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Remarkably mild and efficient catalytic Sakurai reaction of *N*-alkoxycarbonylamino sulfones with allyltrimethylsilane using indium(III) chloride☆

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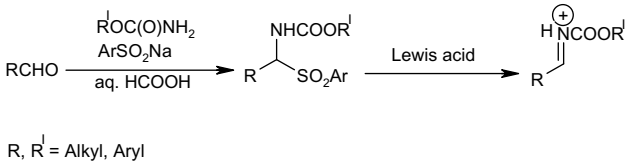
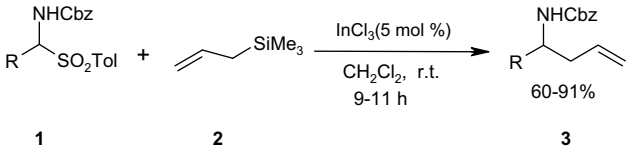
Abstract—The Sakurai reaction of *N*-alkoxycarbonylamino sulfones with allyltrimethylsilane in the presence of a catalytic amount of indium(III) chloride at room temperature produces the corresponding protected homoallylic amines in high yields.

Homoallylic amines possess significant biological activity.[1] A practical approach for the synthesis of these compounds involves the Lewis acid-catalyzed reaction of imines with allylsilanes (Sakurai reaction).[2] As imines are generally unstable, the in situ formation of imines followed by allylation in one-pot is more convenient. However, in this process, several Lewis acids would be deactivated or decompose due to the presence of amine and of water formed in the reaction. It is known that *N*-alkoxycarbonylamino sulfones, prepared[3] from aldehydes, are converted into the corresponding *N*-alkoxycarbonyl imine derivatives on treatment with a Lewis acid[4] (Scheme 1). Thus the Sakurai reaction of these sulfones with allylsilanes in the presence of a suitable Lewis acid constitutes an important method for the synthesis of homoallylic amines.



Scheme 1.



Scheme 2.

In continuation of our work[5] on the development of useful synthetic methodologies we have observed that a catalytic amount of $InCl_3$ is highly effective for the reaction of *N*-alkoxycarbonylamino sulfones with allyltrimethylsilane to afford the corresponding protected homoallylic amines at room temperature (Scheme 2).

Initially we carried out the reaction of *N*-benzyloxycarbonylamino *p*-tolylsulfone **1** (R = Ph) with allyltrimethylsilane in the presence of various Lewis acids (Table 1). Considering the amount of the catalyst, reaction time and yield, $InCl_3$ (5 mol %) was found to be the most effective. Subsequently, this catalyst was utilized for the preparation of a series of protected homoallylic amines (Table 2). The reactions were complete within 9–11 h. The products were formed at room temperature and in high yields. Previously, only one catalytic Sakurai reaction of *N*-alkoxycarbonylamino sulfones with allyltrimethylsilane had been reported, using bismuth triflate.[6] The other catalysts examined such as $TiCl_4$,

Keywords: Sakurai reaction; *N*-Alkoxycarbonylamino sulfone; Allyltrimethylsilane; Protected homoallylic amine; Indium(III) chloride.
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Table 1. Allylation of *N*-benzyloxycarbonylamino *p*-tolylsulfone, **1a** (R = Ph) using different Lewis acids at room temperature (Scheme 2)[a]

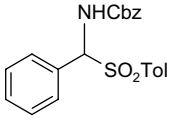
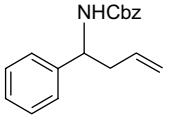
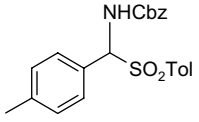
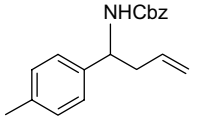
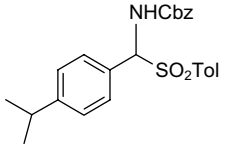
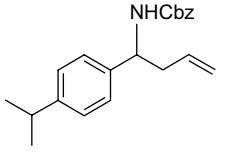
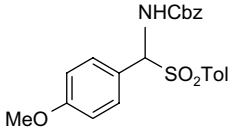
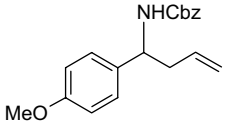
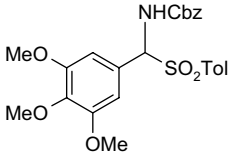
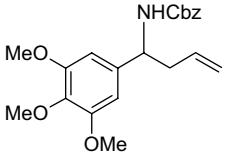
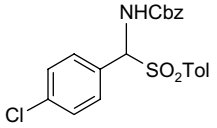
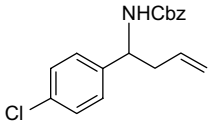
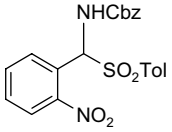
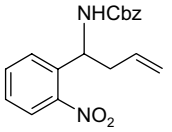
Entry	Lewis acid	*x* mol %	Time (h)	Isolated yield (%)
1	$CeCl_3{\cdot}7H_2O$	5	9	10
2	$CeCl_3{\cdot}7H_2O$	5	24	15
3	$ZrCl_4$	5	9	20
4	$ZrCl_4$	5	24	35
5	VCl_3	5	9	10
6	VCl_3	5	24	20
7	$CuBr_2$	5	9	20
8	$CuBr_2$	5	24	35
9	$InCl_3$	2	9	30
10	$InCl_3$	2	24	45
11	$InCl_3$	5	9	87
12	$InCl_3$	10	9	90

[a] Reaction conditions: *N*-benzyloxycarbonylamino *p*-tolylsulfone (1 mmol), allyltrimethylsilane (1.5 mmol), Lewis acid (*x* mol %).

$SnCl_4$ or $Zn(OTf)_2$ were required in a stoichiometric quantity or in large exess.[4,7,8] With bismuth triflate, several reactions required reflux using excess allyltrimethylsilane. The conversion times were longer (generally around 24 h) and yields were also somewhat lower. For example, for the conversion of *N*-benzyloxycarbonylamino *p*-tolylsulfones **3f** and **3j** the times required were 9 h and 10 h, respectively, and the yields were 86% and 78%, respectively, in the present method (Table 2), but for the same conversion using bismuth triflate, the times were 26 h and 24 h and the yields were 78% and 73%. In the earlier work, the sulfones derived from aliphatic aldehydes required much longer times and yields were lower. For comparison, the homoallylic amine **1n** was previously prepared using catalytic bismuth triflate in a yield of 61% in 44 h while using indium chloride under the present reaction conditions, the same product was formed in a yield of 74% in 10 h.

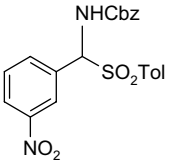
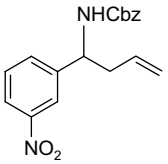
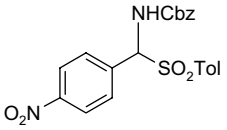
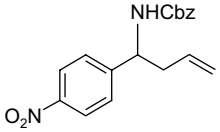
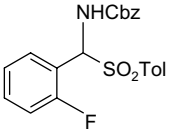
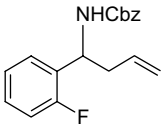
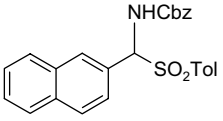
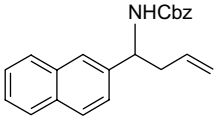
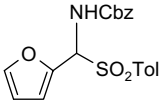
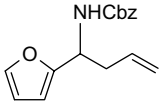
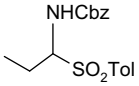
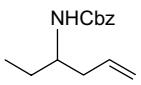
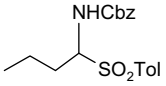
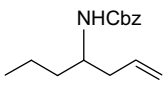
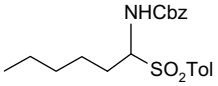
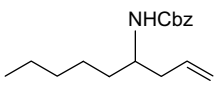
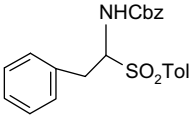
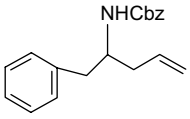
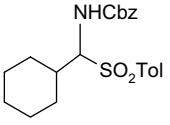
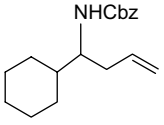
N-Alkoxycarbonylamino sulfones derived from various aldehydes (aromatic and aliphatic) underwent the present conversion smoothly. Aromatic aldehydes containing both electron-donating and electron-withdrawing groups could be used to prepare the sulfones. Open

Table 2. $InCl_3$-catalyzed allylation of *N*-benzyloxycarbonylamino *p*-tolylsulfones, **1**, with allyltrimethylsilane, **2** (Scheme 2)

Entry	Reactant (**1**)	Product (**3**)[a]	Time (h)	Isolated yield (%)
a			9	87
b			9	88
c			9	90
d			9	89
e			9	91
f			9	86
g			11	71

(*continued on next page*)

Table 2 (*continued*)

Entry	Reactant (**1**)	Product (**3**)[a]	Time (h)	Isolated yield (%)
h			11	77
i			11	73
j			10	78
k			10	82
l			11	60[b]
m			9	79
n			10	74
o			10	72
p			11	74
q			10	78

[a] The structures of the products were established from their spectral (IR, ^{1}H, ^{13}C NMR, and MS) and analytical data.
[b] The reaction was run with 2.5 equiv of allyltrimethylsilane.

chain and cyclic aliphatic aldehydes were also used. Various functional groups such as ether, halogen, and nitro remained intact. The sulfones derived from an acid sensitive aldehyde such as furfuraldehyde (entry l) and a sterically hindered aldehyde such as 2-naphthaldehyde (entry k) also formed the corresponding protected homoallylic amines in good yields. The structures of the products were established from their spectral (IR, ^{1}H, ^{13}C NMR, and MS) and analytical data.

In conclusion, we have described here a highly efficient improved protocol for the synthesis of protected homoallylic amines at room temperature and in impressive yields by applying the Sakurai reaction of *N*-alkoxycar-

bonylamino sulfones and allyltrimethylsilane in the presence of a catalytic amount of indium chloride.

General experimental procedure: Allyltrimethylsilane (1.5 mmol) was added drop-wise to a solution of *N*-alkoxycarbonylamino *p*-tolylsulfone (1 mmol) and $InCl_3$ (5 mol %) in CH_2Cl_2 (5 mL) under nitrogen. The mixture was stirred and the reaction was monitored by TLC. After completion, the reaction was quenched with distilled water (5 mL) and the mixture was extracted with EtOAc (3×10 mL). The combined organic portions were washed with water (2×10 mL) and saturated aqueous NH_4Cl (2×10 mL), dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was subjected to column chromatography (silica gel, hexane–EtOAc, 92:8 to 95:5) to obtain pure protected homoallylic amine.

The spectral and analytical data of the previously unknown homoallylic amines are given below.

Compound **3b**: White solid; mp 62–64 °C; IR (KBr): ν_{max} 3352, 1690, 1526, 1457, 1259 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.36–7.23 (5H, m), 7.15–7.07 (4H, m), 5.63 (1H, m), 5.12–4.92 (5H, m), 5.71 (1H, br s), 2.59–2.48 (2H, m), 2.32 (3H, s); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 156.2, 137.1, 136.8, 134.4, 129.2, 128.6, 128.0, 126.1, 118.8, 100.0, 67.5, 54.5, 40.8, 21.2; FABMS: *m/z* 318 $[M+Na]^{+\bullet}$; Anal. Calcd for $C_{19}H_{21}NO_2$: C, 77.29; H, 7.12; N, 4.75. Found: C, 77.38; H, 7.04; N, 4.86.

Compound **3e**: White solid; mp 68–70 °C; IR (KBr): ν_{max} 3348, 1703, 1593, 1507, 1238 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.40–7.22 (5H, m), 6.47–6.39 (2H, m), 5.65 (1H, m), 5.18–4.97 (5H, m), 4.66 (1H, br s), 3.82 (6H, s), 3.81 (3H, s), 2.58–2.47 (2H, m); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 156.9, 155.9, 153.4, 138.0, 137.2, 136.5, 133.9, 128.6, 128.3, 118.6, 105.6, 103.3, 67.0, 60.9, 56.2, 54.9, 41.3; FABMS: *m/z* 394 $[M+Na]^{+\bullet}$; Anal. Calcd for $C_{21}H_{25}NO_5$: C, 67.93; H, 6.74; N, 3.77. Found: C, 67.81; H, 6.80; N, 3.69.

Compound **3i**: Oil; IR (KBr): ν_{max} 3324, 1701, 1604, 1521, 1348 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 8.15 (2H, d, $J = 8.0$ Hz), 7.41 (2H, d, $J = 8.0$ Hz), 7.38–7.23 (5H, m), 5.61 (1H, m), 5.19–5.01 (5H, m), 4.82 (1H, br s), 2.57–2.43 (2H, m); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 156.1, 150.0, 147.2, 136.2, 132.5, 128.7, 128.5, 128.0, 127.2, 123.9, 119.8, 67.0, 54.1, 40.8; FABMS: *m/z* 349 $[M+Na]^{+\bullet}$; Anal. Calcd for $C_{18}H_{18}N_2O_4$: C, 66.26; H, 5.52; N, 8.59. Found: C, 66.37; H, 5.48; N, 8.65.

Compound **3k**: White solid; mp 65–67 °C; IR (KBr): ν_{max} 3363, 1687, 1525, 1463, 1251 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.82–7.61 (5H, m), 7.48–7.20 (7H, m), 5.62 (1H, m), 5.12–4.99 (5H, m), 4.80 (1H, br s), 2.62–2.51 (2H, m); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 155.8, 139.9, 135.8, 133.0, 132.7, 132.6, 128.4, 128.0, 127.9, 127.8, 126.0, 125.5, 125.2, 124.6, 118.4, 66.8, 54.3, 40.7; FABMS: *m/z* 354 $[M+Na]^{+\bullet}$; Anal. Calcd for $C_{22}H_{21}NO_2$: C, 79.76; H, 6.34; N, 4.23. Found: C, 79.87; H, 6.28; N, 4.29.

Compound **3o**: White solid; mp 40–42 °C; IR (KBr): ν_{max} 3331, 1700, 1530, 1452, 1276 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.36–7.28 (5H, m), 5.73 (1H, m), 5.10–5.01 (4H, m), 4.43 (1H, d, $J = 8.0$ Hz), 3.68 (1H, m), 2.28–2.10 (2H, m), 1.39–1.20 (8H, m), 0.88 (3H, t, $J = 7.0$ Hz); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 156.2, 136.9, 134.2, 128.6, 128.0, 117.9, 67.0, 50.8, 39.5, 34.6, 31.4, 25.2, 22.6, 14.0; FABMS: *m/z* 298 $[M+Na]^{+\bullet}$; Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.18; H, 9.09; N, 5.09. Found: C, 74.26; H, 9.17; N, 5.01.

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