



**Synthesis, Characterisation and Antimicrobial Activity of Mannich base Transition Metal Complexes derived from 3-(diethanolamin-1-ylmethyl)benzene-1,2-diol**

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**ABSTRACT**

A new Mannich base (HL<sup>1</sup>) was synthesized from catechol/diethanolamine and characterised by IR, UV-Vis, <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy. Co (II), Ni (II) and Cu (II) of the ligand were also prepared in ratio (1:1) and their IR, UV-Vis spectroscopy and TGA data reported. All complexes have octahedral configuration. The biological activities of the metal chelates against fourteen bacteria are also reported. Most of the complexes have higher activities than those of the free Mannich base.

**Keywords:** Mannich reaction, catechol, aminomethylation, thermal analysis, antimicrobial activity

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**INTRODUCTION**

Mannich reaction is one of the most important C-C bond forming reactions in organic chemistry (ligand design) for the preparation of secondary and tertiary amine derivatives [1]. This reaction has been employed in ligand design for various applications. Catechol and phenol complexes are of great importance in bioinorganic and biomedical chemistry [2]. Aminomethylation of catechol with dialkylamine to give products useful as blood platelet aggregation inhibitors have been reported [3]. Also Mannich bases of acetophenones and aminophenols have been disclosed to have antitumour, anticonvulsant and cytotoxic activities [4, 5]. Hussain et al have also reported the antibacterial and antifungal activities of Mannich bases derived from 4,6-diacetylresorcinol [6]. As a general case, this aminomethylation reaction of aromatic compounds is performed in aqueous alcoholic solvents, in benzene, in toluene, or in a mixture of toluene-ethanol. The presence of diethanolamino arm enables the ligand to serve a variety of commercial applications such as corrosion inhibitors, surfactants, gas purification, and herbicides [7].

Studies of Mannich base complexes have grown over the years due to the selectivity and sensitivity of the ligands to various metal ions. The investigation of the biological activities of metal complexes derived from catechol/diethanolamine has not been reported [8]. We report herein the syntheses, characterisation, and antimicrobial studies of a Mannich base obtained from catechol/ diethanolamine and its transition metal(II) complexes. Also the thermogravimetric analysis data of the metal complexes are reported.

**EXPERIMENTAL SECTION**

**2.1. Materials and Methods**

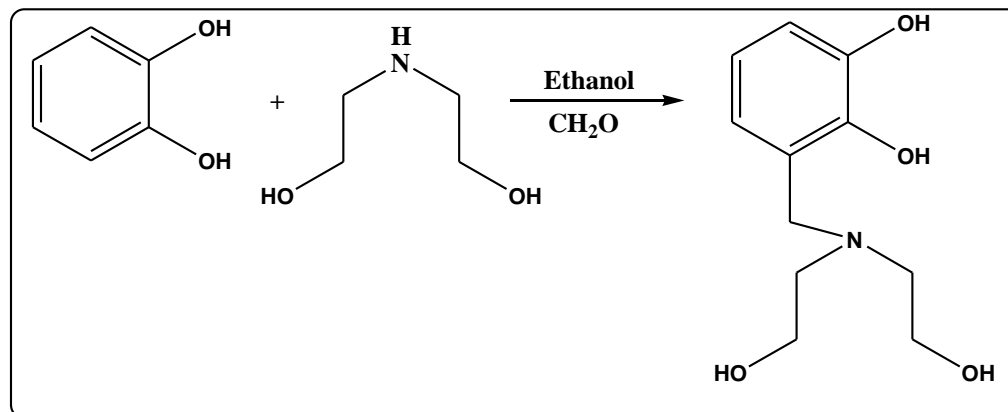
CuCl<sub>2</sub>.2H<sub>2</sub>O, CoCl<sub>2</sub>.H<sub>2</sub>O, NiCl<sub>2</sub>.4H<sub>2</sub>O, catechol, formaldehyde solution and solvents were obtained commercially from Aldrich and were used without further purification. IR spectra were recorded as KBr disc using Shimadzu FTIR spectrophotometer in the range (4000 – 250) cm<sup>-1</sup>. <sup>1</sup>H and <sup>13</sup>C spectra NMR were acquired in DMSO using Bruker AMX300 MHz spectrometer. Electronic spectra were recorded for the solutions of the synthesized compounds in DMSO on a Perkin Elmer UV-Vis spectrophotometer model Lambda 25. The thermogravimetric

analysis (TGA) was carried out in dynamic nitrogen atmosphere ( $20 \text{ mL min}^{-1}$ ) with a heating rate of  $10 \text{ }^\circ\text{C min}^{-1}$  using Thermogravic Analyzer Perkin Elmer TGA 4000.

## 2.2. Synthesis of 3-(diethanolamin-1-ylmethyl)benzene-1,2-diol ( $\text{HL}^1$ )

(2.202g, 20mmol) of catechol was dissolved in 10ml of ethanol, then (3.83ml, 40mmol) of diethanolamine with 2 ml formaldehyde solution in 20ml of ethanol was heated to reflux and kept  $100^\circ\text{C}$  for 20hours. The resulting solution was filtered hot and left to stand at room temperature. Upon slow evaporation of ethanol from the solution, dark purple precipitate was obtained after four days. This was filtered and washed severally with ethanol.  $^1\text{H NMR}$  ( $\text{DMSO}-d_6$ )  $\delta$  ppm: 2.55 (s, 2H), 2.70(t,4H), 2.95 (t,4H), 7.96(t, 1H), 8.23 (d, 1H), 8.15(d, 1H).  $^{13}\text{C NMR}$  ( $\text{DMSO}-d_6$ )  $\delta$  ppm: 58, 59, 60, 163 -164.  $\lambda_{\text{max}}$ (DMSO) 310nm, mp  $>300^\circ\text{C}$ .

The synthesis of the ligand is summarised in scheme 1:



Scheme 1: Preparation of Mannich Base

## 2.3. Synthesis of the Metal complexes

A solution of metal salt dissolved in ethanol was added gradually to a stirred ethanolic/DMF solution of the ligand  $\text{HL}^1$ , in the molar ratio 1:1. The reaction mixture was further stirred at  $80^\circ\text{C}$  for 5hours to ensure complete formation of metal complexes. The resulting solution was filtered hot and kept at room temperature for 3days until solid precipitates were obtained. The precipitate was collected by filtration, washed several times with ethanol and dried in a vacuum desiccator over anhydrous  $\text{CaCl}_2$ .

## 2.4. Antimicrobial Activities

The susceptibility of bacteria to synthesized compounds was determined using bioassay method as described by Beton and co-workers[9]. Solutions of known concentration (2 mg/ml) of the synthesized compounds ( $\text{HL}^1$ ,  $\text{CoHL}^1$ ,  $\text{NiHL}^1$  and  $\text{CuHL}^1$ ) were prepared by reconstituting them in 5% DMSO which was also used as negative control while streptomycin (1 mg/ml) was used as positive control. Mueller Hinton (Himedia) sterile agar plate surface was seeded with standardized inoculum ( $10^6$ cfu/ml) and allowed to stand at room temperature for 3 h. Wells were made on the seeded plates with 6 mm cork borer and these were separately filled with 1 ml each of the solution of the synthesized compounds. The resulting plates were allowed to stand at room temperature for 1 h before they were incubated at  $37^\circ\text{C}$  for 24 h and zones of inhibition were afterwards measured.

## RESULTS AND DISCUSSION

All the complexes were stable at room temperature and were non-hygroscopic. On heating, they decompose at high temperatures ( $> 300^\circ\text{C}$ ). The complexes were insoluble in water, slightly soluble in DMF but soluble in DMSO while demonstrating varying degrees of solubility in ethanol, diethyl ether and chloroform.

Table 1: Characteristic IR bands( $\text{cm}^{-1}$ ) of  $\text{HL}^1$  and its metal complexes

Compound	$\nu$ (O-H)	$\nu$ (C-O)	$\nu$ (C=C)	$\nu$ (C-N)	$\nu$ (M-N)	$\nu$ (M-O)
$\text{HL}^1$	3362(br)	1074(s)	1587	1447(s)	---	---
$\text{CoHL}^1$	3356(br)	1067(s)	1622	1526(s)	431	485
$\text{NiHL}^1$	3363(br)	1072(s)	1616	1522(s)	485	554
$\text{CuHL}^1$	3391(br)	1063(s)	1611	1508(s)	461	470

s:strong, br: broad

### 3.1 The IR spectra of the metal complexes

The IR spectra (Table 1) of the metal complexes showed that band due to the phenolic OH group that appeared in the spectrum of the ligand at  $3362\text{ cm}^{-1}$  has shifted to  $(3391 - 3356)\text{ cm}^{-1}$  in the spectra of the complexes. This is also corroborated by shifts observed in  $\nu(\text{C-N})$  values of the ligand compared to the metal complexes, the  $\nu(\text{C-N})$  stretching frequency occurred at  $1447\text{ cm}^{-1}$  but shifted to higher values  $(1508 - 1526)\text{ cm}^{-1}$  in the metal complexes. Both shifts observed in the functional groups are taken to indicate their involvement in coordination with the central metal ions with the presence of coordinated water also observable [10].

The  $\nu(\text{C=C})$  stretching vibrations appeared at  $1587\text{ cm}^{-1}$  in the spectrum of the ligand but shifted upward to  $(1622 - 1611)\text{ cm}^{-1}$  in the spectra of the metal complexes. This may be attributed to the delocalisation of pi-electrons upon complexation [11].

New bands appeared in the spectra of all metal complexes at  $(470 - 554)$  and  $(431 - 485)\text{ cm}^{-1}$  that would be assigned to  $\nu(\text{M-O})$  and  $\nu(\text{M-N})$  respectively. The  $\nu(\text{M-O})$  stretching usually occur at higher frequency region and usually sharper and stronger than  $\nu(\text{M-N})$ . These observations are in accordance with structure of Co (II), Ni (II) and Cu (II) complexes with HL<sup>1</sup> in which the central metal ions acquire a coordination number of 4 and 6 [12,13].

**Table 2: Electronic spectral data for HL<sup>1</sup> and its metal complexes**

Compound	$\pi-\pi^*$ , $n-\pi^*$ and charge transfer transitions ( $\text{cm}^{-1}$ )	d-d transitions ( $\text{cm}^{-1}$ )
HL <sup>1</sup>	35336, 29940	----
CoHL <sup>1</sup>	37313, 31250	18519
NiHL <sup>1</sup>	34483, 26316, 23810	13459, 11751, 10384
CuHL <sup>1</sup>	34722, 33898	16779

### 3.2 Electronic spectra of the metal complexes

The electronic spectra of the metal complexes are listed in Table 2. Generally, in all spectra of metal complexes, the absorption band due to  $\pi-\pi^*$  and  $n-\pi^*$  transitions that are observed in the spectrum of the free ligand higher than  $29940\text{ cm}^{-1}$  have shifted to lower frequencies due to the coordination of ligand with metal ions [14]. The spectrum of copper complex showed absorption bands at  $16779\text{ cm}^{-1}$  which could be attributed to  $T_{2g} \rightarrow E_g$  transition characterized by Cu(II) ion in a distorted octahedral geometry.

Absorption band at  $18519\text{ cm}^{-1}$  observed in the spectrum of cobalt complex is assigned to  ${}^4T_{1g}(\text{F}) \rightarrow {}^4A_{2g}(\text{F})$  transition which favour octahedral configuration. Nickel complexes generally shows three bands in octahedral environment and these correspond to the following transitions  ${}^3A_{1g}(\text{F}) \rightarrow {}^3T_{2g}(\text{F})$ ,  ${}^3A_{2g} \rightarrow {}^3T_{1g}(\text{F})$  and  ${}^3A_{2g} \rightarrow {}^3T_{1g}(\text{P})$  observed at 13459, 11751 and  $10384\text{ cm}^{-1}$  respectively [15].

### 3.3 Thermal analyses

The TGA results of the solid complexes  $\text{CoL}(\text{H}_2\text{O})_3\text{Cl}$ ,  $\text{NiL}(\text{H}_2\text{O})_3\text{Cl}$  and  $\text{CuL}(\text{H}_2\text{O})_{2.5}\text{Cl}$  are listed in Table 3. Decomposition existed in three stages. First stage involves the loss of water molecules, followed by the loss of the organic ligand and HCl. The last stage represents the formation of metal oxides [16].

**Table 3: Thermal analyses (TGA) results of metal complexes of HL<sup>1</sup>**

Complex	Temp. range ( $^{\circ}\text{C}$ )	$n^{\#}$	Weight loss found (calculated) (%)	Assignment	Metallic residue
$\text{CoL}(\text{H}_2\text{O})_3\text{Cl}$	30 - 120	1	14.14(14.38)	Loss of $3\text{H}_2\text{O}$	CoO
	120 - 762	1	59.20(60.45)	Loss of L, HCl	
$\text{NiL}(\text{H}_2\text{O})_3\text{Cl}$	30 - 125	1	13.84(14.38)	Loss of $3\text{H}_2\text{O}$	NiO
	125 - 762	2	68.50(70.17)	Loss of L, HCl	
$\text{CuL}(\text{H}_2\text{O})_{2.5}\text{Cl}$	30 - 140	1	11.65(12.11)	Loss of $2.5\text{H}_2\text{O}$	CuO
	140 - 862	2	69.00(69.91)	Loss of L, HCl	

$n^{\#}$  = number of decomposition steps

### 3.4 Antimicrobial activity

Table 4 illustrates the result of antimicrobial activities of Mannich base (HL<sup>1</sup>) and its metal complexes against fourteen bacteria. The ligand; its Co, Ni and Cu complexes were active against one, two, five and four of the fourteen organisms tested respectively. The metal complexes exhibited broad spectrum of activity while the ligand shows narrow spectrum of activity suggesting that the complexing metals especially Ni enhanced antibacterial activity of Mannich base. Considering the various bacteria that the various compounds were active against, the various compounds compete favourably with the positive control (1 mg/ml streptomycin). Thus the various compounds could be used to treat infections caused by the pathogen they are active on though this will need further work such as testing it against various strains of the sensitive organisms, toxicity assay, mode and mechanisms of action of the compound etc.

Table 4: Antimicrobial activity of the Mannich base and its metal complexes

Organisms	Zones of Inhibition (mm) **				
	HL <sup>1</sup> (2mg/ml)	CoHL1 (2mg/ml)	NiHL1 (2mg/ml)	CuHL1 (2mg/ml)	Strep (1mg/ml)
<i>Ps. aureginosa</i> (NCIB 950)	00	00	00	00	00
<i>B. stearothermophilus</i> (NCIB 8222)	00	00	00	00	21
<i>B. cereus</i> (NCIB 6349)	00	00	00	14	21
<i>B. polymyxa</i> (LIO)	00	00	00	00	18
<i>C. pyogenes</i> (LIO)	00	00	00	00	20
<i>Ps. fluorescense</i> (NCIB 3756)	00	00	12	00	20
<i>C. sporogenes</i> (NCIB 532)	00	00	14	20	24
<i>M. luteus</i> (NCIB 196)	00	00	00	00	18
<i>E. faecalis</i> (NCIB 775)	00	00	00	00	20
<i>Staph. aureus</i> (NCIB 8588)	18	12	00	00	20
<i>B. subtilis</i> (NCIB 3610)	00	00	16	00	19
<i>K. pneumonia</i> (NCIB 418)	00	00	00	00	00
<i>E. coli</i> (NCIB 86)	00	00	18	14	11
<i>P. vulgaris</i> (LIO)	00	14	10	12	16

Key: LIO; Locally Isolated Organism, NCIB; National Collection of Industrial Bacteriology, (mm)\*\*; Mean of three replicates

Note: The negative control (5 % DMSO) was not active against any of the tested bacterial.

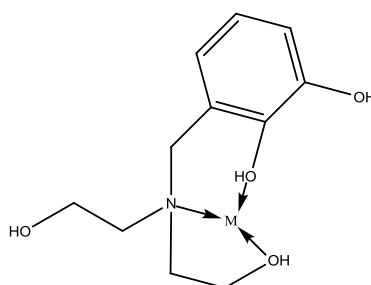


Figure 1: Proposed Structure of metal complexes (M = Co, Ni, Cu)

## CONCLUSION

The Mannich ligand and its metal complexes have been successfully synthesized and characterised. The thermogravimetric analysis shows that the complexes are stable as observed. All the compounds tested exhibited various activities. Evaluation of the antimicrobial activities shows a broader spectrum in the activity of the metal complexes compared to that of the free ligand.

## Acknowledgement

The authors are grateful to the Departments of Chemistry and Microbiology of Obafemi Awolowo University, Nigeria for providing the facilities for this research.

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