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A Study of Formation and Stability of Metal–Isatin Complexes in Solution

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The formation constants of binary ML and ML_2 and ternary MAL complexes where M = Co(II), Ni(II), Cu(II), or Zn(II), L = O, O^- donor isatin or 2,3-indolinedione, and A = (i) N, O^- donor glycine, alanine, or valine, (ii) N, N donor ethylenediamine or 2,2′-bipyridyl, or (iii) O^-, O^- donor oxalic acid or catechol have been determined from solution equilibrium studies by potentiometric pH measurements at 30 ± 1 °C and 0.1 mol·dm^{-3} (KNO_3) ionic strength in 5 vol % ethanol–water. The stepwise formation constants of these complexes followed the sequence $\log K^{M}_{ML} > \log K^{MA}_{MAL} > \log K^{ML}_{ML_2}$. The relative stabilities of the ternary complexes have been characterized in terms of the statistical parameter $\Delta \log K$. The results showed an increasing order of stability with respect to the nature of donor atoms on A as O^-, O^- < N, O^- < N, N. This sequence has been attributed to various astatistical factors. The stabilities of all the complexes also followed the (natural) order Co(II) < Ni(II) < Cu(II) > Zn(II).

Introduction

In recent years there has been interest in the study of metal ion interactions (*1–4*) with various ligands, since they significantly enhance the physiological activity of many organic compounds. Most of these reactions are mediated through a metal ion, resulting in the formation of binary and or mixed ligand (ternary) complexes (*5*, *6*). The ternary complexes provide a model for the metal-directed reactions involving exchange of functional groups and Schiff base formation (*7*, *8*) and in other cases where the reaction is catalyzed by the coordination of the substrates with the metal ion. Leussing et al. (*9–11*) have made extensive studies on many such reactions potentiometrically in solution. Similarly the isatin, an important biochemical reagent used in the determination of amino acids (*12*, *13*), which also exhibits different biological activities (*14–17*), was found to form its Schiff base complexes with amino acids selectively in the presence of metal ions (*18*, *19*). Moreover, the metal–isatin binary complex was found to be advantageous over simple isatin in the chromatographic determination of amino acids (*20*). However, no quantitative information is available regarding the formation and stability of these complexes in solution.

In the present study, the stepwise formation constants of the binary ML and ML_2 and ternary MAL complexes where M = Co(II), Ni(II), Cu(II), or Zn(II), L = O, O^- donor isatin, and A = (i) N, O^- donor glycine, alanine, or valine, (ii) N, N donor ethylenediamine or 2,2′-bipyridyl, or (iii) O^-, O^- donor oxalic acid or catechol have been determined pH-metrically at 30 ± 1 °C and 0.1 mol·dm^{-3} (KNO_3) ionic strength in 5 vol % ethanol–water. The ligands (A) and metals (M) were chosen in view of their known biological and other important roles, so that the different factors affecting the formation and stability of the complexes can be observed.

Experimental Section

Reagents. Isatin was obtained from E. Merck, and all other chemicals used in the experiment were of BDH analar grade. All the solutions were prepared with double-distilled water except that of isatin which was prepared in 5 vol % ethanol–water. The solutions of metal(II) nitrate and carbonate-free potassium hydroxide were standardized by known literature methods (*21*, *22*).

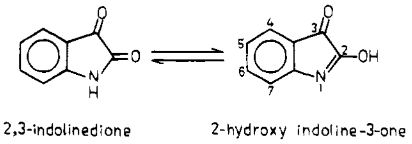

Figure 1. Tautomers of isatin.

Potentiometric pH Measurements. The pH measurements were made with a CENTURY CP 901 (India) digital pH meter consisting of a combined glass and calomel electrode assembly which was calibrated with standard buffers. The experimental method consisted of a potentiometric titration of solutions containing a 1:5 molar ratio of metal–isatin for binary systems and a 1:1:1 molar ratio of metal–A–isatin for ternary systems with 0.1 mol·dm^{-3} standard carbonate-free potassium hydroxide under nitrogen atmosphere. The titrations were carried out in a double jacket cell maintained at 30 ± 1 °C and 0.1 mol·dm^{-3} (KNO_3) ionic strength. All other experimental details are similar to those described earlier (*23*).

Results

Determination of the Formation Constants. The proton–ligand constants (pK_a) of ligands and metal–ligand formation constants ($\log K^{M}_{ML}$ and $\log K^{ML}_{ML_2}$) of binary complexes have been evaluated by analyzing the pH titration curves obtained for the binary systems using the methods of Irving and Rossotti (*24*) with suitable computer programs. The formation of binary complexes was confirmed from the titration curves in which the difference in degree of neutralization between isatin and metal–isatin solutions reveals the release of proton from the (enolic) isatin (Figure 1) due to complex formation. The possibility of the formation of polynuclear complexes or metal hydrolysis was not considered, since excess ligand solution was used in the complexation equilibria. The $\bar{n}$ (degree of formation) values (0.1–1.8) obtained (*24*) for the different binary systems indicate the formation of both 1:1 (ML) and 1:2 (ML_2) complexes. The pK_a values of all the ligands and the binary formation constants obtained under the present experimental conditions are presented in Table 1.

The formation of all the ternary complexes (MAL) occurred in two-step equilibria in which the isatin (L) acted

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Table 1. Proton–Ligand and Metal–Isatin Formation Constants at 30 ± 1 °C and 0.1 mol·dm^{-3} (KNO$_3$) Ionic Strength

ligand/system	pK_{1a}/log K^{M}_{ML}	pK_{2a}/log $K^{ML}_{ML_2}$	ligand/system	pK_{1a}/log K^{M}_{ML}	pK_{2a}/log $K^{ML}_{ML_2}$
isatin		10.62	oxalic acid	1.28	4.08
glycine	2.45	9.67	catechol	9.20	11.54
alanine	2.51	9.78	Co(II)–isatin	4.66	3.98
valine	2.28	9.64	Ni(II)–isatin	4.75	3.92
ethylenediamine	6.94	9.73	Cu(II)–isatin	6.84	5.66
2,2′-bipyridyl	1.51	4.48	Zn(II)–isatin	5.85	4.76

as a secondary ligand in the presence of all other ligands (A). The mixed ligand curves of (MAL) ternary systems closely followed the corresponding binary complex (MA) curves in the lower pH region until the protons of the primary ligands were neutralized, indicating the formation of primary complexes, MA, in the lower pH region. The divergence of the ternary curves from those of the binary systems above this pH region confirms the formation of ternary complexes, MAL, in two-step equilibria: M + A $\rightleftharpoons$ MA (K^{M}_{MA}); MA + L $\rightleftharpoons$ MAL (K^{MA}_{MAL}) (charges omitted). The formation of ternary complexes was also confirmed from a number of observations (*25*), such as a change in the pH range of complexation, a change in intensity of the color (due to complexation), a shift in the pH of precipitation, etc., when compared to the corresponding binary systems. The species distribution curves obtained for some representative systems (Figure 2) using the computer program BEST (*26*) also evidenced the formation of ternary complexes. The percentage variation of the various metal complex species as a function of pH indicates that the formation of ternary complexes increases with an increase in pH. The stepwise formation constants (logK^{MA}_{MAL}) of all the ternary complexes have been calculated (*27, 28*) and are listed in Table 2. The standard deviation for the constants reported is ±0.03 log unit.

Discussion

Binary Systems. The ligand isatin exists in enolic form (Figure 1) in its solution, and the pK_a value determined for this ligand (L) corresponds to its hydroxyl proton. The pK_a values determined for all other ligands (A) under the present experimental conditions were found to be in good agreement with the values reported earlier for these ligands under identical conditions (*23*).

From the results (Table 1) it is found that the isatin forms both 1:1 and 1:2 binary complexes. The results also show that the 1:1 formation constants (logK^{M}_{ML}) are greater than the corresponding 1:2 formation constants (log $K^{ML}_{ML_2}$) for all the binary metal chelates as expected on statistical grounds (*7, 25*). The stabilities of the binary complexes with respect to the metal ions followed the sequence Co(II) < Ni(II) < Cu(II) > Zn(II), which is in accordance with the Irving–Williams (*29*) (natural) order.

Ternary Systems. All the ternary complexes, MAL, were found to form in stepwise equilibria in which the isatin (L) acted as the secondary ligand in the presence of all other ligands (A). The influence of the primary ligand (A) on the binding of the secondary ligand (L) isatin and also the relative stability of the ternary complexes, MAL, when compared to the corresponding binary complexes, ML, have been characterized in terms of the statistical parameter Δ log K_1 calculated from the equation

$$\Delta \log K_1 = \log K^{MA}_{MAL} - \log K^{M}_{ML} \qquad (1)$$

The Δ log K_1 values obtained for all the systems (Table 2) are negative, indicating that the ternary complexes are less stable when compared to their binary complexes, ML. From statistical considerations (*7, 25*) it can be expected that the tendency of the metal ion (M^{2+}) to bind itself to L decreases after being bound to A in MA. Hence, log K^{MA}_{MAL} should be less than log K^{M}_{ML} and should be comparable with log $K^{ML}_{ML_2}$. Thus, negative Δ log K_1 values are expected as observed in the present study. But due to a greater contribution of different astatistical factors, the formation of ternary complexes in the present study is more favored over the ML$_2$ complexes, resulting in greater log K^{MA}_{MAL} values than the corresponding log $K^{ML}_{ML_2}$. Thus, positive Δ log K_2 values (Table 2) can be observed from the following expression:

$$\Delta \log K_2 = \log K^{MA}_{MAL} - \log K^{ML}_{ML_2} \qquad (2)$$

The results also show that the stabilities of the ternary complexes with respect to the donor atoms on A increase in the order O$^-$, O$^-$ < N, O$^-$ < N, N. This can be explained by considering various astatistical factors such as the basicity of the ligand, nature of the donor atoms, charge neutralization in the complex, metal–ligand π-interactions, electrostatic repulsions, steric effects, etc.

Metal–2,2′-Bipyridyl/Ethylenediamine–Isatin Ternary Systems. The higher stabilities of N, N donor systems could be due to the absence of (or less) electrostatic repulsions between the donor atoms of the two ligands (A and L) than in the corresponding complexes containing O$^-$, O$^-$ donor ligands (A). The data in Table 2 indicate that the stability of 2,2′-bipyridyl is greater than that of ethylenediamine. The higher stability of 2,2′-bipyridyl systems can be attributed to its π-acidic nature. Due to metal–2,2′-bipyridyl d_π–p_π interactions (*7*) the effective positive charge or electronegativity of the metal ion in [metal–2,2′-bipyridyl]$^{2+}$ remains almost the same as in aqueous metal ion (M^{2+}), facilitating greater interaction with the (O, O$^-$ donor) secondary ligand isatin. This may also be interpreted (*30*) in terms of Pearson's hard and soft acid–base rule. As a result of back-donation of electrons from the d-orbitals of the metal ion to 2,2′-bipyridyl, the metal ion becomes a (relatively) harder acid, which favors coordination with the O, O$^-$ donor (hard base) isatin in the second step. In case of ethylenediamine no such π-interac-

Table 2. Formation Constants and Δ log *K* Values of Metal–A–Isatin Ternary Complexes at 30 ± 1 °C and 0.1 mol·dm^{-3} (KNO$_3$) Ionic Strength

	Co(II)			Ni(II)			Cu(II)			Zn(II)		
A	log K^{MA}_{MAL}	Δ log K_1	Δ log K_2	log K^{MA}_{MAL}	Δ log K_1	Δ log K_2	log K^{MA}_{MAL}	Δ log K_1	Δ log K_2	log K^{MA}_{MAL}	Δ log K_1	Δ log K_2
glycine	4.33	−0.33	+0.35	4.45	−0.30	+0.53	6.62	−0.22	+0.96	5.58	−0.27	+0.82
alanine	4.31	−0.35	+0.33	4.43	−0.32	+0.51	6.60	−0.24	+0.94	5.56	−0.29	+0.80
valine	4.28	−0.38	+0.30	4.40	−0.35	+0.48	6.56	−0.28	+0.90	5.53	−0.32	+0.77
ethylenediamine	4.37	−0.29	+0.39	4.47	−0.28	+0.55	6.67	−0.17	+1.01	5.59	−0.26	+0.83
2,2′-bipyridyl	4.40	−0.26	+0.42	4.51	−0.24	+0.59	6.72	−0.12	+1.06	5.64	−0.21	+0.88
oxalic acid	4.12	−0.54	+0.14	4.26	−0.49	+0.34	6.38	−0.46	+0.72	5.37	−0.48	+0.61
catechol	4.20	−0.46	+0.22	4.32	−0.43	+0.40	6.45	−0.39	+0.79	5.44	−0.41	+0.68

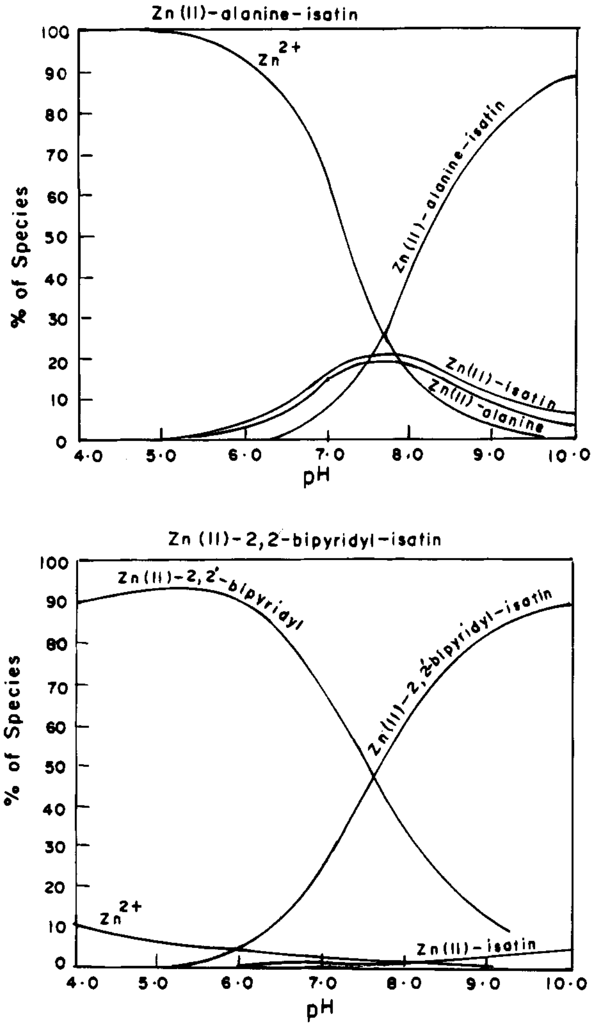

Figure 2. Species distribution curves of zinc(II)–alanine/2,2'-bipyridyl–isatin ternary systems.

tions are possible. Hence, relatively less stable complexes were formed.

Metal–Oxalic Acid/Catechol–Isatin Ternary Systems. The observed trend of stabilities (Table 2) of ternary complexes containing O^-, O^- donor ligands (A) is catechol > oxalic acid. The higher stability of catechol systems can be attributed to its higher basicity and π-interactions, which are absent in oxalic acid. The lower stabilities of both oxalic acid and catechol systems could be due to the formation of negatively charged complexes (MAL) which involves greater electrostatic repulsions, resulting in more negative $\Delta \log K_1$ values.

Metal–Glycine/Alanine/Valine–Isatin Ternary Systems. The stabilities of the N, O^- donor amino acid (A) systems are intermediate to those of both N, N and O^-, O^- donor systems. This may be due to the formation of neutral complexes, MAL, in which the electrostatic repulsions are very minimal. The stabilities of these complexes follow the order glycine > alanine > valine. Glycine forms stable complexes which may be due to the absence of any alkyl side chain which may produce an unfavorable steric effect (*31*). The stabilities of the alanine and valine systems followed the basicity order coupled with steric factors.

During these studies it was also observed that although the Schiff base formation was established in the synthesis (*18, 19*) of transition-metal Schiff base complexes of isatin and amino acids, no such condensation occurred under the present experimental conditions, and instead ternary complexes were formed, as observed in some similar cases (*23*). Even if the formation of Schiff bases in trace quantities cannot be ruled out, the rapid hydrolysis of these Schiff bases has inhibited the formation of binary (tridentate) Schiff base complexes in the present study.

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