SYNTHESIS OF SCHIFF BASES OF SALICYLALDEHYDE WITH CHLORO SUBSTITUTED 2-AMINOBENZOTHIAZOLE, THEIR METAL ION COMPLEXES AND ANTIBACTERIAL EVALUATION.

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Abstract: A series of Chloro substituted 2-aminobenzothiazole were incorporated with salicylaldehyde under acidic condition. The novel synthesized imine products and their metal Ligand complexes have been elucidated by H^1 NMR, IR and mass spectral data. The prepared compound (Ligand) and metal ion complexes were screened against the Gram +Ve and Gram –Ve bacteria. Almost all complexes showed good antibacterial activity. In particular complex of Copper and Nickel showed the best result in the antibacterial evaluation.

Key-words: Chloro Substituted 2-aminobenzothiazole, Salicylaldehyde, Schiff bases, Metal-Ligand complexes, Antibacterial activity.

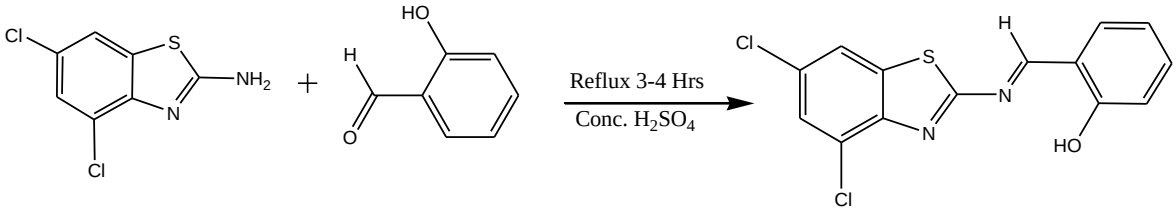
INTRODUCTION

Synthesis and antimicrobial activity of 2-aminobenzothiazole and its derivatives is reported [1]. Further, their other pharmacological activities such as anticancer, antiulcer, antihistaminic, anti-inflammatory activity and analgesic activities also reported [2-6]. It was envisaged that the compounds containing these moieties in their molecular frame work might show enhanced biological activity. Increasing physiological importance of oxygen donor organic compounds and active role played by coordination certain metal ions to them is of interest towards use in synthesizing and studying structural aspects of metal complexes with some oxygen, sulphur and nitrogen donor ligands. The aromatic benzothiazole nucleus is associated with a variety of antihistamine activity, pharmacological actions such as fungicidal and leishmanicides activities The complexes of the ligand 2- amino acetate, 6-chloro benzothiazole with some transition metal ions have been studied. In the present study we now report the synthesis of complexes of 4, 6-dinitrobenzothiazole-2-amine acetate and their study of magnetic properties for the wide range of applications.

MATERIALS AND METHODS

Synthesis of Schiff base (Ligand):

A mixture of 4,6-Dichloro-2-amino benzothiazole (0.1 mol), salicylaldehyde (0.1 mol) and conc.H2SO4 has been refluxed for 3 hrs. The resultant yellow precipitate is filtered and crystallized from ethanol. The steps in the synthesis of Ligand are shown in figure 1

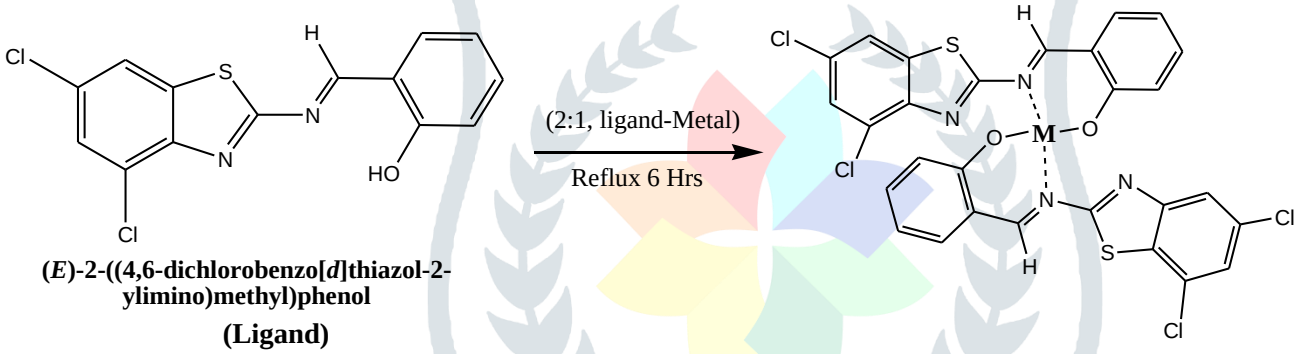


4,6-Dichloro-2-aminobenzothiazole **salicylaldehyde**

(*E*)-2-((4,6-dichlorobenzo[*d*]thiazol-2-ylimino)methyl)phenol
(Ligand)

Preparation of complexes:

All the matal complexes have been prepared by refluxing the ethanol solution of the suitable metal salt (Nickel acetate tetrahydrate, Copper acetate, and Zinc acetate dihydrate) and 2-aminoacetic acid benzothiazole for one hour. The 2:1 ratio of ligand to metal is maintained throughout all the experiments. The obtained crystalline colored precipitates upon cooling the solutions at room temperature were filtered off, washed with distilled water and recrystallized from ethanol.



(*E*)-2-((4,6-dichlorobenzo[*d*]thiazol-2-ylimino)methyl)phenol
(Ligand)

(Metal-Lignd complex)

M - Cd $^{++}$,Ni^{++},Cu^{++},Zn^{++}

INSTRUMENTATION:

FT-IR spectra in the range, 4000-200 cm^{-1}, were recorded on 8300 Shimadzu Spectrophotometer, UV-visible spectra were measured by using Shimadzu 160 spectrophotometer in the range 200-1000 nm. The magnetic susceptibility values of the prepared complexes were obtained at room temperature using Magnetic Susceptibility on Bruker Magnet B.M.6, The ^{1}H nuclear magnetic resonance spectra were recorded on a BRUKER ADVANCED II 400 MHz spectrometer in DMSO as a solvent, relative to the internal standard Tetramethylsilane (TMS). Melting points were recorded on a Tanco Laboratory melting point apparatus.

(E)-2-((4,6-dichlorobenzo[d]thiazol-2-ylimino)methyl)phenol (L):

Solid, mp 195ºC, **UV (λmax) in ethanol:** 258 nm, **(IR) υmax (KBr/cm-1):** 3375.66 (NH), 3181.24(Ar=C-H), 1538(C=N), 1244.85(CN), 1265.12 (C-S). **^{1}H-NMR (δ-ppm):** 3.46 (s, 2H, NH_2), 7.77 (d, aryl H, adjacent to sulphur), 8.88 (d, aryl H, adjacent to Cl).

Bis-(E)-2-((4,6-dichlorobenzo[d]thiazol-2-ylimino)methyl)phenol cadmium(II) Complex (ML1:

Solid, mp 192^{0}C, **UV (λmax) in ethanol :** 256 nm, **(IR) υmax (KBr/cm-1):** NH(3449.82), 3025.78(Ar=CH), 1496.17(C=N),1264.09(C-N), 1276.24(C-S), 1724 and 1048 cm^{-1} (stretching of C = O and C-O of the hydroxyl in the carboxyl ate). **^{1}H-NMR (δ-ppm):** 4.16 (t, 2H, -NH), 6.08 (d, 2H, -CH_2), 7.15(d, 1H, Ar-H), 8.10(d,Ar-H), 8.92 (d,Ar-H).

Bis-(E)-2-((4,6-dichlorobenzo[d]thiazol-2-ylimino)methyl)phenol copper (II) Complex (ML2):

Solid, mp 123^{0}C **UV (λmax) in ethanol:** 277 nm, **(IR) υmax (KBr/cm-1):** 3450.41 (NH), 3107(Ar=C-H), 1425.21 (C=N), 1258.54 (C-N), 1263 (C-S), 573.16, 917.86 (stretching and bending vibration for Cu-O)**,** 1718 and 1030 cm^{-1} (stretching of C = O and C-O of the hydroxyl in the carboxylate). **1H-NMR (δ-ppm):** 4.1 (t, 1H, NH), 8.12 (dd,1H,Ar-H), 5.86 (d, 2H, CH_2), 8.86 (d, 1H, Ar-H), 7.12 (d,1H, Ar-H).

Bis-(E)-2-((4,6-dichlorobenzo[d]thiazol-2-ylimino)methyl)phenol Nickel (II) Complex (ML3):

Solid, mp 133^{0}C **UV (λmax) in ethanol:** 286 nm, **(IR) υmax (KBr/cm-1):** 3345.52 (NH), 3081.68 (Ar=C-H), 1456.61 (C=N), 1288.34 (C-N), 1245.09 (C-S), 525.43, 936.42 (stretching and bending vibration for Ni-O)**,** 1720 and 1035 cm^{-1} (stretching of C = O and C-O of the hydroxyl in the carboxylate). **1H-NMR (δ-ppm):** 4.56 (t, 1H, NH), 8.70 (dd,1H,Ar-H), 5.47 (d, 2H, CH_2), 8.68 (d, 1H, Ar-H), 7.57 (d,1H, Ar-H).

Bis-(E)-2-((4,6-dichlorobenzo[d]thiazol-2-ylimino)methyl)phenol Zinc(II) Complex (ML4):

Solid, mp 158^{0}C **UV (λmax) in ethanol:** 272 nm, **(IR) υmax (KBr/cm-1):** 3469.25 (NH), 3147.73 (Ar=C-H), 1436.47 (C=N), 1289.63 (C-N),, 1285.32 (C-S), 573.90, 989.43 (stretching and bending vibration for Ni-O)**,** 1713 and 1040 cm^{-1} (stretching of C = O and C-O of the hydroxyl in the carboxylate) **1H-NMR (δ-ppm):** 4.26 (t, 1H, NH), 8.13 (dd,1H,Ar-H), 5.89 (d, 2H, CH_2), 8.57 (d, 1H, Ar-H), 7.79 (d,1H, Ar-H).

PHARMACOLOGY

Antibacterial activity

The title compounds (R1a-e) were screened for their antibacterial activity using disc diffusion method.[17] The bacterial organisms used included both gram positive and gram negative strains like Staphylococcus aureus, Escherichia coli, Streptococcus pyogens, Salmonella enteric Ser para typhi, S.entrica ser typhi and Micrococcus luteus.

For antibacterial susceptibility testing of title compounds (R1a-e), the sterile disc of 6 mm diameter (SD067, HiMedia, Mumbai) was loaded with 20µl of title compound solution (1000 µg/ml) in DMF. The discs were then placed at centre on the Mueller-Hinton agar seeded with bacterial inoculums approximately 106 CFU/ ml, incubated at 37° C for 24 hrs and growth inhibition zone formed around disc was measured. Test was done in triplicate and mean value was considered as inhibition zone. Solvents were used as controls and showed no inhibitions in preliminary studies. All the synthesized complexes (R1 a-f) exhibited moderate to good activity against the test organisms. [16] The activity of complexes R1c showed excellent activity against all organisms.

Table 5: antimicrobial activity

Ligand (L), Cd complex (ML1), Cu complex (ML2), Ni complex (ML3), Zn complex (ML4);
+++ = Zone size 16-22 mm; ++ = Zone size 9-15 mm; + = Zone size 6-8 mm; — = No inhibition.

Compound	Gram negative bacteria			Gram positive bacteria		
	S. enterica Ser typhi	Salmonella enterica Serpara typhi	E.Coli	Streptococcus pyrogens	Micrococcus luteus	S.aureus
L	++	-	++	-	++	-
ML 1	+	+	+	-	-	+
ML 2	+++	+++	+	++	+++	++
ML 3	++	++	++	-	++	+
ML 4	+	+	-	++	++	+

CONCLUSION

The ligand 4, 6-dichlorobenzothiazole-2-amine were successfully synthesized by condensation method. The ligand was treated to different metal salts to afford the corresponding transition metal ion (II) complexes. Among ligands and metal ligand complexes copper and Nickel complexes shows best activity against the bacteria where as other complexes and ligand shows moderate activity.

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