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Highly efficient iron-catalyzed allylation of aromatic aldehydes with allyltriethoxysilane: one-pot and practical synthesis of homoallyl ethers

Ming-Song Yang[a], Li-Wen Xu[a,b*], Fei-Bao Zhang[a], Hua-Yu Qiu[a*], Jian-Xiong Jiang[a] and Guo-Qiao Lai[a]

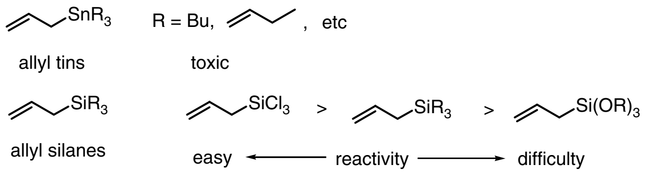
$FeCl_3$ was found to be an active catalyst for the one-pot allylation reaction of aromatic aldehydes with allyltriethoxysilane under mild and simple conditions, which resulted in the direct synthesis of homoallyl ethers with very high chemoselectivity and yields. Various types of homoallyl ethers were obtained in excellent yields (up to 99%). Copyright © 2008 John Wiley & Sons, Ltd.

Keywords: Sakurai reaction; allylation; allyltriethoxysilane; homoallyl ether; iron

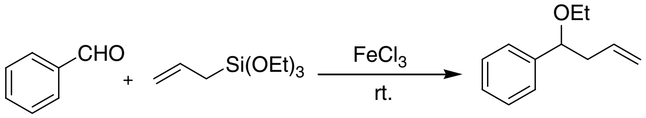
Introduction

Allylation of carbonyl compounds is one of the most interesting processes in organic synthesis, in most cases for the preparation of homoallylic alcohols that can be widely used in the synthesis of biological active compounds.[1,2] The allylation of carbonyl compounds with different organometallic allyl reagents under Lewis acid conditions has been extensively used for the formation of important carbon–carbon bonds.[3] Over the past few decades, many reagents have been developed for such reactions, for example, allyl tins[4–7] and allyl silanes[8–17] (Scheme 1), which are very useful because of their moderate reactivity, which can be increased by catalyst activation and thus allows for application to catalytic enantioslective reactions. In the past, the allylation reaction of carbonyl compounds from allylstannanes and allylsilanes, was always promoted by stoichiometric amounts of a conventional Lewis acid such as $TiCl_4$, $SnCl_4$, $AlCl_3$, fluoride ions (TBAF), lanthanide triflate, trimethylsilyl triflate (TMSOTf), Bronsted acids and Lewis base.[4–21] However, because allylstannanes and chloride allylsilanes are both toxic and moisture-sensitive, trimethyl allylsilanes are generally more desirable for the allylation of carbonyl compounds (the Sakurai–Hosomi reaction) in organic synthesis.[22,23]

The low reactivity of allyltrialkyloxysilanes has limited their synthetic utility.[24–27] Only AgF and CuCl-TMAT, catalyst systems with fluoride anions, have been reported for the allylation of aldehyde using allyltrialkyloxysilanes. However, it is should be noted that there is no report that homoallyl ethers can be prepared from the one-pot allylation of aldehyde using allyltriethoxylsilane. In the past, the homoallyl ethers were prepared by the Lewis acid-catalyzed allylation of acetals.[28–36] Most of these methods involve some problems, such as that the utilization of stoichiometric amounts of catalysts from aldehydes requires a two-step conversion comprising acetalization of aldehydes and subsequent allylation of acetals. Although the allylation reactions have attracted considerable attention, many catalyst systems that are effective in the allylation of aldehydes with allyltrimethylsilane and allyltrichlorosilane often fail with allyltriethoxysilane. As a result, the development of novel catalyst for one-pot synthesis of homoallyl ethers is interesting. In our search for an economical, efficient Sakurai-type allylation with allylsilane, we became intrigued by the idea of using a catalytic



Scheme 1. Different organometallic allyl regeants.



Scheme 2. Iron-catalyzed allylation of benzaldehyde with allyltriethoxysilane.

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* Correspondence to: Li-Wen Xu and Hua-Yu Qiu, Key Laboratory of Organosilicon Chemistry and Material Technology of Ministry of Education, Hangzhou Normal University, Hangzhou 310012, People's Republic of China. E-mail: chmxlw@nus.edu.sg

a Key Laboratory of Organosilicon Chemistry and Material Technology of Ministry of Education, Hangzhou Normal University, Hangzhou 310012, People's Republic of China

b Department of Chemistry, National University of Singapore, 3 Science Drive 3, Singapore 117543, Republic of Singapore

amount of cheap, readily available and low toxicity $FeCl_3$ in this reaction. As an extension of previous studies of $FeCl_3$-catalyzed organic transformations in our group,[37–40] herein, we report our findings for the development of a novel iron-catalyzed allylation using allyltriethoxysilane.

Results and Discussions

To establish an effective catalytic condition, we surveyed many transition metal-based catalysts in this allylation reaction of benzaldehyde with allyltriethoxysilane. Among the Lewis acid and Brønsted acids tested, $FeCl_3$ catalyzed the reaction most efficiently (Table 1, entry 1). The use of 5 and 1 mol% of $FeCl_3$ was not sufficient to carry out the reaction, and the yields of desired products were decreased (up to 20%, entry 8). We studied the reaction under different conditions and the results were satisfactory in most cases (Table 1). Suitable solvents for this reaction were found to be dichloromethane, acetonitrile and nitromethane. Nitromethane was a better solvent in terms of yields than other solvents tested (Table 1, entry 6). However, toluene, methanol and tetrahydrofuran were not suitable solvents for this reaction (Table 1, entries 3–5), and with the increase in the amount of alcohol (for example, EtOH) in the nitromethane, the yield was decreased (entries 10 and 11).

Encouraged by this result, we carried out the reaction with various aldehydes. The results are collected in Table 2. The allylation of aldehydes proceeded cleanly in most cases (up to 99%). To demonstrate the efficiency of the $FeCl_3$ with various aromatic aldehydes, substituted aryl aldehydes were used in the optimized procedures (Table 2). Interestingly, the yields of *p*-methoxylbenzaldehyde were very low;[8] this unexpected finding may be due to the different reactivity in the first transformation to hemiacetal, which will be studied in the next step.

It is well known that the reactivity of allyltrialkyloxysilanes is very low. When methanol or ethanol was used as solvent, acetal [1-(dimethoxymethyl)benzene or 1-(diethoxymethyl)benzene] was obtained in excellent yield. Unfortunately, the allyltriethoxylsilane did not react with the acetal under our conditions (Scheme 3).

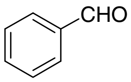
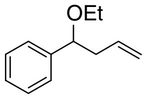
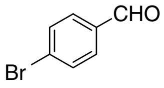
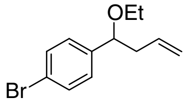
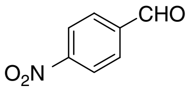
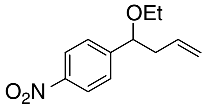
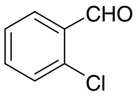
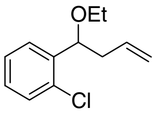
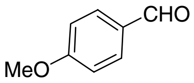
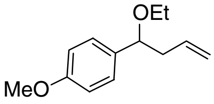
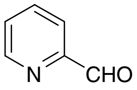
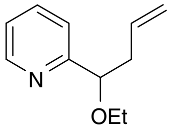
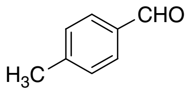
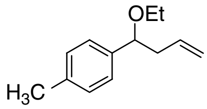
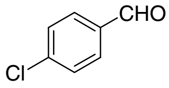
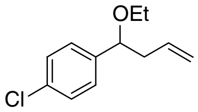
Table 1. $FeCl_3$-catalyzed allylation of benzaldehyde using allyltriethoxysilane under different conditions

Entry[a]	$FeCl_3$ (%)	Allylsilane (equiv.)	Solvent	*T* (h)	Yield (%)[b]
1	10	1.5	CH_2Cl_2	3	80
2	10	1.5	CH_3CN	3	84
3	10	1.5	THF	3	trace
4	10	1.5	CH_3OH	3	trace[c]
5	10	1.5	Toluene	3	0
6	10	1.5	CH_3NO_2	0.5	98[d]
7	1	1.5	CH_3NO_2	3	trace
8	5	1.5	CH_3NO_2	3	20
9	10	1.1	CH_3NO_2	3	97
10	10	1.1	CH_3NO_2	3	98[e]
11	10	1.1	CH_3NO_2	3	70[f]

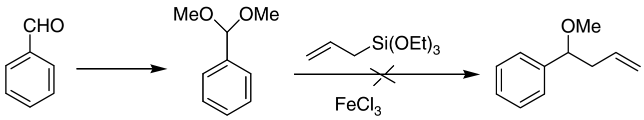
[a] Reaction conditions: 1.0 mmol of aldehyde, 1.5 mmol of allylsilane, 2 ml of solvent (CH_2Cl_2), at room temperature, under atmospheric pressure. [b] GC yield using an initial standard. [c] Acetal was detected and obtained in excellent yield. [d] Isolated yield. [e] Addition of 1 or 10 mol% EtOH. [f] Addition of 100 mol% EtOH.

Although the reaction mechanism of the present catalytic system has not yet been fully elucidated, our studies have suggested that trace water from the atmosphere was crucial to this reaction. When reactions were carried out in a Schlenk tube, which was dried and filled with N_2, none of the desired product was obtained. We also treated the homoallyl alcohol under the reaction conditions, and found that no desired product was obtained, which showed that the homoallyl ethers were not generated from the corresponding homoallic alcohols. From these results, we assumed that the addition was proposed via

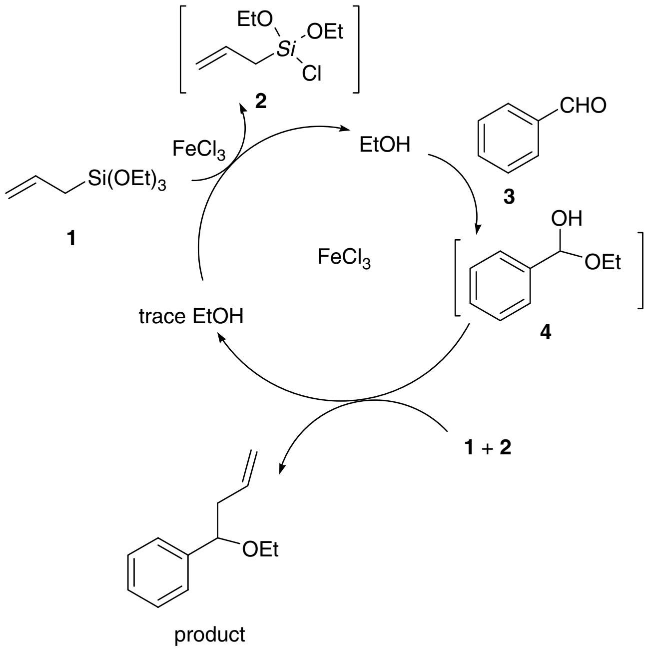
Table 2. $FeCl_3$-catalyzed allylation of aldehyde using allyltriethoxysilane

Entry[a]	Aldehyde	Product	Yield (%)[b]
1			98
2			98
3			97
4			98
5			16
6			NR
7			91[c]
8			90[c]

[a] Reaction conditions: 1.0 mmol of aldehyde, 1.5 mmol of allylsilane, 2 ml of solvent (CH_2Cl_2), at room temperature, under atmospheric pressure. [b] Isolated yield. [c] H-NMR yield.



Scheme 3. Unsuccessful allylation of aldehydes with allyltriethoxysilane in MeOH.



Scheme 4. Possible mechanism of catalytic allylation in the preparation of homoallyl ether.

the intermediate by the Lewis acid catalyst ($FeCl_3$) as well as by activation of the allyltriethoxysilane, as depicted in Scheme 4. At the first step, the allyltriethoxysilane was hydrolyzed to produce ethanol under atmospheric humidity. The trace ethanol reacted easily with aldehyde to produce the unstable and more reactive hemiacetal, which reacted easily with allyltriethoxysilane. To clarify the importance of trace water or ethanol in this reaction, we added trace EtOH (1mol% or 10 mol%) instead of water. We found that the yield of the reaction was very good, and the same result was obtained. It should be noted that larger amounts of water and alcohol were also disadvantageous to this reaction because allyltrialkyloxysilane was hydrolyzed to produce cross-linked product and aldehyde was tranferred to acetal, which did not easily react with each other under the present conditions.

Conclusion

In summary, we have developed a catalytic allylation of aldehydes using allyltriethoxylsilane. $FeCl_3$ was found to be an active catalyst for the allylation, under mild and simple conditions, of aromatic aldehydes with allyltriethoxysilane, which resulted in the unexpected and efficient synthesis of homoallyl ethers with very high chemoselectivity. It is a good example of one-pot synthesis of homoallyl ether via allylation of aldehydes directly. We anticipate that this work will provide a useful and practical method for the preparation of homoallyl ethers.

Experimental Section

General procedure for the allylation of aldehydes with allyltriethoxysilane

$FeCl_3$ (0.1 mmol) was added into a solution of aldehyde (1.0 mmol) and allyltriethoxysilane (1.5 mmol) in CH_2Cl_2 (3 ml). After stirring at room temperature for 3 h, the mixture was diluted with H_2O (10 ml) and extracted with EtOAc (3 × 15 ml). The combined organic layers were washed with aqueous HCl and then washed with aqueous $NaHCO_3$; the organic layer was dried (Na_2SO_4), concentrated *in vacuo* and purified by column chromatography on silica gel (EtOAc-petro ether, 1 : 20) to gain the pure product. All the known products were fully characterized by GC-MS and the usual spectral methods (NMR and IR).

Selected spectra data of products

1-(1-ethoxybut-3-enyl)benzene (Table 2, entry 1): ^{1}H-NMR (400 MHz, $CDCl_3$, ppm), $\delta = 7.30$(m, 5H), 5.77(m, 1H), 5.34(m, 2H), 4.26(t, $J = 8$ Hz, 1H), 3.36 (m, 2H), 2.57(m, 1H), 2.40(m, 1H), 1.18(t, $J = 8$ Hz, 3H).^{13}C-NMR (100 MHz, $CDCl_3$, ppm): $\delta = 142.26$, 134.84, 128.12, 127.28, 126.48, 116.53, 81.64, 63.94, 42.29, 15.12. GC-MS: *m/z* 176(M), 135(100), 107(79), 79(63). 1-Bromo-4-(1-ethoxybut-3-enyl)benzene (Table 2, entry 2): ^{1}H-NMR (400 MHz, $CDCl_3$, ppm), $\delta = 7.46$(d, $J = 8.0$ Hz, 2H), 7.18 (d, $J = 8.0$ Hz, 2H), 5.74 (m, 1H), 5.02 (m, 2H), 4.23 (t, $J = 6.0$ Hz, 1H), 3.34 (m, 2H), 2.54 (m, 1H), 2.35 (m, 1H), 1.17 (t, $J = 8.0$ Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$, ppm): $\delta = 141.33$, 134.28, 131.26, 128.22, 121.02, 116.95, 81.00, 64.08, 42.32, 15.10. GC-MS: *m/z* 254–256(M, 255), 215(92), 213(100), 187(75), 185(89), 157(32), 77(62). 1-(1-ethoxybut-3-enyl)-4-nitrobenzene (Table 2, entry 3): ^{1}H-NMR (400 MHz, $CDCl_3$, ppm), $\delta = 8.21$(d, J = 8 Hz, 2H), 7.47(d, $J = 8$ Hz, 2H), 5.75 (m, 1H), 5.03 (m, 2H), 4.39 (t, $J = 8$ Hz, 1H), 3.39 (m, 2H), 2.57 (m, 1H), 2.41(m, 1H), 1.21 (t, $J = 8$ Hz, 3H).^{13}C-NMR (100 MHz, $CDCl_3$, ppm): $\delta = 150.02$, 147.20, 133.50, 127.18, 123.45, 117.56, 80.76, 64.61, 42.17, 15.09. GC-MS: *m/z* 221(M), 180(85), 152(100). 1-Chloro-2-(1-ethoxybut-3-enyl)benzene (Table 2, entry 4): ^{1}H-NMR (400 MHz, $CDCl_3$, ppm), $\delta = 7.49$(m, 1H), 7.30(m, 2H), 7.20(m, 1H), 5.87(m, 1H), 5.05(m, 2H), 3.87(m, 1H), 3.38(m, 2H), 2.46(m, 2H), 1.19(t, $J = 8$ Hz, 3H).^{13}C-NMR (100 MHz, $CDCl_3$, ppm): $\delta = 139.88$, 134.51, 132.62, 129.13, 128.14, 127.28, 126.83, 116.68, 77.40, 64.40, 40.94, 15.09. GC-MS: *m/z* 210–212 (M, 210), 171(28), 169(84), 141(100), 113(30).

Acknowledgments

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