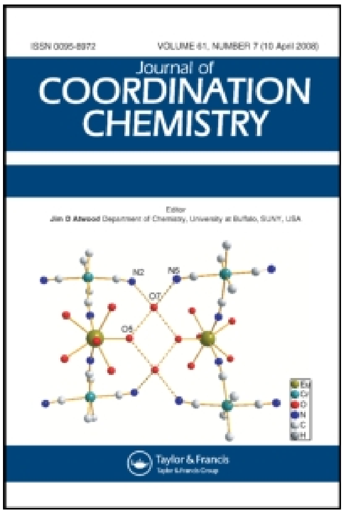

Journal of Coordination Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713455674

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To cite this Article Sridharan, R. and Krishnamoorthy, C. R.(1983) 'EQUILIBRIUM STUDY ON BINARY COMPLEXES OF Cu(II), Ni(II) Co(II) and Mg(II) WITH NUCLEIC ACID BASES', Journal of Coordination Chemistry, 12: 4, 231 — 235
To link to this Article: DOI: 10.1080/00958978308073853
URL: http://dx.doi.org/10.1080/00958978308073853

J. Coord. Chem., 1983, Vol. 12, pp. 231-236
0095-8972/83/1204-0231 $18.50/0

EQUILIBRIUM STUDY ON BINARY COMPLEXES OF Cu(II), Ni(II) Co(II) and Mg(II) WITH NUCLEIC ACID BASES

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(Received May 3, 1982; in final form July 7, 1982)

Formation constants of 1:1 binary complexes of Cu(II), Ni(II), Co(III) and Mg(II) with nucleic acid bases such as adenine, 8-azaadenine, cytosine and uracil are reported at 30° at an ionic strength of 0.1M (KNO_3). The acid dissociation constants of the above ligands are reported at 30 and 60° together with the thermodynamic parameters involved in their dissociation reactions. In general the first dissociation is favourable and the stability of the 1:1 metal complexes decreases in the order Cu(II) > Ni(II) > Co(II) > Mg(II). There is a good correlation between the basicity of the ligands and the stability of the 1:1 metal complexes. No significant interaction is observed in the case of uracil with any of the metal ions investigated.

INTRODUCTION

Recently there have been extensive studies on the transition metal complexes of purines and pyrimidines.[1-6] These studies have been motivated because of the biological relevance of metal binding to DNA constituents. Moreover the carcinostatic activity of some substituted purines and pyrimidines[8-11] also prompted investigations. As a part of a broad programme to study the interaction of metal ions with complicated molecules like polynucleotides it was considered appropriate to start with simple ligands such as nucleic acid bases. Thus the present investigation attempts a detailed study of the interaction of metal ions such as Cu(II), Ni(II), Co(II) and Mg(II) with adenine, 8-azaadenine, cytosine and uracil at 30° in aqueous solution. A similar study was carried out at 45° in this laboratory previously.[12]

EXPERIMENT AND CALCULATIONS

Potentiometric titrations were carried out using an L1-120 Elico digital pH meter with a combined electrode. The electrode system was calibrated and the titrations were carried out as described previously.[12] The reagents were of AnalaR grade and the metal nitrates were standardised by the methods outlined earlier.[13] Carbonate-free sodium hydroxide was prepared and standardised by titration with potassium hydrogen phthalate.

The dissociation reactions of the ligands can be expressed as shown in equations (*1*) and (*2*) and the constants were calculated by a direct algebraic method.[14]

$$H_2L \underset{}{\overset{k_a}{\rightleftharpoons}} HL + H^+;\ k_a = \frac{[HL][H^+]}{[H_2L]} \qquad (1)$$

$$HL \underset{}{\overset{k_{2a}}{\rightleftharpoons}} L + H^+;\ k_{2a} = \frac{[L][H^+]}{[HL]} \qquad (2)$$

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Formation of the 1:1 binary complex is indicated by the following equilibrium.

$$M + L \rightleftharpoons ML;\ K_{ML} = \frac{[ML]}{[M][L]} \qquad (3)$$

Charges in the above equilibrium expressions are omitted for simplicity. The stabilities of the complexes were calculated using methods described earlier.[15]

RESULTS AND DISCUSSION

Acid dissociation constants of the ligands calculated by a direct algebraic method from the potentiometric titration data obtained from Figure 1 and are presented in Table 1. Adenine, 8-azaadenine and cytosine were protonated by adding one equivalent of hydrochloric acid. Titration curves similar to that in Figure 1 were obtained in all other cases.

Thermodynamic parameters associated with the dissociation reactions of the ligands calculated from their corresponding temperature coefficient data are presented in Table 2.

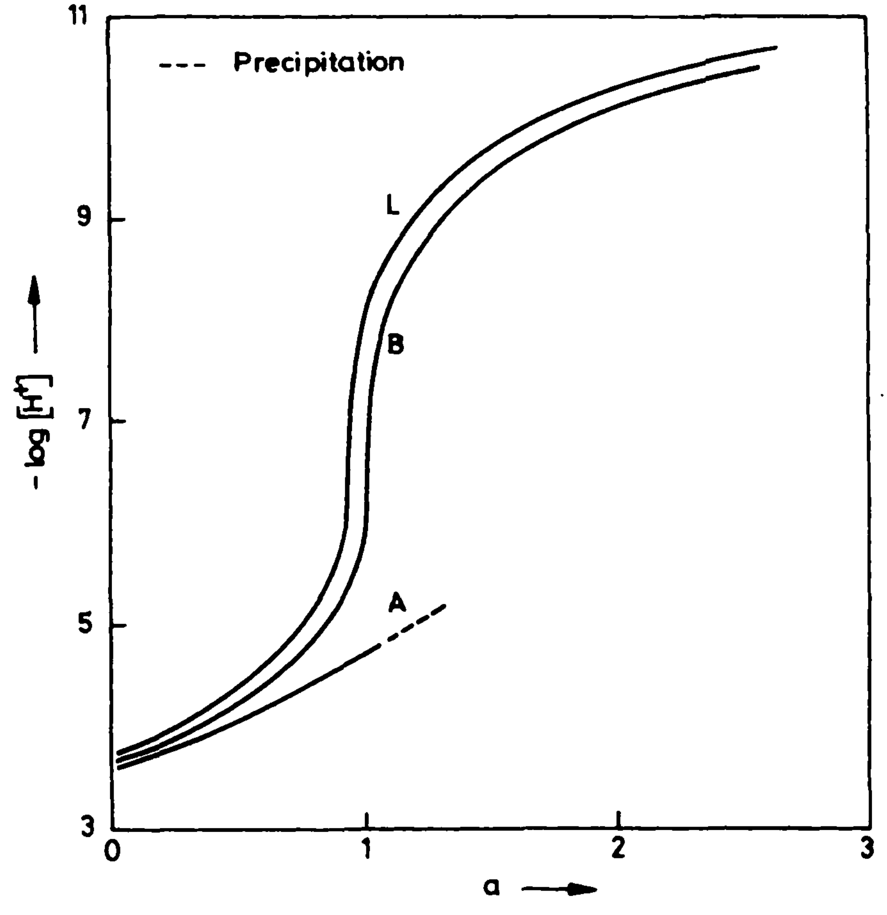


FIGURE 1 Potentiometric titration curves for adenine with Cu(II) and Mg(II) in 1:1 ratio of ligand to metal ion at 30° and μ = 0.1M (KNO_3). L = Free ligand curve, A = Cu(II) – Adenine curve, B = Mg(II) – Adenine curve and a = number of moles of base added per mole of ligand.

TABLE 1
Acid dissociation constants of the purine and pyrimidine bases at $\mu = 0.1$ M(KNO_3).

Ligand	30°		60°	
	pk_a	pk_{2a}	pk_a	pk_{2a}
adenine	4.34 ± 0.01	9.63 ± 0.01	4.09 ± 0.03	9.31 ± 0.06
8-azaadenine	3.51 ± 0.06	6.68 ± 0.06	3.29 ± 0.05	6.35 ± 0.06
cytosine	4.76 ± 0.03	11.55 ± 0.06	4.20 ± 0.03	10.60 ± 0.06
uracil	9.14 ± 0.06	–	8.66 ± 0.06	–

TABLE 2
Thermodynamic parameters associated with the ligand dissociations

Ligand	ΔHi kJ mol^{-1}	ΔGi kJ mol^{-1}	ΔSi J K^{-1} mol^{-1}
adenine	16.1	25.2	−30.0
	20.7	55.9	−116.3
8-azaadenine	14.2	20.4	−20.4
	21.3	38.8	−57.6
cytosine	36.1	27.6	27.9
	61.3	67.1	−19.1
uracil	31.00	53.1	−72.9

The 1:1 formation constants for the interaction of metal ions with the ligands have been calculated at 30°. The titrations could not be completed because of the separation of a solid phase before the inflection point. However calculations were carried out in the region of the titration curve well ahead of the precipitation point. No significant interaction was observed in the case of uracil with any of the metal ions. The reacting species, the anionic form of uracil, is present only in small amounts in the pH range employed in this investigation. The formation constants calculated are given in Table 2.

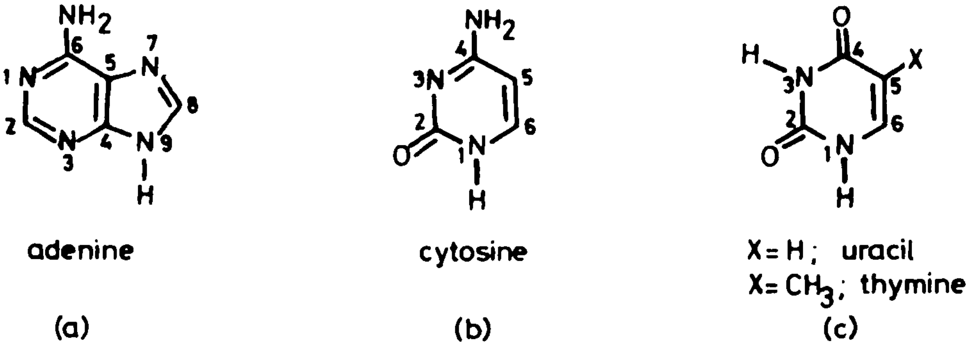
The acid dissociation constants reported in Table 1 fall in line with values reported earlier,[12,16–18] even though different experimental conditions were employed. The thermodynamic parameters reported here clearly show that both enthalpy and entropy factors favour the first dissociation reaction of all the ligands.

The stability of the above 1:1 metal complexes seems to be independent of the metal ion concentration indicating that the possibility of polynuclear species being formed is not important.

TABLE 3
1:1 formation constants for the interaction of the metal ions with the bases at 30° $\mu = 0.1$ M(KNO_3).[a]

Metal ion	Adenine log K	8-Azaadenine log K	Cytosine log K
Cu(II)	7.4	5.7	7.0
Ni(II)	7.1	5.5	5.2
Co(II)	6.8	5.3	5.2
Mg(II)	6.7	5.1	2.2

[a] ±0.1 log K units.



adenine

(a)

cytosine

(b)

X = H ; uracil
X = CH_3; thymine

(c)

FIGURE 2 The bases involved in this study.

Regarding the nature of metal ion binding in these complexes, the ligands act mostly as monodentates in their coordination to transition metal ions though chelation is seen as a possible alternative.[19,20] When chelation is considered as the preferred alternative, purine bases can form stable chelates (a 5-membered ring (Fig. 2a) involving the substituent at position 6, the metal ion and N(7)), whereas metal chelation in pyrimidines involves a less stable 4-membered ring (Fig. 2b, 2c). In the present investigation it is found that the stability of both purine and pyrimidine metal complexes are almost equal. This indirectly suggests that both these ligands may be acting as monodentates making use of the common pyrimidine ring.

Another conclusion which may be drawn here is that the stabilities of the 1:1 binary complexes are in perfect agreement with the basicities of the ligands which decrease in the order adenine > 8-azaadenine > cytosine. Thus the increased basicity of adenine makes its metal complexes more stable. Introduction of an aza-group in position seven decreases the overall basicity of the purine ring system as seen in the case of 8-azaadenine. The absence of an imidazole ring in cytosine likewise decreases its overall basicity. The higher stability of the Cu(II)-cytosine complex compared with that of 8-azaadenine cannot be explained on the basis of our present investigation, but it may be due to the predominant influence of factors other than the basicity of the ligand. Finally, with respect to the metal ions, the stabilities of the 1:1 binary complexes decrease in the order Cu(II) > Ni(II) > Co(II) > Mg(II), as expected.

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