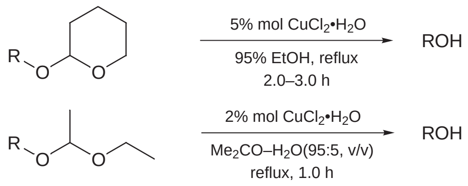
[redacted]

[redacted] condition. As expected, we found it
EE groups and [redacted]
H_2O (95:5 v/v). The removal of
$O-H_2O$ (95:5) as solvent is however,
xing $Me[CH_2]_{21}OTHP$ with 5% mol

[redacted]

$CuCl_2 \cdot H_2O$ in Me_2CO-H_2O (95:5 v/v) for 6 h gave the parent alcohol in only 25% isolated yield.



Scheme 1

In order to gain some insight into the mechanism of this novel deprotection process, we investigated the reaction with anhydrous $CuCl_2$ in anhydrous EtOH. We found that both THP and EE groups could be removed as efficiently as when using $CuCl_2 \cdot 2H_2O$ in H_2O-containing EtOH. Therefore, H_2O is not indispensable for these reactions. However, refluxing of EE protected compound with anhydrous $CuCl_2$ in anhydrous acetone led to decomposition to several unidentified products. Additionally $THF-H_2O$ (95:5 v/v) was an unsuitable solvent for deprotection and led to no reaction after refluxing for several hours. We also tested $CuSO_4 \cdot 5H_2O$ and $Cu(acac)_2$ and found them to be ineffective in the deprotection of THP or EE groups under the same conditions.

Since an aqueous solution of $CuCl_2$ is acidic (pH 3.6 in 0.2 M aqueous solution), it is most possible that these deprotection reactions are simply acid-catalyzed hydrolysis of acetals. However, considering the catalytic amount of $CuCl_2$ in the reaction system, it is also likely that metal complexation is involved in the reaction so as to facilitate. Sen *et al.* recently reported that $FeCl_3 \cdot 6H_2O$ could remove THP protecting groups.[5] It seems likely that these processes have some common feature in the reaction pathway. However, the detailed mechanism for $CuCl_2$-promoted deprotection is still unclear.

In Table 1 (entry 5), both THP and dioxolane groups in the 3β-OH and 17-oxo-protected epiandrosterone were found to be removed under the $CuCl_2$-promoted deprotection conditions. This suggests that dioxolane groups in general might be also removed under the same reaction conditions. We then investigated the ability of $CuCl_2 \cdot 2H_2O$ to cleave cyclic dioxolane derivatives. Thus, ketals and acetals were prepared according to standard procedures,[1] and the deprotection was conducted under the same conditions as for the THP ethers and results are summarized in Table 2. Although the deprotection indeed worked in most of cases, the reaction generally takes longer than for corresponding deprotection of THP or EE groups. In several cases, the reaction did not proceed to completion (Table 2, entries 3, 4 and 5). In one case, the acetal group was not cleaved and the starting material was recovered unchanged (entry 6).

In conclusion, we have discovered an efficient method for the deprotection of THP and EE groups. The reaction is remarkably simple and requires only a catalytic amount of inexpensive and readily available copper(II) chloride dihydrate.

Experimental

$CuCl_2 \cdot 2H_2O$ was obtained from Beijing Chemical Reagent Co., China and anhydrous $CuCl_2$ was purchased from Aldrich. All solvents were distilled prior to use. 100–200 Mesh silica gel (Qingdao, China) was employed for column chromatography purification. THP ethers, EE ethers and dioxolane derivatives were prepared by standard procedures and characterized by ^{1}H (200 MHz) and ^{13}C NMR (50 MHz).

General Procedure for Deprotection with $CuCl_2 \cdot H_2O$. — The protected compound (1 mmol) was dissolved in 95% EtOH (10 mL) or Me_2CO-H_2O (95:5 v/v; 10 mL). To the solution was added $CuCl_2 \cdot H_2O$ (0.05 or 0.01 mmol and the homogenous solution was heated under gentle reflux until completion of the reaction (monitored by TLC). After cooling, the solvent was removed by evaporation. Diethyl ether (30 mL) was added to the residue, and the mixture was washed with H_2O and saturated aqueaus NaCl. The ethereal solution was dried over anhydrous $MgSO_4$. Removal of the drying agent and the solvent gave a crude product, which was purified by column chromatography with silica gel. The pure parent compound was identified by comparison with an authentic sample (TLC, ^{1}H NMR, ^{13}C NMR).

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