A Novel, Efficient, and Selective Cleavage of Acetals Using Bismuth(III) Chloride

Gowravaram Sabitha,* R. Satheesh Babu, E. Veakata Reddy, and J. S . Yadav
Organic Division I, Indian Institute of Chemical Technology, Hyderabad 500 007, India

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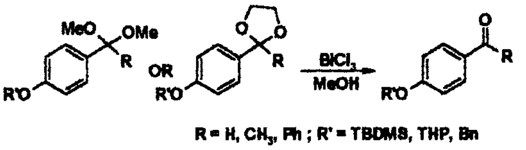
Treatment of acetals with bismuth(III) chloride in methanol provides a simple, convenient and chemoselective process for deprotection, and the parent aldehyde or ketone was obtained in high yield. The acetals have been cleaved selectively in the presence of silyl, benzyl and tetrahydropyranyl ethers.

Acetals are most frequently used protecting groups for carbonyl functionality in organic synthesis. The deprotection of these groups into aldehydes and ketones is an important transformation and usually accomplished by aqueous acid hydrolysis using several acids such as hydrochloric acid, acetic acid, oxalic acid, *p*-toluenesulfonic acid, trifluoroacetic acid etc. Other methods include using Lewis acids,[2] oxidative conditions,[3] phosphorus-based reagents[4] and silicon-based reagents.[5] Recently (trimethylsilyl) bis(fluorosulfinyl)imide[6] and thiourea[7] have been employed for the effective cleavage of these groups. Many of these procedures suffer from one or more drawbacks such as lack of selectivity due to strong acidic conditions, oxidizing nature, non commercially available reagent and unsatisfactory yields. Although all these procedures have their own advantages, there is still a great need to develop an efficient method which is non acidic, anhydrous and mild to cleave the acetals selectively in presence of other ether linked protecting groups.

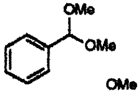
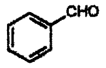
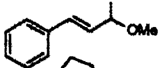
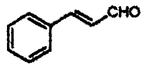
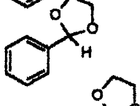
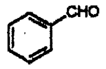
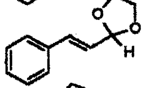
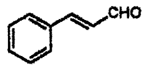
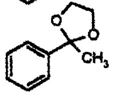
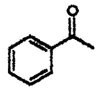
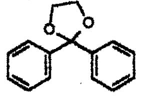
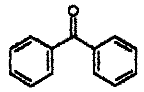
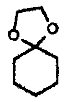
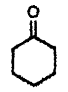
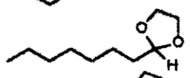
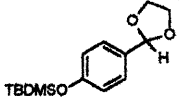
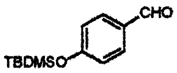
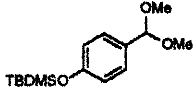
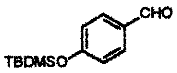
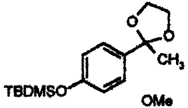
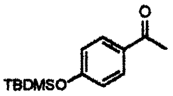
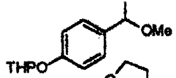
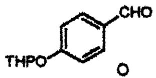
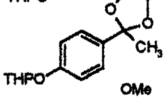
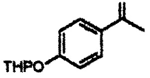
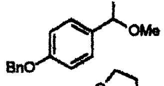
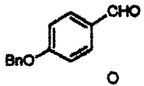
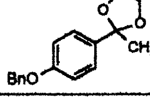
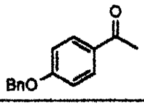
Over recent years, the catalytic activity of bismuth(III) derivatives as Lewis acids has been demonstrated in several reactions such as cyanation and allylation of carbonyl compounds,[8] Friedel–Crafts,[9] enoxysilanes,[10] allylsilanes,[11] cross aldol and Michael reactions. Mukaiyama,[12] carbonyl-ene[13] reactions and carbonyl Diels–Alder reactions[14] reveal the exclusive importance of bismuth(III) salts over other Lewis acids.[15] We herein report a simple, efficient and selective method for the cleavage of acetals using bismuth(III) chloride as catalyst. Even though bismuth(III) halides[16] have been known for thioacetalization, it is justified here to note that we have made a systematic study on the deprotection of acetals and found high selectivity over the other ether linked protecting groups.

Thus, a mixture of benzaldehyde dimethylacetal (entry 1, 1



Scheme 1

Table 1. Cleavage of acetals using $BiCl_3$

Entry	Substrate	Product[a]	Reaction time	Yield[b] %
1			30 min	92
2			45 min	85
3			30 min	90
4			45 min	89
5			30 min	86
6			6 h, reflux	80
7			8 h, reflux	70
8			8 h, reflux	76
9			30 min	85
10			30 min	82
11			30 min	85
12			30 min	80
13			30 min	85
14			30 min	84
15			30 min	85

[a]All products were characterized by ^1H NMR & IR spectra. [b]The yields were determined after chromatographic purification.

eq), bismuth chloride (0.5 eq) and methanol (5 mL) was stirred at room temperature for 30 min, on completion, (monitored by thin layer chromatography) the reaction mixture was subjected to usual workup which yielded 92% of the deprotected product. A wide range of acetals has been subjected to cleavage by this procedure with bismuth chloride to provide the corresponding aldehydes and ketones in good yields (Table 1). It was observed that the cleavage of these groups was faster in methanol rather than in dichloromethane. However, 1,3-dioxolanes of aliphatic compounds required reflux conditions to accelerate the reaction.

With these results, we have extended our studies on doubly protected acid-sensitive substrates for making the procedure more effective. Silyl ethers with acetals (entries 9, 10, 11) were subjected to the cleavage procedure and observed the selective cleavage of acetal group only. Similarly THP ethers of acetal (entries 12, 13) and benzylic ethers of the acetal (entries 14, 15) were also converted to the singly protected compounds without any noticeable deprotection of the other protecting groups.

In conclusion, we have developed a new and efficient selective method for the deprotection of acetals using $BiCl_3$, an inexpensive, commercially available and non-toxic reagent. Moreover, the selectivity of the procedure under mild Lewis acid conditions may find application in organic synthesis.

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17 General Procedure: To an acetal (1 mmol) in MeOH (5 mL), $BiCl_3$ (0.5 mmol) was added and stirred for the specified time and conditions (Table l). On completion, MeOH was removed under reduced pressure and ice was added to quench the catalyst. The reaction mixture was extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with water and dried over Na_2SO_4. The solvent was removed under reduced pressure, and subjected to further purification by column chromatography to give the corresponding aldehyde or ketone.

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