SYNTHESIS, SPECTRAL STUDIES AND ANTIBACTERIAL STUDIES OF TRANSITION METAL COMPLEXES OF NICOTINOYL HYDRAZONE

E. Lakshmi¹, A. Suseelamma*², M. Sandhya Rani³, G.Ramanjaneyulu⁴ and P. Raveendra Reddy*¹
 ¹Department of Chemistry, Sri Krishnadevaraya University, Anantapuramu-515003, INDIA
 ²Department of Chemistry, Hindu P.G. College for Women, Sanath Nagar, Hyderabad-500034
 ³Department of Botany, Sri Krishnadevaraya University, Anantapuramu-515003
 ⁴ Department of Chemistry, S.S.B.N.P.G.College, Anantapuramu-515001

Abstract :

The synthesis and characterization of Fe (II), Co(II) & Ni(II) complexes of 2-Hydroxy acetophenone nicotinoylhydrazone are reported based on elemental analysis, molar conductivity, magnetic susceptibility measurements, infrared and electronic spectroscopy. The ligand was found to behave as monobasic tridentate (NNO donor) manner. All the synthesized complexes are non-electrolytic in nature. Biological activities of the ligand and its complexes were tested against Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus and Bacillus subtilis bacteria.

I. INTRODUCTION

Schiff bases are an important class of ligands in coordination chemistry. Schiff bases derived from hydrazones and aroylhydrazines have been widely used as ligand for the synthesis of transition metal complexes [1]. Schiff bases or their metal complexes have many applications in analysis of water [2]. Hydrazones, heteroaroyl hydrazones ligands and their metal complexes are biologically active[3].

Hydrazones, especially acyl and aroylhydrazones, are multipurpose class of ligands having great biological and chemical activities. Hydrazones exhibit physiological and biological activities in the treatment of several diseases such as tuberculosis [4], Fe overload disease [5–7] and as inhibitors for many enzymes [8]. These properties of the hydrazones are attributed to the formation of stable chelate complexes with transition metals which catalyze physiological processes. They are of interest in the field of electrochromism where a change in the oxidation state of the metal is possible [9,10]. Aroylhydrazone complexes, on the other hand, seem to be a good candidate for catalytic oxidation studies because of their stability to resist oxidation. Acyl and aroylhydrazones contain trigonal N and O-donor atoms that can coordinate to metal ions [11,12]. On the other hand, it is well-known that the azide anion is an efficient and versatile mediator for magnetic coupling and was more commonly employed in the design of polynuclear transition-metal complexes with remarkable diversity in structure and magnetism [13].

Heteroaroyl hydrazones forms stable metal complexes with transition metal ions and inner transition metal ions due to complexing ability of ligand through keto-enol tautomerism and availability of other donor sites in the ligand. i.e., nicotinoylhydrazone has three donor atoms(O,N,N). Hydrazones and their metal complexes are found to have potential application in biology and medicine.

. Nicotinic acid (in large doses) lowers the levels of both cholesterol and triglycerides in the plasma. It has been used as anti-hyperlipoproteinemic drug. It inhibits low-density protein production and of lipolysis in fatty tissue. Nevertheless, it does not have an effect on the general synthesis of cholesterol in the organism. Nicotinic acid in combination with bile acid-reducing drugs can lower the level of cholesterol and triglycerides by 10–30% [14-18].

A few studies of metal complexes of nicotinoylhydrazones have been observed. In this view, we are much interested to prepare a new series of metal complexes of nicotinoylhydrazones. Here in, we report synthesis, spectral studies and antibacterial activity of $C_{14}H_{13}N_3O_2$ ligand and its iron(II), cobalt(II) and nickel(II) complexes.

II. Materials and method

Nicotinic acid hydrazide, 2-methoxyacetophenone, agarose were purchased from Sigma-Aldrich. All other chemicals were of AR grade and used as provided. The solvents used for the synthesis were distilled before use. Elemental analyses were carried out on a Heraeus Vario EL III Carlo Erba 1108 instrument. Magnetic

measurements were taken at 298K using lakeshore VSM 7410 instrument. Molar conductivity measurements at 298 \pm 2K in dry and purified DMF were carried out using a ELICO CM model 162 conductivity meter. The electronic spectra were recorded in DMF with a UV lamda50 (Perkin-Elmer) spectrophotometer. IR spectra were recorded in the range 4,000–400 cm⁻¹ with a Perkin-Elmer spectrum100 spectrometer on KBr discs.

2.1 Preparation of Ligands

Ligand was prepared by reacting niazid with 2-Hydroxy acetophenone. A methanolic solutions of nicotinylhydrazide (5mmol), carbonyl compound (5mmol) were mixed in a 100-ml round bottom flask. Two drops of HCl were added to the reaction mixture and refluxed for 3 hours. On cooling the reaction mixture to room temperature, yellow colored crystalline products were separated. The products were collected, washed with hot water and few drops of hexane and dried in vacuum. Structure of the ligand is shown in **Fig. 1**.



Fig 1: Structure of 2-Hydroxy acetophenone nicotinoylhydrazone(C₁₄H₁₃N₃O₂)

2.1.1. Characterization of 2-Hydroxy acetophenone nicotinoyl hydrazone ($C_{14}H_{13}N_3O_2$):

2-Hydroxy acetophenone nicotinoyl hydrazone ($C_{14}H_{13}N_3O_2$): Yield 72%, M.Pt.242-244 °C, Anal (%) Calc.(found): C-65.97(65.88); H-5.07 (5.04); N-16.68(16.64); ¹H-NMR spectra: δ (13.18) (singlet 1H), δ (11.64) (singlet 1H), δ (8.8)(multiplet 4H), δ (7.3) (multiplet 4H), δ (2.50) (singlet 3H), assigned to –OH, – NH, nicotine H, benzene H, methyl H protons respectively. Mass spectra of C₁₄H₁₃N₃O₂ shows molecular ion peak m/z 255. The mass spectrum of C₁₄H₁₃N₃O₂ is shown in **Fig 2**.



Fig 2: The mass spectrum of C₁₄H₁₃N₃O₂

2.2. Preparation of complexes

All the metal complexes were prepared in a similar way by following method. To a hot solution of ligand $C_{14}H_{13}N_3O_2$ (0.02M) in 25ml of methanol a suspension of respective metal salts [Chlorides of Fe (II), Co (II), Co (II)] was added drop wise with constant stirring. The reaction mixture was refluxed on a water bath for 4-6h. The precipitated complexes were filtered, washed with ethanol. Followed by ether and dried over fused calcium chloride. Yield: 54-60%.

2.3 Antimicrobial Analysis by Disc Diffusion Method.

The 2-Hydroxy acetophenone nicotinoylhydrazone($C_{14}H_{13}N_3O_2$) and its metal complexes were screened for their antimicrobial activity by disc diffusion method [19] against six bacterial strains such as

Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus and *Bacillus subtilis bacteria*. Antibacterial activity was tested by the filter paper disc diffusion technique involving the cultures of the selected organisms for 24h. Mueller Hintonagar number 2 (Hi Media, India) was used as the bacteriological medium and sterile yeast nitrogen base with 2% agar (Hi Media, India) was used as the fungal medium. The test solutions of the ligand and its metal complexes were prepared in sterile dimethyl sulfoxide (DMSO) solvent for the study. The synthesized 2-Hydroxy acetophenone nicotinoylhydrazone($C_{14}H_{13}N_3O_2$) and its metal complexes were tested at different concentrations to find out the minimum concentration of the ligand and its metal complexes required for inhibiting the growth of microbes.

Ampiicillin (100 μ g/mL) was taken as the standard for antibacterial activity. The organism was seeded into sterile nutrient agar medium by mixing one mL of inoculum with 20mL sterile melted nutrient agar kept at 48–50°C in a sterile petri dish. The medium was allowed to solidify first. Then the test solutions, the standard drugs, and the blank were impregnated in whatmann filter paper discs, placed on the solidified medium in the petridish, and left undisturbed for 2 h at room temperature. The petridishes were then incubated at 37°C for 24 h and the zone of inhibition for the test samples, standard, and control (DMSO) was measured.

III. RESULTS AND DISCUSSION

3.1 Elemental analysis, molar conductivity measurements and magnetic moment

All the complexes are stable at room temperature, non-hygroscopic, slightly soluble in water, but more soluble in methanol, ethanol and readily soluble in CH₃CN, DMF and DMSO. The analytical data (**Table 1**) are consistent with the proposed molecular formulae of complexes. Low molar conductivity values of present complexes suggest non-electrolytic nature of the complexes. The effective magnetic moment (μ_{eff}) of the metal complex of FeC₂₈H₂₄N₆O₄ is 5.1B.M. The value suggest high spin octahedral geometry for the complexes [20]. The effective magnetic moments (μ_{eff}) of the CoC₂₄H₂₆N₆O₄ is 4.28 B.M. which is consistent with three unpaired electrons and falls within the range reported for mononuclear cobalt(II) complexes[21]. The magnetic moment of NiC₂₈H₂₄N₆O₄ is 2.95 B.M. The data reveal that the observed magnetic moment values of these complexes are as expected for mono nuclear nickel(II) complexes having two unpaired electrons [22]. Mass spectrum of FeC₂₈H₂₆N₆O₄ is shown in **Fig.3**. Mass spectra of FeC₂₈H₂₆N₆O₄ shows molecular ion peak at m/z 564.

S.NO	Complex	Melting	Ele	μeff	ΛM ^a			
		Point						
		°C	C	Н	N	Μ		
1	FeC ₂₈ H ₂₄ N ₆ O ₄	>300	59.87	4.12	13.84	9.05	5.2	4.8
			(59.57)	(4.15)	(13.78)	(9.09)		
2	CoC ₂₈ H ₂₄ N ₆ O ₄	>300	59.17	4.26	14.84	10.32	4.31	11.2
			(59.16)	(4.22)	(14.79)	(10.37)		
3	NiC ₂₈ H ₂₄ N ₆ O ₄	>300	59.25	4.19	14.78	10.39	2.95	18
			(59.29)	(4.23)	(14.82)	(10.35)		
*			346, 543	9 9781				
		62/25/2/2017						

Table 1: Physico-chemical properties of metal complexes

Fig 3 Mass spectrum of $FeC_{28}H_{24}N_6O_4$

© 2018 JETIR November 2018, Volume 5, Issue 11 3.2 Electronic spectra

Electronic absorption spectra of metal complexes were recorded in DMSO. The important electronic spectral data of metal complexes are presented in **Table 2**. The electronic spectrum of complex $FeC_{28}H_{24}N_6O_4$ is shown in **Fig 4**. The study of magnetic and electronic spectra data are quite informative in characterizing the geometry of the complexes. The UV-visible spectrum of the ligands and their complexes were recorded in DMSO.

All the complexes show strong intense bands in the region 34364-31153 cm⁻¹ attributed due to intraligand and π - π * aromatic ring. Another sharp peak shows in the region of 28328-25445 cm⁻¹ is due to n- π * transition. One medium intensity band observed in the range 21551-20491 cm⁻¹ is due to metal to ligand charge transfer transition (MLCT). A weak band is observed in the region of 16863-15504 cm⁻¹ which can be assigned to d-d transition.

Complex	π-π*	n -π*	СТ	d-d
	transition	transition	transition	transition
FeC ₂₈ H ₂₄ N ₆ O ₄		The second second second		
	34364	28328	21551	16863
$CoC_{28}H_{24}N_6O_4$				
	32581	26564	20491	15504
NiC ₂₈ H ₂₄ N ₆ O ₄	114	1		
	31153	25445	20661	17235

Table 2 Electronic Spectral data(cm⁻¹) of metal complexes



Fig 4 Electronic spectra of FeC₂₈H₂₄N₆O₄

3.3 IR spectra

The important bands in infrared spectra of the ligand and it's metal complexes are discussed. Important IR spectral bands of complexes are presented in **Table 3**. An intense band is observed in the region of 3220 cm⁻¹ in IR spectra of ligand due to phenolic v(-OH) group. The band is disappeared in metal complexes. This indicates deprotonation of phenolic group and bond formation between phenolic oxygen and metal ion [23, 24]. In the IR spectrum of ligand a strong band is observed in the region of 1689 cm⁻¹ which is assigned to v(C=O)group. In the IR spectra of complexes this peak is shifted to lower wave

numbers suggesting the involvement of >C=O group in chelation. The C=N (imine) vibration is observed in 1603 cm⁻¹ range in the IR spectra of ligands. This band is shifted to lower wave number in IR spectra of all the complexes suggesting the participation of azomethine nitrogen atom in coordination with metal ion. The non-ligand absorption bands occurring in the regions 522-538 cm⁻¹ and 403-417 cm⁻¹ are assigned to $v_{(M-O)}$ and $v_{(M-N)}$ vibrations respectively[25]

Compound	v(O-H) cm ⁻¹	v(N-H) cm ⁻¹	v(C=O) cm ⁻¹	v(C=N) cm ⁻¹	v(M-O) cm ⁻¹	v(M-N) cm ⁻¹
C14H13N3O2	3220	3003	1689	1603	_	_
	0220	2002	1007	1000		
FeC ₂₈ H ₂₄ N ₆ O ₄	-	3001	1686	1599	528	417
$CoC_{28}H_{24}N_6O_4$	-	3009	1669	1601	538	414
NiC ₂₈ H ₂₄ N ₆ O ₄	-	3091	1664	1602	522	403

Fable 3:	Important IR	spectral	bands of o	complexes	& ligand
----------	--------------	----------	------------	-----------	----------

Based on the above spectral data we suggest general structure of the metal complexes. It is shown in Fig. 5.



Fig. 5 Structure of metal complexes

3.4 Antibacterial activity

To determine the antibacterial activity of $C_{14}H_{13}N_3O_2$ ligand and its Fe(II), Co(II), and Ni(II) complexes, the disc diffusion method was used, with ampiciillin as the standard antibiotic. The prepared compounds were tested against *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus* and *Bacillus Subtilis bacteria*, *Pseudomonas aerogenosa*, *Candida albicans*, *species* microorganisms. Table 6 contains the screening results corresponding to the $C_{14}H_{13}N_3O_2$ its metal complexes with good inhibition of growth against the tested organisms. The $C_{14}H_{13}N_3O_2$ ligand and its complexes hold a less activity against the *E. coli*. The $C_{14}H_{13}N_3O_2$ ligand and its metal complexes showed a reasonable result against the growth of *Klebsiella*. The ligand and its complexes showed a more activity against the growth of *S. aureus*. The ligand $C_{14}H_{13}N_3O_2$ and complexes showed highest activity against the growth of this bacterium. A comparative account on the effect of antibacterial activity against the chosen microbes indicates that the ligand and its three metal chelates show reasonable activity against *Klebsiella Pneumonia* (19, 18, and 16 mm) and *Bacillus subtilis* (21, 18, and 19 mm) while the growth of other organisms is moderately inhibited by the FeC₂₈H₂₄N₆O₄ ligand and better activity was shown by its Fe(II), Co(II) and Ni(II) The highest antibacterial action (21 mm) has been observed for FeC₂₄H₂₆N₆O₄ complex against *Bacillus Subtilis*.



	Bacterial growth inhibition zone (in mm)											
Compound	S. Aureus			B. Subtilis		K. Pneumonia			E. Coli			
	10 (µg/mL)	20 (µg/mL)	30 (µg/mL)	10 (µg/mL)	20 (µg/mL)	30 (µg/mL)	10 (µg/mL)	20 (µg/mL)	30 (µg/mL)	10 (µg/mL)	20 (µg/mL)	30 (µg/mL)
$C_{14}H_{13}N_3O_2$	8	12	14	9	11	13	7	10	12	6	8	10
FeC ₂₈ H ₂₄ N ₆ O ₄	12	17	20	16	18	21	13	16	19	15	18	20
CoC ₂₈ H ₂₄ N ₆ O ₄	10	13	13	6	15	18	- 11	15	18	12	14	17
NiC ₂₈ H ₂₄ N ₆ O ₄	11	13	15	10	17	19	12	14	16	7	11	14
Standard	16	18	21	17	18	22	15	17	20	18	20	22
Control	-	-	-	-	-	-	-	-	-	-	-	-

Table 4. Antibacterial activity of metal complexes and ligand

Standard: Ampicillin; Control:DMS

IV. Conclusions

2-Hydroxy acetophenone nicotinoylhydrazone($C_{14}H_{13}N_3O_2$) has been synthesized and characterized based on elemental analysis, Mass, IR, NMR and ESR spectral studies. Fe(II), Co(II) and Ni(II) complexes of 2-hydroxy acetophenone nicotinoylhydrazones($C_{14}H_{13}N_3O_2$) have been synthesized and characterized based on various physicochemical and spectral techniques. These studies revealed that the complexes have general formula ML₂ (where L = hydrazone). The hydrazones act as monobasic tridentate ligand. Electronic spectral data suggest that the complexes have octahedral geometry. Antibacterial activity of metal complexes have been studied. Among three complexes FeC₂₈H₂₄N₆O₄ shows better activity.

References

- 1.M. Jayaramudu and K.H.Reddy 1999. Dimeric metal complexes of diacetylmonoxime isonicotinoyl hydrazone. Indian Journal of Chemistry, 38A: 1173-1176.(ref5)
- 2.R. M. Issa, S. A. Abdel-Latif and H. A. Abdel-Salam. 2001. Synthesis and characterization of new Cu(II) complexes derived from benzilic and mandelic hydrazones. Synthesis and Reactivity in Inorganic and Metal-Organic Chemistry, 31(1): 95-105.
- 3.C. Z. Hussain and S. K. Aftab. 1997. Synthesis and spectroscopic studies of biologically active Co(II), Cu(II) and Ni(II) complexes of hydrazine derived Schiff-base ligands. Journal of The Chemical Society of Pakistan, 19(3): 196-200.
- 4.M. Ramesh , K. B. Chandrashekar and K. Hussain Reddy. 2000. Spectrophotometric determination of lead(II) in water samples using benzil α-monoxime isonicotinoyl hydrazone. Indian Journal of Chemistry, Sec A (IJC-A), 39A: 1337-1339.
- 5.B. N. Sivasankar and S. Gavindaragam. 1995. Synthesis, Characterization and Thermal Reactivity of Mixed Metal Hydrazidocarboxylate Hydrazinates. Synthesis and Reactivity in Inorganic and Metal-Organic Chemistry, 25 (1): 127-138.
- 6. A. Ghaib, S. Menager, P. Verite, O. Lafont. 2002. Synthesis of variously 9,9-dialkylated octahydropyrimido [3,4-a]-s-triazines with potential antifungal activity. Farmaco 57(2): 109-116.
- P. M. Gurubasavaraj, P. M. Veeresha. 2008. Synthesis, Characterization, Electrochemistry and Biological Activities of Ni(II) and Cu(II) Complexes of Schiff Bases. Asian Journal of Chemistry 20(4): 2841-2846.
- 8.N. Nawar, N. M. Hosny. 2000. Synthesis, spectral and antimicrobial activity studies of oaminoacetophenone o-hydroxybenzoylhydrazone complexes. Transition Metal Chemistry 25(1):1-8
- 9.R. Castarlenas, Dixneuf. 2003. Highly Active Catalysts in Alkene Metathesis: First Observed Transformation of Allenylidene into Indenylidene via Alkenylcarbyne—Ruthenium Species. Angewandte Chemie International Edition 42(37): 4524-4527.
- 10.R.L. Dutta, A. Syamal, Elements of Magnetochemistry. 2nd ed. New Delhi: Affiliated East- West Press Pvt. Ltd; 1993.
- 11.C.M. Harris, E.D. Mckenzie. 1967. Nitrogenous chelate complexes of transition metals—III: bis-chelate complexes of nickel (II) with 1,10-phenanthroline, 2,2'-bipyridyl and analogous ligands, Journal of Inorganic and Nuclear Chemistry 29(4): 1047-1068.
- 12.R. K. Mohapatra, U. K. Mishra, S. K. Mishra, A. Mahapatra and D. C. Dash. 2011. Synthesis and Characterization of Transition Metal Complexes with Benzimidazolyl-2-hydrazones of o-anisaldehyde and Furfural. Journal of the Korean Chemical Society. 55(6): 926-931.
- 13.R. K. Mohapatra, U. K. Mishra, S. K. Mishra, A. Mahapatra, D. C. Dash, 2014. Synthesis and spectral characterization of transition metal complexes withbenzothiazolyl-2-hydrazones of salicylidene acetoneand salicylidene acetophenone. Acta chimica and pharmaceutica indica 2(4): 156-162.
- 14.C. Mirela, I. Emilia, M. S. Adrian, 2008 Studies on nickel(II) complex compounds with 2-benzothiazolyl hydrazones. Revue Roumaine de Chimie, 53(10): 903-910.
- 15.K. Nakamoto, 4th Ed., Wiley, New York, (1986).
- 16.R. N. Patel, N. Singh, V. L. N. Gundla. 2006. Synthesis, structure and properties of ternary copper(II) complexes of ONO donor Schiff base, imidazole, 2,2'-bipyridine and 1,10-phenanthroline. Polyhedron, 25(17): 3312-3318.
- 17.V. Singh and A. Singh. 2008. Synthesis, spectral studies of cobalt(II) tetrathiocyanoto dicuperate(I) complexes with some acylhydrazones and their antimicrobial activity. Russian Journal of Coordination Chemistry 34(5): 374-381.
- 18.B. Sutariya, S. Mohan, S. Sambasiva and S. Rao. 2007. Synthesis and antimicrobial activity of some new 2-substituted aminothiazoles. Indian Journal of Chemistry, Sec B (IJC-B) 46B: 884-887.
- 19. B. Mounyr, M. Sadiki and S. K. Ibnsouda 2016. Methods for *in vitro* evaluating Antimicrobial activity. Journal of Pharmaceutical Analysis 6(2): 71-79.
- 20.S. Baluja, A. Solanki A and N. Kachhadia. 2006. Evaluation of biological activities of some Schiff bases and metal complexes. Journal of the Iranian Chemical Society 3(4); 312-317.
- 21.G. T. A. Jombo. 2011. Synthesis, Characterisation And Anti Microbial Activity Of Various Schiff Base Complexes Of Zinc (II) And Copper (II) Ions. Asian Journal of Pharmaceutical and Health Sciences. 1(1): 8-11.
- 22. C. M. Harris and E. D. Mckenzie 1967. Nitrogenous chelate complexes of transition metals-III: bis-

chelate complexes of nickel (II) with 1,10-phenanthroline, 2,2'-bipyridyl and analogous ligands.Journal of Inorganic and Nuclear chemistry 29(4):1047-1068.

- 23.M. Shebl, M. E. Saied Khalil, A. Saleh Ahmed and A. A. Hesham Medien 2010. Synthesis, spectroscopic characterization and antimicrobial activity of mono-, bi- and tri-nuclear metal complexes of a new Schiff base ligand. Journal of Molecular Structure 980(1): 39-50.
- 24.A.A. Adel Emara and A. A. Azza Abou-Hussen 2006. Spectroscopic studies of bimetallic complexes derived from tridentate or tetradentate Schiff bases of some di- and tri-valent transition metals. Spectrochimica Acta Part A 64(4):1010-1024.
- 25.K. Nakamoto, (1997). Infrared and Ramman Spectra of Inorganic and Coordination Compounds, 5th ed., John Wiley & Sons, New York, USA.

