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M Jahangir Alam
 Dept. of Chemistry, Bangladesh
 University of Engineering &
 Technology (BUET), Dhaka,
 Bangladesh

MR Ullah
 Dept. of Chemistry, Bangladesh
 University of Engineering &
 Technology (BUET), Dhaka,
 Bangladesh

Mousume Akther
 Dept. of Chemistry, University
 of Chittagong, Chittagong,
 Bangladesh

Comparative Stability of mixed ligand complexes of Ni(II) and Zn(II) metal ions with 2,6-Pyridinedicarboxylic acid (DPA) and Oxalic acid, Ethylenediamine, Glycine, Phenylalanine, Tyrosine

M Jahangir Alam, MR Ullah and Mousume Akther

Abstract

By using SCOG (stability constant of generalised species) computer program we can calculate the value of $\Delta \log K$. If the value of $\Delta \log K$ is more positive then the stability of the complex increases. The formation constant of ternary complexes [MAL], where M = Ni(II), Zn(II); A = 2,6-Pyridinedicarboxylic acid (DPA) and L = Oxalic acid, Ethylenediamine, Glycine, Phenylalanine, Tyrosine have been determined. The analysis of the representative species distribution curves show that the pH range 5-7 [ML] and [MAL] are the major species. The percentage of all other species is less than 1% in case of [M(DPA)(L)] system. This is because DPA forms stable binary complex M-DPA(MA) at low pH and L combines with [MA] to form [MAL] ternary complex. The $\Delta \log K$ value becomes more negative with increasing the charge on the ligand L, e.g. oxalate > glycinate > ethylenediamine. The electronic repulsion is more with the increasing charge on L^p , resulting in more negative $\Delta \log K$ values. It is observed that for the complex [Ni(DPA)L] and [Zn(DPA)L] where L = ph-alanine and tyrosine, $\Delta \log K$ value is less negative or positive than the complexes where L = ox, gly, α -ala. This is because of the intramolecular interligand interaction. More positive values of $\Delta \log K$ for the systems with L = tyrosine because of hydrogen bonding between the phenolic -OH of the side group of tyrosine and the carboxylate (-COO⁻) group of the DPA. Due to the large size of Zn metal ion it can bind firmly the bulky ligand thereby increases the stability of Zn (II) over the stability of Ni (II) complexes. So Zn(II) complexes are more stable compared to Ni(II) complexes.

Keywords: Stability, Mixed Ligand, 2,6-Pyridinedicarboxylic Acid (DPA), SCOG etc

1. Introduction

In a complex where two or more ligands of the same type are bonded with a metal ion is called a binary ligand complex and if the different types of ligand are present, then the complex is said to be mixed ligand complex^[1]. Mixed ligand complexes play an important role in biological processes as exemplified by many instances in which enzymes are known to be activated by metal ions^[2, 3]. Such complexes have been implicated in the strong and transport of active substances through membranes^[4]. Many mixed ligand complexes are finding application in the microelectronic industry, chemical vapors deposition of metals and drugs^[5]. These complexes have been used in the analysis of semiconductor materials. Many mixed complexes have been extensively used in clinical applications as enzyme inhibitors^[6], antibacterial^[7, 8], antiviral^[9-11] and as anti-cancerous^[12-14]. Different kinds of metals have been employed in these complexes including Copper, Nickel, Zinc and many others^[13]. Most of the physiological activities regarding amino acid, nucleic acid interactions are promoted by metal ions through the formation of mixed-ligand complexes^[15-21].

Zinc is involved in numerous aspects of cellular metabolism^[22]. It was estimated that about 10% of human proteins potentially bind zinc, in addition to hundreds which transport and traffic zinc. It is required for the catalytic activity of more than 200 enzymes^[23, 24] and it plays a role in immune function^[24, 25], wound healing^[24], protein synthesis, DNA synthesis and cell division^[26]. Zinc is required for proper sense of taste and smell^[27, 28] and supports normal growth and development during pregnancy, childhood, and adolescence^[29-32].

Nickel is used in many specific and recognizable industrial and consumer products, including stainless steel, alnico magnets, coinage, rechargeable batteries, electric guitar strings,

Correspondence

M Jahangir Alam
 Dept. of Chemistry, Bangladesh
 University of Engineering &
 Technology (BUET), Dhaka,
 Bangladesh

microphone capsules, plating on plumbing fixtures^[33]. Amino acids have important ligation properties due to the presence of several coordination sites and are widely applied in the field of insecticides, medicines and analytical reagents due to their excellent bioactivity^[34]. The formation of metal complexes plays an important role to enhance their biological activity^[35]. The glycine is a neutral, aliphatic nonessential glycolytic amino acid and play an important role in haeme synthesis^[36]. It acts as a inhibitory neurotransmitter in central nervous system in spinal cord, brain stem and retina^[37]. Oxalic acid is a bidented anionic ligand it form mixed ligand complexes with transition metal ion. Ethylenediamine, Phenylalanine, Tyrosine also an important ligands which forms stable complexes with metal ions.

Dipicolinic acid (pyridine-2,6-dicarboxylic acid, DPA) is a chemical compound which composes 5% to 15% of the dry weight of bacterial spores^[38]. It is implicated as responsible for the heat resistance of the endospore^[39]. However, mutants resistant to heat but lacking dipicolinic acid have been isolated, suggesting other mechanisms contributing to heat resistance are at work^[40]. Dipicolinic acid forms a complex with calcium ions within the endospore core. The calcium-dipicolinic acid complex also functions to protect DNA from heat denaturation by inserting itself between the nucleobases, thereby increasing the stability of DNA^[41]. Two genera of bacterial pathogens are known to produce endospores: the aerobic *Bacillus* and anaerobic *Clostridium*^[42]. Transition metal complexes of 2,6-Pyridinedicarboxylic acid(DPA) have gained importance because of their biological significance.

The formation of mixed ligand complexes of Nickel and Zinc with 2,6-Pyridinedicarboxylic acid (DPA) and some biologically important amino acids like Oxalic acid, Ethylenediamine, Glycine, Phenylalanine, Tyrosine as ligands have great socio economic importance and unique significance in the field of biochemistry [43, 44]. The acute action of drug and their complex formation in complex media is dependent on metal ligands selectivity and stability constant^[45]. Many attempts have been made to evaluate different factors affecting the stability of the metal chelates along with their stability constants^[46, 47]. Therefore it is necessary to investigate the mixed ligand complexes of Ni(II) and Zn(II) involving various types of bi- and tri- dented biologically important ligands.

2. Objectives

The aim of the present works is to prepare the mixed ligand complexes [MAL], where M = Ni(II), Zn(II); A = 2,6-Pyridinedicarboxylic acid (DPA) and L = Oxalic acid, Ethylenediamine, Glycine, Phenylalanine, Tyrosine etc. biologically important ligands.

The line of approach of the present works may be summarized below:

(i) Preparation of ternary complexes. (ii) Determination of the stability constant of the complexes.

Stability constant of complex compound is very essential for MRI, Catalysis for RNA cleavage, kinetics of reaction, Radiopharmaceuticals, Molecular recognition, Macrocyclic complexes, Host-guest interactions, Enthalpy determination, Cation and Anion selective complexation, Supramolecular complexes, Action of Drug, Environmental effects, Metallomics (including peptides) etc. For imbalance of stability constant above phenomena would be disorder. So, Studies are required to determine the stability constant. Result obtain from the present work would be helpful in the

development of biological, pharmaceutical and physiological implication in the future.

3. Methodology and Experimental

(a) Preparation of metal perchlorate

Metal perchlorate will be prepared from analytically pure metal carbonate by treatment with 70% perchloric acid (A.R). The resulting solids will be vacuum filtered, washed with ethanol till free from excess acid and recrystallized several times from ethanol (metal perchlorates are partially soluble in alcohol).

(b) Stability Constant determination

Irving Rossotti titration technique has been used to determine the formation constants of the ternary complexes using SCOGS (Stability Constant of Generalized Species) computer program^[48]. The activity coefficient of H⁺ under experimental condition has been considered to be equal to unity and the value of the ionic product of water 14.167 has been used. Potentiometric titration will be carried out in aqueous media using pH meter with accuracy 0.01 pH unit using 0.2 M NaOH solution. The solutions of reagents will be prepared in double distilled and deionized water. The freshly prepared NaOH solution will be used as a titrant for pH metric titrations. It will be standardized with oxalic acid according to the literature method^[49]. The 1.0 M NaClO₄ solutions were prepared to maintain the 0.2 M ionic strength of the titration solutions by taking required amount of sodium perchlorate. The metal solutions also will be standardized according to literature method^[50]. The pH electrode will be calibrated in aqueous solution using buffer solution of pH 4.01 and 6.86. As usual pH metric titration method^[51] will be used for solution works. The stability constant of metal complexes will be determined potentiometrically by using SCOGS^[52] computer program.

For the determination of the protonation constants of the ligands (L) the following sets of solution (50 cm³) were prepared.

- (i) 0.02 M HClO₄, 0.002M ligand and 0.178 M NaClO₄
- (ii) 0.02 M HClO₄, 0.005 M ligand and 0.175 M NaClO₄

For the determination of the formation constants of the binary complexes ML, ML₂ and the following sets of solutions (50cm³) having M:L in the ratio 1:3 and 1:5 were prepared.

- (i) 0.02 M HClO₄, 0.002M metal perchlorate, 0.006M ligand and 0.172 M NaClO₄
- (ii) 0.02 M HClO₄, 0.002M metal perchlorate, 0.01M ligand and 0.168 M NaClO₄

For the determination of the formation constants of the ternary complexes [MAL] the following sets of solutions (50cm³) having M:A:L in the ratio 1:1:1, 1:2:2 and 1:3:3 were prepared.

- (i) 0.02 M HClO₄, 0.002M metalperchlorate, 0.002M ligand(A), 0.002M ligand(L) and 0.174 M NaClO₄
- (ii) 0.02 M HClO₄, 0.002M metalperchlorate, 0.004M ligand(A), 0.004M ligand(L) and 0.170 M NaClO₄
- (iii) 0.02 M HClO₄, 0.002M metalperchlorate, 0.006M ligand(A), 0.006M ligand (L) and 0.166 M NaClO₄

All the prepared sets were titrated against standard alkali. Titrations of each set were carried out twice to check the reproducibility of the data.

All the titration were carried out in aqueous medium and the temperature was maintained at 25°C ± 1°C during the progress of titrations. All titration were carried out under nitrogen atmosphere. The titration vessel was designed such that there were inlet holes for the electrode, the burette and

glass stirrer. Pure nitrogen was obtained by passing the nitrogen through alkaline pyrogallol (for absorption of oxygen if any is traces), concentrated sulphuric acid (for absorption of moisture) and finally through aqueous solution. Pure nitrogen was allowed to pass through the solution through an inert

nozzle fitted at the bottom of the titration vessel. Titration were carried out using ORION RESEARCH microprocessor ionalyzer/901 having an accuracy of ± 0.001 pH unit. The glass electrode was calibrated using buffer solution of pH 4.0 and 9.0. The ionalyzer reading were directly taken by pH.

Table 1: Proton ligand formation constant of ligands and formation constant of their Ni(II) binary complexes in aqueous medium with I = 0.2 M (NaClO₄) at 25 °C \pm 1 °C.

| Ligands | $\log K_1^H$ | $\log K_2^H$ | $\log K_{NiL}^{Ni}$ | $\log K_{NiL_2}^{Ni}$ |
|-------------------------------------|--------------|--------------|---------------------|-----------------------|
| Oxalic acid | 3.88 | 2.33 | 4.27 | 5.58 |
| Ethylenediamine | 10.43 | 7.12 | 7.78 | 14.58 |
| Glycine | 9.58 | 2.42 | 6.00 | 10.46 |
| Phenylalanine | 9.22 | 1.96 | 4.81 | 8.56 |
| Tyrosine | 9.33 | 1.72 | 4.77 | 8.89 |
| 2,6-Pyridinedicarboxylic acid (DPA) | 4.36 | 2.11 | 6.96 | 9.78 |

Table 2: Proton ligand formation constant of ligands and formation constant of their Zn(II) binary complexes in aqueous medium with I = 0.2 M (NaClO₄) at 25 °C \pm 1 °C.

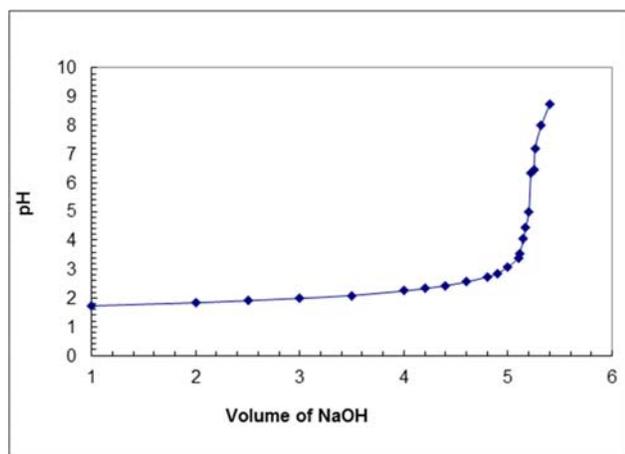
| Ligands | $\log K_1^H$ | $\log K_2^H$ | $\log K_{ZnL}^{Zn}$ | $\log K_{ZnL_2}^{Zn}$ |
|-------------------------------------|--------------|--------------|---------------------|-----------------------|
| Oxalic acid | 3.88 | 2.33 | 4.77 | 5.20 |
| Ethylenediamine | 10.43 | 7.12 | 5.59 | 10.63 |
| Glycine | 9.58 | 2.42 | 4.98 | 9.91 |
| Phenylalanine | 9.22 | 1.96 | 4.30 | 8.37 |
| Tyrosine | 9.33 | 1.72 | 4.18 | 8.30 |
| 2,6-Pyridinedicarboxylic acid (DPA) | 4.36 | 2.11 | 6.36 | 9.88 |

Table 3: Stability constant of mixed ligand complexes [Ni(DPA)(L)] in aqueous medium with I = 0.2 M (NaClO₄) at 25 °C \pm 1 °C.

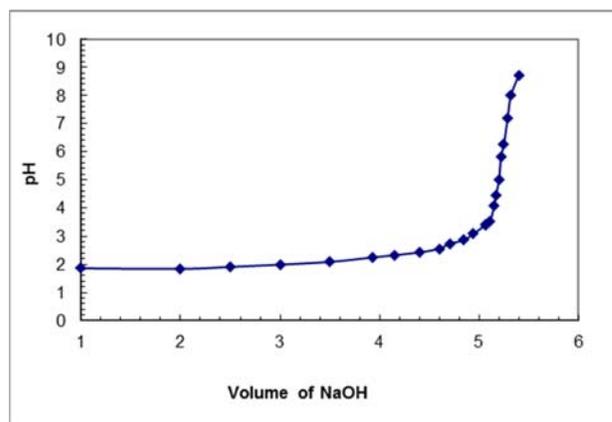
| System | $\log K_{NiAL}^{Ni}$ | $\log K_{NiA}^{Ni}$ | $\log K_{NiAL}^{NiA}$ | $\log K_{NiL}^{Ni}$ | $\Delta \log K$ |
|-------------------|----------------------|---------------------|-----------------------|---------------------|-----------------|
| [Ni(DPA)(Ox)] | 10.7 | 6.96 | 3.74 | 4.27 | -0.53 |
| [Ni(DPA)(en)] | 14.62 | 6.96 | 7.66 | 7.78 | -0.12 |
| [Ni(DPA)(gly)] | 12.42 | 6.96 | 5.46 | 6.00 | -0.54 |
| [Ni(DPA)(Ph-ala)] | 11.32 | 6.96 | 4.36 | 4.81 | -0.45 |
| [Ni(DPA)(Tyr)] | 11.91 | 6.96 | 4.95 | 4.77 | +0.18 |

Table 5: Stability constant of mixed ligand complexes [Zn(DPA)(L)] in aqueous medium with I = 0.2 M (NaClO₄) at 25 °C \pm 1 °C.

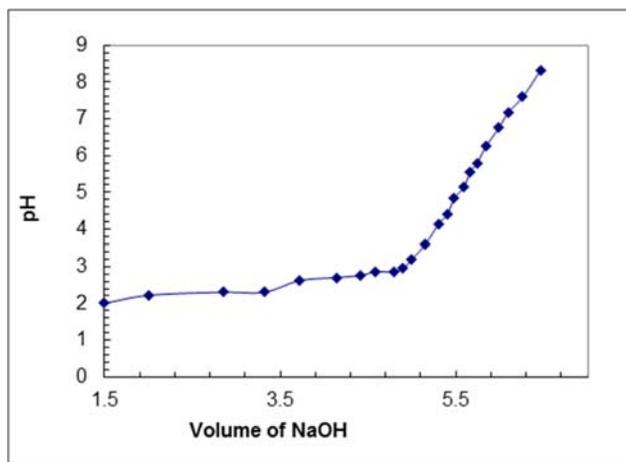
| System | $\log K_{ZnAL}^{Zn}$ | $\log K_{ZnA}^{Zn}$ | $\log K_{ZnAL}^{ZnA}$ | $\log K_{ZnL}^{Zn}$ | $\Delta \log K$ |
|-------------------|----------------------|---------------------|-----------------------|---------------------|-----------------|
| [Zn(DPA)(Ox)] | 10.85 | 6.36 | 4.49 | 4.77 | -0.28 |
| [Zn(DPA)(en)] | 14.28 | 6.36 | 7.92 | 5.59 | +2.33 |
| [Zn(DPA)(gly)] | 12.20 | 6.36 | 5.84 | 4.98 | +0.86 |
| [Zn(DPA)(Ph-ala)] | 11.58 | 6.36 | 5.22 | 4.30 | +0.92 |
| [Zn(DPA)(Tyr)] | 11.48 | 6.36 | 5.12 | 4.18 | +0.94 |



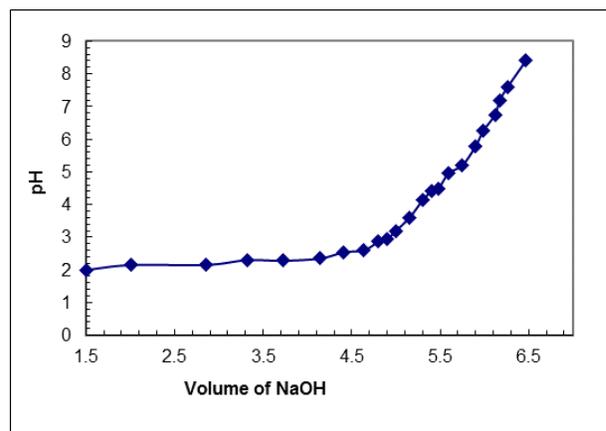
Curve 1: Ni²⁺ + 2,6-Pyridinedicarboxylic acid (DPA) + Oxalic Acid



Curve 2: Ni²⁺ + 2,6-Pyridinedicarboxylic acid (DPA) + Ethylenediamine



Curve 3: Zn^{2+} + 2,6-Pyridinedicarboxylic acid (DPA) + Oxalic Acid



Curve 4: Zn^{2+} + 2,6-Pyridinedicarboxylic acid (DPA) + Ethylenediamine

Fig 1: Potentiometric titration curves of aqueous solutions containing metal ions, 2,6-Pyridinedicarboxylic acid (DPA) and L= Oxalic Acid, Ethylenediamine (each 0.001M).

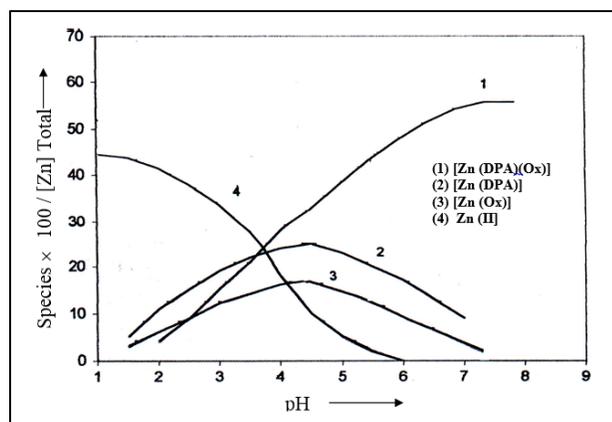


Fig 2: Species distribution diagram for the $[Zn(DPA)(ox)]$ ternary system showing the formation percentages relative to total concentration of the metal as the function of pH.

4. Result and Discussion

The analysis of the representative species distribution curves show that the pH range 5-7, $[ML]$ and $[MAL]$ are the major species. The percentage of all other species is less than 1% in case of $[M(DPA)(L)]$ system. This is because DPA forms stable binary complex M-DPA (MA) at low pH and L combines with $[MA]$ to form $[MAL]$ ternary complex.

It is observed that in general $\Delta \log K$ value for the $[Ni(DPA)L]$ and $[Zn(DPA)L]$ complexes where L= Oxalic acid(ox) studies is negative, as expected from the statistical consideration. The $\Delta \log K$ value becomes more negative with increasing the charge on the ligand L, e.g. oxalate > glycinate > ethylenediamine. The second negative charge faces electronic repulsion in forming the ternary complexes. Hence the tendency of L^{n-} to get bound the neutral $[MA]$ will be less than to get bound with charged M^{2+} ion in the formation of binary complexes $[ML]$, leading to negative $\Delta \log K$ value. The electronic repulsion is more with the increasing charge on L^{n-} , resulting in more negative $\Delta \log K$ values. So, the $[M(DPA)(ox)]$ complexes where M = Ni and Zn are less stable than $[M(DPA)(L)]$ complexes where L= gly, en, ph-ala, and tyr. This is due to the fact that the oxalate ion has doubly negative charge which results in electronic repulsion is forming in mixed ligand complexes.

It is observed that for the complex $[Ni(DPA)L]$ and $[Zn(DPA)L]$ where L= Phenyl alanine and tyrosin, $\Delta \log K$ value is less negative or positive than the complexes where L=ox, gly, α -ala. This is because of the intramolecular interligand interaction. More positive values of $\Delta \log K$ for systems with L= tyrosine because of hydrogen bonding between the phenolic $-OH$ of the side group of tyrosine and the carboxylate ($-COO^-$) group of the ADPA.

It is investigated that the $\Delta \log K$ values for $[Zn(DPA)L]$ complexes are more positive than those of the $\Delta \log K$ values of $[Ni(DPA)L]$ complexes where L= en, ox, gly, α -ala, ph-alanine and tyrosin. The atomic and ionic radii both increases with of atomic number from Ni to Zn. Due to the large size of Zn metal ion it can bind firmly the bulky ligand thereby increases the stability of Zn (II) over the stability of Ni (II) complexes. It is observed that for he complexes $[Zn(DPA)L]$ and $[Ni(DPA)L]$ where L= tyr and ph-ala $\Delta \log K$ value is positive or less negative then the complexes where L= gly, ox, α -ala, and en. This is because of intramolecular interligand interaction. Two carboxylic groups and an amino groups of DPA coordinates with the metal ion. The non-coordinate side group hydroxyphenyl and phenyl ring of tyrosin and phenylalanine respectively comeover the pyridyl of DPA and hence non-covalent hydrophobic interaction is possible. This intamoculler interligand interaction stabilized the ternary complexes, leading to more positive $\Delta \log K$ values.

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