



Research Article

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Synthesis and evaluation of antimicrobial activity of benzofuran derivative and its metal complexes

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ABSTRACT

In the present study O,N,O-donating ligand was prepared from the condensation of 2-aminobenzohydrazide and 5-bromo-2-hydroxybenzaldehyde to give the Schiff base. The structure of the compounds has been confirmed by MASS, IR, NMR, ¹³C NMR, ESI MASS. The synthesized compounds were screened for their antibacterial and antifungal activities.

Keywords: Benzofuran, Schiff base, Metal complexes, Antimicrobial activity

INTRODUCTION

Extensive importance in the chemistry of benzofurans in a natural products has paying attention due to their biological activities and their potential applications as pharmacological agents. Some benzofuran ring bearing different substituents at the Carbon-2 position are broadly spread in nature, e.g., aianthoidol, is a neolignan derivative, has been reported to have antiviral, antioxidant and antifungal activities[1]. Benzofurans occur in a great number of natural products. benzofurans have pharmacological, physiological and poisonous properties. The most recognized of the benzofurans are amiodarone, angelicin, xanthotoxin, bergapten, nodekenetin and usnic acid compounds. The benzofuran ring system is the basic skeleton of numerous compounds possessing cardiovascular activities[2]. benzofuran based fused heterocycles significantly very abundant in nature and have extensive pharmacological activities [3]. According to the literature review in the current years, there has been an increased the importance of benzofuran derivatives as anti-microbial agents, especially 2-substituted [4] or 2,3-disubstituted benzofurans derivatives [5]. In natural compound, the seed oil of the Egonoki plant has contained a benzofuran derivative which known as egonal is an useful synergist for pyrethrum and rotenone against mosquitoes, house flies, aphides and other insects [6].

So, we thought that its very valuable to synthesized and characterized for antimicrobial activities.

EXPERIMENTAL SECTION

TLC(Thin layer chromatography) using silica gel G (E. Merck) plates was used to access the reactions and purity of the synthesized compounds. IR spectra were recorded on Shimadzu IRAffinity-1S fourier transform infrared spectrophotometer. Mass spectra were determined by GCMS-QP2010 mass spectrometer, ¹H NMR spectra were determined by Bruker spectrometer (400 MHz) using TMS (internal standard). Elemental data was recorded on Carlo Erba EA 1108 elemental analyzer.

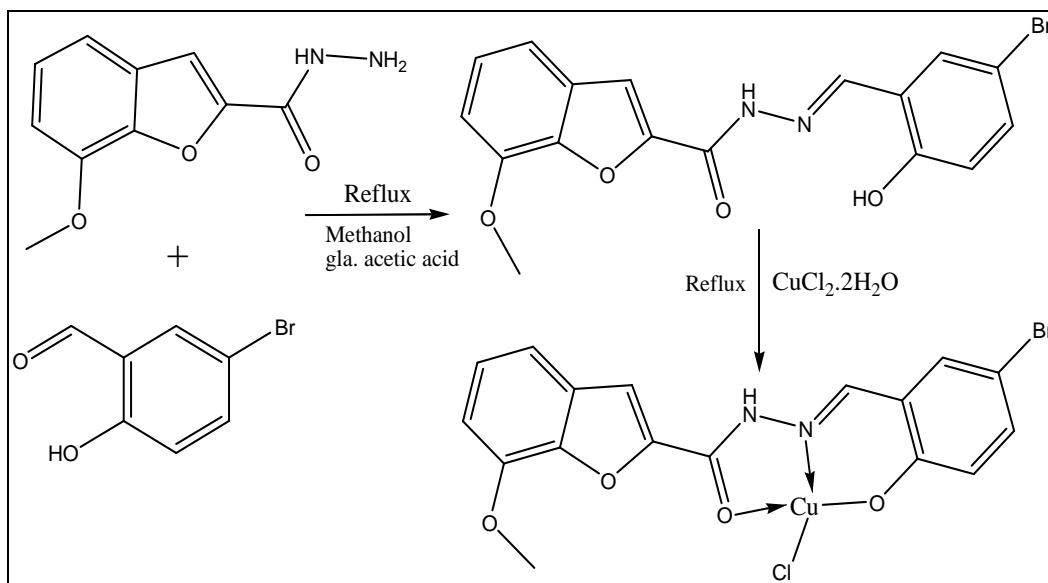


Figure : 1

General procedure for the synthesis of (E)-N'-(5-bromo-2-hydroxybenzylidene)-7-methoxybenzofuran-2-carbohydrazide

To a solution of benzofuran hydrazone (0.01 mole) and glacial acetic acid (10 ml), were added 5-bromo-2-hydroxybenzaldehyde. The reaction mixture heated to 60-65 °C for appropriate time. The reaction is being monitored by TLC using hexane: ethyl acetate (3:7). After completion of the reaction, the mixture was poured into crushed ice. Filtered out the separated solid product and dried under reduced pressure. Colour: White; Anal. Calcd. For $C_{17}H_{13}BrN_2O_4$ (388.2 g/mol): IR (KBr, cm^{-1}): $\nu(OH)$ phenolic 2924; $\nu(NH)$ 3265; $\nu(C=N)$ 1606; $\nu(N-N)$ 942; $\nu(C=O)$ 1696.

Preparation of metal complexes

Cu(II), Ni(II), Co(II) complexes were prepared by mixing of ligand in methanol and an aqueous solution of the metal chlorides in 1 : 1 molar ratio. The reaction mixture was refluxed on oil bath for 3-4 hrs. The reaction was monitored by TLC. When the reaction was completed, the solvent was removed approximately 50%, from hot solution. Then the residue was cooled to room temperature. The solid complexes formed were filtered, washed with hot water (20mL, 3-4 times) and ethyl alcohol (30mL, 3-4 times), and finally dried in vacuum desiccators over anhydrous $CaCl_2$. Colour: Green; Anal. Calcd. For $[Cu(C_{17}H_{12}BrN_2O_4)Cl]$ (487.19 g/mol): IR (KBr, cm^{-1}): $\nu(NH)$ 3266; $\nu(C=N)$ 1586; $\nu(N-N)$ 961; $\nu(C=O)$ 1659; $\nu(OH)$ phenolic not observed. $[Ni(C_{17}H_{12}BrN_2O_4)Cl]$ (482.34 g/mol) Colour: green : IR (KBr, cm^{-1}): $\nu(NH)$ 3269; $\nu(C=N)$ 1582; $\nu(N-N)$ 951; $\nu(C=O)$ 1658; $\nu(OH)$ phenolic not observed. $[Co(C_{17}H_{12}BrN_2O_4)Cl]$ (482.58 g/mol) Colour: Pink: IR (KBr, cm^{-1}): $\nu(NH)$ 3269; $\nu(C=N)$ 1582; $\nu(N-N)$ 951; $\nu(C=O)$ 1658; $\nu(OH)$ phenolic not observed.

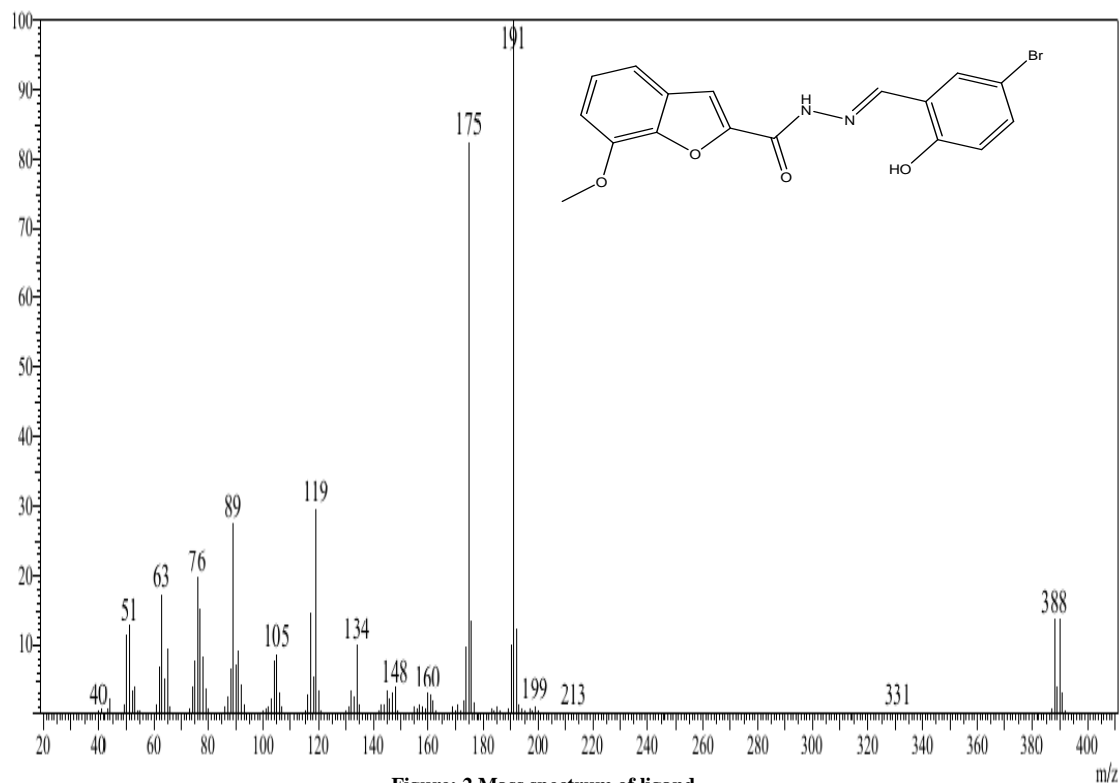


Figure: 2 Mass spectrum of ligand

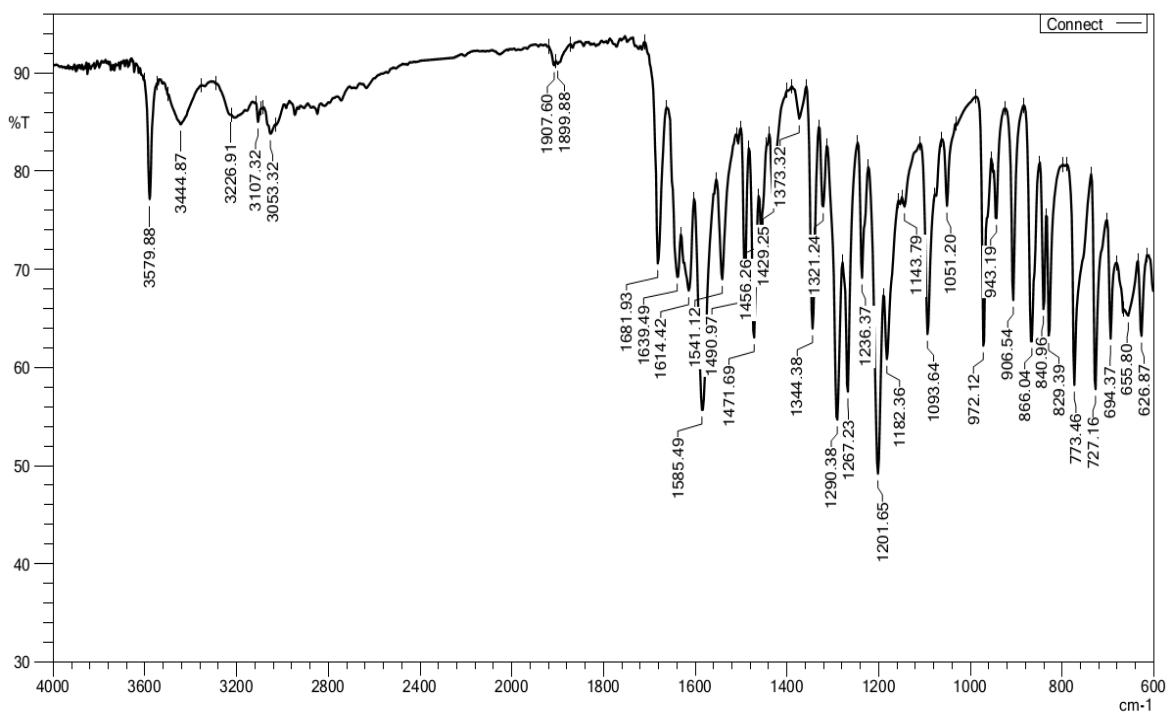


Figure: 3 IR spectrum of ligand

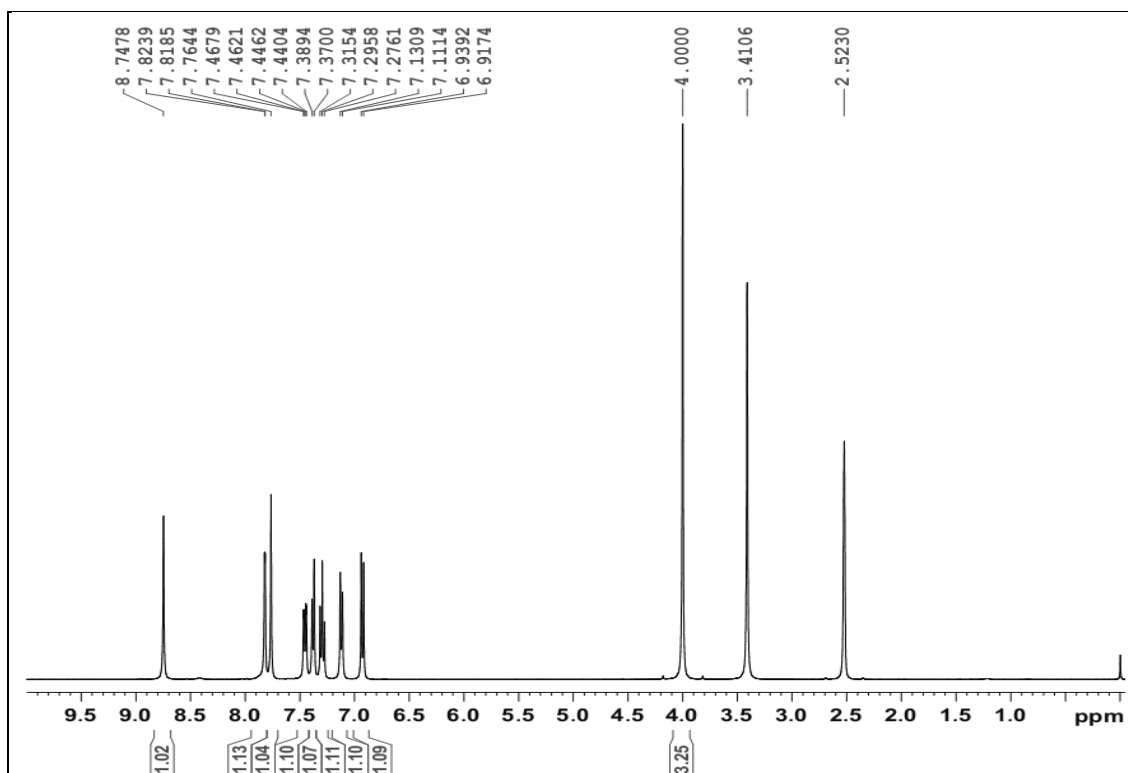
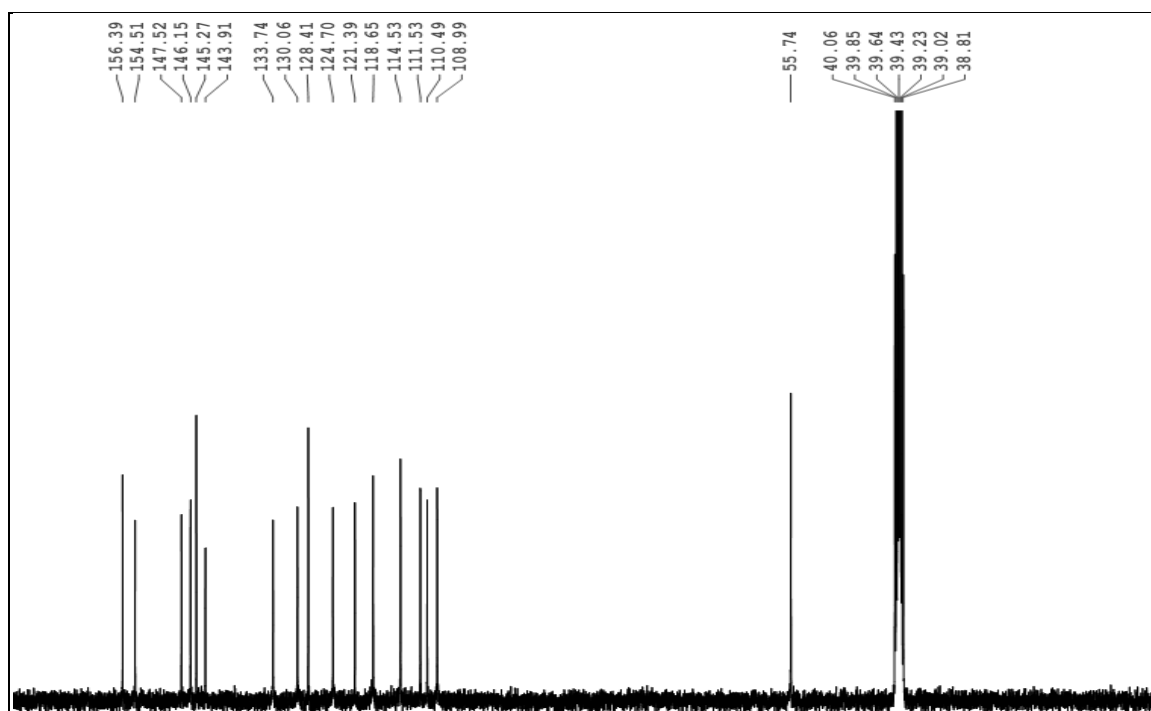


Figure: 4 NMR spectrum of ligand

Figure: 5 ¹³C NMR spectrum of ligand

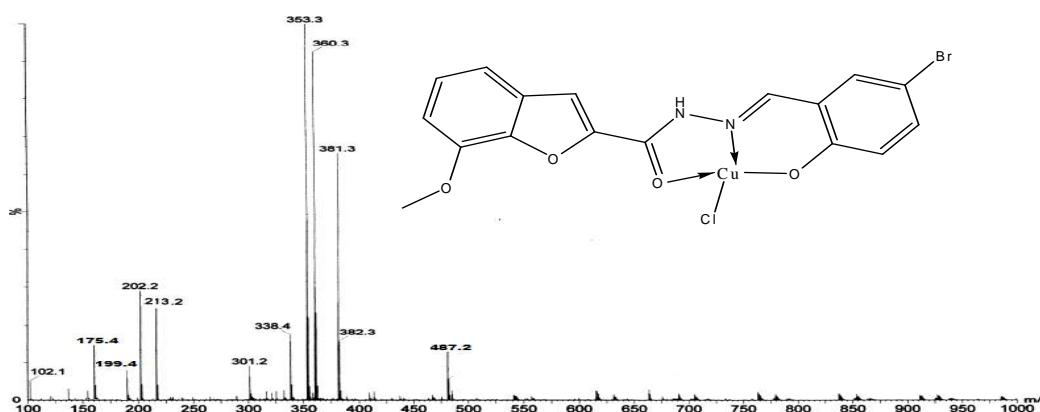


Figure: 6 ESI MASS spectrum of complex

Minimum inhibitory concentrations (MIC) (in $\mu\text{g/ml}$) of compounds by using macrodilution

Compound	Minimum inhibitory concentration values (in $\mu\text{g/ml}$)							
	Antibacterial activity				Antifungal activity			
	<i>E. coli</i>	<i>S. aureus</i>	<i>R. solanacearum</i>	<i>X. vesicatoria</i>	<i>A. niger</i>	<i>A. flavus</i>	<i>F. oxysporum</i>	<i>A. solani</i>
L	128	64	128	128	128	128	64	128
C ₁	64	64	128	64	128	128	64	128
C ₂	64	32	64	64	64	32	64	64
C ₃	128	64	128	128	64	128	64	128
Chloram-phenicol	8	8	8	2	-	-	-	-
Terbinafin	-	-	-	-	8	2	2	2

Antimicrobial activity of ligand and its corresponding metal complexes

Compound	Zone of inhibition (in mm) ^a							
	Antibacterial activity				Antifungal activity			
	<i>E. coli</i>	<i>S. aureus</i>	<i>R. solanacearum</i>	<i>X. vesicatoria</i>	<i>A. niger</i>	<i>A. flavus</i>	<i>F. oxysporum</i>	<i>A. solani</i>
L	15	14	10	13	08	13	11	11
C ₁	18	19	17	18	12	14	13	08
C ₂	22	26	18	17	15	17	15	12
C ₃	19	17	15	13	11	16	11	13
Chloram-phenicol	34	35	32	29	-	-	-	-
Terbinafin	-	-	-	-	22	24	29	25

^a Average of three replicates.

Where *E. coli* = *Escherichia coli*, *S. aureus* = *Staphylococcus aureus*, *R. solanacearum* = *Ralstonia solanacearum*, *X. vesicatoria* = *Xanthomonas campestris* pv. *vesicatoria*, *A. niger* = *Aspergillus niger*, *A. flavus* = *Aspergillus flavus*, *F. oxysporum* = *Fusarium oxysporum*, *A. solani* = *Alternaria solani*.

RESULTS AND DISCUSSION

The ligand was well characterized by Mass, IR, ¹H NMR, ¹³C NMR and ESI Mass spectral studies. The metal complexes were prepared using respective metal chlorides (Cu, Ni, Co) with the ligand in 1:1 molar ratio. All the complexes were non-hygroscopic and stable at room temperature. The antimicrobial studies of metal complexes display moderate activity against bacterial and fungi strain as compare to ligand

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