Synthesis ,characterization and investigation of biological activity of new heterocyclic compounds
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Abstract

A new compounds of 2-amino-5-(m-nitro phenyl)-1,3,4-oxadiazole [1] and 2-amino-5-phenyl-1,3,4-oxadiazole[2], N[(o-hydroxy benzylidene-5-( phenyl-2-y1)-1,3,4-oxadiazole-2-amine][3] or N[(m-nitro benzylidene-5-(m-nitro phenyl-2-y1)-1,3,4-oxazpine][4], 2-(m-nitro phenyl) -3(5-m-nitrophenyl)-1,3,4-oxadiazole]2-yl-thiazolidin-4-one [5], 2-(m-nitro phenyl) -tetrazolo-1-y1)- 5-(m-nitrophenyl)1,3,4-oxadiazole ] [6], 5-(m-nitro phenyl)-2'(m-nitrophenyl)]-2-yl-2,3-dihydro-1,3-oxazine-4,7-dione [7], 4-hydradino nicotinic acid [8], 1-phenyl-4-(nicotinoyl) thiosemicarbazide [9], and 3-hydrazino-5-(pyridyl )-1,2,4- Triazole-4-phenyl [11], 3(p-N,N' dimethyl amino benzylidene)- hydrazino -5-(pyridyl )-1,2,4- Triazole-4-phenyl [12], 4-(3-methyl pyrazol-5-one)- hydrazino -5-(pyridyl )-1,2,4- Triazole-4-phenyl [13], 4-(3,5-dimethyl pyrazol)- hydrazine-5- (pyridyl )-1,2,4- Triazole-4-phenyl [14], ethyl 4-bromo-phenoxyacetate [15], p-bromo pheno-aceto thiosemicabazone [16] ,2- amino-5-(p-brom phenoxymethylene)-1,3,4-thiadiazole [17], 2N( p-nitro benzylidene)-1,3,4-Thiadiazole -5- (p-bromo phenoxy methyl [18]), 5 -(p-bromo phenoxy methyl) 2'-(p-nitro phenyl- 2-y1)-5,6-dimethyl-1,3-oxazine-4,7-dione [19] or5-(p-bromo phenoxy methyl) 3-(p-nitro phenyl- 2-y1)-2,3-dihydro-1,3-oxazine-4,7-dione [20] and imidazoline[21].

The chemical structures of these compounds were identified by FT-IR, H-NMR , Uv spectroscopy and the reaction time ,purity was checked by TLC with determining the melting points. Some of the new compounds were tested against four strains of bacteria ( Klebsiella Pneumoniae ,Pseudomonas aeruginosa ,Staphylococcus Aureus and Bacillus subtilus ) comparing these activities with that of starting material .

Key word: heterocyclic compounds , oxazpine ,imidazoline.
تحضير وتشخيص ودراسة الفعالية الحيوية لمركبات غير هتجانسة الحلقة

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الخلاصة

تتضمن البحث تحضير 2-امينو-5-ميثانيترول فينيل-1,3,4-اوكساسبايزول (1), 2-امينو-5-هيدرازينو-1,3,4-اوكساسبايزول (2), ن-بوزثيدروكسسي-2-أمينو-1,3-اوكساسبايزول (3), ن-بوزثيدروكسسي-2-أمينو-4-أون (4) او 2-ميثانيترول أريل-5-(ميثانيترول ويندلين-5-إيثيل)-1,3,4-اوكساسبايزول (5), 2-ميثانيترول أريل-5-(ميثانيترول ويندلين-5-إيثيل)-1-أون (6), 2-ميثانيترول أريل-5-(ميثانيترول ويندلين-5-إيثيل)-3-أون (7), 3,5-ثنائي هيدرو-1,3,4-اوكساسبايزول (8), 3,5-ثنائي هيدرو-2-أوكساسبايزول (9), 2-أوكساسبايزول (10), 4-هيدرازينو-4-أون (11), 3-(بارابزوييكسً يثٍم) بارابزوييكسً يثٍم (بارابزوييكسً يثٍم)

الفعالية الحيوية لوركبات غير هتجانسة الحلقة.

تم تشخيص التراكيب الكيميائية للمركبات المحضرة بواسطة أطياف الإشعة تحت الحمراء، فوفق البنفسجية واطيفين الرنين النووي المغنطيسي كما تم تحديد زمن التفاعل ونفاوة المركبات بواسطة كراموتوكرافيا الطبقة الرقيقة وتم اختيار الفعالية الحيوية لمركبات ضد اربع انواع من البكتريا.
Introduction
The derivatives of 1,3,4-oxadiazol constitute an important family of heterocyclic compounds (1-5), since many of them display a remarkable biological activity (6). Antifungal (6), analgesic (7), and anti-inflammatory (8) and hypoglycemic activity (9).

A triazolo-thiadiazole system may be viewed as a cyclic analogue of two very important components (10).

Heterocyclic compounds play an important role in biochemical processes (11-15) because the side groups of the most typical and essential constituents of living cells are based on aromatic heterocycles.

Between them, sulfur and nitrogen containing heterocyclic compounds have maintained the interest of researchers through the development of organic synthesis (16).

Oxazepine belongs to non-homologous structures which have 7-homologous atoms (oxygen and nitrogen) (17).

Pyrazole derivatives constitute an important family of compounds due to their applications as pharmaceuticals (analgesics, anti-inflammatory, antibacterial, and antidepressant), agrochemicals (insecticides) and dyestuffs (18-20).

Accordingly, we wish to report herein the synthesis of compound which possesses a chemically important nitrogen heterocyclic nucleus with a view to achieve better antimicrobial activity. Some of the prepared compounds were screened for their in vitro antimicrobial activity against different strains of bacteria.

Experimental part
1- Melting points were measured using hot stage *Gallen Kamp* melting point apparatus and were uncorrected.

2- The FTIR spectra in the range (4000-600) cm\(^{-1}\) were recorded using KBr disk on a *SHIMADZU* F.T.IR 8300 spectrophotometer Japan.

3- UV/vis spectra were recorded on UV/vis varian UV-Cary-100 spectrophotometers in (ISSC).

4- \(^1\)H-NMR spectra were recorded a BRUKER-400 MHz operating at 300 MHz with tetra methyl silane as internal standard in CDCl\(_3\) and DMSO-d\(_6\) as a solvent, measurements were made at Chemistry Department, AL-Baath University-Syria.

5- Elemental Analysis (C.H.N) was carried out with : Euroea Elemental Analyzer Italia by Chemistry Department College of Science, Babylon University.

6- Thin Layer Chromatography (TLC) was carried out using Fertigfollen precoated sheets type PolyGram silg, and the plates were developed with iodine vapor.

7- The biological activity was performed by biology department/college of Science, Tikrit University.
1-Synthesis of 2-amino-5-m-nitro phenyl-1,3,4-oxadiazole [1] and 2-amino-5 phenyl-1,3,4-oxadiazole[2][21].

An equimolar of semicarbazide hydrochloride and benzaldehyde or m-nitro benzaldehyde were dissolved in ethanol in presence of fused sodium acetate. The mixture was refluxed for one hour, then cooled and precipitated by water, filtered to obtain phenyl semicarbazone or m-nitro phenyl semicarbazone. Phenyl semicarbazone or m-nitro phenyl semicarbazone dissolved in glacial acetic acid and fused sodium acetate, bromine (in acetic acid) (0.5ml) was added to this mixture (2g) contained in flat flask. The mixture became warm and rapidly became colorless. This mixture was poured in water, filtered and dried. Re crystallized from mixture of ethanol and acetic acid.

2-Synthesis of Schiff bases N[(m-nitrobenzylidene-5-(m-nitrophenyl-2-yl)-1,3,4-oxadiazole-2-amine][4] or N[(o-hydroxy benzylidene-5-(phenyl-2-yl)-1,3,4-oxadiazole-2-amino][3][22].

A mixture of 2-amino-5-(m-nitro phenyl)1,3,4-oxadiazole [2] or [3] 2-amino-5- phenyl)1,3,4-oxadiazole (0.01mol) and m-nitro benzaldehydes (0.01mol) or o-hydroxy benzaldehyde was refluxed in absolute ethanol (15ml) containing few drops of glacial acetic acid for 3hrs. After cooling to room temperature the precipitate was filtered and dried. The products were re-crystallized from ethanol. Yield 80%,FT IR (cm⁻¹),3100(C-Harm.),2923 and 2868 (C-Haliph.), 1602(C=N).780,720(C-NO₂ m-substituted).

3-Synthesis of 2-m-nitro phenyl)-3- (5-m-nitrophenyl)1,3,4-oxadiazole]-2-yl-thiazolidin-4-one [5][23]:

A (0.01) mole of 2- mercptoacetic acid was added dropwise to (0.01)mole of Schiff base in(20 ml)of dry benzene ,the mixture was refluxed for (24) hours then the solvent was evaporated and the formed precipitate was re crystallized from ethylacetate and benzene,m.p (160) °C,yield (75%).

4-Synthesis of 2-(m-nitro phenyl) –tetrazolo-1-yl)- 5-(m-nitrophenyl )1,3,4-oxadiazole ] [6][24]:

A mixture of (0.01mol) of Schiff bases [4], tetrahydrofuran (THF) (15ml) and sodium azide (0.01mol,0.67gm) was heated on a water bath, the temperature of the water bath was controlled between (50-55)°C. The end of the reaction was checked by (TLC) which showed the disappearance of the starting material.

5- Synthesis of 5-(m-nitro phenyl)-2‘-(m-nitrophenyl)-2-yl-2,3-dihydro-1,3-oxazpine-4,7-dione [7][25].

A mixture of compound [4] (0.01) mole of Schiff base and (0.01 ) mole of maleic anhydride in (20 ml) of benzene was refluxed for (24) hours then the solvent evaporated and the formed precipitate was re crystallized from appropriate solvents ,m.p ( 210) °C,yield (75%).
6- Synthesis of 4-hydrazino nicotinic acid [8]:

A mixture of nicotinamide (0.01 mol) and (99%) (0.32 g, 0.317 ml, 0.01 mol) of hydrazine hydrate was dissolved in ethanol, and the mixture was refluxed for 5 hours, excess solvent was distilled off. The resulting solid was separated out on cooling filtered and re crystallized from ethanol, m.p. (203-205 °C), yield (80%).

7- Synthesis of 1-phenyl-4-nicotinoyl thiosemicarbazide [26] [9]:

A mixture of nicotinic acid hydrazide (0.01mol) and phenyl isothiocyanate (0.01mol, 10ml) in (20 ml) absolute ethanol was refluxed for (7) hours. The solid material obtained on cooling was filtered off, and re crystallized by using ethanol, m.p (200) °C, yield (75%).

8- Synthesis of 5-(pyridyl)-1,2,4-Triazole-4-phenyl -3-thiol [10]:

A stirring mixture of compound [9] (0.01 mol) and (10 ml) of 2N sodium hydroxide solution was refluxed for 4 hours after cooling, the solution was acidified with hydrochloric acid and the precipitate was filtered, the precipitate was re crystallized to give compound [10], m.p (230) °C, yield (68%).

9- Synthesis of 3-hydrazino-5-(pyridyl)-1,2,4-Triazole-4-phenyl [11]:

A mixture of compound [10] (0.01 mol) and (99%) (0.32 g, 0.317ml, 0.01 mol) of hydrazine hydrate was dissolved in ethanol, and the mixture was refluxed for 6 hours, excess solvent was distilled off. The resulting solid then separated out on cooling filtered and re crystallized from ethanol, m.p (207 °C), yield (80%).

10- Synthesis of 3-(p,N,N1 dimethyl amino benzylidene)- hydrazino -5- (pyridyl)-1,2,4-Triazole-4-phenyl [12]:

The same procedure in (2) was used.

11- Synthesis of 4-(3-methyl pyrazol-5-one)- hydrazino -5- (pyridyl)-1,2,4-Triazole-4-phenyl [13].

A mixture of carbohydrazide [5] (0.01 mol) and methyl acetoacetate (0.01 mol) in absolute ethanol was heated under reflux temperature for 5 hours. The reaction mixture cooled and the formed precipitate was filtered off to give the product, m.p 190°C, yield (79%).

12- Synthesis of 4-(3,5-dimethyl pyrazol-5-one)- hydrazine-5-(pyridyl)-1,2,4-Triazole-4-phenyl [14].

A mixture of compound [17] (0.01 mol) and acetylacetone (0.01 mol) in absolute ethanol (15 ml) was heated at reflux temperature for 5 hours. The reaction mixture cooled and the formed precipitate was filtered off to give the product, m.p 200°C, yield (65%).
13- Synthesis of ethyl 4-bromo-phenoxy acetate [15]:

*p*-bromo phenol (0.01mole) was dissolved in absolute ethanol (100ml) with (0.01mol)of (K₂CO₃) and heated in a water bath. The hot solution was cooled. Ethyl chloro acetate (0.01mole ,10ml) was added to the mixture. The addition was performed dropwise with stirring for 1 hr.,the stirring and refluxing continued for 4hrs. The reaction mixture was filtered and evaporated to give a white crystals,which were re crystallized from ethanol to give the ester [15].

Physical properties of the products are listed in Table (1).

14- Synthesis of p-bromo pheno-aceto thiosemicarbazone [16].

A mixture of ethyl p-bromo ethyl phenoxy acetate (0.01mol) and thiosemicabazide (0.01mol) in ethanol (20ml) was refluxed for 3hrs. The reaction mixture was filtered and poured on ice water. The precipitate was filtered and re-crystallized from chloroform petroleum to give white crystals,which were re crystallized from ethanol to give the ester [15]. Physical properties of the products are listed in Table (1).

15-Synthesis of 2- amino-5-[(p-bromo phenoxy methylene)-1,3,4-thiadiazole [17].

A mixture of ethyl p-bromo pheno acetothiosemicarbazone (0.01mole)and (10 ml) phosphorous oxy chloride was refluxed for 5 hrs. The cold reaction mixture was poured on crushed ice and neutralized by adding sodium hydroxide solution. The resulting solid was filtered and re crystallized from chloroform to give a white crystals of amino thiadiazole [17].

16- Synthesis of 2-(p-nitro benzylidene)-1,3,4-Thiadiazole -5-(p-bromo phenoxy methyl [18].

A mixture of compound [17] (0.01mol) and p-nitro benzaldehyde (0.01mol) was refluxed in absolute ethanol (15ml) containing few drops of glacial acetic acid for 3hrs. After cooling to room temperature the precipitate was filtered and dried. The product was re-crystallized from ethanol. Yield 80%.

17 - Synthesis of 5-(p-bromo phenoxy methyl) 2′-(p-nitro phenyl)- 2-yl-5,6-dimethyl-1,3-oxazpine-4,7-dione [19]or 5-(p-bromo phenoxy methyl) 2′-(p-nitro phenyl)- 2-yl-2,3-dihydro-1,3-oxazpine-4,7-dione [20].

A mixture of ( 0.01) mole of Schiff base[18] and (0.01 ) mole of 2,3-dimethyl maleic anhydride or maleic anhydride in (20 ml) of benzene was refluxed for (24) hours then the solvent evaporated and the formed precipitate was re crystallized from appropriate solvents ,m.p (130-132, 157-159) °C,yield (75%).
methyl)-1,3,4-thiadiazol-2-
ylimidazolidine-4-one[21]:

A mixture of Schiff base[18] (0.01) mole and glycine (0.01) mole in (15 ml) of THF was refluxed for (12) hours then cool to room temperature and the formed precipitate was filtrated and re-crystallized from ethanol and THF, m.p (165-168) °C, yield (70%).

Table (1): physical properties of the prepared compounds.

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Molecular formula</th>
<th>Molecular Weight</th>
<th>Yield (%)</th>
<th>M.P (°C)</th>
<th>colour</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C₅H₆N₄O₃</td>
<td>206</td>
<td>68</td>
<td>107-109</td>
<td>Yellow</td>
</tr>
<tr>
<td>2</td>
<td>C₅H₇N₃O</td>
<td>161</td>
<td>82</td>
<td>220</td>
<td>Pale yellow</td>
</tr>
<tr>
<td>3</td>
<td>C₁₅H₃N₅O₅</td>
<td>339</td>
<td>73</td>
<td>85-87</td>
<td>White</td>
</tr>
<tr>
<td>4</td>
<td>C₁₅H₁₁N₂O₂</td>
<td>265</td>
<td>83</td>
<td>146-148</td>
<td>Pale yellow</td>
</tr>
<tr>
<td>5</td>
<td>C₁₉H₁₃N₃O₈</td>
<td>439</td>
<td>75</td>
<td>160</td>
<td>Yellow</td>
</tr>
<tr>
<td>6</td>
<td>C₁₅H₁₆N₆O₅</td>
<td>382</td>
<td>-</td>
<td>-</td>
<td>Brown</td>
</tr>
<tr>
<td>7</td>
<td>C₁₇H₁₁N₅O₆S</td>
<td>413</td>
<td>75</td>
<td>210</td>
<td>White</td>
</tr>
<tr>
<td>11</td>
<td>C₁₃H₁₂N₆</td>
<td>252</td>
<td>80</td>
<td>267</td>
<td>Yellow</td>
</tr>
<tr>
<td>12</td>
<td>C₂₂H₂₁N₇</td>
<td>385</td>
<td>76</td>
<td>200</td>
<td>Yellow</td>
</tr>
<tr>
<td>13</td>
<td>C₁₇H₁₆N₆O</td>
<td>318</td>
<td>79</td>
<td>190</td>
<td>Yellow</td>
</tr>
<tr>
<td>14</td>
<td>C₁₆H₁₆N₆</td>
<td>292</td>
<td>80</td>
<td>230</td>
<td>Yellow</td>
</tr>
<tr>
<td>17</td>
<td>C₉H₈N₃OSBr</td>
<td>289</td>
<td>75</td>
<td>245</td>
<td>White</td>
</tr>
<tr>
<td>18</td>
<td>C₁₆H₁₁N₄O₃SBr</td>
<td>419</td>
<td>87</td>
<td>230</td>
<td>Yellow</td>
</tr>
<tr>
<td>19</td>
<td>C₂₂H₁₇N₃O₆SBr</td>
<td>545</td>
<td>75</td>
<td>130-132</td>
<td>White</td>
</tr>
<tr>
<td>20</td>
<td>C₂₀H₁₅N₃O₆SBr</td>
<td>517</td>
<td>75</td>
<td>157-159</td>
<td>White</td>
</tr>
<tr>
<td>21</td>
<td>C₁₈H₁₂N₃O₄SBr</td>
<td>474</td>
<td>70</td>
<td>165-168</td>
<td>White</td>
</tr>
</tbody>
</table>

Table (2): Re-crystallization solvents and C.H.N analysis for some compounds.

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Re-crystallization solvents</th>
<th>C.H.N.cal./found analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>EtOH</td>
<td>37.76/37.6 2.79/2.7 14.68/13.99</td>
</tr>
<tr>
<td>3</td>
<td>EtOH+AcOH</td>
<td>53.09/53.0 2.65/2.4 20.64/20.33</td>
</tr>
<tr>
<td>6</td>
<td>MeOH</td>
<td>47.12/47.1 2.61/2.4 29.31/29.01</td>
</tr>
<tr>
<td>12</td>
<td>EtOH</td>
<td>68.57/68.33 5.45/5.24 25.45/25.20</td>
</tr>
<tr>
<td>18</td>
<td>EtOH</td>
<td>45.82/45.6 2.62/2.3 13.36/13.21</td>
</tr>
<tr>
<td>19</td>
<td>EtOH</td>
<td>48.44/48.32 3.11/3.0 10.27/10.14</td>
</tr>
</tbody>
</table>

Results and Discussion
The first step in scheme (1) involved the synthesis of phenyl amino oxadiazole and substituted phenyl amino oxadiazole by the reaction of benzaldehyde or substituted benzaldehyde with semicarbazide hydrochloride and bromine in presence of sodium acetate in acetic acid.

These compounds were characterized through the FT-IR, $^1$H-NMR spectra and other physical properties.

The FT-IR spectrum of compound [1], showed the appearance of stretching band of (NH$_2$) group at (3430-3600) cm$^{-1}$ and at (1630) cm$^{-1}$ for (C=N) group. The $^1$H-NMR spectrum of compound [1], fig., (1), showed the peaks at (3.47) ppm due to (CH) group and (7.43-8.54) ppm (m, Ar-H).

Compounds [3] and [4] were prepared from the reaction of compounds [1or2] with m-nitro benzaldehyde or benzaldehyde. The structure of compound [3] was confirmed through the disappearance of absorption bands of (NH$_2$) group at (3430-3600) cm$^{-1}$ and appearance of band sym., and asym., at (1612) cm$^{-1}$ which attributed to (C=N) azomethine group while the $^1$H-NMR spectrum of this compound fig.,(2), showed singlet signal at (2.7) ppm due to (CH) group, singlet signal at (5.0) ppm due to (OH) group and multiplet signals at (7.4-8.2) ppm due to aromatic protons, besides the melting points, colours and T.LC and C.HN analysis.

Thiazolidinone derivative (5) was prepared by the reaction of Schiff base[4] and mercaptoacetic acid in dry benzene, the product was characterized by FT-IR spectroscopy and the melting point, TLC were determined. The FT-IR spectrum of compound (7) showed the appearance of the (C=N) group in 1600 cm$^{-1}$ and the disappearance of (O-H) broad band stretching vibration at 3500-3000 cm$^{-1}$ of mercapto acetic acid.

The suggested mechanism$^{(19)}$ of the reaction is shown in scheme (below):

![Scheme 1, Mechanism steps for the prepared compounds [7,19 and 20].](image-url)
The compound [3] Schiff base was heated in water bath at (55 - 60°C) with sodium azide, to give the desired product [6]. The titled compound was characterized by their melting point, FT-IR table (3), or Uv/vis. spectra and checked by T.L.C also C.H.N analysis.

Scheme 2: Regents and conditions of the preparation of tetrazole.

The mechanism of the reaction systematically investigated as [3+2] cyclo additions which christened as a 1,3-dipolar cycloadditions\(^{28}\). It involved the addition of unsaturated systems, dipolarphiles, to 1,3-dipoles, a molecule possessing resonance contributors in which a positive and negative charge are located in 1,3-position relative to each other. The addition results in a five-member ring. Azides are a prominent class of 1,3-dipoles and azide 1,3-dipolar cycloadditions. They are of great synthetic value and have been studied mechanistically in great detail\(^{12}\). The common features of this type of reactions is best accommodated by a T.S. geometry in which the dipolarphile and its ligands lies in one plane, and the azide lies in a parallel plane above or below, so that the orbitals perpendicular to the planes interact to form bonds, scheme below.
Scheme 3: Approximate transition state geometry for azide addition.

(1612 cm\(^{-1}\)), attributed to (C=N) (imine group) stretching frequency is good evidence for the success of this step of reaction. It also, the FT-IR spectra for these compounds were devoid of a strong band at (2120–2160)cm\(^{-1}\) attributed stretching frequency of a zide group. A band at (1531 cm\(^{-1}\)) was due to the cyclic (N=N) stretching of tetrazole ring. The characteristic data are reported in Table (3).

The FT-IR spectrum of compound [7] was confirmed from the appearance of carbonyl group band at (1720 cm\(^{-1}\)) and (C-H)aliphatic band at (2924-2854)cm\(^{-1}\),besides the (C=N) band of oxadiazole ring at (1610cm\(^{-1}\)) and bands at (1239 and 1118cm\(^{-1}\)) belong to the asymmetric and symmetric (C-O-C) band. All the spectral data for other compounds are listed in table (3).

The FT-IR absorption bands, was utilized to characterize the specific structure of the synthesized compounds. The disappearance of band at The compound [1,3]oxazepine-4,7-dione [7] was synthesized from the reaction of compound [1] with maleic anhydride in dry benzene\(^{17,18}\). This compound was characterized by its melting point,colour,and FT-IR,Uv/vis spectroscopy table (3), and checked by T.L.C.

The FTIR spectrum for hydrazide derivatives (4-hydrrazino nicotinic acid) [8] show the appearance of the characteristic absorption bands in the regions (3332-3276) cm\(^{-1}\) due to asymmetric and symmetric stretching vibration of the (NH-NH\(_2\)) group, while a new band appeared at (1677) cm\(^{-1}\) and (1620) cm\(^{-1}\) due to the stretching vibration of amide I and appearance of amide II bending vibration band at (1523) and (1510) cm\(^{-1}\) respectively.

The triazole [10] was characterized using FT-IR spectrum which showed the disappearance of band of carbonyl at the region (1677) cm\(^{-1}\)due to amide II bending
and the appearance of bands in the region (1643-1612) cm\(^{-1}\) due to stretching vibration of (C=N) group, a band appeared in the region (2534) cm\(^{-1}\) due to \(\nu(C=S)\) stretching vibration. The analytical and spectral data are in accordance with the structures assigned.

Treatment of 3-mercapto-4-phenyl-5-pyridyl-1,2,4-Triazole with hydrazine hydrate in ethanol afford 3-hydrazino-4-phenyl-5-pyridyl-1,2,4-Triazol [11]. The structure of the hydrazine-phenyl-5-pyridyl-1,2,4-Triazol was confirmed from its melting point, colour and FT-IR spectrum.

The F.T.IR spectrum of compound [11] indicates the disappearance of the thiol bond at (2534 cm\(^{-1}\)) and appearance of doublet bands of NH\(_2\) group asymmetric and symmetric at (3313, 3201 and \(\nu\) NH stretching band at 3128 cm\(^{-1}\)).

The title compound [12] was synthesized from the reaction between compound [11] and \(p\)-N,N\(^6\)-dimethyl amino aldehyde in absolute ethanol and glacial acetic acid.

This compound [12] was characterized by the melting point, its colour and FT-IR spectrum. The FT-IR spectrum, shows the disappearance of the two absorption bands due to (-NH\(_2\)) stretching of hydrazino triazole [11], showed all the suggested bonds for (C=C) aromatic, endocyclic (C=N) and exocyclic imine group.

Stretching vibrations in addition to out of plane bending of substituted aromatic ring. All the spectral data for other compounds are listed in table (3). The pyrazol derivatives [13,14] were prepared through the reaction of hydrazine derivatives [11] with acetyl acetone or methyl aceto acetate.

The FTIR spectrum of compound [13] shows the disappearance of NH\(_2\) and NH bands in the region (3332-3276) cm\(^{-1}\) and appearance of (OH) band at (3200) cm\(^{-1}\) of enol form and C=O band at (1740) cm\(^{-1}\) and (1720) cm\(^{-1}\) respectively of the keto form.

From the above mentioned facts, we can indicate compound [13] can exist in equilibrium between keto [I] and enol [II] forms:

Reagents: i-CH\(_3\)COCH\(_2\)COCH\(_3\), abs. EtOH, reflux (5) hrs.
The \( p \)-bromo phenol was treated with ethyl chloroacetate in presence of potassium carbonate in absolute ethanol to give the ester \([15]\).

The structure of compound \([15]\) was confirmed by physical properties which are listed in table (2). FT-IR spectrum shows the band at 1720 cm\(^{-1}\) for (C=O) of ester, 2920 cm\(^{-1}\) for (C-H) aliphatic and disappearance of (O-H) absorption band.

For the product \([16]\), FT-IR spectrum showed absorption band at \(3460\) cm\(^{-1}\) for (\(-\text{NH}_2\)) group which overlap with absorption of (\(-\text{NH}\)) group, and aband appeared at \(1662\) cm\(^{-1}\) for (C=O)amid group. The band appeared at \(1161\) cm\(^{-1}\) due to (C=S) weak band while the \(1\)H-\(NMR\) spectrum fig., (3), of compound (16) \(\delta_{ppm}\) showed the peak at \(2.5(s, 2H, -CH_2); 6.9-7.4(m,4H, Ar-H)\) and at \(4.34(s,2H,NH)\).

The thiosemecarbazone derivative was refluxed with POCl\(_3\) to give thiadiazole \([17]\). The FT-IR spectrum of this compound showed the band at \(3600-3200\) cm\(^{-1}\) broad for (\(-\text{NH}_2\)) ; at \(1631\) cm\(^{-1}\) for (C=N) and the \(1\)H-\(NMR\) spectrum fig., (4), of this product \(\delta_{ppm}\) sho

The FT-IR spectrum of compound \([19]\) as example was confirmed from the appearance of carbonyl group band at \(1710\) cm\(^{-1}\) and (C-H) aromatic band at \(3090\) cm\(^{-1}\) and (C-H) aliphatic band at \(2850\) cm\(^{-1}\) and bands at \(1273\) and \(1080\) cm\(^{-1}\) belong to asymmetric and symmetric (C-O-C) band. All the spectral data for other compounds are listed in table (3) while the \(1\)H-\(NMR\) spectrum for compound (19), fig.,(6 ) exhibited the peaks \(\delta_{ppm}\) at \(2.12(s,3H,CH_3)\) ,at \(5.4(s,2H,CH_2)\) and at \(7.2(s,1H,CH)\) also at \(6.9-7.4(m,8H,2Ar-H)\).

Imidazolidine derivative \([21]\) was prepared by the heating of Schiff base derivative with glycine (\(\alpha\)-amino acetic acid )in THF ,the product was identified by the FT-IR spectrum which shows the appearance of NH
vibration in $3320 \text{ cm}^{-1}$ and the disappearance of $C=N$ band in $1600 \text{ cm}^{-1}$.

**Table (3): FT-IR and UV/Vis spectral data for compounds.**

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>UV,$\lambda_{\text{max}}$ (nm),DMSO</th>
<th>$\nu_{\text{as. CH}}$ vs CH$_2$</th>
<th>$\nu$ C-H Ar.</th>
<th>$\nu$ C=O Ar.</th>
<th>$\nu$ C=N</th>
<th>$\nu$ C=O</th>
<th>N-H</th>
<th>Others</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>260</td>
<td>2950, 2880</td>
<td>3080</td>
<td>1569,1480</td>
<td>1630</td>
<td>-</td>
<td>1550,1350,3600</td>
<td>NO$_2$</td>
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<tr>
<td>3</td>
<td>250</td>
<td>2900, 2870</td>
<td>3097</td>
<td>1470</td>
<td>1612</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>269</td>
<td>2924, 2854</td>
<td>3100</td>
<td>1600,1490</td>
<td>1610</td>
<td>1720</td>
<td>3350</td>
<td>C-O-C$_{2}$1118,1327</td>
</tr>
<tr>
<td>6</td>
<td>295</td>
<td>2900, 2870</td>
<td>3092</td>
<td>1590,1480</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>N=N1531</td>
</tr>
<tr>
<td>7</td>
<td>274</td>
<td>2940, 2870</td>
<td>3099</td>
<td>1600,1490</td>
<td>1600</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>269</td>
<td>2960, 2860</td>
<td>3095</td>
<td>1600,1495</td>
<td>-</td>
<td>1677,1620</td>
<td>3332-3276</td>
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</tr>
<tr>
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<td>3100</td>
<td>1598,1485</td>
<td>1643,1612</td>
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<td>-</td>
<td>C=S 2534</td>
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<tr>
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<td>1610</td>
<td>1596</td>
<td>3460</td>
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<td>13</td>
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<td>3090</td>
<td>1500</td>
<td>-</td>
<td>1740,1720</td>
<td>-</td>
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</tr>
<tr>
<td>15</td>
<td>260</td>
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<td>3100</td>
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<td>1720</td>
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<td>16</td>
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<td>2900,2980</td>
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<td>1500</td>
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<tr>
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<td>1710</td>
<td>-</td>
<td>C-O-C 1273,1080</td>
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<td>21</td>
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<td>1560</td>
<td>-</td>
<td>-</td>
<td>3320</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Biological activity**

The biological activity of compounds was determined by measuring the diameter of the empty region around the well (Inhibition zone). The results of preliminary screening tests are listed in table (4).

**Table (4): Antibacterial activities of the synthesized compound**

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Klebsiella Pneumoniae</th>
<th>Pseudomonas aeruginosa</th>
<th>Staphylococcus aureus</th>
<th>Bacillus subtilus</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>++</td>
<td>-</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>8</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>9</td>
<td>-</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>11</td>
<td>++</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Note:
- = No inhibition = inactive
+ = (5-10) mm = slightly active
++ = (11-20) mm = moderately active

The biological activity test showed that compound [3] with free (-NH₂) and (SH) groups having a biological effect more than other compounds.

**Conclusion**

1. For *Klebsiella Pneumoniae* (G⁻), compounds [3,7,11] showed highest activity, while compounds [9] showed no active on this bacteria.
2. For *Pseudomonas aeruginosa* (G⁻), some compounds have no effect on this bacteria because this bacteria is highly resistant to a wide range of antibiotic because of the slim poly saccharides in cell wall which blocked antibiotics from bacteria and also there are genetic factor.
3. For *Staphylococcus aureus* (G⁺), some compounds have moderate effect on this bacteria.
   For *Bacillus subtilus* (G⁺), all compounds have moderate effect except compounds [3,4] has no effect on these bacteria.
References


Fig.(3): H-NMR for compound [16].

Fig.(5): H-NMR for compound [18].
Fig.(1): H-NMR for compound [1].

Fig.(6): H-NMR for compound [19].
Fig.(2): H-NMR for compound [3].

Fig.(4): H-NMR for compound [17].
Scheme 1
Scheme 2
Scheme (3)