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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF COPPER (II), COBALT (II),NICKEL (II) AND MERCURY (II) COMPLEXES OF SCHIFF BASE DERIVED FROM 2-ACETYL-5-CHLORO THIOPHENE 5-AMINO-1,3,4-THIADIAZOLE-2-THIOL

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ABSTRACT

The biologically active Schiff base (imines) was synthesized by the reaction of 2-acetyl-5-chloro thiophene and 5-amino-1, 3, 4-thiadiazole-2-thiol in the presence of conc. Acid. The characterization of Schiff bases were carried out by using elemental analysis and VSM including IR, ^{1}H -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 1:2 metal to ligand ratio, by chelation of metals Cu (II) Co (II),Ni (II), and Hg (II) with octa-dentate complexes were synthesized.

KEY WORDS: octa-dentate Schiff base, 2-acetyl-5-chloro thiophene-5-amino-1, 3, 4-thiadiazole-2-thiol, VSM, Biological activity.

INTRODUCTION

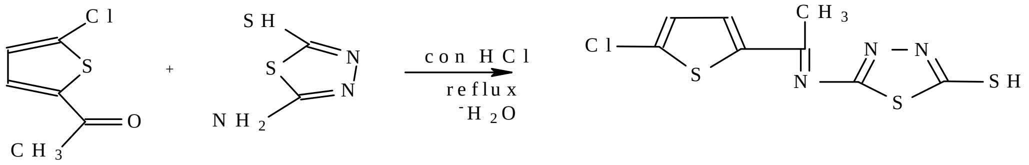
Schiff base complexes have been extensively investigated in recent and past years and have been employed in are a soft catalysis[1], material chemistry[2], and magneto chemistry[3]. Binuclear Schiff base complexes have been of continuing interest because of their roles as biological models, catalyst for organic reaction as components in the formation of new materials [4].Copper complexes are considerably interesting due to their variety in coordination chemistry, technical application, catalysis, spectroscopic properties, anion selectivity, and their biological significance[5, 6]. A wide variety of cobalt(II) complexes are known to bind dioxygen more or less reversibly and are therefore frequently studied as model compounds for natural oxygen carriers and for their use in O_2 storage, as well as in organic synthesis due to their catalytic properties under mild conditions[7]. For these applications, we are extending this field in synthesis of novel binuclear Schiff base complexes. Metal complexes of Schiff bases play a central role in the development of coordination chemistry. 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), Ni (II) and Hg (II) metal complexes of Schiff bases derived from the condensation of 2-acetyl-5-chloro thiophene and 5-amino-1,3,4-thiadiazole-2-thiol. Antifungal and antibacterial activity of Schiff base and its metal complexes have also been explored against different species of bacteria and 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 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) was 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 field strength of 5 KG. The ^1H 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

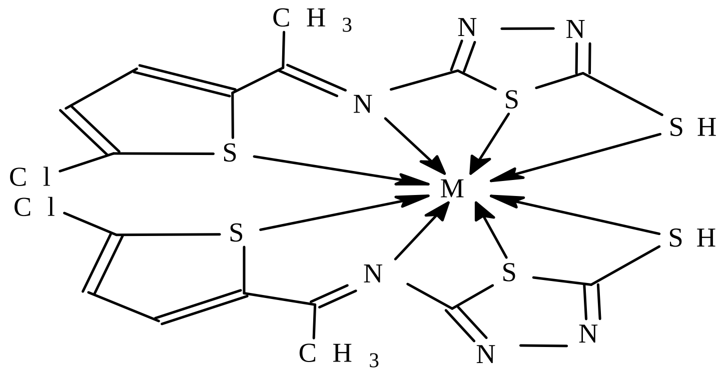
The reaction mixture containing 2-acetyl-5-chlorothiophene(3g,0.0186mol in 10ml of methanol)5-amino1,3,4-thiadizole-2-thiol (2.48g, 0.044mol in 20ml of methanol dissolved in hot condition) was taken in 250-ml round bottom flask and refluxed for 8h. On cooling the reaction mixture, light yellow coloured product was formed. It was collected by filtration and washed with hot water and 50 % cold methanol. This compound was recrystallized from ethanol and dried in vacuo, yield 3.2. g;m.p. 212°C.



Scheme 1: Synthetic route for the preparation of ligand-ACTAT

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.



M=Cu^{2+}, Co^{2+}, Ni^{2+}, Hg^{2+}

Proposed metal-ligand complexes

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[8, 9] 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 1:2metal to ligand ratio.

Characterization of ACTAT

The reagents have been characterized by IR and ^{1}H NMR spectral data. The infrared spectra (Table-2) of ACTAT show bands at 1697 cm-1 for ѴC=N; 722 for ѴC-S; 743 for ѴC-Cl; indicating the Schiff base formation. The lowering of ѴC=N of azomethine group to the extent of 30-50 cm^{-1} in all the complexes suggests the participation[10-12] of azomethine nitrogen in complexation. On coordination, this band is shifted to lower frequency suggests that the ligand is coordinated to metal ion via azomethine nitrogen in all complexes. This change in shift is due to the drift of the lone pair density of azomethine nitrogen towards metal atom[13]. In the far IR spectral region, additional medium to strong bands at 405-420 and 325-355 cm^{-1} are assigned to ѴM-N and ѴM-S modes[14,15] respectively.^{1}H NMR spectra of ACTAT ($CDCl_3$ + DMSO-d6) showed signals at 2.54, (3H,s); 7.15-7.69, (4H,m); 7.69 (1H,s) due to CH_3, C_4H_2S(Thiophene),$C_2H_2N_2S$(Thiadiazole) C=N and =C-NH(hydrazine)proton.

The magnetic moment value of Cu-ACTAT and Hg-ACTAT 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[16-18]. The magnetic moment of Co-ACTAT was found to lie in 2.23 BM which is typically observed for low spin d^7 system of the present type suggest its octahedral geometry. Monomeric cobalt complexes have lower magnetic moment values than would be expected for pure octahedral complexes suggesting flattening towards planar arrangement[19-23]in table-4

The magnetic moments of Ni (II) complex was observed at 3.73 BM. This value is in the range reported earlier for octahedral complexes[24] 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[25].

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

Compound / complex (colour)	M.Pt.^{0}C Yield %	Mol. Wt.	Elemental Analysis Found (calculated)					
			C %	H%	N%	Cl%	S%	M%
ACTAT(light-yellow colour)	212	275.8	34.8	2.1	15.2	12.8	29.7	-
		(80%)	(27.8)	(1.7)	(12.1)	(10.2)	(27.8)	
ACTAT -Co(Light pink colour)	260	334.7	28.6	1.7	12.5	10.5	28.6	17.5
		(85%)	(22.9)	(1.4)	(10)	(8.4)	(22.9)	(14)
ACTAT -Cu(black colour)	250	339.3	28.2	1.7	12.3	10.4	28.3	18.7
		(85%)	(22.6)	(1.4)	(9.9)	(8.3)	(22.6)	(14.9)
ACTAT -Ni (light black colour)	230	334.5	28.6	1.8	12.5	10.3	28.7	17.5
		(80%)	(22.9)	(1.4)	(10)	(8.5)	(23)	(14)
ACTAT -Hg(brown colour)	>300 (dc)	476.4	20.1	1.2	8.8	7.4	20.2	42.1
		(85%)	(16.1)	(1.0)	(7.0)	(5.9)	(5.4)	(33.6)

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

Compound	ѴC=N	ѴC-S	ѴC-Cl	ѴM-N	ѴM-S
ACTAT	1697	722	743	-	-
Cu- ACTAT	1615	650	740	420	355
Co- ACTAT	1608	708	735	415	352
Ni- ACTAT	1610	707	745	412	340

Hg- ACTAT	1623	712	743	405	325

Table 3: Molar conductance data of metal complexes of ACTAT.

ACTAT- **Complex**	**Conductance(Ohm^{-1}Cm^{2}mol^{-1})**
Cu- ACTAT	8.5
Co- ACTAT	8.6
Ni- ACTAT	8.7
Hg- ACTAT	8.5

Table 4: Magnetic moment data of metal complexes of ACTAT

ACTAT- **Complex**	**Magnetic Momentum(B.M)**
Cu- ACTAT	2.11
Co- ACTAT	2.23
Ni- ACTAT	3.73
Hg- ACTAT	2.11

Anti-microbial assay

Biological activity of the ligand and a series of its metal complexes [Cu(II), Ni(II), Co(II) and Hg(II)] were screened for antibacterial activity against S.sureus as gram positive bacteria and E.coli as Gram-negative and the fungi A. fumigatus by using broth micro dilution procedures. From (table-5), the Gram positive bacteria on all metal complexes were found to inhibit all tested bacteria at different rates and the activity as following order Co > Ni > Cu > Hg. In Gram negative bacteria also follows the same order and all complexes have higher bacterial activity than ligand. In fungal activity, the ligand showed activity against Aspergillusfumigatus and metal complexes show activity in the following order Cu > Co > Ni >Hg. It is known that chelation tends to make the ligand to act as more powerful and potent bacterial agent. A possible explanation for this increase in the activity upon chelation is that, in chelated complex, positive charge of the metal is partially shared with donor atoms present on ligands and there is an electron delocalization over the whole chelating ring. This, in turn, increases the lipid layers of the bacterialmembranes. Generally, it is suggested that the chelated complexes deactivate various cellular enzymes, which play a vital role in various metabolic pathways of these microorganisms[26-30].

Table-5: Anti-microbial Activities of Ligand and Metal Complexes

Sample Ligand	**Bacteria**						**Fungi**		
	Gram -positive			**Gram-negative**			**A .Funigatus**		
	S.aureus			**E.Coli**					
	50 µg/mL	**100 µg/mL**	**150 µg/mL**	**50 µg/mL**	**100 g/mL**	**150 µg/mL**	**50 g/mL**	**100 µg/mL**	**150 g/mL**
Ligand (ACTAT)	5	10	14	4	10	12	5	11	14
Cu-ACTAT	11	14	18	10	15	17	12	15	19

Co-ACTAT	10	15	19	13	16	18	10	14	17
Ni- ACTAT	9	13	17	11	15	16	12	15	18
Hg- ACTAT	8	11	15	9	14	15	11	16	19

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