



Allyl Cleavage under Mild Oxidative Conditions

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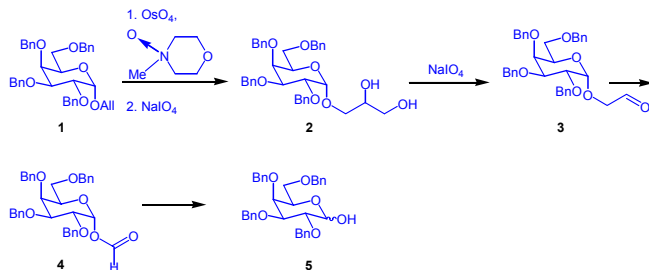
The allyl ether is a common protecting group that permits orthogonal protection strategies with a wide range of protecting groups and is widely employed in multi-step synthetic schemes. We report here a novel and convenient method of *O*- and *N*-allyl deprotection under neutral, mild oxidative conditions.

Two specific oxidating reagents are employed for the reaction: osmium tetroxide with 4-methyl morpholine *N*-oxide as a co-oxidant which specifically oxidizes double bonds, and a periodate salt that cleaves vicinal diols. The reaction conditions were optimized on allyl galactoside **1** as an example (Scheme 1). Heterogeneous conditions in which an aqueous solution of 3 equivalents of sodium or potassium periodate was added to a dioxane solution of **1**, containing 3 equivalent of 4-methyl morpholine *N*-oxide and a catalytic amount of OsO_4 were found to give the best yield. The reaction is rather slow and requires 4-5 days to complete (yield 73%). Increasing the temperature to 50-60°C reduces the time to 5-16 h but the yield is somewhat lower (60%). Over the course of the reaction the allyl group gradually oxidizes to an *O*-formate derivative, which undergoes slow hydrolysis. Intermediates accumulate in the reaction mixture and can be isolated at certain stages of the reaction. Thus, an epimeric mixture of diol **2**, aldehyde **3** and formate **4** were each isolated and characterized.

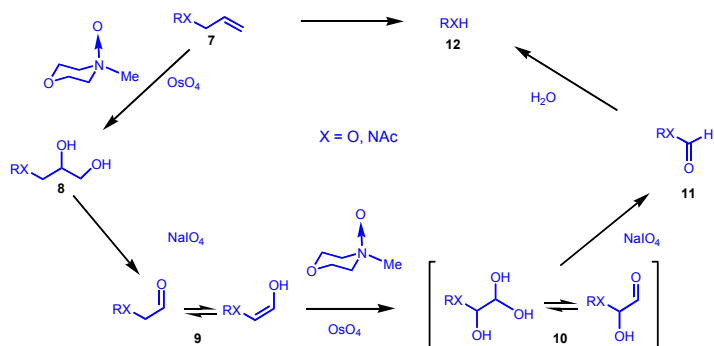
The intermediate aldehyde **2** accumulates in the reaction mixture immediately after NaIO_4 is added and can be isolated. Evidently, the presence of both oxidative agents, 4-methylmorpholine *N*-oxide with a catalytic amount of OsO_4 and NaIO_4 , is necessarily for the conversion of the aldehyde **3** into the free hydroxyl derivative **5**: stirring of a solution of **2** at 60°C and in the presence of any one of the oxidative agents separately led only to unidentified decomposition products, whereas, the reaction with a mixture of both agents gave the target alcohol **5** in 67% yield.

Based on these observations a mechanism for the oxidative removal of the allyl functionality is proposed in Scheme 2. It includes: an initial osmium tetroxide-catalyzed dihydroxylation of the double bond of **7** followed by periodate oxidation of the resulting glycerol derivative **8** to provide the glycolaldehyde ether **9**. The enol tautomeric form of the aldehyde **9** undergoes further osmium tetroxide-promoted oxidation to give a hemiacetal **10**, which may either undergo hydrolysis directly to free hydroxyl **12** or be subjected to one more oxidative cleavage by peroxide to generate the hydrolysis prone formate derivative **11**.

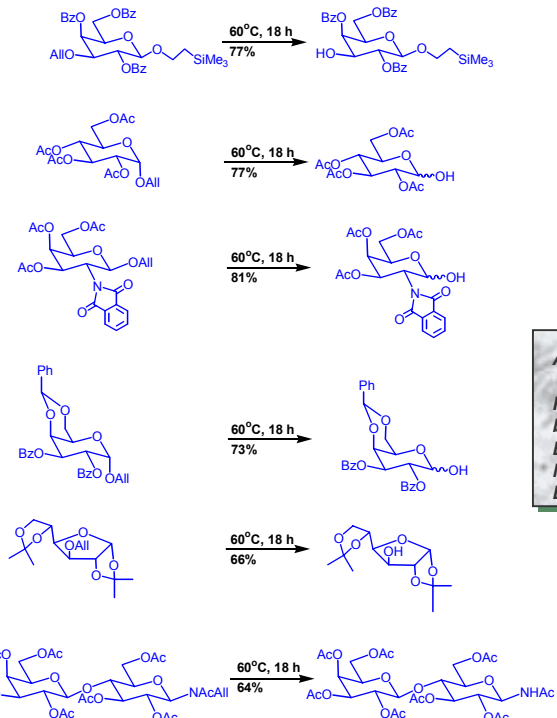
Further examples of oxidative cleavage of allyl groups in different chemical environments are presented in Scheme 3. They include: deprotection of *O*-allyl ethers that substitute sugars at secondary alcohol and anomeric positions in the presence of base labile ester protecting groups as well as acid labile cyclic ketal and acetal protections of diol. The last example demonstrates the possibility of *N*-allyl deprotection.



Scheme 1



Scheme 2



Scheme 3

Acknowledgements
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