Synthesis and Characterization of Some New Heterocyclic Compounds Via Unsaturated Ketone with Evaluating of Their biological Activity

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Abstract

This work includes preparing of some new derivatives of pyrimidine , pyrazole , and isoxazole from the reaction between benzylideneacetophenone (chalcone) (1) and hydrazine derivatives in the presence of sodium acetate and dry acetone to obtain heterocyclic compounds (2-6).

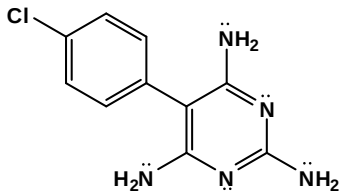
Reaction of (2) with different substituted benzaldehydes in absolute ethanol and drops of glacial acetic acid gave Schiff bases derivatives (8-10) respectively. Schiff bases (8-10) were reacted with sodium azide in THF to give tetrazole derivatives (11-13)**.** Reaction of (2) with sodium nitrate and concentrated hydrochloric acid , then with phenol gave diazo compound (7).

The prepared compounds were diagnosed mediated FT.IR,^{1}H-NMR,UV/Vis spectra, melting points were recorded and the purity was checked through TLC technique. The biological effectiveness were measured for some prepared compounds.

Key wards : Unsaturated ketone, Chalcone, Benzylidenebenzophenone, Heterocyclic compounds, pyrimidine, pyrazole, isoxazole**.**

Introduction

A promising therapeutic efficacy for the management of several diseases is shown in a chemical class which is chalcones[1]. The importance of multi-therapeutic of chalcones includes medical drugs, anti-inflammatory, anti plasmodia, anti tumor, and antioxidant[2].They intervention in the synthesis of flavonoids and isoflavonids[3]. Claisen-Schmidt condensation reaction is main method to synthesis chalcones from aromatic aldehydes and acetophenone [4,5]. Due to the high activity of biological compounds that contain nitrogen structural components of the pharmaceutical and agricultural chemicals such as pyrimidines, pyrazoles, and tetrazoles[6-12]. Of compounds that have biological activity and the importance of medical intervention in the synthesis of nucleic acids and drug zidovudine and HIV medication is pyrimidine [13-15]. Barbiturates Ultra short-acting such as thiophenol sodium "pentothal" are used as hypnotics [16]. Some diaminopyrimidines, such as pyrimethamine are powerful anti malaria drugs [17,18].



Pyrimethamine

Pyrazole derivatives have shown good pharmacological effects they have the potential medical activities, like anti- inflammatory [19], anti- viral [20], anti microbial [21], anti convulsant [22], anti tumor [23], fungicidal activities [24], and anti histamine [25]. The promising structural moiety for drug designing, which are reported to possess anti- bacterial [26], anti convulsant [27], anti psychotic [27], anti-inflammatory [28], anti tumor [29], analgesic [30],insecticidal [31], anti oxidant [32], anti depressant [31,32], and anti microbial activities [32] are isoxazole derivatives. Because of the unique structure and applications as anti hypertensive, anti allergic, anti biotic , and anti convulsant agents [33-37]. Tetrazole and its derivatives have attracted interest.

Experimental

A- Techniques :

1- Uncorrected melting points were measured by digital MP 161 MSRS melting point apparatus

2- The spectra of FTIR were recorded by SHIMADZU FT.IR 8300 spectrophotometer in the range (4000-400) cm^{-1} using KBr disk.
3- The spectra of ^{1}HNMR were \recorded by BRUKER-400 MHz operating at 300 MHz with internal standard "tetramethyl silane" , and DMSO- d^{6} as a solvent in Jordan at Chemistry Department , AL- al-Bayt University, Jordan.
4- UV- Vis. spectra were recorded by SHIMADZU UV spectrophotometer - 1800 using DMSO as solvent.
5- Thin Layer Chromatography (TLC) was carried out using Fertigfollen precoated sheets type polygram silg, and the plates were developed with iodine vapor.
6- The biological activity was performed by environmental laboratory, Baghdad University.

B- Materials :

Chemicals employed were of analytical reagent and used without further purification**.**

C- Methods :

Synthesis of : Benzylideneacetophenone or (*E*) - chalcone (1) [38] .
General Procedure
Chalcones were synthesized by base catalyzed Claisen-Schmidt condensation reaction of acetophenone and aldehyde by known literature method [38,39].

A mixture of benzaldehyde (0.01 mol) and acetophenone (0.01 mol) was dissolved in (10 mL) ethanol in a (100 mL) round-bottomed flask equipped with a magnetic stirrer. Then(10 mL) NaOH solution (1g in 10ml H_2O) was added drop wise to the reaction mixture on vigorous stirring for (30) minutes when solution became turbid. The reaction temperature was maintained between (20-25) ^{0}C using a cold water bath on the magnetic stirrer. After vigorous stirring for (5) hours the reaction mixture was neutralized by (0.1- 0.2N) HCl whereby the precipitation occurred. On filtering off, the crude chalcone were dried in air and re-crystallized by ethanol to obtain pure chalcone , m.p (54-56) ^{0}C, yield (71)%.

Synthesis of : "4,6 - diphenyl -4,5- dihydropyrimidine - 2- amine" (2)., "3,5 - diphenyl - 2,3 - dihydroisoxazole" (3)., "3,5 - diphenyl - 2,3 - dihydro 1*H* - pyrazole" (4)., " 1,3,5 - triphenyl - 2,3 - dihydro - 1H - pyrazole" (5)., " 1- (2,4 - dinitrophenyl) - 3,5 - diphenyl - 2,3 - dihydro - 1*H* - pyrazole" (6) [40,41].

(0.01 mol) of chalcone, hydrazine derivatives, and sodium acetate in (25 mL) of dry acetone were mixed and stirred for (1) hour, then refluxed for (5-6) hours. The reaction mixture was cooled.

A solution of (2%) of sodium bicarbonate then acetone was used to wash the formed precipitate, then filtered and dried. Re-crystallization solvent ethanol , yield (75-83)%.

Synthesis of: " 4-[(4,6- diphenyl - 4,5 - dihydropyrimidine - 2- yl) diazenyl] phenol" (7) [42,43].

Compound (2) (0.005 mol) was added to a mixture of hydrochloric acid and sodium nitrite ($NaNO_2$) in an ice bath with stirring. Then added (0.005 mol) of phenol, dissolved in alkaline medium. For two hours the reaction mixture left to cooling, then acidified with hydrochloric acid whereby a precipitated of color separated out. The filtered crystals were washed by cold water, dried. Re-crystallization solvent ethanol , m.p (263-265) ^{0}C, yield (90)%.

Synthesis of : "N-[4- chlorobenzylidine] -4,6 -diphenyl -4,5- dihydropyrimidine -2- amine" (8) ., "N-[4-(dimethylamino)benzylidine] -4,6 -diphenyl -4,5- dihydropyrimidine -2- amine" (9) .,
N-(4-nitrobenzylidine) -4,6 -diphenyl -4,5- dihydropyrimidine -2-amine" (10) [44-47] ."

The condensation reaction of equimolar quantity of primary amine with the appropriate aromatic aldehydes is the major method to prepare series of Schiff bases.

A mixture of equimolar amounts (0.01 mol) of appropriate substituted aldehydes and pyrimidine - 2- amine derivative (2) in absolute ethyl alcohol (15 mL) with few drops of acetic acid snow was condensed in water bath for (3-4) hours. And then the reaction mixture was allowed to cool at room temperature, the precipitate was filtered, dried and re-crystallized from ethyl alcohol to give a bright crystals, yield (80-86)%

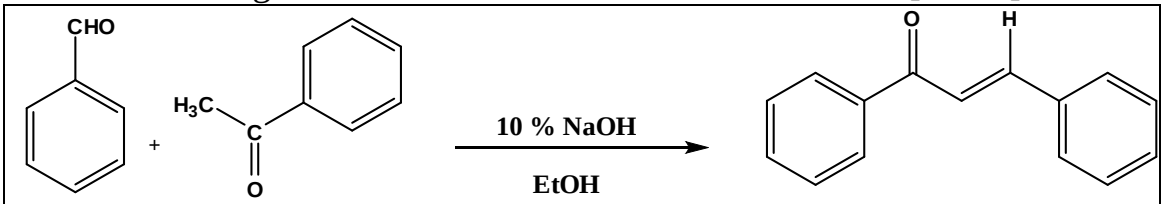
Synthesis of : "2-[5-(4-chlorophenyl) -2,5- dihydro- 1*H* -tetrazole-1 -yl] -4,6- diphenyl -4,5- dihydropyrimidine" (11) ., "4-[1-(4,6-diphenyl-4,5-dihydropyrimidine -2-yl) -2,5-dihydro-1*H*-tetrazole -5-yl] -*N*,*N* -dimethylaniline" (12) ., " 2-[5-(nitrophenyl) -2,5-dihydro-1*H* -tetrazole-1-yl] -4,6-diphenyl-4,5-dihydropyrimidine" (13) [48].

To a stirring solution of Schiff bases (8-10) (0.01 mol) in (10 mL) of tetrahydrofuran , sodium
azide (0.01mol) in (10 mL) of tetrahydrofuran was added drop wise. After the addition ,the mixture was refluxed for (7- 8) hours in water bath at (55-

60) ^{0}C, then cooled at room temperature and the precipitate was filtered , washed with cold water, re-crystallized with benzene petroleum spirit (40-60) ^{0}C., yield (71-77) %

Results and Discussion

The first step in (scheme -1) involved the synthesis of the starting material (trans or *E*- chalcone) by the reaction of benzaldehyde with acetophenone in presence of sodium hydroxide as catalyzed in absolute ethanol according to Claisen-Schmidt condensation reaction[49-54].



benzaldehyde **acetophenone**

trans or (*E*)-chalcone
benzylideneacetophenone
1,3-diaryl-2-propen-1one
phenyl styryl ketone

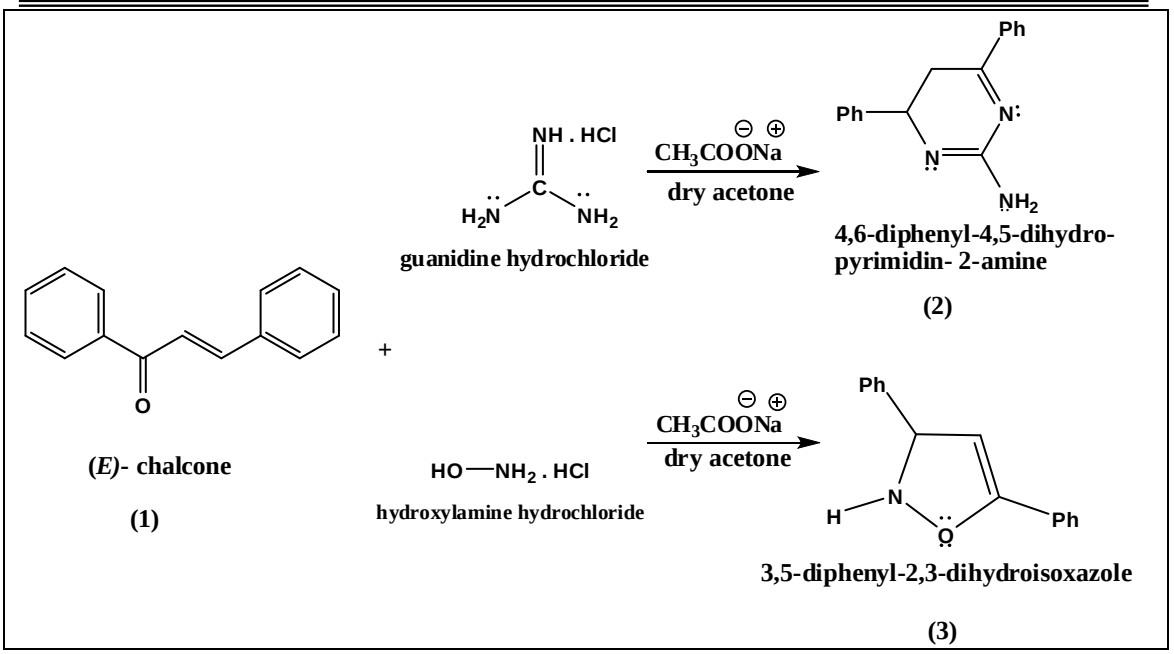
(1)

Scheme - 1

Chalcone or *N*- benzylideneacetophenone was characterized through the FT.IR spectra and other physical properties (table -2).

The spectrum FT.IR of starting material (1) explain the appearance of stretching band of (C=O) group at (1664) cm^{-1} ,also, at (1576) cm^{-1} for (C=C) group (fig.1) [55].

Compounds (2) and (3) were prepared from the reaction of N-benzylideneacetophenone (1) with hydrazine derivatives "guanidine hydrochloride, and hydroxylamine hydrochloride" in presence of sodium acetate in dry acetone (scheme -2).



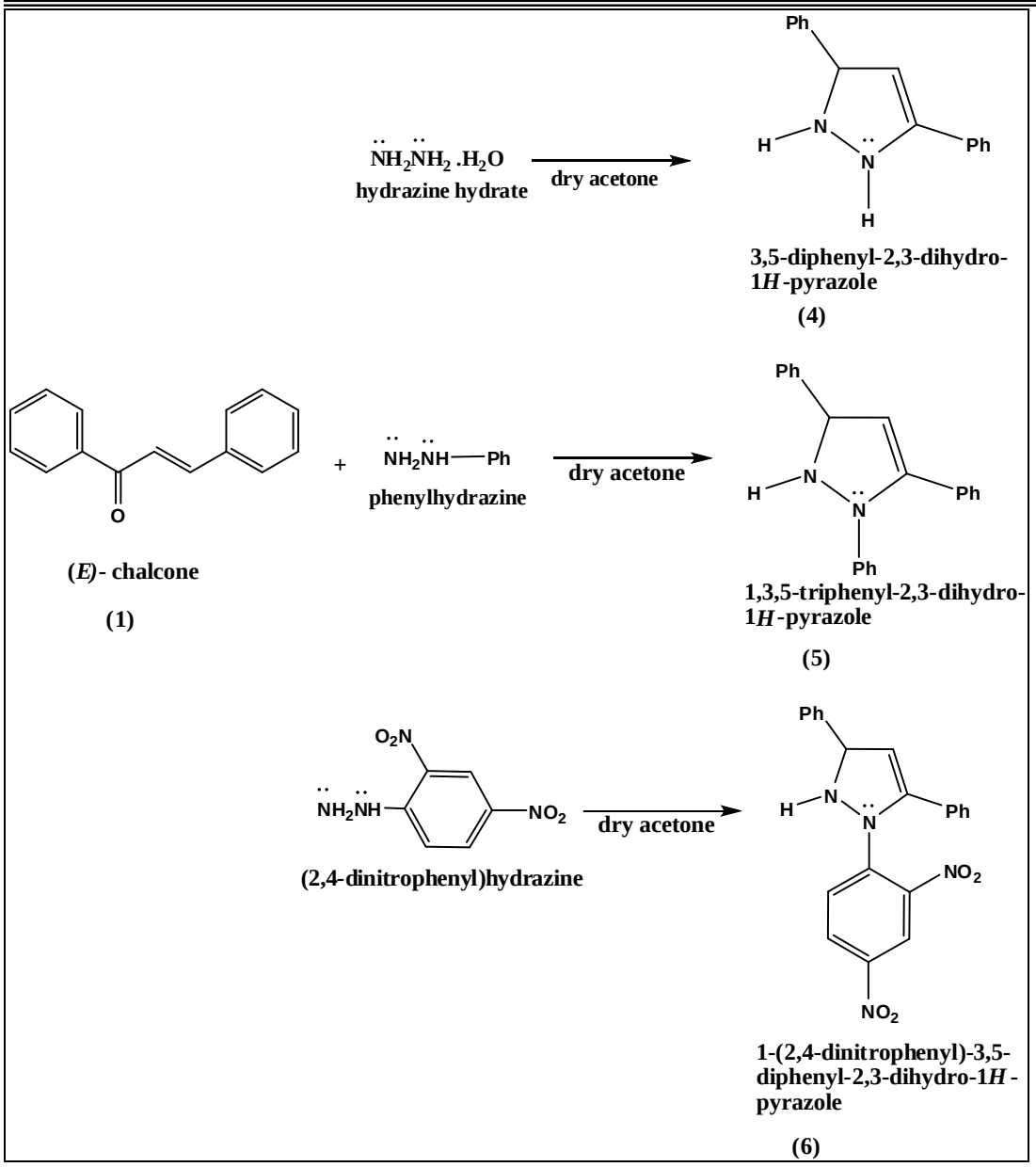
Scheme - 2

The products were characterized by FT.IR spectroscopy and the melting points , TLC were determined.

The reaction mechanisms includes nucleophilic addition on β- carbone in chalcone according to Michael addition reaction , then cyclization reaction, and condensation reaction to form the heterocyclic compounds [56].

The structure of compounds (2) and (3) were confirmed through the disappearance of absorption bands of (C=O) group at (1664) cm^{-1} , (C=C) at (1576) cm^{-1} , and appearance of bands asym., and sym., at (3420, 3312) cm^{-1} which attributed to (NH_2) group , (C=N) at (1685) cm^{-1} in pyrimidine ring , and absorption bands of (N-H) at (3327) cm^{-1},(N-O) at (1465.6) cm^{-1} in isoxazole ring (table -3),(figs. 2 and 3)., While the ^{1}HNMR spectrum of compound (2) showed singlet signal at δ (4.39) ppm due to (NH_2) group protons, δ (1.359 and 2.505) ppm due to methylene group (CH_2) protons, δ (3.924) ppm due to methine group (CH) proton, and signals at δ (7.272-8.025) ppm due to aromatic protons, (fig.14) [57]. The physical properties of these compounds are shown in (table -2).

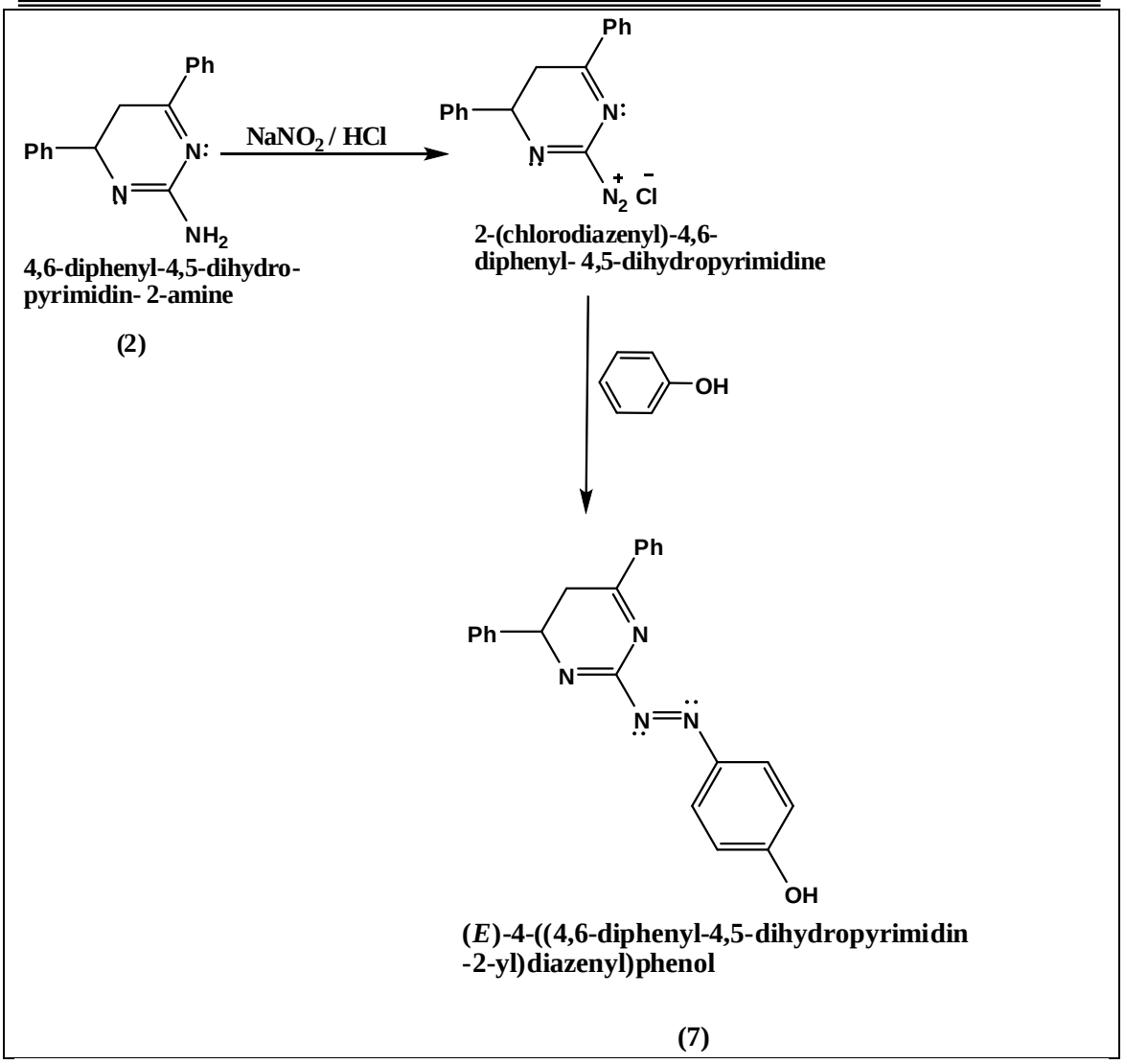
Compounds (4), (5) and (6) were prepared from the reaction of N-benzylideneacetophenone (1) with hydrazine hydrate (90 %), phenyl hydrazine, and 2,4- dinitrophenylhydrazine in dry acetone (scheme -3).



Scheme - 3

The products were characterized by spectroscopy of FT.IR , and the melting points , TLC were determined. The spectra of FT.IR for compounds (4,5, and 6) showed the emergence of a distinctive absorption bands in the region(3374 -3355)cm^{-1} refers to vibration of the (N-H) group (table-3) (figs. 4,5, and 6) [57]., And (table 2) show the physical properties of these compounds.

Compound (7) was prepared from the diazotization reaction of the amine **:** 4,6 - diphenyl-4,5 - dihydropyrimidine-2- amine (2) with sodium nitrate and concentrated hydrochloric acid then coupling reaction with phenol (scheme -4).



4,6-diphenyl-4,5-dihydro-pyrimidin- 2-amine

(2)

2-(chlorodiazenyl)-4,6-diphenyl- 4,5-dihydropyrimidine

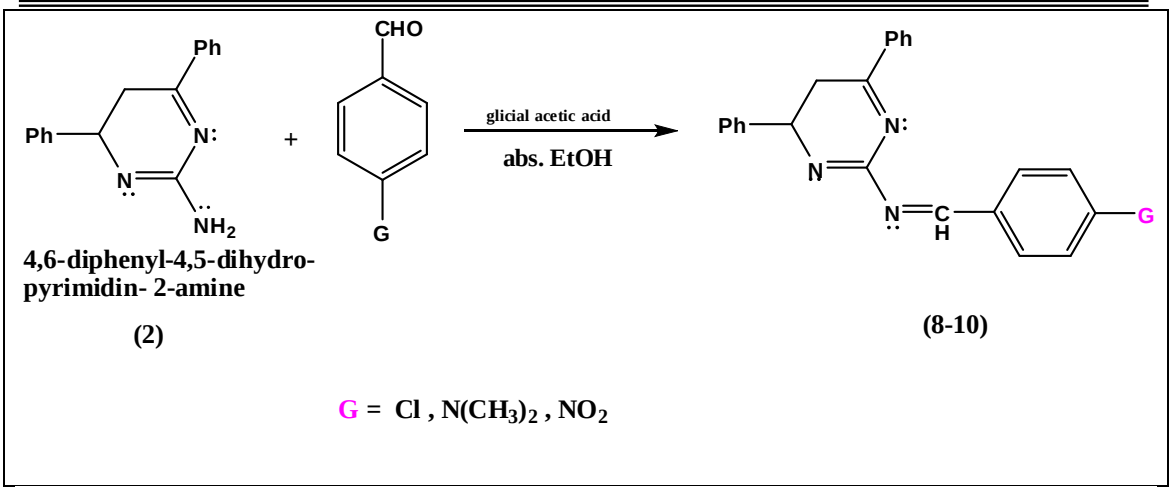
(*E*)-4-((4,6-diphenyl-4,5-dihydropyrimidin -2-yl)diazenyl)phenol

(7)

Scheme - 4

The spectrum FT.IR of compound (7) Showed the emergence of a distinctive absorption in the region packs (3324) cm^{-1} refers to the absorption packages of the (OH) phenolic group , and (1567) cm^{-1} refers to the absorption packages of the trans azo (N=N) group., the disappearance
of absorption packages at (3420, and 3312) cm^{-1} due to the stretching vibration of (NH_2) group of amine (table -4) (fig.7) [58]. The (table-2) show physical properties of these compounds.

Compounds (8-10) were prepared from the reaction of compound (2) with para substituted benzaldehydes (scheme -5).



4,6-diphenyl-4,5-dihydro-pyrimidin- 2-amine

(2)

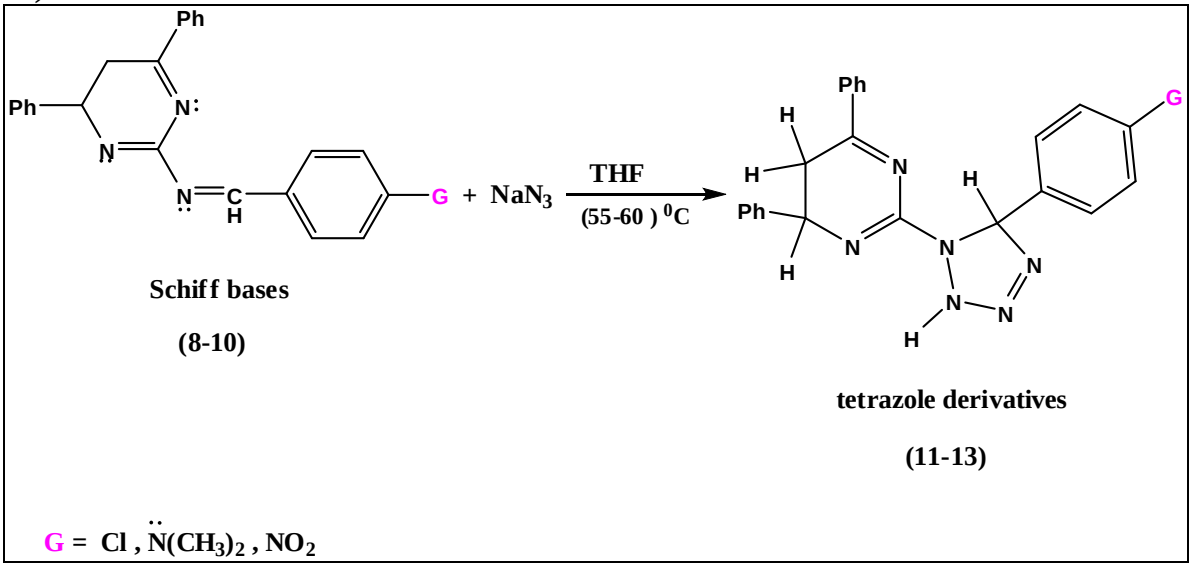
(8-10)

G = Cl , $N(CH_3)_2$, NO_2

Scheme - 5

The structures of compounds (8-10) were conformed through the disappearance of absorption bands of (NH_2) group at (3420,3312) cm^{-1} And the appearance of the package at range (1712-1643) cm^{-1} which refers to (C=N) azomethine group, (table -5), (figs. 8-10) [59,60].The products were characterized by FT.IR spectroscopy and the melting points , TLC were determined. The (table-2) shows physical properties of these compounds.

In water bath at (55-60) ^0C Schiff bases (8-10) were heated with sodium azide in THF to form the desired compounds (11-13). The characterization of these titled compounds were melting points, its colors, FT.IR, ^{1}HNMR, UV-Vis. spectra and checked by TLC technique (scheme -6).



Schiff bases

(8-10)

tetrazole derivatives

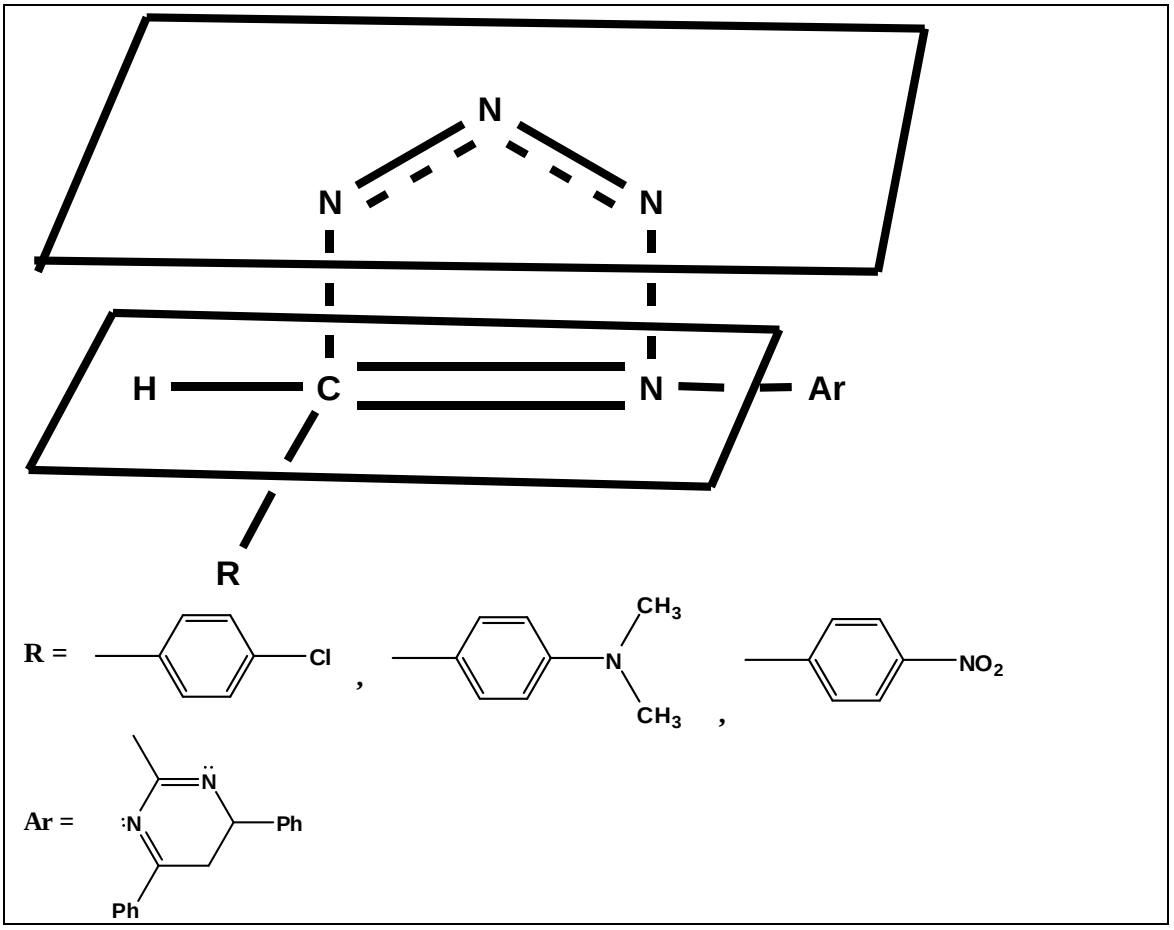
(11-13)

G = Cl , $N(CH_3)_2$, NO_2

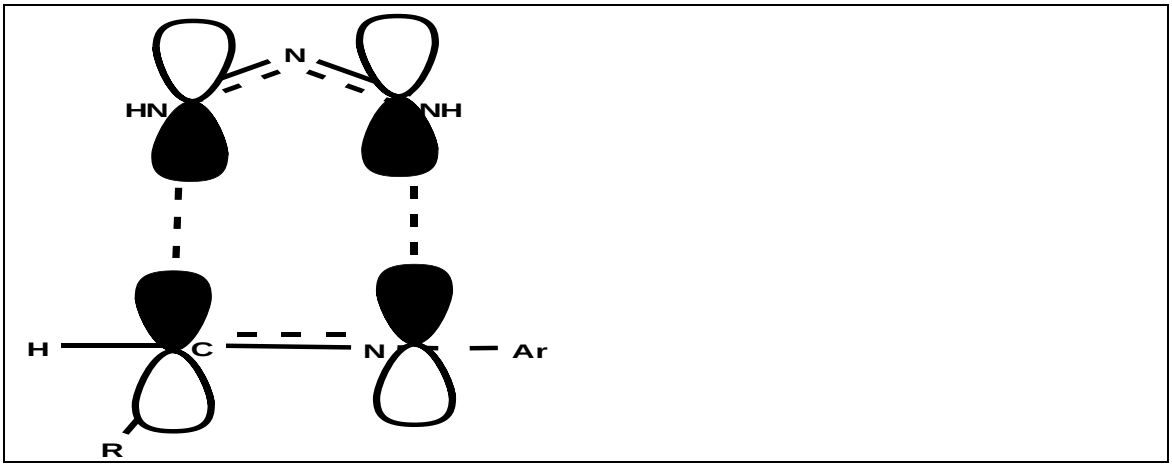
Scheme - 6

The mechanism of this reaction classified as [3+2] cycloadditions, it is one of the types of a 1,3- dipolar cycloadditions[61]. The addition reaction includes addition of unsaturated molecule (dipolarphile) to a molecule type 1,3- dipole which has two charges positive and negative distributed on the 1,3- positions relative to each other.

The five member ring results from cycloaddition reaction. The important and prominent type of 1,3- dipoles are azides which undergo 1,3- dipolar cycloadditions. they possesses great importance of synthetic field and have been studied mechanically in great detail[62]. The mechanism of 1,3- cycloaddition includes T.S. geometry which the azide lies in one plane and in a parallel plan above or below the dipolarphile and its ligands, therefore, orbitals perpendicular to the planes interact to form bonds, as shown in (scheme - 7, and 8) below [63,64]:



Scheme -7



Scheme - 8

The expected transition state for add of azide dipolar : Orbitals perpendicular to
the level of the reactant molecule to form bonds in the cycloaddition

To characterize specific structure of the compounds synthesized were used by spectroscopy of FT.IR. The good evidence for the success of this step of reaction was disappearance of bands at (1712-1643) cm^{-1} which attributed to (C=N) (imine group) stretching frequency., Also the IR spectra of these compounds devoid of powerful bands at (2120-2160) cm^{-1} attributed stretching frequency of azide group bands at (1537- 1507) cm^{-1} were due to the cyclic (N=N) stretching of tetrazole ring., The (N-H) group appears at (3365-3327) cm^{-1} (table -6) (figs.11-13) [57].

The ^{1}HNMR spectrum of compound (13), showed the following characteristic chemical shifts (DMSO- d^{6}, ppm): δ (7.606-10.37) ppm due to aromatic protons, δ (4.368) ppm due to (NH) proton for tetrazole , δ (2.543) ppm due to methylene group (CH_2) protons,
δ (3.39 and 6.673) ppm due to methine group (CH) protons, in pyrimidine ring and tetrazole ring (fig.15) [57,60]. The physical properties of these compounds are shown in (table -2).

UV-Vis. spectra of compounds (11,12, and 13) showed high intense peaks which assigned to overlap of (π- π*) and (n- π*) transitions.,
(table -7) show absorption peaks values of these compounds[57,60].

Microbiological tests

The disc diffusion method was used for study the antibacterial activity in this work. The prepared compounds (2,3,6,12, and 13) were Assayed for

antimicrobial activity in vitro against gram-negative bacteria and Gram-positive bacteria Escherichia coli , and staphylococcus aurous respectively. The sterilized Petri dishes and agar were prepared by autoclaving for (15) min at (121) ^{0}C. The used solvent was DMSO. Both bacteria were incubated in Sterile plates at (37) ^{0}C for (24) hours. The various prepared compounds which were examined cause inhibition zones.

The (table-8) shows results of the Initial examination tests. Biological Effectiveness test showed that prepared compounds with free (-NH_2) groups having moderate biological effect on each of E.Coli and Staph.aureus

Conclusion

1. For *Staphococcus aureus* (G+), compound (2,6, and 12) showed slightly activity, while compounds (3, and13) showed no activity on this bacteria.
2. For *Escherichia coli* (G-), compounds (3) have no effect on this bacteria because this bacteria is highly resistant to a wide range of antibiotic because of the slim polysaccharides in cell wall which blocked antibiotics from bacteria and also there are genetic factor., While compounds (6,12, and 13) have effect on this bacteria, compound (2) showed highest activity.

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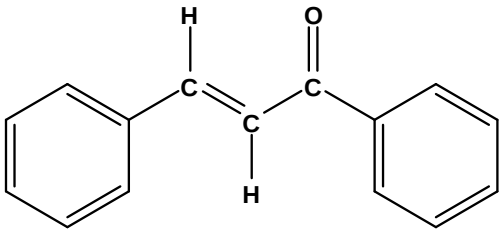
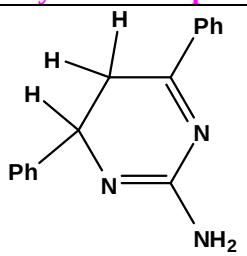
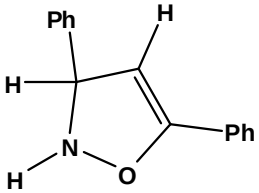
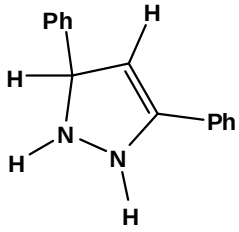
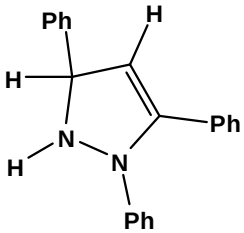
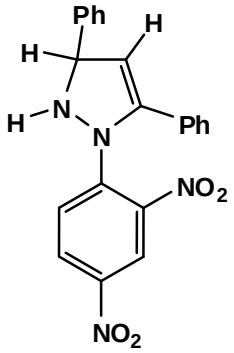
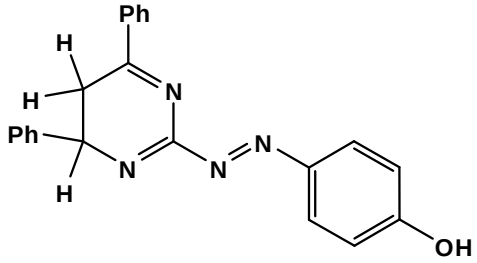
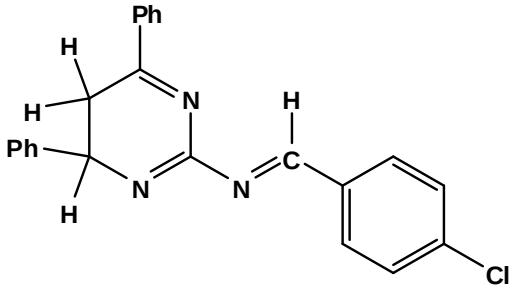
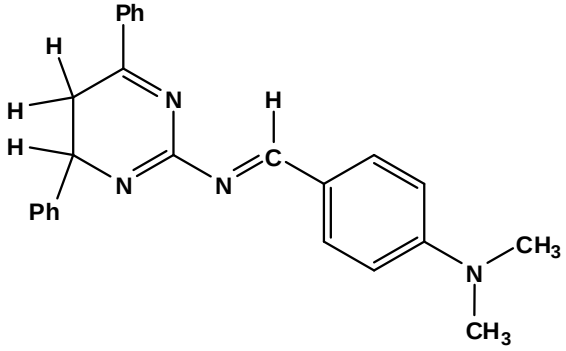
Table no. (1): Structure and nomenclature of the prepared compounds.

Comp. no.	Structure and name
1	 **(*E*)-chalcone** **benzylidineacetophenone**
2	 **4,6-diphenyl-4,5-dihydropyrimidin-2-amine**
3	 **3,5-diphenyl-2,3-dihydroisoxazole**
4	 **3,5-diphenyl-2,3-dihydro-1*H*-pyrazole**
5	 **1,3,5-triphenyl-2,3-dihydro-1*H*-pyrazole**

6	 **1-(2,4-dinitrophenyl)-3,5-diphenyl-2,3-dihydro-1*H*-pyrazole**
7	 **(*E*)-4-((4,6-diphenyl-4,5-dihydropyrimidin-2-yl) diazenyl)phenol**
8	 **(*E*)-*N*-(4-chlorobenzylidene)-4,6-diphenyl-4,5-dihydropyrimidin-2-amine**
9	 **(*E*)-*N*-(4-(dimethylamino)benzylidene)-4,6-diphenyl-4,5-dihydropyrimidin-2-amine**

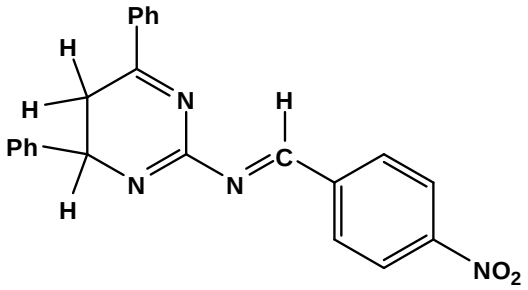
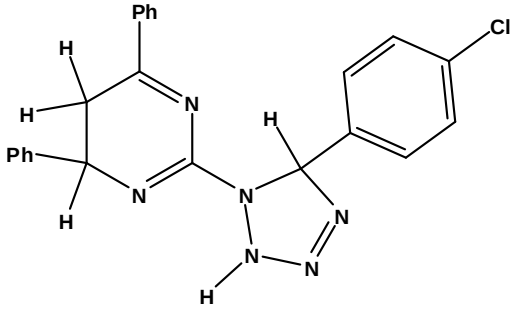
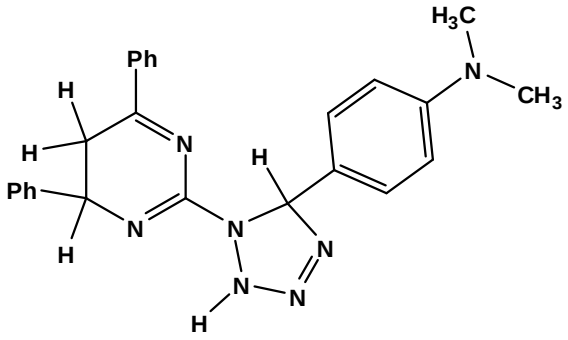
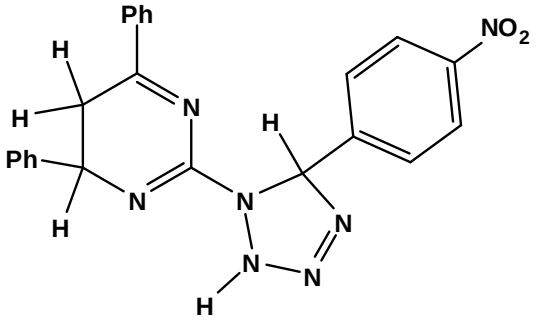
10	 **(*E*)-*N*-(4-nitrobenzylidene)-4,6-diphenyl-4,5-dihydropyrimidin-2-amine**
11	 **2-(5-(4-chlorophenyl)-2,5-dihydro-1*H*-tetrazol-1-yl)-4,6-diphenyl-4,5-dihydropyrimidine**
12	 **4-(1-(4,6-diphenyl-4,5-dihydropyrimidin-2-yl)-2,5-dihydro-1*H*-tetrazol-5-yl)-*N*,*N*-dimethylaniline**
13	 **2-(5-(4-nitrophenyl)-2,5-dihydro-1*H*-tetrazol-1-yl)-4,6-diphenyl-4,5-dihydropyrimidine**

Table no. (2): Physical properties of the compounds prepared.

Comp.	M.p. ^{0}C	Color	%Yield
1	54 -56	Light yellow	71
2	162 -164	Yellow	77
3	153 -155	Yellow	75
4	147 -149	Yellow	80
5	167 - 169	Deep yellow	79
6	173 -175	Deep yellow	83
7	263 -265	Reddish brown	90
8	145 -147	Brown - yellow	85
9	171 -173	Dark - brown	86
10	157 -159	Brown - yellowish	80
11	187 -189	Deep brown	71
12	196 -199	Brown	77
13	175 -177	Light brown - yellow	73

Table no. (3): FT.IR spectral data of the prepared compounds (2-6).

Comp.	CH υ aro.	CHυ ali.	C=Nυ endo	$NH_2\upsilon$ & N-Hυ	C=Cυ aro.	Others
2	3071	2933	1685	3420 Asym., 3312 sym.	1543	N-H $_{bend.}$ 1663 υ
3	3062	2856	-	3327	1511	N-H $_{bend.}$ 1583 υ C=C $_{alkene}$ 1622 υ C-O 1037υ
4	3044	2853	-	3355	1561	N-H $_{bend.}$ 1593 υ C=C $_{alkene}$ 1637υ
5	3037	2867	-	3356	1548	N-H $_{bend.}$ 1591 υ C=C $_{alkene}$ 1631υ
6	3054	2923	-	3374	1557	N-H $_{bend.}$ 1663 υ C=C $_{alkene}$ 1682υ NO_2 υ 1535Asym, 1352 sym.

Table no. (4): FT.IR spectral data of the azo compound (7).

Comp.	O-H υ phenolic	C-H$^{\upsilon}$ aro.	C-H$^{\upsilon}$ ali.	C=N$^{\upsilon}$ endo	C=C$^{\upsilon}$ aro.	N=N$^{\upsilon}$ trans azo
7	3324	3036	2821	1667	1543	1567

Table no. (5): FT.IR spectral data of the Schiff bases (8-10).

Comp.	CH υ aro.	CH$^{\upsilon}$ ali.	C=N$^{\upsilon}$ endo	C=N$^{\upsilon}$ imine	C=C$^{\upsilon}$ aro.	Others
8	3051	2879	1674	1643	1519	C-Cl aromatic 836$^{\upsilon}$ C-H methine 2954$^{\upsilon}$
9	3045	2876	1643	1586	1521	C-N 1255$^{\upsilon}$ C-H methine 2951$^{\upsilon}$
10	3067	2889	1712	1690	1637	NO_2 υ 1557Asym. , 1312 sym. C-H methine 2967$^{\upsilon}$

Table no. (6): FT.IR spectral data of the tetrazoles compounds (11-13).

Comp.	CH υ aro.	CH$^{\upsilon}$ ali.	N-H$^{\upsilon}$	C=N$^{\upsilon}$ endo	N=N$^{\upsilon}$	C=C$^{\upsilon}$ aro.	Others
11	3056	2876	3327	1674	1522	1465	C-Cl aromatic 843$^{\upsilon}$
12	3021	2863	3334	1643	1507	1411	C-N 1241$^{\upsilon}$
13	3073	2893	3365	1712	1537	1473	NO_2 υ 1538 Asym., 1297 sym.

Table no. (7): UV.-Visible spectral data of the prepared compounds.

Comp.	λ_{Max} (nm)

11	233 , 249
12	291, 312
13	343, 367

Table no. (8): Antimicrobial activity for some prepared compounds .

Comp.	***E*scherichia coli**	***S*taphococcus aureus**
2	++	+
3	-	-
6	+	+
12	+	+
13	+	-

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

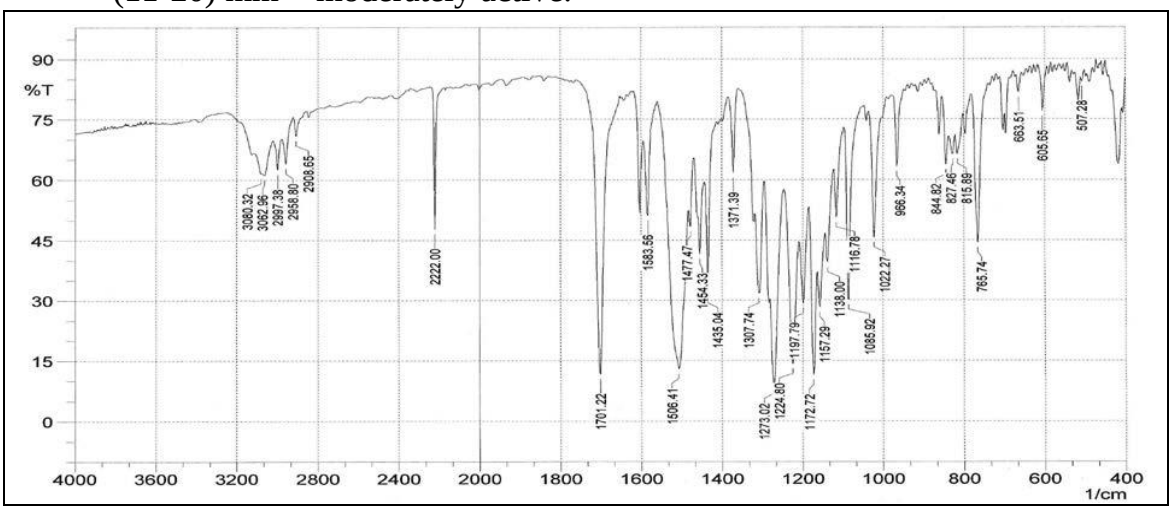


Fig.(1): FT.IR spectrum of starting material (1).

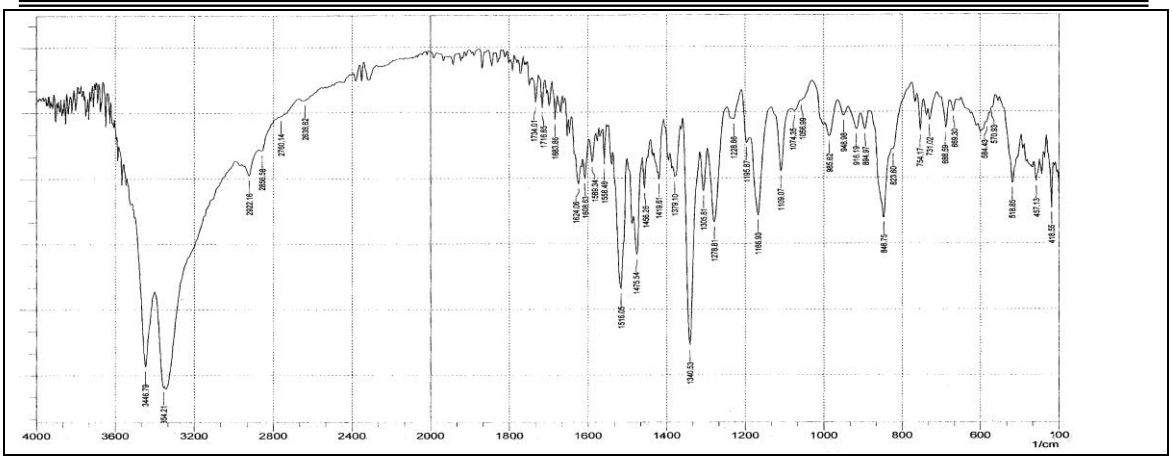


Fig.(2): FT.IR spectrum of compound (2).

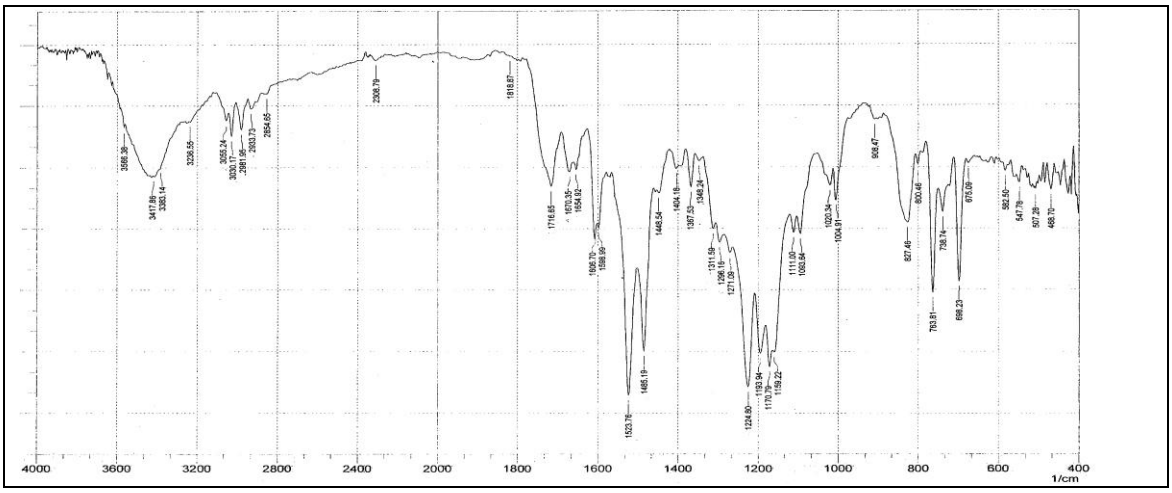


Fig.(3): FT.IR spectrum of compound (3).

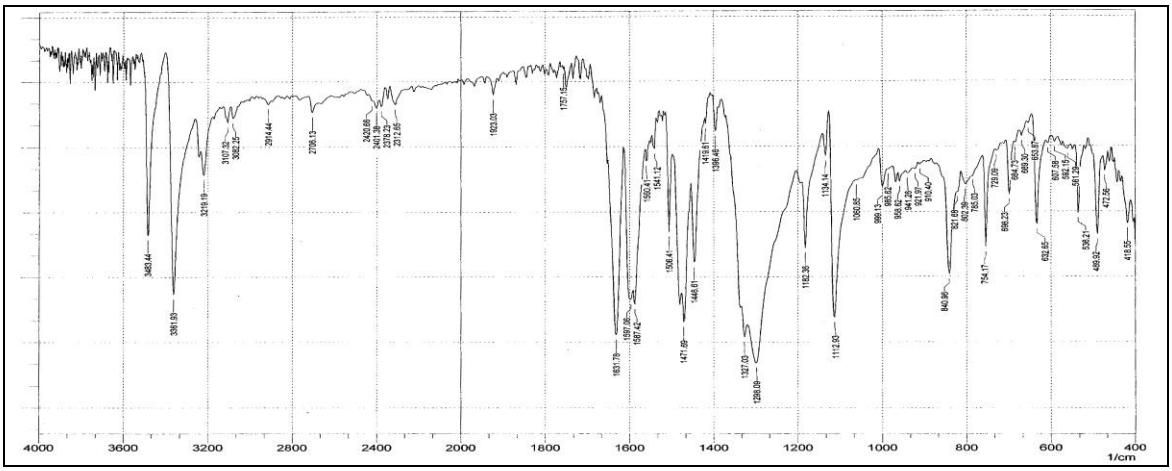


Fig.(4): FT.IR spectrum of compound (4).

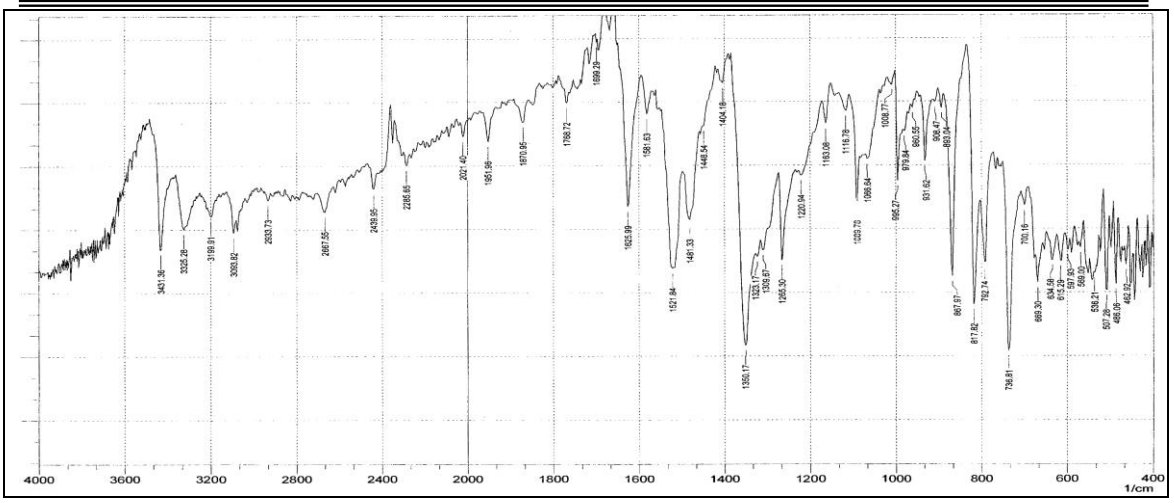


Fig.(5): FT.IR spectrum of compound (5).

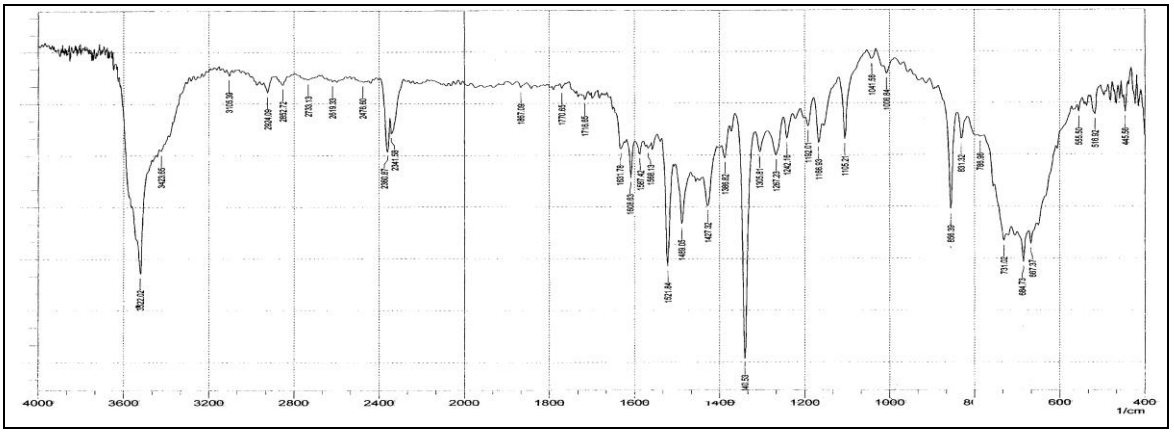


Fig.(6): FT.IR spectrum of compound (6).

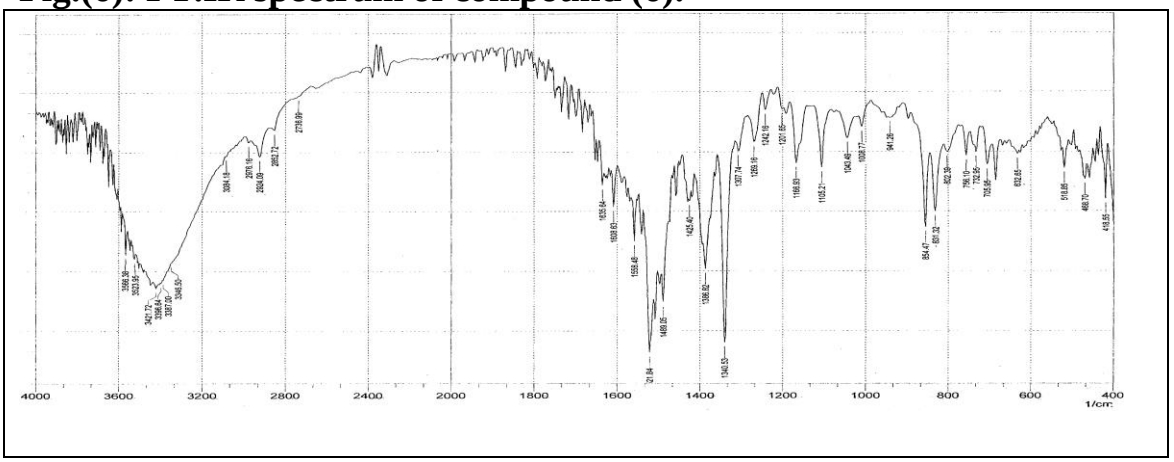


Fig.(7): FT.IR spectrum of compound (7).

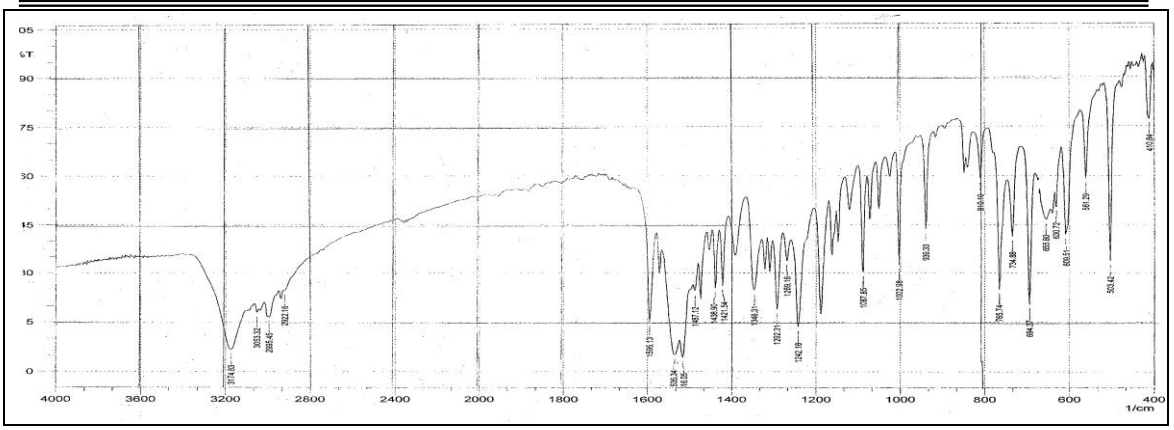


Fig.(8): FT.IR spectrum of compound (8).

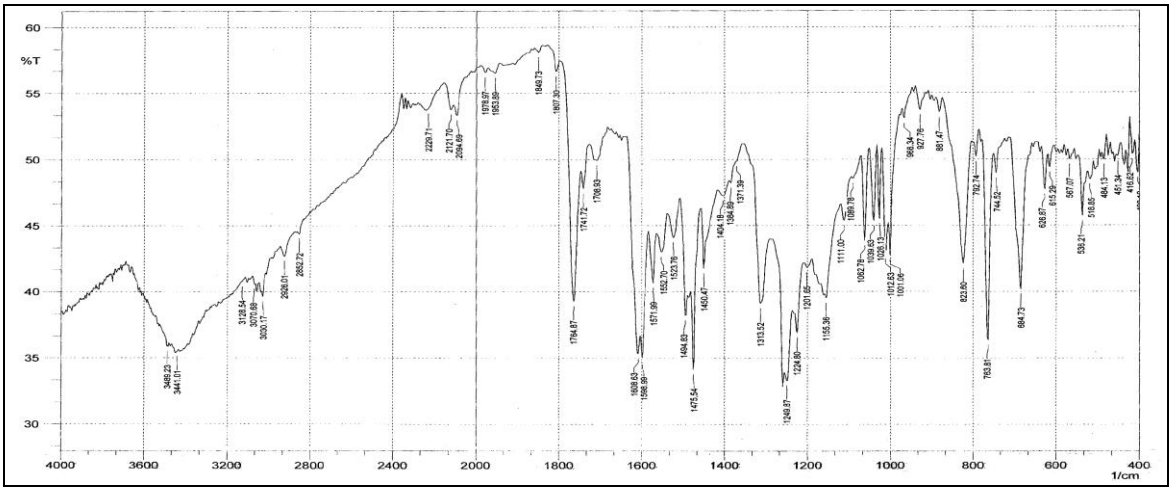


Fig.(9): FT.IR spectrum of compound (9).

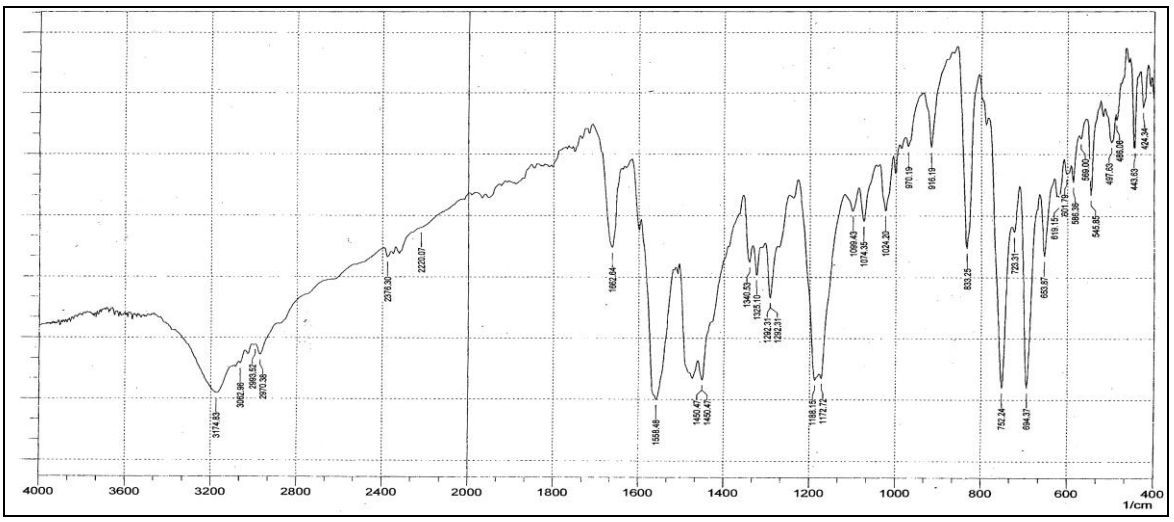


Fig.(10): FT.IR spectrum of compound (10).

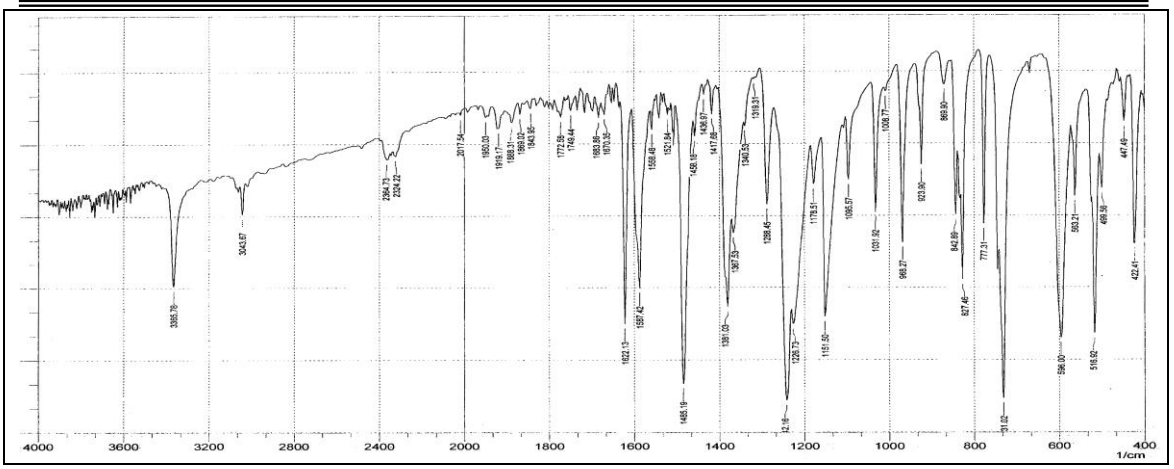


Fig.(11): FT.IR spectrum of compound (11).

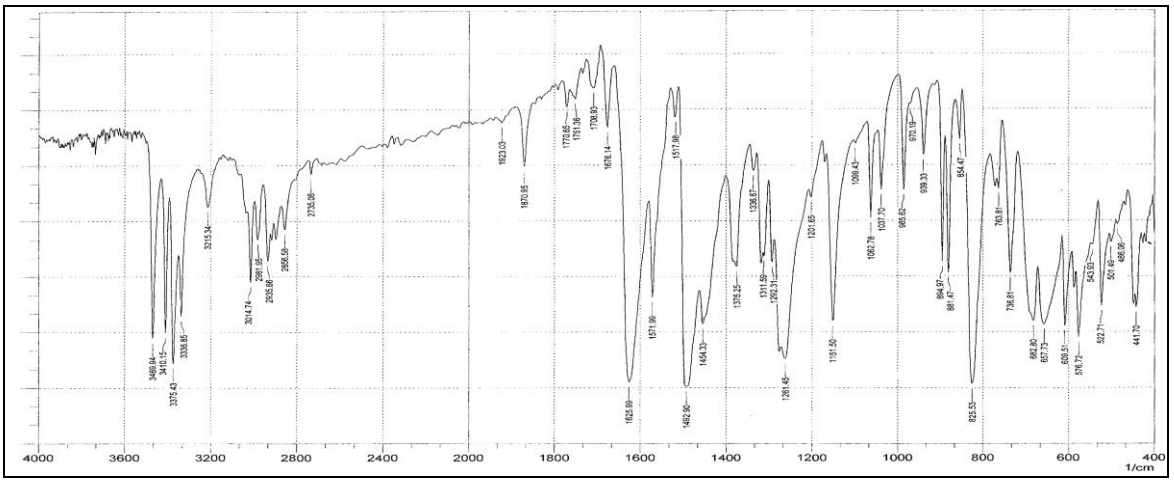


Fig.(12): FT.IR spectrum of compound (12).

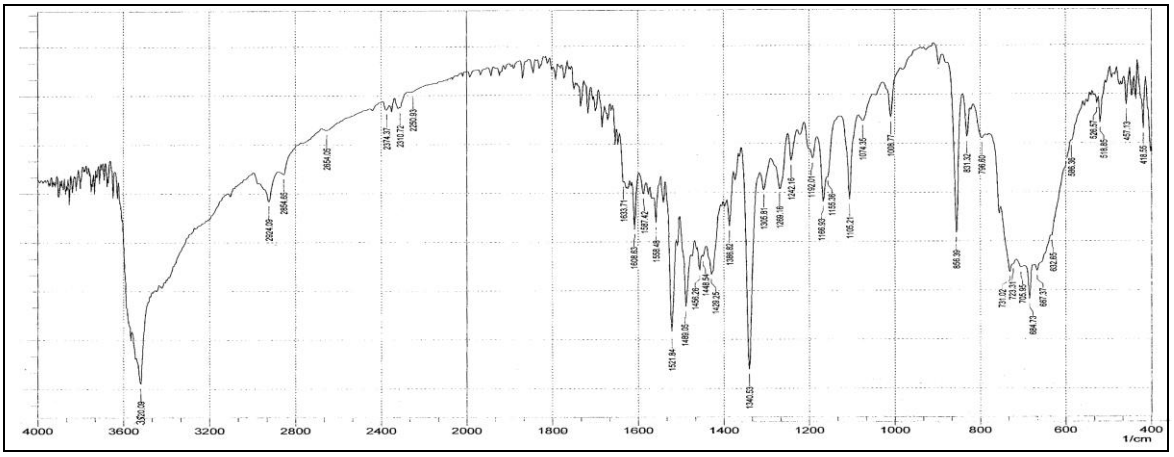


Fig.(13): FT.IR spectrum of compound (13).

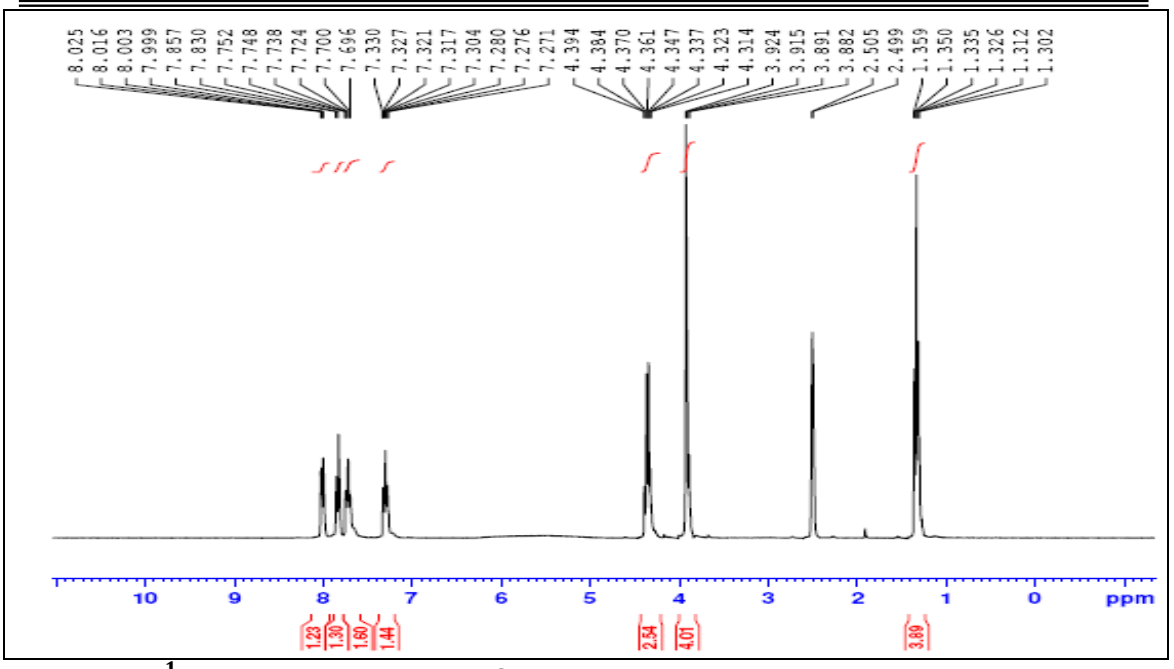


Fig.(14): ^{1}HNMR spectrum of compound (2).

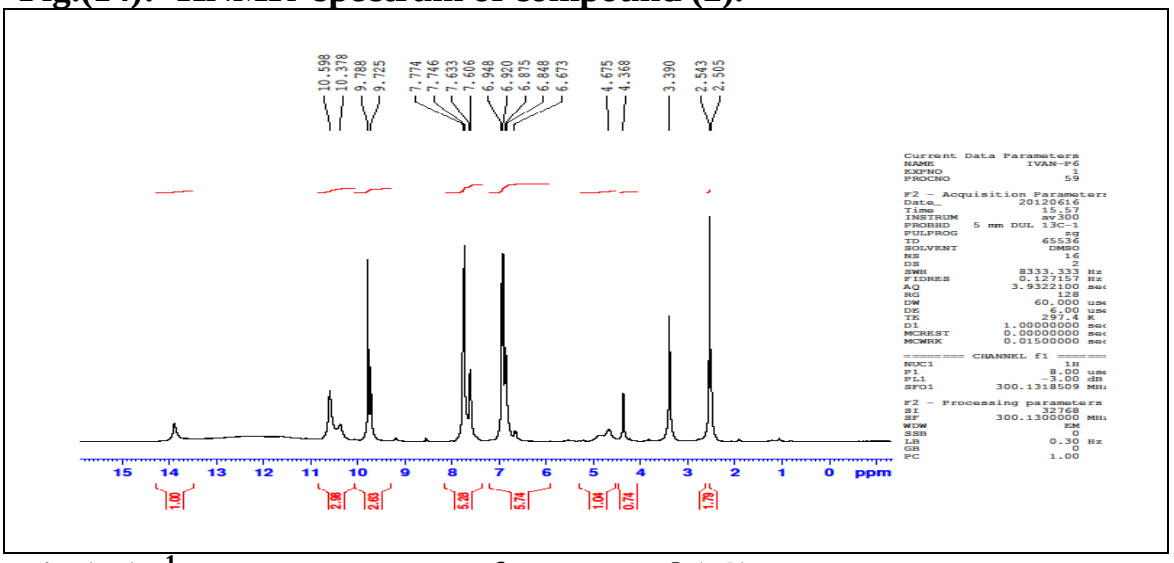
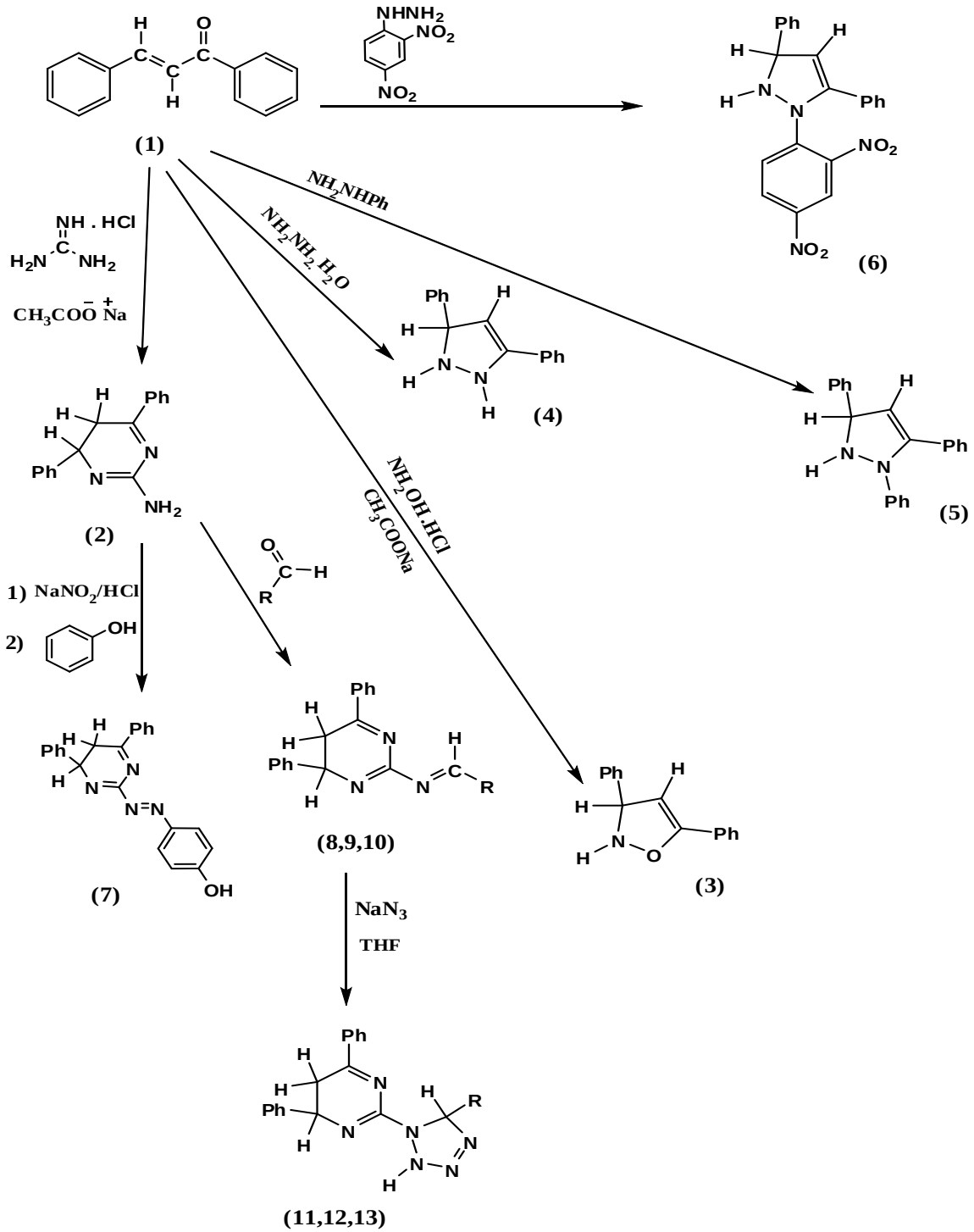


Fig.(15): ^{1}HNMR spectrum of compound (13).



R = 4-Cl- C_6H_4 , 4-$N(CH_3)_2$-C_6H_4 , 4-NO_2-C_6H_4

Scheme -9

تحضير و تشخيص مركبات حلقية غير متجانسة جديدة من كيتون غير مشبع و دراسة الفعالية البيولوجية لها

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أحلام جاسم زاير*

قسم الكيمياء, كلية التربية للعلوم الصرفة – ابن الهيثم, جامعة بغداد

الخلاصة

يتضمن البحث تحضير بعض مشتقات جديدة لل‌پريميدين و ال‌پيرازول و آزوگزازول من تفاعل بنزيليدين أسيتوفينون (چالكون) (1) مع بعض مشتقات الهيدرازين في الأسيتون الجاف بوجود خلات الصوديوم اللامائية لبعض المشتقات للحصول على مركبات حلقية غير متجانسة التركيب (2-6) .

تم مفاعلة المركب (2) بتفاعل تكثيف مع ألديهايدات أروماتية المعوضة في الأيثانول المطلق بوجود قطرات من حامض الخليك الثلجي ليعطي قواعد شيف (8-10) التي تعاني تفاعل تكوين حلقة مع أزيد الصوديوم في رباعي هيدروفيوران لتعطي مشتقات التيترازول (11-13).

يعاني المركب (2) تفاعل ديازة عند مفاعلته مع نتريت الصوديوم بوجود حامض الهيدروكلوريك المركز يتبعه تفاعل ازدواج مع الفينول ليعطي مشتق الدايآزو (7).

تم تشخيص المركبات المحضرة بالطرق الفيزيائية و الطيفية (مطيافية الأشعة تحت الحمراء الرنين النووي المغناطيسي والأشعة فوق البنفسجية - المرئية). وتم متابعتها بوساطة كروموتوغرافيا الطبقة الرقيقة وقياس درجات الانصهار, كما اختبرت هذه المركبات ضد أنواع من البكتريا.

الكلمات المفتاحية : كيتون غيرمشبع, چالكون, بينزيليدين أسيتوفينون, مركبات حلقية غير متجانسة التركيب , پريميدين، پيرازول، آزوگزازول .