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DESIGN, SYNTHESIS, SPECTRUM CHARACTERIZATION AND BIOLOGICAL ESTIMATION OF NOVEL 1,3,4-THIADIAZOLE DERIVATIVE

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ABSTRACT

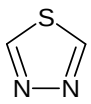
This work report describes the details about the synthesis of 1,3,4-thiadiazole derivative based on reaction between 4-nitro benzoic acid and thiosemicarbazide .The further synthesized compound [E]-N-benzylidene-5-(4-nitrophenyl)-1,3,4 thiadiazol 2-amine was determined by spectrum characterization (UV&IR) and screened for antimicrobial activity.

KEYWORDS: 1,3,4-thiadiazole derivative,4-nitrobenzoicacid,thiosemicarbazide, [E]-N-benzylidene-5-(4-nitrophenyl)-1,3,4 thiadiazol 2-amine , antimicrobial activity.

INTRODUCTION

In the branch of organic chemistry, the medicinal chemistry occupies the chief position because it involves design, development and synthesis of many new drugs. 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.[1,2]

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 and so on. Drugs in market with thiadiazole ring **are Acetazolamide, Methazolamide, Timolol, etc..,**[3,4]



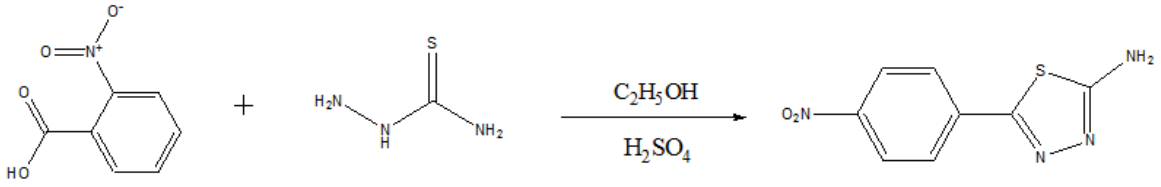
1,3,4-THIADIAZOLE

MATERIALS

- 4-nitrobenzoic acid, con.sulfuric acid, benzaldehyde, Thiosemicarbazide, ethanol and other necessary chemicals were purchased from Best Scientific Company, Dharmapuri.
- The IR spectra of the compounds were recorded on ATR FT-IR spectrometer, BRUKER ALPHA II.
- The absorption of compounds to be visualized in UV spectrophotometer SHIMADZU, model-1601.

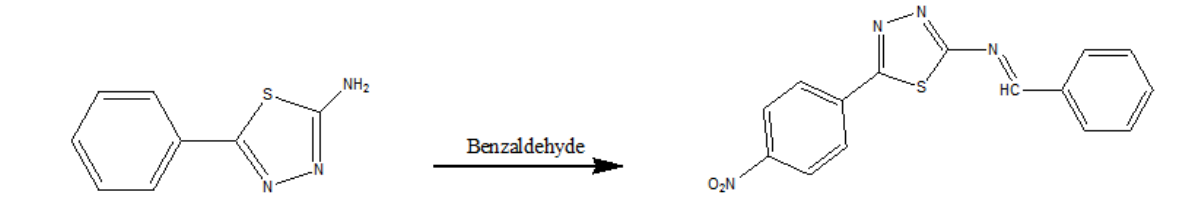
SCHEME

STEP 1: SYNTHESIS OF 5-(4-nitrophenyl)-1,3,4-thiadiazol-2-amine



NITROBENZOIC ACID THIOSEMICARBAZIDE 5-(4-nitrophenyl)-1,3,4-thiadiazol-2-amine

STEP 2: SYNTHESIS OF(*E*)-*N*-benzylidene-5-(4-nitrophenyl)-1,3,4-thiadiazol-2-amine



5-(4-nitrophenyl)-1,3,4-thiadiazol-2-amine

(*E*)-*N*-benzylidene-5-(4-nitrophenyl)-1,3,4-thiadiazol-2-amine

METHOD

1. SYNTHESIS OF 5-(4-NITROPHENYL)-1,3,4-THIADIAZOL-2-AMINE

Thiosemicarbazide (9.11g, 0.1mol), 4-Nitrobenzoic acid (16.7g, 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(E)-N-BENZYLIDENE-5-(4-NITROPHENYL)-1,3,4-THIADIAZOL-2-AMINE[5]

A mixture of 2.22g (0.01mole) of **5-(4-nitrophenyl)-1,3,4-thiadiazol-2-amine**, 1.3ml benzaldehyde (0.01mole) and absolute ethanol was placed in round bottom flask and refluxed for 4 hrs on completion of reaction was monitored by TLC, the reaction mixture was cooled to room temperature and poured into ice cold water with constant stirring. The precipitated product was filtered and washed with cold water and dried. The precipitated product was recrystallized using ethanol.

INSTRUMEMTATION

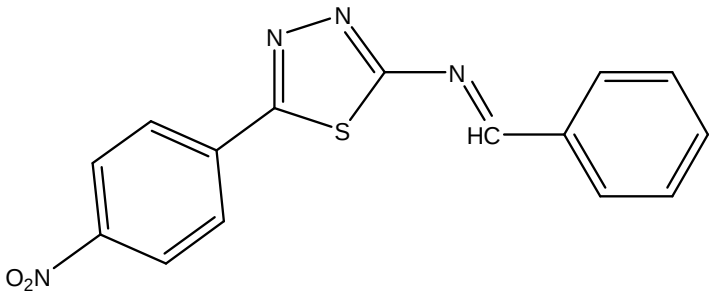
- The completion of the reaction is confirmed by the using TLC method.
- The UV spectrum of newly synthesized compound is determined by using UV spectrophotometer SHIMADZU, model-1601 at Vinayaka mission's college of pharmacy, Salem.
- The structure of compound is confirmed by ATR FT-IR spectrometer, Model-BRUKER ALPHA II at Vinayaka mission's college of pharmacy, Salem.

DETERMINATION OF BIOLOGICAL ACTIVITY[6,7]

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 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. Ciprofloxacin is used as standard drug.

RESULT AND DISCUSSION

The newly synthesized thiadiazole derivative compound is shown in figure: 1. 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.



(*E*)-*N*-benzylidene-5-(4-nitrophenyl)-1,3,4-thiadiazol-2-amine

Figure 1.

IUPAC name: [E]-N-benzylidene-5-(4-nitrophenyl)-1,3,4 thiadiazol 2-amine
Molecular formula: $C_{10}H_9ClN_4O_2$
Appearance: Crystalline powder form
Color: White color

SPECTRUM CHARACTERIZATION

UV SPECTROSCOPY

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.

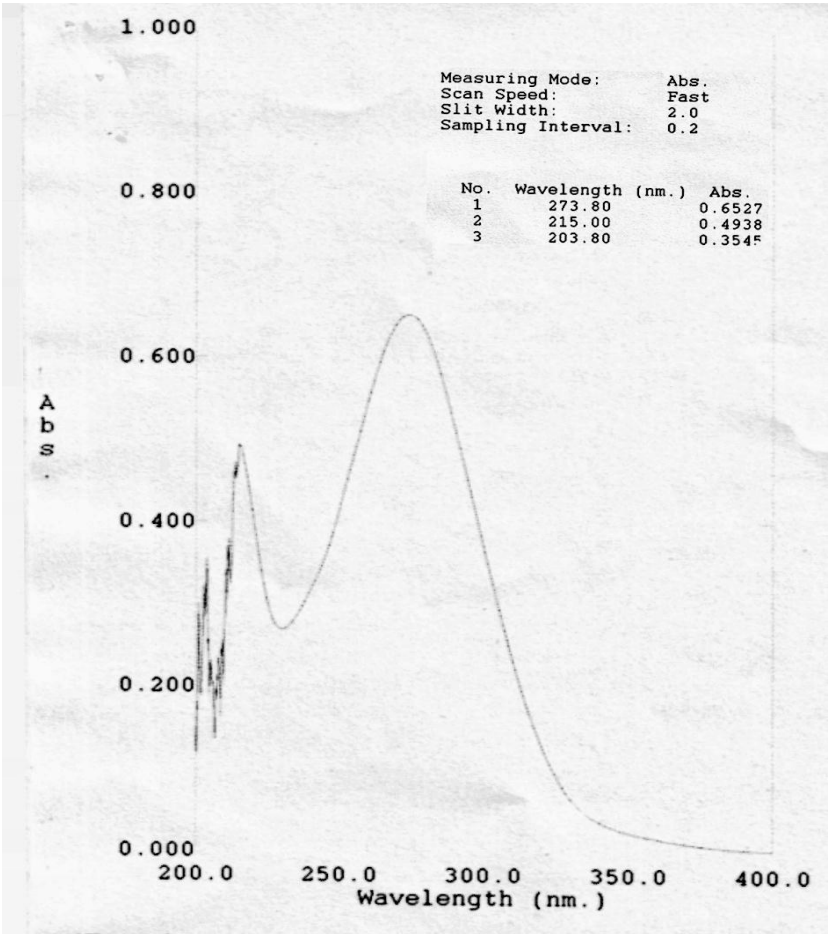


Figure 2: The absorption maximum of compound using NaOH.

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

B) IR SPECTRUM

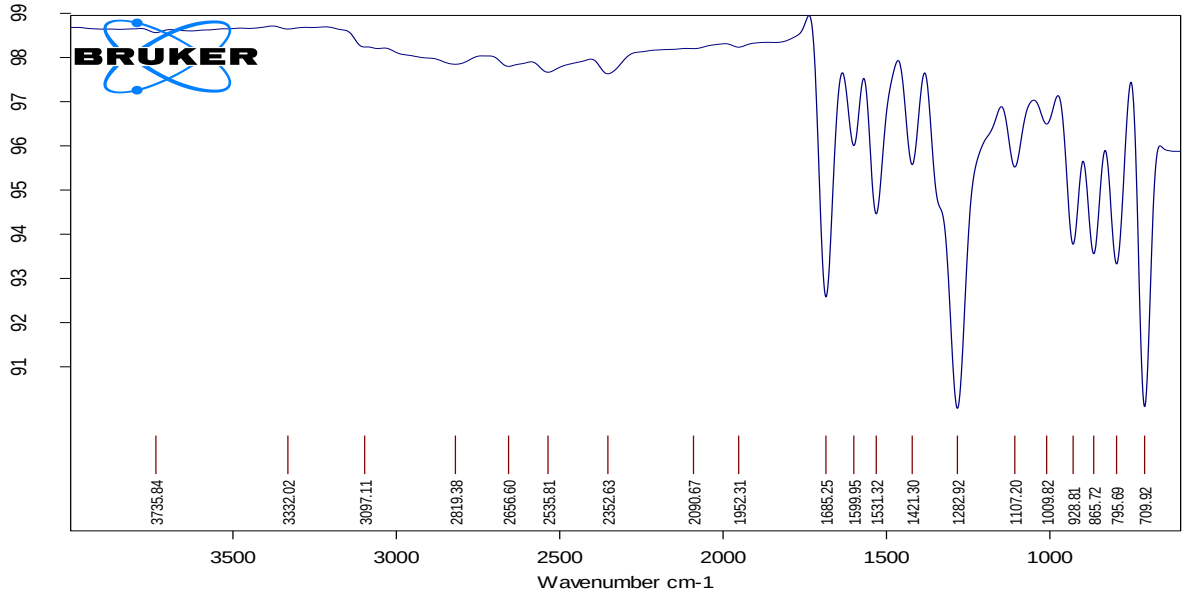


Figure 3: Atr ft-ir analysis of thiadiazole derivative.

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

RADICAL	WAVELENGTH TABLE	ATR FT-IR READINGS	INFERENCE
C=C STRETCHING (AROMATIC)	1450-1600CM^{-1}	1531.32CM^{-1} 1599.95CM^{-1}	C=C BOND IN A MOLECULE
C-H BENDING	700-850CM^{-1}	709.92CM^{-1} 795.69CM^{-1}	C-H BOND IN A MOLECULE
C=N STRETCHING	1630-1690CM^{-1}	1685.25CM^{-1}	C=N BOND IN A MOLECULE
C-N VIBRATION	1000-1400CM^{-1}	1282.92CM^{-1} 1107.20CM^{-1}	C-N BOND IN A MOLECULE
C-S STRETCHING	880-1030cm^{-1}	928.81cm-1 1009.82cm-1	C-S BOND IN A MOLECULE
N-O STRETCHING	1550-1475cm-1	1531.32cm-1	N-O BOND IN A MOLECULE

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

ANTIMICROBIAL ACTIVITY

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

Microorganism	Reference Antibiotic	Concentration(mg)		Zone of inhibition (mm)	
		STD	SAMPLE	STD	SAMPLE
Gram positive bacteria *Staphylococcus aureus*	Ciprofloxacin	50mg 100mg	50mg 100mg	12mm 15mm	9mm 10mm

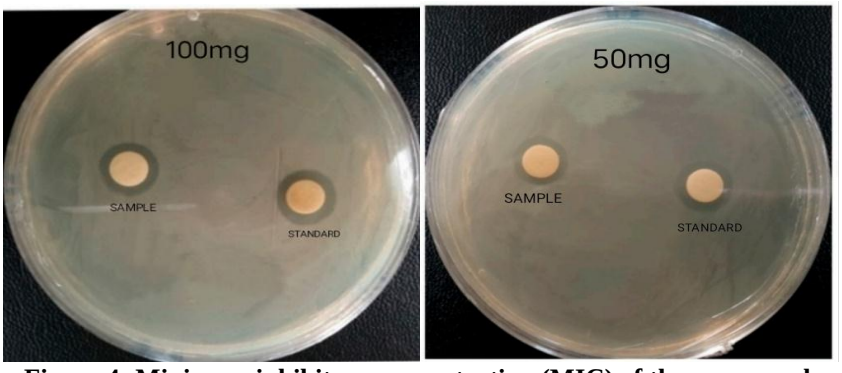


Figure 4: Minimum inhibitory concentration (MIC) of the compound.

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 bacteria has shown a close inhibition effect when compared the standard drug.

ACKNOWLDGEMENT

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