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# $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$ as a simple and efficient catalyst in Biginelli reaction

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A highly efficient and facile procedure for the one-pot three-component synthesis of 3,4-dihydropyrimidin-2-(1*H*)ones/thiones from the one-pot condensation of aldehyde, β-dicarbonyl compound and urea/thiourea was developed. The methodology is applicable to a wide range of substrates with high yield in the presence of $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$. The complex is an air-stable, environmentally friendly and recoverable catalyst and can efficiently catalyze the Biginelli reaction. The catalyst has high catalytic efficiency with low catalyst loading, and can be recycled ten times with only a small loss of activity.

**KEYWORDS**

Biginelli reaction, dihydropyrimidinones (DHPMs), metal complex, multi-component reactions

## 1 | INTRODUCTION

As a one-pot three-component reaction, the Biginelli reaction was reported by Petro Biginelli in 1893.[1] The Biginelli reaction offers an efficient way to access multi-functionalized 3,4-dihydropyrimidin-2-(1*H*)ones (DHPMs) and related heterocyclic compounds. DHPMs have a wide spectrum of biological activities, such as antiviral, antitumor, antibacterial, anticytotoxin, anti-inflammatory and antihypertensive properties.[2] Several alkaloids obtained from marine sources contain the dihydropyrimidine nucleus, and these alkaloids show some interesting biological activities.[3] Thus, the synthesis of DHPMs has been of much importance in recent decades.

A strong acidic catalyst was employed in the original Biginelli reaction, but the yields of products (DHPMs) were low. In order to improve the yields of products, several kinds of catalysts were applied to the reaction process. A Lewis acid was a common catalyst for the Biginelli reaction, such as $SbCl_3$,[4] $CaF_2$,[5] $Fe_3O_4$/SMPA,[6] $Cu(OTf)_2$,[7] $ZnI_2$[8] and $ZrCl_4/ZrOCl_2$. Many ionic liquids have been applied to the Biginelli reaction, including $[Et_3NSO_3H]HSO_4$,[9] $[Hmim]HSO_4$,[10] $[cmmim][BF_4]$[11] and sulfonic acid-functionalized Brønsted acidic ionic liquids.[12] Metal–organic complexes, such as bis[(L)prolinato-N,O]Zn,[13] [Gmim]ClCu(II)[14] and CPs/MOFs,[15] were used as catalysts for the Biginelli reaction and high yields of DHPMs were obtained. Other catalysts such as $PPh_3$,[16] graphite[17] and trypsin[18] can catalyze the Biginelli reaction effectively. At the same time, more and more conditions were applied to the Biginelli reaction, such as microwave irradiation,[19] ultrasound irradiation[20] and solvent-free conditions,[21] and all of these methods have been achieved giving high yields of DHPMs.

Bismuth is the only stable heavy metal element with less toxicity and radioactive in nature, and its compounds have been of great value as metal catalysts in organic synthesis since the discovery of their catalytic activity.[22] Some bismuth salts have been applied to the Biginelli reaction, such as $BiCl_3$,[23] $Bi(OTf)_3$,[24] $Bi(NO_3)_3{\cdot}5H_2O$[25] and $BiONO_3$.[26] All of these were successfully applied for the synthesis of DHPMs. However, there are problems with these methods, such as use of toxic solvent, complex operation, requirement of a large amount of catalyst and difficulty in recycling the catalyst. A new bismuth complex has been studied in our laboratory. The complex is highly stable in air, and has been successfully applied in the one-pot three-component Biginelli reaction. The complex can catalyze a wide range of substrates in ethanol and be recycled ten times with only a small loss of activity. High yields of products can be obtained under simple operation in this method, and the amount of the catalyst required is low (only 1 mol%).

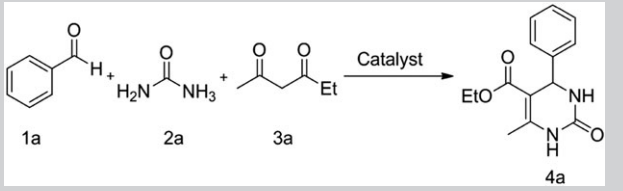
  

## 2 | RESULTS AND DISCUSSION

At the outset of our investigations, a selection of Lewis acids and metal complexes were applied to the model reaction (benzaldehyde (**1a**), urea (**2a**) and ethyl acetoacetate (**3a**)) under prototypical reaction conditions (1 mol%, reflux, 6 h), as summarized in Table 1. Lewis acids could catalyze this reaction alone, but the yields of **4a** were all less than 60% (Table 1, entries 2–4, 6, 8, 10 and 12). When metal–piperazine complexes were used as catalysts of the model reaction (Table 1, entries 5, 7, 9, 11 and 14), the yields of **4a** were all over 60%, and an 87% yield of **4a** was obtained under catalysis with Bi–piperazine complex (Table 1, entry 14). When the ligand of the Bi complex was replaced with other nitrogenous heterocyclic compounds (Table 1, entries 13, 15–20), all these Bi complexes could catalyze the reaction, and the yields were all over 70%. At the same time, when catalyzed by Bi–6-hydroxypurine complex, $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$, the highest yield of **4a** (Table 1, entry 20) was obtained (95%). When complexes of bismuth(III) chloride with oxygen donor ligands (Table 1, entries 21 and 22) or constrained thioether ligand (Table 1, entry 23) catalyzed the model reaction, the yield of **4a** was no more than 60%. These results show that the 6-hydroxypurine ligand also played an important role in the catalysis process. The Bi complex $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$ was a suitable catalyst for the one-pot three-component Biginelli reaction.

As evident from Table 2, with ethanol as the solvent in the model reaction, the yield of **4a** was 95% (Table 2, entry 6). When the solvent was changed to methanol and acetonitrile, the yield was reduced to 80 and 84%, respectively (Table 2, entries 1 and 2). And the yield of **4a** was less than 50% when ethyl acetate, methylene chloride or water served as solvent (Table 2, entries 3–5). The amount of catalyst loading that exhibited the best performance in terms of yield was further examined. It was found that 1 mol% $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$ achieved a yield of **4a** of 95%. When the catalyst loading was lower than 1 mol%, the yield of **4a** increased with increasing amount. There was no further increase in the yield of **4a** when the catalyst loading was over 1 mol%. Thus, 1 mol% $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$ was suitable for the reaction.

**TABLE 1** Optimization of catalysts[a]




| Entry | Metal salt | Ligand | Yield (%)[b] |
|---|---|---|---|
| 1 | — | — | 0 |
| 2 | $AlCl_3$ | — | 45 |
| 3 | $SnCl_4$ | — | 62 |
| 4 | $FeCl_3$ | — | 41 |
| 5 | | Piperazine | 70 |
| 6 | $NiCl_2$ | — | 53 |
| 7 | | Piperazine | 75 |
| 8 | $MnCl_2$ | — | 33 |
| 9 | | Piperazine | 64 |
| 10 | $SbCl_3$ | — | 52 |
| 11 | | Piperazine | 72 |
| 12 | $BiCl_3$ | — | 58 |
| 13 | | Piperidine | 71 |
| 14 | | Piperazine | 87 |
| 15 | | Imidazole | 83 |
| 16 | | 2-Methylimidazole | 84 |
| 17 | | Dalfampridine-$d_4$ | 86 |
| 18 | | Indoline | 81 |
| 19 | | Tetrahydroquinoline | 82 |
| 20 | | 6-Hydroxypurine | 95 |
| 21 | | Tetrahydrofuran | 30 |
| 22 | | Diethyl carbitol | 49 |
| 23 | | *o*-$C_6H_4(SMe)_2$ | 60 |

[a]Reaction conditions: **1a** (1 mmol), **3a** (1 mmol), **2a** (1.5 mmol), catalyst (1 mol %), solvent (EtOH, 5 ml), refluxing, 6 h.

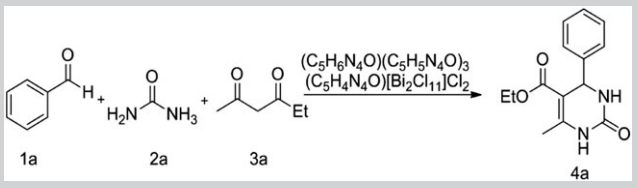
[b]Yields refer to isolated products.

## 3 | EXPERIMENTAL

### 3.1 | Catalyst

6-Hydroxypurine (1.36 g, 10 mmol), $BiCl_3$ (2.15 g, 6.8 mmol) and 35% aqueous HCl (3 ml) were mixed,

**TABLE 2** Optimization of Biginelli reaction conditions[a]




| Entry | Solvent | Catalyst amount (mol%) | Yield (%)[b] |
|---|---|---|---|
| 1 | MeOH | 1 | 80 |
| 2 | MeCN | 1 | 84 |
| 3 | Ethyl acetate | 1 | 42 |
| 4 | Dichloromethane | 1 | 39 |
| 5 | $H_2O$ | 1 | 54 |
| 6 | EtOH | 1 | 95 |
| 7 | EtOH | 0.5 | 23 |
| 8 | EtOH | 0.7 | 49 |
| 9 | EtOH | 0.9 | 71 |
| 10 | EtOH | 1.2 | 94 |
| 11 | EtOH | 1.4 | 95 |

[a]Reaction conditions: **1a** (1 mmol), **3a** (1 mmol), **2a** (1.5 mmol), solvent (5 ml), refluxing, 6 h.

[b]Yields refer to isolated products.

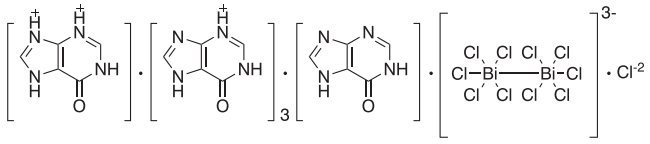
dissolved in water (30 ml) and heated to 80°C to form a clear solution. The mixture was cooled slowly to room temperature. Single crystals of $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$ were collected after 7 days (Scheme 1). The crystal structure of the catalyst is shown in Figure 1.

### 3.2 | Biginelli reaction: General procedure

A mixture of aldehyde (1.0 mmol), β-dicarbonyl compound (1.0 mmol), urea/thiourea (1.5 mmol), $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$ (0.1 mmol) and EtOH (5 ml) was heated to reflux. The course of the reaction was monitored by TLC and complete disappearance of the raw materials was observed within 6 h. The mixture was diluted with EtOH (10 ml) and the catalyst was isolated by simple decantation. After evaporation of the solvent, the crude product was purified by either crystallization (EtOH) or column chromatography (silica gel, EtOAc–petroleum ether). Known products were identified by comparing their spectral data with those of authentic samples. Substrates, products and yields are summarized in Table 3.

Isomerization of the products derived from the condensation reactions involving salicyladehyde (**4c**, **4u**) was found in experiments. Scheme 2 shows the molecular structure.

Simultaneously, urea was replaced by thiourea or derivatives of urea. The results are shown in Table 4. The yields of products when using thiourea were lower than when using urea. Yields of aromatic aldehydes carrying electron-withdrawing groups reacting with thiourea were 78–82% (**4 t**, **4u** and **4×**), and the yields of products of aromatic aldehydes



**SCHEME 1** Structure of catalyst.

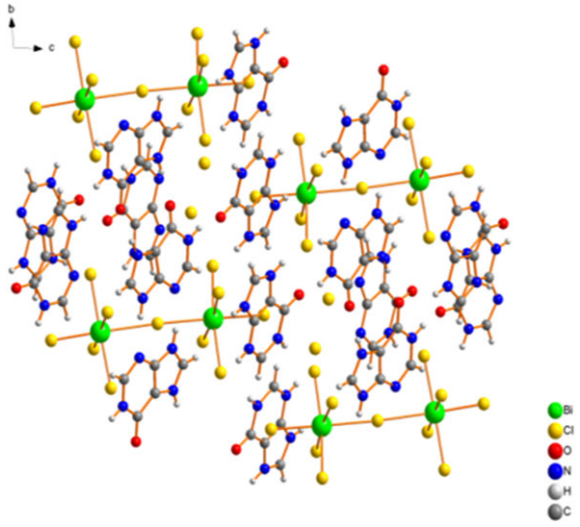
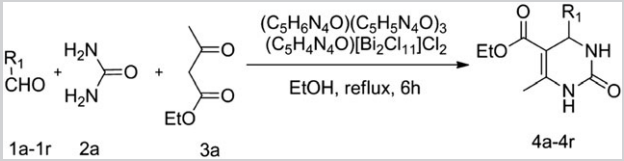


**FIGURE 1** Crystal structures of catalyst.

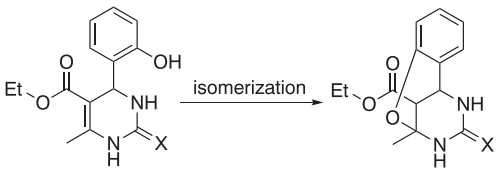
**TABLE 3** Three-component $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$-catalyzed Biginelli reaction with various aldehydes[a]




| Entry | $R_1$ | Product | Yield (%)[b] |
|---|---|---|---|
| 1 | $C_6H_6$ | **4a** | 90 |
| 2 | 2-$ClC_6H_6$ | **4b** | 91 |
| 3 | 2-$OHC_6H_6$ | **4c** | 92 |
| 4 | 3-$NO_2C_6H_6$ | **4d** | 81 |
| 5 | 4-$CH_3C_6H_6$ | **4e** | 96 |
| 6 | 4-$OMeC_6H_6$ | **4f** | 96 |
| 7 | 4-$PhC_6H_6$ | **4 g** | 93 |
| 8 | 4-$NO_2C_6H_6$ | **4 h** | 83 |
| 9 | 3,4-2$OMeC_6H_6$ | **4i** | 96 |
| 10 |  | **4j** | 75 |
| 11 | Me | **4 k** | 91 |
| 12 | Et | **4 l** | 91 |
| 13 | Pr | **4 m** | 89 |
| 14 | Bu | **4n** | 87 |
| 15 | Am | **4o** | 86 |
| 16 |  | **4p** | 87 |
| 17 |  | **4q** | 85 |
| 18 |  | **4r** | 90 |

[a]Reaction conditions: aldehyde (1 mmol), ethyl acetoacetate (1 mmol), thiourea (1.5 mmol), catalyst (1 mol%), solvent (EtOH, 5 ml), refluxing, 6 h.

[b]Yields refer to isolated products.

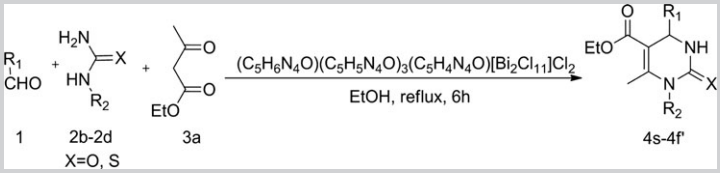



**SCHEME 2** Isomerization of DHPMs to diazatricyclic compounds.

carrying electron-donating groups reached 86, 85 and 83% for **4v**, **4w** and **4y**, respectively. As products of aliphatic aldehydes, yields of **4z**, **4a'** and **4b'** reached 73–80%. As substitutes for urea, methylurea and ethylurea reacted with benzaldehyde or acetaldehyde, and the yields of **4c'**, **4d'**, **4e'** and **4f'** were 77–83% which were lower than those when using urea (**4a**, 95%; **4 k**, 91%).

The scope of the method was extended to β-dicarbonyl compounds. As evident from Table 5, β-carbonyl ester and

**TABLE 4** Three-component $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$-catalyzed Biginelli reaction with various aldehydes, thiourea or derivatives of urea[a]

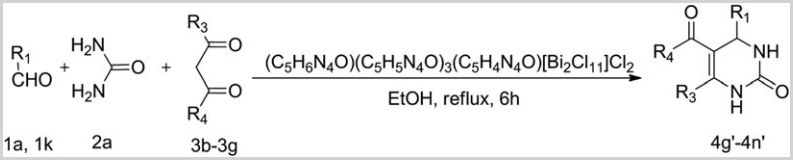


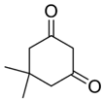

| Entry | Aldehyde | Thiourea/urea | Product | Yield (%)[b] |
|---|---|---|---|---|
| 1 | $R_1 = C_6H_6$ | $R_2$ = H, X = S | **4 s** | 85 |
| 2 | $2\text{-}ClC_6H_6$ | | **4 t** | 80 |
| 3 | $2\text{-}OHC_6H_6$ | | **4u** | 82 |
| 4 | $4\text{-}CH_3C_6H_6$ | | **4v** | 86 |
| 5 | $4\text{-}OMeC_6H_6$ | | **4w** | 85 |
| 6 | $4\text{-}ClC_6H_6$ | | **4×** | 81 |
| 7 | $4\text{-}PhC_6H_6$ | | **4y** | 83 |
| 8 | Me | | **4z** | 75 |
| 9 | Am | | **4a'** | 73 |
| 10 |  | | **4b'** | 80 |
| 11 | $C_6H_6$ | $R_2$ = Me, X = O | **4c'** | 86 |
| 12 | | $R_2$ = Et, X = O | **4d'** | 85 |
| 13 | Me | $R_2$ = Me, X = O | **4e'** | 80 |
| 14 | | $R_2$ = Et, X = O | **4f'** | 87 |

[a]Reaction conditions: aldehyde (1 mmol), ethyl acetoacetate (1 mmol), thiourea (1.5 mmol), catalyst (1 mol%), solvent (EtOH, 5 ml), refluxing, 6 h.

[b]Yields refer to isolated products.

**TABLE 5** Three-component $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$-catalyzed Biginelli reaction with various β-carbonyl esters/ketones[a]




| Entry | Aldehyde | β-Carbonyl ester/ketone | Product | Yield (%)[b] |
|---|---|---|---|---|
| 1 | $R_1 = C_6H_6$ | $R_3$ = Me, $R_4$ = OMe | **4 g'** | 96 |
| 2 | | $R_3$ = Me, $R_4$ = Oi-Pr | **4 h'** | 93 |
| 3 | | $R_3$ = Me, $R_4$ = Me | **4i'** | 85 |
| 4 | | $R_3$ = Ph, $R_4$ = Ph | **4j'** | 80 |
| 5 | |  | **4 k'** | 79 |
| 6 | |  | **4 l'** | 75 |
| 7 | $R_1$ = Me | $R_3$ = Me, $R_4$ = OMe | **4 m'** | 93 |
| 8 | | $R_3$ = Me, $R_4$ = Oi-Pr | **4n'** | 90 |

[a]Reaction conditions: aldehyde (1 mmol), β-carbonyl ester/ketone (1 mmol), urea (1.5 mmol), catalyst (1 mol%), solvent (EtOH, 5 ml), refluxing, 6 h.

[b]Yields refer to isolated products.

β-carbonyl ketone could afford the desired products **4 g'–n'**. For β-carbonyl ester, yields of **4 g'** (96%) and **4 h'** (93%) were similar to that of **4a** (95%) and yields of **4 m'** and **4n'** were similar to that of **4 k**, 93 and 90%, respectively. As substitutes for ethyl acetoacetate, β-carbonyl ketones could be used as substrates for the

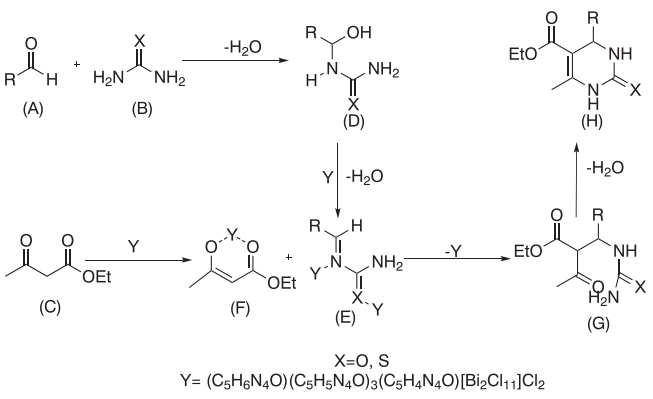
Biginelli reaction, and yields of products were 75–85%. The yields when using β-carbonyl ketones with chain structures (**4i'**, 85%; **4j'**, 80%) were higher than when using annular β-carbonyls (**4 k'**, 79%; **4 l'**, 75%).

### 3.3 | Mechanism

Folkers and co-workers[28] suggested the mechanism for the formation of DHPMs via an acylimine intermediate, and the following mechanism has been proposed (Scheme 3). The mechanism consists of an initial step of a reaction between the respective aldehydes (**A**) and urea/thiourea (**B**) forming their corresponding hemiaminals, *N*-(1-hydroxybenzyl/substituted benzyl)urea/thiourea (**D**), via standard nucleophilic addition reaction. **D** interacts with the Bi complex, forming a highly reactive intermediate (**E**). At the same time, the respective β-ketoesters (**C**) or possibly their enol forms activated by the Bi complex (**F**) attack **E** to afford open-chain intermediates (**G**). **G** after further nucleophilic addition eventually undergoes dehydration to furnish the DHPMs/DHPM thiones (**H**).

### 3.4 | Recyclability and activity of catalyst

In order to examine the recyclability and activity of the catalyst, the one-pot three-component Biginelli reaction of benzaldehyde (**1a**), urea (**2a**) and ethyl acetoacetate (**3a**) catalyzed by $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$ in refluxing ethanol was used as a model reaction. The reaction mixture was stirred under TLC analysis until benzaldehyde disappeared completely. After completion of the reaction, the catalyst was recovered by filtration and washed with hot ethanol. The catalyst was recovered without significant loss. The recovered catalyst was reused directly. As shown in Figure 2, the catalyst was recycled ten times with only a small loss of activity (isolated yield only slightly declined from 95 to 85%).




**SCHEME 3** Mechanism for the (C5H6N4O)(C5H5N4O)3(C5H4N4O)[Bi2Cl11]Cl2-catalyzed Biginelli reaction.

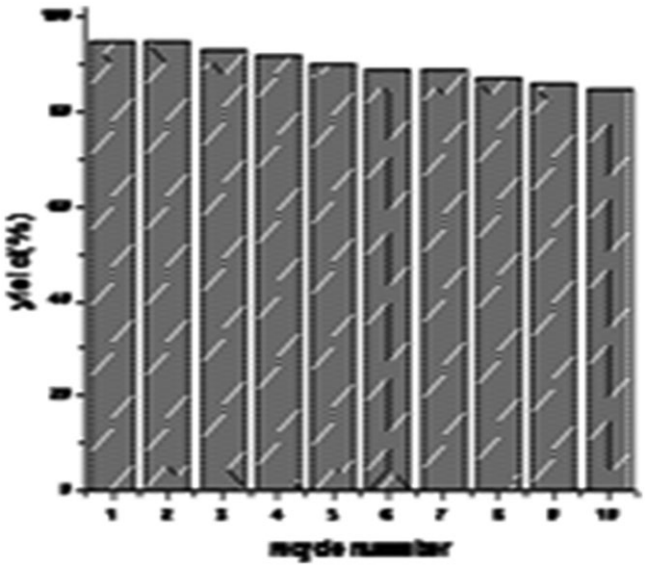


**FIGURE 2** Reusability cycles of catalyst.

## 4 | CONCLUSIONS

We have developed a facile, convenient and environmentally friendly one-pot three-component synthetic method for DHPMs. As an accessible, low-toxicity, stable and recyclable catalyst, $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$ could catalyze the Biginelli reaction efficiently with low catalyst loading and be recycled ten times with only a small loss of activity. The present protocol offers a simple, inexpensive and versatile approach to the synthesis of sterically demanding DHPMs.

## 5 | CHARACTERIZATION DATA

Unless otherwise stated, all reagents and solvents were used without further purification. Flash column chromatography was performed using silica gel (200–300 mesh) under pressure. Analytical TLC was carried out using GF254 commercial silica gel plates. Visualization of the developed chromatogram was performed by UV absorption or aqueous $KMnO_4$. All $^1H$ NMR spectra were recorded in DMSO-$d_6$ or $CDCl_3$ solution. $^1H$ NMR spectra were referenced internally to the residual proton resonance in DMSO (2.5 ppm) and $CDCl_3$ (7.26 ppm).

### 5.1 | Ethyl 6-Methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4a)[5]

White solid. $^1H$ NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.21 (s, 1H), 7.75 (s, 1H), 7.36–7.20 (m, 5H), 5.15 (d, $J$ = 3.2 Hz, 1H), 3.98 (q, $J$ = 7.1 Hz, 2H), 2.25 (s, 3H), 1.09 (t, $J$ = 7.1 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 260.1. Anal. Calcd for $C_{14}H_{16}N_2O_3$ (260.12) (%): C, 64.60; H, 6.20; N, 10.76. Found (%): C, 64.48; H, 6.11; N, 10.81.

### 5.2 | Ethyl 4-(2-Chlorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyri midine-5-carboxylate (4b)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.28 (s, 1H), 7.72 (s, 1H), 7.43–7.24 (m, 4H), 5.63 (d, $J$ = 2.7 Hz, 1H), 3.89 (q, $J$ = 7.0 Hz, 2H), 2.30 (s, 3H), 0.99 (t, $J$ = 7.1 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 294.1. Anal. Calcd for $C_{14}H_{15}ClN_2O_3$ (294.08) (%): C, 57.05; H, 5.13; N, 9.50. Found (%): C, 56.87; H, 5.31; N, 9.65.

### 5.3 | Ethyl 4-(2-Hydroxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyri midine-5-carboxylate (4c)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 7.62 (s, 1H), 7.28–7.16 (m, 3H), 6.88 (ddd, $J$ = 46.4, 26.4, 4.6 Hz, 2H), 4.47 (dd, $J$ = 4.7, 2.9 Hz, 1H), 4.17 (p, $J$ = 3.7 Hz, 2H), 3.29–3.24 (m, 1H), 1.74 (s, 3H), 1.24 (t, $J$ = 7.1 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 276.1. Anal. Calcd for $C_{14}H_{16}N_2O_4$ (276.11) (%): C, 60.86; H, 5.84; N, 10.14. Found (%): C, 60.60; H, 5.51; N, 9.95.

### 5.4 | Ethyl 4-(3-Nitrophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyri midine-5-carboxylate (4d)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.39 (s, 1H), 8.20–8.05 (m, 2H), 7.92 (s, 1H), 7.69 (ddd, $J$ = 19.6, 10.9, 4.6 Hz, 2H), 5.31 (d, $J$ = 3.3 Hz, 1H), 4.16–3.83 (m, 2H), 2.28 (s, 3H), 1.10 (t, $J$ = 7.1 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 305.2. Anal. Calcd for $C_{14}H_{15}N_3O_5$ (305.1) (%): C, 55.08; H, 4.95; N, 13.76. Found (%): C, 55.36; H, 4.78; N, 14.07.

### 5.5 | Ethyl 6-Methyl-2-oxo-4-p-tolyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4e)[17]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.18 (s, 1H), 7.71 (s, 1H), 7.12 (s, 4H), 5.10 (d, $J$ = 2.9 Hz, 1H), 3.97 (q, $J$ = 7.0 Hz, 2H), 2.26 (s, 3H), 2.24 (s, 3H), 1.10 (t, $J$ = 7.0 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 274.1. Anal. Calcd for $C_{15}H_{18}N_2O_3$ (274.13) (%): C, 65.68; H, 6.61; N, 10.21. Found (%): C, 65.79; H, 6.48; N, 9.97.

### 5.6 | Ethyl 4-(4-Methoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyri midine-5-carboxylate (4f)[17]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.16 (d, $J$ = 1.3 Hz, 1H), 7.72–7.63 (m, 1H), 7.20–6.82 (m, 4H), 5.09 (d, $J$ = 3.3 Hz, 1H), 3.98 (q, $J$ = 7.1 Hz, 2H), 3.72 (s, 3H), 2.24 (s, 3H), 1.11 (t, $J$ = 7.1 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 290.2. Anal. Calcd for $C_{15}H_{18}N_2O_4$ (290.13) (%): C, 62.06; H, 6.25; N, 9.65. Found (%): C, 62.09; H, 6.58; N, 9.47.

### 5.7 | Ethyl 4-(Biphenyl-4-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyri midine-5-carboxylate (4 g)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.26 (s, 1H), 7.81 (s, 1H), 7.63 (t, $J$ = 6.6 Hz, 4H), 7.41 (ddd, $J$ = 20.4, 16.3, 10.1 Hz, 5H), 5.20 (d, $J$ = 2.5 Hz, 1H), 4.01 (q, $J$ = 7.0 Hz, 2H), 2.27 (s, 3H), 1.13 (t, $J$ = 7.0 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 336.1. Anal. Calcd for $C_{20}H_{20}N_2O_3$ (336.15) (%): C, 71.41; H, 5.99; N, 8.33. Found (%): C, 71.26; H, 5.85; N, 8.61.

### 5.8 | Ethyl 4-(4-Nitrophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyri midine-5-carboxylate (4 h)[29]

White solid. 1H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.37 (s, 1H), 8.25–8.20 (m, 2H), 7.91 (s, 1H), 7.55–7.46 (m, 2H), 5.28 (d, $J$ = 3.3 Hz, 1H), 3.99 (q, $J$ = 7.1 Hz, 2H), 2.27 (s, 3H), 1.10 (t, $J$ = 7.1 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 305.0. Anal. Calcd for $C_{14}H_{15}N_3O_5$ (305.1) (%): C, 55.08; H, 4.95; N, 13.76. Found (%): C, 55.40; H, 4.74; N, 14.09.

### 5.9 | Ethyl 4-(3,4-Dimethoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4i)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.17 (s, 1H), 7.69 (s, 1H), 6.99–6.60 (m, 3H), 5.10 (d, $J$ = 2.9 Hz, 1H), 4.00 (q, $J$ = 7.0 Hz, 2H), 3.71 (s, 6H), 2.24 (s, 3H), 1.12 (t, $J$ = 7.1 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 320.1. Anal. Calcd for $C_{16}H_{20}N_2O_5$ (320.14) (%): C, 59.99; H, 6.29; N, 8.74. Found (%): C, 60.09; H, 6.05; N, 8.78.

### 5.10 | Ethyl 4-(Furan-2-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4j)[29]

Taupe solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.26 (s, 1H), 7.77 (s, 1H), 7.56 (d, $J$ = 0.8 Hz, 1H), 6.36 (dd, $J$ = 3.0, 1.8 Hz, 1H), 6.09 (d, $J$ = 3.1 Hz, 1H), 5.20 (d, $J$ = 3.3 Hz, 1H), 4.18–3.86 (m, 2H), 2.23 (s, 3H), 1.14 (t, $J$ = 7.1 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 250.1. Anal. Calcd for $C_{12}H_{14}N_2O_4$ (250.1) (%): C, 57.59; H, 5.64; N, 11.19. Found (%): C, 57.46; H, 6.01; N, 8.91.

### 5.11 | Ethyl 4,6-Dimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4 k)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.00 (s, 1H), 7.23 (s, 1H), 4.08 (tdd, $J$ = 17.0, 7.0, 3.5 Hz, 3H), 2.16 (s, 3H), 1.19 (t, $J$ = 7.1 Hz, 3H), 1.09 (t, $J$ = 6.2 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 198.1. Anal. Calcd for $C_9H_{14}N_2O_3$ (198.1) (%): C, 54.53; H, 7.12; N, 14.13. Found (%): C, 54.64; H, 7.03; N, 14.44.

### 5.12 | Ethyl 4-Ethyl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4 l)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 8.94 (s, 1H), 7.31 (s, 1H), 4.14–3.98 (m, 3H), 2.17 (s, 3H), 1.50–1.31 (m, 2H), 1.19 (td, $J$ = 7.1, 2.7 Hz, 3H), 0.79 (t, $J$ = 7.4 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 212.2. Anal. Calcd for $C_{10}H_{16}N_2O_3$ (212.12) (%): C, 56.59; H, 7.60; N, 13.20. Found (%): C, 56.47; H, 7.69; N, 13.54.

### 5.13 | Ethyl 6-Methyl-2-oxo-4-propyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4 m)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 8.95 (s, 1H), 7.35 (s, 1H), 4.06 (pd, $J$ = 7.2, 3.6 Hz, 3H), 2.16 (s, 3H), 1.45–1.22 (m, 4H), 1.19 (t, $J$ = 7.1 Hz, 3H), 0.85 (t, $J$ = 7.0 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 226.1. Anal. Calcd for $C_{11}H_{18}N_2O_3$ (226.13) (%): C, 58.39; H, 8.02; N, 12.38. Found (%): C, 58.09; H, 7.89; N, 12.73.

### 5.14 | Ethyl 4-Butyl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4n)[29]

White solid $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 8.95 (s, 1H), 7.34 (s, 1H), 4.06 (dddd, $J$ = 17.9, 10.9, 7.1, 3.8 Hz, 3H), 2.16 (s, 3H), 1.45–1.21 (m, 6H), 1.19 (t, $J$ = 7.1 Hz, 3H), 0.85 (t, $J$ = 6.7 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 240.2. Anal. Calcd for $C_{12}H_{20}N_2O_3$ (240.15) (%): C, 59.98.; H, 8.39; N, 11.66. Found (%): C, 60.23; H, 8.33; N, 11.85.

### 5.15 | Ethyl 6-Methyl-2-oxo-4-pentyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4o)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 8.94 (s, 1H), 7.34 (s, 1H), 4.14–3.98 (m, 3H), 2.16 (s, 3H), 1.49–1.11 (m, 12H), 0.85 (t, $J$ = 6.8 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 254.2. Anal. Calcd for $C_{13}H_{22}N_2O_3$ (254.16) (%): C, 61.39.; H, 8.72; N, 11.01. Found (%): C, 61.17; H, 8.85; N, 10.94.

### 5.16 | Ethyl 6-Methyl-4-isopropyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4p)[29p]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 8.91 (s, 1H), 7.31 (s, 1H), 4.14–4.00 (m, 2H), 3.95 (t, $J$ = 3.6 Hz, 1H), 2.17 (d, $J$ = 6.9 Hz, 3H), 1.27–1.13 (m, 4H), 0.82 (d, $J$ = 6.9 Hz, 3H), 0.74 (d, $J$ = 6.8 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 226.2. Anal. Calcd for $C_{11}H_{18}N_2O_3$ (226.13) (%): C, 58.39; H, 8.02; N, 12.38. Found (%): C, 58.46; H, 8.07; N, 12.66.

### 5.17 | Ethyl 4-*sec*-Butyl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4q)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 8.89 (d, $J$ = 9.4 Hz, 1H), 7.27 (d, $J$ = 39.9 Hz, 1H), 4.19–3.86 (m, 3H), 2.17 (d, $J$ = 2.2 Hz, 3H), 1.47–1.06 (m, 6H), 0.90–0.67 (m, 6H). MS (ESI, 70 eV): $m/z$ = 240.2. Anal. Calcd for $C_{12}H_{20}N_2O_3$ (240.15) (%): C, 59.98.; H, 8.39; N, 11.66. Found (%): C, 60.15; H, 8.61; N, 11.42.

### 5.18 | Ethyl 4-Cyclohexyl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4r)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 8.89 (s, 1H), 7.29 (d, $J$ = 1.5 Hz, 1H), 4.13–3.99 (m, 2H), 3.93 (t, $J$ = 3.8 Hz, 1H), 2.17 (s, 3H), 1.64 (dd, $J$ = 33.1, 10.0 Hz, 4H), 1.32 (dd, $J$ = 19.3, 16.4 Hz, 2H), 1.19 (t, $J$ = 7.1 Hz, 3H), 1.09 (dd, $J$ = 23.5, 10.5 Hz, 4H), 0.85 (dt, $J$ = 12.3, 7.5 Hz, 1H). MS (ESI, 70 eV): $m/z$ = 266.1. Anal. Calcd for $C_{14}H_{22}N_2O_3$ (266.16) (%): C, 63.13; H, 8.33; N, 10.52. Found (%): C, 63.35; H, 8.13; N, 10.37.

### 5.19 | Ethyl 6-Methyl-4-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4 s)[17]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 10.36 (s, 1H), 9.67 (d, $J$ = 1.6 Hz, 1H), 7.44–7.15 (m, 5H), 5.18 (d, $J$ = 3.7 Hz, 1H), 4.01 (q, $J$ = 7.0 Hz, 2H), 2.30 (s, 3H), 1.16–1.07 (m, 3H). MS (ESI, 70 eV): $m/z$ = 276.0. Anal. Calcd for $C_{14}H_{16}N_2O_2S$ (276.09) (%): C, 60.85; H, 5.84; N, 10.14; S, 11.60. Found (%): C, 60.49; H, 5.88; N, 10.32; S; 11.73.

### 5.20 | Ethyl 4-(2-Chlorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyri midine-5-carboxylate (4 t)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 10.38 (s, 1H), 9.62 (s, 1H), 7.52–7.24 (m, 4H), 5.64 (d, $J$ = 3.2 Hz, 1H), 3.92 (q, $J$ = 7.1 Hz, 2H), 2.33 (s, 3H), 1.06 (t, $J$ = 7.0 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 310.3. Anal. Calcd for $C_{14}H_{15}ClN_2O_2S$ (310.05) (%): C, 54.10; H, 4.86; N, 9.01; S, 10.32. Found (%): C, 54.44; H, 4.72; N, 9.15; S, 10.18.

### 5.21 | Ethyl 4-(2-Hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydro pyrimidine-5-carboxylate (4u)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.39 (dd, $J$ = 5.1, 1.8 Hz, 1H), 9.17 (d, $J$ = 1.7 Hz, 1H), 7.10 (dddd, $J$ = 59.2, 52.6, 30.6, 4.8 Hz, 4H), 4.59 (dd, $J$ = 5.2, 2.6 Hz, 1H), 4.04 (q, $J$ = 7.1 Hz, 2H), 3.40 (d, $J$ = 2.6 Hz, 1H), 1.89 (s, 3H), 1.07 (t, $J$ = 7.1 Hz, 3H). MS (ESI, 70 eV): $m/z$ = 292.1. Anal. Calcd for $C_{14}H_{16}N_2O_3S$ (292.09) (%): C, 57.52; H, 5.52; N, 9.58; S, 10.97. Found (%): C, 57.31; H, 5.60; N, 9.81; S, 10.73.

### 5.22 | Ethyl 6-Methyl-4-*p*-tolyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4v)[17]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 10.32 (s, 1H), 9.63 (d, $J$ = 1.7 Hz, 1H), 7.12 (dd, $J$ = 21.3, 8.1 Hz, 4H), 5.13 (d, $J$ = 3.7 Hz, 1H), 4.01 (q, $J$ = 7.1 Hz, 2H), 2.28 (d, $J$ = 7.3 Hz, 6H), 1.11 (t, $J$ = 7.1 Hz, 3H). MS (ESI,

70 eV): *m/z* = 290.1. Anal. Calcd for $C_{15}H_{18}N_2O_2S$ (290.11) (%): C, 62.04; H, 6.25; N. 9.65; S, 11.04. Found (%): C, 62.15; H, 6.11; N, 9.43; S, 11.21.

### 5.23 | Ethyl 4-(4-Methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydro pyrimidine-5-carboxylate (4w)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 10.31 (s, 1H), 9.62 (d, $J$ = 1.7 Hz, 1H), 7.18–7.08 (m, 2H), 6.95–6.85 (m, 2H), 5.11 (d, $J$ = 3.7 Hz, 1H), 4.00 (q, $J$ = 7.1 Hz, 2H), 3.73 (s, 3H), 2.29 (s, 3H), 1.11 (t, $J$ = 7.1 Hz, 3H). MS (ESI, 70 eV): *m/z* = 306.4. Anal. Calcd for $C_{15}H_{18}N_2O_3S$ (306.1) (%): C, 58.80; H, 5.92; N, 9.14; S, 10.47. Found (%): C, 59.00; H, 6.17; N, 9.03; S, 10.11.

### 5.24 | Ethyl 4-(4-Chlorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyri midine-5-carboxylate (4×)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 10.41 (s, 1H), 9.69 (s, 1H), 7.43 (d, $J$ = 8.4 Hz, 2H), 7.22 (d, $J$ = 8.4 Hz, 2H), 5.16 (d, $J$ = 3.4 Hz, 1H), 4.00 (q, $J$ = 6.9 Hz, 2H), 2.29 (s, 3H), 1.09 (t, $J$ = 7.1 Hz, 3H). MS (ESI, 70 eV): *m/z* = 310.0. Anal. Calcd for $C_{14}H_{15}ClN_2O_2S$ (310.05) (%): C, 54.10; H, 4.86; N, 9.01; S, 10.32. Found (%): C, 54.33; H, 4.69; N, 9.21; S, 10.39.

### 5.25 | Ethyl 4-(Biphenyl-4-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyri midine-5-carboxylate (4y)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 10.40 (s, 1H), 9.72 (d, $J$ = 1.9 Hz, 1H), 7.73–7.57 (m, 4H), 7.50–7.28 (m, 5H), 5.23 (d, $J$ = 3.7 Hz, 1H), 4.04 (q, $J$ = 7.1 Hz, 2H), 2.32 (s, 3H), 1.14 (t, $J$ = 7.1 Hz, 3H). MS (ESI, 70 eV): *m/z* = 352.1. Anal. Calcd for $C_{20}H_{20}N_2O_2S$ (352.12) (%): C, 68.16; H, 5.72; N, 7.95; S, 9.10. Found (%): C, 68.30; H, 5.49; N, 7.66; S, 9.30.

### 5.26 | Ethyl 4,6-Dimethyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4z)[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 10.15 (s, 1H), 9.22 (s, 1H), 4.18–4.03 (m, 3H), 2.20 (s, 3H), 1.20 (t, $J$ = 7.1 Hz, 3H), 1.09 (t, $J$ = 5.7 Hz, 3H). MS (ESI, 70 eV): *m/z* = 214.3. Anal. Calcd for $C_9H_{14}N_2O_2S$ (214.08) (%): C, 50.45; H, 6.59; N, 13.07; S, 14.96. Found (%): C, 50.10; H, 6.63; N, 13.44; S, 15.06.

### 5.27 | Ethyl 6-Methyl-2-oxo-4-pentyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4a')[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 10.11 (s, 1H), 9.28 (s, 1H), 4.17–4.00 (m, 3H), 2.20 (s, 3H), 1.29 (ddd, $J$ = 27.9, 13.1, 6.9 Hz, 11H), 0.85 (t, $J$ = 6.6 Hz, 3H). MS (ESI, 70 eV): *m/z* = 270.1. Anal. Calcd for $C_{13}H_{22}N_2O_2S$ (270.14) (%): C, 57.75; H, 8.20; N, 10.36; S, 11.86. Found (%): C, 57.57; H, 8.35; N, 10.46; S, 11.69.

### 5.28 | Ethyl 4-Cyclohexyl-6-methyl-2-thioxo-1,2,3,4-tetrahydropyri midine-5-carboxylate (4b')[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 10.15 (s, 1H), 9.31 (d, $J$ = 2.5 Hz, 1H), 4.22–4.07 (m, 2H), 4.03 (t, $J$ = 4.3 Hz, 1H), 2.27 (s, 3H), 1.71 (dd, $J$ = 29.0, 9.9 Hz, 4H), 1.50–1.32 (m, 2H), 1.26 (t, $J$ = 7.1 Hz, 3H), 1.21–1.07 (m, 4H), 0.90 (t, $J$ = 12.0 Hz, 1H). MS (ESI, 70 eV): *m/z* = 282.5. Anal. Calcd for $C_{14}H_{22}N_2O_2S$ (282.14) (%): C, 59.54; H, 7.85; N, 9.92; S, 11.35. Found (%): C, 59.69; H, 7.98; N, 10.00; S, 11.05.

### 5.29 | Ethyl 1,6-Dimethyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4c')[29]

White solid. $^1$H NMR (400 MHz, $CDCl_3$, $\delta$, ppm): 7.33–7.29 (m, 1H), 7.28–7.22 (m, 4H), 5.73 (s, 1H), 5.39 (d, $J$ = 2.3 Hz, 1H), 4.11 (q, $J$ = 7.1 Hz, 2H), 3.23 (s, 3H), 2.52 (s, 3H), 1.19 (t, $J$ = 7.1 Hz, 3H). MS (ESI, 70 eV): *m/z* = 274.2. Anal. Calcd for $C_{15}H_{18}N_2O_3$ (274.13) (%): C, 65.68; H, 6.61; N, 10.21. Found (%): C, 65.79; H, 6.77; N, 10.00.

### 5.30 | Ethyl 1-Ethyl-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyri midine-5-carboxylate (4d')[29]

White solid. $^1$H NMR (400 MHz, $CDCl_3$, $\delta$, ppm): 7.29 (dd, $J$ = 10.0, 4.1 Hz, 2H), 7.26–7.20 (m, 3H), 5.71 (d, $J$ = 7.4 Hz, 1H), 5.35 (d, $J$ = 2.3 Hz, 1H), 4.09 (q, $J$ = 7.1 Hz, 2H), 3.89 (dt, $J$ = 14.2, 7.1 Hz, 1H), 3.75 (dt, $J$ = 14.5, 7.1 Hz, 1H), 2.53 (s, 3H), 1.19 (dt, $J$ = 14.3, 7.1 Hz, 6H). MS (ESI, 70 eV): *m/z* = 288.2. Anal. Calcd for $C_{16}H_{20}N_2O_3$ (288.15) (%): C, 66.65; H, 6.99; N, 9.72. Found (%): C, 66.91; H, 6.68; N, 9.70.

### 5.31 | Ethyl 1,4,6-Trimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4e')[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 7.42 (d, $J$ = 3.5 Hz, 1H), 4.16–4.02 (m, 3H), 3.07 (s, 3H), 2.41 (s, 3H), 1.20 (t, $J$ = 7.1 Hz, 3H), 1.07 (d, $J$ = 6.3 Hz, 3H). MS (ESI, 70 eV): *m/z* = 212.0. Anal. Calcd for $C_{10}H_{16}N_2O_3$ (212.12) (%): C, 56.59; H, 7.60; N, 13.20. Found (%): C, 56.78; H, 7.66; N, 13.12.

### 5.32 | Ethyl 1-Ethyl-4,6-dimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4f')

White solid. IR (KBr, $cm^{-1}$): 3228 (NH), 2985–2873 (C═H), 1681 (C═O), 1624 (C═C). $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 7.36 (d, $J$ = 3.3 Hz, 1H), 4.17–4.01 (m, 3H), 3.76 (dt, $J$ = 14.1, 7.1 Hz, 1H), 3.57 (dd, $J$ = 14.4, 7.1 Hz, 1H), 2.41 (s, 3H), 1.20 (t, $J$ = 7.1 Hz, 3H), 1.11–1.00 (m, 6H). $^{13}$C NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 166.03, 155.39,

149.20, 104.85, 99.99, 59.83, 45.48, 37.17, 23.36, 15.74, 15.27, 14.65. MS (ESI, 70 eV): *m/z* = 226.1. Anal. Calcd for $C_{11}H_{18}N_2O_3$ (226.13) (%): C, 58.39; H, 8.02; N, 12.38. Found (%): C, 58.50; H, 7.92; N, 12.51.

### 5.33 | Methyl 6-Methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4 g')[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.24 (s, 1H), 7.78 (s, 1H), 7.37–7.20 (m, 5H), 5.15 (d, $J$ = 3.4 Hz, 1H), 3.53 (s, 3H), 2.26 (s, 3H). MS (ESI, 70 eV): *m/z* = 246.1. Anal. Calcd for $C_{13}H_{14}N_2O_3$ (246.1) (%): C, 63.40; H, 5.73; N, 11.38. Found (%): C, 63.60; H, 5.85; N, 11.08.

### 5.34 | Isopropyl 6-Methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4 h')[5]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.18 (s, 1H), 7.73 (s, 1H), 7.28 (dt, $J$ = 12.1, 7.7 Hz, 5H), 5.13 (d, $J$ = 3.0 Hz, 1H), 4.81 (dt, $J$ = 12.4, 6.2 Hz, 1H), 2.24 (s, 3H), 1.16 (d, $J$ = 6.2 Hz, 3H), 0.98 (d, $J$ = 6.2 Hz, 3H). MS (ESI, 70 eV): *m/z* = 274.2. Anal. Calcd for $C_{15}H_{18}N_2O_3$ (274.13) (%): C, 65.68; H, 6.61; N, 10.21. Found (%): C, 65.83; H, 6.91; N, 10.00.

### 5.35 | 5-Acetyl-3,4-dihydro-6-methyl-4-phenylpyrimidin-2-(1*H*)one(4i')[5]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.20 (s, 1H), 7.84 (s, 1H), 7.32 (d, $J$ = 6.8 Hz, 2H), 7.26 (d, $J$ = 6.0 Hz, 3H), 5.27 (s, 1H), 2.30 (s, 3H), 2.11 (s, 3H). MS (ESI, 70 eV): *m/z* = 230.1. Anal. Calcd for $C_{13}H_{14}N_2O_2$ (230.11) (%): C, 67.81; H, 6.13; N, 12.17. Found (%): C, 68.00; H, 5.97; N, 12.34.

### 5.36 | 5-Benzoyl-4,6-diphenyl-3,4-dihydropyrimidin-2-(1*H*)one (4j')[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.44 (s, 1H), 8.01 (s, 1H), 7.51–6.94 (m, 15H), 5.34 (d, $J$ = 2.9 Hz, 1H). MS (ESI, 70 eV): *m/z* = 354.0. Anal. Calcd for $C_{23}H_{18}N_2O_2$ (354.14) (%): C, 77.95; H, 5.12; N, 7.90. Found (%): C, 77.85; H, 5.33; N, 7.73.

### 5.37 | 3,4,7,8-Tetrahydro-7,7-dimethyl-4-phenylquinazoline-2,5-(1*H*,6*H*)dione (4 k')[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.47 (s, 1H), 7.77 (s, 1H), 7.37–7.18 (m, 5H), 5.15 (d, $J$ = 2.7 Hz, 1H), 2.42 (d, $J$ = 17.3 Hz, 1H), 2.24 (dd, $J$ = 30.7, 16.7 Hz, 2H), 2.03 (d, $J$ = 16.1 Hz, 1H), 1.03 (d, $J$ = 9.1 Hz, 3H), 0.89 (s, 3H). MS (ESI, 70 eV): *m/z* = 270.0. Anal. Calcd for $C_{16}H_{18}N_2O_2$ (270.14) (%): C, 71.09; H, 6.71; N, 10.36. Found (%): C, 71.33; H, 6.56; N, 10.40.

### 5.38 | 3,4,7,8-Tetrahydro-4,7-diphenylquinazoline-2,5-(1*H*,6*H*)dione (4 l')[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.59 (d, $J$ = 26.5 Hz, 1H), 7.83 (d, $J$ = 21.3 Hz, 1H), 7.29 (ddd, $J$ = 25.1, 15.4, 6.5 Hz, 10H), 5.22 (d, $J$ = 14.8 Hz, 1H), 3.56–3.14 (m, 1H), 2.94–2.53 (m, 3H), 2.38 (dd, $J$ = 36.2, 13.9 Hz, 1H). MS (ESI, 70 eV): *m/z* = 318.1. Anal. Calcd for $C_{20}H_{18}N_2O_2$ (318.14) (%): C, 75.45; H, 5.70; N, 8.80. Found (%): C, 75.61; H, 5.55; N, 8.91.

### 5.39 | Methyl 4,6-Dimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4 m')[29]

White solid. $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 9.02 (d, $J$ = 11.7 Hz, 1H), 7.23 (s, 1H), 4.12 (dd, $J$ = 6.2, 3.4 Hz, 1H), 3.61 (s, 3H), 2.16 (s, 3H), 1.09 (d, $J$ = 6.3 Hz, 3H). MS (ESI, 70 eV): *m/z* = 184.0. Anal. Calcd for $C_8H_{12}N_2O_3$ (184.08) (%): C, 52.17; H, 6.57; N, 15.21. Found (%): C, 52.33; H, 6.61; N, 15.49.

### 5.40 | Isopropyl 4,6-Dimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4n')

White solid. IR (KBr, cm$^{-1}$): 3248 (NH), 3134 (NH), 2979–2941 (C—H), 1735(C═O), 1703 (C═O), 1624 (C═C). $^1$H NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 8.97 (s, 1H), 7.21 (s, 1H), 4.91 (dd, $J$ = 12.0, 5.9 Hz, 1H), 4.11 (s, 1H), 2.15 (s, 3H), 1.19 (d, $J$ = 4.2 Hz, 6H), 1.09 (d, $J$ = 5.8 Hz, 3H). $^{13}$C NMR (400 MHz, DMSO-$d_6$, $\delta$, ppm): 165.31, 153.02, 148.02, 101.18, 66.55, 46.75, 23.87, 22.28, 22.17, 18.10. MS (ESI, 70 eV): *m/z* = 212.0. Anal. Calcd for $C_{10}H_{16}N_2O_3$ (212.12) (%): C, 56.59; H, 7.60; N, 13.20. Found (%): C, 56.70; H, 7.83; N, 13.00.

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