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Journal of Molecular Catalysis A: Chemical 245 (2006) 37–46
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
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# A remarkably rapid regioselective synthesis of β-enaminones using silica chloride in a heterogeneous as well as an ionic liquid in a homogeneous medium at room temperature

Atul R. Gholap, Narayan S. Chakor, Thomas Daniel, Rajgopal J. Lahoti, Kumar V. Srinivasan *

*Organic Chemistry Technology Division, National Chemical Laboratory, Dr. Homi Bhabha Road, Pune 411008, Maharashtra, India*

Received 28 March 2005; received in revised form 5 July 2005; accepted 18 September 2005
Available online 25 October 2005

**Abstract**

Silica chloride as a heterogeneous catalyst has been used for the regioselective synthesis of β-amino-α,β unsaturated esters and ketones. Similar regioselective synthesis was also performed using an ionic liquid 1-*n*-butyl imidazolium tetrafluoroborate [Hbim]$BF_4$ as a recyclable homogeneous medium as well as a promoter without the need for any added catalyst. Both the methods were found to be remarkably rapid and afforded the β-enaminones in excellent isolated yields.


*Keywords:* Silica chloride; Ionic liquid; β-Enaminones; 1,3-Diketones; Amines

## 1. Introduction

The enaminones are an important class of organic synthetic intermediates. They have a very high impact as synthons for the synthesis of various heterocyclic and biologically active analogues [1], including anticonvulsant [2], anti-inflammatory [3] and antitumor agents [4]. Due to their wide range of activity and importance, a simple and high yielding one-pot approach for the synthesis of β-enaminones is highly desirable. The conventional method for the synthesis of enaminones is the azeotropic removal of water by refluxing an amine with 1,3-diketone in an aromatic solvent [5]. Various modified synthetic pathways have been reported in literature such as the addition of metallic esters or amide enolates to nitriles [6], tosyl imines [7] or imidoyl halides [8]. Apart from these, the enamination of 1,3-dicarbonyl compounds has been carried out using catalyst systems such as silica/micro-wave [9], clay$K_{10}$/ultrasound [10] and $NaAuAl_4$ [11]. More recently, $Bi(TFA)_3$ [12] as well as $Zn(ClO_4)_2{\cdot}6H_2O$ [13] have also been reported as effective catalysts. Many of the methods reported so far suffer from one or more drawbacks such as long reaction time, unsatisfactory yields and hazardous and expensive catalysts. Taking into consideration all these limitations, we investigated the progress of the reaction of various amines with 1,3-diketones in a novel heterogeneous as well as a homogeneous medium. For the first time, silica chloride was used as a solid catalyst for the enamination under heterogeneous conditions. For the homogeneous conditions, a recyclable ionic liquid (IL), viz. 1-*n*-butylimidazolium tetrafluoroborate [Hbim]$BF_4$ was used as a reaction medium as well as a promoter for the first time in the absence of any added catalyst. For both the methodologies which were performed under ambient temperature, the reaction rates were significantly higher than those reported so far for the synthesis of β-enaminones at room temperature.

## 2. Results and discussion

### 2.1. Enamination in heterogeneous medium using silica chloride

Recently heterogeneous catalysts like silica chloride, a modified silica, have proven to be useful for various organic transformations [14]. These transformations are affected by the reagents immobilized on the porous solid supports of the modified silica and have advantages such as enhanced reaction rates, higher yields, greater selectivity and ease of manipulation over the con-

* Corresponding author. Tel.: +91 20 25889089; fax: +91 20 25893616.
*E-mail address:* kvsri@dalton.ncl.res.in (K.V. Srinivasan).

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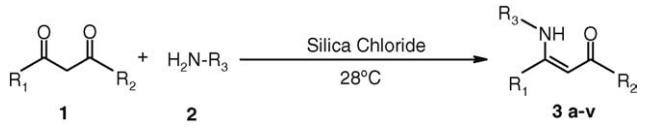
doi:10.1016/j.molcata.2005.09.021




Scheme 1.

ventional solution phase reaction. Consequently, in the case of enamination reaction, we thought there is scope for further innovation towards milder reaction conditions, short reaction time and better yields. This paper reports for the first time a regio- and chemo-selective enamination of β-dicarbonyl compounds under mainly solvent free conditions using silica chloride at room temperature in excellent yields and purity.

A variety of amines including ammonium acetate, aliphatic and aromatic amines were condensed with various 1,3-diketones like ethyl acetoacetate, acetyl acetone and 1,3-cyclohexanedione using silica chloride as a heterogeneous catalyst at 28 °C (Scheme 1). The results are recorded in Table 1.

In majority of the cases, where even one of the reactants is a liquid, the reaction was carried out under solvent free condition. In others, which constitute a minority where both the reactants are solid (entries 3, 6, 12, 15), chloroform was used as the solvent as indicated in Table 1. All the isolated products were well characterized by their IR, $^{1}$H and $^{13}$C NMR spectral analysis and their elemental analysis was in conformity with their structures. It is clear from our results that the silica chloride catalyzed condensation reaction of 1,3-dicarbonyls with the amines provides a remarkably rapid and viable alternative route for the synthesis of β-enaminones. All the reactions were complete in just 5–10 min affording the products **3a–v** in excellent isolated yields. It is observed that both the highly reactive aliphatic and the less reactive aromatic amines undergo the reaction in an equally facile manner. It is noteworthy that by this methodology the reaction of acetyl acetone with ammonium acetate gave the enaminone **3a** in 93% yield in just 10 min (entry 1) instead of long reaction time (24 h) in the previously reported method [15] using silica gel as a catalyst. This highlights the significantly higher Lewis acid character of silica chloride as against silica gel for the enamination reaction. This method has been successfully applied for the enamination of cyclic 1,3-diketones affording potential pharmaceutically important anticonvulsant compounds and appears to be more convenient and superior to the preparative methods reported so far for such compounds. The reported methods take much longer time, make use of hazardous solvents and involve complex isolation procedures. For instance, the enamination of 1,3-cyclohexanedione with aniline showed only 30% conversion to **3i** even after 24 h in the presence of silica gel as catalyst as against 100% conversion with an isolated yield of 92% for **3i** in just 10 min using silica chloride.

The recycle data for the typical reaction of aniline with acetyl acetone using silica chloride as catalyst under the condition of our methodology are recorded in Table 2. There is a progressive decrease in the isolated yields as well as the chlorine content of the recovered catalyst and a corresponding increase in the reaction time.

Based on the above observations, a plausible mechanism for the reaction is postulated as shown in Fig. 1. The Si–Cl bond is labile and can give rise to Lewis acid centers on silica. The Cl is easily displaced selectively by the acetyl oxygen of 1,3-dicarbonyl compounds by a nucleophilic substitution reaction generating a cationic center on the carbonyl carbon, which is easily attacked by the nucleophilic primary amines to form the imine which after tautomerisation forms the enaminone. It is important to note that the original activity of the recovered silica chloride from recycle batch 2 could be restored by treatment with thionyl chloride under reflux.

The reactivity of silica chloride was also checked by taking low catalyst loading for the reaction of aniline with acetyl acetone. It was observed that as wt% of catalyst based on acetyl acetone decreases the reaction time increases, but the low percentage of catalyst does not affect the yields. This proportion of the catalyst was the optimum since any loading beyond 10% (w/w) did not bring about any further decrease in reaction time and increase in yield. The results are summarized in Table 3.

### 2.2. Enamination in a homogeneous medium using ionic liquid

In recent times ionic liquids continue to receive much attention as green solvents, with many excellent reviews available summarizing their preparation, use and advantages compared to traditional solvents [16]. Thus, the non-volatile, non-flammable and thermally stable ionic liquids can be used as replacements for the selected organic solvents for various transformations, since the latter are very often volatile, hazardous and pose problems of recovery. Additionally, some ILs possess inherent Lewis/Brønsted acidity, which can promote and catalyze organic transformation of commercial importance in excellent yields under ambient condition such as acetylation of alcohols [17] and one-pot synthesis of 3,4-dihydropyrimidin-2-(1H)-ones [18] at ambient temperature under ultrasound irradiation reported by us recently.

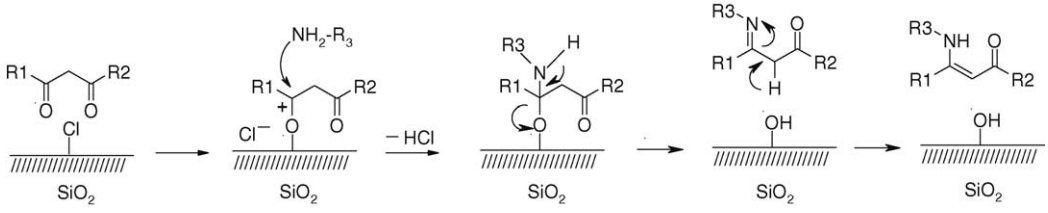



Fig. 1. Plausible mechanisms for the synthesis of enaminones.

Table 1
Synthesis of β-enaminones (**3a–v**) using silica chloride or $[Hbim]BF_4$

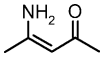
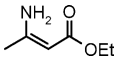
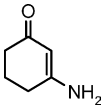
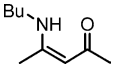
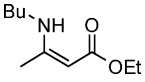
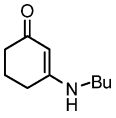
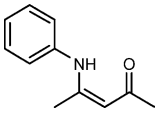
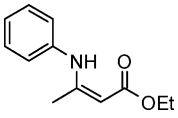
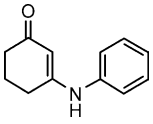
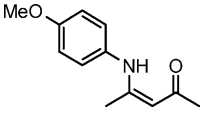
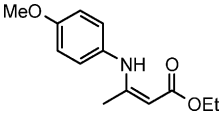
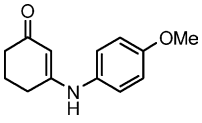
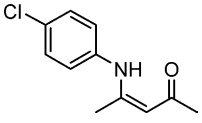
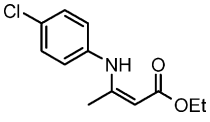
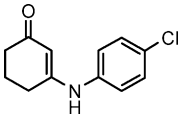
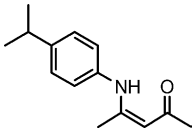
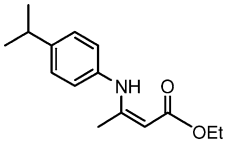
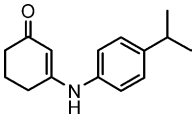
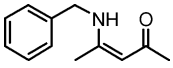
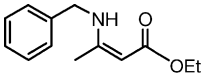
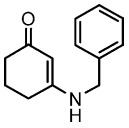
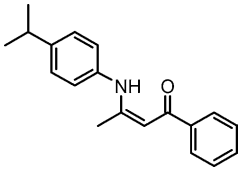
| Entry | **3a–v** | Product | Silica chloride | | $[Hbim]BF_4$ | |
|---|---|---|---|---|---|---|
| | | | Reaction time (min) | Yield[a] (%) | Reaction time (min) | Yield[a] (%) |
| 1 | **3a** |  | 10 | 93 | 30 | 92 |
| 2 | **3b** |  | 15 | 90 | 30 | 90 |
| 3 | **3c**[b] |  | 15 | 90 | 5 | 93 |
| 4 | **3d** |  | 5 | 96 | 5 | 92 |
| 5 | **3e** |  | 5 | 94 | 5 | 92 |
| 6 | **3f**[b] |  | 5 | 93 | 20 | 92 |
| 7 | **3g** |  | 5 | 91 | 25 | 91 |
| 8 | **3h** |  | 8 | 90 | 25 | 93 |
| 9 | **3i** |  | 10 | 92 | 20 | 93 |
| 10 | **3j** |  | 5 | 94 | 25 | 92 |
| 11 | **3k** |  | 5 | 92 | 25 | 92 |
| 12 | **3l**[b] |  | 5 | 90 | 20 | 93 |
| 13 | **3m** |  | 5 | 91 | 30 | 93 |
| 14 | **3n** |  | 8 | 90 | 30 | 92 |

Table 1 (*Continued*)

| Entry | 3a–v | Product | Silica chloride | | [Hbim]$BF_4$ | |
|---|---|---|---|---|---|---|
| | | | Reaction time (min) | Yield[a] (%) | Reaction time (min) | Yield[a] (%) |
| 15 | **3o**[b] |  | 10 | 90 | 30 | 91 |
| 16 | **3p**[c] |  | 5 | 93 | 20 | 92 |
| 17 | **3q**[c] |  | 8 | 92 | 30 | 90 |
| 18 | **3r**[c] |  | 10 | 90 | 30 | 92 |
| 19 | **3s** |  | 5 | 96 | 5 | 90 |
| 20 | **3t** |  | 5 | 93 | 10 | 89 |
| 21 | **3u** |  | 5 | 91 | 10 | 90 |
| 22 | **3v**[c] |  | 15 | 93 | 30 | 91 |

[a] Isolated yields after column chromatography.
[b] Chloroform used as a solvent.
[c] New compound.

The ILs belonging to the 1-*n*-butylimidazolium [Hbim] series were screened for the reaction of aniline with acetyl acetone to afford 4-phenylamino-pent-3-en-2-one (**3g**). All the ILs were subjected to a thorough drying protocol of 80 °C at 10 mmHg for 4 h and their moisture content estimated. The reaction in different ILs was followed by subjecting aliquots of reaction mixture to TLC at 5-min intervals using 10% ethyl acetate in petroleum ether (bp 60–80 °C) as eluent. The time for complete conversion of acetyl acetone was noted at which point the reaction was stopped and the product was isolated. The results are recorded in Table 4.

Table 2
Recycle study of recovered silica chloride

| Batch | Chlorine content (%) | Reaction time (min) | Yield[a] (%) |
|---|---|---|---|
| First batch | 4.26 | 5 | 91 |
| Recycle 1 | 1.62 | 30 | 88 |
| Recycle 2 | 1.05 | 120 | 80 |

[a] Isolated yields after column chromatography.

Table 3
Effect of wt% of silica chloride on reaction rate of aniline with acetyl acetone

| Entry | Silica chloride (wt%) | Time (min) | Yield[a] (%) |
|---|---|---|---|
| 1 | 2 | 20 | 89 |
| 2 | 4 | 16 | 90 |
| 3 | 6 | 12 | 88 |
| 4 | 8 | 8 | 90 |
| 5 | 10 | 5 | 91 |

[a] Isolated yields after column chromatography.

Table 4
Screening of various ILs for reaction of aniline with acetyl acetone

| Entry | Ionic liquid | Moisture content (wt%) | Chemical shift $\delta$ (ppm) –NH proton | Time for complete conversion (min) | Yield[a] (%) |
|---|---|---|---|---|---|
| 1 | [Hbim]$ClO_4$ | 0.014 | 11.83 | 55 | 93 |
| 2 | [Hbim]Cl | 0.013 | 12.17 | 35 | 91 |
| 3 | [Hbim]Br | 0.013 | 12.22 | 35 | 90 |
| 4 | [Hbim]$BF_4$ | 0.012 | 14.59 | 20 | 92 |

[a] Isolated yields after column chromatography.

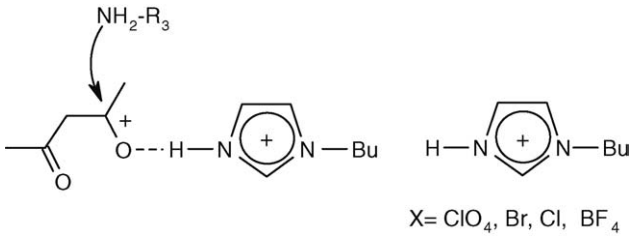



Fig. 2. The hydrogen bond interaction of the imidazolium cation.

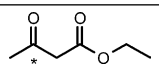
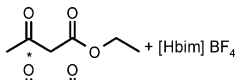
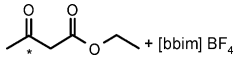
It was observed that the nature of the anion governs the electrophilicity of the imidazolium cation, which in turn influences the acidity of the –NH proton. This is indicated by increasing downfield shift of the –NH proton. This –NH proton is capable of hydrogen bonding with acetyl oxygen generating the cationic center as shown in Fig. 2 which is easily attacked by the nucleophilic amines.

Consequently, it can be observed from Table 4, the IL [Hbim]$BF_4$ with most deshielded –NH proton afforded the best results in terms of time of complete conversion although all the ILs afforded more or less similar isolated yields. Therefore, all further reactions were carried out in this IL.

The IL [Hbim]$BF_4$ acts as a solvent medium and has also promoted the reaction with its inherent Brønsted acidity. The Brønsted acidity is conferred by the –NH proton of [Hbim]$BF_4$ (chemical shift of 14.59 ppm) capable of bonding with carbonyl oxygen of 1,3-dicarbonyl compound as shown in Fig. 2. Evidence for this was obtained by recording the $^{13}C$ NMR spectra of ethyl acetoacetate with an external lock of $D_2O$ and with one equivalent of the IL. The results are recorded in Table 5.

A significance shift of ~3 ppm for the carbonyl carbon of EAA by its interaction with IL was observed. Additional evidence was obtained by recording their IR spectra neat wherein also a significant shift to lower wave number by 7 $cm^{-1}$ was observed.

Table 5
The $^{13}C$ NMR chemical shifts and IR data for the carbonyl

| Entry | Substrate | Chemical shift[a] (ppm) | IR values[b], $\nu$ ($cm^{-1}$) |
|---|---|---|---|
| 1 |  | 214.1 | 1742.1 |
| 2 |  | 217.1 | 1735.5 |
| 3 |  | 214.1 | 1741.2 |

[a] Recorded neat with $D_2O$ as external lock.
[b] Recorded with neat sample.

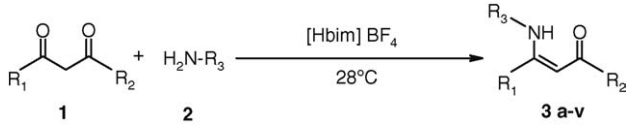
For comparison and to substantiate the above observations, the reaction of aniline with acetylacetone was carried out in the non-acidic IL [bbim]$BF_4$ under similar conditions. The time for complete conversion was considerably longer (5 h) to afford the product in 89% yield. Moreover, no shift in the $^{13}C$ NMR and IR spectra for the carbonyl carbon and C=O stretching frequency, respectively, for the ethylacetoacetate with one equivalent of [bbim]$BF_4$ was observed thereby confirming the poor catalytic activity of the relatively non-acidic [bbim]$BF_4$.

Consequently, all the amines and 1,3-diketones used in the silica chloride catalyzed reaction were subjected to the enamination using ionic liquid 1-*n*-butylimidazolium tetrafluoroborate [Hbim]$BF_4$ as the solvent as well as promoter at 28 °C (Scheme 2) in the absence of any added catalyst. The results are recorded in Table 1.

Both acyclic and cyclic 1,3-dicarbonyl compounds undergo enamination with amines in excellent isolated yields. In majority of the cases, the products were selectively extracted from the ionic liquid medium using 10% ethyl acetate in petroleum ether (bp 60–80 °C) leaving behind the ionic liquid, which was recovered and recycled. In the case of the reaction between 1,3-cyclohexanedione and amines the products were isolated by dilution with water and filtration of the precipitated cyclic enaminones. The aqueous layer containing the IL was subjected to distillation at 80 °C at a reduced pressure of 10 mmHg for 4 h to remove all traces of water. The recovered IL from both the above mentioned procedures could be recycled five times with almost no loss of activity. The IL [Hbim]$BF_4$ was recycled five times for the reaction of acetyl acetone with aniline. The results are recorded in Table 6. It was observed that the IL exhibits only a marginal loss in activity spread over five recycle batches.

The structure of the new cyclic enaminone **3r** was confirmed by X-ray crystallography [19]. The ORTEP diagram is shown in Fig. 3.

The enaminones resulting from the cyclic diketone are reported to be pharmaceutically important potential anticonvulsant compounds [2].




Scheme 2.

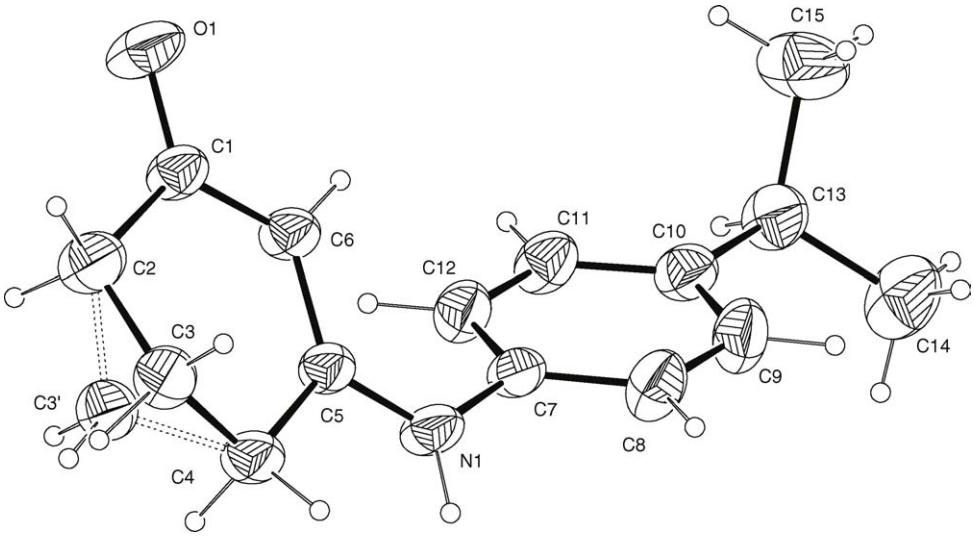



Fig. 3. ORTEP diagram of the X-ray crystal structure of compound **3r** with thermal ellipsoids at 50% probability.

Table 6
Reusability of ionic liquid for synthesis of enaminones (entry 7)

| Entry | Yield[a] (%) |
|---|---|
| 1 | 91 |
| 2 | 91 |
| 3 | 90 |
| 4 | 88 |
| 5 | 90 |

[a] Isolated yields after column chromatography.

The regioselectivity of the methodology was confirmed by performing the reaction of benzoyl acetone with 4-isopropylamine using silica chloride and [Hbim]$BF_4$, respectively, at room temperature to obtain the enaminone **3v** as the only product. This was confirmed by comparing the $^{13}C$ NMR values of the acetyl carbonyl carbon and the benzoyl carbonyl carbon in both the substrate and the product **3v**, respectively. The $^{13}C$ NMR shift of the acetyl carbonyl carbon (193.5 $\delta$) changes to 162.3 $\delta$ retaining the value of the benzoyl carbonyl carbon at 188.2 $\delta$ without any change. The $^{13}C$ NMR spectra (**3v**) are submitted as supplementary material. This clearly indicates that the enamination has taken place regioselectively at the acetyl carbonyl carbon and not at the benzoyl carbonyl carbon. Evidently, this regio-selectivity at acetyl carbonyl carbon has been maintained for the β-keto-esters as well wherein no formation of the amide from the ester was observed.

## 3. Experimental

All chemicals were of research grade and were used as obtained from Aldrich or Fluka. IR spectra were recorded on a Mattson Research Series FT-IR spectrometer 60, NMR spectra were recorded on Bruker AC-200 spectrometer in $CDCl_3$ with TMS as an internal standard. The melting points are uncorrected and recorded on the BUCHI melting point instrument model B-540. Column chromatography was performed using silica gel (60–120 mesh size) purchased from Thomas Baker and TLC was carried out using aluminum sheets pre-coated with silica gel $60F_{254}$ purchased from Merck. Determinations of the moisture content of ionic liquid samples were carried out using a Halogen Moisture Analyzer model METTLER TOLEDO HB 43.

### *3.1. Procedure for the synthesis of silica chloride*

Flame dried silica gel (20 g) and freshly distilled thionyl chloride (100 ml) was refluxed for 50 h under argon atmosphere. The excess unreacted thionyl chloride was distilled out and the resulting greyish silica chloride was flame dried, stored in airtight container and used as it is for the reactions.

#### *3.1.1. Typical procedure for synthesis of β-amino-α,β-unsaturated ketones and esters using silica chloride as a heterogeneous catalyst*

A mixture of 1,3-dicarbonyl compound (2 mmol), amine (2.2 mmol) and silica chloride (10%, w/w) was stirred at room temperature (28 °C). The completion of reaction was followed by TLC using 10% EtOAc in petroleum ether (bp 60–80 °C) as eluent. After completion of reaction, the crude reaction product which is a paste was subjected to column chromatography using 1% EtOAc in petroleum ether (bp 60–80 °C) as eluent to isolate pure products and were fully characterized.

### *3.2. Preparation of 1-n-butylimidazolium tetrafluoroborate [Hbim]$BF_4$*

Tetrafluoroboric acid (1 mmol) as 40% (w/v) solution in water was added slowly over a period of 30 min to 1-butyl imidazole (1 mmol) at 0 °C under stirring. The reaction mixture was stirred for an additional period of 2 h at the same temperature. Water was removed from the reaction mixture by subjecting it to evaporation for 4 h at 80 °C under reduced pressure (10 mmHg) to give the product as colorless liquid (20 g; yield, 96%); IR ($cm^{-1}$) 3607, 3153, 2876, 1580, 1466, 894, 762; $^1H$ NMR ($CDCl_3$, 200 MHz) $\delta$ 0.56 (t, 3H), 0.95 (m,

2H), 1.47 (m, 2H), 3.87 (t, 2H), 7.12 (d, 1H), 7.20 (d, 1H), 8.16 (s, 1H), 14.59 (brs, 1H); $^{13}$C NMR ($CDCl_3$, 50 MHz) $\delta$ 13.1, 19.2, 32.1, 48.5, 120.9, 122.8, 135.2. All the other ionic liquids such as [Hbim]Br, [Hbim]Cl, [Hbim]$ClO_4$, were prepared as above using the corresponding acid of the anion. Care must be exercised in handling [Hbim]$ClO_4$ in large amount for possible explosion hazards although no untoward incident was experienced in handling the IL in the present work. The [bbim]$BF_4$ for comparative studies was synthesized as per the method previously reported by us [21].

### 3.2.1. Typical procedure for synthesis of β-amino α,β-unsaturated ketones and esters in ionic liquid [Hbim]$BF_4$ as a homogeneous medium

A mixture of 1,3-dicarbonyl compound (2 mmol) and amine (2.2 mmol) in [Hbim]$BF_4$ (2 ml) was stirred at room temperature (28 °C). The completion of reaction was followed by TLC using 10% EtOAc in petroleum ether (bp 60–80 °C) as eluent. After completion of reaction the product was selectively extracted using 10% EtOAc in petroleum ether (2× 10 ml) leaving behind the ionic liquid. The immiscible organic layer was separated, dried over anhydrous sodium sulphate and the solvent was evaporated under reduced pressure to afford the crude product. The crude product was purified by column chromatography using 1% EtOAc in petroleum ether (bp 60–80 °C) as eluent. The recovered [Hbim]$BF_4$ was used as such for the recycle studies.

*3.2.1.1. Characterization data for compounds **3a–v**. 4-Amino-pent-3-en-2-one (**3a**)* [15]: The above general procedure, starting from acetyl acetone (0.3 g, 3 mmol) and ammonium acetate (0.27 g, 3.6 mmol) gave compound **3a**: (white solid); mp 32 °C; IR ($cm^{-1}$) 3366, 3013, 1710, 1621, 1535, 1431, 1288, 1216, 754; $^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 1.90 (s, 3H), 2.03 (s, 3H), 5.01 (s, 1H), 9.81 (brs, 2H); $^{13}$C NMR ($CDCl_3$, 50 MHz) $\delta$ 21.7, 28.6, 95.2, 161.7, 196.1; Anal. Calcd for $C_5H_9NO$ (99): C, 60.58; H, 9.15; N, 14.13. Found: C, 60.52; H, 9.13; N, 14.10.

*3-Amino-but-2-enoic acid ethyl ester (**3b**)* [15]: The above general procedure, starting from ethyl acetoacetate (0.3 g, 2.30 mmol) and ammonium acetate (0.21 g, 2.76 mmol) gave compound **3b**: (yellow oil); IR ($cm^{-1}$) 3450, 3336, 2981, 1716, 1621, 1567, 1446, 1288, 1163, 1045, 788, 565; $^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 1.25 (t, 3H, $J$ = 7.2 Hz), 1.90 (s, 3H), 4.12 (q, 2H, $J$ = 7.2 Hz), 4.50 (s, 1H), 7.95 (brs, 2H); $^{13}$C NMR ($CDCl_3$, 50 MHz) $\delta$ 14.0, 21.5, 57.9, 83.0, 159.9, 169.8; Anal. Calcd for $C_6H_{11}NO_2$ (129): C, 55.80; H, 8.58; N, 10.84. Found: C, 55.72; H, 8.51; N, 10.86.

*3-Amino-cyclohex-2-enone (**3c**)* [5a]: The above general procedure, starting from 1,3-cyclohexanedione (0.3 g, 2.67 mmol) and ammonium acetate (0.24 g, 3.21 mmol) gave compound **3c**: (yellow solid); mp 126 °C; IR ($cm^{-1}$) 3262, 2925, 1591, 1569, 1243; $^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 1.92–1.96 (m, 2H), 2.25–2.32 (m, 2H), 2.44–2.48 (m, 2H), 5.40 (s, 1H), 5.96 (brs, 2H); $^{13}$C NMR ($CDCl_3$, 50 MHz) $\delta$ 20.5, 27.1, 34.7, 96.7, 167.0, 194.7; Anal. Calcd for $C_6H_9NO$ (111): C, 64.84; H, 8.16; N, 12.60. Found: C, 64.82; H, 8.20; N, 12.61.

*4-Butylamino-pent-3-en-2-one (**3d**)*: The above general procedure, starting from acetyl acetone (0.3 g, 3 mmol) and butyl amine (0.26 g, 3.6 mmol) gave compound **3d**: (yellow oil); IR ($cm^{-1}$) 3450, 2959, 2932, 1611, 1578, 1299, 1020, 736; $^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 0.96 (t, 3H, $J$ = 7.3 Hz), 1.36–1.40 (m, 2H), 1.45–1.60 (m, 2H), 1.94 (s, 3H), 2.01 (s, 3H), 3.12 (q, 2H, $J$ = 6.5 Hz), 5.35 (s, 1H), 10.90 (brs, 1H); $^{13}$C NMR ($CDCl_3$, 50 MHz) $\delta$ 13.7, 20.5, 27.4, 27.8, 34.7, 49.4 96.7, 156.6, 194.7; Anal. Calcd for $C_9H_{17}NO$ (155): C, 69.63; H, 11.04; N, 9.02. Found: C, 69.55; H, 11.09; N, 9.06.

*3-Butylamino-but-2-enoic acid ethyl ester (**3e**)*: The above general procedure, starting from ethyl acetoacetate (0.3 g, 2.30 mmol) and butyl amine (0.2 g, 2.76 mmol) gave compound **3e**: (yellow oil); IR ($cm^{-1}$) 3141, 3016, 2962, 1644, 1605, 1403, 1275, 1176, 1059, 757, 666; $^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 0.92 (t, 3H, $J$ = 7.3 Hz), 1.24 (t, 3H, $J$ = 7.2 Hz), 1.33–1.38 (m, 2H), 1.42–1.58 (m, 2H), 1.90 (s, 3H), 3.14 (q, 2H, $J$ = 6.5 Hz), 4.10 (q, 2H, $J$ = 7.2 Hz), 4.42 (s, 1H), 8.55 (brs, 1H); $^{13}$C NMR ($CDCl_3$, 50 MHz) $\delta$ 12.7, 13.6, 18.0, 19.0, 31.6, 41.6, 56.9, 81.0, 160.6, 169.4; Anal. Calcd for $C_{10}H_{19}NO_2$ (185): C, 64.83; H, 10.34; N, 7.56. Found: C, 64.82; H, 10.31; N, 7.58.

*3-Butylamino-cyclohex-2-enone (**3f**)*: A mixture of 1,3 cyclohexane dione (0.3 g, 2.67 mmol) and butyl amine (0.23 g, 3.21 mmol) gave compound **3f**: (yellow solid); mp 94–96 °C; IR ($cm^{-1}$) 3262, 2925, 1591, 1569, 1243; $^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 0.91 (t, 3H, $J$ = 7.2 Hz), 1.32–1.38 (m, 2H), 1.55.1.59 (m, 2H), 1.88–1.94 (m, 2H), 2.32–2.42 (m, 4H), 3.05 (q, 2H, $J$ = 6.5 Hz), 5.14 (s, 1H), 5.38 (brs, 1H); $^{13}$C NMR ($CDCl_3$, 50 MHz) $\delta$ 12.7, 19.3, 21.0, 28.4, 29.4, 35.0, 41.8, 94.2, 166.3, 196.1; Anal. Calcd for $C_{10}H_{17}NO$ (167): C, 71.81; H, 10.25; N, 8.37. Found: C, 71.80; H, 10.21; N, 8.33.

*4-Phenylamino-pent-3-en-2-one (**3g**)* [15]: The above general procedure, starting from acetyl acetone (0.3 g, 3 mmol) and aniline (0.33 g, 3.6 mmol) gave compound **3g**: (white solid); mp 50 °C; IR ($cm^{-1}$) 3450, 3032, 3020, 1620, 1571, 1509, 1278, 1188, 1024, 921, 751, 697, 505; $^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 1.97 (s, 3H), 2.09 (s, 3H), 5.18 (s, 1H), 7.07–7.36 (m, 5H). 12.48 (brs, 1H); $^{13}$C NMR ($CDCl_3$, 50 MHz) $\delta$ 19.3, 28.6, 97.2, 124.1, 125.0, 128.6, 138.2, 159.7, 195.5; Anal. Calcd for $C_{11}H_{13}NO$ (175): C, 75.40; H, 7.48; N, 7.99. Found: C, 75.43; H, 7.46; N, 7.92.

*3-Phenylamino-but-2-enoic acid ethyl ester (**3h**)*: The above general procedure, starting from ethyl acetoacetate (0.3 g, 2.30 mmol) and aniline (0.25 g, 2.76 mmol) gave compound **3h**: (yellow oil); IR ($cm^{-1}$) 3563, 3018, 2928, 1649, 1615, 1596, 1272, 1166, 1059, 757, 698; $^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 1.28 (t, 3H, $J$ = 7.2 Hz), 1.99 (s, 3H), 4.17 (q, 2H, $J$ = 7.2 Hz), 4.69 (s, 1H), 7.05–7.34 (m, 5H). 10.38 (brs, 1H); $^{13}$C NMR ($CDCl_3$, 50 MHz) $\delta$ 14.2, 19.8, 58.3, 86.0, 124.0, 124.5, 128.7, 139.2, 158.4, 170.0; Anal. Calcd for $C_{12}H_{15}NO_2$ (205): C, 70.22; H, 7.37; N, 6.82. Found: C, 70.19; H, 7.35; N, 6.84.

*3-Phenylamino-cyclohex-2-enone (**3i**)*: The above general procedure, starting from 1,3-cyclohexanedione (0.3 g,

2.67 mmol) and aniline (0.3 g, 2.67 mmol) gave compound **3i**: (yellow solid); mp 178–180 °C; IR ($cm^{-1}$) 3262, 2925, 2855, 1591, 1569, 1526, 1451, 1243, 1182, 670; $^1H$ NMR ($CDCl_3$, 200 MHz) $\delta$ 1.98–2.02 (m, 2H), 2.29–2.36 (m, 2H), 2.48–2.54 (m, 2H), 5.29 (s, 1H). 5.55 (brs, 1H), 7.11–7.34 (m, 5H); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 21.6, 29.2, 36.2, 98.6, 123.8, 125.1, 128.9, 138.2, 163.7, 198.2; Anal. Calcd for $C_{12}H_{13}NO$ (187): C, 76.98; H, 7.00; N, 7.48. Found: C, 76.95; H, 7.02; N, 7.50.

*4-(4-Methoxy-phenylamino)-pent-3-en-2-one (**3j**)*: The above general procedure, starting from acetyl acetone (0.3 g, 3 mmol) and 4-methoxy aniline (0.3 g, 2.67 mmol) gave compound **3j**: (yellow oil); IR ($cm^{-1}$) 3438, 3000, 2960, 2836, 1607, 1568, 1515, 1440, 1278, 1187, 1033, 843, 750; $^1H$ NMR ($CDCl_3$, 200 MHz) $\delta$ 1.90 (s, 3H,), 2.08 (s, 3H,), 3.80 (s, 3H,), 5.15 (s, 1H), 6.8 (d, 2H, $J$ = 8Hz), 7.03 (d, 2H, $J$ = 8Hz), 12.28 (brs, 1H); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 19.5, 28.9, 55.3, 96.7, 114.1, 126.5, 131.3, 157.6, 161.1, 195.7; Anal. Calcd for $C_{12}H_{15}NO_2$ (205): C, 70.22; H, 7.37; N, 6.82. Found: C, 70.28; H, 7.35; N, 6.82.

*3-(4-Methoxy-phenylamino)-but-2-enoic acid ethyl ester (**3k**)*: The above general procedure, starting from ethyl acetoacetate (0.3 g, 2.30 mmol) and 4-methoxy aniline (0.34 g, 2. 76 mmol) gave compound **3k**: (yellow oil); IR ($cm^{-1}$) 3265, 2949, 2836, 1655, 1613, 1514, 1247, 1164, 1035, 786; $^1H$ NMR ($CDCl_3$, 200 MHz) $\delta$ 1.27 (t, 3H, $J$ = 7.2 Hz), 1.87 (s, 3H,), 3.78 (s, 3H,), 4.15 (q, 2H, $J$ = 7.2 Hz), 4.64 (s, 1H), 6.84 (d, 2H, $J$ = 8.2 Hz), 7.01 (d, 2H, $J$ = 8.2 Hz), 10.20 (brs, 1H); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 14.2, 19.7, 55.0, 58.2, 84.4, 113.8, 126.4, 131.8, 157.1, 159.6, 170.1; Anal. Calcd for $C_{13}H_{17}NO_3$ (235): C, 66.36; H, 7.28; N, 5.95. Found: C, 66.39; H, 7.21; N, 5.98.

*3-(4-Methoxy-phenylamino)-cyclohex-2-enone (**3l**)*: The above general procedure, starting from 1,3-cyclohexanedione (0.3 g, 2.67 mmol) and 4-methoxy aniline (0.39 g, 3.2 mmol) gave compound **3l**: (yellow solid); mp 166–168 °C; IR ($cm^{-1}$) 3417, 3255, 3019, 1579, 1509, 1242, 1215, 1185, 1035, 758, 668; $^1H$ NMR ($CDCl_3$, 200 MHz) $\delta$ 1.94–1.98 (m, 2H), 2.27–2.29 (m, 2H), 2.44–2.48 (m, 2H), 3.77 (s, 3H), 5.33 (s, 1H), 6.81 (d, 2H, $J$ = 8 Hz), 7.02 (d, 2H, $J$ = 8 Hz); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 21.7, 29.1, 36.2, 55.3, 98.0, 114.2, 125.9, 130.9, 157.3, 164.4, 197.8; Anal. Calcd for $C_{13}H_{15}NO_2$ (217): C, 71.87; H, 6.96; N, 6.45. Found: C, 71.84; H, 7.02; N, 6.47.

*4-(4-Chloro-phenylamino)-pent-3-en-2-one (**3m**)*: The above general procedure, starting from acetyl acetone (0.3 g, 3 mmol) and 4-chloro aniline (0.45 g, 3.6 mmol) gave compound **3m**: (white solid); mp 61–63 °C; IR ($cm^{-1}$) 3335, 3017, 1615, 1570, 1508, 1282, 1215, 1024, 758, 668; $^1H$ NMR ($CDCl_3$, 200 MHz) $\delta$ 2.01 (s, 3H), 2.13 (s, 3H), 5.24 (s, 1H,), 7.08 (d, 2H, $J$ = 8Hz), 7.33 (d, 2H, $J$ = 8Hz), 12.46 (brs, 1H); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 19.4, 29.0, 98.1, 116.5, 124.6, 126.9, 135.5, 159.3, 196.6; Anal. Calcd for $C_{11}H_{12}ClNO$ (209): C, 63.01; H, 5.77; Cl, 16.91; N, 6.68. Found: C, 63.03; H, 5.72; Cl, 16.87; N, 6.62.

*3-(4-Chloro-phenylamino)-but-2-enoic acid ethyl ester (**3n**)*: The above general procedure, starting from ethyl acetoacetate (0.3 g, 2.30 mmol) and 4-chloro aniline (0.35 g, 2.76 mmol) gave compound **3n**: (yellow oil); IR ($cm^{-1}$) 3374, 3262, 3019, 2983, 1651, 1621, 1504, 1277, 1249, 1170, 1058, 754, 667; $^1H$ NMR ($CDCl_3$, 200 MHz) $\delta$ 1.28 (t, 3H, $J$ = 7.2 Hz), 1.95 (s, 3H), 4.16 (q, 2H, $J$ = 7.2 Hz), 4.72 (s, 1H), 7.10–7.34 (m, 4H), 10.28 (brs.1H); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 14.4, 19.9, 58.8, 87.2, 116.5, 124.3, 126.7, 136.1, 158.1, 170.2; Anal. Calcd for $C_{12}H_{14}ClNO_2$ (239): C, 60.13; H, 5.89; Cl, 14.79; N, 5.84. Found: C, 60.17; H, 5.84; Cl, 14.81; N, 5.79.

*3-(4-Chloro-phenylamino)-cyclohex-2-enone (**3o**)* [20]: The above general procedure, starting from 1,3-cyclohexanedione (0.3 g, 2.67 mmol) and 4-chloro aniline (0.41 g, 3.21 mmol) gave compound **3o**: (grayish solid); mp 188–190 °C; IR ($cm^{-1}$) 3416, 3253, 1603, 1575, 1522, 1251, 1215, 1014, 758, 668; $^1H$ NMR ($CDCl_3$, 200 MHz) 1.92–1.96 (m, 2H), 2.25–2.27 (m, 2H), 2.43–2.49 (m, 2H), $\delta$ 5.39 (s, 1H), 6.99 (d, 2H, $J$ = 8.2 Hz), 7.19 (d, 2H, $J$ = 8.2 Hz); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 21.5, 29.0, 36.1, 98.6, 125.0, 129.0, 130.4, 136.8, 164.1, 198.3; Anal. Calcd for $C_{12}H_{12}ClNO$ (221): C, 65.02; H, 5.46; Cl, 15.99; N, 6.32. Found: C, 65.00; H, 5.52; Cl, 15.94; N, 6.38.

*4-(4-Isopropyl-phenylamino)-pent-3-en-2-one (**3p**)*: The above general procedure, starting from acetyl acetone (0.3 g, 3 mmol) and 4-isopropyl aniline (0.48 g, 3.6 mmol) gave compound **3p**: (yellow oil); IR ($cm^{-1}$) 3338, 2960, 2928, 1617, 1568, 1518, 1355, 1277, 1186, 1017, 750; $^1H$ NMR ($CDCl_3$, 200 MHz) $\delta$ 1.30 (d, 6H, $J$ = 7.2 Hz), 1.97 (s, 3H,), 2.09 (s, 3H,), 2.90 (sept, 1H, $J$ = 6.9 Hz), 5.17 (s, 1H), 7.03 (d, 2H, $J$ = 8 Hz), 7.19 (d, 2H, $J$ = 8 Hz), 12.45 (brs, 1H); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 19.7, 23.8, 28.9, 33.5, 97.1, 124.7, 126.9, 136.2, 146.3, 160.3, 195.7; Anal. Calcd for $C_{14}H_{19}NO$ (217): C, 77.38; H, 8.81; N, 6.45. Found: C, 77.35; H, 8.78; N, 6.44.

*3-(4-Isopropyl-phenyl amino)-but-2-enoic acid ethyl ester (**3q**)*: The above general procedure, starting from ethyl acetoacetate (0.3 g, 2.30 mmol) and 4-isopropyl aniline (0.37 g, 2.76 mmol) gave compound **3q**: (yellow oil); IR ($cm^{-1}$) 3260, 2961, 2931, 1654, 1619, 1518, 1360, 1331, 1272, 1162, 1058, 758, 668, 544; $^1H$ NMR ($CDCl_3$, 200 MHz) $\delta$ 1.28 (t, 3H, $J$ = 7.2 Hz), 1.39 (d, 6H, $J$ = 7.2 Hz), 1.97 (s, 3H), 2.92 (sept, 1H, $J$ = 6.9 Hz) 4.20 (q, 2H, $J$ = 7.2 Hz), 5.10 (s, 1H,), 7.01 (d, 2H, $J$ = 8 Hz), 7.17 (d, 2H, $J$ = 8 Hz), 10.28 (brs, 1H); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 14.4, 19.9, 23.7, 33.3, 58.3, 85.4, 124.4, 126.7, 136.9, 145.5, 158.9, 170.1; Anal. Calcd for $C_{15}H_{21}NO_2$ (247): C, 72.84; H, 8.56; N, 5.66. Found: C, 72.87; H, 8.58; N, 5.70.

*3-(4-Isopropyl-phenyl amino)-cyclohex-2-enone (**3r**)*: The above general procedure, starting from 1,3 cyclohexane dione (0.3 g, 2.67 mmol) and 4-isopropyl aniline (0.43 g, 3.21 mmol) gave compound **3r**: (yellow solid); mp 153–155 °C; IR ($cm^{-1}$) 3241, 3178, 3098, 2958, 1602, 1537, 1417, 1361, 1249, 1185, 817, 754; $^1H$ NMR ($CDCl_3$, 200 MHz) $\delta$ 1.38 (d, 6H, $J$ = 7.2 Hz), 1.97–2.03 (m, 2H), 2.30–2.36 (m, 2H), 2.47–2.53 (m, 2H), 2.90 (sept, 1H, $J$ = 6.9 Hz), 5.50 (s, 1H), 7.06 (d, 2H, $J$ = 8 Hz), 7.18 (d, 2H, $J$ = 8 Hz); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 21.7, 23.7, 29.2, 33.4, 36.2, 98.3, 124.0, 126.8, 135.9, 146.0, 164.1, 198.0; Anal.

Calcd for $C_{15}H_{19}NO$ (229): C, 78.56; H, 8.35; N, 6.11. Found: C, 78.61; H, 8.29; N, 6.06.

*4-Benzylamino-pent-3-en-2-one (**3s**)* [15]: The above general procedure, starting from acetyl acetone (0.3 g, 3 mmol) and benzylamine (0.34 g, 3.20 mmol) gave compound **3s**: (yellow viscous oil); IR ($cm^{-1}$) 3417, 3030, 1607, 1573, 1356, 1295, 1027, 736, 697; $^1H$ NMR ($CDCl_3$, 200 MHz) $\delta$ 1.90 (s, 3H), 2.03 (s, 3H), 4.45 (d, 2H, $J = 5.5$ Hz), 5.04 (s, 1H), 7.23–7.37 (m, 5H), 11.17 (brs. 1H); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 19.0, 27.4, 46.0, 96.3, 125.7, 127.0, 129.2, 137.4, 162.4, 194.5; Anal. Calcd For $C_{12}H_{15}NO$ (189): C, 76.16; H, 7.99; N, 7.40. Found: C, 76.15; H, 7.90; N, 7.32.

*3-Benylamino-but-2-enoic acid ethyl ester (**3t**)* [15]: The above general procedure, starting from ethyl acetoacetate (0.3 g, 2.30 mmol) and benzylamine (0.29 g, 2.76 mmol) gave compound **3t**: (colorless liquid); IR ($cm^{-1}$) 3291, 3030, 2978, 1651, 1607, 1453, 1272, 1235, 1171, 1059, 784, 697; $^1H$ NMR ($CDCl_3$, 200 MHz) $\delta$ 1.26 (t, 3H, $J = 7.2$ Hz), 1.92 (s, 3H), 4.13 (q, 2H, $J = 7.2$ Hz), 4.41 (d, 2H, $J = 5.5$ Hz), 4.51 (s, 1H), 7.32–7.45 (m, 5H), 8.97 (brs, 1H); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 14.3, 19.0, 46.5, 58.1, 82.9, 126.4, 127.0, 128.5, 138.5, 161.5, 170.3; Anal. Calcd for $C_{13}H_{17}NO_2$ (219): C, 71.21; H, 7.81; N, 6.39. Found: C, 71.27; H, 7.79; N, 6.41.

*3-Benzylamino-cyclohex-2-enone (**3u**)* [20]: The above general procedure, starting from 1,3-cyclohexanedione (0.3 g, 2.67 mmol) and benzylamine (0.30 g, 3.21 mmol) gave compound **3u**: (yellow solid); mp 123–125 °C; IR ($cm^{-1}$) 3426, 3261, 3018, 2952, 1577, 1525, 1260, 1216, 757, 667; $^1H$ NMR ($CDCl_3$, 200 MHz) $\delta$ 1.91–2.01 (m, 2H), 2.24–2.30 (m, 2H), 2.36–2.42 (m, 2H), 4.21 (d, 2H, $J = 5.5$ Hz), 5.13 (s, 1H), 5.59 (brs, 1H), 7.27–7.32 (m, 5H); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 21.5, 28.7, 35.9, 46.3, 96.0, 126.9, 128.1, 136.7, 165.4, 196.7; Anal. Calcd For $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.56; H, 6.90; N, 6.91.

*3-(4-Isopropyl-phenylamino)-1-phenyl-but-2-en-1-one (**3v**)*: The above general procedure, starting from benzoylacetone (0.3 g, 1.85 mmol) and 4-isopropyl aniline (0.3 g, 2.21 mmol) gave compound **3v**: (yellow solid); mp 76–78 °C; IR ($cm^{-1}$) 3410, 3054, 2958, 1588, 1545, 1319, 852, 744, 686; $^1H$ NMR ($CDCl_3$, 200 MHz) $\delta$ 1.39 (d, 6H, $J = 7.2$ Hz), 2.26 (S, 3H), 3.05 (sept, 1H, $J = 6.9$ Hz), 6.00 (s, 1H), 7.24 (d, 2H, $J = 8.2$ Hz), 7.35 (d, 2H, $J = 8.2$ Hz), 7.55–7.57 (m, 3H), 8.05 (dd, 2H, $J = 2.2$ Hz, 8.2 Hz), 13.18 (brs, 1H); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 20.1, 23.7, 33.4, 93.8, 124.6, 126.9, 128.0, 130.5, 136.2, 140.0, 146.4, 162.3, 188.3; Anal. Calcd for $C_{19}H_{21}NO$ (279): C, 81.68; H, 7.58; N, 5.01. Found: C, 81.69; H, 7.54; N, 5.06.

## 4. Conclusion

A remarkably rapid, efficient and regioselective synthesis of β-amino-α,β unsaturated esters and ketones has been achieved at ambient temperature using for the first time silica chloride as solid catalyst and an ionic liquid, viz. 1-*n*-butylimidazolium tetrafluoroborate, respectively. The reactions proceeded to completion in just 5–30 min giving rise to the β-enaminones in excellent isolated yields. For the reactions involving the IL, the IL acted both as a recyclable reaction medium as well as promoter and did not require any additional catalyst. The enamination in both the cases takes place regioselectively at the acetyl carbonyl carbon in the case of β-keto esters and benzoyl acetone, respectively. The methodologies described have been proven to be a superior alternative to existing methods of enamination of cyclic 1,3-diketones, which give rise to pharmaceutically important anticonvulsant compounds. The short reaction times, recyclability of solid catalyst as well as the IL and easy work up procedures make these methodologies generally environment friendly and amenable for scale up.

## Acknowledgments

A.R.G. thanks CSIR, New Delhi for the award of a Senior Research Fellowship. The authors also acknowledge financial assistance from the Department Science and Technology (DST), New Delhi, vide Project No. (SR/S5/OC-23/2002).

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molcata.2005.09.021.

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