

Facile and Highly Selective Deprotection of *tert*-Butyldimethyl Silyl Ethers using Sulfated SnO₂ as a Solid Catalyst

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Abstract: Highly selective deprotection of *tert*-butyldimethylsilyl ethers at room temperature has been described using sulfated SnO₂ as an efficient solid catalyst.

Keywords: deprotection, sulfated SnO₂, TBDMS ethers

INTRODUCTION

Sulfated metal oxides belong to the class of solid superacids (stronger than 100% sulfuric acid, i.e., acid strength $H_0 \leq -12$). Study of sulfated metal oxides, first reported in 1976, has become an interesting and active area of research because of the high catalytic activity for acid-catalyzed reactions.^[1] Although sulfated metal oxides have been widely employed in the petroleum industry, their effective use as a catalyst for organic transformations remain relatively unexplored.

Temporary protection and deprotection of functional groups play key roles in the synthesis of complex organic molecules of biological significance.^[2] Since the introduction of *tert*-butyldimethylsilyl (TBDMS) group

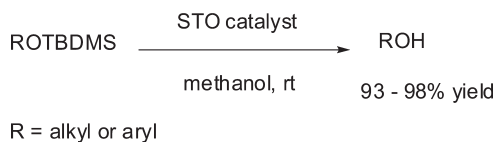
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by E. J. Corey in 1972, silyl ethers have been extensively used as protecting groups for hydroxyl functionality in various organic transformations.^[3] Several reports are available on the use of acidic, basic, reducing, oxidizing, and fluoride-based conventional reagents for the deprotection of TBDMS group.^[4] Protocols involving various Lewis acids such as TMSOTf, TMSCl, BF₃-OEt₂, BCl₃, Sc(OTf)₃, InCl₃, ZnBr₂, Zn(BF₄)₂, Ce(OTf)₄, CeCl₃ · 7H₂O/NaI, BiBr₃, BiOCIO₄, SbCl₃, and Ni(II)Cl₂ · 6H₂O have also been reported for the deprotection of TBDMS ethers.^[5]

Recently, tetra-butyl ammonium tribromide (TBATB), TiCl₄-Lewis base complexes, and NaHSO₄ on silica have also been reported for the deprotection of TBDMS ethers.^[6] However, most of these methods require hazardous reagents and cumbersome workup procedures that are detrimental to the environment. Moreover, in nearly all cases, the reagent cannot be recovered and recycled except for NaHSO₄ on silica, for which catalyst-to-substrate weight ratio was very high. Hence, there is still a need to develop a highly active and selective solid catalyst that can offer operational simplicity together with mild reaction conditions.

In continuation of our efforts to develop building blocks for some of the naturally occurring iminosugars, we could achieve highly selective and quantitative deprotection of TBDMS ethers using a solid superacid such as sulfated SnO₂(STO) at room temperature with very fast reaction rates. It was found that STO catalyzed the selective deprotection of several other TBDMS ethers, giving high yields (Scheme 1).

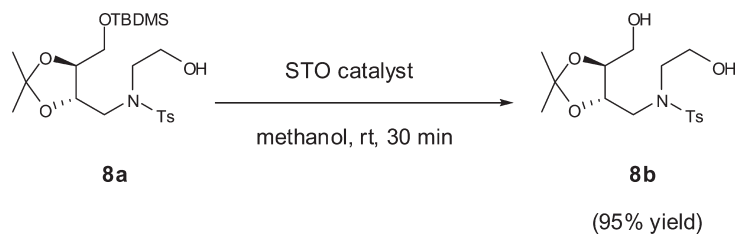


Scheme 1. Deprotection of TBDMS ethers at room temperature using STO catalyst.

RESULTS AND DISCUSSION

Initial experiments indicated that under heterogeneous conditions, the cleavage of TBDMS ether **8a** to **8b** with STO in methanol was very facile (95% yield, Scheme 2) with easy separation and recovery of the catalyst.

Encouraged by this observation, several structurally varied TBDMS ethers with different acid labile functional groups were subjected to these conditions, and the results are summarized in Table 1. Deprotection of TBDMS ethers of primary alcohols with our catalyst resulted in excellent yields within a few minutes (entries 1–8 and 12, Table 1). Deprotection of TBDMS ethers of secondary alcohols (entries 9–11, Table 1) also resulted in almost quantitative yields (>93%), but with longer reaction times as



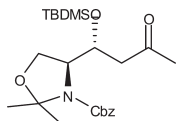
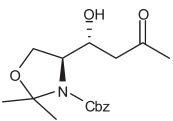
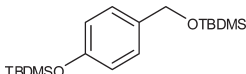
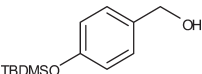
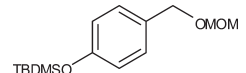
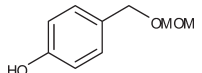
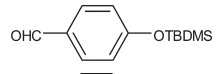
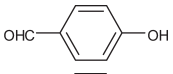
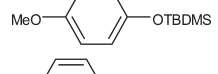
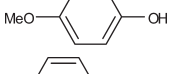
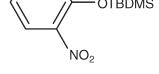
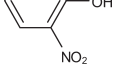
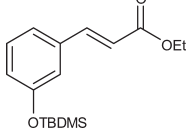
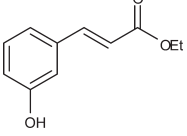
Scheme 2. Deprotection of TBDMS ethers **8a** to **8b** at room temperature using STO catalyst.

Table 1. Deprotection of TBDMS ethers at room temperature using STO in methanol^a

Entry	Substrate ^b	Product ^c	Time (min)	Yield (%) ^d
1			10	98
2			10	96
3			15	98
4			10	97
5			15	95
6			30	96
7			20	95
8			30	95
9			35	96
10			60	93

(continued)

Table 1. Continued

Entry	Substrate ^b	Product ^c	Time (min)	Yield (%) ^d
11			45	94
12			15	96
13			15.5 h	95
14			17 h	96
15			10	98
16			10	96
17			15	98

^aCatalyst-to-substrate weight ratio was 0.01.

^bTBDMS ethers.

^cProducts after deprotection.

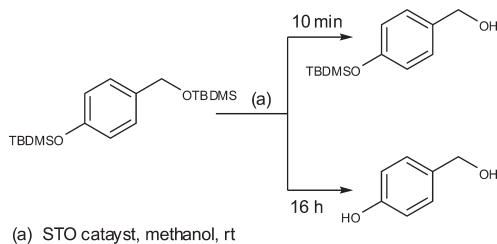
^dIsolated yield.

compared to TBDMS ethers of primary alcohols. It was interesting to note that our catalyst also showed a chemoselective cleavage of TBDMS ether in the presence of TBDPS ether (entry 3, Table 1). In addition, selective deprotection of aliphatic TBDMS ether was readily achieved in the presence of aryl TBDMS ether within a few minutes over the STO catalyst. In case of the deprotection of aryl TBDMS ethers, longer reaction times (several hours) were required than for alkyl TBDMS ethers (entries 12–17, Table 1) as shown in Scheme 3. Furthermore, several other functional groups, such as alkene, alkyne, methoxy, aldehydic, nitro, α - β unsaturated ester, and azide, and sensitive protective groups, such as OMOM, OAc, Oallyl, acetonide, N-tosyl, N-Cbz, OBn, and benzylidene, were found to be unaffected by the catalyst. Thus, the catalyst selectively performs the deprotection of TBDMS ether without affecting several other sensitive protections. All the substrates

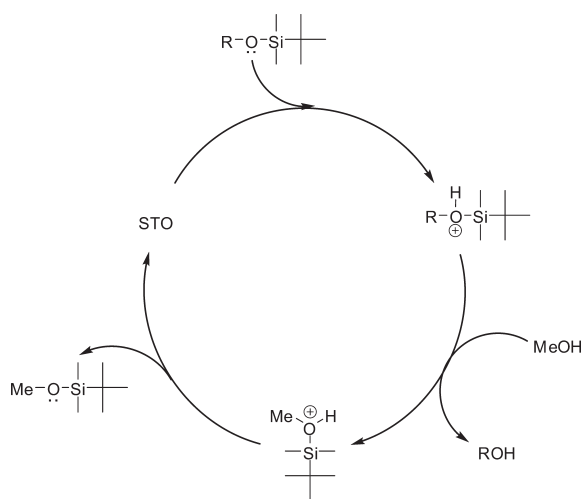
and products of respective reactions carried out in this work were isolated in pure form, and their structures were confirmed by spectroscopic means. (See the supporting information).

After having performed a deprotection reaction of TBDMS ether **8a**, the catalyst was recovered by filtration, washed with methanol and dichloromethane, dried, and then reused for three consecutive runs under the same reaction conditions, which gave an average yield of 93%.

The plausible mechanism underlying the cleavage of TBDMS ether is shown in Scheme 4. It is likely that the STO protonates the TBDMS ether, which in turn could facilitate the attack of methanol present in the reaction, leading to the formation of product.



Scheme 3. Selective deprotection of aliphatic TBDMS ether in the presence of aryl TBDMS ether.



Scheme 4. Proposed plausible mechanism for the cleavage of TBDMS ether.

CONCLUSION

In conclusion, we have demonstrated that STO serves as an efficient solid catalyst for the facile and mild deprotection of TBDMS ethers. The superiority and flexibility of our protocol over existing methods is due to the faster reaction rate at room temperature, minimum catalyst-to-substrate weight ratio (0.01), high selectivity, excellent yields, ease of operation, and the simplicity in the workup, which involves mere filtration of the catalyst, which can then be reused. This method will find widespread application, particularly in the synthesis of complex organic molecules containing more than one protecting groups.

EXPERIMENTAL

Preparation of STO Catalyst

STO has been prepared by the standard procedure reported in the literature.^[7] Stannous chloride (22.56 g) was dissolved in 200 ml, of deionized water to get a clear solution. Aqueous ammonium hydroxide (25 ml) was added to this solution with stirring until pH 8. The yellowish precipitate thus obtained was washed well with deionized water, then dried at 110°C for 12 h to get stannous hydroxide (18 g). Dry hydroxide powder (5 g) was then equilibrated with 25 ml of 2 N H₂SO₄ for 2 h and then it was evaporated to dryness and calcined at 500°C for 4 h to get the catalyst.

Typical Experimental Procedure for Deprotection of TBDMS Ether

A mixture of TBDMS ether **8a** (0.473 g, 1 mmol) and STO catalyst (0.00473 g) in methanol (5 ml) was stirred at room temperature. After completion of the reaction, as indicated by thin-layer chromatography (TLC), the reaction mass was filtered. The filtrate was concentrated under reduced pressure, and the crude compound was purified by column chromatography over silica gel (100–200 mesh) to afford the pure alcohol **8b** (95% yield).

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