Research Paper

1- (3, 4 - Dichlorobenzensulfonyl) -3-methyl-1H-imidazolium chloride: An Efficient Catalyst for Biginelli Reaction

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Abstract: 1-(3, 4-Dichlorobenzensulfonyl)-3-methyl-1H-imidazolium chloride is used as an effective catalyst for biginelli reactions in the synthesis of octahydroquinazololones in water. The catalyst could be easily recovered and reused without significant decrease of the catalytic activity. All compounds have been synthesized and characterized using melting points, IR Spectra, NMR spectra and ESI-MS.

Keywords: Biginelli reaction, ionic liquid, microwave, water

Introduction

In recent years, Biginelli reaction is ranked as one of the powerful route for the synthesis of octahydroquinazololones. These derivatives have considerable attention since they exhibit potent antibacterial activity against Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa [1] and calcium antagonist activity [2]. Due to its biological and pharmacological importance, several methods have been developed for the preparation of quinazolinone derivatives. These routes usually involves the reaction of aldehydes with SOCl₂ and pyridine, then with 2-amino benzylamine in a refluxing solvent such as benzene or xylene with azeotropic water removal [3], refluxing ethanol/acetic acid mixture [4], and by in alkali media, there are few reports for the synthesis of octahydroquinazolinone derivatives using catalysts such as TMSCl [5], Nafion-H [6], conc. H₂SO₄ [7], NH₄VO₃ [8], ZrOCl₂-8H₂O [9], silica-sulfuric acid [10] and also in ionic liquids [HMM][HSO₄] in presence of TMSCl [11], [BMIM][Br]-[BMIM][BF₄] [12]. All the methods have their own advantages with some disadvantages such as low yields, requirement of organic solvents, use of expensive catalysts, tedious workup procedure, etc.

Due to environmental concern use of benign solvents as alternative to volatile organic solvents is of much interest to organic chemists. The use of water as reaction media and catalyst as ionic liquids in microwaves can offer a solution to solvent emission and catalyst recycle problems[13]. Ionic liquids are of considerable interest as they can serve as catalyst and green media in Lewis acid catalyzed biginelli reactions [14] and also due to their unique properties such as non-volatility, non-flammability, etc. It can be thought of ubiquitous among ionic liquids due to their ionic conductivity. Recently a variety of ionic liquids have been demonstrated as practical alternative to organic solvents as well as catalyst in organic reactions/transformations [15-17]. Ionic liquids are capable of facilitating the formation of the key catalytic intermediate and of stabilizing them through ion-pairing formation. The aldehyde activation is more efficient in presence of ionic liquids [18]. In particular Sulfonyl imidazolium salts have been demonstrated as reagents in the synthesis of nucleoside polyphosphates [19] aryl sulfonamides and aryl sulfonates [20].

As our keen ongoing research interest in microwaves synthesis [21], sulfonyl imidazolium salts and in continuation of our effort to develop the catalytic applicability of an acidic ionic liquid 1-(3, 4-dichloro benzene sulfonyl)-3-methyl imidazolium chloride ([3, 4-dcbmim][Cl]) [22] (Figure 1). A catalytic application was developed for the beginsi synthesis of octahydroquinazololones (OHQ) (Table 1) in the microwave reaction of aromatic aldehydes, dimedone and urea/thiourea using 5mol% of [3, 4-dcbmim][Cl], products obtained with good yields.
Material and Methods

General procedure for the synthesis of octahydraquinazolinone under aqueous media: A mixture of aldehyde (1 mmol), dimedone (1 mmol), urea or thiourea (1.5 mmol) and [3, 4-dcbsmim][Cl] (5 mol%) was added with 5 ml of water in a closed vessel and irradiated with Microwaves of 150 W at 100°C and pressure of 100 psi till the completion of the reaction (Table 1). After the completion of the reaction indicated by TLC, the reaction mixture was allowed to cool to room temperature. The obtained precipitate was filtered off, washed with distill water. Further the filtrate (water) was evaporated for dryness to get a crude catalyst and the resulting catalyst was reused directly for the next run without purification. All the products are known compounds and were characterized by melting point, IR, NMR and mass spectrometry and comparison of their physical data with literature data. The isolated yields of the products were 88-95%.

The Spectral Data of the few compounds
4-(4-Chlorophenyl)-7,7-dimethyl-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (4b)
MP = 291 °C IR (KBr) = 3237, 2954, 1624, 1565, 1450 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ = 0.96 (s, 3H), 1.08 (s, 3H), 2.13 (m, 2H), 2.46 (s, 2H), 4.69 (s, 1H), 7.14 - 7.23 (m, 4H), 7.26 (b, 2H) ¹³C NMR (CDCl₃, 100 MHz) δ = 27.2, 29.2, 31.4, 32.0, 40.8, 50.7, 115.0, 129.1, 129.7, 129.8, 131.9, 142.5, 162.5, 196.2. ESI-MS calcd for C₁₆H₁₈ClN₃O₂ m/z 343.06 [M+K], found 343.2.

Results and Discussion

First the reaction was carried out without use of any catalyst under microwave irradiation conditions in aqueous medium by using the model reaction of benzaldehyde (1 mmol), dimedone (1 mmol) with Urea (1.5 mmol) and 40-46 % amount of product was observed at different temperatures between 80-100 °C. In presence of 10 mol % of [bmm][Cl] and 10 mol % of
we obtained 44% and 95% of yield respectively under microwave irradiation at 100°C (Table 2).} 

Table 2. Screening of ionic liquid in aqueous medium

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Temperature</th>
<th>Time(min)</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>Water</td>
<td>80</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>Water</td>
<td>100</td>
<td>7</td>
<td>46</td>
</tr>
<tr>
<td>3</td>
<td>[Bmmim][Cl]</td>
<td>Water</td>
<td>100</td>
<td>6</td>
<td>44</td>
</tr>
<tr>
<td>4</td>
<td>[3, 4-dcbismim][Cl]</td>
<td>Water</td>
<td>100</td>
<td>5</td>
<td>94</td>
</tr>
</tbody>
</table>

a Reaction condition: Benzaldehyde (1 mmol), Dimedone (1 mmol), Urea (1.5 mmol) catalyst (10 mol %) in aqueous medium.
b Isolated Yield

In order to demonstrate the reusability of [3, 4-dcbismim][Cl] the experiment was performed using benzaldehyde as a model substrate under aqueous condition. After the reaction crude solid was recrystallized from 95% ethanol to obtain the desired product in pure form. The water layer consisting of [3, 4-dcbismim][Cl] along with some residual reactants and byproducts, which were vacuumed to remove solvent. The resulting catalyst was directly used in subsequent runs without further treatment (Table 4).

Table 3. Effect of catalyst concentration on model reaction

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol %)</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>80</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>95</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>95</td>
</tr>
</tbody>
</table>

a Reaction Condition: Benzaldehyde (1 mmol), Dimedone (1 mmol), Urea (1.5 mmol)
b Isolated Yield.
Table 5
Comparison of catalyst for the synthesis of octahydroquinazolinone with different reaction condition

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ionic liquid</th>
<th>Conditions</th>
<th>Time</th>
<th>Yield(%)b</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[Hmim][HSO₄] / TMSCI</td>
<td>Microwave</td>
<td>10min</td>
<td>89</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>[bmim]Br</td>
<td>reflux</td>
<td>10hr</td>
<td>30</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>[bmim] Br / TMSCI</td>
<td>100°C</td>
<td>2.5hr</td>
<td>92</td>
<td>12</td>
</tr>
<tr>
<td>4</td>
<td>[bmim][BF₄] / TMSCI</td>
<td>60-70°C</td>
<td>6.5hr</td>
<td>94</td>
<td>12</td>
</tr>
<tr>
<td>5</td>
<td>[3, 4-dcbsmim][Cl]</td>
<td>Water, Microwave</td>
<td>6min</td>
<td>94</td>
<td>Present work</td>
</tr>
</tbody>
</table>

aReaction Condition: Benzaldehyde (1 mmol), Dimedone (1mmol), Urea (1.5 mmol)
bIsolated yield

Conclusion
In conclusion, we demonstrate the application of [3, 4-dcbsmim][Cl] is as an efficient catalyst for the synthesis of octahydroquinazolinone derivatives in aqueous media. The advantages offered by this method are green reaction media, short reaction time, product isolation was easy with good yields.

List of abbreviations
[bmim][Br]: 1-Butyl-3-methylimidazolium bromide
[bmim][Cl]: 1-Butyl-3-methylimidazolium chloride
[bmim][HSO₄]: 1-Benzyl-3-methyl imidazolium hydrogen sulphate
[Hmim] [HSO₄]: 1-Methylimidazolium hydrogen sulfate
TMSCI: Chlorotrimethylsilane
[3, 4-dcbsmim][Cl]: 1-(3, 4-Dichloro benzene sulfonyl)-3-methylimidazolium chloride
OHQ: Octahydroquinazolinone

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