

Research Article

Synthesis and Antimicrobial Evaluation of Schiff Bases Derived from 2-amino-4, 6-dimethyl benzothiazole with 2-Hydroxy-naphthalene-1-carbaldehyde, 3-Methyl-thiophene-2-carbaldehyde and their Metal Complexes

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ABSTRACT

The studies of 12 transition metal complexes of Schiff bases are discussed, Schiff bases are obtained by condensation of 2-amino-4, 6-dimethyl benzothiazole with 2-Hydroxy-naphthalene-1-carbaldehyde, 3-Methyl-thiophene-2-carbaldehyde and Cu (II), Co (II), Mn (II), Fe (II), Cr (II) and Ni (II) chloride were chosen to synthesize new complexes. The Schiff bases and the complexes were characterized on the basis of physicochemical studies viz. spectral studies like IR, ¹H NMR, Mass studies. The ligands and their metal complexes were screened for antibacterial activity against various bacteria like *Escherichia Coli*, *Salmonella typhi*, *Staphylococcus aureus*, *Bacillus subtilis* and fungicidal activity against various fungi like *Aspergillus niger*, *Penicillium chrysogenum*, *Fusarium moneliforme*, *Aspergillus flavus*.

Keywords: Benzothiazole, Schiff bases, metal complexes, spectral study, antimicrobial activity.

INTRODUCTION

Benzothiazoles are bicyclic ring system with multiple applications which have been the subject of great interest because of their biological activities. The presence of Heterocyclic Benzothiazole is one of the oldest and potent heterocyclic compounds. Literature review revealed Benzothiazole having anthelmintic activity¹, anti tumor², analgesic and anti-inflammatory³, antimalarial⁴, antifungal⁵, anticandidous activities⁶ and various CNS activities⁷ of benzothiazoles, including antimicrobial,⁸⁻⁹ antiviral¹⁰⁻¹¹, analgesics¹², and anticytotoxic¹³⁻¹⁴. Schiff bases derived from an amino and carbonyl compound are an important class of ligands that coordinate to metal ions via azomethine nitrogen and have been studied extensively¹⁵. In azomethine derivatives, the C=N linkage is essential for biological activity, several azomethines were reported to possess remarkable antibacterial, antifungal, anticancer and diuretic activities¹⁶. Schiff bases have wide applications in food industry, dye industry, analytical chemistry, catalysis, fungicidal, agrochemical and biological activities¹⁷.

Schiff bases are known to possess variety of biological properties. They are useful syntheses for many compounds. They can be used for synthesis of bioactive molecules. Heterocyclic Schiff bases are used for synthesis of pyrazolines, azetidinones, oxazolines which are potent anti-microbial molecules. Schiff bases of hydroxy aldehydes and ketones were widely used in co-ordination chemistry for the preparation of metal complexes¹⁸⁻¹⁹. Schiff bases and their co-ordination compounds have been gained importance now-a-days as they are useful in biochemical²⁰, anti-cancer²¹, anti-inflammatory²², and antipyretic²³, among others. Some of them have been used as complexing agent²⁴⁻²⁵ and powerful corrosion inhibitors²⁶. A Schiff base of hydroxy acetophenone and its complexes has a variety of applications in biological, clinical, analytical and pharmacological areas²⁷⁻²⁹. Earlier work has shown that some drugs showed increased activity when administered as metal chelates rather than as organic compounds³⁰⁻³¹ and that the co-ordinating possibility of hydroxy acetophenone has been improved by

condensing with a variety of carbonyl compounds.

Here in this paper we report the synthesis of Schiff bases as ligand and their metal complexes Cu (II), Co (II), Mn(II), Fe(II), Cr(II) and Ni(II) . All the synthesized compounds were screened for their antimicrobial activity. Further the structures of synthesized compounds were confirmed by elemental analysis and spectral studies. The structures of the ligands are shown in **scheme-I** and **scheme-II**.

EXPERIMENTAL

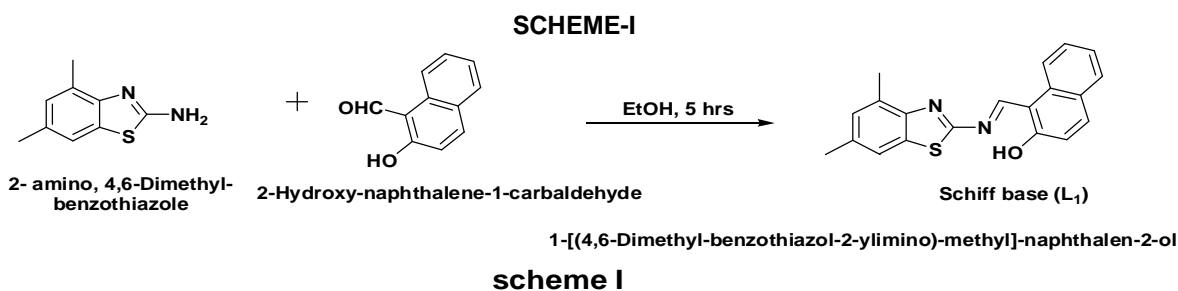
All the melting points were determined in an open capillary tube and are uncorrected; completion of the reaction was monitored by thin layer chromatography on precoated sheets of silica gel G. All the reagents used were chemically pure and are of AR grade. The ligand selected in the preparation of metal complexes are 1-[(4,6-Dimethyl-benzothiazol-2-ylimino)-methyl]-naphthalen-2-ol (L_1), (4,6-

Dimethyl-benzothiazol-2-yl)-(3-methyl-thiophen-2-ylmethylene)-amine (L_2). Transition metals Cu (II), Co (II), Mn(II), Fe(II), Cr(II) and Ni(II) were used for the synthesis of metal complexes with corresponding Schiff base ligands.

Synthesis of ligands

Synthesis of Schiff base 1-[(4,6-Dimethyl-benzothiazol-2-ylimino)-methyl]-naphthalen-2-ol (L_1)

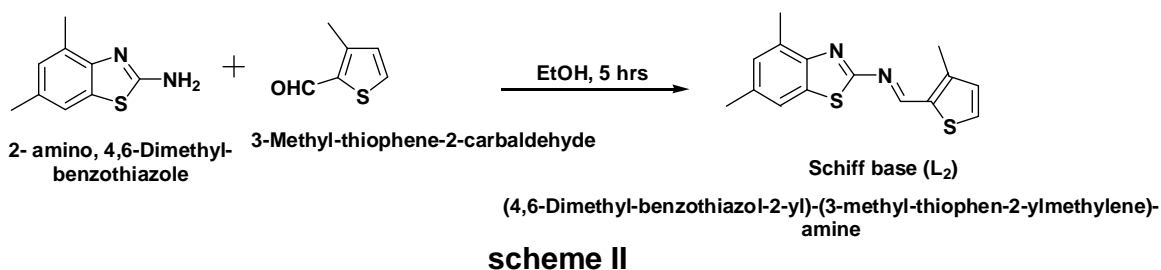
2-amino, 4, 6-dimethyl benzothiazole and 2-Hydroxy-naphthalene-1-carbaldehyde, were dissolved in distilled ethanol in equimolar quantities. The reaction mixture was refluxed on water bath for about 4-5 hours; the progress of the reaction was monitored by TLC. The hot reaction mixture was then poured on ice cold water the solid thus separated was filtered washed with water and dried. The solid then recrystallised from ethanol.



Synthesis of Schiff base (4,6-Dimethyl-benzothiazol-2-yl)-(3-methyl-thiophen-2-ylmethylene)-amine (L_2)

2-amino, 4, 6-dimethyl benzothiazole and 3-Methyl-thiophene-2-carbaldehyde, were dissolved in distilled ethanol in equimolar quantities. The reaction mixture was refluxed

on water bath for about 4-5 hours; the progress of the reaction was monitored by TLC. The hot reaction mixture was then poured on ice cold water the solid thus separated was filtered washed with water and dried. The solid then recrystallised from ethanol.



Preparation of complexes

The ligand (0.02 moles) and the metal salt (0.01 moles) in 50 ml ethanol were mixed. The pH of the mixture solution was raised up to 5 using alcoholic ammonia. The solution was then concentrated on steam bath in a china bowl. Solid complex thereafter separate out washed with acetone to remove excess of ligand and dried over CaCl₂ overnight.

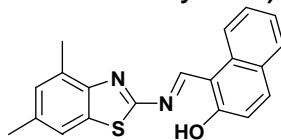
RESULT AND DISCUSSION

All the complexes at room temperature are insoluble in water and the most of the common organic solvent but soluble in DMF and DMSO. The analytical data of the complexes (Table-1) indicate that their stoichiometry may be represented as 1:2 metal to ligand ratio.

Table 1: Physical data of Synthesized Ligands and Metal complexes

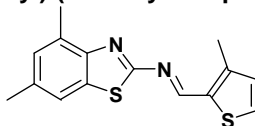
Entry	Molecular Formula	Color	Yield (%)	Melting Point (°C)
L ₁	C ₂₀ H ₁₆ N ₂ OS	Yellow	67	218°C
L ₁ M ₁	[CuC ₄₀ H ₃₂ N ₄ S ₂ O ₂].nH ₂ O	Brown	56	>280°C
L ₁ M ₂	[Co C ₄₀ H ₃₂ N ₄ S ₂ O ₂].nH ₂ O	Green	74	>280°C
L ₁ M ₃	[Ni C ₄₀ H ₃₂ N ₄ S ₂ O ₂].nH ₂ O	Light yellow	66	>280°C
L ₁ M ₄	[Fe C ₄₀ H ₃₂ N ₄ S ₂ O ₂].nH ₂ O	Coffee brown	64	>280°C
L ₁ M ₅	[Mn C ₄₀ H ₃₂ N ₄ S ₂ O ₂].nH ₂ O	Termeric yellow	67	>280°C
L ₁ M ₆	[Cr C ₄₀ H ₃₂ N ₄ S ₂ O ₂].nH ₂ O	Ash color	62	>280°C
L ₂	C ₁₅ H ₁₄ N ₂ S ₂	Orange	73	128°C
L ₂ M ₁	[Cu C ₃₀ H ₂₈ N ₄ S ₄].nH ₂ O	Brown	64	>280°C
L ₂ M ₂	[Co C ₃₀ H ₂₈ N ₄ S ₄].nH ₂ O	Vanilla	65	>280°C
L ₂ M ₃	[Ni C ₃₀ H ₂₈ N ₄ S ₄].nH ₂ O	Parrot green	62	>280°C
L ₂ M ₄	[Fe C ₃₀ H ₂₈ N ₄ S ₄].nH ₂ O	Light green	69	>280°C
L ₂ M ₅	[Mn C ₃₀ H ₂₈ N ₄ S ₄].nH ₂ O	Brown	71	>280°C
L ₂ M ₆	[Cr C ₃₀ H ₂₈ N ₄ S ₄].nH ₂ O	ash	66	>280°C

L₁ and L₂ are ligands M₁ = Cu, M₂ =Co, M₃ =Ni, M₄ =Fe, M₅ = Mn, M₆ =Cr

Spectroscopic data of selected compounds**1-[(4,6-Dimethyl-benzothiazol-2-ylimino)-methyl]-naphthalen-2-ol (L₁)**

Schiff base (L₁)

IR (KBr): 3448 cm⁻¹(O-H), 1597cm⁻¹(C=N), 3086 cm⁻¹ 2916 cm⁻¹(CH₃), ¹HNMR: δ 2.45 (s,3H), δ 2.75 (s,3H), δ 10.089 (s,1H), δ 14.1 (s,1H), δ 6.3-7.8 (m,8H); M.S. (m/z): 332

(4,6-Dimethyl-benzothiazol-2-yl)-(3-methyl-thiophen-2-ylmethylene)-amine (L₂)

Schiff base (L₂)

IR (KBr): 1581cm⁻¹(C=N), 2989 cm⁻¹ 2929cm⁻¹(CH₃) ¹HNMR: δ 2.49 (s,3H), δ 2.52 (s,3H), 2.57 (s,3H), δ 9.15 (s,1H), δ 7.1-7.9 (m,4H); M.S. (m/z): 286

The IR spectra of the complexes were compared with those of the free ligand in order to determine the coordination sites that may

be involved in coordination. Upon comparison it was determined that the ν(C=N) stretching vibration is found in the Schiff base at 1597 in

L_1 and 1581 in L_2 cm^{-1} . This band shifted to lower wave numbers in the complexes indicating the participation of nitrogen in coordination³². The new bands at ν M-N stretching vibrations were appeared at 540 - 525 cm^{-1} in the spectra of metal complexes.³³

^1H NMR spectra of the transition complexes were recorded, unfortunately, however due to the presence of a metal ion, proton resonance was not affected and one could observe only broad peaks indicating the formation of the complex.

ANTIMICROBIAL ACTIVITY

Antibacterial Activity

Procedure

The antibacterial activity was measured by agar cup method. Nutrient agar (Himedia) was prepared and sterilized at 15 Psi for 15 minutes in the autoclave. It was allowed to cool below 45 $^\circ\text{C}$ and seeded with turbid suspension of test bacteria separately, prepared from 24 hours old slant cultures. 3% inocula were used every time. The bacterial cultures selected were, two gram negative cultures viz. *Escherichia coli*, *salmonella typhi* and two Gram positive cultures Viz.

Staphylococcus aureus, *Bacillus subtilis*. This seeded preparation was then poured in sterile petri plate under aseptic condition and allowed it to solidify

Cups of 10 mm diameter were bored in the agar plate with sterile cork borer. 100 μl of compound solution prepared in the cup under aseptic condition with the help of micropipette. 100 μl of DMSO was also placed in one of the cup as blank (negative control). A standard antibiotic disk impregnated with 10 units of penicillin was also placed on the seeded nutrient agar surface as standard reference antibiotic (positive control).

The plates were kept in refrigerator for 15 minutes to allow diffusion of the compound from agar cup into the medium. Then the plates were shifted to incubator at 37 $^\circ\text{C}$ and incubated for 24 hours.

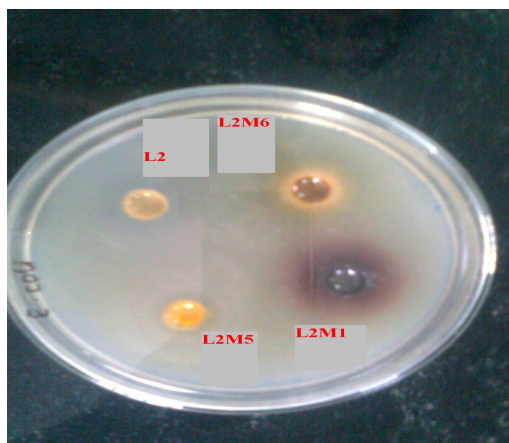
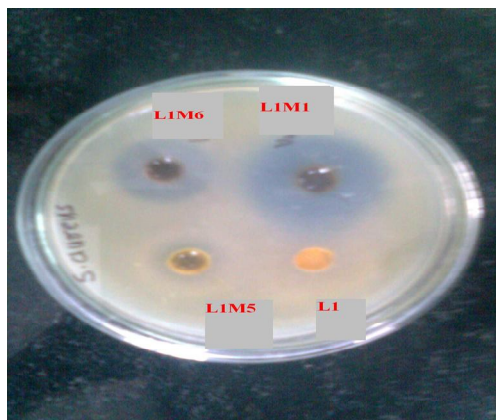
After incubation plates were observed for the zone of inhibition of bacterial growth around the agar cup. Results were recorded by measuring the zone of inhibition in millimeter (mm) using zone reader³⁴.

Antibacterial Activity of the synthesized ligand and their metal complexes are given in table 2.

Table 2: Antibacterial activity of the synthesized ligand and their metal complexes

S.No.	Compound	<i>Escherichia coli</i>	<i>Salmonella typhi</i>	<i>Staphylococcus aureus</i>	<i>Bacillus subtilis</i>
1	L_1	11 mm	-ve	-ve	13 mm
2	L_1M_1	19 mm	21 mm	32 mm	35 mm
3	L_1M_2	16 mm	20 mm	24 mm	26 mm
4	L_1M_3	18 mm	19 mm	26 mm	26 mm
5	L_1M_4	16 mm	26 mm	25 mm	25 mm
6	L_1M_5	13 mm	-ve	18 mm	19 mm
7	L_1M_6	-ve	24 mm	24 mm	24 mm
8	L_2	10 mm	-ve mm	-ve	12 mm
9	L_2M_1	26 mm	22 mm	33 mm	33 mm
10	L_2M_2	17 mm	19 mm	22 mm	27 mm
11	L_2M_3	16 mm	25 mm	25 mm	23 mm
12	L_2M_4	17 mm	23 mm	26 mm	26 mm
13	L_2M_5	13 mm	19 mm	17 mm	25 mm
14	L_2M_6	16 mm	22 mm	22 mm	22 mm
	DMSO	-ve	-ve	-ve	-ve
	Peniciline	13 mm	18 mm	36 mm	18 mm

Ligands - -ve = No antibacterial activity
Zone of inhibition in mm



Antifungal Activity Procedure

Antifungal activity was performed by poison plate method. The medium used was Potato Dextrose Agar (Himedia). The medium was prepared and sterilized at 10 Psi in autoclave for 15 minutes. Then the compound to be tested is added to the sterile medium in aseptic condition so as to get final concentration as 1%. Griseofulvin was prepared as standard reference plate(positive control)

Aspergillus niger, *penicillium chrysogenum*, *Fusarium moneliforme*, *Aspergillus flavus* were selected as test fungal cultures. They were allowed to grow on slant for 48 hours so as to get profuse sporulation. 5ml of 1:100 aqueous solution of Tween 80 was added to the slant and spores were scraped with the help of nicrome wire loop to form suspension.

The fungal suspension was spot inoculated on the plate's prepared using compound with the help of nicrome wire loop. The plates were incubated at room temperature for 48 hours.

After incubation plates were observed for the growth of inoculated fungi. Results were recorded as growth of fungi (no antifungal activity) reduced growth of fungi (moderate antifungal activity) and no growth of inoculated fungi (antifungal activity) ³⁴.

Antifungal Activity of the synthesised ligand and their metal complexes are given in table 3.

Table 3: Antifungal activity of the synthesized ligand and their metal complexes

S. No.	Compound	<i>Aspergillus niger</i>	<i>Penicillium chrysogenum</i>	<i>Fusarium moneliforme</i>	<i>Aspergillus flavus</i>
1	L ₁	+ve	+ve	-ve	+ve
2	L ₁ M ₁	-ve	-ve	-ve	-ve
3	L ₁ M ₂	-ve	-ve	-ve	-ve
4	L ₁ M ₃	-ve	-ve	-ve	-ve
5	L ₁ M ₄	-ve	-ve	-ve	-ve
6	L ₁ M ₅	+ve	+ve	-ve	+ve
7	L ₁ M ₆	-ve	-ve	-ve	+ve
8	L ₂	-ve	-ve	-ve	-ve
9	L ₂ M ₁	-ve	-ve	-ve	-ve
10	L ₂ M ₂	-ve	-ve	-ve	+ve
11	L ₂ M ₃	-ve	-ve	-ve	-ve
12	L ₂ M ₄	-ve	-ve	-ve	-ve
13	L ₂ M ₅	-ve	-ve	-ve	-ve
14	L ₂ M ₆	-ve	-ve	-ve	+ve
	+ve control	+ve	+ve	+ve	+ve
	-ve control (Griseofulvin)	-ve	-ve	-ve	-ve

Ligands +ve - Growth (No Antifungal Activity)
-ve - No Growth (Antifungal Activity Observed)



CONCLUSION

It is clear from the present result that preliminary studies showed their good inhibitory properties. In general the transition metal complexes of the corresponding Schiff bases are more active than their parent ligand and hence may serve as vehical for activation of the ligand as principle cytotoxic species.

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