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Simple and Efficient Method for Deprotection of Tetrahydropyranyl Ethers by Using Silica Supported Sodium Hydrogen Sulphate

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Tetrahydropyranyl (THP) ethers have been efficiently and simply deprotected by using Silica supported sodium hydrogen sulphate ($NaHSO_4$-SiO_2) in methanol at room temperature to regenerate the parent alcohols in high yields.

Keywords THP ethers, deprotection, $NaHSO_4$-SiO_2, methanol, reusable catalyst

Introduction

Protection of hydroxyl groups and subsequent deprotection are frequently applied in multistep transformations and synthesis of complex organic molecules.[1] The tetrahydropyranyl (THP) group is widely used as a hydroxyl protecting group, because it can easily be introduced and is stable under a variety of reaction conditions, including strongly basic conditions like Grignard reagent, lithium alkyls, alkylting, acylating reagents and reactions involving oxidation and reduction by inorganic hydrides. Commonly cleavage of THP ethers can be carried out under aqueous acidic condition such as acetic acid, *p*-toluene sulphonic acid, or HCl, *etc*. In recent years, a number of different methods have been reported for the deprotection of THP groups.[2] Although these methods are useful in organic synthesis, but there is still a need for an efficient and excellent yielding catalysts that can work under mild conditions and have shorter reaction time periods.

In recent years, heterogeneous catalysts have gained importance in several organic transformations due to their interesting reactivity as well as for economic and environmenttal reasons. In recent works[3] and their applications for deprotections with this heterogeneous catalysts we observed that silica supported sodium hydrogen sulphate was a highly efficient catalyst for THP ethers and this was a good reusable catalyst.

Several THP ethers were cleaved to produce the parent alcohols in excellent yields (Table 2). The conversion occurred at room temperature. THP ethers were not deprotected with this silica supported sodium hydrogen sulphate in CH_2Cl_2 at room temperature. In our present work we carried out for deprotection using methanol at room temperature for 10 min, to give the corresponding alcohols in high yields. The solvent plays an important role in the cleavage reaction; it was found that methanol is the best one among the solvents tested with THP ether of 4-nitrobenzyl alcohol.

Scheme 1

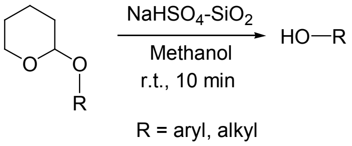

Table 1 Deprotection of 4-nitrobenzyl alcohol THP ether in various solvents[a]

Entry	Solvent	Time	Yield/%
1	Methanol	10 min	99
2	Ethanol	1.5 h	92
3	Acetonitrile	4 h	90
4	1,4-Dioxane	Incomplete after 10 h	—
5	Acetone	Incomplete after 10 h	—
6	THF	Incomplete after 10 h	—
7	CH_2Cl_2	No reaction	—

[a] All reactions were carried out at room temperature.

Methanol gave the best results and is generally recommended. Ethanol and acetonitrile solvents are less efficient solvents. Whereas the reaction was slow in THF, acetone and 1,4-dioxane. The reaction was totally ineffective in dichloromethane.

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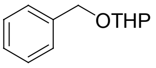
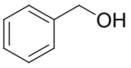
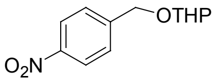
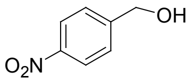
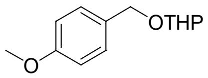
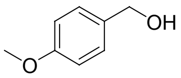
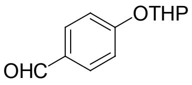
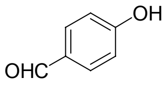
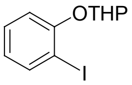
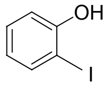
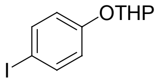
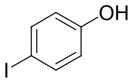
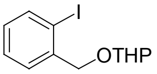
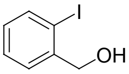
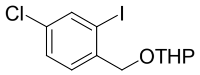
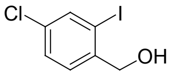
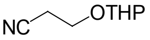
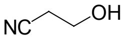
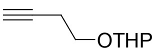
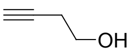
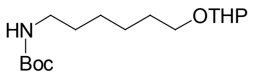
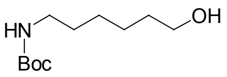
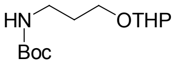
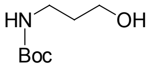
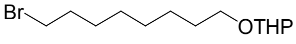
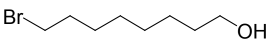
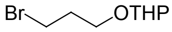
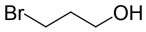
Table 2 Deprotection of THP ethers using $NaHSO_4$-SiO_2^{a} in methanol at r.t.

Entry	Substrate	Product	Time/min	Yield/%
a			10	98
b			10	99
c			10	98
d			10	96
e			10	98
f			10	98
g			10	95
h			12	93
i			15	92
j			15	91
k			10	88
l			10	87
m			15	92
n			15	93

^{a} The structures of the products were established by direct comparison of their spectral (^{1}H NMR) data with those of the parent.

The catalyst $NaHSO_4$-SiO_2 can easily be prepared[4] from the readily available $NaHSO_4$ and silica gel (230—400 mesh) and these are inexpensive and non-toxic. As the reaction is heterogeneous in nature, the catalyst can easily be removed by simple filtration. The filtered catalyst was dried and again reused for deprotection. First time we used fresh catalyst to give 99% yield in 10 min with 4-nitrobenzyl alcohol THP ether, after second time reuse we got 90% yield in 45 min and also we tried for third time reuse to get 78% yield in 2 h.

Experimental

$NaHSO_4$ was obtained from Finar Chemicals Ltd. All solvents were distilled prior to use. 100—200 mesh silica gel was employed for column purification. THP ethers were prepared by standard procedures.[5]

To a stirred solution of THP ether of 4-nitro benzyl alcohol (200 mg, 1.30 mmol) in methanol (10 mL) was added activated (while hot) $NaHSO_4$-SiO_2 (200 mg) at room temperature (the catalyst was kept in an oven at 120 ℃ for 48 h before using it). After completion of the reaction (monitored by TLC), the catalyst was filtered and washed with methanol (5 mL). The filtrate and washings were combined and the solvents were removed under vaccum. The residue was purified by column chromatography using hexane/EtOAc (4∶1) over silica gel to afford the parent alcohol 4-nitrobenzyl alcohol (128 mg, 99% yield).

Conclusions

In conclusion, we have developed a simple, inexpensive and efficient protocol for deprotection of THP ethers using $NaHSO_4$-SiO_2 at room temperature. The reaction completed within 10—15 min. Experimental simplicity, utilization of cheap heterogeneous catalyst and excellent yields are the main advantages of the present procedure.

The present deprotection method is highly efficient. The THP ethers can be easily cleaved in presence of wide range of functional groups present in phenols and alcohols. Aldehyde, boc, nitro, nitrile groups, halogens, and methoxy groups are unaffected. Moreover, the conversions occurred at room temperature and therefore the experimental procedure is simple. The structures of generated alcohols were established by direct comparison of their spectral (^{1}H NMR, 400 MHz) data with that of the authentic alcohols.

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