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Research Article

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Synthesis and antibacterial activity of transition metal complexes of 2-amino acetate, 6-nitro benzothiazole

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ABSTRACT

A Series of coordination complexes of the ligand 2- amino acetate, 6-nitro benzothiazole with some metal ions Ni (II), Cu (II), Zn (II), Cd (II) and Sn (II) has been successfully prepared and evaluated for their anti-bacterial activity. The prepared complexes were characterized by elemental analysis, electronic spectra, infrared spectra, magnetic moment, and conductivity measurement. From spectral measurement, monomer structures for the complexes were proposed. Square planar geometry was proposed for copper complex. The other complexes were proposed to be tetrahedral. The anti-bacterial activities against Gram-positive and Gram-negative pathogenic bacteria were investigated using disc diffusion method. and appreciate activity were observed.

Keywords: metal complexes, amino acetate benzothiazole, anti-bacterial activity

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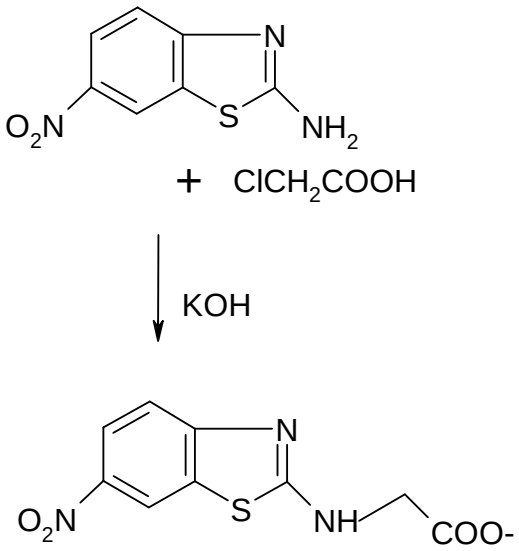
INTRODUCTION

Benzothiazoles are bicyclic ring system with multiple applications. In particular 2-amino benzothiazole were intensively studied as central muscle relaxants. Biologist's attention was drawn to this series when pharmacological profile was discovered. The aromatic benzothiazole [15] nucleus is associated with variety of antihistamine activity, pharmacological activities,[9,10] such as fungicidal, anti-inflammatory, anti-microbial, and anti-convulsant.[2] These activities are probably due to presence of the –N=C-S group.[13]Substituted benzothiazole have been reported to show diverse application as metal complexing agents. [1,5] and photostabliser. The wide range of application of the ligand and its complexes aroused our interest for assaying their antimicrobial activity against gram positive and gram negative micro-organism

EXPERIMENTAL SECTION

Synthesis of 2-amino acetate, 6-nitro benzothiazole:
A solution of p-nitro aniline (0.085 mol) in 95% acetic acid (50 ml) was added to a solution of KSCN (0.308 mol) in 95% acetic acid (100ml). The mixture was cooled to 0^0C & a solution of Br_2 (7.5 ml) in acetic acid (30ml) was added slowly with stirring so that temperature between 0 &10^0C. After addition was complete, the stirring was continued for 1hr. at 5^0C and then mixture was poured into water. The solid was collected & re-crystallized from ethanol. The product (0.036mol), conc. HCl (27ml) and water (50 ml) were refluxed for 2 hr. The solution was cooled and the product was filtered off, washed with water & re-crystallized from ethanol.

The steps of synthesis of 2-amino acetate, 6-nitro benzothiazole can be shown below



Preparation of complexes:
Addition of ethanol solution of the suitable metal salt (Nickel acetate tetra hydrate, Copper acetate, Cadmium acetate dihydrate, stannous chloride and Zinc acetate dihydrate) to an ethanol solution of 2-amino acetate, 6-nitro benzothiazole in 2:1(ligand: metal [3, 4] molar ratio was carried out. After refluxing for half an hour, crystalline colored precipitates formed at room temperature. Washed with distilled water, dried and recrystallized from ethanol and dried at $46^0{}_{C.}$ Table 1: Shows the melting point of the prepared compounds

Instrumentation:
The FTIR spectra in the range (4000-200) cm^{-1} were recorded as CsI disc on FTIR and the magnetic susceptibility values of prepared complexes were obtained at room temperature using Magnetic Susceptibility Balance of Bruke Magnet B.M. 6. The 1H nuclear magnetic resonance spectra were recorded on a Jeol 400 MHz spectrometer with tetra methyl silane (TMS) as internal standard. Melting points were recorded on a hot stage Gallen Kamp melting point apparatus.

Table 1. Physical data for ligand and metal complexes (melting point)

Compound	Melting point ^{0}C
L_H	182
$Ni(L_H)_2$	185
$Cu(L_H)_2$	215
$Sn(L_H)_2$	Above 310
$Zn(L_H)_2$	255
$Cd(L_H)_2$	261

L_H *- 2-amino acetate, 6-nitro benzothiazole*

RESULTS AND DISCUSSION

Infra- red spectroscopy: The ligand was prepared by the reaction of one mole of 2-amino, 6-nitro benzothiazole with one mole of chloroacetic acid in presence of KOH.

Table 1 shows the physical data (m.p.) for the ligand and the prepared complexes he FTIR spectrum of the ligand shows a characteristics stretching absorption band at 3250, 1710, 1560, and 675 cm^{-1} assigned to secondary amine, carbonyl, C=N of the thiazole ring and stretching of C-S group respectively.[11]

The reaction between this ligand with Ni(II), Cu(II), Sn(II), Zn(II) and Cd(II) Gave different types of complexes. In the free ligand, the band at 1710 and 1030 cm^{-1} were assigned to the stretching of C=O and C-O of the carboxylate group. On complexation these bands were shifted to a lower frequency region.

The shift is probably due to the complexation of the metal to the ligand through oxygen of the carbonyl group. Stretching of metal –oxygen bands of the complexes appeared in low frequency region (415-450) cm^{-1}. [12] The IR data of the complexes are shown in **Table 2**

The table lists of stretching frequency (**ν**) for some the group exhibited by ligand and complexes.

Table 2: Characteristics absorption band of 2-amino acetate, 6-nitro benzothiazole and its complexes

Compound	ν(C=O) cm^{-1}	ν (C-O) cm^{-1}	ν (M-O) cm^{-1}
L_H	1710	1030	
$Ni(L_H)_2$	1560	1005	450
$Cu(L_H)_2$	1670	988	420
$Sn(L_H)_2$	1645	990	415
$Zn(L_H)_2$	1575	996	440
$Cd(L_H)_2$	1580	965	435

L_H - 2-amino acetate, 6-nitro benzothiazole

Magnetic Susceptibility and conductivity measurement

The experimentally determined value of magnetic moment for each complexes is listed in **Table 3**. Magnetic measurements are widely used in studying transition metal complexes. The magnetic properties are due to the presence of unpaired electrons in partially filled d-orbital in outer shell of the metal ion in the complex.

The magnetic moment for Ni (II) complexes is approximately 1.09 B.M. this value refers to high spin tetrahedral structure, while the value of Cu (II) is approximately 0.7 led to suggest the square planar structure. Other complexes have no magnetic moment because it is diamagnetic. Molar conductivity measurement in DMF solvent at 25 ^{0}C showed that complexes were non –electrolyte.

Table 3: Magnetic moment, conductivity measurement in DMF solvent

Symbol	Name	Conductivity ($ohm^{-1}cm^2 mol^{-1}$)	μ_m (B.M.)	Suggested Structure
L_H	2-amino acetate, 6-nitro benzothiazole			
$Ni(L_H)_2$	Bis(2-amino acetate, 6-nitro benzothiazole) nickel(II)	15	1.09	Tetrahedral
$Cu(L_H)_2$	Bis(2-amino acetate, 6-nitro benzothiazole) copper(II)	25	0.7	Square planar
$Sn(L_H)_2$	Bis(2-amino acetate, 6-nitro benzothiazole) tin(II)	32	0	Tetrahedral
$Zn(L_H)_2$	Bis(2-amino acetate, 6-nitro benzothiazole) zinc(II)	16	0	Tetrahedral
$Cd(L_H)_2$	Bis(2-amino acetate, 6-nitro benzothiazole) cadmium(II)	14	0	Tetrahedral

NMR Spectroscopy: The data of 1H NMR of the 2-amino, 6-nitro benzothiazole and its complexes displayed good solubility in DMSO. The proton nuclear magnetic resonance spectral data gave additional support for the composition of the complexes. [7] **Table 4**

The δ 6.35-8.19 ppm resonance signal protons of the aromatic ring shifted to higher field upon complexation. While proton of the CH_2 aliphatic group shifted to higher field also.

Table 4 ^{1H}NMR spectral data (δ ppm) of the ligand and complexes

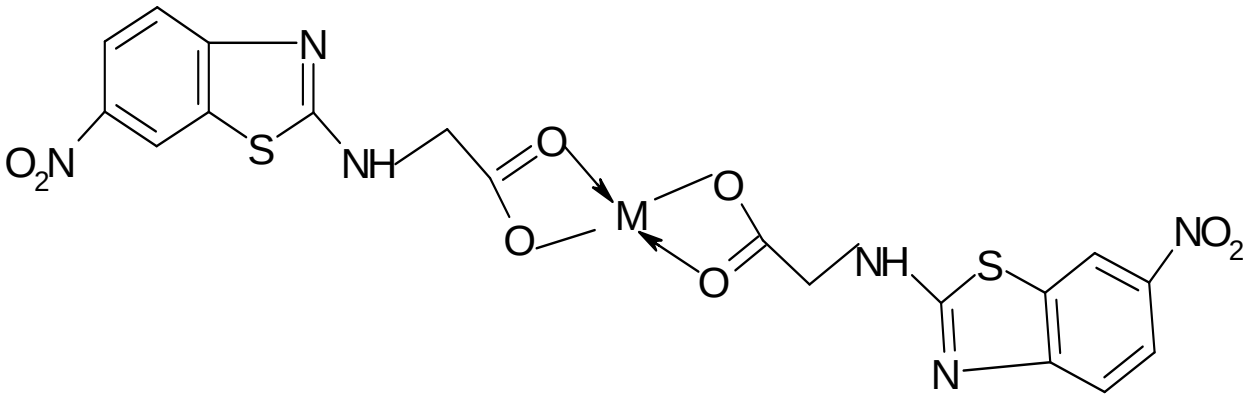
Symbol	-CH_2 aliphatic	Aromatic
L_H	4.18	7.40-8.19
$Ni(L_H)_2$	4.17	6.50-7.19
$Cu(L_H)_2$	4.24	6.47-7.93
$Sn(L_H)_2$	4.18	6.69-7.87
$Zn(L_H)_2$	4.26	6.35-7.97
$Cd(L_H)_2$	4.25	6.59-7.70

Study of Complex formation in solution:

Mole ratio [M/L] in the complex was determined using **Mole ratio method**. [8] The complexes of L_H with metal ions were studied in solution using ethanol as a solvent.

The [M/L] ratio was determined from absorbed light [A]for metal salt and ligand.

The result of complexes in ethanol, Suggestion that metal to ligand ratio was [1/2] for all complexes. On the basis of preceding discussion, the structure of the complexes suggested as follows,



Pharmacology

Antibacterial activity

The title compounds (R1a-e) were screened for their antibacterial activity using cup-plate diffusion method. The bacterial organisms used included both gram positive and gram negative strains like Staphylococcus aureus subsp. Escherichia coli, Staphylococcus pyrogens,B. subtilis, P. vulgaris and micrococcus luteus. Sensitivity plates were seeded with bacterial inoculums of 1×10^6 CIU/ml and each well diameter (10mm) was loaded with 0.1ml of test compound solution (1000 µg/ml) in DMF.So that concentration of each test compounds was 100 µg/ml. The zones of inhibition were recorded after incubation for 24 h using vernier caliper. Inhibition zone record of the compounds clearly indicated that R1c, R1d, R1e highly active against M.leteus and R1b, R1c, R1d, R1e highly active against S.aureus. The result are presented in table 4.

Compound	**Gram negative bacteria**			**Gram positive bacteria**		
	Salmonella enterica Ser typhi	*Salmonella enterica Ser para typhi*	*E.Coli*	*Streptococcus pyrogens*	*Micrococcus luteus*	*S.aureus*
R1 a	—	—	—	—	—	—
R1 b	+	+	+	—	—	+
R1 c	+++	+++	+	—	+++	++
R1 d	++	++	—	—	++	+
R1 e	+	+	—	++	++	+
R6 f	+	+	—	—	+	—
R7 g	—	—	—	—	—	—
R8 h	—	—	—	—	—	—

+++ = Zone size 16-22 mm.
++ = Zone size 9-15 mm.
+ = Zone size 6-8 mm.
— = No inhibition.

CONCLUSION

The novel complexes were successfully synthesized with ligand 2-amino acetate, 6-nitro benzothiazole by condensation method. The ligand was treated with different metal salt to formed corresponding complexes. Square planar geometry was for the copper complexes. [18] The other complexes were proposed to be tetrahedral. Significant anti-bacterial activity was observed with complex **R1c.**

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