

An Efficient Cleavage of 1,3-Dioxolane Using $\text{ZnCl}_2/\text{THF}/\text{H}_2\text{O}$

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Abstract: A new, mild and efficient method for the cleavage of 1,3-dioxolane is reported.

Keywords: 1,3-Dioxolane, ketal, deprotection

Selective reactions on a functional group of polyhydroxy compounds are extremely useful in organic synthesis, especially in the field of carbohydrate and nucleoside chemistry. Indirect methods for the selective reaction on a functional group of polyhydroxy compounds involve the use of protective groups. In order to utilize this methodology efficiently, selective protection and deprotection of certain hydroxy groups within the polyhydroxy compound are required.

Ketal formation is most commonly used for protecting 1,2- and 1,3-diols. Great effort has been invested in the selective cleavage of these protective groups¹. Most of the methods widely used now to cleavage ketals can be categorized into two groups: acid catalyzed hydrolysis and oxidative cleavage. The selective cleavage of ketals by these methods is difficult if the substrates contain other acid- and oxidation-labile groups. So, milder condition for their cleavage is still in need to be developed².

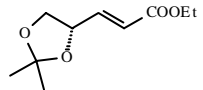
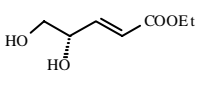
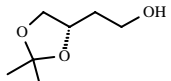
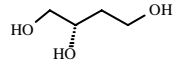
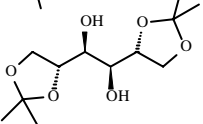
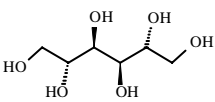
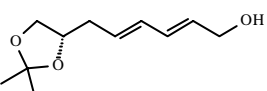
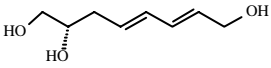
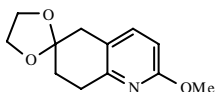
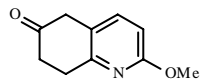
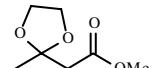
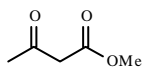
Recently, we found $\text{ZnCl}_2/\text{THF}/\text{H}_2\text{O}$ is of choice for this end. Typical procedure is as follows: Ketal (1 mmol) was dissolved in THF- H_2O (5 mL, 4 : 1). ZnCl_2 (40 mg) was then added. The pH value of the media is 6.5-7. The mixture was refluxed for 30 minutes. It was then cooled to r.t. and then ether or ethyl acetate (50 mL) was added. The organic layer was washed with water (10 mL), saturated aq. NaHCO_3 (10 mL) and brine (10 mL) successively. The organic phase was dried over anhydrous Na_2SO_4 . Removal of the solvent under reduced pressure gave the deprotected product in 85-97% yield.

A variety of ketals were used to test its generality and the results are shown in **Table 1**.

Some compounds with other acid labile protective groups, such as TBS, THP, were also treated under the same conditions. Their cleavages were very slow. Accordingly, we consider that $\text{ZnCl}_2/\text{THF}/\text{H}_2\text{O}$ is selective to the cleavage of ketals in the presence of other acid sensitive protecting groups.

In summary, zinc chloride in aqueous THF is a method of choice in the selective cleavage of ketals.

Table 1. Selective Deprotection of Acetonides and 1,3-Dioxolanes

Substrate*	Product*	Yield (%)
		90
		92
		85
		87
		95
		97

* All are known compounds

References

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