

Mild and efficient one-pot three-component synthesis of benzopyrimidoquinoline-tetraone derivatives in ionic liquids

Bai-Xiang Du, Bo Zhao, Gan Cai, Yu-Ling Li* and Xiang-Shan Wang

School of Chemistry and Chemical Engineering, Jiangsu Key Laboratory of Green Synthetic Chemistry for Functional Materials, Xuzhou Normal University, Xuzhou Jiangsu 221116, P. R. China

An efficient one-pot synthesis of 5-aryl-5,12-dihydrobenzo[*g*]pyrimido[4,5-*b*]quinoline-2,4,6,11(1*H*,3*H*)-tetraone derivatives via three-component reaction of aromatic aldehydes, 2-hydroxy-1,4-naphthoquinone and 6-aminouracil in ionic liquid [bmim]BF₄ is reported. This method had the advantages of easier work-up, environmentally benign procedure, high yields and ease of recovery and reuse of reaction media.

Keywords: multicomponent reactions, ionic liquid, pyrimidoquinoline

Over the past decade, multicomponent reactions (MCRs) have become one of the most efficient tools for synthesising highly complex molecules and introducing molecular diversity from simple starting materials in a single synthetic operation.¹ MCRs have been widely used in organic, combinatorial, and medicinal chemistry because of their advantages such as convenience and high degree of atom economy.²

Heterocyclic compounds containing nitrogen atoms are widespread in nature, and are valuable in the design and discovery of new biologically active compounds. Their applications to pharmaceuticals, agrochemicals, and functional materials are becoming increasingly important. For example, pyrimidoquinolines have diverse pharmacological activities such as anticancer,³ antibacterial,⁴ antimicrobial,⁵ antiallergic,⁶ anti-inflammatory,⁷ and antimalarial activity.⁸ For the preparation of these complex molecules much effort has been directed towards the synthetic manipulation of pyrimidoquinolines.

Zoorob synthesised pyrimidoquinolines by the reaction of benzoylthylbarbituric acids with aniline derivatives by refluxing in xylene in the presence of a catalytic amount of *p*-toluene sulfonic acid.⁹ Shi synthesised pyrimido[4,5-*b*]quinoline derivatives via the three-component reaction in water in the presence of triethylbenzylammonium chloride (TEBAC).¹⁰ Tu reported a simple and efficient synthesis of benzoquinolinopyrimidine derivatives via a three-component reaction in mixed solvent of acetic acid and glycol under microwave irradiation at 120 °C.¹¹ Singh reported the synthesis of pyrimidoquinolines via *t*-BuOK catalysed cyclisation reaction of 2-chloroquinoline-3-carbonitriles and guanidine hydrochlorides in high yields in ethyl alcohol at 90 °C.¹² These methods usually require forcing conditions, long reaction times, complex synthetic pathways and often react in organic solvents or by catalysis. Therefore, development of simple and safe methodologies for the synthesis of pyrimidoquinolines is of prime interest from the synthetic and environment points of view. Recently ionic liquids have been used as environmentally benign solvents for a broad range of inorganic and organic reactions.¹³ A nice feature of ionic liquid is that yields can be optimised by changing the anions or properties of the cation. In addition, several ionic liquids show enhancement in reaction rates and selectivity, compared to organic solvents

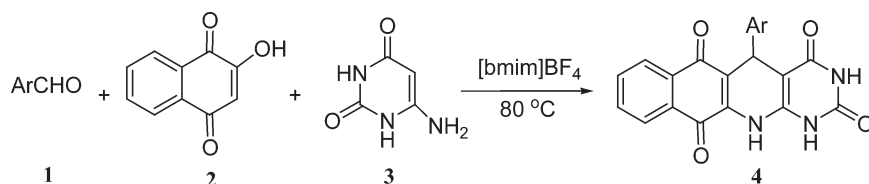
with the added benefit of the ease of recovery and reuse of these ionic liquids.¹⁴

In view of the importance of pyrimidoquinolines for diverse therapeutic activity and in continuation of developing environmentally benign methodologies for synthesis of heterocyclic compounds, we now report a novel three-component one-pot synthesis of well functionalised pyrimidoquinolines in ionic liquid medium (Scheme 1).^{15–17} When three components of aromatic aldehyde **1**, 2-hydroxy-1,4-naphthoquinone **2** and 6-aminouracil **3** were treated in ionic liquids [bmim]BF₄ at 80 °C for a few hours (Scheme 1), the pyrimidoquinolines derivatives **4** were obtained in high yields (80–95%). To the best of our knowledge, this is the first report on such a synthesis of 5-aryl-5,12-dihydrobenzo[*g*]pyrimido[4,5-*b*]quinoline-2,4,6,11(1*H*,3*H*)-tetraone derivatives.

Results and discussion

The study was initiated by using 4-chloroaldehyde, 2-hydroxy-1,4-naphthoquinone and 6-aminouracil as model substrates for the preparation of **4a** in various reaction conditions (Table 1). We examined several traditional solvents and ionic liquids. It was found that no conversion to product occurred even after 24 h in organic solvent such as EtOH, DMF, CH₃CN at reflux temperature (Table 1, entry 1). There was a remarkable temperature effect in this reaction; for the ionic liquid [bmim]BF₄, no conversion to the product occurred even after 24 h at room temperature, but the yield of product **4a** improved and the reaction time was shortened as the temperature increased. The yield levelled off when temperature was further increased to 90 °C (Table 1, entries 4–8). Therefore, 80 °C was chosen as the most suitable reaction temperature. The effect of reaction time on the yields of product **4a** in ionic liquid [bmim]BF₄ was also investigated. The reactions were performed in ionic liquid [bmim]BF₄ for 8, 10, or 12 h at 80 °C (Table 1, entries 7, 9 and 10), leading to **4a** in 88%, 95%, and 93% yields, respectively. Thus, the optimal reaction time is 10 h. Different ionic liquids were also studied at 80 °C as shown in Table 1. On the basis of results in Table 1, we could conclude that [bmim]BF₄ was the best ionic liquid for this reaction.

To generalise the feasibility of this protocol, a range of structurally diverse aldehydes bearing electron donating and



Scheme 1 The reaction of **1**, **2** and **3** in ionic liquid [bmim]BF₄.

* Correspondent. E-mail: ylli19722@163.com

Table 1 Optimisation of the reaction conditions for synthesis of **4a**^a

| Entry | Temp/°C | Medium | Time/h | Yield/% ^b |
|-------|---------|-----------------------|--------|----------------------|
| 1 | Reflux | EtOH | 24 | 0 |
| 2 | Reflux | DMF | 24 | 0 |
| 3 | Reflux | CH ₃ CN | 24 | 0 |
| 4 | rt | [bmim]BF ₄ | 24 | 0 |
| 5 | 40 | [bmim]BF ₄ | 24 | 30 |
| 6 | 60 | [bmim]BF ₄ | 12 | 55 |
| 7 | 80 | [bmim]BF ₄ | 10 | 95 |
| 8 | 90 | [bmim]BF ₄ | 10 | 94 |
| 9 | 80 | [bmim]BF ₄ | 8 | 88 |
| 10 | 80 | [bmim]BF ₄ | 12 | 93 |
| 11 | 80 | [emim]Br | 10 | 35 |
| 12 | 80 | [pmim]Br | 10 | 40 |
| 13 | 80 | [bmim]Br | 10 | 30 |
| 14 | 80 | [emim]BF ₄ | 10 | 80 |
| 15 | 80 | [pmim]BF ₄ | 10 | 82 |
| 16 | 80 | [bmim]PF ₆ | 10 | 85 |

^aReaction condition: 2 mL of ionic liquid, 1 mmol 4-chloroaldehyde, 1 mmol 2-hydroxy-1,4-naphthoquinone, 1 mmol 6-aminouracil.

^bIsolated yields.

Table 2 Synthesis of **4** in ionic liquid [bmim]BF₄^a

| Entry | Ar | Products | Time/h | Yields/% ^b |
|-------|--|-----------|--------|-----------------------|
| 1 | 4-ClC ₆ H ₄ | 4a | 10 | 95 |
| 2 | 3-OCH ₃ C ₆ H ₄ | 4b | 10 | 86 |
| 3 | 2-OHC ₆ H ₄ | 4c | 16 | 84 |
| 4 | 3-BrC ₆ H ₄ | 4d | 13 | 98 |
| 5 | 3,4-(OCH ₃) ₂ C ₆ H ₃ | 4e | 13 | 90 |
| 6 | 4-OHC ₆ H ₄ | 4f | 15 | 85 |
| 7 | 3,4-(OCH ₂ O)C ₆ H ₃ | 4g | 15 | 83 |
| 8 | 4-BrC ₆ H ₄ | 4h | 9 | 91 |
| 9 | 3-ClC ₆ H ₄ | 4i | 12 | 85 |
| 10 | 2-BrC ₆ H ₄ | 4j | 13 | 86 |
| 11 | 2-OCH ₃ C ₆ H ₄ | 4k | 15 | 80 |
| 12 | 3,4-Cl ₂ C ₆ H ₃ | 4l | 10 | 86 |
| 13 | 2-ClC ₆ H ₄ | 4m | 12 | 90 |
| 14 | 3-OHC ₆ H ₄ | 4n | 12 | 90 |
| 15 | 4-CH ₃ C ₆ H ₄ | 4o | 18 | 95 |

^aReaction condition: 2 mL ionic liquid, 1 mmol aromatic aldehyde, 1 mmol 2-hydroxy-1,4-naphthoquinone, 1 mmol 6-aminouracil, 80 °C.

^bIsolated yields.

withdrawing substituents were transformed in ionic liquid [bmim]BF₄ with 2-hydroxy-1,4-naphthoquinone and 6-aminouracil under optimised conditions. The results indicated that aldehydes carrying both electron-withdrawing and electron-donating substituents were converted to their corresponding derivatives in good yields under optimal conditions described above. At the same time, we have also observed delicate electronic effects: aldehydes with electron-withdrawing groups reacted rapidly, while electron donating groups decreased the reactivity, requiring longer reaction times. The results are summarised in Table 2. All the products were characterised by melting points, ¹H NMR, IR and HRMS.

To explain the mechanism of this one-pot, multicomponent reaction, we tentatively propose a plausible reaction mechanism which is illustrated in Scheme 2. Firstly, Knoevenagel condensation of aromatic aldehyde **1** with 2-hydroxy-1,4-naphthoquinone **2** could lead to the formation of intermediate **5**. Then, nucleophilic addition between **5** and **3** would give Schiff's base **6** which would undergo a electrocyclic reaction to give intermediate **7**. Finally, the product **4** was obtained by a rapid imine–enamine tautomerisation.

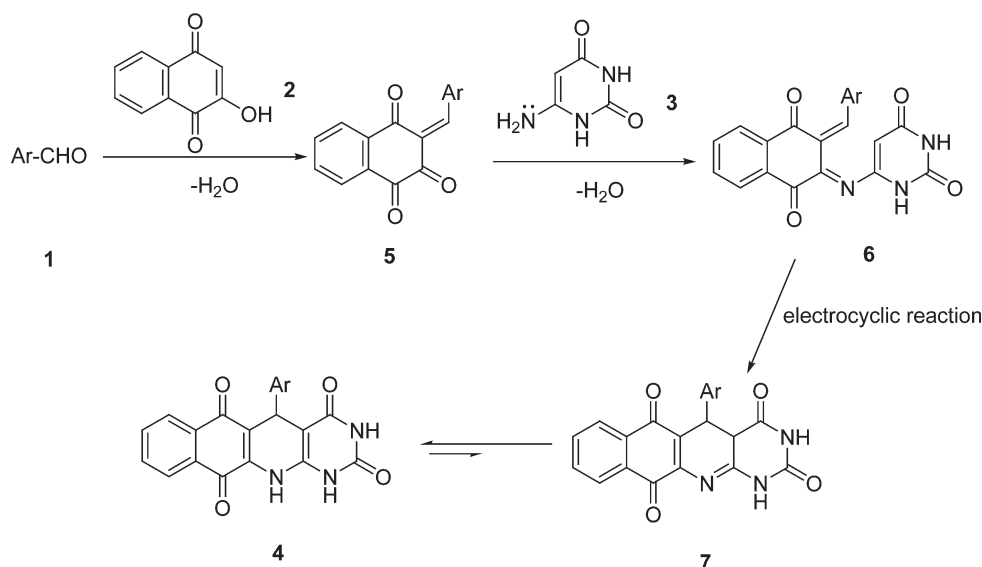
In our studies, the recycling of the ionic liquid [bmim]BF₄ has also been investigated by using the preparation of **4a** as a model. Since the poor solubility of products in ionic liquids and water, they were easily separated by simple filtration from mixture of water and ionic liquid, the filtrate was then extracted with ether and dried at 90 °C in vacuum for several hours to be recycled. As shown in Fig. 1, the reaction medium could be recycled at least six times without significant decrease of the yields, which ranged from 95 to 88%.

Experimental

Melting points were determined in open capillaries without further correction. IR spectra were recorded on a Tensor 27 spectrometer in KBr. ¹H NMR spectra were obtained from solution in DMSO-*d*₆ with Me₄Si as an internal standard using a Bruker-400 spectrometer. HRMS data were obtained using a MicroTOF-QII instrument.

Synthesis of **4**; general procedure

A mixture of aromatic aldehyde **1** (1 mmol), 2-hydroxynaphthalene-1,4-dione **2** (1 mmol), 6-aminouracil **3** (1 mmol) was stirred at 80 °C for 9–18 h in ionic liquid [bmim]BF₄ (2 mL). After completion of the reaction as indicated by TLC, water (5 mL) was added and the product was filtered off and washed with water. The remaining aqueous layer containing the ionic liquid was extracted with ether (8 mL) for three

**Scheme 2** Reaction mechanism of **1**, **2** and **3** in ionic liquid [bmim]BF₄.

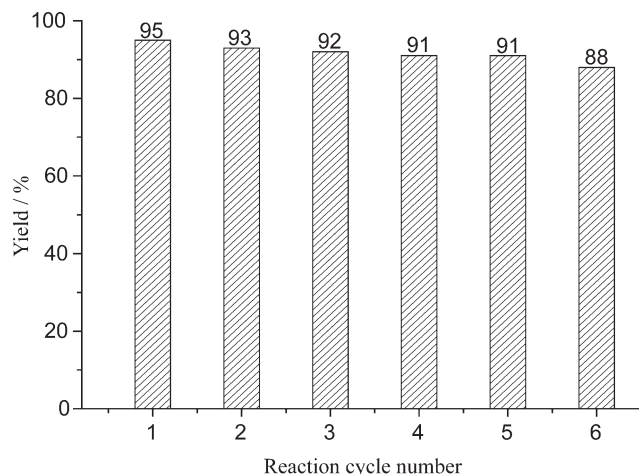


Fig. 1 Reusability of ionic liquid [bmim]BF₄.

times to remove organic impurity, and then dried under vacuum at 90 °C for about 15 h to afford ionic liquid, which was used in the subsequent runs without further purification. The crude product was purified by recrystallisation from DMF and H₂O to give **4** as a red powder.

5-(4-Chlorophenyl)-5,12-dihydrobenzo[g]pyrimido[4,5-b]quinoline-2,4,6,11(1H,3H)-tetraone (4a): M.p. >300 °C; ¹HNMR (DMSO-*d*₆, δ, ppm): 10.98 (s, 1H, NH), 10.21 (s, 1H, NH), 9.35 (s, 1H, NH), 8.05 (d, 1H, ArH, *J* = 7.2 Hz), 7.91 (d, 1H, ArH, *J* = 7.2 Hz), 7.81–7.84 (m, 2H, ArH), 7.36 (d, 2H, ArH, *J* = 8.4 Hz), 7.28 (d, 2H, ArH, *J* = 8.4 Hz), 5.09 (s, 1H, CH); IR (KBr, ν, cm⁻¹): 3563, 3479, 3417, 3235, 1772, 1716, 1638, 1616; HRMS Calcd for C₂₁H₁₁ClN₃O₄ (M–H)⁻ requires 404.0437; found: 404.0447.

5-(3-Methoxyphenyl)-5,12-dihydrobenzo[g]pyrimido[4,5-b]quinoline-2,4,6,11(1H,3H)-tetraone (4b): M.p. >300 °C; ¹HNMR (DMSO-*d*₆, δ, ppm): 10.95 (s, 1H, NH), 10.20 (s, 1H, NH), 9.36 (s, 1H, NH), 8.05 (d, 1H, ArH, *J* = 7.2 Hz), 7.93 (d, 1H, ArH, *J* = 7.6 Hz), 7.81–7.85 (m, 2H, ArH), 7.14 (d, 1H, ArH, *J* = 8.0 Hz), 6.88 (d, 2H, ArH, *J* = 8.4 Hz), 6.73 (d, 1H, ArH, *J* = 8.4 Hz), 5.07 (s, 1H, CH), 3.69 (s, 3H, OCH₃); IR (KBr, ν, cm⁻¹): 3649, 3553, 3416, 3235, 1718, 1638, 1617; HRMS Calcd for C₂₂H₁₄N₃O₅ (M–H)⁻ requires 400.0934; found: 400.0957.

5-(2-Hydroxyphenyl)-5,12-dihydrobenzo[g]pyrimido[4,5-b]quinoline-2,4,6,11(1H,3H)-tetraone (4c): M.p. >300 °C; ¹HNMR (DMSO-*d*₆, δ, ppm): 10.95 (s, 1H, NH), 10.23 (s, 1H, NH), 9.30 (s, 2H, NH+OH), 8.03 (d, 1H, ArH, *J* = 6.8 Hz), 7.92 (d, 1H, ArH, *J* = 7.2 Hz), 7.78–7.85 (m, 2H, ArH), 7.01 (t, 1H, ArH, *J* = 8.0 Hz), 6.74 (d, 2H, ArH, *J* = 6.8 Hz), 6.52 (t, 1H, ArH, *J* = 8.4 Hz), 5.01 (s, 1H, CH); IR (KBr, ν, cm⁻¹): 3553, 3480, 3414, 3235, 1719, 1638, 1616; HRMS Calcd for C₂₁H₁₂N₃O₅ (M–H)⁻ requires 386.0777; found: 386.0802.

5-(3-Bromophenyl)-5,12-dihydrobenzo[g]pyrimido[4,5-b]quinoline-2,4,6,11(1H,3H)-tetraone (4d): M.p. >300 °C; ¹HNMR (DMSO-*d*₆, δ, ppm): 10.99 (s, 1H, NH), 10.22 (s, 1H, NH), 9.40 (s, 1H, NH), 7.82–8.05 (m, 4H, ArH), 7.52 (s, 1H, ArH), 7.34 (d, 2H, ArH, *J* = 6.0 Hz), 7.20 (t, 1H, ArH, *J* = 6.8 Hz), 5.06 (s, 1H, CH); IR (KBr, ν, cm⁻¹): 3551, 3478, 3411, 3235, 1730, 1654, 1614; HRMS Calcd for C₂₁H₁₁BrN₃O₄ (M–H)⁻ requires 447.9933; found: 447.9937.

5-(3,4-Dimethoxyphenyl)-5,12-dihydrobenzo[g]pyrimido[4,5-b]quinoline-2,4,6,11(1H,3H)-tetraone (4e): M.p. >300 °C; ¹HNMR (DMSO-*d*₆, δ, ppm): 10.94 (s, 1H, NH), 10.19 (s, 1H, NH), 9.32 (s, 1H, NH), 8.05 (d, 1H, ArH, *J* = 7.6 Hz), 7.93 (d, 1H, ArH, *J* = 7.6 Hz), 7.81–7.85 (m, 2H, ArH), 6.93 (s, 1H, ArH), 6.77 (s, 2H, ArH), 5.04 (s, 1H, CH), 3.70 (s, 3H, OCH₃), 3.66 (s, 3H, OCH₃); IR (KBr, ν, cm⁻¹): 3563, 3478, 3416, 1714, 1638, 1617; HRMS Calcd for C₂₃H₁₆N₃O₆ (M–H)⁻ requires 430.1038; found: 430.1048.

5-(4-Hydroxyphenyl)-5,12-dihydrobenzo[g]pyrimido[4,5-b]quinoline-2,4,6,11(1H,3H)-tetraone (4f): M.p. >300 °C; ¹HNMR (DMSO-*d*₆, δ, ppm): 10.92 (s, 1H, NH), 10.17 (s, 1H, NH), 9.28 (s, 2H, NH+OH), 8.03 (d, 1H, ArH, *J* = 7.2 Hz), 7.93 (d, 1H, ArH, *J* = 8.4 Hz), 7.80–7.86 (m, 2H, ArH), 7.09 (d, 2H, ArH, *J* = 8.4 Hz), 6.60 (d, 2H, ArH, *J* = 8.0 Hz), 4.98 (s, 1H, CH); IR (KBr, ν, cm⁻¹): 3551, 3479, 3416, 3235, 1717; HRMS Calcd for C₂₁H₁₂N₃O₅ (M–H)⁻ requires 386.0777; found: 386.0783.

5-(3,4-Methylenedioxyphenyl)-5,12-dihydrobenzo[g]pyrimido[4,5-b]quinoline-2,4,6,11(1H,3H)-tetraone (4g): M.p. >300 °C; ¹HNMR (DMSO-*d*₆, δ, ppm): 10.94 (s, 1H, NH), 10.18 (s, 1H, NH), 9.33 (s, 1H, NH), 8.05 (d, 1H, ArH, *J* = 7.6 Hz), 7.94 (d, 1H, ArH, *J* = 7.2 Hz), 7.83–7.85 (m, 2H, ArH), 6.88 (s, 1H, ArH), 6.75–6.77 (m, 2H, ArH), 5.92 (s, 2H, OCH₂O), 5.02 (s, 1H, CH); IR (KBr, ν, cm⁻¹): 3551, 3478, 3416, 3235, 1716, 1638, 1616; HRMS Calcd for C₂₂H₁₂N₃O₆ (M–H)⁻ requires 414.0725; found: 414.0738.

5-(4-Bromophenyl)-5,12-dihydrobenzo[g]pyrimido[4,5-b]quinoline-2,4,6,11(1H,3H)-tetraone (4h): M.p. >300 °C; ¹HNMR (DMSO-*d*₆, δ, ppm): 10.96 (s, 1H, NH), 10.21 (s, 1H, NH), 9.38 (s, 1H, NH), 8.06 (d, 1H, ArH, *J* = 7.2 Hz), 7.92 (d, 1H, ArH, *J* = 7.2 Hz), 7.82–7.85 (m, 2H, ArH), 7.21–7.38 (m, 4H, ArH), 5.09 (s, 1H, CH); IR (KBr, ν, cm⁻¹): 3553, 3475, 3416, 3235, 1773, 1719, 1638; HRMS Calcd for C₂₁H₁₁BrN₃O₄ (M–H)⁻ requires 447.9933; found: 447.9937.

5-(3-Chlorophenyl)-5,12-dihydrobenzo[g]pyrimido[4,5-b]quinoline-2,4,6,11(1H,3H)-tetraone (4i): M.p. >300 °C; ¹HNMR (DMSO-*d*₆, δ, ppm): 10.96 (s, 1H, NH), 10.21 (s, 1H, NH), 9.38 (s, 1H, NH), 8.05 (d, 1H, ArH, *J* = 7.2 Hz), 7.81–7.91 (m, 3H, ArH), 7.38 (s, 1H, ArH), 7.21–7.30 (m, 3H, ArH), 5.07 (s, 1H, CH); IR (KBr, ν, cm⁻¹): 3552, 3481, 3415, 3235, 1719, 1662, 1637, 1617; HRMS Calcd for C₂₁H₁₁ClN₃O₄ (M–H)⁻ requires 404.0437; found: 404.0454.

5-(2-Bromophenyl)-5,12-dihydrobenzo[g]pyrimido[4,5-b]quinoline-2,4,6,11(1H,3H)-tetraone (4j): M.p. >300 °C; ¹HNMR (DMSO-*d*₆, δ, ppm): 10.83 (s, 1H, NH), 10.17 (s, 1H, NH), 9.39 (s, 1H, NH), 8.04 (d, 1H, ArH, *J* = 6.8 Hz), 7.79–7.83 (m, 3H, ArH), 7.39–7.46 (m, 2H, ArH), 7.24 (d, 1H, ArH, *J* = 7.2 Hz), 7.04 (d, 1H, ArH, *J* = 7.2 Hz), 5.43 (s, 1H, CH); IR (KBr, ν, cm⁻¹): 3552, 3475, 3414, 3235, 1720, 1638, 1616; HRMS Calcd for C₂₁H₁₁BrN₃O₄ (M–H)⁻ requires 447.9933; found: 447.9967.

5-(2-Methoxyphenyl)-5,12-dihydrobenzo[g]pyrimido[4,5-b]quinoline-2,4,6,11(1H,3H)-tetraone (4k): M.p. >300 °C; ¹HNMR (DMSO-*d*₆, δ, ppm): 10.77 (s, 1H, NH), 10.11 (s, 1H, NH), 9.37 (s, 1H, NH), 8.03 (d, 1H, ArH, *J* = 7.2 Hz), 7.78–7.85 (m, 3H, ArH), 7.31 (d, 1H, ArH, *J* = 7.2 Hz), 7.12 (t, 1H, ArH, *J* = 7.6 Hz), 6.83–6.89 (m, 2H, ArH), 5.21 (s, 1H, CH), 3.67 (s, 3H, OCH₃); IR (KBr, ν, cm⁻¹): 3552, 3480, 3415, 3238, 3067, 1721, 1654, 1616; HRMS Calcd for C₂₂H₁₄N₃O₅ (M–H)⁻ requires 400.0934; found: 400.0949.

5-(3,4-Dichlorophenyl)-5,12-dihydrobenzo[g]pyrimido[4,5-b]quinoline-2,4,6,11(1H,3H)-tetraone (4l): M.p. >300 °C; ¹HNMR (DMSO-*d*₆, δ, ppm): 10.98 (s, 1H, NH), 10.21 (s, 1H, NH), 9.40 (s, 1H, NH), 8.06 (d, 1H, ArH, *J* = 6.8 Hz), 7.91 (d, 1H, ArH, *J* = 6.8 Hz), 7.81–7.85 (m, 2H, ArH), 7.58 (d, 1H, ArH, *J* = 1.6 Hz), 7.48 (d, 1H, ArH, *J* = 8.4 Hz), 7.37 (dd, 1H, ArH, *J*₁ = 8.4 Hz, *J*₂ = 1.6 Hz), 5.08 (s, 1H, CH); IR (KBr, ν, cm⁻¹): 3553, 3482, 3415, 3235, 1725, 1655, 1638, 1616; HRMS Calcd for C₂₁H₁₀Cl₂N₃O₄ (M–H)⁻ requires 438.0049; found: 438.0041.

5-(2-Chlorophenyl)-5,12-dihydrobenzo[g]pyrimido[4,5-b]quinoline-2,4,6,11(1H,3H)-tetraone (4m): M.p. >300 °C; ¹HNMR (DMSO-*d*₆, δ, ppm): 10.93 (s, 1H, NH), 10.10 (s, 1H, NH), 9.30 (s, 1H, NH), 8.06 (d, 1H, ArH, *J* = 7.6 Hz), 7.93 (d, 1H, ArH, *J* = 7.2 Hz), 7.79–7.87 (m, 2H, ArH), 7.01 (t, 1H, ArH, *J* = 8.0 Hz), 6.74 (s, 2H, ArH), 6.52 (d, 1H, ArH, *J* = 8.0 Hz), 5.03 (s, 1H, CH); IR (KBr, ν, cm⁻¹): 3551, 3481, 3413, 3236, 1717, 1660, 1637, 1616; HRMS Calcd for C₂₁H₁₁ClN₃O₄ (M–H)⁻ requires 404.0437; found: 404.0444.

5-(3-Hydroxyphenyl)-5,12-dihydrobenzo[g]pyrimido[4,5-b]quinoline-2,4,6,11(1H,3H)-tetraone (4n): M.p. >300 °C; ¹HNMR (DMSO-*d*₆, δ, ppm): 10.95 (s, 1H, NH), 10.11 (s, 1H, NH), 9.30 (s, 2H, NH+OH), 8.04 (d, 1H, ArH, *J* = 6.8 Hz), 7.93 (d, 1H, ArH, *J* = 6.8 Hz), 7.80–7.86 (m, 2H, ArH), 7.01 (t, 1H, ArH, *J* = 7.0 Hz), 6.75 (s, 2H, ArH), 6.53 (d, 1H, ArH, *J* = 6.8 Hz), 5.02 (s, 1H, CH); IR (KBr, ν, cm⁻¹): 3553, 3480, 3414, 3235, 1719, 1638, 1616; HRMS Calcd for C₂₁H₁₂N₃O₅ (M–H)⁻ requires 386.0777; found: 386.0779.

5-(4-Methylphenyl)-5,12-dihydrobenzo[g]pyrimido[4,5-b]quinoline-2,4,6,11(1H,3H)-tetraone (4o): M.p. >300 °C; ¹HNMR (DMSO-*d*₆, δ, ppm): 10.92 (s, 1H, NH), 10.20 (s, 1H, NH), 9.25 (s, 1H, NH), 8.03 (d, 1H, ArH, *J* = 6.8 Hz), 7.90 (d, 1H, ArH, *J* = 7.2 Hz), 7.78–7.85 (m, 2H, ArH), 7.20 (d, 2H, ArH, *J* = 8.0 Hz), 7.02 (d, 2H, ArH, *J* = 7.6 Hz), 5.05 (s, 1H, CH), 2.19 (s, 3H, CH₃); IR (KBr, ν, cm⁻¹): 3550, 3482, 3414, 3230, 1719, 1616; HRMS Calcd for C₂₂H₁₄N₃O₄ (M–H)⁻ requires 384.0985; found: 384.1002.

Conclusion

In summary, an efficient one-pot synthesis of 5-aryl-5,12-dihydrobenzo[g]pyrimido[4,5-*b*]quinoline-2,4,6,11(1*H*,3*H*)-tetraone derivatives via three-component reaction of aromatic aldehyde, 2-hydroxy-1,4-naphthoquinone and 6-aminouracil in ionic liquid [bmim]BF₄ is reported. The ionic liquid plays a dual role as solvent and the promoter in this conversion. The simple experimental and product isolation procedures combined with ease of recovery and reuse of this reaction media is expected to contribute to the development of a green strategy for the synthesis of highly fictionalised pyrimido [4,5-*b*]quinolines.

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