# ONN DONORS
# Chapter -4: Synthesis, characterization, crystal structure and biological evaluation of ONN donor Schiff bases and their metal complexes

# 4.Synthesis, characterization, crystal structure and biological evaluation of Schiff bases and metal complexes derived from o-vanillin& Heterocyclic amines

## 4.1 INTRODUCTION

Heterocyclic chemistry is a very important branch of chemistry accounting for about two third of organic compounds. A cyclic organic compound containing all carbon atoms in ring formation is referred to as a carbocyclic compound. If at least one atom other than carbon forms a part of the ring system, then it is designated as a heterocyclic compound. Nitrogen, oxygen and sulfur are the most common hetero-atoms. There are *aliphatic* and *aromatic*cyclic compounds. The aliphatic heterocyclesare three to eight membered systems, with certain strains in the lower membered rings that areanalogous to cyclic amines, ethers, thio ethers and amides [291-293].

The aromatic heterocyclic compoundsare those ring systems with a heteroatom thatresembles benzeneand its analogues in some of their properties. They obey Huckel's 4n+2 rule of aromaticity [294].

Besides being the largest portion of natural products, heterocyclics are the major components of biological molecules such as DNA and RNA, the most important macromolecules of life containing information to carry out each and every function in the cell. Nucleotides, monomers of nucleic acids, the building blocks of our genes are known to have phosphate group, ribose of deoxy-ribose and nitrogenous base. These nitrogenous bases are purines (e.g. cytosine, thymine, and uracil) and pyrimidines (e.g. adenine and guanine). Chlorophylls and hemoglobin, the most important pigments in plant and animal respectively are derivatives of large porphyrin rings [295, 296].

Heterocycles are abundant in nature as drugs, vitamins, natural products and biomolecules [297]. They are having a number of physiological and pharmacological activities; antitumor [298-301], antibiotic [302-305], anti-inflammatory [306-308], antidepressant [309,310], antitubercular [311], antimalarial [312], anti-HIV [313, 314], antibacterial [315-317] antifungal [318], antiviral [319, 320], antidiabetic [321, 322], herbicidal [323-326] and insecticidal [327]. They play very important role in pharmaceuticals [328] and agrochemicals [329]. Some heterocycles have significant solvatochromic [330, 331], photochromic [332] and biochemi-luminescence

properties andthus found applications in industry as dyestuff, fluorescent sensor, brightening agents, information storage, plastics and analytical reagents [333]. They have applications also in polymer chemistry, especially in conjugated polymers. In the electronics industry they play a major role as an integral part of organic conductors, semiconductors, molecular wires, photovoltaic cells and organic light-emitting diodes (OLEDs), light harvesting systems, optical data carriers, chemically controllable switches and liquid crystalline compounds [334].Heterocycles are again used in synthesis as synthetic intermediates, protecting groups, chiral auxiliaries, organic catalysts and metal ligands in asymmetric catalytic inorganic synthesis. Heterocycles, therefore, are an attractive field of chemical research.

Pyridine, discovered by the Scottish chemist Thomas Anderson in 1849, is a basic heterocyclic compound with the chemical formula $C_5H_5N$, structurally related to benzene, with one methine group (=CH-) replaced by a N atom [335]. Russian chemist Aleksei Chichibabin invented a pyridine synthesis reaction in 1924, which was based on inexpensive reagents, which is used for the industrial production of pyridine [336, 337]. It is used in industry as a precursor for making pesticides [338] and act as a good solvent also [339, 340]. Pyridine is added to ethanol to make it unsuitable for drinking and in low doses to foods to give them a bitter flavor[341]. The pyridine ring occurs in many important compounds, including the vitamins: niacin and pyridoxal.

**Pyridine Schiff base**

Schiff bases derived from pyridine-2-aldehyde and primary amines, are known to function as Bidentate ligands, while bis-Schiff bases of pyridine-2,6- dialdehyde function as atridentate [342-348]. Derivatives of pyridine Schiff base are acting as antioxidants [349], DNA binding and cleavage agents [350]. Gudasi et al have reported the synthesis and characterization of dioxouranium(II) and thorium(IV) complexes of Schiff bases derived from 2-aminopyridine and acetophenones with biological activity [351].

Henri et al synthesized two Schiff bases and eight transition metal complexes derived from 2, 3-diminopyridine and ortho-vanillin and found it to have antibacterial activity [352]. Gupta and Barhate synthesized a tridentate ligand derived from o-hydroxybenzaldehyde and 2-aminopyridine and its transition metal complexes with Fe(II), Cu(II), Ru(III) and Rh(III) with antimicrobial activity [353]. Kalshetty et al

synthesized new Schiff base ligands formed by the condensation of 3-Aldehydosalicylic acid with equimolar quantities of 2-Amino-5-methyl pyridine and found it to have antimicrobial activity [354]. Al-omar and Amar synthesized Schiff bases from pyridine-2,6-carboxamide and found it as potential antimicrobial agents [355]. Attia et al synthesized 2-chloro-6-ethoxy-4-acetylpyridine and found that Schiff base as biologically active [356]. Amar synthesized a Schiff base using 2,6-diacetylpyridine as synthon and found it to have biological activity [357]. Abou-Ghalia et al (2003) synthesized a Schiff base, (Nα-dipicolinoyl)-bis-Lleucyl-DL-norvalyl with linear tetra and cyclic octa bridged peptides and found it to have anti-inflammatory property [358]. Abou-Ghalia and Amr synthesized Schiff base containing cyclo-(Nα-dipicolinoyl) pentapeptide with breast and CNS cytotoxicity [359]. Gupta et al synthesized Salicylaldehyde Schiff bases of 2-aminopyridine and found it to have good antimicrobial activity [360,361].

In the following section we describe the synthesis, characterization, crystal study and biological activity of o-vanillin-2-aminopyridine Schiff bases and their metal complexes by using spectroscopic, thermo gravimetric and other analytical methods alongside a study of their biological activity.

## 4.2 EXPERIMENTAL SECTION

### 4.2.1 Materials

The Chemicals and solvents were obtained from Spectrochem and Merck. Absolute alcohol was obtained from Baroda Chem. Industries Ltd., Baroda.

### 4.2.2 Single crystal X-ray structure determination

Crystals having good morphology were chosen for three-dimensional intensity data collection. X-ray intensity data of some of the complexes were collected at room temperature on Bruker CCD area-detector diffractometer equipped with graphite monochromated MoKα radiation (α=0.71073 Å). The crystals used for data collection was of suitable dimensions. The unit cell parameters were determined by least-square refinements of all reflections in both cases. All the structures were solved by direct method and refined by full-matrix least squares on $F^2$. Data were corrected for Lorentz, polarization and multi-scan absorption correction[152]. The structures were solved by direct methods using SHELXS97 [152]. All non-hydrogen atoms of the molecule were located in the best E-map. Full-matrix least-squares refinement was carried out using SHELXL97 [152]. Hydrogen atoms were placed at geometrically

fixed positions and allowed to ride on the corresponding non-H atoms with C-H = 0.93-0.96Å, and Uiso=1.5 Ueq of the attached C atom for methyl H atoms and 1.2 Ueq for other H atoms. Atomic scattering factors were taken from International Tables for X-ray Crystallography (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4). An ORTEP [153]view of the both the complexes with atomic labeling are shown in further section. The geometry of the molecule was calculated using the software PLATON[1544] and PARST [155].

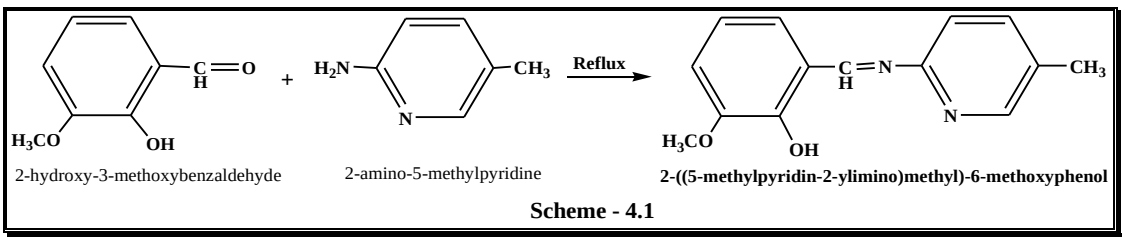
### *4.2.3Antibacterial screening*

The test organism was activated by inoculating a loop full of the strain in 25 ml of Nutrient Broth and kept overnight on a rotary shaker. The assay was performed by agar well diffusion method [362]. 200 µl inoculums ($1\times10^8$ cfu/ml), was introduced into molten nutrient agar and poured into Petri dishes when temperature reached 40-42°C. The media was solidified and wells were prepared in the seeded agar plates with the help of a cup borer (8.5 mm). 100 µl of test compound was introduced into the well and the plates were incubated at 37°C for 24 h. DMSO (dimethylsulphoxide) was taken as negative control.

## 4.3 Preparation of Schiff base ligands and metal complexes

### *4.3.1Synthesis of 2-(5-methylpyridin-2-ylimino)methyl)-6-methoxyphenol [MMM]*

Equimolar (25 mmol) ethanolic solution (50 mL) of 2-hydroxy-3-methoxybenzaldehyde (3.8 gm) and 2-amino-5-methylpyridine (2.7 gm) was refluxed for 6 hours in round bottom flask. During the reflux a microcrystalline orange compound was separated, which was isolated by filtration and dried in air and finally purified by crystallizing in appropriate solvent. (Scheme-4.1)




**Scheme - 4.1**

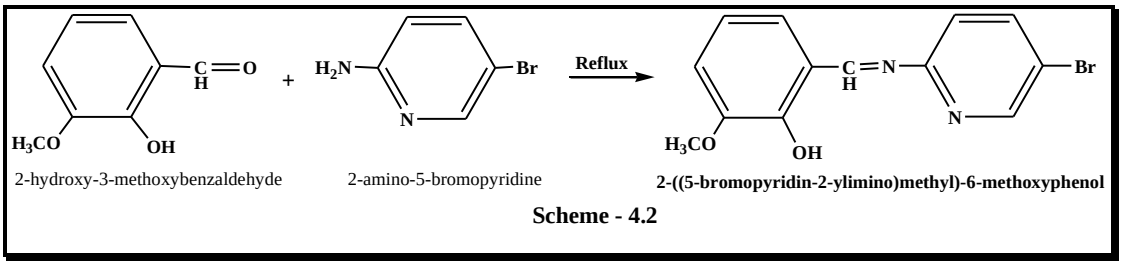
MMM is dark orange crystalline compound. Yield: 82%, m.p.: 210°C.Anal. Calc. for $C_{14}H_{14}N_2O_2$ M.W.: 242.27, C (69.41%), H (5.82%), N (11.56%), found: C (69.48%), H (5.75%), N (11.61%).

IR (KBr, $cm^{-1}$): 3460-3390 (m) (O-H Hydrogen bonded), 1604 (s) (C=N azomethine), 3046 and 2832 $cm^{-1}$ (m) (C–H of ali/aro), 2927 $cm^{-1}$(m) (–$OCH_3$).$^1$H NMR ($CDCl_3$,

400 MHz, TMS): δ2.36 (s, 3H, -$CH_3$), δ3.90 (s, 3H, -$OCH_3$), δ6.85-8.31 (m, 6H, Ar-H), δ9.41 (s, -CH=N-), δ 14.00 (s, 1H, O-H). MASS: m/z = 242 [$C_{14}H_{14}N_2O_2$], 225 [$C_{14}H_{14}N_2O$]$^+$, 214 [$C_{13}H_{12}N_2O$] $^+$, 199 [$C_{12}H_{10}N_2O$]$^+$, 183 [$C_{12}H_{10}N_2$]$^+$, 168 [$C_9H_{11}NO_2$]$^+$, 150 [$C_8H_9NO_2$]$^+$, 135 [$C_8H_9NO$]$^+$, 121 [$C_8H_{10}O$]$^+$, 109 [$C_7H_8O$]$^+$, 78 [$C_6H_6$]$^+$, 65 [$C_5H_5$]$^+$.

### *4.3.2Synthesis of 2-(5-bromopyridin-2-ylimino)methyl)-6-methoxyphenol [BMM]*

Equimolar (25 mmol) ethanolic solution (50 mL) of 2-hydroxy-3-methoxybenzaldehyde (3.8 gm) and 2-amino-5-bromopyridine (4.3 gm) was refluxed for 6 hours in round bottom flask. During the reflux a microcrystalline orange compound was separated, which was isolated by filtration and dried in air and finally purified by crystallizing in appropriate solvent. (Scheme – 4.2)




**Scheme - 4.2**

BMM is orange brown crystalline compound. Yield: 89%, m.p.: 192$^o$C.Anal. Calc. for $C_{13}H_{11}BrN_2O_2$ M.W.: 307.14, C (50.84%), H (3.61%), N (9.12%), found: C (50.88%), H (3.58%), N (9.16%).

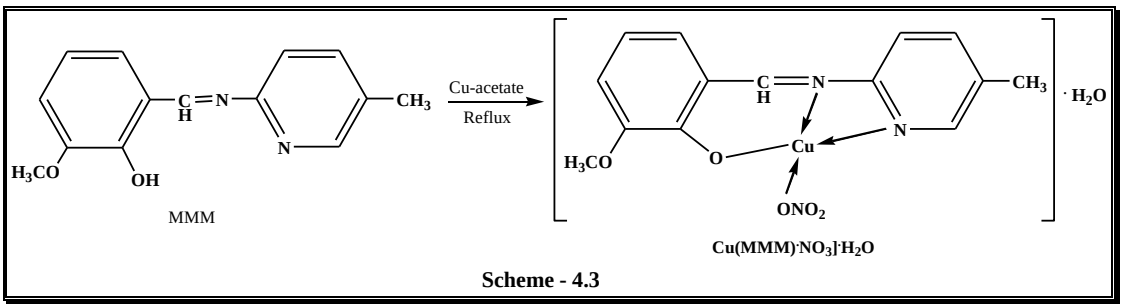
IR (KBr, cm$^{-1}$): 3470-3420 (m) (O-H Hydrogen bonded), 1605 (s) (C=N azomethine), 3048 and 2830 cm$^{-1s}$ (m) (C–H of ali/aro), 2930 cm$^{-1}$(m) (–$OCH_3$).$^1$H NMR ($CDCl_3$, 400 MHz, TMS): δ 3.92 (s, 3H, -$OCH_3$), δ6.87-8.19 (m, 6H, Ar-H), δ 9.32 (s, -CH=N-), δ 13.92 (s, 1H, O-H).MASS: m/z = 308 [$C_{13}H_{11}BrN_2O_2$], 289 [$C_{13}H_{11}BrN_2O$]$^+$, 278 [$C_{12}H_9BrN_2O$] $^+$,263 [$C_{12}H_9BrN_2$]$^+$, 247 [$C_{11}H_{11}BrN_2$]$^+$,235 [$C_{10}H_9BrN_2$]$^+$, 212 [$C_8H_9BrN_2$]$^+$,199 [$C_7H_7BrN_2$]$^+$, 184[$C_6H_5BrN_2$]$^+$, 150 [$C_9H_{10}O_2$]$^+$, 138 [$C_8H_{10}O_2$]$^+$, 106 [$C_7H_8O$]$^+$, 92 [$C_7H_8$]$^+$, 78 [$C_6H_6$]$^+$, 64 [$C_6H_5$]$^+$.

## Preparation of Schiff base metal complexes

### *4.3.3 Synthesis of [Cu(MMM)·$NO_3$]·$H_2O$*

Cupric nitrate (0.2 gm, 1 mmol) was dissolved in minimum amount of distilled water and the solution was added to hot ethanolic solution of the 2-(5-methylpyridin-2-ylimino)methyl)-6-methoxyphenol (0.2 gm, 1 mmol) with constant shaking. After

the complete addition, small amount of sodium acetate was added and the reaction mixture was refluxed for 4 h. A crystalline solid was formed which was filtered, washed with hot distilled water and then ethanol and dried under vacuum. (Scheme – 4.3)

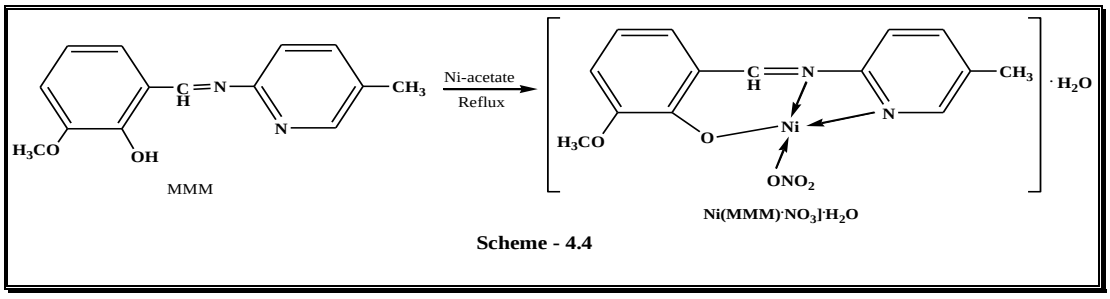



**Scheme - 4.3**

*[Cu(MMM)·NO$_3$]·H$_2$O* is Deep green colored crystalline compound. Yield: 75%, m.p.: >300$^o$C, Solubility: DMF. Anal. Calc. for $C_{14}H_{15}CuN_3O_6$ M.W.: 385, C (43.69%), H (3.93%), N (10.92%), Cu (16.51%) found: C (43.65%), H (3.89%), N (11.00%), Cu (16.44%).

### *4.3.4 Synthesis of [Ni(MMM)·NO$_3$]·H$_2$O*

Nickel nitrate (0.3gm, 1 mmol) was dissolved in minimum amount of distilled water and the solution was added to hot ethanolic solution of the 2-(5-methylpyridin-2-ylimino)methyl)-6-methoxyphenol (0.3gm, 1 mmol) with constant shaking. On completing the addition, a small amount of sodium acetate was added and the reaction mixture was refluxed for 4 h. A crystalline solid was formed which was filtered, washed with hot distilled water and then ethanol and dried under vacuum. (Scheme – 4.4)

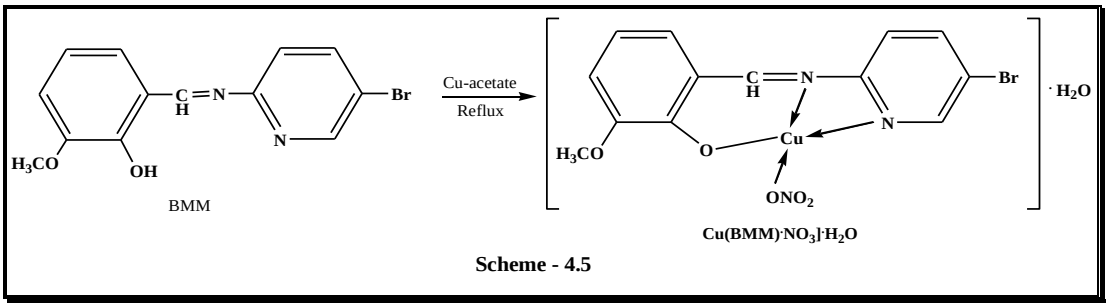



**Scheme - 4.4**

*[Ni(MMM)·NO$_3$]·H$_2$O* is reddish crystalline compound. Yield: 82%, m.p.: >300$^o$C, Solubility: DMF. Anal. Calc. for $C_{14}H_{15}N_3NiO_6$ M.W.: 380, C (44.25%), H (3.98%), N (11.06%), Cu (15.45%) found: C (44.21%), H (3.93%), N (11.01%), Cu (15.39%).

### *4.3.5 Synthesis of [Cu(BMM)·NO$_3$]·H$_2$O*

Cupric nitrate (1 mmol) was dissolved in minimum amount of distilled water and the solution was added to hot ethanolic solution of the 2-((5-bromopyridin-2-ylimino)methyl)-6-methoxyphenol (1 mmol) with constant shaking. On completing addition, a small amount of sodium acetate was added and the reaction mixture was refluxed for 4 h. A crystalline solid was formed which was filtered, washed with hot distilled water and then ethanol and dried under vacuum. (Scheme – 4.5)



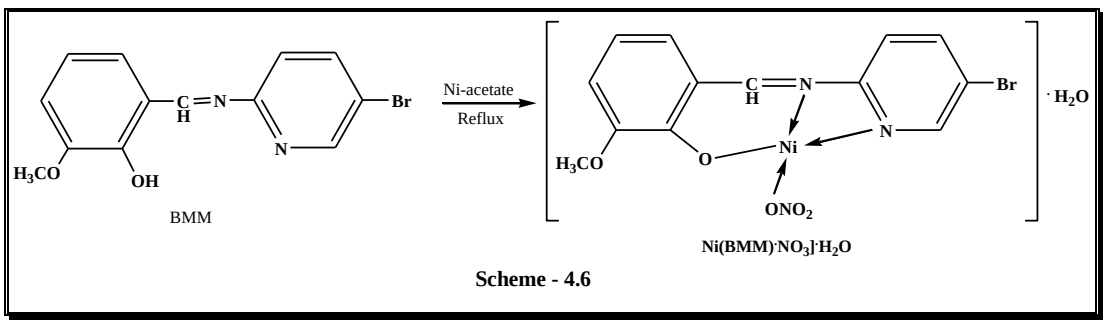

**Scheme - 4.5**

*[Cu(BMM)·NO$_3$]·H$_2$O* is green crystalline compound. Yield: 79%, m.p.: >300$^o$C, Solubility: DMF. Anal. Calc. for $C_{13}H_{12}BrCuN_3O_6$ M.W.: 447, C (34.72%), H (2.69%), N (9.34%), Cu (14.13) found: C (34.68%), H (2.73%), N (9.37%), Cu (14.17%).

ESI-MS: 447[$C_{13}H_{12}BrCuN_3O_6$], 430 [$C_{13}H_{10}BrCuN_3O_5$]$^+$, 413 [$C_{13}H_{10}BrCuN_3O_4$]$^+$, 399 [$C_{12}H_8BrCuN_3O_4$]$^+$, 338 [$C_{12}H_8BrCuN_2O$]$^+$, 307 [$C_{13}H_{11}BrN_2O_2$]$^+$, 260 [$C_{12}H_9CuN_2O$]$^+$, 227 [$C_{13}H_{12}N_2O_2$]$^+$, 196 [$C_{13}H_{12}N_2$]$^+$.

### *4.3.6 Synthesis of [Ni(BMM)·NO$_3$]·H$_2$O*

Nickel nitrate (1 mmol) was dissolved in minimum amount of distilled water and the solution was added to hot ethanolic solution of the 2-((5-bromopyridin-2-ylimino)methyl)-6-methoxyphenol (1 mmol) with constant shaking. After the complete addition, small amount of sodium acetate was added and the reaction mixture was refluxed for 4 h. A crystalline solid was formed which was filtered, washed with hot distilled water and then ethanol and dried under vacuum. (Scheme – 4.6)




**Scheme - 4.6**

*[Ni(BMM)·NO$_3$]·H$_2$O* is reddish crystalline compound. Yield: 80%, m.p.: >300$^o$C, Solubility: DMF. Anal. Calc. for $C_{13}H_{12}BrN_3NiO_6$ M.W.: 444, C (35.10%), H (2.72%), N (9.45%), Cu (13.19%) found: C (35.17%), H (2.70%), N (9.41%), Cu (13.23%).

ESI-MS: 442 $[C_{13}H_{12}BrN_3NiO_6]$, 430 $[C_{13}H_{10}BrNiN_3O_5]^+$, 417 $[C_{13}H_{10}BrNiN_3O_4]^+$, 399 $[C_{12}H_8BrNiN_3O_4]^+$, 338 $[C_{12}H_8BrNiN_2O]^+$, 309 $[C_{13}H_{11}BrN_2O_2]^+$, 260 $[C_{12}H_9CuN_2O]^+$, 227 $[C_{13}H_{12}N_2O_2]^+$, 196 $[C_{13}H_{12}N_2]^+$.

## 4.4Characterization of Schiff base ligands and metal complexes

### *4.4.1 Physico-chemical properties of synthesized Schiff base ligands and metal complexes*

The Schiff base ligands and the metal complexes of O-vanillinwere synthesized in a very facile and essentially identical way. All these compounds are intensively colored, air and moisture free crystalline solids. They are soluble in common organic solvents. The structures of the ligands and metal complexesareconfirmed by spectroscopic and crystallographic studies as well as some important analytical techniques.

IR spectra (4000–400 cm$^{-1}$) of the ligands and metal complexes were recorded using KBr discs on 8400 FT-IR Shimadzu spectrometer. The mass spectra of the ligands were recorded on a Trace GC ultra DSQ II. $^1$H NMR spectra of ligands were recorded on Bruker Avance-II 400 MHz FT-NMR spectrometer using TMS as an internal standard and $CDCl_3$ as a solvent.X-ray intensity data were collected on Bruker CCD area-detector diffractometer equipped with graphite monochromated Mo Kα radiation (λ= 0.71073 Å). ESI-Mass spectra of complexes were recorded VG-70S spectrometer. Electronic spectra of the metal complexes in DMF were recorded on a Perkin-Elmer Lambda 19 spectrophotometer. Elemental analysis (C, H and N) were carried out on elemental analyzer Perkin-Elmer 2400, while analysis of copper was determined by EDTA after decomposing the complexes with $HNO_3$. Magnetic susceptibility measurements of the complexes were carried out by Gouy balance using $Hg[Co(SCN)_4]$ as calibrant. Purity of the ligands and their complexes was evaluated by thin layer chromatography. The analytical and physical data of ligands and metal complexes are listed in Table 4.1.

**Table 4.1: The physical and analytical data of ligands and their metal complexes**

| Ligand or complex | Formula | M W | Color | % Yield | M.P. | Elemental analysis, % Found/(Calcd.) | | | | $\mu_{eff}$ Found/( Calcd.) BM |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | C | H | N | M | |
| MMM | $C_{14}H_{14}N_2O_2$ | 242 | Orange | 82 | 210 | 69.35 (69.41) | 5.79 (5.82) | 11.60 (11.56) | - | - |
| BMM | $C_{13}H_{11}BrN_2O_2$ | 307 | Orange | 89 | 192 | 50.90 (50.84) | 3.57 (3.61) | 9.09 (9.12) | - | - |
| [Cu(MMM)·$NO_3$]·$H_2O$ | $C_{14}H_{15}CuN_3O_6$ | 385 | Deep green | 75 | >300 | 43.65 (43.69) | 3.89 (3.93) | 11.00 (10.92) | 16.44 (16.51) | 1.94 (1.73) |
| [Ni(MMM)·$NO_3$]·$H_2O$ | $C_{14}H_{15}N_3NiO_6$ | 380 | Reddish | 82 | >300 | 44.21 (44.25) | 3.93 (3.98) | 11.01 (11.06) | 15.39 (15.45) | 2.80 (2.82) |
| [Cu(BMM)·$NO_3$]·$H_2O$ | $C_{13}H_{12}BrCuN_3O_6$ | 447 | Green | 79 | >300 | 34.68 (34.72) | 2.73 (2.69) | 9.37 (9.34) | 14.17 (14.13) | 1.80 (1.73) |
| [Ni(BMM)·$NO_3$]·$H_2O$ | $C_{13}H_{12}BrN_3NiO_6$ | 445 | Reddish | 80 | >300 | 35.17 (35.10) | 2.70 (2.72) | 9.41 (9.45) | 13.23 (13.19) | 2.90 (2.82) |

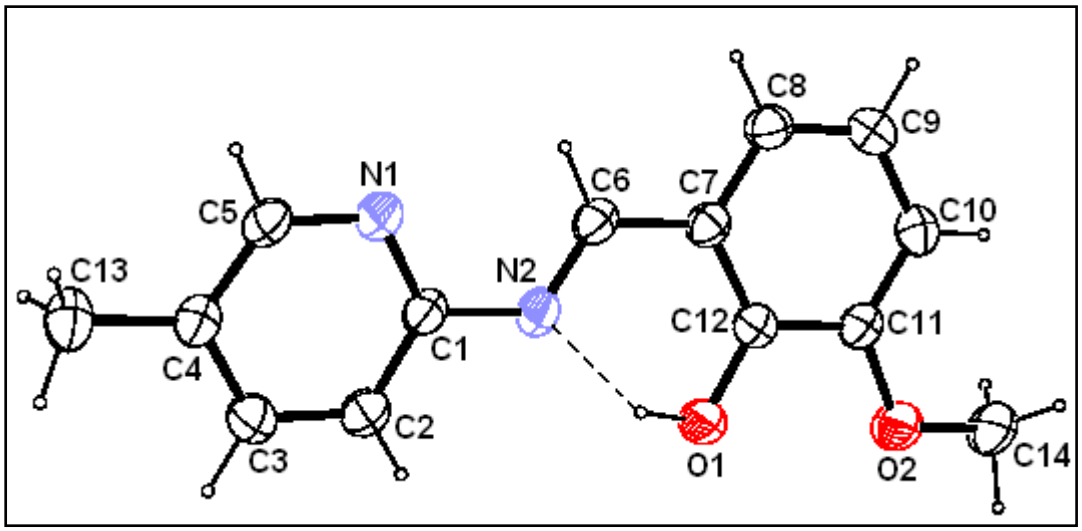
### 4.4.2 Crystal structure of Schiff base ligands

#### 4.4.2.1*The Crystal structure of Schiff base ligand MMM*

The X-ray intensity data of a well defined crystal (0.3 x 0.2 x 0.2 mm) were collected at room temperature (293K) by using a CCD area-detector diffractometer (*X'calibur system – Oxford diffraction make, U.K.*) which is equipped with graphite monochromated MoKα radiation (α=0.71073 Å). A total number of 11484 reflections were collected of which 1686 reflections were treated as observed ($I > 2\sigma(I)$). Data were corrected for Lorentz and polarization and absorption factors.The structure was solved by direct methods using SHELXS97. All non-hydrogen atoms of the molecule were located from the E-map. Full-matrix least-squares refinement was carried out by using SHELXL97 software. All the hydrogen atoms were located from a difference electron density map and their positional and isotropic thermal parameters were included in the refinement. The final refinement cycle yielded an R- factor of 0.0476 [wR ($F^2$) = 0.1218] for the observed data. The residual electron density ranges from -0.197 to0.165eÅ$^{-3}$. Atomic scattering factors were taken from International Tables for X-ray Crystallography (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4). An ORTEP view of the title compound with atomic labeling is shown in Fig.4.1.

The single crystal X-ray diffraction study on this compound clearly indicates that the compound has strong intramolecular O-H---N hydrogen bond. The strong intramolecular O-H---N hydrogen bond is an evidence of the preference for the phenol-imine tautomeric form in the solid state. The Hydrogen bonding geometry parameters of the ligand are also shown in Table 4.2-4.4.

**Figure- 4.1: ORTEP view of Schiff base ligand MMM**




***ORTEP* view of the molecule, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.**

**Table4.2: Crystallographic data of Schiff base ligand MMM**

| | |
|---|---|
| CCDC Number | 834633 |
| Crystal description | Orange rectangular |
| Crystal size | 0.30 x 0.20 x 0.20 mm |
| Empirical formula | $C_{14}$ $H_{14}N_2O_2$ |
| Formula weight | 242.27 |
| Radiation, Wavelength | Mo *K*α, 0.71073 Å |
| Unit cell dimensions | a=11.6052(4),b=4.9569(2), c=21.2962(10)Å, β = 91.318(4)$^o$ |
| Crystal system, Space group | Monoclinic, $P2_1/n$ |
| Unit cell volume | 1224.76(9)Å$^3$ |
| No. of molecules per unit cell, Z | 4 |
| Absorption coefficient | 0.089 mm$^{-1}$ |
| F(000) | 512 |
| θ range for entire data collection | 3.51 < θ < 25.00 |
| Reflections collected / unique | 11484 / 2131 |
| Reflections observed (I > 2σ(I)) | 1686 |
| No. of parameters refined | 215 |
| Final R-factor | 0.0476 |

| | |
|---|---|
| wR($F^2$) | 0.1218 |
| Goodness-of-fit | 1.017 |
| $(\Delta/\sigma)_{max}$ | -0.001 for x H131 |
| Final residual electron density | $-0.197 < \Delta\rho < 0.165$ eÅ$^{-3}$ |

**Table4.3: Selected bond lengths and bond angles of MMM**

| Bond distances (Å)with esd's in parentheses | | Bond angles(°)with esd's in parentheses | |
|---|---|---|---|
| N1 C1 | 1.334(2) | C1 N1 C5 | 116.37(15) |
| N1 C5 | 1.342(2) | C6 N2 C1 | 121.72(15) |
| N2 C6 | 1.283(2) | C11 O2 C14 | 116.93(16) |
| N2 C1 | 1.414(2) | N1 C1 C2 | 122.73(16) |
| O1 C12 | 1.338(2) | N1 C1 N2 | 119.88(16) |
| O2 C11 | 1.370(2) | C2 C1 N2 | 117.38(15) |
| O2 C14 | 1.421(2) | N1 C5 C4 | 125.37(16) |
| C6 C7 | 1.447(2) | N2 C6 C7 | 120.73(16) |
| C7 C12 | 1.404(2) | N2 C6 H6 | 122.0(12) |
| C7 C8 | 1.404(2) | O2 C11 C10 | 125.71(16) |
| C10 C11 | 1.373(3) | O2 C11 C12 | 114.35(16) |

**Table 4.4: Hydrogen–bonding geometry (e.s.d.`s in parentheses)**

| **D–H…A** | **D–H(Å)** | **D…A(Å)** | **H…A(Å)** | **D–H…A(°)** |
|---|---|---|---|---|
| O1-H1...N2 | 0.82 | 2.556(2) | 1.83(3) | 147(3) |
| C3-H3...O2 $^{i}$ | 0.99(2) | 3.571(2) | 2.58(2) | 178(2) |
| **Symmetry code** : (i) 1–x, 2-y, -z | | | | |

### 4.4.3 IR spectral studies

The IR spectra of the ligands show a broad band at 3410-3450 $cm^{-1}$ due to the stretching vibrations of phenolic hydroxyl group. The broadness is due to intermolecular hydrogen bonding between the phenolic group and the azomethine group. The strong band observed at 1605& 1604 $cm^{-1}$ is assigned to the stretching vibrations of the azomethine (-C=N-) group. Two moderately intense bands observed at 3046/3048 and 2832/2830 $cm^{-1}$, are due to aromatic and aliphatic $\upsilon$(C–H), respectively. Whereas Band appeared in range of 2927-2930 $cm^{-1}$ is due to stretching vibrations of the $–OCH_3$ group.The IR spectra of metal complexes show sharp band in the range 1600-1550 $cm^{-1}$, which is shifted to lower frequency as compared to ligand, suggesting coordination of the azomethine nitrogen to the metal ion. The disappearance of$\upsilon$(O–H) shows the deprotonation of the –OH group and its subsequent coordination to the central metal atom. Two new bands observed at 578–

564 and 481-470 $cm^{-1}$ are characteristic of M–O and M–N absorptions, respectively[362-364]. (Figure 4.2-4.4)

**Figure 4.2: IR spectrum of Schiff base ligand MMM**

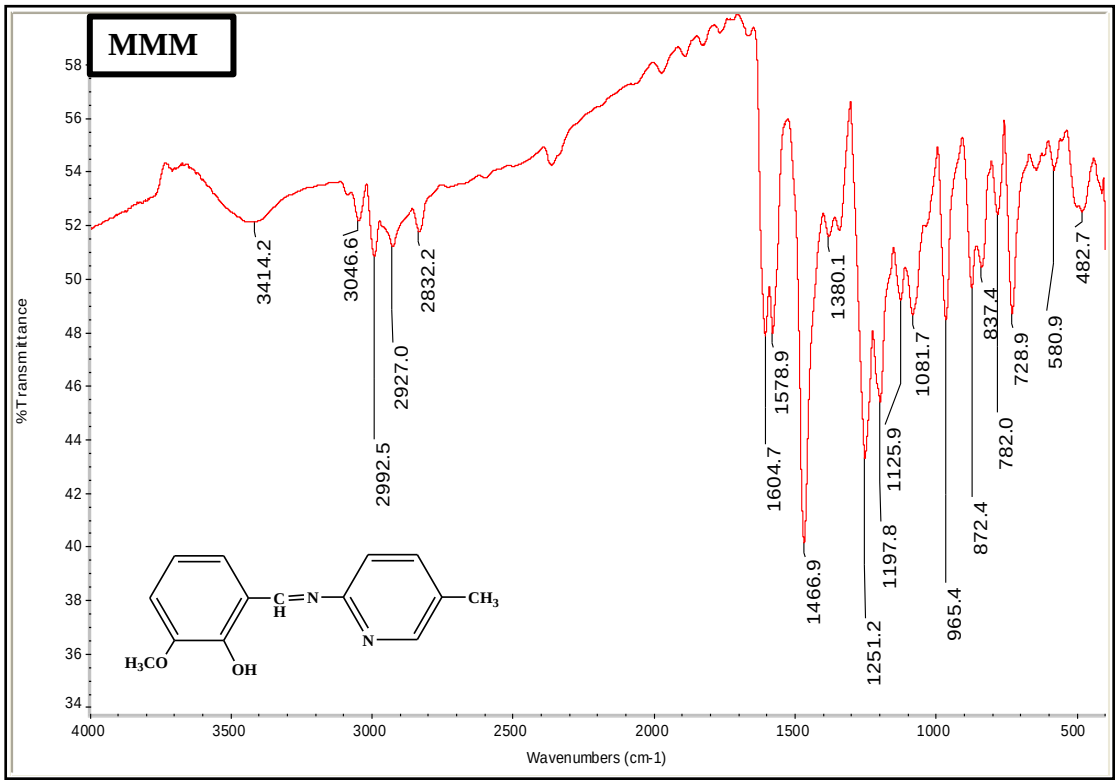



**Figure 4.3: IR spectrum of Schiff base ligand MMM**

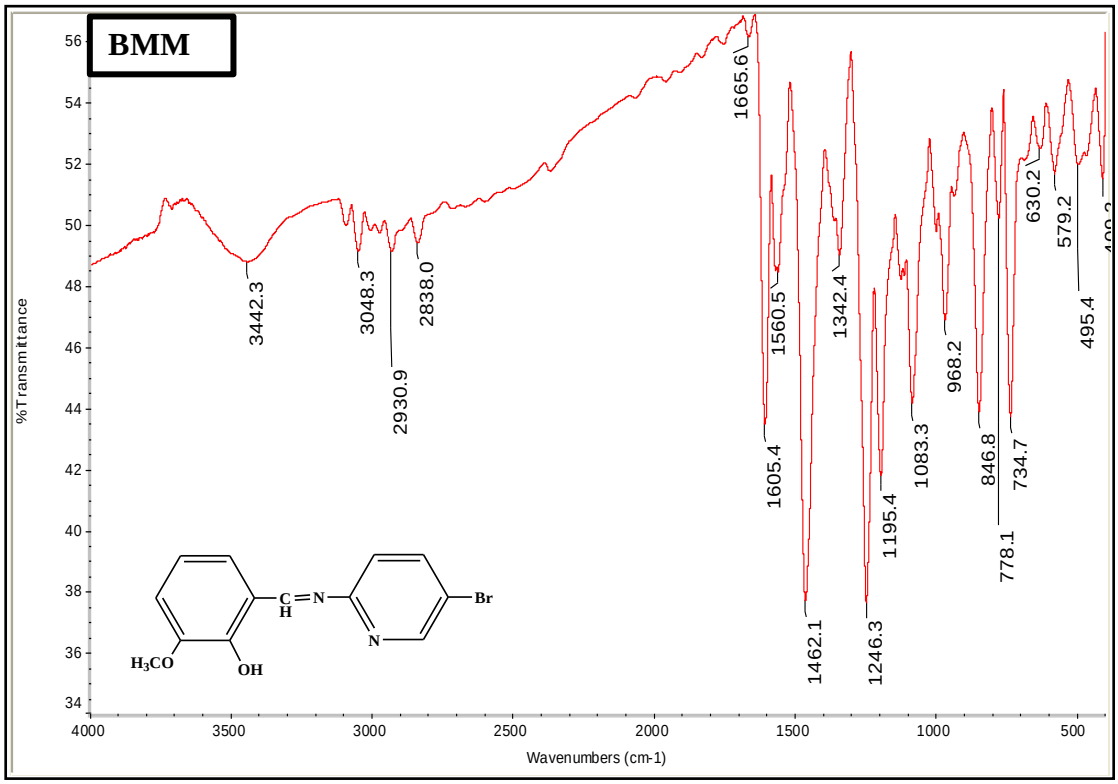
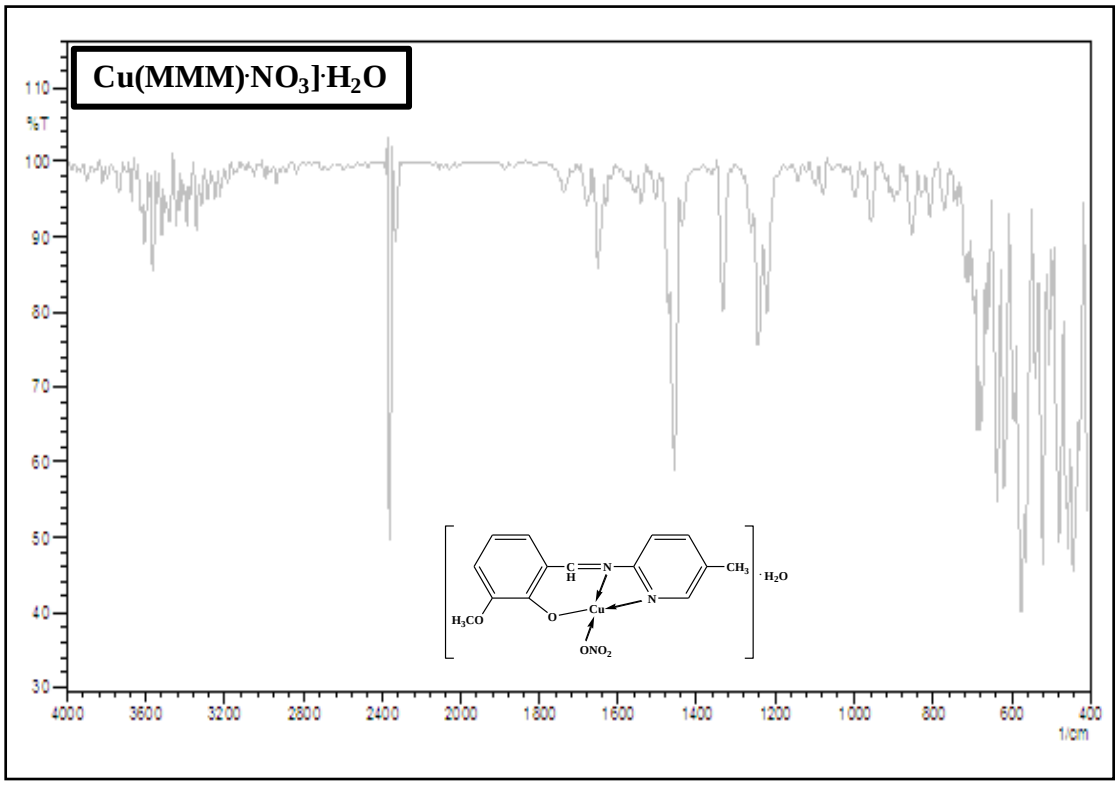


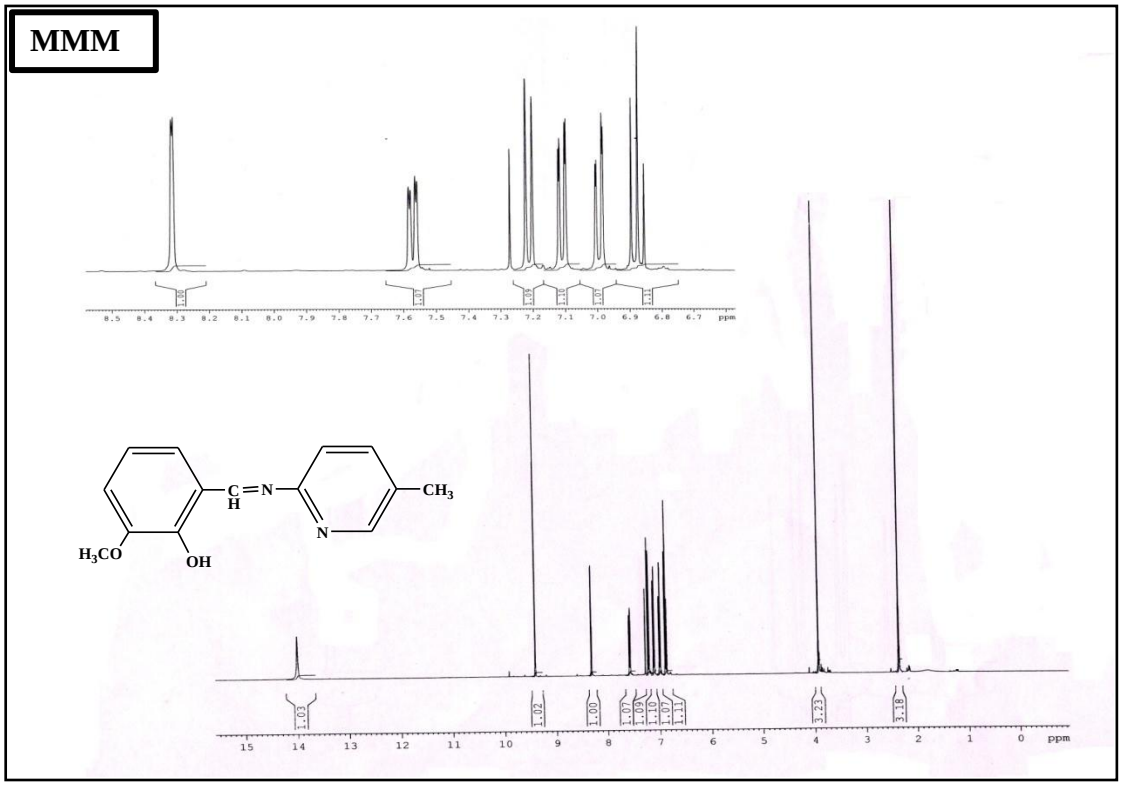

**Figure 4.4: IR spectrum of Schiff base ligand MMM**




### 4.4.4 NMR spectral studies

The synthesized Schiff base ligands were characterized by the $^{1}H$ NMRspectra in $CDCl_3$. All the spectra are in good agreement with theproposed structure of the ligands. The signal due to methyl protons (Ligand MMM) appeared as singlet at δ 2.36 *ppm*[365], whereas signal due to methoxy protons appeared as singlet in the range δ 3.89-3.93 *ppm*. In the aromatic region, a few doublets and in some cases overlapping doublets/multiplets are observed in the range δ 6.85-8.31 *ppm*. These signals are due to aryl protons of benzene/pyridine rings. The signals due to azomethine proton (-CH=N-) appeared as singlet at δ 9.41 ppm. Another singlet corresponding to one proton is observed in the range δ 13.92-14.00 *ppm*. This signal disappeared in the complexes [366]. (Figure 4.5)

**Figure 4.5: $^{1}H$ NMR spectrum of Schiff base ligand MMM**




### 4.4.5 Mass spectral studies

The mass spectra of Schiff base ligands were in good agreement with the proposed structures. Schiff base ligands show molecular ion peakscorresponding to their molecular masses. The other peaks appeared in the mass spectrum (abundance range 1–100%) are attributed to the fragmentation of ligand molecule obtained from the rupture of different bonds inside the molecule. Melting point of each metal complex is very high, as a result of this, the mass spectra were carried out by ESI. TheESI–Mass spectra of complexesshow molecular ion peakscorresponding to their molecular weights. The mass spectra of ligands MMM & BMM revealed the molecular ion peak at m/e 242 and 308 respectively, which are consistent with the formula weights and support the identity of the structures [367]. (Figure 4.6-4.11)

**Figure 4.6: Mass spectrum of Schiff base ligand MMM**

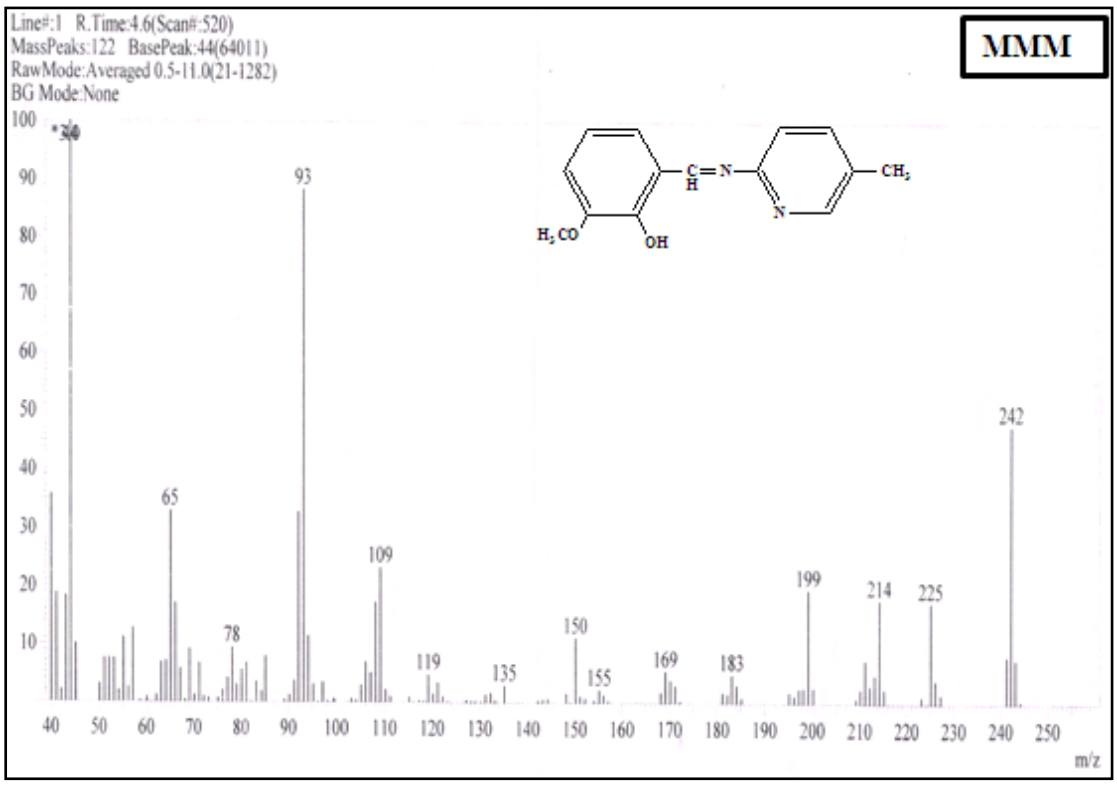



**Figure 4.7: Mass spectrum of Schiff base ligand BMM**

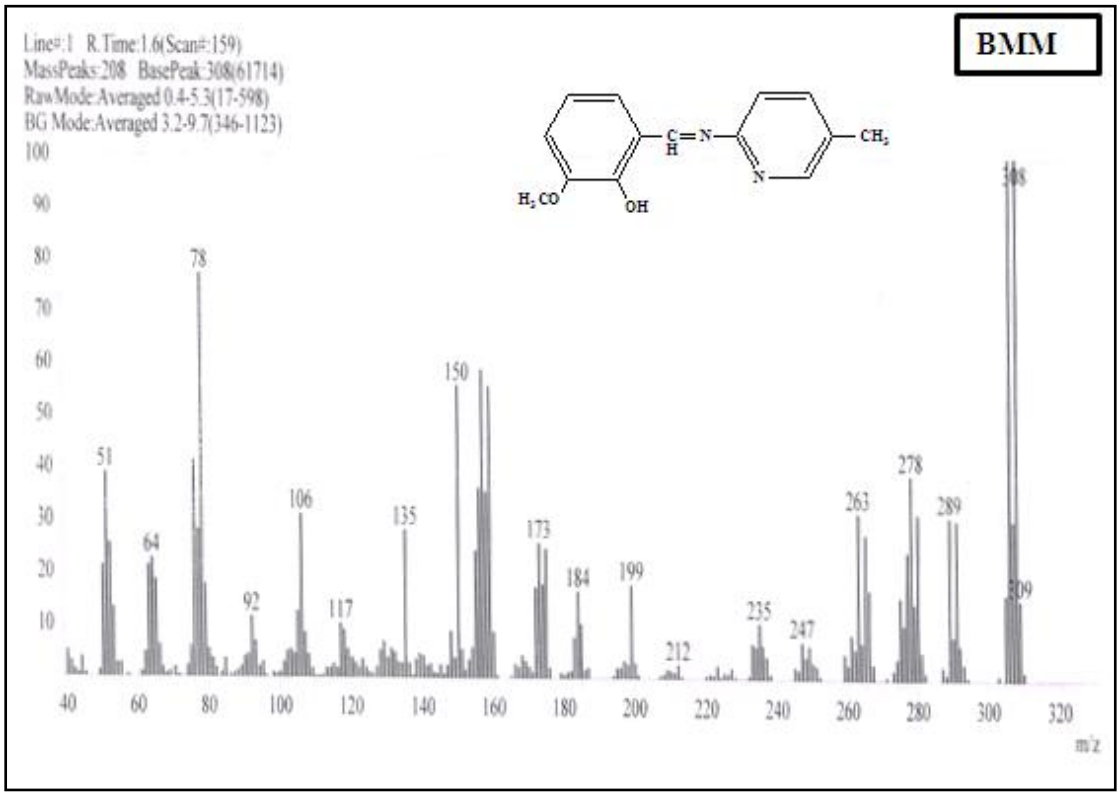



**Figure 4.8: Mass spectrum of metal complex $[Cu(BMM)NO_3]H_2O$**

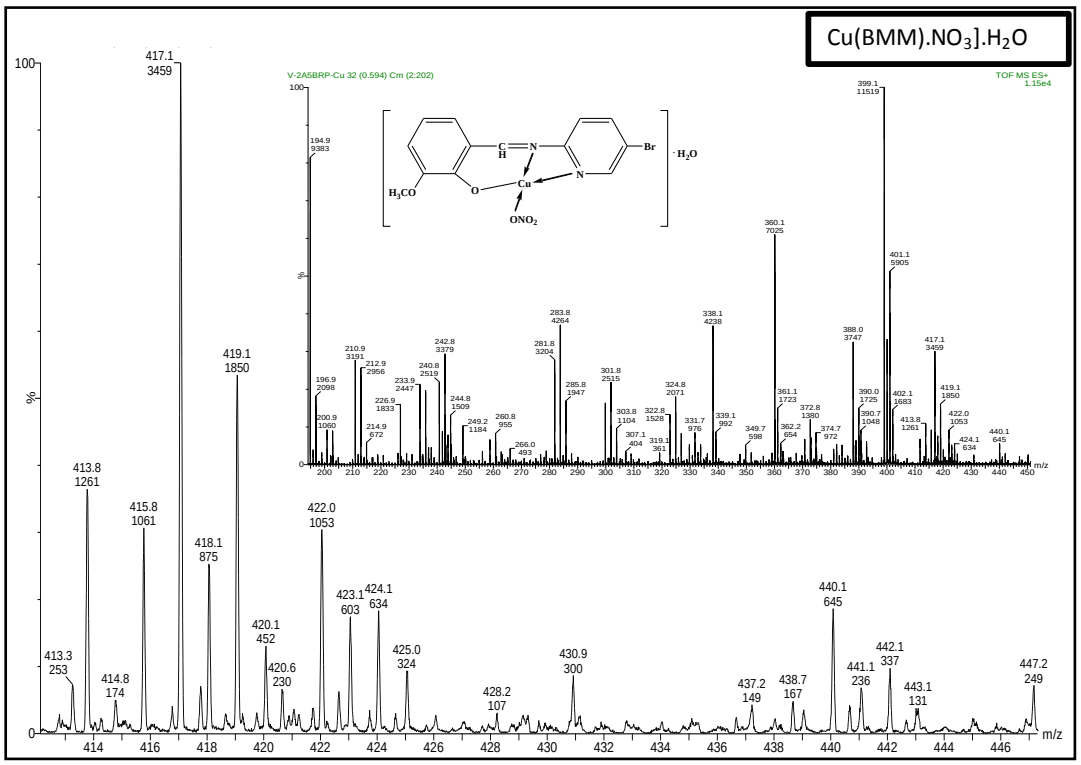



**Figure 4.9: Mass spectrum of metal complex $[Ni(BMM)NO_3]H_2O$**

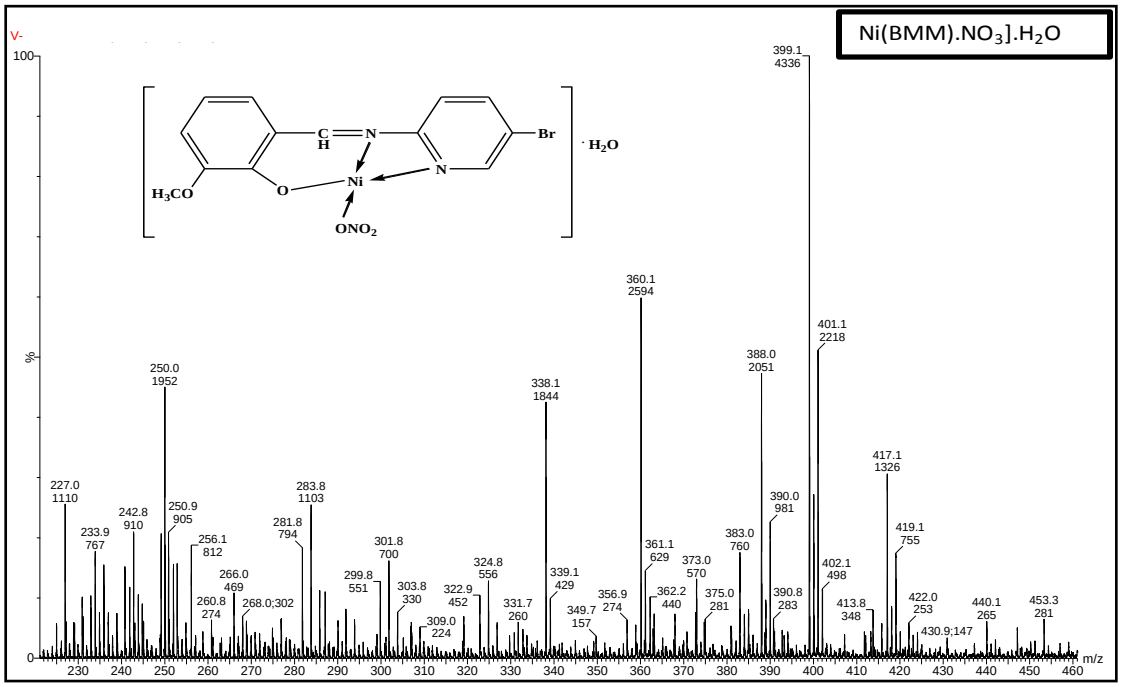



**Figure 4.10: Massfragmentation of Schiff base ligand MMM**

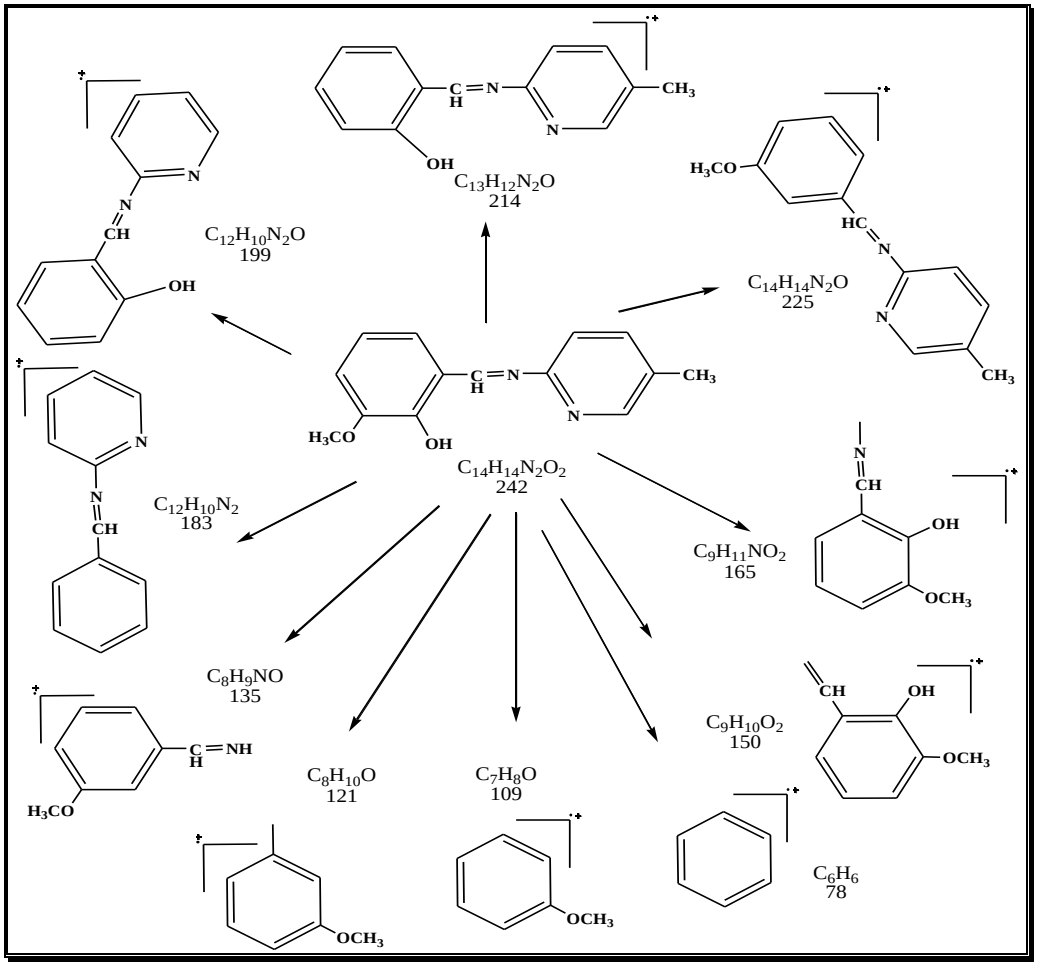
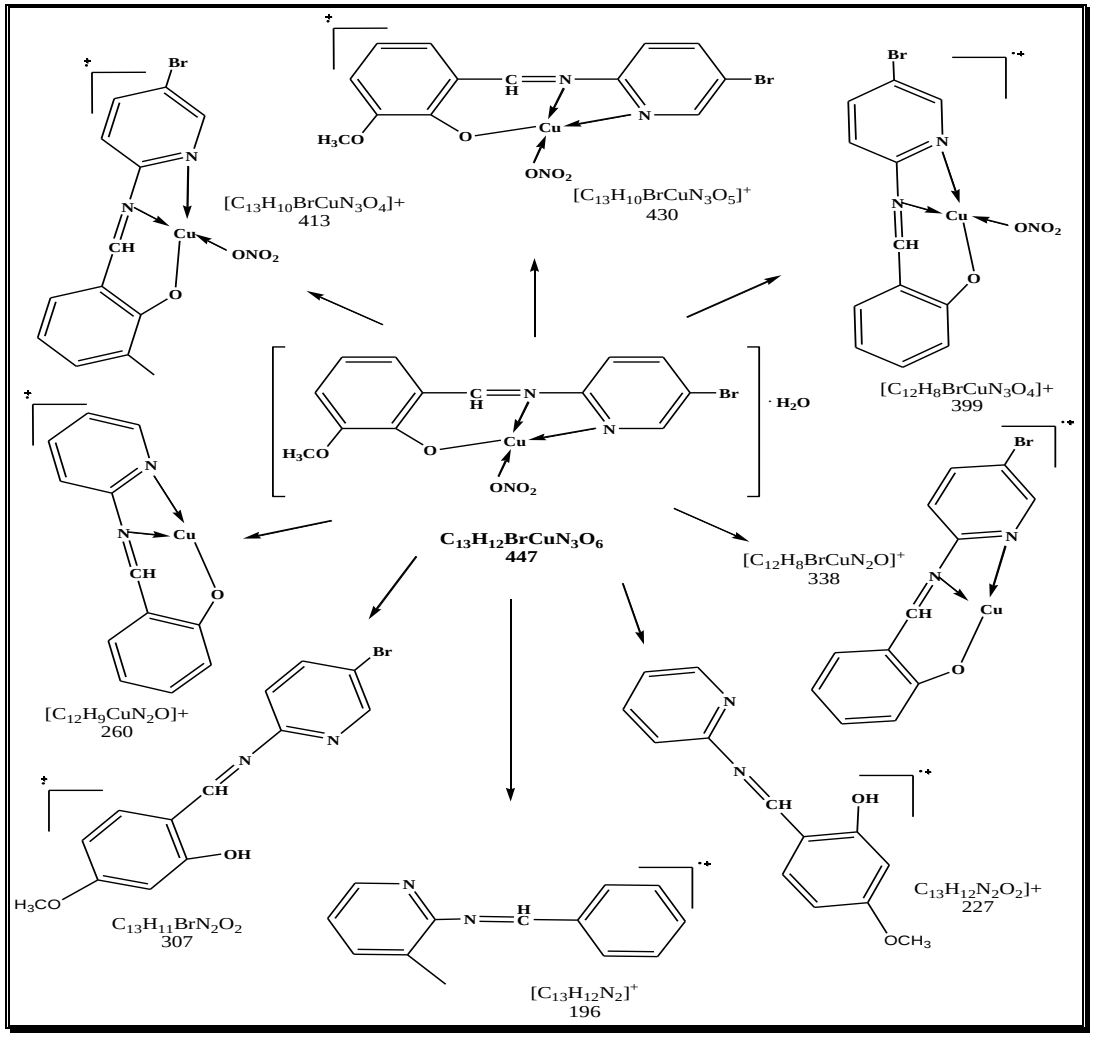



**Figure 4.11: Massfragmentation of $[Cu(BMM)NO_3]H_2O$**




### 4.4.6 Thermal studies

Thermal analyses of all the complexes were carried out by the TG-DTA techniques. The experimental results revealed that the degradation occurred in multiple stages, following a complex mechanism. Thermal behavior of all complexes can be explained as follows. In the present investigation, heating rates were suitably controlled at 10°Cmin$^{-1}$ and mass loss followed upto 60-550°C. The simultaneous TG-DTG-DTA curves of the Cu(II) and Ni(II) complexes are presented in following Figures. The TG curve follows the decrease in sample mass with increase in temperature. The decomposition of the complexes undergoes in two stages. The degradation of Lattice water molecule takes place in the first stage at 65-69ºC and 98-100ºC with a mass loss of 4.64% (calcd.: 4.67%) and 4.73% (calcd.: 4.72%), respectively[369]. The maximum of mass loss is indicated by the DTG peak at 64°C in case of Cu-complex and 94°C in case of Ni-complex. The maximum rate of mass loss is indicated by the DTA trace at 60°C and 92°C respectively. The degradation of

one -$NO_3$ molecule takes place in the second stage at 269ºC and 309ºC with a mass loss of 16.05% (calcd.: 16.07%) and 16.26% (calcd.: 16.27%) ,respectively. The maximum rate of mass loss is indicated by the DTG peak at 279°C in case of Cu-complex and 321°C in case of Ni-complex. The maximum rate of mass loss is indicated by the DTA trace at 288°C and 313°C, respectively. (Table 4.5& Figures 4.12-4.15)

**Table 4.5: Thermo-analytical data of the complexes**

| Complexes | TG range (°C) | DTGmax (°C) | DTAmax (°C) | Mass loss(%) obs.(calcd.) | Assignments |
|---|---|---|---|---|---|
| Copper complex | 65-69 | 64 | 60 | 4.64 (4.67) | Loss of Lattice $H_2O$ molecule |
| | 269 | 279 | 288 | 16.05 (16.07) | Loss of Coordinated -$NO_3$ molecule |
| Nickel Complex | 98-100 | 94 | 92 | 4.73 (4.72) | Loss of Lattice $H_2O$ molecule |
| | 309 | 321 | 313 | 16.26 (16.27) | Loss of Coordinated -$NO_3$ molecule |

**Figure 4.12: TG-DT analysis of metal complex[Cu(MMM)$NO_3$]$H_2O$**

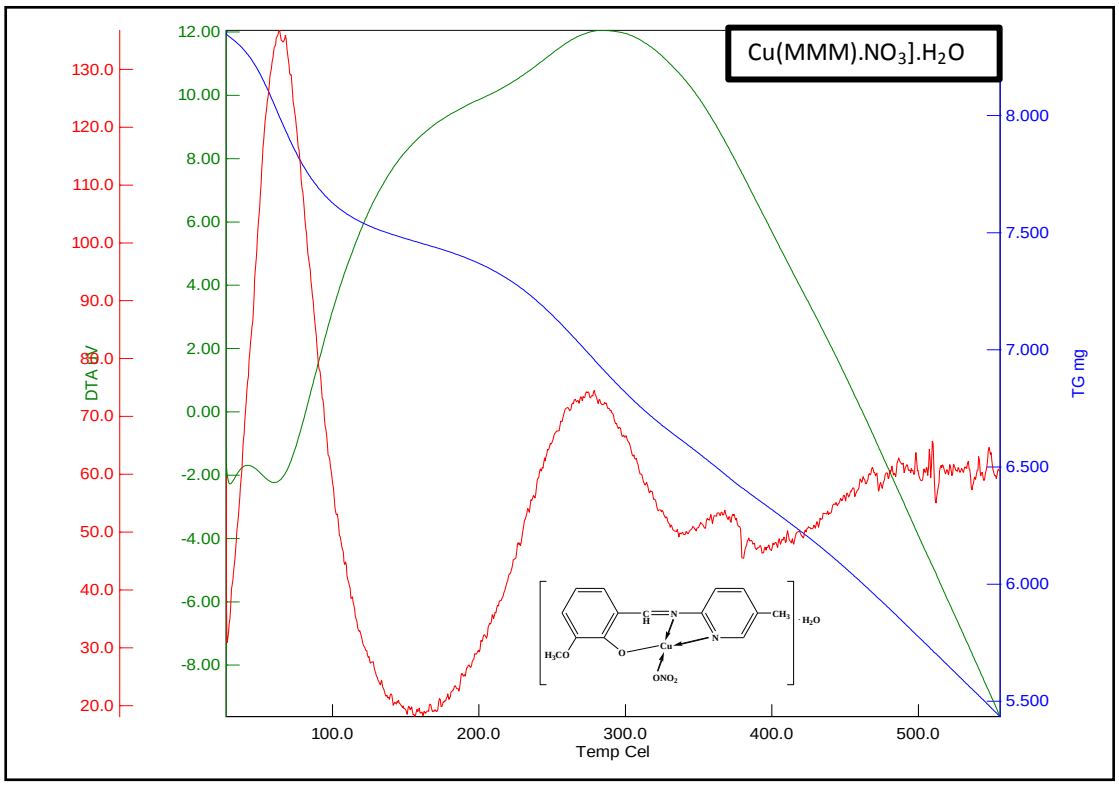



**Figure 4.13: TG-DT analysis of metal complex[Ni(MMM)$NO_3$]$H_2O$**

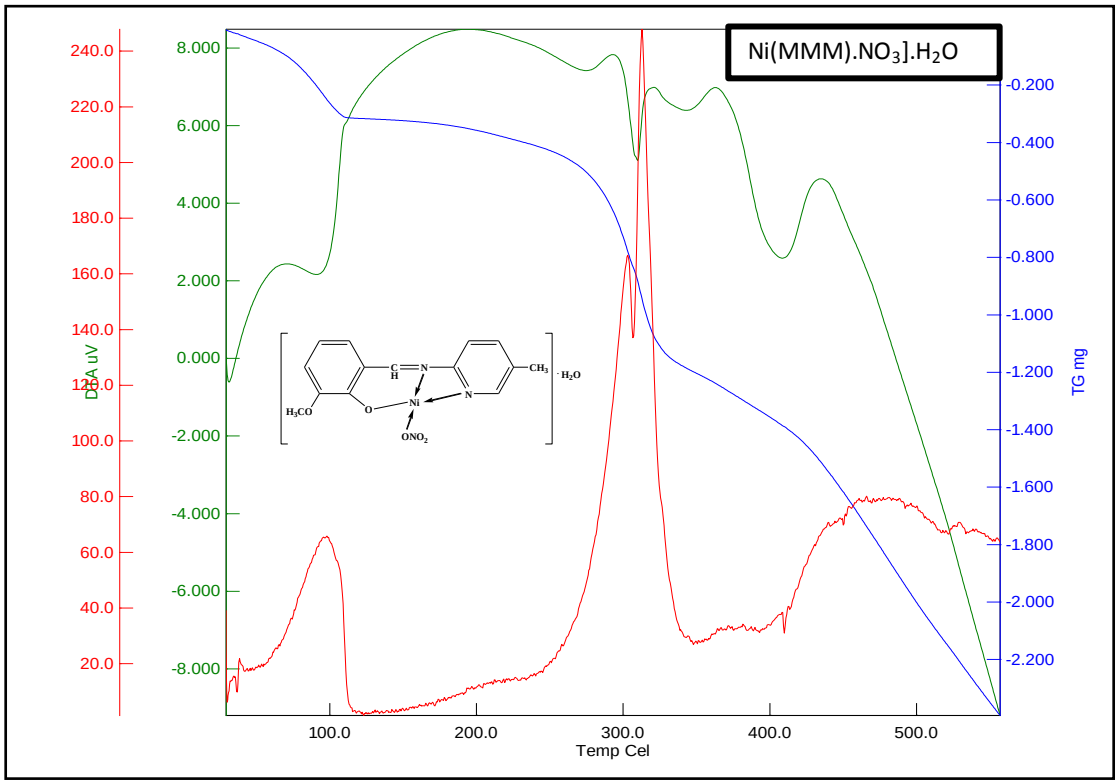



**Figure 4.14: TG-DT analysis of metal complex[Cu(BMM)$NO_3$]$H_2O$**

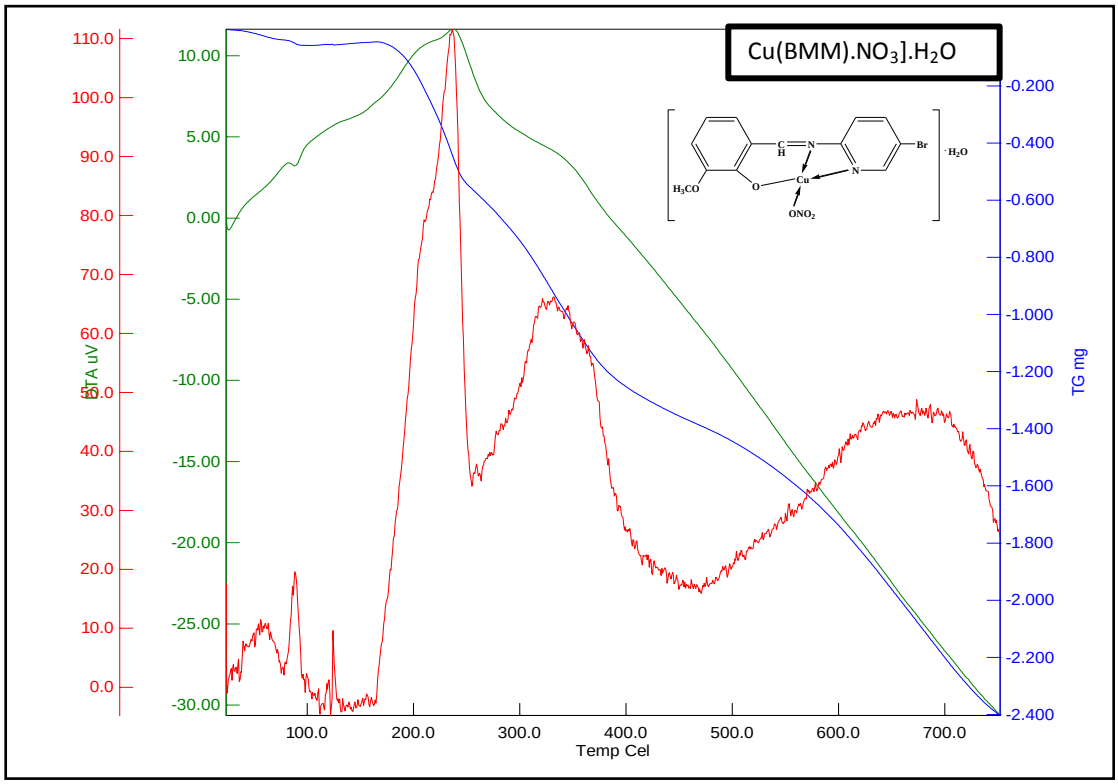
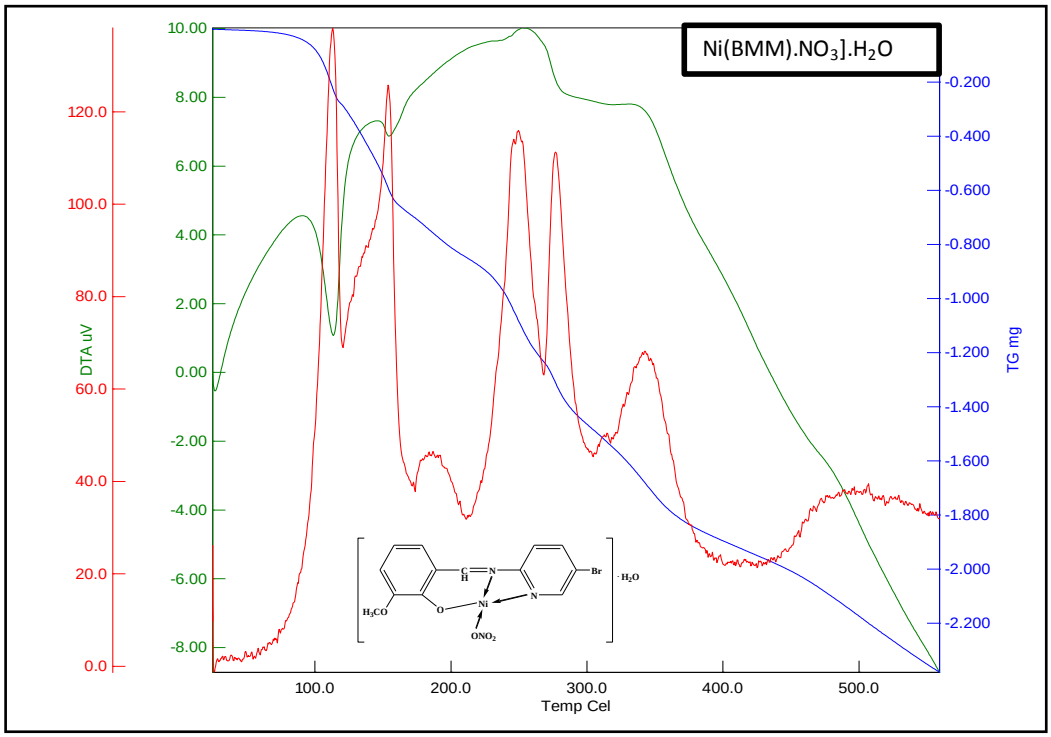



**Figure 4.15: TG-DT analysis of metal complex[Ni(BMM)$NO_3$]$H_2O$**




### 4.4.7 UV – Visible Spectral studies

Electronic spectra of all the complexes were recorded in dimethylformamide (DMF). For square planer Cu(II), the expected transition is $^{2}B_{1g} \rightarrow {}^{2}A_{1g}$ with absorption at 450-460 nm. Due to Jahn–Teller (J-T) distortions, square planar Cu(II) complexes give a broad absorption between 600 and 700nm and the peak at 450–460 nm merges with the broad band and thus only one broad band is observed [368]. The Ni(II) complexes showed one strong band at 435-445 nm, which is assigned to the square planar $^{1}A_{1g} \rightarrow {}^{1}A_{2g}$ transition.

### 4.4.8. Conductivity

The observed molar conductance of the metal(II) complexes in $10^{-3}$M DMF solution are in the range 8-19 $\Omega^{-1}$ $cm^{2}$ $mol^{-1}$. The molar conductance values are consistent with the non-electrolytic nature for all metal complexes [368].

### 4.4.9. Magnetic measurement

Magnetic moment measurements of all Cu(II) complexes show magnetic moment in the range of 1.80-1.94 BM, which corresponds to one unpaired electron and is expected from mononuclear Cu(II) complexes ($d^{9}$) with some orbital contribution. The magnetic moment values of the copper complexes correspond to the spin only value of 1.73 BM for the Cu(II) complexes. The magnetic moment values of

Ni(II) complexes is between 2.80-2.90 BM which is also corresponds to NI(II) calculated value 2.82 [369-370].

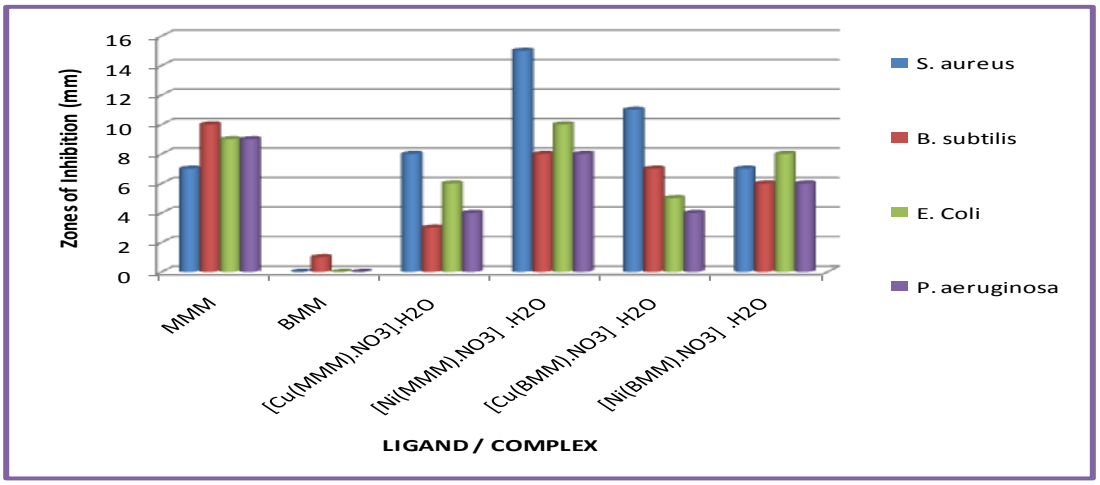
**4.5Antimicrobial activity**

Antimicrobial activity of the ligands and the metal complexes were evaluated against the *Staphylococcus aureus, Bacillus subtilis, Escherichia coli & Pseudomonas aeruginosa*. Metal complexes show better inhibition as compared to their ligands. BMM ligand does not show antibacterial activity. While Cu(II) and Ni(II) complexes of this ligand show remarkable antibacterial activity. It might be due to complexation of metal ions with Schiff base ligand. Such metal complexes might be inhibiting the enzyme activity of the bacterial system. MMM ligand and their metal complexes both show good antibacterial activity, which suggests the ligand inhibits the enzymes of the bacterial system. Antibacterial activity of the ligands and complexes were quite comparable to the standard drugs [371-373].(Table 4.6 & Figure 4.16)

**Table 4.6: Antibacterial activity of Schiff base ligands and their metal complexes**

| **Ligand/complex** | **Microbial species (Zone of Inhibition in mm)** | | | |
|---|---|---|---|---|
| | *S. aureus* | *B. subtilis* | *E. Coli* | *P. aeruginosa* |
| MMM | 7 | 10 | 9 | 9 |
| BMM | - | 1 | - | - |
| $[Cu(MMM)\cdot NO_3]\cdot H_2O$ | 8 | 3 | 6 | 4 |
| $[Ni(MMM)\cdot NO_3]\cdot H_2O$ | 15 | 8 | 10 | 8 |
| $[Cu(BMM)\cdot NO_3]\cdot H_2O$ | 11 | 7 | 5 | 4 |
| $[Ni(BMM)\cdot NO_3]\cdot H_2O$ | 7 | 6 | 8 | 6 |

**Figure 4.16: Antibacterial activity chart of ligands and metal complexes**




**4.6 Conclusion**

Schiff bases of 2-amino-5-methylpyridine (MMM) and 2-amino-5-bromopyridine were synthesized. The crystal structure of MMM was determined by X-ray crystallographic method and both ligands were analysed by other methods such as NMR, IR and mass spectroscopy. The Cu(II) and Ni(II) complexes of both theses ONN donor ligands were prepared and characterized by elemental analysis, conductivity measurement, thermo-gravimetric analysis, IR, UV and Mass spectroscopy. The biological activity of both ligands and complexes were examined by using both Gram positive and Gram negative bacterial species. Both ligands and complexes were found to exhibit antibacterial activity with some complexes showing increased antibacterial activity compared to the respective ligands.

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