Trimethylsilyl Trifluoromethanesulfonate Catalyzed One-Pot Method for the Conversion of Aldehydes to Homoallyl Ethers in an Ionic Liquid

Peter W. Anzalone, Ram S. Mohan*

Laboratory for Environment Friendly Organic Synthesis, Department of Chemistry, Illinois Wesleyan University, Bloomington, IL 61701, USA
E-mail: rmohan@iwu.edu

Received 3 April 2005

Abstract: A mild method for the trimethylsilyl trifluoromethanesulfonate (TMSOTf) catalyzed one-pot synthesis of homoallyl ethers from aldehydes has been developed in the ionic liquid 1-butyl-3-methylimidazolium trifluoromethanesulfonate ([bmim][OTf]). The advantages of this method include the use of a recyclable ionic liquid, facile product isolation without employing excess organic solvent, elimination of an aqueous waste stream, and mild reaction conditions.

Keywords: ionic liquids, homoallyl ethers, aldehydes, allylations

Room temperature ionic liquids are becoming increasingly popular as solvents in organic synthesis for several reasons.[1,2] They are practically nonvolatile and, hence, do not pose the risks associated with volatile organic compounds. In addition, they are nonflammable and can be recycled easily without any significant loss in activity. Although ionic liquids have several attractive features, they do have some drawbacks. Ionic liquids are very expensive and often, reactions carried out in them require the use of generous amounts of organic solvents for product isolation. Hence, ionic liquids are attractive alternatives to organic solvents only when their use promotes new reaction pathways or allows for milder reaction conditions than would be otherwise possible. Herein, we report a versatile one-pot method for the conversion of aldehydes to homoallyl ethers in the ionic liquid 1-butyl-3-methylimidazolium trifluoromethanesulfonate ([bmim][OTf]), an alternative to dichloromethane, which is the typical solvent for allylations using allyltrimethylsilane. In addition, unique solubility properties of ionic liquids are taken advantage of to allow facile product isolation.

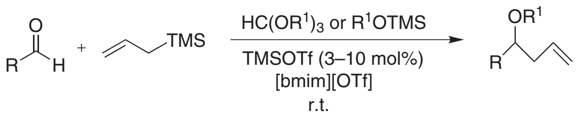
Homoallyl ethers are versatile functional groups amenable to further synthetic manipulation and, hence, their synthesis has attracted considerable attention. The allylation of acetals using organosilicon reagents is a useful method to generate homoallyl ethers and several catalysts have been used to effect this transformation. These include titanium(IV) chloride,[3] aluminum trichloride,[4] boron trifluoride–diethyl ether complex,[4] trityl perchlorate,[5] diphenylboryl trifluoromethanesulfonate,[5] montmorillonite,[6] lead/aluminum,[7] trimethylsilyl bis(fluorosulfonyl)imide,[8] iodotrimethylsilane,[9] trimethylsilyl trifluoromethanesulfonate (TMSOTf),[10] dicyclopentadienylbis(triflyloxy)titanium(IV) [$Ti(Cp)_2(CF_3SO_3)_2$],[11] trifluoroacetic acid,[12] bismuth tribromide,[13] trimethylsilyl bis(trifluoromethanesulfonyl)amide ($TMSNTf_2$),[14] scandium(III) trifluoromethanesulfonate,[15] indium metal,[16] and bismuth(III) trifluoromethanesulfonate.[17] One drawback of using acetals for the synthesis of homoallyl ethers is that they often have poor shelf lives or are not commercially available and need to be synthesized from the corresponding aldehyde. Hence, we were interested in developing a mild, one-pot synthesis of homoallyl ethers from aldehydes.[18]

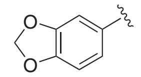
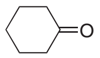
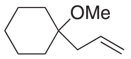
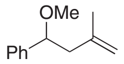
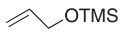
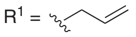
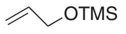
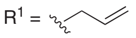
We now report a TMSOTf-catalyzed one-pot synthesis of homoallyl ethers from aldehydes in the ionic liquid [bmim][OTf] that allows facile product isolation and avoids an aqueous workup, thus eliminating an aqueous waste stream. When these reactions were done under solvent-free conditions, often an exothermic reaction occurred accompanied by the formation of black tar. Therefore, ionic liquids offer a convenient medium for these reactions. The results are summarized in Table 1. The reaction was effective with both allyltrimethylsilane and methallyltrimethylsilane (e.g., Table 1, entry 1g). Since the number of trialkylorthoformates that are commercially available is limited, we also investigated the use of alkoxytrimethylsilanes in the reaction; this allowed a wider range of homoallyl ethers to be synthesized. In addition, the reaction could be carried out with just 1.2 equivalents of the alkoxysilane (while 2.0 equivalents of the trialkylorthoformate were needed). The versatility of this method is illustrated by the synthesis of allyl homoallyl ethers (Table 1, entries 4a and 4b), which can serve as useful precursors to cyclic enol ethers via ring-closing metathesis reactions.[19]

The reaction is rapid at room temperature. The aldehydes are soluble in the ionic liquid, but the crude reaction product is only partially soluble and, hence, the bulk of the product separates rapidly from the ionic liquid as the reaction progresses. Besides the expected homoallyl ether, the crude product was found to contain unreacted allyltrimethylsilane and trialkylorthoformate or alkoxysilane. Although the bulk of crude product separates as a distinct layer, the recovered ionic liquid did contain up to 10% of the homoallyl ether product. In order to achieve complete separation, the ionic liquid was extracted with a minimal amount of diethyl ether (3 × 5 mL). If a homoallyl ether

SYNTHESIS 2005, No. 16, pp 2661–2663
Advanced online publication: 04.08.2005
DOI: 10.1055/s-2005-872112; Art ID: M02005SS

Table 1 One-Pot Method for the Conversion of Aldehydes to Homoallyl Ethers in [bmim][OTf][a]



Entry	Aldehyde R	TMSOTf (mol%)	Reagent	Homoallyl ether[b] R^1	Time (min)	Yield[c] (%)
1a	Ph	5	$HC(OMe)_3$	Me	10	78
1b	Tol	5	$HC(OMe)_3$	Me	30	88
1c	4-ClC_6H_4	5	$HC(OMe)_3$	Me	25	82
1d		3	$HC(OMe)_3$	Me	5	77
1e	$PhCH_2CH_2$	10	$HC(OMe)_3$	Me	120	48
1f[d]		5	$HC(OMe)_3$		80	44
1g[e]	Ph	0.5	$HC(OMe)_3$		10	74
2[f]	Tol	3	MeOTMS	Me	10	74
3	3-BrC_6H_4	6	EtOTMS	Et	10	97
4a[g]	Ph	3			5	81
4b[g]	4-ClC_6H_4	3			5	83

[a] Two equivalents of trialkylorthoformate or allyltrimethylsilane were used, unless otherwise mentioned.

[b] All products have been reported previously in the literature and were characterized by ^1H and ^{13}C NMR spectroscopy (see ref. 18e for entry 1e and 18f for all others).

[c] Refers to the yield of the isolated and purified product.

[d] Reaction was carried out using cyclohexanone as substrate; the full substrate and product are shown in this entry.

[e] Reaction was carried out using methallyltrimethylsilane in place of allyltrimethylsilane and 0.5 mol% TMSOTf; the full product is shown in this entry.

[f] Reaction was carried out using 1.2 equivalents of MeOTMS and 1.2 equivalents of allyltrimethylsilane.

[g] Reaction was carried out using 1.2 equivalents of allyloxytrimethylsilane and 1.2 equivalents of allyltrimethylsilane.

product is needed on a large scale, this procedure is especially attractive because the product can be easily separated from the ionic liquid using a separatory funnel. To the best of our knowledge, this is the first example of a reaction in an ionic liquid wherein product isolation can be achieved by taking advantage of the differential solubility of the starting material and product in the ionic liquid. The recovered ionic liquid was found to be effective in catalyzing subsequent reactions, although with each run the reaction took longer unless additional TMSOTf (1–2 mol%) was added, suggesting that some catalyst was being removed in the diethyl ether extractions.

The results with aliphatic aldehydes were less promising and the allylation required the use of 10 mol% catalyst. A moderate yield of the expected homoallyl ether product was obtained from 3-phenylpropionaldehyde (Table 1, entry 1e). Similarly, the results were less promising using cyclohexanone (Table 1, entry 1f) and complete conversion to the homoallyl ether could not be obtained even with increased catalyst loading. In summary, a mild method for the direct conversion of aldehydes into homoallyl ethers has been developed using TMSOTf as the catalyst in the ionic liquid [bmim][OTf].

1-Butyl-3-methylimidazolium trifluoromethanesulfonate was purchased from Acros Chemicals and stored in a vacuum desiccator (15 mmHg) at r.t. It was dried prior to use at 80 °C (0.1 mmHg) for 12 h. Reaction progress was followed by gas chromatography using a Varian CP 3800 capillary GC instrument equipped with a fused silica column (30 m × 0.25 mm ID). Products were analyzed by NMR spectroscopy on a JEOL 270 MHz (67.5 MHz for ^{13}C NMR) NMR spectrometer. Crude products were purified by flash column chromatography using silica gel.

Methyl 1-Phenylbut-3-enyl Ether; Typical Procedure:
A mixture of benzaldehyde (0.509 g, 4.80 mmol), $HC(OMe)_3$ (1.05 mL, 1.02 g, 9.59 mmol), and allyltrimethylsilane (1.51 mL, 1.10 g, 9.59 mmol) in [bmim][OTf] (2.0 mL, 2.59 g) was stirred at r.t. in a flame-dried round-bottom flask under N_2 as TMSOTf (43.4 μL, 0.2399 mmol) was added. After 10 min, the product (top layer) was separated from the ionic liquid using a separatory funnel. The ionic liquid was extracted with Et_2O (3 × 5 mL). The combined Et_2O extracts and the product layer were stirred with solid Na_2CO_3 (0.3 g) for 5 min, and then filtered and concentrated on a rotary evaporator to yield the crude product (1.13 g) as a clear, yellow oil [in an alter-

native workup, the reaction mixture was directly extracted with Et_2O (3 × 5 mL)]. The crude product was purified by column chromatography [silica gel (20 g), EtOAc–hexane 5:95] to yield the homoallyl ether as a colorless oil; yield: 0.604 g (78%) (>98% pure by ^1H and ^{13}C NMR spectroscopy and GC). The recovered ionic liquid (2.49 g) was stirred with powdered 4-Å sieves for 2 h, filtered, and heated under vacuum overnight (80 °C, 0.1 mmHg) prior to re-use.

Acknowledgment

We gratefully acknowledge funding from the National Science Foundation (RUI grant) and Research Corporation (Cottrell College Science Award). R.M. would also like to thank The Camille and Henry Dreyfus Foundation for a teacher-scholar award.

References

(1) (a) *Ionic Liquids in Organic Synthesis*; Wasserscheid, P.; Welton, T., Eds.; Wiley-VCH: Weinheim, **2003**. (b) *Ionic Liquids as Green Solvents*; Rogers, R. D.; Seddon, K. R., Eds.; ACS Symposium Series 856, American Chemical Society: Washington DC, **2003**.

(2) For reviews on ionic liquids, see: (a) Luo, S.; Peng, Y.; Zhang, B.; Wang, P.; Cheng, J. *Curr. Org. Synth.* **2004**, *1*, 405. (b) Forsyth, S.; Pringle, J.; MacFarlane, D. *Aust. J. Chem.* **2004**, *57*, 113. (c) Zhao, H.; Malhotra, S. V. *Aldrichimica Acta* **2002**, *35*, 75. (d) Gordon, C. M. *Appl. Catal., A* **2001**, *222*, 101. (e) Butler, R. *Chem. Ind. (London)* **2001**, *17*, 532. (f) Wasserscheid, P. *Nachr. Chem.* **2001**, *49*, 12.

(3) Hosomi, A.; Masahiko, E.; Sakurai, H. *Chem. Lett.* **1976**, 941.

(4) Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1978**, 499.

(5) Mukaiyama, T.; Nagaoka, H.; Murakami, M.; Ohshima, M. *Chem. Lett.* **1985**, 980.

(6) Kawai, M.; Onaka, M.; Izumi, Y. *Chem. Lett.* **1986**, 381.

(7) Tanaka, H.; Yamashita, S.; Ikemoto, Y.; Torii, S. *Tetrahedron Lett.* **1988**, *14*, 1721.

(8) Trehan, A.; Vij, A.; Walia, M.; Kaur, G.; Verma, R. D.; Trehan, S. *Tetrahedron Lett.* **1993**, *34*, 7335.

(9) Sakurai, H.; Sasaki, K.; Hosomi, A. *Tetrahedron Lett.* **1981**, *22*, 745.

(10) (a) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 71. (b) For allylation of acetals using TMSOTf as a catalyst in ionic liquids, see: Leonard, N. M.; Zerth, H. M.; Mohan, R. S. *Org. Lett.* **2003**, *5*, 55.

(11) Hollis, T. K.; Robinson, N. P.; Whelan, J.; Bosnich, B. *Tetrahedron Lett.* **1993**, *34*, 4309.

(12) McCluskey, A.; Mayer, D. M.; Young, D. J. *Tetrahedron Lett.* **1997**, *38*, 5217.

(13) Komatsu, N.; Uda, M.; Suzuki, H.; Takahashi, T.; Domae, T.; Wada, M. *Tetrahedron Lett.* **1997**, *38*, 7215.

(14) Ishii, A.; Kotera, O.; Saeki, T.; Mikami, K. *Synlett* **1997**, 1145.

(15) Yadav, J. S.; Subba Reddy, V. B.; Srihari, P. *Synlett* **2001**, 673.

(16) (a) Yadav, J. S.; Subba Reddy, B. V.; Reddy, G. S. K. K. *Tetrahedron Lett.* **2000**, *41*, 2695. (b) Kwon, J. S.; Pae, A. N.; Choi, K.; Koh, H. Y.; Kim, Y.; Cho, Y. S. *Tetrahedron Lett.* **2001**, *42*, 1957.

(17) Wieland, L. C.; Zerth, H. M.; Mohan, R. S. *Tetrahedron Lett.* **2002**, *43*, 4597.

(18) For examples of one-pot syntheses of homoallyl ethers in organic solvents, see: (a) Sakurai, H.; Sasaki, K.; Hayashi, J.; Hosomi, A. *J. Org. Chem.* **1984**, *49*, 2808.
(b) Mekhalfia, A.; Markó, I. E. *Tetrahedron Lett.* **1991**, *32*, 4779. (c) Wang, M. W.; Chen, Y. J.; Wang, D. *Synlett* **2000**, 385. (d) Yadav, J. S.; Subba Reddy, B. V.; Srihari, P. *Synlett* **2001**, 673. (e) Watahiki, T.; Akabane, Y.; Mori, S.; Oriyama, T. *Org. Lett.* **2003**, *5*, 3045. (f) Anzalone, P. W.; Baru, A. R.; Danielson, E. M.; Hayes, P. D.; Panico, A. F.; Smith, R. C.; Mohan, R. S. *J. Org. Chem.* **2005**, *70*, 2091.

(19) Sutton, A. E.; Seigal, B. A.; Finnegan, D. F.; Snapper, M. L. *J. Am. Chem. Soc.* **2002**, *124*, 13390.