



## **METAL LIGAND STABILITY CONSTANT OF SUBSTITUTED 3,5-DIARYL ISOXAZOLINES COMPLEXES IN 70% DIOXANE SOLVENT MEDIA**

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### **ABSTRACT**

The complex formation between Pr(III) & Sm(III) metal ions and 3-(2-hydroxy-3-nitro-5-methylphenyl)-5-(3-nitrophenyl)isoxazoline L<sub>1</sub>, 3-(2-hydroxy-3-nitro-5-methylphenyl)-5-(4-chlorophenyl) isoxazoline L<sub>2</sub>, 3-(2-hydroxy-3-nitro-5-methylphenyl)-5-(2-furyl)isoxazoline L<sub>3</sub> have been studied at 0.1 M ionic strength (26 ± 0.1°C) in 70% dioxane water mixture by Bjerrum method as adopted by Calvin & Wilson. It is observed that Pr(III) & Sm(III) metal ions form 1:1 & 1:2 complexes with ligand L<sub>1</sub>, L<sub>2</sub> & L<sub>3</sub>. The data obtained were used to estimate & compare the values of proton ligand stability constant (p<sup>K</sup>) & metal ligand stability constant (log K). From estimated data (p<sup>K</sup> & log K), the effect of substituents were studied.

**Key words:** Substituted 3,5-diarylisoxazoline, Dioxane-water mixture, Stability constant.

### **INTRODUCTION**

Metal complexation not only brings the reacting molecules together to give activated complex<sup>1</sup> but also polarized electrons from the ligand towards the metal. The relation between stability and basicity of ligands is indicated by the formation constant and free energy change value Bulkier group increases the basicity of ligands as well as stability. The stability of complexes is determined by the nature of central metal atom and ligands. The studies in metal ligand complexes in solution of a number of metal ion with carboxylic acids, oximes, phenol etc. would be interesting, which throw light on the mode of storage and transport of metal ions in biological Kingdom. Metal with the view to understand the bioinorganic chemistry of metal ions, Banerjee and Rao<sup>2</sup> have synthesized a number of mixed ligand alkaline earth metal complexes. Bjerrum et al.<sup>3</sup> have taken the initiative to develop field. Tekade et al.<sup>4</sup> investigated stability constants of some substituted pyrazolines, isoxaline and diketone Shivaraj et al.<sup>5</sup> have studied formation constants and thermodynamic parameters of bivalent metal ion complexes with 3-amino-5-ethyl isoxazole Schiff bases and N, N; N, O and O<sub>2</sub>O donar ligands in solution. Recently, Thile<sup>6</sup> studied interaction between Cu(II), Cr(II), Nd(II) and Pr(II) metal ions and substituted hydroxyl chalcones at 0.1 M ionic strength pH metrically. Thakur et al.<sup>7,8</sup> have studied the influence of dielectric constants of medium on the complex equilibrium of substituted hydroxyl-1,3-propandiones with Cr(II) metal ions and studies on interaction between Cu(II), Cr(II) and Ni(II) metal ions at 0.1 M ionic strength pH metrically. β-diketone have gained a lot of interest

due to their importance as good ligands and its complexes have been widely used in diverse areas because of their unique structural features, chemical functionalities<sup>9</sup>. It shows chelating behavior towards transition metal ion. 1,3-diketone are very important compound in organic synthesis, because they exhibit some biological activity such as antioxidant, antitumor, antibacterial activities and are also key intermediation to various heterocyclic compound<sup>10-13</sup>.  $\beta$ -diketone and its keto-enol form is also importance pharmacophores of HIV-1 integrase inhibitors<sup>14</sup>. Isoxazolines possess medicinal activities such as anti-inflammatory<sup>15</sup>, antibacterial, anticonvulsant<sup>16</sup>, antibiotic<sup>17</sup>, antitubercular<sup>18</sup>, antifungal<sup>19</sup> and anxiolytic activity<sup>20</sup>.

In present work, an attempt has been made to study the interactions between Pr(III) & Sm(III) cations at 0.1 M ionic strength with ligand at 0.1 ionic strength, pH metrically in 70% dioxane-water mixture.

## EXPERIMENTAL

### Materials and methods

The ligand L<sub>1</sub> [HNMP3NI], L<sub>2</sub> [HNMP4CI], & L<sub>3</sub> [HNMP2FI] was synthesized in the laboratory by known literature method. The purity of these compounds exceeds 99.5% and structures were confirmed by NMR, IR and melting points. The stock solutions of the ligand was prepared by dissolving required amount of ligand in a minimum volume of dioxane subsequently diluted to final volume. Metal ion solution was prepared by dissolving metal nitrate (Sigma-Aldrich) and standardized by EDTA titration method as discussed in literature. Carbonate free sodium hydroxide solution was prepared by dissolving the Analar pellets in deionised water and solution was standardized. The stock solution of perchloric acid was prepared and used after standardization.

### Measurements

All measurements were carried out at  $(26 \pm 0.1^\circ\text{C})$ . Systronic microprocessor based pH meter with magnetic stirrer and combined glass and calomel electrode assembly used for pH measurements. The sensitivity of pH meter is 0.01 units. The instrument could read pH in the range 0.00 to 14.00 in the steps of 0.005. The pH meter was switched on half an hour before starting the titration for initial warm up of the instrument. It was calibrated before each titration with an aqueous standard buffer solution of pH 7.00 and 9.20 at  $(26 \pm 0.1^\circ\text{C})$  prepared from a 'Qualigens' buffer tablets. The hydrogen ion concentration was measured with combined glass electrode.

### Procedure

The experimental procedure involved the titrations of –

- (i) Free acid HClO<sub>4</sub> (0.01 mol.dm<sup>-3</sup>)
- (ii) Free acid HClO<sub>4</sub> (0.01 mol.dm<sup>-3</sup>) and ligand ( $20 \times 10^{-4}$  mol.dm<sup>-3</sup>)
- (iii) Free acid HClO<sub>4</sub> (0.01 mole dm<sup>-3</sup>) and ligand ( $20 \times 10^{-4}$  mol.dm<sup>-3</sup>) and metal ion ( $4 \times 10^{-4}$  mol.dm<sup>-3</sup>) against standard carbonate free sodium hydroxide (0.15 mol.dm<sup>-3</sup>) solution using Calvin-Bjerrum and Calvin-Wilson pH titration techniques. The ionic strength of all the solutions were maintained constant by adding appropriate amount of NaClO<sub>4</sub> solution. All titrations were carried out in 70 percentages of dioxane-water mixtures and reading were recorded for each 0.1 mL addition. The curves of pH against volume of NaOH solution were plotted (Fig. 1-3). The Proton-Ligand constants were calculated from pH values obtained from the titration curves using the Irvin-Rossotti method and MATLAB computer program (Table 1).

**Table 1: Proton ligand formation number ( $E_A$ ) at ( $26 \pm 0.1^\circ\text{C}$ ) and at ionic strength  $\mu = 0.1 \text{ mol dm}^{-3}$   $\text{NaClO}_4$  in 70% dioxane-water mixture**

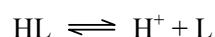
pH	$V_1$	$V_2$	$V_2 - V_1$	$E_A$
<b>System: HNMP3NI (<math>L_1</math>)</b>				
5.14	3.2743	3.4453	0.1710	0.7432
5.21	3.2743	3.5219	0.2476	0.6282
5.42	3.3000	3.5479	0.2479	0.6279
5.63	3.3330	3.5810	0.2480	0.6278
6.00	3.3330	3.6040	0.2710	0.5932
6.14	3.3330	3.6660	0.3330	0.5004
6.21	3.3413	3.6813	0.3400	0.4899
6.35	3.3572	3.7078	0.3506	0.4742
6.37	3.3589	3.7178	0.3589	0.4617
6.42	3.3660	3.7330	0.3670	0.4497
6.49	3.3661	3.7331	0.3670	0.4498
6.70	3.3662	3.7332	0.3670	0.4498
6.84	3.4496	3.8363	0.3867	0.4212
7.00	3.4582	3.8582	0.4000	0.4013
7.35	3.4662	3.8992	0.4330	0.3521
7.42	3.4662	3.9322	0.4660	0.3027
7.56	3.4867	3.9717	0.4852	0.2740
7.70	3.4867	3.9867	0.5000	0.2518
8.00	3.5000	4.0330	0.5330	0.2029
8.35	3.5000	4.0660	0.5660	0.1536
<b>System: HNMP4CI(<math>L_2</math>)</b>				
6.42	3.3660	3.4524	0.0864	0.8705
6.49	3.3661	3.4643	0.0982	0.8528
6.70	3.3662	3.4662	0.1000	0.8500
6.84	3.4496	3.5783	0.1287	0.8074
7.00	3.4582	3.5912	0.1330	0.8011
7.35	3.4662	3.6202	0.1540	0.7695
7.42	3.4662	3.6209	0.1540	0.7685
7.56	3.4867	3.6424	0.1550	0.7671
7.70	3.4867	3.6647	0.1780	0.7338
8.00	3.5000	3.7000	0.2000	0.7009
8.35	3.5000	3.7500	0.2500	0.6262
8.70	3.5660	3.8960	0.3300	0.5072
9.00	3.6330	4.0330	0.4000	0.4025
9.35	3.6660	4.0990	0.4330	0.3545

Cont...

pH	V <sub>1</sub>	V <sub>2</sub>	V <sub>2</sub> - V <sub>1</sub>	E <sub>A</sub>
<b>System : HNMP2FI(L<sub>3</sub>)</b>				
5.21	3.2743	3.5403	0.2660	0.6005
5.42	3.3000	3.5700	0.2700	0.5947
5.63	3.3330	3.6067	0.2737	0.5892
6.00	3.3330	3.6067	0.2737	0.5892
6.14	3.3330	3.6067	0.2737	0.5892
6.21	3.3413	3.6161	0.2748	0.5890
6.28	3.3413	3.6161	0.2748	0.5890
6.35	3.3572	3.6322	0.2750	0.5877
6.37	3.3589	3.6379	0.2790	0.5816
6.42	3.3660	3.6474	0.2814	0.5780
6.49	3.3661	3.6528	0.2867	0.5700
6.70	3.3662	3.6593	0.2931	0.5613
6.84	3.4496	3.7448	0.2952	0.5577
7.00	3.4582	3.7580	0.2998	0.5509
7.35	3.4662	3.7662	0.3000	0.5509
7.42	3.4662	3.7782	0.3120	0.5330
7.56	3.4867	3.8146	0.3279	0.5092
7.70	3.4867	3.8156	0.3289	0.5077
7.91	3.4998	3.8328	0.3330	0.5020
8.35	3.5000	3.8342	0.3342	0.5003
8.42	3.5330	3.8719	0.3389	0.4935
8.56	3.5332	3.9330	0.3998	0.4025
8.70	3.5660	3.9660	0.4000	0.4024
9.00	3.6330	4.0350	0.4020	0.4020

## RESULTS AND DISCUSSION

The extent of deviation may be the dissociation of -OH group. 3-(2-hydroxy-3-nitro-5-methylphenyl)-5-(3-nitrophenyl)isoxazoline L<sub>1</sub>, 3-(2-hydroxy-3-nitro-5-methylphenyl)-5-(4-chlorophenyl)isoxazoline L<sub>2</sub>, 3-(2-hydroxy-3-nitro-5-methylphenyl)-5-(2-furyl)isoxazoline L<sub>3</sub> may be considered as a monobasic acid having one replaceable H<sup>+</sup> ion from phenolic -OH group and can be represented as –



The titration data were used to construct the curves [acid curve (A), acid + ligand curve (A + L) and acid + ligand + metal ion curve (A + L + M)] between volume of NaOH against pH. The proton-ligand formation number  $\bar{n}_A$  were calculated by Irving and Rossotti expression (Table 1).

$$\bar{n}_A = \gamma - \frac{(V_2 - V_1)(N + E^0)}{(V^0 + V_1)(T_L^0)} \quad \dots(1)$$

Where  $\gamma$  denotes the number of dissociable protons, N is the concentration of sodium hydroxide (0.15 mol.dm<sup>-3</sup>), (V<sub>2</sub>-V<sub>1</sub>) is the measure of displacement of the ligand curve relative to acid curve, where V<sub>2</sub> and V<sub>1</sub> are the volume of alkali added to reach the same pH reading to get accurate values of (V<sub>2</sub>-V<sub>1</sub>): the

titration curves were drawn on an enlarged scale:  $E^0$  and  $T_L^0$  are the resultant concentration of perchloric acid and concentration of ligand, respectively.  $V_0$  is the initial volume of reaction mixture ( $50 \text{ cm}^3$ ). Proton-ligand stability constant  $p^k$  values of Ligand were calculated by algebraic method point wise calculation and also, estimated from formation curves (Fig. 4-6)  $n_A$  Vs pH (Half integral method) by noting pH at which  $n_A = 0.5$  [Bjerrum 1957] (Table 2).

**Table 2: Proton ligand stability constant  $p^k$**

System	$p^k$	
	Half integral method	Pointwise calculation method
HNMP3NI ( $L_1$ )	6.1406	6.3177
HNMP4CI ( $L_2$ )	8.7125	8.3992
HNMP2FI ( $L_3$ )	7.9134	7.9837

Metal-Ligand stability constants ( $\log k$ ) were determined by the half integral method by plotting  $E$  Vs  $pL$ . The experimental  $E$  values determined using expression

$$\bar{n} = \frac{(V_3 - V_2) (N + E^0)}{(V^0 + V_2) \bar{n}_A T_M^0} \quad \dots(2)$$

Where  $N$ ,  $E^0$ ,  $V_0$  and  $V_2$  have same significance as in equation (1),  $V_3$  is the volume of NaOH added in the metal ion titration to attain the given  $p^H$  reading and  $T_M^0$  ( $4 \times 10^{-4} \text{ mol dm}^{-3}$ ) is the concentration of metal ion in reaction mixture. The stability constants for various binary complexes have been calculated (Table 3).

**Table 3: Metal ligand stability constant (Log K)**

System	Log $K_1$	Log $K_2$	Log $K_1 - \text{Log } K_2$	Log $K_1/\text{Log } K_2$
<b>(a) HNMP3NI (<math>L_1</math>)</b>				
Pr(III)	7.1884	4.8341	2.3543	1.4870
Sm(III)	5.5325	3.9829	1.5496	1.3891
<b>(b) HNMP4CI (<math>L_2</math>)</b>				
Pr(III)	9.0219	4.5226	4.4993	1.9948
Sm(II)	9.7899	7.1674	2.6225	1.3659
<b>(c) HNMP2FI(<math>L_3</math>)</b>				
Pr(III)	8.8345	5.3495	3.4850	1.6514
Sm(III)	8.4049	3.7820	4.6229	2.2223

### Metal ligand stability constant (Log K)

It is observed that (Table 3) sufficiently large difference between  $\log K_1$  &  $\log K_2$  values of Pr(III) for ligand  $L_1$ ; Pr(III), for ligand  $L_2$  & Sm(III) for ligand  $L_3$  indicates the stepwise formation of complex between metal ion and ligand except Sm(III) for ligand  $-L_1$ ; Sm(III), for ligand  $L_2$  & Pr(III) for ligand  $L_3$ . It showed that less difference between  $\log K_1$  &  $\log K_2$  values indicates complexes are occurring simultaneously. The higher value of ratio (Log  $K_1/\text{Log } K_2$ ) for Pr(III)- Ligand- $L_1$  &  $-L_2$  & Sm(III)-ligand- $L_3$  complex indicates the more stable stepwise complex formation as compare to Sm(III) -Ligand- $L_1$  &  $L_2$  & Pr(III)-Ligand  $L_3$  complexes.

### Proton-ligand stability constant ( $p^K$ )

It is observed from titration curve in (Fig. 1, 2, 3) shows that the ligand curves starts deviating from free acid ( $\text{HClO}_4$ ) curves at  $\text{pH} > 2.17, 2.25$  &  $2.49$ , respectively. The extent of deviations may be the dissociation of  $-\text{OH}$  group completely.

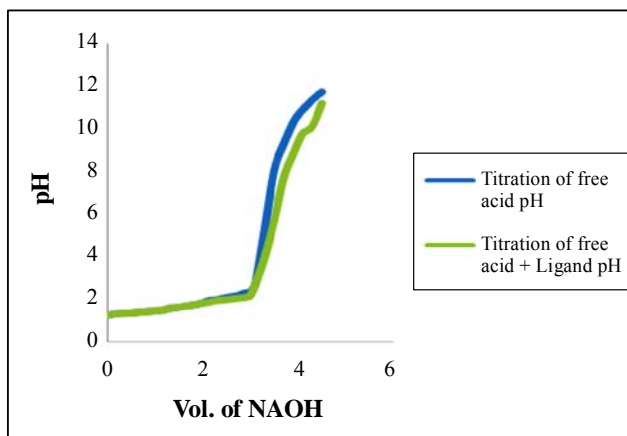


Fig. 1: System: HNMP3NI L1

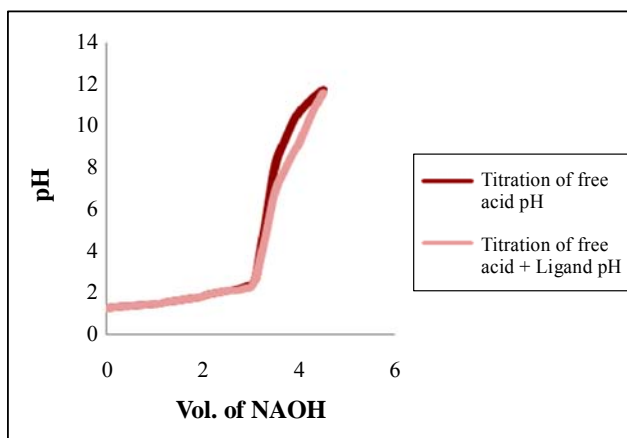


Fig. 2: System: HNMP4CI L2

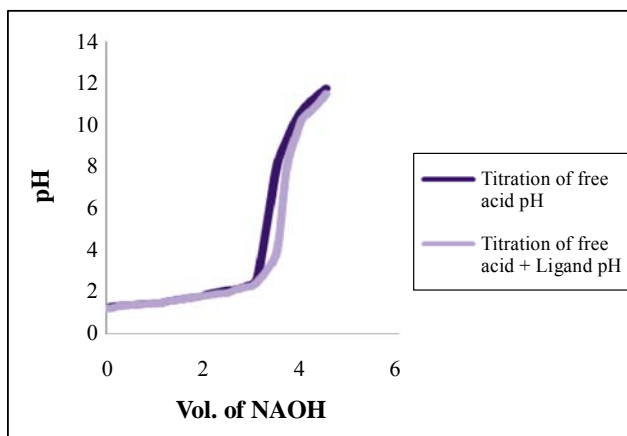
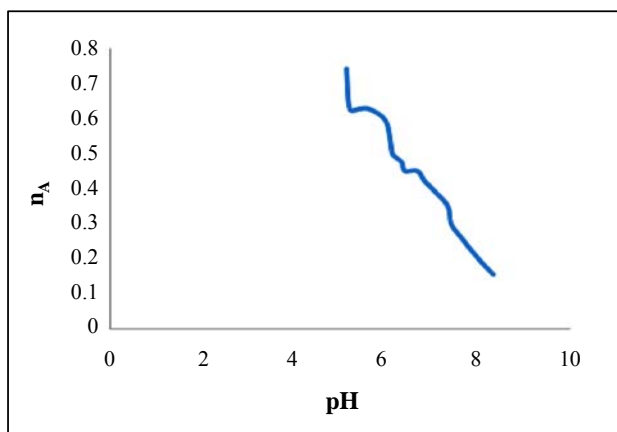
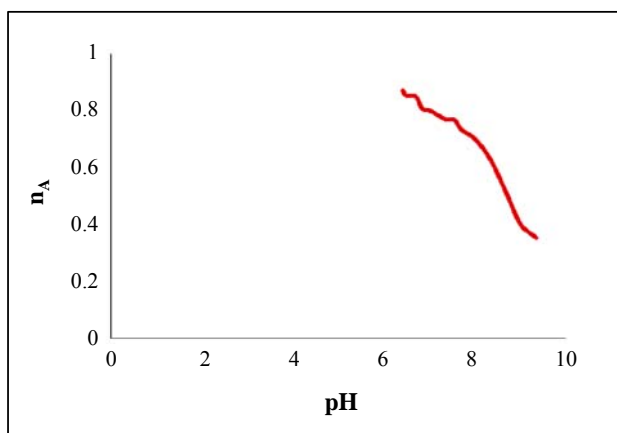


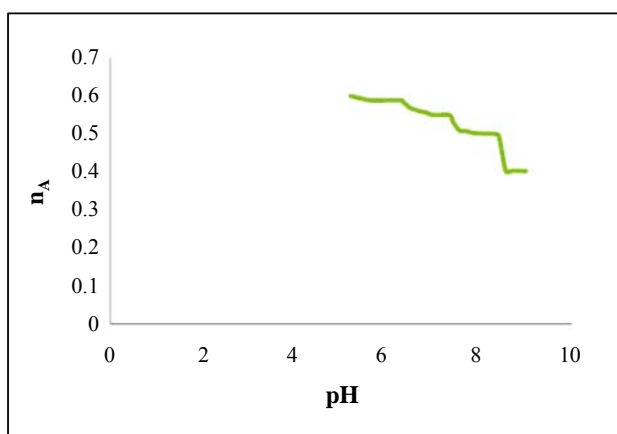
Fig. 3: System: HNMP2FI L3



**Fig. 4: Formation of  $n_A$  Vs pH ligand-L1**



**Fig. 5: Formation of  $n_A$  Vs pH ligand-L2**



**Fig. 6: Formation of  $n_A$  Vs pH ligand-L3**

## CONCLUSION

From the titration curve, it is observed that the departure between (Acid + Ligand) curve & (Acid + Ligand + Metal) curve for all system of  $L_1$ ,  $L_2$  &  $L_3$  started from pH = 2.17 to 3.35, this indicate the commencement of complex formation. Also change in color from yellow to brown in pH range from 3.35 to 9.81 during the titration showed the complex formation between metal & ligand.

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