Sulfamic Acid: An Efficient and Recyclable Solid Acid Catalyst for the Synthesis of Quinoline-4-Carboxylic Acid Derivatives in Water

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Abstract

A simple, cost-effective, environmentally, and convenient procedure for the synthesis of quinoline-4-carboxylic acid derivatives is described through a one-pot MCR condensation of pyruvic acid, various aniline derivatives, and differentially substituted aryl aldehydes in the presence of sulfamic acid (NH$_2$SO$_3$H) (SA) as an efficient and recyclable catalytic system under mild reaction conditions in water.

Keywords: Quinoline-4-carboxylic acid derivatives; One-pot MCR; Sulfamic acid; Recyclable catalyst; Green chemistry

Introduction

Quinoline [1] 1-aza-naphthalene and benzo[b]pyridine are nitrogen containing heterocyclic aromatic compounds. Quinolines are very important compounds due to their wide spectrum of biological activities behaving as anti-malarial, anti-bacterial, anti-fungal, anti-asthmatic, anti-hypertensive, anti-inflammatory, anti-platelet activity [2-9]. In addition quinolines have been employed in the study of bioorganic and bio-organic-metallic processes [10,11]. Considering the significant applications in the fields of medicinal, bioorganic, industrial, and synthetic organic chemistry, there has been tremendous interest in developing efficient methods for the synthesis of quinolines. Some derivatives of such as quinoline-4-carboxylic acid elicited profound changes in the morphology of typical tips of Botrytis cinerea [12]. Quinoline-4-carboxylic acids are one of the most important series of quinoline derivatives because they exhibit a wide variety of medicinal effects and are applied as active components in industrial antioxidants [13,14]. Meanwhile, quinoline-4-carboxylic acids are the key precursors for the synthesis of other useful quinolone derivatives [15]. Despite remarkable efforts in the last decade [16-19] the development of effective methods for the synthesis of quinoxaline ring is still an important challenge and much in demands. In recent years, many methods for the synthesis of these quinoline acids have successively been reported. The conventional synthesis involves the Pfitzinger reaction [20,21], Doebner reaction [22,23], Friedlander and Combes methods [24-31]. However, these synthetic methods require expensive and hazardous solvents and chemicals, as well as harsh reaction condition. Therefore, the development of simple, convenient, and environmentally benign approaches for the synthesis of quinolines is still desirable. In recent years, the use of solid acids as heterogeneous catalysts has received tremendous interest in various areas of organic synthesis [32-34]. Heterogeneous solid acids are advantageous over conventional homogeneous acid catalysts as they can be easily recovered from the reaction mixture by simple filtration and can be reused after activation or without activation and more importantly without appreciable lose in activities. SA has emerged as a substitute for conventional Bronsted- and Lewis acid catalysts. This catalyst is an amino acid containing sulfur element with mild acidity. It is fast coming up as a stable, white odorless crystalline, commercially available, also not volatile and corrosive, thus can be considered as green catalyst in organic synthesis [35-37]. Interestingly, sulfamic acid exists not only in its amino sulfonic acid form, but also as H N SO$_2$ + zwiterionic units [38] immiscible with commonly employed non-polar organic solvents [35]. Also, it is a white crystalline solid [39]. In recent years, SA has been extensively used as an efficient heterogeneous catalyst for acid catalyzed reactions, such as, acetalization, [40] esterification, [41-43] functional group protections and deprotections [44] the Michael addition [45] amino Diels–Alder reactions [46], Biginelli condensations [47] and Beckmann rearrangement [48].

As the aforesaid conditions are not compatible with heat- or acid-sensitive substrates, there is a need to develop an effective synthesis of quinoxalines employing more ecofriendly conditions and catalysts [49-60]. With considering green chemistry principles, especially using water greenest and most abundant solvent [61-70]. We have recently reviewed the application of Doebner reaction in synthesis of heterocycles including quinolone-4-carboxylic acids [71]. We also frequently used Sulfamic acid as an efficient catalyst in different organic transformations [72-80] and published a review highlighting the application of Sulfamic acid in organic synthesis [81,82]. Armed with these experiences, in response to the need for the facile, efficient and green synthesis of quinolone-4-carboxylic acid derivatives, herein we wish to report the high yielding, one pot MCRs synthesis of this heterocyclic via condensation of pyruvic acid, various amines and aryl benzaldehyde in the presence of SA as a relatively inexpensive and available catalyst in water under mild reaction conditions. These eco-friendly protocols offer several advantages such as green, convenient and cost-effective procedures with high yield, shorter reaction time, simpler work-up, recovery, and reusability of solid acid heterogeneous catalyst (SA) in subsequent reactions.

Results and Discussion

To optimize the reaction conditions, a mixture of pyruvic acid (1.2 mmol), aniline (1.1 mmol), and benzaldehyde (1.0 mmol) was selected as a model reaction (Scheme 1) and was examined under different conditions. Initially, we examined various catalysts such as NH$_2$SO$_3$H, H$_3$P$_2$Mo$_{18}$O$_{61}$, HNO$_3$, DABCO, Nano-Fe$_3$O$_4$ and also tested the un-catalyzed reaction (Table 1). Because of type of reaction that needs acidic or basic catalyst, or in another word needs a stimulus to begin a reaction and also base on previous work [82] we choose these catalysts to examine to in this reaction (Scheme 1). As shown in Table 1, among the catalysts tested, NH$_2$SO$_3$H(SA) gave the highest yield for the corresponding quinoline derivative (Table 1) [83-85].

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Experimental Section

Materials and equipment’s

Chemicals and solvents were purchased from Merck-Aldrich and used directly with high-grade quality, without any purification. TLC

Table 1: Synthesis of 4a in presence of different catalysts in reflux condition. Synthesis of 4a in presence of different catalysts in reflux condition, a 1.2 mmol (1), 1.1 mmol (2a) and 1.0 mmol (3a) in presence of 3 mol% of catalyst and 5 mL of H₂O. Refers to the isolated yield.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst mol (%)</th>
<th>Time (hr)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NH₄SO₃H</td>
<td>3</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>H₃P·Mo₃O₁₄</td>
<td>3</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>HNO₂</td>
<td>3</td>
<td>81</td>
</tr>
<tr>
<td>4</td>
<td>DABCO</td>
<td>4.5</td>
<td>59</td>
</tr>
<tr>
<td>5</td>
<td>Nano-Fe₃O₄</td>
<td>6</td>
<td>68</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>18</td>
<td>Trace</td>
</tr>
</tbody>
</table>

Table 2: Synthesis of 4a in presence of different solvents. Synthesis of 4a in presence of different solvents: a 1.2 mmol (1), 1.1 mmol (2a) and 1.0 mmol (3a) in presence of 3 mol% of catalyst (Sulfamic acid) and 5 mL of solvent. Refers to the isolated yield.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time (hr)</th>
<th>Temperature (°C)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H₂O</td>
<td>3</td>
<td>Reflux</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>CH₂CH₂OH</td>
<td>6.5</td>
<td>Reflux</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>CH₂CN</td>
<td>18</td>
<td>Reflux</td>
<td>Trace</td>
</tr>
<tr>
<td>4</td>
<td>-</td>
<td>26</td>
<td>100</td>
<td>69</td>
</tr>
</tbody>
</table>

Table 3: Synthesis of 4a in presence of different amount of catalyst and temperature. Synthesis of 4a in presence of different amounts of catalyst (Sulfamic acid) and temperature: a 1.2 mmol (1), 1.1 mmol (2a) and 1.0 mmol (3a). Refers to the isolated yield. In solvent-free condition.

<table>
<thead>
<tr>
<th>Entry</th>
<th>R¹</th>
<th>R²</th>
<th>Product</th>
<th>Time (hr)</th>
<th>Yield (%)</th>
<th>Mp (°C)</th>
<th>Lit. Mp [Ref]</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>H</td>
<td>4a</td>
<td>3</td>
<td>90</td>
<td>211-212</td>
<td>212-214       [82]</td>
</tr>
<tr>
<td>2</td>
<td>4-Me</td>
<td>H</td>
<td>4b</td>
<td>4</td>
<td>88</td>
<td>213-214</td>
<td>218-219       [83]</td>
</tr>
<tr>
<td>3</td>
<td>4-NO₂</td>
<td>H</td>
<td>4c</td>
<td>11</td>
<td>43</td>
<td>233-235</td>
<td>238-239       [84]</td>
</tr>
<tr>
<td>4</td>
<td>3-Cl</td>
<td>H</td>
<td>4d</td>
<td>4</td>
<td>80</td>
<td>256-259</td>
<td>256-260       [85]</td>
</tr>
<tr>
<td>5</td>
<td>H</td>
<td>4-OMe</td>
<td>4e</td>
<td>7</td>
<td>83</td>
<td>213-215</td>
<td>216-217       [86]</td>
</tr>
<tr>
<td>6</td>
<td>H</td>
<td>4-OH</td>
<td>4f</td>
<td>3</td>
<td>89</td>
<td>268-270</td>
<td>271-273       [87]</td>
</tr>
<tr>
<td>7</td>
<td>H</td>
<td>4-NO₂</td>
<td>4g</td>
<td>3</td>
<td>90</td>
<td>319-322</td>
<td>324/32 [88]</td>
</tr>
<tr>
<td>8</td>
<td>4-Me</td>
<td>4-OMe</td>
<td>4h</td>
<td>3.5</td>
<td>79</td>
<td>231-233</td>
<td>235-237       [89]</td>
</tr>
<tr>
<td>9</td>
<td>4-Me</td>
<td>4-NO₂</td>
<td>4i</td>
<td>5.5</td>
<td>91</td>
<td>263-265</td>
<td>266-268       [82]</td>
</tr>
</tbody>
</table>

Figure 1: The recyclability of the SA in the preparation of 4a.
Scheme 2: Synthesis of quinoline-4-carboxylic acid derivatives.

Scheme 3: Proposed mechanism of the synthesis of 4.
analyses were done using percolated TLC silica gel 60 F254 (Merck) plates. The $^1$H NMR spectra were recorded by Bruker Ultrashield 500 MHz respectively advance instrument, with CDCl3 used as solvent. Proton resonances are designated as singlet (s), doublet (d), triplet (t) and multiplet (m). FT-IR spectra were recorded using KBr disks on FTIR Bruker Tensor 27 instrument in the 500-4000 cm$^{-1}$ region. The vibration transition frequencies are reported in wave numbers (cm$^{-1}$). Band intensities are assigned as weak (w), medium (m), and strong (s). Melting points were measured using a capillary tube method with a Barnstead Electrothermal 9200 apparatus. All products were known and identified by comparison of their physical and spectrosopic data with those of authentic compounds and found being identical. All yields refer to isolated products.

The synthesis of quinoline-4-carboxylic acid derivatives (4a-i)

**General procedure:** A mixture of pyruvic acid (1.2 mmol), amine (1.1 mmol), and benzaldehyde (1.0 mmol) in 5 ml of water was well stirred with NH$_4$SO$_4$ (3 mol%). This mixture was magnetically stirred under reflux for appropriate time according to Table 4. The progress of reaction was monitored by TLC (7.3, n-hexane/ethyl acetate). Upon completion of the reaction, the mixture was cooled to room temperature. After filtration, the catalyst which remained in the aqueous phase can be recovered simply by removing the water through heating and the aqueous phase, and stored for use in subsequent run under the same conditions without any treatment.

The remaining solution is concentrated by increasing slightly CH$_2$Cl$_2$, and was magnetically stirred for 5 min. The precipitate was filtered to give quinoline-4-carboxylic acid as a crude. This crude was recrystallized with acetic acid to get pure product (Table 4; 4a-i) All the products were known and identified by comparison of their physical and spectrophotometric data with those of authentic compounds and found being identical. All yields refer to isolated products.

**References**


