Highly efficient synthesis of homoallylamines from aldimines with allylstannane promoted by MgI_2 etherate

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We describe a mild and efficient procedure for the synthesis of homoallylamines by addition of allyltributylstannane to aldimines with promoted by MgI_2 etherate (MgI_2•$(OEt_2)_n$) in good to excellent yields.

Keywords: aldimine, allyltributylstannane, homoallylamine, MgI_2 etherate

Lewis acid-catalysed carbon–carbon bond forming reactions are of great importance in organic synthesis due to their high rate of reaction and selectivity under mild reaction conditions.[1–3] Lewis acid-promoted nucleophilic addition of allylic organometallics to aldimines is one of the most important carbon–carbon bond forming reactions, and it provides a useful method for the preparation of homoallylamines.[4] Homoallylamines are important building blocks for the preparation of various biologically active molecules.[5] Generally, the preparation of homoallylamines is accomplished either by nucleophilic addition of organometallic reagents[6,7] or by addition of allylsilane, allyltin, allylboron or allylgermane reagents to imines in the presence of a variety of Lewis acids,[8–10] transition metallic reagents,[11,12] lanthanide triflates,[13,14] or other catalysts.[15] Recently, Li and Zhao have developed the allylation of allyltributyltin promoted by the recoverable and reusable polymer-supported sulfonamide of *N*-glycine.[16] However, the traditional methods using Lewis acids such as $TiCl_4$, BF_3•Et_2O and $SnCl_4$ must be carried out under strictly anhydrous conditions, which are difficult to achieve especially on a large scale. Palladium complexes and water-tolerant Lewis acids lanthanide triflates are rather expensive. From the above, it is clear that the development of less expensive, environmentally benign, and easily handled promoters for allylation of aldimines is highly desirable.

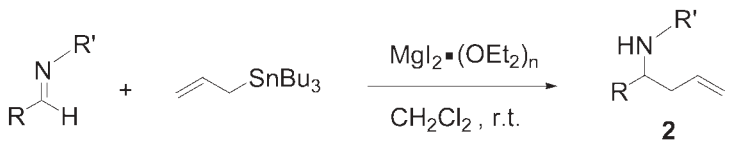
In our previous paper,[17] we have demonstrated that MgI_2 etherate could efficiently promote the allylation of aldehydes with allyltributylstannane. In the continuation of our research, we now wish to describe a simple and efficient allylation of aldimine with allyltributylstannane promoted by MgI_2 etherate under mild reaction conditions in good to excellent yields (Scheme 1).

Results and discussion

Initially, we preformed a variety of imines derived from aromatic aldehydes and aromatic amines. We carried out our first studies into the allylation of benzylideneaniline **1a** with allyltributylstannane using an equimolar amount of freshly prepared MgI_2 etherate in CH_2Cl_2 at room temperature. After stirring for 1.0 h, the desired homoallylamine was afforded in 92% yield. Then, under the similar reaction conditions, the allylation of aldimine **1b** and **1c**, prepared from benzaldehyde and 4-methylaniline or benzylamine, respectively, was examined, (Table 1, entries 2 and 3). The aromatic imine **1b** also produced the corresponding homoallylamine **2b** in 95% yield (entry 2). Furthermore, the allylation of imine **1c** gave the desired product in good yield (entry 3). Inspired by the above results, we applied the MgI_2 etherate catalyst system to the allylation of a variety of imines. The results are summarised in Table 1. As shown in Table 1, the reaction proceeded smoothly at room temperature and provided good to excellent yields. The reaction of the aldimines **1d** and **1e**, derived from *p*-anisaldehyde and *p*-nitrobenzaldehyde, also proceded very smoothly and provided the homoallylamines **2d** and **2e** respectively in nearly quantitative yields (Table 1, entries 4 and 5). The use of *o*-aminophenol as the imine component was examined and the allylation products **2f–i** were obtained in good yields (Table 1, entries 6–9). The allylation of the imine **1l** derived from cinnamaldehyde and p-methoxyaniline produced the homoallylamine **2l** in 90% yield (Table 1, entry 12). Morever, the reaction of heteroaromatic imines **1j** and **1k** derived from 2-thiophenealdehyde also proceeded in good yields (Table 1, entries 10 and 11). Apparently, the use of aromatic amines as the imine component gave, in general, better results than the use of benzylamine. The reactions of allyltributylstannane with chiral imines, promoted by MgI_2 etherate, were also studied (Table 1, entries 13 and 14). The allylation with chiral imines involving the *S*-l-phenylethylamine auxiliary afforded moderate stereoselection in excellent yield. In addition, various ketoimine substrates are unreactive toward to allyltributylstannane in the presence of MgI_2 etherate (Table 1, entries 15–17).

To examine the halide anion effect, $MgCl_2$ etherate and $MgBr_2$ etherate were compared under parallel reaction conditions (100 mol % of catalyst) in the allylation reaction of benzylideneaniline **1a** with allyltributylstannane. $MgCl_2$ etherate is almost inactive and $MgBr_2$ etherate is less effective in terms of substrate conversion and yield. The unique reactivity of MgI_2 etherate is attributed to the dissociative character of the iodide counterion and a more Lewis acidic cationic $[MgI]^+$ species as a result of Lewis base activation of Lewis acid.[13]

In conclusion, we have found an efficient and smooth allylation of imines with allyltributylstannane in the presence of the MgI_2 etherate system. This catalytic reaction enables the allylation to be carried out under essentially neutral conditions at room temperature in good to excellent yields. We are still working with other chiral imines to enhance the level of the diastereoselectivity. We intend to study the addition of stereogenic and heterosubstituted stannanes and an enantioselective variant of this reaction.



Scheme 1 MgI_2 etherate-promoted allylation of aldimines with allyltributylstannane.

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Table 1 The allylation of aldimine with allyltributylstannane promoted by $MgI_2•(OEt_2)_n$[a]

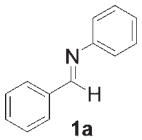
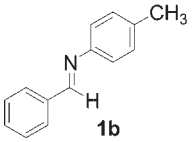
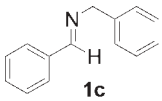
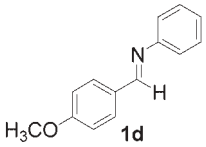
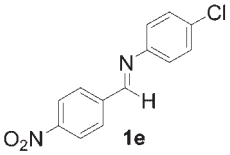
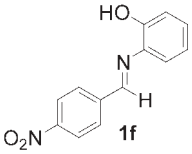
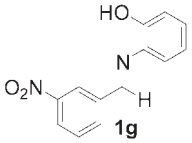
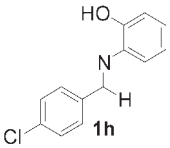
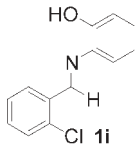
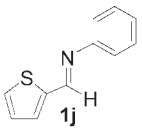
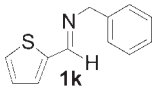
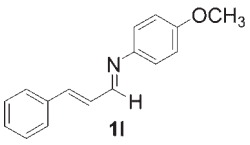
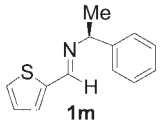
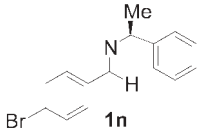
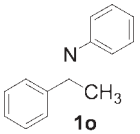
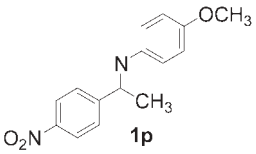
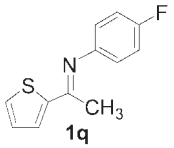
Entry	Aldimine	Time/h	Product[b]	Yield/%[c]
1	 **1a**	1	**2a**	92
2	 **1b**	0.5	**2b**	95
3	 **1c**	2	**2c**	89
4	 **1d**	1	**2d**	98
5	 **1e**	0.5	**2e**	97
6	 **1f**	0.5	**2f**	90
7	 **1g**	0.5	**2g**	91
8	 **1h**	0.5	**2h**	87
9	 **1i**	0.5	**2i**	88
10	 **1j**	0.5	**2j**	93
11	 **1k**	1	**2k**	86
12	 **1l**	1	**2l**	90

Table 1 *Continued*

Entry	Aldimine	Time/h	Product[b]	Yield/%[c]
13	 **1m**	2	**2m**	92 (dr 74:26)[d]
14	 **1n**	2	**2n**	94 (dr 62:38)[d]
15	 **1o**	8	**NA**[e]	NR[f]
16	 **1p**	8	**NA**	NR
17	 **1q**	8	**NA**	NR

[a] The reaction was carried out by addition of imine and allyltributylstannane promoted by 1.0 equivalent of MgI_2•$(OEt_2)_n$ at room temperature in CH_2Cl_2.
[b] All products were identified by their ^{1}H NMR spectra.
[c] Yields of products isolated by column chromatography.
[d] The ratio of *dr* value was determined by ^{1}H NMR analysis.
[e] NA = Not available.
[f] NR = No reaction.

Experimental

For product purification by flash column chromatography, silica gel (200–300 mesh) and light petroleum ether (PE, b.p. 60–90 °C) were used. ^{1}H NMR spectra were taken on a Bruker AM-500 spectrometer with TMS as an internal standard and $CDCl_3$ as solvent. The reactions monitoring was accomplished by TLC on silica gel polygram SILG/UV 254 plates. All compounds were identified by ^{1}H NMR and the spectra are in good agreement with those reported in the literature.

Synthesis of homoallylamines; typical procedure

To a stirred benzylideneaniline **1a** solution of (0.5 mmol) in CH_2Cl_2 (3 mL) was added freshly prepared MgI_2 etherate (0.5 mmol) at room temperature. After stirring for 10 min, a solution of allyltributylstannane (0.6 mmol) in CH_2Cl_2 (2 mL) was added dropwise by a syringe. The resulting homogeneous reaction mixture was stirred at r.t. for 1.0 h and quenched by saturated $NaHCO_3$ aqueous solution. Extractive workup with ethyl acetate and chromatographic purification of the crude product on silica gel gave the homoallylamine **2a** in 92% yield. All the homoallylic amine products are pale yellowish to yellowish oils.

4-Phenyl-4-(N-phenyl)aminobut-1-ene (**2a**):[16] δ_H 2.60–2.65 (m, 1H), 2.71–2.75 (m, 1H), 4.29 (br s, 1H), 4.50–4.53 (m, 1H), 5.26–5.33 (m, 2H), 5.85–5.92 (m, 1H), 6.63 (d, 2H, *J* = 7.5 Hz), 6.78 (t, 1H, *J* = 7.5 Hz), 7.19–7.22 (m, 2H), 7.35–7.37 (m, 1H), 7.42–7.50 (m, 4H).

4-Phenyl-4-(N-4′-methyl-phenyl)aminobut-1-ene (**2b**):[20] δ_H 2.28 (s, 3H), 2.56–2.60 (m, 1H), 2.67–2.71 (m, 1H), 4.14 (br s, 1H), 4.43–4.46 (m, 1H), 5.22–5.29 (m, 2H), 5.82–5.90 (m, 1H), 6.52 (d, 2H, *J* = 8.5 Hz), 6.99 (d, 2H, *J* = 8.0 Hz), 7.30–7.33 (m, 1H), 7.39–7.42 (m, 2H), 7.42–7.47 (m, 2H).

4-Phenyl-4-(N-benzyl)aminobut-1-ene (**2c**):[21] δ_H 2.46–2.51 (m, 1H), 2.50–2.60 (m, 1H), 3.78 (s, 3H), 4.12 (s, 1H), 4.32–4.35 (m, 1H), 5.12–5.19 (m, 2H), 5.71–5.80 (m, 1H), 6.48–6.50 (m, 2H), 6.62–6.65 (m, 1H), 6.84–6.87 (m, 2H), 7.05–7.09 (m, 2H) 7.26–7.28 (m, 2H).

4-(4′-Methoxy-phenyl)-4-(N-phenyl)aminobut-1-ene (**2d**):[22] δ_H 2.48–2.52 (m, 1H), 2.58–2.61 (m, 1H), 3.68 (s, 3H,), 4.30 (dd, 1H, *J* = 5.0, 8.0 Hz), 5.12–5.19 (m, 2H), 5.71–5.78 (m, 1H), 6.46 (d, 2H, *J* = 8.5 Hz), 6.67 (dd, 2H, *J* = 2.5, 7.0 Hz), 7.22–7.24 (m, 1H), 7.29–7.33 (m, 2H), 7.34–7.36 (m, 2H).

4-(4′-Nitrophenyl)-4-(N-4′-chloro-phenyl)aminobut-1-ene (**2e**):[23] δ_H 2.45–2.52 (m, 1H), 2.59–2.64 (m, 1H), 4.26 (br s, 1H), 4.42–4.45 (m, 1H), 5.18–5.22 (m, 2H), 5.67–5.74 (m, 1H), 6.34 (d, 2H, *J* = 10.0 Hz), 7.01 (d, 2H, *J* = 10.0 Hz), 7.51 (d, 2H, *J* = 10.0 Hz), 8.17 (d, 2H, *J* = 10.0 Hz).

4-(4′-Nitrophenyl)-4-(N-2′-hydroxy-phenyl)aminobut-1-ene (**2f**):[24] δ_H 2.55–2.65 (m, 2H), 4.47 (t, 1H, *J* = 6.8 Hz), 5.18–5.24 (m, 2H), 5.71–5.82 (m, 1H), 6.23 (d, 1H, *J* = 8.0 Hz), 6.59 (t, 1H, *J* = 7.6 Hz), 6.67 (t, 1H, *J* = 7.6 Hz), 6.72 (d, 1H, *J* = 4.4 Hz), 7.55 (d, 2H, *J* = 9.2 Hz), 8.18 (d, 2H, *J* = 8.4 Hz).

4-(3′-Nitrophenyl)-4-(N-2′-hydroxy-phenyl)aminobut-1-ene (**2g**):[24] δ_H 2.57–2.62 (m, 2H), 4.48 (t, 1H, *J* = 6.8 Hz), 5.17–5.23 (m, 2H), 5.73–5.78 (m, 1H), 6.27 (d, 1H, *J* = 7.6 Hz), 6.55–6.59 (m, 1H), 6.64–6.70 (m, 1H), 6.72 (d, 1H, *J* = 7.6 Hz), 7.47 (t, 1H, *J* = 8.0 Hz), 7.72 (d, 1H, *J* = 7.6 Hz), 8.08 (dd, 1H, *J* = 1.6, 8.0 Hz), 8.24 (dd, 1H, *J* = 1.6, 4.0 Hz).

4-(4′-Chlorophenyl)-4-(N-2′-hydroxy-phenyl)aminobut-1-ene (**2h**):[24] δ_H 2.50–2.60 (m, 2H), 4.36 (t, 1H, *J* = 7.6 Hz), 5.13–5.21 (m, 2H), 5.71–5.76 (m, 1H), 6.34 (d, 1H, *J* = 8.0 Hz), 6.60 (t, 1H, *J* = 7.6 Hz), 6.72 (d, 2H, *J* = 8.0 Hz), 7.26–7.31 (m, 4H).

4-(2′-Chlorophenyl)-4-(N-2′-hydroxy-phenyl)aminobut-1-ene (**2i**):[24] δ_H 2.45–2.53 (m, 1H), 2.67–2.74 (m, 1H), 4.86 (m, 1H), 5.15–5.25 (m, 2H), 5.76–5.89 (m, 1H), 6.25 (d, 1H, *J* = 7.6 Hz), 6.56 (t, 1H, *J* = 6.8 Hz), 6.67 (t, 2H, *J* = 7.2 Hz), 7.14–7.21 (m, 2H), 7.36–7.39 (m, 1H), 7.41–7.45 (m, 1H).

4-(2′-Thiophene)-4-(N-phenyl)aminobut-1-ene (**2j**):[14] δ_H 2.64–2.68 (m, 2H), 4.12 (br s, 1H), 4.71 (t, 1H, *J* = 7.5 Hz), 5.15–5.21 (m, 2H), 5.76–5.83 (m, 1H), 6.60 (d, 2H, *J* = 9.0 Hz), 6.68–6.71 (m, 1H), 6.93–6.98 (m, 2H), 7.11–7.17 (m, 3H).

4-(2′-Thiophene)-4-(N-benzyl)aminobut-1-ene (**2k**):[22] δ_H 2.52–2.55 (m, 2H), 3.62 (d, 1H, *J* = 13.0 Hz), 3.81 (d, 1H, *J* = 13.0 Hz), 4.02 (t, 1H, *J* = 7.0 Hz), 5.05–5.12 (m, 2H), 5.67–5.76 (m, 1H), 6.97 (t, 2H, *J* = 5.3 Hz), 7.24–7.26 (m, 2H), 7.29–7.33 (m, 4H).

6-Phenyl-4-(N-4′-methoxy-phenyl)aminohexa-1,5-diene (**2l**):[21] ^{1}H NMR ($CDC1_3$) δ 2.43–2.50 (m, 2H), 3.73 (s, 3H), 3.95–3.99 (m, 1H), 5.14–5.20 (m, 2H), 5.81–5.89 (m, 1H), 6.19 (dd, 1H, *J* = 6.0, 16.0 Hz), 6.57–6.64 (m, 3H), 6.75 (dd, 2H, *J* = 2.5, 6.5 Hz), 7.19–7.36 (m, 5H).

4-(2′-Thiophene)-4-(N-α-methyl-phenyl)aminobut-1-ene (**2m**): δ_H 1.33 (d, 2.2H, *J* = 5.5 Hz), 1.36 (d, 1.8H, *J* = 6.5 Hz), 2.45 (m, 1.48H), 2.55–2.57 (m, 0.52H), 3.67–3.72 (m, 2H), 3.86–3.87 (m, 1H), 4.03 (t, 1H, *J* = 6.0 Hz), 5.04–5.11 (m, 2H), 5.59–5.64 (m, 0.74H), 5.70–5.73 (m, 0.26H), 6.80 (s, 0.74 H), 6.88 (s, 0.26H), 7.18–7.35 (m, 8H). *m/z* (EI): 257 ([M+1]$^+$, 12), 216 (54), 121 (7), 112 (100), 77 (43). HRMS (EI) Calcd for $C_{16}H_{19}NS$: 257.1238. Found for [M]$^+$: 257.1225.

4-(4′-Bromophenyl)-4-(N-α-methyl-phenyl)aminobut-1-ene (**2n**): δ_H 1.25 (d, 1.86H, *J* = 5.5 Hz), 1.33 (d, 1.14H, *J* = 6.5 Hz), 2.28 (m, 1.24H), 2.39–2.43 (m, 0.76H), 3.33–3.36 (m, 1H), 3.43–3.47 (q, 1H, *J* = 7.0 Hz), 3.68–3.74 (m, 1H), 5.01–5.05 (m, 2H), 5.55–5.65 (m, 1H), 7.10–7.46 (m, 9H). *m/z* (EI): 329 ([M]$^+$ for ^{79}Br, 6), 331 ([M]$^+$ for ^{81}Br, 6), 288 (24), 184 (49), 105 (100), 77 (42). HRMS (EI) Calcd for $C_{18}H_{20}BrN$: 329.0779. Found for [M]$^+$ for ^{79}Br: 329.0768.

Zhejiang University of Technology Scholars Program is gratefully acknowledged.

Received 27 April 2010; accepted 10 May 2010
Paper 1000090 doi:10.3184/030823410X12756737135354
Published online: 2 July 2010

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