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Selective deprotection of alkyl *t*-butyldimethylsilyl ethers in the presence of aryl *t*-butyldimethylsilyl ethers with bismuth bromide

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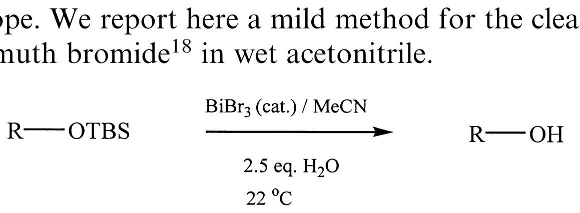
Abstract

Alkyl *t*-butyldimethylsilyl ethers can be selectively cleaved in the presence of aryl ethers using a catalytic amount of bismuth bromide in wet acetonitrile at ambient temperatures. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: alkyl ethers; aryl ethers; selective hydrolysis; bismuth bromide; group transformation.

The transformation of an alcohol to its corresponding *t*-butyldimethylsilyl (TBS) ether has been a common and useful method[1] for protecting the hydroxyl group since its introduction by Corey[2] in 1972. The alkyl TBS ethers are stable towards basic and mildly acidic conditions.[1] Although tetra-*n*-butylammonium fluoride is the most common reagent for the cleavage of TBS ethers, the strong basicity of the fluoride anion makes it inappropriate for base-sensitive substrates.[3] There are several other methods for the deprotection of TBS ethers, some of which include catalytic transfer hydrogenation using Pd,[4] reductive cleavage by DIBAL-H,[5] ultrasonic cleavage in MeOH/CCl_4,[6] DDQ,[7] CAN,[8] I_2,[9] K_2CO_3/EtOH,[10] LiCl/DMF/H_2O/90°C,[11] DMSO/H_2O/90°C,[12] CBr_4/MeOH/65°C,[13] TASF/DMF,[14] I_2/MeOH,[15] TMSCl/MeCN/H_2O[16] and $Sc(OTf)_3$.[17] However, these methods involve basic, reducing, oxidizing or high-temperature conditions that limit their scope. We report here a mild method for the cleavage of TBS ethers using a catalytic amount of bismuth bromide[18] in wet acetonitrile.



$$\text{R—OTBS} \xrightarrow[\text{2.5 eq. } H_2O,\ 22\ ^{\circ}C]{BiBr_3\text{ (cat.) / MeCN}} \text{R—OH}$$

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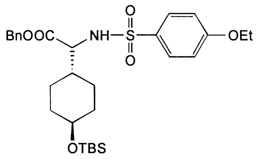
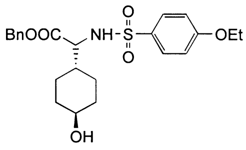
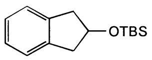
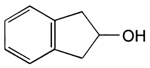
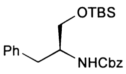
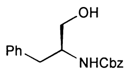
Table 1 contains a few representative examples which demonstrate the mildness of this procedure. Esters, ethers, sulfonamides and benzyl carbamates are inert under the conditions employed.

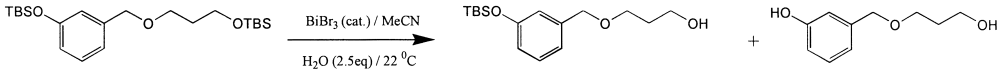
Table 1
Deprotection of TBS ethers with $BiBr_3$ in wet MeCN at room temperature

Entry	TBS ether	Reaction time (h)[a]	Alcohol[b]	Yield (%)[c]
1		0.3		85
2		0.5		83
3		0.5		87

[a]The reaction was carried out following the general procedure described in the text. [b]All products were fully characterized by spectroscopic methods. [c]Isolated yields.

Since few methods exist for the selective deprotection of alkyl TBS ethers in the presence of aryl TBS ethers,[15–17,19] we also examined the use of the $BiBr_3$ procedure for this purpose. Initially, the experiment was performed with bis-TBS ether **3**, and the reaction was followed by HPLC (Table 2). It is apparent from the results in Table 2 that the hydrolysis of the alkyl TBS ether is fast, and the optimum time for the selective hydrolysis of alkyl TBS ether is around 15–30 min. Longer reaction times increase the yield of dideprotected compound **5** at the expense of mono-TBS ether **4**. After 24 hours, dideprotected compound **5** is obtained in 58% yield.

Table 2
Selective deprotection of bis-TBS diethers with $BiBr_3$ in MeCN at room temperature



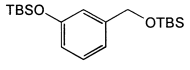
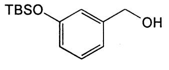
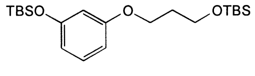
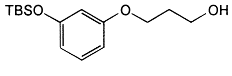
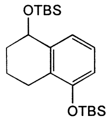
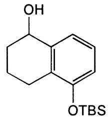
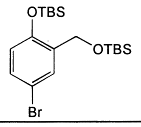
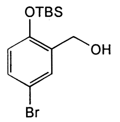
3 **4** **5**

Entry	Reaction time (min)[a]	Product **4** (%)[b]	Phenol **5** (%)[b]	Unreacted bis-TBS ether **3** (%)[b]
1	5	84	4	12
2	15	93	5	2
3	30	94	5	1
4	45	93	6	1
5	90	90	9	1
6	24 h	42	58	<1

[a]The reaction was carried out following the general procedure described in the text. [b]The yields were determined by HPLC.

For the examples illustrated in Table 3, it can be seen that this procedure works well on more complex substrates as well as those which contain electron-rich aromatic rings. In all cases, independent of the aryl group and the substitution pattern, monodesilylation of the *alkyl* TBS group was observed.

Table 3
Selective deprotection of bis-TBS diethers with $BiBr_3$ in MeCN at room temperature

Entry	TBS diether	Reaction time (min)[a]	Product alcohol[b]	Yield (%)[c]
1		20		85
2		20		80
3		90		72
4		20		88

[a]The reaction was carried out following the general procedure described in the text. [b]All products were fully characterized by spectroscopic methods. [c]Isolated yields.

Recently, Lipshutz[15] and Grieco[16] have reported on the use of I_2/MeOH and TMSCl/H_2O/MeCN, respectively, to effect a similar deprotection of an alkyl TBS ether. It was shown[15] that HI generated in situ in the above case might be the species responsible for the hydrolysis of the alkyl TBS ethers. Also in our case, the hydrolysis may be catalyzed[20] by HBr that is generated in situ from the reaction of bismuth bromide with water.[21]

$$BiBr_3 + H_2O \longrightarrow BiOBr + 2\,HBr \qquad (1)$$

In summary, the use of bismuth bromide in wet acetonitrile provides a mild and effective means of removing alkyl TBS ethers in the presence of aryl TBS ethers. Bismuth bromide is a bright-yellow stable solid, readily available commercially and is much easier to handle than iodine or chlorotrimethylsilane.

Typical experimental procedure: To a solution of bis-TBS ether **3** (3.96 g, 10.0 mmol) in acetonitrile (25 mL) was added bismuth bromide (0.14 g, 0.31 mmol) followed by the addition of water (0.46 mL, 25.5 mmol). The reaction mixture was stirred at 22°C, and the progress of the reaction was monitored by TLC. After 20 min, TLC indicated completion of the reaction. The reaction mixture was quenched with water. The product was isolated by extraction with ethyl acetate. The combined organic extracts were washed with water and concentrated in vacuum. The crude product was purified on silica gel. Elution with hexane:ethyl acetate (20:1) afforded 2.25 g (80%) of **4**.

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