

# Microwave Assisted Synthesis and Biological Evaluation of Transition Metal Complexes of p-methyl isonitrosophenyl Acetate

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## ABSTRACT

The shorter reaction times offered by microwave assisted deals with the synthesis of p-methyl isonitrosophenyl acetate using p-cresol, acetic anhydride and n-amyl nitrite. The Fe(II), and Fe(III) complexes of Schiff base derived from p-methyl isonitrosophenyl acetate have been synthesized. The complexes of the type ML<sub>2</sub> 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 non electrolytic nature. The biological activity of Schiff base and their metal complexes are studied against gram positive and gram negative bacteria by disc diffusion technique which shows that complex exhibit promising antibacterial activity than that of Schiff base against tested bacteria.

**Keywords:** p-methyl isonitrosophenyl acetate, complexes, spectroscopy, antimicrobial activity

## INTRODUCTION

Chemist are looking for cleaner, more environmentally benign ways to make targeted synthesis. In industry the shorter reaction times offered by microwave assisted synthesis are suited to explore the wide range of applications. Schiff bases are considered to be the important class of chelating agents especially when -OH functional group also present with azomethine group. In recent years, researcher shows much interest in the synthesis and characterization of Schiff bases metal complexes due to their importance as catalyst in many reactions (Huges, 1984; Chatterjee *et al.*, 2000; Ali *et al.*, 2002). Transition metals are essential for normal functioning of living organism and are, therefore, of great interest as potential drugs [Malhotra *et al.*, 2006]. Coordination compounds derived from numerous Isonitroso ketones have been reported because of their anti-tuberculosis, antimicrobial and corrosion inhibitors [Fouda *et al.*, 2008; Ali *et al.*, 1988; Ferrari *et al.*, 1999]. 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. It was also established that the biological activity of Schiff bases is altered many folds on coordination with metal ions [Malik *et al.*, 2010]. Keeping the above fact in our mind and in continuation of work on transition metal complexes with Schiff bases [Saraf *et al.*, 2012(a)] the ligand p-methyl isonitrosophenyl acetate (L) has been synthesized. and its metal complexes with Fe(II) , and Fe(III) were synthesized. The structure of ligand and metal complexes had been characterized by FTIR, H NMR and UV spectroscopy. The biological activity also studied against gram positive and gram-negative bacteria for ligand and metal complexes.

## MATERIALS AND METHODS

All chemical used were of analytical grade and of highest purity available and used without further purification. P-cresol and n-amyl alcohol were obtained from M/S Merck chemicals. Metal (II) chlorides and acetate salts were also obtained from Merck. Solvents used were distilled and purified before used.

### Synthesis of p- Methyl isonitroso phenyl acetate

p-cresol (100ml) and acetic anhydride(120ml) was taken in round bottom flask. Fused sodium acetate (4g) was added to it and reflux for 1hour. The reaction mixture was cooled and poured into ice cold water. Liquid layer was separated by separating funnel and distilled to obtain pure p-methyl phenyl acetate at 210°C-212°C.

Dissolved 12g of sodium in 250ml of absolute alcohol and to this solution, added in small portion, and with cooling, first 60ml n-amyl nitrite and then 70ml of p-methyl phenyl acetate. This mixture was allowed to stand for 2 days in well stopper bottle in a refrigerator. At the end of this time, the brown sodium salt was filtered and dried in air. The dried sodium salt was dissolved in a minimum quantity of ice cold water and treated with a calculated quantity of glacial acetic acid. Precipitate p-methyl Isonitroso phenyl acetate was then filtered through suction, and dried in vacuum. The crude product was recrystallised from benzene.

### Synthesis of Metal Complexes:

#### 1.Preparation of Fe(P-MINPA) <sub>2</sub>:

00.358g of P-MINPA was dissolved in minimum quantity of alcohol was added. Similarly 0.392g of ferrous

ammonium sulphate was dissolved in water. The FAS solution was added to reagent solution drop by drop with constant stirring. The pH was adjusted to 5.5-6.0 with buffer tablets. This solution was refluxed on sand bath at 100°C for 2hrs. and then kept in vaccum desicator for overnight. A blue coloured complex was formed, filtered and recrystallised from chloroform.

#### 2.Preparation of Fe(P-MINPA) <sub>3</sub>:

Aqueous solution of Ferric Chloride and P-MINPA was mixed in the molar ratio of 1:3 and pH of solution was maintained 5-6 by HCl/NH<sub>4</sub>OH. On putting in microwave oven for 4 to 5 hour yellow colour complex was formed, filtered and recrystallised from chloroform.

## 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 Nicolet 400 D FT- IR spectrophotometer using KBr pellets from. The electronic spectra of the metal complexes in DMF were recorded on JASCO 7800 Elico SL-159 and Shimadzu UV-160A UV-VIS spectrophotometer. Magnetic susceptibility measurements of the complexes in the solid state were determined by Gouy balance using CuSO<sub>4</sub> as the calibrant at room tempera-ture. Molar conductance measurements were made in anhydrous DMF on a Systronic model 305 conductivity bridge.

Above synthesized compounds and ligands (Schiff base) were screened against bacteria Escherichia coli by the filter paper disc method [Dubey amd Maheswari, 2002] at various concentrations using nutrient agar as medium. Sterilized filter paper of 5 mm diameter was soaked in solutions of different concentrations of test samples and introduced on nutrient agar plates. These plates were incubated for 48 hours at 35°C.

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 Fe(II), Ni(II) and Co(II) complexes are paramagnetic in nature. The molar conductance values for all the complexes in 10<sup>-3</sup>M DMSO are in the range of 9.5-14 W<sup>-1</sup> cm<sup>2</sup> mol<sup>-1</sup> suggesting their non-electrolytic nature[Kumar *et al.*, 1994] 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: Elemental analysis data and molar conductance value for ligand and metal complexes**

Sr. no.	Ligand/ Complexes	Elemental analysis (%) Found/ (Calculated)				Colour	Yield (%)	$\mu_{\text{eff}}$
		C	H	N	M			
1	P-MINPA	60.24 (60.34)	5.33 (5.03)	7.66 (7.82)	.....	Colourless	98%	.....
2	Fe(P-MINPA) <sub>2</sub>	52.17 (52.19)	4.25 (4.34)	6.65 (6.71)	13.40 (13.48)	Blue	87%	5.18
3	Fe (P-MINPA) <sub>3</sub>	51.22 (51.81)	4.24 (4.31)	6.66 (6.71)	14.22 (14.12)	Yellow	94%	4.63

**Infrared Spectroscopy:**

The infrared spectral data of Schiff base ligand and its metal complexes are listed in Table 3.

- 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-MINPA shows sharp band observed for ligand at 1640 cm<sup>-1</sup>, is due to azomethine >C=N linkage which is shifted to lower frequency (1590-1560 cm<sup>-1</sup>) on going from ligand to its metal complexes due to coordination of azomethine nitrogen with metal ion [Sece *et al.*, 2000]. 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.
- In the spectra of P-MINPA show pick at 1680 cm<sup>-1</sup> which may be attributed to the  $\nu$  C=O, The disappearance of this band in all the metal complexes indicating the involvement of this group in complex formation [Saraf *et al.*, 2011(b)].
- Metal-ligand vibration is observed in far-IR region usually give information regarding the bonding of ligand with metal ion. The new band is appear in the region of 510 cm<sup>-1</sup> due the >M-O suggest the coordination of oxygen with metal ion.
- The presence of sharp band in the region 575 cm<sup>-1</sup> in all the complexes due to the >M-N coordination of azomethine nitrogen [Ghosh *et al.*, 2012; Saraf *et al.*, 2012(c)]. The appearance of  $\nu$ M-N and  $\nu$ M-O vibration support the involvement of N and O atoms in complexation with metal ions under investigation [Thomas *et al.*, 1995]

The IR spectra of ligand and its complexes, the band at 1210-1220cm<sup>-1</sup> can be attributed to C-O bond [Ibrahim Dermir, *et al.*, 2008].

The N → O stretching vibration due to N—O of =NOH Which found near 930-960 cm<sup>-1</sup> [Palm and Werbin 1954] metal complexes have coordination through the oxime oxygen or nitrogen atom only.

**Electronic Spectra and magnetic measurements**

The electronic spectral measurements were used for assigning the stereochemistry of the metal ions in the complexes based on position and number of d-d transition peaks. Electronic spectra of ligand and its metal complexes were displayed in DMF (Dimethylformamide) solution. Electronic spectra of ligand shows absorption in UV/ visible region two high intensity base bands at 273 nm (40421 cm<sup>-1</sup>) and 270 nm (37037 cm<sup>-1</sup>) which indicate  $\Pi$  and  $\Pi^*$  transition of azomethine group in the ligand [Boghaei *et al.*, 2000]. The electronic spectra of Fe(II) complex exhibits two bands. The bands at 11350cm<sup>-1</sup> may be assigned to  $^5T_{2g} \rightarrow ^5E_g$  (G) transition [Dwivedi and Dhakarey, 2003] and the other at 19700cm<sup>-1</sup> to charge transfer. Similar types of transitions are reported for octahedral Fe(II) complexes [Aswar *et al.*, 2006]. The magnetic moment value of Fe(II) complex is 5.40 B.M. indicating an octahedral geometry [Patel, *et al.*, 2000] of this complex.

The electronic spectra of the Fe(III) complex exhibits two bands at 10242 cm<sup>-1</sup> and 19945 cm<sup>-1</sup> assigned to [ $^3A_{2g} \rightarrow ^3T_{1g}(P)$ ] and [ $^3A_{2g} \rightarrow ^3T_{1g}(F)$ ] transitions respectively, expected for octahedral geometry. The observed magnetic moment value of Fe (III) complex (4.63 B.M.) is in good agreement with this geometry [Aryane *et al.*, 2009].

**Table 2: IR spectra of Schiff base ligand and its metal complexes in cm<sup>-1</sup>**

Sr. No	Compound	C=N	C=O	C-O	M-N	M-O	N--O
1	P-MINPA	1640	1680	1220	-	-	-
2	Fe(P-MINPA) <sub>2</sub>	1560	-	1220	575	420	955
3	Fe (P-MINPA) <sub>3</sub>	1590	-	1210	560	280	965

**Table 3: Electronic spectral data of complexes**

Ligand/Complexes	Geometry	Band Assignments	$\lambda_{max}$
P-MINPA	-	$\pi \rightarrow \pi^*$ $n \rightarrow n^*$	40421 cm <sup>-1</sup> 37037 cm <sup>-1</sup>
Fe(P-MINPA) <sub>2</sub>	Octahedral	<sup>5</sup> T <sub>2g</sub> $\rightarrow$ <sup>5</sup> E <sub>g</sub> (g) ligand $\rightarrow$ metal charge transfer	11350 cm <sup>-1</sup> 19700 cm <sup>-1</sup>
Fe (P-MINPA) <sub>3</sub>	Octahedral	<sup>5</sup> T <sub>2g</sub> $\rightarrow$ <sup>5</sup> E <sub>g</sub> (g) ligand $\rightarrow$ metal charge transfer	10242cm <sup>-1</sup> 19945 cm <sup>-1</sup>

**Table-4: NMR Spectra of P-MINPA and complexes**

Sr.No	Compound	=NOH	-CH=N-	CH <sub>3</sub>	Aomatic ring
1	P-MINPA	8.60 $\delta$	8.40 $\delta$	2.2 $\delta$	7.60 $\delta$
2	Fe(P-MINPA) <sub>2</sub>	-	8.20 $\delta$	1.6 $\delta$	7.10 $\delta$
3	Fe(P-MINPA) <sub>3</sub>	-	8.20 $\delta$	1.6 $\delta$	7.20 $\delta$

**Table 5: Antibacterial activity of ligand and its complexes**

Ligand/Complexes	Gram + ve		Gram -ve	
	<i>S.aureus</i>	<i>S.Pneumoniae</i>	<i>E. coli</i>	<i>P.aeruginosa</i>
P-MINPA	+	+	+	+
Fe(P-MINPA) <sub>2</sub>	+++	+++	+++	+++
Fe (P-MINPA) <sub>3</sub>	+++	+++	+++	++++
Amoxicillin	++	++	++	++

**H NMR Spectra:**

H NMR Spectra of Schiff base (P-MINPA) and their complexes were recorded in DMSO (Dimethyl sulfoxide) solution and TMS (Tetramethylsilane) used as internal standard. The azomethine proton (-CH=N-) appears at 8.4 $\delta$ , it has been shifted to down field in metal complexes and appear at ~8.2 which confirm coordination of ligand with metal by azomethine nitrogen [Vashi, et al., 2013]. NMR spectrum of (P-MINPA) show a peak around 8.60  $\delta$  due to the=NOH group. Two groups of band corresponding to -CH<sub>3</sub> and the aromatic proton in (P-MINPA) appears at 2.2  $\delta$  and 7.60  $\delta$  respectively. It may be mentioned that etyl- $\alpha$ -isonitrosoacetate(HEINA), Isonitrosoacetylacetone [Thakkar and Deshmukh, 1994] (HINAA), Isonitrosoacetophenone [Pathak and Haldar, 1994] (HINAP) and p-chloroisonitrosoacetophenone [Raut et al., 2011] (HP-CIINAP), show =NOH proton resonance at -9.27  $\delta$ , 8.65  $\delta$ , 8.6  $\delta$  and -8.64  $\delta$  respectively. NMR spectra of Fe(P-MINPA)<sub>2</sub>, Fe (P-MINPA)<sub>3</sub>, in DMSO solution exhibit peak due to methyl,

azomethine proton (-CH=N-) and aromatic ring proton and do not show any proton signal due to the =NOH group. This suggests that their complexes have been formed by the replacement of the proton of the =NOH group by the metal ion. It is interesting to note that the peak due to methyl proton Fe(P-MINPA)<sub>2</sub> exhibit at lower value compared to that of methyl proton in the reagent (P-MINPA). Further peak due to aromatic ring proton in these complexes occur at higher field side with respect to that of aromatic ring proton signal in (P-MINPA).

**Antimicrobial Activity:**

The antibacterial activity data is presented in Table 4. The antibacterial activity of ligand and their metal complexes were screened on gram positive bacteria: Staphylococcus aureus and Streptococcus pneumoniae and gram negative bacteria: Escherichia coli and Pseudomonas aeruginosa by disc diffusion technique. The diameter of susceptibility zones measured in mm

[Rehman *et al.*, 2001]. Filter paper disc of diameter 6 mm were used for the incresults were recorded. The antibacterial activity of ligandubation period of 60 hours at 25-30°C and and their complexes were tested by measuring inhibition zone observed around material. Ligand showed significant range of activity on growth of all selected bacterial stain. The results suggest that complexes increase the antibacterial activity [Valarathy and Subbalakshami, 2013].

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**Conflicts of interest:** The authors stated that no conflicts of interest.

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