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Tetrahedron Letters 47 (2006) 5041–5044
Tetrahedron Letters

(Bromodimethyl)sulfonium bromide catalyzed efficient multicomponent one-pot synthesis of homoallylic amines☆

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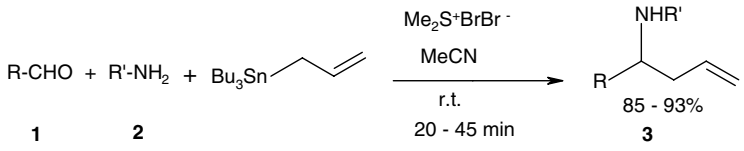
Received 16 February 2006; revised 9 May 2006; accepted 17 May 2006

Abstract—Three-component reactions of aldehydes, amines and allyltributylstannane in the presence of a catalytic amount of (bromodimethyl)sulfonium bromide have been accomplished in short reaction times to afford the corresponding homoallylic amines in excellent yields.

Allylation of imines with allyl organometallics in the presence of a catalyst constitutes an important reaction for the preparation of homoallylic amines.[1] Various Lewis acids such as $TiCl_4$, $BF_3{\cdot}OEt_2$, $PdCl_2(Ph_3P)_2$ or $PtCl_2(Ph_3P)_2$ have been used for this reaction.[2] A one-pot procedure involving the in situ formation of imines (from aldehydes and amines) followed by allylation is more convenient for this transformation.[3] However, some of the methods employed earlier for this one-pot conversion are associated with certain drawbacks such as long reaction times, unsatisfactory yields (especially with aliphatic aldehydes) and requirement of a surfactant or molecular sieve (along with the catalyst) or a nitrogen atmosphere. In continuation of our work[4] on the development of useful synthetic methodologies, we observed that (bromodimethyl)sulfonium bromide[5] catalyzed efficiently the three-component reactions[6] of aldehydes, amines and allyltributylstannane to form the corresponding homoallylic amines at room temperature (Scheme 1).

Imines (formed in situ from aldehydes and amines in the presence of the catalyst) underwent facile reaction with allyltributylstannane to form homoallylic amines in excellent yields.[7] The reaction proceeded at room temperature and the products were formed within 20–45 min (Table 1). Aldehydes containing both electron-donating and electron-withdrawing groups in the aromatic rings were found to undergo the conversion smoothly. An acid sensitive aldehyde such as furfuraldehyde and a sterically hindered aldehyde such as 1-naphthaldehyde also formed the corresponding homoallylic amines. Aliphatic aldehydes underwent the transformation cleanly. Other methods[3d] have been found to be unsuitable for the preparation of homoallylic amines from enolizable aldehydes. The present method is highly selective for aldehydes as ketones did not form products under the reaction conditions. No homoallylic alcohol was isolated from the reaction as the formation of the imines occurred rapidly and the selective activation of imines rather than aldehydes was achieved. The



Scheme 1.

Keywords: Homoallylic amine; (Bromodimethyl)sulfonium bromide; Multicomponent reaction.
☆ Part 87 in the series 'Studies on novel synthetic methodologies.' IICT Communication No. 060515.
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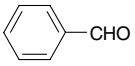
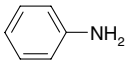
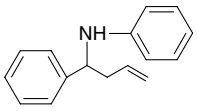
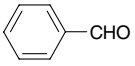
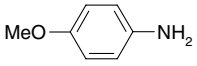
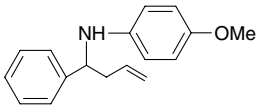
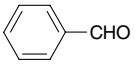
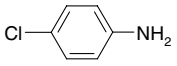
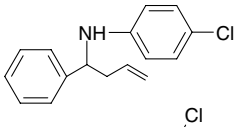
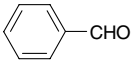
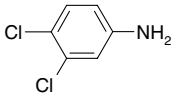
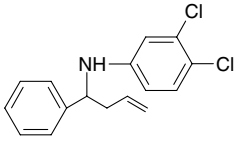
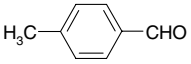
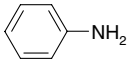
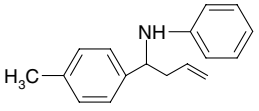
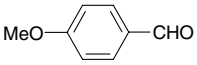
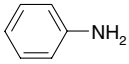
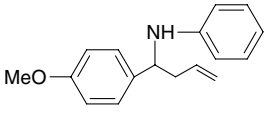
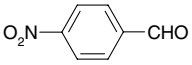
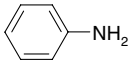
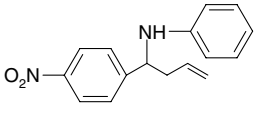
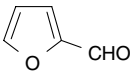
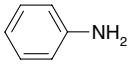
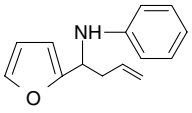
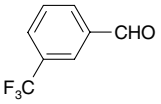
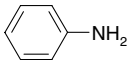
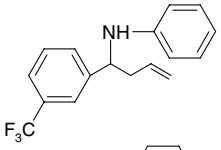
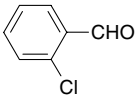
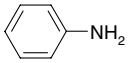
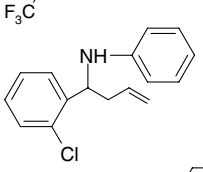
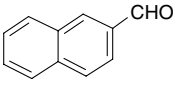
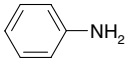
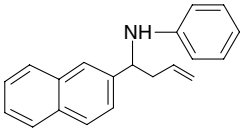
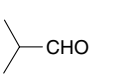
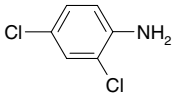
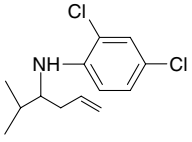
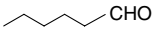
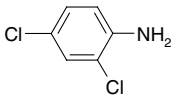
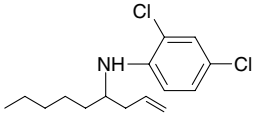
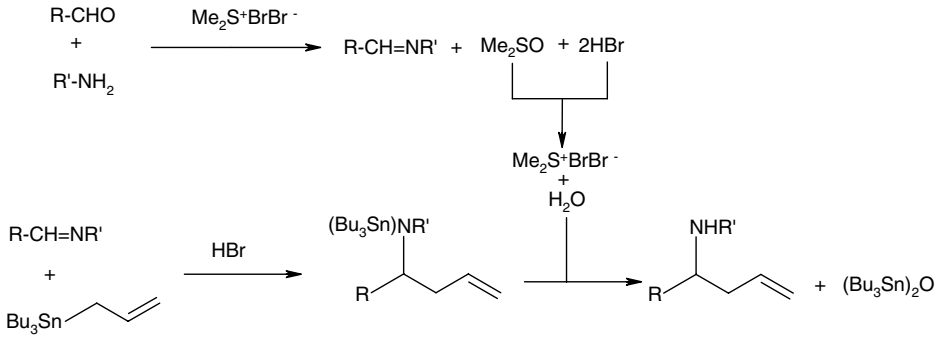
doi:10.1016/j.tetlet.2006.05.101

Table 1. (Bromodimethyl)sulfonium bromide catalyzed synthesis of homoallylic amines[a]

Sl. no	Aldehyde (**1**)	Amine (**2**)	Product (**3**)	Time (min)	Isolated yield (%)
a				20	90
b				25	88
c				30	92
d				30	90
e				20	87
f				20	93
g				45	85
h				25	90
i				20	91
j				25	88
k				30	91
l				40	87
m				45	89

[a] The structures of the prepared homoallylic amines were settled from their spectral (IR, ^{1}H NMR and MS) data.



Scheme 2.

structures of the homoallylic amines were established from their spectral (IR, ^{1}H NMR and MS) data.[7]

The catalyst, (bromodimethyl)sulfonium bromide, is an inexpensive reagent. It catalyzed the present conversion with the rapid formation of imines along with its simultaneous transformation into Me_2SO and HBr (Scheme 2). The nucleophilic addition of allyltributylstannane to these imines in the presence of HBr followed by subsequent hydrolysis afforded homoallylic amines and bis(tributyltin)oxide. The reaction of Me_2SO with HBr regenerated the catalyst, (bromodimethyl)sulfonium bromide, as the formation of bis(tributyltin)oxide consumed water.[5a] In the absence of the catalyst, only a trace amount of product was formed even after 1 h. The catalyst had been used[5] earlier for other synthetic conversions but its uses have not been fully explored. The reaction was also attempted with a catalytic amount of trimethylsulfonium bromide. However, the yields of the homoallylic amines were low, indicating the requirement of a bromodimethyl group of the sulfonium salt in the catalyst to carry out an efficient transformation.

Acknowledgements

The authors thank CSIR and UGC, New Delhi, for financial assistance.

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7. General procedure for the synthesis of homoallylic amines: To a mixture of an aldehyde (1 mmol) and an amine (1 mmol), allyltributylstannane (1.2 mmol) in MeCN (5 mL) and $Me_2S^+BrBr^-$ (10 mol %; prepared by reported method[5b]) were added. The mixture was stirred at room temperature and the reaction was monitored by TLC. After completion, the solvent was evaporated and H_2O (10 mL) was added. The mixture was extracted with EtOAc (3×10 mL) and the extract was concentrated. The residue was purified by column chromatography over silica gel using hexane as an eluent to obtain pure homoallylic amine. The spectral (IR, ^{1}H NMR and MS) data of some representative compounds are given below.
Compound **3c**: IR (KBr): ν_{max} 3414, 1600, 1499, 1312 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.38–7.10 (5H, m), 6.97 (2H, d, $J = 8.0$ Hz), 6.35 (2H, d, $J = 8.0$ Hz), 5.71 (1H, m), 5.25–5.10 (2H, m), 4.32 (1H, br t, $J = 5.5$ Hz), 4.08 (1H, br s), 2.69–2.38 (2H, m); FABMS: m/z 260, 258 ($M^{+\cdot}+1$). Anal. Calcd for $C_{16}H_{16}ClN$: C, 74.56; H, 6.21; N, 5.44%. Found: C, 74.68; H, 6.27; N, 5.32%.
Compound **3f**: IR (KBr): ν_{max} 3418, 1612, 1507, 1220 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.27 (2H, d, $J = 8.0$ Hz), 7.03 (2H, t, $J = 8.0$ Hz), 6.82 (2H, d, $J = 8.0$ Hz), 6.59 (1H, t, $J = 8.0$ Hz), 6.42 (2H, d, $J = 8.0$ Hz), 5.75 (1H, m), 5.21–5.09 (2H, m), 4.31 (1H, td, $J = 5.5$, 1.5 Hz), 4.03 (1H, m), 3.78 (3H, s), 2.61–2.40 (2H, m); FABMS: m/z 254 ($M^{+\cdot}+1$). Anal. Calcd for $C_{17}H_{19}NO$: C, 80.63; H, 7.51; N, 5.53%. Found: C, 80.69; H, 7.45; N, 5.58%.
Compound **3h**: IR (KBr): ν_{max} 3412, 1603, 1505, 1315 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.30 (1H, d, $J = 1.8$ Hz), 7.06 (2H, t, $J = 8.0$ Hz), 6.64 (1H, t, $J = 8.0$ Hz), 6.52 (2H, d, $J = 8.0$ Hz), 6.23 (1H, dd, $J = 2.0$, 1.8 Hz), 6.09 (1H, d, $J = 2.0$ Hz), 5.72 (1H, m), 5.20–5.08 (2H, m), 4.52 (1H, t,

$J = 5.5$ Hz), 3.89 (1H, br s), 2.64 (2H, t, $J = 5.5$ Hz); FABMS: m/z 214 ($M^{+\cdot}+1$). Anal. Calcd for $C_{14}H_{15}NO$: C, 78.87; H, 7.04; N, 6.57%. Found: C, 78.93; H, 7.12; N, 6.64%.

Compound **3l**: IR (KBr): ν_{max} 3417, 1618, 1504, 1353 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.51 (1H, d, $J = 2.0$ Hz), 7.20 (1H, dd, $J = 8.0$, 2.0 Hz), 6.48 (1H, d, $J = 8.0$ Hz), 5.79 (1H, m), 5.15–5.03 (2H, m), 4.24 (1H, d, $J = 8.0$ Hz), 3.24 (1H, m), 2.41–2.15 (2H, m), 1.91 (1H, m), 1.02 (3H, d, $J = 7.0$ Hz), 0.99 (3H, d, $J = 7.0$ Hz); FABMS: m/z 262, 260, 258 ($M^{+\cdot}+1$). Anal. Calcd for $C_{13}H_{17}Cl_2N$: C, 60.46; H, 6.59; N, 5.43%. Found: C, 60.55; H, 6.67; N, 5.38%.