Synthesis of Pyrimidines Fused with Azaheterocyclic Five and Six Membered Rings

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Abstract:

5-Arylidine barbituric acid derivatives 1(a-h) were prepared from the reaction of this acid with proper aromatic aldehydes in present of acetic acid (also, 5-benzylidine barbituric acid 1a was prepared as an authentic sample from the reaction of benzaldehyde with 1,3-diphenyl-2-propen-1-one in present of pyrimidine).To increase the yields of these derivatives a modified procedure was followed using solvent – free grindstone technique.

These arylidines were used as synthons in preparation of the titled compounds by 1,4-Michael addition, thus 2-aryl-5-spirooxiran-1-yl-barbituric acid 2(a-h) were obtained via epoxidation of the proper arylidine by hydrogen peroxide in presence of anhydrous sodium carbonate. The reaction of these oxirans with hydrazine hydrate gave 3-aryl-pyrazolo[3,4-d]pyrimidine-4,6-diones3(a-h).The refluxing of compound(1h) with hydrazine hydrate in presence of pyridine gave 3-(2,6-dichlorophenyl) pyrazolino[3,4-d] pyrimidin- 4,6-dione(4), which on oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) gave the authentic sample of compound(3h).

Also, 3-aryl-dihydroisoxazolo[3,4-d]pyrimidine - 4,6-diones 6(a-b and g) were prepared by the reaction of proper arylidine with hydroxyl amine salt in pyridine and oxidation of the products 3-aryl-3,3a-dihydroisoxazolo [3,4-d] pyrimidine-4,6-diones 5(a-b and g) with (DDQ) .

7- Amino-5-arylpyrimido[4,5-d]pyrimidine-2,4-diones 7(a-b and g) were prepared by the reaction of proper arylidine and guanidine hydrochloride in ethanol.

Finally, 5-arylpyrimido[4,5-d] pyrimidine-2,4,7-trione 8(a-c) and 5-arylpyrimido[4,5-d]pyrimidine-2,4-dione -7-thione 9(a) were prepared by the reaction of proper arylidine with urea or thiourea in refluxing ethanol. This procedure was modified to increase the yield using phase-transfer catalytic (PTC) technique using catalytic amount of tetraethylammmonium iodide and aqueous sodium hydroxide solution .

The structures of these compounds were confirmed by H^1NMR of representative samples in addition to IR ,UV Spectra and authentic samples .

Introduction:

Fused azaheterocyclic five or six membered rings and their thio-analogs (such as thiouric acid and thioquanine) played important roles as immunosuppressive agent in organ transplants[1].Therapeutically, these compounds were used in treatment of hyperuricemia,chronic gout(antiurolithic) [2]and male erectile dysfunction -(the fames drug sildenafil citrate (Viagra))[3]. Also pyrimidines exhibit in vitro growth inhibitory activity against gram positive and gram negative bacteria and yeast [4].

Recently , it has reported that the reaction of aromatic chalcons (or aromatic aldehydes) with barbituric acid or thiobarbituric acid may afford arylidine barbitiuric acid [5]. Also, the using of α,β- unsaturated heterocyclic arylidines as synthone in preparation of fused azaheterocyclic five or six membered rings with different reaction conditions were investigate in our previous works[5]. Finally, many derevatives of isoxazolo were prepared recently by the reaction of proper arylidine with hydroxyl amine salt in pyridine[6].

As part of continuous program directed toward the studies with polyfunctionally substituted heterocyclic's [7-8], it was became of interest to investigate preparative routs to synthesis of pyrimidines fused with azaheterocyclic five or six membered rings of anticipated biological activity[9-10].

Experimental:

All melting points were determined on a Gallen Kamp and Electro thermal 1A9300 Digital-Series (1998) apparatus and were uncorrected. The IR – spectra (vmax cm^{-1} KBr disc) were recorded on Perkin – Elmer 590B Spectrophotometer. UV-On Shimadzu UV-160 spectrophotometer using EtOH as solvent. All NMR spectra were obtained on a BRUKER AVANCE DPX 400 MHz. spectrometer in DMSO-d6 solutions using TMS as an internal standard at Department of Chemistry, Donnan and Robert Robinson Laboratories, University of Liverpool,U.K. except that of compounds 8(a) and 9(a) they were recorded on a Bruker 300 MHz , in (Al – al – Bayt university , Jordan) using $CDCl_3$ as a solvent .

5-Arylidine barbituric acid derivatives 1(a-h) :

Method (A) : Conventional procedure [5] :

A mixture of barbituric acid (1.28g; 0.01mol) and proper aromatic aldehyde (0.01 mol) in glacial acetic acid (30 mL.) was heated under reflux for 3h. The reaction mixture was concentrated, diluted with ice cold water. The solid deposited was filtered off, dried and recrystallized from an EtOAc.to yield compounds (1a-f). The physical and spectral data were listed in Table(1).

Method (B) , Solvent – free grindstone procedure [6]:

A mixture of (0.01mole) of barbituric acid (1.28g), appropriate aromatic aldehyde and solid pellets of

sodium hydroxide was grinded by means of mortar in which the yellow mixture was gathered to form a sticky solid which finally converted a powder after about (30) minutes. The resulting solid was washed thoroughly with water. The solid was then dried and recrystallized from an EtOAc.to yield compounds 1(a-h). The physical and spectral data were listed in Table(1).

Table (1): The physical and spectral data of 5-arylidine barbitiuric acid 1(a-f)

Compd. No.1	Ar	m.p. °C (lit.)*	Yield % method		IR (KBr) υ(cm^{-1})		UV ($CHCl_3$) λmax(nm)
			A	B	C=O	C=C	
a	C_6H_5-	263-265 (264)	66	68	1679	1580	334
b	4-$CH_3OC_6H_4$-	280dec.	70	75	1653	1604	330
c	4-$NO_2C_6H_4$-	256-57 (255)	70	75	1674	1645	364
d	4-BrC_6H_4-	199-201	55	50	1689	1601	333
e	4-$CH_3OC_6H_4$-	280-82 (275)	60	76	1689	1620	360
f	4-$CH_3C_6H_4$-	222-24	60	70	1635	1620	360
g	4-$CH_3CH_2OC_6H_4$-	190-92	44	50	1670	1600	340
h	2,4-$Cl_2C_6H_3$-	244-46	35	50	1670	1600	340

*[10]

Formation of an authentic sample of (1a)[5]:
A mixture of 1,3-diphenyl-2-propen-1-one (chalcone) (2.08 g; 0.01mol). and barbituric acid (1.28g.; 0.01mol) in pyridine (30 mL.) was refluxed for 3h. The reaction mixture was concentrated, cooled, and acidified with ice cold acetic acid. The solid which was separated out was filtered off, washed with water, dried and recrystallized from the suitable solvent to give 1a (25% yield) . This compound has the same melting point, mixed melting point and spectral data with that from the previous method.

2-Aryl-5-spirooxiran-1-yl barbituric acids 2(a-h) [7]**:**
To a mixture of (1 g) sodium carbonate dissolved in (1 mL.) water and 30% hydrogen peroxide(1 mL.) ,a hot ethanolic solution of (0.01mole) of proper 5-arylidine barbitiuric acid (1a-f) in (10 mL.) was added. The mixture was allowed to stand for 24h at room temperature. The solid was removed by filtration, washed with water to be neutralized, dried and crystallized from aqueous ethanol to give compounds 2(a-h). The physical and spectral data were listed in Table (2).

Table (2): The physical and spectral data of 2-aryl-5-spirooxiran-1yl-barbituric acid 2(a-h)

Compd. No.2	Ar	m.p. °C	Yield %	IR (KBr) υ (cm^{-1})			UV ($CHCl_3$) λmax(nm)
				C=O	C-O-C		
					Asymm	Symm	
a	C_6H_5-	293-95	77	1688.6	1220	1100	332
b	4-$CH_3OC_6H_4$-	300 (dec.)	80	1690	1220	1100	333
c	4-$NO_2C_6H_4$-	278-300	67	1690	1222	1100	300
d	4-BrC_6H_4-	277-79	40	1700	1222	1100	343
e	4-$CH_3OC_6H_4$-	288-90	45	1688	1233	1105	333
f	4-$CH_3C_6H_4$-	300 (dec.)	43	1690	1233	1105	339
g	4-$CH_3CH_2OC_6H_4$-	270-72	55	1690	1230	1110	350
h	2,4-$Cl_2C_6H_3$-	290 (dec.)	50	1690	1230	1105	330

3-Arylpyrazolo[4,3-d]pyrimidin- 4,6-dione 3(a-h)[13]:

To a mixture of proper spirobarbituric acid 2(a-h),(0.06 mole) dissolved in chloroform (10 mL.) and acetic acid (2mL.) , hydrazine hydrate (0.68 gm, 0.6 mole) was added . After 4 hours reflux, the solution was cooled and washed with diluted hydrochloric acid, and then with diluted sodium carbonate solution. The organic layer was dried and concentrated under vacuum to give an oil product, which was crystallized from benzene to give compound s 3 (a-h). The physical and spectral data were listed in Table (3).

Formation of an authentic sample of (3h): 3-Phenyl-pyrazolo[3,4-d]pyrimidine-4,6-dione(4)[14]:

A mixture of 1(h) (2.16gm, 0.01mole) in ethanol (25), hydrazine hydrate (0.68,0.06 mole) and pyridine (4 mL.) was refluxed for 6 hours, cooled, concentrated under vacuum, then poured into water and acidified with acetic acid .The residue was filtered off ,washed with water and crystallized from methanol to afford compound 4. m.p.(293-95 °C),yield (60%).

Table (3): The physical and spectral data of 3-arylpyrazolo [3,4-d]pyrimidin- 4,6-diones 3(a-h)

Compd. No.3	Ar	m.p. °C	Yield %	IR (KBr) υ(cm^{-1})		UV ($CHCl_3$) λmax(nm)
				C=N	N-H	
a	C_6H_5-	240-42	56	1617.5	3400	328
b	4-$CH_3OC_6H_4$-	210 (dec.)	56	1618	3400	296
c	4-$NO_2C_6H_4$-	220 (dec.)	40	1612	3400	322
d	4-BrC_6H_4-	160 (dec.)	35	1612	3410	344
e	4-$CH_3OC_6H_4$-	188-90	55	1612	3410	334
f	4-$CH_3C_6H_4$-	196 (dec.)	55	1610	3410	333
g	4-$CH_3CH_2OC_6H_4$-	158-60	50	1618	3410	323
h	2,4-$Cl_2C_6H_3$-	166-68	50	1618	3400	330

3-Phenylpyrazolo[3, 4-d]pyrimidin- 4,6-dione 3(h) [14] :

To a solution of compound 4 in 50 mL. benzene was added of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (D.D.Q.) (1g), then the reaction mixture was refluxed for 8 hours and concentrated under vacuum. The crude product was chromatographed over Al_2O_3 60g .The column was eluted with benzene until the yellow color in benzene disappears. The benzene was removed under pressure and the solid product was crystallized from acetic acid to give compound 3(h). This compound has the same melting points, mixed melting point and spectral data with that via the peroxidation method.

3-Aryl-3,3a-dihydroisoxazolo[3,4-d]pyrimidine -4,6-dione 5(a-b and g)[15]:

A reaction mixture of 24% aqueous solution of hydroxylamine hydrochloride (2.5mL.) and a proper arylidene (2.14 mmole) in pyridine (5mL.) was refluxed for 4hrs. The mixture was then acidified with dilute acetic acid, and left overnight. The solid, thus obtained was recrystallized from ethanol to give the titled compounds. The physical and spectral data were listed in Table (4).

Table (4):The physical and spectral data of 3-aryl-isoxazolo[3,4-d]pyrimidine -4,6-diones 5(a-b and g)

Compd. No.5	Ar	Yield %	IR (KBr) υ(cm^{-1})		UV ($CHCl_3$) λmax(nm)
			C=N	C=C	
a	C_6H_5-	67	1606	1405	266
b	4-$CH_3OC_6H_4$-	67	1600	1400	276
g	4-$CH_3CH_2OC_6H_4$-	70	1600	1400	260

3-Aryl-dihydroisoxazolo[3,4-d]pyrimidine - 4,6-dione 6(a-b and g)[16]:

To a solution of compound (5) (0.014 mole) in benzene (50 mL.)was added of 2,3-dichloro-5,6-

dicyano-1,4-benzoquinone(D.D.Q.) (1g),then the reaction mixture was stirred for 10 hrs and concentrated under vacuum. The crude product was chromatographed over Al_2O_3 (60g).

The column was eluted with benzene until the yellow color in benzene disappears. The benzene was removed under pressure and the solid product was crystallized from acetic acid to give compounds 6(a-b and g). The physical and spectral data were gave in Table (5).

Table (5): The physical and spectral data of 3-aryl-isoxazolo[3,4-d]pyrimidine -4,6-diones 6(a-band g)

Compd. No.6	Ar	Yield %	IR (KBr) υ(cm^{-1})		UV ($CHCl_3$) λmax(nm)
			C=O	C=N	
a	C_6H_5-	67	1645	1610	266
b	4-$CH_3OC_6H_4$-	67	1645	1600	276
g	4-$CH_3CH_2OC_6H_4$-	70	1640	1600	260

7- Amino-5-arylpyrimido[4,5-d]pyrimidine-2,4-diones 7(a-b and g):

To a mixture of proper 5-arylidine barbitiuric acid1(a-b and g) (3.4 mmole) and guanidine hydrochloride (3.4 mmole) in ethanol (17 mL.), 80% solution of sodium hydroxide was added portion – wise during (2) hrs. Refluxing was continued for further 20hrs . The reaction mixture was then diluted with water and left overnight. The resulting product was filtered off and washed with a mixture of water / ethanol (1:1) then recrystallized from benzene to give off the title compounds. The physical and spectral data were listed in Table (6).

Table (6): The physical and spectral data of 7- amino-5-arylpyrimido[4,5-d]pyrimidine-2,4-diones 7(a-b and g)

Compd. No.7	Ar	m.p. °C	Yield %	IR (KBr) υ(cm^{-1})			UV ($CHCl_3$) λmax(nm)
				NH_2	C=O	C=C	
a	C_6H_5-	223-24	55	3420	1690	1580	331
b	4-$CH_3OC_6H_4$-	190-92	65	3440	1690	1580	331
g	4-$CH_3CH_2OC_6H_4$-	167-69	66	3440	1680	1575	344

5-Aryl-pyrimido[4,5-d] pyrimidine -2,4,7-trione 8(a-c) and thione 9(a):

Method (a)(Homogenous reaction)[11]:

A mixture of 5-phenylidine barbitiuric acid (0.01mole), sodium ethoxide solution (0.01mole of sodium metal in 5 mL.. of absolute ethanol), urea or thiourea(0.01mole) in 100 mL. of absolute ethanol was refluxed for 6 h, cooled, concentrated under vacuum. The precipitated product was filtered ,dried and crystallized from ethanol to afford compounds 8(a-c) and compound 9(a). The method, yields, physical and spectral data were listed in Table (7).

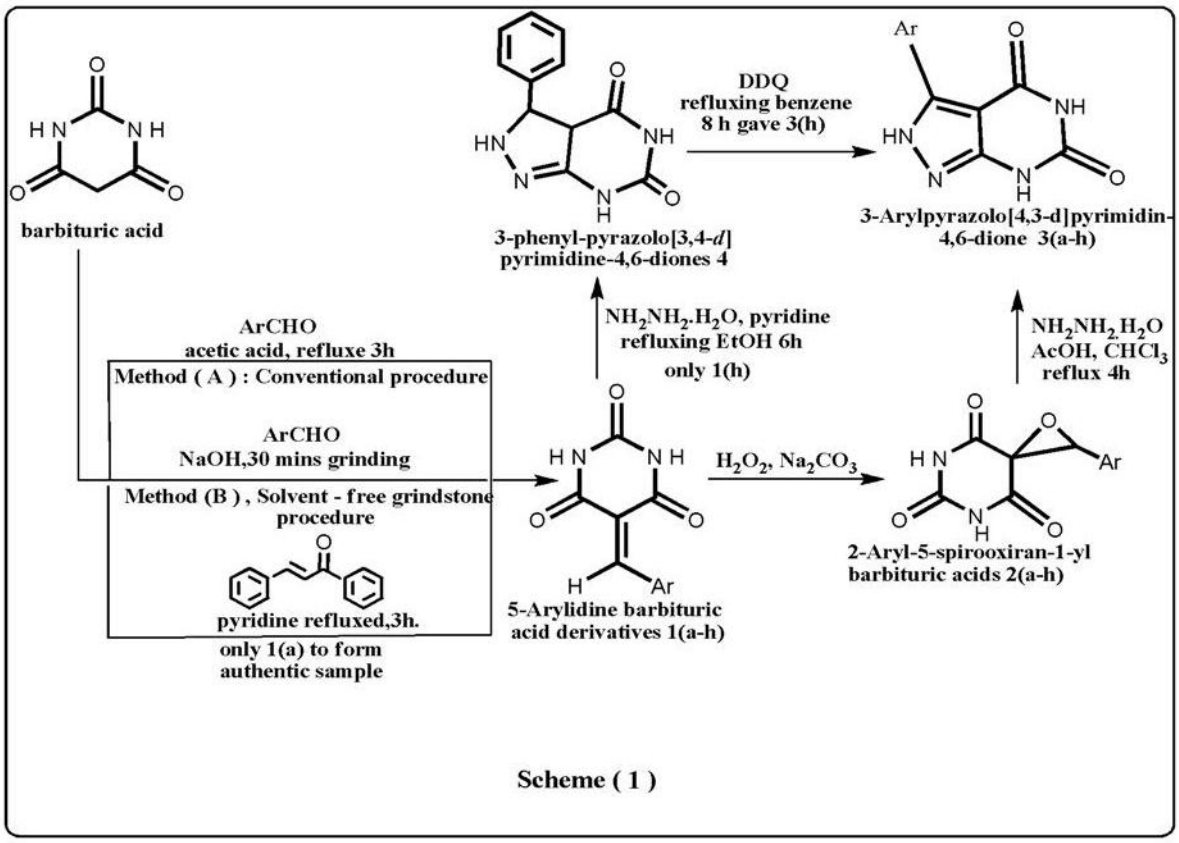
Method(b)(Phase Transfer Catalysis)[6]:

A mixture of benzene (60 mL.),water(20 mL.), sodium hydroxide(10 g), tetraethyl ammonium iodide (1 g) and urea or thiourea (0.01mole) were stirred by mechanical stirrer until a clear solution was obtained. 5-Phenylidine barbitiuric acid (0.01mole)was added and the two – phases mixture was heated in a water bath (60-65 ^{O}C)with vigorous stirring for 2 hours. The resulting mixture was cooled, the layers were separated and the benzene phase washed with 3x25 mL. water, dried over anhydrous $MgSO_4$ .Evaporation under vacuum and the residual solid was recrystallized from aqueous ethanol to give compounds 8(a-c)and 9(a). The yields were listed in Table (7).

Table (7):The physical and spectral data of 5-arylidine barbitiuric acid 8 (a-c) and thione 9(a):

Compd. No.8 and 9	X	Ar	m.p. °C	Yield % method		IR (KBr) υ(cm^{-1})			UV ($CHCl_3$) λmax(nm)
				A	B	C=O	C=C	C=S	
8a	O	C_6H_5-	263-66	44	88	1676	1617	----	334
8b	O	4-$CH_3OC_6H_4$-	280 (dec.)	46	90	1664	1618	----	330
8c	O	4-$NO_2C_6H_4$-	256-58	50	90	1674	1601	----	364
9a	S	C_6H_5-	267-68	35	86	1741	1600	1676	330

Results and Discussion: Scheme (1) was summarized the synthetic route followed for the preparation of the designed 3-arylpyrazolo[4,3-d]pyrimidin- 4,6-dione 3(a-h).



5-Arylidine barbituric acid derivatives 1(a-h) were prepared via Claisen – Schmidt condensation by refluxing aldehyde with barbituric acid in presence of pyridine[5]. The presence of conjugated carbonyl group showed the IR frequencies of these compounds at(1653- 1689cm^{-1}) with the exocyclic double bond (1580-1620cm^{-1})[17] .The UV spectra for these compounds gave λ max at (330-360 nm) due to the conjugation that cause bathochromic shift ,Table (1). The ^{1}HNMR spectra of compounds 1(b-d) which were selected as a representative for this series came in a good agreement with the proposed structure . Compound 1(b) showed characteristic signals as the following : two singlet at δ 11.30 and 11.18 assigned to two pyrimidintrione protons, a singlet at δ 7.07 for one proton due to vinyl– H , a singlet at δ 8.39 and 8.26 assigned to four protons due to Ar H and finally a singlet at δ 3.88 for three protons due to OCH_3. Compound 1(c) showed characteristic signals as the following : two singlet at δ 11.42 and 11.27 assigned to two pyrimidintrione protons, a singlet at δ 8.24 for one proton due to vinyl– H , a singlet at δ 7.99 and7.68 assigned to four protons due to ArH . Finally, compound 1(d) showed characteristic signals as the following : two singlets at δ 11.50 and 11.53 assigned to two pyrimidintrione protons, a singlet at δ 8.03 for one proton due to vinyl– H , a singlet at δ 8.26 and δ 8.34 assigned to four protons due to Ar H .

The direct epoxidation of arylidine with hydrogen peroxide in presence of anhydrous sodium carbonate gave 2-aryl-5-spirooxiran-1-yl barbituric acids 2(a-h) via 1,4-Michael addition [7]. The IR spectra showed frequency of C-O-C (1200-1230 cm^{-1}) and (1110-1105) for asymmetrical and symmetrical stretching vibrational bands specific for epoxides and the disappearance of double bond frequency and relative increase of carbonyl frequency to (1681- 690 cm^{-1}) indicated the absence of conjugation and this was confirmed by decreasing the absorption in UV spectra of these compounds to 260-270 nm, Table(3)[5].The ^{1}HNMR spectrum of compound 2(b) which was selected as a representative for this series were in a good agreement with the proposed structure, it showed characteristic signals as the followings : two singlet at δ 11.31 and 11.18 assigned to two pyrimidintrione protons, a singlet at δ 8.25 for one proton due to C2 of oxiran ring , a singlet at δ 8.38 and7.07 assigned to four protons due to ArH and a singlet at δ 3.89 assigned to three protons due to 4-MeO .

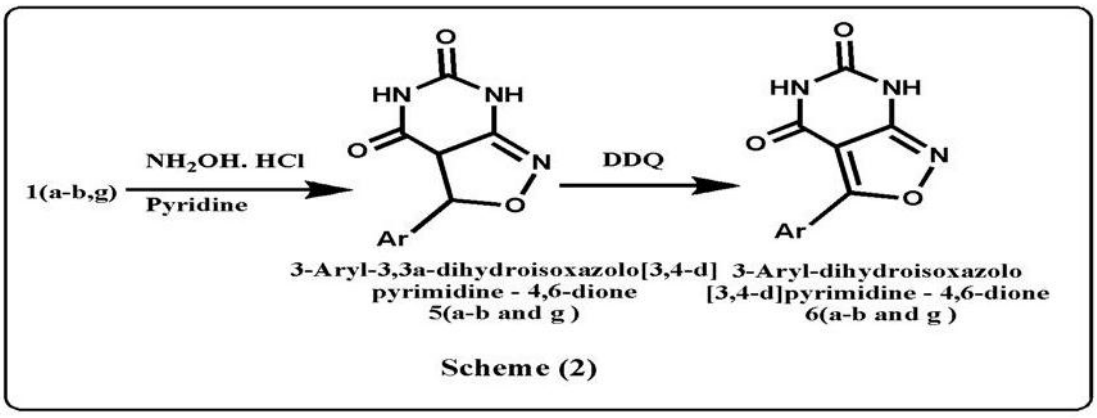
2-Aryl-5-spirooxiran-1-yl-barbituric acid 2(a-h) were converted to 3-arylpyrazolo[4,3-d]pyrimidin- 4,6-dione 3(a-h) as they refluxed with hydrazine hydrate in chloroform and acetic acid as catalyst[5],this pyrazoline rings were assigned from their UV and IR spectra ,which came in agreement with these moieties. The UV absorptions were in the range (330-345 nm)[18],while the IR spectrum showed a new band at (1617 cm^{-1}) of C =N str. The ^{1}HNMR spectra of compound 3(d) which was selected as a representative for this series was in a good agreement with the proposed structure, it showed characteristic signals as the following : two singlet at δ 11.27 and 11.43 assigned to two pyrimidindione protons, a singlet at δ 8.25 for one proton due to pyrazoline proton , a singlet at δ 8.08 and7.54 assigned to four protons due to Ar H .

Attentions has been given as a part of efforts to develop this work , as the structure skeleton of these compounds was established spectroscopically it was also established by their c hemical behavior (authentic samples).

The starting compound 5-phenylidine barbitiuric acid 1(a) was synthesized by refluxing of a mixture of barbituric acid and benzaldehyde was identical (lR, TLC, m.p and mixed m.p) with an authentic sample prepared from 1,3-diphenyl-2-propen-1-one (chalcone) according to a reported procedure [5] . The correct assignment for compound (1a) was indicated by the formation of the same product from the two different compounds .

In the same way compounds 3 (h) was also selected for authentic study, thus reaction of compound 1(h) with hydrazine hydrate in presence of pyridine gave pyrazoline derivative 4 [14], this ring was assigned from its UV and IR spectra ,which came in agreement with these moieties. The UV spectrum showed band at (330 nm), while the IR spectrum showed a new band at (1620 cm^{-1}) of C=N str. The ^{1}HNMR spectra of compound 4 came in a good agreement with the proposed structure, it showed characteristic bands as the following : one singlet at δ 12.30 assigned to CONHCO pyrimidindione proton , one singlet at δ 7.92 assigned to the two protons of the second pyrimidindione NH proton and pyrazoline NH proton , two singlet at δ 4.26 assigned to two ring protons and a singlet at δ 7.50 assigned to three protons due to ArH . Oxidation of these pyrazoline rings by 2,3-dichloro-5,6-dicyano-1,4-enzoquinone(D.D.Q.) gave the same products identical (lR, TLC, m.p and mixed m.p) from that via epoxidation [17].

3-Aryl-3,3a-dihydroisoxazolo[3,4-d]pyrimidine-4,6-diones 5(a-b and g) were prepared by the reaction of proper arylidine 1(a-b and g) with hydroxyl amine salt in pyridine[15], which in oxidation by 2,3-dichloro-5,6-dicyano-1,4-enzoquinone(D.D.Q.) gave compounds 6(a-b and g), Scheme (2).



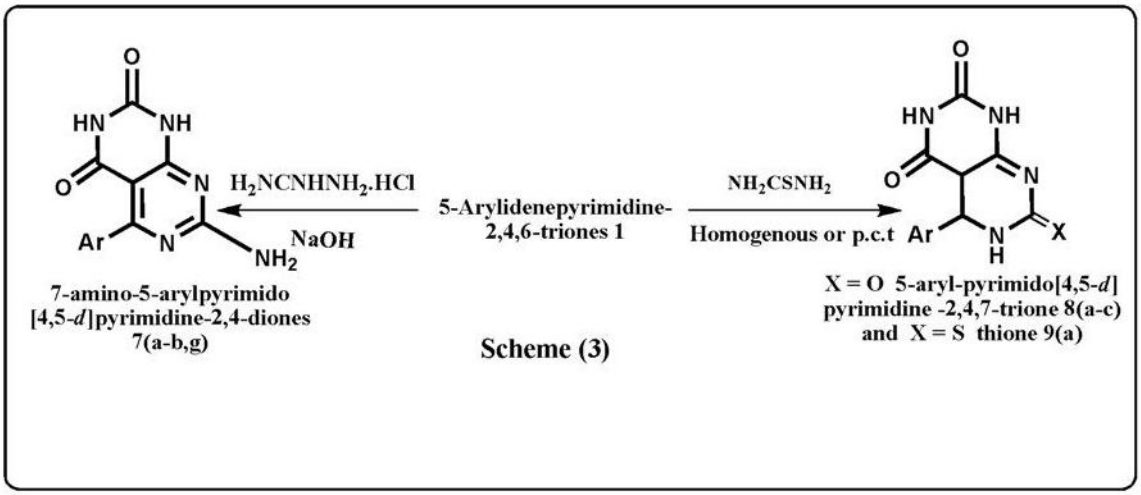
Scheme (2)

These isoxazole rings were assigned from their UV and IR spectra ,which were in agreement with these moieties.

The UV absorptions were in the range (266-276 nm)[15],while the IR spectrum showed absorption band at (1620 cm^{-1}) of C =N str and the presence of a new characteristic absorption band of heterocyclic C=C at (1400cm^{-1}) and the absence of aliphatic protons indicate the oxidation of oxazole ring .

The ^{1}HNMR spectra of compound 6(g) which was selected as a representative for this series came in a good agreement with the proposed structure, it showed characteristic bands as the following : one singlets at δ 12.32 assigned to CONHCO pyrimidindione proton , one singlet at δ 7.92 assigned to the two protons of the second pyrimidindione NH proton and one ArH proton while the others three aromatic protons at δ 7.54 , quartet at δ 4.26 assigned to two protons due CH_2 and triplet at δ 1.28 assigned to three protons due to CH_3 .

7- Amino-5-arylpyrimido [4,5- d]pyrimidine -2,4-diones 7 (a-b and g) were prepared by the reaction of proper arylidine 1(a-b,g) with guanidine hydrochloride in basic medium Scheme(3).



Scheme (3)

The IR spectra of these compounds reflecte the presence of the characteristic absorption band at (3490 and 3310 cm^{-1}) for (NH_2) function in addition to (1633 cm^{-1}) for (C=N) function . Furthermore , the absence of vinylic absorption frequencies clearly indicate the formation of pyrimidine ring . The UV absorptions λ max(Me OH) were in the range(340nm) resemble to the published for similar compounds[12]. The ^{1}HNMR spectra of compound 7(g) which was selected as a representative for this series came in a good agreement with the proposed structure, it showed characteristic bands as the following : δ 7.00-7.50 assigned to two NH_2 and four protons due to Ar – H , quartet at δ 4.21 assigned to two protons due CH_2 and triplet at δ 1.27 assigned to three protons due to CH_3 .

Finally,5-arylpyrimido[4,5-d]pyrimidine-2,4,7-trione8(a-c)and5-arylpyrimido[4,5-d]pyrimidine-2,4-dione -7-thione 9(a) were prepared by the reaction of proper arylidine with urea or thiourea in refluxing ethanol. This procedure was modified to increase the yield using phase-transfer catalytic (PTC) techniqe using catalytic amount of tetraethylammmonium iodide and water as solvent,Scheme (3) .The IR spectra of these compounds reflected a strong band in the region (1676 cm^{-1}) for C=O or (1174cm^{-1}) for C=S vibrations, and finally the (C=N) function at (1615 cm^{-1}) , this low value due to conjucation..

The UV absorptions λ max(Me OH) were in the range(300-305 nm) resemble to the published for similar compounds[12]. 1H-NMR ($CDCl_3$) δ (ppm) of compound 8(a) showed two singlet at 8.62 and 8.20 assigned to two pyrimidinedione ring NH protons (the starting barbituric ring); 8.18 assigned of the other pyrimidine NH proton, and 7.54 assigned of the five aromatic pprotons; and 3.38 assigned for for two aliphatic protons.

Finally, the 1H-NMR ($CDCl_3$) δ (ppm) of compound 9(a) showed 8.7 and 8.6 of two NH pyrimidinedione ring and 2.30 one NH pyrimidinethione ring .7.25-7.70 of 5H , ArH); 1.60 and 1.35two aliphatic protons.

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تحضير بريميدينات ملتحمة مع حلقات حاوية على النتروجين غير متجانسة خماسية وسداسية

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الملخص

حضرت مشتقات 5–اريليدين حامض الباربتيوريك 1 (h-a) من تفاعل هذا الحامض مع الالديهايدات الاروماتية المناسبة بوجود حامض الخليك(كذلك حضر5– بنزايليدين حامض الباربتيوريك (1a) (لعمل نموذج توثيقي لهذه المركبات) من تفاعل البنزالديهايد مع الجالكون(3،1– ثنائى فنيل –2– بروبين –1–اون).ولزيادة نسبة منتوج هذه المشتقات استخدمت تقنية السحن الخالي من المذيب.

استخدمت هذه الاريليدينات كمادة اساسية لتحضير المواد المذكورة بالعنوان بوساطة إضافة مايكل 4،1. فقد حضرت مشتقات 2 – اريل– 5 سبايرو حامض اوكسيران –1–يل حامض الباربتيوريك 2(h–a) عن طريق الاكسدة الفوقية للاريدينات بوساطة بيروكسيد الهيدروجين وبوجود كربونات الصوديوم اللامائية، أعطى تفاعل هذه الاوكسيرينات مع الهايدرازين المائي 3–أريل بايرازولو(4،3–d) بريميدين –6،4– داى اون3 (h-a) . ان تصعيد المركب 1(h) مع الهايدرازين المائي وبوجود البريدين أعطى 3– فنيل بايرازولينو (4،3–d) بريميدين –6،4– داى اون (4) ، والذي عند أكسدته باستخدام3– ثنائي كلورو–5،6– ثنائي سيانو –1،4– بنزوكوينون أعطى نموذج توثيقي للمركب 3(h) .

كذلك حضرت المركبات 3–اريل– 3 ،a3 ثنائى هيدرو ايزواكسازولو(3،4–d) بريميدين 6,4 (5 ,H 7H ثنائى – اون 6(a-c و g) من اكسدة مشتقات 3– أريل 3،3 a ثنائى هيدرو ايزواوكسازول (3،4–d) بريميدين –6،4– ثنائى اون 5(a-c و g) (والتى حضرت بتفاعل الاريدين المناسب مع ملح الهدروكسيل امين فى البيريدين) .

حضرت البريميدينات الامينية 7(a-c و g) من تفاعل الاريلدين المناسب مع هيدروكلوريد الكواندين بوسط قاعدي. اما المركبات5– اريل بريميدو (5،4– d) بريميدين 7،4،2– تراي اون 8(d-a) و5– اريل بريميدو(5،4– d) بريميدين 4،2 داى اون – 7- ثايون9 فقد حضرت من تفاعل الاريدين المناسب مع اليوريا أو الثايوريا بالتصعيد بالإيثانول. طورت هذه الطريقة لزيادة المنتوج باتباع تقنية التحفيز بانتقال الطور وباستخدام كميات محفزة من(رباعي اثيل بوديد الامونيوم) وبوجود محلول مائي لهيدروكسيد الصوديوم.

تم إثبات التراكيب الكيميائية للمركبات بوساطة اطياف الرنين النووي المغناطيسي لنماذج ممثلة للسلاسل المحضرة اضافة الى أطيافها في منطقة الأشعة تحت الحمراء وفوق البنفسجية وبعمل النماذج التوثيقية .