[Bmim]BF₄ Ionic Liquid: A Novel and Recyclable Reaction Media for the Synthesis of Homoallylic Amines

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Abstract: The imines derived in situ from aldehydes and amines undergo smoothly nucleophilic addition with allyltinylstannane in 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF₄) ionic liquid to afford the corresponding homoallylic amines in high yields with high selectivity. The recovered ionic liquid can be recycled in four to five runs with gradual decrease in activity.

Key words: allylation, ionic liquids, imines, homoallylic amines

The stereoselective addition of allylmetal reagents to aldehydes and imines is one of the most important carbon–carbon bond formation reactions in organic synthesis.¹ There is significant current interest in amine synthesis, because of the growing importance of chiral amines as bases in asymmetric syntheses² and as components of P–N ligand architectures.³ Generally, homoallylic amines are prepared either by the addition of organometallic reagents to imines⁴ or by the nucleophilic addition of allylsilane or allyltin or allyltin-boron or allylgermane reagents to imines in the presence of acid catalysts.⁵ Lewis acids such as TiCl₄, BF₃·OEt₂, and PdCl₂(Ph₃P)₂ or PtCl₂(Ph₃P)₂ have been employed for this transformation.⁶ However, many of these reagents are expensive, hygroscopic and difficult to handle especially on large scale. Furthermore, most of these reagents are deactivated or decomposed during aqueous workup and hence they cannot be recovered and recycled in subsequent runs. In order to circumvent some of these problems recently one-pot procedures have also been developed for this transformation.⁷ The use of solvents like water, supercritical fluids and ionic liquids have received a lot of attention in recent times in the area of green synthesis. In this respect, ionic liquids (Figure 1) have emerged as a set of ‘green’ solvents with unique properties such as tunable polarity, high thermal stability, and immiscibility with a number of organic solvents, negligible vapor pressure and recyclability.⁸ As a result of their green credentials and potential to enhance reaction rates and selectivities, ionic liquids are finding increasing applications in organic synthesis. Their non-volatile character and thermal stability makes them potentially attractive alternatives to environmentally unfavorable organic solvents, notably chlorinated hydrocarbons. They are particularly promising as solvents for the immobilization of transition metal based catalysts, Lewis acids and enzymes.⁹

Because of the distinct advantages of room temperature ionic liquids as environmentally benign reaction media for catalytic processes, much attention has been currently focused on organic reactions promoted by ionic liquids.¹⁰ In view of the emerging importance of the imidazolium based ionic liquids as novel reaction media, we wish to explore the use of ionic liquids as promoters and recyclable solvent system for the synthesis of homoallylic amines under mild conditions (Scheme 1).

Scheme 1

The treatment of benzaldehyde and aniline with allyltinylstannane in 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF₄) or 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim]PF₆) (Figure 1) at room temperature afforded the corresponding homoallylic amine in 92% yield. In a similar fashion, various imines (formed in situ from aldehydes and amines in ionic liquid) reacted smoothly with allyltinylstannane to afford the corresponding homoallylic amines in excellent yields. The reactions proceeded smoothly at room temperature and were complete within 4.5–8.5 hours (Table 1). Both electron-rich and electron-deficient aldehydes produced the homoallylic amines in excellent yields (80–93%) with high selectivity, whereas ketones did not yield any product under these reaction conditions. This method is equally effective even with aldehydes bearing electron-withdrawing substituents in the aromatic ring (entry m). Furthermore, acid sensitive aldehydes such as fururaldehyde and cinnamaldehyde worked well without any decomposition or polymerization under these reaction conditions (entries g, k and l). Even sterically hindered aldehydes such as 1-naphthaldehyde and 2-hydroxy benzal-

Figure 1 Structures of [Bmim]PF₆ and [Bmim]BF₄ ionic liquids
dehyde also gave the corresponding homoallylic amines in high yields (entries c, d, e, h, and o). In all cases, no homoallylic alcohol (an adduct between the aldehyde and allyltributylstannane) was obtained under these reaction conditions. This is due to the rapid formation of imines from aldehydes and amines in ionic liquids. In this reaction, the efficiency of ionic liquid was strongly influenced by the nature of the anion. The reactivity of hydrophilic [bmim]BF$_4$ and hydrophobic [bmim]PF$_6$ ionic liquids was studied for this conversion. Among these ionic liquids, [bmim]BF$_4$ was found to be superior in terms of yields and reaction rates. Since the products were weakly soluble in the ionic phase, they were easily separated by simple extraction with ether. The rest of the ionic liquid was thoroughly washed with diethyl ether and recycled in subsequent reactions. Second and third reactions using recovered ionic liquid afforded similar yields to those obtained in the first run. In the fourth and fifth runs, the yields were gradually decreased. For example, benzaldehyde, aniline and allyltributylstannane in [bmim]BF$_4$ afforded 92%, 90%, 89%, 85%, and 79% over five cycles. However, the activity of ionic liquid was consistent in runs and no decrease in yield was obtained when the recycled ionic liquid was activated at 80 °C under vacuum in each cycle. Furthermore, the products obtained were of the same purity as in the first run. However, in the absence of ionic liquid, the reaction did not proceed in polar organic solvents such as acetonitrile and methanol even after a long reaction time. In further reactions, the efficiency of various quaternary ammonium salts was studied. The three-component coupling reaction was not successful in other molten salts such as tetrabutylammonium chloride (Bu$_4$NCl) or 1-butyl-3-methylimidazolium chloride ([bmim][Cl]). The simple experimental and product isolation procedures combined with ease of recovery and reuse of this novel reaction media is expected to contribute to the development of clean process for the synthesis of homoallylic amines. The scope and generality of this process is illustrated with respect to various aldehydes and amines and the results are presented in Table 1. The use of [bmim]BF$_4$ ionic liquid as reaction media for this transformation avoids the use of additives or acidic promoters and also eliminates aqueous workup to isolate the products.

In summary, this paper demonstrates the successful use of ionic liquids as novel and convenient reaction media for three-component coupling reactions of aldehydes, amines

| Entry | Aldehyde RCHO | Amine R’NH$_2$ | Product $^a$ | Time (h) | Yield (%) $^b$
|-------|--------------|--------------|-------------|---------|-------------
| a     | R = Ph       | R’ = Ph      | 3a          | 4.5     | 92          |
| b     | R = 4-ClC$_6$H$_4$ | R’ = Ph      | 3b          | 5.0     | 90          |
| c     | R = α-naphthyl | R’ = piperonyl | 3c          | 6.5     | 85          |
| d     | R = α-naphthyl | R’ = Ph      | 3d          | 5.5     | 89          |
| e     | R = α-naphthyl | R’ = 4-BrC$_6$H$_4$ | 3e          | 6.0     | 83          |
| f     | R = Ph       | R’ = 4-FC$_6$H$_4$ | 3f          | 4.5     | 92          |
| g     | R = PhCH=CH  | R’ = Ph      | 3g          | 5.0     | 85          |
| h     | R = 2-HOC$_6$H$_4$ | R’ = 4-MeC$_6$H$_4$ | 3h          | 6.5     | 87          |
| i     | R = 4-MeC$_6$H$_4$ | R’ = 4-BrC$_6$H$_4$ | 3i          | 5.5     | 90          |
| j     | R = 4-MeC$_6$H$_4$ | R’ = 4-FC$_6$H$_4$ | 3j          | 5.5     | 92          |
| k     | R = PhCH=CH  | R’ = 4-FC$_6$H$_4$ | 3k          | 5.0     | 84          |
| l     | R = 4-NO$_2$C$_6$H$_4$ | R’ = Ph      | 3l          | 4.5     | 90          |
| m     | R = 4-NO$_2$C$_6$H$_4$ | R’ = Ph      | 3m          | 8.5     | 80          |
| n     | R = 4-MeOC$_6$H$_4$ | R’ = Ph      | 3n          | 5.5     | 91          |
| o     | R = α-naphthyl | R’ = 4-FC$_6$H$_4$ | 3o          | 6.5     | 82          |
| p     | R = 4-MeC$_6$H$_4$ | R’ = Ph      | 3p          | 4.5     | 93          |

$^a$ All products were characterized by $^1$H NMR, $^{13}$C NMR, IR and mass spectroscopy.

$^b$ Isolated and unoptimized yields.
and allyltributylstannane to produce homoallylic amines under mild conditions. This method is very useful for the synthesis of homoallylic amines especially from acid sensitive aldehydes. The notable features of this procedure are mild reaction conditions, simplicity in operation, improved yields and reaction rates, cleaner reaction profiles and recyclability of ionic liquids making this method convenient process for the synthesis of homoallylic amines.

IR spectra were recorded on a Perkin-Elmer FT-IR 240-c spectrophotometer using KBr optics. 1 H NMR spectra were recorded on a Finning MAT 1020 mass spectrometer operating at 70 eV. 1-Butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF 4 ) and 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim]PF 6 ) ionic liquids were prepared according to the procedures reported in the literature. 11

**Homoallylic Amines 3a-p; General Procedure**

A mixture of aldehyde 1 (2 mmol), amine 2 (5 mmol) and allyltributylstannane (2 mmol) in [bmim]BF 4 (2.0 mL) was stirred at r.t. for the appropriate time (Table 1). After completion of the reaction, as indicated by TLC, the reaction mixture was extracted with Et 2 O and the resulting product was directly charged onto a small silica column. /c180

**Aromatic amines via reductive alkylation of aromatic aldehydes with allyltributylstannane**

A mixture of aldehyde 2 (2 mmol), amine 3 (5 mmol) and allyltributylstannane (2 mmol) in [bmim]BF 4 (2.0 mL) was stirred at r.t. for the appropriate time (Table 1). After completion of the reaction, as indicated by TLC, the reaction mixture was extracted with Et 2 O and the resulting product was directly charged onto a small silica column. /c180


**1 H NMR (CDCl 3 ):**

1 H NMR (CDCl 3 ) of the reaction products showed the presence of the characteristic 2-H, 3-H, and 4-H protons of the homoallylic amines. The spectra were recorded using TMS as internal standard.

**IR (neat):** The IR spectra of the reaction products were recorded on a Perkin-Elmer FT-IR 2000 spectrometer using KBr optics. The IR bands were assigned based on the literature.

**13 C NMR (CDCl 3 ):**

The 13 C NMR spectra of the reaction products were recorded on a Gemini-200 spectrometer in CDCl 3 using TMS as internal standard. The spectra were analyzed to determine the structure of the reaction products.

**EI-MS:** The mass spectra were recorded on a Finning MAT 1020 mass spectrometer using KBr optics. The mass spectra were analyzed to determine the molecular weight and the fragmentation pattern of the reaction products.
EI-MS: m/z = 318 (M+ + 2), 316 (M+), 276, 274, 182, 155, 141, 105, 91.

4-Fluoro-N-[4-(methyl)phenyl]-but-3-enylamine (3j)
Liquid.
IR (neat): 3411, 3034 2981, 2922, 1701, 1627, 1518, 996, 921, 818, 787, 704 cm⁻¹.
1H NMR (CDCl₃): δ = 7.15 (d, 2 H, J = 8.0 Hz), 7.02 (2 H, J = 8.0 Hz), 6.60–6.65 (m, 2 H), 6.30–6.35 (m, 2 H), 5.60–5.79 (m, 1 H), 5.05–5.17 (m, 2 H), 4.20 (dd, 1 H, J = 7.9 Hz), 7.90 (d, 1 H, J = 8.0 Hz), 7.65 (d, 1 H, J = 8.0 Hz), 7.40–7.58 (m, 3 H), 7.34–7.40 (m, 1 H), 6.65–6.78 (m, 2 H), 6.30–6.40 (m, 2 H), 5.79–5.85 (m, 1 H), 5.20–5.25 (m, 2 H), 5.10 (t, 1 H, J = 5.6 Hz), 4.15 (br s, 1 H, NH), 2.80–2.90 (m, 1 H), 2.50–2.60 (m, 1 H).
EI-MS: m/z = 273 (M+), 232, 165, 127, 104, 77.

N-[4-(methyl)phenyl]-but-3-enylaniline (3p)
Liquid.
IR (neat): 3415, 3077, 2930, 1640, 1600, 993, 915, 755 cm⁻¹.
1H NMR (CDCl₃): δ = 7.25 (d, 2 H, J = 8.1 Hz), 7.0–7.18 (m, 4 H), 6.60 (t, 1 H, J = 7.9 Hz), 6.45 (d, 2 H, J = 8.1 Hz), 5.70–5.85 (m, 1 H), 5.10–5.25 (m, 2 H), 4.38 (t, 1 H, J = 6.5 Hz), 4.05 (br s, 1 H, NH), 2.50–2.65 (m, 2 H), 2.30 (s, 3 H).
EI-MS: m/z = 237 (M+), 198, 118, 104, 91, 77, 65, 51.

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References