Mild and Efficient Allylation of Aldehydes with Allyltributylstannane Promoted by MgI_2·$(OEt)_n$ Etherate

Xingxian Zhang*

College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou, Zhejiang 310032, P. R. of China
Fax +86(571)88320320; E-mail: zhangxx@zjut.edu.cn

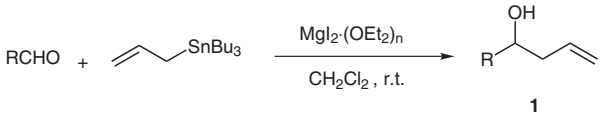
Received 23 May 2007

Abstract: Allylation of aldehydes with allyltributylstannane was promoted in the presence of MgI_2·$(OEt)_n$ to give homoallylic alcohols. The iodide anion and a noncoordinating reaction medium (CH_2Cl_2) are the key features of this catalytic system.

Key words: magnesium iodide, allylation, aldehyde, allyltributylstannane

Lewis acid catalyzed carbon–carbon bond-forming reactions are of great importance in organic synthesis due to their high reactivity and selectivity under mild reaction conditions.[1–3] Among them, Lewis acid catalyzed allylation of aldehydes[4–6] has been widely utilized in the construction of carbon–carbon bonds to generate homoallylic alcohols, which are important building blocks for the synthesis of many natural products and pharmaceuticals.[7] Generally, the preparation of homoallylic alcohols can be accomplished either by nucleophilic addition of organometallic reagents or by addition of allylsilane, allyltin or allylborane reagents in the presence of a variety of Lewis acids, Brønsted acids, transition metallic reagents, lanthanide triflates, and other catalysts.[5,6,8] Recently, there was a report on carrying out these reactions in the presence of $CeCl_3$·$7H_2O$[9] or $CeCl_3$·$7H_2O$/NaI.[10] However, many of these reagents are rather expensive and difficult to be handle on a large scale. From the viewpoints described above, the development of less expensive, environmentally benign and easily handled promoters for allylation of aldehydes is still highly desirable.

In our previous paper[11] we have demonstrated that MgI_2·$(OEt)_n$ could efficiently catalyze Mukaiyama-type aldol addition of aromatic aldehydes with silyl enolates. In continuation of our work, we wish to report herein a mild and efficient allylation of aldehydes with allyltributylstannane mediated by MgI_2·$(OEt)_n$ in good to excellent yields (Scheme 1).



Scheme 1 MgI_2·$(OEt)_n$-catalyzed allylation

We initiated our studies by carrying out the allylation of benzaldehyde with allyltributylstannane using freshly prepared MgI_2·$(OEt)_n$ (1.0 M in Et_2O–benzene, 1:2)[12] in CH_2Cl_2 at room temperature. It was noticed that the amount of MgI_2·$(OEt)_n$ catalyst had an effect on the yield of addition products. The optimal condition was to use 100 mol% of MgI_2·$(OEt)_n$ to give the desired homoallylic alcohol in good yield (92%). Furthermore, among the various solvents screened, good yield was obtained in a noncoordinating reaction medium such as CH_2Cl_2. Moderate yield was obtained in nonpolar solvents such as benzene or toluene. However, no reaction was noted when it was carried out in the polar solvents, such as Et_2O, DMF, THF and MeCN.

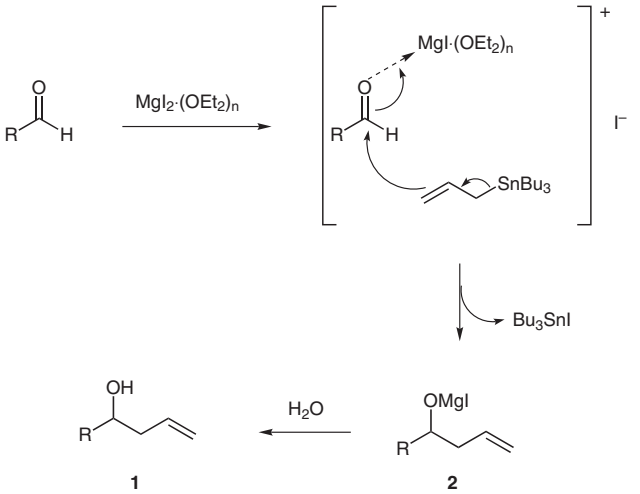
Encouraged by these results, allylation of a variety of aldehydes has been investigated. The results are summarized in Table 1. As shown in Table 1, the reaction proceeded smoothly at room temperature and provided good product yields. Among the various aldehydes chosen, we observed that aromatic aldehydes were good substrates, and provided the corresponding adducts in good to excellent yields (Table 1, entries 1–7). Moreover, allylation of unsaturated aldehydes (Table 1, entries 8 and 9) and aliphatic aldehydes (Table 1, entries 10–12) also afforded products in good yields, whereas aromatic and aliphatic ketones were unreactive towards allyltributylstannane in the presence of MgI_2·$(OEt)_n$. This was probably due to the lower reactivity of ketones, as compared to aldehydes, towards allylstannanes.[13] The higher coordinating ability of the magnesium(II) towards oxygen atoms of the carbonyl moiety[14] is presumably responsible for the effective activation of aldehydic carbonyl.

The key advantage of this method was the selective allylation of aldehydes in the presence of the highly acid-sensitive acetonide and Boc protecting groups (Table 1, entries 13 and 14), which normally do not survive under strongly acidic conditions.[15] We found that, allylation of Boc-L-phenylalanine exclusively afforded 1,2-*anti*-allylic alcohol **1m** in 78% yield (Table 1, entry 13). Furthermore, this method was also useful for the selective allylation of D-glyceraldehyde without affecting the acetonide moiety (Table 1, entry 14) to afford a mixture of diastereoisomers in a 1:2 ratio.

SYNLETT 2008, No. 1, pp 0065–0068
Advanced online publication: 03.12.2007
DOI: 10.1055/s-2007-990919; Art ID: W10207ST

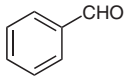
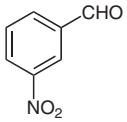
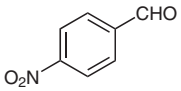
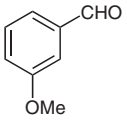
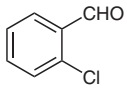
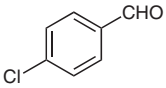
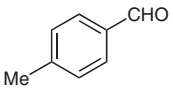
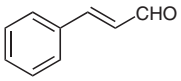
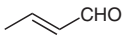
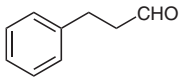
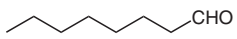
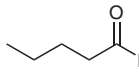
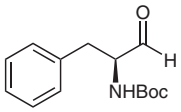
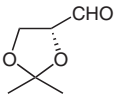
To examine the halide anion effect, halogen analogues of $MgI_2·(OEt)_n$, $MgCl_2·(OEt)_n$ and $MgBr_2·(OEt)_n$, were compared under parallel reaction conditions (100 mol% of catalyst) in the allylation reaction of aryl aldehydes with allyltributylstannane. It was found that $MgCl_2·(OEt)_n$ was almost inactive, while $MgBr_2·(OEt)_n$ was less effective in terms of substrate conversion and yield. Apparently, the unique catalytic reactivity of $MgI_2·(OEt)_n$ can be attributed to the dissociative character of iodide counterion to give a more acidic cationic $[MgI]^+$ species as a result of Lewis base activation of Lewis acid.[16] We proposed the following pathway for this allylation reaction (Scheme 2), which suggests that the activation of the aldehydes probably occurs via formation of an oxonium salt with $MgI_2·(OEt)_n$ due to its high oxophilic character. The cationic character[17] of this more Lewis acidic Mg(II) coordination with peripheral ethereal ligands results from the ready dissociation of iodide ion in accordance with the coordination of the Lewis basic formyl group. Then, rapid protonation of magnesium alkoxide **2** by quenching with water generates the desired homoallylic alcohol. In addition, this allylation needed a stoichiometric amount of $MgI_2·(OEt)_n$ because of the above strong interaction with the oxygen function.[14]

In summary, we have demonstrated the unique catalytic reactivity of $MgI_2·(OEt)_n$ in the allylation of aromatic aldehydes, unsaturated aldehydes and aliphatic aldehydes with allyltributylstannane. This magnesium-catalyzed allylation addition is mild, efficient, operationally simple and highly selective. Iodide counterion, weakly coordinating peripheral ethereal ligands for Mg(II), and a noncoordinating reaction medium are critical factors for the unique reactivity of this catalytic system. Further investigations on the catalytic reactivity of $MgI_2·(OEt)_n$ in other C–C bond-constructing reactions are underway.



Scheme 2 The proposed mechanism of $MgI_2·(OEt)_n$-catalyzed allylation

Table 1 Allylation of Aldehydes with Allyltributylstannane Promoted by $MgI_2·(OEt)_n$[18,19]

Entry	Aldehyde	Time (h)	Product[a]	Yield (%)[b]
1		4	**1a**	92
2		1	**1b**	97
3		1	**1c**	95
4		5	**1d**	80
5		3	**1e**	95
6		3	**1f**	94
7		5	**1g**	62
8		4	**1h**	82
9		5	**1i**	66
10		3	**1j**	80
11		5	**1k**	81
12		5	**1l**	74
13		4	**1m**	78[c]
14		4	**1n**	70[d]

[a] All products were identified by their ^1H NMR spectra.
[b] Yields of products isolated by column chromatography.
[c] Only *anti*-configuration allylic alcohol was obtained.
[d] The product was obtained as a mixture of *syn* and *anti* isomers in a 1:2 ratio.

Acknowledgment

Zhejiang University of Technology Scholars Program is gratefully acknowledged.

References and Notes

(1) Corma, A.; Garcia, H. *Chem. Rev.* **2003**, *103*, 4307.
(2) Yamamoto, H. *Lewis Acids in Organic Synthesis*; Wiley-VCH: Weinheim, **2000**.
(3) Kobayashi, S.; Sugiura, M.; Kitagawa, H.; Lam, W. W. L. *Chem. Rev.* **2002**, *102*, 2227.
(4) Nishigaichi, Y.; Takuwa, A.; Naruta, Y.; Maruyama, K. *Tetrahedron* **1993**, *49*, 7395.
(5) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207.
(6) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31.
(7) (a) Nicolaou, K. C.; Kim, D. W.; Baati, R. *Angew. Chem. Int. Ed.* **2002**, *41*, 3701. (b) Hornberger, K. R. C.; Hamblet, L.; Leighton, J. L. *J. Am. Chem. Soc.* **2000**, *122*, 12894. (c) Felpin, F. X.; Lebreton, J. *J. Org. Chem.* **2002**, *67*, 9192. (d) Jaber, J. J.; Mitsui, K.; Rychnovsky, S. D. *J. Org. Chem.* **2001**, *66*, 4679. (e) Balskus, E. P.; Mendez-Andino, J.; Arbit, R. M.; Paquette, L. A. *J. Org. Chem.* **2001**, *66*, 6695. (f) Chen, G. M.; Brown, H. C.; Ramachandran, P. V. *J. Org. Chem.* **1999**, *64*, 721. (g) Lee, K. Y.; Oh, C.-Y.; Ham, W.-H. *Org. Lett.* **2002**, *4*, 4403.
(8) (a) Nishiyama, Y.; Kakushou, F.; Sonoda, N. *Tetrahedron Lett.* **2005**, *46*, 787. (b) Yanagisawa, A.; Morodome, M.; Nakashima, H.; Yamamoto, H. *Synlett* **1997**, 1309. (c) Yadav, J. S.; Reddy, B. V. S.; Krishna, A. D.; Sadasiv, K.; Chary, C. J. *Chem. Lett.* **2003**, *32*, 248. (d) Teo, Y. C.; Tan, K. T.; Loh, T. P. *Chem. Commun.* **2005**, 1318. (e) Aspinall, H. C.; Bissett, J. S.; Greeves, N.; Levin, D. *Tetrahedron Lett.* **2002**, *43*, 319. (f) Andrade, C. K. Z.; Azevedo, N. R.; Oliveira, G. R. *Synthesis* **2002**, 928. (g) Choudary, B. M.; Sridhar, C.; Sekhar, C. V. R. *Synlett* **2002**, 1694. (h) Hamasaki, S.; Chounan, Y.; Horino, H.; Yamamoto, Y. *Tetrahedron Lett.* **2000**, *41*, 9883. (i) Kobayashi, S.; Iwamoto, S.; Nagayama, S. *Synlett* **1997**, 1099. (j) Kobayashi, S.; Aoyama, N.; Manabe, K. *Synlett* **2002**, 483.
(9) Yadav, J. S.; Reddy, B. V. S.; Kondaji, G.; Reddy, J. S. S. *Tetrahedron* **2005**, *61*, 879.
(10) Bartoli, G.; Bosco, M.; Guiliani, A.; Marcantoni, E.; Palmieri, A.; Petrini, M.; Sambri, L. *J. Org. Chem.* **2004**, *69*, 1290.
(11) (a) Li, W. D.; Zhang, X. X. *Org. Lett.* **2002**, *4*, 3485. (b) Zhang, X. X.; Li, W. D. *Chin. Chem. Lett.* **2003**, *14*, 800.
(12) Arkley, V.; Attenburrow, J.; Gregory, G. I.; Walker, T. *J. Chem. Soc.* **1962**, 1260.
(13) For examples of allylation reactions of ketones, see: (a) Kobayashi, S.; Aoyama, N.; Manabe, K. *Synlett* **2002**, 483. (b) Hanawa, H.; Kii, S.; Maruoka, K. *Adv. Synth. Catal.* **2001**, *343*, 57. (c) Hamasaki, R.; Chounan, Y.; Horino, H.; Yamamoto, Y. *Tetrahedron Lett.* **2000**, *41*, 9883.
(14) (a) Tobe, M. L.; Burgess, J. *Inorganic Reaction Mechanisms*; Addison Wesley Longman: New York, **1999**, Chap. 7. (b) Wehmschulte, R. J.; Twamley, B.; Khan, M. A. *Inorg. Chem.* **2001**, *40*, 6004.
(15) (a) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207. (b) Nishigaichi, Y.; Takuwa, A.; Naruta, Y.; Maruyama, K. *Tetrahedron* **1993**, *49*, 7395. (c) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31. (d) Inoue, K.; Yasuda, M.; Baba, A. *Synlett* **1997**, 699. (e) Andrade, C. K. Z.; Azevedo, N. R.; Oliveira, G. R. *Synthesis* **2002**, 928. (f) Choudary, B. M.; Sridhar, C.; Sekhar, C. V. R. *Synlett* **2002**, 1694.
(16) (a) Corey, E. J.; Li, W. D.; Reichard, G. A. *J. Am. Chem. Soc.* **1998**, *120*, 2330. (b) Denmark, S. E.; Stavenger, R. A. *Acc. Chem. Res.* **2000**, *33*, 432. (c) Denmark, S. E.; Wynn, T. *J. Am. Chem. Soc.* **2001**, *123*, 6199.
(17) (a) Corey, E. J.; Ishihara, K. *Tetrahedron Lett.* **1992**, *33*, 6807. (b) Corey, E. J.; Imai, N.; Zhang, H. Y. *J. Am. Chem. Soc.* **1991**, *113*, 728.
(18) **Typical Procedure for the Synthesis of Homoallylic Alcohols**: To a stirred solution of benzaldehyde (0.5 mmol) in CH_2Cl_2 (3 mL) was added a freshly prepared solution of MgI_2·$(OEt)_n$ in Et_2O–benzene (1:2, 1.0 M, 0.5 mL) at r.t. After stirring for 10 min, a solution of allyltributylstannane (0.6 mmol) in CH_2Cl_2 (2 mL) was added dropwise via a syringe. The resulting homogeneous reaction mixture was stirred at r.t. for 3 h and quenched with distillated H_2O. Extractive workup with Et_2O and chromatographic purification of the crude product on silica gel gave the homoallylic alcohol **1a** in 92% yield.
(19) **Selected spectroscopic data**: Compound **1a**:[20] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.13 (br s, 1 H), 2.47–2.52 (m, 2 H), 4.72 (t, *J* = 6.5 Hz, 1 H), 5.11–5.19 (m, 2 H), 5.76–5.85 (m, 1 H), 7.25–7.29 (m, 1 H), 7.32–7.35 (m, 4 H). Compound **1b**:[10] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.15 (br s, 1 H), 2.43–2.52 (m, 1 H), 2.54–2.62 (m, 1 H), 4.85–4.89 (m, 1 H), 5.18–5.22 (m, 2 H), 5.75–5.84 (m, 1 H), 7.53 (t, *J* = 8.0 Hz, 1 H), 7.70 (d, *J* = 7.6 Hz, 1 H), 8.14 (d, *J* = 8.1 Hz, 1 H), 8.25 (s, 1 H). Compound **1c**:[10] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.48–2.63 (m, 2 H), 2.82 (br s, 1 H), 4.90 (t, *J* = 6.2 Hz, 1 H), 5.17–5.22 (m, 2 H), 5.77–5.87 (m, 1 H), 7.56 (d, *J* = 8.0 Hz, 2 H), 8.21 (d, *J* = 8.0 Hz, 2 H). Compound **1d**:[21] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.45–2.49 (m, 2 H), 3.77 (s, 3 H), 4.65 (t, *J* = 6.5 Hz, 1 H), 5.08–5.16 (m, 2 H), 5.72–5.82 (m, 1 H), 6.78 (d, *J* = 8.2 Hz, 1 H), 6.88–6.91 (m, 2 H), 7.23 (t, *J* = 8.0 Hz, 1 H). Compound **1e**:[22] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.32–2.41 (m, 2 H), 2.58–2.63 (m, 1 H), 5.12–5.20 (m, 3 H), 5.79–5.90 (m, 1 H), 7.16–7.33 (m, 3 H), 7.54 (d, *J* = 7.6 Hz, 1 H). Compound **1f**:[9] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.31 (d, *J* = 2.9 Hz, 1 H), 2.41–2.49 (m, 2 H), 4.67–4.69 (m, 1 H), 5.12–5.16 (m, 2 H), 5.72–5.79 (m, 1 H), 7.25–7.31 (m, 4 H). Compound **1g**:[10] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.21 (br s, 1 H), 2.33 (s, 3 H), 2.45–2.50 (m, 2 H), 4.66 (t, *J* = 6.5 Hz, 1 H), 5.08–5.16 (m, 2 H), 5.74–5.82 (m, 1 H), 7.14 (d, *J* = 7.7 Hz, 2 H), 7.22 (d, *J* = 7.5 Hz, 2 H). Compound **1h**:[20] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.09 (br s, 1 H), 2.35–2.44 (m, 2 H), 4.34 (br s, 1 H), 5.14–5.19 (m, 2 H), 5.79–5.90 (m, 1 H), 6.23 (dd, *J* = 7.9, 15.9 Hz, 1 H), 6.59 (d, *J* = 15.9 Hz, 1 H), 7.21–7.37 (m, 5 H). Compound **1i**:[23] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.66 (br s, 1 H), 1.70 (d, *J* = 6.5 Hz, 3 H), 2.24–2.35 (m, 2 H), 4.08–4.15 (m, 1 H), 5.11–5.17 (m, 2 H), 5.51 (dd, *J* = 6.8, 15.2 Hz, 1 H), 5.65–5.73 (m, 1 H), 5.75–5.85 (m, 1 H). Compound **1j**:[10] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.73–1.81 (m, 2 H), 1.89 (br s, 1 H), 2.14–2.21 (m, 1 H), 2.26–2.32 (m, 1 H), 2.64–2.71 (m, 1 H), 2.75–2.83 (m, 1 H), 3.64–3.70 (m, 1 H), 5.10–5.15 (m, 2 H), 5.74–5.85 (m, 1 H), 7.15–7.30 (m, 5 H). Compound **1k**:[24] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.0 Hz, 3 H), 1.21–1.50 (m, 12 H), 1.65 (br s, 1 H), 2.05–2.21 (m, 1 H), 2.27–2.38 (m, 1 H), 3.58–3.72 (m, 1 H), 5.12–5.19 (m, 2 H), 5.77–5.95 (m, 1 H). Compound **1l**:[22] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.0 Hz, 3 H), 1.24–1.48 (m, 6 H), 1.72 (br s, 1 H), 2.12–2.16 (m, 1 H), 2.15–2.33 (m, 1 H), 3.60–3.65 (m, 1 H), 5.10–5.17 (m, 2 H), 5.77–5.90 (m, 1 H). Compound **1m**:[25] $[\alpha]^{24}_D$ –21.2 (*c* = 1.02, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35 (s, 9 H), 2.20–2.30 (m, 2 H), 2.83–2.94 (m, 2 H), 3.59 (td, *J* = 1.5, 7.0 Hz, 1 H), 3.73 (br q, *J* = 8.0 Hz, 1 H), 4.88 (d, *J* = 9.5 Hz, 1 H), 5.10–5.15 (m, 2 H), 5.70–5.80 (m, 1 H), 7.18–7.32 (m, 5 H).

Compound **1n**:[26] $[\alpha]^{24}_{D}$ +15.1 (*c* = 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.36 (s, 3 H), 1.43 (s, 3 H), 2.16–2.24 (m, 1 H), 2.25–2.37 (m, 1 H), 2.41 (br s, 1 H, OH), 3.62–3.78 (m, 1 H), 3.90–3.95 (m, 1 H), 3.98–4.06 (m, 2 H), 5.10–5.17 (m, 2 H), 5.80–5.91 (m, 1 H).

(20) Keck, G. E.; Tarbet, K. H.; Geraci, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 8467.

(21) Watahiki, T.; Oriyama, T. *Tetrahedron Lett.* **2002**, *43*, 8959.

(22) Shen, K. H.; Yao, C. F. *J. Org. Chem.* **2006**, *71*, 3980.

(23) Miyamoto, H.; Daikawa, N.; Tanaka, K. *Tetrahedron Lett.* **2003**, *44*, 6963.

(24) Li, G. L.; Zhao, G. *Org. Lett.* **2006**, *8*, 633.

(25) Bonini, B. F.; Comes-Franchini, M.; Fochi, M.; Laboroi, F.; Mazzanti, G.; Ricci, A.; Varchi, G. *J. Org. Chem.* **1999**, *64*, 8008.

(26) (a) Roush, W. S.; Walts, A. E.; Hoong, L. K. *J. Am. Chem. Soc.* **1985**, *107*, 8186. (b) Yadav, J. S.; Reddy, B. V. S.; Kondaji, G.; Reddy, J. S. S. *Tetrahedron* **2005**, *61*, 879.