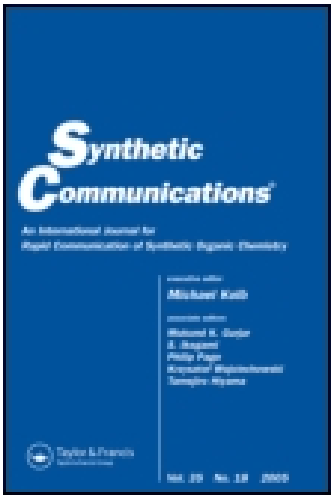

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Three-Component Synthesis of Homoallylic Carbamates

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Three-Component Synthesis of Homoallylic Carbamates

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Abstract: Scandium triflate catalyzed three component condensation of aldehyde, benzyl carbamate, and allyltrimethylsilane to afford the corresponding N-Cbz protected homoallylic amine is described.

Keywords: Homoallylic amine, allyltrimethylsilane, scandium triflate, aldehyde, benzylcarbamate

Nucleophilic addition of allylic organometallic to imine constitutes an important reaction for the preparation of homoallylic amine.[1] The homoallyl amines and derivatives are useful intermediate in natural product synthesis.[2–4] Usually, synthesis of homoallylic amines is achieved by allylation of aldimines using allyl stannane in the presence of a Lewis acid.[5–12] Other allylic metals such as allylgermane,[13,14] allylgalium,[15] and allylsilane[16–20] were used in the presence of Lewis acid catalyst for this synthetic protocol. Most of these methodologies are fraught with limitations such as excess use of catalyst (or co-catalyst), moisture sensitive conditions, and poor substrate selectivity. Although our recent process involving iodine[21] as catalyst was efficient, substrates bearing TBDMS protecting group could not be used.[22] In recent years, scandium trifluoromethane sulfonate is emerging as attractive Lewis acid catalyst for various organic transformations.[23] Herein, we wish to report the synthesis of N-Cbz protected homoallyl amine using scandium triflate as a catalyst (Scheme 1).

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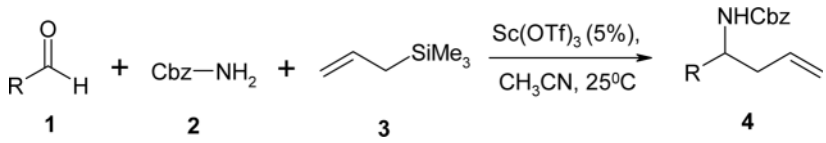


Scheme 1.

The reaction of benzaldehyde, benzylcarbamate, and allyltrimethylsilane in the presence of 5% $Sc(OTf)_3$ in acetonitrile at ambient temperature resulted in the formation of the homoallylic amine in high yield (Table 1). Rate enhancement was not significant when 10 mol% of catalyst was used, while rate of reaction was slow when 2 mol% of catalyst was used. Simultaneous formation of homoallylic alcohol due to addition of allyltrimethylsilane with aldehyde was not observed. Both aromatic and aliphatic aldehydes undergo homoallylation with very good yield irrespective of the nature of the substrate. With 4-nitrobenzaldehyde and isobutaraldehyde, yields were relatively poor.

In conclusion, synthesis of Cbz protected homoallyl amines were achieved using allyltrimethylsilane as allylating agent in presence of $Sc(OTf)_3$ as catalyst.

EXPERIMENTAL

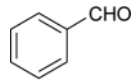
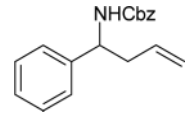
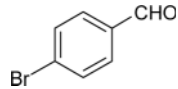
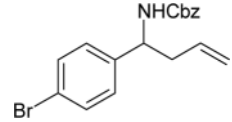
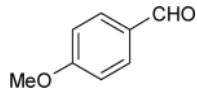
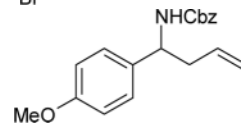
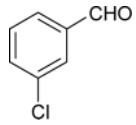
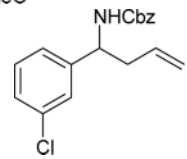
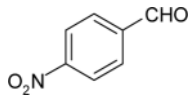
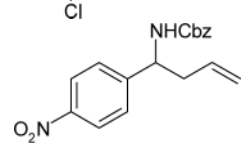
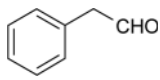
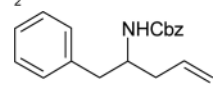
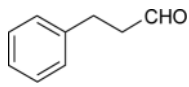
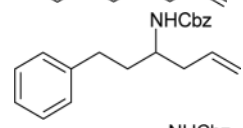
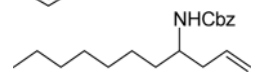
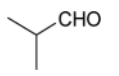
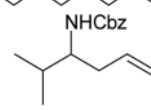
^1H NMR and ^{13}C NMR spectra were recorded in Bruker 400 MHz instrument. Chemical shifts are given in δ units relative to the tetramethylsilane (TMS) signal as an internal reference in $CDCl_3$. Coupling constants (J) are reported in hertz. IR spectra were recorded in Perkin-Elmer Spectrum RXI FT-IR spectrometer. Mass spectra were recorded on a Finnigan mass spectrometer using ionisation energy of 70eV and elemental analysis was carried out in Perkin-Elmer 2400 Series II elemental analyser. Silica gel (230–400 mesh, SRL) was used for column chromatography.

Typical procedure for the synthesis of homoallylic amine: The solution of aldehyde (1 mmol) and $Sc(OTf)_3$ (0.05 mmol) in benzyl carbamate (1 mmol) and allyltrimethylsilane (1 mmol) in CH_3CN (2 mL) was stirred and monitored by TLC. The reaction mixture was diluted with ether, washed with brine, dried (Na_2SO_4), and concentrated. The crude product was purified by flash chromatography on silica gel (230–400 mesh) with petroleum ether–EtOAc (10–20%) as eluent to give the pure product (65–85%).

Spectral Data

N-Benzyloxycarbonyl-1-phenylbut-3-enylamine (4a):[24] White solid; mp. 67–68°C (Lit.[24] mp (for R (+)-enantiomer 68–69°C). IR (Nujol, cm^{-1}):

Table 1. Synthesis of Cbz protected homoallyl amine

Entry	Aldehyde (**1**)	Time (h)	Product[a](**4**)	Yield[b] (%)
a		2		83
b		3		78
c		3.5		83
d		2.5		85
e		5		67
f		3.5		78
g		4		78
h		4.5		80
i		4.5		65

[a]All products are characterized by IR, NMR, mass spectroscopy and elemental analysis.
[b]Isolated yield after chromatographic purification.

3056, 1714, 1423, 1262, 739. ^{1}H NMR (400 MHz, $CDCl_3$): 7.36–7.24 (m, 5H), 7.24–7.13 (m, 5H), 5.67–5.50 (m,1H), 5.10-4.94 (m 5H), 4.81–4.65 (m, 1H), 2.55–2.37 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 155.6, 141.9, 136.4, 133.7, 128.5, 128.4, 128.1, 127.3, 126.2, 118.4, 66.7, 54.4, 41.0. MS (m/z, % rel. intensity): 240 (31), 196 (28), 129 (3), 107 (9), 104 (14), 91 (100), 77 (11), 65 (8).

N-Benzyloxycarbonyl-1-(4-bromophenyl) but-3-enylamine (4b): White solid; mp 87–88°C. IR (Nujol, cm^{-1}): 3055, 1714, 1598, 1418, 1266, 748. ^1H NMR (400 MHz, $CDCl_3$): 7.44 (d, J = 8.1 Hz, 2H), 7.40–7.25 (m, 5H), 7.13 (d, J = 7.7 Hz, 2H), 5.72–5.54 (m, 1H), 5.22–4.96 (m, 5H), 4.82–4.65 (m, 1H), 2.60–2.36 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 155.6, 141.0, 136.2, 133.2, 131.6, 128.5, 128.2, 127.9, 121.1, 118.9, 66.9, 53.9, 40.8. MS (m/z, % rel. intensity): 320 (8), 274 (10), 253 (6) 185 (36), 105 (34), 91 (100), 77 (41), 65 (6). Anal. Calcd for $C_{18}H_{18}BrNO_2$: C, 60.01; H, 5.03; N, 3.89. Found: C, 59.97; H, 5.07; N, 3.84.

N-Benzyloxycarbonyl-1-(4-methoxyphenyl)but-3-enylamine (4c): White solid; mp 70–71°C (Lit.[24] mp (for S-(−)-enantiomer 67–68°C). IR (Nujol, cm^{-1}): 3055, 1719, 1506, 1427, 1266, 739. ^1H NMR (400 MHz, $CDCl_3$): 7.41–7.29 (m, 5H), 7.19 (d, J = 7.8 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 5.77–5.58 (m, 1H), 5.20–5.00 (m, 5H), 4.80–4.70 (m, 1H), 3.79 (s, 3H), 2.60–2.54 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 158.7, 155.6, 136.4, 133.9, 128.4, 128.0, 127.3, 118.2, 113.8, 86.7, 55.2, 53.9, 40.9. MS (m/z, % rel. intensity): 270 (40), 226 (54), 162 (6), 134 (6), 107 (2), 91 (100), 77 (2), 65 (4). Anal. Calcd for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.25; H, 6.82; N, 4.54.

N-Benzyloxycarbonyl-1-(3-chlorophenyl)but-3-enylamine (4d): White solid; mp 62–63°C. IR (Nujol, cm^{-1}): 3055, 1714, 1506, 1266, 739, 702. ^1H NMR (400 MHz, $CDCl_3$): 7.41–7.17 (m, 8H), 7.12 (d, J = 6.3 Hz, 1H), 5.72–5.51 (m, 1H), 5.21–4.93 (m 5H), 4.82–4.68 (m, 1H), 2.59–2.36 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 155.6, 136.2, 134.4, 133.1, 129.8, 128.5, 128.2, 127.5, 126.3, 124.5, 119.0, 66.9, 53.9, 40.9. MS (m/z, % rel. intensity): 274 (12), 230(18), 166 (5),141 (67), 113 (25), 91 (100), 77 (42), 65 (5). Anal. Calcd for $C_{18}H_{18}ClNO_2$: C, 68.46; H, 5.74; N, 4.43. Found: C, 68.42; H, 5.69; N, 4.48.

N-Benzyloxycarbonyl-1-(4-nitrophenyl)but-3-enylamine (4e): White solid; mp 88–89°C. IR (Nujol, cm^{-1}): 3047, 2307, 1719, 1516, 1266, 739. ^1H NMR (400 MHz, $CDCl_3$): 8.1 (d, J = 7.8 Hz, 2H), 7.50–6.92 (m, 7H), 5.65–5.45 (m, 1H), 5.23–4.91 (m, 5H), 4.86–4.72 (m, 1H), 2.56–2.30 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 155.5, 149.6, 147.1, 132.4, 128.5, 128.3, 128.2, 127.0, 123.8, 119.7, 67.7, 54.1, 40.7. MS (m/z, % rel. intensity): 285 (6), 241 (13), 191 (2), 177 (2), 152 (16), 108 (4), 91 (100), 77 (4), 65 (4). Anal. Calcd. for $C_{18}H_{18}N_2O_4$: C, 66.25; H, 5.56; N, 8.58. Found: 66.29; H, 5.51; N, 8.63.

N-Benzyloxycarbonyl-1-benzylbut-3-enylamine (4f): White solid; mp 86–87°C. IR (Nujol, cm^{-1}): 3065, 1701, 1520, 1446, 1252, 1040, 744. ^1H NMR (400 MHz, $CDCl_3$): 7.52–7.07 (m, 10H), 5.88–5.70 (m, 1H), 5.17-5.00 (m, 4H), 4.65 (d, J = 6.8 Hz, 1H), 4.06–3.88 (m, 1H), 2.91–2.68 (m, 2H), 2.36–2.23 (m, 1H), 2.21 = 2.04 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 155.7, 137.8, 136.6, 134.1, 129.4, 128.5 128.4, 128.0, 128.0, 126.4, 118.2, 66.5, 51.6, 40.4, 38.1. MS (m/z, % rel. intensity): 254 (4),

204 (19), 160 (23), 107 (8), 91 (100), 71 b(6), 65 (5). Anal. Calcd for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.19; H, 7.25; N, 4.79.

N-Benzyloxycarbonyl-1-(2-phenylethyl)but-3-enylamine (4g): White solid; mp 50–51°C. IR (Nujol, cm^{-1}): 3065, 1696, 1534, 1451, 1243, 1045, 739, 698. ^1H NMR (400 MHz, $CDCl_3$): 7.32–7.16 (m, 7H), 7.13–7.06 (m, 3H), 5.77–5.60 (m, 1H), 5.10–4.95 (m, 4H), 4.54 (d, J = 7.8 Hz, 1H), 3.79–3.63 (m, 1H), 2.68–2.50 (m, 2H), 2.29–2.09 (m, 2H), 1.83–1.70 (m 1H), 1.70–1.55 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 156.2, 141.7, 136.6, 133.9, 128.5, 128.4, 128.3, 128.1, 125.9, 118.1, 66.6, 50.5, 39.5, 36.5, 32.3. MS (m/z, % rel. intensity): 268 (22), 224 (57), 207 (6), 181 (3), 157 (2), 132 (3), 114 (11), 91 (100), 77 (3), 65 (6). Anal. Calcd for $C_{20}H_{23}NO_2$: C, 77.63; H, 7.49; N, 4.53. Found: C, 77.45; H, 7.45; N, 4.59.

N-Benzyloxycarbonyl-1-heptylbut-3-enylamine (4h): White solid. mp 51–52°C IR (Nujol, cm^{-1}): 3055, 1710, 1511, 1432, 1261, 739. ^1H NMR (400 MHz, $CDCl_3$): 7.43–7.26 (m, 5H), 5.86–5.66 n(m, 1H), 5.19–4.97 (m, 4H), 4.63–4.47 (m,1H), 3.81–3.56 (m, 1H), 2.34–1.99 (m, 2H), 1.5–1.18 (m, 12H), 0.87 (t, J = 6.31 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 156.0, 136.7, 134.3, 128.5, 128.0, 117.8, 66.5, 50.7, 39.4, 34.6, 31.8, 29.4, 29.2, 25.8, 22.6, 14.0. MS (m/z, % rel. intensity): 262 (9), 218 (43), 197 (94), 154 (26), 129 (16), 103 (23), 91 (100), 86 (37), 69 (75), 55 (39), 43 (80). Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.21; H, 9.63; N, 4.62. Found: C, 75.27; H, 9.55; N, 4.68.

N-Benzyloxycarbonyl-1-isopropylbut-3-enylamine (4i):[24] Colourless oil. IR (Nujol, cm^{-1}): 3074, 1696, 1534, 1248, 739. ^1H NMR (400 MHz, $CDCl_3$): 7.41–7.27 (m, 5H), 5.84–5.65 (m, 1H), 5.19–4.98 (m, 4H), 4.67–4.52 (m, 1H), 3.66–3.48 (m, 1H), 2.33–2.19 (m, 1H), 2.17–2.04 (m, 1H), 1.80–1.69 (m, 1H), 0.92 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 156.3, 136.7, 134.7, 128.5, 128.3, 128.0, 117.4, 66.5, 55.7, 36.8, 31.4, 19.2, 17.7. MS (m/z, % rel. intensity): 206 (16), 162 (20), 107 (3), 91 (100), 77 (2), 65 (5), 43 (4). Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.80, H, 8.60, N, 5.61.

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