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Novel Zinc(II) Complexes with Thiadiazole Containing Schiff Bases: Syntheses and Structural Characterization

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RESEARCH ARTICLE

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ABSTRACT

Herein we describe the synthesis of three zinc(II) complexes of thiadiazole derived Schiff base ligand. All the reported complexes were characterized by analytical and spectroscopic techniques. The data obtained from the characterization techniques confirmed the structures of synthesized complexes. The antibacterial activity of the reported compounds were studied using *E. coli*, *B. subtilis* and *S. aureus*. The results obtained from antibacterial investigations revealed that the tested zinc(II) complexes showed potent microbial growth inhibition than their respective thiadiazole Schiff base ligands. The growth inhibition was compared with standard antibacterial drug Streptomycin.

INTRODUCTION

Thiadiazole derived Schiff bases are important and most versatile type of ligands due to their potential donor atoms, among which nitrogen is of paramount importance in the metal-ligand linkage. Moreover, the π -delocalization and configurational flexibility create the possibility of a variety of co-ordination modes ^[1]. Furthermore, thiadiazole derivatives are known for their biological potency viz., antibacterial and antifungal ^[2]. Metal-chelate Schiff-base complexes have continued to play the role of one of the most important stereochemical models in main group and transition metal coordination chemistry due to their preparative accessibility, diversity and structural variability ^[3].

Many reports have been published on sulfur coordinating to a metal atom ^[3]. The thio-metal coordination has shown effective biological activities ^[4]. Since, involvement of sulfur played a crucial role in the biological investigations ^[5].

In this research paper, we describe the synthesis, characterization and antimicrobial studies of Zinc(II) complexes with a Schiff base ligand derived from 5-ethyl-1,3,4-thiadiazol-2-amine and aromatic substituted aldehydes.

EXPERIMENTAL

Materials and Methods

All chemicals were procured from Merck and Loba chemical companies. Solvents were used without further purification. Thin layer chromatography was done with Silica Gel G (Merck Index) pre-coated plates and the spots were visualized UV light. Infrared spectra were recorded in the range 4000-200 cm^{-1} on a JASCO FTIR-8400 spectrophotometer using Nujol mulls between polyethylene sheets. $^1\text{H-NMR}$ spectra were obtained on a Varian AC 400 spectrometer. ESI-MS were determined on Waters mass spectrometer.

General Synthesis

The synthesis of ligands have been previous reported by our research group [2]. To a methanolic solution of 5-ethyl-1,3,4-thiadiazol-2-amine (1.38 g, 10 mmol) was added 4-chlorobenzaldehyde, 4-bromobenzaldehyde and 4-hydroxybenzaldehyde in methanol separately. The reaction mixture was stirred for 30 min and then refluxed for 4 h. The completion of reaction was monitored by TLC. The solvent was removed by distillation to obtain L_1 - L_3 .

N-(4-chlorobenzylidene)-5-ethyl-1,3,4-thiadiazol-2-amine (L_1)

Yield : 61%; mp: 174 °C; FT-IR (nujol, v/cm^{-1}): 3079, 2988, 2353 (C-H), 1655 (C=N), $^1\text{H-NMR}$ (400 MHz, DMSO-d_6) δ : 1.18 (s, CH_3 , 3H), 4.21 (dd, CH_2 , 2H), 8.14 (s, CH, 1H, -N=CH-), 7.56-7.05 (m, Ar-H, 7H, Aromatic protons); Mass(m/z): 251 [M^+ , 81%].

N-(4-bromobenzylidene)-5-ethyl-1,3,4-thiadiazol-2-amine (L_2)

Yield : 65%; mp: 185 °C; FT-IR (nujol, v/cm^{-1}): 3074, 2928, 2157 (Ar-C-H), 1614 (C=N); $^1\text{H-NMR}$ (400 MHz, DMSO-d_6) δ : 1.76 (s, OCH_3 , 3H), 4.21 (dd, CH_2 , 2H), 8.05 (s, CH, 1H, -N=CH-), 7.48-7.73 (m, Ar-H, 8H, Aromatic protons); Mass(m/z): 295 [M^+ , 81%].

4-(((5-ethyl-1,3,4-thiadiazol-2-yl)imino)methyl)phenol (L_3)

Yield : 67%; mp: 212 °C; FT-IR (nujol, v/cm^{-1}): 3069, 2984, 2906 (Ar-C-H), 1593 (C=N), 3458 (O-H); $^1\text{H-NMR}$ (400 MHz, DMSO-d_6) δ : 1.76 (s, OCH_3 , 3H), 4.15 (dd, CH_2 , 2H), 8.72 (s, CH, 1H, -N=CH-), 10.12 (s, OH, 1H), 7.48-7.12 (m, Ar-H, 7H, Aromatic protons); Mass(m/z): 233 [M^+ , 76%].

Synthesis of Metal Complexes

The Zinc(II) complexes of Schiff base were prepared in 1:1:1 [metal:ligand:1,10-phenanthroline] stoichiometric ratio.

To a 25 mL hot methanolic solution of metal chloride (0.170 g, 1 mM), ligand solution (L_1 or L_2 or L_3) was added (1 mM) and stirred for 20 min at room temperature. To the above reaction mixture, a methanolic solution of 1,10-phenanthroline (0.198 g, 1 mM) was added dropwise with continuous stirring. After the complete addition, the mixture was refluxed for 8 h at 60°C. The product was precipitated by pouring into ice cold water and filtered, washed thoroughly with cold ethanol and dried in vacuo. The analytical and physical data were reported in **Table 1**. The tentative structures are depicted in **Figure 1**.

Table 1. Analytical and physical data of the compounds.

Compound	Molecular formula	Yield (%)	Calcd. (found), %					Molar conductance $\text{Scm}^2\text{mol}^{-1}$
			C	H	N	S	M	
L_1	$\text{C}_{11}\text{H}_{10}\text{N}_3\text{SCL}$	61	52.44 (53.13)	3.97 (4.1)	16.68 (16.81)	12.71 (12.85)	-	-
L_2	$\text{C}_{11}\text{H}_{10}\text{N}_3\text{SBr}$	65	44.44 (44.63)	3.38 (3.47)	14.23 (14.37)	10.84 (10.97)	-	-
L_3	$\text{C}_{11}\text{H}_{11}\text{N}_3\text{OS}$	67	56.65 (56.94)	4.72 (4.79)	18.02 (18.13)	13.73 (13.86)	-	-
1	$\text{ZnC}_{23}\text{H}_{18}\text{N}_5\text{SCL}$	57	55.75 (55.89)	3.36 (3.41)	14.14 (14.21)	6.46 (6.53)	12.80 (12.93)	12.47
2	$\text{ZnC}_{23}\text{H}_{18}\text{N}_5\text{SBr}$	60	51.2 (51.31)	3.33 (3.42)	12.98 (13.07)	5.93 (6.02)	12.13 (12.27)	12.26
3	$\text{ZnC}_{23}\text{H}_{19}\text{N}_5\text{OS}$	53	57.85 (57.96)	3.98 (4.03)	14.67 (14.77)	6.7 (6.76)	13.7 (13.78)	14.23

Antibacterial studies

The biological studies involved the antibacterial potency of the ligands and their Zinc(II) complexes. The activity was evaluated against three bacterial species namely, *E. coli*, *B. subtilis* and *S. aureus* by paper disc diffusion method [6]. Streptomycin was used as a standard drug for reference.

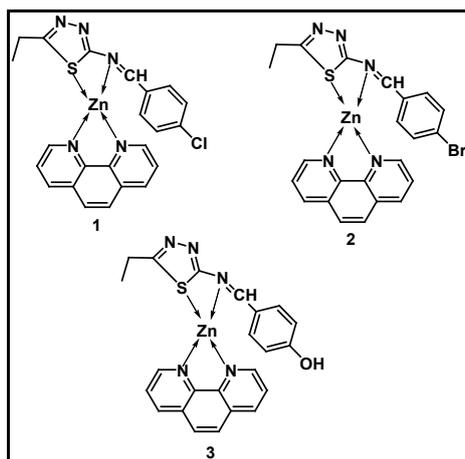


Figure 1. Tentative structures of reported Zinc(II) complexes.

The tested compounds were dissolved in DMF (no inhibition activity observed) to get concentration of 1 mg/mL. The bacterial species were sub-cultured in agar medium and the Petri dishes were incubated for 24 h at 37 °C. Standard antibacterial drug, Streptomycin was also screened under similar conditions for comparison. The wells were dug into the agar media using a sterile metallic borer. Activity was determined by measuring the diameter of the zone showing complete inhibition (mm).

RESULTS AND DISCUSSION

The Schiff base ligands were obtained by 1:1 condensation of 5-ethyl-1,3,4-thiadiazol-2-amine with 4-chlorobenzaldehyde or 4-bromobenzaldehyde or 4-hydroxybenzaldehyde to yield N-(4-chlorobenzylidene)-5-ethyl-1,3,4-thiadiazol-2-amine (L_1) or N-(4-bromobenzylidene)-5-ethyl-1,3,4-thiadiazol-2-amine (L_2) or N-(4-hydroxybenzylidene)-5-ethyl-1,3,4-thiadiazol-2-amine (L_3), respectively. The formation of the Zinc(II) complexes was achieved by reaction of above prepared ligands with Zinc(II) salts in 1:1:1 [M:L:1,10-phen] ratio. The analytical and physical data are presented in **Table 1**.

IR Spectral Analysis

The significant shifts in the IR spectrum of complex 3 is shown in **Figure 2**. The bands of the imine (C=N) stretching vibrations and donor nitrogen coordinating to metal center confirmed the formation of complex. The expected mode of interaction between the ligand and the Zinc(II) ion was via coordination of the Zinc(II) ion to the azomethine nitrogen group and sulfur of thiadiazole ring^[7]. The IR spectra of Zinc(II) complexes showed the characteristic band in the region 1583-1578 cm^{-1} , attributed to imine group which was shifted to lower frequencies due to complexation. The appearance of additional weak bands in the region 474-467 and 565-537 cm^{-1} due to $\nu(\text{M-O})$ and $\nu(\text{M-N})$ respectively, confirmed complexation. A broad band in the region 3486 cm^{-1} was due to hydroxyl group which was also observed in L_3 . This clearly indicates the non-participation of OH group in complexation.

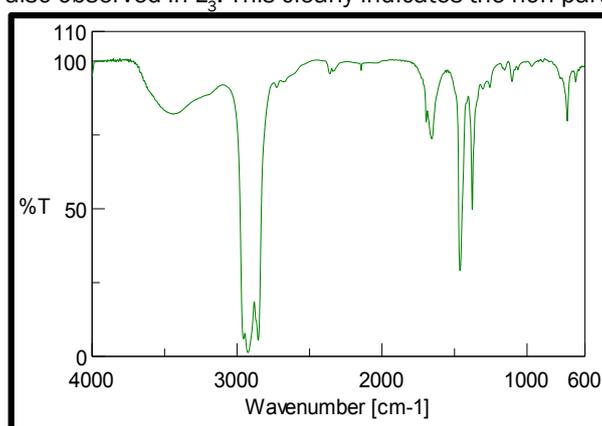


Figure 2. IR spectrum of Complex 3.

Conductivity Measurements

The molar conductance values of the Zinc(II) complexes in DMF (10^{-3} M solutions) were measured at room temperature and the results are tabulated in **Table 1**. The conductance values of Zinc(II) complexes fall in the range 14.3-12.2 $\text{Scm}^2\text{mol}^{-1}$, indicating the non-electrolytic nature of complexes.

Electronic Spectra

The electronic absorption spectra of the ligands and their Zn(II) complexes were recorded in DMSO at room temperature. The ligand showed the absorption bands in the region 289-312 nm, which are assigned to $\pi-\pi^*$ transition of the C=N chromophore.

Upon complexation, this band was shifted to lower wavelength region, suggesting the coordination of nitrogen (C=N) with Zinc(II) ion. Zinc(II) complex does not exhibit d-d electronic transition due to the non-availability of d-electrons. An absorption band observed in the complexes was mainly due to M→L charge-transfer transitions which confirms their tetrahedral geometry^[8].

Mass Spectroscopy

The mass spectra of complexes were obtained by ESI-MS technique. The representative mass spectrum of complex 3 is shown in **Figure 3**. The peak at m/z 476.6 corresponds to molecular ion peak [M⁺]. In addition to the molecular ion peak, many other peaks can be seen which corresponds to the fragment ions obtained from the complex molecule.

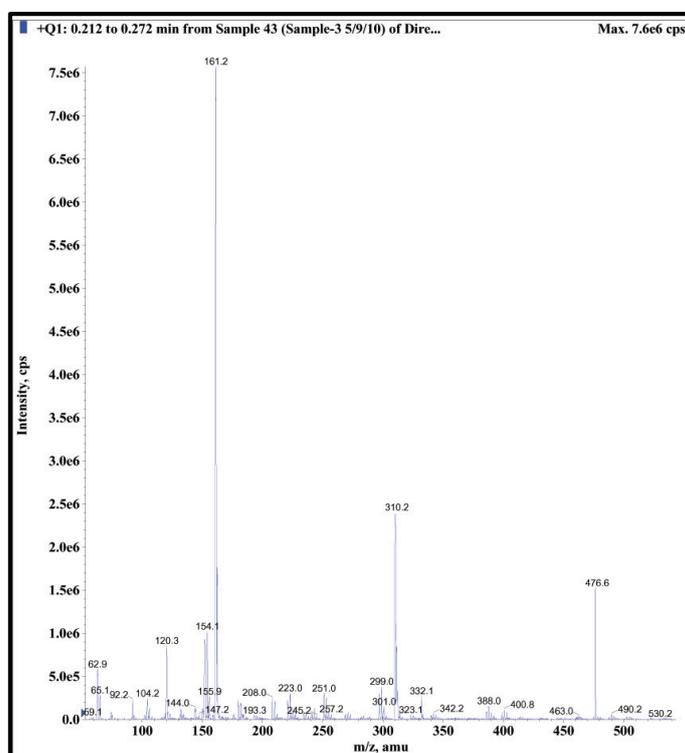


Figure 3. Mass spectrum of complex 3.

Thermal Studies

The TG/DTG curves of complex 3 are illustrated in **Figure 4**. The decomposition of the complex in the temperature range 20-200 °C are usually due to loss of water of moisture, hydration and coordination. The first stage between 150 and 200 °C corresponds to the dehydration. The anhydrous complex is stable up to 200 °C. The observed weight loss indicates the loss of two lattice water molecules present in proximity of the complex. The second stage of decomposition was continuous and mass loss occurs in the range 220-390 °C (TG=45.3%), suggesting the evaporation of the ligand. The third stage between 390-560 °C, (TG=37.8%) corresponds to the remaining organic molecule of the ligand leaving behind metal oxide as the end product^[8].

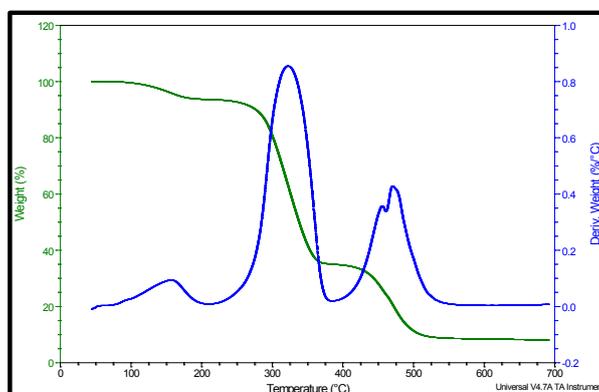


Figure 4. Thermo gravimetric [TGA (green line) and DTG (blue line)] curves of complex 3.

Antimicrobial Activity

The antimicrobial activity results are tabulated in **Table 2** and graphically represented in **Figure 5**. The observation of zone of inhibition can reveal the potentiality of the compound towards microbial growth inhibition. From **Table 2**, it was concluded that the Zn(II) complexes are more potent antimicrobials than their free ligands, which indicates that the metallation increases

antimicrobial activity. The obtained antimicrobial results depicts that the Zn(II) complexes were active against all the selected microorganisms. The complexes showed moderate activity against other selected species of microorganisms. This would suggest that the chelation could facilitate the ability of a complex to cross a cell membrane and can be explained by Tweedy's chelation theory^[9]. All the test compounds show lesser activity than the standard antibiotics.

Table 2. Antibacterial activity of Schiff base and its Zinc (II) complexes.

Compound	Zone of inhibition (in mm)*		
	Antibacterial activity		
	<i>B. subtilis</i>	<i>S. aureus</i>	<i>R. solanacearum</i>
L ₁	08	09	07
L ₂	08	08	07
L ₃	07	10	06
1	21	17	19
2	19	18	22
3	16	20	18
Streptomycin	32	29	26

*average of three replicates

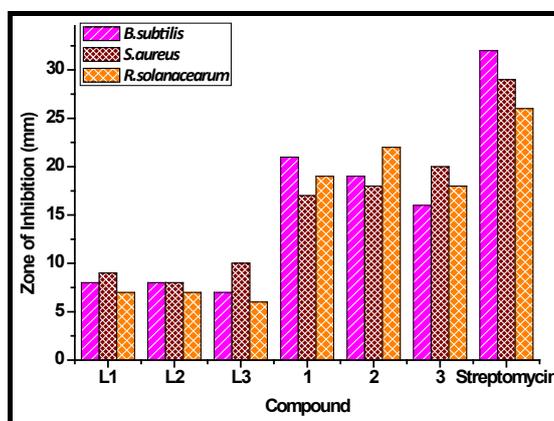


Figure 5. Graphical representation of Antibacterial activity.

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