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Enthalpy and Entropy Changes Associated with the Ternary Complexes of Xanthosine in Solution

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Potentiometric equilibrium measurements have been made at 5, 25, 35, and 45 °C for the formation of ternary complexes of xanthosine and Cu(II), Ni(II), Zn(II), Co(II), Mn(II), Mg(II), and Ca(II) with bipyridyl (bpy), *o*-phenanthroline (*o*-phen), 5-sulfosalicylic acid (SSA), and *N,N,N',N'*-tetramethylethylenediamine (TMEN) in a 1:1:1 ratio. The ionic strength was maintained constant by using 0.10 M KNO_3 as the supporting electrolyte. The ternary complexes of the above systems were found to be more stable than the corresponding binary complexes. The enthalpy ($\Delta H_\mathrm{f}^\circ$) and entropy ($\Delta S_\mathrm{f}^\circ$) changes associated with the ternary complexes of xanthosine were calculated from the 1:1:1 stability constants by temperature coefficient data. With the aid of these parameters (enthalpy and entropy changes), we have evaluated new quantities, $\Delta\Delta H_\mathrm{f}^\circ$ and $\Delta\Delta S_\mathrm{f}^\circ$, to explain the extra stability found in these ternary complexes. $\Delta\Delta H_\mathrm{f}^\circ$ and $\Delta\Delta S_\mathrm{f}^\circ$ are the differences between the enthalpy and entropy changes associated with the ternary and binary complexes, respectively. Various factors have been attributed to account for this extra stability found in these systems. Of these, the stacking interaction, which is expected to occur between the purine part of xanthosine and the aromatic secondary ligands, seems to be most effective.

Introduction

Ternary complexes of nucleosides and nucleotides have received much attention during the last decade, because of their importance in biological systems.[1-7] Such studies will help toward understanding the nature of similar species that are present in biological systems. They also provide useful information in understanding the specific and selective interactions that take place in many biochemical processes. Ternary complexes of nucleosides and nucleotides are found to be more stable than the corresponding binary complexes,[8-13] a fact which is contrary to the statistical considerations. Then the question arises as to what the factors are that are responsible for the extra stability of ternary complexes. It is difficult to attribute any single factor to this; in fact, there are many factors that are responsible for the extra stability of ternary complexes. One such factor is the π-accepting capacity of the secondary ligands concerned. It has been observed that in ternary complexes ligands containing O as a donor atom form stabler complexes with π-accepting ligands and metal ions.[14] However, there is equally strong evidence that ligands containing mixed N and O as donor atoms form stabler complexes than ligands containing pure N or O as donor atoms with π-accepting ligands and metal ions.[7,15] In addition to this, it is an established fact that purine and pyrimidine bases, nucleosides, and nucleotides associate extensively in aqueous solution by a mechanism involving vertical stacking of bases.[16] This stacking interaction has also been observed in biological systems.[17] The influence of divalent metal ions on the self-association tendency of nucleoside 5'-triphosphates has been reported by Sigel recently.[18] Therefore, in the case of nucleosides similar effects are also expected, though to a lesser extent. In most of the papers on ternary complexes the extra stability is measured in terms of $\Delta \log K$ values (where $\Delta \log K$ is the difference in stabilities between ternary and binary complexes). But, the values of $\Delta \log K$ itself vary with temperature. Since the values of $\Delta \log K$ vary with temperature, there is a need to measure this extra stability in ternary complexes by other parameters, such as $\Delta\Delta H_\mathrm{f}^\circ$ and $\Delta\Delta S_\mathrm{f}^\circ$, which directly measure the extent of extra interaction in these systems. $\Delta\Delta H_\mathrm{f}^\circ$ and $\Delta\Delta S_\mathrm{f}^\circ$ are the differences between the enthalpy and entropy changes associated with the ternary and binary complexes, respectively; i.e., $\Delta\Delta H_\mathrm{f}^\circ = \Delta H_\mathrm{T}^\circ - \Delta H_\mathrm{B}^\circ$ and $\Delta\Delta S_\mathrm{f}^\circ = \Delta S_\mathrm{T}^\circ - \Delta S_\mathrm{B}^\circ$, where $\Delta H_\mathrm{T}^\circ$, $\Delta S_\mathrm{T}^\circ$ and $\Delta H_\mathrm{B}^\circ$, $\Delta S_\mathrm{B}^\circ$ are the enthalpy and entropy values associated with the ternary and binary complexes, respectively. In this paper we report the enthalpy and entropy changes associated with the ternary complexes of xanthosine in solution. With the aid of these parameters we have evaluated the $\Delta\Delta H_\mathrm{f}^\circ$ and $\Delta\Delta S_\mathrm{f}^\circ$ to explain the extra stability found in ternary complexes. This type of correlation, we hope, will lead to a more comprehensive understanding of ternary complexes of biomolecules in solution.

Experimental Section

Xanthosine was obtained from Sigma Chemicals, St. Louis, MO, and *o*-phenanthroline (*o*-phen), α,α'-bipyridyl (bpy), 5-sulfosalicylic acid (SSA), and *N,N,N',N'*-tetramethylethylenediamine (TMEN) were obtained from E. Merck, Darmstadt, West Germany.

Stock solutions of *o*-phen and bpy, in the diprotonated form, and SSA and TMEN were prepared from double-distilled water. For every titration, fresh solid ligand (xanthosine) was weighed out into the reaction cell to avoid possible hydrolysis. Metal salts of Cu(II), Ni(II), Co(II), Zn(II), Mn(II), Mg(II), and Ca(II) were of AnalaR grade, and the metal ions were standardized volumetrically by titration with the sodium salt of EDTA in the presence of a suitable indicator as outlined by Schwarzenbach.[19] Carbonate-free sodium hydroxide was

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prepared by the method of Schwarzenbach and Biedermann[20] and was standardized by titration with potassium hydrogen phthalate.

The experimental method employed consisted of potentiometric titration of the ligand with a standard sodium hydroxide solution, in the absence and presence of the above-mentioned metal ions being investigated. The ionic strength was maintained constant by using 0.10 M KNO_3 as the supporting electrolyte and relatively low concentrations of the ligand and metal ion (1×10^{-3} M). During the course of titrations a stream of nitrogen is passed over the solution to eliminate the adverse effect of atmospheric carbon dioxide.

An ECIL digital pH metal (Model pH 5651) with a combination electrode was used to determine the hydrogen ion concentration. The electrode system was calibrated by direct titration of acetic acid, and the observed pH meter reading was compared with the actual hydrogen ion concentration. The pH regions below 3.5 and above 10.5 were calibrated by measurement in HCl and NaOH solutions, respectively.

Calculations

The proton dissociation constants of ligands TMEN, bpy, *o*-phen, and SSA at different temperatures are related to the usual equilibrium dissociations[7] as

$$H_2L \rightleftharpoons HL^- + H^+$$

$$HL \rightleftharpoons L^{2-} + H^+$$

Formation of Mixed-Ligand 1:1:1 Complexes. In the case of ternary complexes of metal ions, xanthosine, and TMEN in a 1:1:1 ratio the following equation was used

$$M^{2+} + H_2L + H_2A \rightleftharpoons MH_2LA + 2H^+$$

together with the related equilibria (charges omitted)

$$M + HL + HA \xrightleftharpoons{K^{M}{}_{MH_2LA}} MH_2LA$$

$$K^{M}{}_{MH_2LA} = \frac{T_M - [HL]X}{[HL]^3X^2} \qquad (1)$$

where

$$[HL^-] = \frac{(2-m)T_M - [H^+] + [OH^-]}{\dfrac{[H^+]}{K_a(L)} + \dfrac{X}{Y}\dfrac{[H^+]}{K_a(A)}}$$

$$X = ([H^+]/K_a(L)) + 1 \text{ (using } K_a \text{ value of xanthosine)}$$

$$Y = ([H^+]/K_a(A)) + 1 \text{ (using } K_a \text{ value of TMEN)}$$

For the ternary complexes of Cu(II), Ni(II), Zn(II), and Co(II) of xanthosine with bpy or *o*-phen the following equations were used (charges omitted)

$$M + A \rightleftharpoons MA$$

$$MA + HL \rightleftharpoons MHLA$$

A = bpy or *o*-phen, HL = xanthosine

$$K^{MA}{}_{MHLA} = \frac{[MHLA]}{[MA][HL]} \qquad (2)$$

where MA denotes the 1:1 metal–bpy or metal–*o*-phen complex. The calculation of $K^{MA}{}_{MHLA}$ is similar to the calculation of the 1:1 metal–xanthosine complex.[6]

However, in the case of Mn(II), Mg(II), and Ca(II) complexes of xanthosine with bpy and *o*-phen separate equations were used as they form different type of complexes (charges omitted). For the *o*-phen system

$$M + A + HL \xrightleftharpoons{K^{M}{}_{MHLA}} MHLA$$

$$K^{M}{}_{MHLA} = \frac{T_M - [L]X_A}{[L]^3X_A{}^2}X_L \qquad (3)$$

where

$$[L] = \frac{6T_M - (2mT_M - 2[H^+] + 2[OH^-])}{\alpha_A + (3\alpha_LX_A/X_L) + (X_A/X_L)}$$

$$X_A = [H^+]^2/(K_aK_{2a}) + ([H^+]/K_{2a}) + 1$$

$$\alpha_A = (3[H^+]^2/K_aK_{2a}) + ([H^+]/K_{2a}) - 1$$

$$\alpha_L = [H^+]/K_a$$

$$X_L = ([H^+]/K_a) + 1$$

where the subscripts A and L represents for the ligands *o*-phen and xanthosine, respectively. For the bpy system

$$M + A + HL \xrightleftharpoons{K^{M}{}_{MHLA}} MHLA$$

$$K = \frac{T_M - [L]X}{[L]^3X^2}Y \qquad (4)$$

where

$$[L] = \frac{(3-m)T_M - [H^+] + [OH^-]}{\dfrac{[H^+]}{K_{2a}(A)} + \dfrac{[H^+]}{K_a(L)}\dfrac{X}{Y}}$$

$$X = \frac{[H^+]}{K_{2a}(A)} + 1 \quad \text{(using } K_{2a} \text{ value of bpy)}$$

$$Y = \frac{[H^+]}{K_a(L)} + 1 \quad \text{(using } K_a \text{ value of xanthosine)}$$

The stability constant for the ternary complexes of metal–xanthosine–SSA in a 1:1:1 ratio was calculated by the equation

$$MHA + HL \xrightleftharpoons{K^{MHA}{}_{MH_2LA}} MH_2LA$$

The constant $K^{MHA}{}_{MH_2LA}$ was calculated in a manner similar to that described for the Cu(II), Ni(II), Zn(II), and Co(II)–xanthosine–bipyridyl system. MHA represents the 1:1 metal–SSA system.

Thermodynamic Constants. Values of the enthalpy of complex formation $\Delta H_f°$ were obtained at each temperature interval by the relationship

$$\Delta H_f° = \frac{2.303RT_1T_2 \log (K_2/K_1)}{T_2 - T_1}$$

The above equation gave better statistical variation of $\Delta H_f°$ than those obtained by a plot of log K against $1/T$. Values of $\Delta G_f°$ and $\Delta S_f°$ for the various reactions involved were calculated by the relationships

$$\Delta G_f° = -RT \ln K$$

$$\Delta S_f° = \frac{\Delta H_f° - \Delta G_f°}{T}$$

where

$\Delta H_f°$ = standard enthalpy change
R = gas constant
T = absolute temperature
K = equilibrium constant
$\Delta G_f°$ = standard free energy change
$\Delta S_f°$ = standard entropy change

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Table I. Proton Dissociation Constants of Ligands (μ = 0 10 M (KNO_3))

ligand	temp, °C	pK_a	pK_{2a}
TMEN	5	6.40 ± 0.02	9.76 ± 0.02
	25	5.93 ± 0.01	9.20 ± 0.02
	35	5.83 ± 0.01	9.03 ± 0.03
α,α′-bpy	5		4.93 ± 0.03
	25		4.47 ± 0.02
	35		4.36 ± 0.02
o-phen	5	2.96 ± 0.02	5.37 ± 0.02
	25	2.40 ± 0.03	5.12 ± 0.03
	35	2.16 ± 0.03	4.99 ± 0.03
ligand	**temp, °C**	**pK_{2a}**	**pK_{3a}**
SSA	5	2.74 ± 0.02	11.95 ± 0.06
	25	2.46 ± 0.03	11.58 ± 0.06
	35	2.41 ± 0.03	11.05 ± 0.05

The values of $\Delta\Delta H_f°$ and $\Delta\Delta S_f°$ are calculated by the equations

$$\Delta\Delta H_f° = \Delta H_T° - \Delta H_B°$$

$$\Delta\Delta S_f° = \Delta S_T° - \Delta S_B°$$

where, $\Delta H_T°$, $\Delta S_T°$ and $\Delta H_B°$, $\Delta S_B°$ are the enthalpy and entropy values associated with the ternary and binary complexes, respectively.

Results and Discussion

The proton dissociation constants of the ligands TMEN, bpy, *o*-phen, and SSA calculated at different temperatures are given in Table I.

Metal–Xanthosine–*N,N,N′,N′*-Tetramethylethylenediamine (TMEN) System (1:1:1). Titrations of equimolar amounts of xanthosine–TMEN and Cu(II), Ni(II), Zn(II), Co(II), Mn(II), Mg(II), and Ca(II) at 45 °C gave an inflection at $m = 2$ (where "m" is the moles of base added per mole of metal ion) corresponding to the formation of the diprotonated species with the stability constant $K^{M}{}_{MH_2LA}$. The titration curves of the above-mentioned metal ions with xanthosine and TMEN at 5, 25, and 35 °C are similar[7] to those at 45 °C. Accordingly, the diprotonated constants were calculated with the help of eq 1. The constants thus calculated are presented in Table II and the corresponding thermodynamic parameters in Table III.

Metal–Xanthosine–α,α′-Bipyridyl (bpy) System (1:1:1). The mixed-ligand titration curves of Cu(II), Ni(II), Zn(II), and Co(II) with xanthosine and bipyridyl in a 1:1:1 ratio gave inflections at $m = 2$ and $m = 3$ at 45 °C.[7] Similar titration curves were obtained for the above systems at 5, 25, and 35 °C, also indicating the formation of a monoprotonated 1:1:1 species from the normal 1:1 metal–bipyridyl complex in the buffer region between $m = 2$ and $m = 3$. The stability constants calculated with the help of eq 2 are listed in Table IV. However, in the case of Mn(II), Mg(II), and Ca(II) metal ions with xanthosine and bipyridyl inflections were obtained at $m = 3$ at 45 °C[7] and similar trends were seen at other temperatures studied. This indicates simultaneous formation of the 1:1:1 complex in the entire buffer region, i.e. between $m = 0$ and $m = 3$. The stability constants, $K^{M}{}_{MHLA}$, calculated by eq 4 are listed in Table IV. The thermodynamic quantities associated with the above system are given in Table V.

Metal–Xanthosine–*o*-Phenanthroline (*o*-phen) System (1:1:1). Mixed-ligand titration curves for Cu(II), Ni(II), Zn(II), and Co(II) with xanthosine and *o*-phen in an equimolar ratio showed inflections at $m = 2$ and $m = 3$ at 45,[7] 5, 25, and 35 °C. The stability constants $K^{MA}{}_{MHLA}$ were calculated in a manner similar to that for the metal–xanthosine–bpy system. In the case of the Mn(II)–xanthosine–*o*-phen system, however, an inflection was obtained at $m = 3$, indicating the formation of a monoprotonated 1:1:1 complex at all the temperatures under investigation. Accordingly, the stability constants were calculated with the help of eq 3 and are presented in Table IV and their thermodynamic quantities in Table V. However, no complexation was observed for Mg(II) and Ca(II) metal ions with xanthosine and *o*-phen at any temperature studied.

Metal–Xanthosine–5-Sulfosalicylic Acid (SSA) System (1:1:1). Potentiometric titration curves for the ternary complexes of Cu(II), Ni(II), Zn(II), Co(II), Mn(II), Mg(II), and Ca(II) with xanthosine and SSA showed inflections at $m = 2$ and $m = 3$ at 45 °C.[7] Accordingly, it was assumed that a diprotonated 1:1:1 complex was formed from the protonated 1:1 metal–SSA complex in the buffer region between $m = 2$ and $m = 3$. Similar results were obtained at 5, 25, and 35 °C also for this system. The constants $K^{MHA}{}_{MH_2LA}$ were calculated, and the data are given in Table II. The corresponding thermodynamic constants are tabulated in Table III.

The stability constants of 1:1:1 metal–xanthosine–bpy, *o*-phen, and SSA are higher than the corresponding 1:1 met-

Table II. Stability Constants of 1:1:1 Metal–Xanthosine–TMEN and Metal–Xanthosine–SSA Complexes (μ = 0.10 M (KNO_3))

metal(II) ion	metal–xanthosine–TMEN (1:1:1)			metal–xanthosine–SSA (1:1:1)		
	log $K^{M}{}_{MH_2LA}$			log $K^{MHA}{}_{MH_2LA}$		
	5 °C	25 °C	35 °C	5 °C	25 °C	35 °C
Cu	7.56 ± 0.09	7.24 ± 0.06	7.16 ± 0.06	3.84 ± 0.05	3.70 ± 0.05	3.84 ± 0.05
Ni	6.03 ± 0.08	5.86 ± 0.10	5.38 ± 0.10	3.11 ± 0.06	2.92 ± 0.02	3.01 ± 0.04
Zn	5.68 ± 0.16	5.47 ± 0.11	5.43 ± 0.11	2.71 ± 0.10	2.37 ± 0.04	2.81 ± 0.06
Co	5.44 ± 0.10	5.27 ± 0.06	5.19 ± 0.06	2.72 ± 0.15	2.56 ± 0.05	2.84 ± 0.04
Mn	5.52 ± 0.07	5.22 ± 0.07	4.92 ± 0.05	2.97 ± 0.10	2.79 ± 0.05	3.02 ± 0.02
Mg	4.98 ± 0.06	5.18 ± 0.04	5.11 ± 0.04	2.18 ± 0.04	2.08 ± 0.02	2.17 ± 0.04
Ca	5.40 ± 0.10	5.34 ± 0.09	5.12 ± 0.09	2.38 ± 0.04	2.26 ± 0.05	2.20 ± 0.03

Table III. Thermodynamic Parameters Associated with the Interaction of Metal Ions with Xanthosine–TMEN and Xanthosine–SSA Systems (μ = 0.10 M (KNO_3))

metal(II) ion	metal–xanthosine–TMEN (1:1:1)			metal–xanthosine–SSA (1:1:1)		
	$\Delta H_f°$, kcal/mol	$\Delta G_f°$(25 °C), kcal/mol	$\Delta S_f°$(25 °C), eu	$\Delta H_f°$, kcal/mol	$\Delta G_f°$(25 °C), kcal/mol	$\Delta S_f°$(25 °C), eu
Cu	−5.3 ± 0.8	−9.87 ± 0.06	+15.3 ± 2.5	−2.7 ± 0.4	−5.05 ± 0.06	+8.1 ± 1.2
Ni	−6.2 ± 0.2	−7.99 ± 0.10	+5.9 ± 3.7	−1.8 ± 0.4	−3.98 ± 0.05	+7.2 ± 1.2
Zn	−2.8 ± 0.6	−7.46 ± 0.10	+15.6 ± 1.8	−2.1 ± 0.8	−3.23 ± 0.02	+3.6 ± 2.4
Co	−1.8 ± 0.3	−7.19 ± 0.11	+17.9 ± 0.7	−2.0 ± 0.3	−3.49 ± 0.04	+4.8 ± 1.0
Mn	−5.4 ± 0.3	−7.12 ± 0.66	+5.7 ± 0.7	−1.4 ± 0.4	−3.80 ± 0.05	+8.1 ± 1.2
Mg	+2.3 ± 0.4	−7.06 ± 0.04	+31.4 ± 1.2	+0.5 ± 0.1	−2.84 ± 0.05	+11.0 ± 0.3
Ca	−2.5 ± 0.06	−7.21 ± 0.09	+16.2 ± 1.8	−1.2 ± 0.2	−3.08 ± 0.06	+6.4 ± 0.8

Table IV. Stability Constants of 1:1:1 Metal-Xanthosine-bpy and Metal-Xanthosine-*o*-phen Complexes[a] (μ = 0.10 M (KNO_3))

metal(II) ion	metal-xanthosine-bpy (1:1:1)						metal-xanthosine-*o*-phen (1:1:1)					
	5 °C		25 °C		35 °C		5 °C		25 °C		35 °C	
	K^{MA}_{MHLA}	K^{M}_{MHLA}	K^{MA}_{MHLA}	K^{M}_{MHLA}	K^{MA}_{MHLA}	K^{M}_{MHLA}	K^{MA}_{MHLA}	K^{M}_{MHLA}	K^{MA}_{MHLA}	K^{M}_{MHLA}	K^{MA}_{MHLA}	K^{M}_{MHLA}
Cu	3.19		3.11		3.08		3.12		3.00		3.16	
Ni	2.78		2.63		2.81		2.86		2.80		2.90	
Zn	2.66		2.61		2.58		2.62		2.76		2.79	
Co	2.79		2.40		2.52		2.68		2.57		2.63	
Mn		7.02		6.45		6.71		7.58		7.14		
Mg		6.31		6.38		6.52						
Ca		6.47				6.30						

[a] The deviations are omitted for clarity. The *K* values are log *K* values.

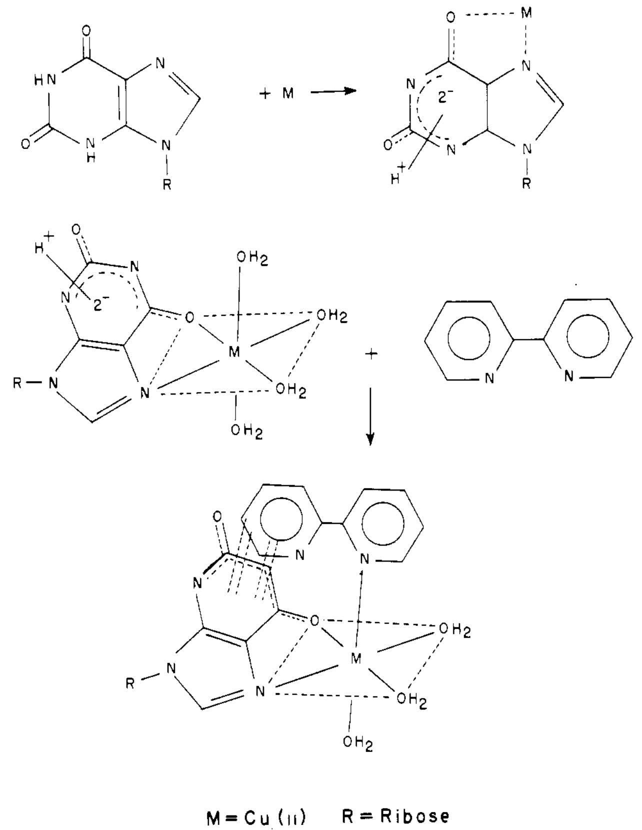

Figure 1. Model illustrating the stacking interaction followed by coordination in H_2O.

al–xanthosine complex constants as is evident from Table VI. This is contrary to statistical considerations,[21] according to which the stability constant for the formation of the 1:1:1 mixed-ligand complex. The higher stability of ternary complexes as compared to that of binary complexes can be attributed to the stacking interaction between the purine part of the xanthosine and the aromatic secondary ligands in the ternary complexes. This fact is further exemplified when one compares the ternary complexes of metal–xanthosine–bpy, –*o*-phen, or –SSA with the metal–xanthosine–TMEN complexes. The former complexes are more stable as compared to the latter. This is because of the fact that the former ligands (bpy, *o*-phen, and SSA) can take part in stacking interactions with xanthosine whereas TMEN, which is an aliphatic ligand, cannot take part in stacking interactions. Another reason for this increased stability of ternary complexes of bpy, *o*-phen, and SSA as compared to those of TMEN is the differences in π-accepting capacities of the ligands concerned. bpy, *o*-phen, and SSA are good π acceptors whereas TMEN is not. Similar results were also obtained in the case of another non-π-accepting ligand, glycine.[15]

The thermodynamic data that are summarized in Tables III and V show negative enthalpy values and positive entropy values for all the 1:1:1 mixed-ligand systems studied. However, they do not exhibit a regular trend. The positive enthalpy value for the Mg(II) ion is due to a very high heat of hydration of Mg(II) ion as compared to that for the rest of the metal ions. The entropy values for the formation of ternary complexes of xanthosine with bpy, *o*-phen, SSA, and TMEN are more positive, which indicates that the complexes are stabilized by an entropy contribution. This is also reflected in the Δ log *K* values (Table VI), which are positive. The positive Δ log K values in these systems may be due to the differences in the

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Table V. Thermodynamic Parameters Associated with the Interaction of Metal Ions with Xanthosine-bpy and Xanthosine-*o*-phen Systems (μ = 0.10 M (KNO_3))

	metal-xanthosine-bpy (1:1:1)			metal-xanthosine-*o*-phen (1:1:1)		
metal(II) ion	$\Delta H_f°$, kcal/mol	$\Delta G_f°$(25 °C), kcal/mol	$\Delta S_f°$(25 °C), eu	$\Delta H_f°$, kcal/mol	$\Delta G_f°$(25 °C), kcal/mol	$\Delta S_f°$(25 °C), eu
Cu	−2.1 ± 0.5	−4.24 ± 0.04	+7.2 ± 1.6	−1.5 ± 0.6	−4.09 ± 0.05	+8.8 ± 1.8
Ni	−1.5 ± 0.2	−3.39 ± 0.06	+7.0 ± 0.6	−1.7 ± 0.7	−3.82 ± 0.06	+7.0 ± 2.3
Zn	−3.2 ± 0.4	−3.56 ± 0.06	+1.2 ± 0.5	−0.8 ± 0.4	−3.68 ± 0.06	+9.6 ± 1.2
Co	−0.3 ± 0.1	−3.38 ± 0.06	+10.5 ± 1.9	−1.5 ± 0.5	−3.50 ± 0.04	+6.7 ± 1.7
Mn	−2.5 ± 0.4	−9.46 ± 0.31	+23.4 ± 1.4	−4.9 ± 0.6	−9.74 ± 0.13	+16.4 ± 1.7
Mg	+2.3 ± 0.4	−8.80 ± 0.27	+37.4 ± 3.1			
Ca	−0.3 ± 0.1	−8.70 ± 0.33	+28.3 ± 1.7			

Table VI. Δ log *K* Values of 1:1:1 Metal-Xanthosine-SSA, Metal-Xanthosine-bpy, and Metal-Xanthosine-*o*-phen Complexes (μ = 0.10 M (KNO_3))

system	temp, °C	Cu(II)	Ni(II)	Zn(II)	Co(II)	Mn(II)	Mg(II)	Ca(II)
metal-xanthosine-SSA	5	+0.73	+0.14	+0.37	+0.08	+0.08	−0.26	−0.04
	25	+0.79	+0.04	+0.11	+0.33	+0.31	−0.14	−0.11
	35	+0.74	+0.09	+0.60	+0.33	+0.15	−0.06	−0.01
	45	+0.09	+0.07	+0.17	+0.23	+0.26	−0.24	−0.07
metal-xanthosine-bpy	5	+0.08	−0.19	+0.32	+0.15	+1.33	+1.53	
	25	+0.20	−0.25	+0.35	+0.37	+0.25	+1.84	
	35	+0.02	−0.11	+0.37	+0.61	+1.24		
	45	+0.17	−0.23	+0.25	+0.42	+1.81	+0.53	+1.04
metal-xanthosine-*o*-phen	5	+0.10	−0.11	+0.21	+0.04	+0.34		
	25	+0.09	−0.08	+0.44	+0.34			
	35	+0.10	−0.02	+0.58	+0.12	+0.28		
	45	+0.15	−0.13	+0.42	+0.28	+0.52		

Table VII. Differences of Enthalpy and Entropy Changes between the Binary and Ternary Complexes of Xanthosine in Solution (μ = 0.10 M (KNO_3))

	$\Delta\Delta H_f°$		$\Delta\Delta S_f°$	
	$K^{MA}{}_{MHLA} - K^{M}{}_{MHL}$		$K^{MA}{}_{MHLA} - K^{M}{}_{MHL}$	
metal(II) ion	M-xanthosine-bpy	M-xanthosine-*o*-phen	M-xanthosine-bpy	M-xanthosine-*o*-phen
Cu	−0.2	+0.4	+0.3	+1.9
Ni	+0.3	+0.1	−0.1	−0.1
Zn	−1.0	+1.4	−1.9	+6.5
Co	+0.3	−1.0	+1.9	−1.9
Mg				
Ca				

solvation energies between the ternary and binary systems, where the entropy values, rather than enthalpy values, may be responsible for the control of stabilities.

In Table VII are given the $\Delta\Delta H_f°$ and $\Delta\Delta S_f°$ values. It can be seen from the table that the $\Delta\Delta H_f°$ and $\Delta\Delta S_f°$ values, which are small, are both positive and negative for the metal–xanthosine–bpy and –*o*-phen systems. The more negative values of the bpy system, as compared to those of the *o*-phen system, is in accord with the flexibility of the ligands concerned. The more flexible bpy will stack with the larger area of the binary metal–xanthosine complex, thus resulting in more stable ternary complexes in solution. The kinetic results obtained by Cayley and Margerum on stacking interactions of ternary complexes[22] are worth mentioning here. They have observed that the formation rate constants of $[Ni(o\text{-}phen)(H_2O)_4]^{2+}$ were increased 2 and 25 times with *o*-phen and bpy ligands, respectively. This tremendous enhancement of the rate constant in the case of the bpy system was attributed to the greater flexibility of bpy as compared to *o*-phen.

The values for other systems could not be computed as the similar data are not available in both binary and ternary systems. The low values of $\Delta\Delta H_f°$ can be associated with the energy of the stacking interaction, which is purely a van der Waals type of interaction and is expected to have a low value of energy of interaction. This interaction is much smaller than a hydrogen bond formation, which has energies in the range of 5–10 kcal/mol. Thus the stacking interaction seems to favor the formation of these ternary complexes in solution.

In conclusion, it is clear from the above discussion that the extra stability found in ternary complexes of xanthosine cannot be attributed to any single factor. In fact, there is more than one factor that is responsible for this extra stability of ternary complexes in solution. Of these, the stacking interaction seems to be most effective. This agrees well with the earlier observations[16,23] that the stacking interaction is far more effective in purine bases than in pyrimidine bases.

On the basis of our conclusions we propose the tentative and simplified stacking model for the metal–xanthosine–bpy system given in Figure 1.

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