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**AN IONIC LIQUID-BASED GREEN SYNTHESIS STRATEGY:  
SYNTHESIS OF DIHYDROPYRIMIDINONES BY THREE-COMPONENT  
BIGINELLI-TYPE REACTION OF ALIPHATIC ALDEHYDES,  
AROMATIC ALDEHYDES AND UREA**

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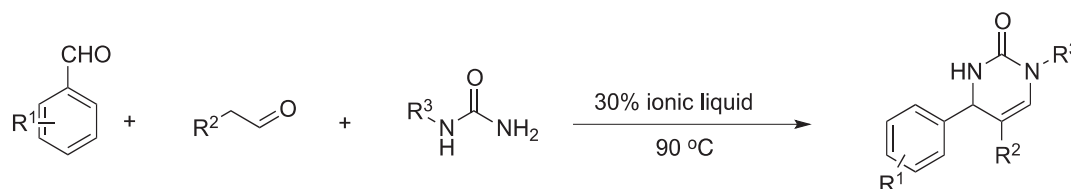
**Abstract** – A Biginelli-type reaction involving aliphatic aldehydes, aromatic aldehydes, and urea was performed at high concentration with high regioselectivity to give a range of highly diverse 3,4-dihydropyrimidin-2-(1*H*)-one products in 58-88% yields, where a 30% aqueous solution of ionic liquid (1-ethyl-3-methylimidazolium tetrafluoroborate) was employed as a green reaction medium. The catalyst can be easily recycled and reused with similar efficacy for at least four cycles.

Multicomponent reactions (MCRs) have evolved into an effective method in modern synthetic organic chemistry because complex organic molecules were synthesized from simple and readily available substrates, and could be obtained in a very fast and efficient manner without the isolation of any intermediates.<sup>1-5</sup> Particularly, the Biginelli reaction is an example of such multicomponent reactions.<sup>6-8</sup> In 1893, Biginelli reported the first synthesis of dihydropyrimidinones (DHPMs) by a simple one-pot condensation reaction of ethyl acetoacetate, benzaldehyde and urea.<sup>9</sup> In recent years, DHPMs and their derivatives have received much attention because they exhibited diverse biological and pharmacological properties such as calcium channel blockers, anti-HIV and anti-hypertensive, etc.<sup>10-13</sup> Therefore, several methods have been reported for the preparation of DHPMs using various catalysts such as Fe<sub>3</sub>O<sub>4</sub>,<sup>14</sup> Ti,<sup>15</sup> HClO<sub>4</sub>-SiO<sub>2</sub><sup>16</sup> and H<sub>3</sub>BO<sub>3</sub>,<sup>17</sup> etc. However, several of these catalysts suffer from some drawbacks such as strong acidic conditions, long reaction times, high reaction temperature and low yields of products.

Moreover, most of these methods employ organic solvents as the reaction medium. Hence, the development of a new protocol toward this direction is an active area of research.

Currently, ionic liquids (ILs) have been one of the most studied subjects in academic and industrial fields owing to their attractive “green” characteristics, such as high thermal and chemical stabilities, environmental safety, as well as the possibility of their recycling.<sup>18-24</sup> Furthermore, ionic liquids are considered as an excellent alternative to organic solvents. These green solvents are also used as catalysts in the Biginelli reaction for the preparation of DHPMs.

Herein, we report a convenient method for the synthesis of DHPMs via a three-component Biginelli-type reaction involving a substituted aromatic aldehyde, substituted urea, and an aliphatic aldehydes at 90 °C for 6 h using a 30% aqueous solution of ionic liquid as an environmentally friendly reaction medium (Scheme 1).



**Scheme 1.** Preparation of dihydropyrimidinones via Biginelli-type reaction

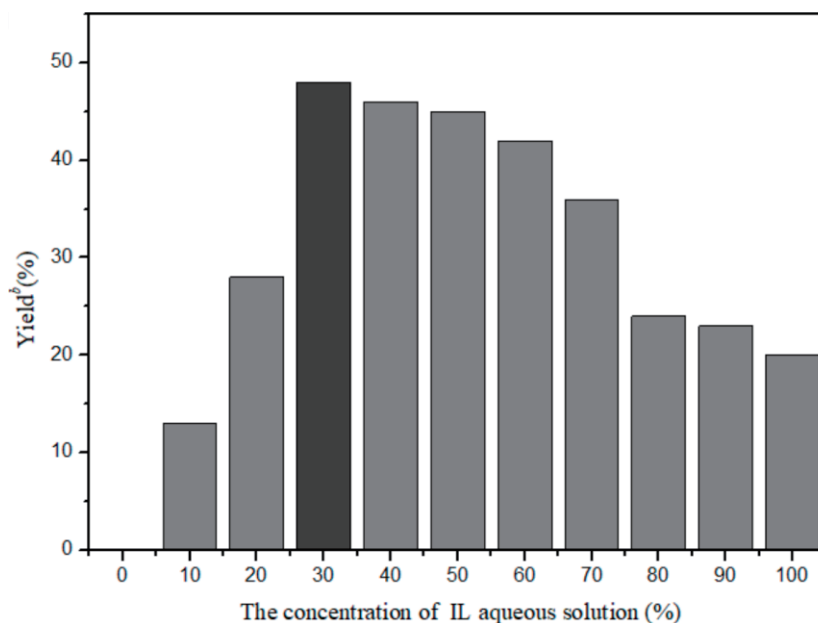
The catalytic activity of 10 different ionic liquids were investigated in our model reaction using 1 mmol of 4-nitrobenzaldehyde, 1.3 mmol of methylurea, and 1.5 mmol of *n*-hexanal as substrates (Table 1). As shown in Table 1, only the ionic liquids containing tetrafluoroborate exhibit some catalytic effect in the model reaction (Table 1, Entries 1-4), while hexafluorophosphate, chloride, and bromine containing ionic liquids have no catalytic effect on the reaction (Table 1, Entries 5-10). 1-Ethyl-3-methylimidazolium tetrafluoroborate ([EMIM][BF<sub>4</sub>]) showed significant catalytic activity to give the desired product in 48% yield after 16 h. When water was used as the reaction medium without a catalyst, no target product was detected (Table 1, Entry 11). In addition, the reaction was catalyzed with hydrochloric acid at the same pH, and a yield of 17% of product was obtained at 60 °C for 16 h (Table 1, Entries 1 and 12). So, we speculate that [BF<sub>4</sub>]<sup>-</sup> provides an acidic condition that catalyzes the reaction with [EMIM]<sup>+</sup>. Upon comparison to the control experiment, it is found that the catalytic effect of the ionic liquid gradually decreased depending on increasing the size of the alkyl substituent in the cation of the ionic liquid. Therefore, [EMIM][BF<sub>4</sub>] was selected as the optimal ionic liquid for our subsequent experiments.

**Table 1.** Effect of different ionic liquid on the yield of reaction<sup>a</sup>

Entry	Ionic Liquid (IL)	pH	Yield (%) <sup>b</sup>
1	1-ethyl-3-methylimidazolium tetrafluoroborate	3.73	48
2	1-butyl-3-methylimidazolium tetrafluoroborate	3.81	40
3	1-hexyl-3-methylimidazolium tetrafluoroborate	3.94	34
4	1-octyl-3-methylimidazolium tetrafluoroborate	4.53	33
5	1-ethyl-3-methylimidazolium hexafluorophosphate	8.75	0
6	1-butyl-3-methylimidazolium hexafluorophosphate	8.99	0
7	1-hexyl-3-methylimidazolium hexafluorophosphate	9.13	0
8	1-octyl-3-methylimidazolium hexafluorophosphate	9.32	0
9	1-butyl-3-methylimidazolium chloride	8.71	0
10	1-butyl-3-methylimidazolium bromide	8.69	0
11	3 mL H <sub>2</sub> O	-	0
12	3 mL (H <sub>2</sub> O+HCl)	3.73	17

<sup>a</sup>Reaction conditions: 4-nitrobenzaldehyde (1 mmol), *n*-hexanal (1.5 mmol), methylurea (1.3 mmol), 1 mL 50% (IL/(IL+H<sub>2</sub>O)), v/v, 60 °C. <sup>b</sup>Yields of pure products isolated by chromatography.

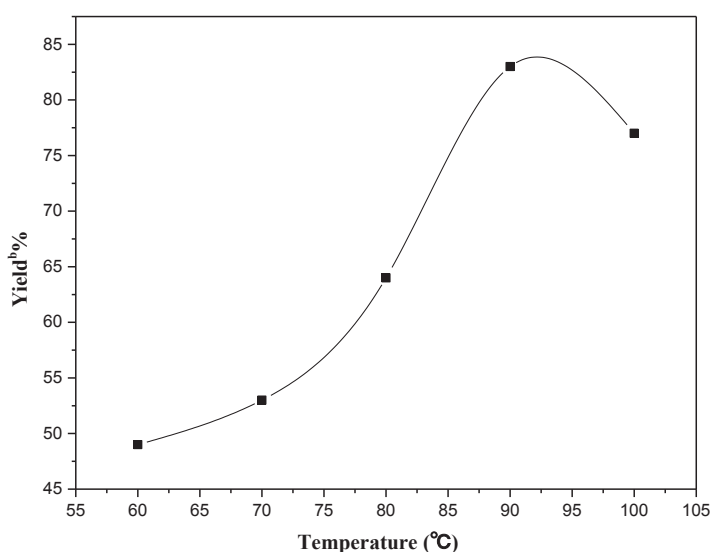
In order to implement the concept of green chemistry and increase the reaction yield, the effect of the ionic liquid concentration on the model reaction was investigated. Table 1 shows that the yield of the target product obtained in a 50% aqueous solution of ionic liquid was low, therefore the influence of the ionic liquid to water ratio on the reaction was further explored, and the results shown in Figure 1. Different concentrations of ionic liquid have a significant effect on the model reaction, showing an initial increase then decrease in the product yield. When the proportion of ionic liquid was 30-50%, an yield of 48-49% was obtained. However, as the concentration of ionic liquid continued to increase, the yield decreases. In addition, Figure 1 shows that when pure water was used as the solvent, no product was formed and the solubility of the substrate was poor. When a certain amount of ionic liquid is added to water, the yield was significantly increased and the solubility of the substrate also improved. Therefore, it was inferred that the ionic liquid acts both as a catalyst and reaction medium in the reaction. Consequently, a 30% aqueous solution of ionic liquid was selected as the optimal reaction medium.



**Figure 1.** Effect of ionic liquid concentration on the yield of reaction<sup>a</sup>

<sup>a</sup>Reaction conditions: 4-nitrobenzaldehyde (1 mmol), *n*-hexanal (1.5 mmol), methylurea (1.3 mmol), 60 °C. <sup>b</sup>Yields of pure products isolated by chromatography.

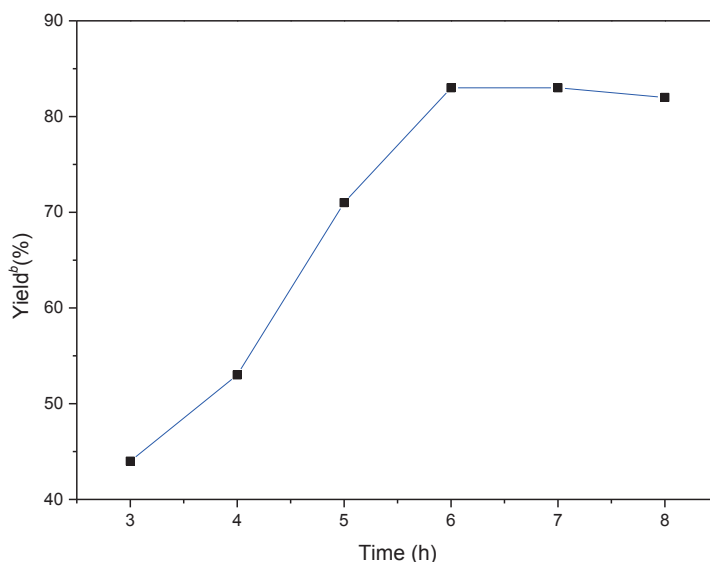
Temperature is a vital parameter that can affect the reaction rate. Therefore, we investigated the effect of the reaction temperature on the reaction yield.<sup>25,26</sup> As shown in Figure 2, the target product was obtained in 82% yield at 90 °C. Upon further increasing the temperature to 100 °C, the yield decreases. After the reaction was complete, as indicated by TLC, many by-products were detected upon increasing the reaction temperature. Therefore, 90 °C was chosen as the optimum reaction temperature.



**Figure 2.** Effect of temperature on the yield of reaction<sup>a</sup>

<sup>a</sup>Reaction conditions: 4-nitrobenzaldehyde (1 mmol), *n*-hexanal (1.5 mmol), methylurea (1.3 mmol), 16 h, 1 mL 30% ([EMIM][BF<sub>4</sub>]/(H<sub>2</sub>O+[EMIM][BF<sub>4</sub>]), v/v). <sup>b</sup>Yields of pure products isolated by chromatography.

The influence of the reaction time on the yield of the model reaction was also investigated, as shown in Figure 3. The best result (up to 83% yield) was achieved by carrying out the reaction at 90 °C for 6 h. Despite increasing the reaction time to 8 h, the yield did not change significantly. Therefore, for the purpose of saving energy, 6 h was chosen as the optimal reaction time.



**Figure 3. Optimization of reaction time<sup>a</sup>**

<sup>a</sup>Reaction conditions: 4-nitrobenzaldehyde (1 mmol), *n*-hexanal (1.5 mmol), methylurea (1.3 mmol), 90 °C, 1 mL 30% ionic liquid aqueous solution. <sup>b</sup>Yields of pure products isolated by chromatography.

The molar ratio of the substrates used in the reaction is also an important factor affecting the reaction yield. Therefore, the effect of the molar ratio of the substrates on the reaction yield was investigated and the results shown in Table 2, where the yield reached a maximum when the molar ratio of *n*-hexanal:*p*-nitrobenzaldehyde:methylurea was 1.5:1:1.5 (Table, entry 5), which was chosen as the optimal molar ratio.

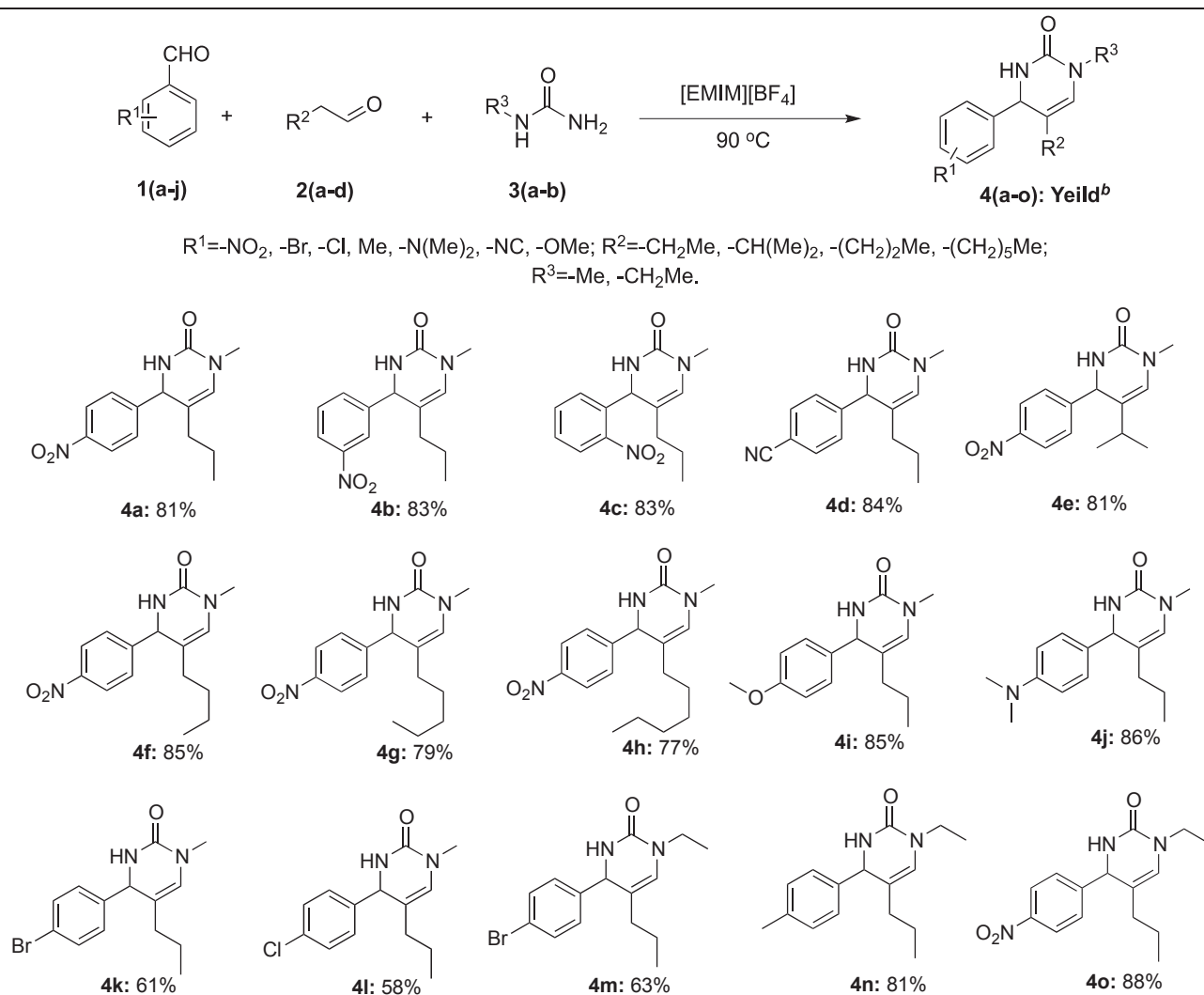
**Table 2.** Effect of molar ratio of substrate on the yield of reaction<sup>a</sup>

Entry	<i>n</i> -Hexanal (mmol)	4-Nitrobenzaldehyde (mmol)	Methylurea (mmol)	Yield <sup>b</sup> /%
1	1	1	1	61
2	1	1	1.5	71
3	1	1.5	1	74
4	1.5	1	1	78
5	1.5	1	1.5	85
6	2	1	1	82
7	2	1	1.5	83

<sup>a</sup>Reaction conditions: 90 °C, 6 h, 1 mL 30% ([EMIM][BF<sub>4</sub>]/(H<sub>2</sub>O+[EMIM] [BF<sub>4</sub>]), v/v). <sup>b</sup>Yields of pure products isolated by chromatography.

With these optimized conditions in hand, a series of aromatic aldehydes, aliphatic aldehydes, and substituted ureas were selected to investigate the substrate scope of our method and the results summarized in Table 3. The aqueous solution of [EMIM][BF<sub>4</sub>] exhibits excellent catalytic activity in the Biginelli-type reaction of aromatic aldehydes, aliphatic aldehydes, and substituted urea. The as-obtained results indicate that electron-donating or withdrawing groups on the aromatic ring do not appear to have a significant effect on the reaction in terms of the product yield. In addition, the target product yield did not change significantly when the position of the substituent on the aromatic aldehyde was changed, indicating that steric hindrance had no significant effect on the reaction (Table 3, **4a–c**). Furthermore, the reaction also achieved good yields when increasing the chain length of the aliphatic aldehyde (Table 3, **4f–h**). However, it was notable that only moderate yields of product were produced with a halogen substituent on the aromatic ring (Table 3, **4l–m**).

**Table 3.** Ionic liquid catalyzed synthesis of dihydropyrimidinones via Biginelli-type reaction<sup>a</sup>



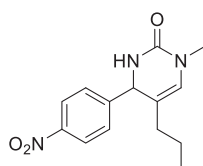
<sup>a</sup>Reaction conditions: 4-nitrobenzaldehyde (1 mmol), *n*-hexanal (1.5 mmol), methylurea (1.5 mmol), 90 °C, 6 h, 1 mL 30% ionic liquid aqueous solution. <sup>b</sup>Yields of pure products isolated by chromatography.

In summary, a novel, green, and environmentally friendly method for the synthesis of a series of novel DHPMs using aromatic aldehydes, aliphatic aldehydes, and substituted urea as substrates employing an aqueous solution of ionic liquid as a catalyst and reaction medium has been reported. The catalyst can be recovered for repeated use (up to four times, Table S1). In addition, this method offers several advantages over those using metal-based catalysts, which include high yield, short reaction time, and environmental-friendliness. What's more, this green reaction process increases the possibility of its application and applicability.

## EXPERIMENTAL

**General procedure for ionic liquid aqueous solution catalyzed synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones:** A mixture of aromatic aldehydes **1** (1 mmol), aliphatic aldehydes **2** (1.5 mmol), substituted ureas **3** (1.5 mmol), 1 mL 30% ([EMIM][BF<sub>4</sub>]/(H<sub>2</sub>O+[EMIM] [BF<sub>4</sub>]), v/v) was incubated at 90 °C for 6 h. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature and then extracted with EtOAc [10 mL × 3]. The organic phase was concentrated under reduced pressure to afford the crude product, which was then purified by column chromatography on silica gel (petroleum ether:EtOAc = 1:1) to give the pure product **4**. See Supporting Information for full experimental details.

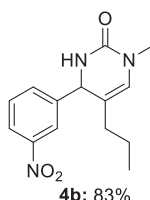
### 1-Methyl-4-(4-nitrophenyl)-5-propyl-3,4-dihydropyrimidin-2(1*H*)-one<sup>27</sup>



**4a:** 81%

Yellow solid, <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.20 (d, *J* = 8.5 Hz, 2H), 7.46 (d, *J* = 8.5 Hz, 2H), 5.82 (s, 1H), 5.46 (s, 1H), 5.03 (s, 1H), 3.08 (s, 3H), 1.86 – 1.54 (m, 2H), 1.34 – 1.11 (m, 2H), 0.85 (t, *J* = 7.3 Hz, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 153.48, 149.99, 147.72, 129.37, 127.99, 125.21, 124.23, 59.06, 39.21, 31.63, 22.63, 14.15.

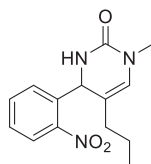
### 1-Methyl-4-(3-nitrophenyl)-5-propyl-3,4-dihydropyrimidin-2(1*H*)-one<sup>27</sup>



**4b:** 83%

Yellow solid,  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.09 (dt,  $J = 3.5, 1.5$  Hz, 2H), 7.59 (d,  $J = 7.8$  Hz, 1H), 7.48 (t,  $J = 7.9$  Hz, 1H), 5.79 (s, 1H), 5.42 (s, 1H), 4.99 (s, 1H), 3.03 (s, 3H), 1.65 (t,  $J = 8.8$  Hz, 2H), 1.41 – 1.27 (m, 2H), 0.79 (t,  $J = 5.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  153.50, 150.01, 147.74, 129.39, 128.01, 124.25, 123.70, 113.02, 59.08, 34.48, 31.65, 22.65, 14.17.

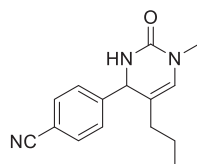
#### 1-Methyl-4-(2-nitrophenyl)-5-propyl-3,4-dihydropyrimidin-2(1H)-one<sup>27</sup>



4c: 83%

Yellow solid,  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.86 (d,  $J = 7.1$  Hz, 1H), 7.59 (t,  $J = 7.6$  Hz, 1H), 7.52 (d,  $J = 7.8$  Hz, 1H), 7.40 (t,  $J = 7.7$  Hz, 1H), 6.01 (s, 1H), 5.57 (s, 1H), 5.27 (s, 1H), 3.03 (s, 3H), 1.71 – 1.65 (m, 2H), 1.26 – 1.16 (m, 2H), 0.79 (t,  $J = 7.3$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  153.48, 149.99, 147.72, 129.37, 127.99, 125.21, 124.23, 113.00, 59.06, 34.46, 31.63, 22.63, 14.15.

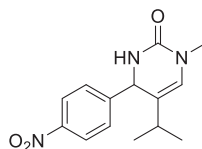
#### 4-(1-Methyl-2-oxo-5-propyl-1, 2, 3, 4-tetrahydropyrimidin-4-yl)benzonitrile<sup>27</sup>



4d: 84%

Yellow solid,  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.53 (d,  $J = 7.6$  Hz, 2H), 7.30 (t,  $J = 17.5$  Hz, 2H), 6.37 (s, 1H), 5.72 (s, 1H), 4.86 (s, 1H), 2.90 (s, 3H), 1.60 (t,  $J = 14.3$  Hz, 2H), 1.25 (ddd,  $J = 20.6, 13.2, 6.7$  Hz, 2H), 0.76 (t,  $J = 6.9$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  153.51, 147.75, 129.40, 128.02, 125.24, 124.26, 116.45, 113.03, 59.09, 34.49, 31.66, 22.66, 14.18.

#### 5-Isopropyl-1-methyl-4-(4-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one<sup>27</sup>



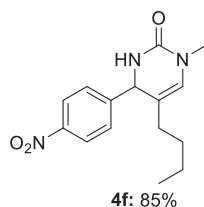
4e: 81%

Yellow solid,  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.11 (d,  $J = 8.7$  Hz, 2H), 7.40 (d,  $J = 8.7$  Hz, 2H), 6.40 (s, 1H), 5.81 (s, 1H), 5.00 (s, 1H), 3.01 (s, 3H), 1.89 (dt,  $J = 13.5, 6.7$  Hz, 1H), 0.93 (d,  $J = 6.8$  Hz, 3H), 0.89



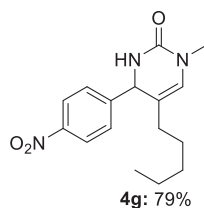
(d,  $J = 6.8$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  153.49, 150.00, 147.73, 129.38, 128.00, 125.22, 124.24, 59.07, 34.47, 31.64, 22.64.

#### 5-Butyl-1-methyl-4-(4-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one<sup>27</sup>



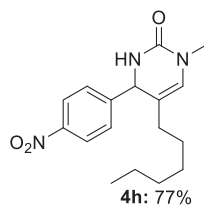
Yellow solid,  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.13 (d,  $J = 8.7$  Hz, 2H), 7.40 (d,  $J = 8.7$  Hz, 2H), 5.79 (s, 1H), 5.75 (s, 1H), 4.97 (s, 1H), 2.99 (s, 3H), 1.67 (t,  $J = 11.9$  Hz, 2H), 1.23 – 1.11 (m, 4H), 0.78 (t,  $J = 6.2$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  153.48, 149.99, 147.72, 127.99, 125.21, 124.23, 123.68, 59.06, 34.46, 31.63, 30.34, 22.63, 14.15.

#### 1-Methyl-4-(4-nitrophenyl)-5-pentyl-3,4-dihydropyrimidin-2(1H)-one<sup>27</sup>

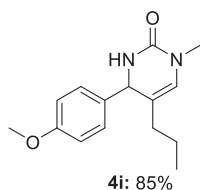


Yellow solid,  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.09 (d,  $J = 8.6$  Hz, 2H), 7.39 (d,  $J = 8.5$  Hz, 2H), 6.01 (s, 1H), 5.75 (s, 1H), 4.97 (s, 1H), 2.98 (s, 3H), 1.64 (t,  $J = 7.5$  Hz, 2H), 1.09 (d,  $J = 10.0$  Hz, 6H), 0.76 (t,  $J = 6.9$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  153.48, 149.99, 147.72, 127.99, 125.21, 124.23, 113.00, 59.06, 34.46, 31.63, 30.34, 26.99, 22.63, 14.15.

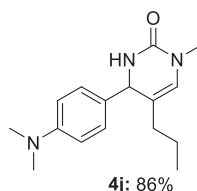
#### 5-Hexyl-1-methyl-4-(4-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one<sup>27</sup>



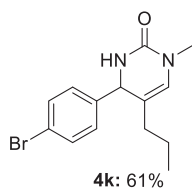
Yellow solid,  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.18 (d,  $J = 8.4$  Hz, 2H), 7.44 (d,  $J = 8.4$  Hz, 2H), 5.88 (s, 1H), 5.80 (s, 1H), 5.02 (s, 1H), 3.05 (s, 3H), 1.70 (t,  $J = 7.2$  Hz, 2H), 1.18 (d,  $J = 7.3$  Hz, 8H), 0.83 (t,  $J = 6.9$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  153.40, 149.91, 147.64, 127.91, 125.13, 124.15, 112.92, 58.98, 34.38, 31.56, 30.27, 28.78, 26.91, 22.55, 14.07.

**4-(4-Methoxyphenyl)-1-methyl-5-propyl-3,4-dihydropyrimidin-2(1H)-one<sup>27</sup>**

Yellow oily liquid, <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.12 (d, *J* = 8.6 Hz, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 5.68 (s, 1H), 5.11 (s, 1H), 4.80 (s, 1H), 3.72 (s, 3H), 2.99 (s, 3H), 1.69 – 1.56 (m, 2H), 1.31 (dd, *J* = 14.6, 7.2 Hz, 2H), 1.14 (t, *J* = 7.0 Hz, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 153.46, 149.97, 129.35, 127.97, 125.19, 124.21, 112.98, 59.04, 54.17, 34.44, 31.61, 22.61, 14.13.

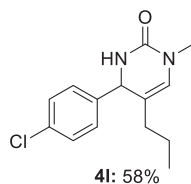
**4-(4-(Dimethylamino)phenyl)-1-methyl-5-propyl-3,4-dihydropyrimidin-2(1H)-one<sup>27</sup>**

Yellow solid, <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.05 (d, *J* = 8.7 Hz, 2H), 6.60 (d, *J* = 8.7 Hz, 2H), 5.66 (s, 1H), 5.09 (s, 1H), 4.75 (s, 1H), 2.99 (s, 3H), 2.86 (s, 6H), 1.70 – 1.54 (m, 2H), 1.26 – 1.12 (m, 2H), 0.77 (t, *J* = 7.3 Hz, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 153.48, 152.38, 129.37, 127.99, 125.21, 124.23, 113.00, 59.06, 39.02, 34.46, 31.63, 22.63, 14.15.

**4-(4-Bromophenyl)-1-methyl-5-propyl-3,4-dihydropyrimidin-2(1H)-one<sup>27</sup>**

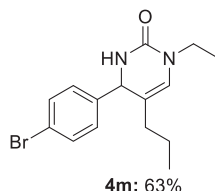
White solid, <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.44 (d, *J* = 8.3 Hz, 2H), 7.14 (d, *J* = 8.3 Hz, 2H), 5.75 (s, 1H), 5.34 (s, 1H), 4.87 (s, 1H), 3.04 (s, 3H), 1.78 – 1.59 (m, 2H), 1.45 – 1.25 (m, 2H), 0.83 (t, *J* = 7.3 Hz, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 153.50, 147.74, 129.39, 128.01, 125.23, 124.25, 123.70, 59.08, 34.48, 31.65, 22.65, 14.17.

#### 4-(4-Chlorophenyl)-1-methyl-5-propyl-3,4-dihydropyrimidin-2(1H)-one<sup>27</sup>



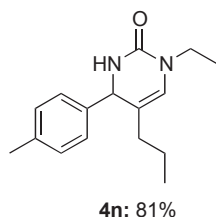
White solid, <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.30 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 5.76 (s, 1H), 5.23 (s, 1H), 4.89 (s, 1H), 3.06 (s, 3H), 1.69 (dd, *J* = 16.9, 8.7 Hz, 2H), 1.38 (dt, *J* = 14.8, 7.4 Hz, 2H), 0.83 (t, *J* = 7.3 Hz, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 153.48, 147.72, 129.37, 127.99, 125.21, 124.23, 123.68, 59.06, 34.46, 31.63, 22.63, 14.15.

#### 4-(4-Bromophenyl)-1-ethyl-5-propyl-3,4-dihydropyrimidin-2(1H)-one<sup>27</sup>

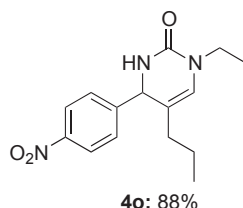


White solid, <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.47 (d, *J* = 8.3 Hz, 2H), 7.16 (d, *J* = 8.5 Hz, 2H), 5.80 (s, 1H), 5.29 (s, 1H), 4.87 (s, 1H), 3.61 – 3.30 (m, 2H), 1.79 – 1.61 (m, 2H), 1.50 – 1.27 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 7.4 Hz, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 152.74, 142.10, 131.90, 128.70, 123.16, 121.95, 113.61, 59.01, 41.62, 32.48, 20.23, 14.24, 13.67.

#### 1-Ethyl-5-propyl-4-(*p*-tolyl)-3,4-dihydropyrimidin-2(1H)-one<sup>27</sup>



Yellow solid, <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.18 (d, *J* = 13.8 Hz, 4H), 5.79 (s, 1H), 4.87 (s, 1H), 3.94 (s, 1H), 3.62 – 3.40 (m, 2H), 2.35 (s, 3H), 1.85 – 1.63 (m, 2H), 1.48 – 1.30 (m, 2H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 6.2 Hz, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 152.82, 140.13, 137.83, 129.32, 126.86, 122.59, 114.38, 59.35, 41.57, 32.55, 21.06, 20.23, 14.26, 13.69.

**1-Ethyl-4-(4-nitrophenyl)-5-propyl-3,4-dihydropyrimidin-2(1H)-one**<sup>27</sup>

Yellow solid, <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.13 (d, *J* = 8.6 Hz, 2H), 7.38 (d, *J* = 8.6 Hz, 2H), 5.78 (s, 1H), 5.59 (s, 1H), 4.94 (s, 1H), 3.47 – 3.37 (m, 2H), 1.72 – 1.57 (m, 2H), 1.38 – 1.31 (m, 2H), 1.12 (t, *J* = 7.1 Hz, 3H), 0.79 (t, *J* = 7.3 Hz, 2H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 152.71, 150.04, 147.64, 127.86, 124.16, 123.80, 112.89, 58.87, 41.73, 32.45, 20.25, 14.23, 13.63.

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