A DESIGN OF NOVEL SYNTHESIS OF P- PHENYL ISONITROSO ACETOPHENONE AND THEIR ANTIMICROBIAL ACTIVITY

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A B S T R A C T

p-phenyl- isonitroso -acetophenone was synthesized. The Co(II), Ni(II) and Cu(II) complexes of ligand p-Phenyl- isonitroso-acetophenone (p-PINAP) have been synthesized and characterized on the basis of elemental analysis, conductivity, magnetic measurement, IR and electronic spectral studies. The conductivity data of the complexes suggests their nonelectrolyte nature. On the basis of these studies complexes of formula $Co(P\text{-}PINAP)_2$, $Ni(P\text{-}PINAP)_2$, and $Cu(P\text{-}PINAP)_2$ have octahedral geometry

Keywords: $Cu(P\text{-}PINAP)_2$, p-phenyl-isonitroso- actophenone , metal, complexes, spectroscopy, antimicrobial activity

1 Introduction

The inclusion of biologically active ligand into organometallic complexes offers much scope for the design of novel drug with enhanced targeted activity.

Isonitroso ketones are of great interest since it has the ability to chelate metal ion through nitrogen and or oxygen donor centers. The interaction of metal ion with ligand containing oxygen and nitrogen as donor atom were undertaken by many chemist. Studies on such complexes indicate that new mechanism of action are possible when combining the bioactivity of the ligand with the properties inherent to the metal by Tomar et al.[1]. With significant development in the field of biological activity of metal chelates plays important role in treatment of biological disorder shown by Mahajan and Patil [2] .

The ligand p-bromo-isonitroso-acetophenone (p-BrINAP) and p-chloro-isonitroso-acetophenone (P-ClINAP) have also been studied by Bhandrakar [3] for few transition metals . Many researchers have screened Pd complexes for anticancer by Ali et al. [4] and antitumor by Malik et al, [5] activities with more or less success. Versatility of Schiff base ligands and biological, analytical and industrial applications of their complexes make further investigations in this area highly desirable. It was also established that the biological activity of Schiff bases is altered many folds on coordination with metal ions shown by Saraf et al. [6]. Keeping the above fact in our mind and in continuation of work on transition metal complexes with Schiff bases.

However, structural studies of the complexes of transition metals with p-phenyl-isonitroso-acetophenone have not been reported yet. The present paper describes the synthesis and characterization of complexes of transition metals Co(II), Ni(II) and Cu(II) with isonitroso p-phenyl-acetophenone on the basis of elemental analysis, IR Spectra, NMR Spectra, Magnetic properties and Antimicrobial activity.

1.1 Material and methods

All chemical used were of analytical grade and of highest purity available and used without further purification. Metal (II) chlorides and acetate salts were also obtained from Merck. Solvents used were distilled and purified before used.

1.1.1: Preparation of Cu (p-PINAP) $_2$: Copper acetate solution was prepared by dissolving 0.199 g. in a minimum quantity of alcohol and equal volume of water was added. Similarly 0.450 g. of p-PINAP was dissolved in a minimum quantity of alcohol. The copper solution was added to the reagent solution drop by drop with constant stirring in conical flask.

The mixed solution was refluxed on sand bath for 4 hrs. On cooling, it was filtered through filter paper, washed with 50% alcohol and analaysed for copper, carbon, hydrogen, and nitrogen.

1.1.1:Preparation of Co (p-PINAP) $_2$: Aqueous solution of Cobalt nitrate and P-PINAP was mixed in the molar ratio of 1:2 and pH of solution was maintained 5-6 by HCl/NH_4OH. On refluxing for an hour yellow colour complex was formed, filtered and recrystalised from chloroform. and analaysed for cobalt, carbon, hydrogen, and nitrogen.

1.1.1: Preparation of Ni (p-PINAP) $_2$: 0.450g of P-PINAP was dissolved in minimum volume of alcohol and equal volume of water was added. Similarly 0.237g Nickel acetate was dissolved in alcohol and water (1:1). The nickel solution was added to reagent solution drop wise with constant stirring. The pH was adjusted to 5-6 with HCl/NH4OH. A green colour solid complex was formed, separated, recrystalised from chloroform. and analaysed for nickel, carbon, hydrogen, and nitrogen.

1.2: Results and discussion

Elemental analyses were carried out on a model 240 Perkin elemental analyzer. Metal contents were determined gravimetrically. The infrared spectra were measured on a Bukar FT-IR spectrophotometer using KBr pellets. Magnetic susceptibility measurements of the complexes in the solid state were determined by Gouy balance using $CuSO_4$ as the calibrant at room temperature . Molar conductance measurements were made in anhydrous DMF on a Systronic model 305 conductivity bridge. Synthesized compounds and ligands were screened against bacteria by the disc dilution method used by Dube [7] at various concentrations using nutrient agar as medium. On the basis of physicochemical characteristics it has been found that the complexes are non-hygroscopic, stable at room temperature, insoluble in water but fairly soluble in DMSO. The magnetic moment data indicates that the complexes are paramagnetic in nature. The molar conductance values for all the complexes suggesting their non-electrolytic nature by Kumar et al,[8] and that no anion are present outside the coordination sphere. Elemental analysis data and molar conductance value for ligand and metal complexes given in table 1 .

Table 1: Quantitative analysis for ligand and metal complexes

COMPLEX	COLOUR	% C	% H	% N	% M
P-PINAP		66.60 (66.68)	3.84 (3.97)	5.60 (5.57)	11.20 (11.08)
Co (p-PINAP)$_2$	Yellow	66.47 (66.28)	3.90 (3.95)	5.60 (5.53)	11.52 (11.63)
Ni (p-PINAP)$_2$	Green	66.25 (66.29)	3.80 (3.94)	5.60 (5.52)	11.60 (11.62)
Cu (p-PINAP)$_2$	Green	65.47 (65.68)	3.20 (3.91)	5.50 (5.47)	12.50 (12.42)

1.2.1: Infrared spectroscopy:

. The ν_{O-H} of the oxime group observed at 3340 cm^{-1} in (p-PINAP) is absent in the spectra in complexes suggesting replacement of H- of OH group of oxime by the metal ion during complex formation through metal ion by Lever [9].The IR spectra of the complexes indicate that the ligand behaves as bidentate and coordinates with metals via azomethine nitrogen and C=O group. The IR spectra of Schiff base ligand P-PINAP shows sharp band observed for ligand at 1710 cm−1, is due to azomethine >C=N linkage which is shifted to lower frequency (1601 cm^{-1}) on going from ligand to its metal complexes due to coordination of azometine nitrogen with metal ion by Sece et al. [10]. It is expected that coordination of nitrogen to the metal atom would reduce the electron density in the azomethine link and thus lower -HC=N absorption.

A band appears in the range 1200-1160 cm^{-1} is reported by Hurst [11] that N-oxide (N→O) stretching mode in aromatic ring compounds . The peak observed near 1625, 1612, 1630 cm^{-1} in spectrum of M (p-PINAP)$_2$ may be assigned to the perturbed $\nu_{C=0}$ and /or $\nu_{C=N}$ stretching vibration involving bonding through oxygen, and nitrogen donor atoms The bands at 1260, 123and 1260 in M(p-PINAP)$_2$ are attributed to

the N-O stretching in the ligand by Deshmukh [12]..The presence of sharp band in the region 601-698 cm−1 in all the complexes due to the >M-N coordination of azomethine nitrogen observed by Ghosh et al. ,Saraf et al. and Thoms [13-15]. The appearance of vM-N and vM-O vibration support the involvement of N and O atoms in complexation with metal ions under investigation by Thakkar et al. [16]. The infrared spectral data of Schiff base ligand and its metal complexes are listed in table 2

Table 2: Infrared spectral frequencies of ligand and metal complexes

p-PINAP	Co (II)	Ni (II)	Cu (II)	Assi. of group
3340	---	---	---	OH, of N-OH
3040	3050	3035	3040	Ar-H
1710	---	---	---	C=O
1606	1625	1612	1630	C=N
---	1260	1235	1260	N O
1040	1055	1081	1080	C-H
763	759	756	757	Para Sub.
----	698	601	695	M-N

1.2.2 : H NMR spectra:

NMR spectra of Co(p-PINAP)$_2$, Ni(p-PINAP)$_2$ & Cu(p-PINAP)$_2$ in DMSO solution exhibit peaks due to –CH group, phenyl group & aromatic ring protons & does not show any proton signal due to =NOH group. This suggest that their complexes have been formed by the replacement of the proton of the =NOH group by the metal ion. NMR spectrum of (P-PINAP) show a peak around 8.90 δ due to the=NOH group. Two groups of band corresponding to phenyl and the aromatic proton in (P-PINAP) appears at 7.89 δ and 7.26 δ respectively. It may be mentioned that etyl-ά-isonitroso-acetoacetate(HEINA), and p-chloro-isonitroso-acetophenone of Raut et al,[17] (HP-CIINAP), show =NOH proton resonance at -9.27 δ, and-8.64 δ respectively.

Table 3: NMR signals in ligand & metal complexes

Complex	=NOH group	Aromatic Ring	-CH group	Phenyl group
p-PINAP	8.9	7.89 & 7.25	2.5	7.26
Cu(p-PINAP)$_2$	---	7.3 & 7.5	7.5	7.48, 7.32,
Co (p-PINAP)$_2$		7.3& 7.5	7.5	7.48,7.32,
Ni (p-PINAP)$_2$	---	7.3 & 7.5	7.5	7.48,7.32,

All values in δ scale

1.2.3 : Antimicrobial activity:

All the synthesized complexes are effective at concentration of 500 µg/ml as Rehaman [18]. Antibacterial activity of the synthetic metal complexes of p-Phenylisonitroso Acetophenone was examined against *E.coli, S.aureus,P.aeruginosa ,B.subtilis, B. cereus and K. pneumonae.* Antifungal activity of the same compounds was evaluated against *Candida albicans* and *A.nigar*

The results showed that the ligand and complexes of p-PINAP exhibited poor to good antimicrobial activities against all the tested strains. Complexes of Co, Ni and Cu were shown maximum zone of inhibition and hence were found to control the growth of all strains of bacteria and fungi examined. Though the ligand exhibited antibacterial and antifungal activity against all the tested strains, but metal complexes are found more active and hence suggested its unsuitability against all the strains.

Table.4: Zone of inhibition antibacterial results of p-PINAP& synthesized complexes

Compound	Bacteria along with zone of inhibition (mm)					
	E. coli	***S. aureus***	***P. aeruginosa***	**B. subtilis**	**B. cereus**	**K. pneumonae**
p-PINPA	10	12	11	14	12	15
Co(p-PINPA)$_2$	14	22	15	14	23	21
Ni(p-PINPA)$_2$	22	15	16	13	15	20
Cu(p-PINPA)$_2$	13	20	18	12	22	22
Gentamicne	20	20	20	20	20	20

Table 5: Antifungal activity of p-PINAP & complexes

Compound	*C. albicans*	*A. niger*
p-PINPA	13	11
Co(p-PINPA)$_2$	19	18
Ni(p-PINPA)$_2$	22	16
Cu(p-PINPA)$_2$	22	17
Miconazole	22	21

1.3 Conclusion

The metal ligand composition was found to be 1: 2. by analytical, IR, NMR spectral data and magnetic property. . The geometry of complex octahedral geometry has been assigned to Co(II), Ni(II),) and Cu(II) Complex. Invitro, Antibacterial and Antifungal screening of these relived that most of the compounds exhibited potted inhibited potential activity.

1.4 References

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