

Rapid Communication

Stannous chloride catalyzed deprotection of tetrahydropyranyl ethers[†]

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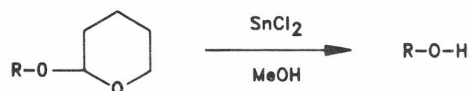
An efficient and mild methodology for the deprotection of tetrahydropyranyl ethers using anhydrous stannous chloride in methanol is described.

Selective introduction and removal of protecting groups is of great significance in organic synthesis. Tetrahydropyranyl ethers are well established as protecting groups for alcohols because of their ease of formation and stability to most non-acidic reagents¹, such as lithium alkyls, metal hydrides, grignard reagents and acylating reagents, etc.

Generally the deprotection of tetrahydropyranyl (THP) ethers is carried out by aqueous acids such as acetic acid, hydrochloric acid, boric acid, etc. The weaker acids invariably require high temperature². Large number of reagents known for the cleavage of the tetrahydropyranyl ethers to corresponding alcohols include $MgBr_2$ ³, Me_2AlCl ⁴, $(NCSBu_2Sn)_2O$ ⁵, $ph_3P.Br_2$ ⁶, and DDQ ⁷, etc. Recently a highly regioselective reductive cleavage of THP ethers using $NaCNBH_3/BF_3.OEt_2$ ⁸ in dry THF has been reported with more than molar stoichiometry of the reagent. In a very recent paper⁹ Maity and Roy have reported that THP ethers can efficiently be deprotected by treatment with excess of $LiCl$ in H_2O -DMSO at 90°C giving the corresponding alcohols in excellent yields.

In this communication we wish to report that anhydrous stannous chloride in methanol can efficiently catalyze the deprotection of tetrahydropyranyl ethers to the corresponding alcohols under mild conditions.

Stannous chloride¹⁰ ($SnCl_2$) is a reducing agent for many functional groups, lewis acid catalyst for C-C bond formations, de-oxygenation of 1,4-endoperoxides, protection of dicarboxylic acids as 1,3-dithianes and selective cleavage of *p*-methoxybenzyl ethers, etc.



R = Alkyl, Benzyl, etc.

Tetrahydropyranyl ethers are efficiently cleaved by catalytic amounts of anhydrous stannous chloride in methanol at room temperature and the results are shown in the Table I. The reaction conditions are mild enough not to effect reduction or isomerization of multiple bonds. Similarly functional groups such as ester, methoxy and methylenedioxy, etc. remain un-affected; however, the tertiary butyl dimethylsilyl ether function is cleaved to the corresponding alcohol¹¹ (cf. Scheme I).

The typical method consists of stirring a mixture of tetrahydropyranyl ether and catalytic amount of anhydrous stannous chloride (20 mole%) at room temperature in methanol. The reaction is usually completed with in 1-3 hr affording alcohols in excellent yields. The efficacy of the methodology can be gauged from Table I where in a wide range of tetrahydropyranyl ethers are deprotected.

The reaction rate is not altered much when catalytic amount of stannous chloride is changed to stoichiometry. The reaction is very sluggish in solvents like acetonitrile, dichloromethane, diethyl ether etc., but very smooth in methanol. Although the mechanism of the reaction is not clear to us, the deprotection may be probably caused by the acidity of the reaction medium (pH 1.3) and a complex formation between stannous chloride and methanol can not be ruled out. Alternatively, the reaction may be proceeding through transacetalisation mechanism similar to PPTS in methanol.

The mildness of the method which works in non-aqueous conditions together with ease of operation and high yields of the products should largely extend the scope of the reagent, which is safe and inexpensive.

All the yields refer to pure isolated products, fully characterized by IR, ¹H NMR, mass spectra and comparison with authentic samples. The tetrahydropyranyl ethers were prepared by copper(II) chloride¹² catalyzed reaction of alcohols with 3,4-dihydro-2H-pyran in dichloromethane as solvent. Anhydrous stannous chloride was pre-

Table I—Stannous chloride catalyzed deprotection of tetrahydropyranyl ethers

Entry	Alcohols	Products	Yield(%)
1			90
2			86
3			88
4			82
5			85
6			75
7			85
8			83
9			80
10			68
11			70
12			85
13			95

pared by adding the dihydrate salt to acetic anhydride (120 g of the salt per 100 g of the anhydride) and stirring the solution vigorously. After an hour the anhydrous stannous chloride was washed free from acetic acid with dry ether and dried *in vacuo*. Methanol used for the reaction was distilled over CaO heated at 600°C in the furnace.

Experimental Section

General procedure for the deprotection of the tetrahydropyranyl ethers. A mixture of the tetrahydropyranyl ether (10 mmoles) and anhydrous stannous chloride (2 mmoles) was stirred in methanol (3 mL) and the progress of the reaction monitored by TLC. After the reaction was completed, the solvent was removed on a rotavac and extracted with solvent ether (15 mL). The ether layer was washed with water (3 × 15 mL) to remove the stannous chloride and concentrated. The residue was column chromatographed over silica-gel using hexane and ethyl acetate (95:5) to get the pure alcohol.

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