



## Synthesis, Characterization and Antimicrobial Activity of Novel Benzimidazole Containing Metal Chelates

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### ABSTRACT

The reaction between 1-(1H-benzo[d]imidazol-1-yl)-2-chloroethanone with aniline gives 2-(4-aminophenyl)-1-(1H-benzo[d]imidazol-1-yl)ethanone(BI), The diazotization of 2-(4-aminophenyl)-1-(1H-benzo[d]imidazol-1-yl)ethanone(BI) couple with salicylic acid, they afford the ligand compound and named as 5-((4-(2-(1H-benzo[d]imidazol-1-yl)-2-oxoethyl)phenyl)diazonyl)-2-hydroxybenzoic acid(BIASA). The transition metal complexes of  $\text{Cu}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Mn}^{2+}$  and  $\text{Zn}^{2+}$  of BIASA have been prepared and characterized by elemental analyses, spectral studies, magnetic moment determination, molar conductivity measurement and microbicidal activity.

**Keywords:** Benzimidazole, salicylic acid, metal chelates, spectral studies, magnetic moment, antibacterial and antifungal activity.

### INTRODUCTION

Benzimidazoles belonging to the fused heterocyclic system prepared from amino acids are associated with diverse pharmaceutical activities such as antibacterial[1], insecticidal[2], fungicidal[3], antimicrobial[4], asvitronectial receptes, antagonist[5], anthelmintic[ 6-8], anti-inflamatory[9], etc. Recently the benzimidazole derivative has been reported with remarkable antimicrobial activity[10]. The compound having benzimidazole –phenyl acetyl chloride-salicylic acid moieties has not been reported. salicylic acid is well known precursor for useful drugs. Hence it was thought interesting to prepare the ligand having benzimidazole–acetyl chloride-salicylic acid moieties. Thus the present communication comprises the studies on benzimidazole-salicylic acid combined molecule and its metal chelates. The research work is illustrated in scheme-1.

### EXPERIMENTAL SECTION

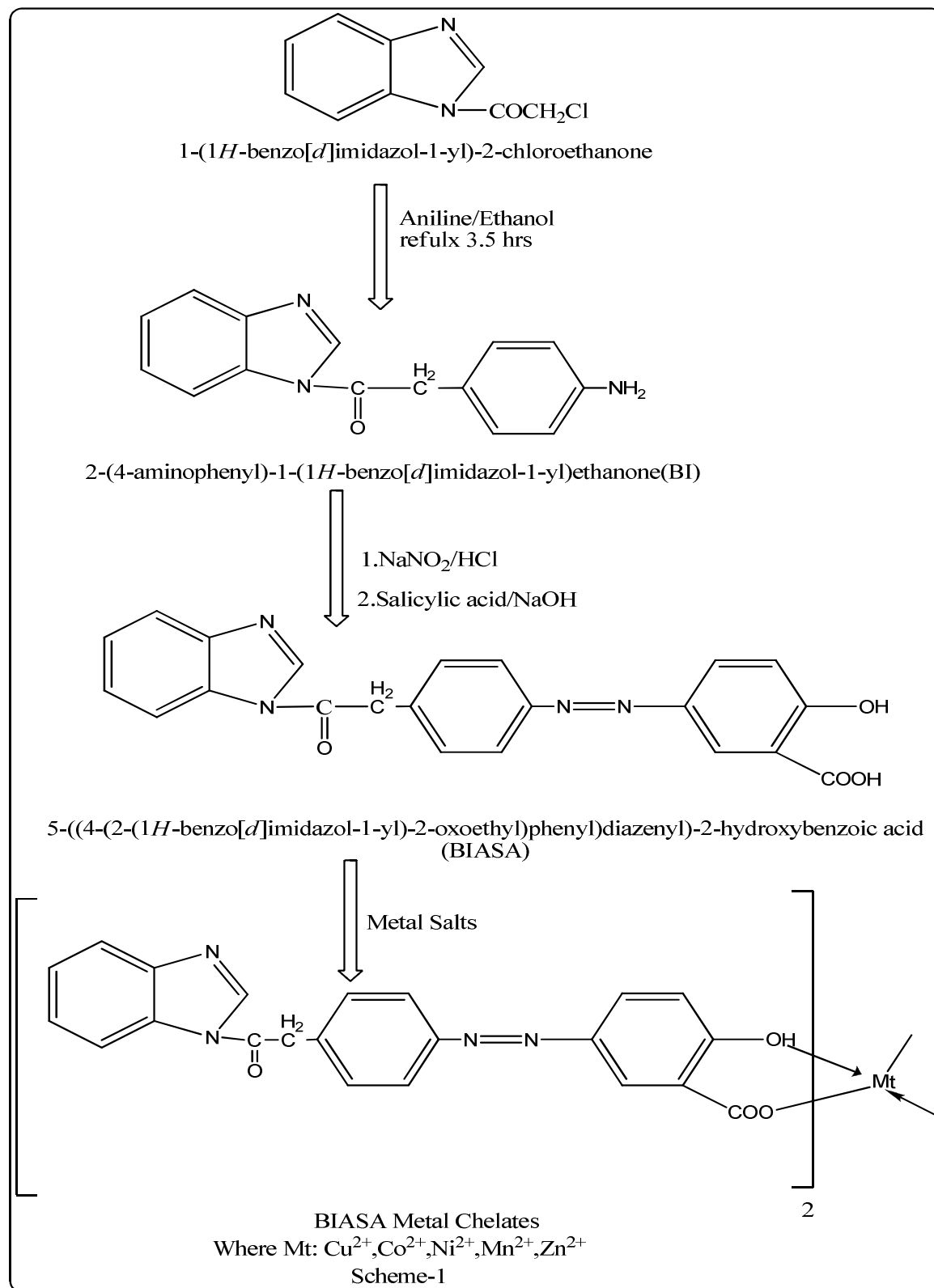
#### Materials

Benzimidazole was prepared by method reported in literature [11]. Salicylic acid was obtained from local dealer. All other chemicals used were of analytical pure grade.

**Synthesis of 5-((4-(2-(1H-benzo[d]imidazol-1-yl)-2-oxoethyl)phenyl)diazonyl)-2-hydroxy benzoic acid (BIASA):**The 5-((4-(2-(1H-benzo[d]imidazol-1-yl)-2-oxoethyl)phenyl) diazenyl) -2-hydroxybenzoic acid(BIASA) was prepared as follows:

A mixture of 1-(1H-benzo[d]imidazol-1-yl)-2-chloroethanone (0.02 mole) and aniline (0.02 mole) in ethanol (70 ml) was heated under reflux for 3.5hrs. Subsequently ethanol was distilled off and the lump mass obtained. It was

trituated with petroleum ether (40-60° C). The solid designated as PEMS was isolated and dried in air. Yield was 76%. It's m.p. was 173-75°C (uncorrected).



A solution of sodium nitrite (0.01) is added dropwise to a stirred and cold solution of 2-(4-aminophenyl)-1-(1*H*-benzo[*d*]imidazol-1-yl)ethanone(BI) (0.01mole) in a mixture of con.HCl and water. The reaction mixture is kept in ice-bath. These diazonium salts poured with stirring into a cold solution of salicylic acid (0.01mole) in sodium

hydroxide solution. The reaction mixture was kept in ice-bath for 30minutes. The separated product are known as 5-((4-(2-(1H-benzo[d]imidazol-1-yl)-2-oxoethyl)phenyl)diazanyl)-2-hydroxybenzoic acid (BIASA) filtered, wash and crystallized from ethanol. Yield was 70%. It's m.p. was 171-73°C (uncorrected).

**Elemental Analysis:** C<sub>22</sub>H<sub>16</sub>O<sub>4</sub>N<sub>4</sub> (400)

	C%	H%	N%
<b>Calculated:</b>	66.00	4.03	13.99
<b>Found :</b>	65.9	4.0	13.9

**Acid Value**            Theoretical: 194.5 mg KOH/1g. Sample.  
                               Found: 195 KOH/1g Sample.

<b>IR Features</b>		
1480-1520 cm <sup>-1</sup> .		Benzimidazole
3030, 1500, 1600 cm <sup>-1</sup>		Aromatic
1680 cm <sup>-1</sup>		CO of COOH
1720cm <sup>-1</sup>		CO of CH <sub>2</sub> CO
3200-3600 cm <sup>-1</sup>		OH
2850, 2920 cm <sup>-1</sup>		CH <sub>2</sub> of COCH <sub>2</sub>

<b>NMR</b>		$\delta$ ppm	
(DMSO)	8.4 – 7.3 (11H)	Multiplet	Aromatic
	6.4 (2H)	Singlet	CH <sub>2</sub>
	11.3 (1H)	Singlet	(COOH)
	5.6 (1H)	Singlet	(OH)

### Synthesis of metal chelates of BIASA

The Cu<sup>2+</sup>, Co<sup>2+</sup>, Ni<sup>2+</sup>, Mn<sup>2+</sup> and Zn<sup>2+</sup> metal ion chelates of BIASA have been prepared in a similar manner. The procedure is as follow.

To a solution of BIASA (40g 0.1 mole) in ethanol-acetone (1:1v/v) mixture (150 ml), 0.1N KOH solution was added dropwise with stirring. The pasty precipitates were obtained at neutral pH. These were dissolved by addition of water up to clear solution. It was diluted to 250 ml. by water and was known as stock solution. 25 ml of the stock solution (which contains 0.01 mole BI-SA) was added drop wise to the solution of metal salt in water at room temperature. Sodium acetate or ammonia was added up to complete precipitation. The precipitates were digested on water bath at 80° C for 2h. The digested precipitates of chelates were filtered washed with water and air dried. It was amorphous powder. Yield was almost quantitative. The detail are given in Table-1

### Measurements

The elemental analysis for C, H and N were carried out on elemental analyzer TF-EA. 1101 (Italy). IR spectra of BIASA and its metal complexes were scanned on a Nicolet 760 FTIR spectrophotometer in KBr. The NMR spectrum of BIASA was scanned on Bruker NMR spectrophotometer using DMSO solvent. The metal content of the metal chelate were performed by decomposing a weighed amount of each metal complexes followed by EDTA titration as reported in literature [12]. Magnetic susceptibility measurement of the entire metal complex was carried out at room temperature by the Gouy method. Mercury tetrathiocyanatocobalate (II) Hg [Co (NCS)<sub>4</sub>] was used as a calibrant. The diffused reflectance spectra of solid metal complex were recorded on a Beckman DK Spectrophotometer with a solid reflectance attachment, MgO was employed as the reflectance compound. The electrical conductivity of all the complexes was measure in acetonitrile at 10<sup>-3</sup> M concentration.

### Antifungal activity

The fungicidal activity of all the compounds was studied at 1000 ppm concentration in vitro plant pathogenic organisms listed in Table-3. The antifungal activities of all the samples were measured by cup plate method [13]. Each of the plant pathogenic strains on potato dextrose agar (PDA) medium. Such a PDA medium contained potato 200 gms, dextrose 20gms, agar 20gms and water 1 litre. 5 days old cultures were employed. The compounds to be tested were suspended (1000ppm) in a PDA medium and autoclaved at 120° C for 15 min. at 15 atm pressure. These medium were poured into sterile Petri plate and the organisms were inoculated after cooling the Petri plate. The percentage inhabitation for fungi was calculated after 5 days using the formula given below.

$$\text{Percentage of inhibition} = 100 (X-Y)/X$$

Where, X: Area of colony in control plate  
 Y: Area of colony in test plate

The fungicidal activity all compound are shown in Table-3

## RESULTS AND DISCUSSION

The parent ligand BIASA was an amorphous brown powder, soluble in various solvents like DMSO and DMF. The results of elemental analysis of the ligand are reported in experimental part. They are consistent with the predicted structure as shown in Scheme-1.

Examination of IR spectrum (not shown) of BIASA reveals that broad band of phenolic hydroxyl stretching is observed at 3200-3600  $\text{cm}^{-1}$  as well as additional absorption bands at 3030, 1500 and 1600 are characteristics of the salicylic acid [10,11]. The strong bands at 1680 for C=O and band at 3400 for sec. NH. The NMR data (shown in experimental part) also confirm the structure of BIASA.

The metal chelate of BIASA with ions  $\text{Cu}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Mn}^{2+}$  and  $\text{Zn}^{2+}$  vary in colours. On the basis of the proposed structure as shown in Scheme-1, the molecular formula of the BIASA ligand is  $\text{C}_{22}\text{H}_{16}\text{O}_4\text{N}_4$ , Which upon complexation coordinates with one central metal atom at four coordination sites and with two water molecules. Therefore the general molecular formula of the resulting metal chelate is  $[\text{C}_{22}\text{H}_{15}\text{O}_4\text{N}_4]_2 \text{M} \cdot 2\text{H}_2\text{O}$  for divalent metal ions. This has been confirmed by results of elemental analysis reported in Table-1. The data are in agreement with the calculated values.

Table-1. Analytical Data of the Metal Chelates of HL (i.e. BIASA)

Compound	Empirical Formula	Mol. Cal. gm/mol	Yield (%)	Elemental Analysis							
				C%		H%		N%		M%	
				Cald	Found	Cald	Found	Cald	Found	Cald	Found
HL (BIASA)	$\text{C}_{22}\text{H}_{16}\text{O}_4\text{N}_4$	400	60	66.00	65.9	4.03	4.0	13.99	13.9	--	--
(L) <sub>2</sub> Cu <sup>2+</sup>	$\text{C}_{44}\text{H}_{30}\text{N}_8\text{O}_8 \text{Cu}^{2+} \cdot 2\text{H}_2\text{O}$	897.54	62	58.82	58.8	3.78	3.7	12.47	12.4	7.07	6.9
(L) <sub>2</sub> Co <sup>2+</sup>	$\text{C}_{44}\text{H}_{30}\text{N}_8\text{O}_8 \text{Co}^{2+} \cdot 2\text{H}_2\text{O}$	892.94	59	59.13	59.1	3.80	3.8	12.54	12.5	6.60	6.6
(L) <sub>2</sub> Ni <sup>2+</sup>	$\text{C}_{44}\text{H}_{30}\text{N}_8\text{O}_8 \text{Ni}^{2+} \cdot 2\text{H}_2\text{O}$	892.71	57	59.14	59.1	3.80	3.7	12.54	12.5	6.57	6.5
(L) <sub>2</sub> Mn <sup>2+</sup>	$\text{C}_{44}\text{H}_{30}\text{N}_8\text{O}_8 \text{Mn}^{2+} \cdot 2\text{H}_2\text{O}$	888.94	63	59.39	59.3	3.82	3.8	12.59	12.5	6.18	6.0
(L) <sub>2</sub> Zn <sup>2+</sup>	$\text{C}_{44}\text{H}_{30}\text{N}_8\text{O}_8 \text{Zn}^{2+} \cdot 2\text{H}_2\text{O}$	899.38	61	58.70	58.6	3.78	3.7	12.45	12.4	7.26	7.2

Inspection of the IR Spectra (not shown) of metal chelates reveals that all the spectra are identical in all respects. The comparison of IR spectrum of the parent ligand BIASA with that of its each metal chelates has revealed certain characteristics differences.

Table -2 Magnetic Moment and Reflectance Spectral data of Metal Chelates of BIASA ligand

Metal chelates	Magnetic Moment $\mu_{\text{eff}}$ (B.M.)	Molar Conductivity $\Omega\text{m} \text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$	Absorption band ( $\text{cm}^{-1}$ )	Transitions
Cu-HL	1.94	37.3	22695 15870	C.T ${}^2\text{T} \rightarrow {}^2\text{T}_{2g}$
Ni-HL	3.85	36	14700 22993	3 A <sub>2g</sub> → 3 T <sub>1g</sub> (p) 3 A <sub>1g</sub> → 3 T <sub>1g</sub> (F)
Co-HL	4.54	35.4	15385 22725	4 T <sub>1g</sub> (F) → 4 T <sub>2g</sub> (F) 4 T <sub>1g</sub> (F) → 3 A <sub>2g</sub>
Mn-HL	5.12	37.8	15384 17660 22970	6 A <sub>1g</sub> → 4 T <sub>1g</sub> (4E <sub>g</sub> ) 6 A <sub>1g</sub> → 4 T <sub>2g</sub> (4G) 6 A <sub>1g</sub> → 4 T <sub>1g</sub> (4G)
Zn-HL	Diamagnetic	-----	-----	-----

One of the significant differences to be expected between the IR spectrum of the parent ligand and its metal chelates is the presence of more broadened bands in the region of 3200-3600  $\text{cm}^{-1}$  for the metal chelates as the oxygen of the O-H group of the ligands forms a coordination bond with the metal ions [13-15]. This is explained by the fact that water molecule might have strongly absorbed to the metal chelates samples during their formation. Another noticeable difference is that the bands due to the COO<sup>-</sup> anion at 1600  $\text{cm}^{-1}$  in the IR spectrum of the each metal chelates. The band at 1400  $\text{cm}^{-1}$  in the IR Spectrum of HL assigned to inplane OH determination [13-15] is shifted towards higher frequency in the spectra of confirmed by a weak bands at 1105  $\text{cm}^{-1}$  corresponding to C-O-M

starching [13-15]. Thus all of these characteristics features of the IR studies suggested the structure of the metal chelates as shown in scheme.

Examination of data of the metal content in each compound revealed a 1:2 metal: ligand (M: L) stoichiometry in all of the chelate of divalent metal ions. Magnetic moment ( $\mu_{\text{eff}}$ ) of each of the metal chelates is given in Table-2. Examination of these data reveals that all chelates other than that of  $\text{Zn}^{2+}$  are para magnetic while those of  $\text{Zn}^{2+}$  are diamagnetic.

**Table 3. Antifungal Activity of Ligand HL<sub>1</sub> and its metal chelates**

Sample	Zone of inhibition of fungus at 1000ppm (%)					
	PE	BT	N	T	RN	AN
HL	64	63	64	66	67	63
(HL)-Cu <sup>2+</sup>	76	80	79	84	77	74
(HL)-Co <sup>2+</sup>	73	74	75	77	75	77
(HL)-Mn <sup>2+</sup>	66	73	73	73	73	73
(HL)-Ni <sup>2+</sup>	73	75	77	76	74	71
(HL)-Zn <sup>2+</sup>	70	79	74	75	73	73

PE= *Penicillium expansum*; BT= *Botrydepladia thiobromine*;  
N= *Nigrospra sp.*; T= *Trichothesium sp.*; RN= *Rhizopus nigricans*;  
AN= *Aspergillus niger*.

The diffuse electronic spectrum of the [Cu HL (H<sub>2</sub>O)<sub>2</sub>] metal complex shows broad bands at 15870 and 22695 cm<sup>-1</sup> due to the <sup>2</sup>T→<sup>2</sup>T<sub>2g</sub> transition and charge transfer, respectively suggesting a distorted octahedral structure [16-18] for the [Cu HL (H<sub>2</sub>O)<sub>2</sub>] complex. Which is further confirmed by the higher value of  $\mu_{\text{eff}}$  of the [Cu HL (H<sub>2</sub>O)<sub>2</sub>] complex. The [Ni HL (H<sub>2</sub>O)<sub>2</sub>] and [Co HL (H<sub>2</sub>O)<sub>2</sub>] complex gave two absorption bands respectively at 14700, 22993, and 15385, 22725 cm<sup>-1</sup> corresponding to <sup>4</sup>T<sub>1g</sub>→<sup>2</sup>T<sub>1g</sub> and <sup>4</sup>T<sub>1g</sub> (p) transitions. Thus absorption bands at the diffuse, reflectance spectra and the value of the magnetic moments  $\mu_{\text{eff}}$  indicate an octahedral configuration for the [NiHL (H<sub>2</sub>O)<sub>2</sub>] and [Cu HL (H<sub>2</sub>O)<sub>2</sub>] complex. The spectra of [Mn HL (H<sub>2</sub>O)<sub>2</sub>] shows weak bands at 15385, 17665 and 22975cm<sup>-1</sup> assigned to the transitions <sup>6</sup>A<sub>1g</sub>→<sup>4</sup>T<sub>1g</sub> (4G), <sup>6</sup>A<sub>1g</sub>→<sup>4</sup>T<sub>2g</sub> (4G) and <sup>6</sup>A<sub>1g</sub> (F) →<sup>4</sup>T<sub>1g</sub>, respectively suggesting an octahedral structure for the [Mn HL (H<sub>2</sub>O)<sub>2</sub>] chelate. As the spectrum of the [Zn HL (H<sub>2</sub>O)<sub>2</sub>] polymer is not well resolved, it is not interpreted but its  $\mu_{\text{eff}}$  value shows that it is diamagnetic as expected.

Conductivities of all the complexes were measured in acetonitrile solvent and all the complexes were found to be electrolytic [19] in nature of 1:2 type and molar conductivity values are in the range of 36 -37.8 Ohm<sup>-1</sup> Cm<sup>-1</sup>.

The antifungal activity of all the compounds measured for various plant pathogens. Inspection of the result shown in Table-3 indicates that all compounds are good toxic for fungi. Out of all the compounds copper chelates is more toxic than other. These compounds almost inhibit the fungi about 79%. Hence produced metal chelates can be employed as garden fungicides. Further work in the direction is in progress.

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