# Formation, Spectral Characterization, Thermal Analysis and Biological Assay of Bis (Thiadiazole-Schiff Base)- Ligands

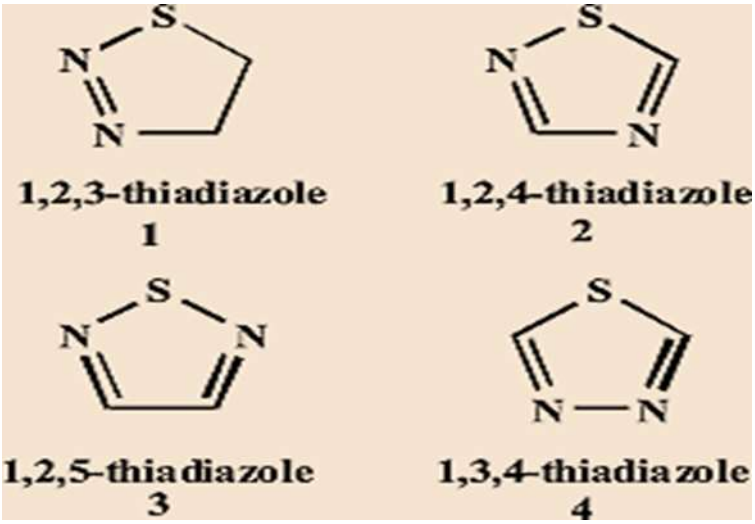
*Muhammed Abdel Hasan Shallal*
*M.Sc in Chemistry , Assist .Lecturer ,Thiqar Government .,Iraq .*

***ABSTRACT***
***Our work includes formation of five new ligands through series reactions such as condensation reaction of bis thiadiazole- amine with aromatic aldehyde to produce Schiff base compound which reacts in azotation reaction as diazonium salt , then coupling step with phenol derivatives and replacement of heteroatom (nitrogen) with (oxygen ) ., the products contain ( bis- Schiff groups , Schiff-azo group , thidizole- schiff ligands , thiadiazole azo- schiff ligands.***
***The formatted ligands were identified by chemical methods like spectrophotometric techniques ( FTIR , $^1$HNMR , Mass ) , Thermal Measurements and biological assay.***

**Keywords: replace , atom , bis .**

## I.INTRODUCTION

There are (four) structures for thiadiazole depending on the positions of the atoms ( sulfur , nitrogen ); these structures do not interconvert and hence are structural isomers and are not tautomers. The compounds themselves are rarely prepared and possess no particular uses and application, however compounds bearing them as a structural motif are fairly common in pharmacology[1-6] .




**Picture .1: Structures of Thiadiazole**

All studies and the literature summarized that differently substituted 1,3,4-thiadiazoles and annelated 1,3,4-thiadiazoles have a great applications of pharmacological activities like antimicrobial , antifungal, antituberculosis , antileishmanial, anti-inflammatory, analgesic, CNS depressant, anticancer, antitumor , antidiabetic , molluscicidal, antihypertensive, diuretic, analgesic, antimicrobial, antitubercular, and anticonvulsant activities[7-18] . These important biological activities encouraged several papers groups to find out many methods for formation of new thiadiazoles using many synthones[19-30] , Thidiazole compound used in several fields[31-40] in preparation of many derivatives[41-47] .

## II. EXPERIMENTAL PART:

The thiadiazole – Schiff ligands were synthesized from chemical compounds ( BDH and SIGMA COMPANIES), I.R spectra were recorded on a Perkin Elmer-spectrum by KBr – disc . 1H.NMR spectra were

recorded 300 MHz spectrometer in using dimethyl sulphoxide . , Mass spectra , Thermal measurements . The methods of synthesis were carried out according to papers[21-24] :

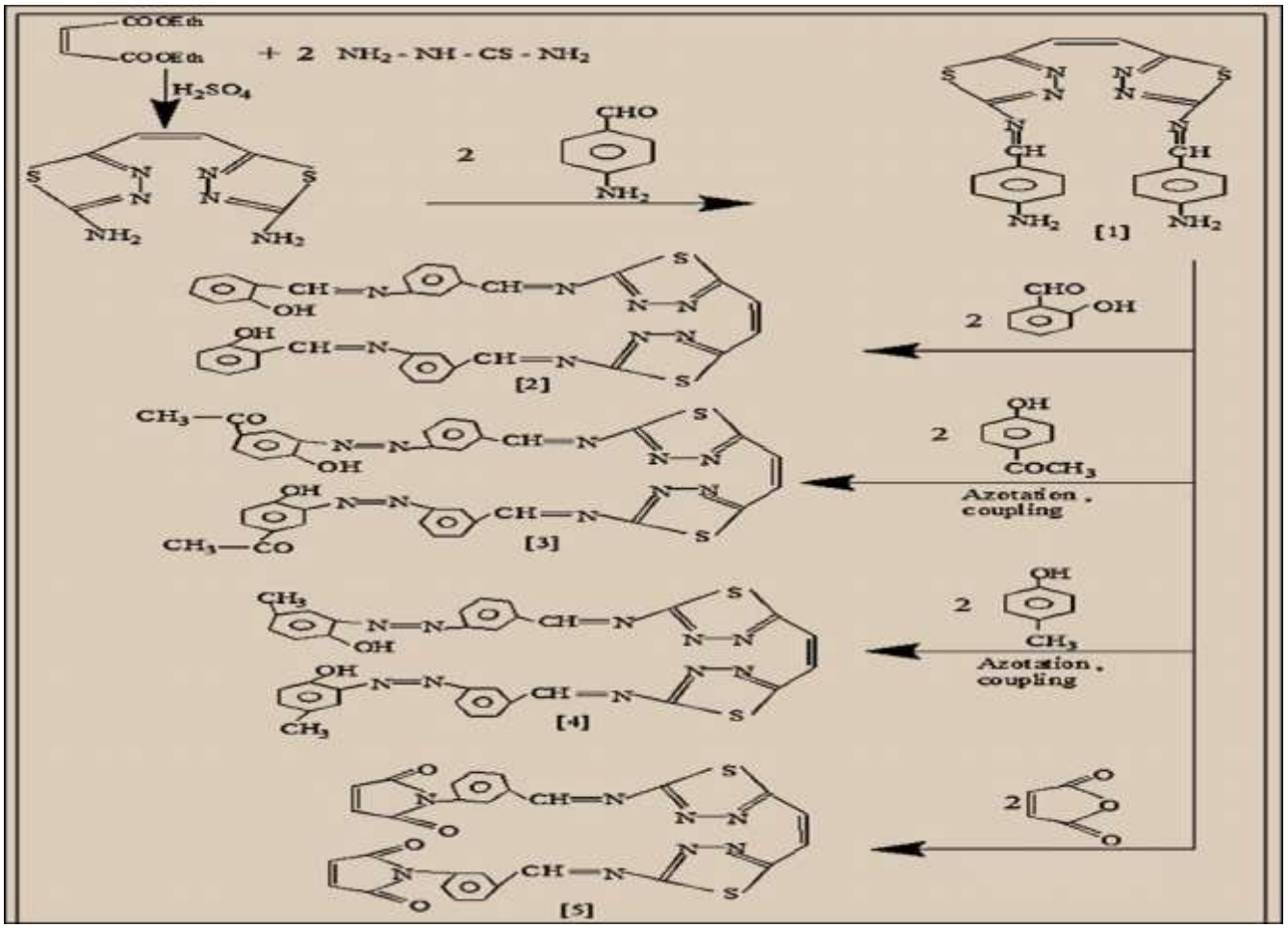
**Preparation of Bis –Thiadiazole Schiff derivative – Ligand (1 ):**
Diethyl maleate (0.01 mole) refluxed with (0.2 mole ) of thio semicarbazide compound in acid medium for completing reaction for (18 hrs) to produce amino-thiadiazole , then the precipitation filtered and dried , which refluxed with (0.02 mole) of 4-amino benzaldehyde according to method[21] to give 76 % ligand (1 ).

**Preparation of Bis –Thiadiazole Schiff derivative – Ligand (2 ):**
Compound (1) (0.01 mole ) refluxed with (0.02 mole) of 2-hydroxy benzaldehyde according to method[21] to give 70 % ligand (2 ).

**Preparation of Bis –Thiadiazole Schiff Azo derivative – Ligand (3 ):**
The compound (1) (0.01 mole ) dissolved in (3 ml )concentrated acid then addition of solution of (sodium nitrite ) in ice path , then addition (0.02 mole) of para-aceto phenol according to method[21] to yield 72 % ligand (3 ).

**Preparation of Bis –Thiadiazole Schiff Azo derivative – Ligand (4 ):**
The compound (1) (0.01 mole ) dissolved in (3 ml )concentrated acid then addition of solution of (sodium nitrite ) in ice path , then addition (0.02 mole) of para-methyl phenol according to method[21] to yield 80 % ligand (4 ).

**Preparation of Bis –Thiadiazole Schiff derivative – Ligand (5 ):**
Compound (1) (0.01 mole) reacted with maleic anhydride (0.02 mole) in presence of acetone according to method[21] to yield 70 % ligand (5 ).




**Scheme.(1) :Preparation of Bis-Thiadiazole Schiff Ligands [ 1 - 5 ]**

## III. RESULTS AND DISCUSSION

The synthesized thiadiazole - schiff ligands identified by chemical techniques:

**Identification of Ligands by Spectra:**

**Identification by FT.IR :** It indicated to many bands at (CH=N)Imine: (1619) , (C=N)Indocycle: 1651 , ($NH_2$): (3316 , 3333) in compound(1) , bands are appeared at (OH-)Phenol: 3423 .,(CH=N)Imine: (1614) , (C=N)Indocycle: 1641 in compounds ( 2 ) ,while other bands appeared at (OH-)Phenol: 3421 .,(CH=N)Imine: (1617) , (C=N)Indocycle: 1646 , (-N=N-) Azo : 1522 , (CO-$CH_3$ )Ketone : 1703 in compound ( 3 ) ., (OH-)Phenol: 3414 .,(CH=N)Imine: (1624) , (C=N)Indocycle: 1666 ,(-N=N-) Azo : 1500 in compound (4) ,bands at (CH=N)Imine: (1643) , (CO-N)Amide: 1681 ,(-N=N-) Azo : 1504 in compound (5) .,Other bands abstracted in Table (1) .

**Table (1): FT.IR- data ($cm^{-1}$) of Ligands (1-5).**

| Ligands | Other Groups |
|---|---|
| **( 1 )** | (CH=N)Imine: (1619) , (C=N)Indocycle: 1651 , ($NH_2$): (3316 , 3333) . |
| **( 2 )** | (OH-)Phenol: 3423 .,(CH=N)Imine: (1614) , (C=N)Indocycle: 1641 . |
| **( 3 )** | (OH-)Phenol: 3421 .,(CH=N)Imine: (1617) , (C=N)Indocycle: 1646 , (-N=N-) Azo : 1522 , (CO-$CH_3$ )Ketone : 1703 |
| **( 4 )** | (OH-)Phenol: 3414 .,(CH=N)Imine: (1624) , (C=N)Indocycle: 1666 , (-N=N-) Azo : 1500 . |
| **( 5 )** | (CH=N)Imine: (1643) , (CO-N)Amide: 1681 ,(-N=N-) Azo : 1504 . |

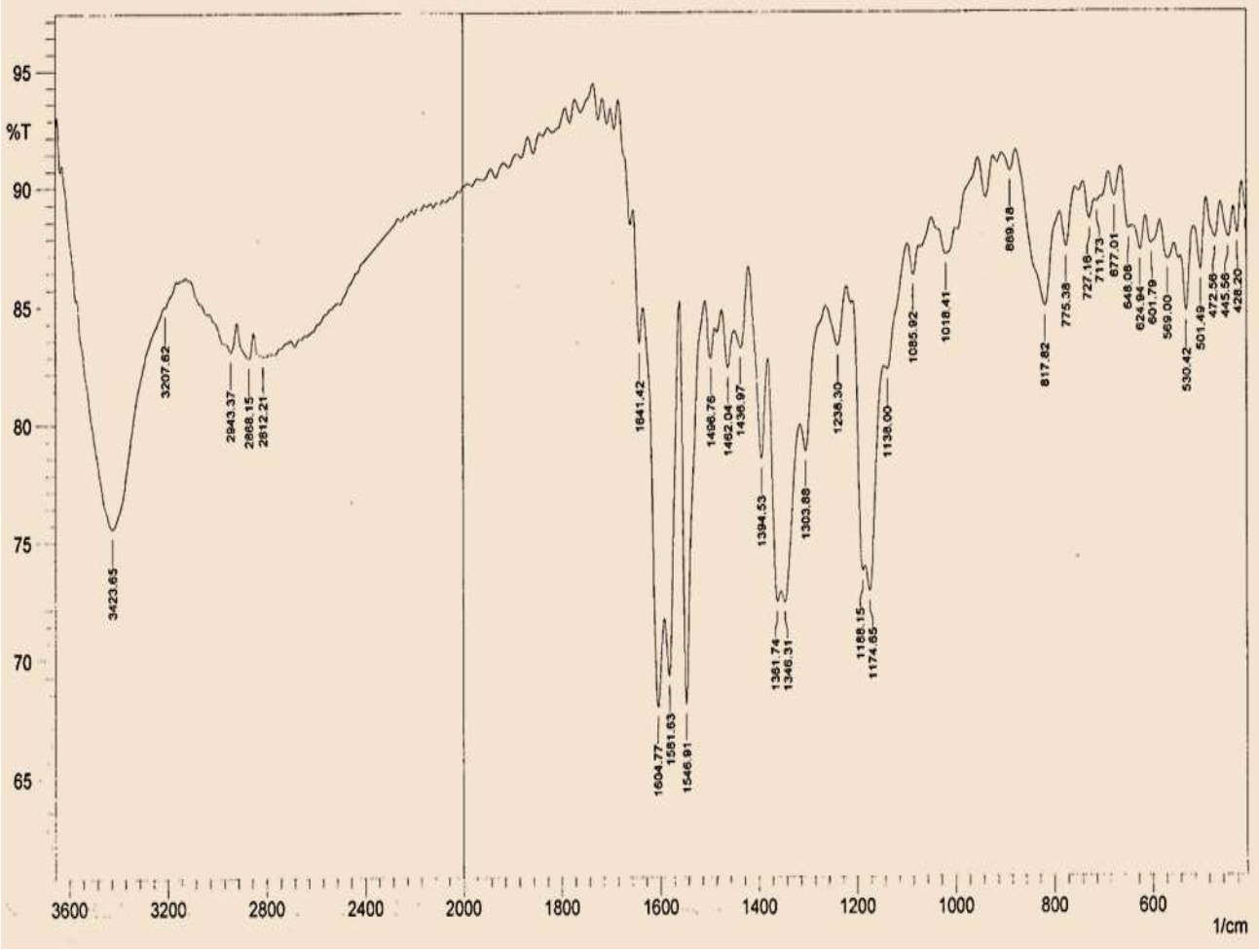



**Fig .(1) : FT.IR of Ligand [ 2 ].**

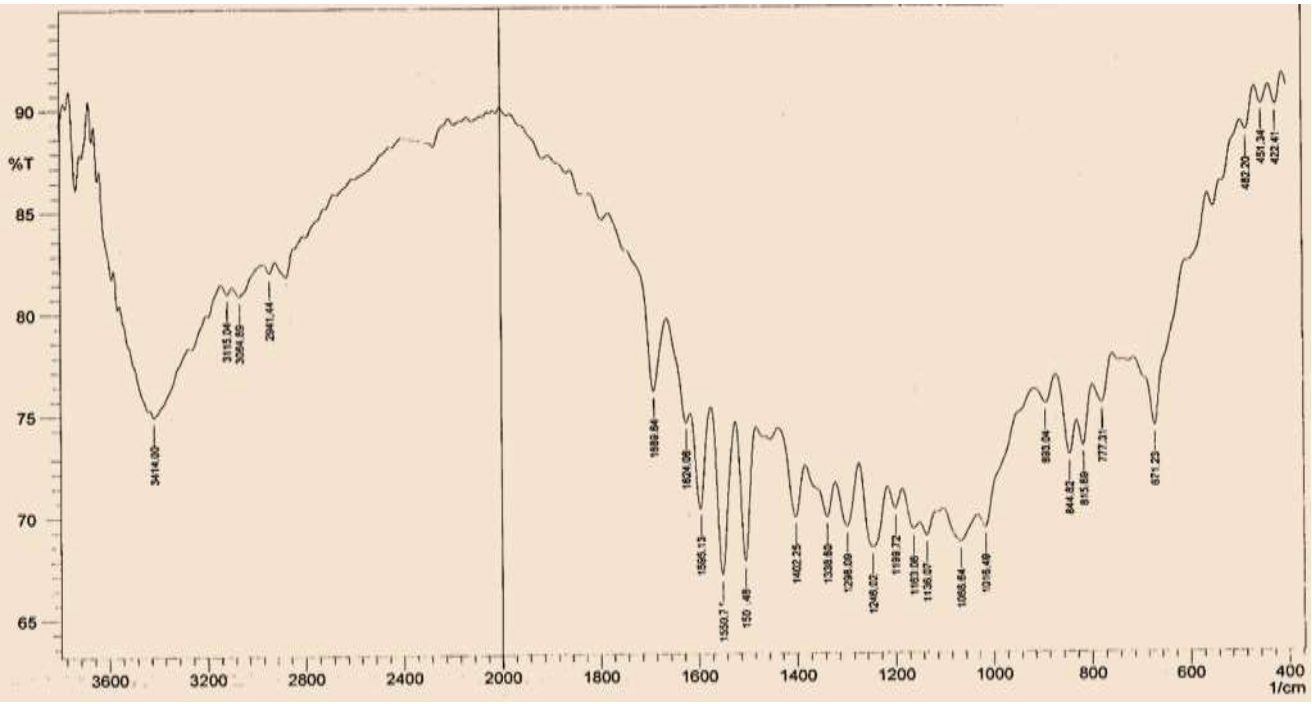



**Fig .(2) : FT.IR of Ligand [ 4 ].**

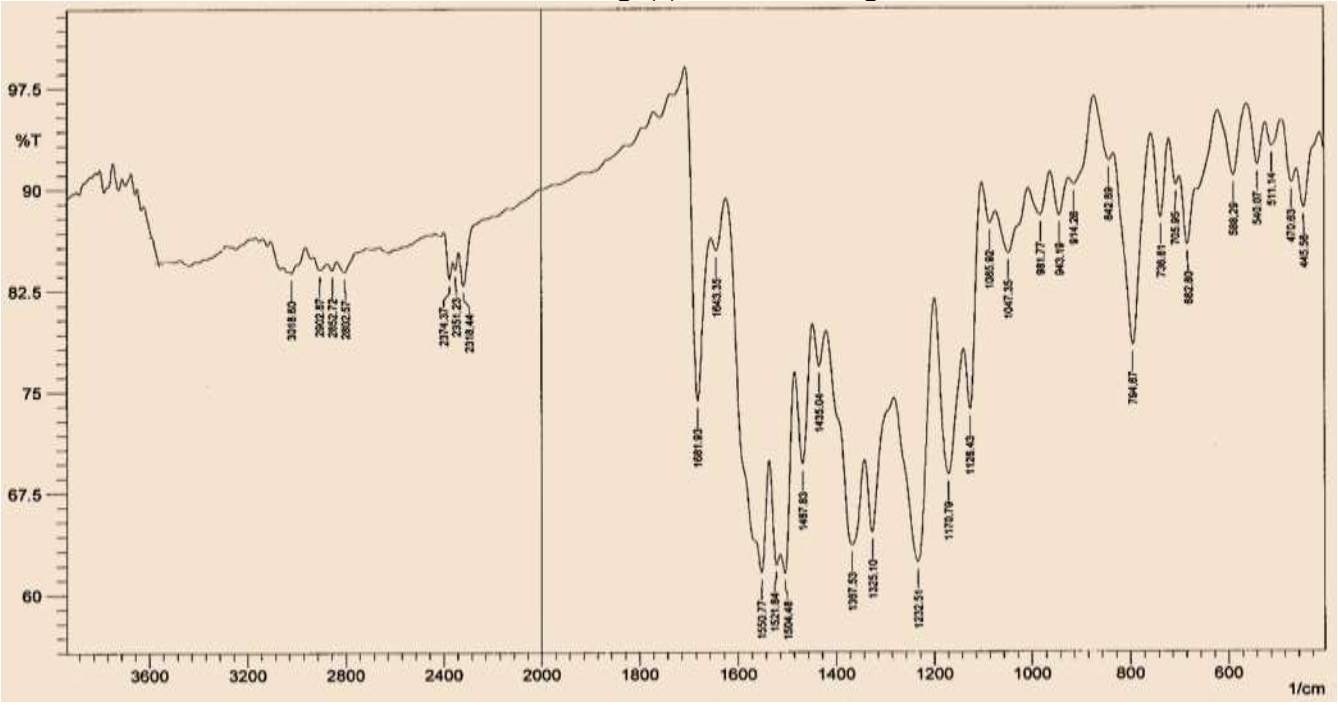



**Fig .(3) : FT.IR of Ligand [ 5 ].**

**Identification by $^{1}$H.NMR** : Which gave many signals at ϭ DMSO-d6(solvent ): 2.50 ., (OH) Proton of Phenol: 10.66 .,Protons of Aromatic ring : (6.70 -7.99) ,(-$CH_2$ =$CH_2$-) proton of Alkene : (6.14 , 6.33) ., (CH=N)Proton of Imine : 8.92 in ligand (1 ) ,but ligand (2) gave peaks at (OH) Proton of Phenol: 10.52 .,Protons of Aromatic ring : (6.91 -7.63) ,(-$CH_2$ =$CH_2$-) proton of Alkene : (6.09 , 6.22) ., (CH=N)Proton of Imine : 8.36 ., ligand(3) appeared peak at (OH) Proton of Phenol: 10.73 .,Protons of Aromatic ring : (6.85 - 7.91) ,(-$CH_2$ =$CH_2$-) proton of Alkene : (6.07 , 6.13) ., (CH=N)Proton of Imine : 8.77 ., (CO-$CH_3$)Ketone: 2.38 ,while ligand ( 4 )showed signals at Protons of (OH) Proton of Phenol: 10.34 .,Protons of Aromatic ring : (6.72 -7.97) ,(-$CH_2$ =$CH_2$-) proton of Alkene : (6.05 , 6.16) .,(CH=N)Proton of Imine : 8.95 ., While ligand (5) showed signals Protons of Aromatic ring : (6.96 -7.89) ,(-$CH_2$ =$CH_2$-) proton of Alkene : (6.00 , 6.10) .,

(CH=N)Proton of Imine : 8.45 ., and other signals in table (2) .

**Table (2): H.NMR-data (δ - ppm) of Ligands (1-5)**

| Comp | Other groups |
|---|---|
| **( 1 )** | DMSO-d6(solvent ): 2.50 ., (OH) Proton of Phenol: 10.66 .,Protons of Aromatic ring : (6.70 - 7.99) ,(-$CH_2$ =$CH_2$-) proton of Alkene : (6.14 , 6.33) ., (CH=N)Proton of Imine : 8.92 . |
| **( 2 )** | DMSO-d6(solvent ): 2.50 ., (OH) Proton of Phenol: 10.52 .,Protons of Aromatic ring : (6.91 - 7.63) ,(-$CH_2$ =$CH_2$-) proton of Alkene : (6.09 , 6.22) ., (CH=N)Proton of Imine : 8.36 . |
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| **( 4 )** | DMSO-d6(solvent ): 2.50 ., (OH) Proton of Phenol: 10.34 .,Protons of Aromatic ring : (6.72 - 7.97) ,(-$CH_2$ =$CH_2$-) proton of Alkene : (6.05 , 6.16) ., (CH=N)Proton of Imine : 8.95 . |
| **( 5 )** | DMSO-d6(solvent ): 2.50 .,Protons of Aromatic ring : (6.96 -7.89) , (-$CH_2$ =$CH_2$-) proton of Alkene : (6.00 , 6.10) ., (CH=N)Proton of Imine : 8.45 . |

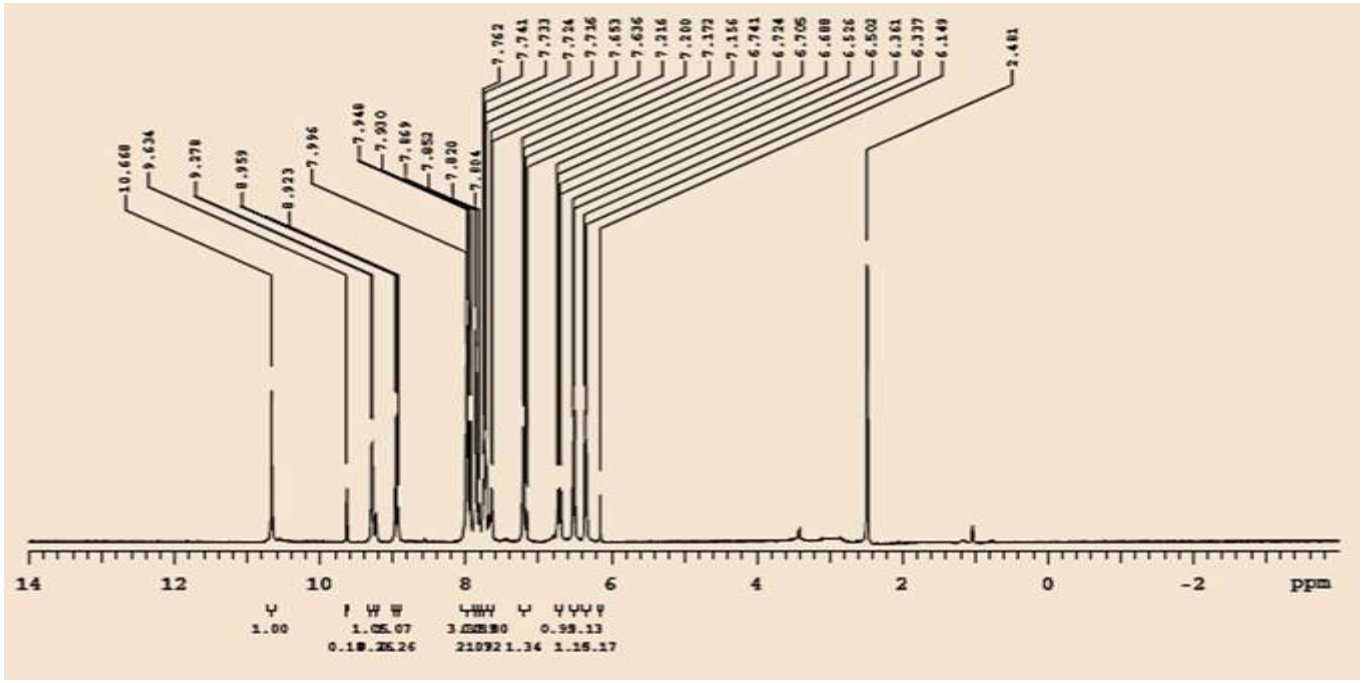



**Fig. (4): H.NMR of Ligand [ 2 ]**

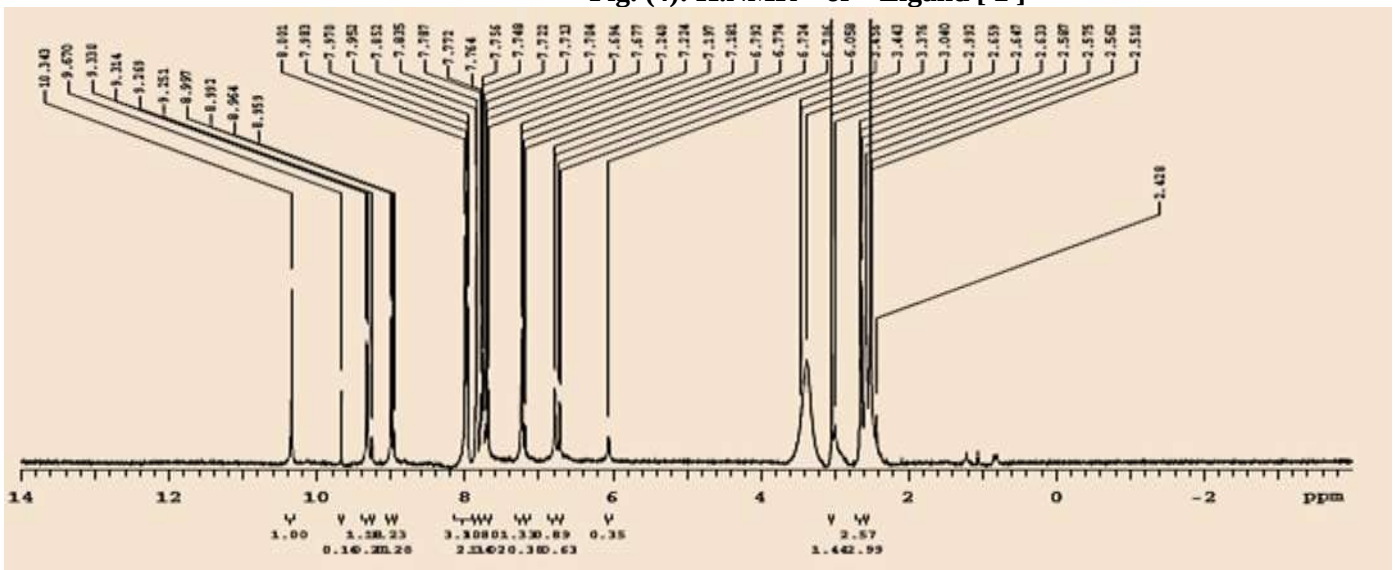



**Fig. (5): H.NMR of Ligand [ 4 ]**

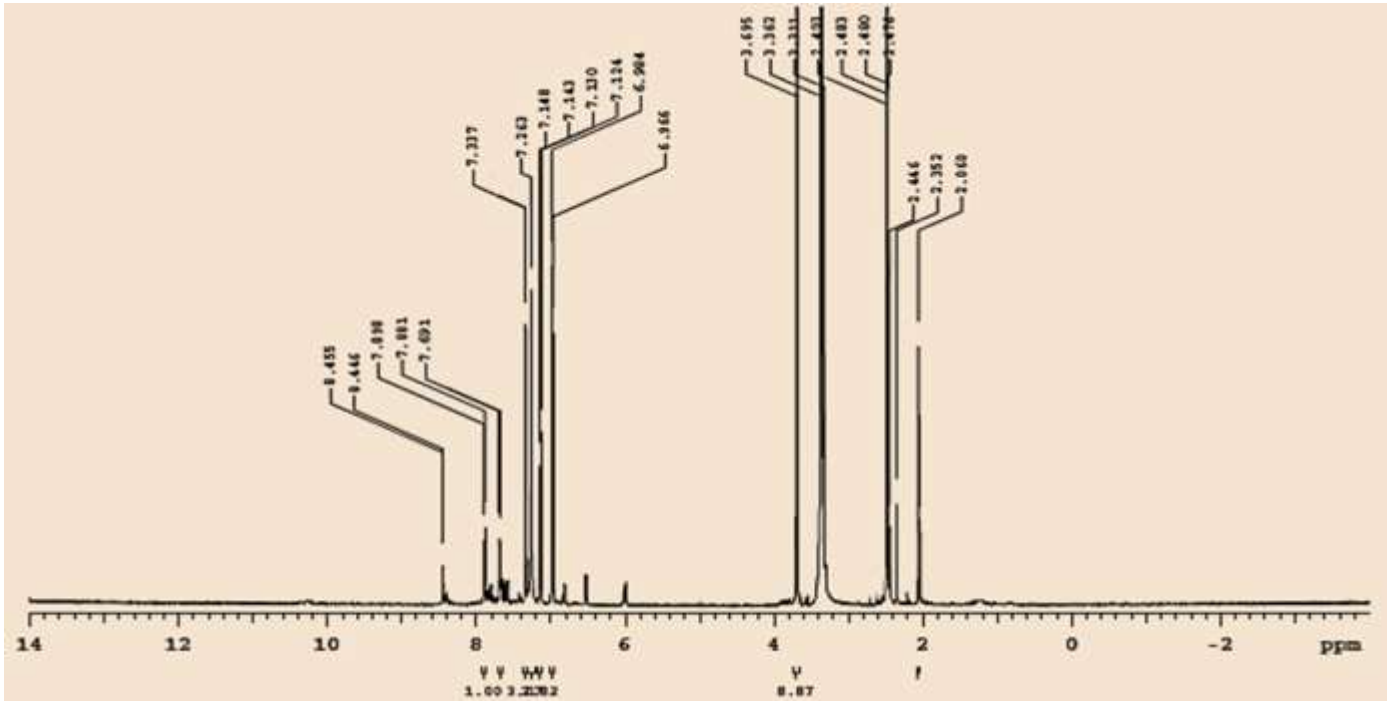
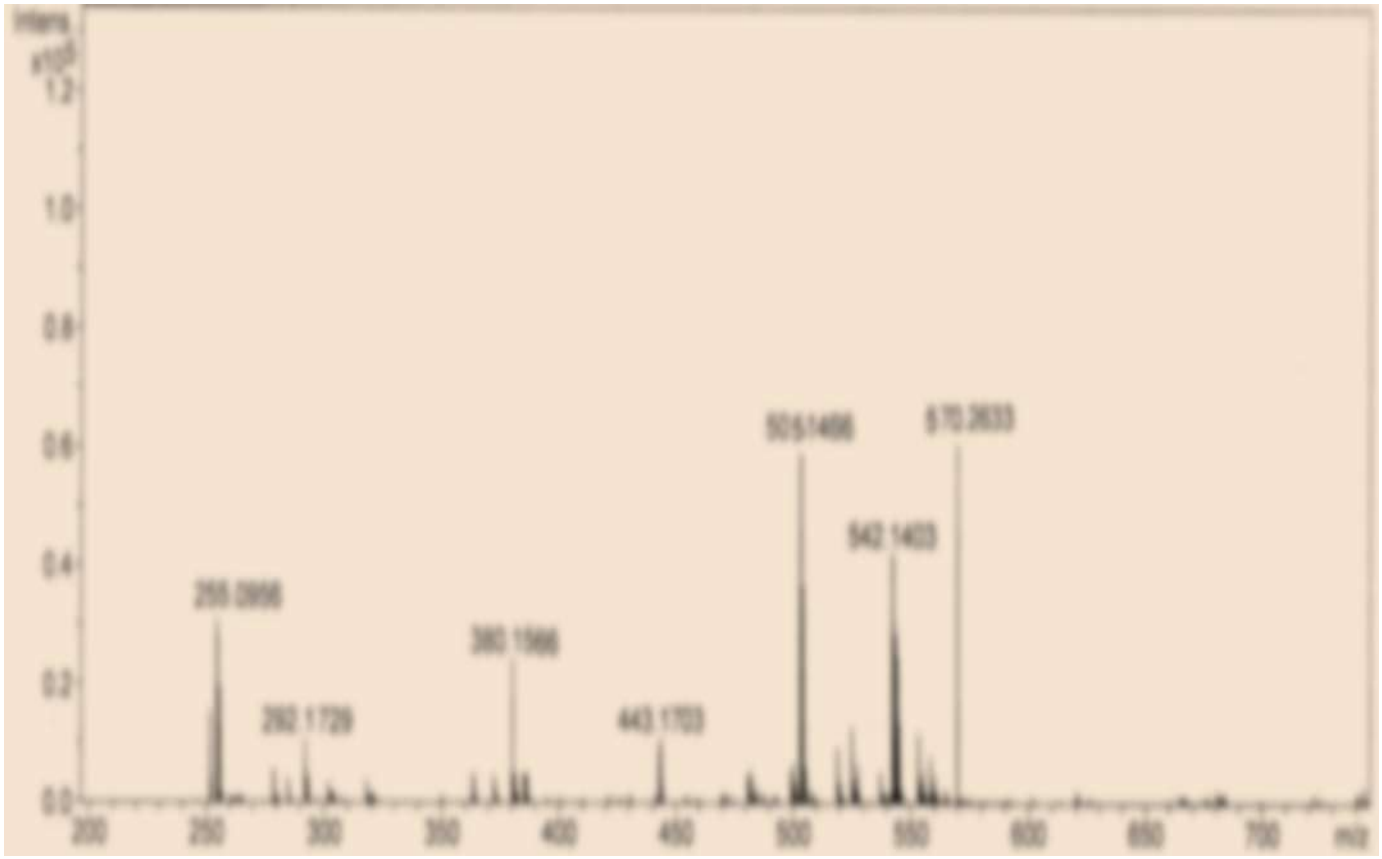
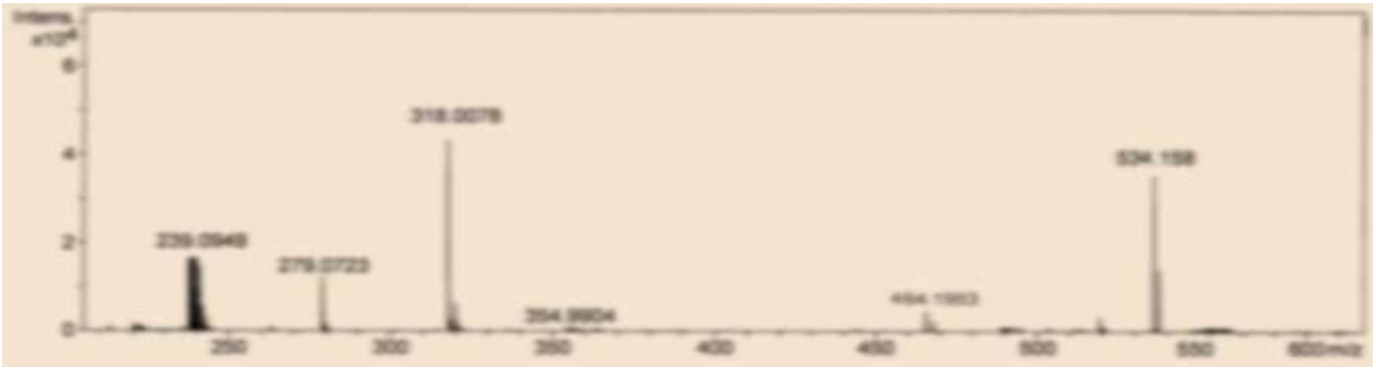



**Fig. (6): H.NMR of Ligand [ 5]**

**Studying of Mass Spectroscopy :**It appeared good indicator about structures of or new ligands by showing figures(7 - 9 ):




**Fig(7): Mass Spectrum of Ligand (3)**



**Fig(8): Mass Spectrum of Ligand (4)**

**Thermo - Measurements :**

All thermal curves appeared high stability at varouse temeratures because of their structure (( schiff – Azo ) with thiadazole ring .Thier results in figures (9 , 10 )

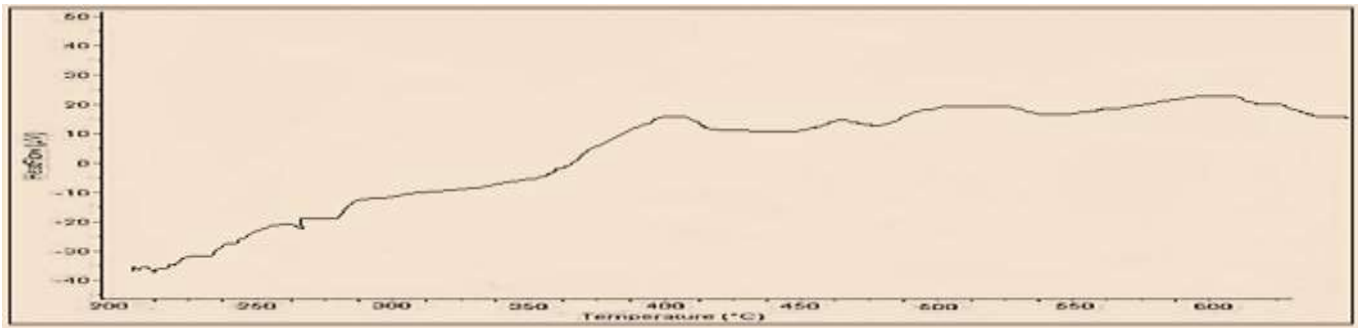



**Fig .(9) :Thermal Analysis of Ligand [ 3 ]**

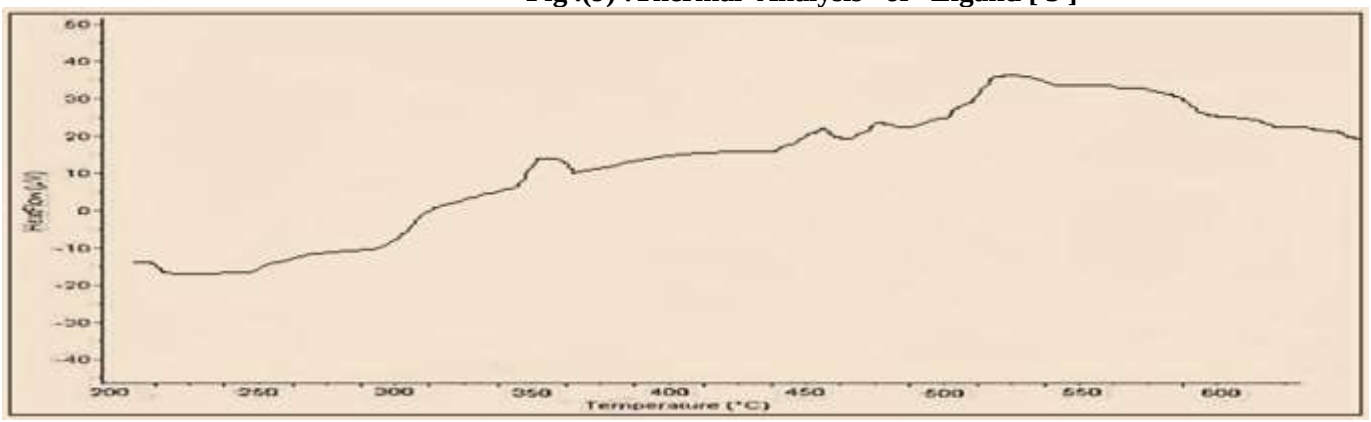



**Fig .(10) :Thermal Analysis of Ligand [ 4 ]**

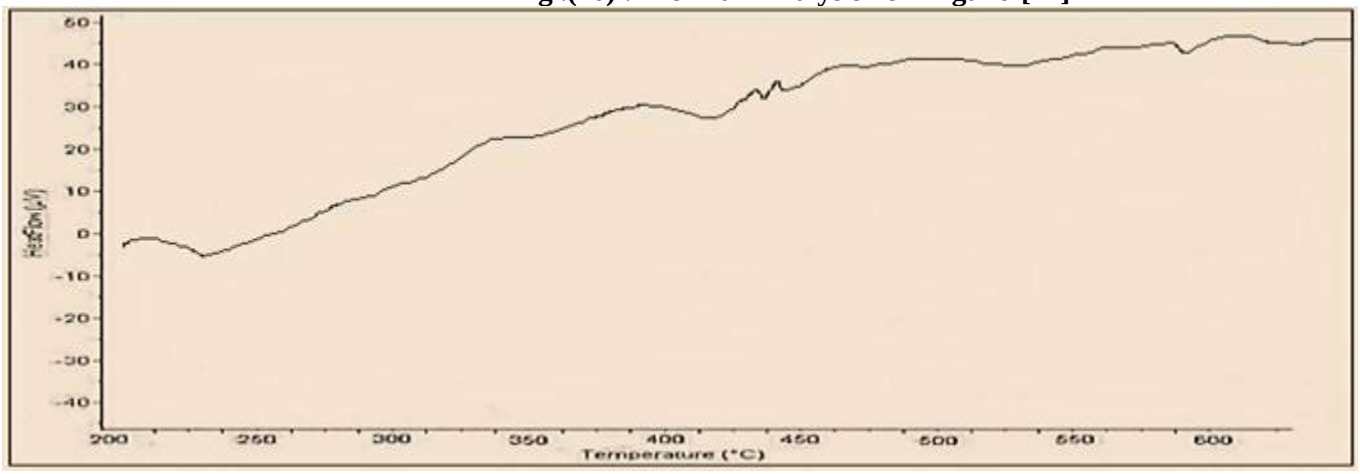



**Fig .(11) :Thermal Analysis of Ligand [ 5 ]**

**Behavior of Compounds on Bacteria :**

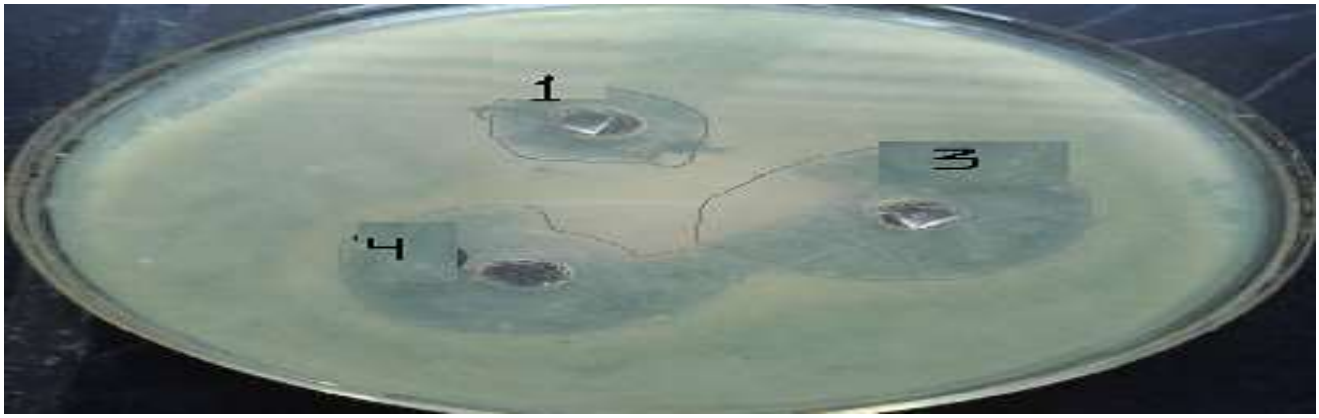
Schiff- Azo ligands [1- 5 ] tested against types of bacteria are showed in table (3 ). The presence of functional groups like: (Schiff- azo) increase antibacterial effect of our compounds against bacteria through using agar biological method[16] . Assay of activities were done at Three concentrations (($1x\ 10^{-2}$ , $1x\ 10^{-3}$ ,$1x10^{-4}$)M ) in (DMSO) - solvent with types of bacteria ((*Streptococcus Salivarius* ,*E- Coli* )) which incubated for 48 hrs at $37^{o}C$ .

Results of antimicrobial studying are abstracted in table (3) at optimal concentration at (**$1x\ 10^{-3}$ M** ) from three concentrations . From results of antibacterial studies we found to be potentially activity against towards two types of bacteria ,which gave good inhibition from the results that the biological activity of all compounds have high biological activity which inhibit the growth of bacteria .

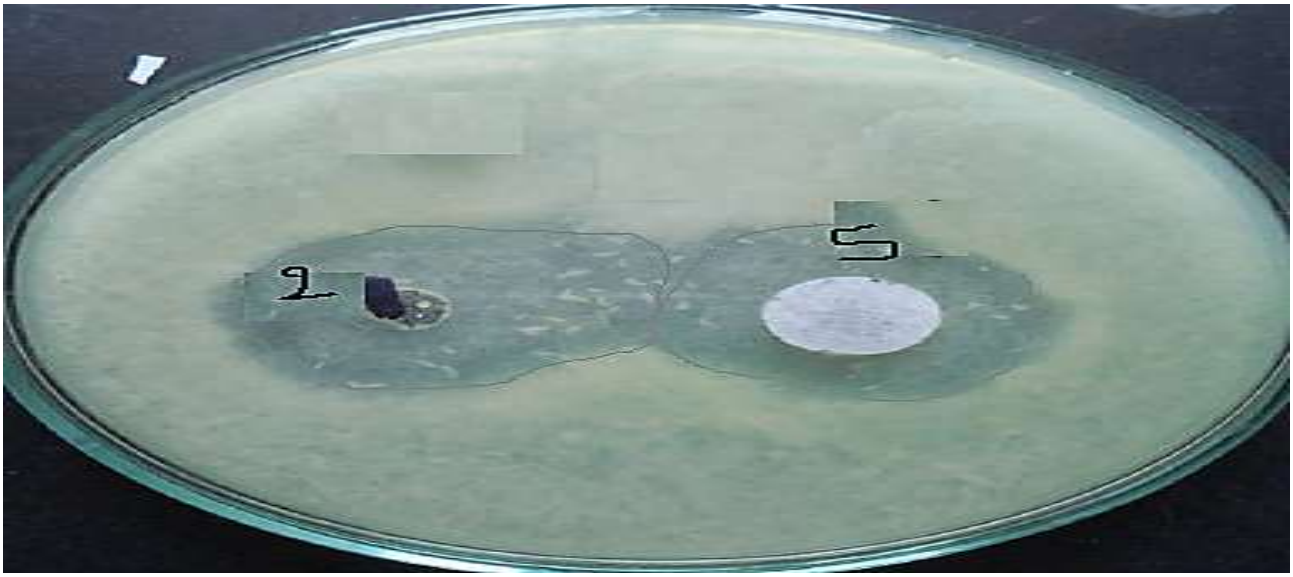
Our compounds [ 3, 4 , 2] have higher activity than other compounds [ 1 , 5 ] which due to presence of (Schiff - azo) in their structures[18-20] ,the mechanism of action for new compounds involved inhibition of growth in bacteria.

**Table(3):Antibacterial Activity of ligands (Inhibition Zone in (mm))as average of ($1x\ 10^{-3}$ ) M**

| Ligands | (average of three Measurements) *Streptococcus Salivarius* | (average of three Measurements) *E- Coli* |
|---|---|---|
| **[ 1 ]** | 6 | 4< |
| **[ 2 ]** | 6 | 4 |
| **[ 3 ]** | 12 | 8 |
| **[ 4 ]** | 12 | 6 |
| **[ 5 ]** | 10 | 6 |




**Picture.(2):The inhibition of Compounds(3, 4 , 1) on *Streptococcus Salivarius***




**Picture. (3):The inhibition of the Compound(2, 5) on *Streptococcus Salivarius***

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