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Iron(III) *p*-toluenesulfonate catalyzed synthesis of homoallyl ethers from acetals and aldehydes

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Abstract—Iron(III) *p*-toluenesulfonate, $Fe(OTs)_3 \cdot 6H_2O$, is an inexpensive, versatile and commercially available catalyst for the allylation of acetals using allyltrimethylsilane to yield homoallyl ethers in moderate to good yields. The one-pot conversion of aldehydes to homoallyl ethers using alkoxysilanes has also been accomplished using $Fe(OTs)_3 \cdot 6H_2O$ as a catalyst. The use of mild reaction conditions and a relatively non-corrosive catalyst make this method an attractive option for the synthesis of a range of homoallyl ethers.

The synthesis of homoallyl ethers from acetals and aldehydes has attracted considerable attention. The allylation of acetals using organosilicon reagents is a useful method to generate homoallyl ethers and hence several catalysts have been used to effect this transformation. These include $TiCl_4$,[1] $AlCl_3$,[2] $BF_3 \cdot Et_2O$,[2] trityl perchlorate,[3] diphenylboryltriflate,[3] montmorillonite,[4] trimethylsilylbis(fluorosulfonyl)imide,[5] $(CH_3)_3SiI$,[6] TMSOTf,[7] $TiCp_2(CF_3SO_3)_2$,[8] tris(*p*-bromophenyl)aminium hexachloroantimonate,[9] triarylpyrilium salts,[10] trimethylsilylbis(trifluoromethanesulfonyl)amide,[11] $BiBr_3$,[12] $Sc(OTf)_3$,[13] and $Bi(OTf)_3 \cdot xH_2O$.[14] Many acetals are not commercially available and must be synthesized from the corresponding aldehyde. In addition, most of these methods only report allylation of dimethyl or diethyl acetals, which results in the formation of homoallyl methyl or ethyl ethers. Although the alkene moiety of homoallyl alkyl ethers can be easily transformed into other groups, alkyl ethers are somewhat inert and not amenable to easy synthetic manipulation. Another disadvantage of this approach is that many acetals have poor shelf lives. Hence the synthesis of homoallyl ethers directly from aldehydes would be advantageous. However, there are very few reports of the one-pot syntheses of homoallyl ethers from aldehydes.[15] Further, many of these methods require the use of corrosive catalysts such as TMS triflate, $TiCl_4$ or rather moisture-sensitive catalysts such as $AlCl_3$ or $Sc(OTf)_3$. An environmentally friendly approach to the synthesis of homoallyl benzyl ethers in which the acetal is generated in situ from the corresponding aldehyde using $FeCl_3$ as the catalyst has been reported.[16] Our continued interest in developing synthetic methodology using mild and efficient Lewis acid catalysts[17] prompted us to investigate the utility of iron(III) *p*-toluenesulfonate, $Fe(OTs)_3 \cdot 6H_2O$, as a catalyst for allylation reactions using allyltrimethylsilane. Although the synthesis of several transition metal tosylates has been described[18] and iron(III) tosylate is commercially available, there are only a few reports of the use of transition metal tosylates as catalysts in organic synthesis. Herein we report the use of iron(III) tosylate as an efficient catalyst for the allylation of acetals and also for the one-pot conversion of aldehydes to a range of homoallyl ethers. The mild reaction conditions and the use of a relatively non-toxic catalyst make this method attractive for the synthesis of homoallyl ethers.

We first investigated the allylation of acetals using allyltrimethylsilane catalyzed by $Fe(OTs)_3 \cdot 6H_2O$ (2.0–10.0 mol %) in CH_3CN at room temperature (Table 1). The reaction worked with a range of acetals in relatively short reaction times. The reactions worked better in CH_3CN than in CH_2Cl_2.

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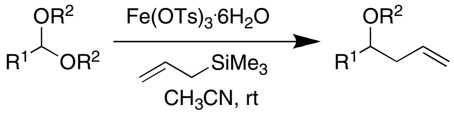
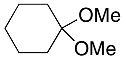
Table 1. Iron(III) tosylate catalyzed allylation of acetals[19]



Entry	R^1[a]	R^2	Allylsilane (equiv)	Mol % cat	Time	Yield[b,c] (%)
1	Ph	Me	2.0	10.0	1 h 20 min	70[16]
2	m-$\mathrm{BrC_6H_4}$	Et	1.5	5.0	1 h 10 min	89[d,14b]
3	p-$\mathrm{ClC_6H_4}$	Me	1.5	5.0	4 h	79[20]
4	p-$\mathrm{MeOC_6H_4}$	Me	1.5	2.0	1 h 30 min	76[16]
5	$\mathrm{PhCH_2}$–	Me	2.0	5.0	18 h	61[e,20]
6	$\mathrm{CH_3(CH_2)_{10}}$–	Me	1.7	2.0	19 h	97[d,21]
7		Me	2.0	10.0	23 h	55[20]

[a] Acetals were purchased commercially or synthesized in laboratory by literature methods.[22]

[b] Isolated yield. Unless otherwise mentioned, the crude product was found to be >97% pure and hence further purification was deemed unnecessary.

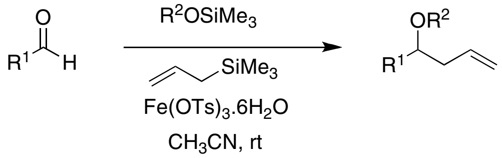
[c] All products have been previously reported in the literature. Superscript numbers against yields refer to literature reference for the product.

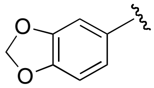
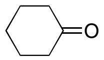
[d] Purified by flash chromatography.

[e] Product was determined to be 95% pure by GC and NMR analysis.

The methodology was then extended to the one-pot conversion of aldehydes to homoallyl ethers using alkoxysilanes. Since a wide range of alkoxysilanes is commercially available, this approach allowed the synthesis of a variety of homoallyl ethers (Table 2). The reaction worked with both aromatic and aliphatic aldehydes. The reaction of cinnamaldehyde (Table 2, entry 1d) afforded the corresponding monoallylation product. In contrast, the use of $\mathrm{TiCl_4}$ as a catalyst for allylation of cinnamaldehyde dimethyl acetal gave only a mixture of diallylated products.[2a] Equal amounts of products arose from both 1,2 and 1,4 additions. Although the methodology was successful with cyclohexanone dimethyl acetal (Table 1, entry 7), attempts to allylate the dimethyl acetal of acetophenone resulted only in deprotection of the acetal to give acetophenone. Cyclohexanone (Table 2, entry 1f) was the only ketone with which the one-pot methodology was successful. As can be seen from Table 2, the methodology was successful with several alkoxysilanes that allowed the convenient

Table 2. Iron(III) tosylate catalyzed conversion of aldehydes to homoallyl ethers[23]



Entry	R^1	Alkoxysilane R^2 (equiv)	Allylsilane (equiv)	Mol % cat	Time	Yield[a,b] (%)
1a	p-$\mathrm{MeOC_6H_4}$	Me, 2.0	2.0	1.0	2 h	79
1b	p-$\mathrm{ClC_6H_4}$	Me, 1.5	1.7	5.0	1 h 30 min	86[c]
1c		Me, 1.7	1.7	5.0	5 h	69[c,d,10]
1d	PhCH=CH	Me, 1.7	1.7	5.0	15 h 15 min	66[16]
1e	$\mathrm{CH_3(CH_2)_8}$–	Me, 2.0	2.0	5.0	18 h	71[c,24]
1f		Me, 2.0	2.0	10.0	5 h	57
2	m-$\mathrm{BrC_6H_4}$	Et, 2.0	2.0	1.0	19 h	84
3a	p-$\mathrm{BrC_6H_4}$	$\mathrm{PhCH_2}$, 2.0	2.0	10.0	15 h 15 min	77[c,16]
3b	p-$\mathrm{MeO_2CC_6H_4}$	$\mathrm{PhCH_2}$, 2.0	2.0	5.0	16 h	72[c,16]
4a	Ph	Allyl, 1.5	1.5	5.0	3 h	88[25]
4b	p-$\mathrm{ClC_6H_4}$	Allyl, 1.5	1.5	5.0	21 h	84[25]

[a] Isolated yield. Unless otherwise mentioned, the crude product was found to be >97% pure and hence further purification was deemed unnecessary.

[b] All products have been previously reported in the literature. Superscript number against yield refers to literature reference for the product.

[c] Purified by flash chromatography.

[d] Although the product has been reported in the literature, its spectral data have not been previously reported ($\mathrm{CDCl_3}$, 270 MHz) δ 2.32–2.39 (m, 1H), 2.47–2.55 (m, 1H), 3.18 (s, 3H), 4.05 (t, 1H, $J = 6.18$ Hz), 4.97–5.06 (m, 2H), 5.71–5.78 (m, 1H), 5.94 (s, 2H), 6.72–6.80 (m, 3H); ^{13}C NMR (12 peaks) (67.5 MHz) δ 147.77, 146.91, 135.61, 134.67, 120.25, 116.79, 107.82, 106.67, 100.86, 83.31, 56.32, 42.42.

synthesis of homoallyl methyl ethers, homoallyl ethyl ethers, homoallyl allyl ethers and homoallyl benzyl ethers.

In summary, the synthesis of a range of homoallyl ethers from acetals and aldehydes has been accomplished using a commercially available, inexpensive and relatively non-corrosive catalyst, iron(III) tosylate.

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Supplementary data

General experimental section and copies of ^{1}H NMR and ^{13}C NMR spectra of all products. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.10.026.

References and notes

1. Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1976**, 941.
2. (a) Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1978**, 499; (b) Ojima, I.; Kumagai, M. *Chem. Lett.* **1978**, 575.
3. Mukaiyama, T.; Nagaoka, H.; Murakami, M.; Ohshima, M. *Chem. Lett.* **1985**, 977.
4. Kawai, M.; Onaka, M.; Izumi, Y. *Chem. Lett.* **1986**, 381.
5. Trehan, A.; Vij, A.; Walia, M.; Kaur, G.; Verma, R. D.; Trehan, S. *Tetrahedron Lett.* **1993**, *34*, 7335.
6. Sakurai, H.; Sasaki, K.; Hosomi, A. *Tetrahedron Lett.* **1981**, *22*, 745.
7. Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 71.
8. Hollis, T. K.; Robinson, N. P.; Whelan, J.; Bosnich, B. *Tetrahedron Lett.* **1993**, *34*, 4309.
9. Kamata, M.; Yokoyama, Y.; Karasawa, N.; Kato, M.; Hasegawa, E. *Tetrahedron Lett.* **1996**, *37*, 3483.
10. Kamata, M.; Nagai, S.; Kato, M.; Hasegawa, E. *Tetrahedron Lett.* **1996**, *37*, 7779.
11. Ishii, A.; Kotera, O.; Saeki, T.; Mikami, K. *Synlett* **1997**, 1145.
12. Komatsu, N.; Uda, M.; Suzuki, H.; Takahashi, T.; Domae, T.; Wada, M. *Tetrahedron Lett.* **1997**, *38*, 7215.
13. Yadav, J. S.; Subba Reddy, B. V.; Srihari, P. *Synlett* **2001**, 673.
14. (a) Anzalone, P. W.; Baru, A. R.; Danielson, E. M.; Hayes, P. D.; Nguyen, M. P.; Panico, A. F.; Smith, R. C.; Mohan, R. S. *J. Org. Chem.* **2005**, *70*, 2091; (b) Wieland, L. C.; Zerth, H. M.; Mohan, R. S. *Tetrahedron Lett.* **2002**, *43*, 4597.
15. (a) Sakurai, H.; Sasaki, K.; Hayashi, J.; Hosomi, A. *J. Org. Chem.* **1984**, *49*, 2808; (b) Mekhalfia, A.; Marko, I. E. *Tetrahedron Lett.* **1991**, *32*, 4779; (c) Wang, M. W.; Chen, Y. J.; Wang, D. *Synlett* **2000**, 385.
16. Watahiki, T.; Akabane, Y.; Mori, S.; Oriyama, T. *Org. Lett.* **2003**, *5*, 3045.
17. We have previously reported the bismuth(III) triflate catalyzed allylation of acetals and aldehydes (Ref. 14). Bismuth compounds are environmentally friendly catalysts because of their remarkably low toxicity.
18. Heintz, R. A.; Smith, J. A.; Szalay, P. S.; Weisberger, A.; Dunbar, K. R. In *Inorganic Syntheses*; Coucouvanis, D., Ed.; Wiley-Interscience: New York, NY, 2002; Vol. 33, Chapter 2, p 75.
19. *Typical procedure for allylation of acetals*: A solution of *p*-anisaldehyde dimethyl acetal (1.128 g, 6.190 mmol) in CH_3CN (20.0 mL) was stirred at rt as allyltrimethylsilane (1.060 g, 1.48 mL, 9.277 mmol, 1.50 equiv) and $Fe(OTs)_3\cdot 6H_2O$ (0.0838 g, 0.1237 mmol, 2.0 mol %) were added. The heterogeneous mixture was stirred at rt and the reaction progress was followed by GC. After 1 h 30 min, the reaction mixture was concentrated on a rotary evaporator and the residue was partitioned between ether (20.0 mL) and aqueous 10% Na_2CO_3 (15.0 mL). The aqueous layer was extracted again with ether (20.0 mL) and the combined organic extracts were washed with aqueous saturated NaCl (15.0 mL), dried (Na_2SO_4) and concentrated on a rotary evaporator to yield 1.124 g of a yellow oil. The crude product was purified by flash chromatography on 50 g of silica gel (EtOAc/hexanes, 5/95) to yield 0.899 g (76%) of the homoallyl methyl ether product as a colorless liquid. The product was determined to be >98% pure by GC, ^{1}H and ^{13}C NMR spectroscopy.
20. Jung, M. E.; Maderna, A. *J. Org. Chem.* **2004**, *69*, 7755.
21. Yoshida, J.; Sugawara, M.; Tatsumi, M.; Kise, N. *J. Org. Chem.* **1998**, *63*, 5950.
22. Leonard, N. M.; Oswald, M. C.; Freiberg, D. A.; Nattier, B. A.; Smith, R. C.; Mohan, R. S. *J. Org. Chem.* **2002**, *67*, 5202.
23. *Typical procedure for the one-pot conversion of aldehydes to homoallyl ethers*: A solution of *p*-bromobenzaldehyde (2.0320 g, 10.982 mmol) in CH_3CN (40.0 mL) was stirred at rt as allyltrimethylsilane (2.509 g, 3.49 mL, 21.959 mmol, 2.0 equiv), benzyloxytrimethylsilane (3.961 g, 4.32 mL, 21.967 mmol, 2.0 equiv), and $Fe(OTs)_3\cdot 6H_2O$ (0.7441 g, 1.0983 mmol, 10.0 mol %) were added sequentially. The heterogeneous mixture was stirred at rt and the reaction progress was followed by GC. After 15 h 15 min, the reaction mixture was concentrated on a rotary evaporator and the residue was partitioned between ether (25.0 mL) and aqueous 10% Na_2CO_3 (20.0 mL). The aqueous layer was extracted again with ether (25.0 mL) and the combined organic extracts were washed with aqueous saturated NaCl (20.0 mL), dried (Na_2SO_4) and concentrated on a rotary evaporator to yield 4.4105 g of a brownish liquid. The crude product was purified by flash chromatography on 250 g of silica gel (EtOAc/hexanes, 3/97) to yield 2.670 g (77%) of the homoallyl benzyl ether product as a colorless liquid. The product was determined to be >97% pure by GC, ^{1}H and ^{13}C NMR spectroscopy.
24. Miura, T.; Masaki, Y. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2155.
25. Huang, Y.-Z.; Liao, Y. *Heteroat. Chem.* **1991**, *2*, 297.