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Synthesis, characterization and antimicrobial activity studies of 2-(2-(5-benzoyl-1-H-1,2,3-benzotriazole-1-yl)2-oxoethylamino) acetic 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 2-amino acetic acid (Glycine). The resulting 2-(2-(5-benzoyl-1H-1,2,3-benzotriazole-1-yl)2-oxoethylamino) acetic 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, Glycine, Metal chelates, IR/NMR Spectroscopies, 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. In view of the above facts and in continuation of our interest in studying the ligating behavior of such compounds [7-10] , therefore the present paper comprise the synthesize and characterize the solid complexes of the newly ligand containing the triazole moieties, 2-(2-(5-benzoyl-1H-1,2,3-benzotriazole-1-yl)2-oxoethylamino) acetic 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.

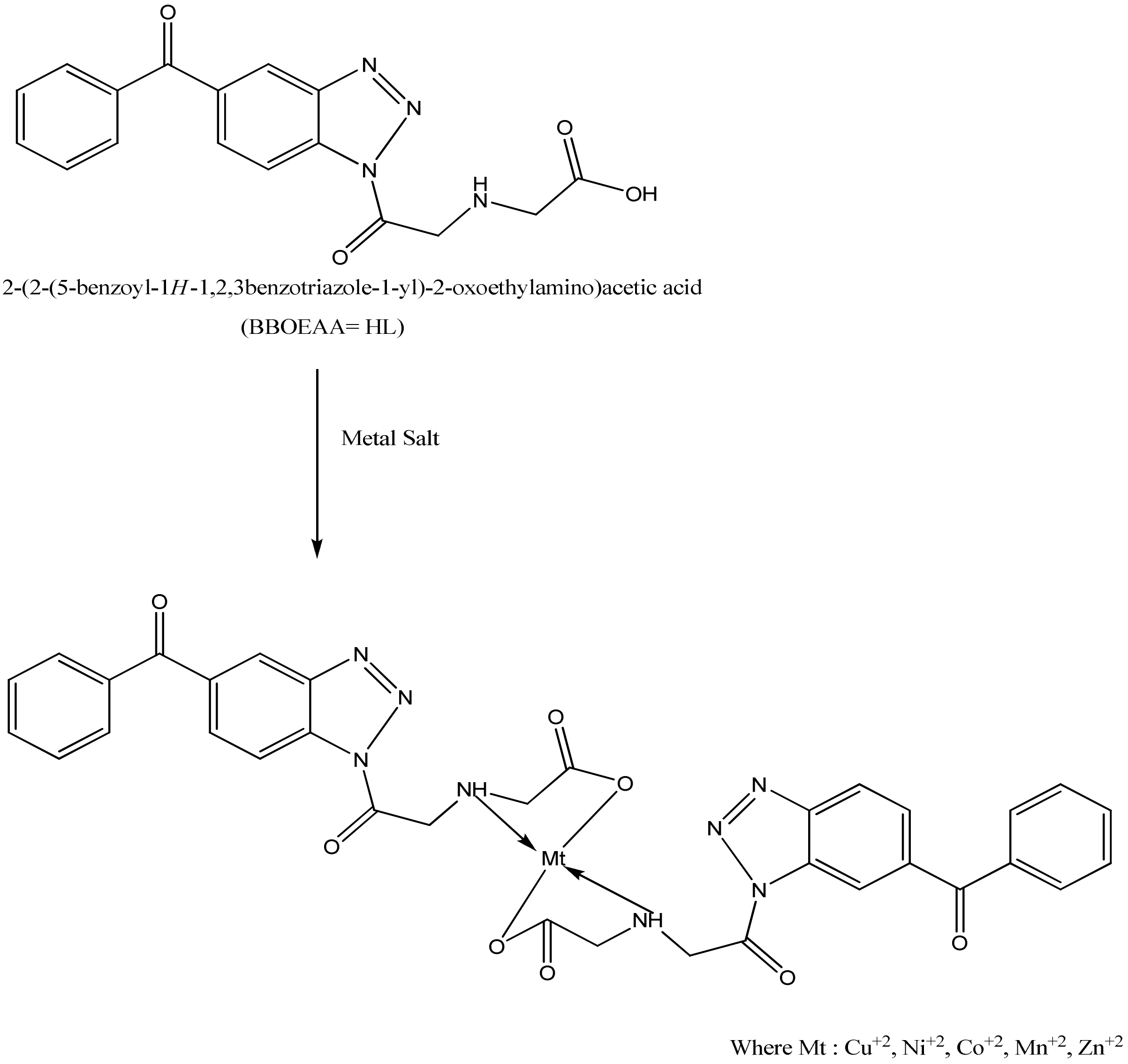
Synthesis of ligand HL

A mixture of 1-(5-benzoyl-1H-1,2,3-benzotriazole-1-yl)2-chloroethanone (BBCE) (0.01mol) and glycine (0.01mol) in ethanol 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 Cu^{2+} , Co^{2+} , Ni^{2+} , Mn^{2+} and Zn^{2+} metal ion complexes of BBOEAA have been prepared in a similar manner. The procedure is as follow.

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 Cu^{+2}), pH 6.0 (for Ni^{+2} and Co^{+2}) and pH 5.6 (Mn^{+2} and Zn^{+2}) 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 50-60 %. All the chelates were powdered well and dried at 70 ^{0}C over a period of 24 h.



2-(2-(5-benzoyl-1*H*-1,2,3benzotriazole-1-yl)-2-oxoethylamino)acetic acid

(BBOEAA= HL)

Where Mt : Cu^{+2}, Ni^{+2}, Co^{+2}, Mn^{+2}, Zn^{+2}

BBOEAA- Metal Chelates

Measurements

The C, H and N contents of metal chelates were determined on elemental analyzer Thermofiniggan 1101 Flash EA (ITALY). The metal contents were estimated using standard methods [11]. The halogen content was determined by Carius method [12]. The infrared spectra (KBr) were recorded in the range 4000-600 cm^{-1} with a nicolet -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 [13] at room temperature (300 K) using Hg [Co $(CNS)_4$] as calibrant [14], and the effective magnetic moment from relation [15], $\mu eff = 2.84\sqrt{Xm \times T}$, 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 [16]. Five days old cultures were suspended in potato dextrose agar (PDA) medium and autoclaved at 1200 ^{0}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.

The antimicrobial activity of each extracts was measured by paper disc diffusion method [17]. In this technique sterilized hot nutrient agar medium and 5 mm diameter paper discs of Whatman were used [18]. 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 ^{o}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 subtills, Staphylococcus aureus gram-positive (+) and Escherichia coli, Salmonella typhi gram-negative (—) organism. All experiments were performed in triplicate and ciprofloxacin was used as standard drug [19].

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 multiplate between 7.5-8.4 δ ppm for aromatic protons, singlet at 2.0 δ ppm for alkyl amines (R-NH-) , singlet at 11.0 δ ppm for –COOH and singlet at 3.6 δ ppm due to the aliphatic $–CH_2$ 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.

Table 1 Analytical and physical data of ligand and complexes

Ligand / Complexes	Molecular Formula	M.W. g/mol	Yield (^{0}C)	Elemental Analysis (%) Found (Calc.)				μ_{eff} B.M.
				C	H	N	M	
HL	$C_{17}H_{14}N_4O_4$	338	52.66	60.32 (60.35)	4.15 (4.17)	16.54 (16.56)	-	-
$(HL)_2$ Cu^{+2}	$C_{34}H_{30}N_8O_9$ Cu^{+2}	757.54	57.04	53.83 (53.85)	3.94 (3.96)	14.77 (14.78)	8.36 (8.38)	1.94
$(HL)_2$ Ni^{+2}	$C_{34}H_{30}N_8O_9$ Ni^{+2}	752.69	52.00	54.19 (54.20)	3.96 (3.98)	14.86 (14.87)	7.78 (7.79)	2.92
$(HL)_2$ Co^{+2}	$C_{34}H_{30}N_8O_9$ Co^{+2}	752.93	54.12	54.15 (54.18)	3.97 (3.98)	14.85 (14.87)	7.80 (7.82)	3.94
$(HL)_2$ Zn^{+2}	$C_{34}H_{30}N_8O_9$ Zn^{+2}	759.38	60.44	53.70 (53.72)	3.93 (3.95)	14.73 (14.74)	8.58 (8.60)	-
$(HL)_2$ Mn^{+2}	$C_{34}H_{30}N_8O_9$ Mn^{+2}	748.93	53.05	54.46 (54.47)	3.98 (4.00)	14.94 (14.95)	7.32 (7.33)	5.68

Infrared spectra

The IR spectrum of ligand HL, the sharp bands due to 5-benzoyl benzotriazole. The bands were observed at 2360 and 1376 cm^{-1} [20]. The inflextious at 1458 cm^{-1} are due to $-CH_2-$ group. The strong band at 2982 and 3055 cm^{-1} is attributed to -OH of carboxylic group of glycine. Several bands appeared between 1500-1600 cm^{-1} region may arised from aromatic breathing. The IR band at 1121 cm^{-1}due to aliphatic secondary –NH– group.

Magnetic moment and electronic spectra

Examination of data of the metal content in each compound revealed a 1:2 metal: ligand (M : L) stoichiomery in all of the complex of divalent metal ions. Magnetic moment (μ_{eff}) of each of the metal complex is given in Table-2. Examination of these data reveals that all complexes other than that of Zn^{2+} are paramagnetic while those of Zn^{2+} are diamagnetic.

Table-2 Magnetic moment of ligand HL and it's metal complex

Heterochelates	**μ_{eff} (BM)**	**Electronic spectral data (cm^{-1})**	**Transition**
$(HL)_2$-Cu^{2+}	1.94	24616 14966	Charge transfer $^{2}B_{1g}\rightarrow{}^{2}A_{1g}$
$(HL)_2$-Ni^{2+}	2.92	22314 15725	$^{3}A_{2g}\rightarrow{}^{3}T_{1g}(P)$ $^{3}A_{1g}\rightarrow{}^{3}T_{1g}(F)$
$(HL)_2$-Co^{2+}	3.94	24936 19890 8417	$^{4}T_{1g}(F)\rightarrow{}^{4}T_{2g}(F)$ $^{4}T_{1g}(F)\rightarrow{}^{4}A_{2g}$ $^{4}T_{1g}(F)\rightarrow{}^{4}T_{2g}(P)$
$(HL)_2$-Mn^{2+}	5.68	23755 18408 16718	$^{6}A_{1g}\rightarrow{}^{6}A_{2g}\ {}^{4}E_{g}$ $^{6}A_{1g}\rightarrow{}^{4}T_{2g}$ (4G) $^{6}A_{1g}\rightarrow{}^{4}T_{1g}$(PG)
$(HL)_2$-Zn^{2+}	Diamagnetic	-------	-------

The diffuse electronic spectrum of the Cu^{+2} metal complex shows broad bands at 14966 and 24616 cm^{-1} due to the $^{2}B_{1g}\rightarrow{}^{2}A_{1g}$ transition and charge transfer, respectively suggesting a distorted octahedral structure [21-23] for the Cu^{+2} complex which is further confirmed by the higher value of μ_{eff} of the Cu^{+2} complex. The Ni^{+2} complex gave two absorption bands at 22314, 15725 corresponding to $^{3}A_{2g}$ → $^{3}T1g$ (P) and $^{3}A_{1g}$ → $^{3}T_{1g}$ (F) transitions. Co^{+2} complex gave three absorption bands at 24936, 19890 and 8417 cm^{-1} Thus absorption bands at 24936, 19890 and 8417 cm^{-1} corresponding to $^{4}T_{1g}$ (F) → $^{4}T_{2g}$ (F), $^{4}T_{1g}$ (F) → $^{4}A_{2g}$, $^{4}T_{1g}$ (F) → $^{4}T_{2g}$ (P) The diffuse, reflectance spectra and the value of the magnetic moments (μ_{eff}) indicate and octahedral configuration for the Ni^{+2} and Co^{+2} complex. The spectra of Mn^{+2} shows weak bands at 23755, 18408 and 16718 cm^{-1} assigned to the transitions $^{6}A_{1g}$ → $^{4}T_{1g}$ (4Eg), $^{6}A_{1g}$ → $^{4}T_{2g}$ (4G) and $^{6}A_{1g}$ → $^{4}T_{1g}$ (4G) respectively suggestion an octahedral structure for the Mn^{+2} chelate. As the spectrum of the Zn^{+2} is not well resolved, it is not interpreted but its μ_{eff} value shows that it is diamagnetic as expected.

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 Cu^{2+} chelate is more active against organism used.

Table-3 Antimicrobial activity of ligand HL and it's metal complex

Compound	**Zone of inhibition (in mm)**						
	Antifungal Activity			**Antibacterial Activity**			
	Penicillium expansum	**Asperginus Niger**	**Nigros Pora sp.**	**Bacillus substilis**	**S.aureus**	**S. typhi**	**Escherichia coli**
Ligand(HL)	12	16	17	13	16	12	17
$(HL)_2$-Cu^{2+}	27	28	29	33	39	31	31
$(HL)_2$-Ni^{2+}	24	26	22	27	28	27	23
$(HL)_2$-Co^{2+}	20	22	23	28	30	23	28
$(HL)_2$-Mn^{2+}	18	25	20	29	22	21	21
$(HL)_2$-Zn^{2+}	20	24	21	25	27	19	20

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 chelate is more toxic that other. These compounds almost inhibit the fungi about 70%. Hence produced metal chelate can be employed as garden fungicides. Further work in the direction is in progress [24].

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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