

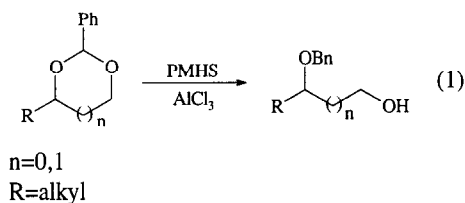
Regioselective Reductive Ring Opening of Cyclic 1,2- and 1,3-Benzylidene Acetals

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A combination of polymethylhydrosiloxane (PMHS) and AlCl_3 was found to be a superior hydride source for reductive ring opening of cyclic benzylidene acetals of both 1,2- and 1,3-diols.

Benzylidene acetals of 1,2- and 1,3-diols form an important class of organic compounds because of their ability to selectively liberate one hydroxyl group, while blocking the other as a stable benzyl ether.¹ The importance of these acetals is more pronounced especially when one of the hydroxyl groups is primary and the other secondary. The selective opening of these benzylidene acetals to either 1° or 2° benzylated alcohols is generally achieved by various reducing agents. These include LiAlH_4 - AlCl_3 ,² DIBAL-H,³ $\text{BH}_3 \cdot \text{Me}_2\text{NH} \cdot \text{BF}_3 \cdot \text{Et}_2\text{O}$,⁴ $\text{NaCNBH}_3 \cdot \text{HCl}$,⁵ $\text{Et}_3\text{SiH} \cdot \text{TFA}$,⁶ as well as others.⁷ All these reagents offer their own advantages as well as limitations depending on the nature of substrate and reaction conditions. Also most of these reagents are either expensive, need specialised reaction conditions or are pyrophoric. In this paper, we describe, a very mild regioselective reductive ring opening of 4,5-*O*-benzylidene acetals of glucopyranosides and a few 1,2-*O*-benzylidene acetals, using $\text{PMHS} \cdot \text{AlCl}_3$. It is pertinent to mention that polymethylhydrosiloxane (PMHS)⁸ is an inexpensive and unexplored reduction reagent (1).



To make us believe the fact that $\text{PMHS} \cdot \text{AlCl}_3$ combination is an effective reducing reagent, methyl 2,3-di-*O*-benzyl 4,6-*O*-benzylidene- α -D-glucopyranoside (entry 1, Table 1) was subjected to the reductive opening protocol using PMHS and AlCl_3 in ether : CH_2Cl_2 mixture for 12 h at ambient temperature. This resulted in the clean formation of methyl 2,3,4-tri-*O*-benzyl- α -D-glucopyranoside without any traces of the other regioisomer. The regioselectivity achieved in the case of entry 2 demonstrates that the bulkiness of the protecting group at C-3 has no role to play. Otherwise sensitive substrate, methyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene- α -D-glucopyranoside furnished 4-*O*-benzyl-2,3-diacetyl compound (entry 3) in 82% yield. This substrate was sensitive to LiAlH_4 - AlCl_3 and acetates were cleaved. Identical selectivity was achieved on azido substrate (entry 4) and carboxylic ester substrate (entry 5). Entry 6 clearly demonstrates that even silyl ethers resist the reaction protocol. The benzylidene acetal (entry 7) having an adjacent ester group also reacted with ease under the described conditions and selective reductive ring opening to yield methyl 3-benzyloxy-2-hydroxy-5-phenylpentanoate in

Table 1. Reductive ring opening of cyclic benzylidene acetals with $\text{PMHS} \cdot \text{AlCl}_3$

Entry	Substrate	Product	Yield /%
1			80
2			78
3			72
4			69
5			70
6			65
7 ^a			68

^aThe compound is racemic and relative stereochemistry is defined.

68% yield. This example gives an access to selectively differentiate two 2° alcohols.⁹

In conclusion, it is pertinent to mention that the reductive ring opening of cyclic benzylidene acetals (both 1,2 and 1,3) has been achieved for the first time using polymeric hydride source namely polymethylhydrosiloxane (PMHS).¹⁰

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- 9 The structures of the products were unambiguously confirmed by comparing with literature data and / or by acetylating the resulting free alcohols.
- 10 Experimental Procedure : Typically, to a solution of methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene- α -D-glucopyranoside (entry 1, 3 mmol) and 0.7 ml of PMHS, in 1:1 ether: CH₂Cl₂ (20 ml), was added AlCl₃ (3 mmol) in 1:1 ether: CH₂Cl₂ mixture (5 ml). The reaction mixture was stirred at ambient temperature for 12 h, ice cold water (50 ml) was added and stirred for further 30 min. The reaction mixture was extracted with CH₂Cl₂ (3x50 ml), washed with water, brine and dried over sodium sulphate. The solvent was removed under reduced pressure and the pure product was isolated by simple column chromatography (silica gel 100-200 mesh, 25: 2 hexane : ethyl acetate) in 80% yield.

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