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LETTERS

An Efficient Method for Deprotection of Acetals

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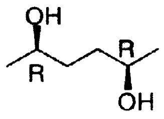
Abstract: A variety of acetonides and acetals were efficiently cleaved using $CuCl_2.2H_2O$ in MeCN. The method was effectively used in synthesis of chiral diols which are important in asymmetric synthesis.

Recently we reported a short and convenient synthesis of (2*R*,5*R*)-2,5-hexanediol **1** from mannitol *via* a tetraol **3**.[1] One of the drawbacks in the synthesis was the moderate yield (45-60 %) during the conversion of an acetonide **2** into the tetraol **3**, which was done using acetyl chloride in methanol. The major problem with the reaction was inconsistency in the yield due to partial conversion into the desired product. In view of the importance of the diol **1** in asymmetric synthesis and our own need for the chiral base chemistry programme, there was a need for a clean method for the above conversion. While working on a part of our programme on allylic oxidation of olefins using copper salts, we discovered that the reaction of the acetonide **2** with $CuCl_2.2H_2O$ (2 equiv.) in MeCN at reflux temperature for 4h gave the tetraol **3** in 94% yield.



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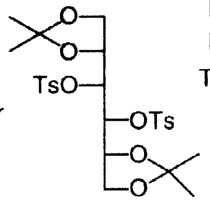

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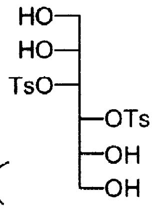

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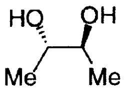
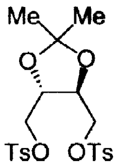


(2*S*,3*S*)-**4**



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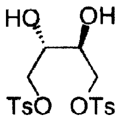

6

In order to show versatility of the reagent in deprotection of acetonide, we carried out deprotection of an acetonide **5**[2a] into a diol **6** in quantitative yield under the above condition. The compound **6**[2b] is a precursor for a chiral diol (2*S*,3*S*)-**4** which is a very useful chiral auxilliary in asymmetric synthesis.[2c] The cleavage of acetonide with cupric chloride prompted us to see its utility on cleavage of other kind of acetals as well. Although many methods have been examined for removal of acetals,[3] cupric chloride has not been used for this purpose.[4] The known acetals were prepared and reacted with $CuCl_2.2H_2O$ in MeCN at rt. It was gratifying to see that most of the acetals were cleaved into aldehydes/ketones in short time in high yield. The results are summarized in the Table.[5] The deprotection reaction worked even with a catalytic amount of copper chloride, but the reaction time was longer. For example, cleavage of acetophenone acetal (entry 4) with 10 mole% of the copper chloride in MeCN took 5 h for completion of the reaction (isolated yield 85 %). Similarly, camphor acetal (entry 9) was deprotected with 10 mole% of the reagent in 5h, and the yield was 75 %. The pH 2 to 3 of the reaction mixture indicated that the deprotection under the present condition was probably acid catalyzed reaction.[6]

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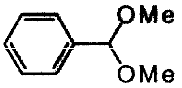
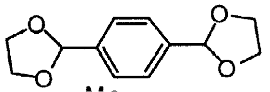
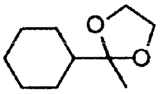
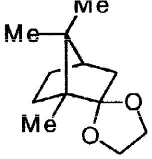
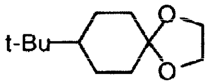
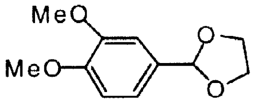
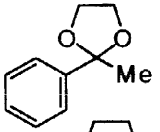
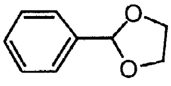
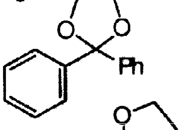
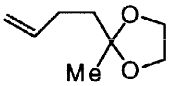
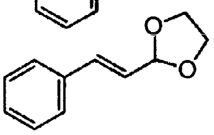
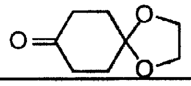
Table: Cleavage of Acetals with 2 equiv. of $CuCl_2.2H_2O$ in Acetonitrile at rt.

Entry	Substrates	Time (min)	% Yield	Entry	Substrates	Time (min)	% Yield
1.		30	85	8.		90	88
2.		30	85	9.		30	78
3.		30	90	10.		30	93
4.		30	96	11.		30	95
5.		30	98	12.		30	74
6.		30	98				
7.		30	95				

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3. For some recent methods for deprotection of acetals, see: (a). Sen, S. E.; Roach, S. L.; Boggs, J. K.; Ewing, G. J.; Magrath, J. *J. Org. Chem.* **1997**, *62*, 6684. (b). Gautier, E. C. L.; Graham, A. E.; McKillop, A.; Standen, S. P.; Taylor, R. J. K. *Tetrahedron Lett.* **1997**, *38*, 1881. (c). Mandal, P. K.; Dutta, P.; Roy, S. C. *Tetrahedron Lett.* **1997**, *38*, 7271.
4. To the best of our knowledge, $CuCl_2$ has not been used in literature for deprotection of acetals. However, it has been used for preparation of acetals. For references, see: (a). Matsumura, K.; Aono, T. Eur. Pat. Appl. **1997**, EP 82-305053 820924; CA 99: 71129. (b). Satoh, J. Y.; Yokoyama, C. T.; Haruta, A. M. *Chem Lett.* **1974**, 1521.
5. After deprotection reaction was over, most of the solvent was removed and the crude was taken in ether. The ethereal layer was washed with aq. $NaHCO_3$ solution, brine, and dried. Solvent removal and purification over silica gel gave pure product.
6. In a preliminary experiment it was found that $CuCl_2.2H_2O$ also cleaved TBDMS ether in an efficient manner. For example, decanol-TBDMS ether was cleaved in 30 min. into alcohol in 92% yield. Similarly, decanol THP ether was cleaved in 90 min. into the alcohol in 50% yield.