

Co(II) Metal Complexes of Oximes Derived from Salicyloyl Pyrazoles: Synthesis, Spectroscopic Characterization and Antimicrobial Activities.

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Abstract

*A series of complexes of Co(II) have been synthesized by the reaction of Cobalt sulphate with salicyloyl pyrazole oximes in 1:2 stoichiometry. The oximes have been derived from the condensation reaction of hydroxylamine hydrochloride and salicyloyl pyrazole in 1:1 molar ratio in ethanol. The possible structure of these newly synthesized complexes have been proposed on the basis of elemental analysis, molar conductance and various spectral (IR, UV-Visible and ¹H NMR) studies and four coordination geometries have been assigned to these complexes. The powder XRD studies confirm the polycrystalline nature of the complexes. Studies were conducted to assess the growth of inhibition potential of the complexes and oximes bacterial strains *S. aureus*, *B. Subtilis* Gram +ve and *Klebsiella P. aeruginosa* Gram -ve bacteria. All complexes and oximes possess moderate inhibitory action against microorganisms.*

Keywords: Synthesis, Condensation reaction, polycrystalline, bacterial strains, microorganisms.

Introduction

A metal complexes or coordination compounds consist of central metal atom or ion bonded by a set of ligands that have one or more atom(s) having lone pair of electron(s). These atoms are bonded electrostatically and covalently to the central metal atom or ion. The ligands which bound to central metal atom or ion are generally lewis bases having lone pair on Nitrogen, Oxygen, Sulphur etc. These lewis bases can be classified as monodentate, bidentate and multidentate types, according to whether one, two or more atoms involved in such bonding¹⁻⁶. Ligands are also grouped as N-donor and O-donor. Such division is based on selection of metal ions for complexation. For smaller transition metal ions like Sc, Ti, V, Cr, Mn, Fe, Co, Ni and Cu the N-donor ligands bind well where as the O-donor ligands complex with metal ions having larger size like alkali, alkaline earth metal ions and large post transition metal ions^{2,4,7}. Some ligands bonded to the metal ion through two or more atoms forms a heterocyclic ring (usually five or six member) in which metal ion is one of the members such complexes are called as metal chelate.

A number of scientists in the past have tried to find some correlation between chemical structure and physiological or biological properties. It is now well established fact that the activity of a compound depends upon three factors. The first and perhaps most important is the heterocyclic moiety present in the particular compound. The second factor is the nature of the substituent and the third factor is the position of the substituents in these compounds. All literature review revealed that compound containing pyrazole moiety, fluorinated compounds showed good biological applications⁸⁻¹¹. Metal complex also plays an essential role in agriculture¹²⁻¹⁴ and industrial chemistry¹⁵.

Adnan S. Abu-Surrah¹⁶ *et al.* (2010) reported the Palladium(II) complexes which showed the cytotoxic effect on SQ20B head and neck cancer cells is dose dependent and varies by cell type. Paulmony Tharmaraj¹⁷ *et al.* (2009) synthesized 1-(2-hydroxyphenyl)-3-phenyl-2-propen-1-one, *N*²[(3,5-

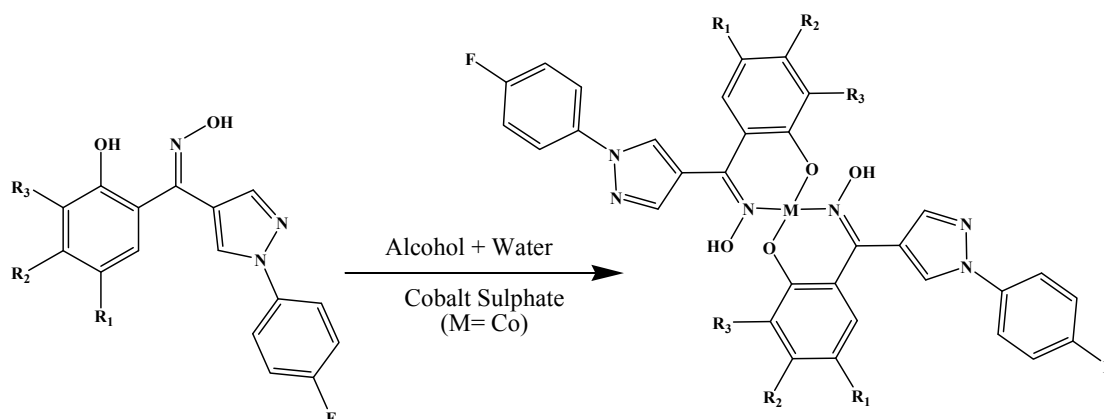
dimethyl-1H-pyrazol-1-yl)methyl] hydrazone and its Cu(II), Co(II) and Ni(II) complexes. The antimicrobial activity of the Ligand and its metal complexes were studied against *S. aureus*, *S. enteriticyphi*, *E. coli* and *B. subtilis* by the well diffusion method. The metal complexes showed enhanced antimicrobial activity compared with that of the free Ligand.

The literature survey suggests that, the transition metal containing pyrazole moiety, oxime group and fluorine substituent has great importance in the field of chemistry and large applications in agriculture, industrial and biological studies. By considering huge applications of transition metal complexes we planned for synthesis of Co(II) complexes with salicyloylpyrazoleoximes.

Experimental work

Material and methods

All the chemicals were commercial available, solvents are research grade and used after purification. Distilled water and ethanol always used. Melting points are recorded on open capillary method and uncorrected. The progress of reaction was studied using thin layer chromatography. The percentage of metal was carried out by volumetric method¹⁸. The ligand salicyloyl pyrazole oxime was prepared using the method reported in our previous investigation¹⁹.



Scheme-1: Synthetic route for synthesis of Co(II) complexes of salicyloylpyrazoleoxime.

Compound	R ₁	R ₂	R ₃
Co-1	Cl	H	H
Co-2	CH ₃	H	H
Co-3	Br	H	H
Co-4	Cl	CH ₃	H
Co-5	Cl	H	Cl

General Procedure for Synthesis of Metal Complexes

One equivalent of metal sulphate (CoSO₄) solutions was prepared in distilled water and acidified by concentrated hydrochloric acid. The resulting acidic solution was made warm using hot water bath. It was further treated with 2 equivalents of alcoholic ligand solution. The addition of ligand solution was made slowly drop after drop. Slight excess of ligand solution was added to ensure the complete complexation. The resulting solution was then treated with alcoholic ammonia to make it alkaline. The solution was then

digested on boiling water bath where coloured complex precipitated out. The product was filtered, washed first with little hot distilled water and then by ethyl alcohol to remove excess of ligand. It was dried under ambient conditions.

Table-1: Physical, Analytical, molar conductance and magnetic moment data of Co (II) complexes.

Complex (M. Formula)	Colour	M. P. (°C)	% Yield	Found (Calcd.) %				ΛM ($\text{ohm}^{-1} \text{cm}^2$ mol^{-1})	μ_{eff} . (BM)
				M	C	H	N		
Co-1 ($\text{C}_{32}\text{H}_{20}\text{Cl}_2\text{F}_2\text{CoN}_6\text{O}_4$)	Gray	264- 266	71	8.34 (8.18)	52.44 (53.35)	2.94 (2.80)	11.46 (11.67)	62.7	1.99
Co-2 ($\text{C}_{34}\text{H}_{26}\text{F}_2\text{CoN}_6\text{O}_4$)	Gray	218- 220	84	8.43 (8.67)	60.38 (60.09)	3.91 (3.86)	12.12 (12.37)	18.8	1.92
Co-3 ($\text{C}_{32}\text{H}_{20}\text{Br}_2\text{F}_2\text{CoN}_6\text{O}_4$)	Gray	264- 266	73	7.48 (7.28)	47.76 (47.49)	2.81 (2.49)	10.51 (10.38)	42.2	2.21
Co-4 ($\text{C}_{34}\text{H}_{24}\text{Cl}_2\text{F}_2\text{CoN}_6\text{O}_4$)	Gray	236- 238	77	7.78 (7.87)	54.33 (54.56)	3.44 (3.23)	11.46 (11.23)	62	2.36
Co-5 ($\text{C}_{32}\text{H}_{18}\text{Cl}_4\text{F}_2\text{CoN}_6\text{O}_4$)	Gray	230- 232	65	7.68 (7.47)	48.52 (48.70)	2.48 (2.30)	10.89 (10.65)	40.9	2.06

Result and Discussion

All the synthesized Co(II) complexes of salicyloylpyrazoleoximes are non-hygroscopic, air stable and prepared by the stoichiometric reaction of the corresponding metal salts with new Schiff's base ligands in a molar ratio (M:L) of 1:2. The elemental analysis data was also found to be in agreement with the proposed formulae and also confirmed the ML_2 composition of the complexes. All the metal complexes are coloured solids which is different than colour of free ligand. The melting points of all metal complexes were determined by open capillary method and uncorrected. All the complexes were found to melt with decomposition at higher temperature which is more than free ligand this supports the complex formation. The solubility of these complexes was examined in different solvents like water, polar and non-polar organic solvents. All the synthesized complexes are soluble in dimethylformamide (DMF), dimethyl sulfoxide (DMSO) and insoluble in water, ethyl alcohol, acetone, chloroform and dichloromethane. Solubility behavior and elemental analysis data of complexes suggest that the synthesized complexes are monomers.

Solution conductivity

The solution conductivities of all metal complexes were measured using Elico digital conductivity meter (Model CM-180) at Department of Chemistry, Ahmednagar College, Ahmednagar. The molar conductance values for all synthesized complexes indicated that the complexes are non-electrolyte and covalent in nature²⁰. This non-electrolyte nature of complexes supports chelating structure in complexes. The molar conductance values are represented in table-1.

Magnetic moments

The observed magnetic moments of Co(II) complexes are given in table-1. The observed values of magnetic moment for complexes are generally diagnostic of the coordination geometry around the metal ion. Room temperature effective magnetic moment of all Co(II) complexes reported here lie in the range 1.92-2.36 BM corresponding to one unpaired electron for square planar stereochemistry.

IR spectra

The comparison of IR spectra of ligands and their metal complexes indicate that the free ligand exhibit broad band in the range 3391-3248 cm^{-1} assignable to free $\nu(\text{O-H})$ stretching frequency which is obviously absent in the spectra of metal complexes indicating deprotonation followed by the formation of metal oxygen bond of phenolic group^{21,22}. The band in the range 3166-3131 cm^{-1} assignable to hydrogen bonded $\nu(\text{O-H})$ stretching frequency which undergone a slight hypsochromic shift in the complexes, indicative of the coordination of nitrogen atom and presence of strong hydrogen bonding. Evidence for this coordination also arise from the small shift towards lower frequency of the band in the range 1563-1542 cm^{-1} assigned to azomethine linkage $\nu(\text{C=N})$ stretching and $\nu(\text{N-O})$ stretching in the range 1282-1226 cm^{-1} . The shifting of these bands in metal complexes happens because in the metal ligand complex the C=N groups becomes conjugations along with the metal-ligand bonds²³⁻²⁵.

The medium to strong absorption peaks due to $\nu(\text{C-O})$ observed in the 1097-1073 cm^{-1} region. The spectra of free ligand moved towards low frequency in the spectra of the complexes²⁶. The observed downward shift of this band on chelation supports bonding of the metal ions to the phenolic OH after deprotonation²⁷⁻²⁸. Further conclusive evidence of the coordination of salicyloylpyrazoleoxime ligand with the metal ion was proved by appearance of weak bands in the low frequency region 557-540 cm^{-1} and 464-447 cm^{-1} which was assigned to $\nu(\text{M-O})$ and $\nu(\text{M-N})$ respectively²⁹⁻³¹. These frequencies were observed only in the spectra of complexes and not in spectra of free ligand, thus confirming participation of the oxygen and nitrogen atoms in the coordination to the metal ion. The significant peaks in FTIR spectra of synthesized ligands and their metal complexes are summarized in Table-2.

Table-2: The significant peaks in FTIR spectra of free ligand and its Co(II) complexes.

Frequency Compound	$\nu_{\text{O-H}}$	$\nu_{\text{C=N}}$	$\nu_{\text{N-O}}$	$\nu_{\text{C-O}}$	$\nu_{\text{M-O}}$	$\nu_{\text{M-N}}$
HL1	3391, 3131	1563	1232	1097	-	-
Co-1	3140	1543	1228	1031	543	468
HL2	3350, 3134	1542	1231	1097	-	-
Co-2	3142	1538	1221	1042	538	445
HL3	3248, 3163	1546	1282	1073	-	-
Co-3	3148	1532	1258	1052	561	451
HL4	3327, 3157	1548	1226	1093	-	-
Co-4	3145	1541	1215	1060	557	460
HL5	3310, 3166	1545	1242	1088	-	-
Co-5	3149	1541	1226	1033	551	430

¹H NMR spectra

¹H NMR spectra of selected compounds was recorded in DMSO-*d*₆ as solvent and TMS as internal standard. However due to presence of metal ion, proton resonance was not effected and gave broad peaks indicating the formation of metal complexes.

The ¹H NMR spectra of salicyloylpyrazoleoximes showed two D₂O exchangeable proton signals at ~12 δ ppm and 10 δ ppm assignable to phenolic and oxime protons respectively. In ¹H NMR spectra of complexes the proton signal at ~12 δ ppm disappears, indicating deprotonation followed by the formation of metal oxygen bond of phenolic group. The proton signals at ~10 δ ppm shifted to higher value. But the chemical shift is smaller indicating the involvement of nitrogen atom in the formation of metal nitrogen bond and intramolecular hydrogen bonding between ligands. The aromatic protons in the metal complexes are appearing in the range 6.5 to 9 δ ppm.

Powder X-ray diffraction

XRD pattern of metal complexes were obtained in solid form. The powder X-ray diffraction of some selected synthesized metal complexes were scanned on Goniometer powder diffraction PW 3050/60 with Cu-K-alpha-1 radiation ($\lambda=1.5406 \text{ \AA}$). The powder XRD patterns were measured in 2 theta range between 5.0084 and 89.9744 with step size 0.0170. The X-ray diffractogram of all complexes showed broad peak, which indicate polycrystalline nature³². Though polycrystalline nature of complexes was observed they were generally not soluble in non polar solvents.

Thermal Analysis

Thermal behaviors for some selected metal complexes have been studied using TGA in air as atmosphere by heating the system at 10⁰C per minute. The weight loss was recorded as a function of time when the temperature was increased at uniform rate. The temperature range used in thermal analysis was from 30⁰C to 900⁰C. Considering percent loss in weight the thermal decomposition behavior of Co(II) complexes of salicyloylpyrazoleoxime are discussed on the basis of their TG curves as follows.

In Co complexes with salicyloylpyrazoleoximes a significant weight loss begins at 250⁰C. There is no significant weight loss below 250⁰C supports for no lattice or coordinated water molecules in the complexes³³⁻³⁴. The anhydrous compound does not remain stable at higher temperature. The decomposition start slowly and then become rapid in the temperature range 250-690⁰C with percent weight loss corresponding to decomposition of organic part. The decomposition is complete when stable residue of Cobalt oxide is left behind.

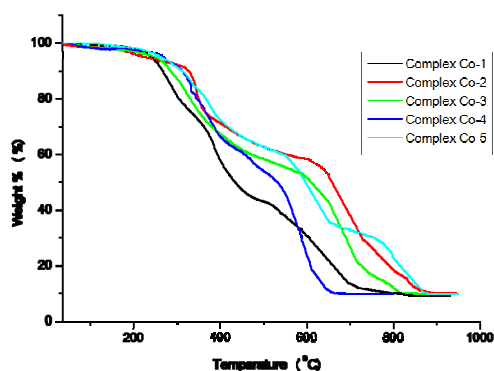


Fig.- 1: TGA profile of complex Co-1 to Co-5.

Electronic absorption spectra

Electronic spectral data of Co(II) complexes were recorded in DMF as solvent and presented in Figures. The UV-Visible spectra gave support in establishing geometry of the synthesized complexes. In the present investigation, the absorption bands observed in the range 280nm and 360nm are attributed to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions due to organic ligands. The shift in absorption frequencies of these bands supports for involvement of oxygen atom of phenol and nitrogen atom of azomethine linkage in coordination with metal. Electronic absorption spectra of Co(II) complexes also showed absorption bands in the region 500-620nm which are assignable to charge transfer band suggesting square planar geometry around Co(II) ion.

Biological Activity

The antimicrobial activity of salicyloyl pyrazole oxime and their metal complexes were screened against bacterial strains *S. aureus*, *B. Subtilis* Gram +ve and *Klebsiella*, *P. aeruginosa* Gram -ve bacteria by the well diffusion method³⁵. All compounds were dissolved in DMF at 100 μ g/ml. DMF was used as solvent and also for control, nutrient agar was used as culture medium. The standard antibiotic used was Penicillin. The activity was reported by measuring the diameter of zone of inhibition in mm. presented table-3.

Table-3: Antibacterial of salicyloylpyrazoleoxime and their Co(II) complex.

Compound	Substituents				Bacteria			
					Gram-positive		Gram-negative	
	R ₁	R ₂	R ₃	R	Sa	Bs	Ks	Pa
HL1	Cl	H	H	F	20	19	23	--
HL2	CH ₃	H	H	F	--	18	--	25
HL3	Br	H	H	F	18	18	23	--
HL4	Cl	CH ₃	H	F	17	18	--	21
HL5	Cl	H	Cl	F	--	16	26	--
Co-1	Cl	H	H	F	26	21	22	25
Co-2	CH ₃	H	H	F	15	19	--	--
Co-3	Br	H	H	F	--	20	--	24
Co-4	Cl	CH ₃	H	F	22	23	26	23
Co-5	Cl	H	Cl	F	17	14	25	--
Control	-	-	-	-	10	08	22	20
Penicillin	-	-	-	-	43	42	32	38

Antimicrobial screening of synthesized Schiff base metal complexes were found comparatively much more active than free ligands. The antimicrobial activity of metal complexes showed considerable zone of inhibition compared to that standard drugs. Most of the synthesized complexes showed antimicrobial activity against all test bacteria. After coordination with metal ion, the compounds which are biologically inactive becomes active and biologically less active compounds becomes more active³⁶⁻³⁸. Such introduction and enhancement in the activity of metal complexes were explained on the basis of Overtone's concept³⁹ and Tweedy's chelation theory⁴⁰. The dissimilarity in the activity of the different metal complexes against different bacteria depends either on the impermeability of the cells of the microbes or difference in the ribosomes in the microbial cells^{41,42}. The metal complexes may also be a vehicle for activation of the ligand as a cytotoxic agent. Moreover, complexation may lead to significant reduction of drug resistant⁴³. Besides this other factor such as solubility, conductivity and dipole moment influenced by the presence of metal ions may also be the possible reason causing enhancement of the antimicrobial activity of chelate complex as compared to free Schiff base compounds⁴⁴.

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