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Synthesis of new schiff bases and their transition metal complexes (Co^{II} , Ni^{II} , Cu^{II} & Zn^{II}) and their characterization stability constant and microbial activities

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Abstract

A series of Schiff bases have been synthesized by reacting 4(P-fluro phenyl) 2-aminothiazole and 2-Hydroxyacetophenone (R-H, 5-Me, 5-cl). The bases and their metal complexes were characterized by elemental analysis, UV-visible and Infra-red spectra, magnetic susceptibility and conductivity measurement. The Schiff base complexes act as monomeric and have octahedral in geometry. The ligand coordinated through oxygen atom of phenolic -OH group and the nitrogen atom of azomethine group. The complexes are non-electrolytic in nature.

The stability constants and thermodynamic parameters (ΔH , ΔG & ΔS) were recorded. The -ve ΔG in each cases indicates the complexation is spontaneous. The enthalpy change is exothermic. The positive value of ΔS indicates the reactions are entropically favored.

The Schiff bases and their metal complexes were screened for antibacterial, anti-fugal and pesticidal activity.

Keywords: Schiff base, metal complexes, biological activity, stability constant

Introduction

The Schiff bases and their transition metal complexes have been amongst the widely studied as a coordination compound in few past years. The Schiff base ligands are able to stabilize many different metals in various oxidation state and controlling the performance of metals in a large variety of useful applications in biological, clinical, analytical and industrial in addition to their important role in catalysis and organic synthesis. Schiff base ligands containing various donor atoms like N, O and S show broad biological activity and are of special interest because of the variety of ways in which they are bonded to metal ion. Now in recent year new interesting applications found in the field of pesticide and medicine. The metal complexes with tridentate O, N, N type of alternative structure have attracted the attention of chemist^[1-5]

In present communication here we report synthesis, characterization, biological activity, stability constant and thermodynamic parameter of a Schiff base derived from 4-(P-Fluorophenyl)-2-aminothiazole and transition metal (Co^{II} , Zn^{II} , Cu^{II} , Zn^{II}) ion complexes.

Result and Discussion

Proton-ligand stability constant (pk) values of ligands. 2H5MPFPAT, 2H5MPMPFPAT and 2H5CPMFPAT were calculated by using half-integral and graphical method.

Values of ligand contains only one pk values due to dissociable proton of the phenolic-OH group. The protonation of imino nitrogen (HC=N) does not take place in the pH range under study. The pk values are summarized in table No. 1.

The pk values follows the trend

2H5MPFPAT > 2H5MPMPFPAT > 2H5CPMFPAT

This is explained on the ground of basic nature of azomethine nitrogen and phenolic oxygen^[6, 7]

Higher values of 2H5CPMFPAT as compared to 2H5MPFPAT may be due to the presence of C1 in the aromatic ring where it behaves more as electron releasing group via stronger mesomeric effect (+M) rather than electron withdrawing group through the donor ability of azomethine nitrogen in 5CSFPAT relative to SFPAT and hence proton-ligand stability constant value increase.

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In ligand 2H5MPMFPAT methyl group is substituted in phenyl ring methyl group has (+I) effect and therefore electron density on phenyl ring increases. Thus azomethine nitrogen and phenolic oxygen becomes more basic due to increase in electron density over them and therefore stability constant values of this ligand is higher that of 2H5CPMFPAT.

Metal-ligand stability constant

The titration curves of acid, ligand and the metal ions are studied. The metal ion curves shows departure from ligand curves at pH much lower than the pH of hydrolysis of metal ion and therefore the libration of the proton is due to chelation. The metal ligand stability constants were determined by using half integral and graphical method. The values are summarized in table No. 2

The order of stability of Schiff base metal complexes follows the trend. $Zn^{II} > Co^{II} > Ni^{II} > Cu^{II}$ and it is found to be in

accordance with the order suggested by Irving and Williams [8]

Effect of temperature

To study the effect of temperature on complexation, the metal ion, The metal ion $Zn^{II} > Co^{II} > Ni^{II} >$ and Cu^{II} and Schiff bases. 2HPMFPAT, 2H5MPMFPAT and 2H5CPMFPAT complexes for determination of metal ligand stability constant at 25, 35 and 45 °C in ethanol water (50:50%) (v/v) medium and at constant ionic strength $\mu = 0.1 M(NaClO_4)$.

As thermodynamic parameter (ΔG , ΔH and ΔS) have been calculated and are summarized in table No. 1.

The logk values decreases with increasing in temperature for complexation. The ΔG , ΔH are negative, while ΔS values are positive.

Table 1: Thermodynamic parameters of Schiff base metal complexes.

Sr. No.	Complex	Log K1			-ΔG(KJM01 ⁻¹)			-ΔH(KJM01 ⁻¹)			ΔS(KJM01 ⁻¹)		
		25	35	45	I	II	III	I	II	I	II	III	
1.	2HPMFPAT	Zn ^{II}	8.40	8.35	8.30	46.77	48.04	49.29	26.79	28.58	67.21	61.94	65.32
		Co ^{II}	8.35	8.29	8.24	46.49	46.92	48.52	32.70	27.52	46.47	64.22	66.23
		Ni ^{II}	8.10	8.05	8.01	45.07	46.04	47.53	26.80	29.63	61.50	54.35	56.45
		Cu ^{II}	7.80	7.75	7.69	43.36	44.17	45.59	28.76	35.93	49.19	27.39	30.47
2.	2H5MPMFPAT	Zn ^{II}	8.00	7.96	7.91	44.50	45.76	46.93	21.87	29.63	76.13	53.43	54.60
		Co ^{II}	7.75	7.70	7.66	43.08	44.22	45.41	27.78	30.68	51.54	44.88	46.52
		Ni ^{II}	7.57	7.50	7.46	42.06	43.05	44.20	41.57	25.42	1.84	58.38	54.25
		Cu ^{II}	7.50	7.47	7.40	41.66	42.87	43.84	17.93	44.34	79.83	05.05	1.77
3.	2H5CPMFPAT	Zn ^{II}	7.73	7.71	7.67	43.08	44.28	45.47	27.48	24.37	79.83	65.90	66.55
		Co ^{II}	7.65	7.61	7.56	42.51	43.21	44.81	23.84	30.68	65.20	41.55	44.63
		Ni ^{II}	7.58	7.53	7.50	42.11	43.51	44.44	29.75	19.12	40.99	80.69	79.82
		Cu ^{II}	7.51	7.48	7.43	41.72	42.93	44.02	12.02	31.73	99.86	37.16	38.84

Electronic spectra of complexes

The electronic spectra of the Co^{II} complexes exhibit band at ~8640, ~18300, ~2200 and ~26500 Cm^{-1} occurrence of the first three bands, attributing to transition $^4T_{2g} \leftarrow ^4T_{1g}$ (v_1) $^4A_{2g} \leftarrow ^4T_{1g}$ (v_2) and $^4T_{2g}$ (p) $\leftarrow ^4T_{1g}$ (v_3) respectively, suggests an octahedral geometry for the complexes. An intense band at ~26650 cm^{-1} ($\epsilon \sim 1000 dm^3 mole^{-1} cm^{-1}$) may be due to ligand to metal (metal \leftarrow ligand) charge transfer.

The Ni^{II} complexes display band at ~8300, ~13800, ~25000 and 26500 cm^{-1} . The first three bands corresponding to transitions $^3T_{2g}$ (F) $\leftarrow ^3A_{2g}$ (v_1), $^3T_{2g}$ (F) $\leftarrow ^3A_{2g}$ (v_2) and $^3T_{2g}$ (p) $\leftarrow ^3A_{2g}$ (v_3) respectively, indicates an octahedral geometry for the complexes. The band occurring at 26500 cm^{-1} is sharp and intense ($\epsilon \sim 1000 dm^3 mol^{-1} cm^{-1}$) and may be due to ligand to metal (metal \leftarrow ligand) charge transfer.

The Cu^{II} complexes display three bands in the region 16300-17500 cm^{-1} , 22250-3700 cm^{-1} and 27565-28300 cm^{-1} . The low energy band may be assigned for Cu^{II} in an octahedral configuration [9, 10]. Corresponding to the transition $^4T_{2g} \leftarrow ^2E_g$ and to the symmetry forbidden metal \leftarrow ligand charge transfer. The Zn^{II} complexes exhibits a high intensity band at 28300-28756 cm^{-1} assigned to metal \leftarrow ligand charge transfer and band at 13340-14900 cm^{-1} due to transitions $^2T_{2g} \leftarrow ^2E_g$ in a distorted octahedral environment [10].

IR of Schiff base complexes

IR spectra of the Schiff base showed the absence of bands at

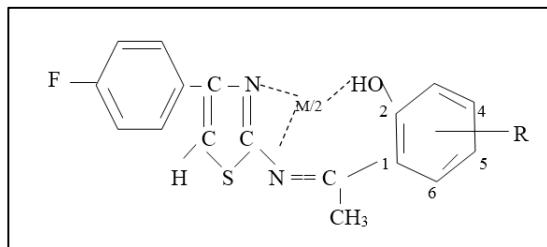
1740 and 3430 cm^{-1} due to carbonyl $v(c=O)$ and $v(NH_2)$ stretching, vibration and instead the appearance of a strong new band at 1625 cm^{-1} assigned [11-13] to the azomethine $v(C=N)$ linkage. This suggested that the amino and ketone moieties of the starting reagents no more exist and have been converted in to respective Schiff base linkage. The comparison of infrared spectra of ligand and their metal chelates indicated that the ligand were coordinates to the metal atom in three ways. Thus representing ligands acts as tridentates. The band appearing at 1625 and 1610 cm^{-1} Assigned to azomethine and thiazole ring vibration Schiffed to lower frequency by 15 cm^{-1} indicating the participation of azomethine nitrogen in chelation, further conclusive evidence of the coordination of these tridentate ligands with the metal was shown by the appearance of high frequency new band at 450-462 and 525-540. There were in turns assigned to metal oxygen $v(M-O)$ and metal- nitrogen (M-N) the obsance of v_{OH} frequency in the complexes indicates the involvement of phenolic-OH in metal-oxygen band formation.

Magnetic moments of complexes

The values of magnetic moments (Gouy) of Co^{II} , Ni^{II} , Cu^{II} and Zn^{II} metal ion complexes. The Co^{II} complexes lies in the range 4.8-5.1 BM indicative¹⁴ of three unpaired electrons on per Co^{II} ion in octahedral environment, the Ni^{II} complexes lies in the range 3.0-3.2 BM indicative¹⁵ of two unpaired electrons on per Ni^{II} ion in octahedral environment, the Cu^{II} complexes lies in the rang 1.7-1.9 BM showing one unpaired electron on

per Cu^{II} ion suggesting a distorted octahedral geometry. Zn^{II} complexes are diamagnetic.

From above parameters i.e. IR, UV and magnetic movement and molecular weight, the proposed structure of metal complexes are as follows.



Where M = Co^{II}, Ni^{II}, Cu^{II} and Zn^{II} ions

Biological activities

The compounds were tested *in vitro* for their antibacterial activity against E.coli, Bacillus and Staphylococcus and antifungal activity against A.niger and A.flaves at 50mg/ml concentration using DMF as the solvent by cup plate method. The zone of inhibition were measured. The activity of ligands was compared with that displayed by ampicillin (antibacterial activity) and griseofulvin (antifungal activity) as the standard drugs.

Antibacterial activity

E coli and ligands 2HPMFPAT, 2H5MPMPAT and 2H5CPMFPAT exhibited zone of inhibition 6-12 mm where as the standard drug Amphicillin exhibited zone of inhibition 20mm.

Bacillus and *Staphylococcus* and ligand exhibited zone of inhibition 6-14mm against 20mm for amphicillin. Hence concluded to amphicillin for antibacterial activity of ligands. 2HPMFPAT, 2H5MPMPAT and 2H5CPMFPAT against the above organism by serial dilution technique^[16] in DMF in the concentration 5-50 mg/ml.

MIC values of ligands were fund. The values lie in the range 15-20mg/ml. The activity of ligands is explained on the grounds of chelation theory^[17].

Antifungal activity

All the ligands i.e. SFPAT, 5MSPAT and 5CSFPAT tested against A. flavus and A. niger. The ligand 2H5MPMBPAT exhibit zone of inhibition 8mm and the standard drug Griseofulvin exhibited zone of inhibition 20mm. Concluded that ligand possesses lower antifungal activity as compared to Griseofulvin other ligands are inactive.

Pesticidal activity

The insecticide and pesticide activity of Schiff base were tested against some sessional edible plants chilli. (*Capsicum annum L*) Okra (*Abelmoschus esculents (L) moench*) Lay's Finger or Bhendi, Tomato. Pesticidal and insecticidal

activities of Schiff bases and their Cu^{II} complexes shows much more activity on poisoning^[18-21]

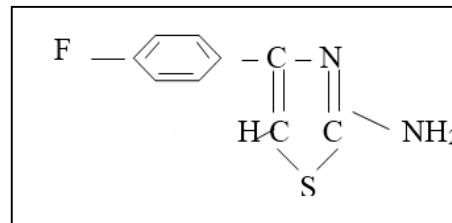
In present report Schiff bases and Cu^{II} and Zn^{II} shows complexes shows pesticidal and insecticidal activities. The rate of prisoning is lower than commercial pesticide and insecticide.

Experimental

Preparation of Schiff bases

Synthesis of aminothiazole

4-(p-Fluorophenyl)-2-aminothiazole, Synthesised as reported method^[22-24].



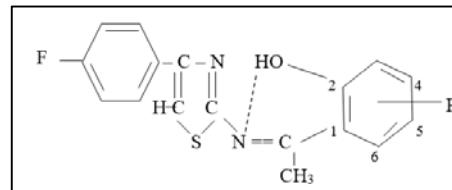
1. 2-Hydroxyacetophenone
2. 2-Hydroxy-5-Methylacetophenone
3. 2-Hydroxy-5-chloroacetophenone

Synthesis of amino thiazole Schiff base (ligand)

A solution of *Salicyladehyde* in ethanol was added to the ethanolic solution of 4-(p-fluorophenyl)-2-aminothiazole in equimolar quantity. The mixture was refluxed on a water bath for 2 hrs. The Schiff base, thus formed was filtered and recrystallized from ethanol and dried under vacuum purity of the Schiff base was checked by molecular weight determination, elemental analysis and TLC. IR-Frequencies in table 2.

Following Schiff base were prepared

1. N-(2-Hydroxyphenyl-methylidene-4(p-fluorophenyl)-2-aminothiazole) 2HPMFPAT
2. N-(2-Hydroxy-5-methylphynyl-methylidene-4(p-fluorophenyl)-2-aminothiazole) 2H5MPMPAT
3. N-(2-Hydroxy-5-chlorophenyl-methylidene-4(p-fluorophenyl)-2-aminothiazole) 2H5CPMFPAT



Sr. No.	Ligand	R
1.	2HPMFPAT	H
2.	2H5MPMPAT	5-CH ₃
3.	2H5CPMFPAT	5-Cl

Table 2: Important IR. Frequencies of the Schiff bases (cm⁻¹)

Sr. No.	Schiff base	V _{O-H}	V _{C=N}	V _{C-O}	Phenyl and thiazole ring vibrations
1.	2HPMFPAT	~2900bd	1625s	1276s	1580m 1515sh 1479s 1370m 1345m 1200m 1165m 1151s
2.	2H5MPMPAT	~2900bd	1625s	1278s	1575m 1505sh 1477s 1375m 1345m 1205m 1180m 1157s
3.	2H5CPMFPAT	~2900bd	1625s	1278s	1577m 1500sh 1410s 1387m 1355m 1210m 1185m 1160s

bd= broad, S=strong, m=medium, w=weak, sh=shoulder

Preparation of metal complex

An ethanol solution 10ml of the appropriate metal salts (II) (0.001M) was added to a stirred ethanol solution (25ml) of the respective Schiff base (0.002M). The mixture was refluxed for 2.5 hrs. The resulting mixture was cooled, filtered and reduced to nearly half its volume. The concentrated mixture was kept overnight at room temperature, which resulted in the formation of solid product. The product thus obtained was filtered washed with ethanol then with ether and dried and crystallized from ethanol gave the desired metal complexes of metal salt. Co^{II}, Ni^{II}, Cu^{II} and Zn^{II} etc.

Determination of stability constants

Proton ligand stability constant

The method of Bjerrum and calvin as modified by Irving and Rossotti [25] has been used to determine n⁻ and P^L values. The experimental procedure involved the pH-metric titrations of the following solutions against at 0.1M ionic strength to determine n⁻ and P^L values of the complexes at 25 ± 1 °C

Table 3: Proton-ligand Stability constants of Schiff bases at constant ionic strength $\mu = 0.1\text{M NaClO}_4$ at temperature 25, 35 and 45 °C.

Sr. No.	Ligand	Temperature °C	Proton ligand stability constant – pK ₁	
			Hall-integral	Graphical
1.	2HPMFPAT	25	10.65	10.67
		35	10.58	10.57
		45	10.51	10.49
2.	2H5MPMFPAT	25	11.20	11.19
		35	11.16	11.16
		45	11.12	11.13
3.	2H5CPMFPAT	25	10.88	10.87
		35	10.80	10.81
		45	10.76	10.77

Table 4: Metal-ligand Stability constants of divalent 3d-metal complexes of Schiff bases at constant ionic strength $\mu = 0.1\text{M NaClO}_4$ at different temperature 25, 35 and 45 °C.

Sr. No.	Ligand	Metal ion	Metal-ligand Stability constant			
			Half Integral		Graphical	
			PK ₁ 253545 °C	PK ₂ 253545 °C	PK ₁ 253545 °C	PK ₂ 253545 °C
1.	2HPMFPAT	Zn ^{II} Co ^{II}	8.00, 7.95, 7.90	6.95, 6.90, 6.87	8.01, 7.95, 7.90	6.96, 6.90, 6.88
		Ni ^{II}	7.95, 7.89, 7.84	6.89, 6.86, 6.81	7.96, 7.90, 7.85	6.90, 6.86, 6.82
		Cu ^{II}	7.70, 7.65, 7.61	6.61, 6.55, 6.45	7.71, 7.65, 7.62	6.60, 6.56, 6.45
2.	2H5MPMFPAT	Zn ^{II} Co ^{II}	7.60, 7.56, 7.51	6.70, 6.46, 6.40	7.61, 7.56, 7.52	6.51, 6.46, 6.41
		Ni ^{II}	7.35, 7.30, 7.26	6.50, 6.26, 6.20	7.35, 7.32, 7.27	6.31, 6.25, 6.20
		Cu ^{II}	7.17, 7.10, 7.06	6.35, 6.04, 6.00	7.18, 7.10, 7.05	6.15, 6.05, 6.00
3.	2H5CPMFPAT	Zn ^{II} Co ^{II}	7.10, 7.07, 7.00	6.21, 5.97, 5.90	7.12, 7.06, 7.01	6.00, 5.96, 5.90
		Ni ^{II}	7.35, 7.31, 7.27	6.53, 6.24, 6.20	7.35, 7.30, 7.28	6.35, 6.25, 6.21
		Cu ^{II}	7.25, 7.21, 7.16	6.41, 6.15, 6.10	7.25, 7.20, 7.15	6.20, 6.16, 6.10

Conclusion

Proton-ligand Stability constants of metal ions have been calculated by using half integral and graphical method. The reported values of proton-ligand stability constants follows trend.

2HPMFPAT, 2H5MPMFPAT and 2H5CPMFPAT

The proposed order of stability of the complexes which follows the trend. Zn^{II}>Co^{II}>Ni^{II}>Cu^{II}.

The effect of elevated temperature on the determination of metal-ligand stability constants has been studied. It was observed that as the temperature increases the values of stability constants decreases. This suggest that low temperature is favorable for complex formation. The

1. Free acid titration

A mixture of 2.0 ml of NaClO₄ (0.02M) + 1.0ml (0.1M) + 12ml water + 15ml ethanol.

2. Schiff base titration

A mixture of 2.0 ml of HClO₄ (0.02M) + 1.0 ml NaClO₄ (0.1M) + 5ml of Schiff base solution (0.02M) + 12ml water + 10ml ethanol.

3. Metal titration

A mixture of 2.0 ml of NaClO₄ (0.02M) + 1.0ml NaClO₄ (0.1M) + 5ml of Schiff base solution (0.02M) + 2.0 ml metal perchlorate solution + 10ml water + 10ml ethanol.

In other sets a requisite amount of NaClO₄ was added to maintain the ionic strength at $\mu = 0.1\text{M}$ was also individually titrated against NaOH at different temperature 35 and 45 °C.

temperature parameter (ΔH , ΔG and ΔS) have been calculated. The ΔH and ΔG values are negative whereas ΔS values are positive. The negative values of ΔH and ΔG suggest that the complex formation is thermodynamically favoured. The positive values of ΔS indicates that entropy effect is found to be predominant over enthalpy effect.

The structures of Schiff bases and of their complexes also have been determined on the basis of their physical and spectral data (i.e. IR and UV visible spectra) and magnetic moments.

The Co^{II}, Ni^{II}, Cu^{II} and Zn^{II} complexes are monomeric, non-electrolytic and covalent in nature having 1:2 (metal-legand) stoichiometry and an octahedral geometry. The coordination

takes place through the oxygen of phenolic – OH, nitrogen of the azomethine group and a nitrogen of thiazole moiety and thus the ligands behave as tridentate with NNO donor set. The $\hbar\chi$ -values indicate the ligands should be placed in between urea and ammonia in the nephelauxetic series.

Ligands have been screened for the evaluation of antibacterial and antifungal activities by cup plate method. The MIC values have been reported the ligands are found to possess good antibacterial activity. Cu^{II} complexes show some pesticidal activities.

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