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Note

Efficient deprotection of tetrahydropyranyl ethers by silica sulfuric acid

Abdol R Hajipour[*, †, ††], Amin Zarei[††], Leila Khazdooz[††],
Seied A Pourmousavi[††], Saeed Zahmatkesh[††] &
Arnold E Ruoho[†]

[†]Dept. of Pharmacology, University of Wisconsin,
Medical School, 1300 University Avenue,
Madison, 53706-1532, WI, USA

[†, ††]Pharmaceutical Research Laboratory, College of Chemistry,
Isfahan University of Technology, Isfahan 84156, IR Iran

E-mail: haji@cc.iut.ac.ir

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Treatment of tetrahydropyranyl (THP) ethers with silica sulfuric acid in methanol provides a simple and efficient process for deprotection of these ethers and the parent alcohols are obtained in excellent yields.

Keywords: Deprotection, tetrahydropyranyl ethers, silica sulfuric acid

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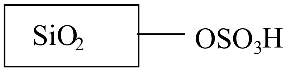
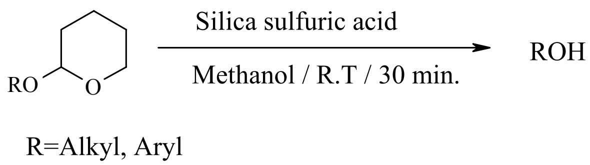
The protection of alcohols as their tetrahydropyranyl ethers is a useful and representative method in modern synthetic chemistry due to their stability towards basic media, Grignard reagent, lithium alkyls, alkylating and acylating reagents and reaction involving oxidation and reduction by inorganic hydrides[1]. Deprotection of these ethers to their corresponding alcohols under mild conditions is also of practical importance and many methods and catalysts have already been applied for this conversion[2-10]. Although some of these methods are useful, 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.

Silica gel reacts with chlorosulfonic acid to give silica sulfuric acid **I**. It is interesting to note that the reaction is easy, clean and no work-up procedure is needed, because HCl gas is evolved from the reaction vessel immediately. So, we also find that silica sulfuric acid **I** is an excellent candidate for sulfuric acid replacement in organic reactions without any limitations such as destruction of acid sensitive functional groups[11].

In ongoing project for deprotection of THP ether under mild conditions herein we report a new method for deprotection of THP ether with silica sulfuric acid in methanol as an efficient cleaving agent (**Scheme I**).



I



Scheme I

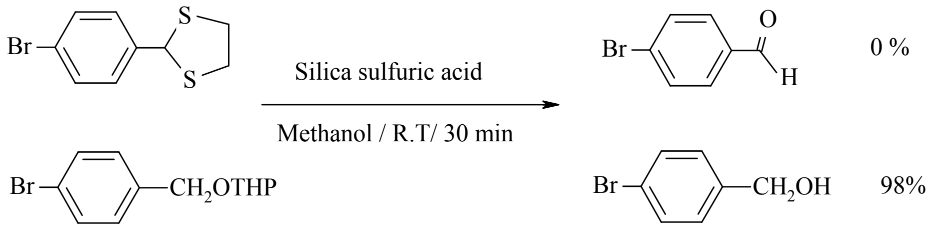
To evaluate the efficiency of the reagent, one equimolar mixture of 2-(*p*-bromophenyl)-1,3-dithiane and *p*-bromobenzyl tetrahydropyranyl ether or one equimolar mixture of *p*-bromobenzaldehyde oxime and *p*-bromobenzyl tetrahydropyranyl ether was treated with catalytic amount of silica sulfuric acid.The results are shown in **Schemes II** and **III**. The reaction was monitored by GC and TLC analysis. As shown in **Schemes II** and **III** and **Table I,** the reagent is suitable for deprotection of OTHP ethers in the presence of other functional groups.

In conclusion, the present procedure provides an efficient and convenient method for deprotection of THP ethers. In addition, high yields and short reaction time periods, straightforward work-up, availability, stability and non-toxicity are advantages of this procedure to the reported methods.

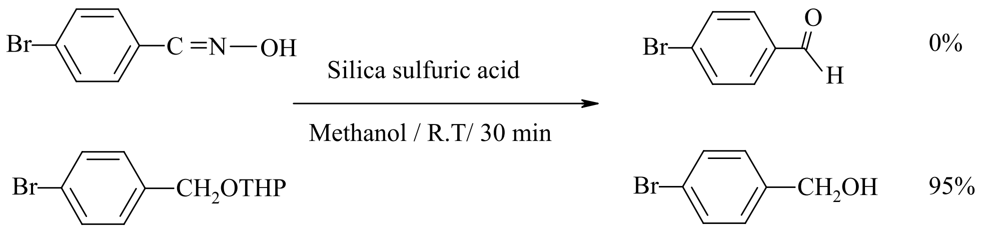
Experimental Section

All yields refer to isolated products. Products were characterized by comparison with authentic samples (IR, ^{1}H NMR spectrum and TLC/GC analysis)[1-10]. All ^{1}H NMR spectra were recorded on a 500 MHz spectrometer in $CDCl_3$ and CCl_4 relative to TMS (chemical shifts in δ, ppm).

Preparation of silica sulfuric acid. A 500 mL suction flask was used. It was equipped with a constant-pressure dropping funnel containing chlorosulfonic acid (46.6 g, 0.4 mole) and gas inlet tube for conducting HCl gas over an adsorbing solution, i.e., water. Into it were charged 60.0 g of

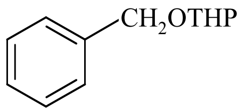
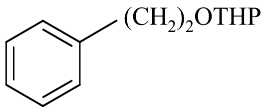
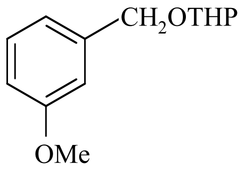
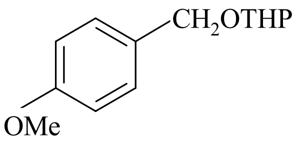
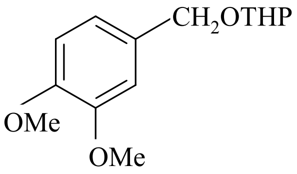
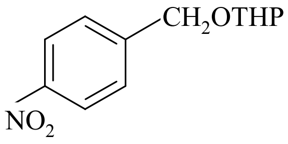


Scheme II



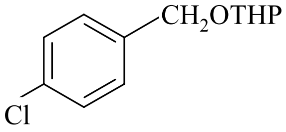
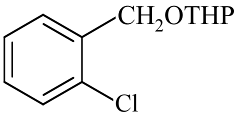
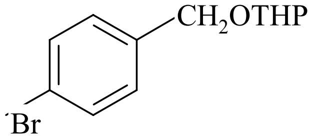
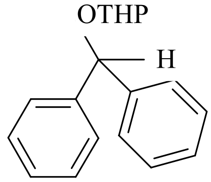
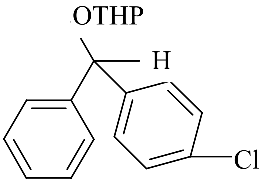
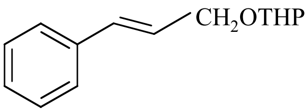
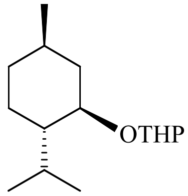
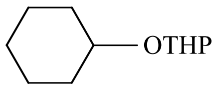
Scheme III

Table I — Deprotection of THP ethers catalyzed by silica sulfuric acid[a]

Entry	Substrate	Deprotection yield (%)[b]
1		98
2		95
3		95
4		98
5		96
6		94

— *Contd*

Table I — Deprotection of THP ethers catalyzed by silica sulfuric acid[a] — *Contd*

Entry	Substrate	Deprotection yield (%)[b]
7		98
8		95
9		98
10		90
11		85
12		94
13		90
14		98
15	$CH_3(CH_2)_7OTHP$	97
16	$(CH_3)_3COTHP$	90
17	$Cl(CH_2)_2OTHP$	98

[a] Products were characterized by comparison with authentic samples (IR and ^{1}HNMR spectrum, TLC) [1-10]. [b] Isolated pure product.

silica gel. Chlorosulfonic acid was added dropwise over a period of 40 min at r.t. HCl was evolved from the reaction vessel immediately after the addition. The mixture was shaken for 30 min at room temperature to obtain a white solid (silica sulfuric acid, 92.0 g)[11].

Detetrahydropyranylation of OTHP ethers of alcohol. General procedure. To a solution of THP ether (2 mmoles) in methanol (5 mL) was added silica sulfuric acid (0.06 g, 0.24 mmoles) and the resulting solution was left at room temperature for 30 min. The progress of the reaction was monitored by GC/TLC. On completion of the reaction, methanol was removed under vacuum and product was purified through a short column of silica gel to obtain pure alcohol. GC retention time was identical with that of an authentic sample and IR and ^{1}HNMR data were in good agreement with the published spectral data.

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