

DESIGN, SYNTHESIS, SPECTRUM CHARACTERIZATION AND BIOLOGICAL ESTIMATION OF NEW HETEROCYCLIC THIADIAZOLE DERIVATIVE

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ABSTRACT

This work report describes the details about the synthesis of 1,3,4-thiadiazole derivative based on reaction between Salicylic acid and thiosemicarbazide. The further synthesized compound 2-chloro-N-(5-(2-Hydroxyphenyl)-1,3,4-Thiadiazol-2-yl)acetamide was determined by spectrum characterization (UV&IR) and screened for antimicrobial activity.

KEYWORDS: 1,3,4-thiadiazole derivative, Salicylic acid, thiosemicarbazide, 2-chloro-N-(5-(2-Hydroxyphenyl)-1,3,4-Thiadiazol-2-yl) acetamide, antimicrobial.

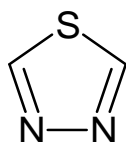
INTRODUCTION

Heterocyclic compounds are cyclic compounds which contains one/more hetero atoms (S, N, O, etc...) along with carbon atoms. In this number of heterocyclic compounds thiadiazole is one of the promising nucleus for the wide variety of biological activity.

1,3,4-thiadiazole moiety is a five membered heterocyclic nucleus bearing nitrogen (N) and sulfur (S) group.

Thiadiazole derivatives possess anti-microbial, analgesic, antiparasitic, antifungal activities.

In the branch of organic chemistry, the medicinal chemistry occupies the chief position because it involves design, development and synthesis of many new drugs.



1,3,4-THIADIAZOLE

MATERIALS

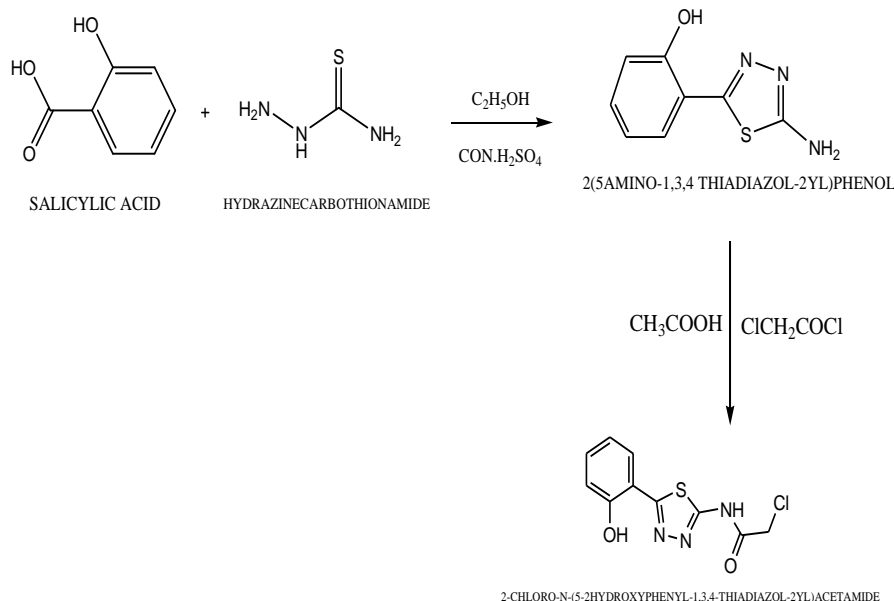
Salicylic acid, conc. sulfuric acid, benzaldehyde and other necessary chemicals were taken in Sri Vijay Vidyalaya college of Pharmacy, Nallampalli.

Thiosemicarbazide, ethanol were purchased from Best Scientific Company, Dharmapuri.

The IR spectra of the compounds were recorded on ATR FT-IR spectrometer (BRUCKER ALPHA II).

The absorption of compounds to be visualized in UV spectrophotometer SHIMADZU, mode-1601.

SCHEM



METHOD

1. SYNTHESIS OF 2-(5-AMINO-1,3,4 THIADIAZOL-2-YL) PHENOL

Thiosemicarbazide (9.11g, 0.1mol), Salicylic acid (13.8g, 0.1 mol) and conc. Sulphuric acid (5 ml) in 50 ml of ethanol are mixed together and the mixture was refluxed for 1.5 hour and poured onto crushed ice. The solid separated out was filtered, washed with cold water and recrystallized from ethanol to separate the first step product.

2. Synthesis of 2-CHLORO-N-(5-2-HYDROXYPHENYL-1,3,4 THIADIAZOL 2-YL)ACETAMIDE

A mixture of 1.15gm (0.01mole) of, 2-chloro-N-(5-(2-Hydroxyphenyl) 1,3,4-Thiadiazol-2yl)acetamidewas dissolved in 10 ml of glacial acetic acid, to this 1.12gm of 0.01mole of chloro acetyl chloride was added and the reaction mixture was refluxed for 1 hr. Cool the mixture to room temperature and pour into ice cold water, the precipitated product was filtered and washed with water and dried. Then was recrystallised from ethanol.

Instrumentation

- The completion of the reaction is confirmed by the using TLC method.
- The UV spectrum of newly synthesized compound is determined by using UV spectrophotometer SHIMADZU, model-1601.
- The structure of compound is confirmed by FT-IR spectrometer (BRUCKER ALPHA II at Vinayaka Mission College Of Pharmacy, Salem.

Determination of Biological Activity

A different concentration of hetero cyclic compounds were tested against the microorganism to determine their MIC, for their anti-microbial activity. Gram positive bacteria *Staphylococcus aureus* and Gram Negative Bacteria *Escherichia coli* is used for this test, culture media is prepared aseptically using standard procedure. Agar well diffusion method used for introduce the sample and standard in bacterial culture plates that previously inoculated on the two petri dish using streak method. The drug with various concentration and the standard is introduced in the culture plates. After 24 hrs of incubation inhibition zones are measured & results are compared. Amoxicillin is used as standard drug.

RESULT AND DISCUSSION

The newly synthesized thiadiazole derivative compound is shown in figure:-----. The compound is chemically named by using chemdraw software. The TLC method is used for confirm the reaction completion and the structure of the compound is determined by spectrum characterization.

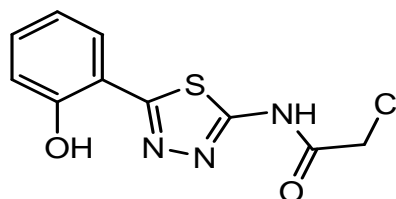


Figure 1:

IUPAC name: 2-Chloro-N-(5-(2-hydroxyphenyl)-1,3,4-thiadiazol-2-yl)acetamide
Molecular formula: C₁₀H₈ClN₃O₂S
Molecular weight: 269.71
Boiling point: 88.51(K)
Appearance: Fine powder
Color: White powder

Spectrum Characterization

A) UV Spectrum

The UV spectrum of newly synthesized THIADIAZOLE DERIVATIVE compound is determined by using UV spectrophotometer SHIMADZU, model-1601, at room temperature using 0.1N NaOH solution as solvent within the range of 200-400 nm.

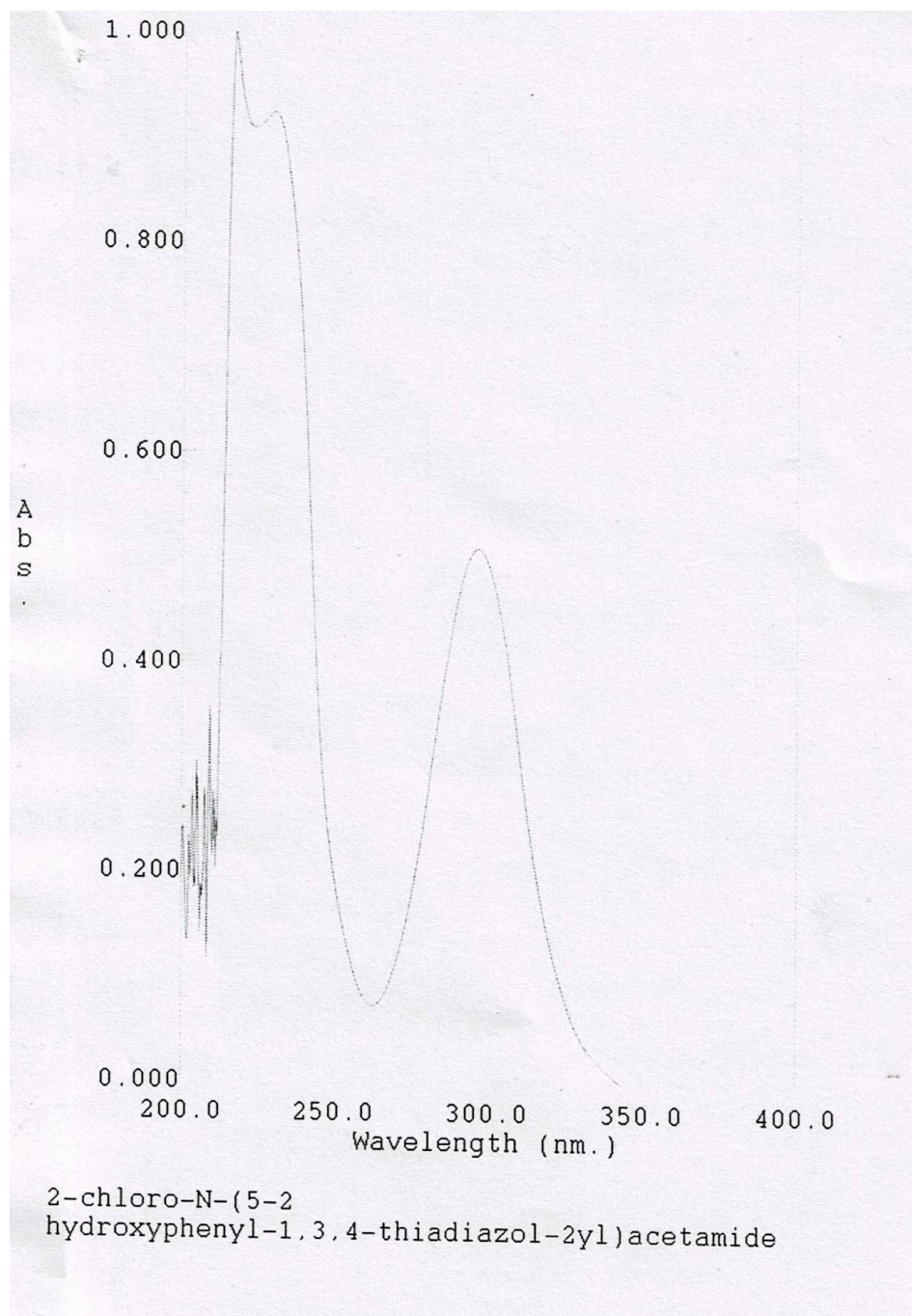


Figure 2: The absorption maximum of compound using NaOH.

In figure 2 shows the absorption spectrum of the thiadiazole compound using NaOH as a solvent gives maximum wavelength at 273 nm.

B) IR Spectrum

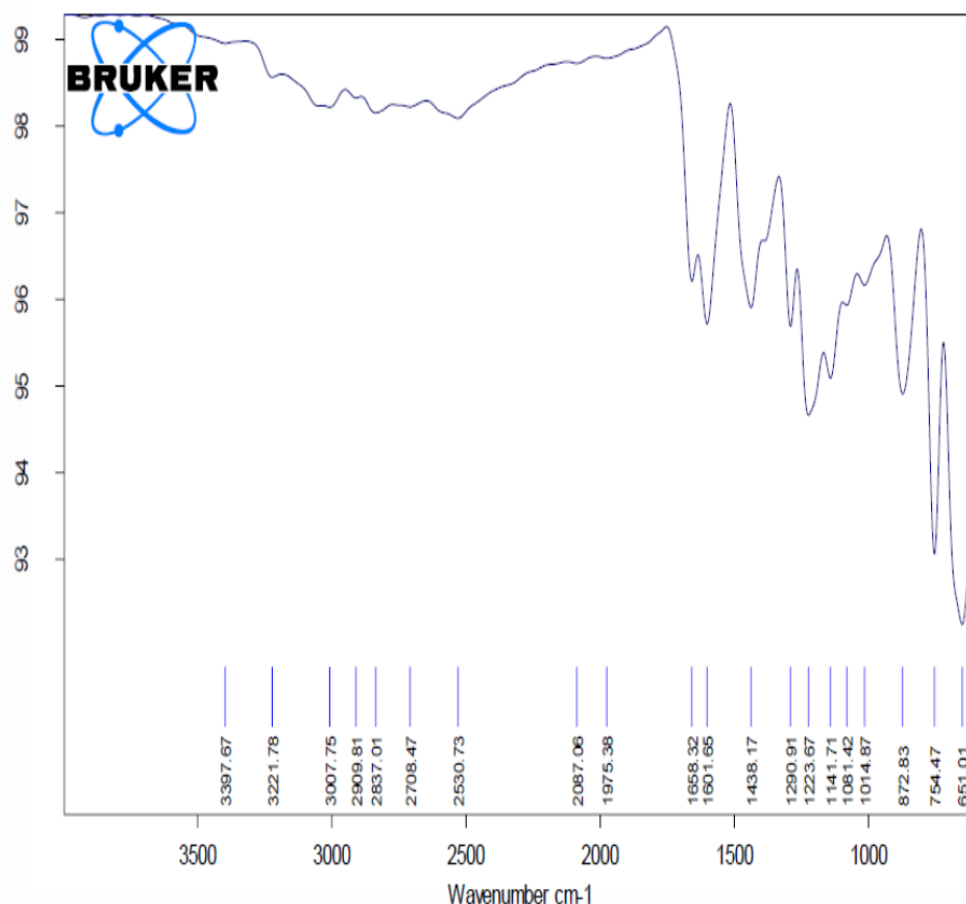


Figure 3: ATR FT-IR Analysis Of Thiadiazole Derivative.

Table 1: ATR FT-IR interpretation of synthesized thiadiazole derivatives.

RADICAL	WAVELENGTH TABLE	ATR FT-IR READINGS	INFERENCE
C=C STRETCHING (AROMATIC)	1700-1500 CM^{-1}	1658.32 CM^{-1} 1601.65 CM^{-1}	C=C BOND IN A MOLECULE
C-H BENDING	860-680 CM^{-1}	754.47 CM^{-1}	C-H BOND IN A MOLECULE
N=C STRETCHING	1630-1690 CM^{-1}	1658.32 CM^{-1}	C=N BOND IN A MOLECULE
C-N VIBRATION	1200-1025 CM^{-1}	1014.87 CM^{-1} 1081.42 CM^{-1}	C-N BOND IN A MOLECULE
C=O STRETCHING	1650-1700 CM^{-1}	1658.32 CM^{-1}	C=O BOND IN A MOLECULE
N-H STRETCHING	1500-1650 CM^{-1}	1601.65 CM^{-1}	N-H BOND IN A MOLECULE
C-Cl BENDING	850-550 CM^{-1}	754.47 CM^{-1} 651.01 CM^{-1}	C-Cl BOND IN A MOLECULE

Based on ATR FT-IR interpretation reading the structure of the newly synthesized compound are confirmed.

Antimicrobial Activity

Different concentration of heterocyclic compounds are tested against the gram positive bacteria and gram negative bacteria to determine their minimum inhibition concentration [MIC] as shown as below and amoxicillin used as standard.

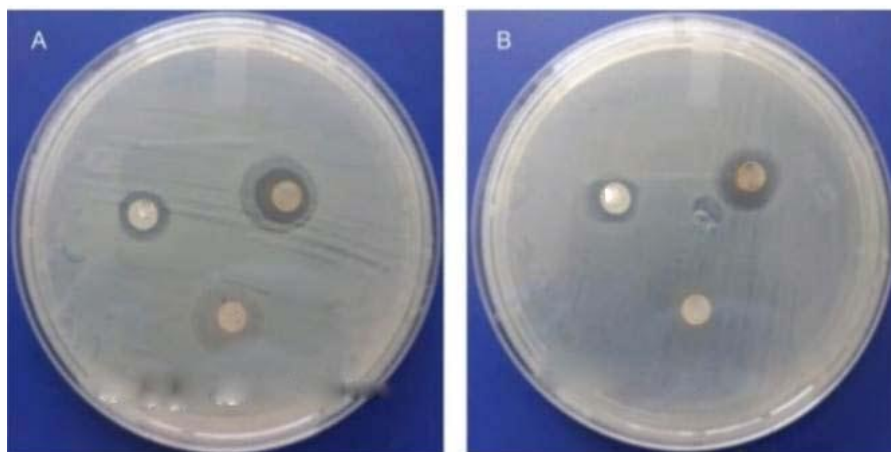


Figure 4: Minimum inhibitory concentration (MIC) of the compound.

BACTERIA	ZONE OF INHIBITION	
	50mg	100mg
Concentration	50mg	100mg
Amoxicillin(standard)	14mm	17mm
Gram positive bacteria <i>Staphylococcus aureus</i>	9mm	12mm
Gram negative bacteria <i>Escherichia coli</i>	6mm	9mm

CONCLUSION

We conclude that, a new thiadiazole derivative was successfully synthesized. The biological estimation of a compound reveals that the new hetero moiety has good biological activity. Then in vitro anti-microbial assay performed against gram positive and gram negative bacteria has shown a close inhibition effect when compared the standard drug.

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