# An Efficient Chemoselective Synthesis of Pyrido[2,3-*d*]pyrimidine Derivatives under Microwave Irradiation

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**Abstract:** A facile and selective synthesis of poly-substituted pyrido[2,3-*d*]pyrimidines is accomplished via microwave-assisted multicomponent reactions controlled by the nature of solvent. In addition, a possible mechanism accounting for the reaction is proposed.

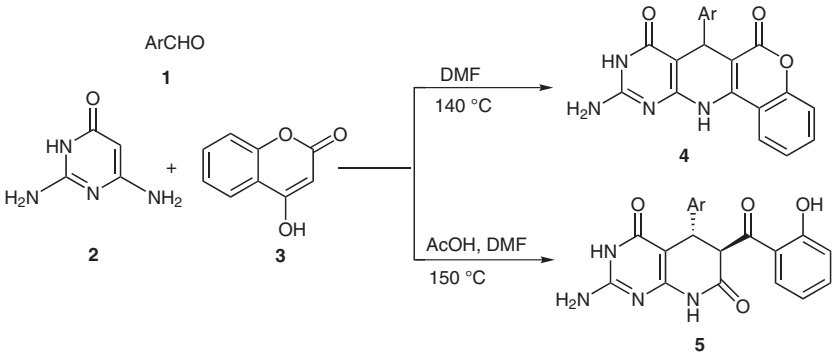
**Key words:** solvent-dependent chemoselectivity, pyrido[2,3-*d*]pyrimidines, microwave irradiation, heterocycles, multicomponent reaction

Selectivity is a key issue to be controlled in organic synthesis. In particular, chemoselectivity is synthetically useful because it gives one of several products selectively from the same substrate without the need to separate the product(s) from the product mixture. It continues to be developed as organic synthesis strives for ever-increasing levels of efficiency. As a result, many studies have focused on the chemoselectivity of reactions.[1] In recent years, many reports have dealt with the control of chemoselectivity reactions with metal catalysts,[1a–e] while solvent-dependent chemoselective reactions have been researched in relatively few papers.[1g–i] Therefore, the development of highly solvent-dependent chemoselective reactions remains a challenge.

Pyrido[2,3-*d*]pyrimidine and its derivatives are useful as antitumor,[2] antibacterial,[3] anti-inflammatory,[4] and antifungal agents.[5] In particular, the pyrido[2,3-*d*]pyrimidin-7-one template has been identified previously as a privileged structure for the inhibition of ATP-dependent kinases, and good potency against Cdks has been reported for representative examples.[6–8] Obtaining selectivity for individual Cdk enzymes, particularly Cdk4, has been challenging. Many extensive investigations of the structure–activity relationships for pyrido[2,3-*d*]pyrimidin-7-one inhibition of Cdk4 have been initiated. Therefore, to obtain the new potential inhibitors of Cdk4, the synthesis of pyrido[2,3-*d*]pyrimidin-7-one should be of great significance. For the preparation of these molecules large efforts have been directed toward the synthetic manipulation of pyrido[2,3-*d*]pyrimidine derivatives. As a result, a number of reports have appeared in the literature[9] that generally require long reaction times and complex synthetic pathways. Thus, new routes for the synthesis of these molecules have attracted considerable attention in the search for a rapid entry to these heterocycles.

In the context of our interest in the design and development of useful tactics and strategies for the synthesis of heterocyclic compounds,[10] herein, we wish to report a new microwave-assisted chemoselective reaction controlled by the nature of solvents for the synthesis of pyrido[2,3-*d*]pyrimidine derivatives using aldehydes **1**, 2,6-diaminopyrimidin-4(3*H*)-one (**2**), and 4-hydroxy-2*H*-chromen-2-one (**3**) (Scheme 1). To the best of our knowledge to date, the solvent-dependent chemoselective synthesis of pyrido[2,3-*d*]pyrimidine derivatives has not yet been reported.

Choosing an appropriate solvent is of crucial importance not only for successful microwave-promoted (MW) syn-




**Scheme 1**

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**Table 1** Optimization of Chemoselectivity Conditions in the Synthesis of **4a** and **5a**

| Entry | Solvent[a] | Ratio | Yield[b] (%) | |
|---|---|---|---|---|
| | | | **4a** | **5a** |
| 1 | $H_2O$ | | 16 | 0 |
| 2 | none | | 0 | 0 |
| 3 | ethylene glycol | | 81 | 0 |
| 4 | EtOH | | 18 | 0 |
| 5 | AcOH | | 33 | 51 |
| 6 | AcOH–DMF | 1:1 | 28 | 54 |
| 7 | AcOH–DMF | 1:2 | 25 | 70 |
| 8 | AcOH–DMF | 1:3 | 9 | 80 |
| 9 | AcOH–DMF | 1:4 | 0 | 88 |
| 10 | AcOH–DMF | 1:5 | 12 | 77 |
| 11 | AcOH–DMF | 1:6 | 28 | 62 |
| 12 | AcOH–DMF | 1:7 | 66 | 32 |
| 13 | DMF | | 92 | 0 |

[a] The volume of solvent was 2.0 mL.
[b] Isolated yields.

thesis, but also for the effective control of chemoselective reactions. In order to choose the optimum solvent, the microwave-assisted reaction of 4-fluorobenzaldehyde (**1a**), 2,6-diaminopyrimidin-4(3*H*)-one (**2**), and 4-hydroxy-2*H*-chromen-2-one (**3**) was examined at 140 °C under solvent-free conditions and using water, ethylene glycol, *N*,*N*-dimethylformamide, acetic acid, and ethanol as solvent. All the reactions were carried out under microwave irradiation (initial power 100 W and maximum power 200 W). The results of the screening of solvents are presented in Table 1 (entries 1–5, 13). As can be seen in Table 1, none of the desired product was detected under solvent-free conditions, and incomplete reactions were observed in the case of water and ethanol as the solvent, respectively. When ethylene glycol was selected as the solvent, the reaction occurred and product **4a** (Ar = 4-$FC_6H_4$) was obtained in relatively good yield, but the product **4a** was obtained with the best yield and the shortest reaction time in *N*,*N*-dimethylformamide, which is an ideal polar aprotic solvent.[11] Furthermore, it was noteworthy that this reaction afforded two products when acetic acid was used as the solvent. On the basis of the $^1$H NMR and $^{13}$C NMR, the two compounds were identified as **4a** and **5a**, and these were easily distinguished from one another. Compound **5a** may give two possible diastereomers, the *trans*- and *cis*-isomers, but only the *trans*-isomer was obtained. The $^1$H NMR spectrum of **5a** showed two singlets at $\delta = 4.73$ and $\delta = 4.34$ assigned to C5 and C6, respectively, which is similar to our recent report.[12]

This influence of solvents on product composition in the reaction is a novel observation and warranted further investigation. A study on the effect of different ratios of acetic acid to *N*,*N*-dimethylformamide was conducted with the same substrates as described in Table 1 (entries 5–13).

Surprisingly, totally different chemoselectivity was observed in both solvents (Scheme 1). The products **4a** and **5a** were generated exclusively in *N*,*N*-dimethylformamide and the mixed solvent *N*,*N*-dimethylformamide–acetic acid (1:4), respectively. The dramatically different results from the two reaction conditions highlight the importance of the amount of acetic acid in controlling chemoselectivity and, thus, the outcome of the reactions.

Thus, the question is, why does the selective formation of **5** occur in the mixed solvent acetic acid–*N*,*N*-dimethylformamide (1:4) whereas only **4** is obtained in *N*,*N*-dimethylformamide?

The chemoselectivity of the reaction should be attributed to the nature of solvent. In *N*,*N*-dimethylformamide, the reactive position of intermediate **9** is the ketone carbonyl, which is attracted by the $NH_2$ groups to form product **4**, while in the mixed solvent acetic acid–*N*,*N*-dimethylformamide, the reactive position of intermediate **11** is the ester carbonyl, which is attracted by the $NH_2$ groups to yield open-ring compound **5**. Therefore, the suggested pathway for the formation of **4** and **5** via route *i* and route *ii*, respectively, is depicted in Scheme 2.

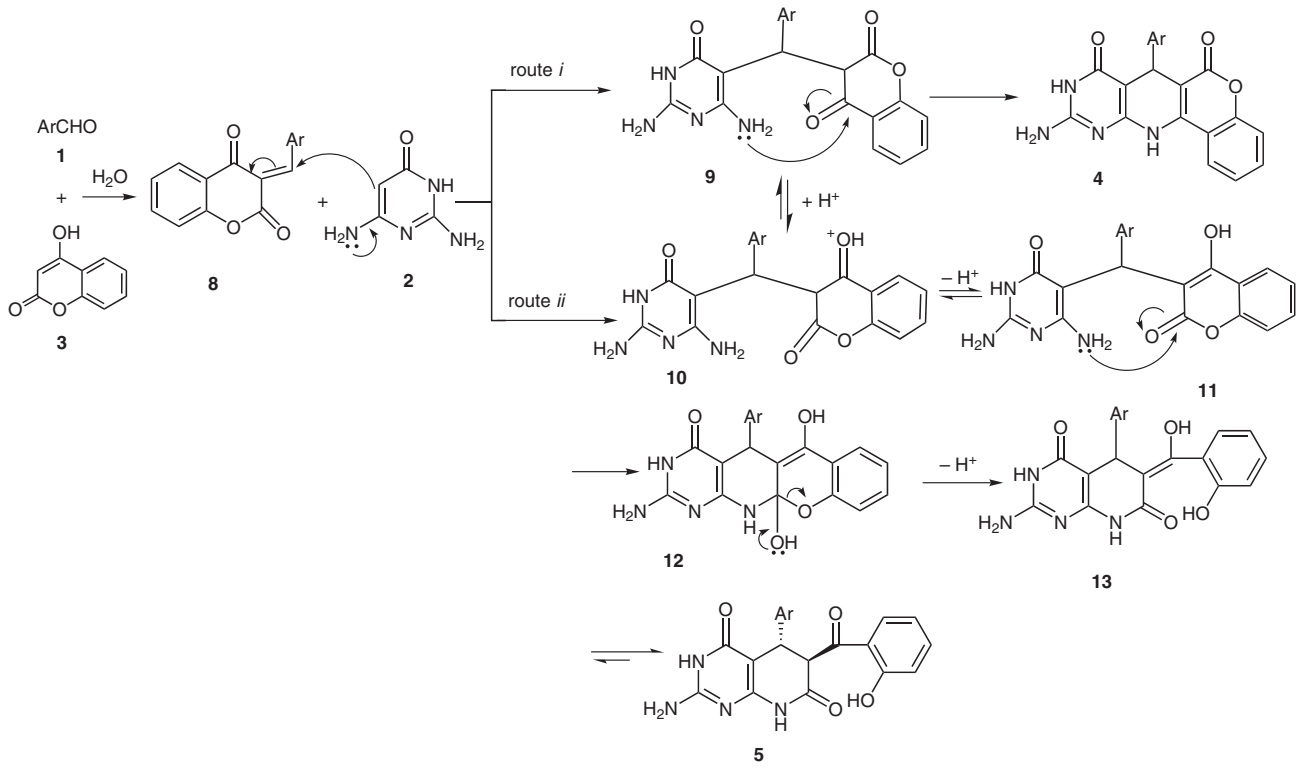
The effect of temperature on the reaction using the same reagents, in *N*,*N*-dimethylformamide and the mixed solvent acetic acid–*N*,*N*-dimethylformamide (1:4), at temperatures ranging from 100 °C to 170 °C in increments of 10 °C, was investigated respectively. The results are summarized in Table 2.

As can be seen in Table 2, we found that the yield of **4a** improved and the reaction time was shortened as the temperature increased from 100 °C to 140 °C (Table 2, entries 1–5). The yield reached a plateau when the temperature

**Table 2** Temperature Optimization for the Synthesis of **4a** and **5a**

| Entry | Temp (°C) | Time (min) | | Yield[c] (%) | |
|---|---|---|---|---|---|
| | | **4a**[a] | **5a**[b] | **4a**[a] | **5a**[b] |
| 1 | 100 | 15 | 13 | 78 | 69 |
| 2 | 110 | 12 | 11 | 82 | 75 |
| 3 | 120 | 11 | 10 | 87 | 79 |
| 4 | 130 | 8 | 9 | 89 | 82 |
| 5 | 140 | 5 | 6 | 92 | 88 |
| 6 | 150 | 7 | 6 | 92 | 90 |
| 7 | 160 | 6 | 6 | 88 | 90 |
| 8 | 170 | 6 | 5 | 86 | 85 |

[a] MW irradiation in DMF.
[b] MW irradiation in AcOH–DMF (1:4).
[c] Isolated yields.




**Scheme 2**

was further increased from 150 °C to 170 °C (Table 2, entries 5–8). Therefore, a reaction temperature of 140 °C was considered to be the most suitable for the synthesis of **4**. In addition, we found that the yield of **5a** increased and the reaction time was shortened as the temperature was increased from 100 °C to 150 °C (Table 2, entries 1–6). However, further increase of the temperature to 160 °C and 170 °C failed to improve the yield of product **5a** (Table 2, entries 7 and 8). Hence, 150 °C was chosen as the reaction temperature for the synthesis of **5**.

Furthermore, the volume of solvent was found to be important for the yields of the two reactions. The synthesis of **4a** [**1a** (1 mmol), **2** (1 mmol), and **3** (1 mmol)] and **5a** [**1a** (1 mmol), **2** (1 mmol), and **3** (1 mmol)] in different volumes of solvent was tested under microwave irradiation conditions. The yield was found to be the highest when 2.0 mL of solvent was used for both reactions.

Under these optimized reaction conditions, a series of pyrido[2,3-*d*]pyrimidine derivatives **4** and **5** were synthesized. The results are presented in Table 3.

**Table 3** Synthesis of **4a** and **5a** under MW Conditions

| Entry | 4 | 5 | Ar | Time (min) | | Yield[c] (%) | | Mp (°C) | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | **4**[a] | **5**[b] | **4**[a] | **5**[b] | **4** | **5** |
| 1 | **4a** | **5a** | 4-$FC_6H_4$ | 5 | 6 | 92 | 90 | 295–296 | 294–295 |
| 2 | **4b** | **5b** | 4-$ClC_6H_4$ | 4 | 5 | 96 | 86 | 287–289 | >300 |
| 3 | **4c** | **5c** | 4-$BrC_6H_4$ | 6 | 5 | 91 | 90 | >300 | 292–294 |
| 4 | **4d** | **5d** | 3-$O_2NC_6H_4$ | 5 | 6 | 92 | 90 | >300 | >300 |
| 5 | **4e** | **5e** | Ph | 6 | 6 | 92 | 89 | 286–288 | 290–291 |
| 6 | **4f** | **5f** | 4-$MeOC_6H_4$ | 8 | 7 | 89 | 85 | >300 | >300 |
| 7 | **4g** | **5g** | 4-$MeC_6H_4$ | 7 | 8 | 88 | 86 | >300 | 262–263 |
| 8 | **4h** | **5h** | 3,4-$(MeO)_2C_6H_3$ | 9 | 8 | 82 | 83 | >300 | >300 |
| 9 | **4i** | **5i** | 2-thienyl | 6 | 7 | 90 | 89 | >300 | >300 |

[a] MW irradiation in DMF.
[b] MW irradiation in AcOH–DMF (1:4).
[c] Isolated yields.

In order to expand the scope of the method, we employed 4-hydroxyquinolin-2(1*H*)-one (**6**) instead of 4-hydroxy-2*H*-chromen-2-one (**3**) in the reaction of **1a** and 2,6-diaminopyrimidin-4(3*H*)-one (**2**) in different solvents such as acetic acid, *N*,*N*-dimethylformamide, and mixtures thereof. The results are described in Table 4. The reaction proceeded smoothly. To our satisfaction, only product **7a** was obtained with the best results in *N*,*N*-dimethylformamide (Scheme 3). With optimized conditions in hand, a series of pyrido[2,3-*d*]pyrimidine derivatives **7** were synthesized. The results are summarized in Table 5.

**Table 4** Screening Solvents for the Synthesis of **7a**

| Entry | Solvent[a] | Time (min) | Yield[b] (%) |
|---|---|---|---|
| 1 | AcOH | 9 | 76 |
| 2 | DMF | 6 | 90 |
| 3 | AcOH–DMF (1:4) | 11 | 70 |

[a] The volume of solvent is 2.0 mL.
[b] Isolated yields.

**Table 5** Synthesis of **7** under MW Conditions

| Entry | 7 | Ar | Time (min) | Yield[a] (%) | Mp (°C) |
|---|---|---|---|---|---|
| 1 | **7a** | 4-$FC_6H_4$ | 6 | 90 | 298–299 |
| 2 | **7b** | 4-HO-3-$O_2NC_6H_3$ | 5 | 93 | 291–292 |
| 3 | **7c** | 4-$ClC_6H_4$ | 7 | 91 | 293–295 |
| 4 | **7d** | 3-$O_2NC_6H_4$ | 6 | 92 | 273–275 |
| 5 | **7e** | Ph | 6 | 89 | 266–268 |
| 6 | **7f** | 4-$MeOC_6H_4$ | 8 | 89 | >300 |
| 7 | **7g** | 4-$MeC_6H_4$ | 9 | 88 | >300 |
| 8 | **7h** | 3,4-$(OCH_2O)C_6H_3$ | 9 | 86 | >300 |
| 9 | **7i** | 2-thienyl | 9 | 88 | 278–279 |

[a] Isolated yields.

As shown in Tables 3 and 5, this methodology can be applied not only to aromatic aldehydes either with electron-withdrawing groups (such as nitro or halide groups) or with electron-donating groups (such as alkoxy groups), but also to heterocyclic aldehydes with excellent yields under the same conditions. Therefore, we concluded that the electronic nature of the substituents of the aldehydes had no significant effect on the two reactions.

Additionally, for comparison, we performed the synthesis of some examples of **4**, **5**, and **7** using classical heating methods under otherwise identical conditions (reaction vessel, temperature, etc.). A comparison of the results for six compounds are listed in Table 6, which indicated that the reactions were efficiently promoted by microwave irradiation and the reaction time was strikingly shortened to 4–9 minutes from the several hours required under conventional heating conditions, the yields were also higher. In addition, it should be noted that small amounts of **4** were detected when compounds **5** were synthesis under traditional heating conditions in mixed solvents *N*,*N*-dimethylformamide–acetic acid (1:4). Therefore, to some extent, the reaction chemoselectivity was improved when the syntheses of **5** were conducted under microwave irradiation conditions.

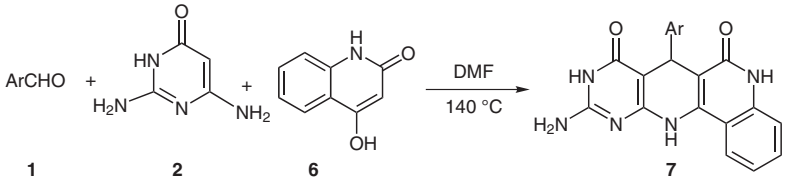
**Table 6** Synthesis of Various **4**, **5**, and **7** Using Conventional Heating

| Entry | Product | Time (h) | Yield[a] (%) |
|---|---|---|---|
| 1 | **4a** | 4 | 68 |
| 2 | **4g** | 6 | 66 |
| 3 | **5a** | 5 | 52 |
| 4 | **5g** | 6 | 49 |
| 5 | **7c** | 6 | 70 |
| 6 | **7f** | 7 | 67 |

[a] Isolated yields.

All the products were characterized by IR spectra and $^1$H NMR as well as elemental analyses. Some compounds were also characterized by $^{13}$C NMR and MS. The IR spectrum of compound **5c** showed strong absorptions at 3463, 3326 and 3159 cm$^{-1}$ due to OH, NH, and $NH_2$ groups and at 1700, 1685, 1635 cm$^{-1}$ due to C=O functionality. The $^1$H NMR spectrum of **5c** showed two singlet at δ = 4.72 (s, 1 H, CH) and δ = 4.31 (s, 1 H, CH) due to CH, and three singlet at δ = 11.19, 10.60, and 10.53 due to OH and NH protons (exchanged with $D_2O$).

In conclusion, we have demonstrated an efficient and practical method for the synthesis of a wide range of pyrido[2,3-*d*]pyrimidine derivatives under microwave irradiation and have shown the effect of the nature of solvent on chemoselectivity. In addition, efforts to expand the reaction with the help of theoretical and spectroscopic studies are in progress in our laboratory.




**Scheme 3**

Microwave irradiation was performed with microwave oven Emrys Creator from Personal Chemistry, Uppsala, Sweden. Melting points were determined in open capillaries and were uncorrected. IR spectra were taken on a FT-IR-Tensor 27 spectrometer in KBr pellets and reported in $cm^{-1}$. $^1H$ NMR ($^{13}C$ NMR) spectra were measured on a Bruker DPX 400 MHz (100 MHz) spectrometer in DMSO-$d_6$ relative to TMS as internal standard. ESI-MS was determined by using the LCQ Advantage HPLC/MS instrument (Thermo Finnigan). Elemental analysis was determined by using a Perkin-Elmer 240c elemental analysis instrument.

### 10-Amino-7-aryl-7,12-dihydro-6*H*-chromeno[3′,4′:5,6]pyrido[2,3-*d*]pyrimidine-6,8(9*H*)-diones 4; General Procedure under Microwave Irradiation

In a 10-mL reaction vial, aldehyde **1** (1 mmol), 2,6-diaminopyrimidin-4(3*H*)-one (**2**, 126 mg, 1 mmol), 4-hydroxy-2*H*-chromen-2-one (**3**, 162 mg, 1 mmol), and DMF (2.0 mL) were mixed and then the vial was capped. The mixture was irradiated for the specified time (Table 3) at 100 W (initial power) and 200 W (maximum power) and 140 °C. Upon completion (TLC), the mixture was cooled to r.t. and then poured into cold $H_2O$. The solid product was filtered, washed with $H_2O$ and 95% EtOH, dried, and recrystallized (95% EtOH) to give the pure product.

### 7-(4-Fluorophenyl) Derivative 4a

IR (KBr): 3472, 3417, 3343, 3233, 3052, 2856, 1662, 1626, 1607, 1536, 1507, 1468, 1380, 1301, 1245, 1199, 1038, 909, 791, 752 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 10.80 (s, 1 H, NH), 10.09 (s, 1 H, NH), 7.84 (d, *J* = 7.6 Hz, 1 H, ArH), 7.63 (t, *J* = 7.6 Hz, 1 H, ArH), 7.43 (d, *J* = 8.0 Hz, 1 H, ArH), 7.36 (t, *J* = 7.6 Hz, 1 H, ArH), 7.15–7.03 (m, 4 H, ArH), 6.58 (s, 2 H, $NH_2$), 5.48 (s, 1 H, CH).

$^{13}C$ NMR (100 MHz, DMSO-$d_6$): δ = 161.8, 160.6, 159.4, 153.8, 152.2, 147.8, 135.4, 132.3, 128.4, 128.3, 124.2, 123.9, 117.8, 116.2, 114.9, 114.7, 104.9, 89.8, 35.0.

Anal. Calcd for $C_{20}H_{13}FN_4O_3$: C, 63.83; H, 3.48; N, 14.89. Found: C, 63.78; H, 3.62; N, 14.97.

### 7-(4-Chlorophenyl) Derivative 4b

IR (KBr): 3490, 3463, 3195, 2962, 1661, 1633, 1570, 1485, 1454, 1356, 1284, 1042, 900, 784, 767 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 10.72 (s, 1 H, NH), 10.16 (s, 1 H, NH), 7.84 (d, *J* = 7.6 Hz, 1 H, ArH), 7.65 (t, *J* = 7.6 Hz, 1 H, ArH), 7.42 (d, *J* = 8.4 Hz, 3 H, ArH), 7.36 (t, *J* = 7.6 Hz, 1 H, ArH), 7.07 (d, *J* = 8.4 Hz, 2 H, ArH), 6.63 (s, 2 H, $NH_2$), 5.46 (s, 1 H, CH).

Anal. Calcd for $C_{20}H_{13}ClN_4O_3$: C, 61.16; H, 3.34; N, 14.26. Found: C, 59.94; H, 3.48; N, 14.18.

### 7-(4-Bromophenyl) Derivative 4c

IR (KBr): 3492, 3423, 3357, 3231, 3066, 2980, 1662, 1625, 1580, 1489, 1447, 1373, 1345, 1280, 1052, 877, 792, 751 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 10.68 (s, 1 H, NH), 10.10 (s, 1 H, NH), 7.84 (d, *J* = 7.6 Hz, 1 H, ArH), 7.65 (t, *J* = 7.6 Hz, 1 H, ArH), 7.43 (d, *J* = 8.4 Hz, 1 H, ArH), 7.36 (t, *J* = 7.6 Hz, 1 H, ArH), 7.27 (d, *J* = 8.4 Hz, 2 H, ArH), 7.12 (d, *J* = 8.4 Hz, 2 H, ArH), 6.60 (s, 2 H, $NH_2$), 5.48 (s, 1 H, CH).

Anal. Calcd for $C_{20}H_{13}BrN_4O_3$: C, 54.94; H, 3.00; N, 12.81. Found: C, 55.07; H, 3.16; N, 12.86.

### 7-(3-Nitrophenyl) Derivative 4d

IR (KBr): 3498, 3433, 3373, 3231, 3066, 2974, 1662, 1621, 1592, 1520, 1491, 1351, 1247, 1109, 899, 842, 792, 751 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 10.62 (s, 1 H, NH), 10.11 (s, 1 H, NH), 8.45 (d, *J* = 8.0 Hz, 1 H, ArH), 8.03–7.95 (m, 2 H, ArH), 7.67 (d, *J* = 7.6 Hz, 1 H, ArH), 7.59 (d, *J* = 8.0 Hz, 1 H, ArH), 7.48 (d, *J* = 8.0 Hz, 1 H, ArH), 7.37–7.32 (m, 2 H, ArH), 6.43 (s, 2 H, $NH_2$), 5.05 (s, 1 H, CH).

$^{13}C$ NMR (100 MHz, DMSO-$d_6$): δ = 161.6, 160.4, 154.7, 154.2, 152.5, 148.4, 147.7, 144.5, 134.6, 132.3, 129.7, 124.2, 123.8, 122.3, 121.5, 116.9, 113.2, 104.5, 90.7, 36.0.

MS (ESI): *m*/*z* = 402.4 $[M - H]^-$, 353.4, 332.6.

Anal. Calcd for $C_{20}H_{13}N_5O_5$: C, 59.56; H, 3.25; N, 17.36. Found: C, 59.44; H, 3.12; N, 17.47.

### 7-Phenyl Derivative 4e

IR (KBr): 3479, 3411, 3339, 3228, 2860, 2738, 1664, 1625, 1491, 1446, 1377, 1374, 1352, 1207, 1055, 879, 821, 751, 695 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 10.79 (s, 1 H, NH), 10.20 (s, 1 H, NH), 7.84 (d, *J* = 7.6 Hz, 1 H, ArH), 7.65 (t, *J* = 7.6 Hz, 1 H, ArH), 7.43 (d, *J* = 8.4 Hz, 1 H, ArH), 7.36 (t, *J* = 7.6 Hz, 1 H, ArH), 7.24 (t, *J* = 7.6 Hz, 2 H, ArH), 7.17–7.10 (m, 3 H, ArH), 6.57 (s, 2 H, $NH_2$), 5.51 (s, 1 H, CH).

Anal. Calcd for $C_{20}H_{14}N_4O_3$: C, 67.03; H, 3.94; N, 15.63. Found: C, 67.17; H, 3.81; N, 15.56.

### 7-(4-Methoxyphenyl) Derivative 4f

IR (KBr): 3451, 3343, 3198, 2838, 1657, 1635, 1591, 1509, 1441, 1363, 1249, 1181, 1033, 835, 761 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 10.76 (s, 1 H, NH), 9.81 (s, 1 H, NH), 7.89–7.83 (m, 1 H, ArH), 7.63 (t, *J* = 8.0 Hz, 1 H, ArH), 7.43–7.34 (m, 1 H, ArH), 7.14 (d, *J* = 7.6 Hz, 1 H, ArH), 7.00 (d, *J* = 8.4 Hz, 2 H, ArH), 6.80 (d, *J* = 8.4 Hz, 2 H, ArH), 6.56 (s, 2 H, $NH_2$), 5.45 (s, 1 H, CH), 3.71 (s, 3 H, $OCH_3$).

Anal. Calcd for $C_{21}H_{16}N_4O_4$: C, 64.94; H, 4.15; N, 14.43. Found: C, 65.21; H, 3.98; N, 14.48.

### 7-(4-Methylphenyl) Derivative 4g

IR (KBr): 3462, 3326, 3203, 2921, 1660, 1629, 1592, 1573, 1479, 1437, 1356, 1190, 1043, 795, 759 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 10.77 (s, 1 H, NH), 10.11 (s, 1 H, NH), 7.83 (d, *J* = 7.6 Hz, 1 H, ArH), 7.64 (t, *J* = 7.6 Hz, 1 H, ArH), 7.42 (d, *J* = 8.4 Hz, 1 H, ArH), 7.36 (t, *J* = 7.6 Hz, 1 H, ArH), 7.04 (t, *J* = 7.6 Hz, 2 H, ArH), 6.98 (d, *J* = 8.0 Hz, 2 H, ArH), 6.56 (s, 2 H, $NH_2$), 5.46 (s, 1 H, CH), 2.25 (s, 3 H, $CH_3$).

$^{13}C$ NMR (100 MHz, DMSO-$d_6$): δ = 161.2, 160.0, 157.9, 153.7, 152.2, 147.6, 138.9, 134.5, 132.2, 128.8, 126.4, 123.9, 121.8, 113.9, 112.2, 104.9, 90.5, 35.1, 20.7.

MS (ESI): *m*/*z* = 389.9 $[M + NH_4]^+$.

Anal. Calcd for $C_{21}H_{16}N_4O_3$: C, 67.73; H, 4.33; N, 15.05. Found: C, 67.70; H, 4.41; N, 15.11.

### 7-(3,4-Dimethoxyphenyl) Derivative 4h

IR (KBr): 3495, 3413, 3358, 2934, 1699, 1645 1520, 1450, 1391, 1262, 1192, 1137, 1022, 768 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 10.66 (s, 1 H, NH), 10.02 (s, 1 H, NH), 8.45 (d, *J* = 8.0 Hz, 1 H, ArH), 7.62 (t, *J* = 7.6 Hz, 1 H, ArH), 7.39–7.36 (m, 2 H, ArH), 6.96 (s, 1 H, ArH), 6.78 (d, *J* = 8.0 Hz, 1 H, ArH), 6.64 (d, *J* = 8.0 Hz, 1 H, ArH), 6.41 (s, 2 H, $NH_2$), 4.93 (s, 1 H, CH), 3.67 (s, 6 H, $OCH_3$).

$^{13}C$ NMR (100 MHz, DMSO-$d_6$): δ = 161.7, 160.6, 154.3, 154.1, 152.3, 148.3, 147.5, 143.7, 139.2, 132.0, 124.2, 123.5, 119.3, 116.9, 113.4, 112.2, 111.9, 100.6, 91.7, 55.7, 55.6, 34.6.

MS (ESI): *m*/*z* = 419.3 $[M + H]^+$, 383.4, 363.3.

Anal. Calcd for $C_{22}H_{18}N_4O_5$: C, 63.15; H, 4.34; N, 13.39. Found: C, 63.03; H, 4.51; N, 13.44.

**7-(2-Thienyl) Derivative 4i**

IR (KBr): 3469, 3339, 3185, 2872, 1625, 1528, 1479, 1439, 1358, 1206, 758, 698 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 10.47 (s, 1 H, NH), 10.11 (s, 1 H, NH), 7.87 (d, *J* = 8.4 Hz, 1 H, ArH), 7.65 (t, *J* = 8.0 Hz, 1 H, ArH), 7.44–7.35 (m, 3 H, ArH), 7.27–7.24 (m, 1 H, ArH), 6.87–6.86 (m, 1 H, ArH), 6.65 (s, 2 H, $NH_2$), 5.63 (s, 1 H, CH).

Anal. Calcd for $C_{18}H_{12}N_4O_3S$: C, 59.33; H, 3.32; N, 15.38; S, 8.80. Found: C, 59.19; H, 3.47; N, 15.43; S, 8.92.

**2-Amino-5-aryl-6-(2-hydroxybenzoyl)-5,8-dihydropyrido[2,3-*d*]pyrimidine-4,7(3*H*,6*H*)-dione 5; General Procedure under Microwave Irradiation**

In a 10-mL reaction vial, aldehyde **1** (1 mmol), 2,6-diaminopyrimidin-4(3*H*)-one (**2**, 126 mg, 1 mmol), 4-hydroxy-2*H*-chromen-2-one (**3**, 162 mg, 1 mmol), AcOH (0.4 mL), and DMF (1.6 mL) were mixed and then the vial was capped. The mixture was irradiated for the specified time (Table 3) at 100 W (initial power) and 200 W (maximum power) and 150 °C. Upon completion (TLC), the subsequent workup was the same as that given for the general procedure under microwave irradiation for **4**.

**5-(4-Fluorophenyl) Derivative 5a**

IR (KBr): 3443, 3337, 3177, 2913, 1700, 1647, 1507, 1453, 1359, 1301, 1241, 1159, 840, 754 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 11.18 (s, 1 H, OH), 10.60 (s, 1 H, NH), 10.51 (s, 1 H, NH), 7.66 (d, *J* = 7.2 Hz, 1 H, ArH), 7.51 (t, *J* = 7.2 Hz, 1 H, ArH), 7.30–7.26 (m, 2 H, ArH), 7.16 (t, *J* = 8.8 Hz, 2 H, ArH), 7.04 (d, *J* = 8.0 Hz, 1 H, ArH), 6.95 (t, *J* = 7.6 Hz, 1 H, ArH), 6.63 (s, 2 H, $NH_2$), 4.73 (s, 1 H, CH), 4.34 (s, 1 H, CH).

Anal. Calcd for $C_{20}H_{15}FN_4O_4$: C, 60.91; H, 3.83; N, 14.21. Found: C, 60.77; H, 3.62; N, 14.29.

**5-(4-Chlorophenyl) Derivative 5b**

IR (KBr): 3460, 3322, 3182, 2934, 1698, 1644, 1536, 1488, 1456, 1485, 1355, 1299, 1214, 1158, 1092, 997, 931, 815, 791, 754 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 11.19 (s, 1 H, OH), 10.62 (s, 1 H, NH), 10.52 (s, 1 H, NH), 7.65 (d, *J* = 7.2 Hz, 1 H, ArH), 7.51 (t, *J* = 8.0 Hz, 1 H, ArH), 7.40 (d, *J* = 8.0 Hz, 2 H, ArH), 7.26 (d, *J* = 8.4 Hz, 2 H, ArH), 7.04 (d, *J* = 8.0 Hz, 1 H, ArH), 6.94 (t, *J* = 8.4 Hz, 1 H, ArH), 6.65 (s, 2 H, $NH_2$), 4.72 (s, 1 H, CH), 4.33 (s, 1 H, CH).

MS (ESI): *m*/*z* = 409.4 $[M - H]^-$.

Anal. Calcd for $C_{20}H_{15}ClN_4O_4$: C, 58.47; H, 3.68; N, 13.64. Found: C, 58.33; H, 3.79; N, 13.75.

**5-(4-Bromophenyl) Derivative 5c**

IR (KBr): 3463, 3326, 3159, 2942, 1700, 1685, 1635, 1536, 1486, 1457, 1353, 1296, 1243, 1159, 1009, 997, 813, 789, 754 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 11.19 (s, 1 H, OH), 10.60 (s, 1 H, NH), 10.53 (s, 1 H, NH), 7.66 (d, *J* = 7.6 Hz, 1 H, ArH), 7.52 (t, *J* = 8.4 Hz, 2 H, ArH), 7.51–7.49 (m, 1 H, ArH), 7.21 (d, *J* = 8.4 Hz, 2 H, ArH), 7.04 (d, *J* = 8.4 Hz, 1 H, ArH), 6.95 (t, *J* = 7.6 Hz, 1 H, ArH), 6.64 (s, 2 H, $NH_2$), 4.72 (s, 1 H, CH), 4.31 (s, 1 H, CH).

$^{13}C$ NMR (100 MHz, DMSO-$d_6$): δ = 197.1, 168.7, 161.4, 158.5, 157.1, 155.4, 142.1, 135.6, 131.7, 131.0, 129.1, 121.5, 120.0, 119.9, 117.7, 89.3, 60.2, 36.9.

MS (ESI): *m*/*z* = 455.5 $[M]^+$, 387.8.

Anal. Calcd for $C_{20}H_{15}BrN_4O_4$: C, 52.76; H, 3.32; N, 12.31. Found: C, 52.71; H, 3.21; N, 12.39.

**5-(3-Nitrophenyl) Derivative 5d**

IR (KBr): 3411, 3338, 3227, 3022, 1706, 1624, 1491, 1447, 1352, 1312, 1248, 1208, 1159, 1010, 863, 791, 751 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 11.21 (s, 1 H, OH), 10.64 (s, 1 H, NH), 10.60 (s, 1 H, NH), 8.12 (d, *J* = 8.4 Hz, 2 H, ArH), 7.85 (d, *J* = 7.6 Hz, 1 H, ArH), 7.66 (t, *J* = 7.6 Hz, 1 H, ArH), 7.45–7.35 (m, 4 H, ArH), 6.65 (s, 2 H, $NH_2$), 4.78 (s, 1 H, CH), 4.46 (s, 1 H, CH).

Anal. Calcd for $C_{20}H_{15}N_5O_6$: C, 57.01; H, 3.59; N, 16.62. Found: C, 57.20; H, 3.66; N, 16.49.

**5-Phenyl Derivative 5e**

IR (KBr): 3434, 3317, 3174, 2906, 2862, 1652, 1601, 1537, 1490, 1451, 1393, 1359, 1276, 1159, 932, 791, 750, 698 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 11.14 (s, 1 H, OH), 10.55 (s, 1 H, NH), 10.45 (s, 1 H, NH), 7.66 (d, *J* = 7.6 Hz, 1 H, ArH), 7.53–7.49 (m, 1 H, ArH), 7.34–7.22 (m, 5 H, ArH), 7.04 (d, *J* = 8.8 Hz, 1 H, ArH), 6.95 (t, *J* = 8.0 Hz, 1 H, ArH), 6.58 (s, 2 H, $NH_2$), 4.75 (s, 1 H, CH), 4.34 (s, 1 H, CH).

$^{13}C$ NMR (100 MHz, DMSO-$d_6$): δ = 197.5, 169.0, 161.5, 158.5, 157.1, 155.3, 142.6, 135.6, 130.9, 128.8, 126.9, 126.8, 121.5, 119.8, 119.9, 117.7, 89.7, 60.5, 37.4.

Anal. Calcd for $C_{20}H_{16}N_4O_4$: C, 63.82; H, 4.28; N, 14.89. Found: C, 63.61; H, 4.11; N, 14.97.

**5-(4-Methoxyphenyl) Derivative 5f**

IR (KBr): 3433, 3343, 3199, 2938, 2840, 1699, 1637, 1537, 1510, 1485, 1363, 1299, 1250, 1177, 997, 825, 798, 757 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 11.17 (s, 1 H, OH), 10.56 (s, 1 H, NH), 10.46 (s, 1 H, NH), 7.65 (d, *J* = 8.0 Hz, 1 H, ArH), 7.51 (t, *J* = 7.6 Hz, 1 H, ArH), 7.16 (d, *J* = 8.4 Hz, 2 H, ArH), 7.04 (d, *J* = 8.0 Hz, 1 H, ArH), 6.95 (t, *J* = 7.6 Hz, 1 H, ArH), 6.87 (t, *J* = 8.4 Hz, 2 H, ArH), 6.59 (s, 2 H, $NH_2$), 4.71 (s, 1 H, CH), 4.28 (s, 1 H, CH), 3.71 (s, 3 H, $OCH_3$).

$^{13}C$ NMR (100 MHz, DMSO-$d_6$): δ = 197.6, 169.0, 161.5, 158.6, 158.3, 156.9, 155.2, 135.6, 134.5, 130.9, 127.9, 121.5, 119.8, 117.7, 114.1, 90.1, 60.7, 55.3, 36.7.

Anal. Calcd for $C_{21}H_{18}N_4O_5$: C, 62.06; H, 4.46; N, 13.79. Found: C, 61.84; H, 4.61; N, 13.84.

**5-(4-Methylphenyl) Derivative 5g**

IR (KBr): 3421, 3321, 3163, 2915, 2770, 1689, 1651, 1540 1487, 1451, 1357, 1241, 1158, 795, 751 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 11.15 (s, 1 H, OH), 10.55 (s, 1 H, NH), 10.45 (s, 1 H, NH), 7.64 (d, *J* = 8.0 Hz, 1 H, ArH), 7.50 (t, *J* = 8.0 Hz, 1 H, ArH), 7.15–7.10 (m, 4 H, ArH), 7.04 (d, *J* = 8.0 Hz, 1 H, ArH), 6.95 (t, *J* = 7.6 Hz, 1 H, ArH), 6.59 (s, 2 H, $NH_2$), 4.71 (s, 1 H, CH), 4.30 (s, 1 H, CH), 2.26 (s, 3 H, $CH_3$).

$^{13}C$ NMR (100 MHz, DMSO-$d_6$): δ = 197.6, 169.0, 161.5, 158.5, 157.0, 155.2, 140.0, 136.0, 135.6, 130.9, 129.3, 126.7, 121.5, 119.8, 117.7, 89.9, 60.6, 37.1, 20.7.

MS (ESI): *m*/*z* = 389.7 $[M - H]^-$, 352.7, 339.0.

Anal. Calcd for $C_{21}H_{18}N_4O_4$: C, 64.61; H, 4.65; N, 14.35. Found: C, 64.72; H, 4.82; N, 14.09.

**5-(3,4-Dimethoxyphenyl) Derivative 5h**

IR (KBr): 3420, 3306, 3187, 2939, 1691, 1638, 1561 1514, 1455, 1420, 1321, 1123, 1002, 782, 757 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$d_6$): δ = 11.13 (s, 1 H, OH), 10.42 (s, 1 H, NH), 10.37 (s, 1 H, NH), 7.78 (d, *J* = 7.6 Hz, 1 H, ArH), 7.46 (t, *J* = 8.0 Hz, 1 H, ArH), 7.39–7.35 (m, 2 H, ArH), 6.71 (d, *J* = 8.0 Hz, 1 H, ArH), 6.64–6.62 (m, 2 H, ArH), 6.37 (s, 2 H, $NH_2$), 4.69 (s, 1 H, CH), 4.21 (s, 1 H, CH), 3.71 (s, 6 H, $OCH_3$).

$^{13}$C NMR (100 MHz, DMSO-$d_6$): δ = 197.7, 168.9, 161.2, 158.8, 154.7, 154.2, 152.3, 149.8, 135.6, 134.3, 131.1, 129.7, 126.6, 121.3, 119.8, 117.7, 114.5, 90.4, 60.7, 55.8, 55.6, 36.6.

Anal. Calcd for $C_{22}H_{20}N_4O_6$: C, 60.55; H, 4.62; N, 12.84. Found: C, 60.59; H, 4.47; N, 12.77.

**5-(2-Thienyl) Derivative 5i**

IR (KBr): 3489, 3339, 3194, 3065, 2956, 1689, 1633, 1542, 1491, 1439, 1359, 1206, 1106, 899, 758 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 11.15 (s, 1 H, OH), 10.78 (s, 1 H, NH), 10.45 (s, 1 H, NH), 7.84 (d, *J* = 7.6 Hz, 1 H, ArH), 7.57 (t, *J* = 8.0 Hz, 1 H, ArH), 7.41–7.28 (m, 3 H, ArH), 6.83 (s, 1 H, ArH), 6.71–6.83 (m, 1 H, ArH), 6.43 (s, 2 H, $NH_2$), 4.73 (s, 1 H, CH), 4.28 (s, 1 H, CH).

Anal. Calcd for $C_{18}H_{14}N_4O_4S$: C, 56.54; H, 3.69; N, 14.65; S, 8.39. Found: C, 56.70; H, 3.86; N, 14.59; S, 8.27.

**10-Amino-7-aryl-7,12-dihydrobenzo[*h*]pyrimido[4,5-*b*][1,6]naphthyridine-6,8(5*H*,9*H*)-dione 7; General Procedure under Microwave Irradiation**

In a 10-mL reaction vial, aldehyde **1** (1 mmol), 2,6-diaminopyrimidin-4-one (**2**, 126 mg, 1 mmol), 4-hydroxyquinolin-2(1*H*)-one (**6**, 160 mg, 1 mmol), and DMF (2.0 mL) were mixed and then the vial was capped. The mixture was irradiated for the specified time (Table 5) at 100 W (initial power) and 200 W (maximum power) and 140 °C. Upon completion (TLC), the subsequent workup was the same as that given for the general procedure under microwave irradiation for **4**.

**7-(4-Fluorophenyl) Derivative 7a**

IR (KBr): 3436, 3345, 3160, 2902, 1652, 1633, 1506, 1444, 1387, 1292, 1222, 1157, 1098, 1062, 862, 844, 807, 782, 760, 667 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 13.80 (s, 1 H, NH), 11.65 (s, 1 H, NH), 10.54 (s, 1 H, NH), 7.82 (d, *J* = 8.0 Hz, 1 H, ArH), 7.53–7.44 (m, 1 H, ArH), 7.34 (d, *J* = 8.0 Hz, 1 H, ArH), 7.19–7.01 (m, 5 H, ArH), 6.45 (s, 2 H, $NH_2$), 5.71 (s, 1 H, CH).

Anal. Calcd for $C_{20}H_{14}FN_5O_2$: C, 64.00; H, 3.76; N, 18.66. Found: C, 64.06; H, 3.59; N, 18.73.

**7-(4-Hydroxy-3-nitrophenyl) Derivative 7b**

IR (KBr): 3426, 3340, 3328, 3149, 2928, 1689, 1638, 1533, 1487, 1341, 1248, 1155, 1100, 791, 752 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 13.78 (s, 1 H, NH), 11.66 (s, 1 H, NH), 10.69 (s, 1 H, OH), 10.61 (s, 1 H, NH), 7.82 (d, *J* = 7.6 Hz, 1 H, ArH), 7.54–7.50 (m, 2 H, ArH), 7.34 (d, *J* = 8.4 Hz, 1 H, ArH), 7.25 (d, *J* = 8.0 Hz, 1 H, ArH), 7.19 (t, *J* = 7.6 Hz, 1 H, ArH), 7.02 (d, *J* = 8.4 Hz, 1 H, ArH), 6.47 (s, 2 H, $NH_2$), 5.68 (s, 1 H, CH).

Anal. Calcd for $C_{20}H_{14}N_6O_5$: C, 57.42; H, 3.37; N, 20.09. Found: C, 57.46; H, 3.49; N, 20.16.

**7-(4-Chlorophenyl) Derivative 7c**

IR (KBr): 3430, 3335, 3178, 3095, 2908, 1673, 1636, 1605, 1487, 1436, 1385, 1272, 1094, 875, 847, 792, 755 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 13.77 (s, 1 H, NH), 11.64 (s, 1 H, NH), 10.54 (s, 1 H, NH), 7.82 (d, *J* = 7.6 Hz, 1 H, ArH), 7.52 (t, *J* = 7.6 Hz, 1 H, ArH), 7.33 (d, *J* = 8.0 Hz, 1 H, ArH), 7.27 (d, *J* = 8.0 Hz, 2 H, ArH), 7.20–7.12 (m, 1 H, ArH), 7.07 (d, *J* = 8.0 Hz, 2 H, ArH), 6.45 (s, 2 H, $NH_2$), 5.70 (s, 1 H, CH).

Anal. Calcd for $C_{20}H_{14}ClN_5O_2$: C, 61.31; H, 3.60; N, 17.87. Found: C, 61.26; H, 3.51; N, 17.79.

**7-(3-Nitrophenyl) Derivative 7d**

IR (KBr): 3411, 3344, 3190, 3091, 2918, 1665, 1631, 1526, 1493, 1445, 1349, 1258, 1094, 862, 793 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 13.76 (s, 1 H, NH), 11.71 (s, 1 H, NH), 10.65 (s, 1 H, NH), 8.05 (s, 1 H, ArH), 7.86–7.83 (m, 2 H, ArH), 7.55–7.52 (m, 3 H, ArH), 7.36 (d, *J* = 8.4 Hz, 1 H, ArH), 7.20 (t, *J* = 7.6 Hz, 1 H, ArH), 6.51 (s, 2 H, $NH_2$), 5.83 (s, 1 H, CH).

Anal. Calcd for $C_{20}H_{14}N_6O_4$: C, 59.70; H, 3.51; N, 20.89. Found: C, 59.78; H, 3.29; N, 20.61.

**7-Phenyl Derivative 7e**

IR (KBr): 3419, 3344, 3182, 3025, 2997, 2929, 1658, 1637, 1608, 1491, 1437, 1385, 1257, 1100, 875,825, 793, 755 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 13.79 (s, 1 H, NH), 11.61 (s, 1 H, NH), 10.50 (s, 1 H, NH), 7.82 (d, *J* = 8.0 Hz, 1 H, ArH), 7.51 (t, *J* = 7.6 Hz, 1 H, ArH), 7.34 (d, *J* = 8.0 Hz, 1 H, ArH), 7.23–7.06 (m, 6 H, ArH), 6.43 (s, 2 H, $NH_2$), 5.74 (s, 1 H, CH).

$^{13}$C NMR (100 MHz, DMSO-$d_6$): δ = 165.5, 164.0, 161.0, 153.7, 140.3, 137.5, 130.5, 128.0, 126.5, 125.3, 123.4, 121.6, 116.7, 115.2, 110.8, 90.3, 34.2.

Anal. Calcd for $C_{20}H_{15}N_5O_2$: C, 67.22; H, 4.23; N, 19.60. Found: C, 67.10; H, 4.33; N, 19.87.

**7-(4-Methoxyphenyl) Derivative 7f**

IR (KBr): 3423, 3337, 3172, 2835, 1645, 1607, 1508, 1438, 1387, 1247, 1177, 1032, 841, 803, 758 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 13.77 (s, 1 H, NH), 11.57 (s, 1 H, NH), 10.46 (s, 1 H, NH), 7.81 (d, *J* = 8.4 Hz, 1 H, ArH), 7.52–7.33 (m, 1 H, ArH), 7.33 (d, *J* = 8.4 Hz, 1 H, ArH), 7.17 (t, *J* = 7.6 Hz, 1 H, ArH), 6.95 (d, *J* = 8.4 Hz, 2 H, ArH), 6.77 (d, *J* = 8.0 Hz, 2 H, ArH), 6.40 (s, 2 H, $NH_2$), 5.68 (s, 1 H, CH), 3.71 (s, 3 H, $OCH_3$).

Anal. Calcd for $C_{21}H_{17}N_5O_3$: C, 65.11; H, 4.42; N, 18.08. Found: C, 64.98; H, 4.27; N, 18.16.

**7-(4-Methylphenyl) Derivative 7g**

IR (KBr): 3402, 3342, 3177, 2923, 1640, 1633, 1508, 1490, 1369, 1254, 1099, 1010, 841, 801, 757 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 13.77 (s, 1 H, NH), 11.61 (s, 1 H, NH), 10.49 (s, 1 H, NH), 7.81 (d, *J* = 8.4 Hz, 1 H, ArH), 7.50 (t, *J* = 7.6 Hz, 1 H, ArH), 7.33 (d, *J* = 8.4 Hz, 2 H, ArH), 7.17 (t, *J* = 7.6 Hz, 1 H, ArH), 7.01 (d, *J* = 8.0 Hz, 1 H, ArH), 6.94 (d, *J* = 8.0 Hz, 2 H, ArH), 6.41 (s, 2 H, $NH_2$), 5.68 (s, 1 H, CH), 2.24 (s, 3 H, $CH_3$).

$^{13}$C NMR (100 MHz, DMSO-$d_6$): δ = 165.5, 165.4, 163.9, 160.9, 153.6, 137.5, 137.2, 134.0, 130.5, 128.6, 126.4, 123.3, 121.6, 116.7, 115.2, 111.2, 90.4, 33.9, 20.7.

MS (ESI): *m*/*z* = 388.7 $(M + NH_4)^+$.

Anal. Calcd for $C_{21}H_{17}N_5O_2$: C, 67.91; H, 4.61; N, 18.86. Found: C, 68.11; H, 4.68; N, 18.77.

**7-[3,4-(Methylenedioxy)phenyl] Derivative 7h**

IR (KBr): 3416, 3345, 3180, 2929, 2742, 1636, 1631, 1608, 1486, 1439, 1322, 1235, 1010, 928, 828, 783, 762 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 13.77 (s, 1 H, NH), 11.54 (s, 1 H, NH), 10.46 (s, 1 H, NH), 7.83 (d, *J* = 8.0 Hz, 1 H, ArH), 7.50 (t, *J* = 7.6 Hz, 1 H, ArH), 7.33 (d, *J* = 8.0 Hz, 1 H, ArH), 7.17 (t, *J* = 7.6 Hz, 1 H, ArH), 6.74 (d, *J* = 8.0 Hz, 1 H, ArH), 6.56–6.52 (m, 2 H, ArH), 6.52 (s, 2 H, $NH_2$), 5.94 (s, 2 H, $CH_2$), 5.67 (s, 1 H, CH).

Anal. Calcd for $C_{21}H_{15}N_5O_4$: C, 62.84; H, 3.77; N, 17.45. Found: C, 62.58; H, 3.88; N, 17.29.

**7-(2-Thienyl) Derivative 7i**

IR (KBr): 3432, 3342, 3178, 2873, 1637, 1603, 1485, 1431, 1373, 1267, 828, 757, 695, 670 cm$^{-1}$.

$^1$H NMR (400 MHz, DMSO-$d_6$): δ = 14.08 (s, 1 H, NH), 11.62 (s, 1 H, NH), 10.57 (s, 1 H, NH), 7.85 (d, *J* = 8.0 Hz, 1 H, ArH), 7.52 (d, *J* = 7.6 Hz, 1 H, ArH), 7.34 (d, *J* = 8.0 Hz, 1 H, ArH), 7.24–7.16 (m, 2 H, ArH), 6.85–6.83 (m, 1 H, ArH), 6.57 (s, 1 H, ArH), 6.47 (s, 2 H, $NH_2$), 5.86 (s, 1 H, CH).

Anal. Calcd for $C_{18}H_{13}N_5O_2S$: C, 59.49; H, 3.61; N, 19.27; S, 8.82. Found: C, 59.43; H, 3.39; N, 19.20; S, 8.65.

**Synthesis of 4 and 7 with Conventional Heating; General Procedure**

A mixture containing aldehyde **1** (1 mmol), 4-hydroxy-2*H*-chromen-2-one (**3**, 162 mg, 1 mmol) [or 4-hydroxyquinolin-2(1*H*)-one (**6**, 160 mg, 1 mmol)], 2,6-diaminopyrimidin-4(3*H*)-one (**2**, 126 mg, 1 mmol), and DMF (2.0 mL) was introduced into a 10-mL Emrys reaction vial, the vial was capped, and the mixture was then stirred at 140 °C (oil-bath temperature) for the specified time. When the reaction was completed (TLC), workup was the same as that given for the general procedure under microwave irradiation for **4**.

**Synthesis of 5 under Classical Heating Conditions; General Procedure**

A mixture containing aldehyde **1** (1 mmol), 4-hydroxy-2*H*-chromen-2-one (**3**, 162 mg, 1 mmol), 2,6-diaminopyrimidin-4(3*H*)-one (**2**, 126 mg, 1 mmol), AcOH (0.4 mL), and DMF (1.6 mL) were mixed into a 10-mL Emrys reaction vial, the vial was capped, and the mixture was then stirred at 150 °C (oil-bath temperature) for the specified time. When the reaction was completed (TLC), workup was the same as that given for the general procedure under microwave irradiation for **4**.

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