

# A New Mannich Base and its transition metal(II) complexes - Synthesis, Structural Characterization, DNA Cleavage and Anti-oxidant Studies

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## Abstract:

A new Mannich base ligand formed by the condensation of tetrahydrocarbazole, phthalimide and *p*-dimethylaminobenzaldehyde and its complexation with transition metal ion Co(II), Ni(II) and Cu(II) are studied. The structures of the complexes have been elucidated on the basis of analytical chemistry, electrical conductivity and spectral study. The complexes were found to adopt square planar geometry. The molar conductance for the metal complexes reveals the nature of the complexes as 1:2 electrolyte. The <sup>1</sup>H NMR spectrum of the ligand was recorded in CDCl<sub>3</sub> and the mass spectrum of the ligand reveals the molecular weight of the ligand to be  $m/z = 435.03$ . The EPR spectrum of the Cu(II) Complex was recorded at 77 K which confirms the existence of the complexes in square planar geometry.

**Keywords:** Mannich base, tetrahydrocarbazole, phthalimide, *p*-dimethylaminobenzaldehyde, transition metal (II) complexes, spectral study, Anti-oxidant activity DNA cleavage study.

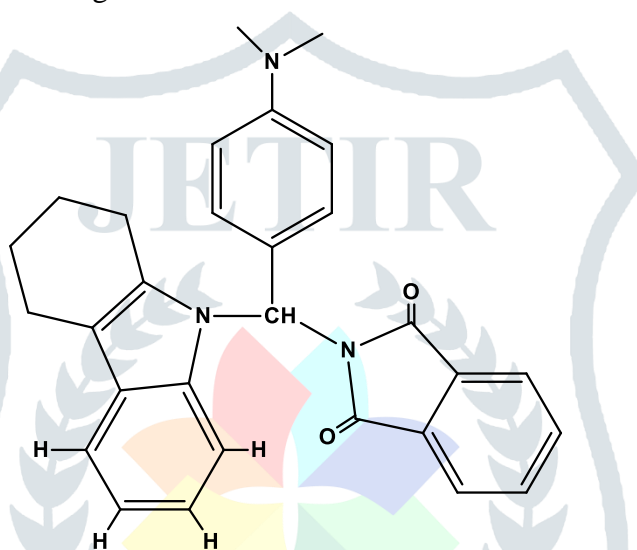
## 1.Introduction:

Metal complexes of Mannich bases have received special attention in the recent years due to their extensive applications in various areas such as analytical chemistry, therapeutic chemistry and utility in synthetic chemistry.<sup>1-4</sup> Mannich bases are the product of aminomethylation involving three-component condensation between compound with active hydrogen atom (phthalimide), aldehyde (*p*-dimethylaminobenzaldehyde) and secondary amine (tetrahydrocarbazole). In the field of therapeutics, metal complexes of Mannich base ligands are widely known for their potent anti-bacterial, anti-fungal, anti-oxidant, anti-cancer activity that are primarily derived from the synergistic action of the pharmacophore, that is Mannich base, in conjunction with the coordinating metal ion.<sup>5-7</sup>

Phthalimides represents organic compounds with imide functionality which can be regarded as the nitrogen analogue of anhydride as much as the diacyl derivative of ammonia and it is well-known in the field of therapeutics for various potent medicinal effects such as anti-convulsant, antimicrobial, hypoglycaemic, anti-inflammatory and anti-tumour activities.<sup>8-10</sup> A search through the literature reveals that no work has been done on the condensation of tetrahydrocarbazole, phthalimide and *p*-dimethylaminebenzaldehyde. In the present study, we have purposed to synthesise metal complexes of the Mannich base and to investigate its bonding characteristics.

## 2. Experiment:

All the reagents used for the preparation of the ligand and the complexes were obtained from Merck and were used as such without further purification. Spectroscopic grade solvents were used for the spectral measurements. The infrared spectra of the solid samples were recorded in JASCO/FT-IR 410 spectrometer in the range of 4000-400  $\text{cm}^{-1}$ . Potassium bromide disc method was employed for sample preparation. The  $^1\text{H}$  NMR spectrum of the ligand was recorded on Bruker-500 Spectrometer in  $\text{CDCl}_3$  solution. The mass spectrum of the ligand was recorded on ThermoExactiveOrbitrap Instrument. Molar conductance measurements were carried out in DMSO solvent using a Coronation digital Conductivity meter. The EPR spectra of the copper complex in DMSO were recorded at liquid nitrogen temperature on a Varian E-4 X-band spectrometer using DPPH as the g-marker.



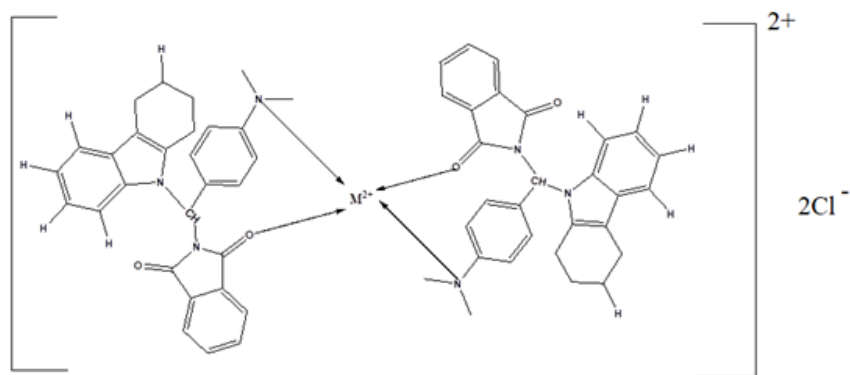
**Scheme 1.** Structure of the Mannich base ligand.

### 2.1 Synthesis of Mannich base:

Equimolar quantities of tetrahydrocarbazole, phthalimide and *p*-dimethylaminobenzaldehyde were taken as the starting materials. Tetrahydrocarbazole was mixed in 20 mL of methanol and then phthalimide and *p*-dimethylaminobenzaldehyde mixed in methanol were added dropwise in a round bottom flask. The contents of the flask were refluxed for 2-3 h. Then ice cubes were added to it, filtered, washed with ether and dried in vacuum desiccator over anhydrous calcium chloride. The proposed structure of the synthesized Mannich base is given in scheme 1.

### 2.2 Synthesis of Metal Complexes:

The Mannich base ligand (L) and the respective metal (II) chlorides were taken in the ratio of 2:1 to synthesize  $\text{ML}_2$  complexes. The mixture was dissolved in 20 mL of methanol and subjected to constant stirring for 1 h. It was then refluxed and the product obtained was then filtered, washed several times with ether and then dried in vacuum over anhydrous  $\text{CaCl}_2$ . The proposed structure of the complexes is given in scheme 2.



**Scheme 2.** The proposed structure of the metal (II) complexes

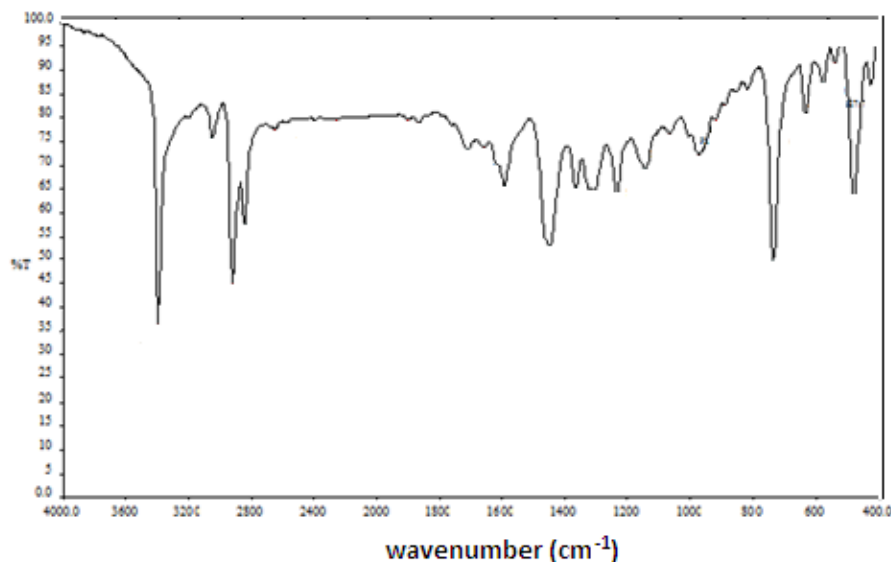
### 3. Results and Discussion:

The elemental analysis show 1:2 (M:L) stoichiometry for all the complexes. The analytical data of ligand and the complexes are given in table 1. They correspond well with the general formula  $ML_2$ , where M= Co(II), Ni(II) and Cu(II). L=  $C_{29}H_{27}N_3O_2$ . The presence of chloride outside the co-ordination sphere is evident from the Volhard's test. The high conductance of the chelates supports the electrolytic nature of the synthesized metal complex.

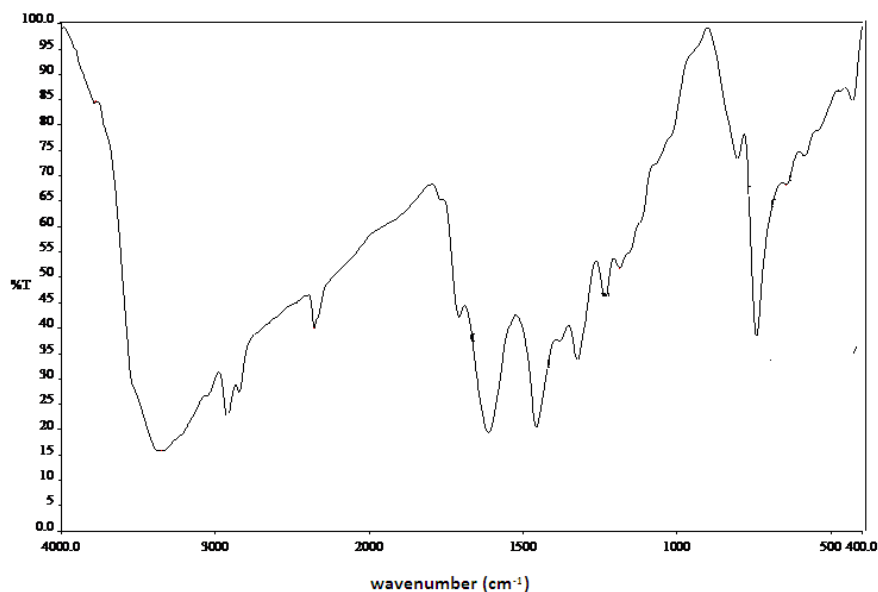
#### 3.1 Infrared Spectra:

The FT-IR spectrum of the Mannich base ligand is shown in Fig.1. The peak at  $3396\text{ cm}^{-1}$  is assigned to  $\nu_{(N-H)}$ . The spectrum of the ligand shows the band at  $1656\text{ cm}^{-1}$  which is assigned to  $\nu_{(C=O)}$ . In addition, at  $735\text{ cm}^{-1}$ , it shows the strong aromatic band. The band at  $1447.81\text{ cm}^{-1}$  is for ring C=C stretch. The bands at  $2924.49\text{ cm}^{-1}$ ,  $2847.10\text{ cm}^{-1}$  indicate the presence of cyclohexenyl moiety.

In order to study the binding mode of the Mannich base to the metal ion in the complexes, the IR spectrum of the free ligand (Mannich base) was compared with the spectra of the complex. The FT-IR spectrum of the Mannich cobalt complex is shown in Fig.2. The band at  $3351\text{ cm}^{-1}$  indicates the shifting of  $-NH$  group of the ligand from  $3396\text{ cm}^{-1}$ . The band at  $1656\text{ cm}^{-1}$  for  $\nu_{(C=O)}$  for the ligand has been shifted to  $1613\text{ cm}^{-1}$ .<sup>11,12</sup> Thus, it indicates the coordination of  $-NH$  and  $-C=O$  group of the ligand with the metal. It also shows the strong aromatic band at  $744\text{ cm}^{-1}$ .

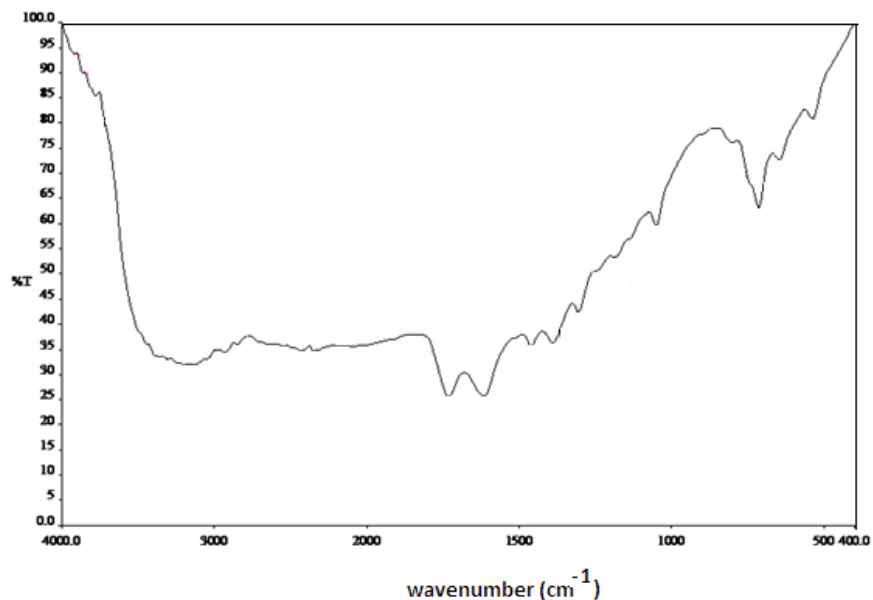


**Fig :1 FT IR Spectrum of the Mannich base ligand**



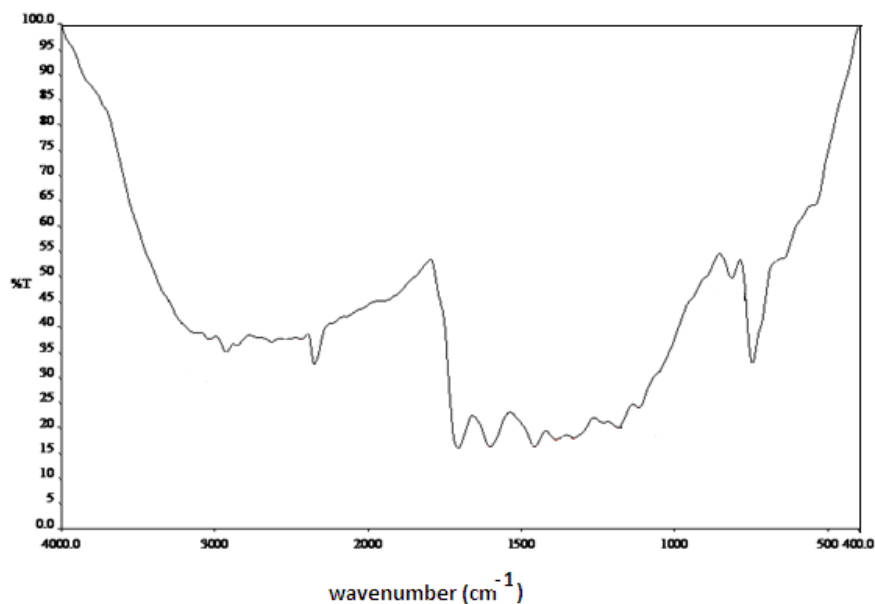
**Fig.2 FT-IR spectrum of the Mannich base derived cobalt complex**

The FT-IR spectra of Mannich base nickel complex is shown in Fig.3. The band at  $3396\text{ cm}^{-1}$  for the  $\text{NH}$  group of the ligand has been shifted to  $3359\text{ cm}^{-1}$ . The band at  $1617\text{ cm}^{-1}$  shows the shifting of  $\nu_{\text{C=O}}$  of the ligand.<sup>11,12</sup> Thus, the shifting indicates the coordination of the of the ligand with the metal. The bands at  $2934$  and  $2855\text{ cm}^{-1}$  are assigned for cyclohexenyl moiety.



**Fig.3 FT-IR spectrum of the Mannich base derived nickel complex**

The FT-IR spectrum of Mannich base copper complex is shown in Fig.4. The band at  $3041\text{ cm}^{-1}$  indicates the shifting of  $\nu(\text{N-H})$  of the ligand. The band at  $1656\text{ cm}^{-1}$  for  $\nu(\text{C=O})$  of the ligand has been shifted to  $1604\text{ cm}^{-1}$  signifying the coordination of ligand with the metal through the carbonyl group.<sup>11,12</sup> The bands at  $2927\text{ cm}^{-1}$  and  $2857\text{ cm}^{-1}$  indicates the presence of cyclohexane. The band at  $748\text{ cm}^{-1}$  confirms the presence of aromatic ring.



**Fig.4 FT-IR spectrum of Mannich base derived copper complex**

### 3.2<sup>1</sup>H NMR spectrum

The <sup>1</sup>H NMR spectrum of the ligand is shown in Fig.5. The multiplet observed in the range 7.8-7.05 ppm is due to protons in the aromatic moiety of the Mannich base ligand. The methyl (-CH<sub>3</sub>) protons exhibit signals at 2.7 ppm, the methylene(-CH<sub>2</sub>-) protons of cyclohexane exhibits signals at 1.8 ppm whereas the methine (-CH) protons in the ligand exhibit signals at 6.7 ppm.

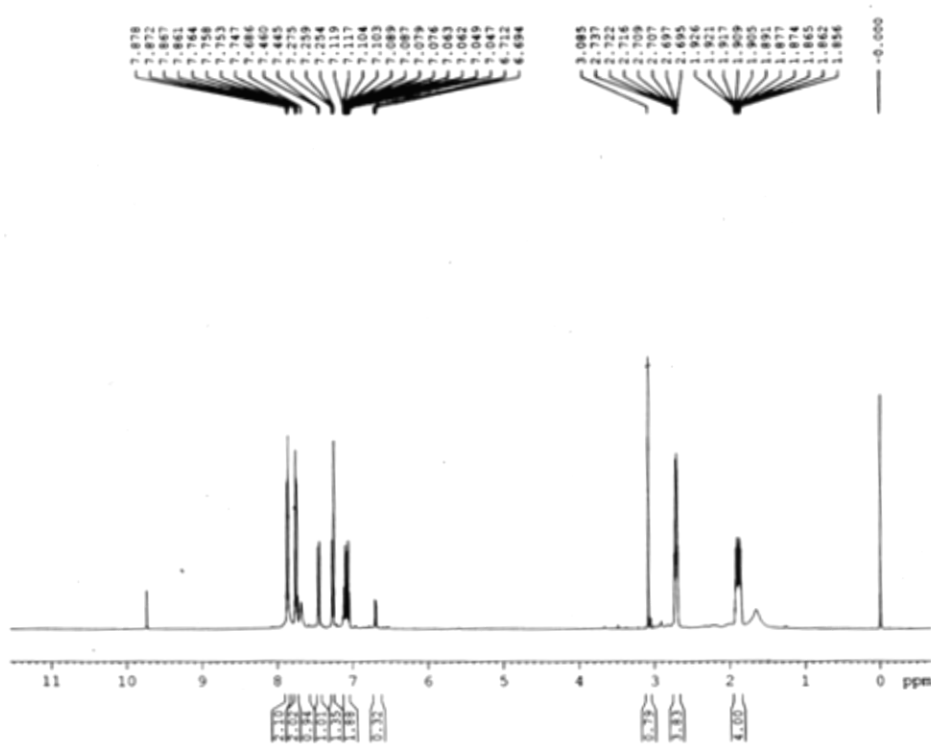


Fig.5 <sup>1</sup>H NMR spectrum of mannich base ligand

### 3.3 Mass spectrum

The Mass spectrum of the ligand is shown in Fig. 6. It exhibits a well-defined molecular ion peak for the aforesaid Mannich base at  $m/z = 435.03$ . Moreover, the mass spectra of the synthesized ligand exhibits peaks at  $m/z$  341.20, 281.16, 170.09, 120.08 corresponding to the various fragments  $[C_{21}H_{17}N_2O_2]$ ,  $[C_{17}H_{15}N_2O_2]$ ,  $[C_{12}H_{12}N]$ ,  $[C_8H_{10}N]$  respectively.

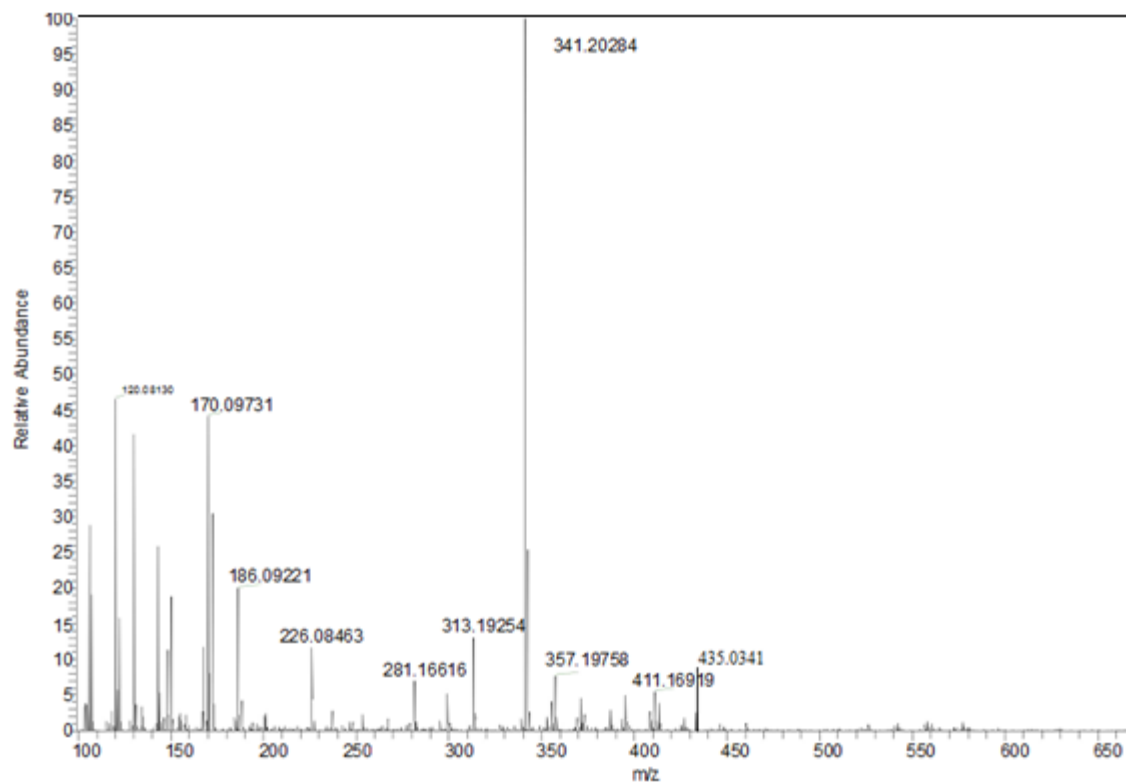


Fig.6 Mass spectra of Mannich base ligand

### 4.3 Elemental Analysis

The Mannich base ligand was synthesized from tetrahydrocarbazole, phthalimide and N,N-dimethylaminobenzaldehyde according to the procedure given above. The ligand was found to be soluble in common organic solvents such as chloroform, methanol, ethanol, DMF and DMSO, but insoluble in diethyl ether. The complexes are soluble in DMSO. The physico-chemical data of the ligand and its complexes are given in the following Table 1.

Table.1 Physico-chemical data of Mannich base ligand and its complexes

Compounds	Empirical Formula	Colour	Mol. wt.	Calc. (%)						
				C	H	N	O	Metal		
								Co	Ni	Cu
Ligand (AB)	C <sub>29</sub> H <sub>27</sub> N <sub>3</sub> O <sub>2</sub>	Brown	449.54	77.48	6.05	9.35	7.12	-	-	-
Co(AB) <sub>2</sub>	C <sub>59</sub> H <sub>58</sub> N <sub>6</sub> O <sub>4</sub> Co	Dark	974.06	72.75	6.00	8.63	6.57	6.05	-	-
Ni(AB) <sub>2</sub>	C <sub>59</sub> H <sub>58</sub> N <sub>6</sub> O <sub>4</sub> Ni	Dark	973.82	72.77	6.00	8.63	6.57	-	6.03	-
Cu(AB) <sub>2</sub>	C <sub>59</sub> H <sub>58</sub> N <sub>6</sub> O <sub>4</sub> Cu	Dark	978.68	72.41	5.97	8.59	6.54	-	-	6.49

### 3.4 EPR spectral analysis

The Electron spin resonance spectrum of the Cu(II) complex was recorded at liquid nitrogen temperature and is displayed in Fig. 7. The spectrum exhibits 4 lines and the analysis of spectrum gives  $g_{\parallel} = 2.29$  and  $g_{\perp} = 2.20$ . The calculated  $g_{\parallel}$  and  $g_{\perp}$  values for the copper(II) complex are greater than 2 which are in agreement with the covalent character of M-L bond.<sup>13</sup> The relationship  $g_{\parallel} > g_{\perp} > 2$  indicates square planar geometry for the copper complex.

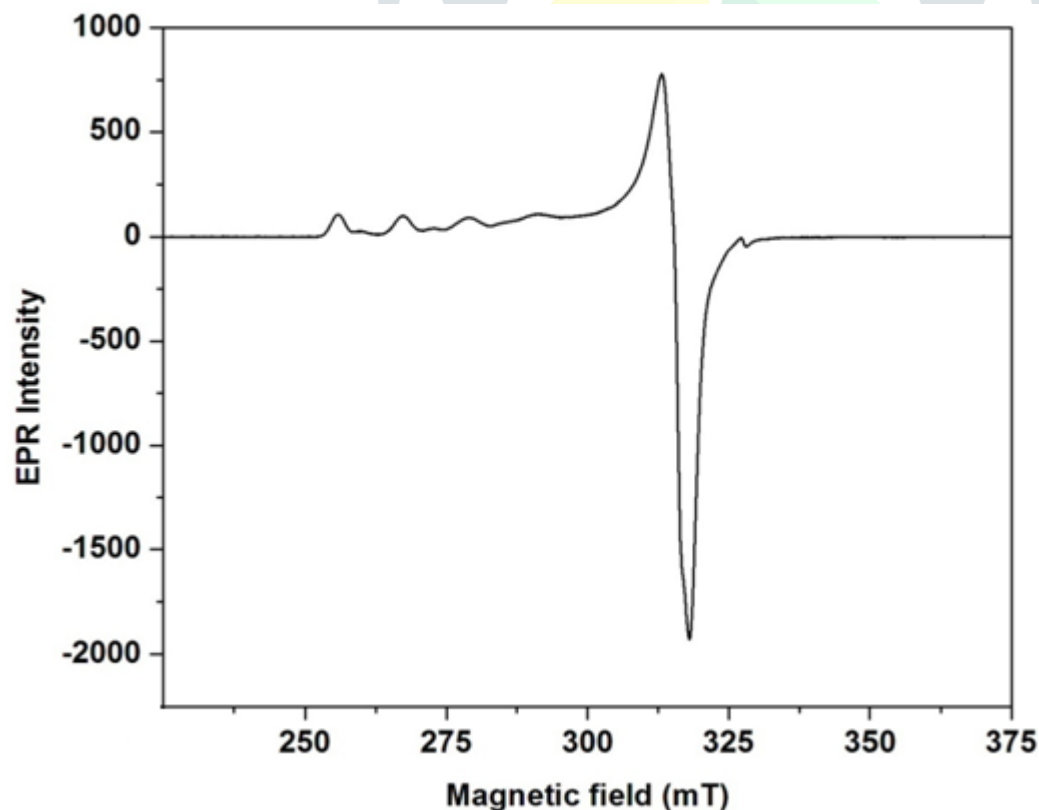
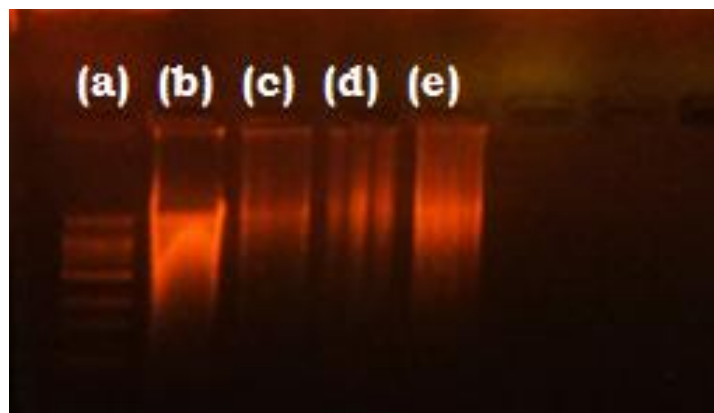


Fig.7 EPR spectrum of Mannich base copper complex



### 3.5 DNA cleavage studies

The DNA cleavage activity of Mannich base complexes have been examined by gel electrophoresis and a representative photograph is shown in Fig.8. The Co-complex has shown partial cleavage at 50 $\mu\text{g}$  and complete cleavage at 100  $\mu\text{g}$ . The complex of Ni has shown partial DNA cleavage at both concentrations. The complex of Cu has shown complete cleavage of DNA even at the concentration of 50 $\mu\text{g}$ .<sup>14-17</sup>The DNA cleavage activity of the synthesized Cu(II) complex was effective while comparing with the other two metal complexes.

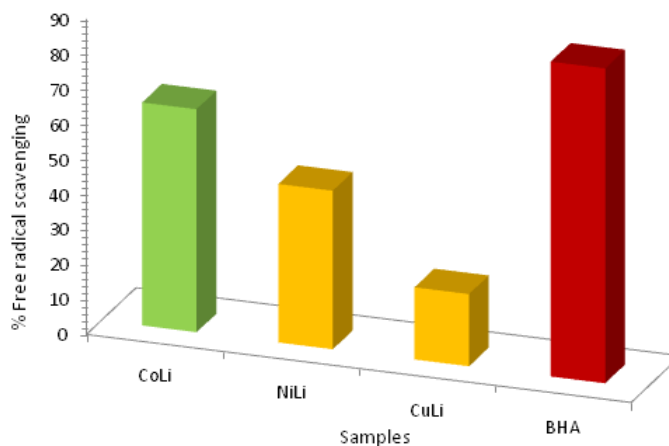


**Fig 8.DNA cleavage of Mannich base metal complexes**

(a) 50  $\mu\text{g}$   $\text{CoL}_2$  (b) 100  $\mu\text{g}$   $\text{CoL}_2$  (c) 50  $\mu\text{g}$   $\text{NiL}_2$  (d) 100  $\mu\text{g}$   $\text{NiL}_2$  (e) 50  $\mu\text{g}$   $\text{CuL}_2$

### 3.6 Anti-oxidant studies

The comparison of the anti-oxidant activity of Butylated hydroxy Anisole (BHA) and metal complexes is shown in Fig.9. The metal ion chelation plays an important role in antioxidant abilities.



**Fig. 9 Comparison of antioxidant activities of BHA and metal complexes**

The percentage of antioxidant activity by free radical scavenging method is given in the table 2. All the complexes showed varying antioxidant (free radical scavenging) activities when compared to BHA. It was found that the cobalt complexes show better antioxidant activity compared to others. The decreasing orders of the antioxidant activity of the complexes are as follows,



**Table2. Percentage Free radical scavenging activity**

Sample	% Activity
Co(AB) <sub>2</sub>	63.78
Ni(AB) <sub>2</sub>	45.34
Cu(AB) <sub>2</sub>	20.64
BHA	90.00

#### 4. Conclusion

A new Mannich base and its transition metal based complexes have been synthesized and characterized by elemental analyses and spectral studies. The synthesized metal complexes were screened for potent DNA cleavage activity and anti-oxidant activity and the obtained results are reported.

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