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SYNTHESIS, CHARACTERISATION AND ANTIFUNGAL STUDIES OF Cu (II) HALIDE COMPLEXES OF SOME STERYL DERIVATIVES OF SUBSTITUTED BENZIMIDAZOLES

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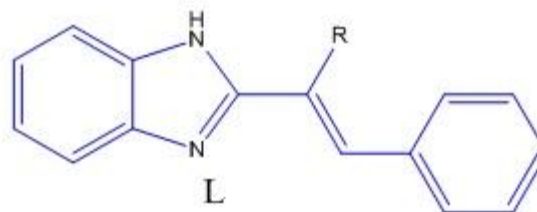
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ABSTRACT: Complexes of Copper (II) halides with steryl derivative of 2- methylbenzimidazole (stmbz), 2-ethylbenzimidazole (stebz) and 2-benzylbenzimidazole (stbbz) of composition CuL_2X_2 (L = stmbz, stebz and stbbz and X = Cl, Br) have been prepared and characterised. The magnetic susceptibility e.p.r. data, electronic absorption pattern and i.r. spectral studies of complexes indicated distorted octahedral environment of ligand around copper (II) atom. Steryl derivatives and their copper (II) complexes were screened for their antifungal activity in dilute aqueous ethanolic media where bromide complexes show higher antifungal activity than free ligands.

INTRODUCTION: Benzimidazole substituent of a molecule is an important pharmacophore and a privileged structure in medicinal chemistry¹⁻³. One of the prominent benzimidazole compound in nature is α -ribosyl-dimethyl benzimidazole which is an axial ligand for Cobalt in Vitamin- B₁₂ whose imidazole part provide an important binding sites in biological systems, displaying a vital role in metal - protein interaction³.

The wide spectrum of pharmacological and medicinal properties of benzimidazole derivatives and their metal complexes aroused huge interest to study the preparation and characterisation of complexes of benzimidazole derivatives⁴⁻¹².

In pursuance of interest of one of us^{8, 9}, we here report antifungal activity of the complexes of copper (II) halide with steryl derivatives of 2-alkyl/aryl of benzimidazole (L).



(R= H, CH₃, C₆H₅)

MATERIAL AND METHODS: Metal salts and solvents used were extra pure reagent of E. Merck or Anal-R grade chemical of B.D.H. The ligands were prepared by known procedure⁹. The metal content of complexes was determined by standard procedure. The elemental analyses were performed as reported earlier⁸⁻⁹. The results of IR and U-V were obtained from I.I.T, Patna and C.D.R.I. Lucknow.

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Preparation of CuL₂X₂ (L= Steryl derivatives of benzimidazole derivatives, X=Cl or Br): About 0.01 mole of copper (II) halides were dissolved in 20-25 ml dry methanol and treated with hot solution of steryl benzimidazole derivative (0.02 mole) in 30-35 ml methanol. The mixed solutions were heated for 15-20 minutes with constant stirring and resulting solution cooled at room temperature, when light ash or brown coloured dihalo-copper (II) complexes separated gradually. The products were collected on a filter, washed with cold methanol and dried in air oven CaCl₂. The complexes were analysed for Cu^{II}, halogens nitrogen contents, and results of analysis are given in **Table 1**. The e.p.r. spectra of complexes were recorded on Varian EPR (E-112) Spectrophotometer in micro crystalline form at LNT. The magnetic susceptibility was determined by Gouy method making diamagnetic correction using Pascal's constants.

RESULTS AND DISCUSSION: The elemental analysis of Cu (II) halides complexes correspond to composition CuL₂X₂ (L= steryl derivatives of 2-methyl, 2- ethyl and 2- benzylbenzimidazole and X

TABLE 1: ANALYTICAL RESULTS AND PHYSICAL DATA OF COMPLEXES

Compounds	Colours	% Metal	% Carbon	%Nitrogen	%Hydrogen	%Halogen Analysis Found (Calc)
CuA ₂ Cl ₂	Grey	11.69(11.58)	62.78(62.65)	9.82(9.74)	4.32(4.17)	12.21(12.35)
CuA ₂ Br ₂	Brown	9.92(9.72)	54.31(54.27)	8.61(8.44)	3.72(3.61)	24.13(24.08)
CuB ₂ Cl ₂	Grey	10.41(10.54)	63.89(63.74)	9.36(9.29)	4.71(4.60)	11.83(11.79)
CuB ₂ Br ₂	Brown	9.31(9.18)	55.69(55.53)	8.18(8.09)	4.16(4.04)	23.21(23.10)
CuC ₂ Cl ₂	Yellow- brown	8.82(8.75)	69.48(69.37)	7.63(7.70)	4.52(4.40)	19.72(19.59)
stmbz= A	White	-----	81.69(81.81)	12.26(12.72)	5.53(5.45)	-----
stebz= B	White	-----	81.11(82.05)	12.01(11.96)	6.03(5.98)	-----
stbbz= C	White	-----	85.23(85.16)	9.55(9.45)	5.48(5.40)	-----

The electronic absorption spectrum of complexes in ethanol display strong absorption band below 400nm attributed to charge transfer transition. A broad shoulder near 440-460nm and weak broad band near 680-700nm was observed in spectrum of [Cu(stebz)₂ Cl₂] and [Cu(stmbz)₂ Cl₂] attributed to ²B_{1g} → ²E_g and ²B_{1g} → ²A_{1g}, ²B_{1g} → ²B_{2g} transitions in distorted octahedral field¹⁵.

In case of dibromo complexes [CuL₂Br₂], (L=stmbz, stebz and stbbz), the spectra display much stronger absorption below 420nm and a broad bands shoulder near 630-680nm attributed to combination of ²B_{1g} → ²A_{1g}, ²B_{1g} → ²B_{2g} transition in tetragonally distorted field¹⁵.

= Cl or Br). The dichloro complexes CuL₂Cl₂ has less solubility in methanol or ethanol than dibromo product CuL₂Br₂. The complexes dissolve appreciably in DMF yielding greenish yellow or brownish yellow solutions. The freshly prepared DMF solution of dihalo complexes show negligible electrical conductance value (6-8 ohm⁻¹ mol⁻¹ cm²) suggesting coordinated nature of halide ions in complexes¹¹. The magnetic susceptibility of complexes occurs in the range 1.79-1.86 BM at 304K (Table 1). The magnetic moment values do not indicate antiferromagnetism in complexes at room temperature¹². The E.P.R. Spectra of Cu(stebz)₂ Cl₂ and Cu(stebz)₂ Br₂ have been interpreted according to Kneubuhl's method¹³. The calculated g_⊥ and g_∥ value of Cu(stebz)₂ Cl₂ was found to be 2.062 and 2.151 and g_{av} equal to 2.091 which gives G value 2.43. The g_⊥ and g_∥ value of Cu (stebz)₂ Br₂ was found as 2.032 and 2.121 and calculated g_{av} was found 2.062, which gave G value 3.78. The G value of bromo complexes [Cu(stebz)₂ Br₂] are greater than that of dichloro complexes indicated lower exchange coupling in dibromo product¹⁴.

The i.r. spectrum of stebz and other steryl derivatives display broad band between 3030-3250 cm⁻¹ attributed from ν(C-H) phenyl ring and ν(N-H) of benzimidazole ν(N-H) group. A medium band at 2928-2875 cm⁻¹ is assigned to CH₃ group ν(C=H) vibrations. These i.r. bands are retained in Cu(II) complexes with slight change in positions and intensities.

The benzimidazole ring ν(C=N) and steryl group (C=C) stretching bands were observed at 1605±5 cm⁻¹ and 1635-1640 cm⁻¹. The ν(C=N) band near 1605±5 of ligand shifted to lower frequency by 10-15 cm⁻¹ in their complexes suggesting the bonding of imidazole ring (C=N) nitrogen to metal atom.

In finger print regions the steryl derivatives show a large number of prominent and medium to strong i.r. bands originated from phenyl ring skeletal, $\nu(\text{C-N})$, $\nu(\text{C-C})$, $\delta(\text{C-H})$, out of plane and in plane bending band and these bands are retained in complexes. The $\delta(\text{NH})$ of benzimidazole part located near 1535 ± 5 in steryl derivatives are not affected appreciably indicating that (N-H) nitrogen is not involved in bonding with Copper (II) halide ¹⁶⁻¹⁸.

Antifungal activity of the ligands and their copper(II) halide complexes were evaluated by Radial growth method ¹⁹ using Czapek's agar medium having composition 20g starch, 20 agar agar, 20g glucose dissolved in 1000ml. To this solution 50, 100 and 200 ppm concentration of

ligands and complexes were made with ethanolic solution of products.

The medium was then poured in petri plate and then spores of fungi (*F. oxysporum*, *A. flavus*, *A. niger* and *R. phaseoli*) were placed on the medium with the help of an inoculum needle. These petri plates were wrapped in polythene bags containing a few drops of ethanol and placed in an incubator at $30\pm 1^{\circ}\text{C}$. The linear growth of fungi was obtained by measuring the fungal colony diameter after five days. The percentage (%) inhibition was calculated as $100(\text{C-T})/\text{C}$ where C and T are the diameter of the fungus colony in the control and test plates respectively. The antifungal activities of metal complexes were much larger than free ligand and shown in **Table 2**. The bromo derivatives have larger activity than chloro complexes.

TABLE 2: ANTIFUNGAL ACTIVITY OF LIGAND AND COMPLEXES AFTER 120 HOUR INCUBATION AT $30\pm 1^{\circ}\text{C}$

Fungi	Conc in ppm	stmbz	stbbz	stebz	CuL ² /2Cl ₂	CuL ² /2Br ₂	CuL ² '/2Cl ₂	CuL ² '/2Br ₂	CuL ² L ₂ Cl ₂	CuL ² L ₂ Br ₂	Ref
<i>A.flavus</i>	50	31	34	28	39	43	40	45	38	46	72
	100	50	52	42	50	58	52	63	58	60	82
	200	61	70	64	66	72	70	74	70	74	96
<i>A.niger</i>	50	38	41	38	45	46	42	46	40	45	70
	100	52	61	58	65	68	58	62	54	60	91
	200	68	76	72	78	81	76	81	73	76	100
<i>R. phaseoli</i>	50	40	40	36	45	46	42	45	42	47	71
	100	50	58	50	62	63	55	60	55	61	86
	200	72	70	58	72	79	71	76	72	76	100
<i>F. oxysporum</i>	50	40	36	38	42	45	42	43	42	48	69
	100	52	51	52	56	60	58	60	54	61	86
	200	72	72	73	76	81	73	79	76	82	98

The reference Antifungal material is Mycostatin; L=stmbz, L¹=stebz and L²=stbbz

CONCLUSION: The ligand coordinates as unidentate nitrogen donor forming distorted octahedral structure with halogen bridging atom. The bromo complexes show higher microbial activity than the free ligand.

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REFERENCES:-

1. Ozkay Y, Tunali Y, Karaca H Isikdag I, : Antimicrobial activity and a SAR study of some novel benzimidazole derivatives bearing hydrazone moiety. European Journal of Medicinal Chemistry 2010; 45 8: 3293
2. b. Pandey D, Shabh R, *et al*: Synthesis Characterisation and Pharmacological screening of novel benzimidazole derivatives. Arabian Journal of Chemistry 2011; 4: 13
- c. Li YF, Wang GF, He P L, Huang W G, Gao FH, Tang W, *et al*: Synthesis and antihepatitis B virus activity of novel benzimidazole derivatives. J. Med. Chem. 2006; 49: 4770-4794.
- d. Podunavac-Kuzmanovic SO, Cvetkovic DM: Antibacterial Evaluation of some benzimidazole derivatives and their Zn (II) complex. J. Serb. Chem. Soc. 2007; 72(5): 459-466
2. a. Walia R, Md. Hedaitullah, Syeda Farha Naaz, Iqbal Khalid, Lamba H S: A newer benzimidazole derivatives; an overview. International Journal of Research in Pharmacy and Chemistry 2011; 1: 3 565.
- b. Yu Luo, Jia-Ping Yao, Li Yang, Chun-Lan Feng, Wei Tang, Gui-Feng Wang, Jian-Pin Zuo, Wei Lu, :Synthesis and Antihepatitis B virus activity of Novel class of thiozolybenzimidazole derivatives:. Arch Pharm Chem. Life Sci 2011; 2: 78-83.
- c. Kadam SS, Mahadik KR, Bolhara KG: Principles of Medicinal Chemistry. Edition 13, 2005; 233.

3.
 - a. Ansari KF, Lal C: Synthesis, Physicochemical properties and Antimicrobial activity of some new benzimidazole derivative. *European Journal of Medicinal Chemistry* 2009; 44: 2294.
 - b. Kucukbay H, Yilmaz U, Sireci N, Onganer AN: Synthesis and Antimicrobial activities of some bridged bis(benzimidazole) derivatives. *Turk J. Chem.* 2011; 35: 561-571
4. Pandey R, Pandey Daya S: Reactions and structural studies of 4-(1H-benzimidazol-2-yl)-benzonitrile with metal nitrates. 2012; 89: 1123-1134
5. Payra P, Zhang H, Kwok WH, Duan M, Gallucci J, Chan MK, :Structural Trends in First Row Transition Metal Bis (benzimidazole) complexes. *Inorg Chem* 2000; 39: 1076-1080.
6. Saha N, Misra A, :Synthesis, Characterisation and a coordinating properties of a new benzimidazolypyrazole: Cobalt(II), Nickel(II) and Copper(II) complexes of 5-methyl-3-(2-benzimidazolyl)pyrazole. *J. Indian Chem. Soc.* 1993; 70: 1035.
7. Tripathi AK, Mathur Pavan, : A Binuclear Iron (III) complexes of N, N, N' N' Tetrakis(2-benzimidazolyl)1,2 Ethanediamine. *J. Indian Chem. Soc.* 1993; 70: 991.
8.
 - a. Ghosh SP, Mishra LK: Complexes of Iron (II &III) with 2-(2'-Pyridyl)-benzimidazole. *Inorg. Chim. Acta* 1973; 7: 545-549
 - b. Choudhary CK, Choudhary RK, Mishra LK :Complexes of Rhodium (III), Palladium (II) and Platinum(II) with 2-(2'-Pyridyl)benzimidazole. *J. Indian Chem. Soc.* 2002; 79: 761-762.
 - c. Ghosh SP, Bhattacharjee P Mishra LK, :Complexes of Rh(III) and Pd(II) with 2-(2'-Pyridyl)benzimidazole. *J. Indian Chem. Soc.*1974; 51: 308.
 - d. Ghosh SP, Bhattacharjee P, Dubey L. and Mishra LK. "Complexes of some Platinum metals with imidazole and benzimidazole". *J. Indian Chem. Soc.* 1975; 52: 230-235.
 - e. Ghosh SP, Mishra LK: Palladium (II) complexes with benzimidazole and 2-methylbenzimidazole. *J. Indian Chem. Soc.* 1970; 47: 1163-1172
 - f. Ghosh SP, Sinha AK, Singh CP, Mishra LK: Oxomolybdenum(V) complexes with 2-(2'-Pyridyl)benzimidazole. *J. Indian Chem. Soc.* 1986; 63: 607-608.
 - g. Sinha AK, Kumari (Mrs.) Urmilla, Singh CP, Mishra LK: Oxovanadium (IV) complexes with imidazole, benzimidazole and substituted benzimidazoles. *J. Indian Chem. Soc.* 1990; 67: 985-986.
 - h. Mishra LK, Gupta SK: Oxovanadium (IV) complexes with 2-(o-Hydroxyphenyl)benzimidazole and imidazoline. *J. Inorg Nucl Chem.* 1979; 41: 980-991.
 - i. Mishra LK, Gupta SK, :Complexes of Copper (II) with 2-(o-Hydroxyphenyl)benzimidazole and related ligands. *J. Indian Chem. Soc.* 1979; 56: 206-208.
 - j. Mishra LK: Complexes of 5-Nitrobenzimidazole with some Metal ions. *J. Indian Chem. Soc.* 1982; 59: 795.
 - k. Ghosh SP, Mishra LK: Complexes of Zn(II), Cd(II) and Hg(II) with Benzimidazole and 2-methylbenzimidazole. *J. Indian Chem. Soc.* 1983; 60: 212-214.
1. Mishra LK, Jha MM, Jha BK: Stable complexes of Oxochromium(V). *J. Indian Chem Soc.* 1989; 66: 818-819.
- m. Mishra LK, AnilRoy KK: Complexes of Rh(III) and Pd(II) with N-Vinylimidazole. *J. Indian Chem. Soc.* 1987; 64: 503-505
9.
 - a. Bala M, Ahmad K, Sharma SR, Mishra LK: Synthesis Characterisation and Derivatographic studies of 1-(1H-benzimidazol-2-yl)ethanone and 1-(1H-benzimidazol-2-yl)phenone with Co(II), Ni(II) and Cu(II). *IOSR-Journal of Applied Chemistry* 2012; 3(1): 46-52
- b. Bala M, Ahmad K, Sharma SR, Mishra LK: Preparation, Characterisation and Anti-fungal activity of 1E-1-(1H-benzimidazol-2-yl)-N-hydroxyethanimine and 1E-1-(1H-benzimidazol-2-yl)-N-hydroxy-1-phenylmethanimine with Co(II), Ni(II), Cu(II), Zn(II) and Cd(II). *IOSR-Journal of Applied Chemistry* 2012; 3(2): 21-29.
- c. Bala M, Mishra LK, :Synthesis, Characterisation and Anti-amoebic activity of 1E-1-(1H-benzimidazol-2-yl)-N-hydroxyethanimine and 1E-1-(1H-benzimidazol-2-yl)-N-hydroxy-1-phenylmethanimine with Oxovanadium (IV), Mn(II), Fe(II). *IJETCAS* 2013; 4(4): 347-353
10.
 - a. Tripathi AK, Sharma KK, Mathur P: Monomeric and Dimeric Mn(II) complexes of N,N,N',N', tetrakis(2-benzimidazolyl) methyl-1,1,2'-ethylenediamine and its derivatives. *Indian J. Chem. Sect A* 1991; 68: 519-525.
 - b. Tehlan S, Hundal MS, Mathur P: Copper(II) complexes of N-Octalated Bis(benzimidazole)diamide Ligand and their Peroxide-Dependent oxidation of Aryl Alcohols. *Inorg Chem.* 2004; 43: 6589-6595
11. Geary W J: The use of Conductivity Measurements in Organic Solvent for the Characterisation of Coordination Compounds" *Coord. Chem. Rev*1971; 7: 81-122
12.
 - a. Andras T, Carlo F, Angiola Chiesi-Villa, Carlo Guastini: Copper (I) benzimidazole Adducts from Mononuclear to Polymeric Complexes. *Inorg Chem.* 1987; 26: 3897-3902.
 - b. Elder MS, Melson GA, Bush DH :The synthesis of O-benzylene-2,1-benzimidazole in the presence of Nickel(II) ions and a study of some of its Metal complexes. *Inorg Chem.* 1966; 5(1): 74-77.
 - c. Liu Qin-De, Jia Wen-Li, Wang suning, :Blue Luminescent 2-(2'-Pyridyl)benzimidazole Derivative Ligands and their Orange Luminescent Mononuclear and Polynuclear Organoplatinum(II) complexes. *Inorg Chem.* 2005; 44: 1332-1343.
 - d. Maurya MR, Kumar A, Martin E, Rehder D, :Synthesis, Characterisation, Reactivity and Catalytic Potential of Model Vanadium (IV, V) complexes with benzimidazole-Derived O,N,N Donor Ligands. *Inorg Chem.* 2006; 45: 5924-5937.
 - e. Zhou Yan-Ling, Meng Fa-Yan, Zhang Jian Zeng Ming-Hun, Liang Hong, :Mononuclear, Tetra, Penta-3d Molecular cluster Based on the variability of SS-1, 2-bis(1H-benzimidazol-2-yl)-1,2-ethanediol ligand arising from Hydroponic and Hydrothermal conditions structure, Crystal growth and Magnetic properties. *Crystal Growth & Design* 2009; 9(3): 1402-1410.
 - f. Tsotakos T, Tsoukalas C, Patsis G, Panagiotopoulon A, Nikolic N, Jankovic D, Djokic D, Raptopoulou CP, Terzis A, Papagiannopoulou, Pelecanou M, Papadopoulos M, Pirmertis L, :Benzimidazole derivatives as N, S, O, Ligands for the fac-[M(CO)₃]⁺ (M= Re⁺, Te⁺). *Inorg Chim Acta* 2011; 377: 62-68.
 - g. Saha D, Das S, Dutta Maity, Dutta S, Baitalik S, :Synthesis, Structural, Characterisation and Phytophysical Electrochemical, Intercomponent Energy- Transfer and Anion- sensing studies of imidazole 4,5-bis(benzimidazole)-Bridged Os^{II} Os^{II} and Ru^{II} and Os^{II} Bipyridine complexes. *Inorganic Chemistry* 2011; 50: 46-61.
 - h. Serratrice M, Cinellu MA, Maiore L, Maria P, Antonio Z, Gabbiani C, Guerri A, Ida L, Stefania N, Mini E, Messori L: Synthesis, Ctructural Characterisation, solution Behaviour and *in-vitro* Antiproliferative properties of a

- series of Gold complexes with 2-(2'-Pyridyl)benzimidazole as Ligand: complexes of Gold(III) versus Gold(I) and Mononuclear versus Binuclear Derivatives. *Inorg Chem.* 2012; 51: 3161-3171.
- i. Molander GA, Ajayl K: Oxidative condensation to form benzimidazole-substituted Potassium Organotrifluoroborates. *Organic Letters* 2012; 14(16): 4242-4255
 13. Kneubuhl FK: Line Shapes of Electron Paramagnetic Resonance Signals produced by Powders, Glasses and viscous Liquids. *J. Chem. Phys* 1960; 33: 1074
 14. Procter IM, Hathaway BJ, Nicholis PJ: Square planar adducts of Cu(II) & Ni(II) complexes of some 2-hydroxyacetophenone thiosemicarbazone with Nitrogen donors. *Indian J. Chem. Sect (A)* 1968; 1678.
 15. Lever A B P: *Inorganic Electronics Spectroscopy* Elsevier Amsterdam, 1968; 357.
 16. Das AK, Nath M, Zulkerman Z: Complexes with Tridentate Ligands: Dimethyl(IV) complexes with N-Salicylidene derivatives of Aroylhydrazines, 5-Methyl hydrazine Carbothioate and 4-substituted thiosemicarbazides. *Inorg Chim. Acta* 1983; 21: 49.
 - 17.
 - a. Nakamoto K: *The Infrared and Raman Spectra of Inorganic and Coordination Compounds* Wiley, New York, 1978.
 - 18.
 - a. Preston PN: Synthesis, Molecular structure Determination and Antitumour Activity of Pt(II) and Pd(II) complexes of 2-Substituted benzimidazole". *Chem. Rev* 1974; 74: 279.
 - b. Cheeseman GWH: Cobalt(II), Nickel(II) and Copper(II) with 2-Substituted Benzimidazole complexes: Potential radiosensitizing agent, 5,2-Substituted benzimidazole Derivatives. *J.Chem. Soc* 1964; 4645.
 19. Nerie Y L Thapual P N: *Fungicides in plant disease control.* Oxford and IBH Publishing Co, New Delhi, 1993.

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