# Chemoselective and Practical Deprotection of Alkyl Trialkylsilyl Ethers in the Presence of Aryl Trialkylsilyl Ethers by a Catalytic Amount of $Sc(OTf)_3$

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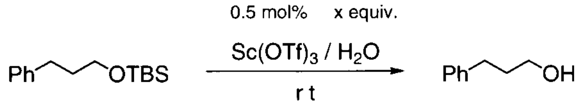
**Abstract:** Treatment of alkyl trialkylsilyl ethers with 0.5 mol% of $Sc(OTf)_3$ combined with 5 equivalents of water in acetonitrile provides an efficient and practical method for the deprotection of silyl ethers. Alcoholic trialkylsilyl ethers have been cleaved selectively in the presence of phenolic trialkylsilyl ethers.

Trialkylsilyl ether is a very important hydroxyl protecting group in synthetic organic chemistry and various silyl ethers have been devised[1] and extensively utilized in synthetic sequences of complex natural products. *t*-Butyldimethylsilyl ethers[2] are one of the most commonly used trialkylsilyl ethers and are very easy to introduce and to remove. A variety of reagents exist for its removal,[1] and very recently several methods for the deprotection of silyl ethers under various reaction conditions have been reported in the literature.[3] However, only scattered procedures for the selective cleavage of alkyl silyl ethers over aryl silyl ethers have been reported.[3d,4] On the other hand, scandium trifluoromethanesulfonate ($Sc(OTf)_3$) was discovered by Kobayashi *et al.* to be a new type of water-soluble Lewis acid,[5] and many useful reactions using $Sc(OTf)_3$ have been developed.[6]

In this paper we report a highly selective and convenient procedure for the new deprotection of trialkylsilyl ethers using a catalytic amount of $Sc(OTf)_3$.

First, we attempted the reaction of *t*-butyldimethylsilyl ether of 3-phenylpropanol with 0.5 mol% of $Sc(OTf)_3$ in acetonitrile. After 1 h, usual work-up of the reaction mixture gave the corresponding alcohol in 48% yield. Screening the amount of water in the reaction revealed that 5 equivalents of water gave the best result as shown in Table 1 (Runs 1, 2, 3, and 4).

**Table 1.** Deprotection of TBS Ether of 3-Phenylpropanol

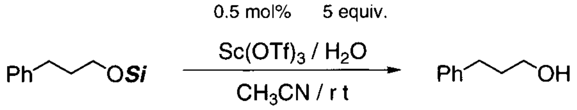


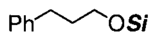
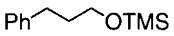
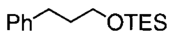
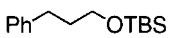
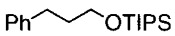
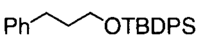
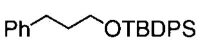
| Run | x / equiv. | Solvent | Time / h | Yield [a] / % |
|---|---|---|---|---|
| 1 | 0 | $CH_3CN$ | 1 | 48 |
| 2 | 2 | $CH_3CN$ | 1 | 89 |
| 3 | 5 | $CH_3CN$ | 1 | 96 |
| 4 | 10 | $CH_3CN$ | 1 | 95 |
| 5 | 5 | THF | 24 | 74 |
| 6 | 5 | $CH_2Cl_2$ | 6 | 0 |

a) Isolated yield of purified product.
(TBS = *t*-$BuMe_2Si$-, TfO = $CF_3SO_3$-)

Next, we examined the effect of the trialkylsilyl moiety of silyl ethers. In the case of trimethylsilyl (TMS), triethylsilyl (TES), and *t*-butyldimethylsilyl (TBS) ether, the deprotection was completed within 1 h at room temperature to give the corresponding alcohols in excellent yield by employing only 0.5 mol% of $Sc(OTf)_3$ (Table 2, Runs 1, 2, and 3). On the other hand, the reactions of more sterically bulky silyl ethers, triisopropylsilyl (TIPS) ether and *t*-butyldiphenylsilyl (TBDPS) ether, did not proceed smoothly under comparable reaction conditions. Longer reaction time (24 h) and/or usage of a larger amount of $Sc(OTf)_3$ (10 mol%) gave the parent alcohols in 97% and 93% yield, respectively (Runs 4 and 6).

**Table 2.** Deprotection of Various Silyl Ethers of 3-Phenylpropanol



| Run |  OSi | Time / h | Yield [a] / % |
|---|---|---|---|
| 1 |  OTMS | 1 | 97 |
| 2 |  OTES | 1 | 98 |
| 3 |  OTBS | 1 | 96 |
| 4 |  OTIPS | 24 | 97 |
| 5 |  OTBDPS | 1 | 5 |
| 6 [b] |  OTBDPS | 24 | 93 |

a) Isolated yield of purified product. b) 10 mol% of $Sc(OTf)_3$ was used. (TMS = $Me_3Si$-, TES = $Et_3Si$-, TIPS = *i*-$Pr_3Si$-, TBDPS = *t*-$BuPh_2Si$-)

The deprotection was conducted with various TBS ethers of primary, secondary, and phenolic alcohols and the results are collected in Table 3.[7] Although the deprotection of aliphatic TBS ethers showed considerable success, phenolic TBS ethers remained unchanged with the recovery of the starting TBS ethers. The reaction of TBS ether of *p*-bromophenol with 1.5 mol% of TfOH for 6 h afforded the *p*-bromophenol in 62% yield, which means the actual species of this deprotection of aliphatic silyl ethers is not TfOH.

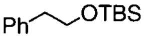
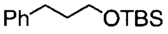
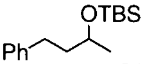
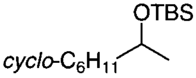
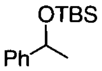
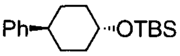
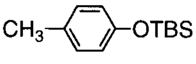
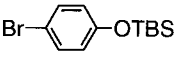
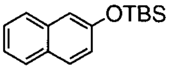
Finally, we examined the chemoselective deprotection of aliphatic TBS ether in the presence of phenolic TBS ether and the result was very satisfactory as shown in Scheme 1. Similar chemoselective deprotection was also successful with the TBDPS group, that is, between aliphatic TBDPS ether and aromatic TBDPS ether (Scheme 2). Additionally, more subtle intermolecular chemoselectivity of deprotection between TBS ether and TBDPS ether of a secondary alcohol was also successfully performed as shown in Scheme 3.

The salient features of the present deprotection of trialkylsilyl ethers include: 1) the ease of operation 2) high efficiency 3) mild reaction conditions 4) chemoselectivity. The deprotection of aliphatic trialkylsilyl ethers described here adds a new and convenient method for the chemistry of protecting groups.

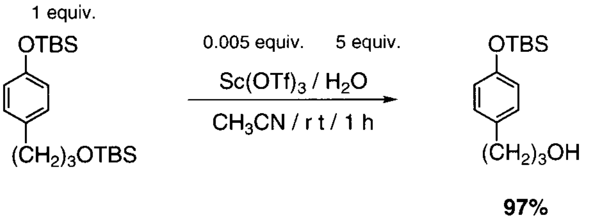
**Table 3.** Deprotection of Various TBS Ethers

0.5 mol% 5 equiv.

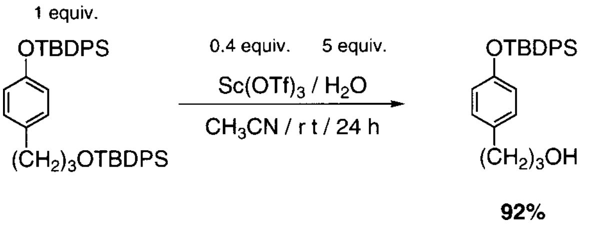
$$\text{ROTBS} \xrightarrow[\text{CH}_3\text{CN / r t}]{\text{Sc(OTf)}_3\text{ / H}_2\text{O}} \text{ROH}$$

| Run | ROTBS | Time / h | Yield [a] / % |
|---|---|---|---|
| 1 |  | 1 | 91 |
| 2 |  | 1 | 98 |
| 3 |  | 1 | 96 |
| 4 [b] | | 12 | 98 |
| 5 |  | 2 | 94 |
| 6 |  | 4 | 97 |
| 7 |  | 12 | 93 |
| 8 |  | 1 | 95 |
| 9 |  | 6 | 0 |
| 10 |  | 6 | 0 |
| 11 |  | 6 | 0 |

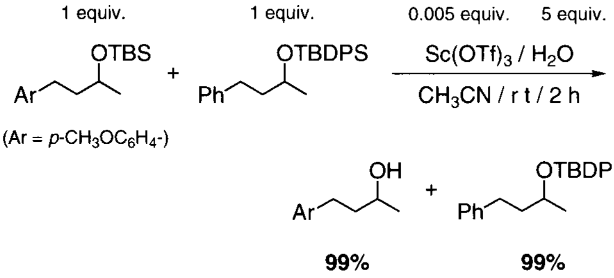
a) Isolated yield of purified product.
b) 0.1 mol% of $Sc(OTf)_3$ was used



**Scheme 1**



**Scheme 2**



**Scheme 3**

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## References and Notes

(1) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd Ed., John Wiley & Sons : New York, 1991; Kocienski, P. J. *Protecting Groups*, Georg Thieme Verlag : New York, 1994.

(2) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.*, **1972**, *94*, 6193.; Corey, E. J.; Snider, B. B. *J. Am. Chem. Soc.*, **1972**, *94*, 2549.; Corey, E. J.; Cho, H.; Rücker, C.; Hua, D. H. *Tetrahedron Lett.*, **1981**, *22*, 3455.

(3) (a) Wilson, N. S.; Keay, B. A. *Tetrahedron Lett.*, **1997**, *38*, 187. (b) Maiti, G.; Roy, S. C. *Tetrahedron Lett.*, **1997**, *38*, 495. (c) Farràs, J.; Serra, C.; Vilarrasa, J. *Tetrahedron Lett.*, **1998**, *39*, 327. (d) Lipshutz, B. H.; Keith, J. *Tetrahedron Lett.*, **1998**, *39*, 2495. (e) Bartoli, G.; Bosco, M.; Marcantoni, E.; Sambri, L.; Torregiani, E. *Synlett*, **1998**, 209.

(4) Collington, E. W.; Finch, H.; Smith, I. J. *Tetrahedron Lett.*, **1985**, *26*, 681.

(5) Kobayashi, S.; Hachiya, I.; Araki, M.; Ishitani, H. *Tetrahedron Lett.*, **1993**, *34*, 3755.

(6) Hachiya, I.; Kobayashi, S. *J. Org. Chem.*, **1993**, *58*, 6958.; Kawada, A.; Mitamura, S.; Kobayashi, S. *Synlett*, **1994**, 545.; Kobayashi, S. *Synlett*, **1994**, 689.; Kobayashi, S.; Ishitani, H.; Nagayama, S. *Synthesis*, **1995**, 1195.; Ishihara, K.; Kubota, M.; Kurihara, H.; Yamamoto, H. *J. Am. Chem. Soc.*, **1995**, *117*, 4413.; Ishihara, K.; Kubota, M.; Kurihara, H.; Yamamoto, H. *J. Org. Chem.*, **1996**, *61*, 4560.; Kobayashi, S.; Nagayama, S. *J. Am. Chem. Soc.*, **1997**, *119*, 10049.; Kajiro, H.; Mitamura, S.; Mori, A.; Hiyama, T. *Synlett*, **1998**, 51.

(7) Typical experimental procedure is as follows (Table 3, Run 4): To a solution of scandium trifluoromethanesulfonate (6.4 mg, 0.013 mmol) in $CH_3CN$ (15 ml) was added 1-(1,1-dimethylethyl)dimethylsiloxy-3-phenylpropane (3.23 g, 12.9 mmol) in $CH_3CN$ (50 ml) and water (1.15 ml, 63.8 mmol) at room temperature. The resultant mixture was stirred for 12 h at room temperature and quenched with a phosphate buffer (pH 7). The organic materials were extracted with dichloromethane (3 x 20 ml) and the combined extracts were washed with brine and dried over anhydrous sodium sulfate. The solvent was evaporated and 3-phenylpropanol (1.72 g, 98%) was isolated by column chromatography on silica gel (ether : hexane = 1 : 1). The product gave satisfactory $^1H$ NMR and IR spectra.