

2-Methylprenyl Group as Acid Labile Alcohol Protection

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Prenyl group is used as an alcohol protection that can be cleaved in a variety of conditions (transition metal catalyst, DDQ, pTsOH, TMSOTf, I₂/Zn). Nevertheless, many of the known methods used for deprotection of prenyl ethers suffer from drawbacks such as unsatisfactory yields, long reaction time, costly catalysts and by-product formation. Recently we have reported the use of 2-methylprenyl group as *O*-protecting group for hydroxamic acids that could be cleaved in relatively mild acid conditions generating volatile by-products [1].

Herein, we report the synthesis of 2-methylprenyl ethers and conditions for protecting group cleavage in acidic conditions. The synthesis of 2-prenylmethyl ethers **3** from alcohols **1** was implemented using Williamson ether synthesis with tosylate **2a** or bromide **2b** as alkylating agents. Screening of cleavage conditions with **3a** as a model substrate revealed that the use of 1 M TFA in DCM is optimal to achieve quantitative deprotection in reasonable reaction time (1.5 h).

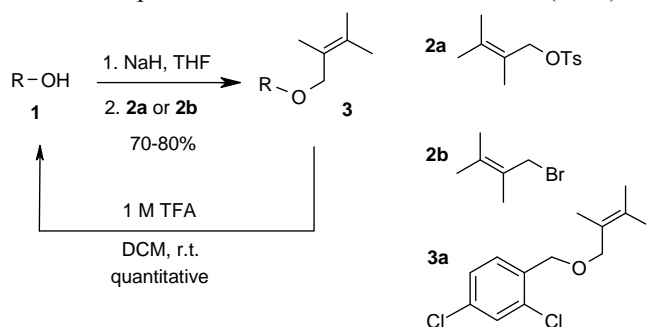
Stability of **3a** under various reaction conditions commonly used for the cleavage of prenyl ethers was also investigated. We observed that 2-methylprenyl group is stable in the presence of metal catalyst [2]; however, the 2-methylprenyl protection was unstable in the presence of DDQ [3], pTsOH [4] or I₂/Zn [3].

To conclude, 2-methylprenyl protection of alcohols offers attractive features such as high yields and short deprotection time in relatively mild acidic conditions. Other applications of the 2-methylprenyl group are currently under studies.

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Scheme 1. Synthesis of 2-methylprenyl ethers **3** and their acidic deprotection