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An efficient synthesis of 3,4-dihydropyrimidin-2(1*H*)-one and 5,6-diphenylpyrimidine derivatives under solvent-free and base conditions

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Abstract An efficient and convenient Biginelli-like reaction one-pot synthesis of a series of 4-aryl-5,6-diphenyl-3,4-dihydropyrimidin-2(1*H*)-one and 4-aryl-5,6-diphenylpyrimidine derivatives under solvent-free conditions from the reaction of aromatic aldehydes, 1,2-diphenylethanone, urea, guanidine carbonate or acetamidine hydrochloride has been reported. This methodology has the advantages of short reaction time, mild reaction conditions, easy work-up and environmental friendliness. Moreover, 4-aryl-5,6-diphenylpyrimidine derivatives were first reported in this process. The structures of the title compounds were further determined by X-ray diffraction. More importantly, different from general Biginelli reaction, this reported method was carried out under base conditions.

Keywords 3,4-Dihydropyrimidin-2(1*H*)-one · 5,6-Diphenylpyrimidine · 1,2-Diphenylethanone · Solvent-free · Synthesis

Introduction

As we all know, *N*-heterocyclic compounds, such as pyrimidines and dihydropyrimidinones, are very important synthetic intermediates in organic synthesis. Pyrimidines show diverse biological activities, such as antiviral [1, 2], antitumor [3], antioxidant [4], and other activities [5–8]. In addition, dihydropyrimidinones

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and their derivatives have also attracted considerable attention due to their wide range of biological activities [9–16]. Thus, it is of great significance to synthesize these types of compounds. The Biginelli reaction is one of the most important procedures for the synthesis of dihydropyrimidinones [17]. The improved Biginelli-like reaction was reported by Wang et al. [18] using $FeCl_3{\cdot}6H_2O$ and TMSCl as catalysts. Many other improved Biginelli-like reactions have been reported by several groups [19–25]. However, many of the established methods still suffer from high reaction temperatures, expensive metal precursors, acid catalysts, or prolonged reaction time.

Organic reactions under solvent-free conditions are ideal protocols for the development of environmentally friendly and economically advantageous chemical processes [26–28]. Such methods not only meet the requirements of sustainable development, but also reflects the concept of low-carbon economy. Herein, we describe a novel mild base-promoted (NaOH) one-pot synthesis of 3,4-dihydropyrimidin-2(1*H*)-one (or 2-amine-5,6-diphenylpyrimidine) via a three-component condensation of aromatic aldehyde, 1,2-diphenylethanone and urea (guanidine carbonate or acetamidine hydrochloride) with excellent yields under solvent-free conditions.

Results and discussion

Initially, we investigated the reaction of aromatic aldehyde, 1,2-diphenylethanone and urea in reported literatures. It was found that only several approaches were reported by some research groups. Kefayati reported this reacton could be operated in DMF using Me_3SiCl and $Co(OAc)_2$ $4H_2O$ as catalysts [29] or carried out this reaction catalyzed by Me_3SiCl in ionic liquid [30]. In 2014, Lokwani completed this reaction in EtOH using K_2CO_3 as catalyst under reflux condition [31]. In 2010, Ji and his co-workers reported this Biginelli-type reaction in the presence of ^{t}BuOK as catalyst in refluxing EtOH [32]. However, this process must be carried out under anhydrous conditions, and the reaction time is very long (7–24 h). Therefore, other simpler methods for the synthesis of these kinds of compounds are still needed.

In order to find a simple operation and to easily obtain the catalyst, we initiated our studies by investigating the effect of different solvents, temperatures, and catalysts using 4-chlorobenzaldehyde, 1,2-diphenylethanone and urea as standard materials. The results are summarized in Table 1. It is shown that the Lewis acids such as $ZnCl_2$, $FeCl_3$, $HgCl_2$, and I_2 had no effect on the reaction (Table 1, entries 1–4). Using proton acid (HCl, 37%) as catalyst, the yield is still poor (Table 1, entry 5). Our attention then turned to investigate the effect of common alkalic catalysts like $Ba(OH)_2$, K_2CO_3, NaOH. Initially, we found that the yields were poor when Na_2CO_3 or $Ba(OH)_2$ was used in model reaction (Table 1, entries 6–7). When NaOH was used as catalyst in different solvents (EtOH, DMF, THF, MeOH, or toluene), the yields are still lower than expected (Table 1, entries 8–12). Surprisingly, excellent yield is obtained when the reaction is carried out under solvent-free conditions using NaOH as a catalyst (Table 1, entry 13). Further study found that the similar yields can be obtained when the loading amount of NaOH is

Table 1 Optimization of reaction conditions using different catalysts and temperatures

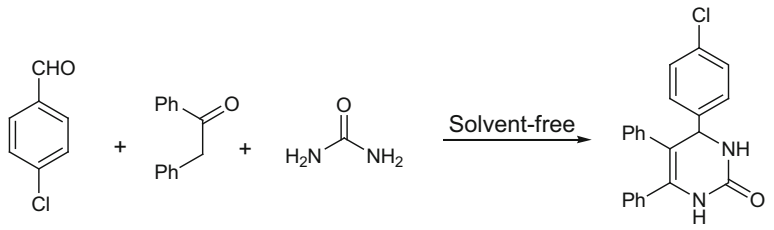
Entry	Conditions	Yield (%)
1	$ZnCl_2$ (1 equiv), EtOH, 70 °C, 30 min	0
2	$HgCl_2$ (1 equiv), EtOH, 70 °C, 30 min	0
3	$FeCl_3$ (1 equiv), EtOH, 70 °C, 30 min	0
4	I_2 (1 equiv), EtOH, 70 °C, 30 min	0
5	HCl (37%, 1 equiv), EtOH, 70 °C, 30 min	Trace
6	Na_2CO_3 (1 equiv), EtOH, 70 °C, 30 min	20
7	$Ba(OH)_2$ (1 equiv), EtOH, 70 °C, 30 min	15
8	NaOH (1 equiv), EtOH, 70 °C, 30 min	40
9	NaOH (1 equiv), DMF, 100 °C, 30 min	32
10	NaOH (1 equiv), toluene, 100 °C, 30 min	20
11	NaOH (1 equiv), MeOH, 70 °C, 30 min	44
12	NaOH (1 equiv), THF, 70 °C, 30 min	18
13	NaOH (1 equiv), solvent-free, 70 °C, 30 min	88
14	NaOH (0.5 equiv), solvent-free, 70 °C, 30 min	90
15	NaOH (0.3 equiv), solvent-free, 70 °C, 30 min	89
16	NaOH (1 equiv), solvent-free, 50 °C, 60 min	30

The reaction conditions: 4-chlorobenzaldehyde (1 mmol), 1,2-diphenylethanone (1 mmol), urea (1.5 mmol), solvents (5 mL)

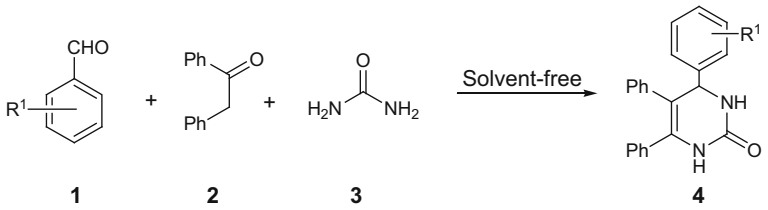
reduced to 0.5 or 0.3 equiv (90 and 89% yields, Table 1, entries 14–15) under the same reaction conditions. The study also found that low temperature is not conducive to the completion of the model reaction (Table 1, entry 16; Scheme 1).

Therefore, taking overall factors of reaction time, temperature, solvent, and amount of catalyst into consideration, we will perform the reaction at 70 °C using a catalytic amount of NaOH (30 mol%) under solvent-free conditions. In order to examine the substrate scope of this Biginelli-like reaction, we applied the approach to various aromatic aldehydes carrying electron-withdrawing or electron-donating substituents under the above-optimized reaction conditions (Scheme 2). From the results, it can be seen that aromatic aldehydes with different substituted groups can be successfully applied to this synthesis method. The results are listed in Table 2.

In order to expand the scope of this study, and to obtain other nitrogen-containing heterocyclic compounds, guanidine carbonate was also invovled in this process; the novel 4-aryl-5,6-diphenylpyrimidine derivatives were obtained with high yields



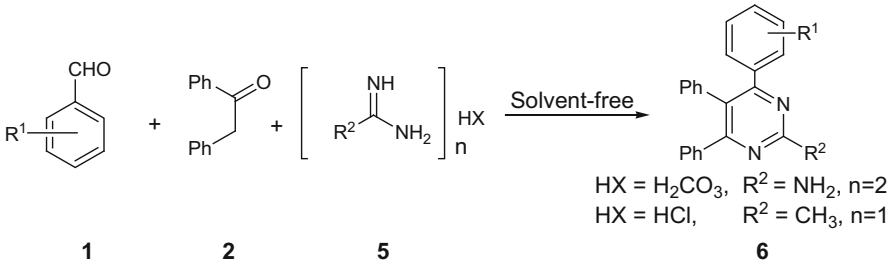
Scheme 1 The model reaction of compound **4d**



Scheme 2 Synthesis of 3,4-dihydropyrimidin-2(1*H*)-one derivatives

Table 2 The results of synthesis of 3,4-dihydropyrimidin-2(1*H*)-one derivatives

Entry	R^1	Product	Time (min)	Yields (%)
1	4-FC_6H_4	**4a**	30	85
2	2-ClC_6H_4	**4b**	30	94
3	3-ClC_6H_4	**4c**	30	92
4	4-ClC_6H_4	**4d**	30	89
5	2,4-$Cl_2C_6H_3$	**4e**	30	86
6	3,4-$Cl_2C_6H_3$	**4f**	30	88
7	3-BrC_6H_4	**4g**	30	92
8	C_6H_5	**4h**	35	83
9	3,4-$(CH_3)_2C_6H_3$	**4i**	45	89
10	2-$CH_3OC_6H_4$	**4j**	35	91
11	4-$CH_3OC_6H_4$	**4k**	35	88
12	2,5-$(CH_3O)_2C_6H_3$	**4l**	30	96
13	3,4-$(CH_3O)_2C_6H_3$	**4m**	40	94
14	3,4-OCH_2O-C_6H_3	**4n**	30	88
15	2-pyridyl	**4o**	30	89



Scheme 3 Synthesis of 2-amine-5,6-diphenylpyrimidine derivatives

(Scheme 3). At the same time, we found that acetamidine hydrochloride was not suitable for this research method; only two corresponding products were obtained. The results are listed in Table 3.

The structures of all the products were confirmed by spectroscopic data, particularly IR, ^{1}H NMR, ^{13}C NMR and HRMS. For example, in ^{1}H-NMR of **4i**, it shows two singlets signals at delta 2.19 and 2.20 due to the two CH_3 protons and

Table 3 The results of synthesis of 2-amine-5,6-diphenylpyrimidine derivatives

Entry	R^1	R^2	Product	Time (min)	Yields (%)
1	C_6H_5	NH_2	**6a**	45	90
2	4-FC_6H_4	NH_2	**6b**	35	88
3	3,4-$Cl_2C_6H_3$	NH_2	**6c**	40	90
4	4-BrC_6H_4	NH_2	**6d**	40	91
5	4-$CH_3C_6H_4$	NH_2	**6e**	38	85
6	3,4-$(CH_3)_2C_6H_3$	NH_2	**6f**	42	95
7	2,5-$(CH_3O)_2C_6H_3$	NH_2	**6g**	50	87
8	3,4-$(CH_3O)_2C_6H_3$	NH_2	**6h**	40	89
9	3,4-$OCH_2OC_6H_3$	NH_2	**6i**	45	83
10	4-$CH_3OC_6H_4$	CH_3	**6j**	40	90
11	3,4-$(CH_3)_2C_6H_3$	CH_3	**6k**	35	86

two singlets at delta 7.45 and 8.65 due to the –NH– protons. A doublet signal at 5.04 ppm is a proton of C^4-H. The 13 aromatic hydrogen protons distribute from 6.79 to 7.26 ppm. In ^{13}C-NMR, the chemical shifts of 24 carbon atoms show at 19.1, 19.6, 59.0, 109.5, 124.4, 125.8, 127.7, 128.0, 128.1, 128.2, 129.2, 129.4, 129.7, 134.6, 135.1, 135.3, 136.2, 138.2, 141.3 and 153.1 respectively. In the HRMS spectrum, the calculated m/z for $C_{24}H_{22}N_2O$ $[M + Na]^+$ is 377.1624, and we found m/z to be 377.1640.

In IR of **6f**, the wave numbers of $–NH_2$ could be found at 3495, 3282 and 3155 cm^{-1}. In its ^{1}H-NMR, the two singlets appear at delta 2.10 and 2.15 due to the two CH_3 protons. The 13 aromatic hydrogen protons could be found from 6.82 to 7.25 ppm. The ^{13}C chemical shifts are 19.1, 19.3, 120.3, 126.4, 126.7, 127.3, 127.8, 127.9, 128.3, 129.1, 130.5, 131.4, 135.2, 136.3, 136.4, 137.4, 139.2, 162.2, 165.6 and 165.9 respectively. In the HRMS spectrum, the calculated m/z for $C_{24}H_{21}N_3$ $[M + H]^+$ is 352.1808, and it is found at 352.1807.

The structures of **4o** and **6h** are additionally confirmed by X-ray diffraction analysis. The crystal structures are shown in Figs. 1 and 2.

Conclusions

In summary, we have described a successful, simple and efficient green approach for the preparation of 3,4-dihydropyrimidin-2(1*H*)-one and 2-amine-5,6-diphenyl pyrimidine derivatives involing aromatic aldehydes **1**, 1,2-diphenylethanone **2**, urea **3** or guanidine carbonate and acetamidine hydrochloride **5** under solvent-free conditions. Advantages of this method include mild reaction conditions, low cost, operational simplicity and reduced environmental impact. Moreover, the products were obtained in excellent yields within short reaction times and the starting materials are also inexpensive and commercially available. More importantly, different from general Biginelli reaction, this reported method was carried out under base conditions.

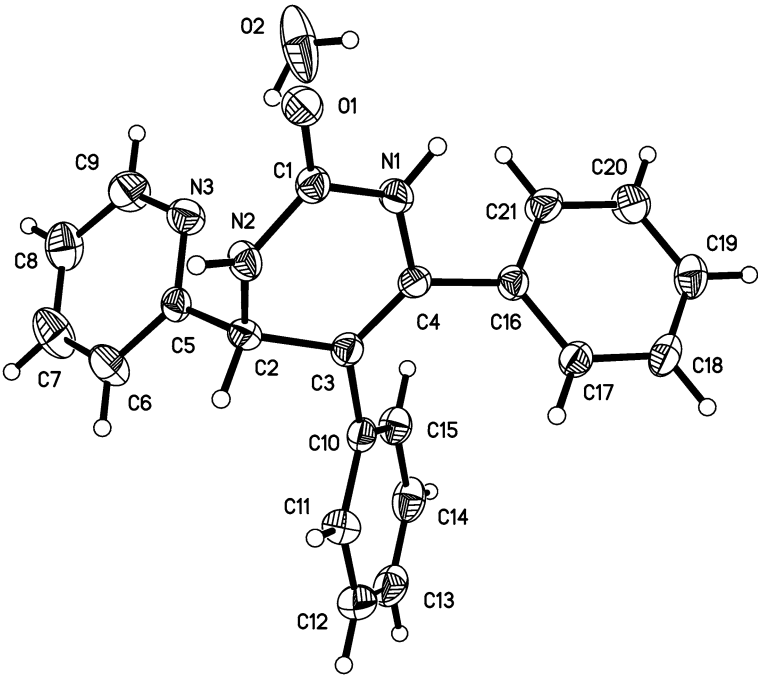


Fig. 1 X-ray structure of **4o**

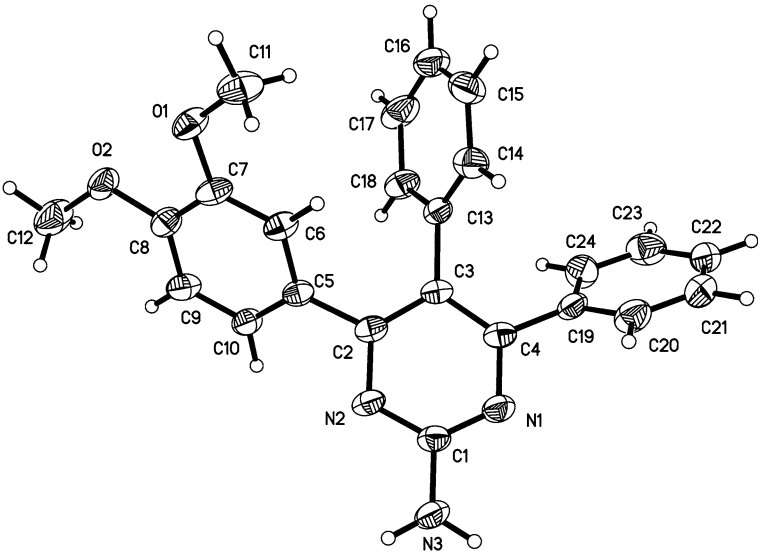


Fig. 2 X-ray structure of **6h**

Experimental

Melting points were determined on an XT-5 microscopic melting point apparatus and were uncorrected. IR spectra were recorded on a FT IR-8101 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were obtained from solution in DMSO-d_6 with Me_4Si as 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. All reagents were purchased from chemical reagent companies and used without further purification.

General Procedure for the synthesis of 3,4-dihydropyrimidin-2(1*H*)-one and 2-amine-5,6-diphenylpyrimidine derivatives

A mixture of aromatic aldehydes **1** (1 mmol), 1,2-diphenylethanone **2** (1 mmol), urea **3** (1.5 mmol) or guanidine carbonate and acetamidine hydrochloride **5** (1 mmol), and NaOH (0.3 mmol) was heated in a round-bottom flask at 70 °C over the course of 30 min. After the reaction was completed (monitored by thin-layer chromatography, TLC), the reaction mixture was poured into water, and then washed with water thoroughly. The product was filtered, dried, and recrystallized from 95% ethanol.

*4-(4-Fluorophenyl)-5,6-diphenyl-3,4-dihydropyrimidin-2(1H)-one (**4a**)*

m.p. 253–255°C; IR (KBr, v, cm^{-1}): 3207, 3082, 1688, 1602, 1508, 1475, 1329, 1276, 1223, 1186, 1155, 1073, 840, 766, 698, 665, 588, 513 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.18 (1H, d, $J = 2.8$ Hz, C^4-H), 6.80 (2H, t, $J = 7.6$ Hz, ArH), 6.98–7.04 (3H, m, ArH), 7.17 (2H, t, $J = 8.8$ Hz, ArH), 7.21–7.25 (5H, m, ArH), 7.40 (2H, dd, $J = 6.0$ Hz, $J = 8.8$ Hz, ArH), 7.54 (1H, s, NH), 8.69 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 58.6, 109.5, 114.5, 114.7, 115.1, 115.2, 115.4, 125.9, 127.0, 127.6, 127.8, 127.9, 128.0, 128.9, 129.1, 129.3, 131.5, 134.7, 134.8, 135.1, 137.9, 140.0, 140.1, 153.2, 160.3, 161.1, 162.7, 163.6; HRMS m/z calculated for $C_{22}H_{17}FN_2O$ [M + Na]$^+$: 367.1223, found: 367.1246.

*4-(2-Chlorophenyl)-5,6-diphenyl-3,4-dihydropyrimidin-2(1H)-one (**4b**)*

m.p. 235–236°C (lit. [32] 237–239 °C); IR (KBr, v, cm^{-1}): 3226, 3100, 1696, 1645, 1495, 1463, 1455, 1267, 1189, 762, 744, 697, 589 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.70 (1H, d, $J = 2.4$ Hz, C^4-H), 6.77 (2H, dd, $J = 2.4$ Hz, $J = 7.6$ Hz, ArH), 6.97–7.01 (3H, m, ArH), 7.19–7.25 (5H, m, ArH), 7.28 (1H, d, $J = 8.4$ Hz, ArH), 7.35–7.40 (2H, m, ArH), 7.48 (1H, s, NH), 7.64 (1H, d, $J = 7.6$ Hz, ArH), 8.72 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 56.6, 108.5, 126.1, 126.6, 127.0, 127.6, 127.7, 127.9, 128.0, 128.2, 128.9, 129.2, 129.3, 129.4, 129.6, 129.7, 131.8, 134.8, 135.0, 137.4, 140.7, 152.8, 162.3; HRMS m/z calculated for $C_{22}H_{17}ClN_2O$ [M + Na]$^+$: 383.0922, found: 383.0943.

*4-(3-Chlorophenyl)-5,6-diphenyl-3,4-dihydropyrimidin-2(1H)-one (**4c**)*

m.p. 214–216°C (lit. [29] 199–201 °C); IR (KBr, *v*, cm^{-1}): 3230, 3085, 1698, 1596, 1573, 1431, 1321, 1267, 1178, 1078, 1000, 851, 765, 699, 590, 512 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.21 (1H, d, $J = 2.8$ Hz, C^4-H), 6.80 (2H, d, $J = 8.0$ Hz, ArH), 6.99–7.05 (3H, m, ArH), 7.19–7.26 (5H, m, ArH), 7.32–7.39 (4H, m, ArH), 7.59 (1H, s, NH), 8.73 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 58.7, 108.9, 125.6, 126.0, 126.9, 127.5, 127.8, 128.1, 128.3, 129.3, 130.6, 133.1, 134.8, 135.1, 137.7, 146.2, 152.9; HRMS m/z calculated for $C_{22}H_{17}ClN_2O$ $[M + H]^+$: 361.1107, found: 361.1143.

*4-(4-Chlorophenyl)-5,6-diphenyl-3,4-dihydropyrimidin-2(1H)-one (**4d**)*

m.p. 253–254°C (lit. [32] 263–265 °C); IR (KBr, ν, cm^{-1}): 3213, 3085, 1689, 1491, 1474, 1409, 1329, 1270, 1189, 1091, 1017, 833, 769, 697, 588 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.19 (1H, d, $J = 2.8$ Hz, C^4-H), 6.79 (2H, d, $J = 7.6$ Hz, ArH), 6.98–7.03 (3H, m, ArH), 7.19–7.25 (5H, m, ArH), 7.36 (2H, d, $J = 8.4$ Hz, ArH), 7.41 (2H, d, $J = 8.4$ Hz, ArH), 7.55 (1H, s, NH), 8.69 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 56.5, 108.5, 126.1, 127.7, 127.8, 127.9, 128.1, 129.3, 129.4, 129.5, 129.7, 131.8, 134.8, 135.0, 137.4, 140.6, 152.8, 162.3; HRMS m/z calculated for $C_{22}H_{17}ClN_2O$ $[M + Na]^+$: 383.0922, found: 383.0945.

*4-(2,4-Dichlorophenyl)-5,6-diphenyl-3,4-dihydropyrimidin-2(1H)-one (**4e**)*

m.p. 197–199°C; IR (KBr, *v*, cm^{-1}): 3223, 3100, 1698, 1644, 1560, 1495, 1464, 1381, 1267, 1184, 1094, 823, 772, 697, 592 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.72 (1H, d, $J = 2.4$ Hz, C^4-H), 6.78 (2H, t, $J = 8.0$ Hz, ArH), 6.97–7.02 (3H, m, ArH), 7.18–7.23 (5H, m, ArH), 7.46 (1H, dd, $J = 1.2$ Hz, $J = 8.4$ Hz, ArH), 7.51 (1H, d, $J = 2.0$ Hz, ArH), 7.53 (1H, s, NH), 7.62 (1H, t, $J = 8.4$ Hz, ArH), 8.76 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 56.4, 108.2, 126.2, 127.8, 127.9, 128.0, 128.2, 128.9, 129.3, 129.4, 131.2, 132.8, 132.9, 134.6, 135.2, 137.2, 139.7, 152.9, 162.3; HRMS m/z calculated for $C_{22}H_{16}Cl_2N_2O$ $[M + H]^+$: 395.0712, found: 395.0711.

*4-(3,4-Dichlorophenyl)-5,6-diphenyl-3,4-dihydropyrimidin-2(1H)-one (**4f**)*

m.p. 235–237°C; IR (KBr, *v*, cm^{-1}): 3224, 3101, 1692, 1655, 1598, 1541, 1472, 1446, 1400, 1324, 1266, 1188, 1131, 1073, 1032, 877, 818, 771, 736, 698, 590 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.27 (1H, d, $J = 2.8$ Hz, C^4-H), 6.81 (2H, dd, $J = 2.0$ Hz, $J = 8.0$ Hz, ArH), 6.97–7.02 (3H, m, ArH), 7.17–7.23 (5H, m, ArH), 7.31 (1H, dd, $J = 2.8$ Hz, $J = 7.2$ Hz, ArH), 7.45 (1H, d, $J = 8.0$ Hz, ArH), 7.56 (1H, s, NH), 7.83 (1H, t, $J = 7.6$ Hz, ArH), 8.68 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 58.7, 108.9, 125.6, 126.0, 126.9, 127.5, 127.8, 128.1, 128.3, 129.3, 130.6, 133.1, 134.8, 135.1, 137.7, 146.2, 152.9; HRMS m/z calculated for $C_{22}H_{16}Cl_2N_2O$ $[M + Na]^+$: 417.0532, found: 417.0543.

*4-(3-Bromophenyl)-5,6-diphenyl-3,4-dihydropyrimidin-2(1H)-one (**4g**)*

m.p. 193–194°C; IR (KBr, *v*, cm^{-1}): 3231, 3098, 1697, 1651, 1599, 1568, 1472, 1319, 1266, 1176, 1071, 764, 699, 590 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.20 (1H, d, $J = 2.8$ Hz, C^4-H), 6.81 (2H, d, $J = 7.6$ Hz, ArH), 7.00–7.05 (3H, m, ArH), 7.21–7.26 (5H, m, ArH), 7.32 (1H, d, $J = 7.6$ Hz, ArH), 7.37 (1H, d, $J = 7.6$ Hz, ArH), 7.47 (1H, d, $J = 7.6$ Hz, ArH), 7.51 (1H, s, ArH), 7.58 (1H, s, NH), 8.72 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 58.7, 108.9, 120.9, 121.8, 126.0, 127.1, 127.7, 127.8, 128.0, 128.1, 128.3, 129.1, 129.2, 129.3, 129.7, 129.9, 130.4, 130.9, 131.5, 131.8, 134.8, 134.9, 135.1, 137.7, 146.4, 153.0, 162.3; HRMS m/z calculated for $C_{22}H_{17}BrN_2O$ $[M + Na]^+$: 427.0421, found: 427.0442.

*4,5,6-Triphenyl-3,4-dihydropyrimidin-2(1H)-one (**4h**)*

m.p. 253–254°C (lit. [32] 241–243 °C); IR (KBr, *v*, cm^{-1}): 3208, 3082, 1688, 1602, 1508, 1475, 1329, 1276, 1223, 1186, 1155, 1092, 840, 766, 698, 664, 588, 513 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.18 (1H, d, $J = 2.8$ Hz, ArCH), 6.79 (2H, d, $J = 7.6$ Hz, C^4-H), 6.97–7.03 (3H, m, ArH), 7.12–7.25 (8H, m, ArH), 7.40 (2H, dd, $J = 5.6$ Hz, $J = 8.4$ Hz, ArH), 7.54 (1H, s, NH), 8.69 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 60.5, 76.7, 77.0, 77.3, 77.4, 111.1, 115.2, 115.7, 115.9, 126.7, 128.1, 128.5, 128.7, 128.8, 129.7, 129.8, 133.1, 134.8, 137.1, 138.7, 161.2, 163.7; HRMS m/z calculated for $C_{22}H_{18}N_2O$ $[M + Na]^+$: 349.1317, found: 363.1494.

*4-(3,4-Dimethylphenyl)-5,6-diphenyl-3,4-dihydropyrimidin-2(1H)-one (**4i**)*

m.p. 208–209°C; IR (KBr, *v*, cm^{-1}): 3228, 3089, 1698, 1649, 1480, 1321, 1268, 1180, 1124, 1094, 1023, 773, 699, 591 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.19 (3H, s, CH_3), 2.20 (3H, s, CH_3), 5.04 (1H, d, $J = 2.8$ Hz, C^4-H), 6.79 (2H, d, $J = 7.6$ Hz, ArH), 6.97–7.02 (3H, m, ArH), 7.10 (2H, s, ArH), 7.13 (1H, s, ArH), 7.21–7.26 (5H, m, ArH), 7.45 (1H, s, NH), 8.65 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 19.1, 19.6, 59.0, 109.5, 124.4, 125.8, 127.7, 128.0, 128.1, 128.2, 129.2, 129.4, 129.7, 134.6, 135.1, 135.3, 136.2, 138.2, 141.3, 153.1; HRMS m/z calculated for $C_{24}H_{22}N_2O$ $[M + Na]^+$: 377.1624, found: 377.1640.

*4-(2-Methoxyphenyl)-5,6-diphenyl-3,4-dihydropyrimidin-2(1H)-one (**4j**)*

m.p. 251–252°C; IR (KBr, *v*, cm^{-1}): 3418, 3271, 1694, 1645, 1598, 1556, 1504, 1486, 1462, 1445, 1268, 1245, 1186, 1030, 758, 697 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.73 (3H, s, OCH_3), 5.48 (1H, d, $J = 2.8$ Hz, C^4-H), 6.77 (2H, dd, $J = 1.6$ Hz, $J = 7.6$ Hz, ArH), 6.96–7.02 (5H, m, ArH), 7.08 (1H, s, NH), 7.22–7.29 (6H, m, ArH), 7.46 (1H, dd, $J = 1.2$ Hz, $J = 7.6$ Hz, ArH), 8.61 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 58.7, 108.9, 120.9, 121.9, 126.0, 127.1, 127.6, 127.7, 127.8, 128.0, 128.1, 128.3, 129.1, 129.3, 129.7, 129.9, 130.4,

130.9, 131.5, 131.8, 134.8, 134.9, 135.1, 137.7, 146.4, 153.0, 153.1, 162.3; HRMS m/z calculated for $C_{23}H_{20}N_2O_2$ $[M + Na]^+$: 379.1417, found: 379.1433.

*4-(4-Methoxyphenyl)-5,6-diphenyl-3,4-dihydropyrimidin-2(1H)-one (**4k**)*

m.p. 211–213°C (lit. [32] 224–226 °C); IR (KBr, *v*, cm^{-1}): 3217, 3085, 1685, 1611, 1512, 1472, 1306, 1254, 1237, 1173, 1035, 832, 771, 697, 588, 517 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.73 (3H, s, OCH_3), 5.07 (1H, d, $J = 2.4$ Hz, C^4-H), 6.79 (2H, d, $J = 7.6$ Hz, ArH), 6.91 (2H, d, $J = 8.4$ Hz, ArH), 6.97–7.03 (3H, m, ArH), 7.21–7.26 (5H, m, ArH), 7.29 (2H, d, $J = 8.4$ Hz, ArH), 7.43 (1H, s, NH), 8.61 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 55.0, 58.6, 109.7, 113.9, 125.9, 127.7, 128.1, 128.2, 129.2, 129.3, 134.5, 135.0, 135.9, 138.1, 153.1, 158.6; HRMS m/z calculated for $C_{23}H_{20}N_2O_2$ $[M + Na]^+$: 379.1417, found: 379.1434.

*4-(2,5-Dimethoxyphenyl)-5,6-diphenyl-3,4-dihydropyrimidin-2(1H)-one (**4l**)*

m.p. 237–239°C; IR (KBr, *v*, cm^{-1}): 3206, 3096, 1683, 1664, 1495, 1460, 1447, 1277, 1241, 1210, 1045, 772, 701 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.67 (3H, s, OCH_3), 3.68 (3H, s, OCH_3), 5.44 (1H, d, $J = 2.8$ Hz, C^4-H), 6.78 (2H, d, $J = 7.6$ Hz, ArH), 6.84 (1H, dd, $J = 3.2$ Hz, $J = 9.2$ Hz, ArH), 6.94 (1H, d, $J = 8.8$ Hz, ArH), 6.98–7.03 (4H, m, ArH), 7.10 (1H, s, NH), 7.20–7.27 (5H, m, ArH), 8.65 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 53.0, 55.2, 56.0, 108.5, 112.5, 112.7, 114.0, 125.8, 127.7, 128.1, 128.2, 129.0, 129.3, 132.1, 135.0, 135.3, 138.0, 150.5, 153.2, 153.4; HRMS m/z calculated for $C_{24}H_{22}N_2O_3$ $[M + Na]^+$: 409.1523, found: 409.1541.

*4-(3,4-Dimethoxyphenyl)-5,6-diphenyl-3,4-dihydropyrimidin-2(1H)-one (**4m**)*

m.p. 206–207°C; IR (KBr, *v*, cm^{-1}): 3236, 3082, 1688, 1657, 1599, 1514, 1449, 1260, 1239, 1181, 1155, 1134, 1084, 1027, 866, 770, 700 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.70 (3H, s, OCH_3), 3.73 (3H, s, OCH_3), 5.06 (1H, d, $J = 2.8$ Hz, C^4-H), 6.81 (2H, d, $J = 6.8$ Hz, ArH), 6.93 (2H, s, ArH), 6.95 (1H, s, ArH), 6.98–7.03 (3H, m, ArH), 7.22–7.27 (5H, m, ArH), 7.46 (1H, s, NH), 8.66 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 55.3, 55.5, 58.9, 109.5, 110.9, 111.8, 118.9, 125.8, 127.8, 128.1, 128.2, 129.2, 129.3, 129.4, 129.5, 134.7, 135.0, 136.1, 138.2, 148.2, 148.8, 153.4, 153.5, 162.3; HRMS m/z calculated for $C_{24}H_{22}N_2O_3$ $[M + Na]^+$: 409.1523, found: 409.1511.

*4-(Benzo[d][1,3]dioxol-5-yl)-5,6-diphenyl-3,4-dihydropyrimidin-2(1H)-one (**4n**)*

m.p. 242–244°C (lit. [32] 249–251 °C); IR (KBr, *v*, cm^{-1}): 3215, 3081, 1687, 1599, 1488, 1372, 1304, 1237, 1190, 1103, 1039, 929, 771, 700, 679, 589, 515 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.05 (1H, d, $J = 2.8$ Hz, C^4-H), 6.00 (2H, d, $J = 4.0$ Hz, OCH_2O), 6.81 (2H, d, $J = 8.0$ Hz, ArH), 6.85 (1H, s, ArH), 6.88 (1H, d, $J = 7.6$ Hz, ArH), 6.92 (1H, s, ArH), 6.98–7.03 (3H, m, ArH), 7.21–7.25 (5H, m,

ArH), 7.48 (1H, s, NH), 8.69 (1H, s, NH); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm): 55.4, 95.9, 96.2, 102.3, 102.6, 103.1, 104.7, 105.8, 115.4, 119.5, 121.3, 122.0, 122.7, 123.1, 123.2, 123.4, 123.7, 124.1, 124.4, 124.5, 126.4, 128.0, 129.7, 131.8, 132.2, 142.0, 142.2, 143.0, 143.7, 148.8; HRMS m/z calculated for $C_{23}H_{18}N_2O_3$ $[M + Na]^+$: 393.1209, found: 393.1220.

*5,6-Diphenyl-4-(pyridin-2-yl)-3,4-dihydropyrimidin-2(1H)-one (**4o**)*

m.p. 216–218°C (lit. [32] 207–209 °C); IR (KBr, v, cm^{-1}): 3219, 3082, 1689, 1590, 1575, 1494, 1473, 1447, 1433, 1331, 1281, 1266, 1189, 765, 747, 698, 591 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.27 (1H, d, $J = 2.8$ Hz, C^4-H), 6.81 (2H, dd, $J = 2.0$ Hz, $J = 8.0$ Hz, ArH), 6.97–7.03 (3H, m, ArH), 7.17–7.23 (5H, m, ArH), 7.30–7.33 (1H, m, ArH), 7.45 (1H, d, $J = 8.0$ Hz, ArH), 7.56 (1H, s, NH), 7.83 (1H, t, $J = 7.6$ Hz, ArH), 8.53 (1H, d, $J = 4.8$ Hz, ArH), 8.69 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 45.7, 61.5, 73.7, 109.0, 121.4, 122.7, 125.8, 125.9, 126.0, 126.7, 127.7, 127.8, 128.0, 128.1, 129.3, 129.5, 134.9, 137.1, 137.9, 139.1, 145.7, 149.1, 153.1, 162.2; HRMS m/z calculated for $C_{21}H_{17}N_3O$ $[M + H]^+$: 328.1450, found: 328.1470.

*4,5,6-Triphenylpyrimidin-2-amine (**6a**)*

m.p. 221–223°C; IR (KBr, v, cm^{-1}): 3486, 3317, 3203, 3055, 1632, 1601, 1583, 1544, 1530, 1493, 1460, 14,386, 1392, 1370, 1275, 1210, 1183, 1077, 1028, 823, 774, 698, 669, 625 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 6.89 (1H, d, $J = 3.6$ Hz, ArH), 6.91 (1H, $J = 2.0$ Hz, ArH), 7.08–7.10 (3H, m, ArH), 7.18–7.26 (10H, m, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 110.4, 120.4, 125.7, 126.4, 127.1, 127.4, 127.6, 127.8, 127.9, 128.0, 128.9, 129.0, 129.1, 129.5, 131.5, 137.1, 139.1, 141.8, 145.9, 162.2, 162.3, 165.9; HRMS m/z calculated for $C_{22}H_{17}N_3$ $[M + H]^+$: 324.1501, found:. 324.1494.

*4-(4-Fluorophenyl)-5,6-diphenylpyrimidin-2-amine(**6b**)*

m.p. 217–219°C; IR (KBr, v, cm^{-1}): 3499, 3294, 3162, 3048, 1630, 1602, 1545, 1530, 1507, 1459, 1438, 1388, 1367, 1227, 1210, 1182, 1159, 1012, 851, 817, 774, 702 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 6.87 (2H, s, NH_2), 6.89 (1H, d, $J = 3.6$ Hz, ArH), 6.91 (1H, d, $J = 2.0$ Hz, ArH), 7.04 (2H, t, $J = 8.8$ Hz, ArH), 7.11 (3H, t, $J = 2.8$ Hz, ArH), 7.19–7.20 (4H, m, ArH), 7.21–7.25 (3H, m, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 120.4, 126.4, 127.4, 127.8, 128.0, 129.1, 129.2, 131.5, 136.2, 137.3, 137.5, 139.2, 162.2, 165.6, 165.9; HRMS m/z calculated for $C_{22}H_{16}FN_3$ $[M + H]^+$: 342.1406, found: 342.1431.

*4-(3,4-Dichlorophenyl)-5,6-diphenylpyrimidin-2-amine (**6c**)*

m.p. 181–184°C; IR (KBr, v, cm^{-1}): 3462, 3290, 3160, 3058, 1669, 1635, 1623, 1576, 1541, 1507, 1496, 1472, 1455, 1397, 1367, 1270, 1210, 1181, 1136, 1030, 895, 812, 771, 700 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 6.93 (2H, s,

NH_2), 6.95 (2H, s, ArH), 7.10–7.15 (4H, m, ArH), 7.19–7.25 (5H, m, ArH), 7.45 (2H, s, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm): 122.2, 127.1, 127.8, 128.1, 128.4, 128.7, 128.8, 129.0, 129.3, 129.6, 129.9, 131.4, 131.5, 132.2, 132.8, 136.2, 138.4, 138.8, 161.8, 164.0, 167.4; HRMS m/z calculated for $C_{22}H_{15}Cl_2N_3$ $[M + H]^+$: 392.0716, found: 392.0721.

*4-(4-Bromophenyl)-5,6-diphenylpyrimidin-2-amine (**6d**)*

m.p. 247–248°C; IR (KBr, v, cm^{-1}): 3483, 3359, 3198, 3054, 1638, 1612, 1583, 1569, 1527, 1485, 1451, 1438, 1399, 1370, 1210, 1180, 1071, 1010, 845, 814, 771, 700 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 6.89 (2H, s, NH_2), 6.90–6.92 (2H, m, ArH), 7.10–7.13 (2H, m, ArH), 7.14 (2H, d, $J = 8.4$ Hz, ArH), 7.19–7.24 (6H, m, ArH), 7.41 (2H, d, $J = 8.0$ Hz, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 111.7, 121.3, 123.4, 126.7, 128.0, 128.2, 128.6, 129.3, 129.4, 130.4, 131.1, 131.8, 133.0, 134.0, 136.8, 141.5, 152.2, 162.3, 170.5, 176.3; HRMS m/z calculated for $C_{22}H_{16}BrN_3$ $[M + H]^+$: 402.0606, found: 402.0628.

*4,5-Diphenyl-6-p-tolylpyrimidin-2-amine (**6e**)*

m.p. 204–206°C; IR (KBr, v, cm^{-1}): 3486, 3356, 3194, 3055, 1640, 1610, 1583, 1573, 1544, 1529, 1511, 1497, 1451, 1438, 1392, 1371, 1272, 1208, 1184, 1020, 812, 768, 699, 644, 627, 508 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.23 (3H, s, CH_3), 6.80 (2H, s, NH_2), 6.88–6.90 (2H, m, ArH), 6.99 (2H, d, $J = 7.6$ Hz, ArH), 7.09–7.11 (5H, m, ArH), 7.17–7.24 (5H, m, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 20.7, 120.4, 126.4, 127.4, 127.8, 128.0, 129.0, 129.1, 129.2, 129.4, 131.4, 136.2, 137.3, 137.5, 139.1, 162.2, 165.6, 165.9; HRMS m/z calculated for $C_{23}H_{19}N_3$ $[M + H]^+$: 338.1652, found: 338.1635.

*4-(3,4-Dimethylphenyl)-5,6-diphenylpyrimidin-2-amine (**6f**)*

m.p. 213–215°C; IR (KBr, v, cm^{-1}): 3495, 3282, 3155, 3058, 1620, 1579, 1544, 1531, 1507, 1495, 1462, 1403, 1369, 1271, 1211, 1194, 1134, 1073,1027, 1010, 817, 769, 700, 642 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.10 (3H, s, CH_3), 2.15 (3H, s, CH_3), 6.82 (1H, dd, $J = 0.8$ Hz, $J = 7.6$ Hz, ArH), 6.89–6.92 (3H, m, ArH), 7.10–7.12 (4H, m, ArH), 7.19–7.25 (5H, m, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 19.1, 19.3, 120.3, 126.4, 126.7, 127.3, 127.8, 127.9, 128.3, 129.1, 130.5, 131.4, 135.2, 136.3, 136.4, 137.4, 139.2, 162.2, 165.6, 165.9; HRMS m/z calculated for $C_{24}H_{21}N_3$ $[M + H]^+$: 352.1808, found: 352.1807.

*4-(2,5-Dimethoxyphenyl)-5,6-diphenylpyrimidin-2-amine (**6g**)*

m.p. 222–223°C; IR (KBr, v, cm^{-1}): 3497, 3268, 3136, 3058, 1660,1651, 1621, 1583, 1550, 1496, 1462, 1421, 1391, 1372, 1300, 1268, 1222, 1184, 1164, 1117, 1049, 809, 774, 751, 701 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.32 (3H, s, OCH_3), 3.64 (3H, s, OCH_3), 6.68 (1H, dd, $J = 2.0$ Hz, $J = 7.6$ Hz, ArH), 6.74–6.77 (2H, m, ArH), 6.82–6.86 (4H, m, ArH, NH_2), 6.99–7.02 (3H, m, ArH),

7.17–7.24 (5H, m, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 55.2, 55.3, 56.1, 111.7, 114.2, 115.3, 121.9, 126.1, 127.1, 127.4, 128.2, 129.1, 129.2, 130.7, 137.0, 138.9, 149.7, 152.3, 162.1, 164.5, 165.5; HRMS m/z calculated for $C_{24}H_{21}N_3O_2$ $[M + Na]^+$: 406.1526, found: 406.1535.

*4-(3,4-Dimethoxyphenyl)-5,6-diphenylpyrimidin-2-amine (**6h**)*

m.p. 200–202°C; IR (KBr, *v*, cm^{-1}): 3438, 3309, 3203, 1660, 1633, 1603, 1542, 1529, 1511, 1495, 1473, 1462, 1418, 1374, 1329, 1264, 1235, 1207, 1186, 1141, 1028, 806, 760, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 3.37 (3H, s, OCH_3), 3.71 (3H, s, OCH_3), 6.66 (1H, d, $J = 2.0$ Hz, ArH), 6.83 (1H, $d = 8.4$ Hz, ArH), 6.93–6.97 (5H, m, ArH, NH_2), 7.12–7.14 (3H, m, ArH), 7.18–7.22 (5H, m, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 55.5, 55.8, 76.9, 77.2, 77.5, 110.4, 113.1, 121.7, 122.6, 126.6, 127.7, 128.1, 128.3, 129.3, 131.1, 131.6, 137.4, 138.9, 147.8, 149.3, 161.9, 165.9, 166.9; HRMS m/z calculated for $C_{24}H_{21}N_3O_2$ $[M + H]^+$: 384.1707, found: 384.1721.

*4-(Benzo[d][1,3]dioxol-5-yl)-5,6-diphenylpyrimidin-2-amine (**6i**)*

m.p. 198–200°C; IR (KBr, *v*, cm^{-1}): 3463, 3298, 3159, 3058, 1619, 1544, 1533, 1503, 1490, 1459, 1445, 1389, 1372, 1338, 1242, 1207, 1180, 1109, 1037, 932, 894, 812, 771, 700, 566 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.97 (2H, s, OCH_2O), 6.72–6.76 (3H, m, ArH), 6.84–6.94 (3H, m, ArH, NH_2), 7.12–7.13 (3H, m, ArH), 7.18–7.19 (4H, m, ArH), 7.20–7.24 (2H, m, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 56.7, 101.1, 107.3, 108.4, 111.7, 120.5, 126.3, 127.4, 127.9, 128.1, 128.3, 129.2, 129.4, 131.4, 136.6, 137.5, 147.0, 147.7, 152.2, 175.8; HRMS m/z calculated for $C_{23}H_{17}N_3O_2$ $[M + H]^+$: 368.1394, found: 368.1398.

*4-(4-Methoxyphenyl)-2-methyl-5,6-diphenylpyrimidine (**6j**)*

m.p. 181–183°C; IR (KBr, *v*, cm^{-1}): 3444, 1608, 1532, 1511, 1436, 1421, 1403, 1299, 1253, 1178, 1029, 844, 818, 766 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.74 (3H, s,CH_3), 3.72 (3H, s, OCH_3), 6.79 (2H, d, $J = 8.8$ Hz, ArH), 7.00–7.02 (2H, m, ArH), 7.19–7.28 (10H, m, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 25.7, 55.1, 113.1, 127.3, 127.6, 127.7, 128.2, 128.3, 129.3, 130.3, 130.8, 131.1, 136.4, 138.5, 159.5, 164.0, 164.8, 165.5; HRMS m/z calculated for $C_{24}H_{20}N_2O$ $[M + H]^+$: 353.1654, found: 353.1666.

*4-(3,4-Dimethylphenyl)-2-methyl-5,6-diphenylpyrimidine (**6k**)*

m.p. 117–119°C; IR (KBr, *v*, cm^{-1}): 3449, 1611, 1579, 1530, 1491, 1442, 1411, 1369, 1074, 1006, 815, 770, 702, 669, 649 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.11 (3H, s,CH_3), 2.16 (3H, s, CH_3), 2.74 (3H, s, CH_3), 6.87 (1H, d, $J = 8.8$ Hz, ArH), 6.94 (1H, d, $J = 8.0$ Hz, ArH), 6.98–7.01 (2H, m, ArH), 7.17 (2H, d, $J = 4.0$ Hz, ArH), 7.19 (2H, d, $J = 1.6$ Hz, ArH), 7.23–7.28 (5H, m, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 19.1, 19.3, 25.7, 127.0, 127.2, 127.6,

128.0, 128.1, 128.4, 128.6, 129.3, 130.6, 130.8, 135.5, 135.6, 136.3, 136.9, 138.4, 164.5, 164.8, 165.6; HRMS m/z calculated for $C_{25}H_{22}N_2$ $[M + H]^+$: 351.1861, found: 351.1844.

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