



## An efficient one pot method for synthesis of carboxylic acids from nitriles using recyclable ionic liquid [bmim]HSO<sub>4</sub>



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Dedicated to my mentor Professor (Mrs.) Krishna Misra on her 76th birthday

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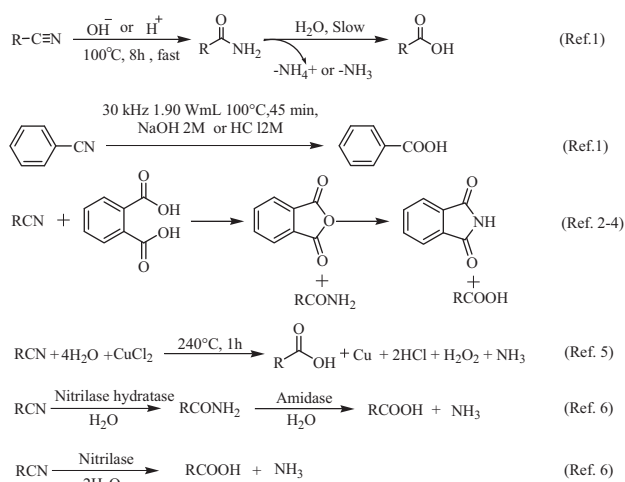
### ABSTRACT

Environmentally benign ionic liquid [bmim]HSO<sub>4</sub> was found suitable for conversion of nitriles into carboxylic acids under mild conditions with excellent purity.

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Several methods have been developed for the synthesis of carboxylic acid-derivatives from various nitriles. Currently, most of the available methods require hydrolysis of nitriles in either strongly acidic or basic medium at elevated temperature and longer reaction time.<sup>1–3</sup> Some of the synthetic methods involve two steps, first step is the formation of amides followed by the second step, which involves their conversion into corresponding acids.<sup>4</sup> The conversion of nitriles into acids using metal salts, such as sodium perborate and copper salts in heterogeneous medium at higher temperatures<sup>5</sup> is also well documented. However, aforementioned approaches involve use of environmentally hazardous solvents/chemicals and lengthy and tedious reaction process. Therefore, a green approach was envisaged to overcome these limitations, in which various enzymes, such as nitrilase hydratase along with amidase and nitrilase were used for the conversion of nitriles into acids (Fig. 1).<sup>6</sup>

Recently, ionic liquids have attracted considerable attention of chemists around the world for their utilities as efficient and green solvent for chemical reactions.<sup>7</sup> Moreover, the use of ionic liquids is environmentally benign and reduces the use of toxic chemicals and reaction time significantly.<sup>8</sup> In addition to this, reusable



**Figure 1.** Schematic representation of previously reported methods for the synthesis of carboxylic acid from nitriles.

property of ionic liquid is an additional advantage over many of the common solvents used in the chemical reactions.<sup>9–12</sup>

Our present study aims at developing a new environmental-friendly practical approach to synthesize carboxylic acids from various nitriles by exploring simple ionic liquid.

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Literature survey reveals that [bmim]HSO<sub>4</sub> has been used in a variety of organic reactions, such as prins reaction,<sup>9</sup> synthesis of coumarins,<sup>13</sup> xanthenes,<sup>14</sup> xanthenedione,<sup>15</sup> nitration of phenol,<sup>16</sup> halogenation of alcohols,<sup>17</sup> acetalization and thioacetalization of carbonyl compounds and their subsequent deprotection,<sup>18</sup> pyranlation of diols,<sup>19</sup> Friedel–Crafts alkylation,<sup>20</sup> synthesis of amid-oalkyl naphthols,<sup>10</sup> formylation of alcohols,<sup>11</sup> conversion of inulin into fructose<sup>12</sup> etc.

The wide spectrum utilization of [bmim]HSO<sub>4</sub> led us to check that if its applicability can be further extended and exploited as a new and more efficient method for the synthesis of acids from nitriles. It is well established that the C-2 proton of the 1,3-dialkylimidazolium cation is acidic,<sup>21–26</sup> ionic liquids are known to contain small amount of water which may act as nucleophile.<sup>7</sup> To prove one more unique application of ionic liquid in organic transformations, we carried out several reactions using different substrates, and found high yield with maximum purity. The scope of ionic liquid-mediated conversion of nitriles into carboxylic acids was investigated by selecting five ionic liquids, such as [bmim]HSO<sub>4</sub>, [bmim]BF<sub>4</sub>, [bmim]Br, [bmim]Cl and [bmim]CH<sub>3</sub>COO. Out of these ionic liquids, only [bmim]HSO<sub>4</sub> showed promising result, while the other ionic liquids did not work in this transformation and thus were eliminated from our present study. On the basis of this observation, we may conclude that counter ion HSO<sub>4</sub><sup>-</sup> of [bmim]HSO<sub>4</sub> is playing an important role in addition to C-2 proton of imidazolium ion.

To establish the utility of the ionic liquid for the conversion of nitriles into acids in single step, preliminary experiment was performed using simple benzonitrile which on treatment with [bmim]HSO<sub>4</sub> at 65 °C for 3 h, yielded benzoic acid up to 94% as white solid<sup>27</sup> with high purity (Table 1, entry 1b). This interesting result encouraged us to extend the same on a series of both aliphatic as well as aromatic nitriles having various substituents (Scheme 1). The nitriles and their respective products, yield and time required for reactions are summarized in Table 1. It is obvious from Table 1 that aromatic nitriles (Table 1, entries 1a–12a), as well as aliphatic nitriles (Table 1, entries 13a–18a) were equally sensible towards transformation in the ionic liquid, and final product yields were found more than 90%.

The electron withdrawing substituents on the benzene ring at ortho/para position were found to enhance the reactivity. The reactivity of hetero-aromatic nitrile (Table 1, entry 12) was also found to be equally sensible and the transformation proceeded with a substantial yield. The idea was further extended using dinitrile compound (Table 1, entry 11), which on ionic liquid treatment gave corresponding dicarboxylic acids with significantly higher yields. It is also evident from this transformation that steric crowding has no considerable effect on the hydrolysis of nitriles (Table 1, entries 9 and 10).

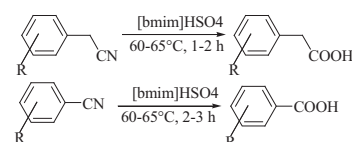
Most conversions of acids into nitriles were highly effective with yields in the range of 90–96%, indicating the utility of new approach. The purity and authenticity of the final products were established by melting point measurement and various analytical techniques such as IR, <sup>1</sup>H and <sup>13</sup>C NMR. The methodology was further authenticated by solving X-ray diffraction data of **15b** (Fig. 2). Further, to test whether the ionic liquid can be used as a highly recyclable solvent/catalyst system, we examined turnover during the conversion reaction. Our analysis and results explicitly reveal that ionic liquid can be recycled and used multiple times (five to six times) without a significant loss in its activity (Fig. 3).

Till date, no nitrile hydrolysis mechanism by ionic liquid is reported. It is estimated that ionic liquids contain approximately 200–600 ppm of water.<sup>7</sup> We proposed that imidazolium salt may trap water molecule on the C-2 position. The HSO<sub>4</sub><sup>-</sup> anion of

**Table 1**The [bmim]HSO<sub>4</sub> catalysed synthesis of aryl/heteroaryl/alkyl nitriles to corresponding carboxylic acid

S. No.	Nitriles (a)	Carboxylic Acids (b)	Time (h)	Yield (%)
1			3.00	94
2			2.20	92
3			2.20	95
4			2.45	90
5			2.45	92
6			2.40	90
7			2.25	90
8			2.50	92
9			2.50	95
10			2.50	95
11			2.45	95
12			2.40	92
13			1.40	94
14			1.25	94
15			1.25	96
16			1.20	95
17			1.40	95
18			1.10	96

Nitriles (a) (2 mmol) were dissolved in 5 ml of [bmim]HSO<sub>4</sub> and the reaction mixture was heated to 60–65 °C for 1–3 h.

**Scheme 1.** Synthesis of various carboxylic acids from nitriles.

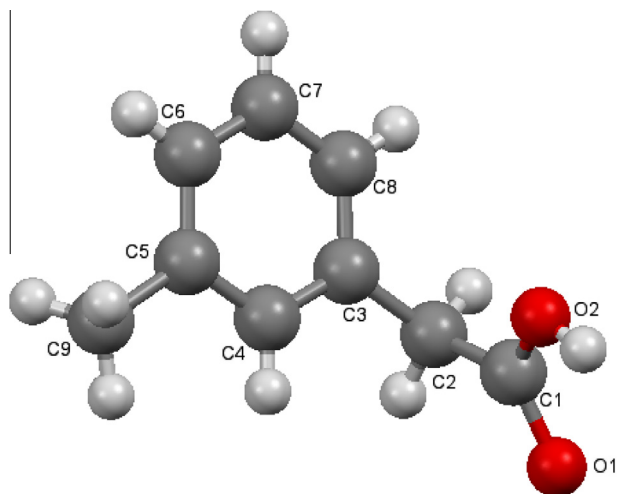


Figure 2. Crystal structure of compound **15b**.

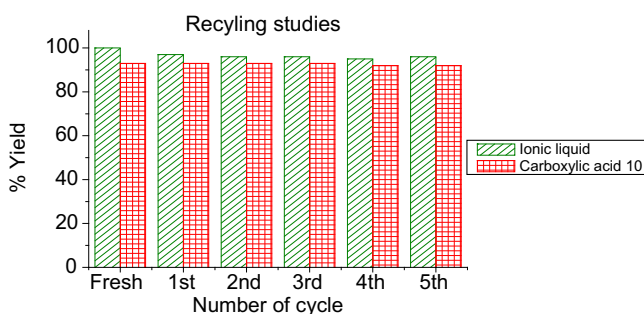


Figure 3. Recycling studies of [bmim]HSO<sub>4</sub>.

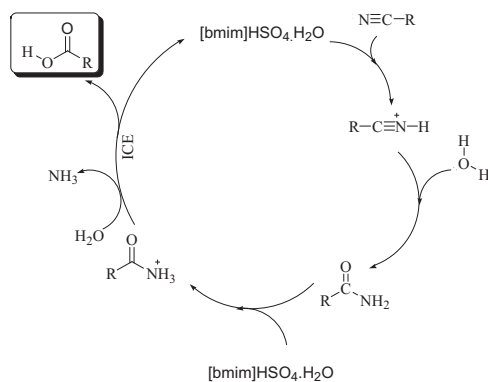


Figure 4. Plausible mechanism.

[bmim]HSO<sub>4</sub> can easily activate the nitrile to nucleophilic attack by associated water, which on partial hydrolysis produces an amide. Subsequently, amide gets protonated with another mole of water associated with [bmim]HSO<sub>4</sub> in a similar manner, which on hydrolysis leads to carboxylic acid. The interaction of [bmim]HSO<sub>4</sub> with nitriles is favored, due to their high solubility in this ionic liquid. The plausible mechanism is depicted in Figure 4.

Thus, it is evident from the above finding that the reported protocol is a convenient, eco-friendly and single-step conversion of nitriles into carboxylic acids by [bmim]HSO<sub>4</sub> with excellent yield in shorter reaction time. In addition, the reaction conditions are

sufficiently mild to allow the survival of different functional groups, such as nitro, amino, alkyl and halogens, except amide. This method is found applicable on a wide variety of nitriles viz. aliphatic, aromatic and heterocyclic nitriles. This approach omitted expensive and tedious purification step, and thus is viable for large scale synthesis of acid from nitrile. Further study on ionic liquids and its potential application in organic synthesis are under way in our laboratory.

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### Supplementary data

Supplementary data (experimental procedures, characterization, full spectroscopic data for all compounds, associated with this article are given in the supplementary material. Crystallographic data for the compound **15b** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. 951369. Copy of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.-cam.ac.Uk) associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.tetlet.2014.05.050>.

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- General procedure for the synthesis of carboxylic acids from nitriles:* Aromatic or aliphatic nitriles (2 mmol) were dissolved in 5 ml of [bmim]HSO<sub>4</sub> and the reaction mixture was heated at 60–65 °C for 1–3 h. The progress of reaction was monitored by TLC. After completion of reaction, as checked by TLC, the reaction mixture was poured into water containing crushed ice. The product was precipitated out, filtered and dried. The yield of the final product was high (>90%) in all cases. All final products obtained were found sufficiently pure so they did not need further purification.