



Metal complexes of 3-(4-Bromophenyl)-3-morpholino-1-phenylpropan-1-one: Their synthesis and characterization

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Abstract : This research paper deals with the synthesis, characterization and antimicrobial studies of a N-Mannich base, 3-(4-bromophenyl)-3-morpholino-1-phenylpropan-1-one and its complexes with variety of transition metals such as Mn(II), Co(II), Ni(II), Cu(II) and Zn(II). The new Mannich base ligand was prepared by the condensation reaction of 4-bromobenzaldehyde, morpholine and acetophenone. The ligand and its metal complexes were characterized using various analytical (Elemental analysis, TLC and Cyclic voltammetry) and spectral studies (FT-IR, UV-Visible, ¹H NMR, and ¹³C NMR). Synthesized ligand and its metal complexes were screened for their potential in antimicrobial activities.

Keywords : Nucleophilic addition reaction, N-Mannich base, transition metal complexes, potential parameters, antimicrobial studies.

1. Introduction

N-Mannich bases play pivotal role in chemical and synthetic organic industries. They also exhibit a broad range of biological activities including antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral, and antipyretic properties¹. The potentiality in biological activities is highly enhanced through the multidentate coordination behavior. Hence, the need for the synthesis of such complexes with a number of transition metals, characterization and biological activities assume paramount importance in the field of medicinal organic chemistry.^{2,3,4,5} Besides, N-Mannich ligands were also encountered with special attention because of their role as catalysts in several reactions such as polymerization reaction, reduction of thionyl chloride, oxidation of organic compounds, reduction reaction of ketones, aldol reaction and epoxidation of alkenes.

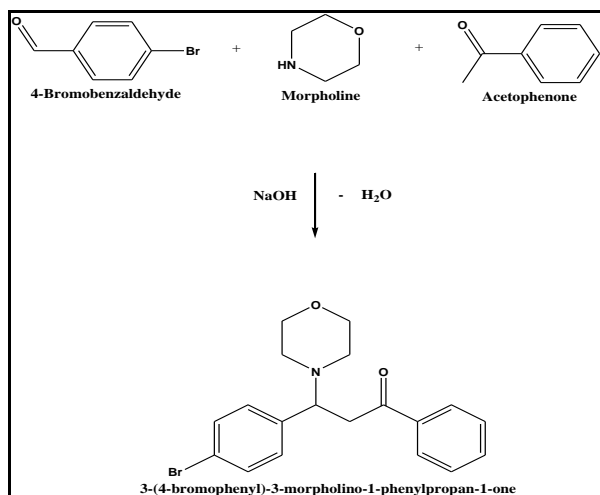
A probe into the literature survey clearly reveals that 4-bromobenzaldehyde, morpholine and acetophenone were not condensed for synthesizing N-Mannich base which augmented our interest for taking these combinations. Hence, we report the synthesis, characterization and antimicrobial studies of a N-Mannich base, 3-(4-bromophenyl)-3-morpholino-1-phenylpropan-1-one and its complexes with a variety of transition metals such as Mn(II), Co(II), Ni(II), Cu(II) and Zn(II).

2. Experimental Methods

All the chemicals were of AR grade and used without further purification unless otherwise stated. All the aromatic aldehydes were obtained from Avra Synthesis Pvt. Ltd., Hyderabad. Melting points of all the compounds were determined in open capillaries and are uncorrected. The homogeneity of compounds was checked by TLC on silica gel 'G' coated glass plates. IR spectra were recorded in KBr on Shimadzu FT-IR 8300 spectrometer and ¹H NMR and ¹³C NMR spectra were recorded in Varian 400 MHz and Bruker Advance II instruments in DMSO-d₆ medium employing TMS as an internal standard. Biological studies were carried out by disc diffusion method with proper incubation.

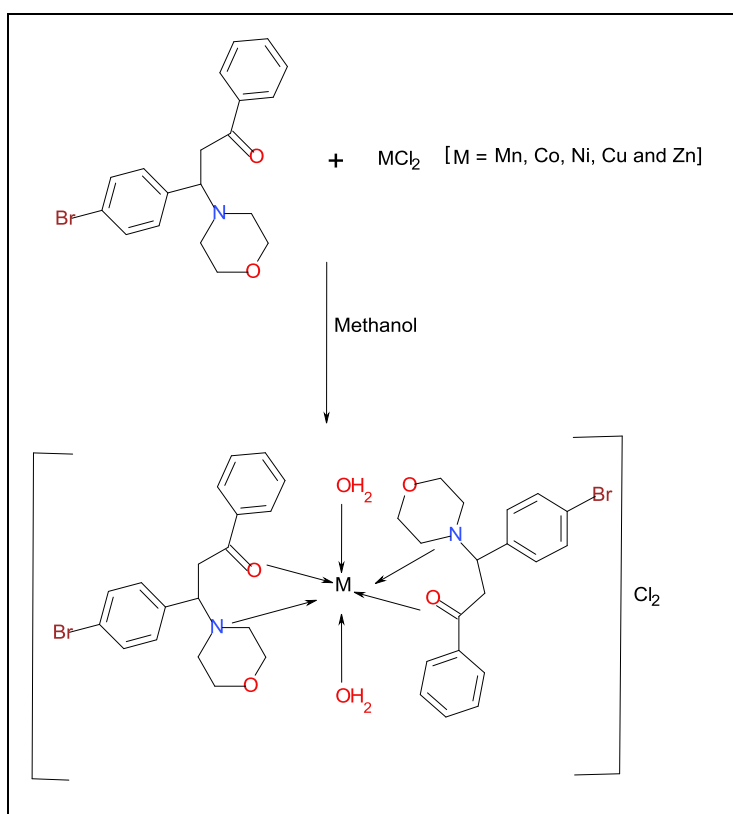
2.1 Synthesis of 3-(4-Bromophenyl)-3-morpholino-1-phenylpropan-1-one (BMA)

4-Bromobenzaldehyde, morpholine and acetophenone were taken in 1:1:1 ratio. 1 g of 4-bromobenzaldehyde was taken in a round bottom flask and 10 mL of ethanol was added. To this solution 0.5 mL of morpholine in ethanol was added and stirred well for 15 min by keeping the reaction mixture on a magnetic stirrer. The solution was made to alkali by adding NaOH pellets. To this solution 0.6 mL of acetophenone in ethanol was added and stirred. Stirring was continued under ice cold condition for about 30 minutes. The compound formed was filtered, washed and recrystallized using ethanol in hot condition (Scheme-1).



Scheme-1 - Synthesis of 3-(4-Bromophenyl)-3-morpholino-1-phenylpropan-1-one (BMA)

2.2 Synthesis of transition metal complexes of 3-(4-Bromophenyl)-3-morpholino-1-phenylpropan-1-one (M-BMA)



Scheme-2 Synthesis of transition metal complexes of 3-(4-Bromophenyl)-3-morpholino-1-phenylpropan-1-one (M-BMA)

A solution of 0.1M of MCl_2 (M=Mn, Co, Ni, Cu and Zn) in methanol and 0.2M of 3-(4-bromophenyl)-3-morpholino-1-phenylpropan-1-one in methanol were added to a round bottom flask and stirred well using magnetic stirrer for an hour (Scheme-2). The complex formed was filtered, washed with distilled water and crystallized from absolute alcohol.

2.3 Biological Activities

Antimicrobial activity for the 3-(4-bromophenyl)-3-morpholino-1-phenylpropan-1-one and its complexes were carried out by disk diffusion technique^{6,7} against the test microorganisms *Staphylococcus aureus* (gram +ve), *Bacillus subtilis* (gram +ve), *Salmonella paratyphi* (gram -ve), *Escherichia coli* (gram -ve) and fungi *Candida albicans* and *Aspergillus niger*. *Ciproflaxacin* and *Clotrimazole* were used as standards for antibacterial and antifungal studies respectively.

2.3.1 Anti-bacterial study

To study the antibacterial activity, nutrient agar was used as a medium. This was prepared by dissolving 5g of yeast extract, 10 g of meat extract, 5 g of peptone, 5 g sodium chloride and 20 g of agar in 100 mL of distilled water in a clean conical flask and the pH was maintained at 7. The solution was boiled to dissolve the medium completely and sterilized. After sterilization, 20 mL media was poured into the sterilized petri plates. These petri dish plates were kept at room temperature for some time. Bacterial inocula containing approximately 10^5 - 10^6 CFU/ml was spread on the surface of the nutrient agar. The recommended concentration of the test sample (100 mg/mL in DMSO) was introduced in the respective wells. Other wells supplemented with DMSO and standard antibacterial drug *Ciproflaxacin*. The plates were incubated at 37°C for 24 h. During this period the test solution diffused and affected the growth of the inoculated microorganisms. A zone was developed on the plate and the inhibition zones were measured by measuring the diameter of inhibited zone in mm. The zone of inhibition values are presented in Table-7 for the classification of the compounds under study.

In order to clarify any participating role of DMSO in the bacterial screening, separate studies were carried out with pure solvent, DMSO and showed no activity against any bacterial strains. In addition to this, a distinct study was also carried out against all the metal salt solutions individually. No appreciable activity was recorded by the individual metal ions.

2.3.2 Antifungal study

The potato dextrose agar (PDA) was used as a medium for antifungal activity. The PDA was prepared by dissolving 20 g of potato extract, 20 g of agar and 20 g of dextrose in one liter of distilled water in a clean conical flask. The solution was boiled to dissolve the media completely and sterilized. After sterilization, 20 mL of media was poured into the sterilized petri plates. These petri plates were kept at room temperature for some time. After a few minutes, the medium got solidified in plate. 0.5 mL of DMSO was used as solvent and 10 µg of *Clotrimazole* as control. It was also done by the same antibacterial activity procedure corresponding with antifungal drug *Clotrimazole* as standard. The zone of inhibition values are presented in Table-8 for the classification of the compounds under study.

3. Results and Discussion

3.1 Elemental Analysis

The elemental analysis data confirms the proposed molecular formula as $C_{19}H_{20}BrNO_2$ for the synthesized Mannich base ligand 3-(4-bromophenyl)-3-morpholino-1-phenylpropan-1-one. The results of elemental analyses show 1:2 (metal: Ligand) stoichiometry for all the complexes with Mn, Co, Ni, Cu and Zn, which confirms the suggested general formula as $[C_{38}H_{44}Br_2O_6N_2M]Cl_2$. The analytical data of ligand and the complexes are given in Table-1. The presence of Chloride ion was confirmed by $AgNO_3$ test. The high molar conductance of the chelates in DMF supports the electrolytic nature of metal complexes^{8,9}.

Table - 1 Physical properties, molar conductance and elemental analysis of BMA and its metal complexes M-BMA

| Compounds | Molecular formula | Molecular weight | Melting point | conductance $\times 10^{-3}$, $\text{ohm}^{-1} \text{cm}^{-2}$ | Elemental analysis % Found (% Calculated) | | | |
|------------|---|------------------|---------------|---|---|----------------|----------------|------------------|
| | | | | | C | H | N | O |
| BMA | $\text{C}_{19}\text{H}_{20}\text{BrNO}_2$ | 373 | 264.7 | - | 60.88 (60.97) | 5.47 (5.39) | 3.68 (3.74) | 8.57 (8.55) |
| Mn(II)-BMA | $[\text{C}_{38}\text{H}_{44}\text{Br}_2\text{O}_6\text{N}_2\text{Mn}]\text{Cl}_2$ | 907.03 | 286 | 204 | 49.82 (50.13) | 4.64 (4.87) | 2.90 (3.08) | 10.30 (10.54) |
| Co(II)-BMA | $[\text{C}_{38}\text{H}_{44}\text{Br}_2\text{O}_6\text{N}_2\text{Co}]\text{Cl}_2$ | 914.41 | 310 | 179 | 49.82 (49.91) | 4.94 (4.85) | 2.92 (3.06) | 10.70 (10.50) |
| Ni(II)-BMA | $[\text{C}_{38}\text{H}_{44}\text{Br}_2\text{O}_6\text{N}_2\text{Ni}]\text{Cl}_2$ | 910 | 286 | 186 | 49.82 (49.93) | 4.64 (4.85) | 2.90 (3.06) | 10.30 (10.51) |
| Cu(II)-BMA | $[\text{C}_{38}\text{H}_{44}\text{Br}_2\text{O}_6\text{N}_2\text{Cu}]\text{Cl}_2$ | 919 | 310 | 169 | 49.82 (49.66) | 4.94 (4.83) | 2.98 (3.05) | 10.70 (10.45) |
| Zn(II)-BMA | $[\text{C}_{38}\text{H}_{44}\text{Br}_2\text{O}_6\text{N}_2\text{Zn}]\text{Cl}_2$ | 920 | 310 | 169 | 49.82 (49.56) | 4.94 (4.86) | 2.98 (3.04) | 10.70 (10.49) |

3.2 FT-IR spectra

The data obtained from the IR spectrum revealed the structural relationship among the constituent atoms and group (Fig-1). The formation of complex was also witnessed by the IR spectrum. IR frequencies corresponding to the respective vibrations are summarized in Table-2. The coordination sites were confirmed by comparing the IR spectrum of ligand and its complexes.

The normal $\nu_{\text{C-H}}$ of alkanes and aromatics are in the range of $3150\text{-}2850 \text{ cm}^{-1}$. The characteristic IR band observed at 3056 cm^{-1} is attributed to the $\nu_{\text{ArC-H}}$. The band appeared at 2922 cm^{-1} is assigned to $\nu_{\text{AliC-H}}$. The $\nu_{\text{C=O}}$ was confirmed by the band observed at 1655 cm^{-1} . The band for $\nu_{\text{C-N}}$ was found at 1109 cm^{-1} . The band retrieved at 1109 cm^{-1} is due to ν_{CNC} of morpholine moiety. The $\nu_{\text{C=O}}$ of the ligand in complex was found at 1606 cm^{-1} which has been shifted from 1655 cm^{-1} indicated the involvement of oxygen atom of carbonyl group of acetophenone with the metal ions. The ν_{CNC} of morpholine lowered by 11 cm^{-1} in the spectra of the complexes suggesting the coordination is through N atom of morpholine. These changes were further advocated by a medium intensity band observed in the range 533 cm^{-1} and 490 cm^{-1} for all the complexes are due to the $\nu_{\text{M-O}}$ and $\nu_{\text{M-N}}$ respectively^{10,11,12}. The above discussions clearly indicate that the nature of the free Mannich base is bidentate and coordination occurs through O and N atoms of the ligand to the metal ions.

Table - 2 Characteristic IR bands (cm^{-1}) of BMA and its metal complexes

| Entry | Compound | Band assignment, cm^{-1} | | | | | | | |
|-------|----------|-----------------------------------|-----------------------|--------------------|----------------------|----------------------|--------------------|--------------------|----------------------------|
| | | ν_{Ar} | $\nu_{\text{Ali-CH}}$ | $\nu_{\text{C=O}}$ | $\nu_{\text{C-N-C}}$ | $\nu_{\text{C-O-C}}$ | $\nu_{\text{M-N}}$ | $\nu_{\text{M-O}}$ | $\nu_{\text{H}_2\text{O}}$ |
| 1. | BMA | 3056 | 2922 | 1655 | 1109 | 1324 | --- | --- | - |
| 2. | Mn-BMA | 3056 | 2925 | 1600 | 1104 | 1326 | 489 | 532 | 3371 |
| 3. | Co-BMA | 3055 | 2925 | 1605 | 1098 | 1326 | 490 | 534 | 3432 |
| 4. | Ni-BMA | 3055 | 2926 | 1606 | 1098 | 1329 | 491 | 533 | 3432 |
| 5. | Cu-BMA | 3055 | 2922 | 1600 | 1070 | 1326 | 488 | 532 | 3340 |
| 6. | Zn-BMA | 3054 | 2872 | 1603 | 1093 | 1320 | 488 | 531 | 3466 |

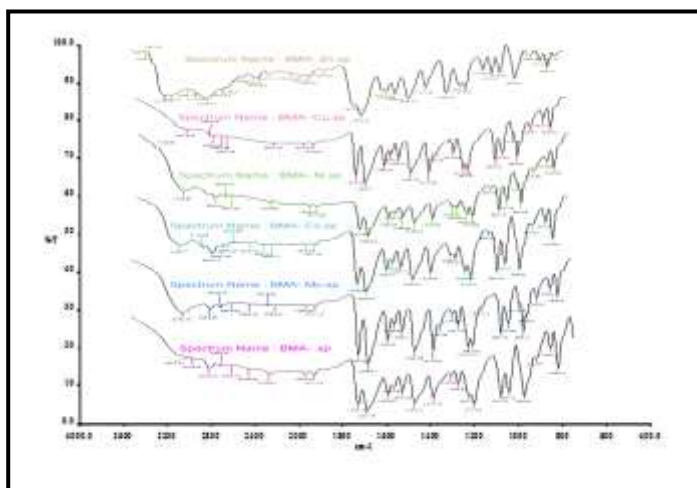


Figure - 1 FT-IR spectrum of BMA and its metal complexes

3.3 Electronic spectra

The electronic absorption spectra supported the results furnished by other analytical and spectral methods of structural investigation (Fig-2). The electronic spectral measurements were used for assigning the structural relationships among the constituent groups of metal complexes based on the position and number of d-d transition peaks ^{7,8,9}. The electronic absorption spectra of BMA and its Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) complexes were recorded at room temperature using DMSO as solvent and in the wavelength range of 250-900 nm. The intensity of absorption and its corresponding electronic transitions ^{13,14,15,16} are summarized in the Table-3.

Table-3 UV-Vis. Spectral and magnetic data of the pure ligand BMA and its metal complexes

| Entry | Compounds | Absorption | | Transition | Magnetic moment (BM) | Geometry |
|-------|-------------|------------|------------------|---|----------------------|------------|
| | | nm | cm ⁻¹ | | | |
| 1. | BMA | 256.4 | 39,002 | - | - | - |
| | | 319.5 | 31,299 | | | |
| 2. | Mn (II)-BMA | 256.4 | 39,002 | ⁶ A _{1g} → ⁴ E _{1g} , | 5.92 | Octahedral |
| | | 318.3 | 31,417 | ⁶ A _{1g} → ⁴ T _{2g} | | |
| 3. | Co (II)-BMA | 256.4 | 39,002 | ⁴ T _{1g} (F) → ⁴ T _{2g} (P) | 3.84 | Octahedral |
| | | 312.1 | 32,041 | ⁴ T _{1g} (F) → ⁴ A _{2g} (F) | | |
| | | 360.4 | 27,747 | ⁴ T _{1g} → ⁴ T _{2g} (F) | | |
| 4. | Ni (II)-BMA | 256.4 | 39,002 | $\pi \rightarrow \pi^*$ | 2.86 | Octahedral |
| | | 263.8 | 37,908 | ³ A _{2g} (F) → ³ T _{1g} (F) | | |
| | | 308.4 | 32,425 | ³ A _{2g} (F)→ ³ T _{1g} (P) | | |
| 5. | Cu (II)-BMA | 256.4 | 39,002 | $\pi \rightarrow \pi^*$ | 2.74 | Octahedral |
| | | 313.3 | 31,918 | | | |
| | | 361.7 | 37,647 | n→ π^* | | |
| 6. | Zn (II)-BMA | 256.4 | 39,002 | $\pi \rightarrow \pi^*$ | 0 | Octahedral |
| | | 320.8 | 31,172 | n→ π^* | | |

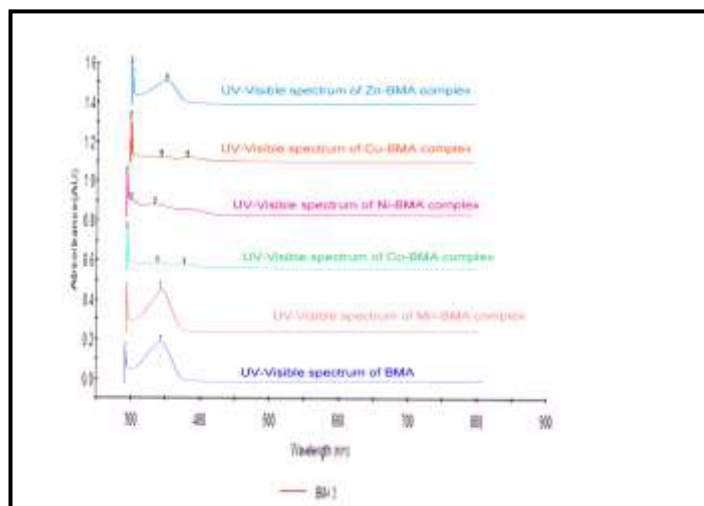


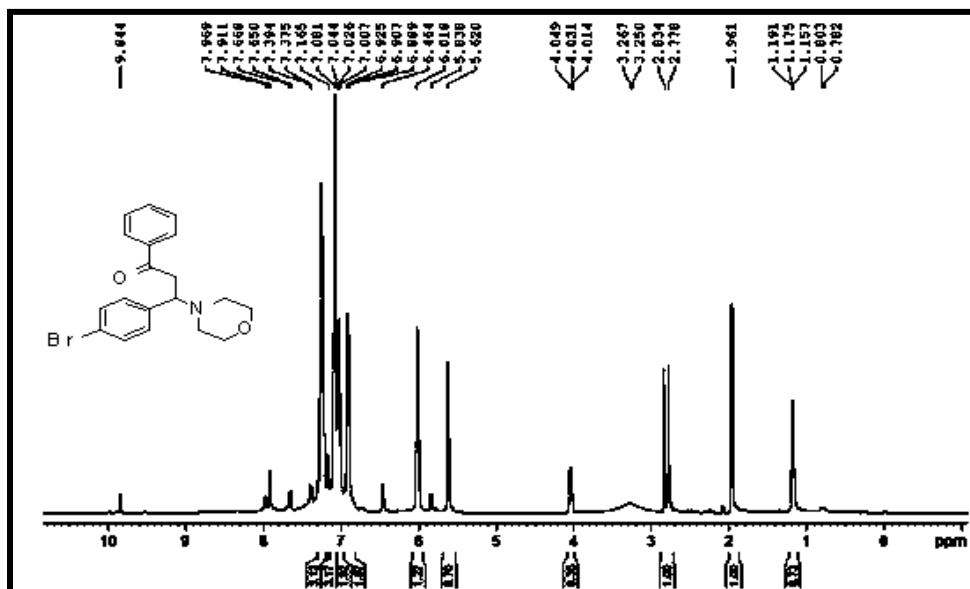
Figure - 2 UV-Visible spectrum of BMA and its metal complexes

3.4 ^1H NMR spectra

^1H NMR spectrum of the ligand was recorded in DMSO- d_6 medium using TMS as an internal standard. The spectrum of the compound is shown in Figure-3. The shift values and the corresponding assignments are summarized in the Table-4.

Table-4 ^1H NMR spectral data and assignments

| S.No. | δ in ppm | Peak | Proton |
|-------|-----------------|----------------|-----------------------------|
| 1. | 7.91 | Doublet (2H) | Br-substitute ring (m) |
| 2. | 7.02 | Doublet (2H) | Br-substituted ring (o) |
| 3. | 7.86 | Doublet (2H) | Acetophenone (o) |
| 4. | 7.37 | Doublet (2H) | Acetophenone (m) |
| 5. | 7.65 | Multiplet (1H) | Acetophenone (p) |
| 6. | 3.25 | Doublet (2H) | CH_2 protons |
| 7. | 4.04 | Triplet (1H) | CH proton |
| 8. | 2.03 | Triplet (4H) | $\text{CH}_2\text{-N-CH}_2$ |
| 9. | 3.26 | Triplet (4H) | $\text{CH}_2\text{-O-CH}_2$ |

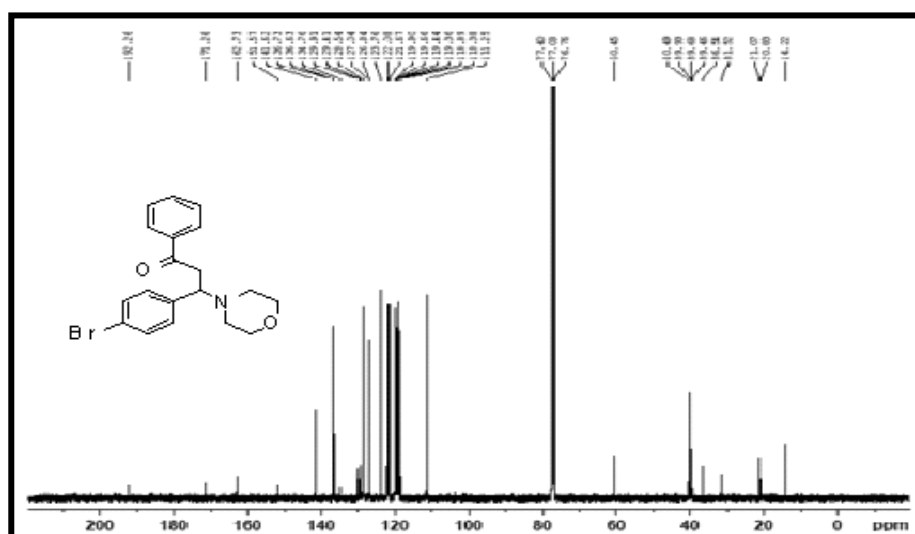
Figure-3 ^1H NMR spectrum of BMA

3.5 ^{13}C NMR spectra

^{13}C NMR spectrum of the synthesized compound was recorded in DMSO- d_6 medium using TMS as an internal standard. The spectrum of the compound is shown in Figure-4. The shift values and the corresponding assignments are summarized in the Table-5.

Table - 5 ^{13}C NMR spectral data and assignments

| S.No. | δ in ppm | No. of | Carbon |
|-------|-----------------|--------|-----------------------------|
| 1. | 134.75 – 134.34 | 4 C | Br-substituted ring (o & m) |
| 2. | 119.75 | 1 C | Br-substituted ring |
| 3. | 136.20 | 1 C | Br-substituted ring |
| 4. | 129.53 – 129.34 | 4 C | Acetophenone (o & m) |
| 5. | 129.80 | 1 C | Acetophenone (p) |
| 6. | 136.80 | 1 C | Acetophenone |
| 7. | 192.24 | 1 C | Carbonyl carbon |
| 8. | 60.45 | 2 C | $\text{CH}_2\text{-O-CH}_2$ |
| 9. | 40.00 | 2 C | $\text{CH}_2\text{-N-CH}_2$ |
| 10. | 40.43 | 1 C | -CH- aliphatic |
| 11. | 36.53 | 1 C | CH_2 |

Figure-4 ^{13}C NMR spectrum of BMA

3.6 Cyclic Voltammetry

Cyclic voltammetry (CV) is an important electro analytical technique in many areas of chemistry. It is widely used to study a class of redox processes, for obtaining stability of reaction products, the presence of intermediates in oxidation-reduction reactions, reaction and electron transfer kinetics and the reversibility of a reaction^{17,18,19,20}. Cyclic voltammetric behaviors of complexes were recorded in the range from +1.5 to -1.5V in DMSO medium. The data obtained from cyclic voltammetry helped us to analyze the redox property of metals in synthesized complex. Complexes, Mn-BMA, Co-BMA, Ni-BMA, Cu-BMA and Zn-BMA showed reduction process and also found to be irreversible in nature (Fig. 15 - 19). The reduction and oxidation potentials are summarized in the Table – 6.

Table - 6 Cyclic Voltammogram data of M-BMA complexes

| Compounds | E _{red} 1/2(V) | E _{ox} 1/2(V) | E _p (V) |
|-------------|-------------------------|------------------------|--------------------|
| Mn (II)-BMA | 0.5891 | -0.9875 | -1.5766 |
| Co (II)-BMA | 0.7621 | -1.2617 | -2.0579 |
| Ni (II)-BMA | 0.2830 | -2.0113 | -2.2943 |
| Cu (II)-BMA | 0.9391 | -0.7011 | -1.6402 |
| Zn (II)-BMA | 0.4959 | -0.7704 | -1.2663 |

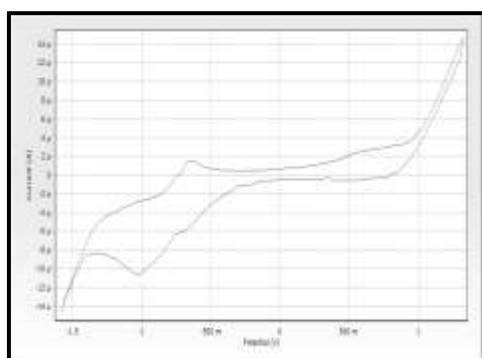


Figure-5 CV curve of Mn-BMA complex

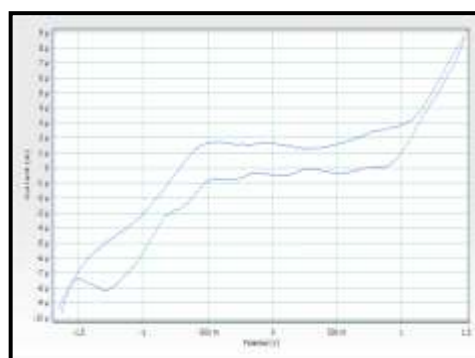


Figure-6 CV curve of Co-BMA complex

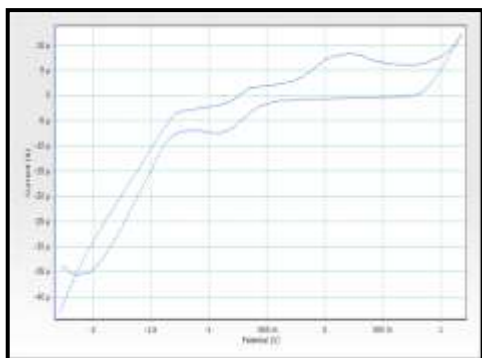


Figure-7 CV curve of Ni-BMA complex

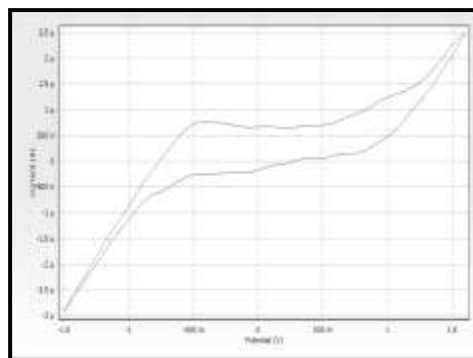


Figure-8 CV curve of Cu-BMA complex

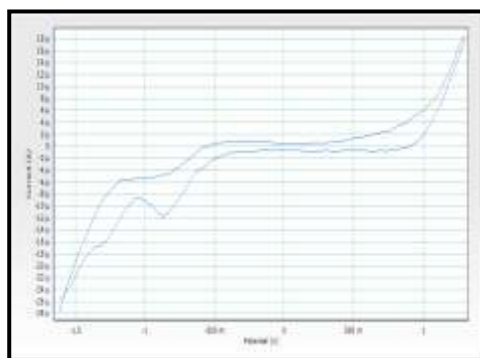


Figure-9 CV curve of Zn-BMA complex

3.7 Antibacterial activity

The prime focus on the production and synthesis of any antimicrobial compound is to inhibit the casual microbe without any side effect on the patients' metabolism. The antimicrobial activity of ligand and its metal complexes were done by in-vitro disc diffusion method in DMSO medium. The metal salts (MCl_2), ligands, metal complexes, the standard drug *Ciprofloxacin*, and the solvent DMSO were screened separately for their antibacterial activities at concentrations of 100 $\mu\text{g}/\text{disc}$, except the standard drug, which was tested at 10 $\mu\text{g}/\text{disc}$. The photographic plates of tested microorganisms are shown in Figure 10-13. The antibacterial activity was estimated on the basis of the size of inhibition zone formed on the seeded agar plates. Growth inhibition was compared with known antibiotics, viz. *Ciprofloxacin*. The N-Mannich base and the complexes exhibited varying degrees of inhibitory effects on the growth of the tested bacterial species.

As observed, the free ligand is moderately active against the bacterial species while the antibacterial activity of the N-Mannich base became more pronounced when it is coordinated to the metal ions. Referring to complexes, we note that the Co (II) complex is more active as compared with other complexes. In conclusion, the antibacterial activity of the complexes follow the order $\text{Co} > \text{Mn} > \text{Ni} > \text{Cu} = \text{Zn}$. Furthermore, the data show that *Staphylococcus aureus gram (+ve)* was inhibited to a greater degree by the Co (II) complex. The complexes prepared with N-Mannich base, 3-(4-bromophenyl)-3-morpholino-1-phenylpropan-1-one, derived from 4-bromobenzaldehyde, morpholine and acetophenone could reasonably be used for the treatment of some common diseases caused by *Staphylococcus aureus gram (+ve)*.

A greater antibacterial activity of metal complexes explained on the basis of Overtone's and Tweedy's concepts^{21,22,23}. According to Overtone's concept of cell permeability, the lipid membrane that surrounds the cell favors only the passage of lipid soluble materials, therefore lipo solubility is considered to be an important factor that controls the antibacterial activity. Drawing on chelation theory, Tweedy's concept explains the increase of lipophilic character of the metal chelate. Upon chelation, the positive charge of the metal ion is partially shared with the donor atom present on the ligand and a π -electron delocalization over the whole chelate ring takes place. In this way, the lipophilic character of the metal chelate increases and favors its permeation through the lipid layers of the bacterial membranes and blocks the metal binding sites in the enzymes of microorganisms²⁴. This penetration disturbs the respiration process of the cell and thus blocks the synthesis of proteins, which restricts further growth of the organisms²⁵.



Figure-10 Antibacterial activities of BMA and its complexes on *Staphylococcus aureus*



Figure-11 Antibacterial activities of BMA and its complexes on *Bacillus subtilis*



Figure-12 Antibacterial activities of BMA and its complexes on *Escherichia coli*



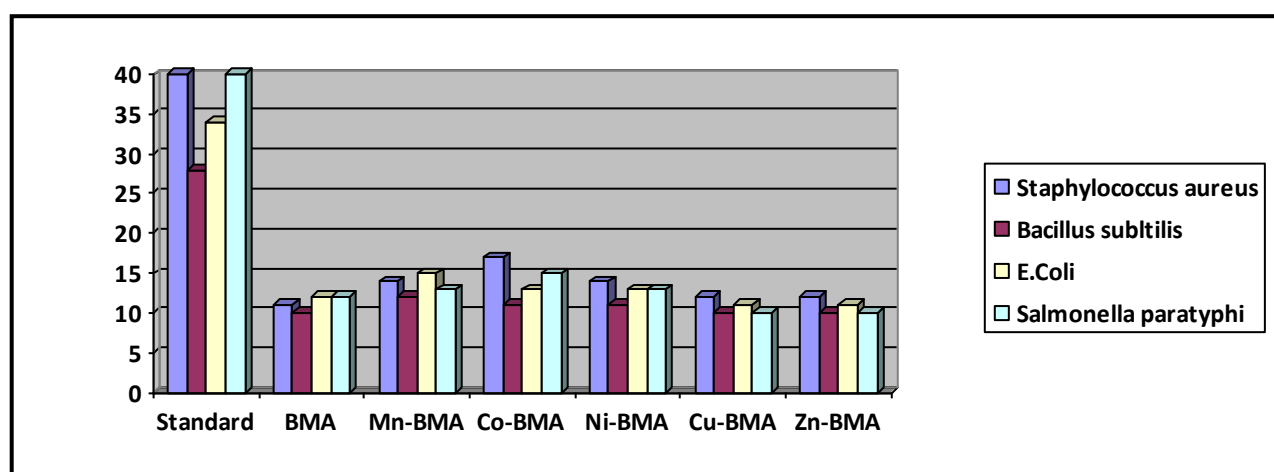
Figure-13 Antibacterial activities of BMA and its complexes on *Salmonella paratyphi*

Table-7 Antibacterial activity of BMA and its complexes

| Compounds | <i>Staphylococcus aureus</i> gram (+ve) | <i>Bacillus subtilis</i> gram (+ve) | <i>Escherichia coli</i> gram (-ve) | <i>Salmonella paratyphi</i> gram (-ve) |
|-----------------|---|-------------------------------------|------------------------------------|--|
| | Zone of Inhibition(mm) | | | |
| BMA* | 11 | 10 | 12 | 12 |
| Mn-BMA* | 14 | 12 | 15 | 13 |
| Co-BMA* | 17 | 11 | 13 | 15 |
| Ni-BMA* | 14 | 11 | 13 | 13 |
| Cu-BMA* | 12 | 10 | 11 | 10 |
| Zn-BMA* | 12 | 10 | 11 | 10 |
| Ciprofloxacin** | 40 | 28 | 34 | 40 |

(*100 µg/disc and **10 µg/disc)

The Table-7 reveals that the inhibition by Cobalt complex is higher than the other complexes. Chelate ring of Co enhances the lipophilicity of the complexes. This increased lipophilicity enhances the penetration of the complexes into lipid membrane and restricts further multiplicity of the microorganisms. The variation in the effectiveness of other complexes (Co>Mn>Ni>Cu=Zn) against different antibacterial organisms is not only depend on the nature of metal but also depends either on the impermeability of the cells of the microbes or on differences in ribosome of microbial cells. The smaller size of Co^{2+} , relative to that of other metals, reduces polarity and increases the lipophilicity of the bacterial membrane, interrupting normal cellular processes and enhancing the antifungal activity of Co^{2+} complex.

Graph-1 Comparative report on antibacterial activity of BMA and its complexes

3.8 Antifungal activity

The antifungal activities of the ligand and its complexes were studied against *Candida albican* and *Aspergillus niger*. The metal salts (MCl_2), ligands, metal complexes, the standard drug *Clotrimazole*, and the solvent DMSO were screened separately for their antifungal activities at concentrations of 100 µg/disc, except the standard drug, which was tested at 10 µg/disc. The photographic plates of tested microorganisms are shown in Figure 14-15. Fungal species were more resistant to treatments with the new complexes. However, our complexes showed activity against these two fungi strains. The results on antifungal activity of the ligands show moderate activity while the complexes show higher activity against the fungi. The Zn-BMA complex shows higher activity when compared to other complexes and the order of activity against the fungi follow the order Zn>Cu>Ni>Mn>Co.

Due to the greater solubility, Zn (II) ions are adsorbed on the surface of the cell wall of microorganisms and disturb the respiration process of the cell and thus block the synthesis of the proteins that restricts further growth of the organisms. So, Zn (II) ions are essential for the growth-inhibitor effect. Such increased activity of the complexes can be explained on the basis of Overtone's concept and Tweedy's Chelation theory. On

chelation, the polarity of Zn (II) 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 zinc ion with donor groups. Further, it increases the delocalization of π -electrons over the whole chelate ring and enhances the lipophilicity of the complexes. This increased lipophilicity enhances the penetration of the complexes into lipid membrane and restricts further multiplicity of the microorganisms.

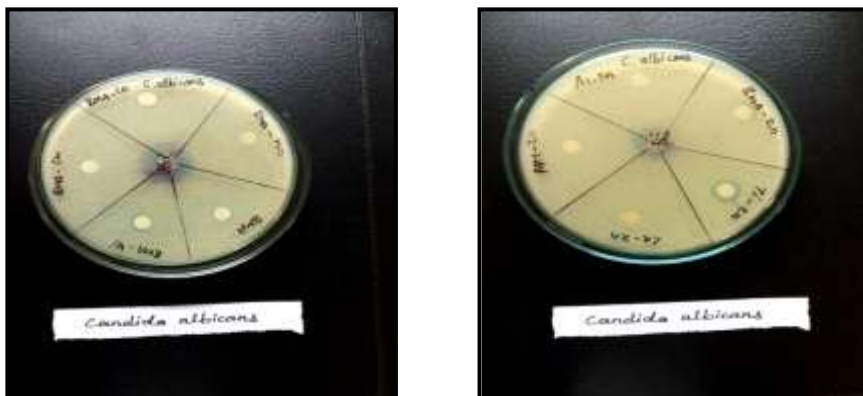


Figure-15 Antifungal activities of BMA and its complexes on *Candida albicans*

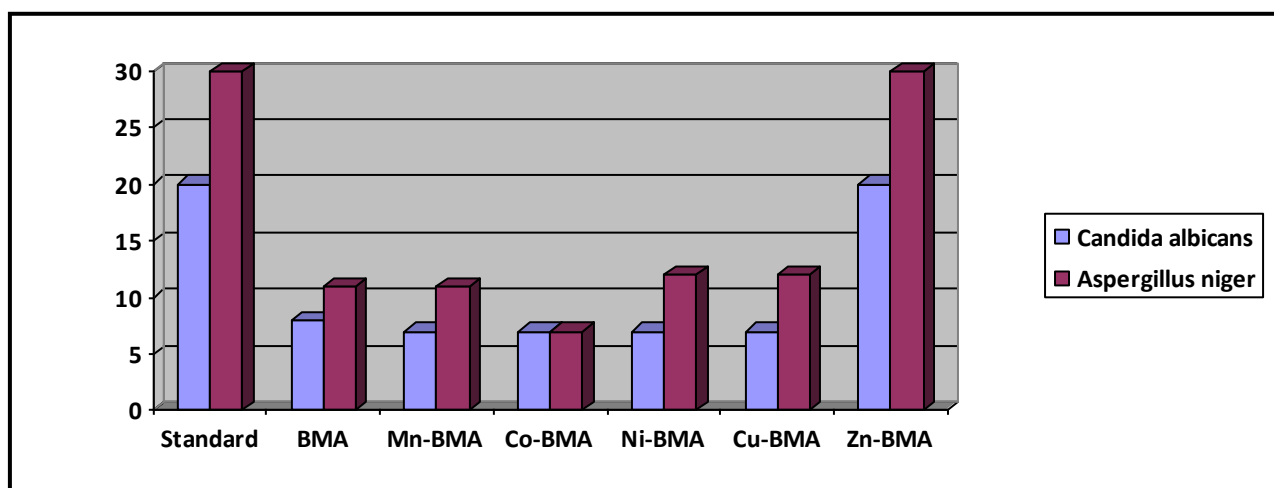


Figure-14 Antifungal activities of BMA and its complexes on *Aspergillus niger*

Table-8 Antifungal activity of BMA and its complexes

| Compounds | <i>Candida albicans</i> | <i>Aspergillus niger</i> |
|----------------|-------------------------|--------------------------|
| | Zone of Inhibition(mm) | |
| BMA* | 08 | 11 |
| Mn-BMA* | 07 | 11 |
| Co-BMA* | 07 | 07 |
| Ni-BMA* | 07 | 12 |
| Cu-BMA* | 07 | 12 |
| Zn-BMA* | 20 | 30 |
| Clotrimazole** | 20 | 30 |

(*100 μ g/disc and **10 μ g/disc)



Graph-2 Comparative report on anti-fungal activity of BMA and its complexes

4 Conclusions

Due to the dynamic nature of N-Mannich bases and its complexes, we have synthesized a N-Mannich base, 3-(4-bromophenyl)-3-morpholino-1-phenylpropan-1-one, derived from 4-bromobenzaldehyde, morpholine and acetophenone. The structural elucidation was done using a range of analytical and spectral studies. The potentiality against microorganisms triggered us to screen the complexes for antimicrobial activities. The complexes have shown greater tendency to prevent the growth of microorganism than the ligand, individual metal ions and medium. The Co-BMA complex has shown greater activity against bacteria than the other complexes. The smaller size of Co^{2+} , relative to that of other metals, reduces polarity and increases the lipophilicity of the bacterial membrane, interrupting normal cellular processes and enhancing the antifungal activity of Co^{2+} complex. The Zn-BMA complex has shown activity tremendously against fungi. The Zn (II) ions are adsorbed strongly on the surface of the cell wall of microorganisms and disturb the respiration process of the cell than the other metal ions, because of its higher solubility.

Thus it blocks the synthesis of the proteins that restricts further growth of the organisms. The Co (II) and Zn (II) complexes prepared with N-Mannich base, 3-(4-bromophenyl)-3-morpholino-1-phenylpropan-1-one, derived from 4-bromobenzaldehyde, morpholine and acetophenone could reasonably be used for the treatment of some common diseases caused by bacteria and fungi respectively.

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