An Efficient and Facile Synthesis of 5-(Thiophene-2-carbonyl)-6-(trifluoromethyl)-tetrahydro-pyrimidin-2(1*H*)-one and 6-(Thiophen-2-yl)-4,5-dihydropyrimidin-2(1*H*)-one from Same Substrates Under Different Conditions

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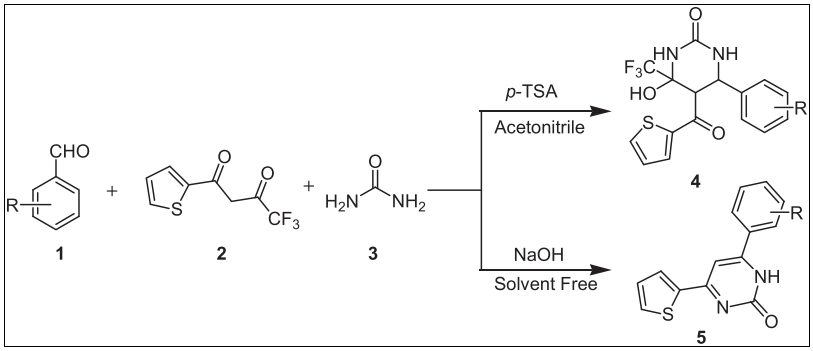

A series of 5-(thiophene-2-carbonyl)-6-(trifluoromethyl)-tetrahydropyrimidin-2(1*H*)-one and 6-(thiophen-2-yl)-4,5-dihydropyrimidin-2(1*H*)-one derivatives have been synthesized from the reactions of aromatic aldehydes, 4,4,4-trifluoro-1-(thien-2-yl)butane-1,3-dione and urea under the different conditions with high yields. In this research, it was found that the *p*-toluenesulfonic acid was an efficient catalyst for obtaining 5-(thiophene-2-carbonyl)-6-(trifluoromethyl)-tetrahydropyrimidin-2(1*H*)-one derivative. At the same time, solvent-free and NaOH were the preferred conditions for the synthesis of 6-(thiophen-2-yl)-4,5-dihydropyrimidin-2(1*H*)-one derivative. Moreover, because of short reaction time, excellent yields, simple setup, this research offered an efficient process for preparing these kind compounds.

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INTRODUCTION

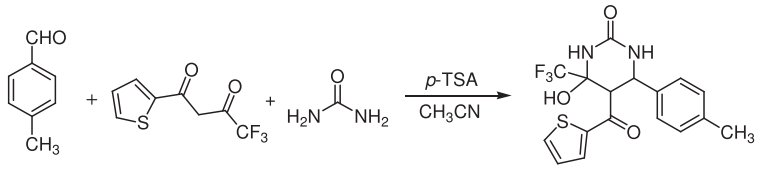
In 1893, Biginelli reported the first synthesis of 3, 4-dihydropyrimidones (DHPMs) by a simple one-pot condensation reaction of ethyl acetoacetate, benzaldehyde, and urea [1]. Because of the wide range of biological activities, such as calcium channel blockers, antihypertensive agents, a_{1a} adrenergic antagonists, and neuropeptide Y antagonists [2], this kind of compound has been extended into many DHPMs-type products by using various 1,3-dicarbonyl compound building blocks, for instance, deuterogenic ethyl acetoacetate [3], cyclic 1,3-dicarbonyl compounds (cyclopentane-1,3-dione, dimedone) [4], heterocyclic compounds (tetronic acid, barbituric acid) [5], 1-tetralone [6], acetophenone [7], 2,4-dioxopentane [8], and so on.

In recent years, we have designed and synthesized some kinds heterocyclic compounds [9], herein, we reported an efficient method for the synthesis of DHPMs-type compounds by the reactions of aromatic aldehyde, 4,4,4-trifluoro-1-(thien-2-yl)butane-1,3-dione, and urea under mild conditions.

RESULTS AND DISCUSSION

In order to carry out our project, we began to explore the reaction about 4-methylbenzaldehyde **1d** (1.0 mmol), 4,4,4-trifluoro-1-(thien-2-yl)butane-1,3-dione **2** (1.0 mmol), and urea **3** (1.0 mmol) to determine the best promoter. Different catalysts or promoters such as HCl[1], $FeCl_3$[6b], polyphosphate ester [10], $ZrCl_4$ [11], heteropoly acids [12], $InBr_3$ [13], NH_2SO_3H [14], and $Cu(OTf)_2$ [15], which were already used as catalysts for Biginelli or Biginelli-type reactions, were applied in this reaction, but no products were observed. However, a satisfactory result (87%) was obtained when the reaction was carried out in the presence of *p*-toluenesulfonic acid (0.5 mmol) in CH_3CN (10 mL) under reflux condition (Scheme 1). The product was characterized by ^{1}H NMR and IR. In its ^{1}H NMR, the singlet at delta 2.15 ppm with three protons is methyl group (CH_3–). Two doublets at 4.25 (1H, d, $J = 11.2$ Hz), 4.90 (1H, d, $J = 11.2$ Hz) with same coupling constant are possible with protons of C-4 and C-5 of pyrimidine ring. In its IR, the wave numbers of more than 3000 cm^{-1}

Scheme 1. Synthesis of 6-hydroxy-5-(thiophene-2-carbonyl)-4-p-tolyl-6-(trifluoromethyl)- tetrahydropyrimidin-2(1*H*)-one[a].



1d **2** **3** **4d**

Entry	Solvent	Catalyst[b]	Temperature °C	Time h	Yields %[c]
1	EtOH	HCl 5%	25	8	Trance
2	EtOH	$FeCl_3$ 0.5	25	8	0
3	EtOH	$ZrCl_4$ 0.5	25	8	0
4	EtOH	HPA 0.5	25	8	0
5	EtOH	$InBr_3$ 0.5	25	8	Trance
6	EtOH	NH_2SO_3 0.5	25	8	Trance
7	EtOH	PE 0.5	25	8	0
8	EtOH	$Cu(OTF))_2$ 0.5	25	8	0
9	EtOH	*p*-TSA 0.5	25	8	20
10	EtOH	*p*-TSA 0.5	50	8	40
11	EtOH	*p*-TSA 0.5	80	5	56
12	CH_3CN	*p*-TSA 0.5	50	8	65
13	CH_3CN	*p*-TSA 0.5	80	5	88
14	CH_3CN	*p*-TSA 0.5	80	3	87
15	CH_3CN	None	80	8	0
16	EtOH	None	80	8	0

[a]Reagents and conditions: aromatic aldehydes **1** (1.0 mmol), 4,4,4-trifluoro-1-(thien-2-yl)butane- 1,3-dione **2** (1.0 mmol), urea **3** (1.0 mmol), solvent (10 mL);

[b]Amount of catalysts;

[c]Isolated yields.

(3438, 3361, 3210, 3113 cm^{-1}) might be hydroxy (–OH) and imino groups (–NH–). Fortunately, we obtained the crystal of this product, and the X-ray of it certified its absolute structure. It was a DHPMs-type product (**4d**) 6-hydroxy-4-(4-methoxyphenyl)-5-(thiophene-2-carbonyl)-6-(trifluoromethyl)tetrahydropyrimidin-2(1*H*)-one. Then, we investigated the background of this kind compound, and we found that only one literature has reported one compound of this structure as its intermediate [3b]. So, this DHPMs-type product has not been effectively reported, and we went to prepare this kind of compound under our reaction conditions.

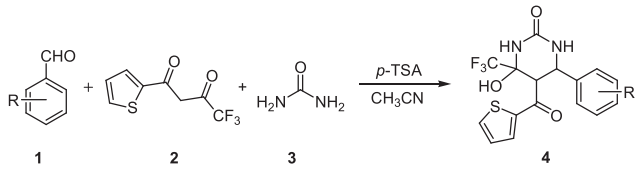
Then, the different aromatic aldehydes with various substituted groups have been chosen to react with 4,4,4-trifluoro-1-(thien-2-yl)butane-1,3-dione and urea under screening conditions and a series of DHPMs-type products have been obtained with high yields. The results showed that either electron-withdrawing groups (such as –F, –Cl, and –Br) or electron-donating groups (such as CH_3–, CH_3O–) had no effect on these syntheses, so all the reactions could be carried out smoothly. The results were listed in Table 1.

Solvent-free organic synthesis has garnered much attention from organic chemists [16]. This method has many advantages, such as high efficiency and selectivity, easy separation and purification, mild reaction conditions, and this benefit industry as well as the environment. In our research, we also went to test this reaction under solvent-free condition.

We also began the reaction about 4-methylbenzaldehyde **1d** (1.0 mmol), 4,4,4-trifluoro-1-(thien-2-yl)butane-1,3-dione **2** (1.0 mmol), and urea **3** (1.0 mmol) in the presence of *p*-toluenesulfonic acid (0.5 mmol) under 70°C about 0.5 h. However, the result exceeded our expectations and no product was gained under this condition. Under screening, we found that other acetic acid catalysts, such as $ZrCl_4$ [11], $InBr_3$ [12], NH_2SO_3H [14], and $Cu(OTf)_2$ [15] also had no effect on this solvent-free reaction. The inorganic alkali, NaOH, was often used in solvent-free organic synthesis, and we wanted to test this reaction in the presence of NaOH (0.5 mmol). To our delight, we found that the reaction could be operated very well, and high yield could be given about 92% (Scheme 2). Then, the product was characterized by IR and ^1H NMR. In its IR, the wave number of more than 3000 cm^{-1} was only 3324 cm^{-1}, and this is different from compound **4d**. In its ^1H NMR, a singlet at delta 2.36 ppm with three protons

Table 1

Synthesis of 5-(thiophene-2-carbonyl)-6-(trifluoromethyl)-tetrahydropyrimidin-2(1*H*)-one derivative[a].



1 2 3 4

Entry	Ar	Product	Yields[b] (%)
1	C_6H_5	**4a**	84
2	4-FC_6H_4	**4b**	82
3	4-BrC_6H_4	**4c**	79
4	4-$CH_3C_6H_4$	**4d**	87
5	3,4-$(CH_3)_2C_6H_3$	**4e**	93
6	3-$CH_3OC_6H_4$	**4f**	90
7	4-$CH_3OC_6H_4$	**4g**	88
8	3,4-$(CH_3O)_2C_6H_3$	**4h**	80
9	3,4,5-$(CH_3O)_3C_6H_2$	**4i**	83
10	3,4-$OCH_2OC_6H_3$	**4j**	90

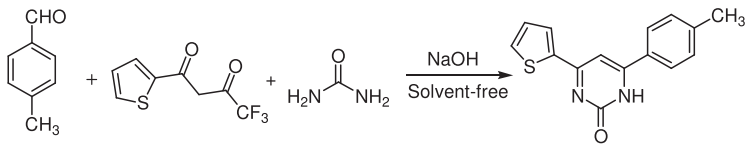
[a]Reagents and conditions: aromatic aldehydes **1** (1.0 mmol), 4,4,4-trifluoro-1-(thien-2-yl)butane-1,3-dione **2** (1.0 mmol), urea **3** (1.0 mmol), and *p*-toluenesulfonic acid (0.5 mmol), CH_3CN (10 mL), reflux.
[b]Isolated yields.

might be a methyl group (–CH_3). However, the chemical shifts at 4.25 ppm and 4.90 ppm were not found in this compoud. In addition, a singlet at delta 11.86 ppm was not found in **4d** ^{1}H NMR. These information could give conclusion that this compound was different from compound **4d**.

Luckily, when 3-methoxybenzaldehyde was used in this synthesis, the crystal of the product was obtained. With the help of X-ray analysis, the structure of the product was confirmed and it was 4-(thiophen-2-yl)-6-p-tolylpyrimidin-2(1*H*)-one. Studying on the product, it could be found that the trifluoromethyl in this reaction was lost. Therefore, it was really different from the aforementioned products.

Under investigation, we found that Jainey P. [17] has reported to synthesize the similar compounds from the reaction of 3-Aryl-1-(thiophen-2-yl)prop-2-en-1-one and urea in reflux EtOH about 16–22 h with moderate yields. However, in our method, the process was very simple and the reaction time was about 0.5 h. So, we decided to use our method to prepare more products. Many aromatic aldehydes with different substituted groups have been used in the reactions, and the 4-(thiophen-2-yl)-6-arylpyrimidin-2(1*H*)-one derivative was obtained with excellent yields. The results were summarized in Table 2.

Scheme 2. Synthesis of 4-(thiophen-2-yl)-6-p-tolylpyrimidin-2(1*H*)-one[a].



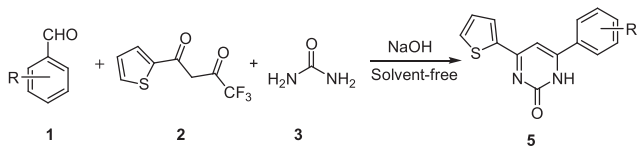
1d 2 3 5e

Entry	Catalyst[b]	Temperature °C	Time h	Yields %[c]
1	*p*-TSA 0.5	40	2	0
2	$ZrCl_4$ 0.5	40	2	0
3	$InBr_3$ 0.5	40	2	0
4	NH_2SO_3 0.5	40	2	0
5	$Cu(OTF))_2$ 0.5	40	2	0
6	NaOH 0.5	40	2	30
7	NaOH 0.5	40	4	36
8	NaOH 0.5	50	2	41
9	NaOH 0.5	60	2	65
10	NaOH 0.5	70	2	90
11	NaOH 0.5	70	1	92
12	NaOH 0.5	70	0.5	92
13	NaOH 0.5	70	0.1	70
14	None	70	2	0

[a]Reagents and conditions: aromatic aldehydes **1** (1.0 mmol), 4,4,4-trifluoro-1-(thien-2-yl)butane- 1,3-dione **2** (1.0 mmol), urea **3** (1.0 mmol), solvent-free conditions;
[b]Amount of catalysts;
[c]Isolated yields.

Table 2

Synthesis of 6-(thiophen-2-yl)-4,5-dihydropyrimidin-2(1*H*)-one derivative[a].



1 2 3 5

Entry	Ar	Product	Yields[b] (%)
1	C_6H_5	**5a**	92
2	3-FC_6H_4	**5b**	78
3	4-FC_6H_4	**5c**	83
4	3,4-$Cl_2C_6H_3$	**5d**	82
5	4-$CH_3C_6H_4$	**5e**	92
6	3,4-$(CH_3)_2C_6H_3$	**5f**	83
7	2-$CH_3OC_6H_4$	**5g**	88
8	3-$CH_3OC_6H_4$	**5h**	90
9	4-$CH_3OC_6H_4$	**5i**	93
10	2,5-$(CH_3O)_2C_6H_3$	**5j**	90
11	3,4,5-$(CH_3O)_3C_6H_2$	**5k**	85
12	4-$CF_3C_6H_4$	**5l**	78
13	3,4-$OCH_2OC_6H_3$	**5m**	86
14	2-pyridyl	**5n**	77
15	4-pyridyl	**5o**	79

[a]Reagents and conditions: aromatic aldehydes **1** (1.0 mmol), 4,4,4-trifluoro-1-(thien-2-yl)butane-1,3-dione **2** (1.0 mmol), urea **3** (1.0 mmol), and NaOH (0.5 mmol), 70°C.
[b]Isolated yields.

The structures of all the products were confirmed on the basis of spectroscopic data, particularly ^{1}H NMR analysis and HRMS spectra. The structures of **4d** and **5h** were additionally confirmed by X-ray single crystal analysis. The crystal structures of **4d** and **5h** were shown in Figures 1 [18] and 2 [19]. The possible reaction mechanisms of **4** and **5** were given in Figures 3 and 4. In Figure 3, first, a Knoevenagel condensation reaction was operated between **1** and **2** to give **6**. Then, the reaction intermediate **7** was obtained from the reaction of urea **3** and intermediate **6**. Compound **4** was achieved after the selective intramolecular cyclization and proton transfer. In Figure 4, initially, a condensation intermediate **6** was produced by reactions **1** and **2**. Under alkaline condition, the OH^- attacked the trifluoromethyl carbonyl to lose TFA, and β-unsaturated carbonyl compound **10** was gained. Then, urea **3** reacted with **10** to give **11**. Compound **5** was formed by sequential intramolecular cyclization, dehydration, and oxidation reaction.

In conclusion, a series of 5-(thiophene-2-carbonyl)-6-(trifluoromethyl)-tetrahydropyrimidin-2(1*H*)-one and 6-(thiophen-2-yl)-4,5-dihydropyrimidin-2(1*H*)-one derivatives have been synthesized from the reactions of aromatic aldehydes, 4,4,4-trifluoro-1-(thien-2-yl)butane-1,3-dione and urea under different conditions with high yields. Under investigation, few methods have been reported for the synthesis of these products. In this research, it was found that the *p*-toluenesulfonic acid was an efficient catalyst for obtaining 5-(thiophene-2-carbonyl)-6-(trifluoromethyl)-tetrahydropyrimidin-2(1*H*)-one derivative. At the same time, solvent-free and NaOH were the preferred conditions for the synthesis of 6-(thiophen-2-yl)-4,5-dihydropyrimidin-2(1*H*)-one derivatives. Moreover, because of short reaction time, excellent yields, and simple setup, this research offered an efficient process for preparing these two kinds of compounds.

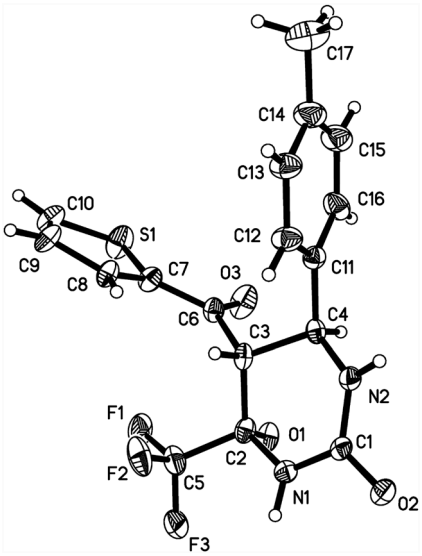


Figure 1. The crystal structure of **4d**.

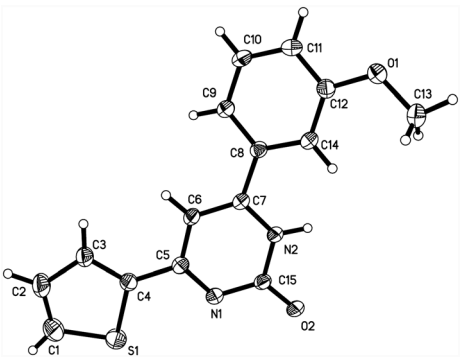


Figure 2. The crystal structure of **5h**.

EXPERIMENTAL

Melting points were determined on XT-5 microscopic melting point apparatus and were uncorrected. IR spectra were recorded on an FT Bruker Tensor 27 spectrometer (Bruker, Germany). ^{1}H NMR and ^{13}C NMR spectra were obtained from a solution in DMSO-d_6 with Me_4Si as an internal standard using a Bruker-400 spectrometer. HRMS spectra were obtained with a Bruker microTOF-Q 134 instrument. X-ray diffractions were recorded on a Siemens P4 or Simart-1000 diffractometer.

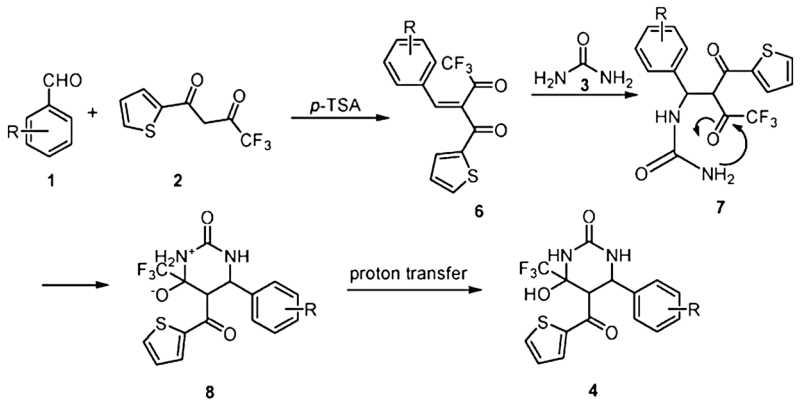


Figure 3. Possible reaction mechanism of compound **4**.

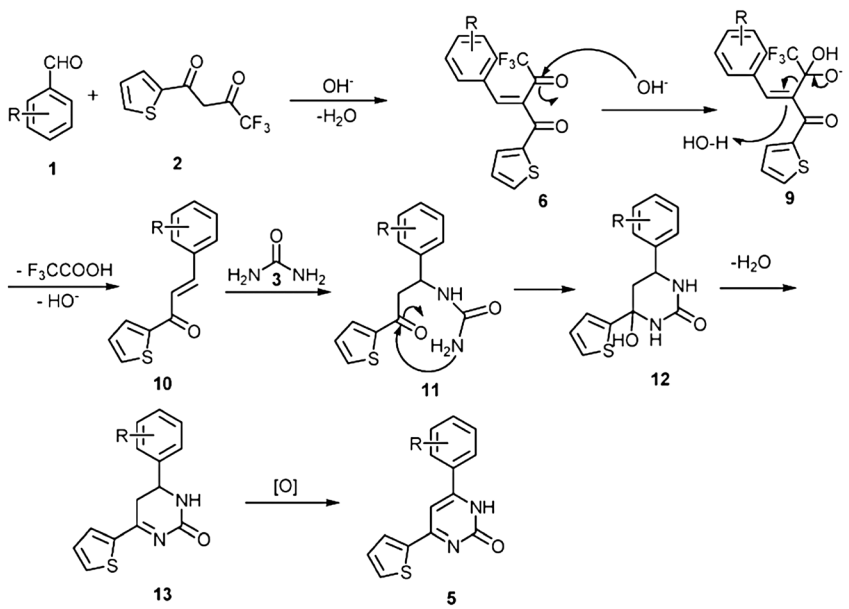


Figure 4. Possible reaction mechanism of compound **5**.

General procedure for the synthesis of 5-(thiophene-2-carbonyl)-6-(trifluoromethyl)- tetrahydropyrimidin-2(1*H*)-one derivative. The mixture of aromatic aldehydes **1** (1.0 mmol), 4,4,4-trifluoro-1-(thien-2-yl) butane-1,3-dione **2** (1.0 mmol), urea **3** (1 mmol), and *p*-toluenesulfonic acid (0.5 mmol) was put in a reaction flask with CH_3CN (10 ml) and let them under reflux conditions about 3 h (monitored by TLC). After completing the reaction, the precipitation was precipitated from CH_3CN solution, then filtered, dried, and bottled.

General procedure for the synthesis of 6-(thiophen-2-yl)-4,5-dihydropyrimidin-2(1*H*)-one derivative. The mixture of aromatic aldehydes **1** (1.0 mmol), 4,4,4-trifluoro-1-(thien-2-yl) butane-1,3-dione **2** (1.0 mmol), urea **3** (1 mmol), and NaOH (0.5 mmol) was put in a reaction flask and let them under solvent-free conditions. The reactions were operated under 70°C about 0.5 h (monitored by TLC). After completing the reaction, the mixture was put into 15 ml H_2O, and the precipitation was precipitated from H_2O solution, then filtered, recrystallized from 95% EtOH, dried, and bottled.

6-Hydroxy-4-phenyl-5-(thiophene-2-carbonyl)-6-(trifluoromethyl)-tetrahydropyrimidin-2(1H)-one (4a). m.p. 242–243°C; IR (KBr, ν, cm^{-1}): 3351, 2360, 2341, 1668, 1516, 1456, 1416, 1360, 1258, 1207, 1184, 1071, 771, 726, 702, 669, 653, 530 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6), (δ, ppm): 4.38 (1H, d, J = 11.2 Hz, CH), 4.83 (1H, d, J = 10.8 Hz, CH), 7.05 (1H, t, J = 4.4 Hz, ArH), 7.13-7.21 (5H, m, ArH), 7.38 (2H, d, J = 7.2 Hz, ArH), 7.82 (1H, br, OH),7.86 (1H, s, NH), 7.95 (1H, s, NH); HRMS m/z calculated for $C_{16}H_{13}F_3N_2O_3S$ $[M]^+$: 370.0599. Found: 370.0570.

4-(4-Fluorophenyl)-6-hydroxy-5-(thiophene-2-carbonyl)-6-(trifluoromethyl)-tetrahydropyrimidin-2(1H)-one (4b). m.p. 236–237°C; IR (KBr, ν, cm^{-1}): 3401, 3222, 3097, 2906, 2361, 2342, 1672, 1608, 1513, 1491, 1417, 1361, 1252, 1232, 1202, 1178, 1110, 1072, 1017, 935, 883, 838, 729, 634, 536 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6), (δ, ppm): 4.29 (1H, d, J = 11.2 Hz, CH), 4.94 (1H, d, J = 10.8 Hz, CH), 7.02 (2H, t, J = 8.8 Hz, ArH), 7.08 (1H, t, J = 4.4 Hz, ArH), 7.27 (1H, s, ArH), 7.34 (1H, s, ArH), 7.45 (2H, t, J = 6.4 Hz, ArH),

7.86(1H, br, OH), 7.88 (1H, s, NH), 7.89 (1H, s, NH); HRMS m/z calculated for $C_{16}H_{12}F_4N_2O_3S$ $[M]^+$: 388.0505. Found: 388.0486.

4-(4-Bromophenyl)-6-hydroxy-5-(thiophene-2-carbonyl)-6-(trifluoromethyl)-tetrahydropyrimidin-2(1H)-one (4c). m.p. 220–221°C; IR (KBr, ν, cm^{-1}): 3438, 3358, 3213, 3107, 2907, 2361, 2342, 1686, 1645, 1489, 1412, 1340, 1273, 1248, 1198, 1107, 1073, 1012, 831, 752, 727, 635, 531 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6), (δ, ppm): 4.31 (1H, d, J = 10.8 Hz, CH), 4.93 (1H, d, J = 11.2 Hz, CH), 7.08 (1H, t, J = 4.0 Hz, ArH), 7.35–7.47 (6H, m, ArH), 7.88 (1H, s, NH), 7.89 (1H, s, NH), 8.00 (1H, br, OH); HRMS m/z calculated for $C_{16}H_{12}BrF_3N_2O_3S$ $[M-H]^-$: 446.9626. Found: 446.9600.

6-Hydroxy-5-(thiophene-2-carbonyl)-4-p-tolyl-6-(trifluoromethyl)-tetrahydropyrimidin-2(1H)-one (4d). m.p. 240–241°C; IR (KBr, ν, cm^{-1}): 3438, 3361, 3210, 3113, 3087, 2900, 2361, 2342, 1920, 1683, 1643, 1518, 1483, 1412, 1308, 1248, 1200, 1186, 1112, 1072, 1027, 998, 827, 812, 770, 751, 719, 681, 656, 636, 533 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6), (δ, ppm): 2.15 (3H, s, CH_3), 4.25 (1H, d, J = 11.2 Hz, CH), 4.90 (1H, d, J = 11.2 Hz, CH), 7.00 (2H, d, J = 8.0 Hz, ArH), 7.07 (1H, t, J = 4.0 Hz, ArH), 7.22 (2H, s, ArH), 7.27 (2H, d, J = 8.0 Hz, ArH), 7.78 (1H, br, OH), 7.85 (1H, s, NH), 7.87 (1H, s, NH); HRMS m/z calculated for $C_{17}H_{15}F_3N_2O_3S$ $[M-H]^-$: 383.0677. Found: 383.0649.

4-(3,4-Dimethylphenyl)-6-hydroxy-5-(thiophene-2-carbonyl)-6-(trifluoromethyl)-tetrahydropyrimidin-2(1H)-one (4e). m.p. 198–199°C; IR (KBr, ν, cm^{-1}): 3433, 3216, 3095, 2923, 2361, 2343, 1686, 1543, 1491, 1414, 1361, 1324, 1250, 1183, 1110. 830, 750, 716, 680, 635, 549 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6), (δ, ppm): 2.06 (3H, s, CH_3), 2.11 (3H, s, CH_3), 4.25 (1H, d, J = 11.2 Hz, CH), 4.85 (1H, d, J = 11.2 Hz, CH), 6.94 (1H, d, J = 7.6 Hz, ArH), 7.08 (1H, s, ArH), 7.09–7.20 (4H, m, ArH), 7.74 (1H, br, OH), 7.87 (2H, s, 2NH); HRMS m/z calculated for $C_{18}H_{17}F_3N_2O_3S$ $[M-H]^-$: 397.0834. Found: 397.0807.

6-Hydroxy-4-(3-methoxyphenyl)-5-(thiophene-2-carbonyl)-6-(trifluoromethyl)-tetrahydropyrimidin-2(1H)-one (4f). m.p. 194–195°C; IR (KBr, ν, cm^{-1}): 3444, 3360, 3207, 3093, 2908, 2831, 2361, 2342, 1686, 1657, 1610, 1588, 1489, 1414, 1362, 1321, 1267, 1194, 1182, 1101, 1073, 1042, 869, 785, 728, 700, 641, 584, 548 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6), (δ, ppm): 3.67 (3H, s, OCH_3), 4.33 (1H, d, J = 11.2 Hz, CH), 4.92 (1H, d, J = 11.2 Hz, CH), 6.69 (1H, d, J = 6.8 Hz, ArH), 6.90 (1H, d, J = 7.6 Hz, ArH), 7.02 (1H, s, ArH), 7.07 (1H, s, ArH), 7.10 (1H, d, J = 8.4 Hz, ArH), 7.21 (1H, s, ArH), 7.32 (1H, s, ArH), 7.85 (1H, s, NH), 7.87 (1H, s, NH), 7.92 (1H, s, OH); HRMS m/z calculated for $C_{17}H_{15}F_3N_2O_4S$ $[M-H]^-$: 399.0626. Found: 399.0601.

6-Hydroxy-4-(4-methoxyphenyl)-5-(thiophene-2-carbonyl)-6-(trifluoromethyl)-tetrahydropyrimidin-2(1H)-one (4g). m.p. 238–239°C; IR (KBr, ν, cm^{-1}): 3436, 3376, 3208, 3103, 2903, 2841, 2359, 2340, 1688, 1636, 1587, 1518, 1412, 1371, 1345, 1308, 1255, 1203, 1181, 1112, 1071, 1040, 996, 837, 820, 768, 751, 719, 681, 657, 635, 541 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6), (δ, ppm): 3.62 (3H, s, OCH_3), 4.27 (1H, d, J = 11.2 Hz, CH), 4.90 (1H, d, J = 11.2 Hz, CH), 6.74 (2H, d, J = 8.4 Hz,ArH), 7.07 (1H, t, J = 4.0 Hz, ArH), 7.25 (1H, s, ArH), 7.32 (3H, m, ArH), 7.86 (1H, s, OH), 7.87 (1H, s, NH), 7.89 (1H, s, NH); HRMS m/z calculated for $C_{17}H_{15}F_3N_2O_4S$ $[M]^+$: 400.0705. Found: 400.0675.

4-(3,4-Dimethoxyphenyl)-6-hydroxy-5-(thiophene-2-carbonyl)-6-(trifluoromethyl)-tetrahydropyrimidin-2(1H)-one (4h). m.p. 233–234°C; IR (KBr, ν, cm^{-1}): 3336, 3211, 3080, 2961, 2935, 2839, 2360, 2341, 1694, 1626, 1517, 1463, 1412, 1360, 1250, 1195, 1141, 1024, 855, 769, 744, 733, 719, 648, 621, 545 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6), (δ, ppm): 3.62 (3H, s, OCH_3), 3.70 (3H, s, OCH_3), 4.40 (1H, d, J = 10.4 Hz, CH), 4.90 (1H, d, J = 10.4 Hz, CH), 6.72 (1H, d, J = 8.4 Hz, ArH), 6.79 (1H, s, ArH), 7.09 (1H, t, J = 4.0 Hz, ArH), 7.14–7.19 (2H, m, ArH), 7.31 (1H, s, ArH), 7.87 (1H, s, OH), 7.99 (1H, s, NH), 8.00 (1H, s, NH); HRMS m/z calculated for $C_{18}H_{17}F_3N_2O_5S$ $[M]^+$: 430.0810. Found: 430.0782.

6-Hydroxy-5-(thiophene-2-carbonyl)-6-(trifluoromethyl)-4-(3,4,5-trimethoxyphenyl)-tetrahydropyrimidin-2(1H)-one (4i). m.p. 212–213°C; IR (KBr, ν, cm^{-1}): 3285, 3215, 3102, 2942, 2836, 2361, 2342, 1695, 1638, 1598, 1499, 1412, 1331, 1242, 1179, 1128, 998, 836, 786, 732, 655, 626, 545 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6), (δ, ppm): 3.49 (3H, s, OCH_3), 3.69 (6H, s, $2\times OCH_3$), 4.38 (1H, d, J = 11.2 Hz, CH), 4.88 (1H, d, J = 11.2 Hz, CH), 6.69 (2H, s, ArH), 7.09 (1H, t, J = 4.0 Hz, ArH), 7.14 (1H, s, ArH), 7.30 (1H, s, ArH), 7.88 (1H, s, NH), 7.90 (1H, s, NH),7.98 (1H, s, OH); HRMS m/z calculated for $C_{19}H_{19}F_3N_2O_6S$ $[M]^+$: 460.0916. Found: 460.0881.

4-(Benzo[d][1,3]dioxol-5-yl)-6-hydroxy-5-(thiophene-2-carbonyl)-6-(trifluoromethyl)-tetrahydropyrimidin-2(1H)-one (4j). m.p. 260–261°C; IR (KBr, ν, cm^{-1}): 3370, 3210, 3090, 2911, 2361, 2342, 1687, 1646, 1490, 1448, 1416, 1361, 1314, 1246, 1209, 1111, 1035, 920, 870, 819, 724, 682, 636, 558, 546 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6), (δ, ppm): 4.29 (1H, d, J = 11.2 Hz, CH), 4.86 (1H, d, J = 11.2 Hz, CH), 5.89 (2H, d, J = 4.0 Hz, CH_2), 6.70 (1H, d, J = 8.0 Hz, ArH), 6.77 (1H, d, J = 8.0 Hz, ArH), 7.12 (3H, d, J = 4.4 Hz, ArH), 7.27 (1H, s, ArH), 7.82 (1H, s, NH), 7.90 (1H, s, NH), 7.93 (1H, br, OH); HRMS m/z calculated for $C_{17}H_{13}F_3N_2O_5S$ $[M-H]^-$: 413.0419. Found: 413.0395.

6-Phenyl-4-(thiophen-2-yl)pyrimidin-2(1H)-one (5a). m.p. 257–258°C; IR (KBr, ν, cm^{-1}): 3309, 3220, 3077, 3034, 2947, 2361, 2342, 1869, 1793, 1634, 1575, 1532, 1497, 1439, 1422, 1393, 1349, 1327, 1261, 1194, 1161, 1089, 1076, 1051, 987, 858, 765, 685, 612, 578 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6), (δ, ppm): 7.27 (1H, t, J = 4.0 Hz, ArH), 7.56–7.62 (4H, m, ArH), 7.88 (1H, d, J = 5.2 Hz, ArH), 8.05 (2H, d, J = 6.8 Hz, ArH), 8.23 (1H, d, J = 3.6 Hz, ArH), 12.02 (1H, s, NH); HRMS m/z calculated for $C_{14}H_{10}N_2OS$ $[M]^+$: 254.0514. Found: 254.0492.

6-(3-Fluorophenyl)-4-(thiophen-2-yl)pyrimidin-2(1H)-one (5b). m.p. 277–278°C; IR (KBr, ν, cm^{-1}): 3318, 3107, 3069, 3013, 2912, 2361, 2342, 1869, 1829, 1772, 1717, 1621, 1586, 1540, 1523, 1489, 1445, 1422, 1395, 1346, 1262, 1189, 1167, 1092, 1078, 1045, 1001, 950, 871, 850, 786, 757, 714, 697, 660, 640, 613, 594, 524 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6), (δ, ppm): 7.28 (1H, t, J = 4.0 Hz, ArH), 7.42–7.47 (1H, m, ArH), 7.59–7.64 (1H, m, ArH), 7.71 (1H, s, ArH), 7.88 (1H, d, J = 4.8 Hz, ArH), 7.96 (2H, d, J = 8.4 Hz, ArH), 8.25 (1H, d, J = 3.6 Hz, ArH), 11.96 (1H, s, NH); HRMS m/z calculated for $C_{14}H_9FN_2OS$ $[M-H]^-$: 271.0342. Found: 271.0328.

6-(4-Fluorophenyl)-4-(thiophen-2-yl)pyrimidin-2(1H)-one (5c). m.p. 245–246°C; IR (KBr, ν, cm^{-1}): 3299, 3115, 3083, 2934, 2361, 2343, 1869, 1845, 1830, 1793, 1772, 1749, 1734, 1717, 1637, 1611, 1587, 1560, 1540, 1523, 1509, 1474, 1444, 1431, 1389, 1350, 1340, 1309, 1260, 1237, 1165, 1104, 1089, 1075, 1050, 1015, 987, 864, 834, 767, 722, 635, 623, 584, 562, 509 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6), (δ, ppm): 7.24 (1H, m, ArH), 7.38 (2H, t, J = 8.8 Hz, ArH), 7.58 (1H, s, ArH), 7.84

(1H, d, $J = 4.8$ Hz, ArH), 8.12 (2H, t, $J = 7.6$ Hz, $J = 6.0$ Hz, ArH), 8.19 (1H, d, $J = 4.8$ Hz, ArH), 11.93 (1H, s, NH); HRMS m/z calculated for $C_{14}H_9FN_2OS$ $[M]^+$: 272.0420. Found: 272.0399.

6-(3,4-Dichlorophenyl)-4-(thiophen-2-yl)pyrimidin-2(1H)-one (5d). m.p. 232–233°C; IR (KBr, ν, cm^{-1}): 3311, 2955, 2361, 2343, 1869, 1845, 1793, 1749, 1717, 1698, 1647, 1638, 1608, 1559, 1541, 1508, 1475, 1438, 1427, 1375, 1339, 1255, 1144, 1086, 1031, 934, 864, 828, 724, 670, 622 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6), (δ, ppm): 7.23 (1H, s, ArH), 7.76 (2H, d, $J = 7.6$ Hz, ArH), 7.82 (1H, d, $J = 4.4$ Hz, ArH), 8.07 (1H, d, $J = 8.4$ Hz, ArH), 8.21 (1H, s, ArH), 8.36 (1H, s, ArH), 12.23 (1H, s, NH); HRMS m/z calculated for $C_{14}H_8C_{12}N_2OS$ $[M - H]^-$: 320.9656. Found: 320.9672.

4-(Thiophen-2-yl)-6-p-tolylpyrimidin-2(1H)-one (5e). m.p. 222–223°C; IR (KBr, ν, cm^{-1}): 3324, 2911, 2365, 2345, 1869, 1845, 1793, 1749, 1717, 1684, 1624, 1571, 1542, 1523, 1509, 1460, 1474, 1449, 1430, 1390, 1352, 1340, 1255, 1187, 1090, 1073, 985, 906, 858, 808, 761, 705, 626, 590 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6), (δ, ppm): 2.36 (3H, s, CH_3), 7.23 (1H, t, $J = 4.0$ Hz, ArH), 7.34 (2H, d, $J = 8.0$ Hz, ArH), 7.48 (1H, s, ArH), 7.83 (1H, d, $J = 4.8$ Hz, ArH), 7.93 (2H, d, $J = 7.6$ Hz, ArH), 8.18 (1H, d, $J = 3.6$ Hz, ArH), 11.86 (1H, s, NH); HRMS m/z calculated for $C_{15}H_{12}N_2OS$ $[M - H]^-$: 267.0592. Found: 267.0602.

6-(3,4-Dimethylphenyl)-4-(thiophen-2-yl)pyrimidin-2(1H)-one (5f). m.p. 167–168°C; IR (KBr, ν, cm^{-1}): 3315, 2915, 2361, 2342, 1845, 1793, 1749, 1698, 1624, 1575, 1559, 1541, 1523, 1507, 1490, 1449, 1429, 1386, 1350, 1336, 1257, 1089, 1074, 990, 903, 879, 808, 762, 703, 625, 590 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6), (δ, ppm): 2.26 (3H, s, CH_3), 2.28 (3H, s, CH_3), 7.23 (1H, t, $J = 3.6$ Hz, ArH), 7.27 (1H, d, $J = 8.0$ Hz, ArH), 7.45 (1H, s, ArH), 7.75 (1H, d, $J = 7.6$ Hz, ArH), 7.83 (2H, s, ArH), 8.18 (1H, s, ArH), 11.81 (1H, s, NH); HRMS m/z calculated for $C_{16}H_{14}N_2OS$ $[M - H]^-$: 281.0749. Found: 281.0756.

6-(2-Methoxyphenyl)-4-(thiophen-2-yl)pyrimidin-2(1H)-one (5g). m.p. 224–225°C; IR (KBr, ν, cm^{-1}): 3401, 3015, 2362, 2343, 1685, 1671, 1654, 1636, 1577, 1542, 1498, 1458, 1438, 1419, 1340, 1256, 1067, 983, 925, 811, 738, 669, 616, 588, 569 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6), (δ, ppm): 3.81 (3H, s, OCH_3), 7.06 (1H, t, $J = 7.2$ Hz, ArH), 7.10 (1H, s, ArH), 7.16 (1H, d, $J = 8.4$ Hz, ArH), 7.20 (1H, t, $J = 4.4$ Hz, ArH), 7.48–7.53 (2H, m, ArH), 7.84 (1H, d, $J = 4.8$ Hz, ArH), 8.04 (1H, d, $J = 3.6$ Hz, ArH), 11.73 (1H, s, NH); HRMS m/z calculated for $C_{15}H_{12}N_2O_2S$ $[M]^+$: 284.0619. Found: 284.0601.

6-(3-Methoxyphenyl)-4-(thiophen-2-yl)pyrimidin-2(1H)-one (5h). m.p. 215–216°C; IR (KBr, ν, cm^{-1}): 3331, 3094, 2995, 2906, 2361, 1342, 1909, 1869, 1772, 1734, 1698, 1626, 1611, 1540, 1508, 1456, 1421, 1392, 1352, 1287, 1274, 1220, 1088, 1042, 995, 947, 917, 872, 842, 781, 757, 724, 694, 669, 635, 618, 596, 546 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6), (δ, ppm): 3.87 (3H, s, OCH_3), 7.16 (1H, d, $J = 8.0$ Hz, ArH), 7.27 (1H, s, ArH), 7.47 (1H, t, $J = 8.0$ Hz, ArH), 7.55 (1H, s, ArH), 7.63 (2H, t, $J = 7.6$ Hz, ArH), 7.88 (1H, s, ArH), 8.24 (1H, s, ArH), 11.96 (1H, s, NH); HRMS m/z calculated for $C_{15}H_{12}N_2O_2S$ $[M]^+$: 284.0619. Found: 284.0604.

6-(4-Methoxyphenyl)-4-(thiophen-2-yl)pyrimidin-2(1H)-one (5i). m.p. 237–238°C; IR (KBr, ν, cm^{-1}): 3295, 3066, 2995, 2912, 2837, 2357, 2330, 1619, 1606, 1572, 1538, 1511, 1475, 1448, 1430, 1392, 1352, 1340, 1298, 1256, 1218, 1178, 1090, 1033, 984, 902, 857, 820, 788, 723, 625 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6), (δ, ppm): 3.86 (3H, s, OCH_3), 7.11 (2H, d, $J = 8.8$ Hz, ArH), 7.27 (1H, s, ArH), 7.48 (1H, s, ArH), 7.86 (2H, d, $J = 3.6$ Hz, ArH), 8.06 (1H, d, $J = 7.6$ Hz, ArH), 8.21 (1H, s, ArH), 11.85 (1H, s, NH); HRMS m/z calculated for $C_{15}H_{12}N_2O_2S$ $[M]^+$: 284.0619. Found: 284.0599.

6-(2,5-Dimethoxyphenyl)-4-(thiophen-2-yl)pyrimidin-2(1H)-one (5j). m.p. 257–258°C; IR (KBr, ν, cm^{-1}): 3319, 3072, 2835, 2362, 2343, 1668, 1621, 1601, 1542, 1506, 1458, 1429, 1386, 1355, 1296, 1267, 1236, 1180, 1135, 1075, 1036, 957, 884, 812, 737, 717, 671, 636, 600, 552 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6), (δ, ppm): 3.74 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 7.08 (2H, t, $J = 2.8$ Hz, ArH), 7.12 (2H, d, $J = 2.8$ Hz, ArH), 7.20 (1H, t, $J = 4.0$ Hz, $J = 4.8$ Hz, ArH), 7.84 (1H, d, $J = 4.4$ Hz, ArH), 8.04 (1H, d, $J = 3.2$ Hz, ArH), 11.71 (1H, s, NH); HRMS m/z calculated for $C_{16}H_{14}N_2O_3S$ $[M - H]^-$: 313.0647. Found: 313.0652.

4-(Thiophen-2-yl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2(1H)-one (5k). m.p. 228–229°C; IR (KBr, ν, cm^{-1}): 3290, 2946, 2839, 2361, 2342, 1671, 1654, 1611, 1582, 1542, 1507, 1455, 1432, 1389, 1346, 1301, 1245, 1175, 1128, 1083, 1045, 1006, 952, 915, 854, 795, 751, 703, 669, 636, 619, 598, 518 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6), (δ, ppm): 3.71 (3H, s, OCH_3), 3.88 (6H, s, $2 \times OCH_3$), 7.25 (1H, m, ArH), 7.31 (2H, s, ArH), 7.47 (1H, s, ArH), 7.85 (1H, t, $J = 5.2$ Hz, $J = 6.0$ Hz, ArH), 8.22 (1H, d, $J = 4.4$ Hz, ArH), 11.90 (1H, s, NH); HRMS m/z calculated for $C_{17}H_{16}N_2O_4S$ $[M - H]^-$: 343.0753. Found: 343.0772.

4-(Thiophen-2-yl)-6-(4-(trifluoromethyl)phenyl)pyrimidin-2(1H)-one (5l). m.p. >280°C; IR (KBr, ν, cm^{-1}): 3305, 3115, 1084, 3030, 2913, 2361, 2342, 1869, 1845, 1772, 1575, 1522, 1474, 1445, 1412, 1390, 1343, 1256, 1244, 1168, 1136, 1119, 1067, 1018, 986, 901, 860, 838, 788, 760, 728, 669, 620, 582 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6), (δ, ppm): 7.28 (1H, t, $J = 4.0$ Hz, ArH), 7.77 (1H, s, ArH), 7.88 (1H, d, $J = 5.2$ Hz, ArH), 7.93 (2H, d, $J = 8.4$ Hz, ArH), 8.24 (1H, d, $J = 4.0$ Hz, ArH), 8.30 (2H, d, $J = 8.0$ Hz, ArH), 12.15 (1H, s, NH); HRMS m/z calculated for $C_{15}H_9F_3N_2OS$ $[M]^+$: 322.0388. Found: 322.0397.

6-(Benzo[d][1,3]dioxol-5-yl)-4-(thiophen-2-yl)pyrimidin-2(1H)-one (5m). m.p. >280°C; IR (KBr, ν, cm^{-1}): 3280, 3096, 2905, 2361, 2342, 1869, 1845, 1793, 1749, 1717, 1698, 1625, 1539, 1523, 1504, 1490, 1448, 1425, 1399, 1339, 1259, 1232, 1159, 1118, 1095, 1077, 1040, 991, 935, 884, 853, 839, 801, 773, 704, 668, 623, 601, 563 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6), (δ, ppm): 6.15 (2H, s, CH_2), 7.10 (1H, d, $J = 8.4$ Hz, ArH), 7.27 (1H, t, $J = 4.4$ Hz, ArH), 7.52 (1H, s, ArH), 7.68 (2H, s, ArH), 7.86 (1H, d, $J = 5.2$ Hz, ArH), 8.22 (1H, d, $J = 3.6$ Hz, ArH), 11.84 (1H, s, NH); HRMS m/z calculated for $C_{15}H_{10}N_2O_3S$ $[M + Na]^+$: 321.0310. Found: 321.0334.

6-(Pyridin-2-yl)-4-(thiophen-2-yl)pyrimidin-2(1H)-one (5n). m.p. 167–168°C; IR (KBr, ν, cm^{-1}): 3289, 3075, 2361, 2342, 1793, 1772, 1934, 1698, 1683, 1647, 1617, 1577, 1541, 1490, 1457, 1429, 1374, 1340, 1262, 1073, 990, 863, 823, 669, 656, 623, 586 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6), (δ, ppm): 7.25 (1H, s, ArH), 7.82 (1H, s, ArH), 7.85 (1H, d, $J = 4.0$ Hz, ArH), 8.03 (2H, d, $J = 4.0$ Hz, ArH), 8.22 (1H, s, ArH), 8.76 (2H, d, $J = 4.0$ Hz, ArH), 12.13 (1H, s, NH); HRMS m/z calculated for $C_{13}H_9N_3OS$ $[M]^+$: 255.0466. Found: 255.0446.

6-(Pyridin-4-yl)-4-(thiophen-2-yl)pyrimidin-2(1H)-one (5o). m.p. 238–239°C; IR (KBr, ν, cm^{-1}): 3301, 3085, 2910, 2360, 2341, 1868, 1844, 1792, 1772, 1716, 1645, 1637, 1616, 1593, 1553, 1539, 1508, 1473, 1427, 1396, 1373, 1341, 1263, 1090, 863,

822, 731, 613 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6), (δ, ppm): 7.29 (1H, t, $J = 4.4$ Hz, ArH), 7.85 (1H, s, ArH), 7.89 (1H, d, $J = 4.8$ Hz, ArH), 8.06 (2H, d, $J = 5.6$ Hz, ArH), 8.25 (1H, d, $J = 3.6$ Hz, ArH), 8.80 (2H, d, $J = 5.2$ Hz, ArH), 12.18 (1H, s, NH); HRMS m/z calculated for $C_{13}H_9N_3OS$ $[M]^+$: 255.0466. Found: 255.0458.

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REFERENCES AND NOTES

[1] Biginelli, P. Gazz Chim Ital 1893, 23, 360.

[2] (a) Kappe, C. O.; Stadler, A. Org React 2004, 63, 1; (b) Kappe, C. O. QSAR Comb Sci 2003, 22, 630; (c) Kappe, C. O. Acc Chem Res 2000, 33, 879; (d) Kappe, C. O. Eur J Med Chem 2000, 35, 1043; (e) Kappe, C. O. Tetrahedron 1993, 49, 6937.

[3] (a) Sabitha, G.; Reddy, K. B.; Yadav, J. S.; Shailajab, D.; Sivudu, K. S. Tetrahedron Lett 2005, 46, 8221; (b) Ma, Y.; Qian, C.; Wang, L.; Yan, M. J Org Chem 2000, 65, 3864; (c) Pisani, L.; Prokopcová, H.; Kremsner, J. M.; Kappe, C. O. J Comb Chem 2007, 9, 415.

[4] (a) Yarım, M.; Sarac, S.; Kilic, F. S.; Erol, K. Il Farmaco 2003, 58, 17; (b) Evans, C. G. E. Gestwicki, J. Org Lett 2009, 11, 2957.

[5] Byk, G.; Gottlieb, H. E.; Herscovici, J.; Mirkin, F. J Comb Chem 2000, 2, 732.

[6] Gao, L.; Ji, H.; Rong, L.; Han, H.; Shi, Y.; Tu, S. J Heterocyclic Chem 2010, 47, 358.

[7] Wang, Z. T.; Xu, L. W.; Xia, C. G.; Wang, H. Q. Tetrahedron Lett 2004, 45, 7951.

[8] (a) Zhu, A. L.; Li, Q. Q.; Li, L. J.; Wang, J. J Catal Lett 2013, 143, 463; (b) Safari, J.; Zarnegar, Z. RSC Adv 2013, 3, 17962; (c) Wang, D. C.; Guo, H. M.; Qu, G. R. Synth Commun 2010, 40, 1115.

[9] (a) Rong, L. C.; Ji, H. L.; Xia, S.; Yin, S.; Shi, Y. H.; Tu, S. J. J Heterocyclic Chem 2012, 49, 696; (b) Gao, L. J.; Ji, H. L.; Rong, L. C.; Tang, D.; Zha, Y. Y.; Shi, Y. H.; Tu, S. J. J Heterocyclic Chem 2011, 48, 957; (c) Rong, L. C.; Xia, S.; Yin, S.; Tao, S. M.; Zha, Y. Y.; Tu, S. J Res Chem Intermed 2013, 39, 3699.

[10] Kappe, C. O.; Falsone, S. F. Synlett 1998, 718.

[11] Reddy, C. V.; Mahesh, M.; Raju, K.; Babu, T. R.; Reddy, V. V. N. Tetrahedron Lett 2002, 43, 2657.

[12] Rafiee, E.; Jafari, H. Bioor Med Chem Lett 2006, 16 2463.

[13] Ramalinga, K.; Vijayalaxmi, P.; Kaimal, T. N. B. Synlett 2001, 863.

[14] Li, J. T.; Hu, J. F.; Liu, T. S. Ultrason Sonochem 2003, 10, 119.

[15] Paraskar, A. S.; Dewkar, G. K.; Sudalai, A. Tetrahedron Lett 2003, 44, 3305.

[16] (a) Tanaka, T.; Toda, F. Chem Rev 2000, 100, 1025; (b) Cave, G. W. V.; Raston, C. L. T. Chem Commun 2000, 2199; (c) Babak Kaboudin, B.; Karimi, M. Bioorg Med Chem Lett 2006, 16, 5324.

[17] Jainey, P. J.; Ishwar, K.; B Indian J Heterocyclic Chem 2011, 20, 309.

[18] X-ray crystallography for **4d**: empirical formula $C_{17}H_{14}F_3N_2O_3S$, Fw = 383.36, T = 296(2) K, monoclinic, space group P2 (1)/n, a = 6.5804 (5) Å, b = 21.9201 (17) Å, c = 15.0638 (12) Å, α = 90°, β = 100.032 (5)°, γ = 90°, V = 2139.6 (3) $Å^3$, Z = 4, Dcalcd. = 1.190 Mg/m^3, λ (MoKα) = 0.71073 Å, μ = 0.192 mm^{-1}, F(000) = 788. 1.66° < θ < 27.61°, R = 0.2601, wR = 0.6380. s = 1.043. Largest diff. peak and hole: 6.903 and −0.987 e. $Å^{-3}$.

[19] X-ray crystallography for **5h**: empirical formula $C_{15}H_{12}N_2O_2S$, Fw = 284.33, T = 296(2) K, monoclinic, space group C2/c, a = 13.802 (2) Å, b = 7.3026(12) Å, c = 13.111(2) Å, α = 90°, β = 94.604 (2)°, γ = 90°, V = 1317.8 (4) $Å^3$, Z = 4, Dcalcd. = 1.433 Mg/m^3, λ (MoKα) = 0.71073 Å, μ = 0.248 mm^{-1}, F(000) = 592. 3.16° < θ <25.20°, R = 0.0406, wR = 0.1167. s = 1.059. Largest diff. peak and hole: 0.277 and −0.256 e. $Å^{-3}$.