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New three-component cyclocondensation reaction: microwave-assisted one-pot synthesis of 5-unsubstituted-3,4-dihydropyrimidin-2(1*H*)-ones under solvent-free conditions

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Abstract—Sixteen 5-unsubstituted-3,4-dihydropyrimidin-2(1*H*)-ones have been synthesized by microwave-assisted Biginelli reactions in a short and concise manner employing ZnI_2 as a catalyst under solvent-free conditions. All products were identified by IR, NMR, elemental analysis and HRMS. The advantages of this novel protocol include the excellent yield, operational simplicity, short time and the avoidance of the use of organic solvents and expensive catalysts.

1. Introduction

It is well known that 3,4-dihydropyrimidin-2-(1*H*)-ones (DHPMs) and their derivatives exhibit a wide range of biological activities, pharmaceutical and therapeutic properties, such as antiviral, antitumour, antibacterial and anti-inflammatory activities.[1–5] Therefore, the preparation of this heterocyclic nucleus has gained great importance in organic synthesis. The simple and direct method for the synthesis of DHPMs known as Biginelli reaction involves the one-pot condensation of an aldehyde, a β-ketoester and urea under strong acidic conditions, which was first reported by Biginelli in 1893.[6] However, the yields of products were very low (just 20–50%). From then on, many new techniques, such as microwave-assisted synthesis technique,[7] ionic liquids,[8] ultrasound irradiation,[9] solvent-free techniques[10] and many new catalysts, such as $InBr_3$,[11] $ZrCl_4$,[12] $CdCl_2$,[13] $BiCl_3$,[14] etc., were used to improve this transformation. In spite of their potential utility, many of these methods involve expensive reagents, strongly acidic conditions, long reaction times, high temperatures and stoichiometric amounts of catalysts and unsatisfactory yields. Furthermore, the scope of substrates was limited to aromatic aldehydes, acetoacetate (or acetylacetone) and urea or thiourea. The first Biginelli-like reaction, reported by Wang et al.,[15] was conducted in CH_3CN by using aldehydes, ketones and urea as substrates and $FeCl_3\cdot 6H_2O$ and TMSCl as catalysts, which remarkably broadened the Biginelli reaction. However, it suffered from its drawbacks, especially the use of highly toxic organic solvent (CH_3CN), long reaction time (12 h) and stoichiometric TMSCl.

With our continuous investigation on the methodology of green synthesis,[16] we report herein, for the first time, Biginelli-like reaction, i.e., three-component cyclocondensation of an aldehyde, acetophenone and urea, can be successfully accomplished by using inexpensive ZnI_2 as catalyst under solvent-free condition and microwave (MW) irradiation, which is an efficient and environmentally friendly preparation of 5-unsubstituted-3,4-dihydropyrimidin-2(1*H*)-ones.

2. Results and discussion

We first began to study the reaction involving benzaldehyde (5.0 mmol), acetophenone (5.0 mmol) and urea (6.0 mmol) by examining the type of catalysts (Scheme 1). Many catalysts or promoters, such as CH_3COOH, $Fe_2(SO_4)_3$, $(CH_3)_3SiCl$, $MgSO_4$, $Mg(ClO_4)_2$, HCl, H_2SO_4, etc., were used to explore the reaction under solvent-free,

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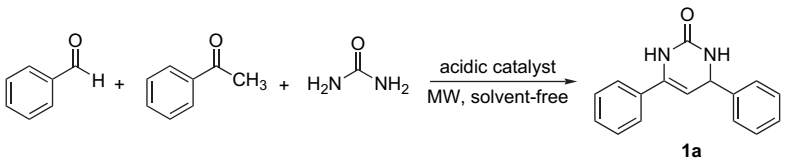


Scheme 1. Microwave-assisted Biginelli-like reactions by various catalysts under solvent-free conditions.

microwave-assisted conditions (Table 1, entries 1–12). From these results, we found that most of the Lewis acids and Brønsted acids could promote the reaction, but the yields were not so high. In comparison with other catalysts, the use of 1.5 mmol of ZnI_2 could make the yield reach 48% under the microwave power (*P*) of 525 W and the irradiation time of 5 min. From the results, we concluded that the reason for ZnI_2 being the best catalyst may be its strongly acidic character. The amount of ZnI_2 was further examined and the results are summarized in Table 1, entries 14–18. It could be seen that 20% molar amount of ZnI_2 gave the best result of this reaction, although other factors could not yet be optimized.

Based on the above optimized results, i.e., 20% molar amount of ZnI_2 as a catalyst, we further examined the effects of the microwave power and the irradiation time on the Biginelli-like reaction, involving 3-methoxyphenaldehyde, acetophenone and urea to afford DHPM **1b**, as shown in Scheme 2. The results are listed in Table 2. It could be found that with the increase of the microwave power from 75 W to 750 W, the yield of **1b** showed a linear increase from 10% to 78% when the irradiation time was 5 min. However, with the microwave power of 750 W, when we increased the microwave irradiation time, the yield of **1b** increased first, then showed a slight decrease when the time was more than 9 min. So the optimized microwave power and the irradiation time were 750 W and 8 min, respectively.

In order to examine the substrate scope of this Biginelli-like reaction, various aromatic aldehydes with different substituents were used under the above-optimized reaction conditions (Scheme 3); the results are shown in Table 3. From the results, we could see that all reactions proceeded smoothly to afford the corresponding DHPMs in moderate to high yields. We also found that all aromatic aldehydes carrying either electron-donating or electron-withdrawing substituents reacted efficiently to give improved yields compared to the classical Biginelli reaction. When some aliphatic aldehydes and all solid materials were used in this protocol under the above-optimized conditions, unfortunately, the expected products could not be obtained. Further investigations are underway.

Table 1. Effects of the type and the amount of catalysts on the formation of **1a**[a]

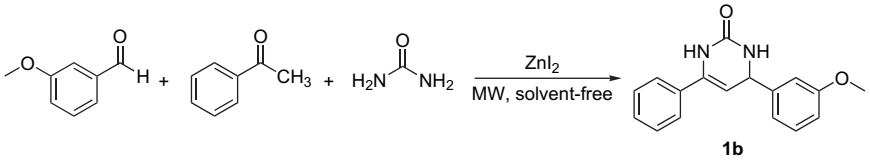
Entry	Catalyst (mmol)	*t* (min)	Yield[b] (%)
1	—	5	—
2	CH_3COOH (1.5)	5	32
3	HCl (1.5)	5	24
4	H_2SO_4 (1.5)	5	40
5	$Fe_2(SO_4)_3$ (1.5)	5	12
6	$FeCl_3$ (1.5)	5	30
7	$AlCl_3$ (1.5)	5	33
8	$(CH_3)_3SiCl$ (1.5)	5	1.6
9	$MgSO_4$ (1.5)	5	—
10	$Mg(ClO_4)_2$ (1.5)	5	24
11	ZnI_2 (1.5)	5	48
12	I_2 (1.5)	5	19
13	Al_2O_3 (1.5)	5	27
14	ZnI_2 (0.1)	5	11
15	ZnI_2 (0.5)	5	34
16	ZnI_2 (1.0)	5	49
17	ZnI_2 (1.2)	5	48
18	ZnI_2 (2.0)	5	47

[a] Reaction conditions: benzaldehyde 5.0 mmol; acetophenone 5.0 mmol; urea 6.0 mmol; *P*=525 W.
[b] Isolated yield.

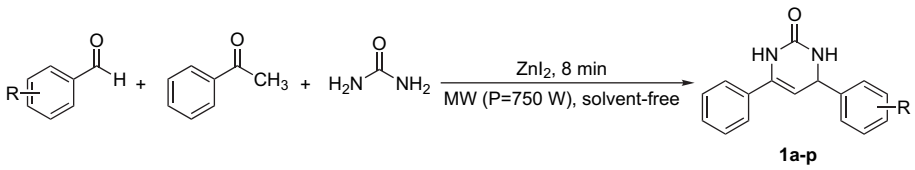
Table 2. Effects of the microwave power and the irradiation time on the formation of **1b**[a]

Entry	*t* (min)	*P* (W)	Yield[b] (%)
1	5	75	10
2	5	150	16
3	5	300	30
4	5	450	45
5	5	600	56
6	5	750	78
7	2	750	17
8	4	750	54
9	6	750	81
10	8	750	89
11	9	750	89
12	10	750	88

[a] Reaction conditions: 3-methoxyphenaldehyde 5.0 mmol; acetophenone 5.0 mmol; urea 6.0 mmol; ZnI_2 1.0 mmol.
[b] Isolated yield.



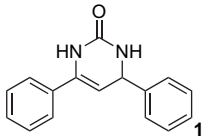
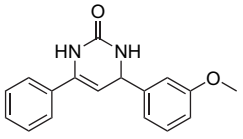
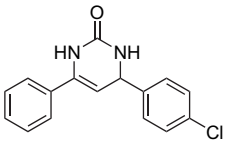
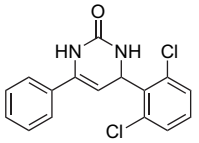
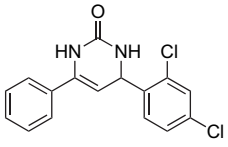
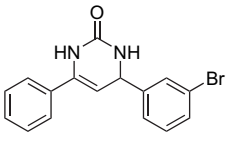
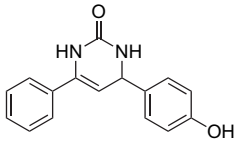
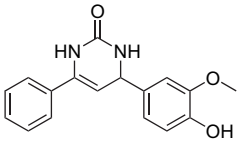
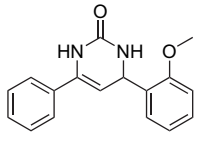
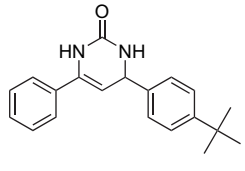
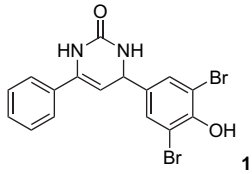
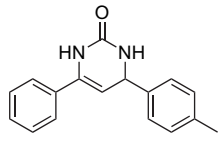
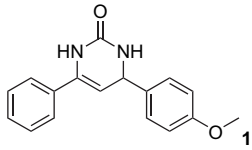
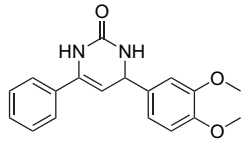
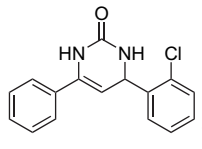
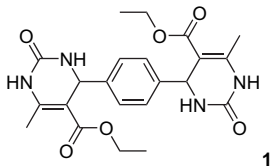
Scheme 2. Microwave-assisted Biginelli-like reactions catalyzed by ZnI_2 under solvent-free conditions.



Scheme 3. Microwave-assisted Biginelli-like reactions of various aromatic aldehydes.

It was noteworthy that highly symmetric Biginelli product **1p** was obtained with excellent yield when acetophenone was replaced by ethyl acetoacetate to react with *p*-phthalaldehyde and urea (Table 3, entry 16). The other Biginelli-like reactions including *p*-phthalaldehyde are under investigation and will be reported in our future work.

Table 3. Cyclocondensation of aromatic aldehydes, acetophenone and urea under microwave irradiation and solvent-free conditions[a]

Entry	R	Product	Yield[b] (%)
1	H	 **1a**	94
2	3-CH_3O	 **1b**	89
3	4-Cl	 **1c**	93
4	2,6-Dichloro	 **1d**	81
5	2,4-Dichloro	 **1e**	83
6	3-Br	 **1f**	88
7	4-OH	 **1g**	77
8	3-CH_3O-4-OH	 **1h**	80
9	2-CH_3O	 **1i**	75
10	4-$(CH_3)_3C$	 **1j**	74
11	3,5-Dibromo-4-OH	 **1k**	71
12	4-CH_3	 **1l**	92
13	4-CH_3O	 **1m**	87
14	3,4-Dimethoxyl	 **1n**	76
15	2-Cl	 **1o**	73
16[c]	4-CHO	 **1p**	96

[a] Reaction conditions: aromatic aldehydes 5.0 mmol; acetophenone 5.0 mmol; urea 6.0 mmol; ZnI_2 1.0 mmol; P=750 W.
[b] Isolated yield.
[c] Acetophenone was replaced by ethyl acetoacetate.

3. Conclusion

In conclusion, an efficient and high-yield protocol for the synthesis of 5-unsubstituted-3,4-dihydropyrimidin-2(1*H*)-ones involving three-component, one-pot condensation of an aromatic aldehyde, acetophenone and urea using ZnI_2 as catalyst under microwave irradiation and solvent-free conditions was developed. High efficiency, short reaction time, solvent-free condition and the use of inexpensive catalyst were the advantages of this protocol. The described procedure expanded the scope of the substrate and improved the yield of three-component Biginelli-like cyclocondensation reactions as compared to classical Biginelli reaction. It is believed that this versatile method applicable to parallel synthesis will be of great value for the rapid generation of structurally related compound libraries.

4. Experimental

4.1. General remarks

All reactions were performed under a nitrogen atmosphere with oven-dried glassware in the refitted stove.[17] All reactants were obtained from commercial sources and freshly distilled prior to use. Reactions were monitored by TLC on silica gel 60H with detection by charring with iodine. Melting points were determined with an X-4 apparatus and were not corrected. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded for DMSO-d_6 solutions with TMS as an internal standard at room temperature unless otherwise specified. HRMS spectra were acquired with the use of APEX II 47e spectrometer; IR spectra were obtained by using an Alpha Centauri FT-IR spectrophotometer.

4.2. Typical experimental procedure for the synthesis of 1a

To a 50 mL flame dried round-bottom flask were added 0.53 g (5.0 mmol) of benzaldehyde, 0.60 g (5.0 mmol) of acetophenone, 0.36 g (6.0 mmol) of urea and 0.319 g (1.0 mmol) of ZnI_2. The resulting mixture was placed into the microwave reactor. After the reaction was completed, distilled water was added into the flask and stirred for several minutes and then filtrated through a sintered funnel to afford the crude product, which was further purified by recrystallization (EtOH).

4.2.1. 3,4-Dihydro-4,6-diphenylpyrimidin-2(1*H*)-one[15] 1a. White solid; mp 245–246 °C; IR (KBr) ν_{max}: 3225, 2922, 1687, 1602, 1451 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.57 (s, 1H, NH), 7.54–7.28 (m, 10H, Ar–H), 5.18 (d, 1H, J=3.6 Hz, C=CH), 5.13 (d, 1H, J=3.6 Hz, CH), 3.43 (br, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 153.5, 145.2, 134.1, 128.5, 128.3, 128.4, 127.2, 126.2, 125.3, 135.4, 98.7, 54.9. Anal. Calcd for $C_{16}H_{14}N_2O$: C 76.78, H 5.64, N 11.19, found C 76.23, H 5.54, N 11.20; HRMS (ESI) for [M+H] found (expected): 251.1183 (251.1179).

4.2.2. 3,4-Dihydro-4-(3-methoxyphenyl)-6-phenylpyrimidin-2(1*H*)-one 2b (firstly reported). White solid; mp 257–258 °C; IR (KBr) ν_{max}: 3209, 2933, 1689, 1598, 1402 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.55 (s, 1H, NH), 7.58–6.83 (m, 9H, Ar–H), 5.18 (d, 1H, J=4.4 Hz, C=CH), 5.10 (d, 1H, J=4.4 Hz, CH), 3.43 (br, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 146.7, 159.4, 135.5, 134.0, 129.6, 128.5, 128.4, 118.3, 113.7, 112.4, 112.0, 143.1, 98.6, 55.0, 54.8. Anal. Calcd for $C_{17}H_{16}N_2O_2$: C 72.84, H 5.75, N 9.99, found C 72.04, H 5.63, N 10.00; HRMS (ESI) for [M+H] found (expected): 281.1289 (281.1285).

4.2.3. 3,4-(4-Chlorophenyl)-3,4-dihydro-6-phenylpyrimidin-2(1*H*)-one[15] 1c. White solid; mp 267–269 °C; IR (KBr) ν_{max}: 3228, 2930, 1680, 1576, 1465 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.69 (s, 1H, NH), 8.11 (s, 1H, NH), 7.50–7.28 (m, 9H, Ar–H), 5.49 (d, J=2.8 Hz, 1H, =CH), 5.15 (d, 1H, J=2.8 Hz, CH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 153.7, 141.7, 136.3, 133.8, 130.3, 129.5, 128.9, 128.6, 128.4, 128.0, 127.8, 125.3, 96.1, 52.4. Anal. Calcd for $C_{16}H_{13}ClN_2O$: C 67.49, H 4.60, N 9.84, Cl 12.45, found C 66.99, H 4.58, N 10.00, Cl 12.52.

4.2.4. 4-(2,6-Dichlorophenyl)-3,4-dihydro-6-phenyl-pyrimidin-2(1*H*)-one 1d (firstly reported). White solid; mp 274–276 °C; IR (KBr) ν_{max}: 3235, 2920, 1650, 1570, 1402 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.57 (s, 1H, NH), 8.20 (s, 1H, NH), 8.16–7.28 (m, 8H, Ar–H), 5.89 (d, J=4 Hz, 1H, =CH), 5.56 (d, J=4 Hz, 1H, CH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 153.3, 142.2, 137.6, 132.3, 131.7, 128.7, 127.7, 126.3, 126.4, 125.6, 96.4, 32.1. Anal. Calcd for $C_{16}H_{12}Cl_2N_2O$: C 60.20, H 3.79, N 8.78, Cl 22.21, found C 59.82, H 4.00, N 8.67, Cl 21.94.

4.2.5. 4-(2,4-Dichlorophenyl)-3,4-dihydro-6-phenylpyrimidin-2(1*H*)-one 1e (firstly reported). White solid; mp 271–274 °C; IR (KBr) ν_{max}: 3279, 2952, 1655, 1587, 1415 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.91 (s, 1H, NH), 7.62–6.76 (m, 8H, Ar–H), 6.26 (d, J=6.4 Hz, 1H, =CH), 5.62 (s, 1H, NH), 5.31 (d, J=6.4 Hz, 1H, CH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.2, 142.7, 135.3, 134.4, 133.2, 129.3, 128.4, 127.4, 127.1, 126.3, 125.4, 95.3, 43.1. Anal. Calcd for $C_{16}H_{12}Cl_2N_2O$: C 60.20, H 3.79, N 8.78, Cl 22.21, found C 60.37, H 3.68, N 9.00, Cl 21.87.

4.2.6. 4-(3-Bromophenyl)-3,4-dihydro-6-phenylpyrimidin-2(1*H*)-one 1f (firstly reported). White solid; mp 256–258 °C; IR (KBr) ν_{max}: 3122, 2923, 1693, 1572, 1401 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.16 (s, 1H, NH), 8.32–7.30 (m, 9H, Ar–H), 7.12 (s, 1H, NH), 5.52 (d, J=5.6 Hz, 1H, =CH), 5.14 (d, J=5.6 Hz, 1H, CH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.9, 147.4, 135.8, 133.7, 130.3, 129.7, 128.7, 128.5, 128.0, 125.1, 124.9, 121.4, 121.3, 97.6, 54.2. Anal. Calcd for $C_{16}H_{13}BrN_2O$: C 58.38, H 3.98, N 8.51, Br 24.27, found C 57.84, H 4.12, N 8.49, Br 24.12.

4.2.7. 3,4-Dihydro-4-(4-hydroxyphenyl)-6-phenylpyrimidin-2(1*H*)-one 1g (firstly reported). Yellow solid; mp 255–257 °C; IR (KBr) ν_{max}: 3389, 2922, 1631, 1515, 1450 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.26 (s, 1H, NH), 8.17–7.53 (m, 9H, Ar–H), 7.38–7.36 (s, 1H, NH), 7.23 (d, J=8.8 Hz, 1H, =CH), 5.50 (s, 1H, OH), 5.13 (d, J=8.8 Hz, 1H, CH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 156.8, 141.6, 131.4, 129.4, 128.9, 127.6, 127.5, 127.3, 124.1, 123.8, 124.9, 96.6, 55.4. Anal. Calcd for

$C_{16}H_{14}N_2O_2$: C 72.17, H 5.30, N 10.52, found C 72.00, H 5.31, N 10.34.

4.2.8. 3,4-Dihydro-4-(4-hydroxy-3-methoxyphenyl)-6-phenylpyrimidin-2(1*H*)-one 1h (firstly reported). White solid; mp 267–268 °C; IR (KBr) ν_{max}: 3226, 2941, 1681, 1589, 1412 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 8.83 (s, 1H, NH), 8.71–7.48 (m, 8H, Ar–H), 8.15 (s, 1H, NH), 7.11 (d, J=4.8 Hz, 1H, =CH), 5.32 (s, 1H, OH), 4.82 (d, J=4.8 Hz, 1H, CH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.6, 163.1, 152.8, 136.6, 131.4, 129.4, 129.0, 128.0, 123.0, 121.5, 112.0, 111.4, 101.6, 55.9, 55.8. Anal. Calcd for $C_{17}H_{16}N_2O_3$: C 68.91, H 5.44, N 9.45, found C 69.12, H 5.33, N 9.63.

4.2.9. 3,4-Dihydro-4-(2-methoxyphenyl)-6-phenylpyrimidin-2(1*H*)-one 1i (firstly reported). White solid; mp 266–267 °C; IR (KBr) ν_{max}: 3208, 2953, 1688, 1593, 1465 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 9.34 (s, 1H, NH), 8.51 (s, 1H, NH), 8.51–6.09 (m, 9H, Ar–H), 5.71 (d, J=6.4 Hz, 1H, =CH), 5.34 (d, J=6.4 Hz, 1H, CH), 3.78 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 156.4, 153.0, 135.6, 134.5, 134.2, 132.5, 129.8, 128.6, 126.3, 126.0, 120.5, 111.2, 110.9, 97.5, 58.3, 55.4. Anal. Calcd for $C_{17}H_{16}N_2O_2$: C 72.84, H 5.75, N 9.99, found C 71.89, H 5.88, N 10.00.

4.2.10. 4-(4-*tert*-Butylphenyl)-3,4-dihydro-6-phenylpyrimidin-2(1*H*)-one 1j (firstly reported). White solid; mp 238–240 °C; IR (KBr) ν_{max}: 3221, 2960, 1695, 1577, 1411 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 8.32 (s, 1H, NH), 7.45–7.12 (m, 9H, Ar–H), 5.27 (d, 1H, J=4.8 Hz, C=CH), 5.14 (d, 1H, J=3.6 Hz, CH), 5.54 (s, 1H, NH), 1.45 (s, 6H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.6, 143.1, 134.3, 128.6, 128.5, 128.2, 127.2, 126.4, 125.3, 136.5, 99.5, 53.5, 42.2, 30.8. Anal. Calcd for $C_{20}H_{22}N_2O$: C 78.40, H 7.24, N 9.14, found C 78.41, H 7.32, N 9.04.

4.2.11. 4-(3,5-Dibromo-4-hydroxyphenyl)-3,4-dihydro-6-phenylpyrimidin-2(1*H*)-one 1k (firstly reported). Slightly red solid; mp 256–260 °C; IR (KBr) ν_{max}: 3276, 3089, 1656, 1553, 1408 cm^{-1}; ^1H NMR (400 MHz, pyridine-d_6): δ 9.214 (s, 1H, NH), 8.21–7.56 (m, 9H, Ar–H), 6.45 (s, 1H, NH), 5.47 (d, J=3.2 Hz, 1H, =CH), 5.23 (d, J=3.2 Hz, 1H, CH), 2.84 (s, 1H, OH); ^{13}C NMR (100 MHz, pyridine-d_6): δ 156.7, 146.2, 136.5, 133.6, 130.5, 128.6, 124.8, 121.4, 113.8, 99.1, 55.4. Anal. Calcd for $C_{16}H_{12}Br_2N_2O_2$: C 45.31, H 2.85, N 6.61, found C 45.25, H 2.78, N 6.55.

4.2.12. 3,4-Dihydro-6-phenyl-4-*p*-tolylpyrimidin-2(1*H*)-one[15] 1l. White solid; mp 248–250 °C; IR (KBr) ν_{max}: 3235, 2920, 1650, 1570, 1402 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 9.24 (s, 1H, NH), 8.48 (s, 1H, NH), 7.84–6.00 (m, 9H, Ar–H), 5.56 (d, J=6.8 Hz, 1H, =CH), 5.31 (d, J=6.8 Hz, 1H, CH), 2.42 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 157.5, 136.4, 133.4, 133.1, 132.5, 129.3, 128.4, 126.2, 125.6, 120.3, 111.1, 110.1, 99.3, 23.1. Anal. Calcd for $C_{17}H_{16}N_2O$: C 77.25, H 6.10, N 10.60, found C 77.32, H 5.99, N 10.61.

4.2.13. 3,4-Dihydro-4-(4-methoxyphenyl)-6-phenylpyrimidin-2(1*H*)-one 1m (firstly reported). White solid; mp 259–261 °C; IR (KBr) ν_{max}: 3381, 2932, 1613, 1515, 1402 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 11.91 (s, 1H, NH), 9.33 (s, 1H, NH), 8.33–7.24 (m, 9H, Ar–H), 6.96 (d, J=8.8 Hz, 1H, =CH), 5.44 (d, J=8.8 Hz, 1H, CH), 3.77 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.1, 159.4, 152.8, 133.2, 131.4, 129.4, 128.7, 127.4, 114.2, 113.8, 79.2, 62.4, 55.5. Anal. Calcd for $C_{17}H_{16}N_2O_2$: C 72.84, H 5.75, N 10.00, found C 72.57, H 5.76, N 10.11.

4.2.14. 3,4-Dihydro-4-(3,4-dimethoxyphenyl)-6-phenylpyrimidin-2(1*H*)-one 1n (firstly reported). Yellow solid; mp 243–245 °C; IR (KBr) ν_{max}: 3275, 2933, 1614, 1512, 1459 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 11.95 (s, 1H, NH), 8.58 (s, 1H, NH), 8.58–7.44 (m, 8H, Ar–H), 7.82 (d, J=8.4 Hz, 1H, =CH), 7.06 (d, J=8.4 Hz, 1H, CH), 3.91 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.3, 151.8, 148.7, 131.3, 128.7, 127.5, 121.2, 111.4, 110.4, 79.1, 55.7, 55.6. Anal. Calcd for $C_{18}H_{18}N_2O_3$: C 69.66, H 5.85, N 15.50, found C 69.65, H 5.84, N 9.01.

4.2.15. 4-(2-Chlorophenyl)-3,4-dihydro-6-phenylpyrimidin-2(1*H*)-one[15] 1o. White solid; mp 260–263 °C; IR (KBr) ν_{max}: 3289, 2942, 1654, 1589, 1418 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 8.60 (s, 1H, NH), 8.15 (s, 1H, NH), 7.42–7.15 (m, 9H, Ar–H), 5.45 (d, J=4.4 Hz, 1H, =CH), 5.12 (d, 1H, J=2.8 Hz, CH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.7, 145.7, 138.3, 135.8, 131.6, 129.5, 128.8, 128.6, 128.4, 128.1, 127.5, 125.5, 94.1, 54.3. Anal. Calcd for $C_{16}H_{12}Cl_2N_2O$: C 60.21, H 3.79, N 8.78, Cl 22.21, found C 60.31, H 3.71, N 9.00, Cl 21.96.

4.2.16. Ethyl-4-(4-(5-(ethoxycarbonyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidin-4-yl)phenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxylate 1p (firstly reported). Slightly yellow solid; mp >350 °C; IR (KBr) ν_{max}: 3355, 2976, 1701, 1646, 1456, 1375 cm^{-1}; ^1H NMR (400 MHz, pyridine-d_6): δ 9.16 (s, 4H, NH), 7.67–7.14 (m, 4H, Ar–H), 5.11–5.14 (m, 2H, CH), 3.99–3.94 (m, 4H, CH_2–R), 2.25–2.19 (m, 6H, H_3C–C=C), 1.13–1.03 (m, 6H, CH_3–C); ^{13}C NMR (100 MHz, pyridine-d_6): δ 165.3, 152.1, 148.3, 143.9, 126.3, 99.2, 59.2, 53.7, 17.7, 14.1; HRMS (ESI) for $C_{22}H_{26}N_4O_6$ [M+Na] found (expected): 465.1756 (465.1759).

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