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Studies on Mixed Ligand Complexes Involving Ligands of Biological Importance [Ni(II), Zn(II) or Cd(II)-1,10-Phenanthroline— or 2,2′-Bipyridyl—Histidine]

By

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With 2 Figures

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The formation of mixed ligand complexes of the title metal ions with 1,10-phenanthroline (*Phen*) or 2,2′-bipyridyl (*Bipy*) in presence of histidine (*His*) has been studied pH-metrically. The stepwise formation of 1 : 1 : 1 mixed ligand complexes has been inferred from the potentiometric titration curves. Initially, a 1 : 1 metal—*Phen* or —*Bipy* complex is formed in the lower buffer region and then the addition of *His* takes place resulting in 1 : 1 : 1 ternary complex formation. The formation constants (K_{MAL}) of the resulting mixed ligand complexes have been calculated at 30 ± 1 °C (μ = 0.1 KNO_3) and the values have been found to be higher than the formation constants of 1 : 2 and lower than those of 1 : 1 metal—*His* complexes. The order of stability in terms of metal ions follows the order, Ni(II) > Zn(II) > Cd(II).

From the view point of the role of metal complexes in biological systems, the information about the concentration of different species of a metal complex in equilibrium mixtures is of considerable importance and can be predicated on the basis of their formation constants. 1,10-Phenanthroline (*Phen*) and 2,2′-bipyridyl (*Bipy*) are well known chelating agents and their metal chelates having biological activity towards varied microorganisms, have been studied quite extensively. The bacteriostatic effects of *Phen* and *Bipy* either alone or in presence of metal ions have been demonstrated on rumen bacteria, acid fast bacteria and a number of gram-positive micro-organisms. Recently, mixed ligand complexes of these ligands with various metal ions[1–7] have also been reported.

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The present paper describes the pH-metric studies on the interaction of Ni(II), Zn(II) or Cd(II) with *Phen* or *Bipy* in presence of an equimolar concentration of *His*. The formation constant data of the resulting 1 : 1 : 1 mixed ligand complexes may be found to be quite useful in studying the role of these complexes in biological systems as well as in analytical chemistry.

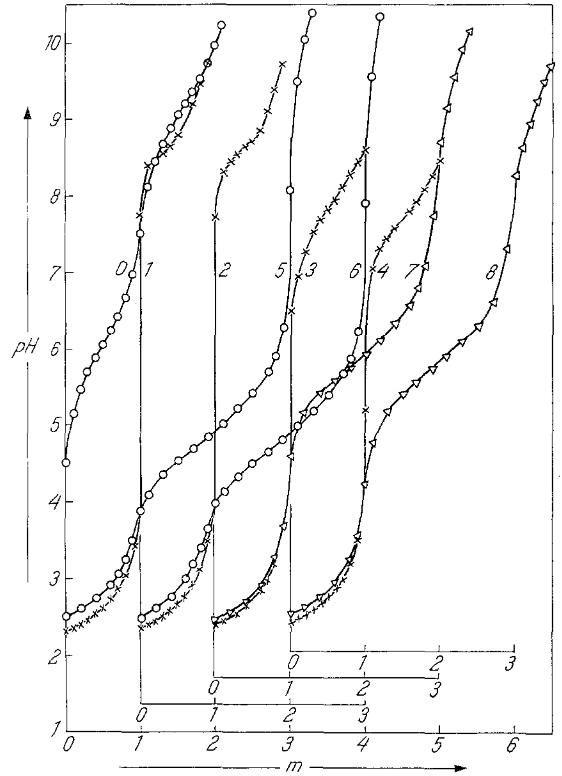

Fig. 1. Potentiometric titration curves of ternary systems, Ni(II) or Zn(II)—*Phen* or -*Bipy*—*His*. Curve 0, *His*; 1. 1 : 1 Ni(II)—*Phen*; 2. 1 : 1 Ni(II)—*Bipy*; 3. 1 : 1 Zn(II)—*Phen*; 4. 1 : 1 Zn(II)—*Bipy*; 5. 1 : 1 : 1 Ni(II)—*Phen*—*His*; 6. 1 : 1 : 1 Ni(II)—*Bipy*—*His*; 7. 1 : 1 : 1 Zn(II)——*Phen*—*His*; 8. 1 : 1 : 1 Zn(II)—*Bipy*—*His*. *m* = Moles of base added per mole of metal ion

Experimental

Stock solutions of the metal nitrates (AnalaR BDH) were prepared in doubly distilled water and standardized with a standard solution of disodium salt of *EDTA* using Murexide [Ni(II)] and Eriochrome black T [Zn(II) and Cd(II)] as indicators. Aqueous solutions of hydrochlorides of *Phen*, *Bipy* and *His* were prepared by direct weighing and their strengths were checked by potentiometric titration against standard KOH (E. Merck) solution.

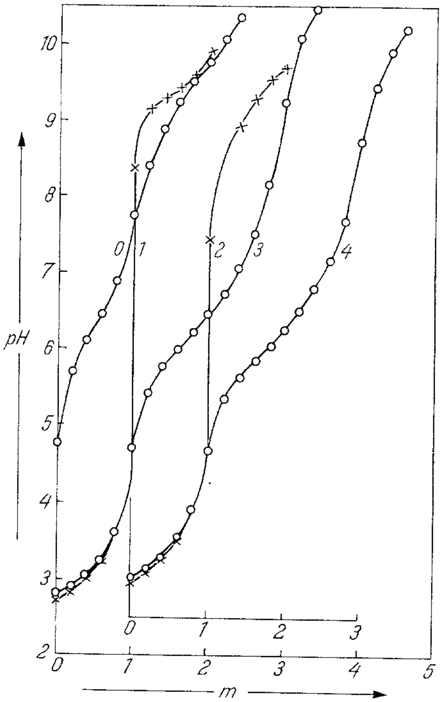

Fig. 2. Potentiomeric titration curves of ternary systems, Cd(II)—*Phen* or -*Bipy*—*His*. Curve 0, *His*; 1. 1 : 1 Cd(II)—*Phen*; 2. 1 : 1 Cd(II)—*Bipy*; 3. 1 : 1 : 1 Cd(II)—*Phen*—*His*; 4. 1 : 1 : 1 Cd(II)—*Bipy*—*His*. *m* = Moles of base added per mole of metal ion

Systronics pH-meter standardized with a 0.05*M* solution of potassium hydrogen phthalate (AnalaR BDH) was used for all the pH measurements. The titrations were carried out at 30 ± 1 °C using a constant temperature bath. In the systems involving Ni(II) and Zn(II), the solutions were prepared in 50 ml and the titrations of the following systems were carried out:

1. 0.005*M*-*Phen* or -*Bipy* + 0.1*M*-KNO_3.
2. 0.005*M*-*His* + 0.1*M*-KNO_3.
3. 0.005*M*-*Phen* or -*Bipy* + 0.005*M*-metal nitrate + 0.1*M*-KNO_3.
4. 0.005*M*-*Phen* or -*Bipy* + 0.005*M*-*His* + 0.005*M*-metal nitrate + + 0.1*M*-KNO_3.

In the systems involving Cd(II), the corresponding solutions were prepared in 50 ml using 0.0025*M* each of *Phen* or *Bipy*, *His* and the metal nitrate because of the low solubility of cadmium complexes in concentrated solutions. The ionic strength of each solution was thus maintained approximately constant ($\mu = 0.1$ KNO_3) and each of the above solutions was titrated against 0.1*M*-KOH solution.

Results and Discussion

Curve 0, Figs. 1 and 2, represents the potentiometric titration of histidine hydrochloride with potassium hydroxide. Its acid dissociation constants ($pk_1 = 6.05$ and $pk_2 = 9.17$) were taken from the literature[8].

The potentiometric titration curves of solutions containing Ni(II), Zn(II) or Cd(II) and *Phen* (Curves 1 and 3, Fig. 1 and Curve 1, Fig. 2) resp. or *Bipy* (Curves 2 and 4, Fig. 1 and Curve 2, Fig, 2) resp. in equimolar proportions exhibit a sharp inflection at $m = 1$ (where m represents the moles of base added per mole of the metal ion) indicating the formation of 1 : 1 binary complexes in the lower buffer region.

When equimolar systems, Ni(II)—*Phen*—*His*, Ni(II)—*Bipy*—*His*, Zn(II)—*Phen*—*His*, Zn(II)—*Bipy*—*His* (Curves 5–8, Fig. 1), Cd(II)—*Phen*—*His* and Cd(II)—*Bipy*—*His* (Curves 3 and 4, Fig. 2) are titrated, two inflections at $m = 1$ and $m = 3$ are observed. In the initial stage, all these curves run slightly above the corresponding 1 : 1 *M*(II)—*Phen* or —*Bipy* titration curves and superimposition starts at $m \approx 1$. This may be due to the presence of free tertiary and secondary amino groups in the histidine hydrochloride which raise the pH of the solution. This indicates that initially a *M*(II)—*Phen* or —*Bipy* (1 : 1) complex is formed in the above systems and the lowering from the *M*(II)—*Phen* or —*Bipy* curve starts after $m = 1$. An inflection at $m = 3$ may be due to the neutralization of the two protons attached to *His* and these are given out during the mixed ligand chelate formation.

On comparing these curves with the corresponding composite curve (which can be drawn by adding the horizontal distance of the secondary ligand curve to the horizontal distance of the *M*(II)—*Phen* or —*Bipy* curve at the same pH) between $m = 1$ and $m = 3$ it can be inferred that the formation of 1 : 1 : 1 mixed ligand chelate, *MAL* is the only possibility in the ternary systems studied during the course of the present investigations. Thus the formation of mixed ligand complexes occurs stepwise and the addition of *His* takes place only after the complete addition of *Phen* or *Bipy*. Further, it gets support by the analysis of the potentiometric data given below.

The equilibria involved in the formation of 1 : 1 : 1 mixed ligand complexes between $m = 1$ and $m = 3$, in the above systems, may be represented as:

$$MA^{2+} + L^{-} \; 11 \; MAL^{+}$$

where M^{2+} stands for metal ion, *A* for *Phen* or *Bipy* and L^- for the secondary ligand anion. The formation constant, K_{MAL} of the ternary chelate may be given by the relation

$$K_{MAL} = \frac{[MAL^+]}{[MA^{2+}][L^-]} \tag{1}$$

and can be determined by the expression:

$$K_{MAL} = \frac{T_M - [L^-]\,X}{[L^-]^2\,X} \tag{2}$$

as derived from the material balance and electroneutrality relations for these systems. In this expression T_M represents the total concentration of all the metal species,

$$X = \frac{[H^+]^2}{k_1 k_2} + \frac{[H^+]}{k_1} + 1$$

and

$$[L^-] = \frac{(3-m)\,T_M - [H^+] + [OH^-]}{\dfrac{2[H^+]^2}{k_1 k_2} + \dfrac{[H^+]}{k_1}}$$

where k_1 and k_2 are the first and second dissociation constants resp. of the secondary ligand.

Table 1. *Formation Constants of Chelates*

System	log K_{MAL}	System	log K_{ML}	log K_{ML_2}
Ni(II)—*Phen*—*His*	7.96 ± 0.20	Ni(II)—*His*	8.62[10]	—
Ni(II)—*Bipy*—*His*	8.03 ± 0.22			
Zn(II)—*Phen*—*His*	5.93 ± 0.09	Zn(II)—*His*	6.67[8]	5.11[8]
Zn(II)—*Bipy*—*His*	6.13 ± 0.10			
Cd(II)—*Phen*—*His*	5.02 ± 0.11	Cd(II)—*His*	5.65[9]	4.14[9]
Cd(II)—*Bipy*—*His*	5.41 ± 0.13			

The calculated values of the formation constants of the ternary complexes are presented in Table 1 and it can be seen that the order of stability in terms of metal ions is Ni(II) > Zn(II) > Cd(II). Further, ternary complexes with *Bipy* as primary ligand and *His* as secondary ligand are found to be more stable than the corresponding complexes involving *Phen* as primary ligand. Since the availability of π-electrons in 1,10-phenanthroline is more than in 2,2′-bipyridyl, so the bond formation with the metal of former is stronger than the latter. Therefore the secondary ligand will form weaker bond in metal—*Phen* system and somewhat stronger in metal—*Bipy* one. A comparison of the formation constants also reveals that the observed values are higher than the formation constants of 1 : 2 and lower than those of 1 : 1 metal—*His* complexes.

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