14.8: PROTECTION OF ALCOHOLS

INTRODUCTION

Often during the synthesis of complex molecules, one functional group in a molecule interferes with an intended reaction on a second functional group on the same molecule. An excellent example is the fact that a Grignard reagent can't be prepared from halo alcohol because the C-Mg bond is not compatible with the acidic -OH group.

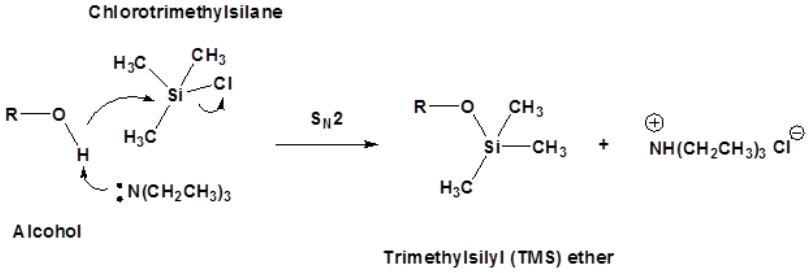
When situations like this occurs, chemists circumvent the problem by protecting the interfering functional group.

Functional group protection involves three steps:

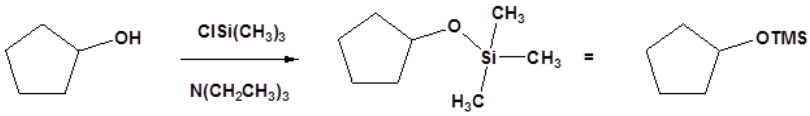
1. Blocking the interfering functionality by introducing a protecting group.
2. Performing the intended reaction.
3. Removing the protecting group and reforming the original functional group.

There are several methods for protecting an alcohol, however, the most common is the reaction with a chlorotrialkylsilane, Cl-SiR_3 This reactions forms a trialkylsilyl ether, R'-O-SiR_3. Chlorotrimethylsilane is often used in conjuction with a base, such as triethylamine, The base helps to form the alkoxide anion and remove the HCl produced by the reaction.

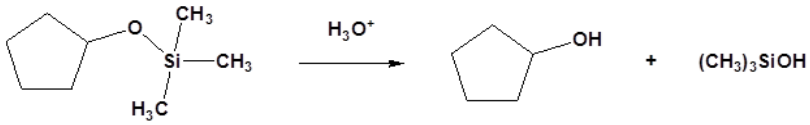
GENERAL REACTION



EXAMPLE

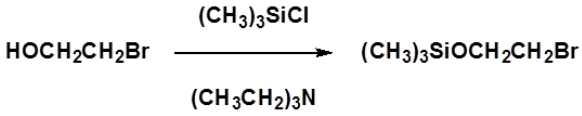


The silyl ether protecting group can be removed by reaction with an aqueous acid or the fluoride ion.

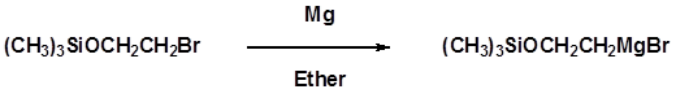


By utilizing a protecting group a Grignad reagent can be formed and reacted on a halo alcohol.

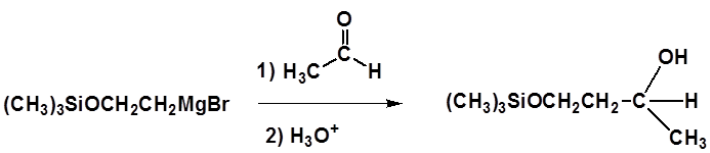
1) Protect the Alcohol



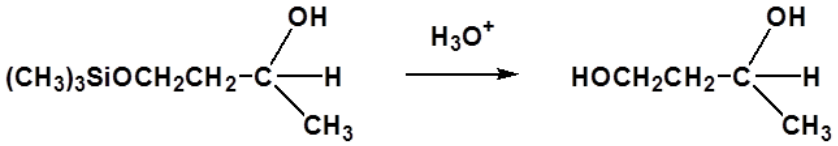
2) Form the Grignard Reagent

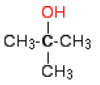


3) Perform the Grignard Reaction

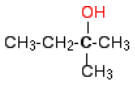


4) Deprotection





2-methylpropan-2-ol



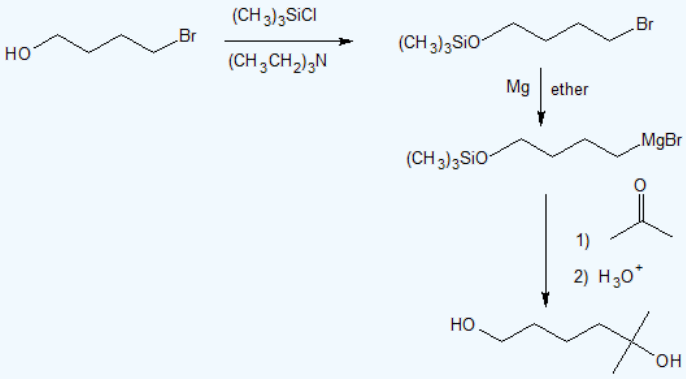
2-methylbutan-2-ol

Exercise

14. Propose a multiple-step synthesis to transform 4-bromo-1-butanol into 5-methylhexane-1,5-diol.

Answer

14.



CONTRIBUTORS AND ATTRIBUTIONS

- Dr. Dietmar Kennepohl FCIC (Professor of Chemistry, Athabasca University)
- Prof. Steven Farmer (Sonoma State University)