



Preparation, Spectroscopic Characterization and Biological Evaluation of Metal Complexes with Schiff Base Derived from Benzofuran and Coumarin Moieties

KEYWORDS

Benzofuran Schiff base, Metal complexes, Spectral, Antimicrobial

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ABSTRACT A series of metal complexes of the type $ML_2 \cdot H_2O$, where $M = Co(II), Ni(II), Cu(II)$ and $MLCl \cdot H_2O$ where $M = Zn(II), Cd(II), Hg(II)$ and $L = BrOCEBFC$, Schiff base derived from the condensation of benzofuran-2-carbohydrazide with 3-acetyl-6-bromo-chromen-2-one have been synthesized. The geometry of the complexes have been proposed by analytical, IR, UV-Vis, 1H NMR, ESR spectral data and magnetic studies. The ΔM values indicate that, the complexes are non-electrolytic in nature. On the basis of these studies octahedral structure has been assigned to $Co(II), Ni(II)$ and $Cu(II)$ complexes and tetrahedral geometry to $Zn(II), Cd(II)$ and $Hg(II)$ complexes. The Schiff base and its metal complexes have been tested for their antimicrobial activities.

INTRODUCTION

Schiff's bases have exhibited higher coordination number and from kinetics and thermodynamic point of view, they are important class of compounds, resulting in an enormous number of publications and literature review, ranging from pure synthetic work to physico-chemical and biochemically relevant studies of metal complexes [1] and found wide range of applications. Schiff's base ligands and their metal complexes exhibit useful biological activities [2]. The seed oil of plant "Egonoki" which is much common in Japan is known to contain a benzofuran derivative called "Egonol". It is an effective synergist for rotenone pyrethrum against houseflies, mosquitoes, aphids and many other insects [3]. Some benzofuran derivatives such as 2-acetylbenzofuran and 2-nitrobenzofuran are well known biodynamic agents possessing various pharmacological properties [4]. Coumarins and its derivatives include antioxidant [5], Pesticidal, nematocidal, DNA-cleavage [6], antituberculosis [7] etc activities.

MATERIALS AND METHODS

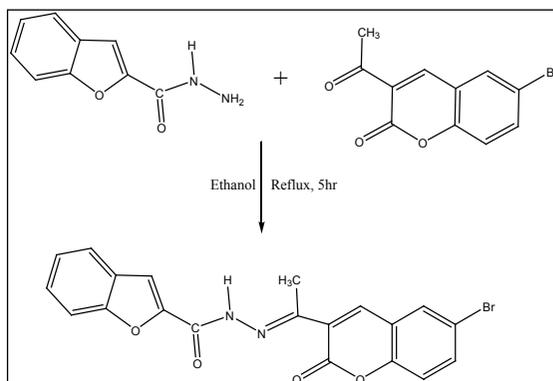
Experimental

All the chemicals used were of analytical reagent grade (AR), and are of highest purity available. Preparation of benzofuran-2-carbohydrazide, elemental analysis and the instruments used were described as reported earlier [8].

Synthesis of the Ligand, BrOCEBFC.

A mixture of equimolar quantities of ethanolic solution (20 mL) of benzofuran-2-carbohydrazide (0.1 mol) and ethanolic solution (20 mL) of 3-acetyl-6-bromo-chromen-2-one (0.1 mol) was refluxed on water bath for about 5 hours. The product that was separated out as intense yellow colored crystalline solid on cooling was filtered, washed with alcohol and recrystallised from hot ethanol (Scheme-1). Yield: 65%, m. p = 272 °C.

Scheme-1



General procedure for the synthesis of $Co(II), Ni(II), Cu(II), Zn(II), Cd(II)$ and $Hg(II)$ complexes.

An ethanolic solution (20 mL) of metal chlorides (0.01 mol) was added to an ethanolic solution (40 mL) of the Schiff's base (0.01 mol). The reaction mixture was refluxed for about 5 h on water bath, on partial removal of the solvent, the separated colored solid complexes were collected by filtration, washed with little hot ethanol and air-dried (yield: 60-65%).

Antibacterial and antifungal assays

The biological activities of synthesized Schiff base and its $Co(II), Ni(II), Cu(II), Zn(II), Cd(II)$ and $Hg(II)$ complexes have been studied for their antibacterial and antifungal activities respectively in DMF solvent. The antibacterial activity of test compounds were assessed against *E. coli* and *S. aureus* organisms and antifungal activity against *A. niger* and *A. flavus* by cup-plate zone inhibition technique [9]. Accurately weighed 10 mg of test compound was dissolved in 10 mL of DMF in serially labeled sterilize test tubes, from the stock solution 0.1 mL (100 mL) of solution was used for antimicrobial assay.

Antibacterial assay

The Nutrient agar prepared by dissolving bacteriological peptone (1g/L), Beef extract (5g/L), Sodium chloride (5g/L) in distilled water and the pH of the solution was adjusted to 7.4 by sodium hydroxide (1M) or hydrochloric acid (1M).

This solution was filtered and agar (20g/L) was added. Then it was sterilized for 15 min at 15 lb/kg pressure. About 15-20 mL of molten nutrient agar was poured into each of the sterilized petri dishes of 3.5 inches diameter, with the help of sterile cork borer two cups of each with 8mm diameter were punched and scooped out the set agar (two cups were numbered for the particular test compounds). The agar plates so prepared are divided into two sets and each set of the plates were inoculated with the suspension of particular organisms by spread plate techniques. The cups of inoculated plates were then filled with 0.1 mL of the test solution, the plates were allowed to stay for 2 hrs in refrigerator further the plates were incubated at 37°C for 24 hrs. The zone of inhibition developed if any, was then measured for the particular compound with particular organisms. Norflaxin (20 mg/mL) was used as a standard and DMF control was also put to know the activity of the solvent.

Antifungal assay

The media used for antifungal activity was the potato-dextrose agar. It was prepared as follows, potato pieces (120g) were dissolved in 10mL distilled water by steaming for 30 min. the solution was filtered while hot and the volume was made up to 400 mL. To this solution dextrose (4g) and agar (8 g) were added and dissolved by steaming for 30 min. The so formed potato-dextrose agar (PDA) media was poured into

two separated conical flasks and were separately inoculated with above fungus using sterile metal wire loop. About 15-20 mL of molten potato-dextrose agar was poured into each of the sterilized petri dishes of 3.5 inches diameter with the help of sterile cork borer, two cups of each with 8 mm diameter were punched and scooped out from the set PBA medium (two cups were numbered for the particular test compounds). The plates so prepared are divided into to separate sets of plates, were inoculated with the suspension particular organism by spread plate technique. The cups of inoculated plates were then filled with 0.1 mL of the test solution the plates were allowed to stay there, as they are in their upright position for two hrs. Further the plates were incubated at 37°C for 72 hrs. The zone of inhibition developed, if any was then measured for the particular compound with particular organism. Chlorometazole (20 mg/mL) was used as a standard. DMF control was also put to know the activity of the solvent.

RESULTS AND DISCUSSION

All the complexes are light colored, soluble in DMF/DMSO and sparingly soluble in common organic solvents. The elemental analysis indicate that the metal complexes of Co(II), Ni(II) and Cu(II) possess the 1:2 type of stoichiometry and 1:1 type of stoichiometry for Zn(II), Cd(II) and Hg(II) complexes. The molar conductance values of all the complexes indicate their non-electrolytic nature (Table-1)

Table-1

Analytical and Physico-Chemical data of the Schiff's base ligand and its Metal Complexes

Ligand / Complexes	Mol. Formula	Mol. Weight	M.P. °C [Yield %]	Elemental Analysis Found(Calcd)						μ_{eff} B.M.	λ_{A}
				%C	%H	%N	%M	%Br	%Cl		
[Br-OCEBFC]	$\text{C}_{20}\text{H}_{13}\text{N}_2\text{O}_4\text{Br}$	424.90	272 [70]	56.10 (56.48)	3.20 (3.06)	6.20 (6.59)	--	18.50 (18.80)	--	--	--
Co(II)	$[\text{Co}(\text{C}_{20}\text{H}_{12}\text{N}_2\text{O}_4\text{Br})_2] \cdot \text{H}_2\text{O}$	925.40	>300 [72]	51.50 (51.92)	2.40 (2.87)	5.98 (6.05)	6.00 (6.35)	17.60 (17.95)	--	4.75	22.10
Ni(II)	$[\text{Ni}(\text{C}_{20}\text{H}_{12}\text{N}_2\text{O}_4\text{Br})_2] \cdot \text{H}_2\text{O}$	925.16	>300 [68]	51.55 (51.93)	2.55 (2.83)	6.52 (6.06)	6.50 (6.34)	16.50 (17.27)	--	3.45	20.84
Cu(II)	$[\text{Cu}(\text{C}_{20}\text{H}_{12}\text{N}_2\text{O}_4\text{Br})_2] \cdot \text{H}_2\text{O}$	930.01	>300 [68]	51.20 (51.66)	2.50 (2.82)	5.88 (6.02)	6.50 (6.83)	17.50 (17.18)	--	1.89	19.48
Zn(II)	$[\text{Zn}(\text{C}_{20}\text{H}_{13}\text{N}_2\text{O}_4\text{Br}) \text{Cl}] \cdot \text{H}_2\text{O}$	561.18	295 [75]	44.00 (44.23)	2.50 (2.60)	5.40 (5.16)	12.50 (12.04)	14.60 (14.71)	6.20 (6.53)	Dia.	19.89
Cd(II)	$[\text{Cd}(\text{C}_{20}\text{H}_{13}\text{N}_2\text{O}_4\text{Br}) \text{Cl}] \cdot \text{H}_2\text{O}$	608.31	298 [68]	40.50 (40.71)	2.00 (2.39)	4.40 (4.75)	18.00 (19.05)	13.10 (13.54)	6.50 (6.01)	Dia.	17.65
Hg(II)	$[\text{Hg}(\text{C}_{20}\text{H}_{13}\text{N}_2\text{O}_4\text{Br}) \text{Cl}] \cdot \text{H}_2\text{O}$	678.28	>300 [75]	35.10 (35.42)	2.40 (2.08)	4.40 (4.13)	29.50 (29.57)	11.60 (11.78)	5.20 (5.23)	Dia.	18.72

^aMelting point/Decomposition Temperature, ^bMolar conductance $\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1} (10^{-3}\text{M})$

IR Spectral Studies

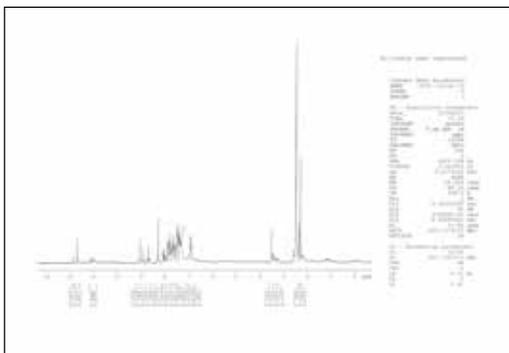
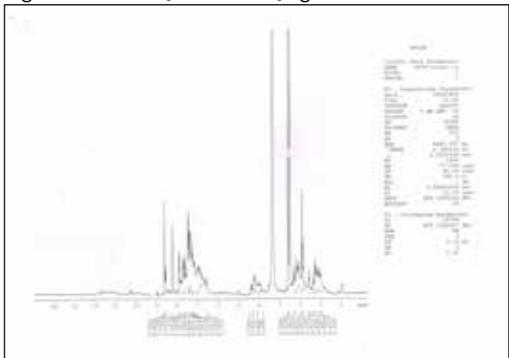
The strong bands at 3274 and 1678 cm^{-1} in free ligand are assigned to $\nu(\text{NH})$ and $\nu(\text{C}=\text{O})$ stretching vibrations respectively. The disappearance of these two bands in the IR spectra of the complexes shows the enolisation of amide carbonyl function and the subsequent coordination of oxygen of the enolised carbonyl with the metal ions. This fact of enolisation of amide carbonyl during complexation was further confirmed by appearance of new sharp bands in the region 1612-1600 cm^{-1} in Co(II), Ni(II) and Cu(II) complexes which are assigned to characteristic azine ($-\text{C}=\text{N}=\text{C}-$) moiety [10] of the coordinated ligand. High intensity sharp band observed at 1736 cm^{-1} is assigned to $\nu(\text{C}=\text{O})$ of lactone [11]. The shifting of this band to lower wave number side in the complexes in the region 1702 cm^{-1} indicates the bonding through oxygen of lactone $\nu(\text{C}=\text{O})$ group.

The Schiff base shows a medium to strong intensity band at

1608 cm^{-1} due to $\nu(\text{C}=\text{N})$ vibration [12]. This band in complexes shifts to lower frequency side and appear in the region 1582 cm^{-1} indicating involvement of azomethine nitrogen in bonding with the metal ions. The medium to strong intensity band observed at 1150 cm^{-1} is attributed to $\nu(\text{C}-\text{O}-\text{C})$ stretching vibration of benzofuran ring in the free ligand [13]. This band shows no shift in the complexes suggesting non participation of 'O' of $\nu(\text{C}-\text{O}-\text{C})$ group. The non-ligand weak intensity bands observed in the complexes in the region 559-560 cm^{-1} and 420-432 cm^{-1} are assigned to $\nu(\text{M}-\text{O})$ and $\nu(\text{M}-\text{N})$ stretching vibrations respectively. $\nu(\text{M}-\text{Cl})$ stretching vibrations are observed in the region 318-321 cm^{-1} in all the complexes.

¹H NMR spectral studies

The ¹H NMR spectrum of ligand (Fig 1) shows a signal at δ 11.28 (s, 1H) and δ 8.95 (s, 1H) due to the presence of amide(CONH) and azomethine($-\text{C}=\text{N}-$) proton respectively. In the spectrum of

Fig-1. ¹H NMR of [BrOCEBFC] ligandFig-2. ¹H NMR of Hg(II) complex of the [BrOCEBFC] ligand

Hg(II) complex (Fig 2) the azomethine proton has shifted from d 8.95 to 9.00 due to its coordination with metal ion. The signal due to amide proton has disappeared in the complex indicates the deprotonation of OH group and bonding through oxygen atom. A singlet at d 3.90 (s, 3H -CH₃) is due to the methyl protons present on the methyliminomethyl function. Nine aromatic protons resonated in the region d 6.70-8.75 (m, 9H) as a multiplet.

MASS SPECTRAL STUDIES

The mass spectrum of the ligand shows a molecular ion peak at m/z 425 which corresponds to the molecular weight of the compound. Thus, supporting the proposed geometry.

ELECTRONIC SPECTRAL STUDIES

The electronic spectra of the Co(II), Ni(II) and Cu(II) complexes were recorded in freshly prepared DMF solution (10⁻³M) at room temperature. The electronic spectra of Co(II) complex show bands at 16260 and 20408 cm⁻¹. These two bands are assignable to ⁴T_{1g} (F) → ⁴A_{2g} (F) (v₂) and ⁴T_{1g} (F) → ⁴T_{2g} (F) (v₂) transitions respectively in an octahedral environment [14]. The Ni(II) complex exhibits two absorption bands at 15625 and 25316 cm⁻¹ assignable to ³A_{2g} (F) → ³T_{1g} (F) (v₂) and ³A_{2g} (F) → ³T_{1g} (P) (v₃) transitions respectively in an octahedral environment. The lowest band v₁ could not be observed due to limited range of the instrument used and is calculated by using band fitting procedure [15]. The Cu(II) complex exhibit a single broad asymmetric band in the region 12820–17544 cm⁻¹. The broadness of the band indicates the three transi-

tions ²B_{1g} → ²A_{1g} (v₁), ²B_{1g} → ²B_{2g} (v₂) and ²B_{1g} → ²E_g (v₃) which are similar in energy and give rise to only one broad absorption band. All of these data suggest a distorted octahedral geometry around Cu(II) ion.

MAGNETIC PROPERTIES

The magnetic measurements for Co(II) and Ni(II) complexes (Table-1) showed magnetic moment values of 4.75 and 3.45 BM, respectively suggesting consistency with their octahedral environment [16]. The Cu(II) complex show magnetic moment value of 1.89 BM (Table-1) which offers possibility of a distorted octahedral geometry [17].

ESR SPECTRUM OF THE Cu(II) COMPLEX

The ESR spectrum of the Copper (II) complex in a polycrystalline state has been recorded at room temperature. The g_{||} and g_⊥ values have been found to be 2.359 and 2.073 respectively. The g_{av} was calculated to be 2.172. The axial symmetry parameter 'G' is determined as G = (g_{||} - 2.00277) / (g_⊥ - 2.00277) = 5.07 is found to be more than 4 suggesting no interaction in the solid state [18].

ANTIBACTERIAL AND ANTIFUNGAL ACTIVITIES

The results of the antibacterial and antifungal activities for the ligand and its complexes are presented in Table 2. The results of antibacterial and antifungal activities reveal that the Schiff base is active and all the complexes have exhibited higher antibacterial and antifungal activities than the ligand. While Hg(II) complex shows higher activity than all the complexes and ligand but lower than the standards used.

Table-2

Antibacterial and antifungal activity results of the ligand and its metal complexes (Zone of inhibition in mm)

Compound	E. coli	S. aureus	A. flavus	A. niger
BrOCEBFC	11	12	14	13
Co(II) -Complex	12	13	15	14
Ni(II) -Complex	12	14	15	15
Cu(II) -Complex	13	14	16	14
Zn(II) -Complex	12	13	15	15
Cd(II) -Complex	13	13	16	14
Hg(II) -Complex	15	16	18	17
Norflaxin	22	24	--	--
Chlorometazole	--	--	22	20

CONCLUSION

In this study, Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) complexes with Schiff base derived from benzofuran-2-carbohydrazide and 3-acetyl-6-bromo-chromen-2-one have been synthesized. Based on the analytical data, magnetic measurements and spectral observations, we have proposed octahedral structures to Co(II), Ni(II) and Cu(II) complexes and tetrahedral structures to Zn(II), Cd(II) and Hg(II) complexes. The Schiff base and all the complexes synthesized have higher antibacterial and antifungal activities against bacterial/fungal strains.

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