

# 1,3-Bis(carboxymethyl)imidazolium Chloride as a Sustainable, Recyclable, and Metal-Free Ionic Catalyst for the Biginelli Multicomponent Reaction in Neat Condition

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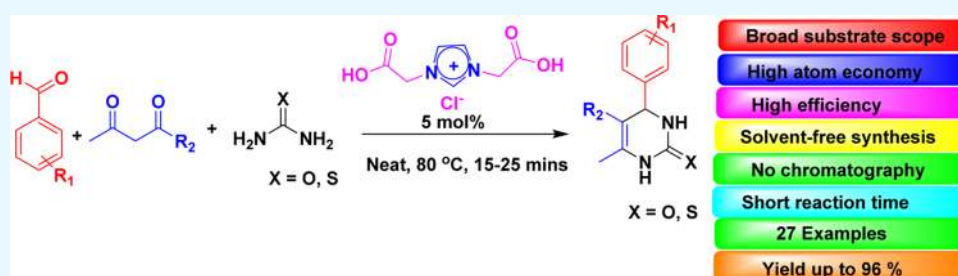
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**ABSTRACT:** A simple and novel methodology has been developed for the synthesis of 1,3-bis(carboxymethyl)imidazolium chloride [BCMIM][Cl] salt. The ionic salt [BCMIM][Cl] catalyzed the reaction among arylaldehydes; the substituted 1,3-dicarbonyl compounds and urea/thiourea at 80 °C with 5 mol % under neat condition provided the substituted dihydropyrimidin-2(1H)-one/thiones in the synthesis step with yields of up to 96%. In addition, we synthesized the commercially available drug Monastrol by employing this methodology. The new synthesis method employs the benefits of a broad substrate scope, short reaction time, and high atom economy along with low catalyst loading in neat conditions, and is devoid of chromatographic purification. The ionic salt [BCMIM][Cl] was recycled and reused up to six cycles without substantial damage of its catalytic efficiency.

## INTRODUCTION

Green chemistry, the term commonly known as sustainable chemistry, is the philosophy of modern-day research that deals with the development of novel environmentally benign synthesis procedures. In the past 2 decades, multicomponent reactions (MCR) have received significant attention, as they largely imply appropriate synthesis methods with a high degree of atom economy to deliver complex molecular architectures in one pot. The multicomponent reaction has numerous advantages such as low cost, process simplicity, low *E*-factor, high atom economy, and complex product formation with a minimum number of synthesis steps.<sup>1–4</sup> In the field of MCRs, the Biginelli multicomponent reaction has gained the special attention of the academic and chemical community because of its efficient generation of dihydropyrimidin-2(1H)-one/thiones and their derivatives.<sup>5–7</sup> Biginelli was first discovered as a simple one-pot multicomponent reaction of benzaldehyde, ethyl acetoacetate, and urea in the presence of a catalytic amount of hydrochloric acid in refluxing condition to produce dihydropyrimidin-2(1H)-ones (DHPMs) as shown in Scheme 1.<sup>8,9</sup> Substituted dihydropyrimidin-2(1H)-one/thiones (DHPMs) were known for their numerous biological and therapeutic possessions, such as anticancer, antibacterial, antiviral, antihypertensive, anti-inflammatory, and calcium

channel blockers (Figure 1).<sup>10–18</sup> Some of the dihydropyrimidiones (DHPMs), such as monastrol (A), enastron (B), dimethylenastron (C) and 5-fluorouracil (D), were clinically used for anticancer medicines such as the Eg<sup>5</sup> inhibitor (Figure 1).<sup>19–22</sup> Methylthiouracil (E) was used as an antithyroid agent,<sup>23</sup> and emivirin (F) was used as a powerful HIV inhibitor.<sup>24</sup> Moreover, riboflavin (Vitamin 2) contains a dihydropyrimidin-2(1H)-one moiety as a key moiety.<sup>25</sup> In the multicomponent Biginelli reactions, a large number of dihydropyrimidin-2(1H)-one/thione libraries could be generated by varying the reactant components (an arylaldehyde, active methylene of 1,3-dicarbonyl compounds, and urea/thiourea) with minimum effort.<sup>26–28</sup>

The various catalysts used in Biginelli reactions are InCl<sub>3</sub>,<sup>29</sup> InBr<sub>3</sub>,<sup>30</sup> ZrCl<sub>4</sub>,<sup>31</sup> IBX,<sup>32</sup> ZnSnO<sub>4</sub>,<sup>33</sup> phytic acid,<sup>34</sup> Fe<sub>3</sub>O<sub>4</sub>@Silica sulfuric acid,<sup>35</sup> in situ generated HBr,<sup>36</sup> L-proline *N*-sulfonic acid-functionalized magnetic nanoparticles,<sup>37</sup> PEG-SANM

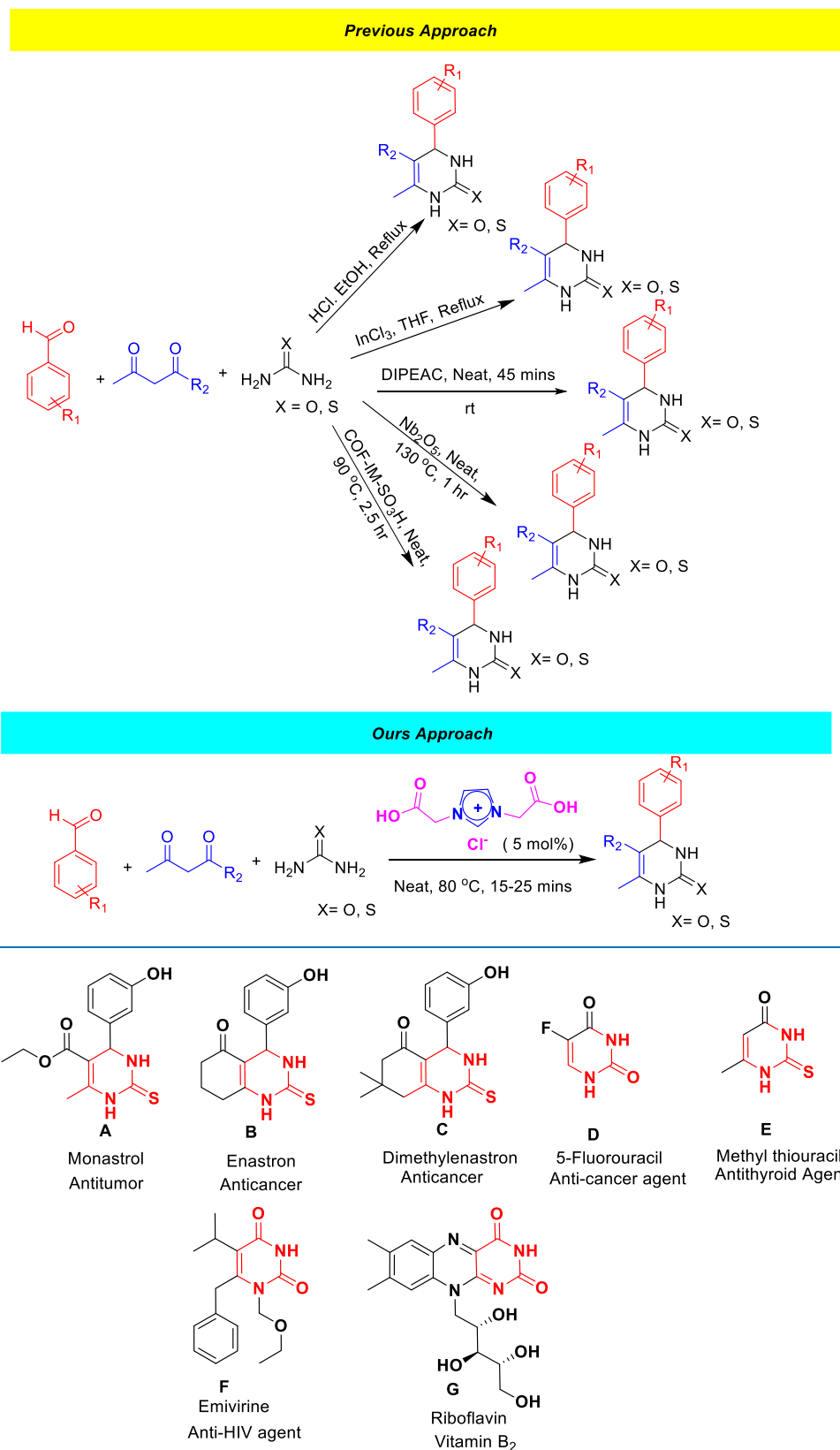
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## Scheme 1. Biginelli Reactions: Previous and Current Approach

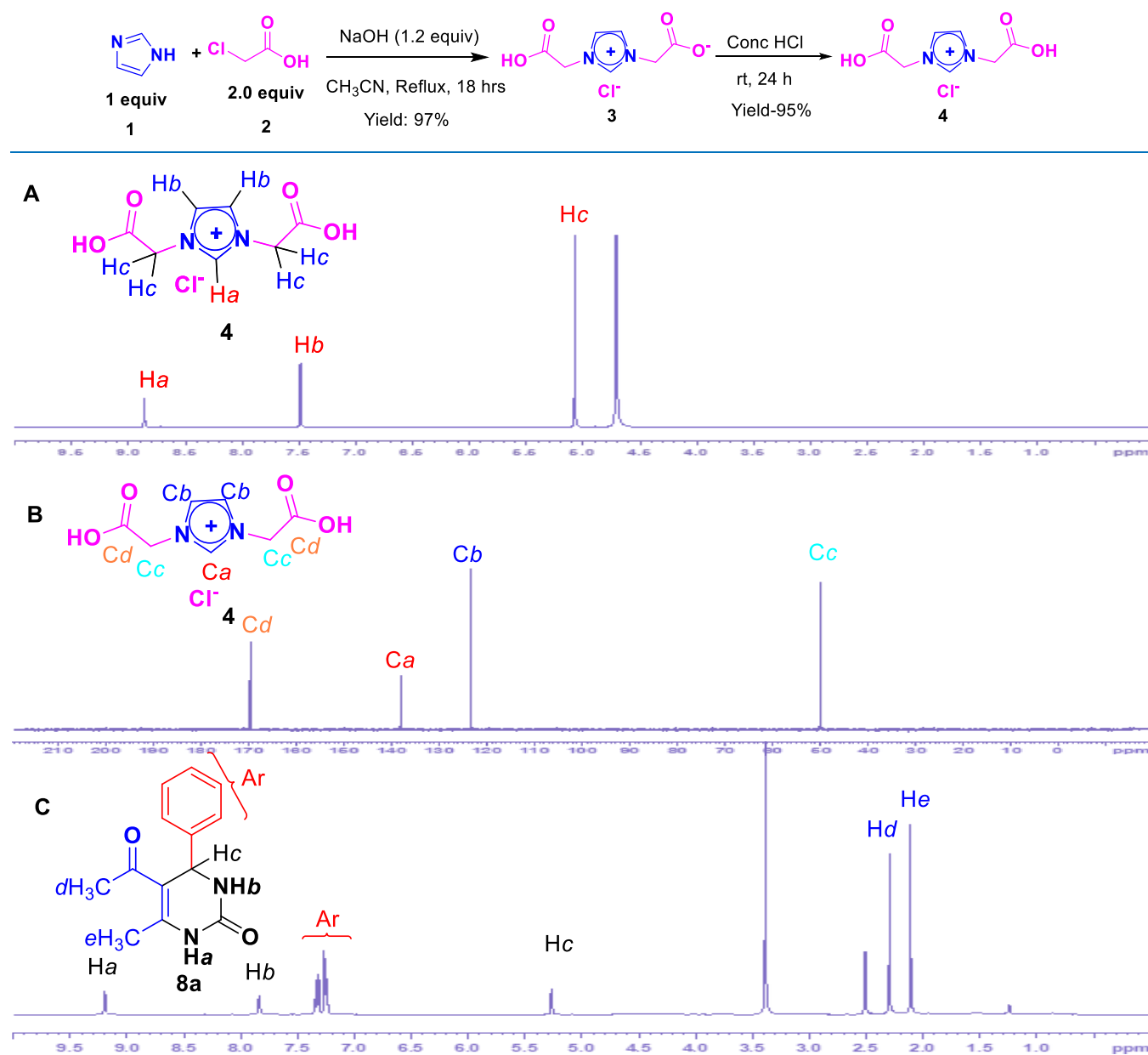


**Figure 1.** Representative biologically active DHPM compounds.

nanocomposite,<sup>38</sup> Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub>-APTMS-Fe(OH)<sub>2</sub>,<sup>39</sup> SO<sub>3</sub>H@imineZCMNPs,<sup>40</sup> titanocene,<sup>41</sup> Bronsted acid in a metal-organic framework,<sup>42</sup> heteropolyacid derivatives,<sup>43</sup> DIPEAC,<sup>44</sup>

Montmorillonite-KSF,<sup>45</sup> CNT-Fe<sub>3</sub>O<sub>4</sub>-TPh,<sup>46</sup> niobium oxides,<sup>47</sup> Zn(II)/Cd(II)-based MOFs,<sup>48</sup> and COF-IM-SO<sub>3</sub>H (Scheme 1).<sup>49</sup> However, synthesis of these catalysts suffers

## Scheme 2. Synthesis of Ionic Salt 1,3-Bis(carboxymethyl)imidazolium Chloride [BCMIM][Cl]

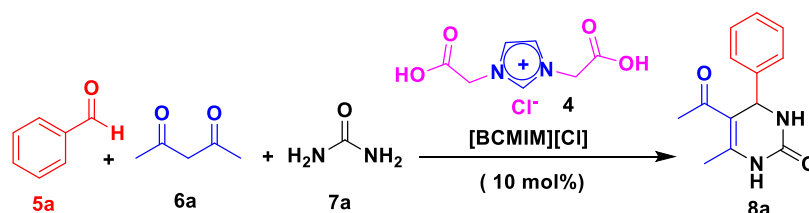


**Figure 2.** NMR spectra: (A) <sup>1</sup>H NMR spectrum of catalyst 4; (B) <sup>13</sup>C NMR spectrum of catalyst 4; and (C) <sup>1</sup>H NMR spectrum of compound 8a.

from several disadvantages such as the use of toxic solvents, expensive metal catalysts, costly or hazardous reagents, harsh reaction environments, lengthy workup procedures, low yields of products, and long reaction times. Thus, from the academic and industrial consideration, the expansion of approaches for the synthesis of dihydropyrimidine-2(1*H*)-ones/thione (DHPM) derivatives using a reusable, inexpensive, nontoxic catalyst, and mild reaction conditions is of enormous importance.<sup>50–57</sup> Currently, the catalysis field is regarded as the core of numerous chemical procedures, since a catalyst lowers the activation energy of the reaction and makes the reaction more feasible.<sup>58–61</sup>

Recently, task-specific ionic liquids (TSILs) have gained significant attention from the research community due to their being a green-substitute preference for catalysis, traditional media, and several chemical tasks. TSILs comprise several distinct properties such as low toxicity, nonvolatility, high

thermal stability, extensive liquid range, excellent solubility, non-flammability, less volatility, and recyclability. TSILs are used as a catalyst as well as an eco-friendly solvent for a wide range of chemical and industrial processes. Thus, the introduction of an inexpensive, active, environmentally friendly, and mild ionic catalyst for MCRs higher than analogs of medicinal and biological eminence is in the mandate. Moreover, there is a huge demand to develop novel approaches for the reduction of further environmental damages.<sup>62–66</sup> Hence, to produce pharmacologically active dihydropyrimidine-2(1*H*)-ones/thiones analogs, competent, advanced, and environmentally benign procedures are still strongly required. Herein, we have reported a modified procedure for the synthesis of 1,3-bis(carboxymethyl)imidazolium chloride [BCMIM][Cl]<sup>67,68</sup> and its application in the one-pot multi-component Biginelli reactions to dihydropyrimidine-2(1*H*)-ones/thiones in solvent-free conditions.

Table 1. Solvent Optimization for the One-Pot Biginelli Multicomponent Reaction<sup>a</sup>

entry	solvent	temperature (°C)	time (h)	yield (%) <sup>b</sup>
1	THF	80	2	30
2	CH <sub>3</sub> CN	80	12	40
3	DMF	80	12	10
4	DMSO	80	12	35
5	CH <sub>2</sub> Cl <sub>2</sub>	80	12	50
6	CHCl <sub>3</sub>	80	12	60
7	CH <sub>3</sub> OH	80	12	40
8	IPA	80	4	70
9	EtOH	80	4	76
10	H <sub>2</sub> O	80	12	10
11	neat	rt	24	50
12	neat	80	0.26	96

<sup>a</sup>The reaction was performed using **5a** (1.66 mmol), **6a** (1.66 mmol), and **7a** (1.66 mmol) in one pot in various solvents. <sup>b</sup>Yield of the isolated product.

## RESULTS AND DISCUSSION

Our synthesis manipulation commenced with the initial synthesis of the targeted bis 1,3-bis(carboxymethyl)-imidazolium chloride [BCMIM][Cl] catalyst as shown in Scheme 2.

At first, the reaction of one equivalent of imidazole **1** with 2 equiv of chloroacetic acid **2** in the presence of 1.2 equivalents of NaOH as base gave the ionic liquid compound **3** in 97% yield after refluxing for 18 h as depicted in Scheme 2. Next, the treatment of crude product **3** with concentrated hydrochloric acid in room temperature for 24 h gave the ionic crystal salt [BCMIM][Cl] **4** with 95% yield. The formation of ionic salt [BCMIM][Cl] **4** was unequivocally supported by analytical techniques. The <sup>1</sup>H NMR spectra of ionic salt [BCMIM][Cl] **4** indicated the appearance of two proton peaks at 8.86 and 7.49 ppm for the Ha and Hb signals of three substituted imidazole protons, and four characteristic proton signals of chloroacetic acid (–CH<sub>2</sub>–) Hc appeared at 5.07 ppm (Figure 2A). The <sup>13</sup>C NMR spectra of the ionic salt [BCMIM][Cl] **4** showed the appearance of Ca, Cb, Cc, and Cd signals at 169.7, 138.2, 123.5, and 50.2 ppm, respectively, as shown in Figure 2B. Next, we employed the ionic salt [BCMIM][Cl] **4** as catalyst for the one-pot multicomponent Biginelli reactions.

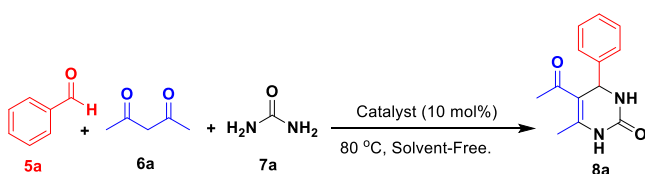
Employing 10 mol % of ionic salt [BCMIM][Cl] **4**, benzaldehyde **5a**, acetylacetone **6a**, and urea **7a** were chosen as the model substrates for the one-pot multicomponent Biginelli reactions. In the solvent optimization reaction, while employing 10 mol % of ionic salt catalyst [BCMIM][Cl] **4**, we have investigated the effect of various solvents in a one-pot Biginelli reaction as depicted (Table 1). Moreover, using a polar aprotic solvent such as tetrahydrofuran (THF), CH<sub>3</sub>CN, dimethylformamide (DMF), and dimethyl sulfoxide (DMSO) at 80 °C for 12 h resulted in the product **8a** with a yield of up to 40% (Table 1, entries 1–4). However, by using the chlorinated solvents such as CH<sub>2</sub>Cl<sub>2</sub> and CHCl<sub>3</sub>, the yield of the product **8a** was not substantially changed (Table 1, entries 5 and 6). Next we turned our attention to polar protic solvents

such as CH<sub>3</sub>OH, IPA, and EtOH, which gradually enhanced the product yield of **8a** up to 76% (Table 1, entries 7–9). However, in an effort to make the reaction medium green, we tried H<sub>2</sub>O as the solvent, which could not significantly enhance the product yield (Table 1, entry 10). Additionally, the Biginelli product yield **8a** was observed up to 50% at room temperature in neat condition after 24 h (Table 1, entry 11). It is interesting to note that the product yield of Biginelli product **8a** was raised up to 96% when we carried out the reaction without using any solvents at 80 °C (Table 1, entry 12) heating condition. The increase in product yield in neat conditions could be due to the enhanced content of the starting materials in the reaction vessel.

Hence, the solvent-free reaction was considered as the best reaction condition for environmental sustainability and cost.<sup>64,65</sup> Next, we also optimized the best catalyst for the multicomponent Biginelli reaction. We examined H<sub>2</sub>SO<sub>4</sub>, PTSA, 1-butyl-3-methyl imidazolium tetrafluoroborate [BMIM][BF<sub>4</sub>] **1D**, 1-carboxymethyl 3-methyl imidazolium tetrafluoroborate [CMMIM][BF<sub>4</sub>] **2D**, and 1,3-bis-(carboxymethyl)imidazolium chloride [BCMIM][Cl] **4** for the multicomponent Biginelli reaction at 80 °C heating condition (Table 2, entries 2–6). However, on employing 1,3-bis(carboxymethyl)imidazolium chloride [BCMIM][Cl] **4**, the Biginelli product yield **8a** was maximum (96%) at 80 °C heating condition in 16 min. Since more than one catalytic center is present in the 1,3-bis(carboxymethyl)imidazolium chloride [BCMIM][Cl] **4**, the reaction time was reduced for the Biginelli reaction as shown in Table 2.

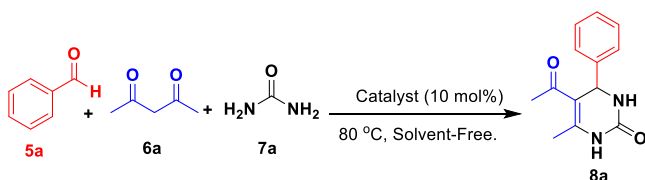
Next, we performed the model Biginelli reaction by changing the mmol ratio of benzaldehyde **5a**, acetylacetone **6a**, and urea **7a** in one pot as shown in Table 3. The reduction of the product yield was perceived on changing the mmol ratios of the starting materials. However, the highest yield was achieved by employing [BCMIM][Cl] catalysts with identical mmol ratio of the starting materials (Table 3, entry 4).

Additionally, we optimized the ionic salt [BCMIM][Cl] catalyst loading mol % to get the best catalytic activity for the

**Table 2. Comparison of Various Catalysts for the Multicomponent Biginelli Reaction<sup>a</sup>**

entry	catalyst	time (min)	yield (%) <sup>b</sup>
1		60	20
2	H <sub>2</sub> SO <sub>4</sub>	60	25
3	PTSA	60	50
4	[BMIM][BF <sub>4</sub> ] 1D	60	30
5	[CMMIM][BF <sub>4</sub> ] 2D	60	60
6	[BCMIM][Cl] 4	16	96

<sup>a</sup>The reaction was performed using 5a (1.66 mmol), 6a (1.66 mmol), and 7a (1.66 mmol) in one pot in various solvents. <sup>b</sup>Yield of the isolated product.

**Table 3. Optimization of mmol Percentage of the Reactants in the One-Pot Biginelli Reaction**

entry	mmol 5a:6a:7a	yield (%) <sup>a</sup>
1	1:0.9:0.9	20
2	1:1.2:1.2	50
3	1: 1.5:1.5	40
4	1:1:1	96

<sup>a</sup>Yield of the isolated product.

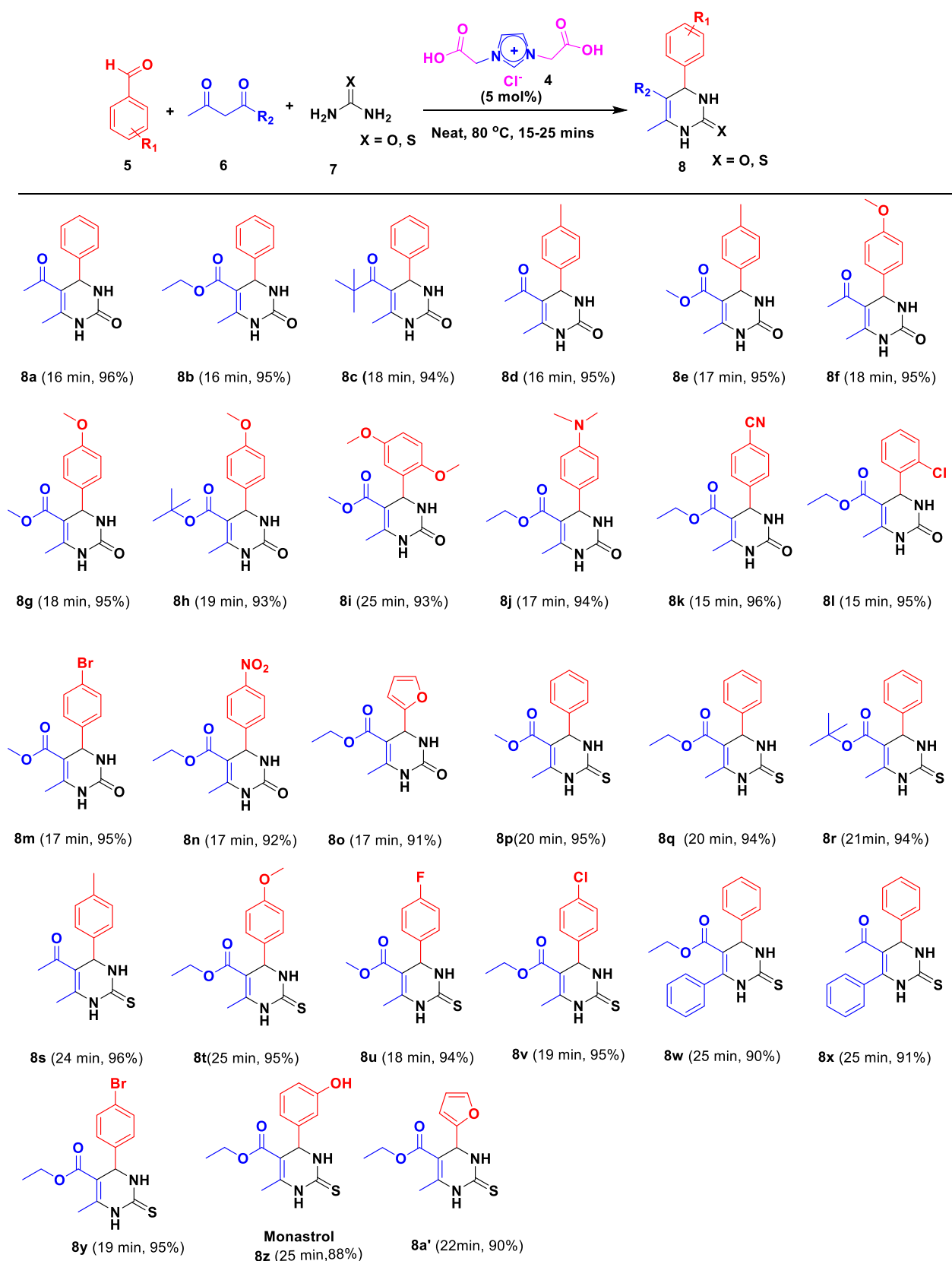
same set of reactions. We observed that the yield of 3,4-dihydropyrimidin-2(1H)-one (DHPM) **8a** was maximum using 5 mol % [BCMIM][Cl] catalyst (Table 2, entries 3). Further increase in the catalyst loading mol % did not influence the yield and time for the reactions (Table 2, entries 4–7). Having the best reaction conditions in hand, the flexibility of the methodology was scrutinized by varying different substituents in the Biginelli reaction. The reactions of the substituted arylaldehyde **5**,  $\beta$ -ketoester/ketone **6**, and urea/thiourea **7** in solvent-free condition at 80 °C heating condition yielded 3,4-dihydropyrimidin-2(1H)-one (DHPM)/thiones in 15–25 min (Scheme 3, **8a–8a'**). Various arylaldehydes containing electron-donating substituent groups such as  $-\text{CH}_3$ ,  $-\text{OCH}_3$ ,  $-\text{OH}$ , and  $-\text{N}(\text{CH}_3)_2$  moieties were well tolerated for this reaction. Arylaldehyde containing electron-withdrawing groups such as  $-\text{CN}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{F}$ , and  $-\text{NO}_2$  yielded the Biginelli product with good yield in a lesser time. Furthermore, the crowded 2,4-dimethoxy benzaldehyde and heteroaryl aldehyde yielded the preferred products with high yields. The Biginelli product 5-acetyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one derivative was confirmed by analytical techniques. Referring to the <sup>1</sup>H NMR spectrum of the characteristic derivatives **8a**, the representative signals at 9.19 and 7.84 ppm indicated two singlets for the two protons of the  $-\text{NH}$  group, the signal at 5.26 ppm indicated a doublet for the  $-\text{CH}$  proton existing in the pyrimidine ring, and the signals at 7.35–7.23 ppm indicated five protons present in the

phenyl ring (Figure 2 spectra C). In the <sup>13</sup>C NMR data, the signals at 194.75 ppm and 152.62 ppm represent acetyl carbonyl carbon and carbonyl carbon in-between two adjacent  $-\text{NH}$  groups, while all other carbons gave the expected peak values (Figure 2 spectra C). Again, the construction of compound **8a** was confirmed by GC-MS:  $m/z$ . The calculated  $m/z$  for compound **8a** (C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub>) is 230.2 and the observed value is 230.1. The Biginelli products **8a–8a'** were confirmed by analytical techniques (Supporting Information) (Table 4).

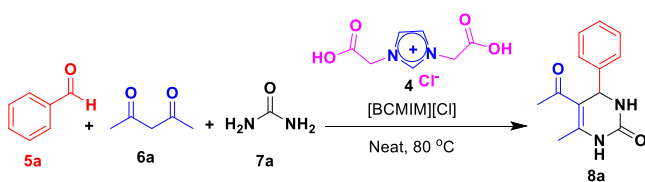
Over the past 2 decades, it has been understood that the concept of sustainable improvement plays a significant part in designing eco-friendly, efficient, and economic strategies for chemical synthesis. In this regard, Sheldon et al. introduced the environmental impact factor or *E*-factor, which helps in determining the quantity of waste generated per kilogram of the product to measure the manufacturing process.<sup>69,70</sup> In addition, our solvent-free green synthesis methods demonstrate lower *E*-factors of 0.17–0.28 for 3,4-dihydropyrimidin-2(1H)-ones (DHPMs)/thiones, which is also in agreement with the principle of atom economy (Supporting Information).

Next, we established the utility of this method in the gram-scale synthesis employing the same set of model reactions by varying the urea/thiourea components. The neat reaction of 10 mmol benzaldehyde **5a**, 10 mmol acetylacetone **6a**, and 10 mmol urea **7a** in the presence of 5 mol % [BCMIM][Cl] could afford 2.08 g of 4-phenyl-3,4-dihydropyrimidin-2(1H)-ones **8a** in the highest yield of 90% (Scheme 4). The neat reaction of 10 mmol benzaldehyde **5p** with 10 mmol acetylacetone **6p** and 10 mmol thiourea **7p** in the presence of 5 mol % [BCMIM][Cl] could afford 2.40 g of 4-phenyl-3,4-dihydropyrimidin-2(1H)-thiones **8p** with 91% yield, establishing the potential synthesis applications of the present protocol for a large-scale synthesis (Scheme S3, Supporting Information).

**Plausible Reaction Mechanism.** Herein, by employing 5 mol % ionic salt catalyst [BCMIM][Cl] **4** in the neat condition, the plausible reaction mechanism of the Biginelli multicomponent reaction is discussed (Figure 3). The Brønsted acid ionic salt [BCMIM][Cl] **4** contains two catalytic centers such as two bifunctional carboxylic acid moieties. Two equivalents of arylaldehyde **a** will be activated by the two carboxylic moieties, which will immediately react with urea/thiourea **b** to yield the adduct **d**. On the other side, substituted 1,3-dicarbonyl compounds will react with Brønsted acidic ionic salt [BCMIM][Cl] **4** to form keto/enol tautomers **c** and **c'**, which will simultaneously react with the adduct **d** to form intermediate **e**. The intermediate **e** will undergo intramolecular cyclization and dehydration to yield the final product **f**. In the Biginelli multicomponent reaction, the effect of hydrogen bonding by the ionic salt [BCMIM][Cl] **4** catalyst is an important parameter.<sup>71–74</sup> The hydrogen-bonding effect of [BCMIM][Cl] **4** catalysts could enhance the electrophilic character of arylaldehyde **a**, 1,3-dicarbonyl compounds **c**, and intermediate **e**. Hence, Brønsted acidic ionic salt [BCMIM][Cl] **4** could enhance the rate of formation of 4-aryl-3,4-dihydropyrimidin-2(1H)-one/(DHP)/4-aryl-3,4-dihydropyrimidin-2(1H)-thione (DHP). The proposed mechanism was described by the imine formation of arylaldehyde with urea/thiourea followed by Michael addition, and then intramolecular cyclization to 4-aryl-3,4-dihydropyrimidin-2(1H)-one/(DHP)/4-aryl-3,4-dihydropyrimidin-2(1H)-thione (DHP) as shown in Figure 3. Since more than one catalytic center is present in the catalyst, it showed higher catalytic

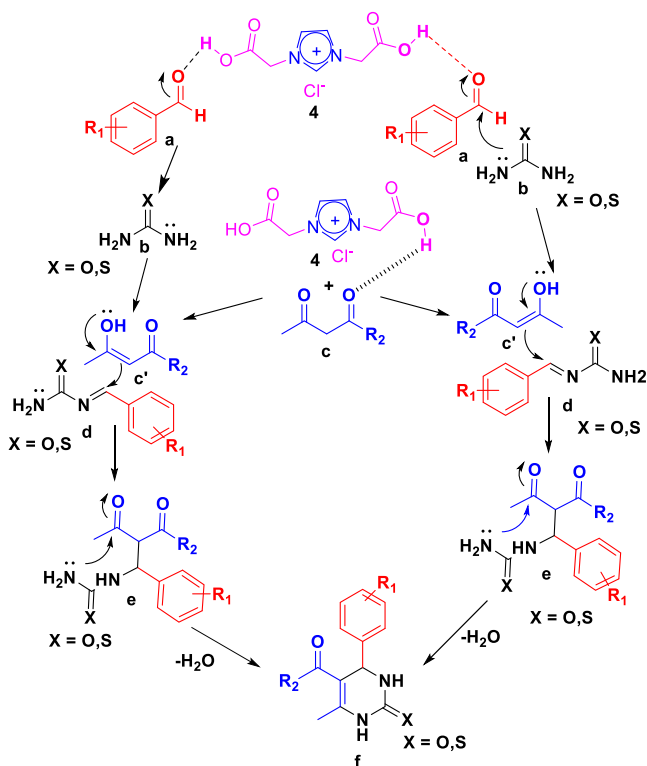
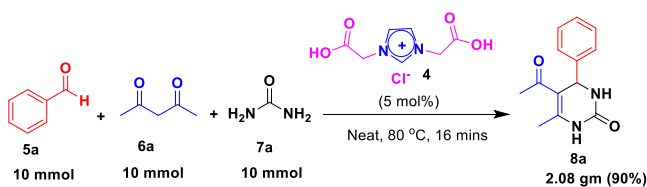
Scheme 3. Substrate Scope for Various 4-Aryl-3,4-dihydropyrimidin-2(1H)-one/4-Aryl-3,4-dihydropyrimidin-2(1H)-thiones (8a–8a')<sup>a,b</sup>

<sup>a</sup>Reaction conditions: The reaction was performed by employing 5 (1.66 mmol), 6 (1.66 mmol), and 7 (1.66 mmol) in one pot at 80 °C in neat condition. <sup>b</sup>Yield of the isolated product.

**Table 4. Optimization of the Ionic Salt Catalyst Loading Percentage<sup>a</sup>**

entry	catalyst	mol %	time (h)	yield (%) <sup>b</sup>
1	[BCMIM][Cl]	0	1	20
2	[BCMIM][Cl]	2	1.5	65
3	[BCMIM][Cl]	5	0.26	96
4	[BCMIM][Cl]	7.5	0.26	96
5	[BCMIM][Cl]	10	0.26	96
6	[BCMIM][Cl]	15	0.26	96
7	[BCMIM][Cl]	20	0.26	96

<sup>a</sup>The reaction was performed using **5a** (1.66 mmol), **6a** (1.66 mmol), and **7a** (1.66 mmol) in one pot in neat condition at 80 °C. <sup>b</sup>Yield of the isolated product.

**Scheme 4. One-Pot Gram-Scale Synthesis of 4-Phenyl-3,4-dihydropyrimidin-2(1H)-ones **8a** Employing the [BCMIM][Cl] **4** Catalyst****Figure 3. Plausible iminium mechanism for the synthesis of 4-aryl-3,4-dihydropyrimidin-2(1H)-ones/4-aryl-3,4-dihydropyrimidin-2(1H)-thiones **8a–8a'**.**

activity to construct various 4-aryl-3,4-dihydropyrimidin-2(1H)-ones/4-aryl-3,4-dihydropyrimidin-2(1H)-thiones **8a–8a'** in a short time.

Since the [BCMIM][Cl] **4** catalyst salt is ionic, it could be recycled and reused several times in the Biginelli reaction. After 4-aryl-3,4-dihydropyrimidin-2(1H)-ones/4-aryl-3,4-dihydropyrimidin-2(1H)-thiones **8a–8a'** product formation, ether was added to the reaction mixture and the suspended solid compound poured into the other beaker washed with hexane and ether to get the pure products.

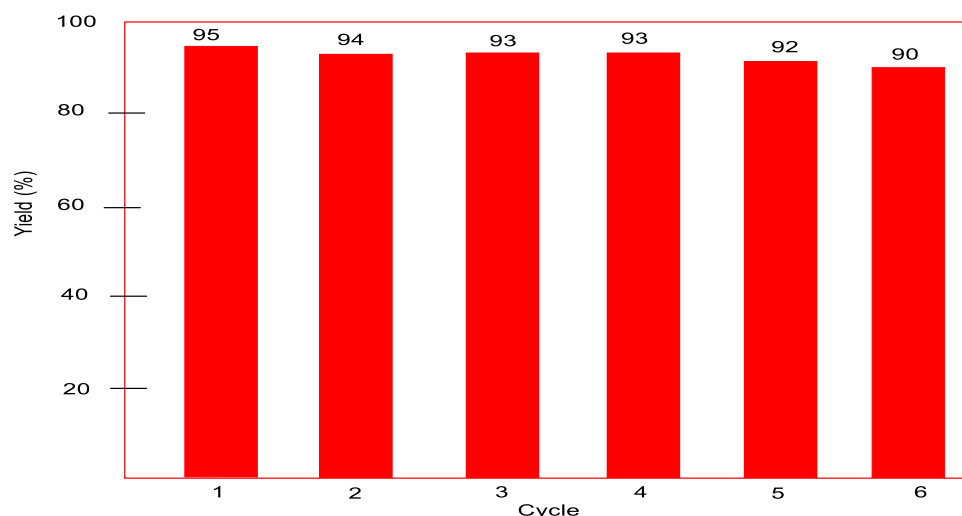
Next, the reaction vessel was washed with ether and dichloromethane. The catalyst was insoluble in ether and dichloromethane due to its ionic nature. It was recycled and reused six times for the same set of model reactions. The catalyst activity was almost the same after six cycles without a noteworthy loss of its catalytic activity (Figure 4). The potential application of the ionic salt-catalyzed Biginelli reaction was found for the synthesis of the commercially available drug monastrol (Scheme 5).<sup>21</sup> In the one-pot reaction, 3-hydroxy benzaldehyde **5z**, ethyl acetoacetate **6z**, and thiourea **7z** were reacted at 80 °C heating in neat condition for 25 min. Interestingly, we were able to achieve the synthesis of monastrol at 80 °C in neat conditions, which confirms the huge advantages of this synthesis methodology for the preparation of important drug molecules like monastrol by an ionic salt catalyst (Scheme 5).

## CONCLUSIONS

In summary, a novel approach for the preparation of 1,3-bis(carboxymethyl) imidazolium chloride [BCMIM][Cl] salt was established for the first time. The Brønsted ionic salt was applied for the synthesis of 4-aryl-3,4-dihydropyrimidin-2(1H)-one/(DHP)/4-aryl-3,4-dihydropyrimidin-2(1H)-thione (DHP) derivatives in the neat condition in a short reaction time. Furthermore, the deterrence from harmful organic solvents and solvent-free synthesis during the Biginelli reaction makes it a suitable and environmentally benign smart method for the synthesis of 4-aryl-3,4-dihydropyrimidin-2(1H)-one/(DHP)/4-aryl-3,4-dihydropyrimidin-2(1H)-thione (DHP) derivatives. The Brønsted acid ionic salt [BCMIM][Cl] was recycled and reused six times without loss of its catalytic efficiency. The important features of this methodology are (1) a novel method to synthesize the Brønsted acid catalyst, (2) broad substrate scope, (3) easy workup procedure, (4) solvent-free synthesis, (5) easy availability of starting materials, (5) low catalyst loading mole percentage, and (6) clean reaction profiles. In addition, the 4-aryl-3,4-dihydropyrimidin-2(1H)-one/(DHP)/4-aryl-3,4-dihydropyrimidin-2(1H)-thione (DHP) derivatives could be useful in medicinal applications.

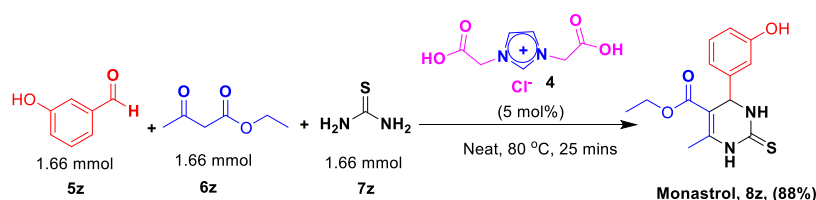
## EXPERIMENTAL SECTION

**General Information:** Substituted aromatic aldehyde, substituted 1,3-dicarbonyl compounds, urea, and thiourea were procured from Sigma-Aldrich, and organic solvents were purchased from commercial suppliers without further purification. Analysis of <sup>1</sup>H NMR and <sup>13</sup>C NMR was recorded using a Bruker DRX400 spectrometer (400 MHz). Relative to the internal standard, the chemical shifts are reported in ppm. Coupling constants (*J*) are calculated in Hz. <sup>1</sup>H NMR multiplicities of peaks are assigned as d (doublet), m (multiplet), s (singlet), and t (triplet). Fourier transform infrared (FT-IR) spectra were documented using a Bomem



**Figure 4.** Catalytic cycle (5 mol % of ionic salt at 80 °C in neat condition recharges each reactant in 1.66 mmol).

**Scheme 5. One-Pot Multicomponent Synthesis of Monastrol 8z Using [BCMIM][Cl] 4 Catalyst**



DA8 3 FTS spectrometer. Mass spectra were recorded using a Perkin Elmer Calrus 600 gas chromatography-mass spectrometry (GC-MS) spectrometer. Thin-layer chromatography (TLC) was performed using 0.25 mm silica gel-coated Kieselgel 60 F254 plates.

**General Procedure for the Synthesis of 1,3-Bis-(carboxymethyl)imidazolium Chloride 4.** In a 500 mL round bottle flask, imidazole **1** (10.0g, 1.0 equiv, 0.15 mol) and chloroacetic acid **2** (27.79 g, 2.0 equiv, 0.30 mol) were dissolved in 200 mL of acetonitrile solvent. NaOH (7.2 g, 1.2 equiv, 0.18 mol) was charged into the reaction mixture. The reaction mixture was refluxed for 18 h. After completion of the reaction, the reaction mixture was cooled and salt was filtered. The filtrate was reduced by the reduced pressure in the rotavaporator to yield the liquid intermediate **3** (31.3 g, 97% yield). The intermediate **3** was treated with cold concentrated HCl for 24 h in rt to provide the crude solid crystal ionic salt **4**. Further washing with dichloromethane and ether yielded the final compound 1,3-bis(carboxymethyl)imidazolium tetrafluoroborate [BCMIM][Cl] ionic salt **4** (29.8 g, 95% yield). The products were characterized by <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR, and GC-MS spectra and were found to be identical to the ones described in the literature.<sup>63,64</sup>

**Representative General Procedure for the Synthesis of 4-Phenyl-3,4-dihydropyrimidin-2(1H)-ones 8a.** In a 100 mL round bottle flask, benzaldehyde **5a** (0.176 g, 1.0 equiv, 1.66 mmol), 1,3-dicarbonyl compound (acetylacetone) **6a** (0.166 g, 1.0 equiv, 1.66 mmol), and urea **7a** (0.099 g, 1.0 equiv, 1.66 mmol) were charged, followed by addition of 5 mol % (11 mg) [BCMIM][Cl] ionic salts to the reaction mixture. The resultant reaction mixture was reacted at 80 °C in heating condition for 16 min. After 16 min, the solid product formation was observed. Next, as monitored by TLC, after completion of the reaction, the reaction mixture was cooled to

ambient temperature. The solid Biginelli product was precipitated and suspended in ether. The solid product was filtered and washed with ice-cooled water (15 mL). The crude product was further washed with ether. The pure products **8a** were obtained without column chromatography with 96% (0.37 g) yield. The products were characterized by <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR, and GC-MS spectra and were found to be identical to the ones described in the literature.

**Representative General Procedure for the Synthesis of 4-Phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate 8p.** In a 50 mL round-bottom flask, benzaldehyde **5p** (0.176 g, 1.66 mmol, 1.0 equiv), 1,3-dicarbonyl compound (methyl acetoacetate) **6p** (0.193 g, 1.66 mmol, 1.0 equiv), and thiourea **7p** (0.126 g, 1.66 mmol, 1.0 equiv) were charged, followed by addition of 5 mol % 1,3-bis(carboxymethyl)imidazolium tetrafluoroborate [BCMIM][Cl] ionic liquids to the reaction mixture. The reaction mixture was stirred at 80 °C in heating conditions for 15 min. After 15 min, the solid product formation was observed. After completion of the reaction as monitored by TLC, the reaction mixture was cooled to room temperature. The solid product was precipitated and suspended in ether. The solid product was filtered and washed with ice-cooled water (15 mL). The crude product was further washed with ether. The pure products **8p** were obtained without column chromatography with 95% (0.41 g) yield. The products were characterized by <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR, and GC-MS spectra and were found to be identical to the ones described in the literature.

**5-Acetyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (8a).**<sup>29</sup> Off-white solid (0.366 g, 96% yield), mp (°C): 194–196, <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 9.19 (s, 1H), 7.84 (s, 1H), 7.35–7.31 (m, 2H), 7.26 (s, 1H), 7.23 (dd, *J* = 5.2, 1.6 Hz, 2H), 5.26 (d, *J* = 3.6 Hz, 1H), 2.30 (s, 3H), 2.11



(s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  194.8, 152.6, 148.6, 144.7, 130.0, 127.8, 126.9, 110.1, 54.3, 30.8, 19.4. GC-MS: 230; FT-IR (KBr,  $\text{cm}^{-1}$ ): 3329, 3253, 1699, 1672, 1595, 1327, 1232.

**Ethyl 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8b).**<sup>29</sup> White solid (0.41 g, 95% yield), mp ( $^{\circ}\text{C}$ ): 196–197,  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.19 (s, 1H), 7.74 (s, 1H), 7.34–7.30 (m, 2H), 7.26 (s, 1H), 7.24 (d,  $J = 8$  Hz, 2H), 5.15 (d,  $J = 2.8$  Hz, 1H), 3.98 (q,  $J = 7.2$  Hz, 2H) 2.25 (s, 3H), 1.09 (t,  $J = 7.2$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  165.8, 152.6, 148.8, 145.3, 128.9, 127.8, 126.7, 99.8, 59.7, 54.4, 18.2, 14.5. GC-MS: 260; FT-IR (KBr,  $\text{cm}^{-1}$ ): 3234, 3113, 1720, 1664, 1217, 1085.

**6-Methyl-4-phenyl-5-pivaloyl-3,4-dihydropyrimidin-2(1H)-one (8c).**<sup>33</sup> White solid (0.471 g, 94% yield), mp ( $^{\circ}\text{C}$ ): 194–196,  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.07 (s, 1H), 7.66 (s, 1H), 7.33 (t,  $J = 7.2$  Hz, 2H), 7.25 (t,  $J = 7.6$  Hz, 3H), 5.09 (d,  $J = 2$  Hz, 1H), 2.51 (s, 3H), 1.29 (s, 9H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  165.3, 152.6, 147.8, 145.4, 128.8, 127.7, 126.8, 101.0, 79.6, 54.8, 28.3, 18.1. GC-MS: 272; FT-IR (KBr,  $\text{cm}^{-1}$ ): 3223, 3093, 1701, 1647, 1234, 1165, 1089.

**5-Acetyl-6-methyl-4-(*p*-tolyl)-3,4-dihydropyrimidin-2(1H)-one (8d).**<sup>49</sup> Off-white solid (0.385 g, 95% yield), mp ( $^{\circ}\text{C}$ ): 140–142,  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.14 (s, 1H), 7.77 (s, 1H), 7.13 (s, 4H), 5.21 (d,  $J = 3.2$  Hz, 1H), 2.28 (s, 3H), 2.26 (s, 3H), 2.08 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  194.8, 152.6, 148.4, 141.8, 137.0, 129.5, 126.8, 110.0, 54.0, 30.7, 21.1, 19.3. GC-MS: 244; FT-IR (KBr,  $\text{cm}^{-1}$ ): 3286, 3118, 1697, 1616, 1327, 1234, 1140.

**Methyl 6-methyl-2-oxo-4-(*p*-tolyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8e).**<sup>47,49</sup> White solid (0.41 g, 95% yield), mp ( $^{\circ}\text{C}$ ): 188–190,  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.15 (s, 1H), 7.68 (s, 1H), 7.12 (s, 4H), 5.11 (s, 1H), 3.53 (s, 3H), 2.26 (s, 3H), 2.25 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  166.3, 152.6, 148.9, 142.2, 136.9, 129.4, 126.5, 99.6, 53.9, 51.2, 21.1, 18.3. GC-MS: 260; FT-IR (KBr,  $\text{cm}^{-1}$ ): 3236, 3113, 2951, 1707, 1681, 1694, 1431, 1240, 1226, 1095.

**5-Acetyl-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (8f).**<sup>29</sup> Brown solid (0.41 g, 95% yield), mp ( $^{\circ}\text{C}$ ): 160–162,  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.08 (s, 1H), 7.69 (s, 1H), 7.10 (d,  $J = 8.8$  Hz, 2H), 6.81 (d,  $J = 8.4$  Hz, 2H), 5.13 (d,  $J = 3.2$  Hz, 1H), 3.65 (s, 3H), 2.21 (s, 3H), 2.01 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  194.9, 159.0, 152.7, 148.3, 136.8, 128.1, 114.3, 110.1, 55.5, 53.8, 30.6, 19.3. GC-MS: 260; FT-IR (KBr,  $\text{cm}^{-1}$ ): 3300, 3213, 1695, 1610, 1510, 1230, 1031.

**Methyl 4-(4-methoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8g).**<sup>29</sup> Off-white solid (0.44 g, 95% yield), mp ( $^{\circ}\text{C}$ ): 194–196,  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.20 (s, 1H), 7.70 (s, 1H), 7.14 (d,  $J = 8.8$  Hz, 2H), 6.87 (d,  $J = 8.4$  Hz, 2H), 5.08 (d,  $J = 3.2$  Hz, 1H), 3.72 (s, 3H), 3.53 (s, 3H), 2.25 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  166.3, 158.9, 152.6, 148.8, 137.3, 127.8, 114.2, 99.7, 55.5, 53.6, 51.2, 18.3. GC-MS: 276; FT-IR (KBr,  $\text{cm}^{-1}$ ): 3345, 3230, 1710, 1678, 1647, 1610, 1433, 1234, 1174, 1093, 1038.

**tert-Butyl 4-(4-methoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8h).** Pale yellow solid (0.49 g, 93% yield), mp ( $^{\circ}\text{C}$ ): 192–194,  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.03 (s, 1H), 7.59 (s, 1H), 7.14 (d,  $J = 8.8$  Hz, 2H), 6.89 (d,  $J = 8.8$  Hz, 2H), 5.03 (d,  $J = 3.2$  Hz, 1H), 3.73 (s, 3H), 2.21 (s, 3H), 1.30 (s, 9H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  165.3, 158.9, 152.6, 147.5, 137.7, 127.9, 114.1,

101.3, 79.5, 55.5, 54.1, 28.3, 18.1. GC-MS: 318; FT-IR (KBr,  $\text{cm}^{-1}$ ): 3237, 3109, 2936, 1701, 1645, 1232, 1165, 1090.

**Ethyl 4-(2,5-dimethoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8i).** White solid (0.49 g, 93% yield), mp ( $^{\circ}\text{C}$ ): 198–200,  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.14 (s, 1H), 7.27 (s, 1H), 6.91 (d,  $J = 8.8$  Hz, 1H), 6.80 (d,  $J = 8.8$  Hz, 1H), 6.60 (s, 1H), 5.45 (s, 1H), 3.94 (q,  $J = 4.4$  Hz, 2H), 3.74 (s, 3H), 3.66 (s, 3H), 2.28 (s, 3H), 1.05 (t,  $J = 7.2$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  165.8, 153.4, 152.6, 151.2, 149.3, 133.3, 114.5, 112.6, 112.4, 98.0, 59.5, 56.4, 55.7, 55.4, 49.6, 18.1, 14.5. GC-MS: 320. FT-IR (KBr,  $\text{cm}^{-1}$ ): 3250, 3109, 1699, 1645, 1494, 1271, 1227, 1209, 1086.

**Ethyl 4-(4-(dimethylamino)phenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8j).** Pale brown solid (0.473 g, 94% yield), mp ( $^{\circ}\text{C}$ ): 188–190,  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.18 (s, 1H), 7.68 (s, 1H), 7.10 (d,  $J = 8.4$  Hz, 2H), 6.72 (d,  $J = 8.4$  Hz, 2H), 5.10 (d,  $J = 2.8$  Hz, 1H), 4.04 (q,  $J = 6.8$  Hz, 2H), 2.92 (s, 6H), 2.29 (s, 3H), 1.18 (t,  $J = 6.8$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  165.9, 152.8, 150.2, 148.0, 133.1, 127.4, 112.7, 100.3, 59.6, 53.8, 18.2, 14.6. GC-MS: 303. FT-IR (KBr,  $\text{cm}^{-1}$ ): 3240, 3111, 2931, 1712, 1674, 1234, 1086.

**Ethyl 4-(4-cyanophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8k).** Off-white solid (0.46 g, 96% yield), mp ( $^{\circ}\text{C}$ ): 154–156,  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.25 (s, 1H), 7.79 (s, 1H), 7.74 (d,  $J = 8.4$  Hz, 2H), 7.36 (d,  $J = 8.4$  Hz, 2H), 5.15 (d,  $J = 3.2$  Hz, 1H), 3.91 (d,  $J = 7.2$  Hz, 2H), 2.20 (s, 3H), 1.01 (t,  $J = 7.2$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  165.6, 152.3, 150.5, 149.7, 133.0, 127.8, 119.2, 110.6, 98.7, 59.8, 54.3, 18.3, 14.5. GC-MS: 285. FT-IR (KBr,  $\text{cm}^{-1}$ ): 3458, 3291, 3227, 3102, 2920, 2230, 1703, 1647, 1217, 1086.

**Ethyl 4-(2-chlorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8l).**<sup>49</sup> White solid (0.46 g, 95% yield), mp ( $^{\circ}\text{C}$ ): 198–200,  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.29 (s, 1H), 7.72 (s, 1H), 7.40 (d,  $J = 7.6$  Hz, 2H), 7.33–7.5 (m, 3H), 5.65 (d,  $J = 2.8$  Hz, 1H), 3.90 (q,  $J = 6.8$  Hz, 2H), 2.31 (s, 3H), 1.00 (t,  $J = 6.8$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  165.4, 151.9, 149.7, 142.2, 132.2, 129.8, 129.7, 129.2, 128.2, 98.4, 59.5, 51.9, 18.1, 14.4. GC-MS: 294; FT-IR (KBr,  $\text{cm}^{-1}$ ): 3230, 3099, 2937, 1701, 1641, 1221, 1078.

**Methyl 4-(4-bromophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8m).** White solid (0.51 g, 95% yield), mp ( $^{\circ}\text{C}$ ): 206–208,  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.18 (s, 1H), 7.71 (s, 1H), 7.46 (d,  $J = 8.4$  Hz, 2H), 7.12 (d,  $J = 8.4$  Hz, 2H), 5.06 (d,  $J = 3.2$  Hz, 1H), 3.92 (q,  $J = 7.2$  Hz, 2H), 2.18 (s, 3H), 1.03 (t,  $J = 7.2$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  165.7, 152.4, 149.2, 144.7, 131.8, 129.0, 120.8, 99.3, 59.8, 53.9, 18.3, 14.5. GC-MS: 339.6529. FT-IR (KBr,  $\text{cm}^{-1}$ ): 3233, 3111, 2955, 1699, 1645, 1217.08, 1084.

**Ethyl 6-methyl-4-(4-nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8n).** Light-yellow solid (0.46 g, 92% yield), mp ( $^{\circ}\text{C}$ ): 211–212,  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.35 (s, 1H), 8.22 (d,  $J = 8.4$  Hz, 2H), 7.89 (s, 1H), 7.51 (d,  $J = 8.4$  Hz, 2H), 5.27 (d,  $J = 3.2$  Hz, 1H), 4.00 (t,  $J = 7.2$  Hz, 2H), 2.27 (s, 3H), 1.10 (t,  $J = 7.2$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  165.5, 152.4, 152.2, 149.8, 147.2, 128.1, 124.3, 98.6, 59.8, 54.1, 18.3, 14.5. GC-MS: 305. 2914. FT-IR (KBr,  $\text{cm}^{-1}$ ): 3219, 3116, 1726, 1697, 1641, 1516, 1346, 1209, 1084.

**Ethyl 4-(furan-2-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8o).** Black solid (0.36 g, 91% yield), mp (°C): 152–154, <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 9.25 (s, 1H), 7.76 (s, 1H), 7.54 (d, *J* = 0.8 Hz, 1H), 6.36 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.10 (d, *J* = 3.2 Hz, 1H), 5.21 (t, *J* = 3.6 Hz, 1H), 4.04–4.02 (m, 2H), 2.23 (s, 3H), 1.14 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 165.5, 156.4, 152.9, 149.8, 142.6, 110.8, 105.8, 97.3, 59.7, 48.2, 18.2, 14.6. GC-MS: 250.2610. FT-IR (KBr, cm<sup>-1</sup>): 3235, 3111, 2976, 1697, 1647, 1232, 1097.

**Methyl 6-methyl-4-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8p).**<sup>47</sup> Off-white solid (0.41 g, 95% yield), mp (°C): 210–212, <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 10.36 (s, 1H), 9.68 (s, 1H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 6.8 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 2H), 5.19 (d, *J* = 3.6 Hz, 1H), 3.56 (s, 3H), 2.30 (s, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 174.7, 166.1, 145.8, 143.8, 129.1, 128.2, 126.8, 100.9, 54.4, 51.6, 17.7. GC-MS: 262.0966. FT-IR (KBr, cm<sup>-1</sup>): 3343, 3314, 3186, 3109, 1662, 1570, 1175, 1111, 1030.

**Ethyl 6-methyl-4-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8q).** Off-white solid (0.43 g, 94% yield), mp (°C): 172–174, <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 10.33 (s, 1H), 9.65 (s, 1H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 6.8 Hz, 1H), 7.24 (t, *J* = 7.6 Hz, 2H), 5.18 (d, *J* = 3.6 Hz, 1H), 4.00 (q, *J* = 7.2 Hz, 2H), 2.30 (s, 3H), 1.10 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 174.7, 165.6, 145.5, 143.9, 129.0, 128.2, 126.8, 101.2, 60.1, 54.5, 17.6, 14.5. GC-MS: 276; FT-IR (KBr, cm<sup>-1</sup>): 3325, 3167, 3103, 2980, 1664, 1572, 1283, 1192, 1173, 1115.

**tert-Butyl 6-methyl-4-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8r).** Off-white solid (0.47 g, 94% yield), mp (°C): 178–180, <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 10.22 (s, 1H), 9.58 (s, 1H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.28 (t, *J* = 7.3 Hz, 1H), 7.22 (d, *J* = 7.2 Hz, 2H), 5.11 (d, *J* = 3.2 Hz, 1H), 2.27 (s, 3H), 1.30 (s, 9H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 180.3, 174.5, 165.0, 144.6, 144.1, 128.9, 128.1, 126.9, 102.4, 80.2, 54.8, 28.2, 17.5. GC-MS: 304; FT-IR (KBr, cm<sup>-1</sup>): 3377, 3175, 2972, 1703, 1476, 1254, 1093.

**1-(6-Methyl-2-thioxo-4-(*p*-tolyl)-1,2,3,4-tetrahydropyrimidin-5-yl)ethan-1-one (8s).** Pale solid brown (0.42 g, 96% yield), mp (°C): 194–196, <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 10.35 (s, 1H), 9.79 (s, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 5.29 (d, *J* = 3.6 Hz, 1H), 2.34 (s, 3H), 2.18 (s, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 195.1, 184.3, 174.7, 145.4, 142.3, 132.7, 129.1, 110.8, 53.5, 31.0, 18.8. GC-MS: 260; FT-IR (KBr, cm<sup>-1</sup>): 3277, 3171, 2995, 1618, 1572, 1180, 1090.

**Ethyl 4-(4-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8t).**<sup>49</sup> White solid (0.48 g, 95% yield), mp (°C): 136–138, <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 10.29 (s, 1H), 9.60 (s, 1H), 7.13 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 5.12 (d, *J* = 3.6 Hz, 1H), 4.00 (q, *J* = 7.2 Hz, 2H), 3.73 (s, 3H), 2.29 (s, 3H), 1.11 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 174.5, 165.6, 159.2, 145.2, 136.2, 128.1, 114.3, 101.5, 60.0, 55.6, 53.9, 17.6, 14.5. GC-MS: 306; FT-IR (KBr, cm<sup>-1</sup>): 3306, 3165, 3106, 2982, 1664, 1572, 1248, 1194, 1170, 1118, 1026.

**Methyl 4-(4-fluorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8u).** Off-white solid (0.44 g, 94% yield), mp (°C): 164–166, <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 10.38 (s, 1H), 9.67 (d, *J* = 1.6 Hz, 1H), 7.27–7.24 (m, 2H), 7.20–7.16 (m, 2H), 5.18 (d, *J* = 4.0 Hz, 1H), 3.56 (s, 3H), 2.30 (s, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ

174.7, 166.0, 163.2, 160.8, 145.9, 140.0, 128.9 (d, *J*<sub>CF</sub> = 9.0 Hz), 115.8 (d, *J*<sub>CF</sub> = 21.0 Hz), 100.8, 53.7, 51.6, 17.7. GC-MS: 280; FT-IR (KBr, cm<sup>-1</sup>): 3306, 3173, 3107, 2995, 1668, 1572, 1180, 1115.

**Ethyl 4-(4-chlorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8v).**<sup>49</sup> White solid (0.49 g, 95% yield), mp (°C): 166–168, <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 10.38 (s, 1H), 9.67 (s, 1H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 5.18 (d, *J* = 4 Hz, 1H), 4.01 (q, *J* = 8.0 Hz, 2H), 2.30 (s, 3H), 1.10 (t, *J* = 8.0 Hz, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 174.7, 165.5, 145.8, 142.8, 132.7, 129.1, 128.8, 100.8, 60.1, 53.9, 17.6, 14.5. GC-MS: 310; FT-IR (KBr, cm<sup>-1</sup>): 3325, 3169, 3102, 2984, 1668, 1570, 1194, 1175, 1117.

**Ethyl 4,6-diphenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8w).** Pale brown solid (0.5 g, 90% yield), mp (°C): 174–176, <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 10.49 (s, 1H), 9.77 (d, *J* = 2.0 Hz, 1H), 7.46–7.24 (m, 10H), 5.28 (d, *J* = 4.0 Hz, 1H), 3.75 (q, *J* = 7.2 Hz, 2H), 0.73 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 174.9, 165.4, 146.3, 143.5, 134.4, 129.6, 129.2, 129.1, 128.3, 128.2, 126.9, 102.3, 59.9, 54.6, 13.8. GC-MS: 338. FT-IR (KBr, cm<sup>-1</sup>): 3310, 3154, 2980, 2895, 1674, 1566, 1277, 1204, 1130, 1103, 1028.

**1-(4,6-diphenyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)ethan-1-one (8x).** Half-white solid (0.47 g, 91% yield), mp (°C): 226–228, <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 10.35 (s, 1H), 9.69 (s, 1H), 7.55–7.43 (m, 5H), 7.34 (t, *J* = 7.4 Hz, 2H), 7.26 (t, *J* = 7.3 Hz, 1H), 7.19 (d, *J* = 7.3 Hz, 2H), 5.31 (d, *J* = 3.4 Hz, 1H), 1.73 (s, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 195.0, 174.7, 143.4, 142.0, 140.6, 132.4, 129.2, 129.1, 128.4, 128.2, 126.7, 110.7, 55.8, 18.3. GC-MS: 308.3120. FT-IR (KBr, cm<sup>-1</sup>): 3188, 2995, 1678, 1645, 1206, 1173, 1107.14, 1080.

**Ethyl 4-(4-bromophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8y).** Off-white solid (0.56 g, 95% yield), mp (°C): 180–182, <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 10.31 (s, 1H), 9.59 (d, *J* = 1.6 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.4 Hz, 2H), 5.09 (d, *J* = 3.6 Hz, 1H), 3.94 (q, *J* = 7.2 Hz, 2H), 2.23 (s, 3H), 1.03 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 174.7, 165.5, 145.8, 143.2, 131.9, 129.1, 121.3, 100.7, 60.1, 53.9, 17.6, 14.5. GC-MS: 355. FT-IR (KBr, cm<sup>-1</sup>): 3323, 3169, 3102, 2982, 1665, 1572, 1194, 1175, 1119.

**Ethyl 4-(3-hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8z).**<sup>21</sup> Off-white solid (0.43 g, 88% yield), mp (°C): 185–186, <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 10.30 (s, 1H), 9.61 (s, 1H), 9.45 (s, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.65 (d, *J* = 8.0 Hz, 3H), 5.09 (d, *J* = 3.6 Hz, 1H), 4.03 (q, *J* = 7.2 Hz, 2H), 2.28 (s, 3H), 1.13 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 174.6, 165.6, 157.9, 145.3, 145.2, 129.9, 117.4, 115.1, 113.7, 101.2, 60.1, 54.4, 14.5. GC-MS: 292. FT-IR (KBr, cm<sup>-1</sup>): 3298, 3179, 3115, 2982, 1663, 1572, 1283, 1188, 1151, 1113, 1024.

**Ethyl 4-(furan-2-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8a').** Black solid (0.40 g, 90% yield), mp (°C): 228–230, <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 10.33 (s, 1H), 9.58 (s, 1H), 7.52 (d, *J* = 0.9 Hz, 1H), 6.32 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.08 (d, *J* = 3.2 Hz, 1H), 5.17 (d, *J* = 4.0 Hz, 1H), 3.98 (m, 2H), 2.21 (s, 3H), 1.07 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 184.3, 175.3, 165.3, 155.0, 146.5, 143.1, 110.9, 106.7, 98.7, 60.1, 48.1, 17.6, 14.5. GC-MS: 266. FT-IR (KBr, cm<sup>-1</sup>): 3308, 3169, 1661, 1609, 1572, 1182, 1113, 1009, 926.

1,3-Bis(carboxymethyl)imidazolium chloride (4).<sup>68,69</sup> White crystal solid (28.9 g, 95% yield), mp (226–228°C): <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O) δ 8.86 (s, 1H), 7.49 (d, J = 0.8 Hz, 2H), 5.08 (s, 4H). <sup>13</sup>C NMR (100 MHz, D<sub>2</sub>O) δ 169.8, 138.2, 123.5, 50.2. FT-IR (KBr, cm<sup>-1</sup>): 3570, 3289, 3163, 3018, 1738, 1178, 1024, 970.

## ■ ASSOCIATED CONTENT

### SI Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acsomega.1c02976>.

<sup>1</sup>H, <sup>13</sup>C NMR, GC-MS, and FT-IR spectra of synthesized compounds 8a–8a' and ionic catalysts 4, 1D and 2D (PDF)

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### Notes

The authors declare no competing financial interest.

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