

Synthesis, characterization and antimicrobial activity studies of 5-(2-(5-benzoyl-1H-1,2,3-benzotriazole-1-yl)2-oxoethylamino)-2-hydroxy benzoic acid and their transition metal chelates

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ABSTRACT

1-(5-benzoyl-1H-1,2,3-benzotriazole-1-yl)2-chloroethanone was condensed with 5-amino-2-hydroxy benzoic acid (5-Amino Salicylic acid). The resulting 5-(2-(5-benzoyl-1H-1,2,3-benzotriazole-1-yl)2-oxoethylamino)-2-hydroxy benzoic acid was characterized by elemental analysis and spectral studies. The transition metal chelates of the same were prepared with Cu^{2+} , Ni^{2+} , Co^{2+} , Mn^{2+} and Zn^{2+} and characterized by IR spectral studies and magnetic properties. The antimicrobial activity of ligand and its metal chelates were screened against various gram-positive (+) and gram-negative (–) organism. The results show that all these samples are more or less active agents against various organisms.

Keywords: 5-benzoyl-1H-benzotriazole, 5-Amino Salicylic acid, Metal chelates, spectral studies, magnetic moment, antibacterial and antifungal activity.

INTRODUCTION

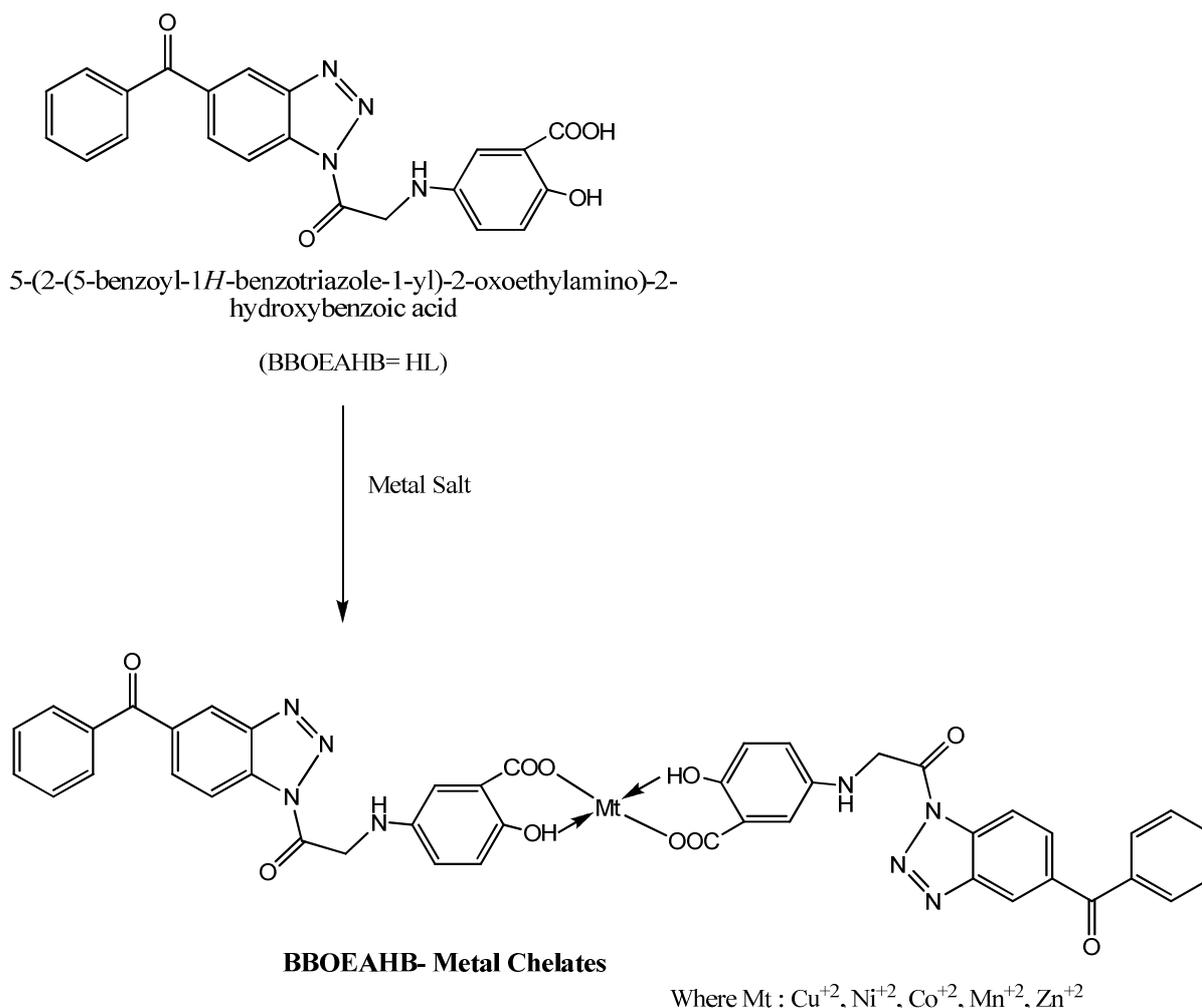
Compounds containing triazole have attracted much interest because of their biological applications[1-4] and are used as dyes and photographic chemicals[5]. Furthermore, triazole appears frequently in the structures of various natural products[6]. Triazole containing compounds appear in many metabolic products of fungi and primitive marine animals. The coordination chemistry of triazole and benzotriazole derivatives was studied due to their importance in industry, agriculture and their biological activity[7-10]. In view of the above facts and in continuation of our interest in studying the ligating behavior of such compounds[11], therefore the present paper comprise the synthesize and characterize the solid complexes of the newly ligand containing the triazole moieties, 5-(2-(5-benzoyl-1H-1,2,3-benzotriazole-1-yl)2-oxoethylamino)-2-hydroxy benzoic acid with Zn^{2+} , Cu^{2+} , Ni^{2+} , Mn^{2+} Co^{2+} and investigate their antimicrobial effects towards some Gram-positive and Gram-negative bacteria. The whole work is summarized in scheme-1.

MATERIALS AND METHODS

All the chemicals used were of pure grade (Merck and B.D.H). The melting points of all complexes were determined by open capillary method and were uncorrected.

Synthesis of ligand HL

A mixture of 1-(5-benzoyl-1H-1,2,3-benzotriazole-1-yl)2-chloroethanone (BBCE) (0.01mol) and 5-amino salicylic acid in ethanol (0.01mol) was added gradually at room temperature. Sodium bicarbonate (0.01mole) was added in the mixture and refluxed it on water bath for 6 h. Subsequently ethanol was distilled off and the lump mass obtained and the air-dried. The ligand used to prepare metal chelates.



Synthesis of Chelates

The Cu²⁺, Co²⁺, Ni²⁺, Mn²⁺ and Zn²⁺ metal ion complexes of BBOEAHB have been prepared in a similar manner. The procedure is as follows:

0.01 mole corresponding ligands were dissolved in alcohol and 0.005 mole metal salts also dissolved in minimum quantity of alcohol. The resultant pH 4-5 (for Cu²⁺), pH 6.0 (for Ni²⁺ and Co²⁺) and pH 5.6 (Mn²⁺ and Zn²⁺) was maintained by adding of sodium acetate and refluxed on water bath for 4 h. The solid mass was filtered, washed with 1:1 mixture of water-ethanol and dried. The percentage yield of chelates was in the range of 60-75 %. All the chelates were powdered well and dried at 70 °C over a period of 24 h.

Measurements

The C, H and N contents of metal chelates were determined on elemental analyzer Thermofinigan 1101 Flash EA (ITALY). The metal contents were estimated using standard methods [12]. The halogen content was determined by Carius method [13]. The infrared spectra (KBr) were recorded in the range 4000-600 cm⁻¹ with a nicoleet -760 spectrophotometer. A reflectance spectrum of ligand was recorded on a Beckman -DK-2A spectrophotometer using MgO as reference. Magnetic susceptibility was measured by Gouy's method[14] at room temperature (300 K) using Hg [Co (CNS)₄] as calibrant[15], and the effective magnetic moment from relation[16], $\mu_{eff} = 2.84\sqrt{Xm \times T}$, where T is the absolute temperature. Diamagnetic corrections were made by using Pascal's constants.

The ligand and their metal chelates were screen at 1000 ppm concentration in vitro for their antifungal activity against three fungi viz. *Penicillium expansum*, *Nigros pora* sp. and *Asperginus niger*. The antifungal activity of the compounds was measured by cup plate method[17]. Five days old cultures were suspended in potato dextrose agar (PDA) medium and autoclaved at 1200 °C for 15 minutes at 15 atmospheric pressure. The percentage inhibition of fungi was calculated after 5 days using the formula given below,

$$\% \text{ of Inhibition} = \frac{100(X - Y)}{X}$$

Where X = area of colony in control plate (without sample)

Y = area of colony in test plate.

To assess the biological potential of the ligands and their macro cyclic complexes, laboratory experiments have been conducted. The following techniques have been used for the antimicrobial activities of these compounds.

In this technique sterilized hot nutrient agar medium and 5 mm diameter paper discs of Whatman were used[18-19]. The agar medium was poured into the petri plates. After solidifications, the petri plates were stored in inverted position so that there was condensation of water in the upper lid. Solutions of test compounds in DMSO in 500 and 1000 ppm concentrations were prepared in which discs were dipped in solution of the test sample placed on seeded plates. The petri plates having these discs on the seeded agar should first be placed at low temperature for two or four hours to allow for the diffusion of chemicals before being incubated at suitable optimum temperature 28 ± 2 °C for 24-30 hours. After the expiry of their incubation period, the zone of inhibition associated with the treated disc was measured in mm. The compounds were tested against Bacillus subtilis, Staphylococcus aureus gram-positive (+) and Escherichia coli, Salmonella typhi gram-negative (−) organism.

RESULTS AND DISCUSSION

The synthesis of ligand was performed by method reported for 5-benzoyl-1-(2-chloro ethanone)-benzotriazole. The C, H and N of ligand are consistent with predicted structure. The NMR spectra of the ligand gave the multiplet between 7.5-8.4 δ ppm for aromatic protons, singlet at 4.0 δ ppm for aryl amines(Ar-NH-), singlet at 5.35 δ ppm for aromatic -OH group (Ar-OH), singlet at 11.0 δ ppm for -COOH and singlet at 4.17 δ ppm due to the aliphatic -CH₂ group protons. Thus the structure of ligand is confirmed. The complexes are microcrystalline coloured powders having melting points higher than the ligands. They are stable in air at room temperature. All compounds gave satisfactory elemental Table-1.

Infrared spectra

The IR spectrum of ligand HL, the sharp bands due to 5-benzoyl benzotriazole. The bands were observed at 2360 and 1379 cm^{-1} [20]. The inflexions at 1489 is due to -CH₂- group. The strong band at 1697 cm^{-1} is attributed to C=O of carboxylic group of salicylic acid. The sharp band at 3127 and 3495 cm^{-1} due to aromatic -OH group. The IR band at 1316 cm^{-1} due to secondary -NH- group.

Magnetic moment and electronic spectra

The room temperature μ_{eff} value for the Co⁺² complex (4.68 B.M.) suggest high spin octahedral geometry, which is further supported by the electronic spectral data. The reflectance spectra bands of the complexes are observed at 7986 – 8965, 15270 -15289 and 22729 -22749 cm^{-1} , assignable to ⁴T_{1g}(F) → ⁴T_{2g}(F) (ν_1), ⁴T_{1g}(F) → ⁴A_{2g}(F) (ν_2) and ⁴T_{1g}(F) → ⁴T_{1g}(P) (ν_3) transitions, respectively[21].

In the Ni⁺² complex, μ_{eff} value at room temperature 3.36 B.M. as expected for four coordinated spin free Ni⁺² species. The reflectance spectra of the Ni⁺² complex, exhibit two strong bands at 15365-15389 cm^{-1} and 22505-22599 cm^{-1} , assignable to ³A_{2g}(F) → ³T_{1g}(F) and ³A_{2g}(F) → ³T_{1g}(P) respectively [22]. The spectral bands are well within the range observed for tetra coordinate octahedral complexes reported earlier[23-24]. The Cu⁺² complex exhibit normal magnetic moment (2.13 B.M.) indicating the distorted octahedral geometry, which is in agreement with data reported by several research workers [25-26]. These complex show broad asymmetric bands in the region 15965-15985 cm^{-1} and at 23266 cm^{-1} assignable to ²B_{1g} → ²A_{1g} and charge transfer transition respectively [27-28]. These results reveal the distorted octahedral geometry for this complex. The former band may be due to ²E_g → ²T_{2g} accounted due to Jahn Teller effect suggesting thereby a distorted octahedral geometry for this complex[29]. Zn⁺² complex is diamagnetic as expected for d10 systems and may have tetrahedral geometry[30-31]. There is no evidence for the characteristic bands of coordinated water in IR spectra.

The electronic spectra of the Mn⁺² exhibited three spin allowed bands in the region 16830 – 16845 cm^{-1} , 18350 – 18364 cm^{-1} and 23870 – 23895 cm^{-1} assigned to the transitions ⁶A_{1g} → ⁴T_{1g}(⁴G), ⁶A_{1g} → ⁴T_{2g}(⁴G) and ⁶A_{1g} → ⁴E_g, ⁴T_{1g}(⁴P) respectively, indicating octahedral geometry [32-33]. The observed magnetic moment (5.45 B.M.) of the complex indicates high spin octahedral environment [34].

Antimicrobial activity

The examination of antimicrobial activity of ligand and its all heterochelates reveals that the ligand is moderately more or less active against various organisms, while all the heterochelates are more active than ligand. Among all the heterochelates the Cu²⁺ chelate is more active against organism used.

The result indicates that the Cu (II) and Zn (II) exhibits higher activity towards most of the plant pathogenic organisms studied than the ligands. The other metal complexes did not show any significant increase in activity as compared to the ligands. The results suggest that variation in structure on coordination affects the growth of micro organisms and may result in to inhibitory or reduction in toxicology of metal ions towards some organisms[35].

Table 1 Analytical and physical data of ligand and complexes

Ligand / Complexes	Molecular Formula	M.W. g/mol	Yield (°C)	Elemental Analysis (%)				μ_{eff} B.M.
				Found (Calc.)				
				C	H	N	M	
HL	C ₂₂ H ₁₆ N ₄ O ₅	416	70	63.45 (63.46)	3.84 (3.85)	13.45 (13.46)	-	-
(HL) ₂ Cu ⁺²	C ₄₄ H ₃₄ N ₈ O ₁₁ Cu ⁺²	913.54	68	57.79 (57.77)	3.71 (3.72)	12.24 (12.25)	6.93 (6.95)	2.13
(HL) ₂ Ni ⁺²	C ₄₄ H ₃₄ N ₈ O ₁₁ Ni ⁺²	908.69	65	58.09 (58.10)	3.73 (3.74)	12.31 (12.32)	6.44 (6.45)	3.36
(HL) ₂ Co ⁺²	C ₄₄ H ₃₄ N ₈ O ₁₁ Co ⁺²	908.93	72	58.07 (58.09)	3.73 (3.74)	12.31 (12.32)	6.98 (6.99)	4.68
(HL) ₂ Zn ⁺²	C ₄₄ H ₃₄ N ₈ O ₁₁ Zn ⁺²	915.38	63	57.67 (57.68)	3.70 (3.71)	12.21 (12.23)	7.13 (7.14)	-
(HL) ₂ Mn ⁺²	C ₄₄ H ₃₄ N ₈ O ₁₁ Mn ⁺²	904.93	66	58.32 (58.34)	3.74 (3.75)	12.36 (12.37)	6.06 (6.07)	5.45

Table-2 Antimicrobial activity of ligand HL and it's metal complex

Compound	Zone of inhibition (in mm)						
	Antifungal Activity			Antibacterial Activity			
	Penicillium expansum	Aspergillus Niger	Nigros Pora sp.	Bacillus subtilis	S.aureus	S. typhi	Escherichia coli
Ligand(HL)	20	15	10	20	13	10	10
(HL) ₂ -Cu ²⁺	34	29	26	22	25	11	23
(HL) ₂ -Ni ²⁺	29	26	24	20	24	12	24
(HL) ₂ -Co ²⁺	20	28	30	18	19	10	19
(HL) ₂ -Mn ²⁺	25	20	21	20	25	09	22
(HL) ₂ -Zn ²⁺	15	10	12	10	12	10	09

CONCLUSION

- The ligand molecule acts as a tetra dentate ligand in all the studied cases of complex.
- Octahedral structures for Ni (II), Co (II), and Mn (II) complexes, tetrahedral polymeric structure for Zn (II), and distorted octahedral for Cu (II) complex have been tentatively proposed.
- Present work will contribute in the field of new antifungal for some plant pathogenic organisms.

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