

### Note

## CuCl<sub>2</sub>·2H<sub>2</sub>O - MeOH, a new reagent system for the deprotection of tetrahydropyranyl ethers<sup>†</sup>

K Joju Davis, U T Bhalerao & B Vittal Rao\*

Organic Chemistry Division-II, Indian Institute of Chemical Technology, Hyderabad-500 007, India

Received 16 September 1998; accepted (revised)  
15 February 2000

Cupric chloride dihydrate in methanol cleave the tetrahydropyranyl ethers to the corresponding alcohols in excellent yields under mild conditions.

Deprotection of functional groups is an unavoidable step in organic synthesis. Hydroxyl function can invariably be protected as tetrahydropyranyl ethers in multistep synthetic operations because of its ease of formation as well as removal.

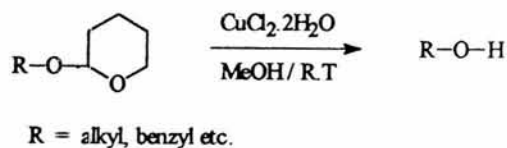
A large number of reagents are known for the deprotection of THP ethers<sup>1</sup>. Recently LiCl in DMSO-H<sub>2</sub>O,<sup>2</sup> SnCl<sub>2</sub>,<sup>3</sup> NH<sub>4</sub>Cl<sup>4</sup> have been reported for the cleavage of THP ethers. However some of these reagents suffer from the disadvantages of high cost, high temperature requirement and being strongly acidic.

Efforts have been made to conduct the reactions under milder conditions as the mild methods are highly desirable to safeguard other functionalities.

Now we would like to present our findings with a new reagent system, i.e., CuCl<sub>2</sub>·2H<sub>2</sub>O in methanol as an efficient cleaving agent for the tetrahydropyranyl ethers.

The typical reaction consists of stirring the tetrahydropyranyl ether with an equimolar quantity of the reagent in methanol for 1-1.5 hr to afford the corresponding alcohol in excellent yields (**Scheme I**).

The salient features of the reagent system are the other functional groups such as methoxy, methoxyethoxymethyl (MEM), Methyleneedioxy ethers, esters etc., are unaffected and also does not result in addition-elimination reactions with the multiple bonds present in the system. However, the tertiarybutyldimethylsilyl (TBDMS) and tertiary-



**Scheme-I**

butyldiphenylsilyl (TBDPS) ether functions are cleaved.

The **Table I**, illustrates the versatility of the new methodology which is capable of cleaving the THP ethers of primary, secondary, allylic and benzylic alcohols in excellent yields.

Best results are obtained when molar stoichiometry of the reagent is used with a reaction time of 1 to 1.5 hr, whereas the reaction requires longer time with less reagent. Although many protic solvents have been tried, methanol is found to be the most suitable polar protic solvent for the efficient deprotection.

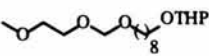
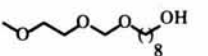
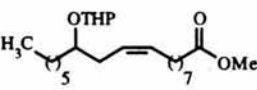
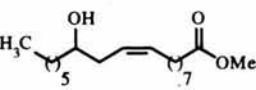
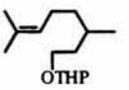
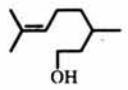
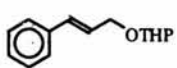
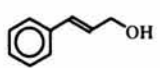
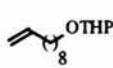
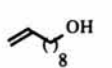
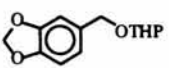
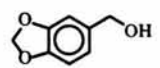
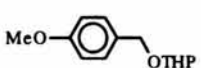
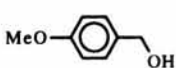
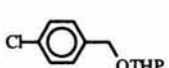
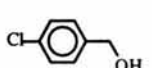
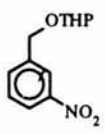
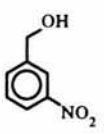
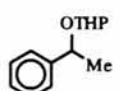
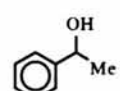
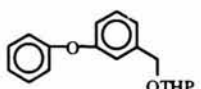
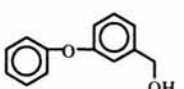
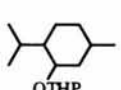
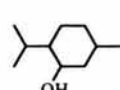
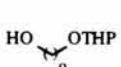
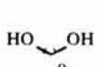
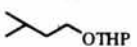
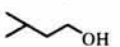
Cupric chloride dihydrate is a mild Lewis acid. The deprotection may be probably caused by the mild acidity of the reaction medium, proceeding through the transacetalisation mechanism similar to PPTS in methanol. With a view to prove the mechanism of the reaction, the reaction mixture was analysed by gas chromatographic method using HP 5890 gas chromatograph equipped with OV.17 S.S. column (10 ft, 10% on chromosorb A). The analysis unequivocally established the formation of 2-methoxytetrahydropyran (prepared by reacting methanol with dihydropyran in presence of catalyst, *p*-toluenesulphonic acid) as a trans acetalization product and in turn the mechanism.

In conclusion cupric chloride dihydrate proved to be an effective reagent system for the cleavage of tetrahydropyranyl ethers. The mild reaction conditions and the excellent yields make the reagent more versatile. The synthetic utility of the reagent is apparent on these grounds as well as, the easy availability of the reagent.

**Note:** All the yields refer to the pure isolated products (**Table I**), fully characterised by IR, <sup>1</sup>H NMR and mass spectra and comparison with authentic samples. Tetrahydropyranyl ethers are obtained by the reaction of alcohol and 3,4-

<sup>†</sup>IICT Communication No. 4126.

**Table I**—Deprotection of tetrahydropyranyl ethers using cupric chloride dihydrate in methanol

Entry	THP ether	Alcohol	Yield (%)
1			82
2			68
3			90
4			89
5			95
6			87
7			85
8			92
9			85
10			85
11			95
12			83
13			95
14			90

dihydro[2H]pyran in presence of catalytic cupric chloride<sup>5</sup> in dichloromethane as solvent. The methanol used for the reactions was distilled over anhyd. calcium oxide.

### Experimental Section

#### General procedure for the deprotection of

**tetrahydropyranyl ethers.** Tetrahydropyranyl ether (10 mmoles) and cupric chloride dihydrate (10 mmoles) were stirred together in methanol (5 mL) for a period of 1-1.5 hr (the progress of the reaction is monitored by TLC). At the end of the reaction period, the solvent was removed under reduced pressure and extracted with ethyl acetate (15 mL). The organic

layer was washed with water (3×15 mL) to remove the cupric chloride and concentrated. The residue was column chromatographed over silica gel using pet. ether-ethyl acetate (3:1) solvent system to get the pure alcohol.

#### Acknowledgement

One of the authors (K.J.D) is thankful to CSIR, New Delhi for financial support in the form of senior research fellowship.

#### References

- 1 a) Greene T W & Wuts P G M, *Protective groups in organic synthesis*, 2nd Edn (John Wiley & Sons Inc, New York), 1991 and references cited therein b) Miyashita M, Yoshikoshi A and Grieco P A, *J Org Chem*, 42, 1977, 3772 c) Kim S & Park J H *Tetrahedron Lett*, 28, 1987, 439 d) Ogava J & Shibasaki M, *Tetrahedron Lett*, 25, 1984, 663 e) Otera J & Nozaki H, *Tetrahedron Lett*, 27, 1986, 5743 f) Srikrishna A, Sattigeri J A, Viswajanani R & Yelamaggad C V, *J Org Chem*, 60, 1995, 2260 g) Wagner A, Heitz M P & Mioskowski C, *J Chem Soc Chem Commun*, 1989, 1619.
- 2 Maiti G & Roy S C, *J Org Chem*, 61, 1996, 6038.
- 3 Davis K J, Bhalerao U T & Vittal Rao B *Indian J Chem*, 36B, 1997, 211.
- 4 Yadav J S, Srinivas D & Reddy G S, *Synth Commun*, 28, 1998, 1399.
- 5 Davis K J, Bhalerao U T & Vittal Rao B, *Synth Commun*, 26, 1996, 3081.