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A Mild, Efficient, Inexpensive, and Selective Cleavage of Primary *tert*-Butyldimethylsilyl Ethers by Oxone in Aqueous Methanol†

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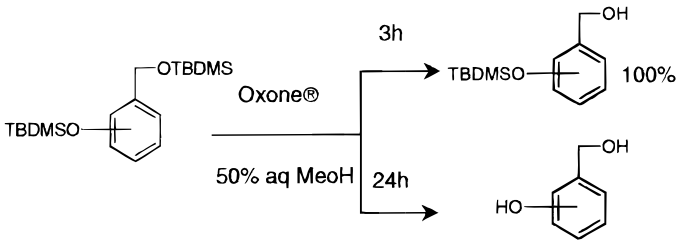
ABSTRACT



The use of a 50% aqueous methonolic solution of Oxone is described for the selective cleavage of primary *tert*-butyldimethylsilyl and aryl ethers at room temperature. This method enables one to deprotect *tert*-butyldimethylsilyl ethers of primary alcohols in the presence of *tert*-butyldimethylsilyl ethers of secondary and tertiary alcohols and phenols. The silyl ethers of phenols were deprotected at longer reaction times.

The *tert*-butyldimethylsilyl (TBDMS)[1] group is one of the most frequently used protecting groups for the hydroxyl function in organic synthesis. This is due to easy installation[1,2] and general stability to basic and mildly acidic reagents.[1] Even though a variety of reagents[3−11] have been developed for the cleavage of TBDMS ethers, most of these methods suffer from the use of basic[3] or strong oxidizing[7,8] and reducing[6] reagents and cumbersome workup. Herein we report a new method for the selective cleavage of primary TBDMS ethers by Oxone ($KHSO_5$ triple salt)[12] under mild conditions which can tolerate a wide variety of other functional groups (Table 1).

Literature shows a number of methods available for the cleavage of alkylsilyl ethers, but there are only a few methods reported[13] for the cleavage of phenolic TBDMS ethers. Most of these methods use basic reagents and required elevated temperatures. Therefore, there still exists a great demand for a mild reagent which works for the cleavage of alkyl as well as phenolic TBDMS ethers with selectivity among these two groups, because the selectivity can be applied to advantage in complex synthetic sequences in which two protected hydroxyl groups must be unmasked at different stages of the synthesis.

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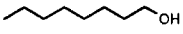
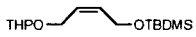
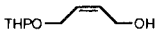
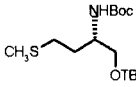
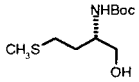
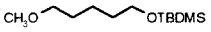
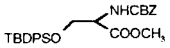
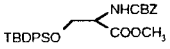
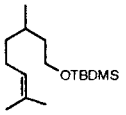
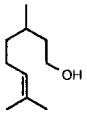
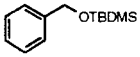
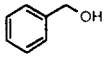
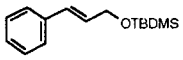
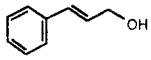
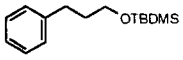
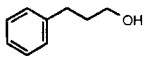
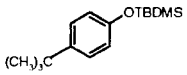
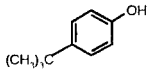
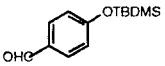
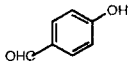
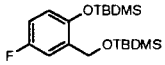
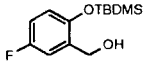
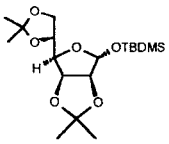
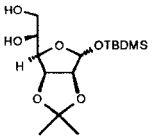
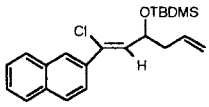
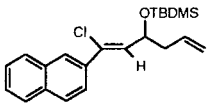
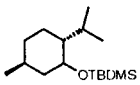
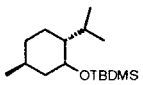
Table 1. Deprotection of *tert*-Butyldimethylsilyl Ethers

Entry	Substrate	Time (h)	Product	Isolated Yield(%)
1		3.0		90
2		2.5		88
3		2.5		85
4		2.5		92
5		3.0		88
6		24.0		No reaction
7		15.0		80
8		2.5		92
9		3.0		88
10		2.5		91
11		24.0		80
12		20.0		75
13		3.0		88
14		3.0		88
15		24.0		No reaction
16		24.0		No reaction

Herein we report that potassium monopersulfate available as Oxone in a 50% aqueous methanolic solution cleaves alkyl and aryl TBDMS ethers with selectivity under mild conditions.[14] The TBDMS ethers of primary alcohols were deprotected within 2.5−3.0 h whereas the phenolic TBDMS

(14) **General Procedure for the Cleavage of the *tert*-Butyldimethylsilyl Group Using Oxone:** The TBDMS ether of 5-benzyloxypentan-1- ol (entry 1) (4.32 m mol) was stirred in a 50% aqueous methanolic solution (30 mL) of Oxone (4.32 m mol) at room temperature for 3 h. The progress of the reaction was monitored by TLC. On completion the methanol was removed under reduced pressure and the residue was extracted twice with ethyl acetate. The combined organic layers were dried on anhydrous sodium sulfate and concentrated in rotary evaporator to afford 5-benzyloxypentan-1-ol in 90% yield, which was identical with the authentic sample. ^{1}H NMR: TBDMS ether of 5-benzyloxypentan-1-ol (200 MHz, $CDCl_3$) δ **0.02 (s, 6H, SiCH$_3$)**, 0.85 (s, 9H, Si-*t*-Bu), 1.35−1.65 (m, 6H, $-CH_2-$), 3.4 (t, 2H, J = 7 Hz), 3.57 (t, 2H, J = 7 Hz), 4.45 (s, 2H, $ArCH_2$), 7.26 (m, 5H, Ar H). 5-Benzyloxypentan-1-ol (200 MHz, $CDCl_3$): δ **1.32**−1.7 (m, 6H, $-CH_2-$), 3.4 (t, 2H, J = 7 Hz), 3.5−3.63 (m, 2H), 4.5 (s, 2H, $ArCH_2$), 7.15−7.4 (m, 5H, ArH).

ethers were unaffected; with prolonged stirring for 20−24 h the cleavage was effected. This reveals the selectivity among alkyl and phenolic TBDMS ethers. On the other hand, the TBDMS ethers of the secondary and tertiary alcholos were unaffected by treatment with Oxone. When the reaction was carried out in the absence of oxidant with 1% dilute HCl and HF adjusted to the same pH as the Oxone (pH 2.8), the cleavage of TBDMS group had not occurred after 2.5−3 h. See comparative data of acid hydrolysis below. Therefore, the real utility of the reagent relative to dilute acids was revealed. Thus, Oxone is an excellent, inexpensive, and mild reagent for the selective cleavage of primary alcoholic TBDMS ethers in the presence of secondary and tertiary alcohols and phenolic TBDMS ethers.

Reagent	Primary TBDMS	Secondary TBDMS	TBDPS	pH	pKa
HF[15a]	Cleaved	Cleaved	Cleaved	-0.7	0.3
HCl[15b]	Cleaved	Cleaved	Cleaved	0.55	1.55
Oxone®	Cleaved	Not Cleaved	Not Cleaved	2.8	3.8
1% HCl &HF (adjusted to pH 2.8)	NotCleaved	Not Cleaved	Not Cleaved	2.8	3.8

We have also demonstrated the selective removal of TBDMS ethers in the presence of *tert*-butyldiphenylsilyl (TBDPS) ethers and certain acid-labile protecting groups (entries 3 and 4) such as THP, N-Boc, etc., and therefore, this method has advantages over other deprotection methods.[15]

In conclusion, we have developed a simple, inexpensive, selective, and mild procedure for the cleavage of primary TBDMS ethers which will have a wide scope in view of the tremendous usefulness of the TBDMS group in organic synthesis.

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