



Research Article

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A New Mannich Base and its Metal Complexes along with their Antimicrobial and Antifungal screening

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ABSTRACT

A new Mannich base, N-(piperidino-1-yl-5-bromophenyl) benzamide, formed by the condensation of Piperadine, benzamide and 5-bromophenyl benzaldehyde and its Ti(III), V(III), VO(IV), Ru(II), Ru(III), MoO(V), MoO₂(VI), UO₂(VI), Co(III), and Mn(III) complexes have been Synthesized. Their probable structures have been proposed on the basis of their microanalytical, IR, UV-vis, ¹H NMR spectral data. All the complexes exhibit octahedral geometry. The biological activities of the ligand and its metal chelates against the bacteria *E.coli*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Salmonella typhi*, *Pseudomonas aeruginosa* and *Shigella flexnri* are also being reported.

Key words: N-(piperidino-1-yl-5-bromophenyl) benzamide, Piperadine, Benzamide, 5-bromophenyl benzaldehyde and their Antimicrobial and Antifungal activity.

INTRODUCTION

The Mannich reaction is an organic reaction which consists of an amino alkylation of an acidic proton placed next to a carbonyl functional group with formaldehyde and ammonia or any primary or secondary amine. The Mannich reaction is also considered a condensation reaction. Mannich reaction is a three-component condensation reaction consisting of active hydrogen containing compound, formaldehyde and a secondary amine. Keeping these facts in view, an attempt has been made to synthesize and characterized the complexes of metals a new Mannich Base, N-(piperidino-1-yl-5-bromophenyl) benzamide which also contains amide moiety. The synthesis of N-(piperidino-1-yl-5-bromophenyl) benzamide and its complexation characteristics with Ti(III), V(III), VO(IV), Ru(II), Ru(III), MoO(V), MoO₂(VI), UO₂(VI), Co(III), and Mn(III) salts. The Mannich reaction is also used in the synthesis of medicinal compounds e.g. rolitetracycline (Mannich base of tetracycline), fluoxetine (antidepressant), tramadol, and tolmetin (anti-inflammatory drug).

EXPERIMENTAL SECTION

All the chemicals and reagents used were of AR grade or equivalent purity, Spectroscopic grade solvents were used for spectral analysis. The carbon, hydrogen, and nitrogen were analysed at CDRI, Lucknow. Conductivity measurements were carried out with Philips conductivity Bridge Model PR 9500 at room temperature and 10⁻³ M dilution. Magnetic susceptibility was determined by Gouy's balance. Copper sulphate was used as the calibrant.

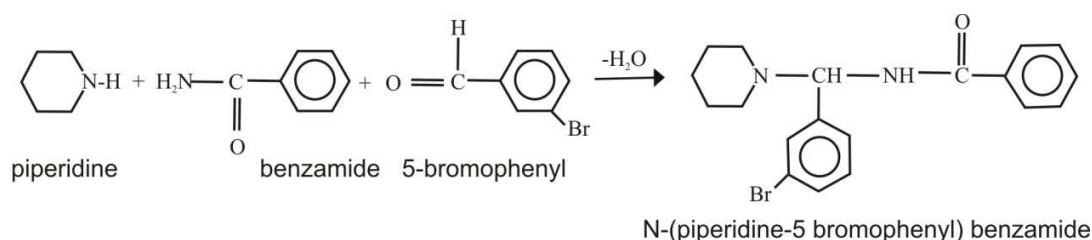
The IR spectra were recorded in KBr pellets using a Perkin-Elmer 783 spectrophotometer. The UV-vis spectra of the complexes were recorded On a Shimadzu UV-1601 spectrophotometer. Ti (III) was prepared by the standard procedure while the other metal salts were used as procured.

ANTIMICROBIAL ACTIVITY

The in vitro biological screening effects of the investigated compounds were tested against the bacteria, *S. aureus*, *S. typhi*, *K. pneumoniae*, *S. flexneri*, *P. aeruginosa*, *E. coli* by the well diffusion method using agar nutrient as the medium. The test solutions were prepared by dissolving the compounds in DMSO. In a typical procedure, a well was made on the agar medium inoculated with microorganisms. The well was filled with the test solution using micropipette and the plate was incubated at 35°C for 25 h., during this period, the test solution was diffused and the growth of the inoculated micro organisms was affected. The inhibition zone developed on the plate was measured. Here ampicillin was used as the control.

SYNTHESIS OF MANNICH BASE

Benzamide (1.21 g, 10 mmol) in 20 ml of ethanol was mixed with piperidine (0.9 ml, 10 mmol) with stirring to get a clear solution under ice cold condition. To the contents, 5-bromophenyl benzaldehyde (1 ml, 10 mmol) was added dropwise using dropper with stirring for 15-20 min. The reaction mixture was then kept at room temperature for 5 days. The colourless solid obtained was filtered and recrystallized from ethanol. The melting point of Mannich base was recorded, it was subjected to elemental analyses and IR spectra was recorded. The preparation of the ligand may be represented as:

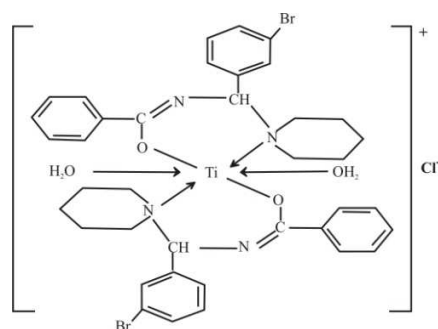
**METAL COMPLEXES**

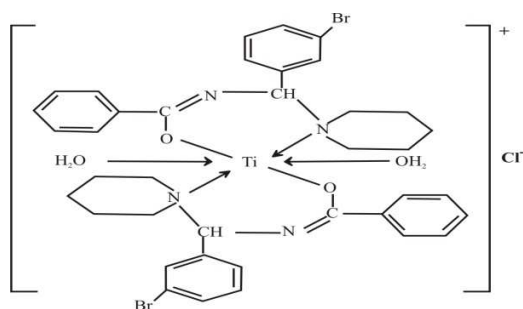
Coordination chemistry is the study of compounds formed between metal ions and other neutral or negatively charged molecules such as $[\text{Co}(\text{NH}_2\text{CH}_2\text{CH}_2\text{NH}_2)_2\text{ClNH}_3]^{2+}\text{Cl}_2^{2-}$. In this formulation, $[\text{Co}(\text{NH}_2\text{CH}_2\text{CH}_2\text{NH}_2)_2\text{ClNH}_3]^{2+}$ is known as a metal complex. Metal complexes are also called coordination compounds. The bonded molecules are called ligand. Ligands are classified in many ways; their charge, size(bulk), the identity of the coordinating atom and the number of electrons donated to the metal.

RESULTS AND DISCUSSION

The analytical data of the synthesized complexes is given in table. The molar conductance values determined at 10^{-3} M dilution and 25°C in both DMF and DMSO suggested 1:1 electrolytic nature for Ti(III), V(III), Ru(III), MoO(V), Co(III), and Mn(III) complexes whereas VO(IV), Ru(II), MoO₂(VI) and UO₂(VI) complexes were non electrolytic in nature.

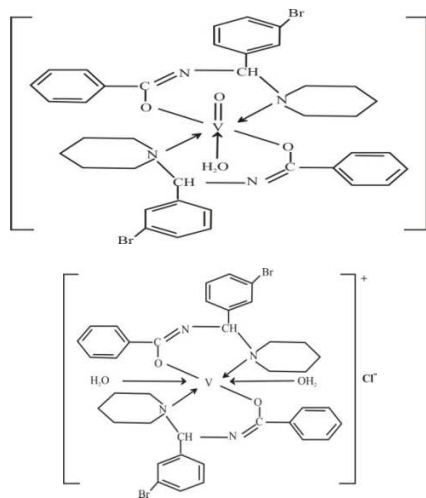
The IR spectrum of the ligand exhibits a number of important bands at 3247, 1673, 1150 and 569 cm^{-1} assignable $\nu_{(\text{NH})}$, amide $\nu_{(\text{C}=\text{O})}$, $\nu_{(\text{C}-\text{N}-\text{C})}$ of piperidine and $\nu_{\text{C}-\text{Br}}$ respectively. The ν_{NH} appeared unchanged whereas the $\nu_{(\text{C}=\text{O})}$ of amide and (C-N-C) of piperidine moiety displayed substantial negative shifts with fairly low intensity in the complex, indicating coordination through the oxygen of amide moiety and nitrogen of piperidine entity present in the Mannich base. The electronic spectrum of the complex exhibits a single broad band at 19570 cm^{-1} assignable to ${}^2\text{T}_{2g} \rightarrow {}^2\text{E}_g$ transition, characteristic of octahedral geometry. The magnetic moment of the complex is 1.71 B.M., which indicated the paramagnetic nature of the complex and t^3 oxidation state of the metal in this complex.





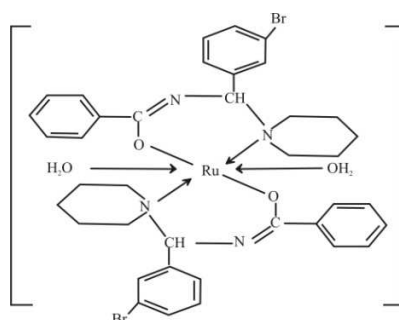
The comparison of IR spectra of the ligand with that of the V (III) complex suggested monobasic bidentate nature for the ligand. The changes in IR frequencies on complexation indicated coordination through oxygen atom of amide C=O and nitrogen atom of piperidine. The other bands appeared unchanged on complexation. The value of magnetic moment calculated from observed value of magnetic susceptibility is 2.94B.M. Which is expected for d^2 system like V^{+3} . The electronic spectrum of the complex exhibits band at 16200 cm^{-1} with a shoulder at 21500 cm^{-1} . The low energy band is assigned to ${}^3T_{1g} \rightarrow {}^3E_{2g}$ and the high energy band to ${}^3T_{1g} \rightarrow {}^3E_{2g} (P)$ respectively. These are characteristic of octahedral V (III) complexes.

The electronic spectrum of the complex displays bands at 11450 , 15940 and 21050 cm^{-1} , which may be assigned to ${}^2B_2 \rightarrow {}^2E$, ${}^2B_2 \rightarrow {}^2B_1$ and ${}^2B_2 \rightarrow {}^2A_1$ transitions respectively, characteristic of octahedral geometry. The only IR spectral bands of the ligand going alterations on complexation are due to $\nu_{C=O}$ of amide and $\nu_{(C-N-C)}$ of piperidine. All other bands remain unaffected. The presence of two non-ligand far IR bands at 525 cm^{-1} and 430 cm^{-1} assignable to ν_{M-O} and ν_{M-N} respectively further supported these coordination sites. The spin value of magnetic moment came out to be 1.76 B.M., which is close to the calculated value of 1.73B.M. for one impaired electron (d^1) like $VO^{+2} (IV)$.

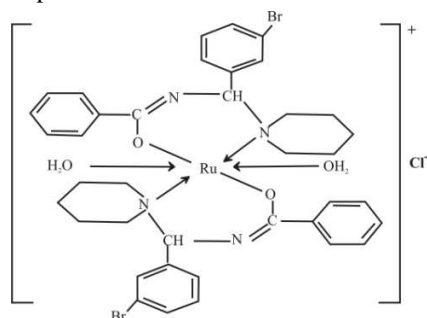


The ground state of Ru (II) in an octahedral environment is ${}^1A_{1g}$ and only two spin allowed transitions, ${}^1A_{1g} \rightarrow {}^1T_{1g}$ and ${}^1A_{1g} \rightarrow {}^1T_{2g}$ are expected. The electronic spectrum of the present complex shows three bands arising from ${}^1A_{1g} \rightarrow {}^1T_{1g}$, ${}^1A_{1g} \rightarrow {}^1T_{2g}$ and ligand ($\pi \rightarrow d \pi$) transitions respectively. The IR spectrum of the ligand exhibits a number of important bands. Most of these bands appeared unaltered in the IR spectrum of the complex except the two bands due to $\nu_{C=O}$ (amide) and $\nu_{(C-N-C)}$ piperidine, which undergo negative shifts on complexation. These coordination sites were further supported by the appearance of two new bands in the far IR region of the complex at 505 cm^{-1} and 410 cm^{-1} assignable to ν_{M-O} and ν_{M-N} respectively.

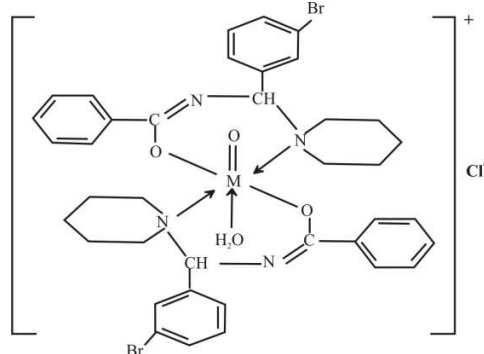
The study of magnetic properties suggested diamagnetic nature of the complex and the presence of +2 oxidation state of ruthenium in this complex.



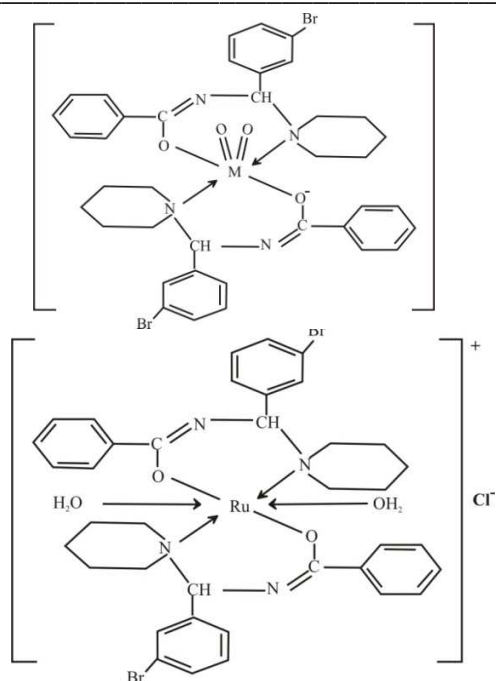
The comparison of both IR and NMR spectra of the ligand with its Ru (III) complex indicated monobasic bidentate nature of the complex. The IR frequencies due to amide $\nu_{C=O}$ and piperidine (C–N–C) undergo substantial negative shift on complexation. This is further supported by the presence of non-ligand bands in complex at 525cm^{-1} and 430cm^{-1} due to ν_{M-O} and ν_{M-N} respectively. The NMR spectra shows that the coordination is occurring via dissociation of –OH proton of the enolic form of the ligand and piperidine nitrogen atom. The electronic spectrum of ruthenium complex displays bands at 13650 , 17630 and 22600cm^{-1} which may be assigned to ${}^2T_{2g} \rightarrow {}^4T_{1g}$, ${}^2T_{2g} \rightarrow {}^4T_{2g}$ and ${}^2T_{2g} \rightarrow {}^2A_{2g}$, ${}^2T_{1g}$ transitions respectively. These are characteristic of octahedral Ru (III) complexes. The spin value of the magnetic moment of the complex is 1.98 B.M. which is expected for Ru (III) and shows paramagnetic character and +3 oxidation state of ruthenium in the complex.



The value of magnetic moment is 1.89 B.M. for the complex, which is expected for d^1 system like M_0O (V). The electronic spectrum of the complex shows three absorption bands at 13610 , 19850 and 26350cm^{-1} assignable to ${}^2B_2 \rightarrow {}^2E$, ${}^2B_2 \rightarrow {}^2B_1$ and ${}^2B_2 \rightarrow {}^2A_1$ transitions respectively. The complex may be considered as octahedral with a strong tetragonal distortion resulting from M_0-O bond. These sites are further supported by the non-ligand bands in the complex due to ν_{M-O} and ν_{M-N} . The value of magnetic moment is 1.89 B.M. for the complex, which is expected for d^1 system like M_0O (V)

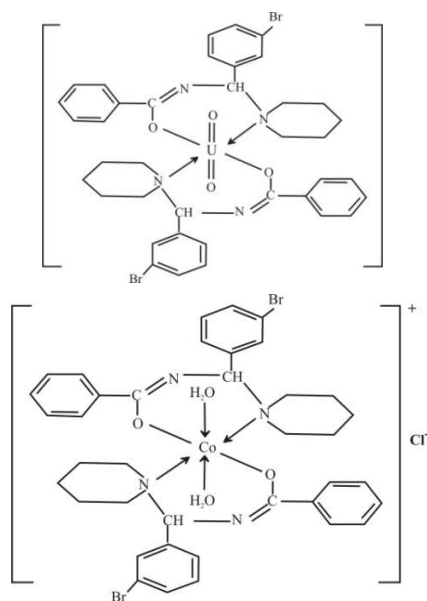


The electronic spectrum of the M_0 (VI) complex shows absorption bands of considerable high intensity at 35000 and 30000cm^{-1} . These bands may be assigned to ligand to metal charge transfer transition possibly superimposed upon other intra ligand transitions. It seems reasonable to assume that characteristic molybdenyl band does not occur in this region. The comparison of IR spectra of the ligand with its corresponding M_0O_2 (VI) complex indicated that the bands due $\nu_{C=O}$ of amide group and $\nu_{(C-N-C)}$ of piperidine get shifted in the complex. The study of magnetic properties suggested diamagnetic nature for this metal chelate as expected for $4d^0$ configuration.



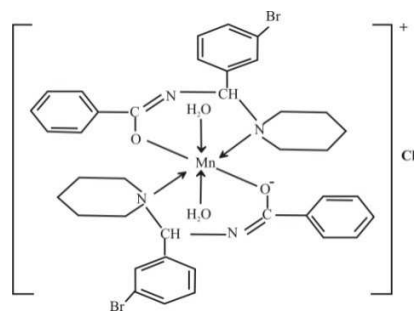
The electronic spectrum of the complex exhibits bands at 22000, 25500 and 37250 cm^{-1} consistent with the vibronic structure of the triatomic UO_2 entity. These altered bands are due to $\nu_{\text{C}=\text{O}}$ of amide moiety and $\nu_{(\text{C}-\text{N}-\text{C})}$ entity of piperidine, suggesting bidentate nature of the ligand. These are further confirmed by two non-ligand bands in the complex due to $\nu_{\text{M}-\text{O}}$ and $\nu_{\text{M}-\text{N}}$. The IR spectrum of the complex also shows new band at 930 cm^{-1} corresponding to symmetrical stretching, confirming the linear nature of the UO_2 group.

The study of magnetic properties suggested diamagnetic nature for the adduct as expected for low spin d^6 Co (III) complexes. The IR spectrum of the complex shows broad medium band at 3510 cm^{-1} , which is assignable to OH stretching vibrations due to the presence of water. That these are coordinated in nature is suggested by two other non-ligand bands at 830 and 720 cm^{-1} assignable to wagging and rocking modes.



The spin only value of magnetic moment of the complex is 4.79 B.M. This value is normal as expected for high spin d^4 system of Mn (III) ion. The electronic spectrum of the complex shows band at 13840, 19450 & 24900 cm^{-1}

assigned to ${}^5B_{1g} \rightarrow {}^5A_{1g}$, ${}^5B_{1g} \rightarrow {}^5B_{2g}$ and ${}^5B_{1g} \rightarrow {}^5E_g$ modes of transitions respectively. The spectral pattern suggests an appreciable splitting of 5E_g ground state of Mn (III) and suggests octahedral geometry for the complex ⁽²³⁾. The comparison of IR spectra of the ligand and the complex revealed that the ligand band due to ν_{NH} remains unaffected in the complex. The band due to amide $\nu_{C=O}$ and $\nu_{(C-N-C)}$ of piperidine are shifted to lower frequencies. This suggested coordination of the ligand with the metal ion through oxygen atom of amide C=O and nitrogen atom of piperidine entity. These coordination sites are further supported by non-ligand bands in the complex at 530cm^{-1} and 415cm^{-1} assignable to ν_{M-O} and ν_{M-N} respectively.



Analytical data of the complexes

Compound/Complex	Colour	M	C	H	N	Cl	Mol Wt.	2M mho $\text{cm}^2 \text{mol}^{-1}$	μ_{eff} (B.M.)
$[(C_{19}H_{20}ON_2Br)_2Ti \cdot 2H_2O]Cl$	Yellow	6.11	58.22	5.62	7.15	4.53	783.26	1:1	1.71
$[(C_{19}H_{20}ON_2Br)_2V \cdot 2H_2O]Cl$	Yellow	6.48	57.99	5.60	7.12	4.51	786.34	1:1	2.94
$[(C_{19}H_{20}ON_2Br)_2VO \cdot H_2O]$	Light yellow	6.80	60.89	5.61	7.48	-	748.84	Non-electrolyte	1.76
$[(C_{19}H_{20}ON_2Br)_2Ru \cdot 2H_2O]$	Green	12.62	56.93	5.49	6.99	-	800.97	Non-electrolyte	Diamagnetic
$[(C_{19}H_{20}ON_2Br)_2Ru \cdot 2H_2O]Cl$	Green	12.08	54.51	5.26	6.69	4.24	836.47	1:1	1.98
$[(C_{19}H_{20}ON_2Br)_2Mo \cdot H_2O]Cl$	Light yellow	11.57	54.98	5.06	6.75	4.28	829.34	1:1	1.89
$[(C_{19}H_{20}ON_2Br)_2MoO_2]$	Light yellow	12.12	57.59	5.05	7.07	-	791.84	Non-electrolyte	Diamagnetic
$[(C_{19}H_{20}ON_2Br)_2UO_2]$	White	25.49	48.83	4.28	6.00	-	933.93	Non-electrolyte	Diamagnetic
$[(C_{19}H_{20}ON_2Br)_2Co \cdot 2H_2O]Cl$	Pinkish yellow	7.42	57.41	5.54	7.05	4.47	794.33	1:1	Diamagnetic
$[(C_{19}H_{20}ON_2Br)_2Mn \cdot 2H_2O]Cl$	Brown	6.95	57.70	5.57	7.09	4.49	790.34	1:1	4.79

Antimicrobial and Antifungal Activity

The in vitro biological screening effects of the investigated compounds were tested against the bacteria, *S. aureus*, *S. typhi*, *K. pneumoniae*, *S. flexneri*, *P. aeruginosa*, *E. coli* by the well diffusion method using agar nutrient as the medium. A comparative study of the ligand and its complexes indicates that the metal chelates exhibit higher activity than the free ligand and the control (ampicillin). The order of activity towards *Shigella flexneri* and *Staphylococcus aureus* is $Mn > Co > Mo > Ru > V > Ti$; *Pseudomonas aeruginosa* is $Co > Mn > Mo > Ru > V > Ti$; *Klebsiella pneumoniae* and *Salmonella typhi* is $Co > Mn > Mo > Ru > V > Ti$; *Escherichia coli* is $Co > Mo > Mn > Ru > V > Ti$. Antimicrobial drugs either kill microbes (microbicidal) or prevent the growth of microbes (microbistatic). Disinfectants are anti-microbial substances used on non-living objects. An antifungal drug is medication used to treat fungal infections such as athlete's foot, ringworm, candidiasis (thrush), serious systemic infections such as cryptococcal meningitis and others. Antifungal work by exploiting differences between mammalian and fungal cells to kill off the fungal organism without dangerous effects on the host. A wide range of chemical and natural compounds are used as antimicrobials. Organic acids are widely used as antimicrobials in food products, e.g. lactic acid, citric acid and their salts.

Antibacterial Activity of the ligands and their complexes

Compound	<i>S. flexneri</i>	<i>S. typhi</i>	<i>P. aeruginosa</i>	<i>S. aureus</i>	<i>E. coli</i>	<i>K. pneumoniae</i>
MBB	9	8	5	7	8	7
Mn (III) Complex	20	17	15	16	17	16
Co (III) Complex	13	12	15	10	12	14
Mo (III) Complex	18	25	14	16	19	22
Ru (III) Complex	15	17	16	15	18	20
V (III) Complex	15	14	15	15	17	18
Ti (III) Complex	14	16	14	12	17	12

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REFERENCES

- [1]A. Syamal, D. Kumar, A.K. Singh, P.K. Gupta, Jaipal and L.K. Sharma, *Indian Journal of Chemistry*, 41A, pp. 1385–1390 (2002).
- [2]N. Raman, R. Vimalaramani & C. Thangaraja, *Indian Journal of Chemistry*, 43A, pp. 2357–60 (2004)
- [3]D.H. Kerridge, *Chem. Soc. Rev.*, 17, p. 181 (1988).
- [4]A.A.E.L. Asmy, M.E. Khalifa & M.M. Hasanian, *Synth. React. Inorg Met- org. Chem*, 28(6), p. 873 (1998).
- [5]B.C. Sharma & C.C. Patel, *Indian J. Chem*, 11, p. 941 (1973).
- [6]S.G. Bhadarye, R.B. Mohad & A.S. Aswar, *Indian Journal of Chemistry*, 40A, pp. 1110–13 (2001).
- [7]Vinod K. Sharma & Shipra Srivastava, *Indian Journal of Chemistry*, 45A pp. 1368–74 (2006).
- [8]S.R. Aswale, P.R. Mandlik, S.S. Aswale & A.S. Aswar, *Indian Journal of Chemistry* 42A, pp. 322–26 (2003).
- [9]D.J. Machni & K.S. Murray, *J. Chem Soc.*, A, 1498 (1961).
- [10]S.J. Swaney, A. Dharma Reddy & K. Bhaskar, *Indian Journal of Chemistry*, 40A, pp. 1166–71 (2001).
- [11]Richa Saxena, Sahdev and Shamim Ahmad, *Oriental Journal of Chemistry*, 26(4), pp 1507–11 (2010).
- [12]A.K. Singh, B.K. Puri and P.K. Rawlley, *Indian Journal of Chemistry*, 28A, pp. 58–62 (1989).
- [13]P. Viswanathamurthi, R. Karvembu, V. Tharaneeswaran and K. Natrajan, *J. Chem. Soc.*, 117, pp. 235–38 (2005).
- [14]M.M. Patel, *Indian J. Chem*, 11, 1177 (1973).
- [15]T. Damil Thangadurai & K. Natrajan, *Indian Journal of Chemistry*, 41A, pp. 741–45 (2002).
- [16]F.N. More & R.E. Rice, *Inorg. Chem.* 7, P. 2510 (1968).
- [17]A. Syamal & M.R. Maurya, *Coord. Chem. Rev*, 95, p. 183 (1989).
- [18]R.N. Pandey, R.N. Sharma, Z.M. Roy Chaudhri & P. Sharma, *J. Indian Chem. Soc.*, 69 p. 719 (1992).
- [19]A.Syamal & M.M. Singh, *React Funct. Polym*, 21, 45 (1993).
- [20]K.S. Nimavat, K.H. Popat, S.L. Vasoya and H.S. Joshi, *Indian Chem. Soc.* 80, pp. 711–13 (2003).
- [21]Kamal M. Ibrahim, Sahar I Mostafa, Nagwa Nawar & Zeinab A Younis, *Indian Journal of chemistry*, 43A, pp. 2294–2300 (2004).
- [22]F.N. Moore & R.E. Rice, *Inorg. Chem.* 7, 2510(1968).
- [23]R.N. Dutta Pur Kayastha *Indian Journal of Chemistry* 37A, pp. 158–160 (1998).