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Synthesis and Characterization of Some New Quinoline-2-one, Schiff bases, Pyrazole and Pyrazoline Compounds Derived From Hydrazide Containing Isoxazoline or Pyrimidine Cycles

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Abstract

The work involves synthesis of new quinolin-2-one Schiff bases $(XIII)_{a,b}$ and $(XIV)_{a,b}$, pyrazoles $(XI)_{a,b}$ and pyrazolines $(XII)_{a,b}$ derivatives containing isoxazoline or pyrimidine cycle starting with chalcones. 3-Aminoacetophenone was reacted with 4-bromobenzaldehyde or 4-N,N-dimethyl aminobenzaldehyde in basic medium to give chalcones $(I)_{a,b}$ by Claisen-Schemidt reaction. These chalcons were reacted with hydroxylamine hydrochloride or with thiourea in basic medium to form isoxazolines $(II)_{a,b}$ or pyrimidine-2-thion $(III)_{a,b}$,respectively.Also the pyrimidine-2-thiones $(III)_{a,b}$ and isoxazolines $(II)_{a,b}$ reacted with 4-or 3-substituted benzaldehyde and coumarin to form Schiff bases $(IV)_{a-f}$ $(V)_{a-f}$ and quinoline derivatives $(VII)_{a-d}$$(VIII)_{a-d}$, respectively. On the other hand, compounds $(V)_{b,f}$ were reacted with ethylchloroacetate in basic medium to give ester compounds $(IX)_{a,b}$ .The condensation of new esters $(IX)_{a,b}$ with hydrazine hydrate led to produce new acid hydrazides $(X)_{a,b}$.The later compound refluxing with 4-substituted benzaldehyde in dry benzene to give Schiff bases $(XIII)_{a,b}$and $(XIV)_{a,b}$ while the reaction of acid hydrazides $(X)_{a,b}$ with acetyl acetone or ethyl aceto acetate led to formation of pyrazole $(XI)_{a,b}$, pyrazoline $(XII)_{a,b}$,respectively. The synthesized compounds were characterized by melting points, FTIR,C.H.N.analysis, Mass and ^{1}H NMR spectroscopy(of someof them) Some of the synthesized compounds have been screened for their antibacterial activities using two types of bacteria; *E. Coli* and *Staph. aureus*. All the examined compounds did not show any biological activity towards *E. Coli* but compound $(VII)_a$ showed activity towards *Staph. aureus.*

Keywords: Chalcones, Schiff bases, Isoxazoline, Pyrimidine, Quinolone, Pyrazole, Pyrazoline.

تحضير و تشخيص بعض مركبات الكوينولين-2-اون و قواعد شف و بايارازول و بايارازولين الجديدة و المشتقة من الهيدرازيد الحاوي على حلقة الأيزوكسازولين أوالبيرمدين

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الخلاصة

يتضمن هذا البحث تحضير مشتقات جديدة لكوينولين-2-اون وقواعد شف$(XIII)_{a,b}$ و$(XIV)_{a,b}$ و بايرازول $(XI)_{a,b}$ وبايرازولين$(XII)_{a,b}$ تحتوي على وحدة الايزوكسازولين و البيريميدين بأستعمال الجالكون كمادة أساسية ،يحضر الجالكون من تفاعل3-أمينوأسيتوفينون مع 4-برومو بنزالديهايد أو4-N,N ثنائي مثيل أمينو بنزالديهايد في وسط قاعدي . يتفاعل الجالكون $(I)_{a,b}$ مع هيدروكسيل أمين هايدروكلورايد او مع الثايويوريا في وسط قاعدي ليعطي الايزوكسازولين $(II)_{a,b}$ أو البيرميدين-2-ثايون على التوالي أيضا تمت

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مفاعلة البيرمدين $(III)_{a,b}$ أو الايزوكسازولين $_{a,b}$ (II) مع الديهايدات اروماتية معوضة أو مع الكيومارين لنحصل على قواعد شف جديدة $(V)_{a-f}$ $(IV)_{a-f}$ ومشتقات الكوينولين $(VII)_{a-d}$, $(VIII)_{a-d}$ ، على التوالي . ومن تكثيف المركبات $(V)_{b, f}$ مع أثيل كلورو أسيتيت في وسط قاعدي حصلنا على مركبات أسترية والتي تم تكثيفها مع الهايدرازين للحصول على الهايدرازايد $_{a,b}$ (X) الذي يصعد مع البنزلديهايد المعوض ليعطي قواعد شيف $(XIII)_{a,b}$ و $(XIV)_{a,b}$.واخيرا تم تحضير مركبات البايارازول $_{a,b}$ (XI) و البايارازولون $_{a,b}$ (XII) من تفاعل الهايدرازايد مع أستيل أسيتون أو أثيل أسيتو أستيت على التوالي. شخصت جميع المركبات المحضرة بوساطة قياس درجات أنصهارها ومن التحليل الدقيق للعناصر و طيف FTIR و طيف الكتلة و ^1H NMR(لبعض منها) كما درست الفعالية البايولوجية لبعض من المركبات المحضرة ضد نوعين من البكتريا وهي*S. aureus* و*E.coli* ولم تظهر جميع المركبات المدروسة اي فعالية بايولوجية تجاة البكتريا السالبة *E.coli* بينما اظهر المركب $(VII)_a$ فعالية تجاة البكتريا الموجبة *S. aureus*.

Introduction

Chalcones were prepared by condensation of acetophenone with aromatic aldehydes in a basic medium [1]. The Chalcone derivatives are important intermediates and also act as precursor for the synthesis of novel cyanopyridines, pyrazolines, isoxazoles, pyrimidines and tetrazole [2]. Five-membered heterocyclic compounds isoxazoline are important for pharmaceutical industry and material science due to their various applications. Isoxazolines are present in the structures of many natural products. In fact, isoxazolines have a broad spectrum of biological and pharmacological activities [3-6]. While, six membered heterocyclic, Pyrimidine can be regarded as a cyclic amine. Pyrimidine is also known 1,3-diazine. It is the parent substance of large group of heterocyclic compounds and plays a vital role in many biological processes. It is found in nucleic acids, several vitamins, co-enzymes and purines [7,8].The derivatives of quinolone have been known to possess various biological activities such as antitumor, antimalarial, antiplatetet, anti-inflammatory and anticonvulsant activities[9,10].
Pyrazoles are one of the important members of heterocyclic compounds with two adjacent nitrogens in a five-membered ring system. Because of their aromaticity and wide application in pharmaceutical and material industry, they have gained significant interest among the scientist [11-14]. Also the pyrazoline showed a wide spectrum of biological activities such as antibacterial, antifungal, anti-choligenic and herbicidal [15-19]. In the view of the varied biological, pharmacological and industry applications .we have planned to synthesize some isoxazoline derivatives and pyrimidine derivatives containing imine, pyrazole or pyrazoline unit.

Experimental

Chemicals

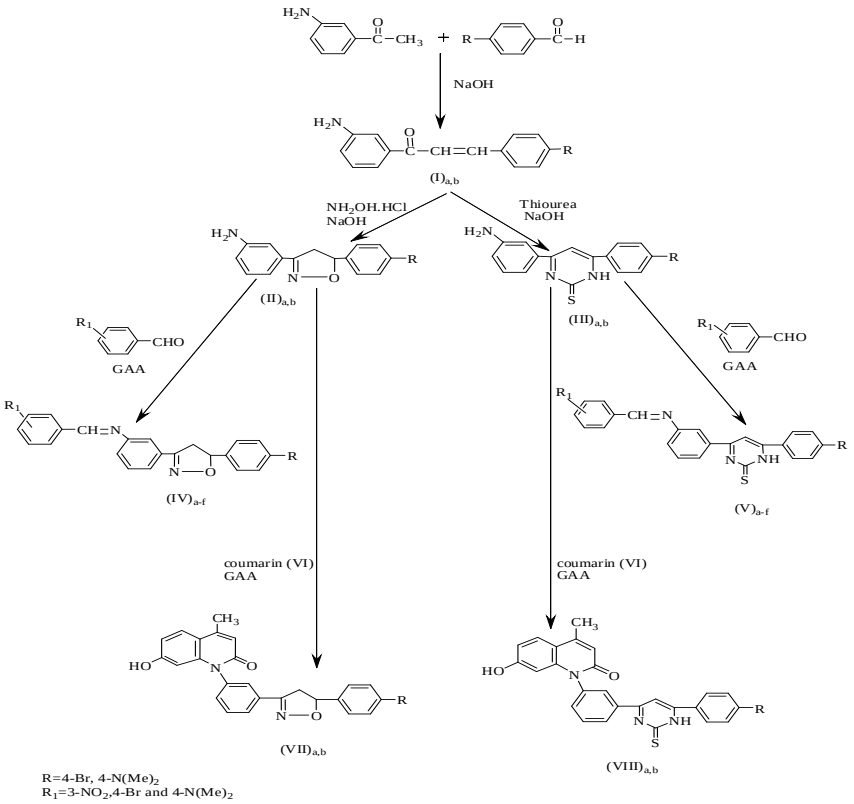
All chemicals were supplied by fluka, GCC, merck and Aldrich chemicals Co. and used as received.

Instruments

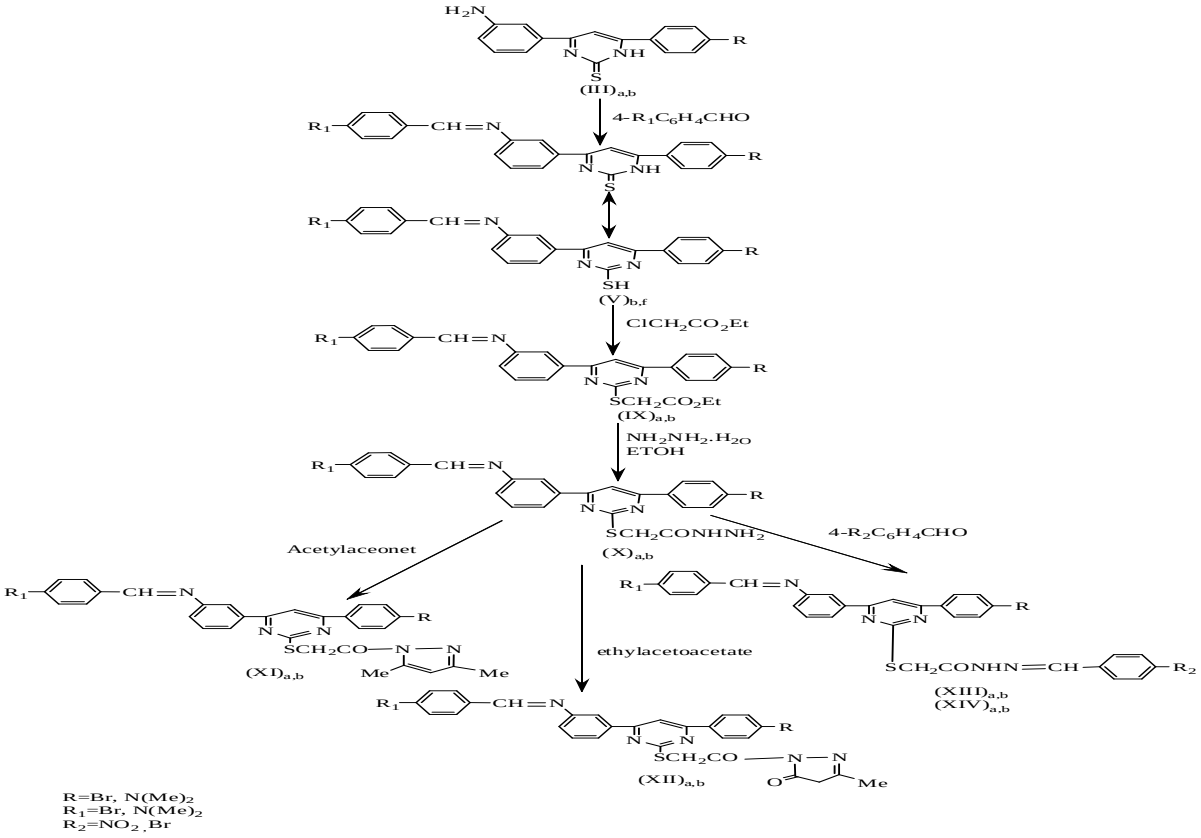
FTIR spectra were recorded using potassium bromide discs on a Shimadzo (IR prestige -21), ^{1}HNMR spectra were recorded on : Bruker , model: ultra-shield 400 MHz , origin : Switzerland and are reported in ppm(δ), DMSO-d_6 was used as a solvent with TMS as an internal standard, were made at chemistry department , Science and Technology University, Jordan and ^{1}HNMR spectra were recorded on: Bruker , model: ultra-shield 300 MHz , origin : Switzerland and are reported in ppm(δ), DMSO –d_6 was used as a solvent with TMS as an internal standard at chemistry department , Al-Bayt University, Jordan . Elemental microanalysis of some compounds were performed on a : Euro vector, model EA 3000 origin : Italy, at University of Baghdad, College of Education for Pure Science (Ibn-Al-Haitham),. The Mass spectrum was recorded on shimadzu model 6CMS QL 1000 EX, made in Japan. Uncorrected melting points were determined using Hot-Stage, Gallen Kamp melting point apparatus.

Synthesis

New compounds are synthesized according to Scheme-1 and 2.



Scheme 1



Scheme 2

Synthesis of (chalcones) 3-[3(4`-bromo or N,N-dimethylaminophenyl)-2-propene-1-one] aniline(I)$_{a,b}$

Equimolar quantities of 3-amino acetophenone (0.01 mol, 1.35g) and 4-substituted benzaldehyde (0.01 mol) were dissolved in minimum amount of alcohol. Sodium hydroxide solution 40% (0.02 mol, 0.78g in 1.95 mL) was added slowly then cooled the mixture. The mixture was poured slowly into 400 mL of ice water with constant stirring and kept in refrigerator for 24 h. The precipitate obtained was filtered [20], washed and recrystallized from ethanol.

Synthesis of 3-(3`-aminophenyl)-5-(4`-bromo or N,N-dimethylaminophenyl)-4,5-dihydroisoxazole (II)$_{a,b}$

A mixture of chalcone (0.02 mol) , hydroxylamine hydrochloride (0.02 mol , 1.39 g) and sodium hydroxide solution (0.5 g NaOH in 25 mL of water) in ethanol (60 mL) was refluxed for 6h. The mixture was concentrated under vacuum and poured on to ice water [6]. The precipitate obtained was filtered, washed and recrystallized from ethyl acetate.

Synthesis of 4-(3`-aminophenyl)-6-(4`-bromo or 4`-N,N-dimethyl amino phenyl)pyrimidine-2(1H)-thione. (III)$_{a, b}$

A mixture of chalcone (0.01mol), thiourea (0.01mol,7.6g) and sodium hydroxide (0.1g) in (25 mL) of 80%(v\v) ethanol was refluxed for 6h. The reaction mixture was concentrated [8] cooled and the solid was filtered off, washed with water, dried and then recrystallized from ethanol. Elemental analysis of compound (III)$_a$:

Calc.: C%= 53.63, H%= 3.35, N%= 11.73

Found: C%=53.99, H%=4.21, N%= 12.69

The physical properties of compounds (I)-(III) are listed in Table-1.

Synthesis of Schiff base derivatives (IV)$_{a-f}$ and (V)$_{a-f}$

A mixture of new amino compound (II)$_{a,b}$, (III)$_{a,b}$ (0.01 mol) and different aromatic aldehyde (0.01 mol) in dry benzene (15 mL) containing 3 drops of glacial acetic acid was refluxed for 6h. [21] The solvent was evaporated under vaccum and the residue crystallized from ethyl acetate.

Synthesis of 7-hydroxy -4-methyl coumarin (VI)

A mixture of resorcinol(0.01 mol, 1.101g) and ethylaceto acetate (0.01mol, 1.274 mL) with 75% H_2SO_4 (10 mL) was heated under reflux for one hour. The resultring dark green solution was cooled and poured over crushed ice .The crude product was filtered off and washed repeatedly with water and dried at100 ^{0}C, for purification it was first dissolved in cold 10% aqueous sodium hydroxide solution and reprecipitated by the addition of dilute hydrochloric acid and it was recrystallized from ethanol to yield pink solid,[9]yield 90% ,m.p=180-182 ^{0}C.

Synthesis of qunoline derivatives (VII)$_{a,b,}$ (VIII)$_{a,b}$

Equimolar amounts of 7-hydroxy-4- methyl coumarin (0.01 mol, 1.76g) and new heterocyclic amine compounds (0.01mol) in glacial acetic acid (10mL) was refluxed for 6h. The excess solvent was distilled off under reduced pressure and poured onto crushed ice to afford the solid .The product obtained was filtered and dried at room temperature [9]. It was purified by recrystallization from ethanol.The physical properties of Schiff bases (IV),(V) and quinolin-2-one derivatives(VII),(VIII)are listed in Table-2.

Synthesis of new ester derivatives (IX)$_{a,b}$

A mixture of compounds (V)$_{b,f}$ (0.01mol) ,ethyl α- chloro acetate (0.01 mol, 1.5mL) and fused sodium acetate (0.03mol,2.46g) in ethanol (25mL) was refluxed for 4h. [22] Then cooled and poured on to cold water, the resulting solid was filtered and recrystallized from ethyl acetat to give a new ester.

Synthesis of hydrazide derivatives (X)$_{a, b}$

A solution of ester (IX)$_{a,b}$ (0.06 mol) and hydrazine hydrate(15mL) in(25mL) of ethanol was heated under reflux during 4h. [23] The mixture was then cooled to room temperature, and the solid obtained was filtered and recrystallized from petroleum ether b.p=60-80^{0}C.

Synthesis of pyrazole and pyrazoline derivatives (XI)$_{a,b}$ and (XII)$_{a,b}$

A mixture of new hydrazide **(X)$_{a,b}$** (0.028 mol) and $CH_3COCH_2COCH_3$ or $CH_3COCH_2CO_2Et$ (0.028 mol) in abs. EtOH(40mL) was refluxed for 3h. [24] The reaction mixture was cooled and the formed precipitate was filtered off and recrystallized to give new pyrazoles (XI)$_{a, b}$ or pyrazoline(XII)$_{a, b}$,respectively. . Elemental analysis of compound (XI)$_b$:

Calc.: C%= 69.26, H%= 5.94, N%= 16.63

Found: C%=68.66, H%=6.91, N%= 15.09

Synthesis of Schiff base derivatives (XIII)$_{a,b}$, (XIV) $_{a,b}$

A mixture of new hydrazide**(X)$_{a,b}$** (0.01 mol) , different aromatic aldehydes (0.012 mol) , in absolute ethanol (10 mL)was refluxed for 3h. [25] The solvent was evaporated under vacuum and the residue recrystallized from chloroform. The physical properties of new compounds (IX)-(XIII) are listed in Table-3.

Table 1- The physical properties of Chalcones (I)$_{a, b}$ and compounds (II)$_{a,b}$-(III)$_{a,b}$

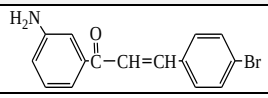
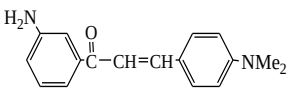
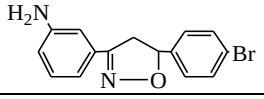
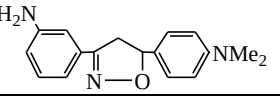
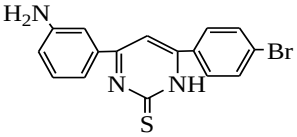
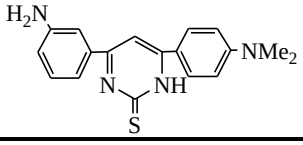
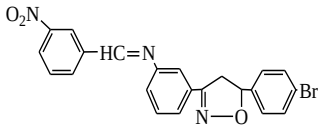
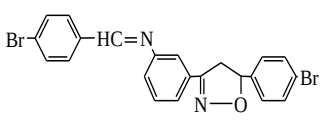
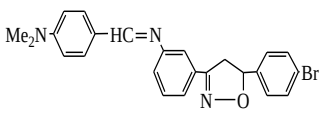
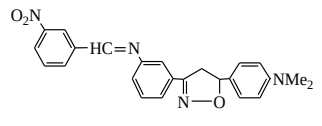
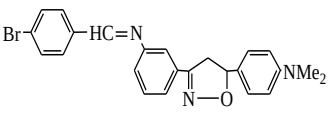
Com No.	Nomenclature	Structural formula	Molecular Formula	M. P ^{0}C	Yield %	Color
(I)$_a$	1-(3`-aminophenyl)-3-(4``-bromophenyl)-2- propene-1-one		$C_{15}H_{12}NOBr$	130-132	90	Yellow
(I)$_b$	1-(3`-aminophenyl)-3-(4``-N,N-dimethylphenyl)-2-propene-1-one		$C_{17}H_{18}N_2O$	115-118	34	Pale Orange
(II)$_a$	3-(3`-aminophenyl)-5-(4``-bromophenyl)-4,5-dihydroisoxazole		$C_{15}H_{13}N_2OBr$	92-93	50	Off white
(II)$_b$	3-(3`-aminophenyl)-5-(4``-N,N-dimethylphenyl)-4,5-dihydroisoxazole		$C_{17}H_{19}N_3O$	64-67	74	orange
(III)$_a$	4-(3`-aminophenyl)-6-(4``-bromophenyl)pyrimidine -2(1H)-thione.		$C_{16}H_{12}N_3SBr$	140-142	80	Yellow
(III)$_b$	4-(3`-aminophenyl)-6-(4``-(N,N-dimethylamino) phenyl)pyrimidine-2(1H)-thione .		$C_{18}H_{18}N_4S$	60-63	50	orange

Table 2- The physical properties of compounds(IV)$_{a-f}$, (V)$_{a-f}$, (VII)$_{a,b}$ and (VIII)$_{a, b}$

Com. No.	Nomenclature	Structural formula	Molecular formula	M. P ^{0}C	Yield %	Color
(IV)$_a$	3[3-(3`-nitrobenzylideneamino) phenyl]-5-(4``-bromophenyl)-4-5-dihydroisoxazole		$C_{22}H_{16}N_3O_3Br$	100-102	42	Yellow
(IV)$_b$	3[3-(4`-bromobenzylideneamino) phenyl]-5-(4``-bromophenyl)-4,5-dihydroisoxazole		$C_{22}H_{16}N_2OBr_2$	170-172	29	Off white
(IV)$_c$	3[3-(4`-N,N-dimethylamino benzylidene amino)phenyl]-5-(4``-bromo phenyl)-4,5-dihydroisoxazole		$C_{24}H_{22}N_3OBr$	120-122	53	Orange
(IV)$_d$	3[3-(3`-nitrobenzylideneamino) phenyl]-5-(4``-N,N-dimethyl amino phenyl)-4-5-dihydroisoxazole		$C_{24}H_{22}N_4O_3$	gummy	31.5	Brown
(IV)$_e$	3[3-(4`-bromobenzylideneamino) phenyl]-5-(4``-N,N-dimethyl amino phenyl)-4,5-dihydroisoxazole		$C_{24}H_{22}N_3OBr$	gummy	55	Black

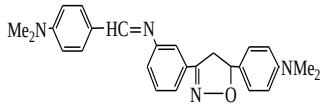
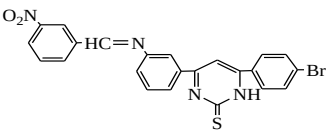
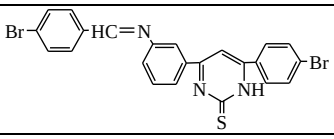
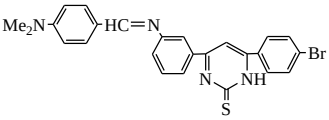
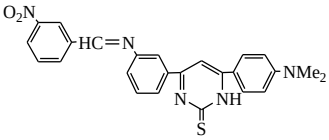
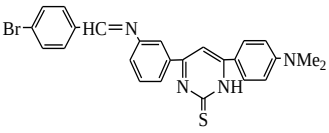
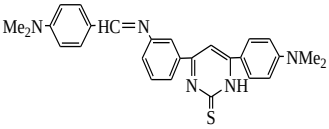
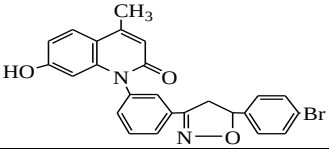
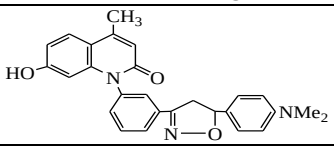
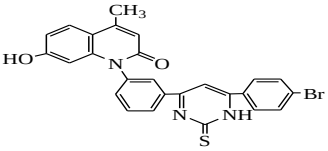
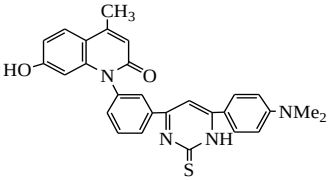
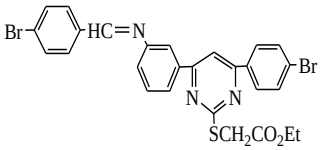
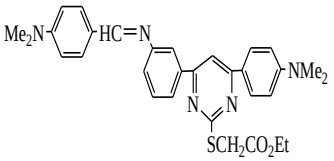
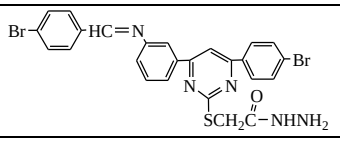
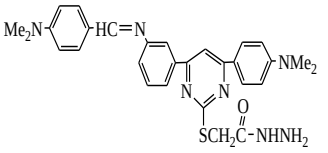
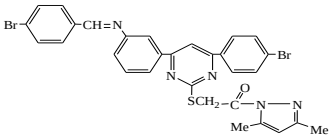
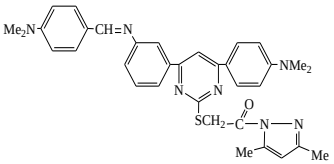
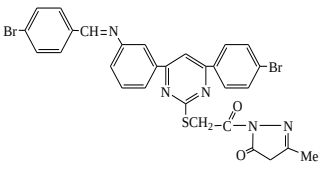
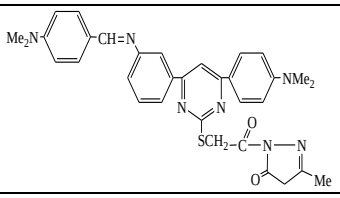
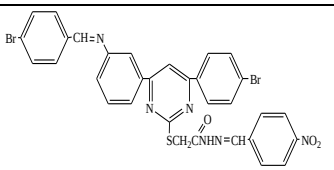
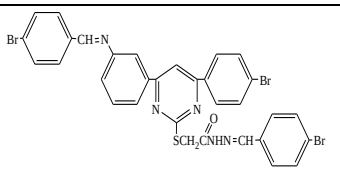
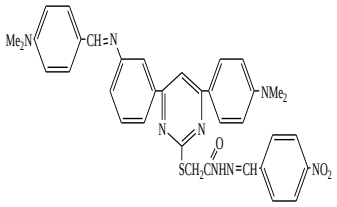
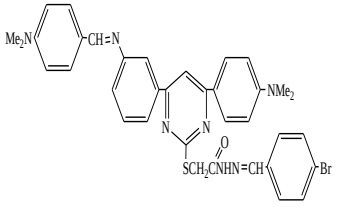
$(IV)_f$	3[3-(4`-N,N-dimethylamino benzylidene amino)phenyl]-5-(4``-N,N-dimethylamino phenyl)-4,5-dihydroisoxazole		$C_{26}H_{28}N_4O$	174-176	54	Brown
$(V)_a$	4-[3-(3`-nitrobenzylideneamino) phenyl]-6-(4``-bromo phenyl) pyrimidine-2(1H)-thione		$C_{23}H_{15}N_4O_2SBr$	280-282	33.5	Off white
$(V)_b$	4-[3-(4`-bromobenzylidene amino) phenyl]-6-(4``-bromo phenyl) pyrimidine-2(1H)-thione		$C_{23}H_{15}N_3SBr_2$	222-224	43	Off white
$(V)_c$	4-[3-(4`-N,N-dimethyl amino benzylideneamino)phenyl]-6-(4``-bromophenyl)pyrimidine-2(1H)-thione		$C_{25}H_{21}N_4SBr$	300-302	42	Orange
$(V)_d$	4-[3-(3`-nitrobenzylidene amino)phenyl]-6-(4``-(N,N- dimethyl amino)phenyl) pyrimidine-2 (1H)-thione		$C_{25}H_{21}N_5O_2S$	98-100	64	Orange
$(V)_e$	4-[3-(4`-bromobenzylidene amino)phenyl]-6-(4``-(N,N-dimethylamino)phenyl) pyrimidine-2 (1H) -thione		$C_{25}H_{21}N_4SBr$	72-73	46	Brown
$(V)_f$	4-[3-(4`- N,N-dimethylamino benzylideneamino)phenyl]-6-(4``-(N,N-dimethylamino) (phenyl)pyrimidine-2(1H)-thione		$C_{27}H_{27}N_5S$	160-162	71	Brown
$(VII)_a$	1-{3-[5-(4-bromophenyl)-4,5-dihydroisoxazol-3-yl]phenyl}-7-hydroxy-4-methylquinolin-2(1H)-one		$C_{25}H_{19}N_2O_3Br$	70-72	75	Off white
$(VII)_b$	1-{3-[5-(4-N,N-dimethylamine) phenyl]-4,5-dihydroisoxazol-3-yl)phenyl}-7-hydroxy-4-methylquinolin-2(1H)-one		$C_{27}H_{25}N_3O_3$	90-91	64	Brown
$(VIII)_a$	1-{3-[6-(4-bromophenyl)-1,2-dihydro-2-thioxopyrimidin-4-yl]phenyl}-7-hydroxy-4-methylquinolin-2(1H)-one		$C_{26}H_{18}N_3O_2SBr$	198-200	90	Pale yellow
$(VIII)_b$	1-{3-[6-(4-N,N-dimethylamine) phenyl)-1,2-dihydro-2-thioxo pyrimidin-4-yl]phenyl}-7-hydroxy-4-methylquinolin-2(1H)-one		$C_{28}H_{24}N_4O_2S$	85-87	62.5	Brown

Table 3- The physical properties of compounds$(IX)_{a,b}$- $(XIV)_{a,b}$

Com. No.	Nomenclature	Structural formula	Molecular formula	M. P ^0C	Yield %	Color
$(IX)_a$	Ethyl-2-(4-[3-(4`-bromo benzylideneamino)phenyl]-6-(4``-bromo phenyl) -1,2-dihydropyrimidin-2-ylthio) acetate		$C_{27}H_{21}N_3O_2SBr_2$	122-124	64	Yellow
$(IX)_b$	Ethyl-2-(4-[3-(4`-N,N-dimethyl amino benzylideneamino) phenyl]-6-(4``-(N,N-dimethyl amino) phenyl) -1,2-dihydro pyrimidin-2-ylthio)acetate		$C_{31}H_{33}N_5O_2S$	200-202	75	Orange
$(X)_a$	2-{4-[3-(4`-bromobenzylidene amino)phenyl]-6-(4``-bromo phenyl)pyrimidin-2-ylthio} aceto hydrazide		$C_{25}H_{19}N_5OSBr_2$	80-82	60	Pale green
$(X)_b$	2-{4-[3-(4`-N,N-dimethyl amino benzylideneamino) phenyl]-6-(4``-(N,N-dimethy lamino)phenyl)pyrimidin-2-ylthio}aceto hydrazide		$C_{29}H_{31}N_7OS$	160-162	62.5	Yellow
$(XI)_a$	2-{4-[3-(4`-bromobenzylidene amino)phenyl]-6-(4``-bromo phenyl)pyrimidin-2-ylthio}-1-(3,5-dimethylpyrazol-1-yl) ethanone		$C_{30}H_{23}N_5OSBr_2$	138-140	50	Pale yellow
$(XI)_b$	2-{4-[3-(4`-N,N-dimethyl amino benzylideneamino) phenyl]-6-(4``-N,N-dimethyl aminophenyl) pyrimidin-2-ylthio}-1-(3,5-dimethyl pyrazol-1-yl) ethanone		$C_{34}H_{35}N_7OS$	75-77	49	Brown
$(XII)_a$	2-{2-[4-(3-(4`-bromo benzylideneamino)phenyl]-6-(4``-bromophenylpyrimidin-2-ylthio)acetyl}-5-methyl pyrazolin-3-one		$C_{29}H_{21}N_5O_2SBr_2$	116-118	81	Off white
$(XII)_b$	2-{2-[4-(3-(4`-N,N-dimethyl aminobenzylideneamino) phenyl]-6-(4``-N,N-dimethyl aminophenylpyrimidin-2-ylthio)acetyl}-5-methyl pyrazolin-3-one		$C_{33}H_{33}N_7O_2S$	100-102	90	Brown
$(XIII)_a$	2-{4-[3-(4-bromobenzylidene amino)phenyl]-6-(4`-bromo phenyl) pyrimidin-2-ylthio}-N- (4``-nitrobenzylidene) acetohydrazide		$C_{32}H_{22}N_6O_3SBr_2$	252-254	37	Off white
$(XIII)_b$	2-{4-[3-(4-bromobenzylidene amino)phenyl]-6-(4`-bromo phenyl)pyrimidin-2-ylthio}-N- (4``-bromo benzylidene) acetohydrazide		$C_{32}H_{22}N_5OSBr_3$	172-174	33	Yellow

$(XIV)_a$	2-{4-[3-(4-N,N-dimethyl amino benzylideneamino) phenyl]-6-(4`-(N,N-dimethy lamino) phenyl) pyrimidine-2-ylthio}-N-(4``-nitro benzylidene) acetohydrazide		$C_{36}H_{34}N_8O_3S$	218-220	25	Orange
$(XIV)_b$	2-{4-[3-(4-N,N-dimethyl amino benzylideneamino) phenyl]-6-(4`-(N,N-dimethyl amino) phenyl) pyrimidin-2-ylthio}-N –(4``-bromo benzylidene) acetohydrazide		$C_{36}H_{34}\ N_7OSBr$	138-140	78	Brown

Results and Discussion

The chalcones $(I)_{a,b}$ were synthesized by Claisen-Schemidt reaction from condensation of aromatic aldehyde with 3-amino acetophenone in presence of NaOH. The compounds $(I)_{a,\ b}$ were characterized by melting points, FTIR spectroscopy .The FTIR spectra of compound $(I)_{a,b}$ showed appearance of two bands in the region (3448-3232)cm^{-1} which attributed to asymmetric and symmetric stretching vibration of NH_2 group, absorption sharp stretching band in the region(1654-1643)cm^{-1}[26] due to C=O group with the appearance of band between (1624-1610) cm^{-1} due to ν C=C of chalcone unit and a stretching band at 692cm^{-1}due to C-Br and νC-NMe_2 appeared at 1342 and 817 cm^{-1} .Besides to disappearance of characteristic absorption bands of starting materials.

The isoxazoline compounds $(II)_{a,b}$ were synthesized by the reaction of equimolar amounts of compounds $(I)_{a,b}$ and hydroxylamine hydrochloride in basic medium .The FTIR spectra showed the disappearance of νC=O and νC=C bands for chalcone moiety, with appearance of new bands for νC-H_{aliph} in the region (2924-2856) cm^{-1} and appearance of a stretching band at (1674-1640) cm^{-1} due to ν C=N of isoxazoline ring (endo cyclic) and ν C-O of isoxazoline ring between (1043-1035) cm^{-1} .

The pyrimidine-2-thiones $(III)_{a,b}$ were synthesized by the reaction of chalcones $(I)_{a,b}$ with thiourea in basic medium. The FTIR spectra exhibited the disappearance of two absorption bands of the νCH=CH group and a band of νC=O groups in the chalcones $(I)_{c,d}$,and appearance of new absorption bands for νNH, νC=N and νC=S groups around (3446-3209) cm^{-1} , (1676-1672) [27] cm^{-1} and 1230 cm^{-1}, respectively .The FTIR absorption bands of compounds (I)-(III) were listed in Table-4. Also the elemental analyses (C.H.N.) of this compound $(III)_a$ are in agreement with the proposed structure.

The Schiff bases type $(IV)_{a-f}$ and $(V)_{a-f}$ were produced from the refluxing of equimolar amounts of amino compound $(II)_{a,b}$ or $(III)_{a,b}$ with different aromatic aldehydes in dry benzene with some drops of glacial acetic acid (GAA) . The FTIR spectra of compounds $(IV)_{a-f}$ showed the disappearance of absorption bands due to νNH_2 and νC=O groups of the starting materials together with appearance of new absorption band in the region (1695-1665) cm^{-1} which is assigned to C=N stretching [28]. The FTIR absorption bands of compounds $(IV)_{a-f}$ were given in Table-5. The ^{1}HNMR spectrum of Schiff base $(IV)_b$ (in DMSO –d_6 as a solvent),Figure-1, exhibited two signals at δ3.90 ppm and δ 5.8 ppm due to two protons at C-4 and one proton at C-5 ,respectively of isoxazoline ring. Twelve aromatic protons appeared in the region δ (7.36-8.1) ppm, finally a singlet signal appeared at δ 8.71ppm could be attributed to one proton of CH=N group.

The FTIR absorption bands of compounds $(V)_{a-f}$ showed the disappearance of absorption bands due to νNH_2 and νC=O groups of the starting materials together with the appearance of new absorption stretching band of C=N group at (1692-1665) cm^{-1}. The FTIR absorption bands of compounds $(V)_{a-f}$ are listed in Table-6. The ^{1}HNMR spectrum of compound $(V)_d$(in DMSO-d_6 as a solvent) Figure-2 exhibited a singlet at δ 9.11ppm that could be attributed to the proton of NH group, a singlet signal at δ 6.757 ppm due to one proton of CH group of pyrimidine ring. Multiplet signal in the region δ (7.13-8.229)ppm that could be attributed to the twelve aromatic protons. The ^{1}HNMR spectrum also showed two sharp signals at δ 8.407 ppm and δ 3.01 ppm for one proton and six protons which could be attributed to the CH=N and N$(CH_3)_2$groups, respectively.

Table 4- Characteristic FTIR absorption bands of compounds $(I)_{a,b}$,$(II)_{a,b}$,$(III)_{a,b.}$

Comp. No.	Characteristic bands FTIR spectra(cm^{-1})							
	ν asy. , sym. NH_2	νC-H aliph.	νC=N endocyclic	νCH=	νC=O	νC=C of chalcone group	νC=C aromatic	Others
$(I)_a$	3448-3232			3070,3061	1654	1624	1583	νC-Br:692
$(I)_b$	3439-3336	2939-2816		3091,3060	1643	1610	1604	νC-NMe_2:1342,817
$(II)_a$	3365-3226	2924-2856	1674				1591	νC-O:1043, νC-O-N:785
$(II)_b$	3442-3221	2891-2856	1640				1606	νC-O:1035, νC-O-N:786
$(III)_a$	3387-3209	2974-2887	1672				1606	νC=S:1230
$(III)_b$	3446-3230	2895-2804	1676				1597	νC=S:1230

Table 5- Characteristic FTIR absorption bands for Schiff bases of isoxazoline compounds $(IV)_{a-f}$

Comp. No.	Characteristic bands FTIR spectra(cm^{-1})			
	νC-H aliph.	νC=N exocyclic	νC=C aromatic	Others
$(IV)_a$	2972-2873	1692	1585	ν3-NO_2:1529,1330
$(IV)_b$	2941-2885	1690	1585	ν4-Br:678
$(IV)_c$	2922-2852	1665	1597	ν4-C-NMe_2:1369,815
$(IV)_d$	2924-2856	1695	1597	ν3-NO_2:1527,1317
$(IV)_e$	2922-2854	1682	1589	ν4-Br:689
$(IV)_f$	2940-2852	1685	1600	ν4-C-NMe_2:1365,813

Table 6- Characteristic FTIR absorption bands for Schiff bases of pyrimidine compounds $(V)_{a-f}$

Comp. No.	Characteristic bands FTIR spectra(cm^{-1})				
	νNH	νC=N exocyclic	νC=C aromatic	νC=S	Others
$(V)_a$	3375	1685	1590	1215	ν3-NO_2:1512,1350
$(V)_b$	3398	1680	1587	1222	ν4-Br:684
$(V)_c$	3395	1665	1587	1226	ν4-C-NMe_2:1365,817
$(V)_d$	3395	1692	1597	1230	ν3-NO_2:1527,1350
$(V)_e$	3421	1681	1597	1228	ν4-Br:688
$(V)_f$	3394	1678	1600	1231	ν4-C-NMe_2:1369,813

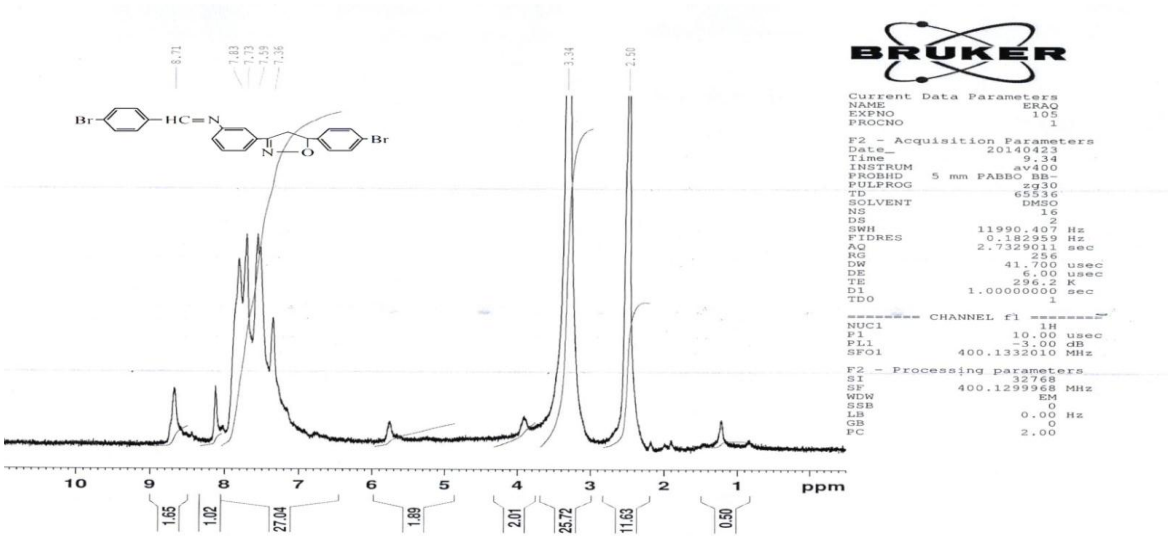


Figure 1- ^{1}HNMR-Spectrum of compound $(IV)_b$

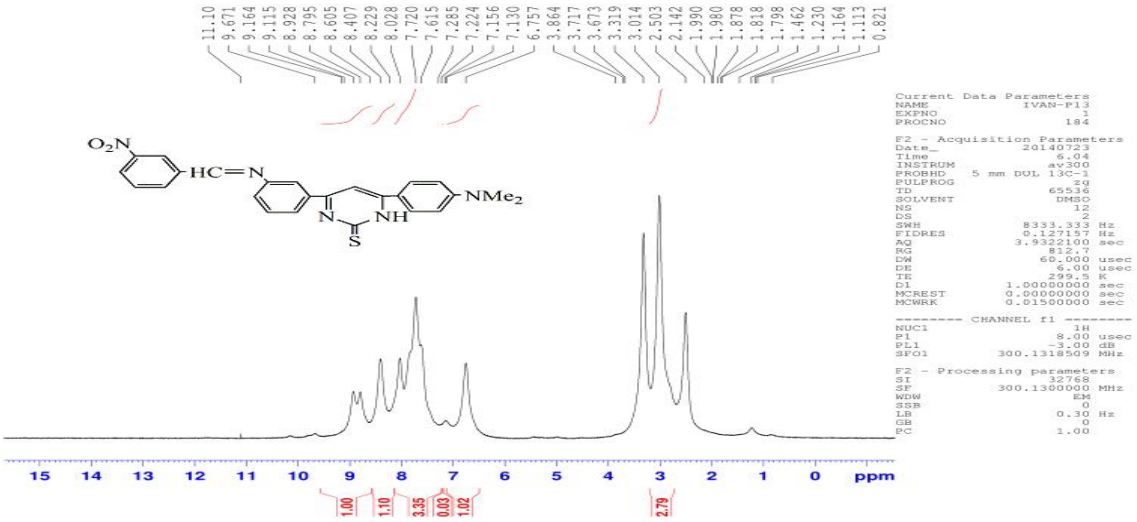
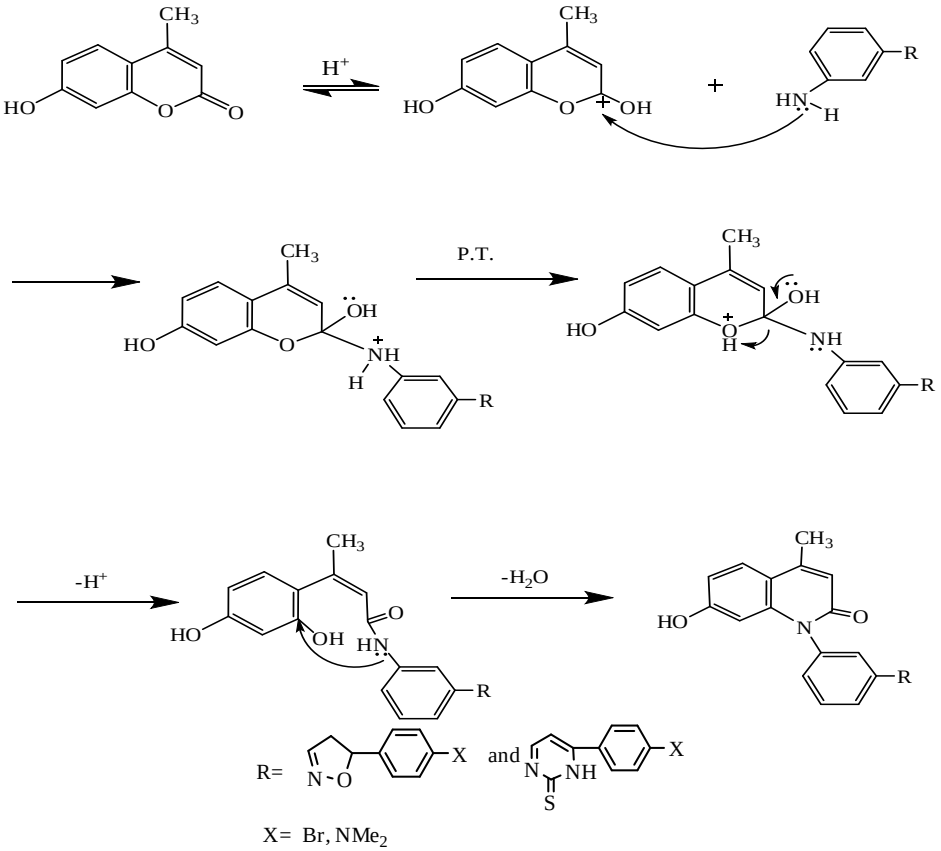


Figure 2- ^{1}HNMR-Specrtum of compound $(V)_d$

7-hydroxy-4-methyl coumarin was prepared by the reaction between resorcinol and ethyl acetoacetate in catalytic amount of sulfuric acid. The characteristic FTIR absorption bands of coumarin (VI) indicated the appearance a band of νO-H at 3502 cm^{-1}, with appearance bands in the region (2954-2880) cm^{-1} due to stretching vibration of C-H aliphatic for CH_3 group with absorption sharp stretching band at 1710 cm^{-1}[29] due to C=O stretching .The spectrum also showed absorption bands for ν C-H aromatic, νC=C and νC-O (lactone) around 3008 cm^{-1}, 1608 cm^{-1} and 1159 cm^{-1}, respectively.

The new quinolin-2-one derivatives were synthesized by refluxing 7-hydroxy-4- methyl coumarin with amino compounds $(II)_{a,b}$ or $(III)_{a,b}$ in glacial acetic acid according to the suggested mechanism Scheme-3.



Scheme 3

The characteristic FTIR absorption bands of qunolin-2-one derivatives $(VII)_{a,b,}$ $(VIII)_{a,b}$ showed a shift in the carbonyl stretching band from lactone group of coumarin to(1712-1697)cm^{-1} for lactam group of qunolin-2-one, appearance new absorption stretching band for νC-N (endocyclic) in the region 1390-1315 cm^{-1} [30] , the band (at 817cm^{-1}) indicated the presence of NMe_2 group. The FTIR absorption bands of compounds (VII),(VIII) are listed in Table-7.

The ^{1}HNMR spectrum of compound $(VIII)_a$ Figure-3 exhibited a broad singlet at δ 3.6 ppm that could be attributed to the OH proton, a sharp singlet signal at δ 6.09 ppm due to proton of CH at C-3 of quinolin-2-one ring. Multiplet signals in the region δ (6.67-7.58)ppm that could be attributed to the eleven aromatic protons and one proton of pyrmidine ring. The ^{1}HNMR spectrum also showed a singlet signals at δ 1.82 ppm due to SH proton and a weak signal at δ 6.45 ppm for NH proton (SH toutomer with NH in pyrimidine unit). Finally this spectrum showed a sharp singlet at δ 2.36ppm for three protons which could be attributed to CH_3 group.

The ester compounds $(IX)_{a, b}$ were synthesized by the reaction of compounds $(V)_{b, f}$ with ethyl-α-chloro acetate in presence of fused sodium acetate. the FTIR spectra of these compounds $(IX)_{a,b}$ showed a significant band between 1728-1697cm^{-1}[31] which could be attributed to stretching vibration of the carbonyl of ester group with disappearance of absorption stretching bands of (S-H, C=S) of compound$(V)_{b,f}$. The ^{1}HNMR spectrum of ester compound $(IX)_a$ Figure-4 showed the following characteristics chemical shifts: a singlet signal at δ 4.11ppm for two protons of SCH_2 group, a quartet signal of two protons of OCH_2 group appear at δ 4.36ppm and a triplet signal in the region δ (1.04-1.06) ppm due to three protons of CH_3 group. Also the spectrum showed multiplet signal in the region δ (6.92-7.85)ppm could be attributed to the twelve aromatic protons and a proton at C5 of pyrimidine ring. Finally this spectrum showed a singlet signal at δ8.65 ppm for azomethine proton.

Table 7- Characteristic FTIR absorption bands of quinoline compounds $(VII)_{a,b}$, $(VIII)_{a,b}$

Comp. No.	Characteristic bands FTIR spectra(cm^{-1})					
	νOH	νC-H aliphatic	νC=O lactam	νC=C aromatic	νC-N	Others
$(VII)_a$	3446	2993-2904	1705	1608	1390	ν4-Br:692
$(VII)_b$	3495	2993-2900	1708	1608	1365	ν4-C-NMe_2:1371,817
$(VIII)_a$	3502	2954-2880	1697	1606	1328	ν4-Br:692, ν C =S:1226
$(VIII)_b$	3493	2920-2902	1712	1598	1315	ν4-C-NMe_2:1371,815 ν C=S:1228

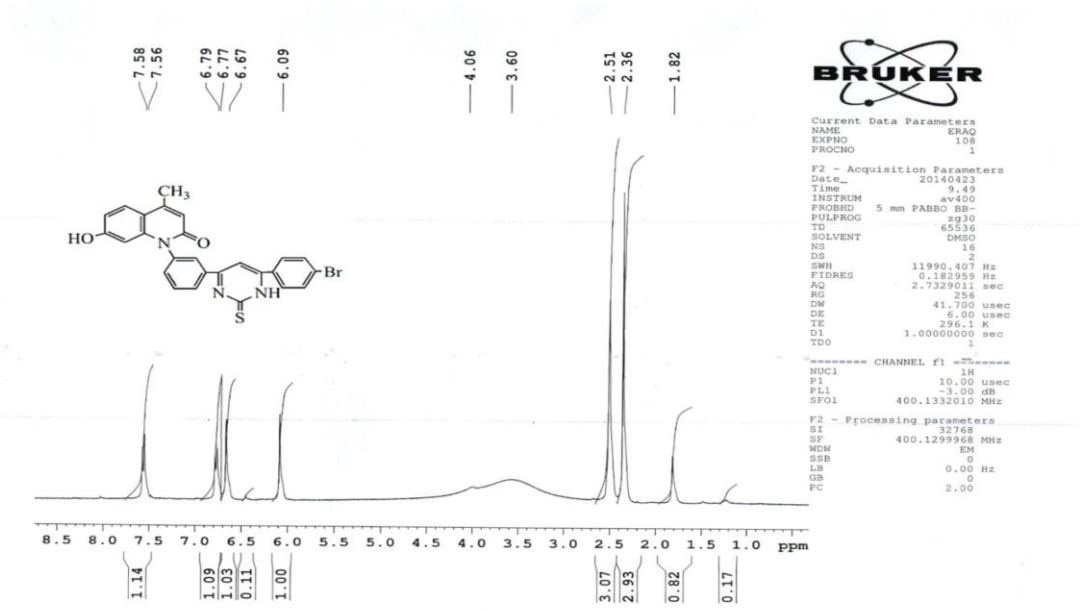


Figure 3- ^{1}HNMR-Spectrum of compound $(VIII)_a$

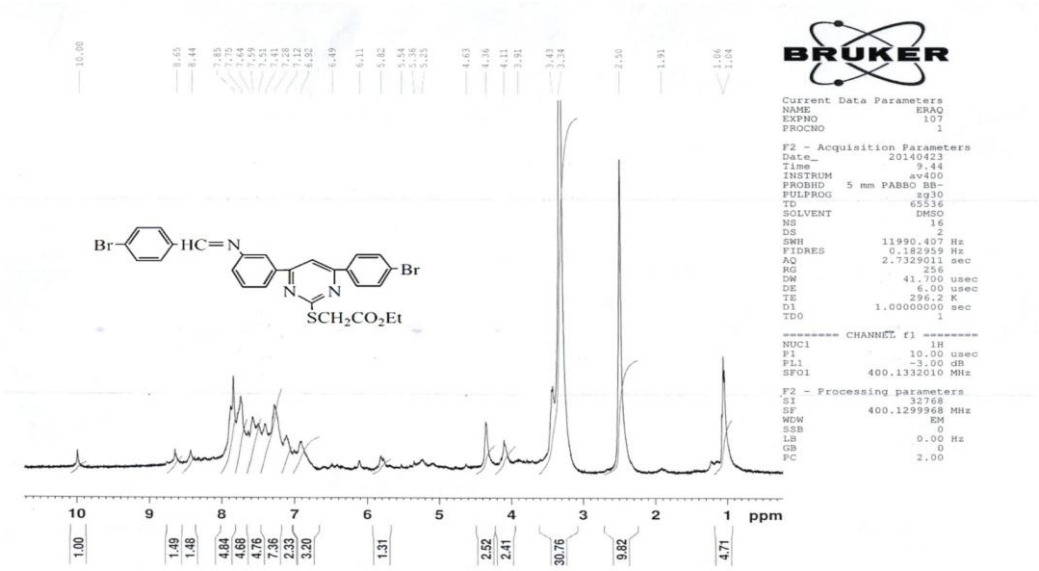


Figure 4- ^{1}HNMR-Spectrum of compound $(IX)_a$

The mass spectrum of compound $(IX)_b$ showed several peaks at m/z= 306(base peak), 206 and 130 gives an excellent diagnostic for presence of pyrimidine ring in the molecule, Scheme-4. An important free cation at m/z= 246 and cation at m/z= 229 [32] are good evidence for the present ester group. Finally the aromatic nature of this compound is evident as a result of the peaks at m/z= 51,65 and 77. The mass spectrum of compound $(IX)_b$ is shown in Figure-5 also the most important fragments of this compound are shown in Scheme-4.

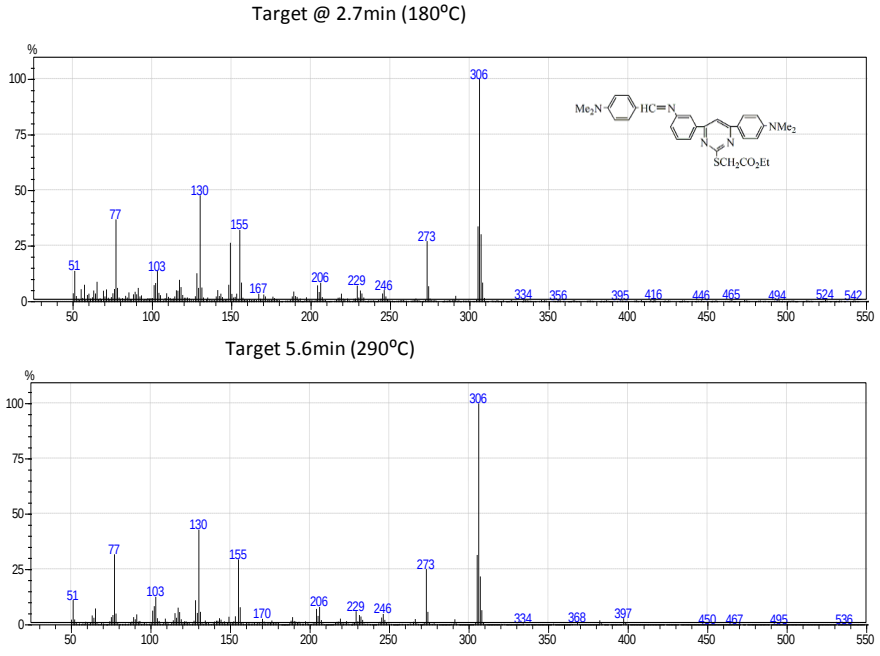
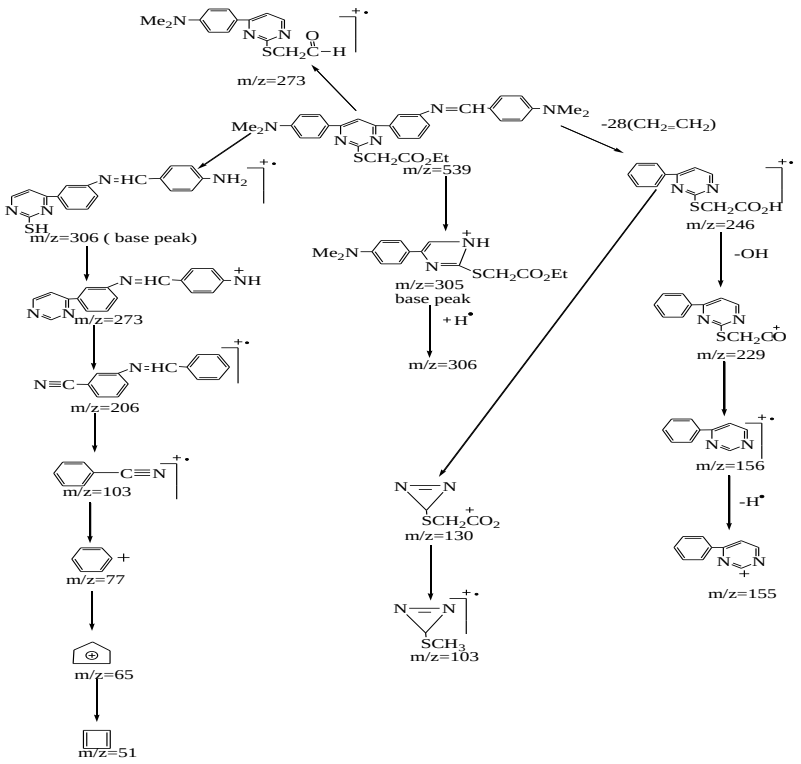


Figure 5- Mass - spectrum of compound $(IX)_b$



Scheme 4- Fragmentation of compound $(IX)_b$

The condensation of ester with hydrazine hydrate led to formation of new acid hydrazides $(X)_{a,b}$ the FTIR spectra exhibited a shift in the carbonyl stretching band of ester group to (1667-1666) cm^{-1} [33] for amide group of new hydrazide $(X)_{a,b}$ together with appearance of three stretching bands in the range(3321-3185) cm^{-1} which are assigned to asymmetric and symmetric bands of νNH_2 and νNH groups. The FTIR absorption bands of compounds (IX),(X) were listed in Table-8.

The new Schiff bases type, $(XIII)_{a,b}$ and $(XIV)_{a,b}$ were synthesized by the refluxing of compounds $(X)_{a,b}$ with different aromatic aldehydes in benzene. These compounds were characterized by melting points and FTIR spectroscopy. FTIR spectra showed the disappearance of two absorption bands due to νNH_2 stretching of acid hydrazide together with the appearance of a stretching bands at (1683-1670)cm^{-1} assignable to ν C=N. The characteristics FTIR absorption bands of new Schiff bases (XIII) , (XIV) , (XI) and (XII) were listed in Table-9.The refluxing of hydrazide $(X)_{a,b}$ with acetyl acetone led to formation of new pyrazoles $(XI)_{a,b}$ .These compounds are characterized by melting points, C.H.N analysis and FTIR spectroscopy. The FTIR spectra showed the disappearance of three absorption bands due to νNH_2 and νNH groups together with the appearance of the stretching bands around (1659-1654) cm^{-1} assignable to ν C=N group and (1433-1380) cm^{-1} due to N-N for pyrazole ring[34]. The elemental analysis (C.H.N.) of this compound $(XI)_b$ are in agreement with its proposed structure.

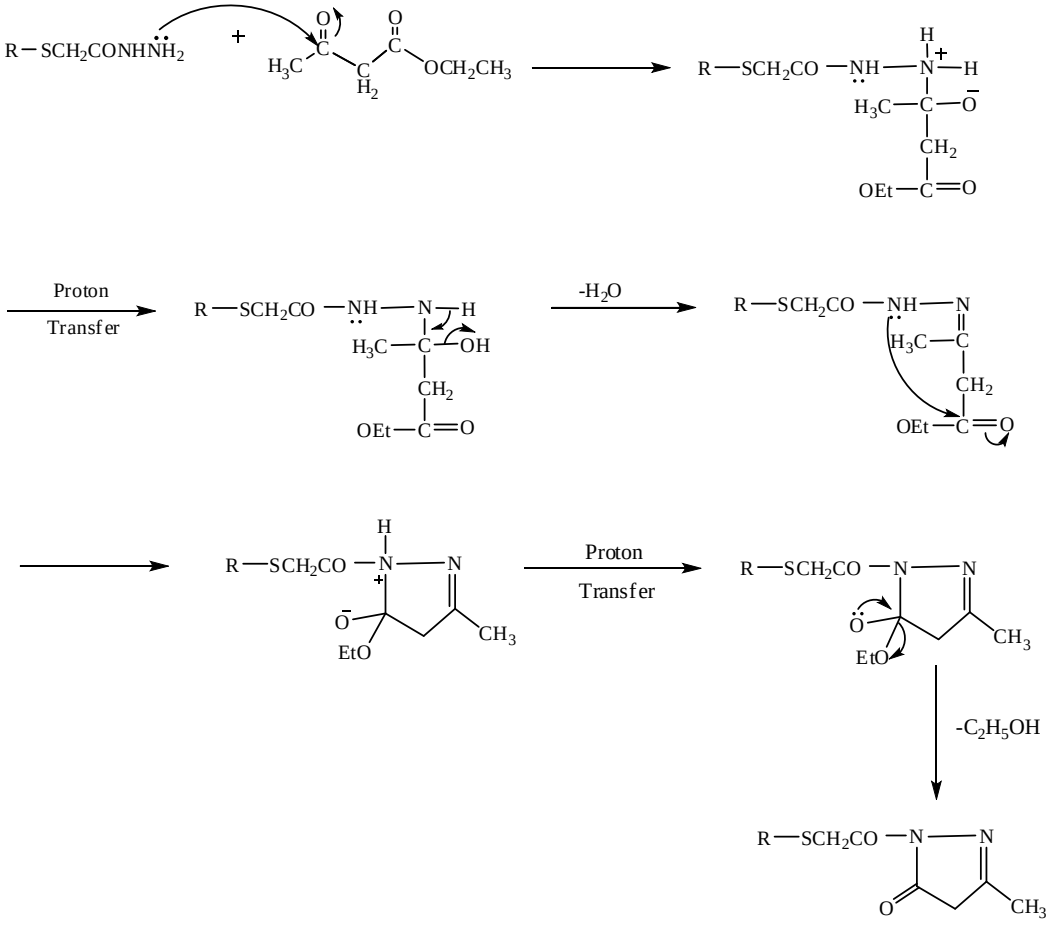
Table 8- Characteristic FTIR absorption bands of compounds $(IX)_{a,b}$ and $(X)_{a,b}$

Comp. No.	Characteristic bands FTIR spectra(cm^{-1})				
	ν asy. , sym. NH_2 and NH	**νC-H aliph.**	**νC=O ester**	**νC=O amide**	**νC=C aromatic**
$(IX)_a$		2980-2879	1728		1589
$(IX)_b$		2889-2858	1697		1604
$(X)_a$	3321-3217	2956-2854		1666	1602
$(X)_b$	3309-3185	2957-2855		1667	1603

Table 9- Characteristic FTIR absorption band of compounds$(XI)_{a, b}$–$(XIV)_{a, b}$

Comp. No.	Characteristic bands FTIR spectra(cm^{-1})					
	νC-H aromatic	**νC-H aliph.**	**νC=O**	**νC=N**	**νC=C aromatic**	**Others**
$(XI)_a$	3061	2954-2852	1670	1654	1606	νN-N 1433, ν C-O :1278
$(XI)_b$	3039	2988-2880	1682	1659	1600	νN-N 1380, ν C-O :1279
$(XII)_a$	3078	2978-2854	1732,1680	1651	1612	νN-N 1438
$(XII)_b$	3072	2950-2852	1730,1705	1676	1604	νN-N 1438
$(XIII)_a$	3092	2900-2866	1653	1679	1596	ν4-NO_2:1549,1342
$(XIII)_b$	3080	2925-2854	1666	1670	1588	ν4-Br:702
$(XIV)_a$	3085	2990-2866	1652	1683	1598	ν4-NO_2:1559,1334
$(XIV)_b$	3090	2924-2855	1649	1678	1605	ν4-Br:701

Also pyrazolines $(XII)_{a,b}$ are produced from the reaction of hydrazide with ethyl aceto acetate, as in the following mechanism, Scheme-5:



Scheme 5

These compounds were identified by melting points and FTIR spectra.The FTIR spectra showed the disappearance of three absorption bands due to νNH_2 and νNH groups together with the appearance of the stretching band around (1676-1651) cm^{-1} due to ν C=N band and new absorption band at (1732-1730)cm^{-1} due to νC=O (endo cyclic). The ^{1}HNMR spectrum of compound$(XII)_b$ Figure-6 exhibited a sharp singlet at δ3.90 ppm for two proton of SCH_2 group, Many signals in the region δ(6.59-7.48)ppm that could be attributed to the twelve aromatic protons and one proton for pyrimidine ring, while the protons of CH_2-(pyrazolone) appeared as a singlet at δ2.31ppm and another singlet signal appeared at δ 1.35 ppm due to three protons of CH_3 group. The ^{1}HNMR spectrum also showed weak signal at δ 7.696ppm for one proton could be attributed to the CH=N and a sharp singlet signal at δ 2.81ppm for twelve protons of two $N(CH_3)_2$groups.

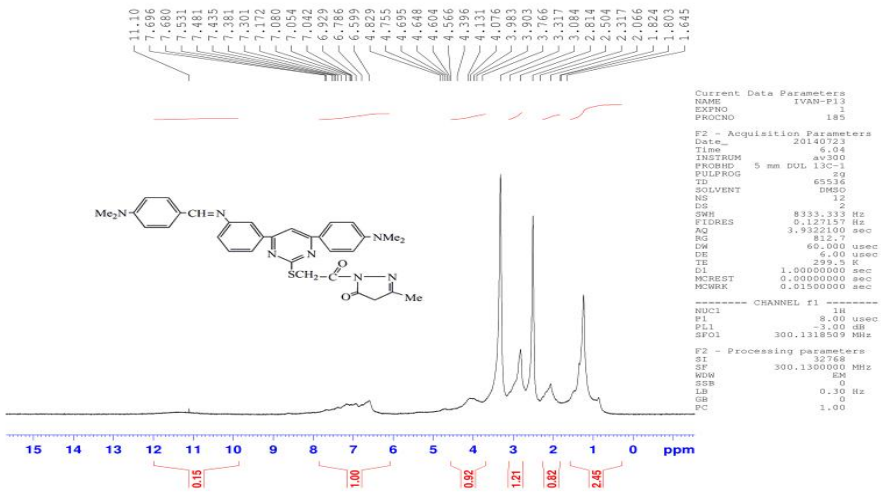


Figure 6- ^{1}HNMR-Specrtum of compound $(XII)_b$

Biological activity

The antibacterial activity of some of the synthesized compounds was performed according to the agar diffusion method , using two types of bacteria; *Escherichia coli* (G-) and *Staphylococcus aureus* (G+).

The antibacterial activities data Table-10 of the examined compounds exhibited:

1. All the compounds did not show any biological activity against *E.coli* (gram-).
2. Compound $(VII)_a$ showed moderate biological activity against *S. aureus* (gram +).

Table 10- Antibacterial activity for some of the synthesized compounds

Comp.No.	*E.Coli* (G-)	*S. aureus* (G+)	Comp.No.	*E.Coli* (G-)	*S.aureus* (G+)
$(II)_b$	Nil	Nil	$(IX)_a$	Nil	Nil
$(III)_a$	Nil	Nil	$(X)_b$	Nil	Nil
$(IV)_d$	Nil	Nil	$(XI)_b$	Nil	Nil
$(VII)_a$	Nil	12mm	$(XII)_a$	Nil	Nil
$(VII)_b$	Nil	Nil	$(XIII)_a$	Nil	Nil

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