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A CONVENIENT AND EFFICIENT SYNTHESIS OF CONDENSED 1,3-DIPHENYLPYRAZOLES : SYNTHESIS OF SOME NEW PYRANOPYRAZOLE , PYRAZOLOPYRANOPYRIMIDINE AND PYRAZOLOPYRANOTRIAZOLOPYRIMIDINE DERIVATIVES

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Abstract

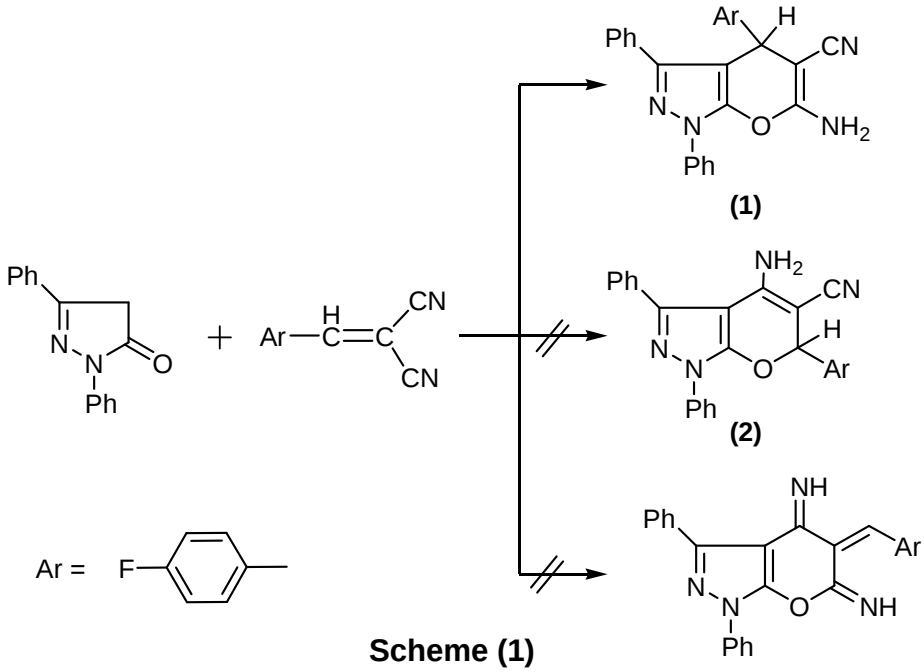
Abstract: Several heterocyclic systems such as pyrano[2,3-c]pyrazole, pyrazolo[4,3:5,6] pyrano[2,3-d]pyrimidine and pyrazolo [4,3:5,6]pyrano-[3,2-e][1,2,4]triazolo[1,5-c]pyrimidine derivatives were obtained from the reaction of 1,3-diphenylpyrazole with 4-fluorobenzylidinemalo-nonitrile to give pyrano[2,3-c]pyrazole(1)as starting material.

Keywords: *pyrazolone, arylidene, enaminonitrile, aminoimino, pyrano-pyrazole*

In continuation of previous work [1-5] dealing with the synthesis and reactions of pyranopyrazole, we report here the utility of 1,3-diphenylpyrazol-5-one in the synthesis of fused pyran derivatives which contain 4H-pyran derivatives [6-10] besides biological activities of pyrazole[11-18] directed the authors to prepare some new 4H-pyrano pyrazole derivatives.

Thus, treatment of 1,3-diphenylpyrazol-5-one with 4-fluoro-benzylidenemalononitrile in refluxing ethanol containing catalytic amount of piperidine afforded 6-amino-5-cyano-1,3-diphenyl-4-(4-fluorophenyl)-1,4-dihydropyrano[2,3-c]pyrazole (1), Scheme 1.

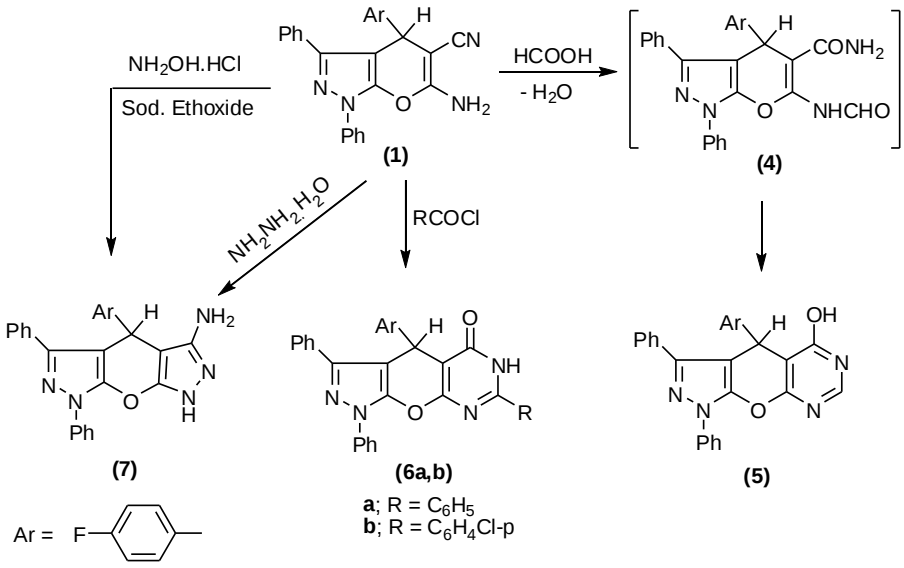
The presence of νCN in the IR spectrum at (2200 cm^{-1}) reject the possible isomer (3) and the appearance of singlet signal at δ = 4.94 due to 4H-pyran in ^{1}HNMR spectrum support the structure (1) and ruled out the other possible isomer (2).



Scheme (1)

Aminonitrile derivative **(1)** was refluxed in boiling formic acid to yield 4-(4-fluorophenyl)-1,3-diphenyl-1,4-dihydropyrazol-o[4',3':5,6]-pyrano[2,3-*d*]pyrimidin-5-ol **(5).** The reaction is prob-ably takes through the formation of 6-formylamino-5 carbox-amide intermediate **(4)**, followed by cyclization, **Scheme 2.**

Benzoylation of aminonitrile **1** with aroyl chlorides afforded the 7-aryl-4-(4-fluorophenyl)-1,3-diphenyl-4,6-dihydropyrazolo [4',3':5,6]pyrano[2,3-*d*]pyrimidin-5(1*H*)-ones (6a,b), **Scheme 2**.



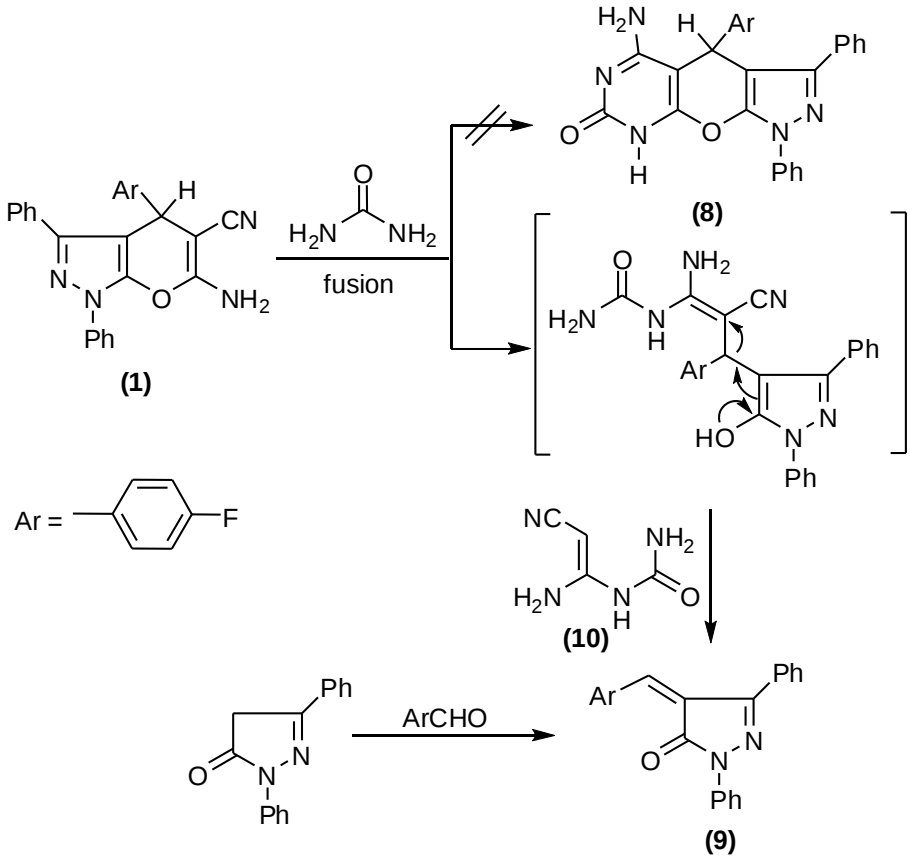
Scheme (2)

Also, reaction of **1** with hydrazine hydrate in refluxing ethanol afforded 4-(4-fluorophenyl)-5,7-diphenyl-4,7-dihydro-1H-pyrazolo[4',3':5,6]pyrano[2,3-c]pyrazol-3-amine **(7)**, **Scheme 2**.

Further confirmation of structure **(7)** was obtained through; its synthesis via authentic route, from the reaction of **1** with hydroxyl amine hydrochloride in sodium ethoxide under reflux.

When aminonitrile derivative **(1)** reacted with ure agives the 4-(4-fluoro-benzylidene)-1,3-diphenyl-1H-pyrazol-5(4H)-one **(9)** was obtained in excellent yield. The formation of compound **(9)** could be rationalized on the basis of formation of an addition product, from which elimination of the non-isolable 1-(1-amino-2-cyanovinyl) urea **(10)** (TLC) gave the p-fluorobenzylidenepyrazolone derivative **(9)**.

Conformation of Structure **(9)** was obtained through its synthesis via another reaction route, thus reaction of pyrazo-lone with p-fluorobenzaldehyde gave a product which identical in all respects (m.p., mixed m.p., and spectral data) with arylidene **(9)**, **Scheme 3**.

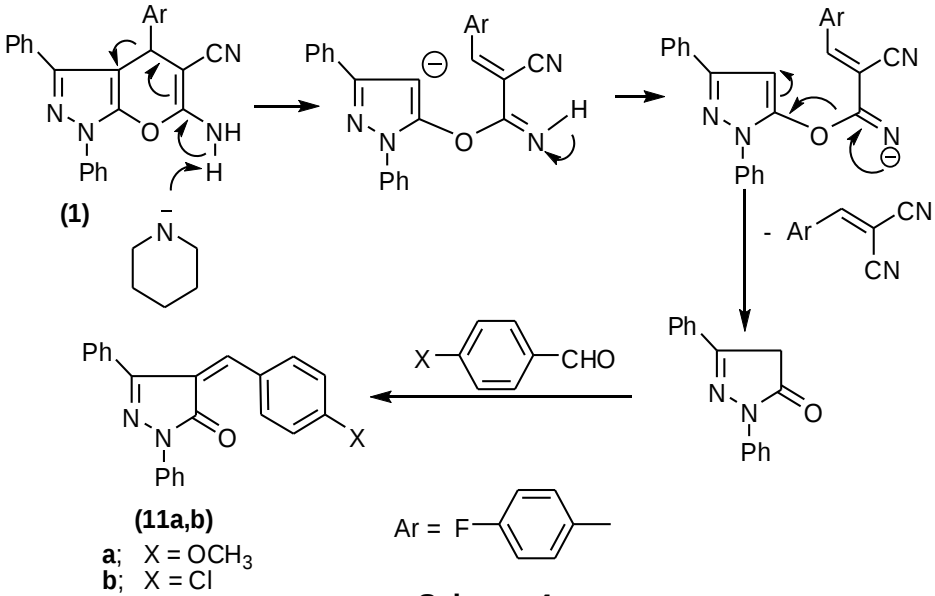


Scheme 3

Interaction of aminonitrile derivative **1** with aromatic aldehydes namely, *p*-anisaldehyde and *p*-chlorobenzaldehyde afforded the unexpected products identified as *p*-methoxy and *p*-chlorobenzylidene pyrazolone derivatives **(11a,b)**.

The formation of compounds **(11a,b)** could be interpreted through a base catalyzed ring opening of the pyran ring and elimination of 2-(4-

fluorobenzylidene)malononitrile to give the pyrazolone which attacks with the aldehyde to give **(11a,b)**[9,10] **Scheme 4**.

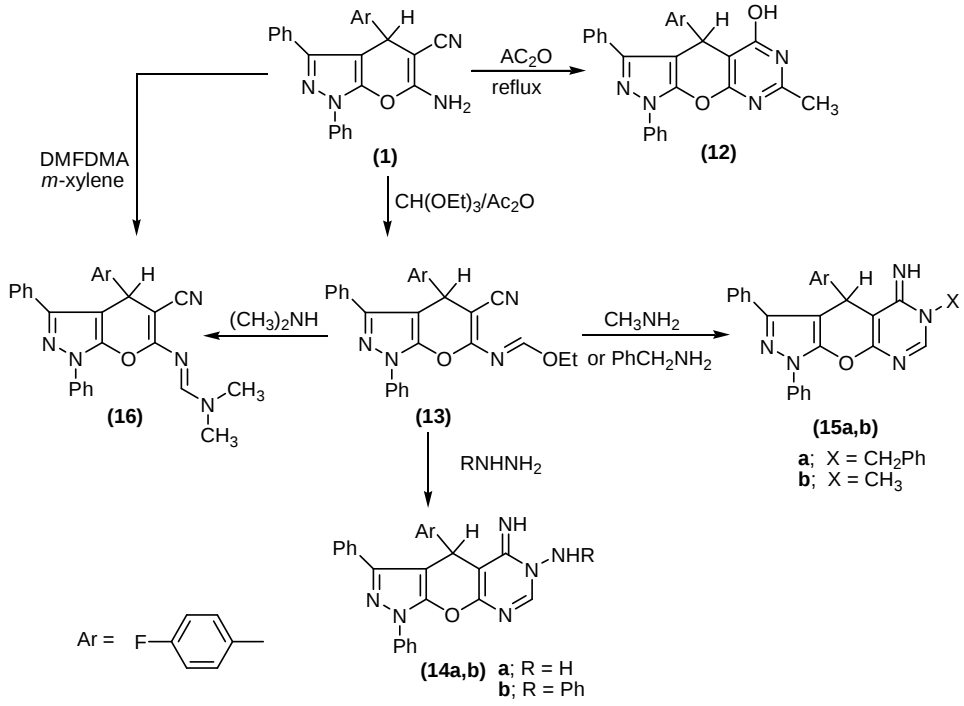


Scheme 4

Further conformation of structure **(11b)** was obtained through its synthesis via authentic route, from the reaction of pyrazolone with *p*-chlorobenzaldehyde to give product which is identical with arylidene **(11b)** (m.p, mixed m.p, and spectral data), **scheme 4.**

The aminonitrile **1** is used as a versatile starting material for synthesis of condensed pyrans. Thus, interaction of **(1)** with acetic anhydride under reflux afforded a product identified as 7-methyl-4-(4-fluorophenyl)-1,3-diphenyl-4,6-dihydropyrazolo[4',3': 5,6]pyrano[2,3-*d*]pyrimidin-5(1*H*)-ole **(12), Scheme 5**.

Compound **1** reacts with triethylorthoformate in refluxing acetic anhydride to give the corresponding ethyl N- [4-(4-fluoro-phenyl)-5-cyano-1,3-diphenyl-1,4-dihydropyrano [2,3-c]pyrazol-6-yl]methanimidate **(13)**, **Scheme 5**.



Scheme 5

Reaction of ethoxymethylideneamino derivative **(13)** with hydrazine hydrate and phenyl hydrazine in absolute ethanol at room temperature afforded 6-amino and 6-phenylamino-4-(4-fluorophenyl)-1,3-diphenyl-5-imino-1,4,5,6-tetrahydropyrazolo[4`,3`:5,6]pyrano[2,3-d]pyrimidines **(14a,b)** respectively, **Scheme 5**.

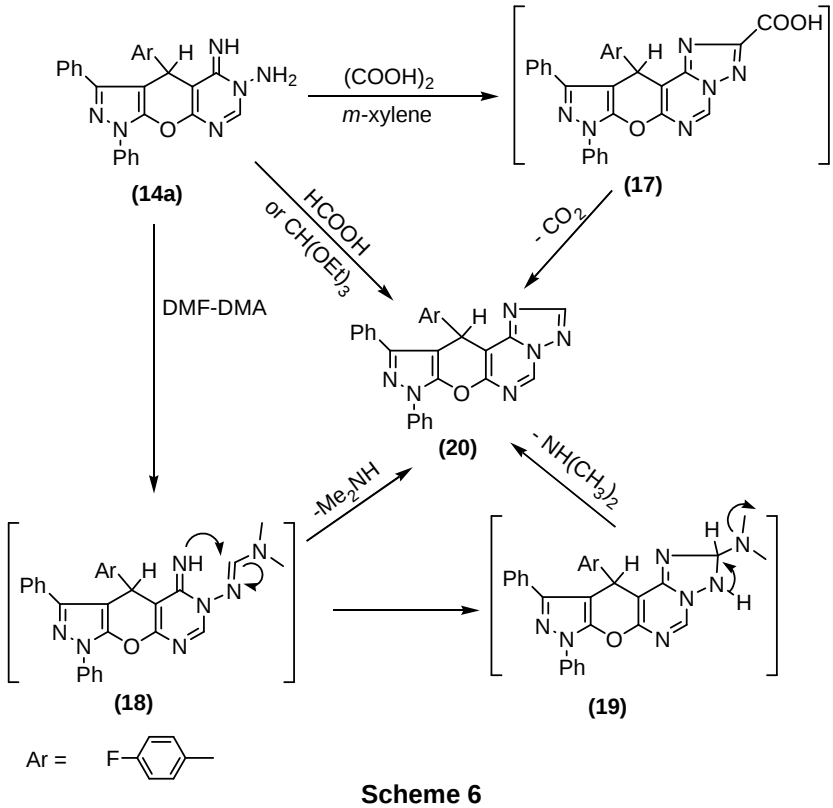
Compound **13** was treated with primary amines namely methyl and benzyl amine in ethanol under stirring afforded 6-substituted-4-(4-fluorophenyl)-1,3-diphenyl-5-imino-1,4,5,6-tetr-ahydropyrazolo[4`,3`:5,6]pyrano[2,3-d]pyrimidine **(15a,b),** respectively**, Scheme 5**.

Interaction of compound **(13)** with dimethylamine in refluxing ethanol afforded *N*'-[5-cyano-4-(4-fluorophenyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-*c*]pyrazol-6-yl]-*N*,*N*-dimethylimi-doformamide **(16).**

The latter compound was also obtained authentically from the reaction of 1 with dimethylformamide-dimethylacetal (DMF-DMA) in refluxing *m*-xylene, **Scheme 5**.

The bifunctional 6-amino-5-iminopyrano[2,3-d]pyrimidine derivative **(14a)** was used as starting material through cyclo-condensation with one carbon donor moiety reagents to give pyranotriazolopyrimidine derivatives. Thus, treatment of amino-imino derivatives **(14a)** with oxalic acid in refluxing *m*-xylene provided a carboxylic acid derivative intermediate **(17)**(TLC), this compound couldn't be isolated and it was soon decarboxylated in the reaction mixture to produce 11-(4-fluorophenyl)-8,10-diphe-nyl-8,11-dihydropyrazolo[4`,3`:5,6]pyrano[3,2-e][1,2,4]triazolo-[1,5-c]pyrimidine **(20), Scheme 6**.

Further confirmation of this structure was obtained through; its synthesis *via* authentic rout. Thus, reaction of **(14a)** with formic acid, triethylorthoformate or DMF-DMA afforded product which was found to be identical with compound **(20)** (m.p., mixed m.p. and spectral data). The formation of the latter compound from reaction of **(14a)** with DMF-DMA could be explained *via* formation of intermediate **(18),** which undergoes spontaneous intramolecular cyclization to produce intermediate **(19)** followed by elimination of dimethylamine, **Scheme 6.**

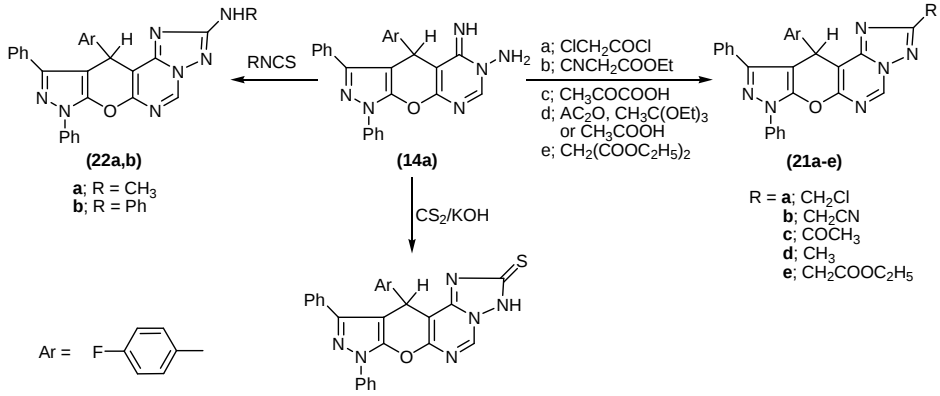


Scheme 6

Reaction of compound **(14a)** with chloroacetyl chloride and ethyl cyanoacetate yielded the corresponding 2-chloromethyl and 2-cyanomethyl derivatives **(21a,b)** respectively, while when reacted with pyruvic acid in refluxing *n*-butanol, 2-acetyl derivative **(21c)** was obtained, **Scheme 7**.

Moreover, the reaction of **(14a)** with acetic anhydride under reflux produced 2-methyltriazole derivative **(21d).** This compound was also obtained from authentically *via* the reaction of **(14a)** with triethylorthoacetate or glacial acetic acid, **Scheme 7**.

Also, cyclocondensation of **(14a)** with diethyl malonate yielded 2-ethoxycarbonylmethyltriazole derivative **(21e)**.



(22a,b)

a; R = CH_3
b; R = Ph

(14a)

(21a-e)

R = **a**; CH_2Cl
b; CH_2CN
c; $COCH_3$
d; CH_3
e; $CH_2COOC_2H_5$

(23)

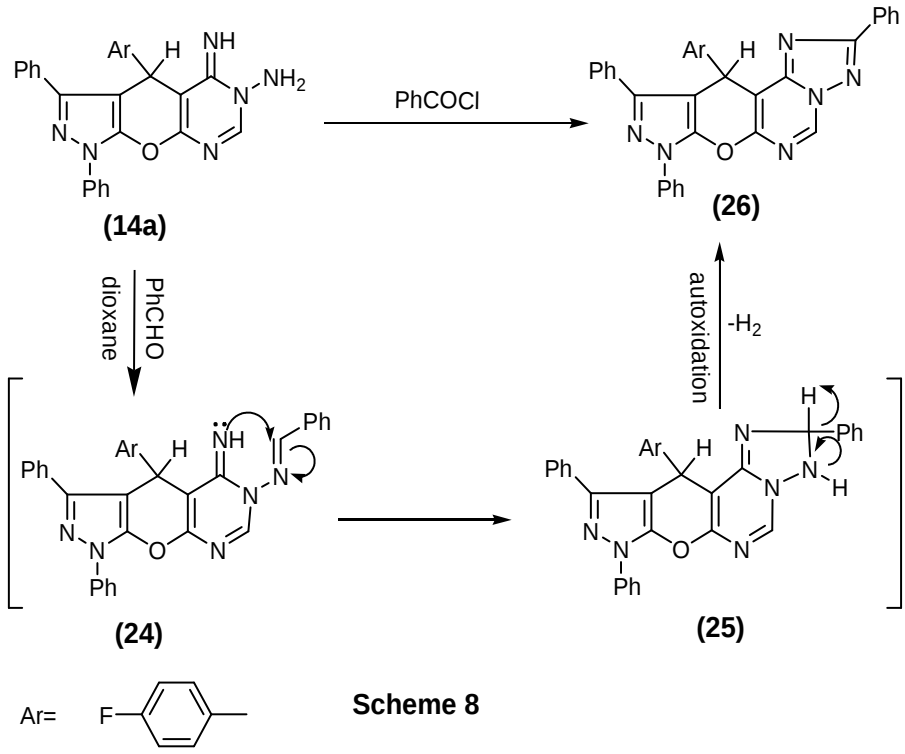
Scheme 7

Reaction of **14a** with methyl isothiocyanate and/or phenyl isothiocyanate afforded 2-methylamino and/or 2-phenylamino derivatives **(22a,b)** respectively, **Scheme 7.**

Reaction of carbon disulphide with 14a in the presence of potassium hydroxide afforded the 2-thione derivative (23), **Scheme 7**.

Aminoimino derivative **14a** reacted with benzaldehyde in refluxing dioxane to give 2-phenylpyranotriazolopyrimidine deri-vative **(26)**. **Scheme 8.**

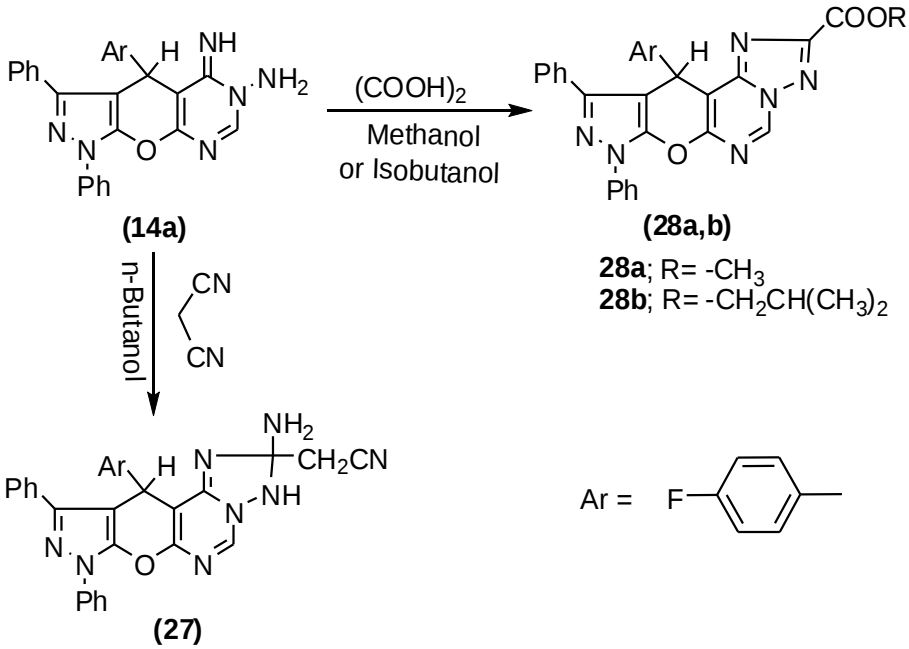
The formation of**(26)** could be explained through formation of benzylideneamino intermediate **(24),** which undergoes intramolecular cyclization to the intermediate **(25),** followed by autoxidation. The structure of **(26)** was further confirmed authetically *via* synthesis through the reaction of **(14a)** with benzoyl chloride.



Scheme 8

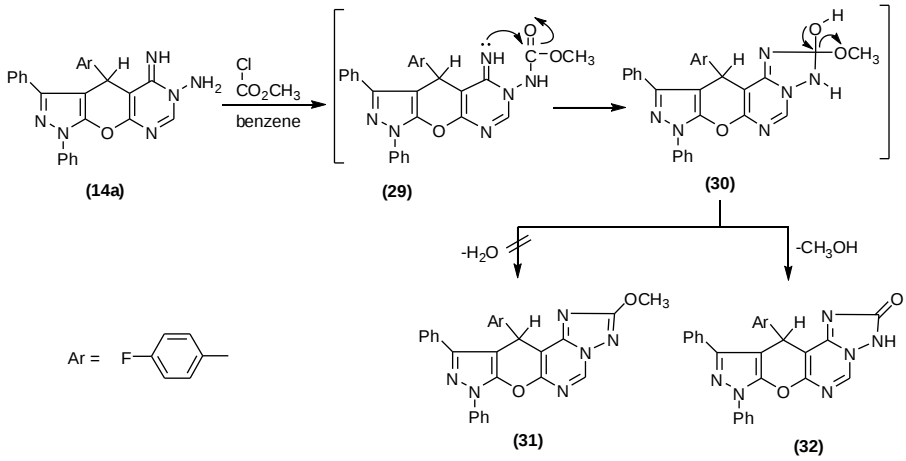
Refluxing compound **14a** with equimolar ratio of malono-nitrile in *n*-butanol resulted in the formation of 2-amino-2-cya-nomethyl-8,l0-diphenyl-11-(4-fluorophenyl)-3,8,11-trihydropyra-zolo[4`,3`:5,6]pyrano[3,2-e][1,2,4]triazolo[1,5-c] pyrimidine **(27), Scheme 9.**

Reaction of **14a** with oxalic acid in refluxing methyl alcohol and in isobutyl alcohol afforded 2-methoxycarbonyl and 2-isobutoxycarbonyl **(28a,b)** derivatives, respectively, **Scheme 9**.



Scheme 9

When **14a** was reacted with methyl chloroformate (1:1 molar ratio) in refluxing dry benzene, the expected 2-oxopyrano-triazolopyrimidine derivative **(32)** was obtained. The formation of **(32)** could be explained by the formation of methyl ester intermediate **(29),** which undergoes spontaneous intramolecular cyclization to give intermediate **(30)** followed by elimination of methanol to yield final isolable product. The other possible structure **(31)** was ruled out on the basis of ^{1}HNMR spectrum which showed the absence of methoxy signal of the isolated product, **(Scheme 10).**



Scheme 10

Experimental

All melting points are uncorrected. IR spectra (KBr) were measured on Shimadzu IR 440 spectrometer. The ^{1}H NMR spectra were performed in $CDCl_3$ or DMSO-d_6 using FX 90 Fourier Transform ^{1}H NMR spectrometer. Mass spectra were measured on a Shimadzu GCMS-QP 1000 EX mass spectrometer using the direct inlet system. Microanalyses were carried out at the Microanalytical Center at Cairo University.

6-Amino-5-cyano-4-(4-fluorophenyl)-1,3-diphenyl-],4-di- hydropyrano [2, 3-c]-pyrazole (1)

A mixture of 1,3-diphenyl pyrazol-5-one (0.01 mol) and 4-fluro-benzylidenemalononitrile (0.01 mol) in ethanol (50 ml), was treated with a few drops of piperidine. The mixture was refluxed for l h. The resulting solid was collected by filtration and recrystallized from ethanol-benzene mixture to give **(1).** (table 1)

4-(4-fluorophenyl)-1,3-diphenyl-4,6-dihydropyrazolo[4',3':5,6] pyrano[2,3-*d*]pyrimidin-5(1*H*)-one (5)

A mixture of (**1**; 0.01mol) and formic acid (30 ml) was refluxed for 5 hrs. The solvent was concentrated till dryness, after cooling the solid product which formed was collected and recrystallized to give **(5)** (table 1).

General procedure for preparation of (6a,b)

A mixture of (**1**; 0.01mol) and p-chlorobenzoylchloride, benzoylchloride (10 ml) was refluxed for 2 hrs. then allowed to cool and treated with petroleum ether (60~80 ºC) (50 ml), where by petroleum ether was decanted, the solid product was separated, collected by filtration and washed with petroleum ether (60~80 ºC) several times, dried and recrystallized to give 7-(4-chlorophenyl)-4-(4-fluorophenyl)-1,3-diphenyl-4,6-dihydropy-razolo[4',3':5,6]pyrano[2,3-*d*]pyrimidin-5(1*H*)-one **(6b)** and 4-(4-fluorophenyl)-1,3,7-triphenyl-4,6-dihydropyrazolo [4',3':5,6] pyra-no[2,3-*d*]pyrimidin-5(1*H*)-one **(6a)**, (table 1).

4-(4-fluorophenyl)-5,7-diphenyl-4,7-dihydro-1*H*-pyrazolo [4',3':5,6]pyrano[2,3-*c*]pyrazol-3-amine (7)

Procedure (1):

A mixture of (1; 0.01mol) and hydrazine hydrate (0.02mol) in ethanol was heated under reflux for 3 hrs. The solvent was removed under vacuum the solid obtained was recrystallized to give **(7)**, (table 1).

Procedure (2):

A mixture of (**1**; 0.01mol) and hydroxylamine hydrochloride (0.02 mol) in sod. ethoxide was heated under reflux for 2 hrs. The solvent was removed under vacuum and the solid obtained was recrystallized, m.p. and mixed m.p. determined with authe-ntic sample gave no depression.

4-(4-fluorobenzylidene)-1,3-diphenyl-1H-pyrazol-5(4H)-one (9).

Procedure (1):

A mixture of (**1**; 0.01mol) and urea (0.02 mol) was heated at (160 ºC) for (20 min). The separated solid was filtered off and recrystallized to give **(9),** (table 1).

Procedure (2):

A mixture of (**1**; 0.01mol) and p-fluorobenzaldehyde (0.01 mol) was refluxed in ethanol/piperidine for 2 hrs. The separated solid was filtered off and recrystallized to give **(9)**, (table 1).

4-(4-chlorobenzylidene)-1,3-diphenyl-1H-pyrazol-5(4H)-one (11).

Procedure (1):

A mixture of (**1**; 0.01 mol) and the p-chlorobenzaldehyde (0.01 mol) in ethanol (40 ml) containing few drops of piperidine were refluxed for 2 hrs. the obtained

product was collected by filtration and recrystallized from the appropriate solvent to give **(11),** (table 1).

Procedure (2):

A mixture of (**1**; 0.01mol) and p-chlorobenzaldhyde (0.01 mol) was refluxed in ethanol/piperidine for 2 hrs. The separated solid was filtered off and recrystallized to give **(11),** (table 1).

7-Methyl-4-(4-fluorophenyl)-1,3-diphenyl-4,6-dihydropyrazo lo[4',3':5,6]pyrano[2,3-*d*]pyrimidin-5(1*H*)-one (12).

A mixture of (**1**; 0.01mol) and acetic anhydride (25 ml) was heated under reflux for 6 hrs. the reaction mixture was concentrated till dryness, the solid which obtained was collected and recrystallized to give **(12),** (table 1).

Ethyl N[4-(4-fluorophenyl)-5-cyano-1,3-diphenyl-1,4-dihydro pyrano[2, 3-c]-pyrazol-6-yl]methanimidate (13).

A mixture of o-aminonitrile (**1**; 0.01 mol), triethylortho-formate (0.01 mol) and acetic anhydride (30 ml) was refluxed for 5 hrs. The solvent was removed under reduced pressure and the separated solid was recrystallized from ethanol-benzene mixture to give the imine **(13),** (table 1).

6-Substituted-4-(4-fluorophenyl)-1,3-diphenyl-5-imino-1,4,5,6-tetra-hydropyrazolo[4',3':5,6]pyrano[2,3-d]pyrimidines (14a,b)

To a solution of (**13**; 0.01 mol) in ethanol (50 ml), hydrazine hydrate and/or phenyl hydrazine (0.01 mol) was added. The reaction mixture was stirred for l h. The solid obtained was filtered off and recrystallized to give **(14a,b),** (table 1).

General procedure for preparation of (15a,b)

To a solution of (**13**; 0.01mol) in absolute ethanol (50 ml), benzylamine and/or methylamine (0.01 mol) was added, the reaction mixture was stirred for 2 hrs. The solid obtained was filtered off and recrystallized to give 6-benzyl-4-(4-fluorophenyl)-1,3-diphenyl-5-imino-1,4,5,6-tetrahydropyrazolo[4',3':5,6]-pyrano[2,3-d]pyrimidine **(15a)** and 6-methyl-4-(4-fluorophenyl)-1,3-diphenyl-5-imino-1,4,5,6-tetrahydropyrazolo[4',3':5,6]pyrano [2,3-d]pyrimidine **(15b),** respectively, (table 1)

N'-[5-cyano-4-(4-fluorophenyl)-1,3-diphenyl-1,4-dihydropyr-ano [2,3-*c*]pyrazol-6-yl]-*N*,*N*-dimethylimidoformamide (16).

Procedure (A):

A mixture of (**1**; 0.01mol) and *N*,*N*-dimethylformamide dimethylacetal (0.01 mol) in xylene (20 ml) was refluxed for 2 hrs. The solvent was removed under reduced pressure the residual solid was collected and recrystallized to give **(16),** (table 1).

Procedure (B):

A solution of (**13**; 0.01mol) and dimethylamine (0.01 mol) in ethanol (50 ml) was stirred for 45 min. the solid obtained was filtered off and recrystallized, m.p. and mixed m.p. determined with authentic sample gave no depression.

11-(4-fluorophenyl)-8,10-diphenyl-8,11-dihydropyrazolo[4',3' :5,6] pyrano [3,2-e] [1,2,4] triazolo [1,5-c]pyrimidine (20).

Procedure A:

A mixture of (**14a**; 0.01 mol) and oxalic acid (0.01 mol) in xylene (20 ml) was refluxed for 8 hrs. The precipitate product was filtered off and recrystallized from benzene to give **(20),** (table 1).

Procedure B:

A mixture of (**14a**; 0.01 mol) and formic acid (10 ml) was refluxed for 6h. the solid obtained was recrystallized to give **(20)**.

Procedure C:

A mixture of (**14a**; 0.01 mol) and triethylorthoformate (0.01 mol) in benzene (50 ml) was refluxed for 5 hrs. The solid obtained was recrystallized to give **(20)**.

Procedure D:

Compound (**14a**; 0.01 mol) reacted with *N*,*N*-dimethyl-formamide-dimethylacetal (DMF-DMA) (0.01) according to produce C to give **(20)**.

2-Chloromethyl-11-(4-fluorophenyl)-8,10-diphenyl-8,11-di-hydropyrazolo[4',3':5,6]pyrano[3,2-e][1,2,4]triazolo[1,5-c]-pyrimidine (21a)

A mixture of (**14a**; 0.01mol) and chloroacetyl chloride (0.01 mol) in benzene (50 ml) was refluxed for 6 hrs. The product obtained was filtered off and recrystallized to give **(21a)** (table 1).

2-Cyanomethyl-11-(4-fluorophenyl)-8,10-diphenyl-8,11-dihydropyrazolo[4',3':5,6]pyrano[3,2-e][1,2,4]triazolo[1,5-c]pyrim-idine (21b)

Compound **(21b)** was prepared from (**14a**; 0.01 mol) and ethyl cyanoacetate (0.01 mol) in ethanol (50 ml) was refluxed for 5 hrs. The solid obtained was collected by filtration and recrystallized to give **(21b),** (table 1).

2-Acetyl-11-(4-fluorophenyl)-8,10-diphenyl-8,11-dihydro pyr-azolo[4',3':5,6] pyrano[3,2-e][1,2,4]triazolo[1,5-c]pyrimidine (21c)

A mixture of (**14a**; 0.01 mol), pyruvic acid (0.01 mol) in *n*-butanol (50 ml) was refluxed for 10 hrs. The product obtained after concentration of reaction mixture, was filtered off and recrystallized to give **(21c)** (table 1)

11-(4-fluorophenyl)-8,10-diphenyl-2-methyl-8,11-dihydro pyrazolo[4',3':5,6] pyrano[3,2-e][1,2,4]triazolo[1,5-c]pyrimi-dine (21d)

Procedure A:

A mixture of (**14a**; 0.01 mol) and acetamide (0.01 mol) in ethanol (50ml) was refluxed for 6 hrs. The solid obtained was filtered off and recrystallized from benzene to give **(21d),** (table 1).

Procedure B:

A mixture of (**14a**; 0.01 mol) and acetic acid (20 ml) was refluxed for 5 hrs. The product was filtered off and recrystallized from benzene (m.p. and mixed m.p. with sample obtained from procedure A gave no depression).

Procedure C:

A mixture of **(21d)** prepared from (**14a**; 0.01 mol) and triethyl orthoacetate (0.01 mol) in benzene (50 ml) was refluxed for 5 hrs. The obtained solid was recrystallized to give **(21)**.

Ethyl 2-(Methoxycarbonyl-11-(4-fluorophenyl)-8,10-diphenyl-8,11-dihydropyrazolo[4',3':5,6]pyrano[3,2-e][1,2,4]triazolo [1,5-c] pyrimidine) acetate (21e)

A mixture of **(14a;** 0.01mol) and diethyl malonate (0.01mol) in ethanol (50 ml) was refluxed for 5hrs. The solid obtained was collected by filtration and recrystallized to give (**21e**), (table 1).

General procedure for preparation of (22a,b).

A mixture of (**14a**; 0.01 mol), methyl isothiocyanate and/or phenyl isothiocyanate (0.012 mol) in ethanol 30 ml. was refluxed for 3 hrs. The obtained products were filtered off and recrystallized to give 2-methylamine and/or phenylamine-11-(4-fluorophenyl)-8,10-diphenyl-8,11-dihydropyrazolo[4',3':5,6] pyra- no [3,2-e] [1,2,4] triazolo [1,5-c]pyrimidine **(22a,b),** (table 1).

2-Thioxo-11-(4-fluorophenyl)-8,10-diphenyl-8,11-dihydro pyrazolo[4',3':5,6]pyrano[3,2-e][1,2,4]triazolo[1,5-c]pyrimi-dine (23).

A mixture of (**14a**; 0.01 mol), 0.3 gm of (KOH) and 3 ml of (CS_2) 30 ml in ethanol was refluxed for 5 hrs. After removal of ethanol, water was added and the alkaline solution was filtered the clear filtrate was acidified with acetic acid and the formed precipitate was collected and recrystallized to give (**23**) (table 1).

11-(4-Fluorophenyl)-8,10-diphenyl-2-phenyl-8,11-dihydro pyrazolo[4',3':5,6]pyrano[3,2-e][1,2,4]triazolo[1,5-c]pyrimi-dine (26)

Procedure (A):

A mixture of (**14a**; 0.01mol) and benzaldehyde (0.012 mol) in dioxane (20 ml) and few drops of piperidine was refluxed for 5hrs. The mixture then cooled and the separated solid was filtered off and recrystallized to give (**26**), (table 1).

Procedure (B):

A mixture of (**14a**; 0.01mol) and benzoyl chloride (10 ml) was refluxed for 3 hrs., the reaction mixture was then diluted with cold NaOH solution and the solid obtained washed with water and recrystallized to give **(26)** m.p. and mixed m.p. determined with authentic sample gave no depression

2-amino-2-cyanomethyl-8,10-diphenyl-11-(4-fluorophenyl)-3,8,11–trihydropyrazolo[4',3':5,6]pyrano[3,2-e][1,2,4]triazolo [1,5-c]pyrimidine (27)

A mixture of (**14a**; 0.01 mol) and malononitrile (0.01 mol) in n-butanol (50 ml) was refluxed for 8 hrs. The precipitated product was filtered off and recrystallized to give **(27).** (table 1)

2-Methoxycarbonyl-11-(4-fluorophenyl)-8,10-diphenyl-8,11-dihydropyrazolo[4',3':5,6]pyrano[3,2-e][1,2,4]triazolo[1,5-c]-pyrimidine (28).

A mixture of (**14a**; 0.01 mol) and oxalic acid (0.01 mol) in methanol (50 ml) was refluxed for 8 hrs. The obtained solid was filtered off and recrystallized from EtOH/benzene to give **(28),** (table 1)

2-Isobutoxycarbonyl-11-(4-fluorophenyl)-8,10-diphenyl-8,11-dihydropyrazolo[4',3':5,6]pyrano[3,2-e][1,2,4]triazolo[1,5-c]-pyrimidine (29)

A mixture of (**14a**; 0.01 mol) and oxalic acid (0.01 mol) in isobutyl alcohol (50 ml) was refluxed for 8 hrs. The solid obtained was filtered off and recrystallized to give **(29)**, (table1).

2-Oxo-11-(4-fluorophenyl)-8,10-diphenyl-8,11-dihydropyrazolo[4',3':5,6]pyrano[3,2-e][1,2,4]triazolo[1,5-c]pyrimidine (33).

A mixture of (**14a**; 0.01mol) and methyl chloroformate (0.01 mol) in benzene (50 ml) was refluxed for 6hrs. The product obtained was filtered off and recrystallized to give **(33),** (table 1).

Table (1): Physical and Analytical Data for the Newly Prepared Comp.:

Com.	m.p. [°C] (recrystallization Solvent)	Colour (Yield [%)	M. Formula (M.Wt.)	Elemental Analyses (%) Calculated/Found		
				C	H	N
1	233-234	White	$C_{25}H_{17}FN_4O$ (408)	73.52	4.20	13.72
	(.Et./B)	(69)		73.50	4.22	13.71
5	130-131	White	$C_{26}H_{17}FN_4O_2$ (436)	71.55	3.93	12.84
	(.Et)	(88)		71.54	3.95	12.85
6a	285-286	Yellow	$C_{32}H_{20}ClFN_4O_2$ (546)	70.27	3.69	10.24
	(.Et./B)	(78)		70.28	3.67	10.25
6b	214-216	Yellow	$C_{32}H_{21}FN_4O_2$ (512)	74.99	4.13	10.93
	(.Et./B)	(89)		74.97	4.10	10.95
7	161-162	Brown	$C_{25}H_{18}FN_5O$ (423)	70.91	4.28	16.54
	(.Et)	(70)		70.93	4.29	16.55
9	112-113	White	$C_{22}H_{15}FN_2O$ (342)	77.18	4.42	8.18
	(.B)	(65)		77.20	4.41	8.17
11	120-121	Brown	$C_{22}H_{15}ClN_2O$ (358)	73.64	4.21	7.81
	(.Et)	(80)		73.63	4.20	7.82
12	238-240	Yellow	$C_{27}H_{19}FN_4O_2$ (450)	71.99	4.25	12.44
	(.Et./B)	(87)		71.98	4.28	12.45
13	160-161	Orange	$C_{28}H_{21}FN_4O_2$ (464)	72.40	4.56	12.06
	(.Et)	(62)		72.41	4.57	12.08
14a	225-226	White	$C_{26}H_{19}FN_6O$ (450)	69.32	4.25	18.66
	(.Et./B)	(75)		69.33	4.26	18.65
14b	265-266	Red	$C_{32}H_{23}FN_6O$ (528)	72.99	4.40	15.96
	(.Et./B)	(74)		72.97	4.42	15.97
15a	280-281	Yellow	$C_{33}H_{24}FN_5O$ (525)	75.41	4.60	13.33
	(.Et./B)	(60)		75.42	4.62	13.35
15b	247-249	Yellow	$C_{27}H_{20}FN_5O$ (449)	72.15	4.48	15.58
	(.Et./B)	(80)		72.17	4.47	15.59
16	132-133	Yellow	$C_{28}H_{22}FN_5O$ (463)	72.56	4.78	15.11
	(.Et)	(89)		72.57	4.79	15.13
20	190-192	White	$C_{27}H_{17}FN_6O$ (460)	70.43	3.72	18.25
	(.B)	(70)		70.45	3.70	18.23
21a	220-222	White	$C_{28}H_{18}ClFN_6O$ (508)	66.08	3.56	16.51
	(.Et./B)	(66)		69.06	3.55	16.53
21b	202-203	White	$C_{29}H_{18}FN_7O$ (499)	69.73	3.63	19.63
	(.Et./B)	(84)		69.75	3.65	19.65
21c	218-220	Yellow	$C_{29}H_{19}FN_6O_2$ (502)	69.32	3.81	16.72
	(.Et./B)	(66)		69.33	3.82	16.73
21d	165-166	White	$C_{28}H_{19}FN_6O$ (474)	70.88	4.04	17.71
	(.Et)	(89)		70.89	4.05	17.72
21e	290-292	Brown	$C_{31}H_{23}FN_6O_3$ (546)	68.12	4.24	15.38
	(.D)	(72)		68.13	4.25	15.39
22a	198-200	White	$C_{29}H_{22}FN_7O$ (503)	69.17	4.40	19.47
	(.Et./B)	(82)		69.18	4.42	19.48
22b	142-143	Yellow	$C_{33}H_{22}FN_7O$ (551)	71.86	4.02	17.78
	(.Et)	(69)		71.85	4.04	17.76
23	253-255	Orange	$C_{27}H_{17}FN_6OS$	65.84	3.48	17.06
	(.Et./B)	(70)	(492)	65.82	3.47	17.04
26	233-235	Orange	$C_{33}H_{21}FN_6O$ (536)	73.87	3.94	15.66
	(.Et./B)	(92)		73.89	3.96	15.67
27	266-267	Yellow	$C_{29}H_{21}FN_8O$ (516)	67.43	4.10	21.69
	(.Et./B)	(89)		67.44	4.12	21.68
28	225-227	Yellow	$C_{29}H_{19}FN_6O_3$ (518)	67.18	3.69	16.21
	(.Et./B)	(80)		67.20	3.68	16.22
29	265-267	Yellow	$C_{32}H_{25}FN_6O_3$ (560)	68.56	4.50	14.99
	(.Et./B)	(80)		68.58	4.52	14.97
33	237-238	Orange	$C_{27}H_{17}FN_6O_2$ (476)	68.06	3.60	17.64
	(.Et./B)	(68)		68.08	3.62	17.65

(B.; benzene, D.; dioxane, DMF; dimethylformamide, Et.; Ethanol).

Table (2): Spectral data for the newly prepared compounds.

Comp.	IR (cm^{-1})	Spectral data (^{1}H-NMR, δ, ppm; Mass spectra: m/z)
1	3322, 3212 (NH_2), 2200 (CN)	^{1}HNMR ($CDCl_3$) :4.69 (s, 2H, NH_2), 4.94 (s, 1H, 4H-pyran), 6.90-7.70 (m, 14H, Ar-H). Mass, m/z (intensity %):342 (100; M^+- $CH_2(CN)_2$), 247 (59.81), 209 (53.20), 183 (12.35), 103 (13.44) , 77 (68.53).
5	3420 (OH)	^{1}H-NMR (DMSO-d_6) 5.49 (s, 1H, 4H-pyran), 6.99-7.89 (m, 15H, ArH + OH), 8.19 (s, 1H, CH-pyrimidine). Mass, m/z (intensity %): 437 (45.2) ,361 (95.2), 323 (85.7), 247 (95.2), 93 (100)
6a	3384 (NH), 1670 (CO).	Mass, m/z (intensity %): 417 (6.6; M^+- *p*-flourophenyl), 205 (11.1),148 (23.6),119 (100), 91 (40.7), 77 (18.9) , 51 (19.4).
6b	3200 (NH), 3068 (CH-aliph.), 1648 (CO),	^{1}H-NMR (DMSO-d_6) 5.53 (s, 1H, 4H-pyran), 6.95-8.12 (m, 18H, ArH) 13.1(b, 1H, NH).
7	3300, 3210 (NH_2, NH)	^{1}H-NMR (DMSO-d_6) 5.29 (s, 1H, 4H-pyran), 6.05 (s, 2H, NH_2), 7.10-7.98 (m, 14H, ArH), 14.34 (b, 1H, NH).
9	3050 (CH-aromatic).	Mass, m/z (intensity %): 343 (2.5) ,237 (1.3), 207 (5.3),183 (4.7), 103 (9.2) , 77 (100).
11	3050 (CH-aromatic)	Mass, m/z (intensity %): 358 (38.2) ,235 (13.8), 189 (14.6), 103 (27.5) , 77 (100).
12	3446 (OH), 1658 (CO)	^{1}H-NMR (DMSO-d_6) 2.34 (s, 3H, CH_3), 5.49 (s, 1H, 4H-pyran), 6.98-7.96 (m, 18H, ArH), 12.71 (s, 1H, NH) disappeared by D_2O.
13	2212 (CN)	^{1}H-NMR (DMSO-d_6) 1.3 (t, 3H, $OCH_2\underline{CH_3}$), 4.4 (q, 2H, $O\underline{CH_2}CH_3$), 5.06 (s, 1H, 4H-pyran), 6.90-7.70 (m, 14H, ArH), 8.27 ppm (s, 1H, CH=N).
14a	3422, 3330, 3301 (NH_2, NH)	Mass, m/z (intensity %):450 (26.3) , 434 (100; M^+-NH_2), 340 (43.8),313 (21.5),218 (6.9), 146 (14.1) , 77 (97.3).
14b	3464 (NH)	Mass, m/z (intensity %):528 (100) , 483 (18.0), 247 (63.5), 171 (12.8).
15a	3360 (NH)	Mass, m/z (intensity %): 525 (38.3) ,434 (73.1), 340 (13.8), 247 (8.2), 207 (7.9), 91 (100; CH_2Ph).
15b	3296 (NH)	^{1}H-NMR (DMSO-d_6) 2.37 (s, 3H, CH_3), 5.20 (s, 1H, 4H-pyran), 7.03-7.98 (m, 18H, ArH), 8.03 (s, 1H, CH-pyrimidine), 17.33 (b, 1H, NH).
16	2198 (CN)	Mass, m/z (intensity %): 463 (25.1) ,368 (100; M^+-*p*-flourophenyl), 247 (14.9), 209 (13.4), and 77 (26.0).
20	3058 (CH-arom)	^{1}H-NMR (DMSO-d_6) 5.51 (s, 1H, 4H-pyran), 7.05-7.89 (m, 18H, ArH), 8.55 (s, 1H, CH-pyrimidine),11.27 (s, 1H, CH-triazole).
21a	3068 (CH-aromatic)	^{1}H-NMR (DMSO-d_6) 4.51 (s, 2H, CH_2), 5.48 (s, 1H, 4H-pyran), 6.79-7.97 (m, 18H, ArH), 9.69(s, 1H, CH-pyrimidine).
21b	2210 (CN)	Mass, m/z (intensity %): 499 (57.7) , 406 (16.8), 311 (53.7), 272 (43.0), 207 (34.9), 142 (26.8) , 77 (100).
21c	1622 (CO)	^{1}H-NMR (DMSO-d_6) 2.78 (s, 3H, CH_3), 6.04 (s, 1H, 4H-pyran), 6.97-7.90 (m, 18H, ArH), 9.6 (s, 1H, CH-pyrimidine).
21d	3078 (CH-aromatic)	^{1}H-NMR (DMSO-d_6) 2.45 (s, 3H, CH_3), 6.01 (s, 1H, 4H-pyran), 6.97-7.95 (m, 14H, ArH), 9.54 (s, 1H, CH-pyrimidine).
21e	1740 (CO)	^{1}H-NMR (DMSO-d_6) 1.16 (t, 3H, $\underline{CH_3}CH_2$), 3.96 (s, 2H, CH_2) , 4.10 (q, 2H, $CH_3\underline{CH_2}$), 5.70 (s, 1H, 4H-pyran), 6.90-7.90 (m, 14H, ArH), 8.10 (s, 1H, CH-pyrimidine).
22a	3304 (NH).	^{1}H-NMR (DMSO-d_6) 2.30 (s, 3H, CH_3), 5.70 (s, 1H, 4H-pyran), 6.97-7.90 (m, 15H, ArH + NH), 8.10 (s, 1H, CH-pyrimidine).

Table (2): Continue.

Compd. No	IR (cm^{-1})	Spectral data (^{1}H-NMR, Mass spectra)
22b	3310 (NH).	Mass, m/z (intensity %): 551 (2.3), 456 (10.2), 435 (36.9), 340 (100), 296 (6.4), 180 (5.4) , 104 (6.2).
23	3322 (NH).	^{1}H-NMR (DMSO-d_6) 1.9 (s, 1H, SH), 5.76 (s, 1H, 4H-pyran), 6.99 -7.92m, 14H, ArH), 8.14 (s, 1H, CH-pyrimidine)
26	1626 (C=N).	Mass, m/z (intensity %): 536 (54.0) ,441 (100; M^+-*p*-flourophenyl), 336 (3.5),273 (3.9),172 (3.5) and 77 (37.6).
27	3430,3320,3200 (NH_2/NH),2170 (CN).	1H-NMR (DMSO-d6) 2.78 (s, 2H, CH2) 5.89 (s, 2H, NH2), 6.03 (s, 1H, 4H-pyran), 6.97-7.90 (m, 19H, ArH + NH), 8.10 (s, 1H, CH-pyrimidine)
28	1738 (CO).	^{1}H-NMR (DMSO-d_6) 3.58 (s, 3H , OCH_3), 6.09 (s, 1H, 4H-pyran), 7.09-7.91 (m, 18H, Ar-H), 8.80 (s, 1H, CH-pyrimidine).
29	1740 (CO).	^{1}H-NMR (DMSO-d_6) 0.81 (d, 6H, $2CH_3$), 1.90 (m, 1H, $\underline{CH}(CH_3)_2$), 4.10 (d, 2H, $\underline{CH_2}CH$) , 6.09 (s, 1H, 4H-pyran), 6.95-7.94 (m, 14H, ArH), 8.37(s, 1H, CH-pyrimidine)
33	1772 (CO).	^{1}H-NMR (DMSO-d_6) 6.22 (s, 1H, 4H-pyran), 6.74 (s, 1H, NH), 7.04-7.90 (m, 14H, ArH), 8.78 (s, 1H, CH-pyrimidine).

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