ( $\Delta G^0$ ), enthalpy ( $\Delta H^0$ ) and entropy ( $\Delta S^0$ ). Linear relationships (Fig. 2–4) are obtained.

#### ACKNOWLEDGEMENT

The authors are grateful to the C.S.I.R. New Delhi for financial assistance.

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