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Research Article

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pH-metric Study of Metal-ligand Stability Constant of Transition Metal Complexes with Pharmacologically Active Ligand N-[(E)-(4-Hydroxy-3-methoxyphenyl)methylene] isonicotinohydrazide.

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ABSTRACT

The interaction of Mn (II), Co (II), Ni (II), Cu (II) and Zn (II) metal ions with organic ligand N-[(E)-(4-Hydroxy-3-methoxyphenyl) methylene] isonicotinohydrazide have been studied by pH-metric technique at 27±1^{0}C in 70% (v/v) ethanol – water medium at 1M ($NaClO_4$) ionic strength. Organic ligand was synthesized by condensation of equimolar mixture of Anti-mycobacterial agent with aromatic aldehyde. The reaction progress and purity of organic ligands were confirmed by thin layer chromatography. Formation of organic ligands was confirmed with the help of MP, IR, ^{1}H NMR, ^{13}C NMR and elemental analysis. The stability constants of these binary complexes were evaluated and order of stability constant found as Cu (II) > Co (II) > Mn (II) > Ni (II) > Zn (II).

KEYWORDS

pH-metric technique, Binary complexation, N-[(E)-(4-Hydroxy-3-methoxyphenyl) methylene] isonicotinohydrazide, transition metals.

1. INTRODUCTION

Schiff bases implement an important function in coordination chemistry because they easily form stable complexes with most transitional metal ions [1]. Schiff bases have a broad variety of applications in different territory such as pharmacological activity, organic and inorganic chemistry[2]. In the field of coordination chemistry, metal ions carry out vital roles in biological processes. Schiff bases containing an amine group (–RC=N–) are usually formed by the condensation of an initial amine with an active carbonyl[3].Isoniazid is anti-mycobacterial drug and used also primarily as a tuberculostatic[4]. It becomes a starting point in the search for new vital derivatives and analogues such as hydrazones which have been informed as active anti-tuberculosis drugs[5]. The chemistry of Metal-drug coordination compounds is more widespread now than before especially in the design of more biologically active drugs[6]. The complexes have been studied with the basic Schiff links to be applied in the clinical, biological, analytical and pharmacological fields[7]. The complexation of Schiff base with transition metals promote the biological activity[8].pH-metric study is one of the best vastly used technique because it has several distinction such as, it is easy to understand and work, cheap technique etc. A pH meter was used to find the stability constant which is advantageous for the formation of a complex in solution[9-10]. Metal ions are known to affect the action of many drugs[11]. The stability of metal complexes with medicinal drugs perform greater role in the biological and chemical activity. The stability constant of complexes has been found to be greater than zero, if all the possible stability constants for a given system have been determined that means it is possible to calculate the equilibrium activity of complexes[12].

Due to these valuable findings observed in literature review and very less work observed on complexation of vanillin. Present work was planned and well executed for the preparation of organic ligands through the condensation of vanillin with isoniazid Complexation of newly synthesized organic ligand was carried out with transition metals [Mn(II), Co(II),Ni(II),Cu(II) and Zn(II)]to determine the order of stability constants by using pH-metric technique.

2. MATERIALS AND METHODS

2.1. Experimental

2.1.1. Synthesis of Schiff base

Take equimolar mix of isoniazid and vanillin (as aromatic aldehyde) in appropriate volume of ethanol, charged 2-3 drops of glacial acetic acid at room temperature. Then raised temperature of reaction mass up to reflux, reaction mass reflux for 3-4 hrs under continuous stirring and progress of reaction check on TLC using Ethyl acetate : Hexane (5:5) as solvents. Then reaction mixture was cooled at room temperature and poured on ice-cold water. The precipitate product was filtered and recrystallized by alcohol. The purity of these compounds were confirmed by TLC, and structures were confirmed by IR, NMR and melting points.

2.1.2. Potentiometric determination of Stability constant

In the present study Calvin-Bjerrum titration technique has been used for the determination of stability constants. The experimental procedure involved pH-metric titration of solutions.

The solution of the ligand (0.01 M) was prepared by dissolving the requisite quantity of the ligand in (mix of 70% of ethanol and 30% of double distilled water). Transition metal solutions (0.01M) was prepared and standardized by the EDTA. The pH-metric titration was carried out at 27±1°Cby using Elico digital pH-meter model L-120 with combined glass-calomel electrode. The pH-meter was standardized against by buffer solution pH 9.2 and pH 4. The solution of complex titration was prepared by three systems[13]:

i) Free $HClO_4$ (A).

0.2N HClO4 (5ml) + 1M NaClO4 (5ml)

ii) Free $HClO_4$ + Ligand (A+L).

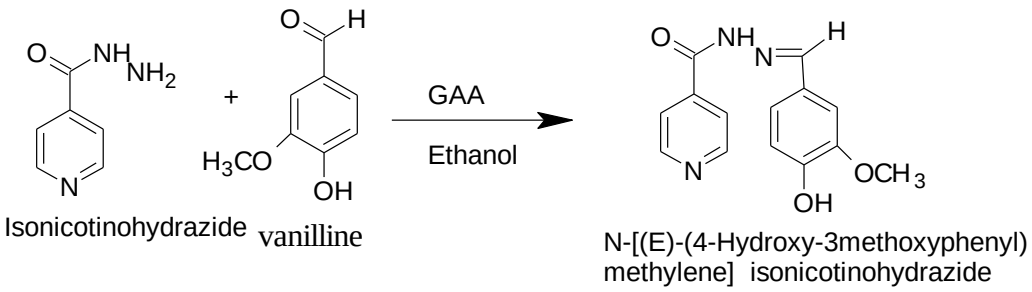
0.2N HClO4 (5ml) + 1M NaClO4 (5ml) + 0.01N ligand (10ml)

iii) Free $HClO_4$ + Ligand + Metal ion (A+L+M).

0.2N HClO4 (5ml) + 1M NaClO4 (5ml) + 0.01N ligand (10ml) + 0.01N transition metal solution (10ml).

3. RESULTS AND DISCUSSION

Organic ligands of the present investigation are prepared as per scheme1:



Scheme 1. Preparation of Organic ligands.

N-[(E)-(4-Hydroxy-3-methoxyphenyl)methylene]isonicotinohydrazide was successfully synthesized through condensation between isoniazid with vanillin. Formation of organic ligand was confirmed with TLC, single spot observed confirms the formation of product. MP was carried out in open capillary tube and elemental analysis was done which is mention in table-1.

3.1. Spectral data

Confirmation of structure was carried out with the help of spectral analysis such as IR, ^{1}H NMR and ^{13}C NMR data mentioned below,

N-[(E)-(4-Hydroxy-3-methoxyphenyl)methylene]isonicotinohydrazide, Nature: solid, yellow color, M.P= 230°C

IR' (cm^{-1}):3445(N-H),1698(C=O), 1663(ali C=N), 1374 (Ar. C=N), 1224 (C-OH), 1031 (O-CH_3),1128 (C-CH).

^{1}H NMR (400MHz, DMSOd_6):11.781δ N-H,9.301δ (s, -OH, 1H),8.303δaliphatic-H, (8.671-8.655)δ [d, 2H, J= 6.4Hz,Pry-H], (7.906-7.900)δ [d,2H, J=2.4Hz, Pry-H], (7.773-7.765)δ [d,2H, J=3.2Hz, Ar-H], 7.333δ (s,1H, Ar-H),3.823δ (s,3H, -OCH_3).
^{13}CNMR (100MHz, DMSO d_6):109.20, 115.53, 121.82, 123.15, (Benzene C), 125.70(Pry-Carbon), 140.97(aliphatic N=CH), 148.33(Benzene C-OCH_3), 149.68 (Pry-Carbon next to N), 150.34 (Benzene C-OH), 162.01 (carbonyl carbon).

The plots of volume of alkali (NaOH) against pH were using to estimate the proton-ligand stability constants of ligand and acid. The proton-ligand stability constant and metal-ligand stability constants and their complexes with Mn(II), Co(II),Ni(II),Cu(II) and Zn(II) metal ions were determined in 70% ethanol-30% water mixture at 27±1°C. The dissociation of OH- clearly indicated by the titrations (acid +ligand) curves deviated from acid curves at pH 2.6 and continued up to pH 11.94. The proton-ligand formation number $\bar{n}_A$ was determined from the titration curves of acid and (acid+ligand). $\bar{n}_A$ defined as hydrogen ions bound to one ligand molecule. This is given by equation,

$$\bar{n}_A = \gamma - \left[\frac{(\varepsilon^0+N)\times(V_2-V_1)}{(V_0-V_1)\times T_L^0}\right] \quad \text{---Equation 1}$$

Where γ denote the replaceable H^+ ion, ε^0 is concentration of acid, T_L^0 is concentration of ligand,N is normality ofalkali,V_1 and V_2 are the volumes of alkali required during the acid and ligand titrations at the given pH andV_0 is the total volume of the mixture. The (acid + ligand + metal) titration curves (A+L+M) deviated from (acid + ligand) titration curves (A+L) in case of metal ion Mn(II) at pH 5.11, metal ion Co(II) at pH 4.63, metal ion Ni(II) at pH 3.24, metal ion Cu(II) at pH 7.46, and metal ion Zn(II) at pH 3.89 and deviation increased continuously up to pH 11.25, pH 11.55, pH 11.64, pH 11.33, and pH 11.56 respectively.

The average number of metal ions associated with the ligand at different of pH values was calculating from the metal ions and ligand titration curves using equation as follows,

$$\bar{n} = \left[\frac{(E^0+N)\times(V_3-V_2)}{(V_0+V_2)\times T_m^0}\right] \quad \text{---Equation 2}$$

Where N, E^0, V_0 and V_2 have the same significance as in Eq. (1), V_3 is the volume of alkali added in the metal titration to attain the given pH reading and T^0 m is the concentration of the metal ion in the reaction mixture. At the time of completion, metal complexes titration curve was observed always at lowest pH values of hydrolysis of metal ion.
The potentiometric titration curve obtained for acid, (acid+ligand) and (acid+ligand+metal) in following graph, from the graph stability constant for proton ligand and metal ligand equilibria has been evaluated. Metal-ligand formation curves and acid-ligand formation curve represented in figure 1.

The deviation of (metal+ ligand) titration curves from ligand curve were found from 3.24 and continued up to11.64. This shows the formation of complexes with respect to change in color and readings related to estimate the value of pH and volume of alkali added presented in table 2.
The protonation constant of ligand and Metal-ligand stability constant are shown in Table 3.
The order of stability constants of complexes with respect to the N-[(E)-(4-Hydroxy-3-methoxyphenyl)methylene]isonicotinohydrazide was found to be Cu (II) > Co (II) > Mn (II) > Ni (II) > Zn (II).

Table 1. Characterization data of Organic ligand.

ligand structure / mol. Formula	**Mol.Wt**	**M.P.**	**Elemental analysis**		
	271.15	230^{o}C	Element	found	Calculated
			C	61.92	61.96
			H	4.76	4.79
			N	15.45	15.49
$[C_{14}H_{13}N_3O_3]$					

Table 2. The pH titration reading of acid, acid + Ligand, Acid + Ligand + Metal at T = 27±1^{0}C, solvent Ethanol-water (70:30).

Vol. of NaOH(ml)	**A**	**A+L**	**A+R+Mn^{+2}**	**A+R+Co^{+2}**	**A+R+Ni^{+2}**	**A+R+Cu^{+2}**	**A+R+Zn^{+2}**
1	2.23	2.12	2.08	2.11	2.09	2.07	2.10
1.6	2.36	2.22	2.14	2.17	2.14	2.13	2.18
2.2	2.54	2.32	2.21	2.25	2.19	2.20	2.27
2.8	2.88	2.46	2.29	2.39	2.24	2.26	2.40
3.4	9.47	2.67	2.45	2.47	2.29	2.35	2.60
4	11.03	3.06	2.83	2.77	2.46	2.87	2.95
4.6	11.27	4.31	3.79	3.25	3.24	3.79	3.62
5.2	11.39	8.82	7.89	7.23	6.39	6.79	6.97
5.8	11.48	10.51	8.52	8.36	7.83	9.39	7.63
6.4	11.57	10.97	9.45	9.66	8.85	9.69	9.39
7	11.63	11.18	10.11	10.15	9.73	9.81	9.80
7.6	11.68	11.31	10.31	10.42	10.25	10.04	10.20
8	11.71	11.38	10.43	10.52	10.42	10.09	10.30

Table 3. Protonation constant of ligand and Metal-Ligand Stability Constant.

Metal	pK	Stability Constant (log K)
Cu(II)	4.22	4.2003
Co(II)	4.22	3.9763
Mn(II)	4.22	3.8135
Ni(II)	4.22	3.4901
Zn(II)	4.22	3.0566

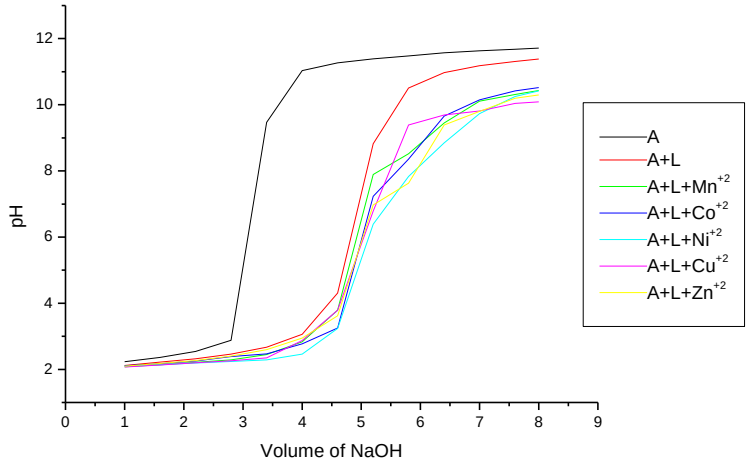


Fig. 1. The pH titration reading of acid, acid + Ligand, acid + Ligand + Metal at T =27±1^{0}C, solvent Ethanol-water (70:30).

4. CONCLUSION

N-[(E)-(4-Hydroxy-3methoxyphenyl)methylene]isonicotinohydrazidehas been successfully and conveniently synthesized, which play the role of organic ligand in the complex formation with transition elements such as Mn (II), Co(II), Ni(II), Cu(II) and Zn(II). The present work describes the effect of organic ligands (Schiff base) on the stability of the complexes.Transition metal complexes of N-[(E)-(4-Hydroxy- 3-methoxyphenyl) methylene] isonicotinohydrazide follows the order of stability constants is Cu (II) > Co (II) > Mn (II) > Ni (II) > Zn (II).

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SUPPLEMENTARY DATA

Symbols

γ*:* Denote the replaceable H^+ ion

ε^0 *:* Concentration of acid

T_L^0 : Concentration of ligand

T^0m: Concentration of the metal ion in the reaction mixture

N: Normality of alkali

V_1 *:* Volume of alkali required during the acid titrations at the given

V_2 *:* Volume of alkali required during the ligand titrations at the given pH

V_3 : Volume of alkali added in the metal titration to attain the given pH reading

V_0 : Total volume of the mixture

$\bar{n}_A$: Hydrogen ions bound to one ligand molecule

$\bar{n}$: Average number of metal ions associated with the ligand at different of pH value