Pergamon

Tetrahedron Letters 43 (2002) 8959–8962

TETRAHEDRON
LETTERS

Iron(III) chloride-catalyzed effective allylation reactions of aldehydes with allyltrimethylsilane

Tsutomu Watahiki and Takeshi Oriyama*

Faculty of Science, Ibaraki University, Bunkyo, Mito 310-8512, Japan

Received 11 September 2002; revised 24 September 2002; accepted 26 September 2002

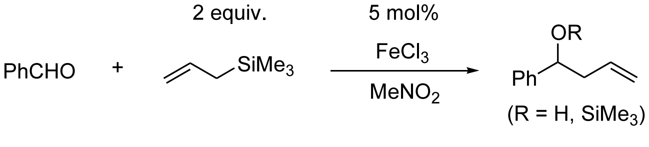
Abstract—Iron(III) chloride-catalyzed allylation reactions of a variety of aldehydes with allyltrimethylsilane proceeded efficiently and smoothly to afford the corresponding homoallyl alcohols in high to excellent yields. This novel method could be suitable especially for the allylation of sterically hindered aliphatic aldehydes. © 2002 Elsevier Science Ltd. All rights reserved.

Lewis acid catalyzed allylations of aldehydes with allylic metal reagents are an important carbon-carbon bond forming reaction, since they give synthetically useful homoallyl alcohols.[1] Among various allylic metal reagents, allyltrialkylsilanes are inexpensive and non-toxic compounds compared to allylstannanes, and many allylation reactions using allylsilanes have been developed.[2] In these reactions, traditional Lewis acids such as $TiCl_4$, $BF_3{\cdot}OEt_2$, and $SnCl_4$ have been generally used, though stoichiometric or near-stoichiometric amounts of Lewis acid were required to perform the reaction completely for the reason that the alcohol oxygen atom coordinates tightly to the Lewis acid.[3] Recently, various rare earth metal triflates such as $Sc(OTf)_3$, $La(OTf)_3$, and $Yb(OTf)_3$ were known to be utilized as Lewis acid catalysts to promote the allylation reactions.[4] However, these cases involve some annoying problems: (1) use of very expensive Lewis acids; (2) longer reaction time; (3) lower yields of allylation products in the case of aliphatic aldehydes; and (4) substrate limitation, and so on. Therefore, we have been interested in developing a highly efficient and widely applicable allylation reaction using an inexpensive Lewis acid catalyst.

Iron is an abundant, cheap, and benign element which exists in nature, and many reactions using iron salts have been developed recently in organic synthesis.[5] Nevertheless, an $FeCl_3$-catalyzed allylation reaction has not been reported so far.[6] Herein we wish to report a highly efficient and convenient procedure for the allylation of various aldehydes with allyltrimethylsilane in the presence of a catalytic amount of $FeCl_3$.

Initially, we examined the reaction of benzaldehyde with 2 equiv. of allyltrimethylsilane in the presence of 5 mol% of anhydrous $FeCl_3$[7] in $MeNO_2$ at room temperature; however, the corresponding homoallyl alcohol was scarcely obtained (Table 1, Run 1), because over-allylation products, such as **1** and **2** (Fig. 1),[4c,8] were formed in moderate yields (48 and 18%, respectively). To control the reactivity of this allylation reaction, we tested the reaction temperature. Predictably, the yields of desired product could be improved and the formation of side products suppressed by lowering the reac-

Table 1. The effect of reaction temperature



Run	Temp. (°C)	Time (h)	Yield[a] (%)
1	rt	2	0
2	0	2	54
3	−20	1	66
4	−29	1	69

[a] Combined yields of alcohol and silyl ether.

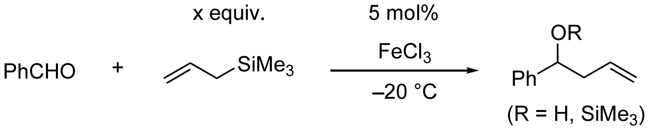
Figure 1. Over-allylation products.

---

* Corresponding author.

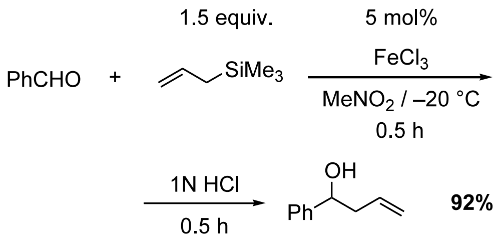
PII: S0040-4039(02)02107-X

Table 2. The effect of solvent



Run	*x* (equiv.)	Solvent	Time (h)	Yield[a] (%)
1	2	$MeNO_2$	1	66
2	2	CH_2Cl_2	1	33
3	2	MeCN	4	0
4	2	THF	4	0
5	1.5	$MeNO_2$	1	81
6	1.1	$MeNO_2$	16	55

[a] Combined yields of alcohol and silyl ether.



Scheme 1. Allylation of benzaldehyde catalyzed by $FeCl_3$.

tion temperature. It was found that the reaction proceeded smoothly at –20°C and the desired allylation product was given in 66% yield (Run 3).

Next, we investigated the effect of solvents and the loading of allyltrimethylsilane, and these experimental results are shown in Table 2. In the case of using CH_2Cl_2, the corresponding allylation product was obtained in lower yield (Run 2). On the other hand, when MeCN and THF were used as a solvent, no reaction occurred (Runs 3 and 4). Thus, $MeNO_2$ turned out to be the most effective solvent in this reaction. Additionally, when the reaction was carried out with 1.5 equivalents of allylsilane, the reaction proceeded very cleanly compared to using 2 equiv. of allylsilane (Run 5). As depicted in the Scheme 1, by shortening the reaction time (0.5 h) and with the treatment of 1N HCl solution for desilylation after allylation, the corresponding homoallyl alcohol could be isolated in excellent yield (92%).

Representative and successful examples for the syntheses of various homoallyl alcohols from aromatic and aliphatic aldehydes are collected in Table 3.[9] Electron-deficient aromatic aldehydes were allylated in excellent yields (Runs 1–6). However, in the case of electron-rich aromatic aldehydes such as *p*-anisaldehyde and *p*-tolualdehyde, over-allylation occurred via a stabilized benzylic cation (Run 8–11). In contrast, $FeCl_3$ catalyzed reaction of acetal with allylsilane gave satisfactory result. That is, the corresponding allylated product was obtained in 92% yield by the treatment of *p*-anisaldehyde dimethyl acetal with allyltrimethylsilane promoted by 5 mol% $FeCl_3$ (Scheme 2). In general, it is anticipated that the allylation of an aliphatic aldehyde is more difficult than that of an aromatic aldehyde because of the higher electron density of the carbonyl group. Fortunately, aliphatic aldehydes could be allylated in high yields with only 5 mol% of $FeCl_3$ at room temperature (Runs 12–17). Especially, it should be noted that sterically hindered aldehydes, such as diphenylacetaldehyde and trimethylacetaldehyde, which branched at the α-position to the carbonyl group, were transformed smoothly into the corresponding homoallyl alcohols in excellent yields (Runs 14–17). Furthermore, we also investigated the diastereoselective allylation of aldehyde having a chiral center (Run 15). Although the stereoselectivity was not satisfactory (*syn*:*anti* = 1.8:1) considering Cram's rule, this was almost equal to the results reported so far on the allylation promoted by $TiCl_4$, $BF_3·OEt_2$, and $SnCl_4$.[10]

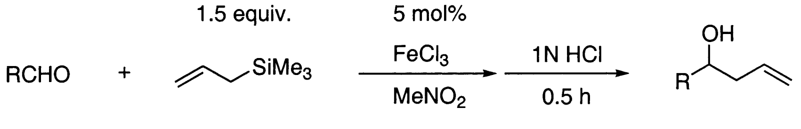
In conclusion, we have presented a highly efficient and powerful method for the allylation of aldehyde with allyltrimethylsilane catalyzed by $FeCl_3$. This reaction took place smoothly using only 5 mol% of $FeCl_3$ and could be applied to a broad range of aldehydes and, especially, very hindered aliphatic aldehydes could be allylated efficiently at room temperature. Additionally, $FeCl_3$ is a very cheap Lewis acid, so this method can be utilized for an economical allylation reaction. These features show that this new method is very practical and will be applicable to the synthesis of various complex natural products.

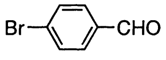
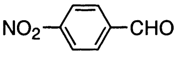
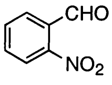
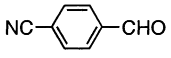
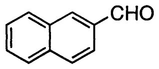
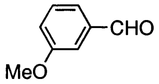
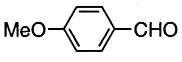
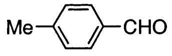
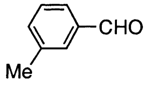
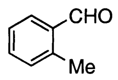
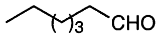
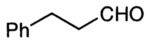
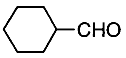
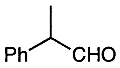
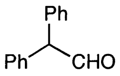
Acknowledgements

T.W. thanks the Sasakawa Scientific Research Grant from The Japan Science Society for generous financial support.

Scheme 2. Allylation of *p*-anisaldehyde dimethyl acetal catalyzed by $FeCl_3$.

Table 3. Allylation of various aldehydes



Run	RCHO	Method a)	Yield b) / %
1	PhCHO	A	92
2		A	98
3		A	98
4		A	99
5		A	99
6 c)		A	86
7		A	92
8		A	0
9 c)		A	18
10 c)		A	80
11 c)		A	70
12		B	89
13		B	94
14		B	92
15 d)		B	99
16		B	92
17	*t*-BuCHO	B	99

a) Method A: –20 °C, 0.5 h. Method B: r t, 1 h. b) Isolated yields of purified product. c) 2 mol% of $FeCl_3$ was used.
d) *Syn* : *anti* = 1.8 : 1 (Determined by ^{1}H NMR analysis.)

References

1. For leading review, see: (a) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207; (b) Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293; (c) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31. (d) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063.
2. (a) Hollis, T. K.; Robinson, N. P.; Whelan, J.; Bosnich, B. *Tetrahedron Lett.* **1993**, *34*, 4309; (b) Maeta, H.; Nagasawa, T.; Handa, Y.; Takei, T.; Osamura, Y.; Suzuki, K. *Tetrahedron Lett.* **1995**, *36*, 899; (c) Gauthier, D. R.; Carreira, E. M. *Angew. Chem.* **1996**, *108*, 2521; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2363; (d) Kaur, G.; Manju, K.; Trehan, S. *Chem. Commun.* **1996**, 581; (e) Komatsu, N.; Uda, M.; Suzuki, H. *Tetrahedron Lett.* **1997**, *38*, 7215; (f) Marx, A.; Yamamoto, H. *Angew. Chem. Int. Ed.* **2000**, *39*, 178; (g) Yasuda, M.; Onishi, Y.; Ito, T.; Baba, A. *Tetrahedron Lett.* **2000**, *41*, 2425; (h) Yadav, J. S.; Chand, P. K.; Anjaneyulu, S. *Tetrahedron Lett.* **2002**, *43*, 3783.
3. (a) Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1976**, 1295; (b) Hayashi, T.; Kabeta, K.; Hamachi, I.; Kumada, M. *Tetrahedron Lett.* **1983**, *24*, 2865; (c) Denmark, S. E.; Henke, B. R.; Weber, E. J. *J. Am. Chem. Soc.* **1987**, *109*, 2512; (d) Nishigaichi, Y.; Takuwa, A.; Jodai, A. *Tetrahedron Lett.* **1991**, *32*, 2383; (e) Yanagisawa, A.; Morodome, M.; Nakashima, H.; Yamamoto, H. *Synlett* **1997**, 1309.
4. Allylation of aldehydes with allylsilanes: (a) Aggarwal, V. K.; Vennall, G. P. *Tetrahedron Lett.* **1996**, *37*, 3745; (b) Yang, Y.; Wang, M.; Wang, D. *Chem. Commun.* **1997**, 1651; (c) Aggarwal, V. K.; Vennall, G. P. *Synthesis* **1998**, 1822. With allylstannanes: (d) Hachiya, I.; Kobayashi, S. *J. Org. Chem.* **1993**, *58*, 6958; (e) Aspinall, H. C.; Browning, A. F.; Greeves, N.; Ravenscroft, P. *Tetrahedron Lett.* **1994**, *35*, 4639; (f) Aspinall, H. C.; Greeves, N.; McIver, E. G. *Tetrahedron Lett.* **1998**, *39*, 9283; (g) Aspinall, H. C.; Bissett, J. S.; Greeves, N.; Levin, D. *Tetrahedron Lett.* **2002**, *43*, 319. With allylgermane: (h) Akiyama, T.; Iwai, J.; Sugano, M. *Tetrahedron* **1999**, *55*, 7499.
5. (a) Iranpoor, N.; Salehi, P. *Synthesis* **1994**, 1152; (b) Christoffers, J. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3141; (c) Barton, D. H. R.; Hill, D. R.; Hu, B. *Tetrahedron Lett.* **1997**, *38*, 1711; (d) Salehi, P.; Iranpoor, N.; Behbahani, F. K. *Tetrahedron* **1998**, *54*, 943; (e) Sen, S. E.;

Roach, S. L.; Smith, S. M.; Zhang, Y. Z. *Tetrahedron Lett*. **1998**, *39*, 3969; (f) Sharma, G. V. M.; Mahalingam, A. K.; Nagarajan, M.; Ilangovan, A.; Radhakrishna, P. *Synlett* **1999**, 1200; (g) Barrett, I. C.; Langille, J. D.; Kerr, M. A. *J. Org. Chem*. **2000**, *65*, 6268; (h) Chibiryaev, A. M.; Kimpe, N. D.; Tkachev, A. V. *Tetrahedron Lett*. **2000**, *41*, 8011; (i) Yus, M.; Pastor, I. M.; Gomis, J. *Tetrahedron* **2001**, *57*, 5799; (j) Sharma, G. V. M.; Kumar, K. R.; Sreenivas, P.; Krishna, P. R.; Chorghade, M. S. *Tetrahedron: Asymmetry* **2002**, *13*, 687; (k) Vidari, G.; Beszant, S.; Merabet, J. E.; Bovolenta, M.; Zanoni, G. *Tetrahedron Lett*. **2002**, *43*, 2687.

6. Nucleophilic additions of allylic metal reagents promoted by stoichiometric amounts of $FeCl_3$: (a) Denmark, S. E.; Weber, E. J. *Helv. Chim. Acta*. **1983**, *66*, 1655; (b) Denmark, S. E.; Weber, E. J.; Wilson, T. M.; Willson, T. M. *Tetrahedron* **1989**, *45*, 1053; (c) Kang, K.-T.; Kim, S. S.; Lee, J. C.; U, J. S. *Tetrahedron Lett*. **1992**, *33*, 3495; (d) Kuroda, C.; Koshio, H.; Koito, A.; Sumiya, H.; Murase, A.; Hirono, Y. *Tetrahedron* **2000**, *56*, 6441.
7. $FeCl_3$ was purchased from Aldrich Company.
8. (a) Ishii, A.; Kotera, O.; Saeki, T.; Mikami, K. *Synlett* **1997**, 1145; (b) Fang, X.; Watkin, J. G.; Warner, B. P. *Tetrahedron Lett*. **2000**, *41*, 447.
9. A typical experimental procedure is as follows (Table 3, Run 1): To a solution of $FeCl_3$ (5.4 mg, 0.033 mmol) in $MeNO_2$ (1.0 ml) were added allyltrimethylsilane (159 μl, 1.00 mmol) and a solution of benzaldehyde (76.3 mg, 0.66 mmol) in $MeNO_2$ (1.0 ml) at −20°C under argon atmosphere. After stirring the reaction mixture for 0.5 h, 1N HCl (2.0 ml) was added and the reaction was allowed to warm to room temperature. The resultant mixture was stirred for an additional 0.5 h and poured into saturated sodium hydrogencarbonate. The organic materials were extracted with Et_2O and dried over anhydrous magnesium sulfate. The solvent was evaporated and 1-phenyl-3-buten-1-ol (90.0 mg, 92%) was isolated by thin-layer chromatography on silica gel (ether:hexane = 1:1). The product gave satisfactory ^1H NMR and IR spectra.
10. (a) Heathcock, C. H.; Kiyooka, S.; Blumenkopf, T. A. *J. Org. Chem*. **1984**, *49*, 4214; (b) Davis, A. P.; Jaspars, M. *J. Chem. Soc*., *Perkin Trans. 1* **1992**, 2111.