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RESEARCH ARTICLE

# Synthesis and Characterization of New Heterocyclic Compounds and Studying the Biological Activity

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## Abstract

New series of some of synthesized compounds derived of the compound (2- (5-(3,5-dinitrophenyl)-1,3,4-thiadiazol-2-yl-substituted benzalidine .The starting material was prepared by the reaction of 3,5-dinitro benzoic acid with thiosemicarbazide in presence of $POCl_3$. The derivatives of Schiff bases were prepared by reaction of 2-amino -5-(3,5dinitro phenyl) 1, 3, 4-thiadiazole with appropriate aldehydes (***m***-nitro, ***p***-N, N-dimethylamino, ***p***-bromo, ***o***-hydroxy, ***p***-hydroxy) benzaldehydes. These Schiff base were synthesized in order to prepare more important compounds which are the quinazolines and oxazepins. These compounds were synthesized from the reaction of Schiff bases (2- 6) with ***o***-amino benzoic acid (anthranilic acid) and phthalic anhydride respectively. The structures of the new compounds were characterized by FT-IR, $^1$H-NMR spectroscopy besides the melting points and other properties. The biological activity (antibacterial activity) in-*vitro* are investigated for the derivatives at prepared concentration (1*10-3 M) and showed inhibition ability against growth of the two types of pathogenic bacteria: [*Staphylococcus aurous*.] as gram positive and *[Escherichia coli*] as gram negative and showed inhibition ability against bacteria. The most of these compounds are effective against both types of bacteria in varying degree, with high activity for quinazolines and oxazepines.

**Keywords**: *Quinazolines, Oxazepines, Biological activity of 1, 3, 4-thiadiazole, Schiff base.*

## Introduction

The five-membered thiadiazole ring contains one sulfur atom at position(1) and two nitrogen atoms, there are four isomeric types of thiadiazole; 1,2,3-Thiadiazole; 1,2,4-Thiadiazole; 1,2,5-Thiadiazole; and 1,3,4-Thiadiazole as shown in Fig.(1) [1].

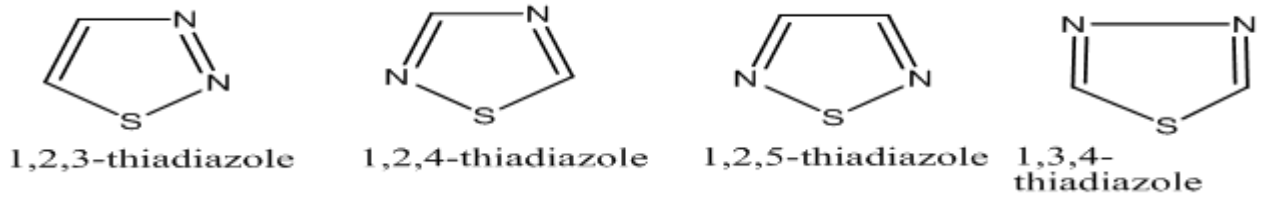



**Figure 1: Structures isomer of Thiadiazole**

The development of 1, 3, 4-thiadiazole chemistry is linked to the discovery of phenylhydrazines and hydrazine in the late 19thcentury. So, the numbering of the 1, 3, 4-thiadiazole ring system was illustrated in Figure 1. The 1,3,4-thiadiazole can be synthesized from cyclization of acylhydrazines including N,N-diacylhydrazines and monoacylhydrazines [2]. Heterocyclic compounds are the most important organic compounds [3]. Pyrimidine is a colorless compound and soluble in water [4]. It is unlike pyridine, it expensive and not readily available and so is seldom used as starting materials for the synthesis. Pyrimidine derivatives play an important role in many biological processes the ring being present in nucleic acid, several vitamin coenzymes, uric acid and other purine compounds.

## Materials and Methods Instruments

- All melting points are uncorrected in degree centigrade and determined on ***Gallen kamp*** electric melting point apparatus.
- FT.IR spectra were recorded on a ***SHIMADZU*** FT.IR 8300

spectrophotometer in the range (4000 -400) cm-1, and using KBr discs.

- 1H-NMR spectrum was recorded on Fourier transformation bruker spectrometer, operating at (400MHz) with (DMSO-d6), measurement was made at Department of Chemistry, Kashan University -Iran.
- The reactions progress was monitored by thin-layer chromatography (TLC) using 4-Fertigfollen precoated sheets type Polygram Silg, the detection was followed by coloring with iodine.
- The biological activity was performed in the central service laboratory, College of Education for Pure Science / Ibn-Al-Haitham, Baghdad University.

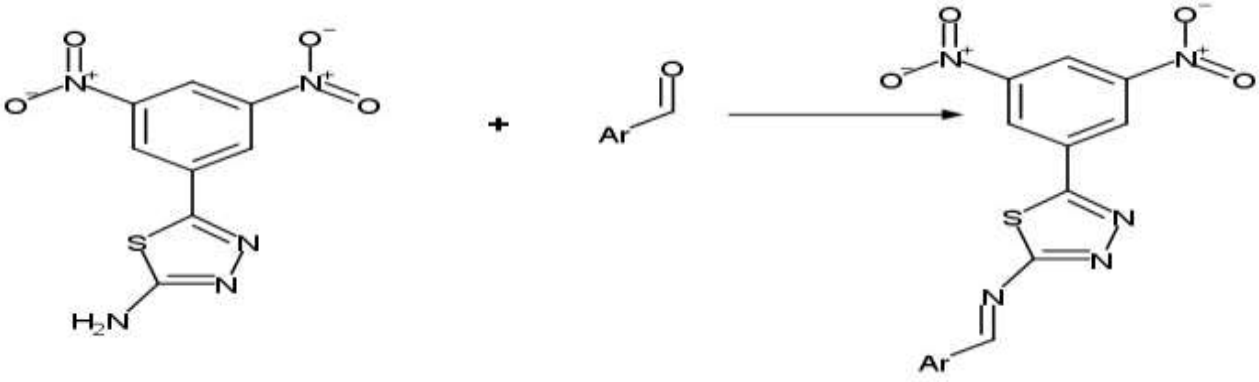
## Experimental

**Synthesis of 2-amino-5-(3,5dinitro phenyl )1,3,4-thiadiazole [1, 5].**

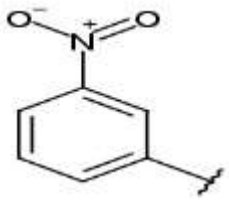
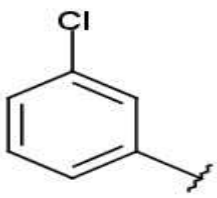
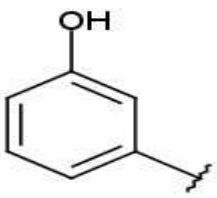
This compound was prepared by the procedure described previously.

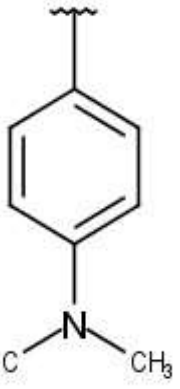
**Synthesis of (2-(((5-(3,5-dinitrophenyl)-1,3,4-thiadiazol-2-yl(*p*-bromo,*p*-N,N-dimethyl,*p*-hydroxy, *m*-nitro, *o*-hydroxy benzylidine )))(2-6)[6]**

A solution of amino compound (1) (0.002 mole, 0.5g) in 15 mL of EtOH was added dropwise into a solution of (0.02 mole) substituted benzaldehyde, in presence of (3) drops of glacial acetic acid then, the mixture was refluxed for 5 hours. After cooling, a precipitate formed which collected by filtration then washed with cold ethanol and recrystallized from ethanol.



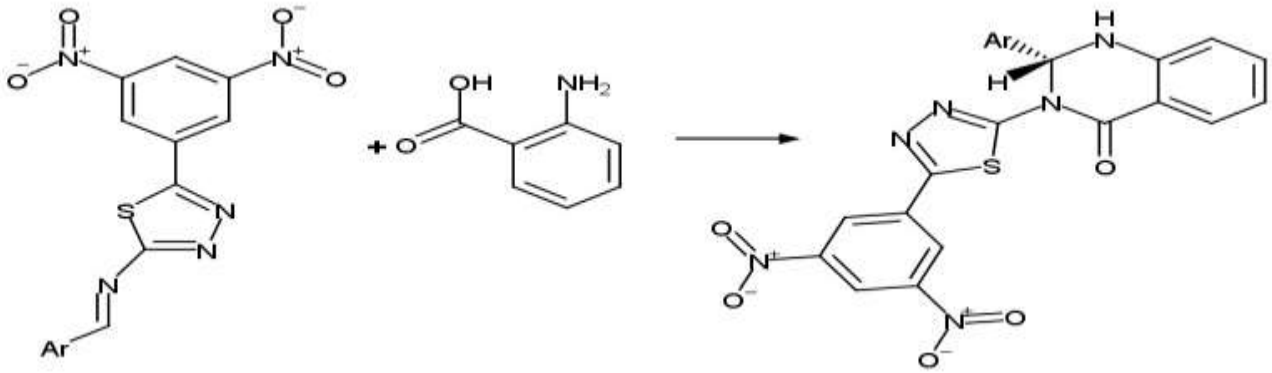

**Equation 1: Synthesis of compound (2-6)**

**Ar=**  **b-**  **c-** 

 **d-**  **e-** .

**Synthesis of (2-(((5-(3,5-dinitrophenyl)-1,3,4-thiadiazol-2-yl(3-(alkyl)2,3-dihydroquinazoline-4(1H)one) (6-10)[7].**



**Equation 2: synthesis of compounds (7-11)**

A solution of 2-aminobenzoic acid (anthranilic acid) (0.02mol) was added to Schiff bases (2-6) (0.02mol) in dioxane. The solution was heated under reflux for (6-8) hour. The solvent was evaporated and the residue was treated with 10% of sodium bicarbonate, then filtered and recrystallized by benzene.

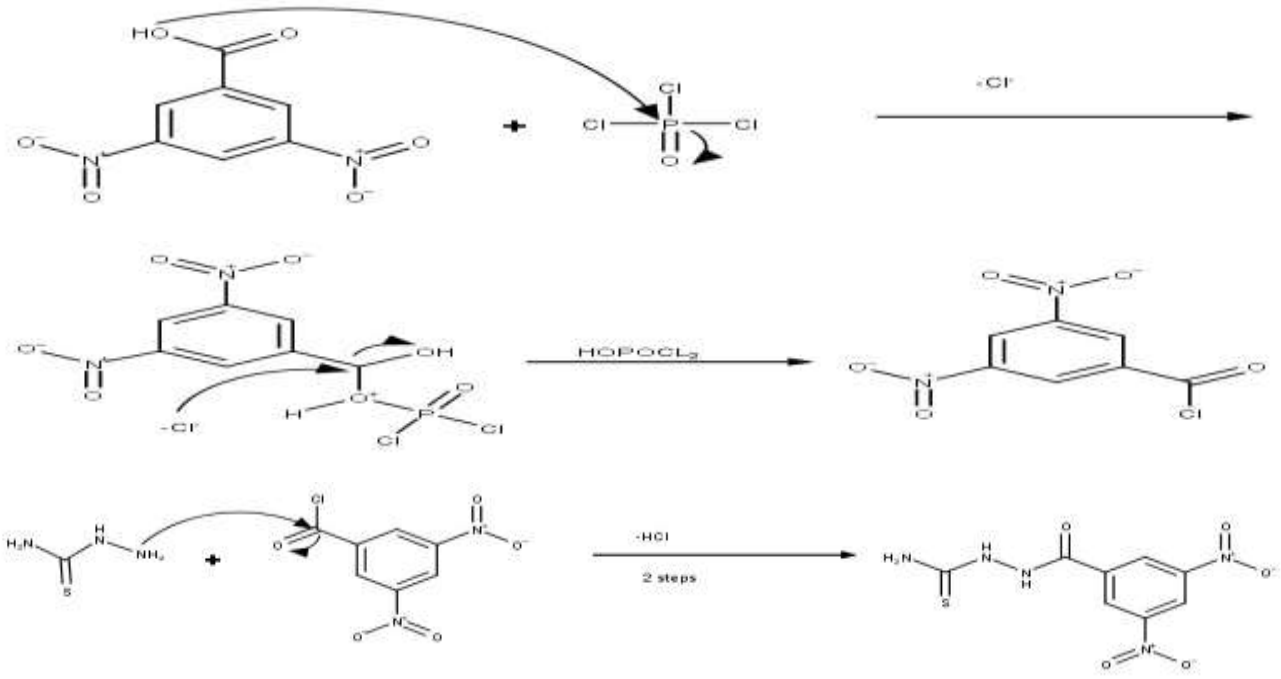
### Synthesis of oxazepines Compounds [2-(((5-(3,5-dinitrophenyl)-1,3,4-thiadiazol-2-yl -2,3-dihydro-1,3-oxazepine-4,7-dione (11-14)[8]:-

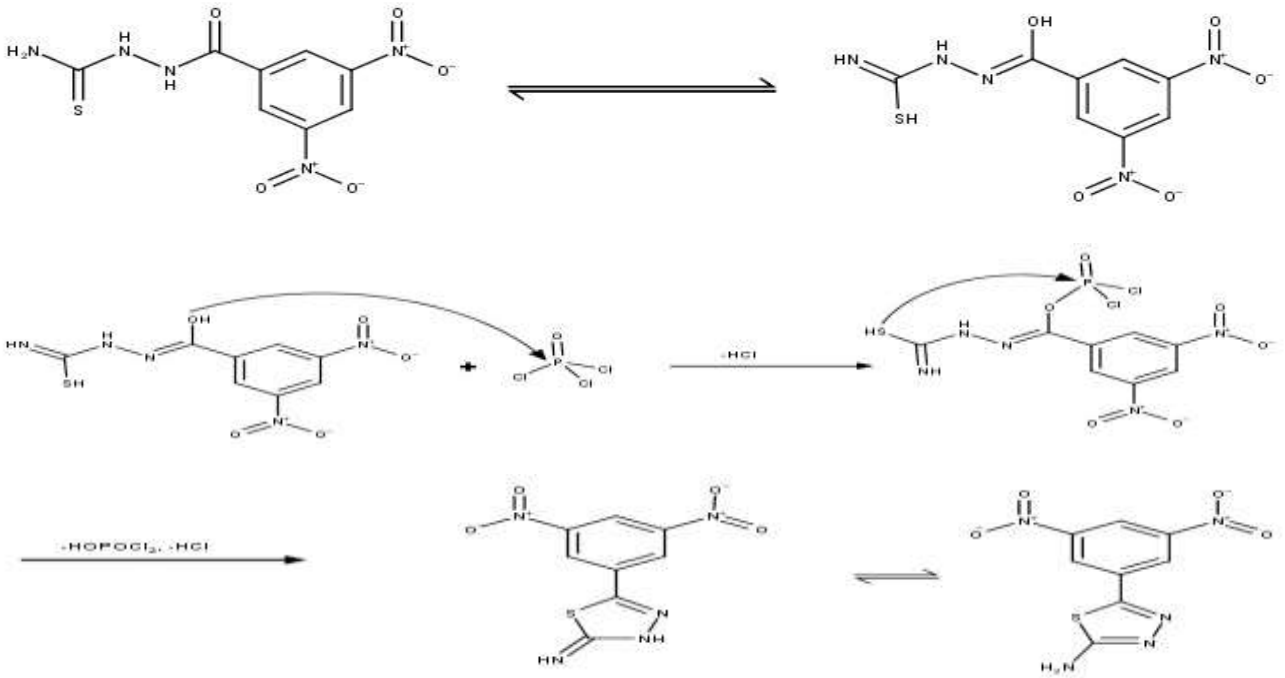
A mixture of compounds (2-6) (0.5 gm., 0.002 mole.) with phthalic anhydride , (0.002 mole) dissolved in(15 ml) dry benzene and then the mixture was refluxed for(6-7) hours , then the mixture was poured on crushed ice, the formed solid product was filtered off and re-crystallized from diethyl ether.

### Results and Discussion

Compound (1) Thiadiazole is characterized by FT.IR and Uv spectroscopy, the melting point is recorded and the purity of this compound is checked by T.L.C. technique.

The FT-IR spectrum of the compound (1) in general, exhibited significant two bands in the region(3469,3415) $cm^{-1}$, which could be attributed to asymmetric and symmetric stretching vibration of $NH_2$ group [9].In addition to a band at about 1620 cm-1 due to cyclic (C=N)stretching is also observed, with symmetrical stretching near 1080 cm-1 band of (3090) $cm^{-1}$ band of (C-H)arom., UV spectrum, shows the transionsn→л and л→л* which confirmed the presence of the un-bonded pair of electrons on sulfur,nitrogen atom and aromatic system (C=C double bond), band of ($NO_2$) asymmetric and symmetric at (1537) $cm^{-1}$ and (1348) $cm^{-1}$ respectively. Other bands of C=Cst. appeared at( 1508,1419)$cm^{-1}$ and band of (C-S-C) at (107,6) $cm^{-1}$[10]. The suggested mechanism for this reaction can be outlined as follow:





**Scheme**: **Mechanism formation for 2- amino -1, 3, 4-thiadiazol derivative**

The spectrum of the Schiff bases (2-6) Table (1),compounds (2-6) showed bands at (3200-3400) cm–[1] assigned for υ(O-H) stretching, the band at (3085) assigned for υ(C-H) aromatic and the band at 1625cm-1 due to υ(C=N) of the Schiff base. Also, the spectrum shows bands at (1589)cm-1 assigned to υ(C=N) cyclic ring stretching and the bands at (1539 and 1355)cm-1, (1506 and 1352)cm-1 ,(1260)cm-1 and (1072)cm-1 attributed to the υ( $NO_2$) asym., and sym., υ(C=C), υ(C -O), υ(C-S-C), stretching frequencies, respectively [11].The Mechanism of this reaction is suggested as below:

**Table 2: FT-IR spectral data of Schiff bases (2-6).**

| *Comp. No.* | *R* | *υ(C=N)* | *υ(C–H)arom.* | *υ(C–H) aliph.* |
|---|---|---|---|---|
| 2 | ***p*-Br(870)** | **1630** | **3050** | **2839,2950** |
| 3 | ***p*-N,N-( 890)** | **1625** | **3087** | **2840,2980** |
| 4 | ***p*-(O-H)3100-3600** | **1625** | **3049** | **2890,2940** |
| 5 | ***m*-($NO_2$)(** 1539 , 1355) | **1627** | **3098** | **2860,2959** |
| 6 | ***o*-(OH)3300-3600** | **1628** | **3041** | **2849,2950** |

Compounds (7-11) were synthesized from the reaction of compounds (2-6) with 2-aminobenzoic acid in dry benzene. The compounds were characterized by their melting points and F.T.IR spectra. The F.T.IR spectrum of compound [9] was confirmed from the appearance of carbonyl group band at (1679$cm^{-1}$) and OH group (3440cm-1) N-H band at (3127$cm^{1}$) and (1022$cm^{-1}$) and C-N stretch (aryl) (1417$cm^{-1}$) belong to the asymmetric and symmetric (C-O-C) band [1].

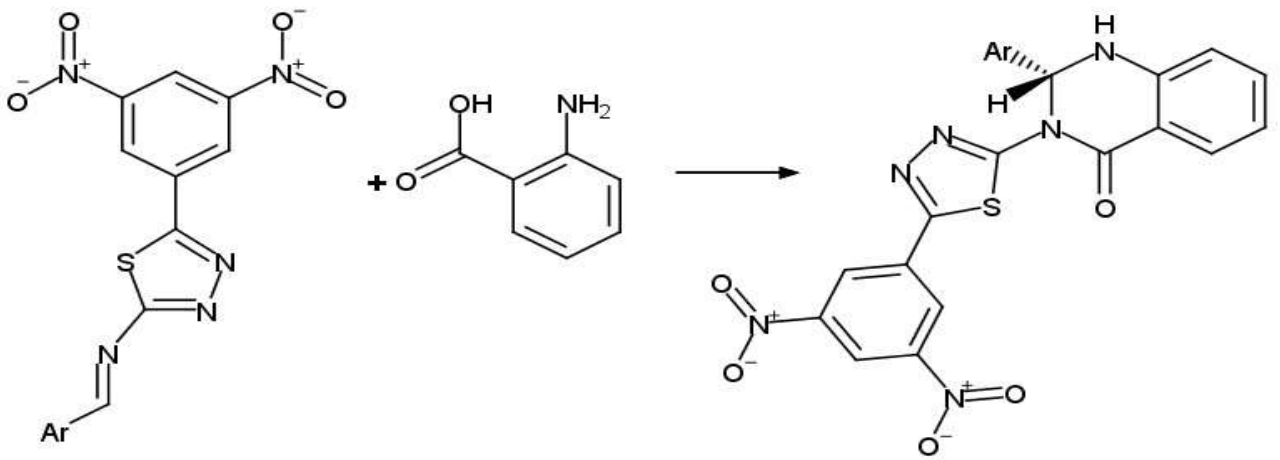


**Table 3: FT-IR spectral data of derivatives (7-11)**

| Comp. No. | R | | υ(C=N) | υ(C–H) arom. | υ(C–H)aliph. |
|---|---|---|---|---|---|
| 7 | ***p*-Br(870)** | | **1625** | **3050** | **2839,2950** |
| 8 | **N,N-(diMethyl** | | **1625** | **3087** | **2840,2980** |
| 9 | ***p*-*(O-H)*3100-3600** | | **1625** | **3049** | **2890,2940** |
| 10 | ***m*-($NO_2$)** | | **1627** | **3098** | **2860,2959** |
| 11 | ***o*-(OH)3300-3600** | | **1625** | **3041** | **2849,2950** |

Reaction of (2-6) derivatives with phthalic anhydride got compounds (12-17), structures of these derivatives were confirmed by the presence of (C=O.) stretching band at (1662) $cm^{-1}$ and(C=C) stretching at(1554)$cm^{-1}$ combined with the vanishing of $NH_2$ stretching band[9].

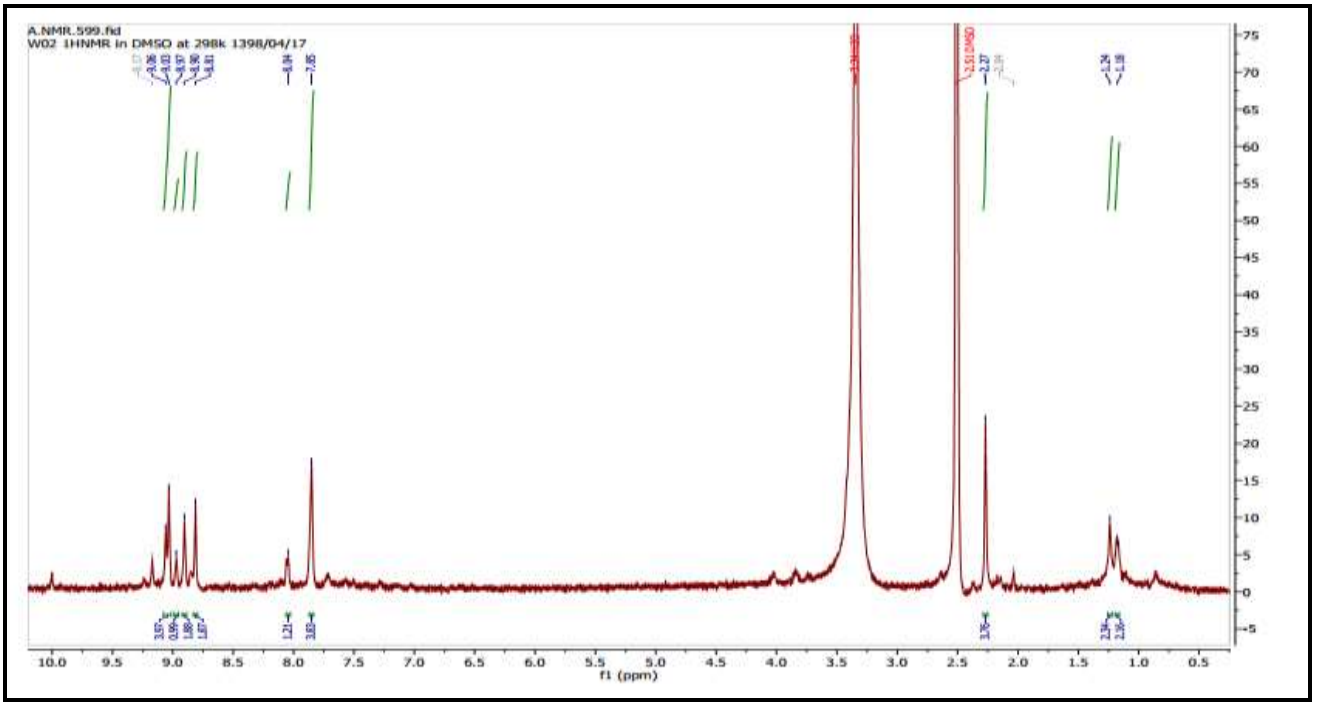



**Fig.2: H-NMR spectrum of compound 2**

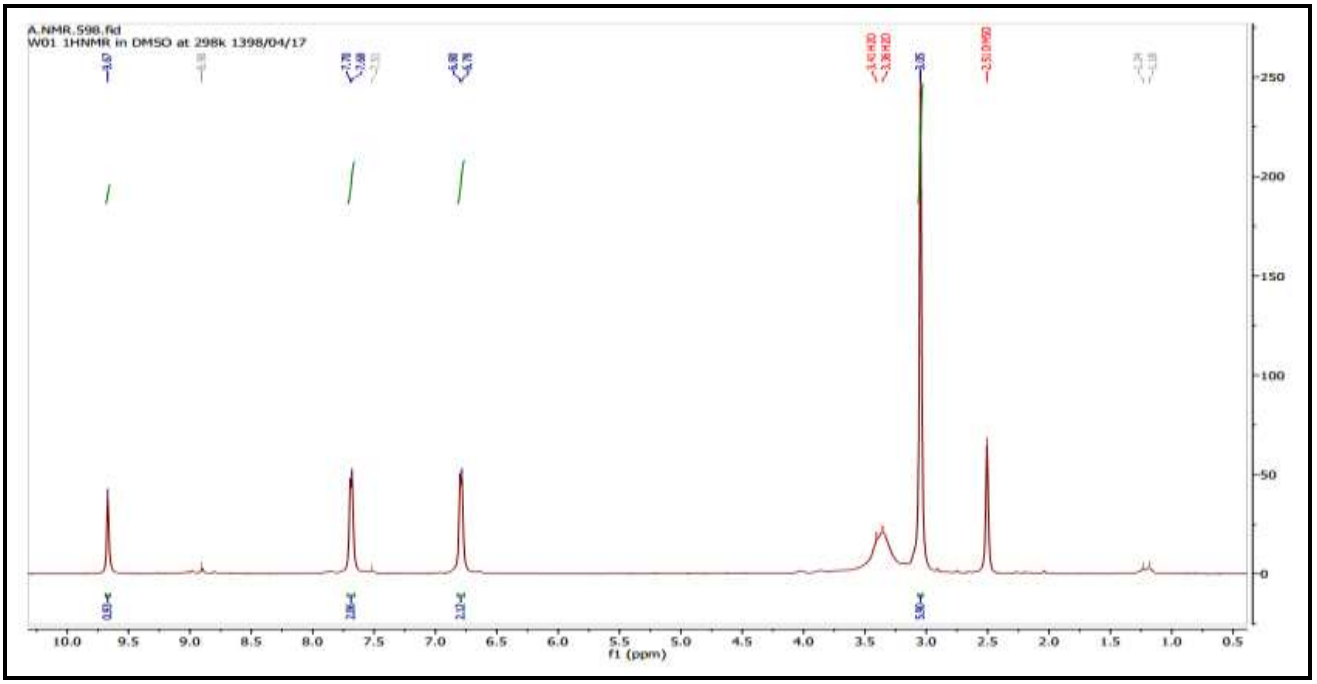



**Fig.3: H-NMR spectrum of compound 3**

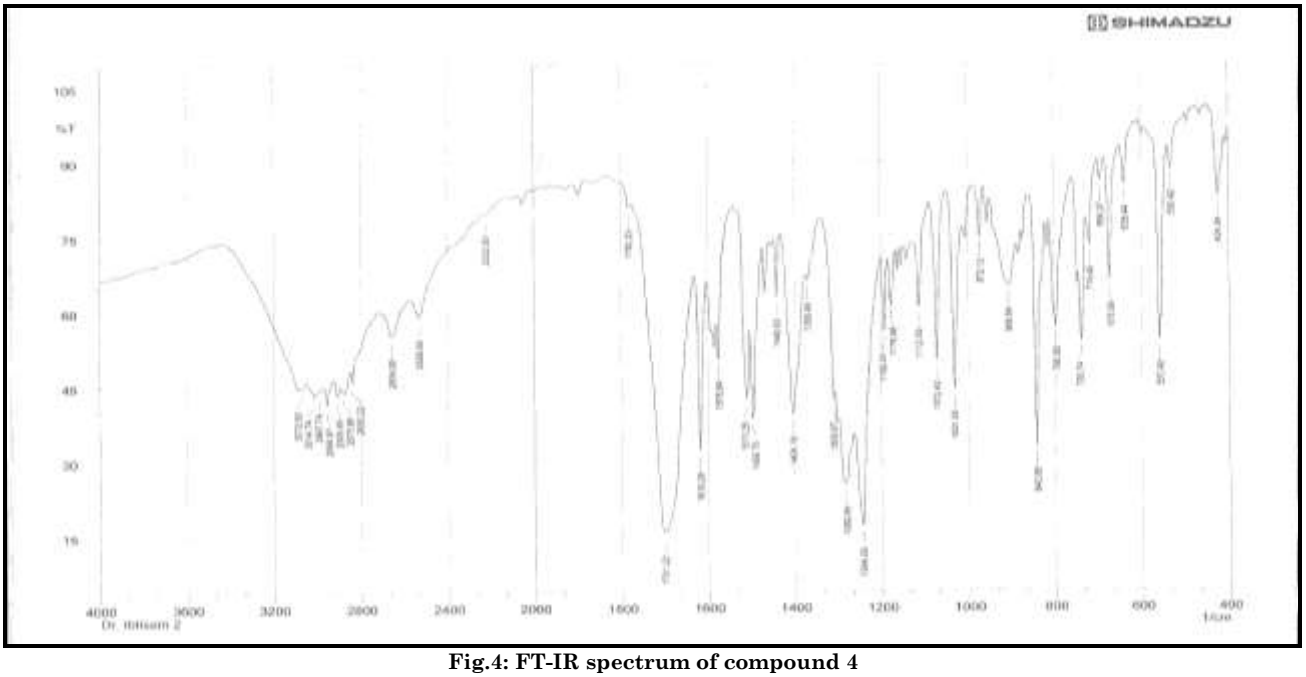



**Fig.4: FT-IR spectrum of compound 4**

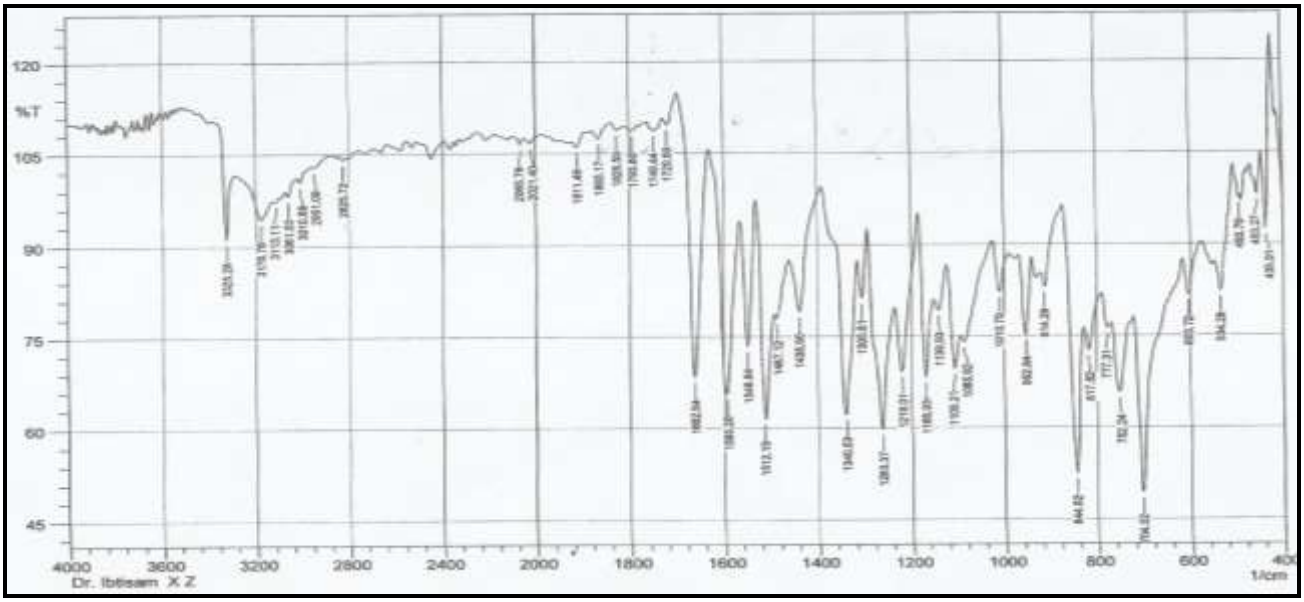



**Fig.5: FT-IR spectrum of compound 5**

## Biological activity

Some heterocyclic derivatives such as tetrazoles or quinazoli nes and oxazepines are considered as chemotherapeutic agents. These (chemotherapeutic agents) are chemicals that intended to be toxic for the infectious organism but innocuous for the host. So it can be given in sufficient dosses to kill or inhibit the microorganism through out the body without harming the body cell. The prepared compounds are known for their antibacterial activity. The prepared agar and petri dishes were sterilized by autoclaving for 15min. at 121 ºC. The agar plates were surface inoculated uniformly from the broth culture of the tested microorganisms. The control used in the disk was DMSO. The same solvent was used for antibiotics [5]. There are some types of bacteria: [*Staphylococcus aurous*.] as gram positive and *[Escherichia coli*] as gram negative. These results of the preliminary screening tests are listed in Table (4).

**Table 4: Antibacterial activites of some of the synthesized compounds**

| Comp. No. | *Staphylococcus aurous* | *Escherichia coli* |
|---|---|---|
| 2 | ++ | + |
| 3 | - | + |
| 5 | -+ | +++ |
| 6 | + | ++ |
| 7 | ++ | + |
| 8 | ++ | ++ |
| 9 | + | + |

**Key to Symbols**

Highly active = +++ (inhibition zone > 20 mm).

Moderately active = ++ (inhibition zone 11-20 mm).

Slightly active = + (inhibition zone 5-10 mm).

Inactive = - (inhibition zone <5 mm).

## Conclusion

In in this work, I noticed that the prepared compounds showed highly activity against ***Escherichia coli*** like compound 5 and some moderately active like 6,8 the others against ***Staphylococcus aurous***. So ,I conclud that the compounds bearing thiadiazol ring possesses a wide range of promising biological activities.

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