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An efficient synthesis of 4,5-diaryl-3,4-dihydropyrimidin-2(1*H*)-one *via* a cesium carbonate-promoted direct condensation of 1-aryl-2-propanone with 1,1′-(arylmethylene)diurea†

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An efficient method for the synthesis of 4,5-diaryl-3,4-dihydropyrimidin-2(1*H*)-one by using 1,1′-(arylmethylene)diurea and 1-aryl-2-propanone as substrates was developed. The reactions proceeded efficiently in the presence of Cs_2CO_3 to give the desired products in moderate to good yields with wide substrate scope and good functional group tolerance, serving as an attractive alternative or complement to the previously reported methods for the facile assembly of biologically and pharmaceutically active 3,4-dihydropyrimidin-2(1*H*)-ones.

1. Introduction

3,4-Dihydropyrimidin-2(1*H*)-ones (DHPMs) are pivotal structural skeletons which widely exist in a variety of natural products[1] and bioactive molecules.[2] These compounds exhibit a wide range of biologically and pharmaceutically relevant activities, such as antibacterial, antitumour, antiviral, antimalarial, antidiabetic, and antiepileptic activities.[2] Normally, 3,4-dihydropyrimidin-2(1*H*)-one could be accessed *via* the Biginelli reaction of aldehyde with ethyl acetoacetate and urea.[3,4] With more than one century of development, tremendous achievements have been made in the Biginelli reaction, especially in the field of organic synthesis, medicinal chemistry, polymer chemistry, and material sciences.[4,5] In addition, the variants of the Biginelli reaction by using other active methylene compounds (or their equivalents), such as 1,3-cyclohexanedione,[6] acetophenone,[7] 1-tetralone,[8] β-oxodithioesters,[9] enaminone,[10] cyclopentanone,[11] alkyl aldehydes,[12] and alkynol,[13] to replace ethyl acetoacetate for accessing diverse 3,4-dihydropyrimidin-2(1*H*)-ones have also been reported. Normally, the Biginelli or Biginelli-like reaction should be performed under acidic conditions in the presence of protic or Lewis acid.[3–5] In 2010, Ji and co-workers reported an efficient method for the synthesis of 4,5,6-triaryl-3,4-dihydropyrimidin-2(1*H*)-ones *via* a three-component Biginelli-type condensation of aldehyde with 2-phenylacetophenone and urea/thiourea under basic conditions in the presence of *t*-BuOK.[14] In the studies, it was observed that the reaction using urea as substrate might proceed *via* the formation of 1,1′-(arylmethylene)diurea as reaction intermediate. Apart from this study, the direct use of pre-prepared 1,1′-(arylmethylene)diurea for the synthesis of 3,4-dihydropyrimidin-2(1*H*)-one has been rarely investigated. In continuation of our interests in the synthesis of heterocycles, herein we report a cesium carbonate-promoted[15] direct condensation of 1-aryl-2-

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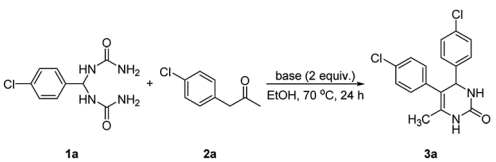
† Electronic supplementary information (ESI) available: Experimental procedures and spectroscopic data of all compounds. See DOI: 10.1039/d0ra05480a

Table 1 Optimization of reaction conditions by using different bases

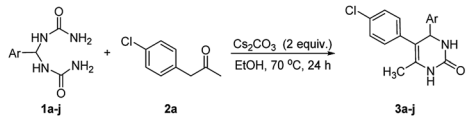


1a 2a 3a

Entry	Base	Yield[a] (%)
1	Pyridine	0
2	DABCO	0
3	DBU	0
4	K_2CO_3	51
5	KOH	60
6	*t*-BuOK	61
7	**Cs_2CO_3**	**75**
8	Cs_2CO_3	22[b]

[a] Isolated yield. [b] Using 0.2 equivalents of Cs_2CO_3.

Table 2 Substrate scope study by using different diureas



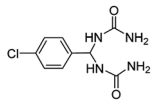
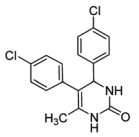
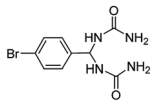
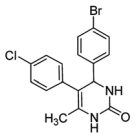
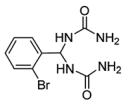
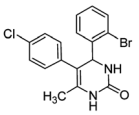
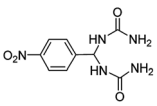
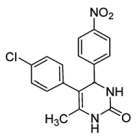
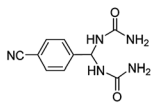
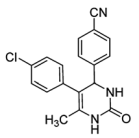
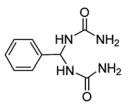
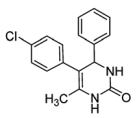
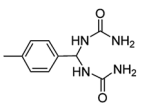
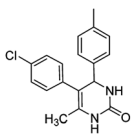
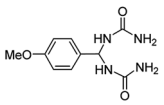
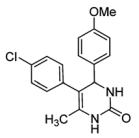
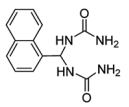
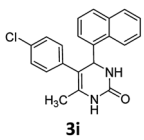
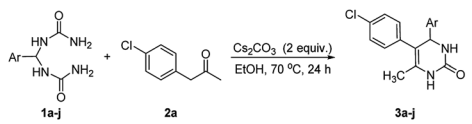
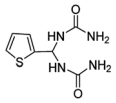
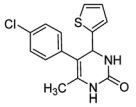
Entry	Diurea **1**	Product **3**	Yield[a] (%)
1	 **1a**	 **3a**	75
2	 **1b**	 **3b**	86
3	 **1c**	 **3c**	67
4	 **1d**	 **3d**	50[b]
5	 **1e**	 **3e**	50
6	 **1f**	 **3f**	65
7	 **1g**	 **3g**	76
8	 **1h**	 **3h**	73
9	 **1i**	 **3i**	64

Table 2 (*Contd.*)



Entry	Diurea **1**	Product **3**	Yield[a] (%)
10	 **1j**	 **3j**	85

[a] Isolated yield. [b] The reaction was performed in *t*-BuOH instead of EtOH at 100 °C.

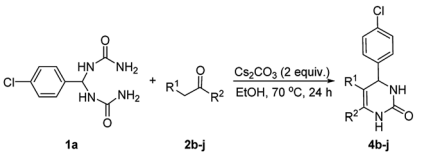
propanone with pre-synthesized 1,1′-(arylmethylene)diurea, leading to the corresponding 4,5-diaryl-3,4-dihydropyrimidin-2(1*H*)-one in moderate to good yields.

2. Results and discussion

To begin with, we chose 1,1′-((4-chlorophenyl)methylene)diurea (**1a**) and 1-(4-chlorophenyl)propan-2-one (**2a**) as model substrates to optimize the reaction conditions by performing the reaction in ethanol at 70 °C for 24 h in the presence of different bases. As shown in Table 1, no desired 4,5-diaryl-3,4-dihydropyrimidin-2(1*H*)-one **3a** was produced when the reaction was performed in the presence of organic bases (entries 1–3). In sharp contrast, the use of inorganic bases (entries 4–7) as reaction promoters were found to promote the condensation with varying performance, with the highest yield (75% yield) being obtained by using Cs_2CO_3 as reaction promoter (entry 7). However, when only a catalytic amount of Cs_2CO_3 (0.2 equiv.) was employed in the reaction, the product yield decreased considerably (entry 8). It should be mentioned that, when D-camphorsulfonic acid (CSA) was introduced into the reaction as a promoter, the corresponding product **3a** could also be obtained, albeit in a relatively poor yield of 32%. In addition, it should be noted that an alternative method for the synthesis of product **3a** *via* the three-component reaction involving 4-chlorobenzaldehyde (0.5 mmol, 1 equiv.), 1-(4-chlorophenyl) propan-2-one (**2a**, 1.2 equiv.), and urea (2 equiv.) proceeded sluggishly in the presence of Cs_2CO_3 (2 equiv.) in ethanol (70 °C, 24 h), leading to the corresponding product **3a** only in 3% yield.

With Cs_2CO_3 being recognized as the optimum base for the condensation, subsequently we investigated the substrate scope of the reaction by using a range of diureas **1a–j** as starting materials. As summarized in Table 2, a variety of aryl substituted diureas could efficiently undergo the intermolecular cyclization under the optimized conditions to afford the expected 4,5-diaryl-3,4-dihydropyrimidin-2(1*H*)-one **3a–j** in 50–86% yields. In addition to phenyl-substituted diureas

Table 3 Substrate scope study by using various ketones



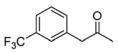
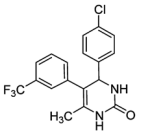
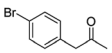
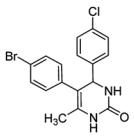
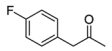
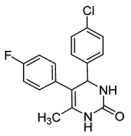
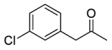
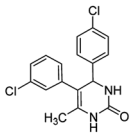
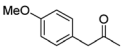
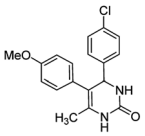
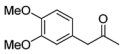
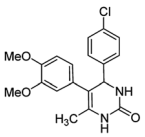
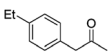
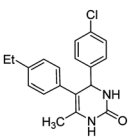
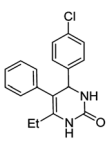
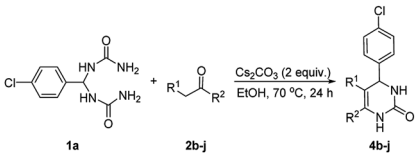
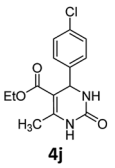
Entry	Ketone **2**	Product **4**	Yield[a] (%)
1	 **2b**	 **4b**	72
2	 **2c**	 **4c**	79
3	 **2d**	 **4d**	88
4	 **2e**	 **4e**	94
5	 **2f**	 **4f**	85
6	 **2g**	 **4g**	89
7	 **2h**	 **4h**	90
8	 **2i**	 **4i**	65

Table 3 (*Contd.*)



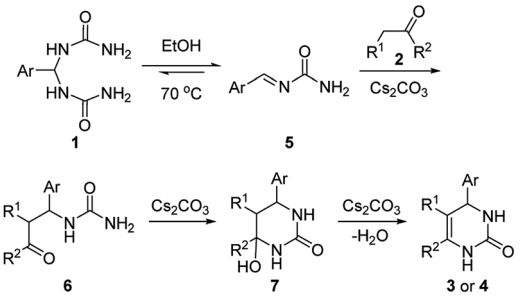
Entry	Ketone **2**	Product **4**	Yield[a] (%)
9	 **2j**	 **4j**	26

[a] Isolated yield.

1a–h, diureas **1i–j** containing naphthenyl and thienyl substituents also efficiently participated in the organic transformation, leading to the anticipated products **3i** and **3j** in 64% and 85% yields, respectively. Especially noteworthy is that, the mild reaction conditions also allowed the reaction to proceed with the tolerance to various functional groups or substituents (*e.g.*, halogen, nitro, cyano, methyl, and methoxy) in the phenyl ring, which could potentially be utilized at a late stage.

Encouraged by the above results, we continued to study the generality of the reaction by utilizing an array of phenylacetones **2b–i** as substrates (Table 3). In all cases, the reactions proceeded efficiently under well-established conditions to deliver the expected products **4b–i** in moderate to good yields. Apart from 1-aryl-2-propanones **2b–e** bearing electron-withdrawing groups which well reacted with substrate **1a** (entries 1–4), substrates **2f–h** possessing electron-donating groups in the aryl ring of 1-aryl-2-propanones were also proven to be suitable candidates for the transformation, giving rise to the desired products **4f–h** in excellent yields (85–90% yields; entries 5–7). In a same manner, 1-phenylbutan-2-one (**2i**) could also be applied in the protocol, furnishing the corresponding product **4i** in 65% yield (entry 8). Moreover, the method could also be applied to the use of ethyl acetoacetate (**2j**) as substrate, albeit in a relatively low yield of 26% (entry 9). Analogously, the reaction also showed good compatibility to different functional groups or substituents, including trifluoromethyl, halogen, and methoxy group.

Mechanistically, the reaction might proceed *via* the initial formation of an imine-type intermediate **5**, which subsequently reacts with 1-aryl-2-propanone **2** in the presence of Cs_2CO_3 leading to compound **6** (Scheme 1).[14] Finally, an ensuing intramolecular cyclization followed by elimination of a hydroxyl group under basic conditions produces the desired product **3** and **4**.



Scheme 1 Proposed mechanism.

3. Conclusions

In summary, we have developed an efficient method for the synthesis of 4,5-diaryl-3,4-dihydropyrimidin-2(1*H*)-one by using 1,1′-(arylmethylene)diurea and 1-aryl-2-propanone as substrates. The reactions proceeded efficiently in the presence of Cs_2CO_3, leading to the desired products in moderate to good yields. The transformation exhibited wide substrate scope and good tolerance to various important functional groups or substituents. We believed that the present protocol employing readily available and pre-synthesized diurea as substrate should serve as an attractive alternative or complement to the existing methods for the facile generation of biologically and pharmaceutically active 3,4-dihydropyrimidin-2(1*H*)-ones.

4. Experimental

4.1 General information

1-Aryl-2-propanone, cesium carbonate, and ethanol were purchased from chemical companies and used directly without further purification (without the need of precautions to exclude air and moisture unless otherwise noted). Starting materials **1a–j** were prepared according to reported methods.[16] Analytical thin layer chromatography (TLC) was performed using silica gel plate (0.2 mm thickness). Subsequent to elution, plates were visualized using UV radiation (254 nm). Flash chromatography was performed using Merck silica gel (200–300 mesh) for column chromatography with freshly distilled solvents. Columns were typically packed as slurry and equilibrated with the appropriate solvent system prior to use. IR spectra were recorded on a FT-IR spectrophotometer using KBr optics. ^{1}H, ^{19}F, and ^{13}C NMR spectra were recorded in d^6-DMSO on Jeol 400 MHz spectrometer. Tetramethylsilane (TMS) served as internal standard for ^{1}H, ^{19}F, and ^{13}C NMR analysis.

4.2 Experimental procedure

General procedure for the preparation of 1,1′-(arylmethylene)diurea:.[16] To a 250 mL round-bottomed flask was sequentially added aryl aldehyde (30 mmol), urea (90 mmol), a catalytic amount of *p*-toluenesulfonic acid (3 mmol) and toluene (100 mL). The reaction mixture was refluxed for overnight. After reaction, the precipitate was collected by filtration, washed with saturated $NaHCO_3$ (10 mL), pure water (20 mL), and Et_2O (20 mL). It was further dried in oven at 120 °C for half an hour to give the desired product of diurea.

Typical procedure for the condensation of 1,1′-(arylmethylene)diurea with 1-aryl-2-propanone. To a mixture of diurea (0.5 mmol) and 1-aryl-2-propanone (0.6 mmol) was added absolute ethanol (3 mL), and it was stirred at room temperature for 5 minutes. Then Cs_2CO_3 (1 mmol) was added and the reaction mixture was stirred vigorously at 70 °C for 24 h. After the completion of the reaction, solvent was removed under vacuum. The residue was purified by silica gel column chromatography by using EtOAc/petroleum ether or CH_2Cl_2/MeOH as eluant to afford the desired product of 4,5-biaryl-3,4-dihydropyrimidin-2(1*H*)-one.

4.3 Characterization data of products

1,1′-((4-Chlorophenyl)methylene)diurea (1a). 6.6 g. Yield = 91%. White solid. Mp: 190.5–191.2 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.40 (d, J = 8.5 Hz, 2H), 7.32 (d, J = 8.5 Hz, 2H), 6.79 (d, J = 8.3 Hz, 2H), 6.08 (t, J = 8.3 Hz, 1H), 5.72 (s, 4H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 157.8, 141.9, 131.6, 128.1, 128.0, 58.6 ppm. FTIR (KBr, neat): ν 3453, 3312, 1667, 1608, 866, 817 cm^{-1}. HRMS (ESI, *m*/*z*): [M + H]$^+$, calcd for $C_9H_{12}ClN_4O_2$: 243.0643, found: 243.0643.

1,1′-((4-Bromophenyl)methylene)diurea (1b). 4.4 g. Yield = 51%. White solid. Mp: 206.6–207.5 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.53 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.4 Hz, 2H), 6.79 (d, J = 8.3 Hz, 2H), 6.06 (t, J = 8.3 Hz, 1H), 5.72 (s, 4H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.2, 142.8, 131.4, 128.8, 120.5, 59.1 ppm. FTIR (KBr, neat): ν 3453, 3312, 1667, 1608, 866, 813 cm^{-1}. HRMS (ESI, *m*/*z*): [M + H]$^+$, calcd for $C_9H_{12}BrN_4O_2$: 287.0138, found: 287.0137.

1,1′-((2-Bromophenyl)methylene)diurea (1c). 6.3 g. Yield = 73%. White solid. Mp: 199.2–199.7 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.60 (d, J = 7.8 Hz, 1H), 7.52 (d, J = 6.7 Hz, 1H), 7.40 (t, J = 7.4 Hz, 1H), 7.23 (t, J = 7.0 Hz, 1H), 6.71 (d, J = 6.9 Hz, 2H), 6.25 (t, J = 7.5 Hz, 1H), 5.63 (s, 4H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 157.4, 141.2, 132.7, 129.4, 128.0, 127.5, 122.4, 59.6 ppm. FTIR (KBr, neat): ν 3430, 3331, 1668, 1612, 750, 719 cm^{-1}. HRMS (ESI, *m*/*z*): [M + H]$^+$, calcd for $C_9H_{12}BrN_4O_2$: 287.0138, found: 287.0140.

1,1′-((4-Nitrophenyl)methylene)diurea (1d). 6.7 g. Yield = 88%. White solid. Mp: 209.8–210.4 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.21 (d, J = 8.8 Hz, 2H), 7.56 (d, J = 8.6 Hz, 2H), 6.98 (d, J = 8.3 Hz, 2H), 6.17 (t, J = 8.2 Hz, 1H), 5.82 (s, 4H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 157.8, 150.8, 146.5, 127.4, 123.4, 58.8 ppm. FTIR (KBr, neat): ν 3459, 3312, 1682, 1516, 1351, 856, 835 cm^{-1}. HRMS (ESI, *m*/*z*): [M + H]$^+$, calcd for $C_9H_{12}N_5O_4$: 254.0884, found: 254.0881.

1,1′-((4-Cyanophenyl)methylene)diurea (1e). 6.3 g. Yield = 90%. White solid. Mp: 222.6–222.9 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.82 (d, J = 8.1 Hz, 2H), 7.49 (d, J = 8.3 Hz, 2H), 6.90 (d, J = 8.2 Hz, 2H), 6.12 (t, J = 8.1 Hz, 1H), 5.76 (s, 4H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.2, 149.1, 132.6, 127.6, 119.5, 110.1, 59.3 ppm. FTIR (KBr, neat): ν 3352, 3300, 2234, 1656, 862, 825 cm^{-1}. HRMS (ESI, *m*/*z*): [M + H]$^+$, calcd for $C_{10}H_{12}N_5O_2$: 234.0986, found: 234.0987.

1,1′-(Phenylmethylene)diurea (1f). 4.0 g. Yield = 64%. White solid. Mp: 190.6–191.2 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.34–7.31 (m, 4H), 7.27–7.23 (m, 1H), 6.72 (d, J = 8.3 Hz, 2H), 6.12 (t, J = 8.3 Hz, 1H), 5.68 (s, 4H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.2, 143.2, 128.6, 127.6, 126.5, 59.6 ppm. FTIR (KBr, neat): ν 3420, 3312, 1667, 1535, 747, 699 cm^{-1}. HRMS (ESI, m/z): [M + H]$^+$, calcd for $C_9H_{13}N_4O_2$: 209.1033, found: 209.1033.

1,1′-(*p*-Tolylmethylene)diurea (1g). 3.7 g. Yield = 55%. White solid. Mp: 196.2–196.8 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.20 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.1 Hz, 2H), 6.67 (d, J = 8.1 Hz, 2H), 6.08 (t, J = 8.3 Hz, 1H), 5.67 (s, 4H), 2.28 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.2, 140.2, 136.6, 129.1, 126.4, 59.4, 21.2 ppm. FTIR (KBr, neat): ν 3458, 3312, 1678, 1532, 864, 814 cm^{-1}. HRMS (ESI, m/z): [M + H]$^+$, calcd for $C_{10}H_{15}N_4O_2$: 223.1190, found: 223.1191.

1,1′-((4-Methoxyphenyl)methylene)diurea (1h). 5.2 g. Yield = 73%. White solid. Mp: 186.6–187.3 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.24 (d, J = 8.6 Hz, 2H), 6.90 (d, J = 8.7 Hz, 2H), 6.70 (d, J = 8.0 Hz, 2H), 6.09 (t, J = 8.1 Hz, 1H), 5.70 (s, 4H), 3.73 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.9, 158.3, 135.1, 127.7, 114.0, 59.2, 55.6 ppm. FTIR (KBr, neat): ν 3428, 3308, 1671, 1515, 1261, 1176, 865, 836 cm^{-1}. HRMS (ESI, m/z): [M + H]$^+$, calcd for $C_{10}H_{15}N_4O_3$: 239.1139, found: 239.1134.

1,1′-(Naphthalen-1-ylmethylene)diurea (1i). 6.8 g. Yield = 88%. White solid. Mp: 221.5–222.7 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.02 (d, J = 8.0 Hz, 1H), 7.96 (d, J = 7.4 Hz, 1H), 7.87 (d, J = 8.1 Hz, 1H), 7.64–7.47 (m, 4H), 6.91 (t, J = 7.8 Hz, 1H), 6.82 (d, J = 7.7 Hz, 2H), 5.66 (s, 4H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 157.4, 138.1, 133.5, 130.3, 128.6, 128.0, 126.3, 125.8, 125.2, 123.4, 122.6, 56.5 ppm. FTIR (KBr, neat): ν 3418, 3297, 1667, 1608, 882, 770 cm^{-1}. HRMS (ESI, m/z): [M + H]$^+$, calcd for $C_{13}H_{15}N_4O_2$: 259.1190, found: 259.1189.

1,1′-(Thiophen-2-ylmethylene)diurea (1j). 4.2 g. Yield = 65%. White solid. Mp: 197.4–198.9 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.41–7.35 (m, 1H), 6.96 (dd, J = 5.0, 3.5 Hz, 1H), 6.91–6.88 (m, 1H), 6.86 (d, J = 8.5 Hz, 2H), 6.32 (t, J = 8.4 Hz, 1H), 5.75 (s, 4H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 157.5, 147.7, 126.8, 124.9, 123.7, 56.2 ppm. FTIR (KBr, neat): ν 3467, 3284, 1671, 1589, 1282, 1123 cm^{-1}. HRMS (ESI, m/z): [M + H]$^+$, calcd for $C_7H_{11}N_4O_2S$: 215.0597, found: 215.0602.

4,5-*bis*(4-Chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (3a). 124.6 mg. Yield = 75%. Yellow solid. Mp: 214.7–215.8 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.50 (s, 1H), 7.38 (s, 1H), 7.35–7.31 (m, 2H), 7.30–7.26 (m, 2H), 7.18–7.14 (m, 2H), 7.11–7.06 (m, 2H), 5.13 (s, 1H), 1.73 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.8, 143.0, 136.7, 131.8, 131.2, 130.9, 130.8, 128.7, 128.4, 128.1, 106.8, 58.5, 16.2 ppm. FTIR (KBr, neat): ν 3265, 1693, 1491, 1241, 1091, 758 cm^{-1}. HRMS (ESI, m/z): [M + H]$^+$, calcd for $C_{17}H_{15}Cl_2N_2O$: 333.0556, found: 333.0558.

4-(4-Bromophenyl)-5-(4-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (3b). 161.6 mg. Yield = 86%. Brown solid. Mp: 206.8–208.2 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.51 (s, 1H), 7.46 (d, J = 8.3 Hz, 2H), 7.39 (s, 1H), 7.30–7.24 (m, 2H), 7.14–7.05 (m, 4H), 5.12 (s, 1H), 1.73 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.8, 143.4, 136.7, 131.3, 131.2, 130.9, 130.8, 129.1, 128.1, 120.4, 106.7, 58.6, 16.2 ppm. FTIR (KBr, neat): ν 3268, 1693, 1489, 1241, 757 cm^{-1}. HRMS (ESI, m/z): [M + H]$^+$, calcd for $C_{17}H_{15}BrClN_2O$: 377.0051, found: 377.0051.

4-(2-Bromophenyl)-5-(4-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (3c). 126.8 mg. Yield = 67%. Yellow solid. Mp: 189.8–191.3 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.56 (s, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.40–7.33 (m, 2H), 7.24 (d, J = 8.2 Hz, 2H), 7.13 (t, J = 7.2 Hz, 1H), 7.01 (d, J = 8.3 Hz, 2H), 5.58 (s, 1H), 1.69 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.5, 142.6, 136.2, 132.6, 131.3, 131.1, 131.0, 129.9, 129.5, 128.5, 128.1, 121.9, 106.3, 58.6, 16.1 ppm. FTIR (KBr, neat): ν 3220, 1694, 1493, 1253, 1095, 737 cm^{-1}. HRMS (ESI, m/z): [M + H]$^+$, calcd for $C_{17}H_{15}BrClN_2O$: 377.0051, found: 377.0050.

5-(4-Chlorophenyl)-6-methyl-4-(4-nitrophenyl)-3,4-dihydropyrimidin-2(1*H*)-one (3d). 88.8 mg. Yield = 50%. Brown solid. Mp: 200.2–201.7 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.51 (s, 1H), 7.44–7.37 (m, 3H), 7.35–7.30 (m, 2H), 7.16 (d, J = 8.3 Hz, 2H), 7.02 (d, J = 8.3 Hz, 2H), 5.13 (s, 1H), 1.73 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.8, 148.5, 136.6, 131.1, 131.0, 130.8, 128.1, 126.6, 125.3, 124.4, 107.4, 54.2, 16.3 ppm. FTIR (KBr, neat): ν 2926, 1721, 1491, 1262, 1093, 1014, 831 cm^{-1}. HRMS (ESI, m/z): [M + H]$^+$, calcd for $C_{17}H_{15}ClN_3O_3$: 344.0796, found: 344.0799.

4-(5-(4-Chlorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidin-4-yl)benzonitrile (3e). 80.3 mg. Yield = 50%. Yellow solid. Mp: 249.3–250.6 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.57 (s, 1H), 7.78–7.72 (m, 2H), 7.47 (s, 1H), 7.33–7.30 (m, 2H), 7.30–7.26 (m, 2H), 7.11–7.06 (m, 2H), 5.24 (s, 1H), 1.73 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.7, 149.3, 136.4, 132.6, 131.3, 131.2, 130.9, 128.2, 127.8, 118.8, 110.1, 106.2, 58.8, 16.2 ppm. FTIR (KBr, neat): ν 3397, 2226, 1679, 1475, 1242, 759 cm^{-1}. HRMS (ESI, m/z): [M + H]$^+$, calcd for $C_{18}H_{15}ClN_3O$: 324.0898, found: 324.0904.

5-(4-Chlorophenyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (3f). 97.4 mg. Yield = 65%. Light yellow solid. Mp: 179.6–180.1 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.45 (s, 1H), 7.34 (s, 1H), 7.29–7.23 (m, 4H), 7.22–7.18 (m, 1H), 7.16 (d, J = 7.9 Hz, 2H), 7.10–7.05 (m, 2H), 5.08 (s, 1H), 1.74 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 153.0, 144.0, 137.0, 131.1, 130.7, 130.7, 128.5, 128.1, 127.3, 126.8, 107.1, 59.2, 16.3 ppm. FTIR (KBr, neat): ν 3055, 1690, 1493, 1014, 744, 698 cm^{-1}. HRMS (ESI, m/z): [M + H]$^+$, calcd for $C_{17}H_{16}ClN_2O$: 299.0946, found: 299.0947.

5-(4-Chlorophenyl)-6-methyl-4-(*p*-tolyl)-3,4-dihydropyrimidin-2(1*H*)-one (3g). 118.2 mg. Yield = 76%. Light yellow solid. Mp: 215.6–216.8 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.44 (s, 1H), 7.30–7.24 (m, 3H), 7.10–7.03 (m, 6H), 5.04 (s, 1H), 2.23 (s, 3H), 1.74 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.9, 141.1, 137.1, 136.4, 131.1, 130.6, 130.5, 129.0, 128.1, 126.8, 107.2, 58.9, 20.7, 16.3 ppm. FTIR (KBr, neat): ν 3271, 1694, 1491, 1241, 832, cm^{-1}. HRMS (ESI, m/z): [M + H]$^+$, calcd for $C_{18}H_{18}ClN_2O$: 313.1102, found: 313.1102.

5-(4-Chlorophenyl)-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (3h). 120.0 mg. Yield = 73%. Yellow solid. Mp: 161.8–163.2 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.42 (s, 1H), 7.29–7.24 (m, 3H), 7.10–7.06 (m, 4H), 6.85–6.80 (m, 2H), 5.02 (s, 1H), 3.69 (s, 3H), 1.74 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.5, 152.9, 137.1, 136.2, 131.1, 130.6, 130.5,

128.1, 128.0, 113.8, 107.3, 58.6, 55.0, 16.3 ppm. FTIR (KBr, neat): ν 3238, 1679, 1510, 1248, 1174, 834 cm^{-1}. HRMS (ESI, *m*/*z*): $[M + H]^+$, calcd for $C_{18}H_{18}ClN_2O_2$: 329.1051, found: 329.1054.

5-(4-Chlorophenyl)-6-methyl-4-(naphthalen-1-yl)-3,4-dihydropyrimidin-2(1*H*)-one (3i). 112.3 mg. Yield = 64%. Light yellow solid. Mp: 250.4–251.6 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.58 (s, 1H), 8.29–8.19 (m, 1H), 7.92–7.86 (m, 1H), 7.82–7.75 (m, 1H), 7.53–7.40 (m, 4H), 7.36 (s, 1H), 7.15 (d, J = 7.8 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 5.99 (s, 1H), 1.81 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.7, 148.0, 144.0, 138.7, 136.9, 133.7, 131.1, 131.0, 130.6, 130.4, 128.6, 128.1, 127.9, 126.0, 125.9, 125.6, 123.6, 106.8, 16.3 ppm. FTIR (KBr, neat): ν 3230, 1703, 1493, 1253, 776 cm^{-1}. HRMS (ESI, *m*/*z*): $[M + H]^+$, calcd for $C_{21}H_{18}ClN_2O$: 349.1102, found: 349.1103.

5-(4-Chlorophenyl)-6-methyl-4-(thiophen-2-yl)-3,4-dihydropyrimidin-2(1*H*)-one (3j). 128.8 mg. Yield = 85%. Light yellow solid. Mp: 193.2–194.4 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.63 (s, 1H), 7.55 (s, 1H), 7.35 (dd, J = 5.0, 1.1 Hz, 1H), 7.33–7.28 (m, 2H), 7.21–7.14 (m, 2H), 6.87 (dd, J = 5.0, 3.5 Hz, 1H), 6.82–6.77 (m, 1H), 5.39 (s, 1H), 1.76 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.9, 148.5, 136.6, 131.1, 131.1, 130.8, 128.1, 126.6, 125.3, 124.4, 107.5, 54.2, 16.3 ppm. FTIR (KBr, neat): ν 3244, 1686, 1490, 1389, 1247, 1091, 839, 698 cm^{-1}. HRMS (ESI, *m*/*z*): $[M + H]^+$, calcd for $C_{15}H_{14}ClN_2OS$: 305.0510, found: 305.0509.

4-(4-Chlorophenyl)-6-methyl-5-(3-(trifluoromethyl)phenyl)-3,4-dihydropyrimidin-2(1*H*)-one (4b). 132.6 mg. Yield = 72%. Yellow solid. Mp: 109.8–110.4 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.60 (s, 1H), 7.51–7.42 (m, 3H), 7.40–7.31 (m, 4H), 7.23–7.14 (m, 2H), 5.22 (s, 1H), 1.74 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.7, 142.9, 139.0, 133.6, 131.9, 131.7, 129.2, 129.0 (q, J = 31.3 Hz), 128.8, 128.5, 125.7 (q, J = 3.8 Hz), 124.2 (q, J = 271.0 Hz), 123.0 (q, J = 4.1 Hz), 106.6, 58.4, 16.2 ppm. ^{19}F NMR (376 MHz, DMSO-d_6): δ −60.98 ppm. FTIR (KBr, neat): ν 3238, 1683, 1490, 1339, 1126, 804, 704 cm^{-1}. HRMS (ESI, *m*/*z*): $[M + H]^+$, calcd for $C_{18}H_{15}ClF_3N_2O$: 367.0820, found: 367.0822.

5-(4-Bromophenyl)-4-(4-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4c). 149.6 mg. Yield = 79%. Light yellow solid. Mp: 209.5–209.8 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.51 (s, 1H), 7.42–7.37 (m, 3H), 7.35–7.30 (m, 2H), 7.18–7.14 (m, 2H), 7.04–7.00 (m, 2H), 5.12 (s, 1H), 1.73 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.8, 143.0, 137.1, 131.8, 131.5, 131.0, 130.9, 128.7, 128.4, 119.3, 106.8, 58.4, 16.2 ppm. FTIR (KBr, neat): ν 3269, 1692, 1490, 1240, 1099, 844, 778 cm^{-1}. HRMS (ESI, *m*/*z*): $[M + H]^+$, calcd for $C_{17}H_{15}BrClN_2O$: 377.0051, found: 377.0050.

4-(4-Chlorophenyl)-5-(4-fluorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4d). 139.5 mg. Yield = 88%. Yellow solid. Mp: 189.0–190.2 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.46 (s, 1H), 7.35 (s, 1H), 7.34–7.31 (m, 2H), 7.18–7.14 (m, 2H), 7.11–7.02 (m, 4H), 5.10 (s, 1H), 1.71 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.6 (d, J = 241.7 Hz), 152.8, 143.0, 134.1 (d, J = 3.3 Hz), 131.7, 131.3 (d, J = 8.0 Hz), 130.4, 128.7, 128.4, 115.0 (d, J = 21.1 Hz), 107.0, 58.8, 16.2 ppm. ^{19}F NMR (376 MHz, DMSO-d_6): δ −115.91 ppm. FTIR (KBr, neat): ν 3259, 1694, 1491, 1242, 1094, 1014, 845, 780 cm^{-1}. HRMS (ESI, *m*/*z*): $[M + H]^+$, calcd for $C_{17}H_{15}ClFN_2O$: 317.0851, found: 317.0851.

5-(3-Chlorophenyl)-4-(4-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4e). 155.9 mg. Yield = 94%. Yellow solid. Mp: 93.8–95.3 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.59 (s, 1H), 7.45 (s, 1H), 7.32–7.29 (m, 2H), 7.22–7.15 (m, 4H), 7.11 (s, 1H), 7.04–6.98 (m, 1H), 5.17 (s, 1H), 1.75 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 153.1, 142.9, 140.2, 133.0, 132.1, 131.5, 130.1, 129.1, 128.9, 128.6, 128.3, 126.4, 107.0, 58.6, 16.4 ppm. FTIR (KBr, neat): ν 3236, 1682, 1489, 1239, 1091, 785 cm^{-1}. HRMS (ESI, *m*/*z*): $[M + H]^+$, calcd for $C_{17}H_{15}Cl_2N_2O$: 333.0556, found: 333.0556.

4-(4-Chlorophenyl)-5-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4f). 140.5 mg. Yield = 85%. Yellow solid. Mp: 184.6–186.2 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.42 (s, 1H), 7.35–7.29 (m, 3H), 7.19–7.14 (m, 2H), 6.99–6.94 (m, 2H), 6.82–6.76 (m, 2H), 5.07 (s, 1H), 3.68 (s, 3H), 1.71 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 157.6, 153.1, 143.3, 131.7, 130.5, 129.8, 129.6, 128.7, 128.3, 113.6, 107.7, 58.9, 54.9, 16.2 ppm. FTIR (KBr, neat): ν 3259, 2924, 1693, 1489, 1249, 842 cm^{-1}. HRMS (ESI, *m*/*z*): $[M + H]^+$, calcd for $C_{18}H_{18}ClN_2O_2$: 329.1051, found: 329.1051.

4-(4-Chlorophenyl)-5-(3,4-dimethoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4g). 160.4 mg. Yield = 89%. Yellow solid. Mp: 151.6–152.7 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.36 (s, 1H), 7.34–7.29 (m, 3H), 7.19–7.15 (m, 2H), 6.78 (d, J = 8.3 Hz, 1H), 6.63 (d, J = 2.0 Hz, 1H), 6.50 (dd, J = 8.2, 2.0 Hz, 1H), 5.10 (s, 1H), 3.67 (s, 3H), 3.64 (s, 3H), 1.73 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 153.0, 148.2, 147.2, 143.4, 131.6, 130.2, 129.6, 128.8, 128.3, 121.9, 113.0, 111.4, 108.0, 58.9, 55.4, 55.3, 16.3 ppm. FTIR (KBr, neat): ν 3343, 1698, 1515, 1457, 1251, 1135, 1011, 766 cm^{-1}. HRMS (ESI, *m*/*z*): $[M + H]^+$, calcd for $C_{19}H_{20}ClN_2O_3$: 359.1157, found: 359.1159.

4-(4-Chlorophenyl)-5-(4-ethylphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4h). 146.5 mg. Yield = 90%. Yellow solid. Mp: 229.8–231.2 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.40 (s, 1H), 7.35–7.29 (m, 3H), 7.19–7.14 (m, 2H), 7.06 (d, J = 8.2 Hz, 2H), 6.97 (d, J = 8.2 Hz, 2H), 5.07 (s, 1H), 2.52 (q, J = 7.6 Hz, 2H), 1.73 (s, 3H), 1.12 (t, J = 7.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 153.0, 143.2, 141.6, 135.1, 131.7, 130.1, 129.2, 128.8, 128.4, 127.5, 107.8, 58.7, 27.7, 16.3, 15.3 ppm. FTIR (KBr, neat): ν 3223, 2928, 1686, 1241, 1088, 842 cm^{-1}. HRMS (ESI, *m*/*z*): $[M + H]^+$, calcd for $C_{19}H_{20}ClN_2O$: 327.1259, found: 327.1260.

4-(4-Chlorophenyl)-6-ethyl-5-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (4i). 101.8 mg. Yield = 65%. Yellow solid. Mp: 184.8–185.7 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.41 (s, 1H), 7.34–7.30 (m, 3H), 7.23 (t, J = 7.4 Hz, 2H), 7.17–7.12 (m, 3H), 7.03–6.98 (m, 2H), 5.05 (d, J = 2.5 Hz, 1H), 2.04–1.94 (m, 2H), 1.03 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 153.2, 143.1, 137.9, 135.5, 131.7, 129.3, 128.7, 128.4, 128.2, 126.5, 107.7, 59.0, 22.7, 13.0 ppm. FTIR (KBr, neat): ν 3235, 1679, 1489, 1227, 1091, 1014, 765, 701 cm^{-1}. HRMS (ESI, *m*/*z*): $[M + H]^+$, calcd for $C_{18}H_{18}ClN_2O$: 313.1102, found: 313.1102.

Ethyl 4-(4-chlorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4j). 38.2 mg. Yield = 26%. White solid. Mp: 212.3–213.6 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.25 (s, 1H), 7.78 (s, 1H), 7.39 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 5.14 (d, J = 3.2 Hz, 1H), 3.98 (q, J = 7.0 Hz, 2H), 2.24 (s, 3H),

1.09 (t, J = 7.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 165.3, 152.0, 148.8, 143.8, 131.8, 128.5, 128.3, 98.9, 59.3, 53.5, 17.9, 14.1 ppm. The characterization data of this product is in accordance with the reported ones.[17]

Conflicts of interest

The authors declare no conflict of interest.

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