Synthesis of new heterocyclic rings including four,five and seven member rings with study their biological activity

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Abstract

A new series of heterocyclic compounds including four, five and seven member rings have been synthesized. These compounds including N,N'-(1,4-phenylenebis(methan-1-yl-1-[1,2], ,4(1,4 phenylene)bis(3-chloro-1-(alkyl)azetidine -2-one(3,4) , 1,4- ylidene))bis(substituted) bis(1-(substituted)-2,5-dihydro-1H-tetrazole-5-yl)benzene (5,6), 2,2-(1,4-phenylene)bis(3-(alkyl)-2H benzo[1,3]thiazine-4(3H-one)(7,8). 2,2-(1,4-phenylene)bis(3-(alkyl)-2,3-dihydroquinazoline-4(1H)one)(9,10). thiazepine derivatives(11,12). (5z,5z)-2,2-(1,4-phenylene)-2,3dihydro-1,3-oxazepine-4,7-dione (13,14) and 3,3-(1,4-phenylene)bis(4-(alkyl)-3,4-dihydrobenzo[1,3]oxazepine-1,5-dione(15,16,17,18) . The structures of these compounds characterized by (FT-IR, H-NMR) spectroscopy and C.H.N analysis ,melting points and checked through T.L.C. The biological activity of these compounds was tested against

Staph. Aureus, E. coli , Sal. typhi and Ps. Aerugenosa bacteria.

Key words : heterocyclic ,oxazepines , Azetidine , tetrazoles.

تحضير مركبات غير متجانسة الحلقة جديدة تشمل حلقات رباعية وخماسية وسباعية مع دراسة فعاليتها الحيوية.

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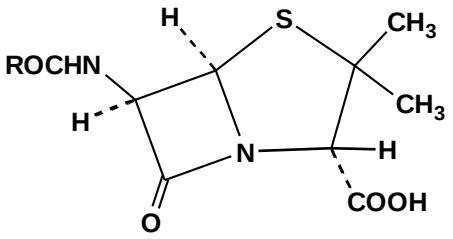
تم في هذا البحث تحضير مركبات غير متجانسة الحلقة تشمل ن ,ن-(1و4-فنيلين بس (ميثان-1-يل-1-(1و2) و4(1و4فنيلين) بس (3-كلورو-1-(الكيل)ازيتيدين-2-اون(3,4) و4,1-يليدين)بس(معوض)بس (1-معوض)-2و5-ثنائي هيدرو-تترازول-5-يل)بنزين (6,5) ,2,2-(4,1-فنيلين)بس (3-الكيل) -2-بنزو(3,1-ثايازين-4(-اون)(6,5) , 2,2-(4,1-فنيلين))بس (3-الكيل)-2-بنزو(3,1)ثايازين-4(3-اون)(8,7) ,2,2-(4,1-فنيلين)بس(3-(الكيل)-3,2—ثنائي هيدروكوينوزولين-4-(1-اون)(10,9) , مشتقات الثليازبين (12,11) , (5,5)-2,2-(4,1-فنيلين) 3,2-ثنائي هيدرو-3,1-اوكسازبين-4و7-دايون (14,13) وكذلك 3,3-(4,1-فنيلين)بس (4-(الكيل)-4,3-ثنائي هيدرو بنزو(3,1)اوكسازبين -5,1-دايون (18,17,16,15). تم تشخيص تراكيب هذه المركبات عن طريق اطياف الاشعة تحت الحمراء والرنين النووي المغناطيسي وتحليل العناصر الدقيق ودرجات الانصهار وكروموتوكرافيا الطبقة الرقيقة كما تمت دراسة تاثيراتها الحيوية ضد اربعة انواع من البكتريا .

Introduction

Heterocyclic compounds have a wide range of applications, but are of particular interest in medicinal chemistry[1] and industrial application. Many Heterocyclic compounds were found in natural products such as alkaloid (alkali-like), this compound is containing nitrogen atom in the ring, for example papaverine from the opium poppy (papaver somniferum) is containing pyridine[2].

Azetidine is an important four-membered heterocyclic β -lactam compound because it is apart of penicillin group compounds which fused with thiazolidine ring.



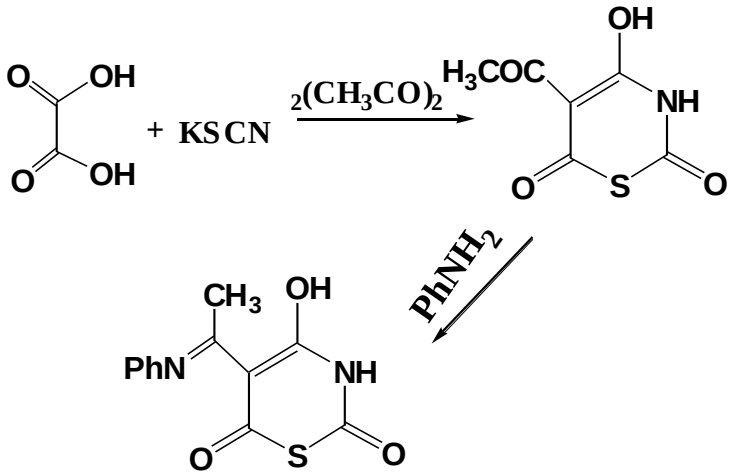
R=-CH_2Ph, -Ph , -$CH_2CH=CHC_2H_5$

Azetidine is a four membered ring containing one nitrogen atom but azetidinone differs from azetdine by the presence of carbonyl group at carbon number two (β-lactam). Many methods have been developed for β -lactam synthesis [3] including cyclization of the corresponding amino acids.

Tetrazole is a five membered-ring containing four nitrogen atoms with one carbon substituted tetrazoles are reported to possess antibacterial, antihypertensive, antiviral, analgesic, anti-inflammatory, anticancer activities [4-5].

Thiazine ; many compounds of 1,4-thiazine are known, most of them derivatives of phenothiazine ($C_{12}H_9NS$), which was discovered in 1883. Phenothiazine has been used as a vermifuge for livestock and also as an insecticide. Drugs of the phenothiazine type include chlorpromazine, a tranquillizer; promethazine hydrochloride (Phenergan), a long-acting antihistaminic; and diethazine hydrochloride (Diparcol), used in treatment of parkinsonis diseases. Thiazines exhibited various kind of biological activity such as Ca^{+2} antagonist ,blood platelet aggregation inhibitors ,antimicrobial and anti hypertensive[6].

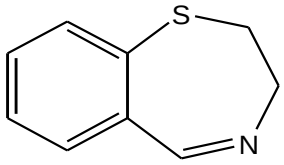
A simple synthesis of 4-hydroxy-5-(1-(phenylimino)ethyl)-2H-1,3-thiazine-2,6(3H)-dione from malonic acid, potassium thiocyanate and acid anhydrides is described[7].



Oxazepine is a seven membered ring that contains two heteroatoms (Oxygen and Nitrogen). Oxazepama (serax) marketed under brand names : Alepam , Serax , Murelax , Serax-Sobril are the first dray of chemical series of compounds , 3-hydroxy benzo diazepines , comprised of two aromatic ring is fused to the seven-membered ring and it contains chloro-substituent or some other electronegative group[8] .

Many examples belong to oxazepines , diazepines are documented ,but very little is known about thiazepine. 1,4 – Benzothiazepine derivatives are of considerable interest because of their biological activity as a muscle relaxants [9] .

Thiazepine contains two hetroatoms (nitrogen and sulphur) in seven membered ring.



4- The biological activity was performed by Biotechnology Department, Tikrit University .

Thiazepine is one of hetrocyclic compounds which have pharmacological interest. Thiazepine is one of drugs which has biological interest due to their activity on the central nervous system , as enzyme inhibitors , anti-cancer , anxiolytic activity ,anticonvulsant, muscle relaxant and other uses .

Experimental part :

1- Melting points are recorded using hot stage Gallen Kamp melting point apparatus and they were uncorrected.

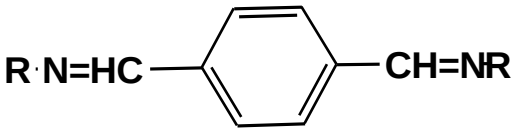
2- Infrared spectra are recorded using Fourier Transform infrared SHIMADZU (8300) (F.T.IR) infrared spectrophotometer, KBr disc .

3- ^{1}H –NMR spectra (DMSO) were recorded on BRUKER-av-300 instrument with TMS as an internal standard.

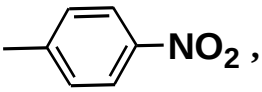
4- Thin layer chromatography (TLC) was carried out, and the plates were developed with iodine vapour.

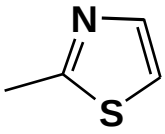
1-Synthesis of Schiff bases(1a,b).

N,N'-(1,4-phenylenebis(methan-1-yl-1-ylidene))bis(substituted) [1,2].



(1,2)

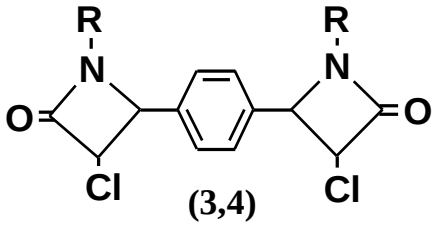
R= 

, 

(a) **(b)**

The Schiff bases (1,2) were prepared according to the reported method[8]. A solution of the primary amine derivatives (0.02 mol)in absolute ethanol (30ml) ,was slowly added to a solution of terephthaldehyde (0.01Mol) in absolute ethanol(20ml).After stirring (3hours for1 and 5hours for 2)) the reaction mixture was cold ,a precipitate was formed which collected by filtration then washed with cold ethanol and re crystallized from ethanol.

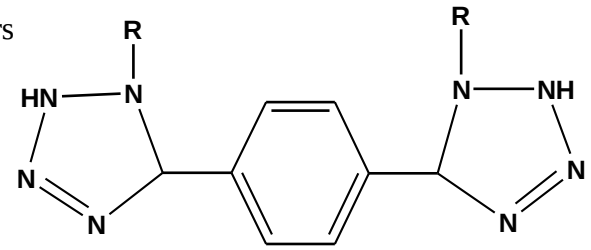
2- Synthesis of 4,4(1,4 phenylene)bis(3-chloro-1-(alkyl)azetidine -2-one(3,4) [10].



(3,4)

Chloro acetyl chloride (0.02mol)in (10ml) of dioxane cooled at 0 ^{0}C , then triethyl amine (0.02mol) in (10ml) dioxane was added ,and Schiff bases (1a,b) (0.01 mol) in 10 ml of dioxane was slowly added then refluxed in water bath for 12hrs . After completion of the reaction (checked by TLC),the reaction mixture poured into ice – cold water to give white precipitate then filtered and dried .Re crystallized by benzene –petrolum ether(50/50).

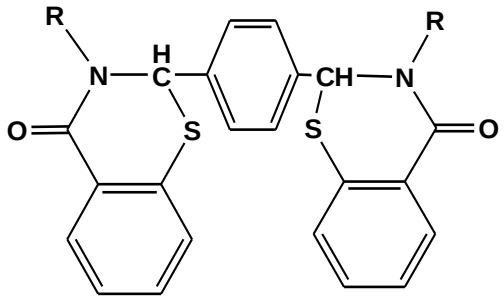
3- Synthesis of 1,4-bis(1-(substituted)-2,5-dihydro-1H-tetrazole-5-yl)phenylene(5,6) [11]



(5,6)

To a stirring solution of Schiff base (1,2)(0.1mol) in 10ml of tetrahydrofuran , sodium azide (0.02mol) in 10 ml of tetrahydrofuran was added. After the addition,the mixture was refluxed for(7-8)hrs., then cooled at room temperature and the precipitate was filtered , washed with cold water. Recrystallized with benzene-petroleum spirit(40-60)^{0}C.

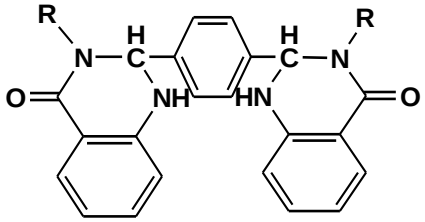
4 -Synthesis of 2,2$^/$-(1,4-phenylene)bis(3-(alkyl)-2H benzo[1,3]thiazine-4(3H -one)(7,8).



(7,8)

A mixture of Schiff base(1,2) (0.01mol) and 2-mercaptobenzoic acid (0.02mol) was stirred with dry benzene (30ml) and 3drops of triethylamine or pyridine. The mixture was refluxed for 3 hrs .then the solvent was removed under reduced pressure. The residue washed with 10% of sodium bicarbonate then filtered and recrystallized with dioxan.

5 -Synthesis of 2,2-(1,4-phenylene)bis(3-(alkyl)-2,3-dihydroquinazoline-4(1H-one)(9,10).

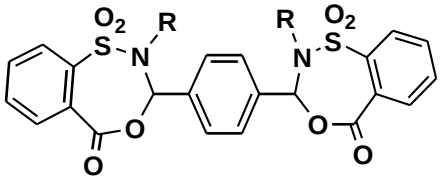


(9,10)

A solution of 2- amino benzoic acid (anthranilic acid) (0.02mol) ,Schiff base(1,2) (0.01mol) in dioxane was added. The solution was heated under reflux temperature for 16hrs., the solvent was evaporated under reduced pressure and the residue was treated with10% of sodium bicarbonate. Then filtered and re crystallized by benzene-petrolum spirit(1:1).

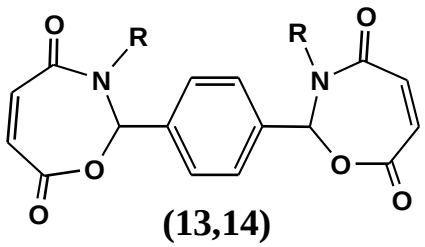
7-Synthesis of (5z,5z)-2,2-(1,4-phenylene)-2,3dihydro-1,3-oxazepine-4,7-dione (1,14)

6 -Synthesis of thiazepine derivatives(11,12).



(11,12)

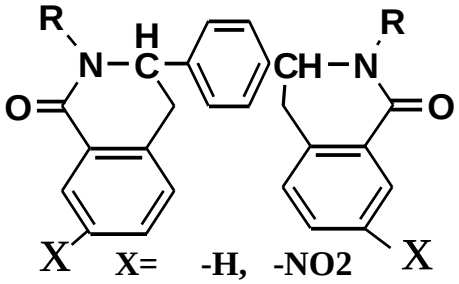
The orthosulfobenzoic acid cyclic anhydride (0.02mol) was dissolved in a small amount of dry benzene and stirred for 30min., Schiff base (1,2) (0.01mol) in 10ml of dry benzene was added with 3-4drops of tetrahydrofuran the mixture was refluxed in water bath 5-6hrs or until the colour changed to green ,the mixture was cooled at room temperature. Green precipitate was collected by filtration and washed with cold dry benzene, re-crystallized by benzene.



(13,14)

A mixture of (0.01mol) of Schiff base (1,2) and (0.02mol) of maleic anhydride dissolved in 10ml of dry benzene and refluxed in a water bath for 4hrs .The solvent was removed and the resulting crystalline solid was re crystallized from dioxin to give the titled compound(13,14).

8- Synthesis of 3,3-(1,4-phenylene)bis(4-(alkyl)-3,4-dihydrobenzo[1,3]oxazepine-1,5-dione(15,16,17,18) [12]**)**



X= -H, -NO2

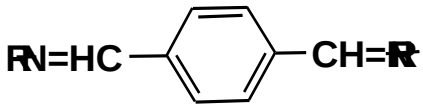
(15,16,17,18)

A mixture of Schiff base (0.01mol) and phthalic or 3-nitro phthalic anhydride(0.02mol) was dissolved in (20ml) of dry benzene and the mixture was refluxed for 5hrs in water bath at 70 ^{0}C .The excess of the solvent was distilled,filtered off and re crystallized from benzene.

Results and Discussion

compounds (1,2). These compounds were tested with 2,4-dinitro phenyl hydrazine this test showed no reaction with this reagent.

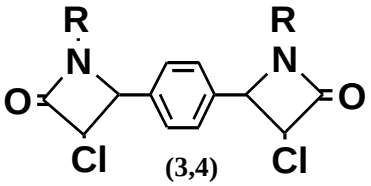
1- Characterization of Schiff basesN,N'-(1,4-phenylenebis(methan-1-yl-1-ylidene)) bis (substituted(1,2)) .

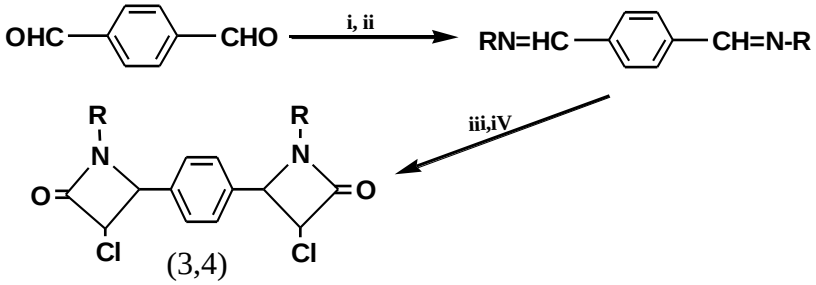


(1)

The reaction of terephthaldehyde with different primary amines is one of the most common reaction to synthesize Schiff bases . The structure of the product is assignment on its melting point and l (FT.IR) spectroscopy besides the C.H.N.S. analysis. The (FT.IR) spectra of Schiff bases (1,2) showed the appearance of the characteristic absorption bands in the region (1618-1600)cm^{-1} due to stretching vibration of the(C=N) for azomethine[13] band besides the disappearance of the absorption band in the region(3290 and 3100 cm-^{1}) due to the symmetric and asymmetric stretching vibration of the (-NH_2) group. Also the (FT.IR) spectra of the compounds (1,2) showed the disappearance of band at (1690) cm-^{1} due to stretching vibration of the carbonyl group of terephthaldehyde , the table (1) showed the FT-IR characteristic bands of

2- Synthesis and Characterization of compounds 4,4(1,4 phenylene)bis(3-chloro-1-(alkyl)azetidine -2-one (3,4) .

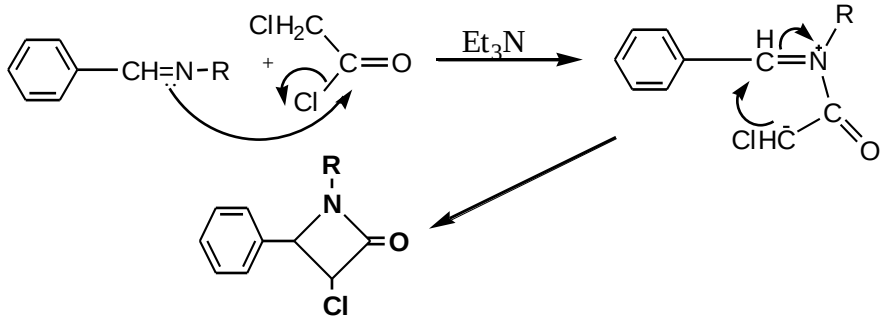




Scheme(2):reagent and condition (i)=primaryamine, ii=GAA, iii=ClCH2COCl iv=Et3N (ii)GAA=glacial acetc acid , (i) p-nitro aniline,2-amino thiazole

These compounds were synthesized according to the sequence in Scheme(2). The Schiff bases (1,2) were treated with chloro acetyl chloride followed by the addition of triethyl amine .These compounds were characterized by their melting points ,FT.IR, H,NMR, ^{13}C-NMR spectra and checked by TLC.

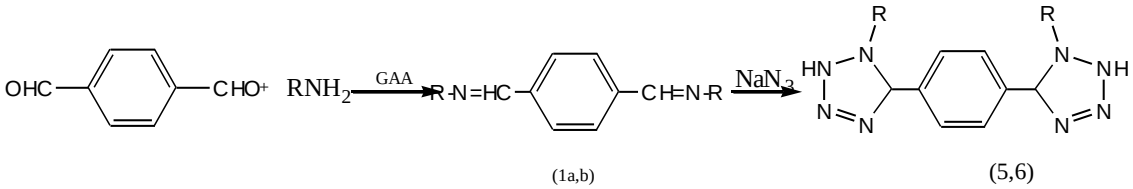
The FT-IR spectra of compounds (3,4) confirmed the appearance of carbonyl group band at (1652-1656)cm-^{1}and(–CH) aromatic band at (3051-3103) cm-^{1} and (C-Cl)cm-^{1} at(852-867) cm^{-1} (CH) aliphatic bands at(2924-2943) cm^{-1}and also bands at(1257-1253)cm^{-} ^{1}belongs to the (C-N) group. ^{1}H NMR spectrum fig(1) shows the following characteristic chemical shifts for compound (4) ,(DMSO) ppm, CH proton in azetidinone ring appeared two signal at(5.397and 5.405)ppm and CH proton fused with chlorine absorbed at (6.371 and 6.486ppm) and (7.6-8.2) ppm for aromatic ring proton. ^{13}C-NMR spectrum fig(2) of compound (3) showed the signal in (101.0)ppm for the carbon in azetidinone fused aryl ring but the signal at (70.230)ppm due to the carbon fused with chlorine in azetidinone ring and at (189.676) ppm for the carbon of carbonyl group. The suggested mechanism of these compounds in scheme(3).



Scheme (3)

3- Synthesis and characterization of 1,4-bis(1-(substituted)-2,5-dihydro-1H-tetrazole-5-yl)benzene (5,6)

The synthesis and interesting pharmacological properties of Tetrazole compounds were recently described. The compounds(1,2) ,Schiff bases were heated in water bath at(55-60C)with sodium azide in THF ,gave the described products(5,6)(4) the titled compounds were characterized by their melting points,its colours, FT.IR, H,NMR, ^{13}C-NMR spectra and checked by TLC technique .



(1a,b) (5,6)

The mechanism of this reaction systematically investigated as [3+2] cyclo additions which christened as a 1,3-dipolar cycloadditions. 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.

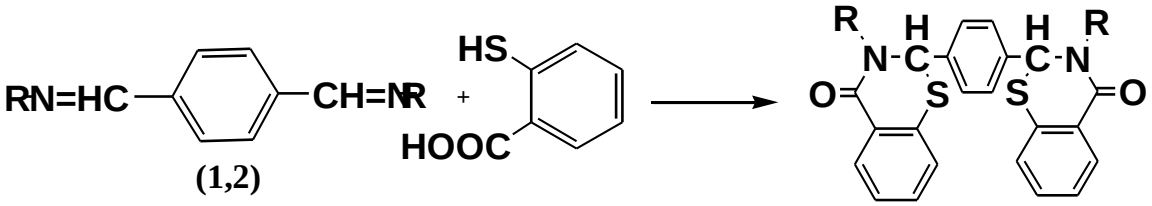
The common features of this type of reactions is best accommodated by a T.S. geometry in which the dipolarphile and its ligands lies in one plane, and the azide lies in a parallel plane above or below, so that the orbitals perpendicular to the planes interact to form bonds.

The FT-IR spectroscopy, were utilized to characterize the specific structure of the synthesized compounds. The disappearacnce of bands at (1600 and 1618 cm^{-1}), attributed to (C=N) (imine group) stretching frequency is good evidence for the success of this step of reaction. It also, the IR spectra for these compounds were devoid of a strong bands at (2120–2160)cm^{-1} attributed stretching frequency of a zide group. bands at (1520-1533 cm^{-1}) were due to the cyclic (N=N) stretching of tetrazole ring. Band at (3371,3390 cm^{-1}) due to (N-H) group . The FT-IR characteristic data are reported in table(2) Table shows the FT-IR spectral data for compounds.

^{1}H-NMR spectrum of compound (6), fig.,(3) shows the following characteristic chemical shifts (DMSO- d_6, ppm):the proton of thiazole ring appeared at the range(δ5.4-5.8)ppm,aromatic ring protons as multiplete at(δ7.3-8.1)ppm , (N-H) proton for tetrazole appeared at (δ 4.9) signal at (δ 9.71) due to the (C-H) proton in tetrazole ring.

^{13}C-NMR spectrum of compound (6) figure (4) showed signal at (95.9,96.021) ppm due to (-CH) in thiazole ring and signal at (175.1) ppm for the carbon in thiazole(C=N) fused with Tetrazole ring and the carbon in aromatic ring gives a signal at(122.0-144.3)ppm.

4 - Synthesis and characterization of 2,2-(1,4-phenylene)bis(3-(alkyl)-2H benzo[1,3]thiazine-4(3H-one)(7,8).



(1,2)

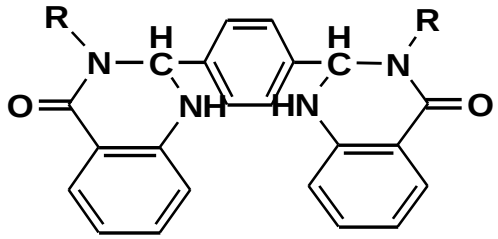
(7,8)

Thiazines derivatives were prepared by the reaction of Schiff bases fig.,(5),compound (7) and 2-mercaptobenzoic acid in dry benzene the products were identified by the FTIR spectra by the appearance of carbonyl group of the thiazines in 1683 cm^{-1} and disappearance of the C=N group in (1600-1618cm-1) and the disappearance of O-H broad band stretching vibration at 3450cm^{-1} of 2-mercaptobenzoic acid.

^{1}H-NMR spectrum of compound (7),figure(6),shows the following characteristic chemical shifts (DMSO- d_6, ppm):the aromatic ring protons as multiplete at(δ6.5-8.2)ppm , signal at (δ 9.9) due to the (C-H) proton in thiazine ring.

^{13}C-NMR spectra of compound (7,8) showed signal at (163.0-168.0) ppm due to (C=O) in thiazine ring and signal at (156.1-157.6)ppm for the (-CH) in thiazine ring and the carbon in aromatic ring gave a signal at(122.4-125.4)ppm.

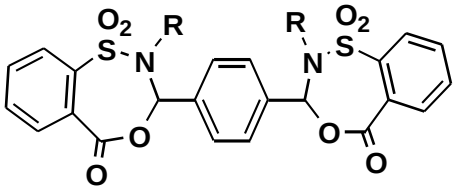
5 -Synthesis and characterization of 2,′2-(1,4-phenylene)bis(3-(alkyl)-2,3-dihydroquinazoline-4(1H)one)(9,10).



pyrimidine derivatives prepared by the heating of Schiff bases derivatives with anthranilic acid(O-amino benzoic acid) in dioxane. The products were identified by the FTIR spectra which show the appearance of NH vibration in (3361-3373) cm^{-1} and the disappearance of C=N band in (1600-1618)cm^{-1},figure(8),compound (10). Also all the FT-IR spectral data for these compounds are listed in table(3).

^{13}C-NMR spectrum of compound (10),fig.,(8) shows singlete signal at 170.0 for (C=O) ,151 for (C=N) in thiazole ring and at 151.9ppm (C-H) in pyrimidine ring and singlet signal at (115and 116) ppm for (-CH) in thiazolie ring.

6- Synthesis and identification of thiazepine derivatives(11,12).



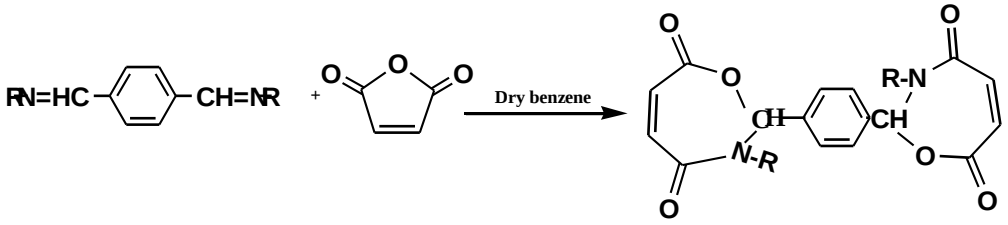
These compounds (11,12) were synthesized from the reaction of compounds (1,2) Schiff bases with O-sulfobenzoicacid cyclic anhydride in dry benzene. These compounds were characterized through the test. In this test the compounds are treated with sodium to form sodium fusion this test used for determinating the presence of sulfur atom in these compounds (11,12) ,it gave a ppositive test ,besides the melting points, FT-IR spectroscopy, and they checked by Gas chromotography. The FT-IR spectrum of compound (11) fig.,(9) as example confirmed the appearance of carbonyl group band at (1701-1716 cm^{-1}) and (C-H) aromatic band at (3091 cm^{-1}) and bands at (1267 and 1080cm^{-1}) belongs to asymmetric and symmetric (C-O-C) band and another band at (1141-1143 cm^{-1}) and (1359-1367 cm^{-1}) for symmetric and asymmetric of SO2 group this band is good evidence for the success of this step of reaction. All the FT-IR spectral data for these compounds are listed in table (4).

^{1}H-NMR spectrum of compound (11),figure(10),shows the following characteristic chemical shifts (DMSO- d_6, ppm):the aromatic ring protons as multiplate at(δ6.6-8.2)ppm , signal at (δ 9.25) due to the (C-H) proton in thiazepine ring.

^{13}C-NMR spectrum of compound (11) shows singlete signal at 167.0ppm for C=O in thiazepine ring,at 155 ppm for (-CH) in the same ring. But the ^{13}C-NMR spectrum of compound (12) shows singlete at 168.0ppm for (-CH) in thiazole ring fused with thiazepine ring,in 170.0ppm for (C=O) in the same ring the signal in 104.0 and 120 ppm due to the carbon atom in thiazole ring figure(12).

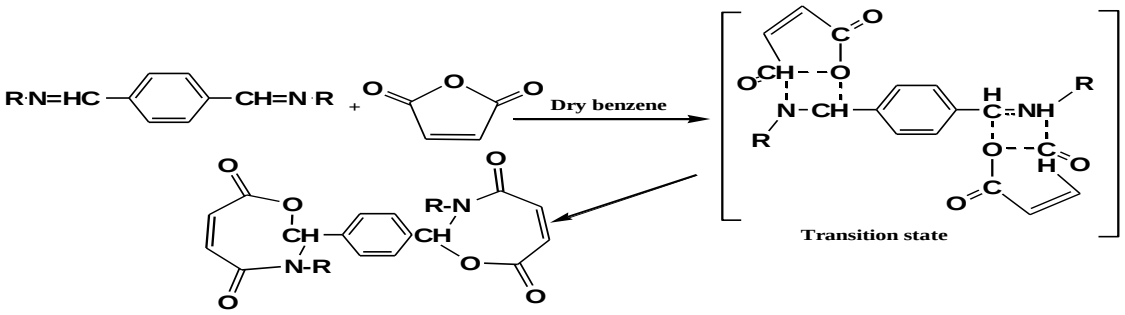
Finally the gas chromatography for compound (11) appeared one peak at retention time (5.00)min figure (13).

7-Synthesis and identification of oxazepine from Schiff base with maleic anhydride(13,14).



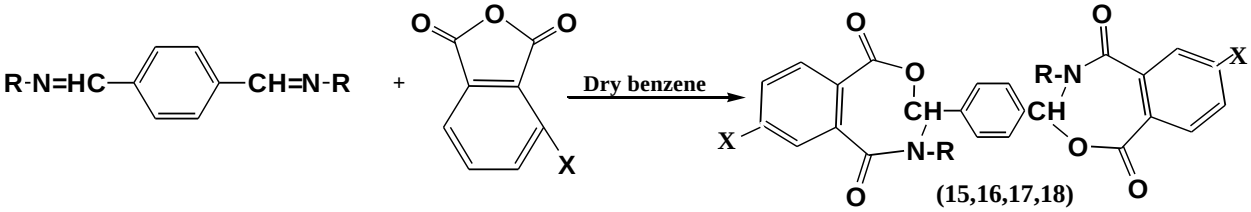
Schiff bases are known to react with cyclicanhydrides to give the corresponding addition products. Therefore, are expected to react with maleic anhydride to give oxazepine derivatives . The reaction of maleic anhydride with Schiff bases is a sort of cycloaddition reaction. Cycloaddition is a ring formation that results from the addition of π bonds to either σ or π bonds with formation of new σ-bonds. This class of reactions and its reverse encompasses a large number of individual types. Huisgen has formulated a useful classification of diverse cycloadditions in terms of the number of new σ bonds, the ring size of the product, and the

number of atoms in the components taking part in the cycloaddition. Our cycloaddition reaction is classified as a 5+2→7, implying 5-atom component plus 2-atom component leading to 7-membered cyclic ring. The suggested mechanism for formation of the oxazepine derivatives as follow in scheme bellow.



The prepared compounds were characterized by their melting points ,its colors, FT-IR spectroscopy ,C.H.N analysis ,and checked by T.L.C technique. The FT-IR spectra of compounds (13,14) , confirmed the appearance of two carbonyl groups lactones and lactam at(1717-1735) $cm^{-1}$for the lactone. The lactam at (1640-1660 cm^{-1}) and (C-H)aliphatic band at(2865-2880 cm^{-1}) and (C-H) aromatic band at (3089-3061 cm^{-1}) and bands at (1265 and 1091 cm^{-1}) belong to asymmetric and symmetric (C-O-C) band .All the FT-IR spectral data for these compounds are listed in table (5).

8- Synthesis and characterization of oxazepine from Schiff base with phthalic and nitro phthlic anhydride(15,16,17,18).



X=-H,-NO_2

Compounds (15,16,17,18 were prepared from the reaction of compound (1,2) Schiff bases with phthalic anhydride or 3- nitro phthalic anhydride in dry benzene. These compounds were characterized by their melting points and FT-IR H,NMR, ^{13}C-NMR spectra, C.H.N.S. analysis for some of them, and checked by T.L.C. The FT-IR spectrum of compound (15), (indicated the appearance of carbonyl group band at (1737-1718cm^{-1}) and (C-H) aliphatic band at (2891cm^{-1}) and bands at (1282 and 1072 cm^{-1}) attributed to the asymmetric and symmetric (C-O-C) band,. All FT-IR characteristic bands of compounds (15,16,17,18) are listed in table (6).

^{1}H-NMR spectrum of compounds (15), Fig. (14), shows the following characteristic chemical shifts, (DMSO-d_6) ppm., aromatic ring protons appeared at the

Microbiological tests:

In this work, the antibacterial test was performed according to the disc diffusion method. Compounds (10,12) were assayed for their antimicrobial activity in vitro against Gram-negative bacteria (*Escherichia coli*) and Gram-positive bacteria (*staphylococcus aurous*). Prepared agar and Petri dishes were sterilized by autoclaving for 15min at 121C°. DMSO was used as a solvent. These plates were incubated at 37C° for 24h for both bacteria. The inhibition zones caused by the various compounds were examined. The results of the preliminary screening tests are listed in table (8). The biological activity test showed that compounds with free (-SH) groups and free ($-NH_2$) groups having a biological effect on each of *E.Coli* and *Staph.aureus*, these compounds are also considered biologically active on *bacteria* while when free ($-NH_2$) and (-SH) groups disappeared the existence of Pyridine lead to increase of the biological activity.

Conclusion

1-Compounds [6] showed slightly activity on Escherichia coli and sale typhi.

2-Compound [15] showed moderate activity on *Staphylococcus aureus* and ps.aerugenosa while compound [8] showed slight activity on this bacteria .

3-Compounds [5] showed no effect on ps.aerugenosa and *Staphylococcus aureus* .

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Table (1): FT-IR spectral data of compounds [1,2].

Comp. No.	υ(C-H) aromatic cm^{-1}	υ(C-H) aliphatic cm^{-1}	υ(C=N) cm^{-1}	υ(C=C) cm^{-1}	Others cm^{-1}
1	3101	2912	1618	1690	υ(NO_2) 1350-1415
2	3100	2974	1600	1589	υ (C-S) 671

Table (2): FT-IR spectral data of compounds [5,6].

Comp. No.	υ(C-H) aromatic cm^{-1}	υ(C=C) aromatic cm^{-1}	υ(N=N) cm^{-1}		Others bands cm^{-1}
5	3040	1595	1506		υ(NO2) 1533and 1367
6	3051	1587	1520		υ(C=N)1649 in thiazoline ring

Table (3): FT-IR spectral data of compounds [9,10].

Comp. No.	υ(C-H) aromatic cm^{-1}	υ(C=C) aromatic cm^{-1}	υ(N-H) cm^{-1}	υ(C=O) cm^{-1}	Others bands cm^{-1}
9	3068	1595	3361	1676	υ(NO2) 1533and 1303
10	3064	1589	3373	1674	υ(C=N)1616 in thiazole ring

Table (4): FT-IR spectral data of compounds [11,12,].

Comp. No.	υ(C-H) aromatic cm^{-1}	υ(C=C) aromatic cm^{-1}	υ(-SO_2) cm^{-1}	υ(C=O) cm^{-1}	Other bands cm^{-1}
11	3091	1597	1143 & 1359	1676	υ(NO_2) 1544and 1348
12	3095	1580	1141& 1367	1645	υ(C=N)1616 in thiazole ring

Table (5): FT-IR spectral data of compounds [13,14,].

Comp. No.	υ(C-H) Aliphatic cm^{-1}	υ(C-H) aromatic cm^{-1}	υ(C=O) cm^{-1} lactone	υ(C=O) cm^{-1} lactam	υ(C=C) cm^{-1}Ar	Others bands cm^{-1}
13	2880	3089,	1717	1640	1568	υ(NO_2) 1336, 1556 υ(C-N) 1182 υ(C-O) 1273
14	2856	3061	1735	1660	1570	υ(C=N) 1660fused with(C=O) υ(C-N) 1133 υ(C-O) 1256

Table (6): FT-IR spectral data of compounds (15,16,17,18).

Comp. No.	υ(C-H) Aliphatic cm^{-1}	υ(C-H) aromatic cm^{-1}	υ(C=O) lactone cm^{-1}	υ(C=O) lactam cm^{-1}	υ(C=C) cm^{-1}Ar	Others bands cm^{-1}
15	2891	3101	1737	1674	1600	υ(NO_2) 1340, 1581 υ(C-N) 1192 υ(C-O) 1282
16	2891	3030	1718	1653	1585	υ(C=N) 1620 υ(C-N) 1153 υ(C-O) 1280

17	2893	3050	1732	1654	1537	υ(NO_2) 1581,1340 υ(C-N) 1155 υ(C-O) 1251
18	2820	3035	1739	1640	1585	υ(NO2) 1533,1350 υ(C-N) 1170 υ(C-O) 1211

Table (7) :Antimicrobial activity for some prepared compounds .

Comp. No.	*Staph. aureus*	*E. coli*	*Sal. typhi*	*Ps. Aerugenosa*
5	-	±	±	-
6	-	±	±	-
7	-	+	-	±
8	+	+	+	±
9	-	±	-	-
10	+	++	-	±
11	+	+	-	+
12	+	++	±	++
13	+	+	-	++
14	+	±	-	++
15	++	±	±	++
17	-	±	-	±
18	-	+	-	+

Key the symbols :(-) = No inhibition , (±) = 6-9 mm, (++) = 15-22 mm.

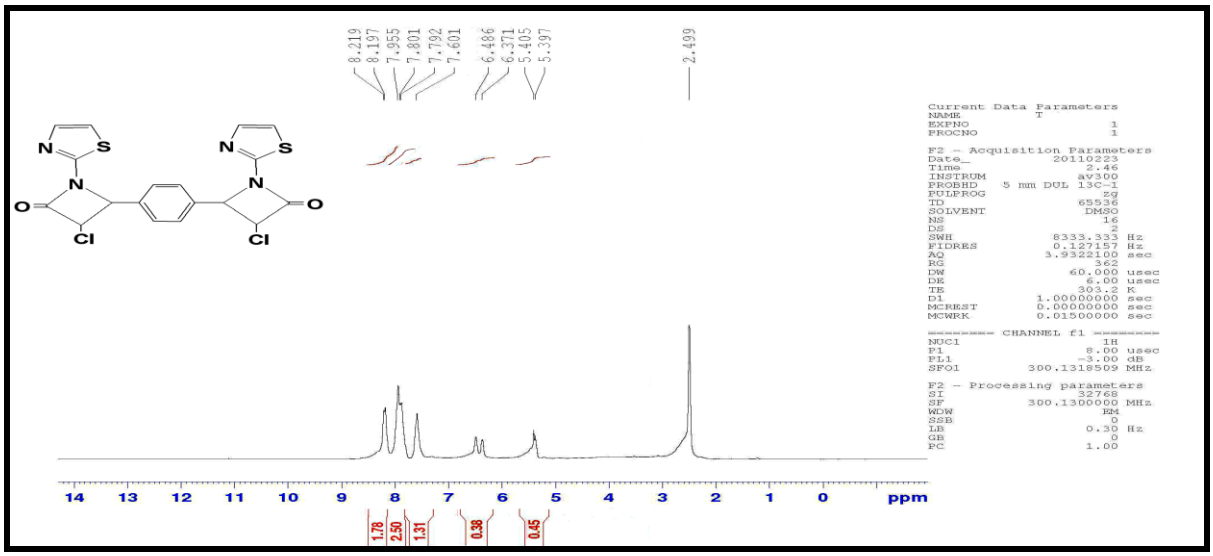


Fig. (1): ^{1}H-NMR spectrum of compound (4).

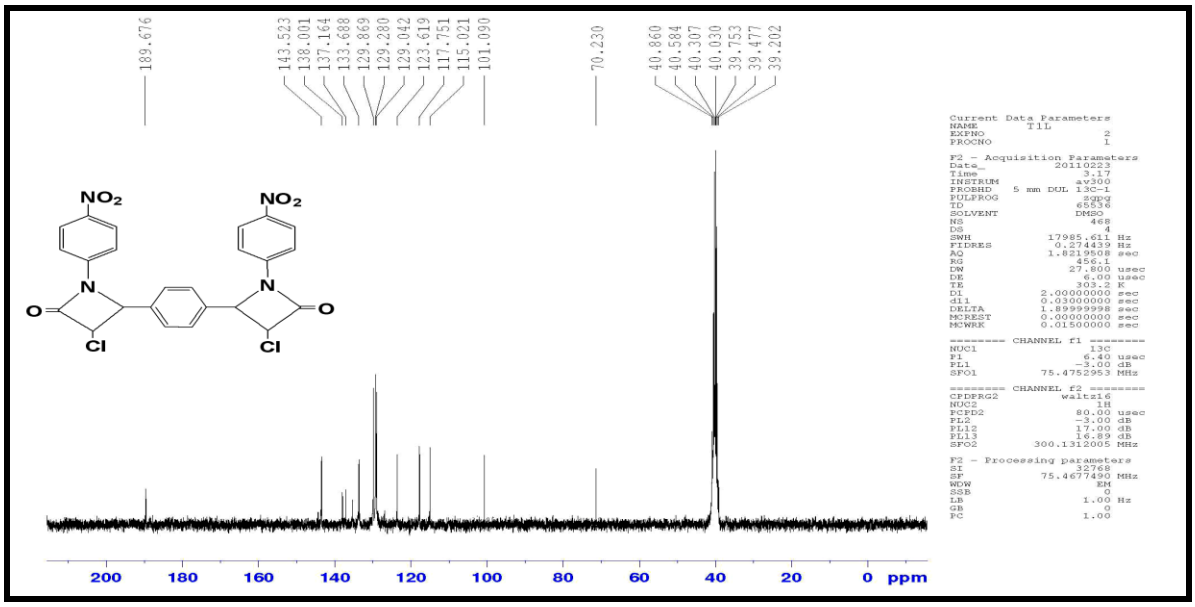


Fig. (2): ^{13}C-NMR spectrum of compound (3).

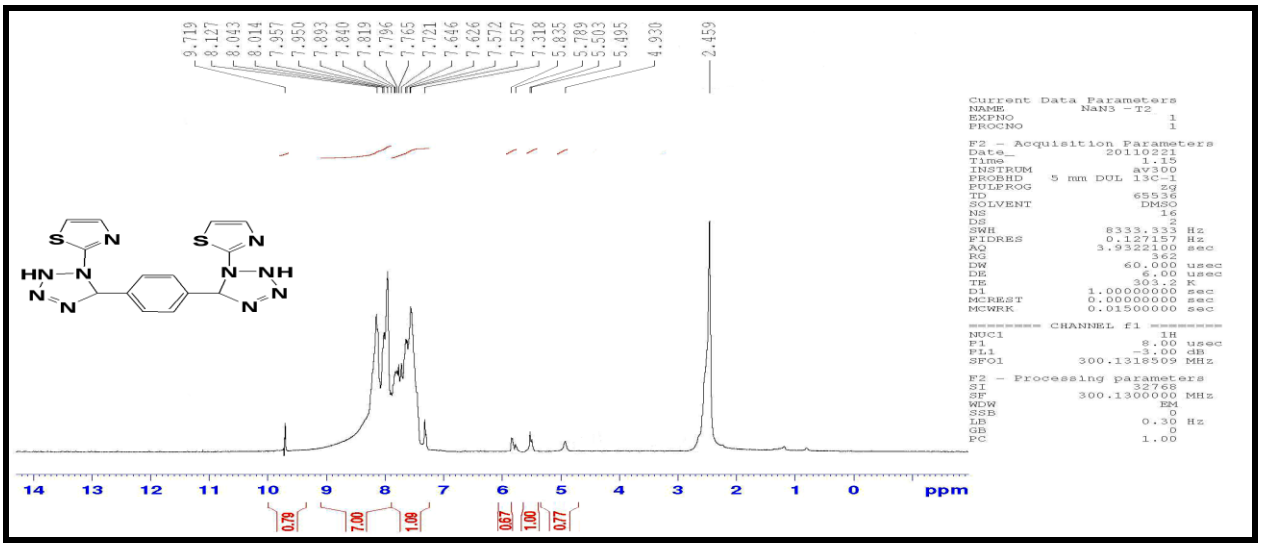


Fig (3): ^{1}H-NMR spectrum of compound (6).

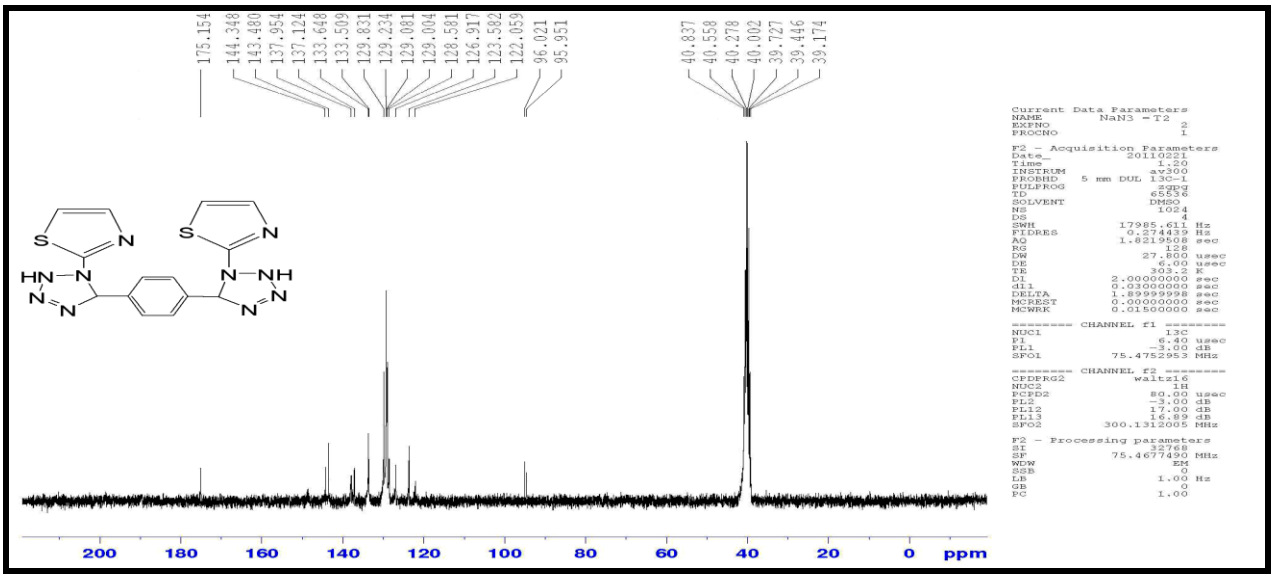


Figure (4) ^{13}C-NMR spectrum of compound 6.

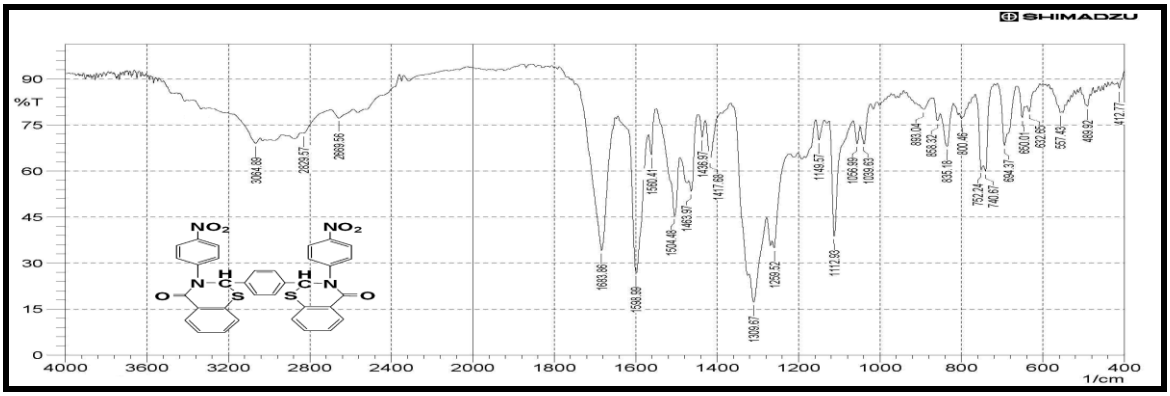
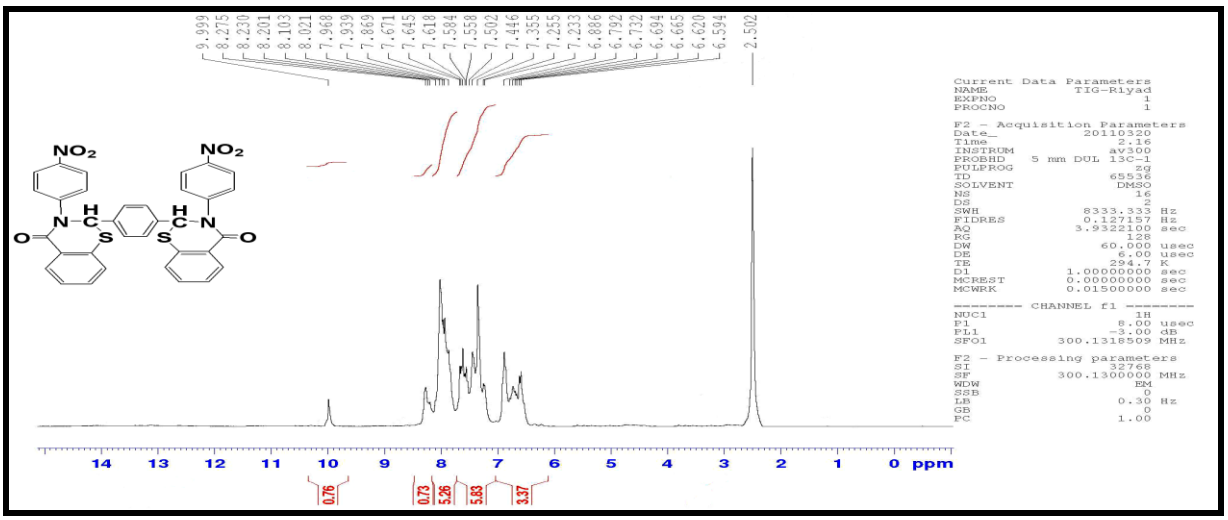


Figure (5) :FT-IR spectrum of compound (7).



figure(6):^{1}H-NMR spectrum of compound (7).

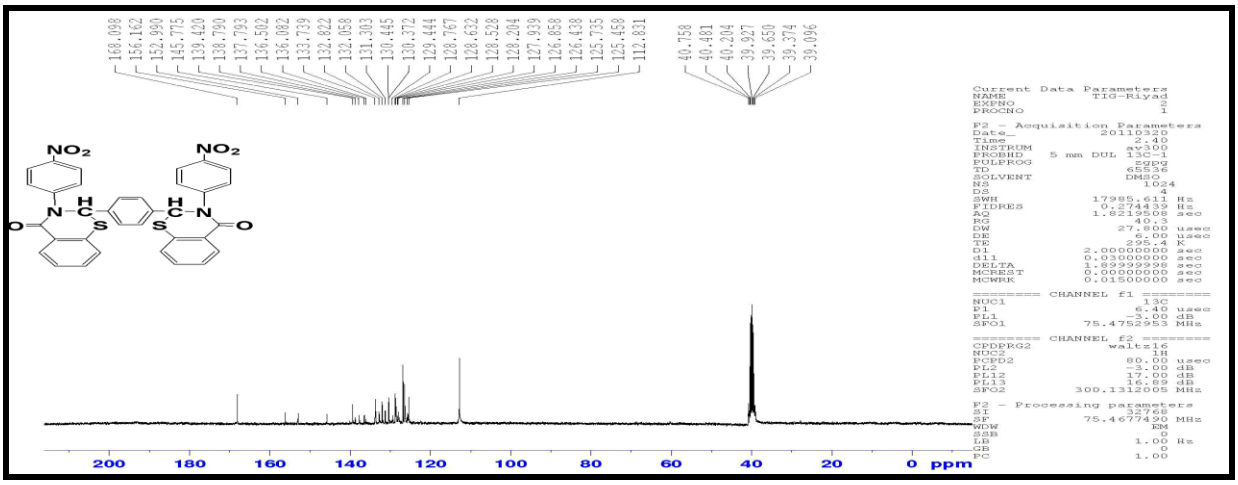


Figure (7): ^{13}C-NMR spectrum of compound (7).

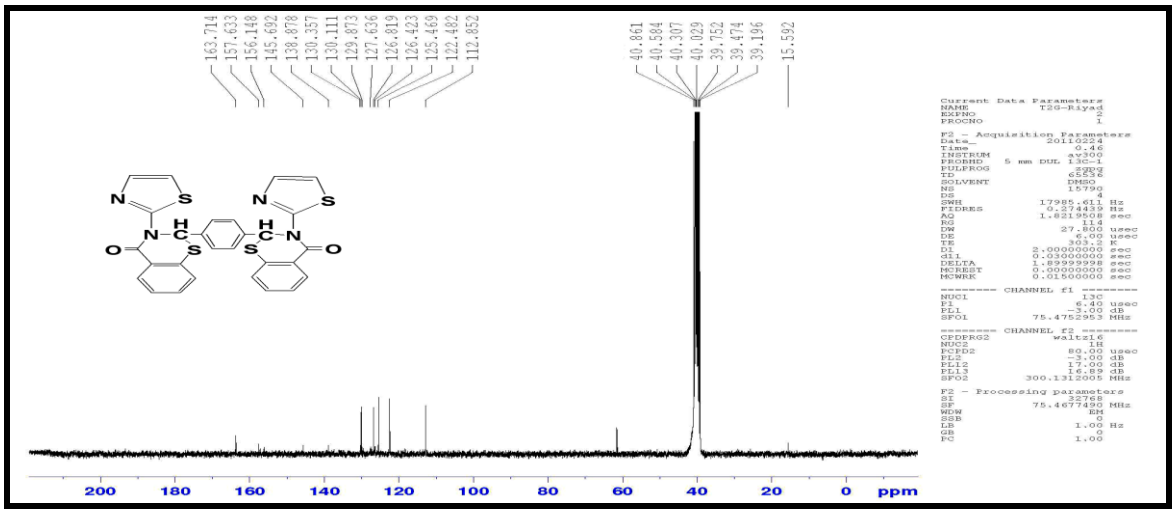


Figure (8): ^{13}C-NMR spectrum of compound (8).

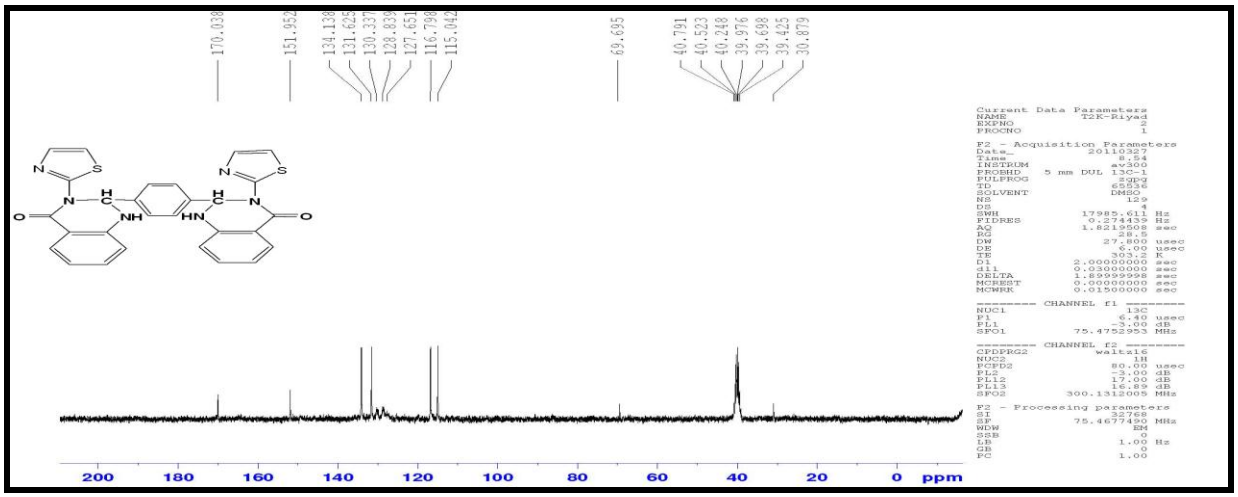


Figure (8): ^{13}C-NMR spectrum of compound (10).

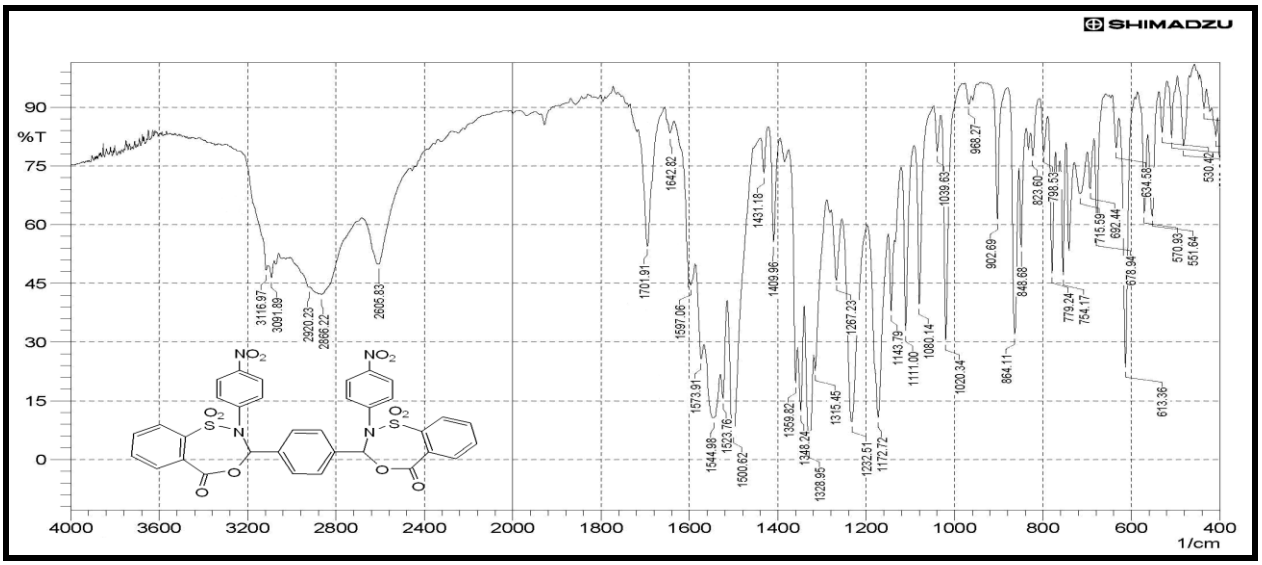
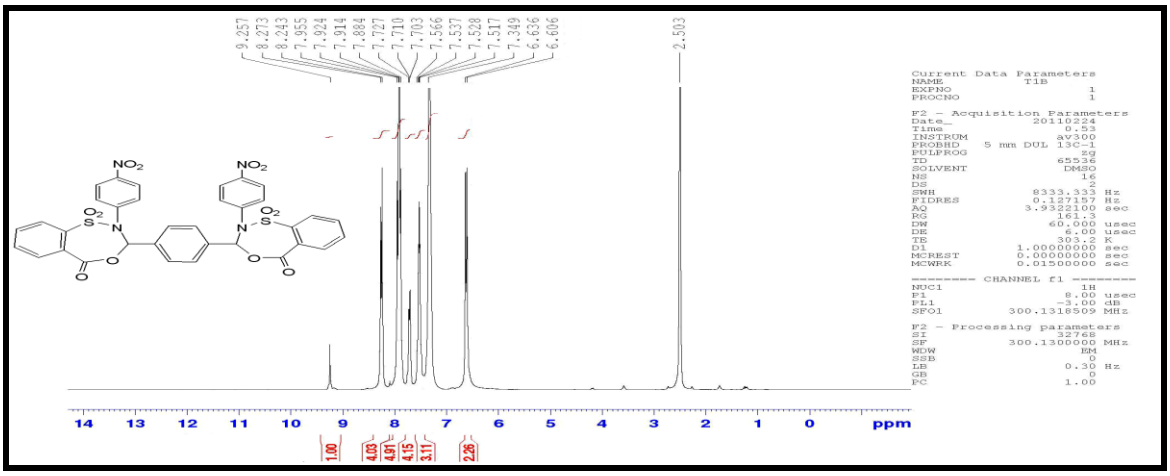


Figure (9) : FT-IR spectrum of compound (11).



figure(10):^{1}H-NMR spectrum of compound (11).

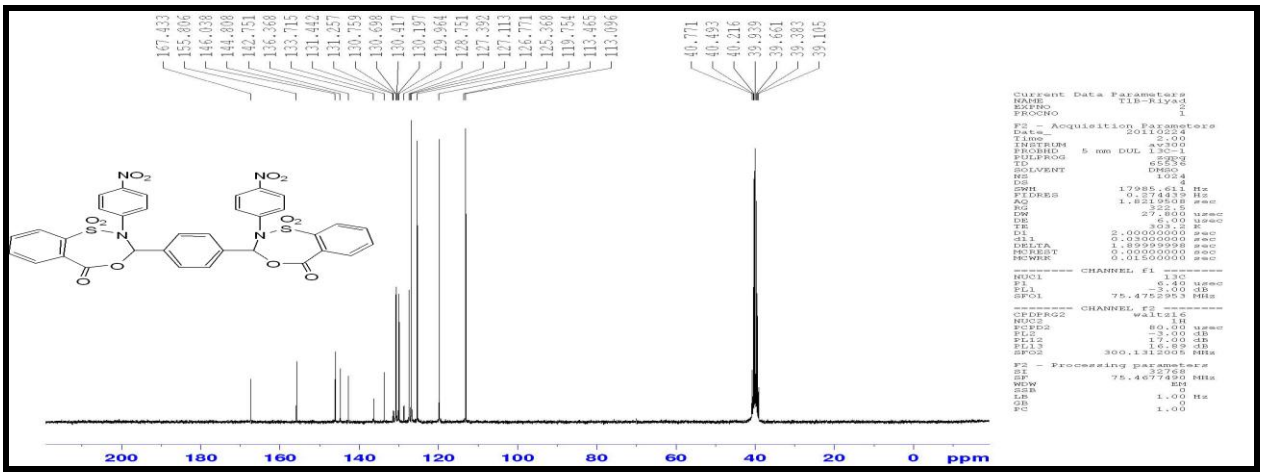


Figure (11): ^{13}C-NMR spectrum of compound (11).

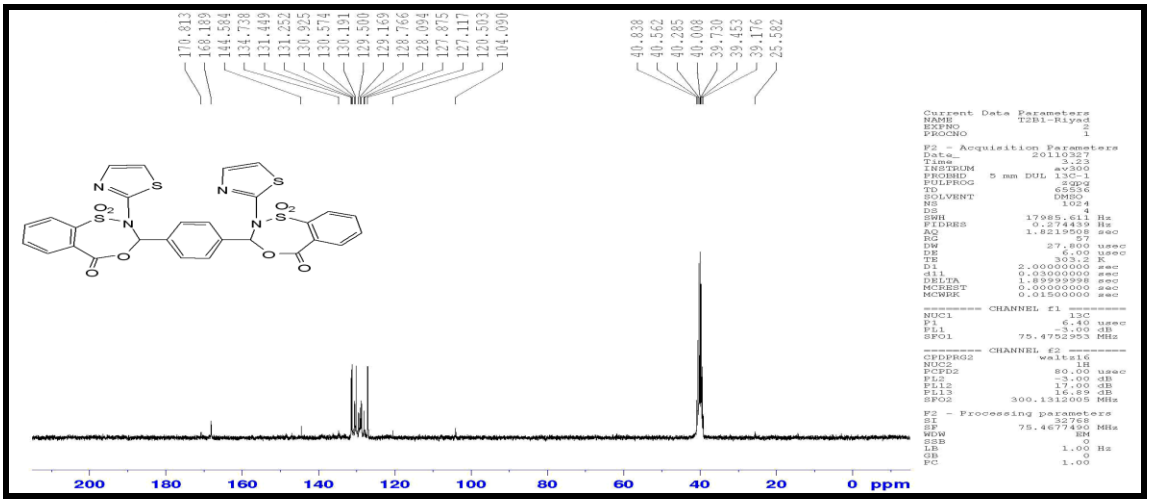
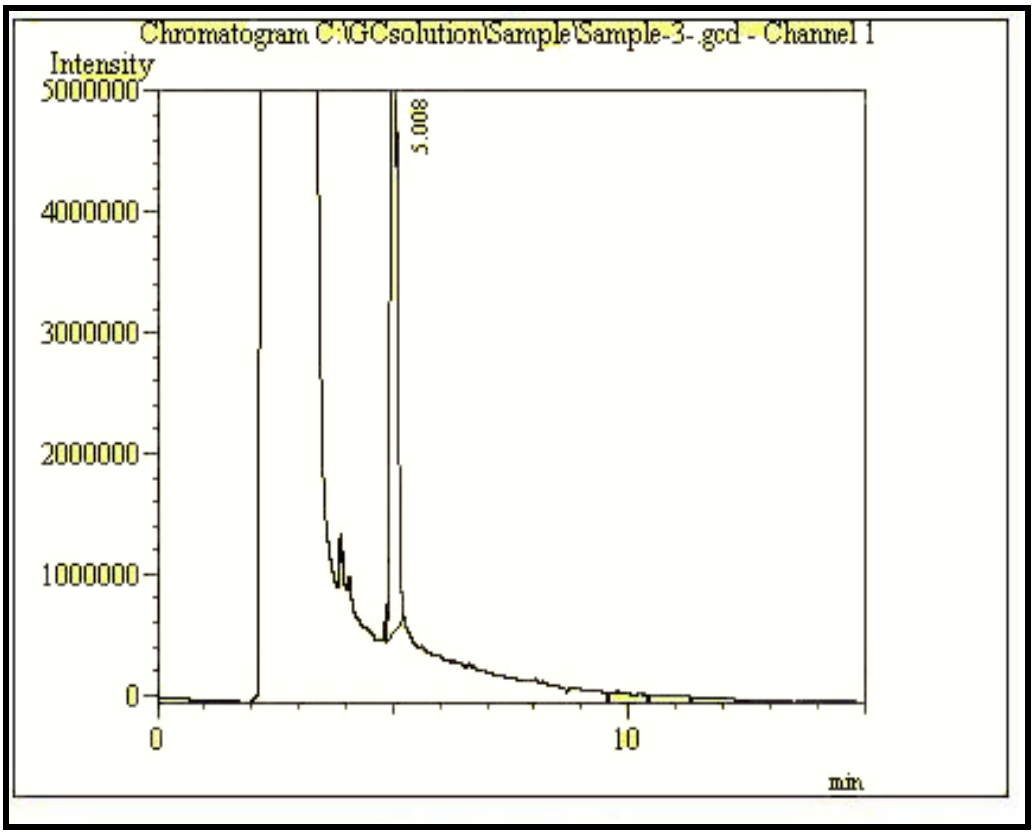
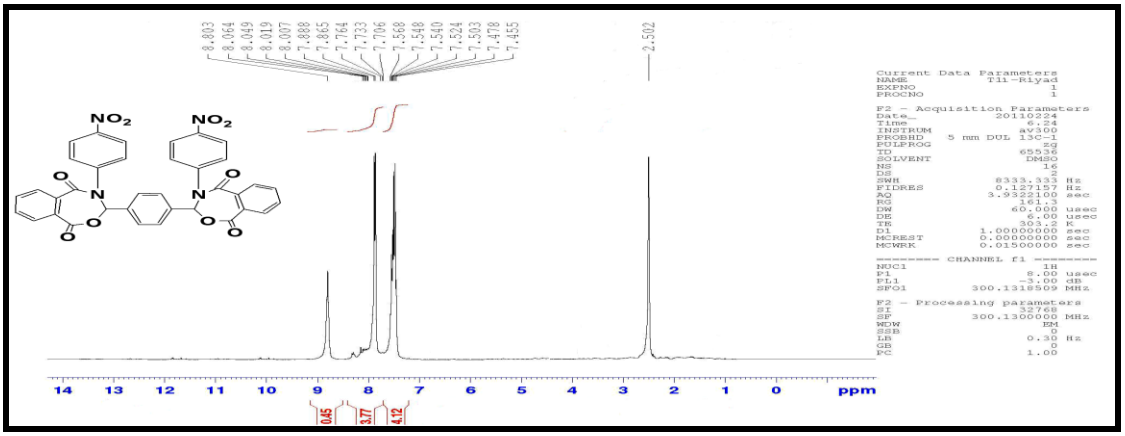


Figure (12): ^{13}C-NMR spectrum of compound (12).



Peak;#	Ret.time	area	Area%	Conc.
1	5.008	6149	100.000	0.000
total	-	7017	100.000	-

Fig (13).



figure(14):^{1}H-NMR spectrum of compound (15).

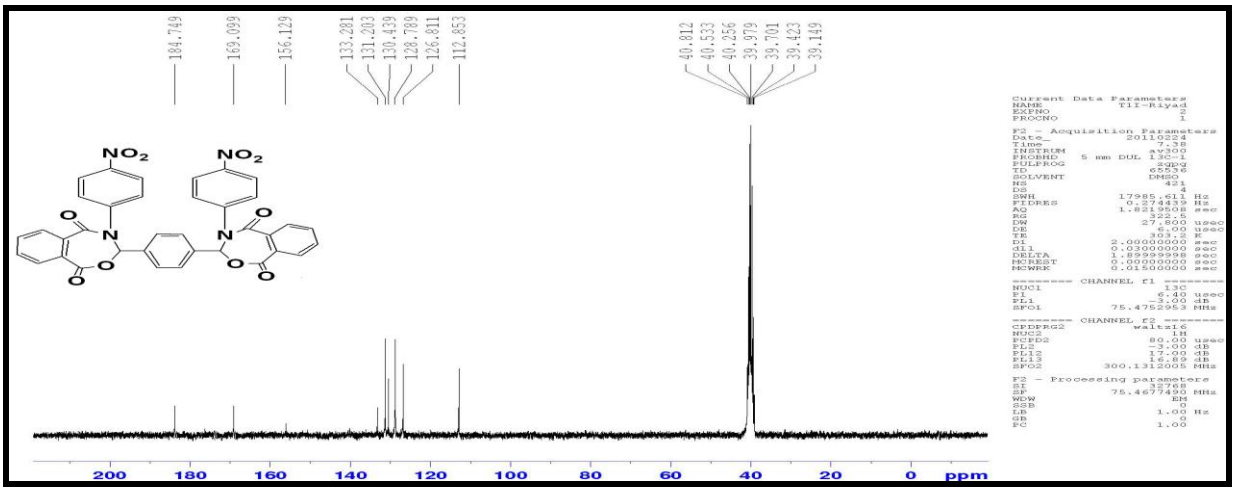


Figure (15): ^{13}C-NMR spectrum of compound (15).