

A Novel, Efficient, and Selective Cleavage of Alkyl *tert*-Butyldimethylsilyl Ethers Using the BiCl₃/NaI System**

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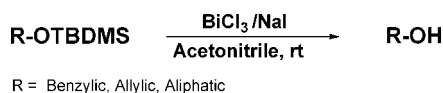
The protection of the hydroxy functional group as a *tert*-butyldimethylsilyl ether (TBDMS)^[1] is most common and useful in organic synthesis, because of its stability towards basic and mild acidic reagents. The importance of any protecting group depends on how easily it can be installed and removed. Tetrabutylammonium fluoride (TBAF)^[1,2] is often used for deprotection of TBDMS ethers, but being a strong base it can alter base-sensitive substrates. Several methods^[3] under various reaction conditions have been reported in the literature for the deprotection of TBDMS ether groups. However, only scattered procedures^[4] exist for the selective cleavage of alkyl TBDMS ethers over aryl TBDMS ethers. Recently, we reported the selective cleavage of primary TBDMS ethers by oxone[®] in aqueous methanol.^[5] But this reagent was inert towards the deprotection of secondary TBDMS ethers. As part of our research program on the synthetic sequences of complex natural products, we needed to deprotect a secondary TBDMS ether group selectively in the presence of an aryl TBDMS ether group. On the other hand, we found that bismuth(III) chloride was an efficient Lewis acid for the selective cleavage of acetals and ketals^[6] and many useful reactions using BiCl₃ have been developed.^[7]

In this paper we report a highly selective and efficient procedure for the selective cleavage of alkyl TBDMS groups in the presence of aryl TBDMS groups using the BiCl₃/NaI system under mild reaction conditions (Scheme 1). Although BiCl₃ is a weak Lewis acid, it was possible to increase the catalytic power of BiCl₃ by addition of sodium iodide. There are many advantages for the use of BiCl₃, no strongly basic or acidic conditions are used, it is a non-toxic,^[8] easy to handle and commercially available compound.

Keywords: alcohols; bismuth(III) chloride; chemoselectivity; deprotection; protecting groups; TBDMS ethers

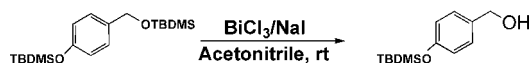
The alkyl TBDMS ethers were cleaved very effectively with 2.5 equiv. of BiCl₃ and 2.6 equiv. of NaI in acetonitrile. The deprotection reaction is

very fast at room temperature and the corresponding alcohols were formed in high yields (Table 1). Under the present reaction conditions the secondary TBDMS ethers were also cleanly deprotected in high yields. The versatility of this procedure has been illustrated by deprotecting the secondary TBDMS group of menthol without loss of the original configuration. ($[\alpha]_D$ observed: -53 , (c 10 in methanol), $[\alpha]_D$ lit.: -50 ± 1 , (c 10 in methanol).



Scheme 1.

We have demonstrated the selective cleavage of primary and secondary alkyl TBDMS groups in the presence of aryl TBDMS groups. Thus, treatment of the bis TBDMS ether with 2.5 equiv. of BiCl₃ and 2.6 equiv. of NaI at room temperature in acetonitrile yielded the mono-deprotected product (Scheme 2). Even after a prolonged reaction time the phenolic TBDMS ether remained unaffected. A number of substrates have been examined using this protocol and we found selectivity in all the cases without affecting the phenolic TBDMS ethers (Table 2). The selective removal of alkyl TBDMS ethers has also been achieved in the presence of other functional groups such as -OTs, -NHBOC, -OMe and -OBn; therefore, the present method offers several advantages over the reported methods.



Scheme 2.

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Table 1. Deprotection of alkyl TBDMS ethers using the BiCl₃/NaI system

Entry	TBDMS Ether	Alcohol	Time (min)	Yield (%) ^[a]
1			30	84
2			30	74
3			30	80
4			45	82
5			45	76
6			45	72
7			30	81
8			90	76
9			30	80
10			120	72

[a] Yields refer to isolated products.

In conclusion, we have described the selective cleavage of primary and secondary *tert*-butyldimethylsilyl ether groups in the presence of aryl *tert*-butyldimethylsilyl ethers. The salient features of the present methodology include 1) the ease of operation, 2) high efficiency, 3) chemoselectivity, and 4) mild reaction conditions. Therefore, this protocol represents a valuable alternative to all of the reagents reported in the literature.

Experimental Section

General Procedure for Cleavage of TBDMS Ether Group

To a mixture of BiCl₃ (2.5 mmol) and NaI (2.6 mmol) in acetonitrile (10 mL) was added the TBDMS ether (1 mmol) in acetonitrile (2 mL) at room temperature. The reaction mixture was stirred at room temperature until TLC indicated that no starting material remained. On completion, the solvent

Table 2. Selective deprotection of alkyl TBDMS ethers

Entry	TBDMS Ether	Alcohol	Time (min)	Yield (%) ^[a]
1			30	81
2			45	86
3			60	82
4			30	84
5			90	80
6			90	85

[a] Yields refer to isolated products.

was removed under reduced pressure and the residue extracted with EtOAc (2 × 10 mL), washed with water and brine. After drying (Na₂SO₄) and solvent removal, the crude product was purified by column chromatography. The alcohols obtained were characterized by IR and ¹H NMR spectroscopy.

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