Montmorillonite Clay-Catalyzed Three-Component Coupling Reactions: A Facile Synthesis of Homoallylic Amines

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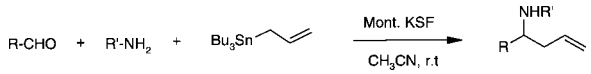
Abstract: Homoallylic amines are synthesized by the three-component coupling reaction of aldehydes, amines and allyltributylstannane using a heterogeneous solid acid catalyst, montmorillonite KSF, under mild reaction conditions to afford the corresponding homoallylic amines in excellent yields.

Keywords: allylstannane; homoallylic amines; imines; solid acids

There is considerable current interest in amine synthesis, because of the growing importance of chiral amines as bases in asymmetric syntheses[1a] and as components of P-N ligand architectures.[1b] The stereoselective addition of allylmetal reagents to aldehydes and imines is one of the most important carbon-carbon bond forming reactions in organic synthesis.[2] Particularly, acid-catalyzed carbon-carbon bonding forming reactions are of great importance in organic synthesis because of their high selectivity and mild reaction conditions.[3] Generally, homoallylic amines are prepared either by addition of organometallic reagents to imines[4] or by nucleophilic addition of allylsilane or allyltin or allylborane or allylgermane reagents to imines in the presence of acid catalysts.[5] Lewis acids such as $TiCl_4$, $BF_3 \cdot OEt_2$, and $PdCl_2(PPh_3)_2$ or $PtCl_2(PPh_3)_2$ have been employed for this transformation.[5,6] However, many of these reagents are expensive, hygroscopic and difficult to handle especially on a large scale. Furthermore, many of these catalysts are deactivated or some times decomposed by amines and water that exist during imine formation. In order to circumvent some of these problems recently one-pot procedures have been developed for this transformation.[7,8] In fact, these procedures do not require the isolation of unstable imines prior to the reactions; metal triflates are strongly acidic and highly expensive. In recent years, the use of solid acid catalysts such as clays and zeolites has received considerable attention in different areas of organic synthesis due to their environmental compatibility, recyclability, greater selectivity, non-corrosiveness, simplicity in operation, low cost and ease of separation.[9] Especially, clay catalysts make the reaction process convenient, economic and act as Brønsted as well as Lewis acids in their natural or ion-exchanged forms, enabling them to function as efficient catalysts for various transformations. In addition, KSF clay has also been employed as an efficient reagent for the preparation of imines.[10]

In view of the emerging importance of the use of solid acids as environmentally friendly and reusable catalysts,[11] we herein describe a simple and efficient protocol for the synthesis of homoallylic amines using a heterogeneous solid acid catalyst, montmorillonite KSF clay, under mild reaction conditions (Scheme 1).

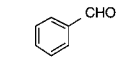
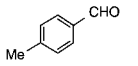
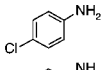
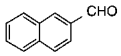
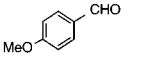
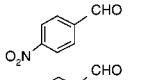
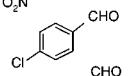
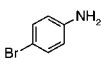
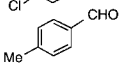
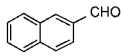
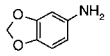
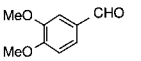
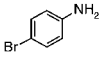
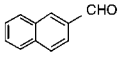
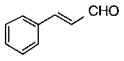
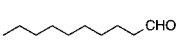
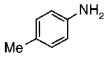
The reaction of benzaldehyde, aniline and allyltributylstannane in the presence of KSF clay in acetonitrile at ambient temperature resulted in the formation of the corresponding homoallylic amine in 90% yield. Similarly, various imines (formed *in situ* from aldehydes and amines on the surface of KSF clay) reacted smoothly with allylstannane to afford the corresponding homoallylic amines in high yields. The reactions proceeded smoothly at ambient temperature and were completed within 3.0–5.5 h. Both aromatic and aliphatic aldehydes afforded excellent yields of products (73–90%) in a short period whereas ketones did not yield any product under these reaction conditions. This method is equally effective with aldehydes bearing electron-withdrawing substituents in the aromatic ring (entry e). Furthermore, acid-sensitive aldehydes such as furfuraldehyde and cinnamaldehyde worked well without any decomposition or polymerization under the present reaction conditions. Enolizable aldehydes such as cyclohexanecarboxaldehyde and octanal also produced the corresponding homoallylic amines in good yields. In all cases, no homoallylic alcohol (an adduct between the aldehyde and allyltributylstannane) was obtained under these reaction conditions. This is because of the rapid formation and activation of imines in the presence of montmorillonite. All the products were characterized



Scheme 1.

  1615-4150/02/34409-938–940 $ 17.50-.50/0

Table 1. Montmorillonite KSF-catalyzed synthesis of homoallylic amines.[a]

Entry	Aldehyde	Amine	Time [h]	Yield [%][b]
a			4.0	90
b			3.5	85
c			5.5	82
d			4.0	87
e			3.5	80
f			4.5	90
g			5.0	85
h			5.5	80
i			4.0	87
j			5.0	90
l			4.0	73
m			3.0	85
n			3.5	88
o			4.0	90
P			5.0	82

[a] All products characterized by ^{1}H NMR, IR and MS.
[b] Isolated, not optimized yields.

by ^{1}H NMR, IR, and mass spectroscopic data. There are several advantages in the use of clay as catalyst for this transformation, which include mild reaction conditions, cleaner reaction profiles, high yields of products, greater selectivity and reusability of the catalyst. The scope and generality of this process is illustrated with respect to various amines and aldehydes including aromatic, α,β-unsaturated, heterocyclic, and aliphatic aldehydes and the results are presented in Table 1. Finally, the clay was recovered by filtration, washed with methanol and recycled for use in subsequent reactions (after activation at 120 °C for 4–5 hours) with a gradual decrease in activity; for example, the reaction of benzaldehyde, aniline and allyltributylstannane under the present reaction conditions afforded 90%, 85% and 81% yields over three cycles. These results clearly show the advantage of our method over protic or Lewis acid-catalyzed procedures.

In summary, this paper describes a simple and convenient method for the synthesis of homoallylic amines involving three-component coupling reactions of aldehydes, amines and allyltributylstannane using montmorillonite clay as solid acid catalyst. The use of an inexpensive and reusable montmorillonite KSF makes this method a useful, convenient, economic and attractive alternative for the synthesis of homoallylic amines of synthetic importance.

Experimental Section

General Remarks

IR spectra were recorded on a Perkin-Elmer FT-IR 240-c spectrophotometer using KBr optics. ^{1}H NMR spectra were recorded on a Gemini-200 spectrometer in $CDCl_3$ using TMS as internal standard. Mass spectra were recorded on a Finnigan MAT 1020 mass spectrometer operating at 70 eV. KSF clay was purchased from Aldrich Co.

General Procedure

A mixture of aldehyde (5 mmol), amine (5 mmol) and allyltributylstannane (5 mmol) as well as montmorillonite KSF clay (1.0 g) in acetonitrile (10 mL) was stirred at ambient temperature for an appropriate time (Table 1). After completion of the reaction as indicated by TLC, the reaction mixture was filtered and washed with ethyl acetate (2 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated under vacuum and purified by column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate/hexane, 1: 9) to afford the pure homoallylamine. The solid clay portion was washed with methanol, dried at 120 °C under reduced pressure and reused in subsequent reactions.

Spectroscopic Data for Products

4c: Liquid; IR (KBr): $\nu = 3420, 3082, 2860, 1645, 1602, 1457, 993, 910, 751$ cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 2.50-2.78$ (m, 2H), 4.25 (br s, 1H, NH), 4.38 (t, 1H, $J = 6.4$ Hz), 5.18–5.25 (m, 2H), 5.75–5.90 (m, 1H), 6.50 (d, 2H, $J = 8.0$ Hz), 6.60 (t, 1H, $J = 7.8$ Hz), 7.10 (t, 2H, $J = 7.8$ Hz), 7.50–7.60 (m, 3H), 7.80–8.0 (m, 4H); EI-MS: $m/z = 273$ (M^+), 232, 165, 127, 104, 77, 51.

4g: Liquid; IR (KBr): $\nu = 3415, 3077, 2930, 1640, 1600, 993, 915, 755$ cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 2.30$ (s, 3H), 2.50–2.65 (m, 2H), 4.05 (br s, 1H, NH), 4.38 (t, 1H, $J = 6.5$ Hz), 5.10–5.25 (m, 2H), 5.70–5.85 (m, 1H), 6.45 (d, 2H, $J = 8.1$ Hz), 6.60 (t, 1H, $J = 7.9$ Hz), 7.0–7.18 (m, 4H), 7.25 (d, 2H, $J = 8.1$ Hz); EI-MS: $m/z = 237$ (M^+), 196, 128, 115, 104, 91, 77, 65, 51.

Acknowledgements

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