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The catalyst-free syntheses of pyrazolo[3,4-*b*]quinolin-5-one and pyrazolo[4′,3′:5,6]pyrido[2,3-*d*]pyrimidin-5,7-dione derivatives by one-pot, three-component reactions

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Graphical Abstract

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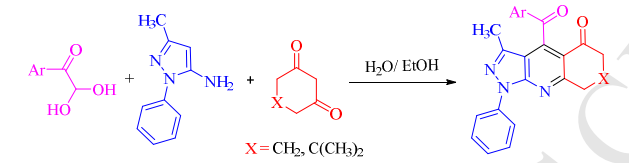

X = CH_2, $C(CH_3)_2$

Ar = C_6H_5, 4-ClC_6H_4, 4-FC_6H_4, 4-MeC_6H_4, 4-$MeOC_6H_4$, 3,4-$(MeO)_2C_6H_3$, 4-$O_2NC_6H_4$, 3-MeO-4-HOC_6H_3

The catalyst-free syntheses of pyrazolo[3,4-*b*]quinolin-5-one and pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidin-5,7-dione derivatives by one-pot, three-component reactions

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ABSTRACT

Herein we report the syntheses of pyrazolo[3,4-*b*]quinolin-5-one and pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidin-5,7-dione derivatives by cyclocondensation of 1,3-diketones, 3-methyl-1-phenyl-1*H*-pyrazole-5-amine and arylglyoxals, under catalyst-free conditions in H_2O/EtOH at reflux in 65-98% and 73-96% yields respectively. This protocol provides mild reaction conditions, good to high yields, non-catalytic, simple procedures and easy isolation of products to structurally diverse tricyclic pyrazolo[3,4-*b*]quinolin-5-one and pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidin-5,7-dione derivatives, which may have biological and pharmacological activities.

Keywords: Arylglyoxals, Pyrazolo[3,4-*b*]quinolines, Pyrido[2,3-*d*]pyrimidines, One-pot, Multi-component reactions

Introduction

The green synthesis of nitrogen-containing heterocyclic compounds using environmentally friendly chemical procedures has attracted much attention due to their various biological and pharmaceutical activities. One-pot, multicomponent reactions (MCRs), which combine three or more substrates concurrently or in sequential addition, lead to domino processes,[1] without isolating intermediate species or changing the solvent. MCRs offer benefits such as simple and convenient operation, facile automation and minimized waste generation due to the decrease in the number of work-up, extraction and purification stages. They play an important role in the synthesis of heterocyclic compounds through environmentally and economically useful one-pot procedures.

Water is the ideal green solvent and the best alternative to organic solvents, because of being non-flammable, non-hazardous, non-toxic, uniquely redox-stable, inexpensive, readily available and environmentally benign.[2] Pyrazoles are important because of their wide range of pharmacological effects[3] and biological activities,[4] such as antidepressant,[5] antibacterial,[6] antihyperglycemic,[7] antimalarial,[8]

antiinflammatory,[9] antimicrobial,[10] antitumor,[11] anticancer,[12] antiviral,[13] and analgesic[14] properties. They also have a wide range of applications in the agrochemicals industry,[15,16] but are relatively scarce in nature.

Pyrazolo[3,4-*b*]quinolones have attracted more attention than other derivatives due to their bioactivities,[17] such as antimycobacterial,[18] antimicrobial,[19] and antiviral.[20] Examples of their use are as inhibitors of herpex simplex virus,[21] oncogenic ras-inhibitors,[22] cyclooxygenase inhibitors,[23] replication,[24] activators of caspases and inducers of apoptosis.[25] Among the several methods available for the synthesis of pyrazolo[3,4-*b*]quinolones,[26-28] the one-pot, three-component reaction of 1,3-diketons, 5-aminopyrazoles and aromatic aldehydes has received much attention.[29]

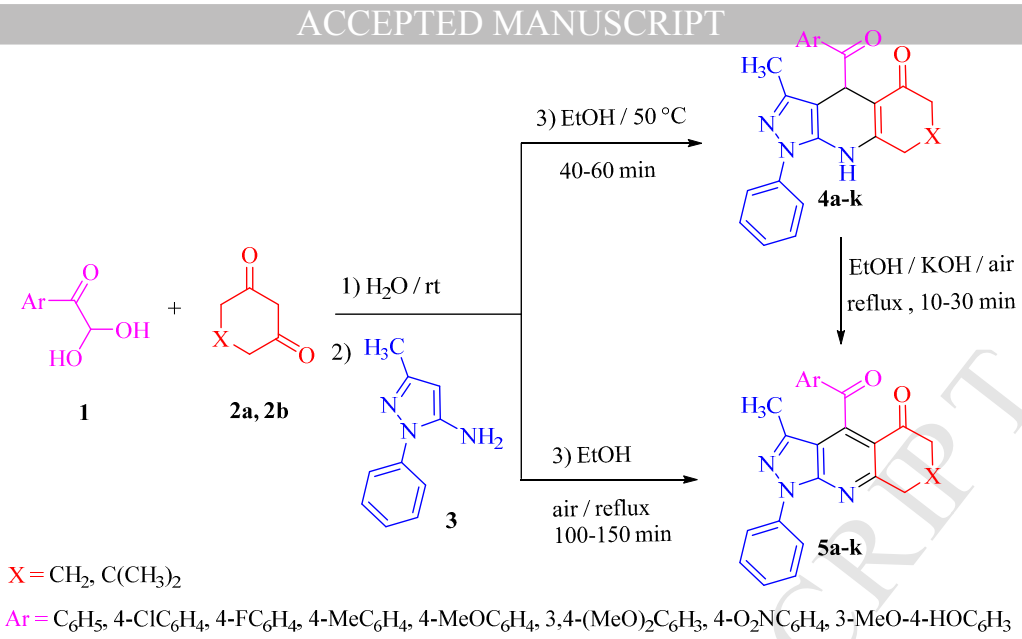
Pyrazolo[3,4-*b*]pyridines are present in numerous natural products and biologically active molecules, such as the anxiolytic drugs cartazolate, etazolate and tracazolate.[30]

Several methods for the synthesis of pyrazoloquinoline derivatives have been reported by diverse procedures,[31-34] but some of the reported methods are limited by the use of expensive reagents, time-consuming multi-step procedures, use of toxic solvents or catalysts. In continuation of our interests in the synthesis of new heterocyclic compounds by one-pot, multi-component reactions,[35-40] herein we report a convenient and rapid method for the synthesis of novel pyrazolo[3,4-*b*]quinoline and pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidine derivatives via a one-pot, three-component reaction, involving intramolecular cyclocondensation of arylglyoxals, 3-methyl-1-phenyl-1*H*-pyrazol-5-amine, 1,3-dicarbonyl compounds such as cyclohexane-1,3-dione, dimedone (5,5-dimethylcyclohexane-1,3-dione) and 1,3-dimethylbarbituric acid using H_2O/EtOH as solvent, without any catalyst.

Results and discussion

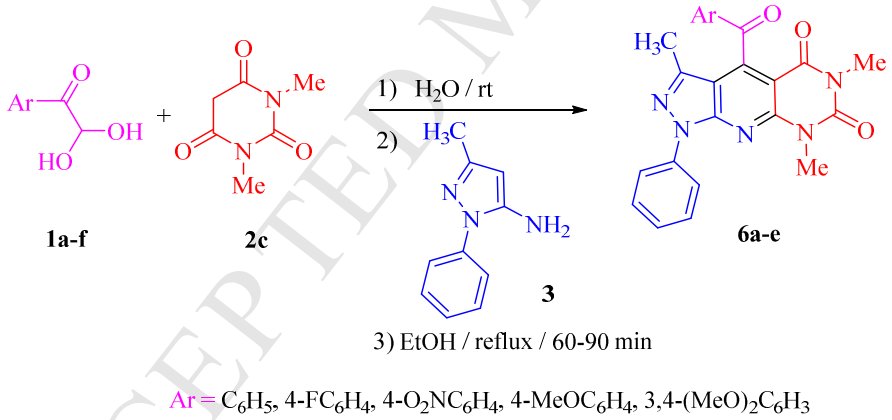
In attempting to develop a simple, one-pot and short reaction route for the synthesis of various heterocyclic compounds, we reported earlier the syntheses of arylquinoxalines, cinnolines, 1*H*-indol-4(5*H*)-ones, acridinediones and diindenopyridine-10,12-diones starting from arylglyoxals.[35-40]

We found that reaction of arylglyoxals **1** with 1,3-diketones [(cyclohexane-1,3-dione (**2a**) and dimedone (**2b**)] and 3-methyl-1-phenyl-1*H*-pyrazol-5-amine **3**, in H_2O/EtOH at 50 ^oC afforded pyrazolo[3,4-*b*]quinolone derivatives **4a-k** by a one-pot, three-component reaction in good to excellent yields. When the reaction was carried out under reflux conditions in the presence of air, the corresponding pyrazolo[3,4-*b*]quinolones **5a-k** were obtained in good to excellent yields (Scheme 1).



Scheme 1. Synthesis of pyrazolo[3,4-*b*]quinolones **5a-k.**

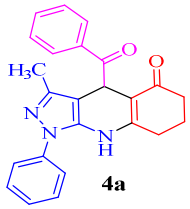
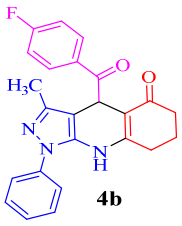
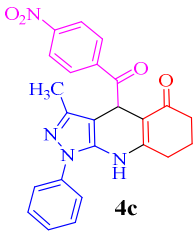
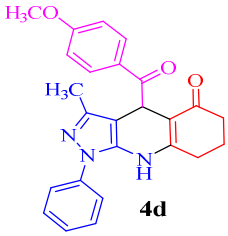
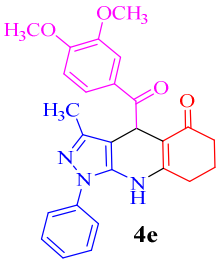
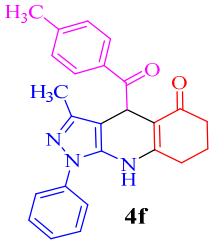
Similarly, the reaction of arylglyoxals **1** with 1,3-dimethylbarbituric acid (**2c**) and 3-methyl-1-phenyl-1*H*-pyrazol-5-amine (**3**) in H_2O/EtOH under reflux conditions gave the desired pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidine-5,7(6*H*,8*H*)-diones **6a-e** in 73-96% yields (Scheme 2).



Scheme 2. Synthesis of pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidine-5,7(6*H*,8*H*)-diones **6a-e.**

The reaction conditions were then applied to a range of different arylglyoxals. The results with various arylglyoxals and product yields and melting points are summarized in Table 1, 2 and 3 (Entry 14). Arylglyoxals with both electron-rich and electron-deficient substituents were well tolerated. Spectral data, TLC and melting points were used to establish that only one product was formed in all cases.

Table 1. Synthesis of 1,4,6,8,9-hexahydro-5*H*-pyrazolo[3,4-*b*]quinolin-5-ones **4a-k.**

Entry	Product	Yield (%)	M.p (^{o}C)
1	 **4a**	67	149-150
2	 **4b**	63	167-168
3	 **4c**	96	197
4	 **4d**	66	148-149
5	 **4e**	84	188-189
6	 **4f**	83	159 (dec.)

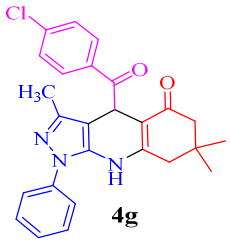
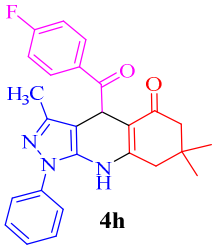
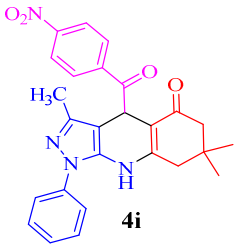
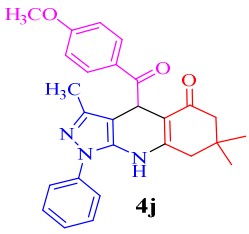
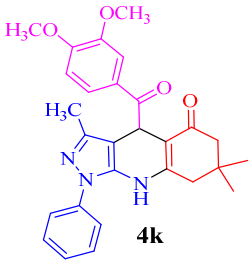
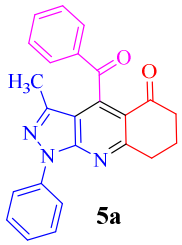
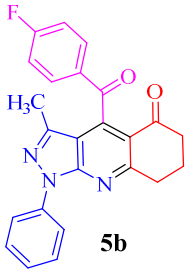
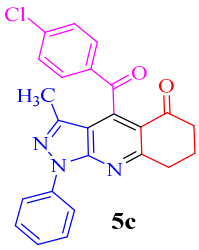
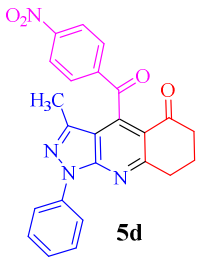
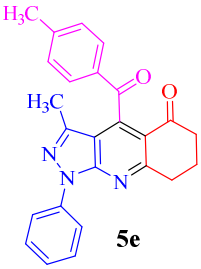
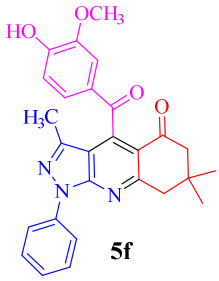
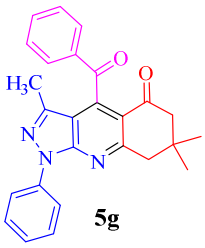
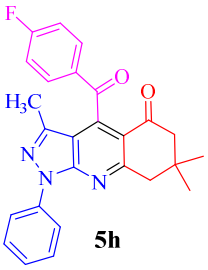
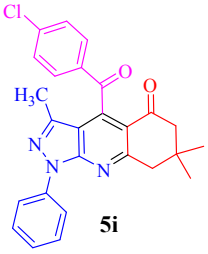
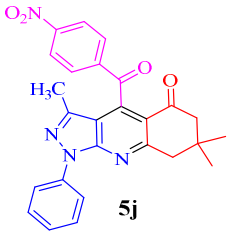
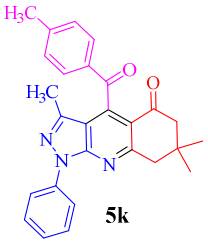
7	 **4g**	94	125-126
8	 **4h**	65	130
9	 **4i**	91	166-167
10	 **4j**	71	159-160
11	 **4k**	87	149

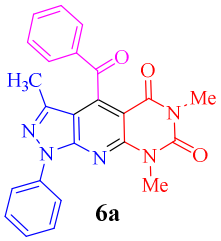
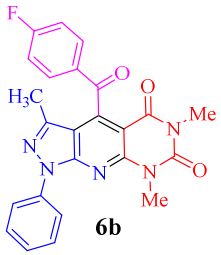
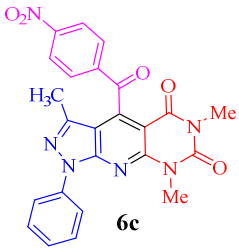
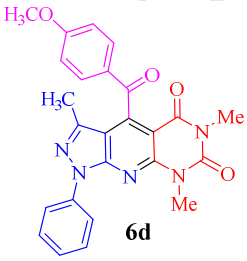
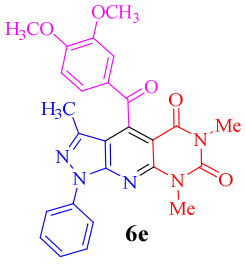
Table 2. Synthesis of 1,6,7,8-tetrahydro-5*H*-pyrazolo[3,4-*b*]quinolin-5-one **5a-k.**

Entry	Product	Yield (%)	M.p (^{o}C)
1	 **5a**	76	170
2	 **5b**	75	176
3	 **5c**	95	183
4	 **5d**	98	210 (dec.)
5	 **5e**	89	159

6	 **5f**	84	224
7	 **5g**	71	173
8	 **5h**	70	171-172
9	 **5i**	94	180
10	 **5j**	95	179
11	 **5k**	83	165

***** The isolated yields refer to the products recrystallized from EtOH.

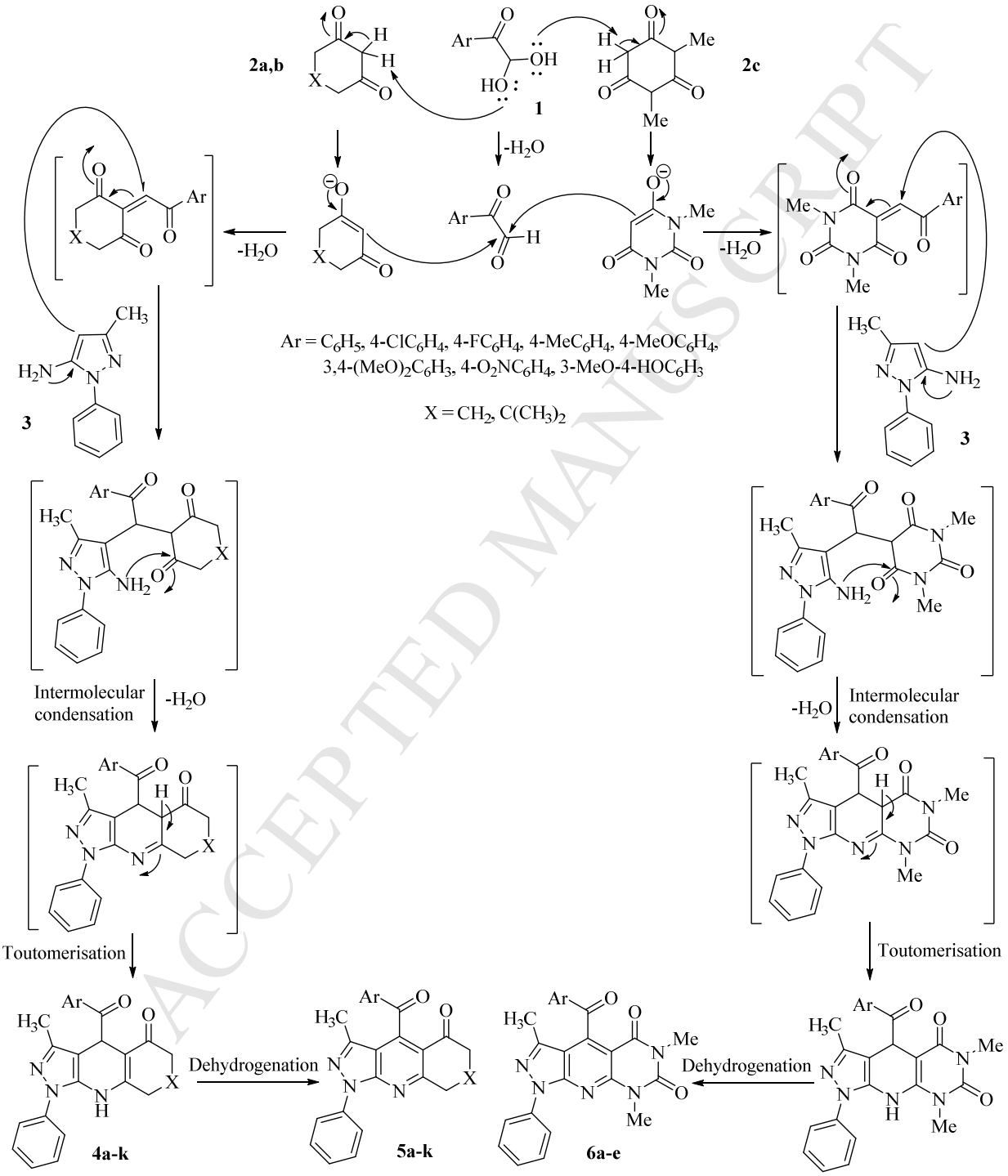
Table 3. Synthesis of 1,8-dihydro-5*H*-pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidine-5,7(6*H*,8*H*)-diones **6a-e.**

Entry	Product	Yield (%)	M.p (^{o}C)
1	 **6a**	73	241
2	 **6b**	75	230
3	 **6c**	96	256
4	 **6d**	75	263
5	 **6e**	90	233

***** The isolated yields refer to the products recrystallized from EtOH.

A plausible mechanism for this reaction is shown in Scheme 3. It involves the initial *Knoevenagel* condensation of arylglyoxals **1** and *β*-diketones **2a,b** or 1,3-dimethylbarbituric acid (**2c**) to form the

corresponding intermediates, followed by Michael addition of 3-methyl-1-phenyl-1*H*-pyrazol-5-amine (**3**) to these intermediates to form the corresponding pyrazolo[3,4-*b*]quinoline and pyrazolo [4',3':5,6]pyrido[2,3-*d*]pyrimidine derivatives through intermolecular cyclization followed by subsequent tautomerization. The initial products were dehydrogenated to give the desired products **5a-k** and **6a-e** under reflux conditions or treatment with ethanolic KOH in the presence of air.



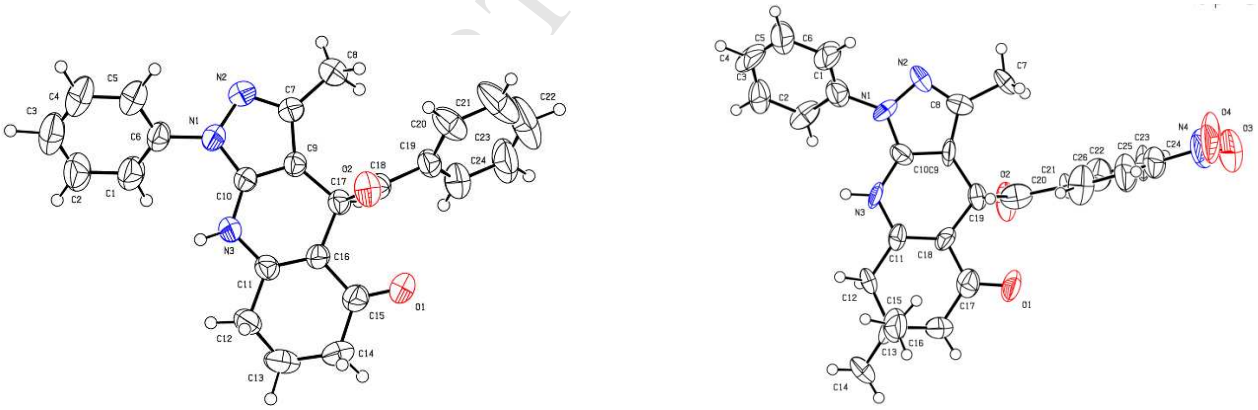
Scheme 3. A plausible mechanistic pathway for formation of **5a-k** and **6a-e.**

The substituted 4-aroyl-3-methyl-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]-5(4*H*)-ones **4a-k** were characterized using ^{1}H-NMR, ^{13}C-NMR and FT-TR spectral data and microanalysis. The characteristic singlet at δ = 5.61-5.82 ppm was ascribed to the CH of the dihydropyridine ring, which was present in all products, and a singlet at δ = 1.67-1.86 ppm which was due to the methyl group attached to the pyrazole ring. In the ^{13}C-NMR spectra of products **4a-k**, signals located around δ = 200.4-202.9 and δ = 194.5-195.7 ppm were attributed to the quinolone and aroyl carbonyl groups respectively. The characteristic absorption bands at 1662-1695 and 1602-1624 cm^{-1} could be assigned to the vibrations of quinolone and aroyl carbonyl groups respectively.

The characteristic singlets at around δ = 2.26-2.29 ppm was attributed to the methyl group attached to the pyrazole moiety and were present in all new products. In the ^{13}C-NMR spectra of the products **5a-k**, signals located around δ = 196.6-199.7 and 192.3-195.1 ppm were due to the quinolone and aroyl carbonyl groups respectively. The absorption bands at around 1662-1679 cm^{-1} could be assigned to the two different carbonyl groups.

In the ^{1}H-NMR spectra of the products **6a-e**, the singlets at around δ = 3.86-3.87, 3.39-3.42 and 2.26-2.27 ppm are attributed to the 3-methyl, 1-methyl and the methyl of pyrazole ring respectively and were present in all new products. In the ^{13}C-NMR spectra of products **6a-e**, signals located around δ = 180.6-192.1 and 159.6-173.5 ppm were due to aroyl and C-4 carbonyl groups respectively. In the FT-IR spectra, the characteristic absorption bands at 1665-1707 cm^{-1} could be assigned to the vibrations of three different carbonyl groups.

The structures of compound **4a** and **4i** were confirmed by single-crystal X-ray analysis (Fig. 1).



4a **4i**

Fig. 1. ORTEP diagram of compounds **4a** and **4i.**

The X-ray single crystal diffraction analysis showed that the carbonyl group of arylglyoxal and the carbonyl group of 1,3-diketones and also the aryl ring of the arylglyoxal and pyrazole moieties are not collimated together.

In the X-ray crystallographic data of compound **4a** the bond lengths of N1-N2, C9-C10, C18-O2 were 1.381, 1.362, 1.222 ° respectively. The bond angles of N2-N1-C6, C7-C9-C17, C11-N3-C10 were 121.04 °, 121.86° and 117.37 °, respectively.

In the X-ray crystallographic data of compound **4i** the bond lengths of C11-N3, C18-C11, C10-N1 were 1.349, 1.379, 1.344 ° respectively. The bond angles of C10-C9-C8, C10-C9-C19, C19-C20-C21 were 105.3 °, 120.7 ° and 121.1 °, respectively.

Conclusions

We have synthesized a new series of pyrazolo[3,4-*b*]quinolin-5-one and pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidin-5,7-dione derivatives by one-pot, three-component reactions of arylglyoxals, 1,3-diketones and pyrazoles under catalyst-free conditions. The reasonable reaction times, mild reaction conditions, good to excellent yields, absence of any catalyst, easy work-up, and ready availability of the starting materials are the merits of this method. Our method provides a new synthesis for pyrazoloquinolines, pyrazolo[3,4-*b*]quinolin-5-ones, and pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidin-5,7-diones with different substituents, which may have pharmaceutical and biological applications.

Experimental

The chemicals used in this work were obtained from Acros and Merck companies and were used without purification. Melting points were measured on a Philip Harris C4954718 apparatus and are uncorrected. The progress of the reaction was monitored by thin layer chromatography (TLC) on Merck's silica plates. Infrared spectra were recorded on a Thermo Nicolet Nexus 670 FT-IR instrument using KBr discs. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance AQS 300 MHz spectrometer at 300 and 75.5 MHz, respectively. Chemical shifts were measured in $CDCl_3$ as solvent relative to TMS as the internal standard. Mass spectra were recorded on a Varian Matt 311 spectrometer and relative abundance of fragments are quoted in parentheses after the *m/z* values. The arylglyoxals were prepared as their hydrates by oxidation of the corresponding acetophenones with SeO_2.[41] The 3-methyl-1-phenyl-1*H*-pyrazole-5-amine **3** was prepared according to the literature method.[42]

General procedure for the synthesis of products:

A) 4-Aroyl-3-methyl-1-phenyl-1,4,6,7,8,9-hexahydro-5*H*-pyrazolo[3,4-*b*]quinolin-5-one derivatives 4a-k:

A mixture of arylglyoxals **1** (1 mmol) and 1,3-diketones [(cyclohexane-1,3-dione (**2a**) or dimedone (**2b**)] (1 mmol) in H_2O (5 mL) was stirred at room temperature and monitored by TLC (CH_2Cl_2 : MeOH / 15:1). After completion of the intermediate formation, 3-methyl-1-phenyl-1*H*-pyrazol-5-amine **3** (1 mmol) in EtOH (2.5 mL) was added to the reaction mixture which was stirred at 50 ^oC for an appropriate time (monitored by TLC, CH_2Cl_2 : Hexane : MeOH / 15:5:1), during which the precipitate was formed and the solid was filtered and washed twice with 2×1 mL of cold H_2O : EtOH (1:1). The desired products were obtained in moderate to excellent yields (63-96%).

B) 4-Aroyl-3-methyl-1-phenyl-1,6,7,8-tetrahydro-5*H*-pyrazolo[3,4-*b*]quinolin-5-one derivatives 5a-k:

Method (I): A mixture of arylglyoxals **1** (1 mmol) and 1,3-diketones [cyclohexane-1,3-dione (**2a**) or dimedone (**2b**)] (1 mmol) in H_2O (5 mL) was stirred and monitored by TLC (CH_2Cl_2 : MeOH / 15:1). After completion of the intermediate formation, 3-methyl-1-phenyl-1*H*-pyrazol-5-amine (1 mmol) in EtOH (5 mL) was added and the reaction mixture was stirred under reflux while passing a fine stream of air through the reaction for an appropriate time (monitored by TLC, CH_2Cl_2 : Hexane : MeOH / 15:5:1). Half of the solvent was evaporated and the obtained precipitate was filtered, washed with cold water and subsequently recrystallized from ethanol to obtain the desired products in high to excellent yields (71-98%).

Method (II): Refluxing the products **4a-k** (1 mmol) in EtOH (5 mL) in the presence of KOH (1 mmol), while passing a fine stream of air over the surface of the solution, for 10-30 min led to the formation of 4-aroyl-3-methyl-1-phenyl-7,8-dihydro-1*H*-pyrazolo[3,4-*b*]quino lin-5(6*H*)-one derivatives **5a-k**.

C) 4-Aroyl-3,6,8-trimethyl-1-phenyl-1*H*-pyrazolo[4',3':5,6]pyrido[2,3-*d*]5,7(6*H*,8*H*)-dione derivatives 6a-e:

A mixture of arylglyoxals **1** (1 mmol) and 1,3-dimethylbarbituric acid (**2c**, 1 mmol) in H_2O (5 mL) was stirred and monitored by TLC (CH_2Cl_2 : MeOH / 15:1). After completion of intermediate formation, 3-methyl-1-phenyl-1*H*-pyrazol-5-amine (1 mmol) in EtOH (5 mL) was added to the mixture and it was stirred under reflux for an appropriate time (monitored by TLC, CH_2Cl_2 : Hexane : MeOH / 15:5:1). After completion of the reaction, half of the solvent was evaporated and the obtained precipitate was filtered,

washed with cold water and recrystallized from ethanol to give the desired products in high to excellent yields (73-96%).

4-Benzoyl-3-methyl-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (4a).

Yellow crystals, 67%, m.p. 149-150 ºC; ν_{max} 3238, 3164, 3037, 2954, 2889, 1662, 1623, 1537, 1460, 1357, 1188, 1113, 1001, 914, 852, 758, 692, 649, 557 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.18 (2 H, d, *J* 7.5 Hz, Ar), 7.94 (1 H, bs, NH, exchanged by D_2O addition), 7.61 (1 H, t, *J* 7.2 Hz, Ar), 7.51 (2 H, t, *J* 7.5 Hz, Ar), 7.40-7.20 (5 H, m, Ar), 5.78 (1 H, s, CH), 2.58-2.40 (2 H, m, CH_2), 2.36-2.21 (2 H, m, CH_2), 1.95 (2 H, quin, *J* 6.3 Hz, CH_2), 1.75 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 202.9, 195.6, 162.3, 1534.0, 153.9, 146.6, 137.7, 137.5, 136.6, 133.1, 129.6, 129.2, 128.5, 127.3, 122.9, 110.2, 100.2, 39.0, 36.3, 28.1, 21.2, 12.9; EIMS : m/z (%) 383 (M, 5), 382 (22), 381 (79), 353 (20), 352 (49), 325 (21), 324 (39), 279 (34), 278 (100), 106 (64), 77 (98), 51 (34); and HRMS *m/z* 383.1618 ($C_{24}H_{21}N_3O_2$ requires 383.1634).

4-(4-Fluorobenzoyl)-3-methyl-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (4b).

Yellow crystals, 63%, m.p. 167-168 ºC; ν_{max} 3232, 3162, 3048, 2957, 2891, 1668, 1610, 1537, 1467, 1358, 1220, 1115, 1005, 852, 760, 596, 522 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.24 (2 H, t, *J* 7.8 Hz, Ar), 7.48-7.26 (6 H, m, Ar + NH, exchanged by D_2O addition), 7.19 (2 H, t, *J* 8.4 Hz, Ar), 5.77 (1 H, s, CH), 2.64-2.45 (2 H, m, CH_2), 2.38 (2 H, t, *J* 6.3 Hz, CH_2), 2.03 (2 H, quin, *J* 6.3 Hz, CH_2), 1.79 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 201.2, 195.6, 167.5, 164.1, 153.3, 146.6, 137.7, 136.4, 134.0, 131.8, 131.7, 129.7, 127.5, 123.0, 115.8, 115.5, 110.4, 100.2, 39.0, 36.4, 28.4, 21.2, 12.9; EIMS : m/z (%) 401 (M, 10), 400 (61), 399 (96), 371 (48), 370 (100), 343 (48), 342 (89), 278 (69), 123 (96), 95 (95), 77 (76), 75 (25), 51 (23); and HRMS *m/z* 401.1528 ($C_{24}H_{20}FN_3O_2$ requires 401.1540).

3-Methyl-4-(4-nitrobenzoyl)-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (4c).

Orange crystals, 96%, m.p. 197 ºC; ν_{max} 3217, 3137, 3028, 2939, 1695, 1604, 1527, 1462, 1350, 1194, 1116, 1000, 851, 769, 689 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.38-8.22 (4 H, m, Ar), 7.50-7.30 (6 H, m, Ar + NH, exchanged by D_2O addition), 5.69 (1 H, s, CH), 2.62-2.44 (2 H, m, CH_2), 2.42-2.22 (2 H, m, CH_2), 2.03 (2 H, quin, *J* 6.3 Hz, CH_2), 1.78 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 201.2, 195.7, 153.4, 150.1, 146.5, 142.7, 137.6, 136.2, 129.8, 127.8, 123.7, 123.1, 110.3, 99.5, 40.0, 36.2, 28.4, 21.2, 13.0; EIMS : m/z (%) 428 (M, 13), 278 (100), 277 (98), 276 (37), 249 (99), 220 (36), 180 (77), 179 (60), 167 (41), 129 (46), 77 (97), 65 (49), 51 (45); and HRMS *m/z* 428.1471 ($C_{24}H_{20}N_4O_4$ requires 428.1485).

4-(4-Methoxybenzoyl)-3-methyl-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (4d).

Yellow crystals, 66%, m.p. 148-149 ºC; ν_{max} 3328, 2955, 2623, 2452, 1680, 1606, 1524, 1459, 1351, 1331, 1232, 1172, 1122, 1046, 1024, 845, 756, 697, 599, 512 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.21 (2 H, d, *J* 8.7 Hz, Ar), 7.89 (1 H, bs, NH, exchanged by D_2O addition), 7.54-7.20 (5 H, m, Ar), 7.00 (2 H, d, *J* 8.7 Hz, Ar), 5.79 (1 H, s, CH), 3.91 (3 H, s, OCH_3), 2.69-2.41 (2 H, m, CH_2), 2.33 (2 H, t, *J* 6 Hz, CH_2), 1.98 (2 H, quin, *J* 6.3 Hz, CH_2), 1.80 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 201.2, 195.6, 163.7, 162.3, 153.8, 146.6, 137.7, 136.7, 131.6, 130.2, 129.5, 127.2, 122.9, 113.7, 110.3, 100.6, 55.5, 38.3, 36.4, 28.2, 21.2, 13.0; EIMS : m/z (%) 413 (M, 7), 336 (44), 277 (100), 249 (66), 217 (20), 135 (78), 77 (93), 51 (40); and HRMS *m/z* 413.1720 ($C_{25}H_{23}N_3O_3$ requires 413.1739).

4-(3,4-Dimethoxybenzoyl)-3-methyl-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (4e).

Pale yellow crystals, 84%, m.p. 188-189 ºC; ν_{max} 3315, 3242, 2941, 1650, 1620, 1525, 1453, 1356, 1255, 1154, 1017, 884, 756, 633 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.06 (1 H, d, *J* 8.4 Hz, Ar), 7.65 (2 H, bs, Ar + NH, exchanged by D_2O addition), 7.50-7.20 (5 H, m, Ar), 6.99 (1 H, d, *J* 8.1 Hz, Ar), 5.82 (1 H, s, CH), 3.99 (3 H, s, OCH_3), 3.96 (3 H, s, OCH_3), 2.54 (2 H, t, *J* 6 Hz, CH_2), 2.36 (2 H, t, *J* 6 Hz, CH_2), 2.00 (2 H, quin, *J* 6 Hz, CH_2), 1.85 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 201.0, 195.6, 153.6, 153.5, 148.9, 146.6, 137.7, 136.6, 130.3, 129.6, 127.3, 124.3, 122.9, 111.2, 110.4, 110.2, 100.6, 56.1, 56.0, 38.3, 36.4, 28.3, 21.2, 13.0; EIMS : m/z (%) 443 (M, 9), 442 (23), 441 (70), 426 (30), 425 (81), 410 (34), 382 (19), 278 (92), 277 (94), 249 (41), 212 (12), 166 (39), 165 (100), 139 (20), 129 (13), 77 (76), 51 (25); and HRMS *m/z* 443.1859 ($C_{26}H_{25}N_3O_4$ requires 443.1845).

3-Methyl-4-(4-methylbenzoyl)-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (4f).

Yellow crystals, 83%, m.p. 159-160 ºC (dec); ν_{max} 3345, 3030, 2955, 1662, 1617, 1527, 1459, 1363, 1189, 1119, 1066, 1004, 847, 754, 694, 599, 521 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 9.51 (1 H, bs, NH, exchanged by D_2O addition), 8.00 (2 H, d, *J* 8.1 Hz, Ar), 7.66-7.35 (5 H, m, Ar), 7.33 (d, *J* 7.8 Hz, 2H, Ar), 5.61 (s, 1H, CH), 2.71-2.55 (2 H, m, CH_2), 2.39 (3 H, s, CH_3), 2.31-2.08 (2 H, m, CH_2), 1.99-1.77 (2 H, m, CH_2), 1.67 (3 H, s, CH_3); δ_C (75.5 MHz, DMSO-d_6) 200.8, 195.0, 155.2, 146.1, 143.4, 138.4, 137.5, 135.3, 129.9, 129.5, 129.2, 127.6, 123.9, 109.4, 99.9, 40.1, 39.9, 36.8, 27.6, 21.6, 13.2; EIMS : m/z (%) 397 (M, 9), 396 (29), 395 (94), 366 (43), 354 (36), 338 (42), 277 (100), 249 (49), 180 (25), 129 (15),

119 (91), 91 (96), 84 (68), 77 (71), 66 (91), 65 (35), 51 (27); and HRMS *m/z* 397.1782 ($C_{25}H_{23}N_3O_2$ requires 397.1790).

4-(4-Chlorobenzoyl)-3,7,7-trimethyl-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (4g).

Pale yellow crystals, 94%, m.p. 124-125 ºC; ν_{max} 3225, 3154, 3044, 2951, 2889, 1687, 1602, 1526, 1467, 1371, 1215, 1113, 993, 861, 813, 765, 642, 607, 546 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.08 (2 H, d, *J* 8.4 Hz, Ar), 7.57-7.24 (8 H, m, Ar + NH, exchanged by D_2O addition), 5.67 (1 H, s, CH), 2.33 (2 H, s, CH_2), 2.25-2.10 (2 H, m, CH_2), 1.78 (3 H, s, CH_3), 1.06 (3 H, s, CH_3), 1.05 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 201.3, 195.5, 151.8, 146.7, 139.3, 137.6, 136.5, 136.1, 130.3, 129.8, 128.8, 127.6, 123.0, 109.0, 99.8, 50.1, 42.0, 39.2, 33.0, 28.4, 28.0, 13.0; EIMS : m/z (%) 447 (M+2, 1), 445 (M, 2), 443 (5), 305 (100), 249 (65), 193 (26), 139 (31), 77 (53), 51 (21); and HRMS *m/z* 445.1557 ($C_{26}H_{24}ClN_3O_2$ requires 445.1557).

4-(4-Fluorobenzoyl)-3,7,7-trimethyl-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (4h).

Pale yellow crystals, 65%, m.p. 130 ºC; ν_{max} 3249, 3172, 3053, 2954, 1681, 1605, 1530, 1464, 1372, 1220, 1156, 1125, 1062, 994, 759, 598 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.30-8.12 (2 H, m, Ar), 7.59-7.25 (6 H, m, Ar + NH, exchanged by D_2O addition), 7.17 (2 H, t, *J* 8.4 Hz, Ar), 5.70 (1 H, s, CH), 2.45-2.28 (2 H, m, CH_2), 2.28-2.10 (2 H, m, CH_2), 1.77 (3 H, s, CH_3), 1.07 (3 H, s, CH_3), 1.06 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 200.9, 195.6, 167.4, 164.0, 146.7, 137.6, 136.6, 134.1, 131.7, 131.5, 129.8, 127.7, 123.1, 115.8, 115.5, 99.9, 50.1, 42.0, 39.1, 33.0, 28.3, 28.0, 13.0; EIMS : m/z (%) 429 (M, 2), 428 (6), 427 (19), 370 (11), 306 (89), 305 (100), 250 (29), 249 (98), 220 (26), 180 (56), 179 (42), 129 (31), 123 (40), 103 (17), 95 (23), 77 (82), 51 (27); and HRMS *m/z* 429.1840 ($C_{26}H_{24}FN_3O_2$ requires 429.1853).

3,7,7-Trimethyl-4-(4-nitrobenzoyl)-1-phenyl-6,7,8,9-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(4*H*)-one (4i).

Yellow crystals, 91%, m.p. 166-167 ºC; ν_{max} 3214, 3147, 3041, 2954, 1694, 1605, 1528, 1466, 1364, 1205, 1120, 1062, 997, 846, 764, 698, 646 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.45-8.20 (4 H, m, Ar), 7.60-7.33 (5 H, m, Ar), 6.58 (1 H, s, NH, exchanged by D_2O addition), 5.71 (1 H, s, CH), 2.58-2.37 (2 H, m, CH_2), 2.35-2.14 (2 H, m, CH_2), 1.82 (3 H, s, CH_3), 1.12 (3 H, s, CH_3), 1.10 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 200.7, 195.6, 151.1, 150.0, 146.7, 143.1, 137.6, 136.2, 130.0, 129.8, 128.0, 123.7, 123.1, 109.2, 99.4, 50.1, 42.3, 40.2, 33.1, 28.8, 27.6, 13.0; EIMS : m/z (%) 456 (M, 8), 455 (47), 454 (100), 435 (27),

383 (14), 351 (26), 332 (13), 305 (49), 249 (24), 150 (15), 105 (30), 77 (64), 51 (14); and HRMS *m/z* 456.1773 ($C_{26}H_{24}N_4O_4$ requires 456.1798).

4-(4-Methoxybenzoyl)-3,7,7-trimethyl-1-phenyl-1,4,6,7,8,9-hexahydro-5*H*-pyrazolo[3,4-*b*]quinolin-5-one (4j).

Yellow crystals, 71%, m.p. 159-160 ºC; ν_{max} 3233, 3162, 3049, 2949, 1679, 1604, 1527, 1465, 1371, 1328, 1223, 1167, 1128, 1026, 760, 600, 558 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.18 (2 H, d, *J* 8.7 Hz, Ar), 7.60-7.30 (5 H, m, Ar), 7.10-6.88 (3 H, m, Ar + NH, exchanged by D_2O addition), 5.77 (1 H, s, CH), 3.90 (3 H, s, OCH_3), 2.38 (2 H, s, CH_2), 2.24 (2 H, s, CH_2), 1.83 (3 H, s, CH_3), 1.12 (3 H, s, CH_3), 1.09 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 200.5, 195.4, 163.5, 151.2, 146.9, 137.8, 136.5, 131.4, 130.6, 129.8, 127.5, 123.0, 113.7, 109.5, 100.4, 55.4, 50.3, 42.3, 38.5, 33.0, 28.4, 28.1, 13.0; EIMS : m/z (%) 441 (M,1), 439 (3), 409 (5), 305 (9), 153 (57), 152 (100), 146 (70), 145 (98), 109 (41), 107 (69), 92 (86), 81 (48), 63 (56), 51 (26); and HRMS *m/z* 441.2069 ($C_{27}H_{27}N_3O_3$ requires 441.2052).

4-(3,4-Dimethoxybenzoyl)-3,7,7-trimethyl-1-phenyl-1,4,6,7,8,9-hexahydro-5*H*-pyrazolo[3,4-*b*]quinolin-5-one (4k).

Pale yellow crystals, 87%, m.p. 149 ºC; ν_{max} 3313, 3062, 2935, 1670, 1624, 1534, 1460, 1346, 1257, 1169, 1124, 1018, 757, 693 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.00 (1 H, d, *J* 8.1 Hz, Ar), 7.62 (1 H, s, Ar), 7.58-7.29 (5 H, m, Ar), 6.97 (1 H, d, *J* 8.4 Hz, Ar), 6.85 (1 H, bs, NH, exchanged by D_2O addition), 5.78 (1 H, s, CH), 3.97 (3 H, s, OCH_3), 3.94 (3 H, s, OCH_3), 2.39 (2 H, s, CH_2), 2.25 (2 H, s, CH_2), 1.86 (3 H, s, CH_3), 1.12 (3 H, s, CH_3), 1.09 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 200.4, 195.5, 153.2, 151.2, 148.9, 146.9, 137.8, 136.5, 130.6, 129.8, 127.6, 123.9, 123.0, 111.1, 110.1, 109.5, 100.4, 56.0, 55.9, 50.3, 42.3, 38.4, 33.0, 28.6, 27.9, 13.1; EIMS : m/z (%) 471 (M, 7), 470 (32), 469 (100), 450 (14), 448 (17), 398 (12), 305 (33), 249 (13), 165 (46), 77 (64), 55 (17); and HRMS *m/z* 471.2139 ($C_{28}H_{29}N_3O_4$ requires 471.2158).

4-Benzoyl-3-methyl-1-phenyl-1,6,7,8-tetrahydro-5*H*-pyrazolo[3,4-*b*]quinolin-5-one (5a).

White crystals, 76%, m.p. 170 ºC; ν_{max} 3059, 2946, 2347, 1676, 1571, 1484, 1431, 1332, 1221, 1129, 1018, 909, 838, 752, 685, 604, 556, 521 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.28 (2 H, d, *J* 8.1 Hz, Ar), 7.81 (2 H, d, *J* 7.5 Hz, Ar), 7.67-7.39 (5 H, m, Ar), 7.35 (1 H, t, *J* 7.5 Hz, Ar), 3.35 (2 H, t, *J* 6.3 Hz, CH_2), 2.75-2.61 (2H, m, CH_2), 2.24 (2 H, bt, *J* 6.3 Hz, CH_2), 2.26 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 196.7, 195.1, 164.7, 151.0, 146.0, 144.5, 138.8, 136.5, 133.6, 129.1, 128.9, 128.5, 126.4, 121.3, 120.7, 113.9, 38.8, 34.1, 21.7, 13.9; EIMS : m/z (%) 381 (M, 23), 380 (53), 352 (37), 338 (29), 306 (55), 305 (100), 249 (92),

220 (24), 180 (44), 129 (26), 105 (65), 77 (96), 51 (35); and HRMS *m/z* 381.1464 ($C_{24}H_{19}N_3O_2$ requires 381.1477).

4-(4-Fluorobenzoyl)-3-methyl-1-phenyl-7,8-dihydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(6*H*)-one (5b).
White crystals, 75%, m.p. 176 ºC; ν_{max} 3078, 2954, 1677, 1599, 1575, 1508, 1480, 1420, 1323, 1232, 1187, 1160, 860, 759, 691, 614 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.27 (2 H, d, *J* 8.1 Hz, Ar), 7.92-7.78 (2 H, m, Ar), 7.55 (2 H, t, *J* 7.8 Hz, Ar), 7.35 (1 H, t, *J* 7.2 Hz, Ar), 7.15 (2 H, t, *J* 8.4 Hz, Ar), 3.35 (2 H, t, *J* 6.3 Hz, CH_2), 2.82-2.60 (2 H, m, CH_2), 2.28 (2 H, t, *J* 6.3 Hz, CH_2), 2.26 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 196.8, 193.5, 167.7, 164.7, 151.0, 145.4, 144.3, 138.7, 133.1, 131.1, 129.1, 126.5, 121.4, 120.7, 116.3, 113.7, 38.8, 34.0, 21.7, 13.8; EIMS : m/z (%) 399 (M, 14), 370 (7), 342 (6), 101 (44), 100 (93), 77 (100), 55 (98), 45 (95); and HRMS *m/z* 399.1396 ($C_{24}H_{18}FN_3O_2$ requires 399.1383).

4-(4-Chlorobenzoyl)-3-methyl-1-phenyl-7,8-dihydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(6*H*)-one (5c).
White crystals, 95%, m.p. 183 ºC; ν_{max} 2942, 1678, 1574, 1484, 1422, 1225, 1088, 1015, 848, 756, 688, 539 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.27 (2 H, d, *J* 8.1 Hz, Ar), 7.74 (2 H, d, *J* 8.1 Hz, Ar), 7.55 (2 H, t, *J* 7.8 Hz, Ar), 7.45 (2 H, d, *J* 8.1 Hz, Ar), 7.36 (1 H, t, *J* 7.2 Hz, Ar), 3.35 (2 H, t, *J* 6 Hz, CH_2), 2.82-2.58 (2 H, m, CH_2), 2.26 (3 H, s, CH_3), 2.24 (2 H, bt, *J* 6 Hz, CH_2); δ_C (75.5 MHz, $CDCl_3$) 196.8, 192.3, 164.7, 145.2, 144.3, 140.1, 138.7, 134.9, 129.8, 129.3, 129.1, 126.5, 121.3, 121.2, 120.6, 112.0, 38.7, 34.0, 21.7, 13.9; EIMS : m/z (%) 417 (M+2, 2), 415 (M, 3), 399 (9), 279 (18), 278 (85), 218 (38), 217 (100), 175 (10), 139 (17), 111 (23), 91 (11), 77 (20), 55 (21), 51 (11); and HRMS *m/z* 415.1062 ($C_{24}H_{18}FN_3O_2$ requires 415.1088).

3-Methyl-4-(4-nitrobenzoyl)-1-phenyl-7,8-dihydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(6*H*)-one (5d).
White crystals, 98%, m.p. 216 ºC (dec); ν_{max} 3098, 2943, 1679, 1574, 1520, 1422, 1343, 1263, 1220, 1128, 1018, 864, 757, 606, 538 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.42-8.16 (4 H, m, Ar), 7.96 (2 H, d, *J* 8.7 Hz, Ar), 7.56 (2 H, t, *J* 7.8 Hz, Ar), 7.38 (1 H, t, *J* 7.2 Hz, Ar), 3.38 (2 H, t, *J* 6 Hz, CH_2), 2.89-2.59 (2 H, m, CH_2), 2.30 (2 H, t, *J* 6 Hz, CH_2), 2.27 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 197.0, 193.3, 164.8, 151.1, 150.5, 144.2, 143.9, 140.9, 138.6, 129.2, 129.1, 126.7, 124.2, 121.4, 120.7, 113.6, 38.6, 33.9, 21.7, 13.9; EIMS : m/z (%) 427 (M+1, 34), 426 (M, 100), 397 (29), 369 (24), 351 (32), 304 (13), 150 (14), 104 (29), 92 (12), 77 (52), 51 (13); and HRMS *m/z* 426.1311 ($C_{24}H_{18}N_4O_4$ requires 426.1328).

3-Methyl-4-(4-methylbenzoyl)-1-phenyl-7,8-dihydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(6*H*)-one (5e).

White crystals, 89%, m.p. 159 ºC; ν_{max} 3044, 2943, 2886, 1675, 1572, 1504, 1426, 1229, 1179, 1126, 1027, 907, 842, 752, 685, 609, 564 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.28 (2 H, d, *J* 8.4 Hz, Ar), 7.70 (2 H, d, *J* 7.5 Hz, Ar), 7.55 (2 H, t, *J* 7.8 Hz, Ar), 7.35 (1 H, t, *J* 7.2 Hz, Ar), 7.26 (2 H, d, *J* 7.5 Hz, Ar), 3.35 (2 H, t, *J* 6.3 Hz, CH_2), 2.82-2.60 (2 H, m, CH_2), 2.43 (3 H, s, CH_3), 2.26 (3 H, s, CH_3), 2.23 (2 H, bt, *J* 6.3 Hz, CH_2); δ_C (75.5 MHz, $CDCl_3$) 196.6, 194.7, 172.5, 164.7, 151.0, 146.2, 144.6, 138.8, 134.1, 129.6, 129.1, 128.7, 126.4, 121.4, 120.6, 113.8, 55.8, 38.8, 34.1, 22.0, 13.9; EIMS : m/z (%) 396 (M+1, 36), 395 (M, 100), 369 (21), 368 (46), 352 (37), 119 (49), 91 (55), 77 (24), 65 (21); and HRMS *m/z* 395.1655 ($C_{25}H_{21}N_3O_2$ requires 395.1634).

4-(4-Hydroxy-3-methoxybenzoyl)-3,7,7-trimethyl-1-phenyl-1,6,7,8-tetrahydro-5*H*-pyrazolo[3,4-*b*]quinolin-5-one (5f).

White crystals, 84%, m.p. 224 ºC; ν_{max} 3150, 2948, 2355, 1662, 1576, 1505, 1434, 1392, 1272, 1176, 1130, 1029, 827, 752, 680, 635, 552 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.28 (2 H, d, *J* 8.1 Hz, Ar), 7.77 (1 H, bs, Ar), 7.54 (2 H, t, *J* 7.8 Hz, Ar), 7.34 (1 H, t, *J* 7.5 Hz, Ar), 7.05-6.69 (2 H, m, Ar), 6.30 (1 H, bs, OH, exchanged by D_2O addition), 4.01 (3 H, s, OCH_3), 3.24 (2 H, s, CH_2), 2.62 (2 H, s, CH_2), 2.28 (3 H, s, CH_3), 1.17 (3 H, s, CH_3), 1.15 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 196.7, 193.7, 163.4, 151.3, 147.3, 145.5, 144.6, 138.8, 129.6, 129.4, 129.1, 126.3, 124.9, 121.3, 119.6, 114.1, 113.9, 109.1, 56.1, 52.4, 47.8, 32.8, 28.4, 28.0, 13.8; EIMS : m/z (%) 456 (M+1, 38), 455 (M, 100), 426 (26), 384 (19), 331 (22), 151 (98), 123 (29), 108 (16), 77 (49), 65 (20), 51 (26); and HRMS *m/z* 455.1825 ($C_{27}H_{25}N_3O_4$ requires 455.1845).

4-Benzoyl-3,7,7-trimethyl-1-phenyl-1,6,7,8-tetrahydro-5*H*-pyrazolo[3,4-*b*]quinolin-5-one (5g).

White crystals, 71%, m.p. 173 ºC; ν_{max} 3068, 2946, 2874, 1678, 1570, 1489, 1426, 1345, 1230, 1130, 1020, 903, 879, 846, 759, 685, 550, 516, 462 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.28 (2 H, d, *J* 8.1 Hz, Ar), 7.79 (2 H, d, *J* 7.2 Hz, Ar), 7.72-7.41 (5 H, m, Ar), 7.35 (1 H, t, *J* 7.2 Hz, Ar), 3.25 (2 H, s, CH_2), 2.60-2.35 (2 H, m, CH_2), 2.26 (3 H, s, CH_3), 1.18 (3 H, s, CH_3), 1.16 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 196.6, 195.1, 163.4, 151.4, 145.4, 144.5, 138.8, 136.5, 133.7, 129.1, 128.9, 128.5, 126.4, 121.3, 119.7, 113.8, 52.2, 47.8, 32.9, 28.4, 28.0, 13.9; EIMS : m/z (%) 410 (M+1, 38), 409 (M, 100), 381 (21), 380 (51), 352 (33), 338 (26), 332 (16), 326 (15), 255 (14), 105 (63), 77 (98), 51 (19); and HRMS *m/z* 409.1778 ($C_{26}H_{23}N_3O_2$ requires 409.1790).

4-(4-Fluorobenzoyl)-3,7,7-trimethyl-1-phenyl-1,6,7,8-tetrahydro-5*H*-pyrazolo[3,4-*b*]quinolin-5-one (5h).

White crystals, 70%, m.p. 171-172 ºC; ν_{max} 2930, 2860, 1674, 1580, 1492, 1463, 1427, 1253, 1168, 1022, 842, 756, 692, 618, 555 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.28 (2 H, d, *J* 8.1 Hz, Ar), 7.75 (2 H, d, *J* 8.1 Hz, Ar), 7.63-7.47 (2 H, m, Ar), 7.34 (1 H, t, *J* 8.1 Hz, Ar), 6.94 (2 H, d, *J* 9.0 Hz, Ar), 3.86 (2 H, s, CH_2), 3.33-3.14 (2 H, m, CH_2), 2.27 (3 H, s, CH_3), 1.17 (3 H, s, CH_3), 1.15 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 196.6, 193.7, 164.0, 163.4, 151.4, 145.6, 144.6, 138.9, 130.8, 129.7, 129.1, 122.0, 121.2, 120.4, 119.6, 114.2, 52.3, 47.8, 32.8, 28.4, 28.0, 13.8; EIMS : m/z (%) 427 (M, 5), 410 (24), 408 (8), 382 (15), 368 (13), 343 (11), 305 (24), 249 (11), 136 (22), 135 (100), 107 (33), 92 (35), 77 (98), 51 (14); and HRMS *m/z* 427.1680 ($C_{26}H_{22}FN_3O_2$ requires 427.1696).

4-(4-Chlorobenzoyl)-3,7,7-trimethyl-1-phenyl-7,8-dihydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(6*H*)-one (5i).

White crystals, 94%, m.p. 180 ºC; ν_{max} 3067, 2940, 2880, 1679, 1573, 1484, 1417, 1226, 1094, 1017, 876, 823, 745, 679, 621, 544 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.28 (2 H, d, *J* 8.1 Hz, Ar), 7.73 (2 H, d, *J* 8.1 Hz, Ar), 7.55 (2 H, t, *J* 7.8 Hz, Ar), 7.44 (2 H, d, *J* 8.4 Hz, Ar), 7.35 (1 H, t, *J* 7.2 Hz, Ar), 3.25 (2 H, s, CH_2), 2.63-2.50 (2 H, m, CH_2), 2.27 (3 H, s, CH_3), 1.18 (3 H, s, CH_3), 1.16 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 196.8, 193.8, 163.4, 151.4, 144.2, 140.1, 138.6, 134.9, 129.7, 129.3, 129.1, 126.5, 121.3, 120.9, 119.7, 113.6, 52.2, 47.7, 32.9, 28.4, 28.0, 13.9; EIMS : m/z (%) 445 (M+2, 22), 443 (M, 18), 307 (100), 306 (93), 300 (25), 249 (34), 195 (29), 140 (27), 139 (70), 111 (55), 77 (65), 51 (18); and HRMS *m/z* 443.1423 ($C_{26}H_{22}ClN_3O_2$ requires 443.1401).

3,7,7-Trimethyl-4-(4-nitrobenzoyl)-1-phenyl-7,8-dihydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(6*H*)-one (5j).

White crystals, 95%, m.p. 179 ºC; ν_{max} 3064, 2949, 2876, 1678, 1570, 1464, 1338, 1226, 1133, 1019, 882, 832, 754, 689, 551 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.40 (1 H, d, *J* 8.4 Hz, Ar), 8.28 (2 H, d, *J* 7.8 Hz, Ar), 8.21 (1 H, d, *J* 8.4 Hz, Ar), 7.91 (2 H, t, *J* 9.3 Hz, Ar), 7.55 (2 H, t, *J* 7.2 Hz, Ar), 7.45-7.30 (1 H, m, Ar), 3.26 (2 H, s, CH_2), 2.71-2.47 (2 H, m, CH_2), 2.29 (3 H, s, CH_3), 1.18 (3 H, s, CH_3), 1.17 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 196.7, 193.9, 163.4, 151. 5, 147.3, 144.3, 139.1, 138.8, 136.7, 129.1, 129.0, 126.4, 123.2, 121.4, 119.8, 113.6, 52.1, 47.7, 32.9, 28.4, 28.1, 13.9; EIMS : m/z (%) 455 (M+1, 11), 454 (M, 36), 424 (56), 395 (13), 379 (15), 367 (14), 331 (44), 120 (100), 92 (41), 77 (52), 65 (26), 51 (12); and HRMS *m/z* 454.1662 ($C_{26}H_{22}N_4O_4$ requires 454.1641).

3,7,7-Trimethyl-4-(4-methylbenzoyl)-1-phenyl-7,8-dihydro-1*H*-pyrazolo[3,4-*b*]quinolin-5(6*H*)-one (5k).

White crystals, 83%, m.p. 165 ºC; ν_{max} 3033, 2939, 2871, 1678, 1572, 1484, 1421, 1230, 1176, 1128, 1023, 881, 817, 752, 679, 614, 548 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.28 (2 H, d, *J* 8.1 Hz, Ar), 7.68 (2 H, d, *J* 7.5 Hz, Ar), 7.54 (2 H, t, *J* 7.8 Hz, Ar), 7.34 (1 H, t, *J* 7.8 Hz, Ar), 7.17-7.30 (2 H, m, Ar), 3.24 (2 H, s, CH_2), 2.51-2.48 (2 H, m, CH_2), 2.42 (3 H, s, CH_3), 2.27 (3 H, s, CH_3), 1.17 (3 H, s, CH_3), 1.16 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 196.6, 194.7, 163.4, 151.4, 145.6, 144.6, 138.8, 134.1, 129.7, 129.1, 128.6, 126.3, 121.3, 119.7, 116.7, 113.8, 52.3, 47.8, 32.9, 28.4, 28.0, 21.8, 13.8; EIMS : m/z (%) 423 (M, 23), 305 (100), 249 (62), 180 (28), 83 (41), 77 (32), 51 (13); and HRMS *m/z* 423.1926 ($C_{27}H_{25}N_3O_2$ requires 423.1947).

4-Benzoyl-3,6,8-trimethyl-1-phenyl-1*H*-pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidine-5,7(6*H*,8*H*)-dione (6a).

White crystals, 73%, m.p. 241 ºC; ν_{max} 3054, 2948, 1689, 1592, 1503, 1454, 1374, 1272, 1116, 1003, 756, 687 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.25 (2H, d, *J* 8.1 Hz, Ar), 7.86 (2 H, d, *J* 7.2 Hz, Ar), 7.74-7.43 (5 H, m, Ar), 7.37 (1 H, t, *J* 8.1 Hz, Ar), 3.86 (3 H, s, CH_3), 3.40 (3 H, s, CH_3), 2.26 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 191.1, 173.5, 164.8, 163.8, 158.4, 150.8, 144.5, 136.1, 134.2, 129.2, 129.1, 128.8, 127.7, 126.5, 120.9, 114.6, 109.4, 53.7, 28.6, 13.7. and HRMS *m/z* 425.1462 ($C_{24}H_{19}N_5O_3$ requires 425.1488).

4-(4-Fluorobenzoyl)-3,6,8-trimethyl-1-phenyl-1*H*-pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidine-5,7(6*H*,8*H*)-dione (6b).

White crystals, 75%, m.p. 230 ºC; ν_{max} 3082, 2948, 1691, 1680, 1593, 1509, 1470, 1375, 1235, 1166, 1005, 834, 753, 691, 509 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.42-8.17 (2 H, m, Ar), 7.98-7.75 (1 H, m, Ar), 7.69-7.47 (2 H, m, Ar), 7.38 (1 H, t, *J* 7.5 Hz, Ar), 7.38-7.23 (2 H, m, Ar), 7.18 (1 H, t, *J* 8.4 Hz, Ar), 3.86 (3 H, s, CH_3), 3.41 (3 H, s, CH_3), 2.26 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 191.9, 168.4, 155.3, 151.3, 144.4, 131.5, 129.2, 129.1, 128.9, 128.7, 126.5, 126.5, 120.9, 116.6, 116.3, 115.5, 115.2, 30. 5, 28.6, 13.7; EIMS : m/z (%) 444 (M+1, 33), 443 (M, 100), 415 (56), 414 (44), 398 (14), 329 (13), 263 (12), 123 (84), 95 (46), 77 (27), 51 (10); and HRMS *m/z* 443.1380 ($C_{24}H_{18}FN_5O_3$ requires 443.1394).

3,6,8-Trimethyl-4-(4-nitrobenzoyl)-1-phenyl-1*H*-pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidine-5,7(6*H*,8*H*)-dione (6c).

White crystals, 96%, m.p. 256 ºC; ν_{max} 3072, 2938, 2875, 1706, 1666, 1585, 1520, 1416, 1359, 1276, 1236, 1157, 1117, 1075, 1024, 975, 876, 833, 799, 753, 690, 585 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.35 (2 H, d, *J* 8.7 Hz, Ar), 8.24 (2 H, d, *J* 7.8 Hz, Ar), 8.02 (2 H, d, *J* 8.4 Hz, Ar), 7.58 (2 H, t, *J* 7.8 Hz, Ar), 7.39 (1 H, t, *J* 7.5 Hz, Ar), 3.87 (3 H, s, CH_3), 3.39 (3 H, s, CH_3), 2.27 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$)

191.8, 160.8, 151.1, 150.9, 150.7, 150.6, 145.8, 144.0, 140.4, 138.5, 129.5, 129.2, 126.7, 124.3, 121.0, 111.6, 103.5, 30.5, 28.6, 13.8; EIMS : m/z (%) 471 (M+1, 32), 470 (M, 100), 442 (15), 395 (15), 348 (17), 263 (16), 150 (13), 104 (19), 77 (25), 51 (10); and HRMS *m/z* 470.1343 ($C_{24}H_{18}N_6O_5$ requires 470.1339).

4-(4-Methoxybenzoyl)-3,6,8-trimethyl-1-phenyl-1,8-dihydro-5*H*-pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidine-5,7(6*H*)-dione (6d).

White crystals, 75%, m.p. 263 ºC; ν_{max} 3066, 2940, 2868, 1665, 1580, 1497, 1420, 1368, 1254, 1159, 1069, 1016, 973, 899, 844, 755, 674, 582, 496, 416 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.25 (2 H, d, *J* 8.1 Hz, Ar), 7.82 (2 H, d, *J* 6.9 Hz, Ar), 7.56 (2 H, t, *J* 8.1 Hz, Ar), 7.37 (1 H, t, *J* 7.2 Hz, Ar), 6.97 (2 H, d, *J* 8.4 Hz, Ar), 3.89 (3 H, s, OCH_3), 3.86 (3 H, s, CH_3), 3.41 (3 H, s, CH_3), 2.27 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 192.0, 164.4, 160.6, 151.3, 150.7, 148.1, 144.6, 138.7, 131.1, 129.4, 129.3, 129.2, 126.4, 120.9, 114.4, 111.8, 103.3, 55.6, 30.4, 28.6, 13.7; EIMS : m/z (%) 456 (M+1, 29), 455 (M, 91), 437 (12), 426 (25), 319 (14), 263 (10), 135 (100), 107 (20), 92 (17), 77 (46); and HRMS *m/z* 455.1578 ($C_{25}H_{21}N_5O_4$ requires 455.1594).

4-(3,4-Dimethoxybenzoyl)-3,6,8-trimethyl-1-phenyl-1,8-dihydro-5*H*-pyrazolo[4',3':5,6]pyrido [2,3-*d*]pyrimidine-5,7(6*H*)-dione (6e).

White crystals, 90%, m.p. 233 ºC; ν_{max} 3068, 2929, 2857, 1707, 1667, 1584, 1505, 1419, 1377, 1269, 1140, 1068, 1021, 756, 576, 492 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.26 (2 H, d, *J* 7.8 Hz, Ar), 7.80 (1 H, bs, Ar), 7.57 (2 H, t, *J* 7.8 Hz, Ar), 7.37 (1 H, t, *J* 7.5 Hz, Ar), 7.06 (1 H, d, *J* 7.2 Hz, Ar), 6.79 (1 H, d, *J* 8.4 Hz, Ar), 4.02 (3 H, s, OCH_3), 3.94 (3 H, s, OCH_3), 3.87 (3 H, s, CH_3), 3.42 (3 H, s, CH_3), 2.27 (3 H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 180.6, 159.6, 154.3, 151.3, 150.7, 149.8, 148.0, 145.1, 144.7, 129.6, 129.2, 126.4, 122.0, 119.0, 117.8, 114.0, 111.3, 110.2, 109.1, 65.2, 56.1, 40.5, 24.6, 13.7; EIMS : m/z (%) 486 (M+1, 35), 485 (M, 100), 457 (27), 455 (31), 348 (16), 319 (20), 263 (17), 252 (16), 200 (28), 166 (29), 165 (97), 137 (27), 91 (15), 86 (20), 78 (25), 77 (67), 51 (15); and HRMS *m/z* 485.1681 ($C_{26}H_{23}N_5O_5$ requires 485.1699).

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