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A Mild and Efficient Method for Selective Deprotection of Tetrahydropyranyl Ethers to Alcohols[†]

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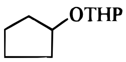
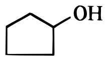
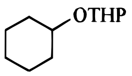
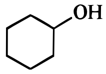
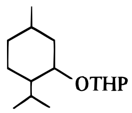
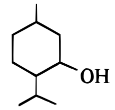
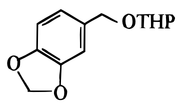
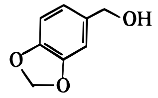
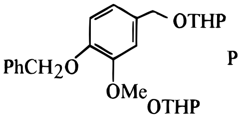
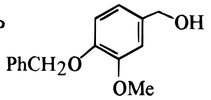
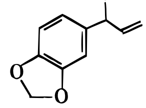
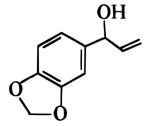
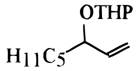
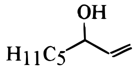
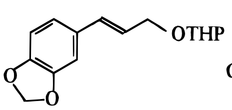
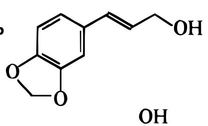
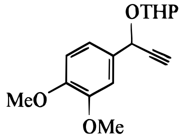
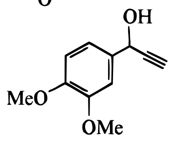
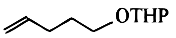
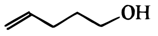
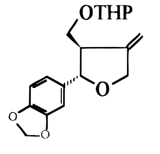
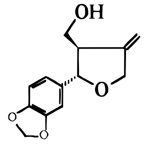
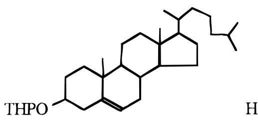
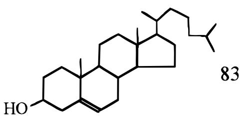
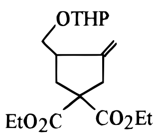
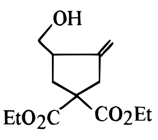
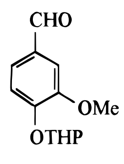
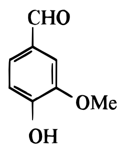
The importance of selective introduction and removal of protecting groups in organic synthesis is well established. Tetrahydropyranylation of hydroxyl groups has been recognized as a useful method for protection of alcohols,[1] because of its easy installation and general stability to most nonacidic reagents. A method that would effect the selective removal of tetrahydropyranyl (THP) ethers in the presence of other sensitive functional groups still remains as a goal. Generally the methods used for the removal of THP ethers employ aqueous reaction media acidified with mineral acids, or nonaqueous media acidified with organic acids.[2] There are few examples which make use of aqueous or nonaqueous neutral reaction conditions,[3] and most of these methods involve some costly and toxic reagents or formation of considerable amounts of side products. We have established that THP ethers can efficiently be deprotected by treatment with excess of LiCl in H_2O−DMSO at 90 °C. This reaction produces the corresponding alcohols in excellent yields, thus providing a mild and efficient aqueous method for the deprotection of THP ethers which does not require the use of acids or generate toxic waste products.

A range of THP ethers were prepared from the corresponding alcohols[4] using the standard procedures [dihydropyran (DHP) and pyridinium *p*-toluenesulfonate (PPTS) in CH_2Cl_2] and subjected to deprotection using an excess of LiCl and H_2O in DMSO at 90 °C for 6 h. The results are summarized in Table 1. All of the products were purified by column chromatography, and the corresponding alcohols were obtained in good yields. This methodology was very effective in removing THP ethers in the presence of other sensitive functional groups such as methylenedioxy ethers (entry 4, 6, 8, and 11), methoxymethyl ethers ($C_5H_{11}CH_2$-OMOM remained unaffected), benzyl ethers (entry 5), methyl ethers (entry 5, 9, and 14), and especially very sensitive aldehyde functionalities (entry 14). It is noteworthy that allylic or styrenyl double bonds and propargylic triple bonds also remain un-

Table 1. Deprotection of THP Ethers[a]

Entry	R-O-THP	Product	Yield (%)
(1)			83
(2)			81
(3)			92
(4)			88
(5)			86
(6)			81
(7)			80
(8)			83
(9)			86
(10)			82
(11)			85
(12)			83
(13)			86
(14)			84

[a] Yields refer to isolated and chromatographically pure products.

[†] This paper is dedicated to Professor U.R. Ghatak on the occasion his 65th birthday.

(1) (a) Reese, C. B. In *Protecting Groups in Organic Chemistry*; McOmie, J. F. W., Ed.; Plenum Press: London, 1973; Chapter 3. (b) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; John Wiley and Sons, Inc.: New York, 1967; Vol. 1, pp 256. (c) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; John Wiley and Sons, Inc.: New York, 1991; p 31.

(2) (a) Bauduin, G.; Bondon, D.; Pietrasanta, Y.; Pucci, B. *Tetrahedron* **1978**, *34*, 3269. (b) Corey, E. J.; Niwa, H.; Knolle, J. *J. Am. Chem. Soc.* **1978**, *100*, 1942. (c) Zimmermann, K. *Synth. Commun.* **1995**, *25*, 2959.

(3) (a) Caballero, G. M.; Gros, E. G. *Synth. Commun.* **1995**, *25,* 395 and references cited therein. (b) Nambiar, K. P.; Mitra, A. *Tetrahedron Lett.* **1994**, *35,* 3033 and references cited therein. (c) Raina, S.; Singh, V. K. *Synth. Commun.* **1995**, *25,* 2395. (d) Srikrishna, A.; Sattigeri, J. A.; Viswajanani, R.; Yelamaggad, C. V. *J. Org. Chem.* **1995**, *60,* 2260.

(4) Some of the alcohols were prepared in our laboratory during the total synthesis of lignans and related compounds; see (a) Adhikari, S.; Roy, S. *Tetrahedron Lett.* **1992**, *33*, 6025. (b) Maiti, G.; Roy, S. C. *J. Chem. Soc., Perkin Trans. 1* **1996**, 403.

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affected under these reaction conditions. Interestingly, the present reaction conditions, although somewhat similar to the Krapcho method,[5] except for lower temperatures, did not affect the *gem*-dicarbethoxy groups while deprotection of THP ethers occurred smoothly (entry 13). The use of NaCl instead of LiCl did not effect the deprotection at all, while it was found that H_2O is essential for the success of the reaction. DMSO was found to be the solvent of choice to provide the maximum yield of the product; use of HMPA or DMF as solvent lowered the yield, while in benzene or THF the reaction did not proceed at all.

In conclusion, we have established a mild, simple, and convenient method for the selective removal of the THP protecting group using a combination of lithium chloride and water in DMSO at 90 °C.

Experimental Section

General Procedure for Deprotection of THP Ethers with LiCl and H_2O in DMSO. A magnetically stirred mixture of THP ether (2 mmol), LiCl (10 mmol), and H_2O (20 mmol) in DMSO (10 mL) was heated at 90 °C for 6 h under N_2. The reaction mixture was allowed to cool to rt, diluted with H_2O (10 mL), and extracted with ether (25 mL × 3). The ether extract was dried over anhydrous sodium sulfate. Evaporation of the solvent followed by purification of the residue on a silica gel (10 g) column using a combination of ethyl acetate and light petroleum (boiling range 60 °C to 80 °C) as eluent furnished hydroxy compounds, which were identified by comparison (TLC, IR, and ^{1}H NMR spectra) with authentic compounds.

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(5) (a) Krapcho, A. P. *Synthesis* **1982**, 805. (b) Krapcho, A. P. *Synthesis* **1982**, 893.