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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF COPPER (II), COBALT (II), LEAD (II) AND MERCURY (II) COMPLEXES OF TETRA DENTATE SCHIFF BASE DERIVED FROM 5-AMINO-1, 3, 4- THIADIAZOLE-2 THIOL AND HYDANTOIN

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ABSTRACT

Two biologically active Schiff bases (imines) were synthesized by the reaction of 5-Amino1, 3, 4 Thiadiazole-2 Thiol with hydentoin in the presence of conc. H_2SO_4. The characterization of Schiff bases were carried out by using elemental analysis and VSM including IR, ^1H - NMR, EI-MS analyses. The Schiff bases were checked for biological screening and found that the compound with -SH group to be more biologically active than the compound with halo (-X) group. Job's continuous variation method and Mole ratio method revealed 1:1 metal to ligand ratio.by chelation of metals Cu (II) Co (II), Pb (II), and Hg (II) with tetra dentate complexes were synthesized.

Keywords: Tetra dentate Schiff base, 5-Amino1, 3, 4- Thiadiazole-2 Thiol and Hydentoin, VSM, Biological activity.

INTRODUCTION

Metal complexes of Schiff bases play a central role in the development of coordination chemistry. Schiff bases provide potential sites for chemical and biological activity of compounds[1-4]. From the survey of existing literature, it appears that 5-Amino1, 3, 4-Thiadiazole-2 Thiol and hydentoin and their complexes have a variety of applications in biological, clinical and analytical fields. More over these ligands form stable complexes with different metal cations[5]. Keeping the above facts in the mind and in continuation of our research work on transition metal (II) complexes with Schiff bases, we report the synthesis

and characterization of Co (II), Cu (II) , Pb (II) and Hg (II) metal complexes of Schiff bases derived from the condensation of 5-Amino1, 3, 4- Thiadiazole-2 Thiol and hydentoin. Antifungal activity of Schiff base and its metal complexes have also been explored against different species of Fungi. Thus the aim of this study is to observe the impact of chelation on the therapeutic value of the organic compounds.

MATERIALS AND METHODS

All the chemicals used were of AR grade and used without further purification. The elemental analyses were performed by the RSIC, CDRI, and Lucknow. The infrared spectra were recorded in the range 4000-180 cm-1 with a Perkin Elmer 983 G spectrophotometer. The electronic spectra were recorded with Cary model 2390 spectrometer. The molar conductance of complexes in DMF (~ 10-3 M) were determined at 27± 20 C using a Systronic 303 direct reading conductivity bridge. The magnetic susceptibility measurements were made using a vibrating sample magnetometer (VSM) operating at a field strength of 5 KG. The ^{1}H NMR spectra was recorded on varian XL-300 MHz high resolution instrument in $CDCl_3$ solvent. The mass spectra were recorded using Fanning Mat 8230 Mass spectrometer.

Synthesis of Ligand

The reaction mixture containing Hydentoin (3g, 0.02976mol in 10ml of methanol) 5-amino1, 3, 4-thiadizole-2-thiol (3.964g.0297mol in 20ml of methanol dissolved in hot condition) was taken in 250-ml round bottom flask and refluxed for 8h. On cooling the reaction mixture, light yellow coloured product was formed. It was collected by filtration and washed with hot water and 50 % cold methanol. This compound was recrystallised from ethanol and dried in vacuo, yield 7.2. g;m.p. 190°C.

Synthesis of metal complexes

To a methanolic solution of the Schiff base, equal moles of metal salts dissolved in the methanol was added followed by 1 ml of 1M NaOAc was added. This reaction mixture was stirred constantly with magnetic stirrer for 20 minutes. Coloured products were formed after allowing to stand for one hour. The solids were collected and washed with n-Hexane and dried.

RESULTS AND DISCUSSION

The analytical data for all the complexes are given in Table- 1. The molar conductivity data of the complexes are consistent with the non-electrolytic nature [6, 7] of the complexes. The ligand and complexes were characterized by elemental analysis to determine percentage of C, N, S and H. The observed and calculated percentages of the elements are in good agreement and support one ligand to a metal ion. The number of coordinated ligands to metal determined by Job's continuous method and Mole ratio method established 1:1 metal to ligand ratio.

Characterization of ATTHT

The reagents have been characterized by IR and ^{1}H NMR spectral data. Infrared spectrum of ATTHT shows bands at [3256(s); 3252(m,br)]; 3143(s), 3135(m); 3060(s), 1670(m); 1610(s), 1431(s);1362(s);1290(s)1202(s),1075(m),:756(δ),722(δ),689(δ); cm-1 respectively corresponding to υNH-symmetric, υC=N symmetric, υ (C-H) aromatic stretch, υ (C=S) stretching υ (C=N) aromatic ring, δ(C-H) of Thiadiazole ring, (HTT and δ (C-H)-oop, bend (aromatic) and δ (C-C)-oop bend aromatic ring vibrations. ^{1}H NMR spectra of HTT ($CDCl_3$ + DMSO-d6) showed signals at 3.34,(2H,s); 7.70, (3H,m); 7.56 (1H,s) , 4.86(1H,s),3.25(1Hs)due$C_3H_2N_2O$(Hydentoin to CH),due to(1H)- $C_2H_3N_3S_2$ (Thiadiazole),) C=N and =C-SH,-C-NH(hydrazine) proton groups.

The magnetic moment value of Cu-ATTHT was 2.11 BM indicates one electron paramagnetism. This value is higher than the spin-only value of 1.73 BM for one unpaired electron. The higher value of the magnetic moment indicates that complexes are monomeric in nature and there is no metal-metal interaction along the axial position in the complex and have distorted octahedral environment[14-16]. The magnetic moment of Co-ATTHT was found to lie in 2.24 BM which is typically observed for low spin d^7 system of the present type suggest its tetrahedral geometry. Monomeric cobalt complexes have lower magnetic moment values than would be expected for pure tetrahedral complexes suggesting flattening towards planar arrangement[17-21].

The magnetic moments of Pb (II) complex was observed at 2.63 BM. This value is in the range reported earlier for octahedral complexes[22] but slightly higher than the spin only value of 2.63 BM probably due to slight distortion from the pure octahedral to D_4h symmetry[23]

Antifungal activity

Potential fungicidal activity of ligands and their metal complexes were screened against the four species of fungi, Fusarium oxysporum, Macrophomina phasealina, Aspergillus flavus and Aspergillus niger by the agar growth food poison technique [24] at four. dilutions (25, 50, 100 and 200 ppm). The percentage inhibition of growth by an inhibitor at different dilutions is determined as $100\times CC-T$ Where C= diameter of fungus colony C in control plate, T= diameter of fungus colony in test plate. The results presented in Table-5 .

The experimental results showed that there is an increase in the toxicity of the complexes as compared to the parent ligands. The results recorded from the antifungal activity were also further compared with the standard fungicide Grisofluvin. The results are quite promising. It is clear from the antifungal screening data, that the metal complexes are more fungi toxic than the chelating agent itself[25].The enhanced activity of the metal complexes may be ascribed to the increased lipophilic nature of these complexes arising due to the chelation. It was also noted that the toxicity of the metal chelates increases on increasing the concentration. The observed toxicity can be explained on the basis of the Tweedy's chelation theory.[26]

Table-1: Analytical Data of AATHT and their metal complex

Compound / complex (colour)	M.Pt.^{0}C Yield %	Mol. Wt.	Elemental Analysis Found (calculated)					
			C %	H %	N%	O%	S%	M%
ATTHT(yellow colour)	190	215.2	27.8	2.3	32.5	8.36	29.7	-
ATTHT-Co(Light pink)	250	274.1	21	1.7	25.1	6.4	22.9	21.4
ATTHT-Cu(black)	230	278.7	21.8	1.8	25.5	6.5	23.3	22.7
ATTHT-Pb (light balck)	205	415.7	24.9	1.2	16.8	4.3	15.3	49.8
ATTHT-Hg(brown)	>300 (dc)	422.4	14.2	1.1	16.5	4.2	15.1	47.4

Table 2: Selected IR bands (cm^{-1}) with tentative assignments

Compound	VC=N	VC-S	VC=O	VM-N	VM-S
ATTHT	1697	722	1670	-	-
Cu-ATTHT	1615	650	1644	420	355
Co- ATTHT	1608	708	1652	415	352
Pb- ATTHT	1610	707	1670	412	340
Hg- ATTHT	1623	712	1630	405	325

Table 3 : Molar conductance data of metal complexes of ATTHT

ATTHT- Complex	Conductance(Ohm^{-1} Cm^{2} mol^{-1})
Cu-ATTHT	8.5
Co- ATTHT	8.6
Pb- ATTHT	8.7
Hg- ATTHT	8.5

Table 4: Magnetic moment data of metal complexes of ATTHT

ATTHT- Complex	Magnetic Momentum(B.M)
Cu- ATTHT	2.11
Co- ATTHT	2.24
Pb- ATTHT	2.63
Cu- ATTHT	2.11

Table- 5 Fungal activity of ATTHT and its metal complexes

Ligand/complex	concentration	F.Oxysporum	M.phaseolina	A.flavus	A.niger
ATTHT	25 ppm	74.55%	72.33%	73.44%	73.33%
	50 ppm	77.76%	76.66%	77.66%	78.77%
	100 ppm	79.70%	77.68%	82.33%	85.55%
	200 ppm	82.10%	77.90%	83.33%	88.77%
ATTHT-Co	25 ppm	80.12%	80.22%	77.76%	80.22%
	50 ppm	82.11%	83.33%	81.88%	84.44%
	100 ppm	85.6%	84.66%	86.88%	86.66%
	200 ppm	88.90%	90.11%	90.11%	88.88%
ATTHT- Cu	25 ppm	83.44%	91.12%	85.66%	84.44%
	50 ppm	86.66%	92.33%	87.88%	87.66%
	100 ppm	91.12%	93.44%	88.44%	89.88%
	200 ppm	92.30%	94.22%	92.11%	92.33%
ATTHT-Pb	25 ppm	77.55%	70.22%	86.66%	74.44%

	50 ppm	78.66%	74.55%	92.33%	77.77%
	100 ppm	87.77%	76.77%	94.44%	83.33%
	200 ppm	93.44%	80.22%	96.66%	94.44%
ATTHT-Hg	25 ppm	95.55%	96.56%	95.66%	96.77%
	50 ppm	96.66%	97.77%	97.77%	97.66%
	100 ppm	97.77%	98.88%	97.77%	97.77%
	200 ppm	98.88%	97.66%	98.88%	98.88%
Grisofluvin (control)	25 ppm	76.66	69.77	86.88%	73.44%
	50 ppm	78.77%	74.66%	92.44%	76.33%
	100 ppm	86.88%	77.77%	94.44%	82.33%
	200 ppm	92.33%	81.22%	96.66%	94.44%

CONCLUSION

A new Schiff base ligand is synthesized using 5-Amino1, 3, 4- Thiadiazole-2 Thiol And Hydentoin. It acts as a tri dentate ligand and forms stable complexes with transition metal (II) ions such as Cobalt (II), Copper (II), Lead (II) and Mercury (II) in methanol. The ligand and its complexes were characterized by spectral and analytical data. From the spectral, stoichiometric analyses, a tetra-dentate geometry were assigned for the monomeric metal complexes. A comparative study of the ligand and its complexes indicates that the complexes exhibit slightly higher antifungal activity than the free ligand.

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