Available on line www.jocpr.com

Journal of Chemical and Pharmaceutical Research

J. Chem. Pharm. Res., 2010, 2(1): 38-46

ISSN No: 0975-7384

Synthesis, characterization and antimicrobial studies on Cobalt (II), Nickel (II), Copper (II) and Zinc (II) complexes of N, O, S donor Schiff bases

R. Shakru, N. J. P. Subhashini, Sathish Kumar K., Shivaraj*

Department of Chemistry, Osmania University, Hyderabad, Andhra Pradesh 500 007, (INDIA)

Abstract

Biologically important Schiff bases L_1 8-nitro-2-{[(5'-methyl-3'-isoxazolyl) imino] methyl} naphtha [NMIIMN], L_2 N-[5'-methyl-3'-isoxazolyl]-N-[(E)-1-(-2 Thiophene)] methylidine] amine [MITMA] have been synthesized. Metal Chelates of NMIIMN and MITMA with Co (II), Ni (II), Cu (II) and Zn (II) metals have been synthesized and the structures of these chelates have been elucidated by elemental analysis, ^{1}H–NMR, Mass, IR electronic spectral data and magnetic moments. From these studies it is found that the ligands NMIIMN and MITMA act as bidentate ligands coordinating through oxygen and nitrogen donor atoms in the case of NMIIMN, sulpher and nitrogen atoms in the case of MITMA. The chelates of Co (II), Ni (II) and Zn (II) appear to be octahedral and Cu (II) appears to be tetragonal geometry. Antimicrobial activity of the ligands and their metal complexes against bacteria (*Bacillus*, *Pseudomonas*) and fungus (*R. Solani*, *A. Niger*) has been carried out. It is found that the metal complexes have higher activities than those of free ligands.

Key words: 5-methyl isoxazole Schiff bases, metal chelate, antimicrobial activity.

Introduction

The chemistry of Schiff base metal complexes had been investigated extensively for the last several decades leading to new synthetic routes variety of structures and their potential biological applications [1-3]. Heterocyclic ring containing oxygen, sulpher and nitrogen impart special biological activity to these Schiff bases and their metal complexes [4-7]. It is well known that several Schiff base complexes have anti-inflammatory, anti-fungal, antibacterial and anti HIV activity [8-12]. Studies on metal complexes of Schiff bases derived from 3-amino 5-methyl isoxazole and substited salicyladehyde have been reported earlier and found that the metal complexes showed more activity than Schiff bases [13]. In the present investigation we report here the synthesis, characterization and antimicrobial studies on Schiff bases NMIIMN and MITMA and their metal complexes.

Materials and Methods

Experimental Section

Physical measurements

^{1}H- NMR spectra of the ligands were recorded at 200 MHz and 300 MHz on Varian Gemini Unity Spectrometer using TMS as internal standard. ^{13}C NMR spectra were recorded at 100.6MHz on Varian Gemini Spectrometer. The EI mass spectra were recorded on a VG micro mass 7070–H Instrument, ESIMS spectra were recorded on VG AUTOSPEC mass spectrometer. IR spectra of the ligand and complexes were recorded using KBr pellets in the range (4000-400cm^{-1}) on Perkin-Elmer Infrared model 337. Electronic spectra of metal complexes in DMSO were recorded on Schimadzu UV-VIS 1601 spectrophotometer. Magnetic susceptibilities of the complexes were determined on Gouy balance model 7550 using Hg [Co (NCS)$_4$] as standard. The diamagnetic correction of the complexes was computed using Pascal's constants. The percentage composition of C, H, N for the complexes and necessary ligands were determined by using micro analytical techniques on Perkin Elmer 240C (USA) elemental analyzer. The percent composition of metal ions in solid metal complexes was determined by EDTA titration procedure. All the chemicals used were analytical reagent grade. 8-nitro-2-hydroxy-1-naphthaldehyde, Thiophene-2-carboxaldehyde and 3-amino-5-methyl isoxazole were prepared by slightly modified techniques [14-15].

Synthesis of Ligand L_1&L_2

NMIIMN (L_1)

A mixture of 3-amino-5-methyl isoxazole (0.05 mol) and 8-nitro 2-hydroxy naphthaldehyde (0.05 mol) was taken in methanol and refluxed for 2 hours. The yellow colored Schiff base obtained was recrystallised from petroleum ether and methanol. Purity of the compound was checked by TLC. Yield: 90-95% .m.p .156-158°C

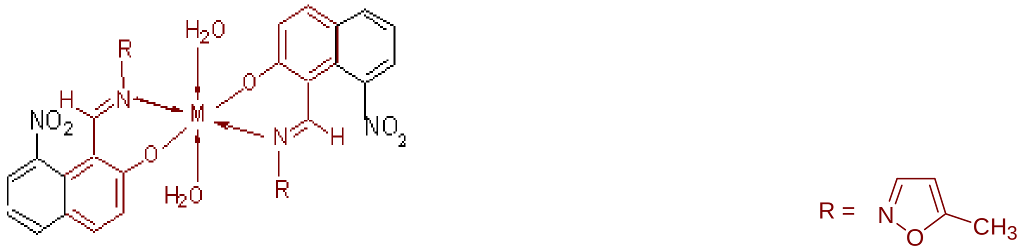
MITMA (L_2)

A mixture of 3-amino-5-methyl isoxazole (0.05 mol) and Thiophene 2-carboxaldehyde (0.05 mol) was taken in methanol and refluxed for 3 hours. The brown colored Schiff base obtained was recrystallised from petroleum ether and methanol. Purity of the compound was checked by TLC. Yield: 75-80%. m.p.76-80°C

General experimental procedure for the preparation of metal complexes

Methanolic solution of MCl_2 nH_20 (M= Co(II) ,Ni(II) ,Cu(II) and Zn(II) salts was added drop wise to methanol solution of Schiff base (1:2) and the resulting mixture was stirred for 30 minutes and refluxed for 2- hrs on water bath and cooled to room temperature. Partial evaporation of solvent with a current of air resulted in the precipitation of colored solids, which was filtered and washed with methanol. The purity of these complexes checked with TLC.

Fig 1 Structure of metal complexes



M=Co (II), Ni (II), Cu (II), Zn (II)

M=Co (II), Ni (II), Cu (II), Zn (II)

Antimicrobial screening

The ligands and their metal complexes were screened against bacteria (*Bacillus, Pseudomonas)* and fungi *(A. Niger, R. solani)* were used. The antimicrobial action was studied by paper disc method. The compounds were dissolved in DMSO. Filter paper discs of 4mm diameter were prepared. The filter paper discs were placed on nutrient medium. These Petri dishes were incubated at 35°C for 48 hrs. The inhibition zone was observed after 48 hrs. The growth of the microbes was measured by recording the diameter of the inhibition zone.

Results and Discussion

Elemental analysis data, formula weight, colours and melting points are given in table-1. The results of the elemental analysis of the Schiff bases NMIIMN and MITMA its complexes are in good agreements with those required by the proposed formula as [M (II) $(L)_2$ $(H_2O)_2$] where M=Co (II), Ni (II), Cu (II) and Zn (II).

TABLE -1 Analytical data of compounds

compounds	m.p (°C)	Colour	C	H	N	Metal	Mol. wt.
NMIIMN	158	yellow	60.48 (60.61)	3.62 (3.70)	14.10 (14.14)	-	297.00
$[Co(NMIIMN)_2(H_2O)_2]$	256	green	52.17 (52.79)	3.28 (3.81)	12.04 (12..32)	7.32 (7.62)	682.00
$[Ni(NMIIMN)_2(H_2O)_2]$	264	green	52.29 (52.48)	3.62 (3.79)	12.12 (12.24)	8.09 (8.16)	686.00
$[Cu(NMIIMN)_2(H_2O)_2]$	243	blue	52.16 (52.33)	4.68 (4.91)	12.42 (12.50)	12.68 (12.95)	688.00
$[Zn(NMIIMN)_2(H_2O)_2]$	186	brown	52.16 (52.25)	3.64 (3.77)	12.12 (12.19)	8.48 (8.56)	689.00
MITMA	76	colorless	55.28 (55.64)	4.02 (4.13)	14.32 (14.43)	-	194.00
$[Co(MITMA)_2(H_2O)_2]^{+2}$	143	Blue green	45.40 (45.47)	4.51 (4.63)	11.19 (11.37)	11.09 (11.16)	475.00
$[Ni(MITMA)_2(H_2O)_2]^{+2}$	165	green	45.40 (45.47)	4.51 (4.63)	11.19 (11.37)	11.09 (11.16)	477.00
$[Cu(MITMA)_2(H_2O)_2]^{+2}$	123	dark blue	45.21 (45.30)	4.41 (4.58)	11.19 (11.25)	11.89 (12.09)	479.00
$[Zn(MITMA)_2(H_2O)_2]^{+2}$	156	Light brown	44.54 (44.67)	4.35 (4.58)	11.16 (11.25)	12.20 (12.27)	481.00

(The value in bracket mentioned is calculated)

Spectral analysis

^{1}H- NMR spectrum of NMIIMN (L_1)

In the ^{1}H NMR ($CDCl_3$). The imine proton appeared as a singlet at δ 8.95.The aromatic protons are in naphthal ring at δ 7.2-7.9 and 5-CH_3 appeared at δ 1.4 as a singlet**.**

^{1}H- NMR spectrum of MITMA (L_2)

In the ^{1}H NMR ($CDCl_3$) (Fig.2.2). The imine proton appeared as a singlet at δ 8.61. Isoxazole H-4 appeared at δ 7.12 as a singlet and 5-CH_3 appeared at δ 2.42 as a singlet**.**

Mass spectrum of NMIIMN (L_1)

The mass spectrum of isoxazole 8-nitro 2-hydroxy 1-naphthaldehyde schiff base showed molecular ion (M^+) peak at m/z 297. The other fragments were observed at m/z 157, 123, 96, and 79.

Mass spectrum of MITMA (L_2)

The mass spectrum of isoxazole Thiophen 2-carboxaldehyde schiff base (Fig.2.3) showed molecular ion (M^{+2}) peak at m/z 194. The other fragments were observed at m/z 179, 165, 152, 111, 99, 55 and 42.

Fig 2 Spectra of ligands

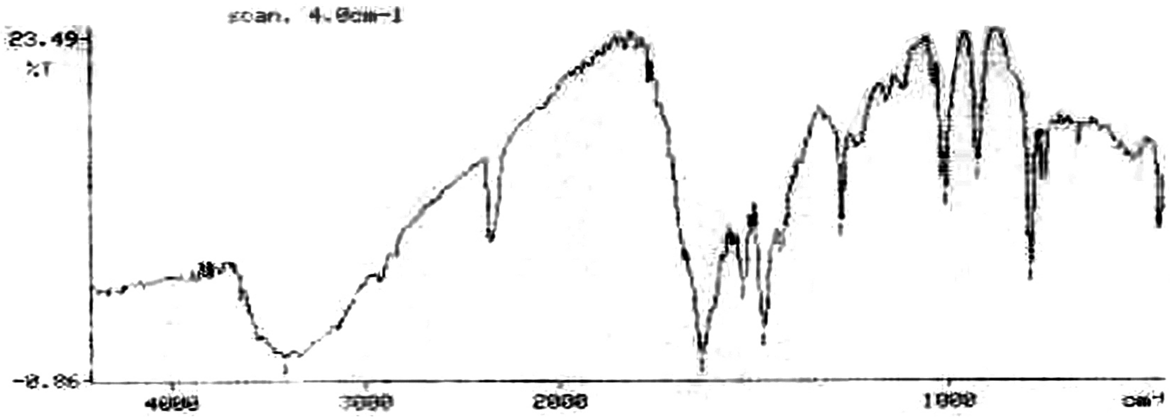


Fig 2.1 IR spectrum of MITMA

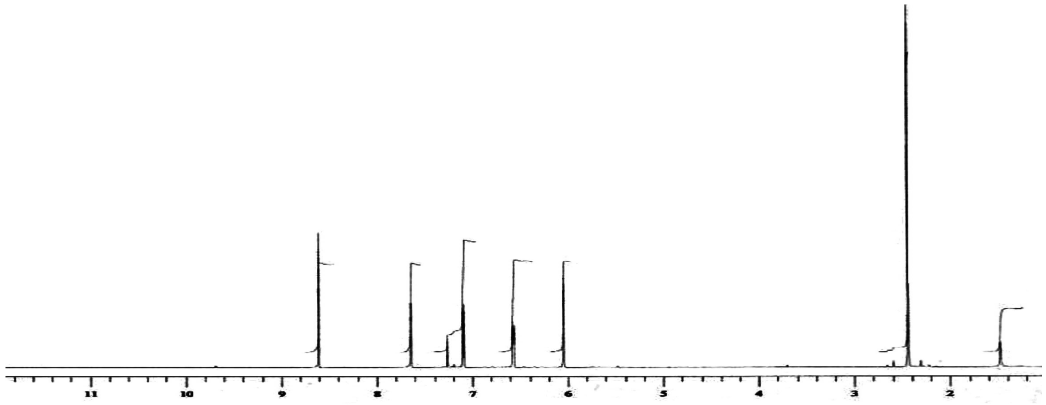


Fig 2.2 ^{1}H-NMR spectrum of MITMA

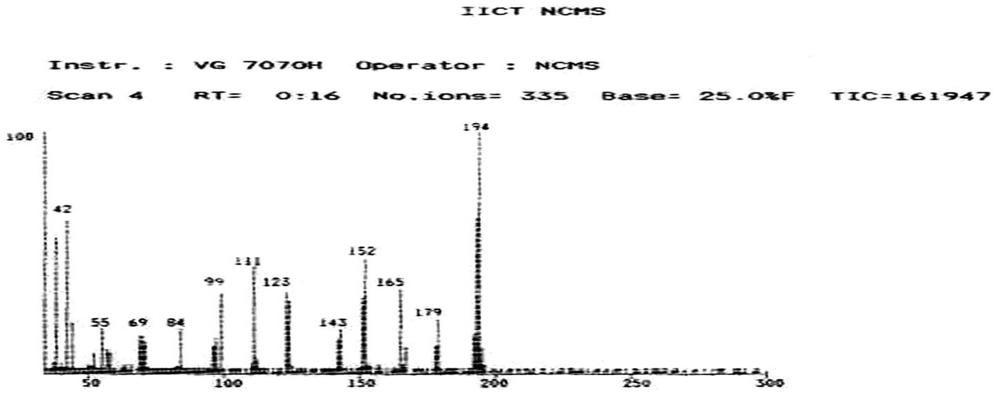


Fig 2.3 Mass spectrum of MITMA

IR spectra of metal complexes

In order to study the binding mode of the Schiff bases to metal ion in complexes, the IR spectra of the free ligands were compared with the spectra of the metal complexes. The IR spectral data is presented in table -2**.** The IR spectra of NMIIMN showed a band at 3413 cm^{-1} assigned to ν (OH) group. The disappearance of this band in complexes indicates the deprotanation of the hydroxyl group and coordination through oxygen .The band observed at 1625 cm^{-1} region in the ligand is assigned to the azomethine group ν (C=N) . The shift of this band in metal complexes towards higher frequencies region to the extent 10-20 cm^{-1} indicates coordination through azomethine nitrogen atom of free ligand. The band at 1273 cm^{-1} due to ν(C –O) of phenolic shifted to higher frequencies region in metal complexes, indicating coordination of phenolic oxygen atom to the metal ion. Two new bands at lower frequencies region 500-529 cm^{-1} and 426-459 cm^{-1} are assigned to ν(M-O) and ν(M-N) respectively [16-18].

Table-2 IR spectra analysis of ligands & metal complexes:

Compounds	ν(C=N) cm^{-1}	ν(OH) cm^{-1}	ν(C-S-C) cm^{-1}	ν(M-O) cm^{-1}	ν(M-N) cm^{-1}	ν(M-S) cm^{-1}
NMIIMN	1625	3413	-	-	-	-
$[Co(NMIIMN)_2(H_2O)_2]$	1636	3341	-	529	459	-
$[Ni(NMIIMN)_2(H_2O)_2]$	1634	3332	-	525	432	-
$[Cu(NMIIMN)_2(H_2O)_2]$	1621	3342	-	500	451	-
$[Zn(NMIIMN)_2(H_2O)_2]$	1632	3340	-	515	426	-
MITMA	1613	-	861	-	-	-
$[Co(MITMA)_2(H_2O)_2]^{+2}$	1636	-	927	-	460	409
$[Ni(MITMA)_2(H_2O)_2]^{+2}$	1633	-	914	-	469	405
$[Cu(MITMA)_2(H_2O)_2]^{+2}$	1639	-	928	-	463	408
$[Zn(MITMA)_2(H_2O)_2]^{+2}$	1636	-	872	-	450	412

The IR spectrum of the ligand MITMA showed (Fig.2.1) a band at at 861 cm^{-1} assigned to ν(C-S-C). This band is shifted to 914-928 cm^{-1} region in metal complexes indicating the involvement of thiophene sulpher in coordination. The new bands at 405-412 cm^{-1} and 450-460 cm^{-1} in the lower frequencies region are assigned to ν (M-S) and imine ν(M-N) respectively [19-21]. In addition, IR spectra of all metal complexes show a diffuse broad band around 3320-3440 cm^{-1} and another band at 771-796 cm^{-1} at lower frequencies region indicating the presence of water molecules in the coordination sphere. This fact is also supported by the results of elemental analysis of complexes.Tentetive structures of representative complexes have shown in Fig.1.

Electronic spectra of metal complexes

The electronic spectra of metal complexes were recorded in DMSO in the range of 200-1100nm. The electronic spectra of Co (II) complexes showed three bands around 12,682-13,563cm^{-1}, 19,601-20,478 cm^{-1} and 25,523-26,822 cm^{-1} corresponding to the transitions $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, $^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ and $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$. The magnetic moment values for these complexes are in the range 4.12-4.69 B.M which suggests an octahedral geometry [22]. The electronic spectra of Ni (II) complexes showed three bands around 10,688-12,486 cm^{-1}, 17,895-20,964 cm^{-1} and 26,769-28,874 cm^{-1} corresponding to the transitions $^3A_{2g}$ (F)$\rightarrow ^3T_{2g}$, $^3A_{2g}$(F)$\rightarrow ^3T_{1g}$(F) and $^3A_{2g}$(F) $\rightarrow ^3T_{1g}$(P). The magnetic moment values for these complexes in the range 3.41-3.72 B.M which suggests an octahedral geometry [23]. The Cu (II) complexes showed a single broad band at 12,462-21,684 cm^{-1} corresponding to the transition $^2E_g \rightarrow ^2T_{2g}$. The magnetic moment values are in the range 1.83-1.98 B.M.which is favoring tetragonal geometry [24]. All Zn (II) complexes are show dia magnetic nature and are found to be octahedral geometry [25-27].

Antimicrobial activity studies

The results of the antibacterial and antifungal screening of the Schiff bases and the metal complexes with *Bacillus*, *Pseudomonas*, *R.Solani* and *A. Niger* at concentration of 25 and 50 g by disc method are given in the table-3. A comparative studies of the ligands and their complexes indicated that metal complexes exhibits higher antimicrobial activity than the free ligands are shown in Fig -3. (Inhibition zone 7-25 mm) the order of the metal complexes follow Cu (II)> Ni (II)> Co (II). The higher activity of metal complexes compare to free ligands can be explained on the basis of Overton s concept and chelation theory [28]. According to Overtons concept of cell permeability, the lipid membranes that surrounds the cell favours the passage of only the lipid soluble material due to which lip solubility is an important factor, which control antimicrobial activity . On chelation the polarity of metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor group. Further it increases the delocalization of pi -electron over the whole chelate ring and enhances the lyophilizes enhances the penetration of the complexes into lipid membranes and blacking of the metal binding sites in the enzymes of microorganisms. These complexes also disturb the respiration process of the cell and thus block the synthesis of protein that restricts further growth of the organism.

The details of the anti –microbial test are given Table -3.

Compounds	*Bacillus*	*Pseudomonas*	*A. Niger*	*R.Solani*
NMIIMN	14	13	12	12
$[Co(NMIIMN)_2(H_2O)_2]$	16	15	13	14
$[Ni(NMIIMN)_2(H_2O)_2]$	17	16	14	15
$[Cu(NMIIMN)_2(H_2O)_2]$	18	17	17	18
$[Zn(NMIIMN)_2(H_2O)_2]$	16	14	15	13
MITMA	15	14	14	14
$[Co(MITMA)_2(H_2O)_2]^{+2}$	16	14	16	16
$[Ni(MITMA)_2(H_2O)_2]^{+2}$	17	15	16	17
$[Cu(MITMA)_2(H_2O)_2]^{+2}$	18	17	18	18
$[Zn(MITMA)_2(H_2O)_2]^{+2}$	15	14	15	15
Gentamycine	16	15	18	17

Fig 3 Biological activity pictures

FIG 3.1 *Pseudomonas* actions on Cu (II)-NMIIMN

FIG: 3.2 *Bacillus* actions on Ni (II)-MITMA

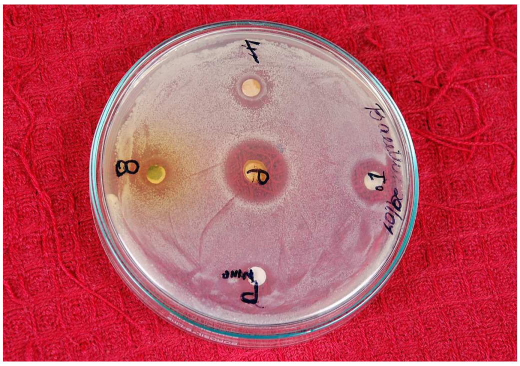


FIG: 3.3 *Bacillus* actions on Cu (II)-MITMA

FIG: 3.4 *Bacillus* actions on Ni (II)-NMIIMN

Conclusion

The Schiff bases NMIIMN and MITMA and their metal complexes have been structurally characterized. The metal: ligand stochiometry in all the complexes is 1:2 associated with two water molecules. The complexes of NMIIMN are non-electrolytes and the complexes of MITMA are electrolytes in DMSO. The ligand NMIIMN acts as mono negative bidentate coordinating through nitrogen azomethane and phenolic oxygen group. The ligand MITMA acts as neutral bidentate coordinating through nitrogen of azomethane and Thiophen sulpher. All complexes are paramagnetic except Zn (II) which is diamagnetic. Based on spectral data and magnetic moments Co (II), Ni (II) and Zn (II) are assigned to octahedral geometry while Cu (II) complexes are assigned to tetragonal geometry.

Acknowledgements

The authors are thankful to The Director, IICT Hyderabad for facilitating ^{1}H- NMR Spectra and Mass spectra.

References

[1] Ferrari , M.B. Capacchi S. Bisaglic F. Pelosi, G.P. *Inorg. chim. Acta*., **2001,** 81, 312 .

[2] Vandim Yu. Kukushkin and Armando J.L. Pombeiro, *Coord Chem. Revewies.*, **1999,** 181**,** 147 .
[3] Vandim Yu. Kukushkin, D.Tudela and A.L.J. Pomberio *Coord. Chem. Revesws.*, **1996,** 156, 333 .
[4] R.H. Holm, G.W. Evereft and A. Chakravorty, ‘*Progress in in Organic chemistry’* Vol.7. P.83 edited by F. Ablest cotton.
[5] B.J. Hathaway, G. Wilkinson, R.D. Gillard and J.A. MC Cleverty; ‘*Compressive Coordination chemistry’*, Pergamon: Oxford., **1987,** Vol. 5, 533.
[6] B. Abolmaali, H.V. Taylor and U. Weser *Structure and bonding (Berlin*)., **1998,** 26, 91.
[7] A. Messerchinidt, *structure and bonding* (Berlin)., **1998,** 37, 90.
[8] A. Tontini, G.Diamatini C. Balsamini, G. Tarzia, L. Perissin and V. Rapozzi, *Eur.J.Med. Chem.*, **1996,** 31, 735**.**
[9] Manish shah, Pankaj patel, Sushil korgaokar and Hansa porekh, *Indian. J. Chem.*, **1996,** 35B, 1282**.**
[10] A.P. Mishra and S.K. Gavtarm, *J. Indian Chem. Soc.*, **2004,** 81**,** 324**.**
[11] Yuejun xiang j. ie chem Raymond F. Schinazi and kang zhao, *Bioorg. Med. Chem. Letter,* **1996,** 6, 1051**.**
[12] N.A. Vekariya M.D. Khunt and A.P. Parikh *Indian. J. Chem.*, **2003,** 42B**,** 421**.**
[13] Y. Prashnthi, K.Kiranmai, N.J.P.Subhashini and Shivaraj. Elsevier, *Spectrochimica Acta Part-A.,* **2008,** 70/1, 30-35.
[14] Vogel A.I. ‘*Text book of Practical Organic Chemistry’*, Longman; London, **1987,** 777.
[15] Kipnis F. and Orn felt J., *J. Am. Chem. Soc.*, **1946,** 68, 273.
[16] Lewis and R.G Wilkins, ‘*Modern Coordination Chemistry’*, Inter science; New York, **1967**.
[17] Svab. A. Zikan V. Danek J spaldonova R Vyzk, Ustar Farm. *Biochemist Prague Czech cesk. Farm* 32. **1983,** (9-10), 316-22.
[18] Pen land R.B. Mizushina S. Curran C, and Onagliano J.V, *J. Am. Chem. Soc.,* **1957,** 79, 1575.
[19] P. Souza F.S. Kaiser, J.R. Mosagar and A. Arquero, *Trans Met Chem.*, **1987,** 12,128.
[20] K.B. Guldasi and M.S. Patil, *Trans Met Chem.*, **2006,** 31, 580.
[21] M.Khare and A.P.Mishra, *J. Indian Chem. Soc.*, **2000,** 77, 256.
[22] N. Mcmdal, O, K, Dcy S. Mitra and K.M. Abdul Malik, *Polyhedron.*, **2000,** 19, 2707.
[23] R.B.Khart, *J. Indian Chem. Soc.*, **1981,** 58, 1056.
[24] E. M. Govge and J.E. Gedard, *Inorganic Chem.,* **1978,** 17, 270.
[25] Smartin, M.R. Bermejo, A.M. G.Deibe, M. Manetlro, C. Lage and A.J.C.Filho, *Polyhedron.*, **2000,** 19, 185.
[26] V.P.Krzyminiewska, H. Litkowska and W.R.Paryzek, *Monatsh. Chem.*, **1999,** 130,243.
[27] K. Bertoncelio, G. D. Fallon K.S. Mury and E.R.T. Tiekine, *Inorg Chem.* **1999,** 130, 243.
[28] Mishra L and Singh V.K, *Indian. J. Chem.*, **1993**, 32A, 446-457.