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A simple, efficient and highly selective deprotection of *t*-butyldimethylsilyl (TBDMS) ethers using silica supported sodium hydrogen sulfate as a heterogeneous catalyst[☆]

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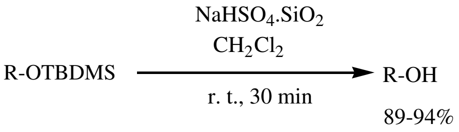
Abstract—*t*-Butyldimethylsilyl (TBDMS) ethers have been efficiently and selectively deprotected using silica supported sodium hydrogen sulfate ($NaHSO_4 \cdot SiO_2$) as a heterogeneous catalyst at room temperature to regenerate the parent alcohols in high yields.

Protection of hydroxyl groups and subsequent deprotection are frequently applied in multistep transformations and syntheses of complex organic molecules.[1] The *t*-butyldimethylsilyl (TBDMS) group is widely used as a hydroxyl protecting group as it can easily be introduced and can withstand a variety of reaction conditions.[2] Cleavage of TBDMS ethers can be carried out using TBAF but this reagent is costly and can cause side reactions.[2] As a result, various other methods including acidic, basic, oxidizing and reducing agents have been introduced for this purpose.[3] Although, these methods are useful in organic synthesis, many of them suffer from drawbacks such as the use of expensive catalysts, prolonged reaction times, complex experimental procedures and disturbance to other functionalities. Thus, there is still a need for an efficient method for selective deprotection of TBDMS ethers in the presence of other functional groups.

In recent years, heterogeneous catalysts have gained importance in several organic transformations due to their interesting reactivity as well as for economic and environmental reasons. In continuation of our work[4] with these catalysts we observed that silica supported sodium hydrogen sulfate ($NaHSO_4 \cdot SiO_2$) is highly efficient for selective cleavage of TBDMS ethers over a wide range of functional groups. Several TBDMS ethers were selectively deprotected to the corresponding alcohols by applying this catalyst at room temperature for 30 min (Scheme 1, Table 1).

The TBDMS ethers prepared from both *primary* and *secondary* alcohols underwent deprotection smoothly to the parent alcohols in high yields. TBDMS protected long chain alcohols (Table 1, entries c and d) also produced the desilylated products in impressive yields. The procedure is suitable for cleavage of TBDMS ethers of unsaturated alcohols (entries f–i) as well as of chiral alcohols (entries j–k). The protocol did not cause isomerization of double or triple bonds nor epimerization of chiral centres. The structures of the products were established from their spectral (^{1}H NMR and MS) data and by direct comparison with authentic samples. The optical rotations of the chiral alcohols were also verified.

The chemoselectivity of the present procedure is interesting. Phenolic TBDMS ethers remained unaffected by the reagent (entries m and n). Such selectivity can be applied in a synthesis in which two protected hydroxyl groups (alcoholic and phenolic) require unmasking



$$\text{R-OTBDMS} \xrightarrow[\text{r. t., 30 min}]{NaHSO_4.SiO_2 \atop CH_2Cl_2} \underset{89\text{-}94\%}{\text{R-OH}}$$

Scheme 1.

Keywords: TBDMS ethers; $NaHSO_4 \cdot SiO_2$; Deprotection; Chemoselectivity; Heterogeneous catalyst.

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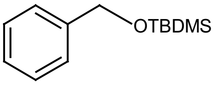
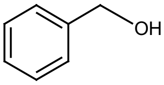
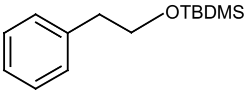
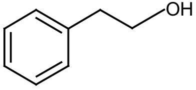
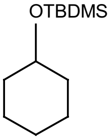
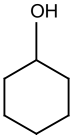
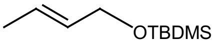
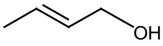
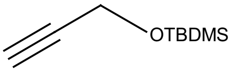
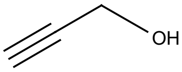
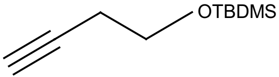
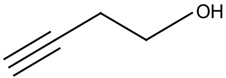
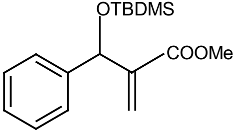
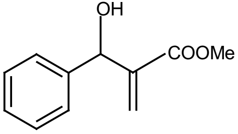
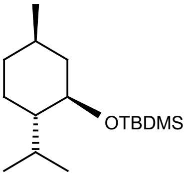
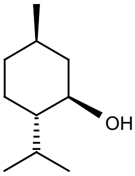
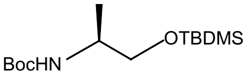
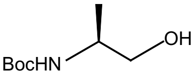
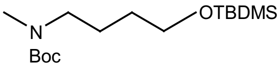
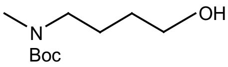
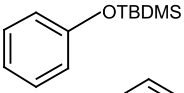
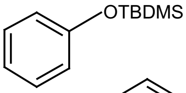
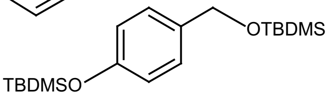
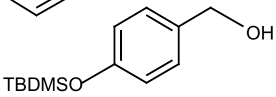
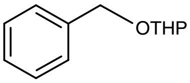
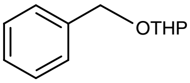
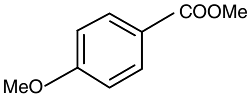
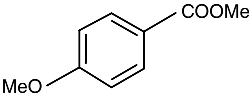
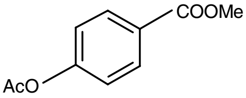
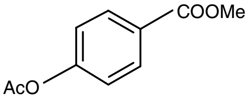
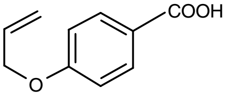
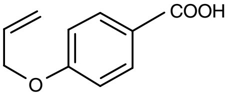
Table 1. Selective cleavage of TBDMS ethers using $NaHSO_4 \cdot SiO_2$[a]

Entry	Substrate	Product	Isolated yield (%)
a			93
b			92
c	$C_{16}H_{33}OTBDMS$	$C_{16}H_{33}OH$	92
d	$C_{18}H_{37}OTBDMS$	$C_{18}H_{37}OH$	92
e			94
f			90
g			93
h			91
i			89
j			90
k			89
l			93
m			—
n			91
o			—
p			—
q			—
r			—

[a] All products were characterized from spectral (^1H NMR, MS) data and by direct comparison with the parent alcohols.

at different stages of the synthetic sequence. Under the present experimental conditions an acid sensitive group such as a THP (entry o) and a base sensitive group such as an acetate (entry q) remained unchanged. Alkyl and allyl ethers (entries p and r) and ester groups (entries i, p and q) were not cleaved under these conditions. Additionally, the TBDMS ethers of *N*-Boc protected amino alcohols underwent facile deprotection without interfering with the amine protecting group (entries k and l).

The catalyst $NaHSO_4 \cdot SiO_2$ can easily be prepared[5] from the readily available starting materials, $NaHSO_4 \cdot SiO_2$ and silica gel and is inexpensive and non-toxic. As the reaction is heterogeneous in nature the catalyst can easily be removed by simple filtration.[6]

In conclusion, we have developed an exceedingly mild, simple and efficient methodology for selective deprotection of TBDMS ethers using $NaHSO_4 \cdot SiO_2$ as a heterogeneous catalyst. The process delivers very high yields of the parent alcohols and is highly chemoselective.

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5. Breton, G. W. *J. Org. Chem.* **1997**, *62*, 8952–8954.
6. *Experimental procedure*: A mixture of TBDMS ether (1 mmol) and $NaHSO_4 \cdot SiO_2$ (200 mg) in CH_2Cl_2 (10 ml) was stirred at room temperature for 30 min (TLC indicated completion of the reaction). The catalyst was removed by filtration and washed with EtOAc (2 × 5 ml). The filtrate and washings were combined and the solvents removed. The residue was subjected to column chromatography (silica gel, hexane–EtOAc) to yield the parent alcohol.