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A Simple and Efficient Procedure for Deprotection of Tetrahydropyranyl Ethers Catalysed by Expansive Graphite†

Zhan-Hui Zhang, Tong-Shuang Li,* Tong-Shou Jin and Jian-Xin Wang

Department of Chemistry, Hebei University, Baoding 071002, Hebei Province, P.R. China

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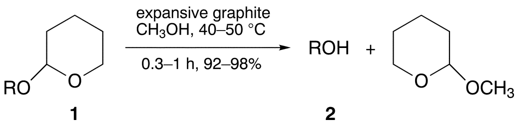
A variety of tetrahydropyranyl ethers of alcohols and phenols are easily deprotected in excellent yield under catalysis by expansive graphite.

Selective introduction and removal of protective groups is of great significance in organic synthesis.[1] The tetrahydropyran-2-yl ether (THPE) functions are one of the most common protecting groups for hydroxy functions owing to their easy installation and remarkable stability towards basic media, Grignard reagents and reactions involving oxidation and reduction by inorganic hydrides.[2]

Tetrahydropyran-2-yl ethers are usually transformed into their parent alcohols or phenols under acid-catalysed conditions. A wide variety of catalysts have been already used for this conversion, including the use of protic acids[3] (acetic acid, toluene-*p*-sulfonic acid, boric acid), Lewis acids[4] (magnesium bromide in diethyl ether, dimethylaluminium chloride), electrogenerated acid,[5] pyridinium toluene-*p*-sulfonate,[6] ion-exchange resins[7] (amberlyst H-15, Dowex 50W-X8, Nafion-H), bis(trimethylsilyl)sulfate,[8] distannoxane,[9] organotin phosphate condensates[10] and triphenylphosphine dibromide (PPh_3Br_2).[11] More recently, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ),[12] mesoporous H-MCM-41 molecular sieve[13] and heteropoly acid[14] have been applied to this reaction. However, some of these procedures suffer from using expensive reagents, strongly acidic conditions and/or necessitate aqueous work-up. Consequently, there is still a demand to develop a mild and efficient alternative procedure for this conversion.

The surface acid character of expansive graphite has been used as an efficient catalyst for organic reactions.[15] Previously we have developed efficient and convenient methods for the preparation[16] and cleavage[17] of 1,1-diacetates and the protection of alcohols by formation of methoxymethyl ethers[18] catalysed by expansive graphite. In connection with our ongoing work on expansive graphite catalysis, herein we wish to report an efficient deprotection of THPEs under catalysis by expansive graphite under mild conditions (Scheme 1).



Scheme 1

As summarised in Table 1, in the presence of expansive graphite the deprotection of THPEs could be carried out rapidly in methanol to afford the corresponding parent hydroxy compounds (**2**) at 40–50; °C in high yields. The present procedure for deprotection of THPEs is quite general as a wide range of THPEs of primary (**1a**–**c** and **1h**), secondary (**1d**–**i**) and benzylic alcohols (**1c**, **1g** and **1i**) as well as phenols and naphthols (**1j**–**1q**) were cleaved in excellent yield. The acid-sensitive functionalities such as methoxy (**1l**) are safe in this procedure. Betulin (**1h**) was not converted into allobetulin under these conditions. The reaction proceeds cleanly and the work-up is simple, involving only the filtration of the catalyst and the removal of solvent to obtain the product in high purity.

The reaction rate is markedly dependent on temperature. We found that at room temperature the reaction proceeds much more slowly; for example, complete conversion of cholesteryl THPE (**1e**) into cholesterol (**2e**) needed 6 h in methanol under catalysis of expansive graphite. The catalyst was easily regenerated by washing with ethanol followed by drying at 120 °C for 1 h. The catalyst could be reused four

Table 1 Deprotection of THPE of alcohols and phenols catalysed by expansive graphite

Substrate	Product	Time (*t*/h)	Yield (%)[a]
n-C_8H_{17}-OTHP (**1a**)	*n*-$C_8H_{17}OH$ (**2a**)	0.70	94
n-$C_{10}H_{21}$-OTHP (**1b**)	*n*-$C_{10}H_{21}OH$ (**2b**)	0.80	96
$PhCH_2$-OTHP (**1c**)	$PhCH_2OH$ (**2c**)	0.50	96
n-$C_6H_{13}CH(OTHP)CH_3$ (**1d**)	*n*-$C_6H_{13}CH(OH)CH_3$ (**2d**)	1.0	97
Cholesteryl-OTHP (**1e**)	Cholesterol(**2e**)	0.60	95
β-Sitosteryl-OTHP (**1f**)	*β*-Sitosterol (**2f**)	0.50	97
Ph_2CH-OTHP (**1g**)	PhCHOH (**2g**)	0.70	92
Lup-20(29)-ene-3*β*,28-diyl-diOTHP (**1h**)	Betulin (**2h**)	1.0	95
PhCH(OTHP)COPh (**1i**)	Benzoin (**2i**)	0.50	94
PhOTHP (**1j**)	PhOH (**2j**)	0.35	96
p-$CH_3C_6H_4OTHP$ (**1k**)	*p*-$CH_3C_6H_4OTHP$ (**2k**)	0.50	96
p-$CH_3OC_6H_4OTHP$ (**1l**)	*p*-$CH_3OC_6H_4OH$ (**2l**)	0.50	96
Resorcinyl-$(OTHP)_2$ (**m**)	Resorcinol (**2m**)	0.50	96
α-Naphthyl-OTHP (**1n**)	*α*-Naphthol (**2n**)	0.30	97
β-Naphthyl-OTHP (**1o**)	*β*-Naphthol (**2o**)	0.65	92
m-$O_2NC_6H_4OTHP$ (**1p**)	*m*-$O_2NC_6H_4OH$ (**2p**)	0.35	98
p-$O_2NC_6H_4OTHP$ (**1q**)	*p*-$O_2NC_6H_4OH$ (**2q**)	0.35	97

[a] Yields refer to isolated pure products.

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*To receive any correspondence (*e-mail:* orgsyn@hbu.edu.cn).

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times for the deprotection of cholesteryl THPE (**1e**) without any loss of catalytic activity.

In conclusion, the present procedure provides a general methodology for the deprotection of THPE from a variety of primary, secondary and benzylic alcohols and phenols. The operational simplicity, use of an inexpensive, non-corrosive and reusable catalyst, high yields and short reaction time can make this procedure a useful and attractive alternative to the currently available methods.

Experimental

The expansive graphite catalyst was prepared according to the literature.[16,19] THPEs were synthesised according to our recent report.[20] The products were characterised by IR and ^{1}H NMR spectra and by comparison of their TLC and mps or bps with authentic samples.

General Procedure for Deprotection of THPE.—A mixture of THPE (2 mmol), methanol (5 ml) and expansive graphite (100 mg) was stirred at 40–50 °C for the length of time indicated in Table 1. The progress of the reaction was monitored by TLC. After completion of the reaction, the catalyst was removed by filtration and washed with CH_2Cl_2 (5 ml). Evaporation of the solvent gave, essentially pure, the corresponding parent hydroxy compound (**2**). Further purification was performed by flash column chromatography on silica gel with light petroleum–diethyl ether as eluent wherever necessary.

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