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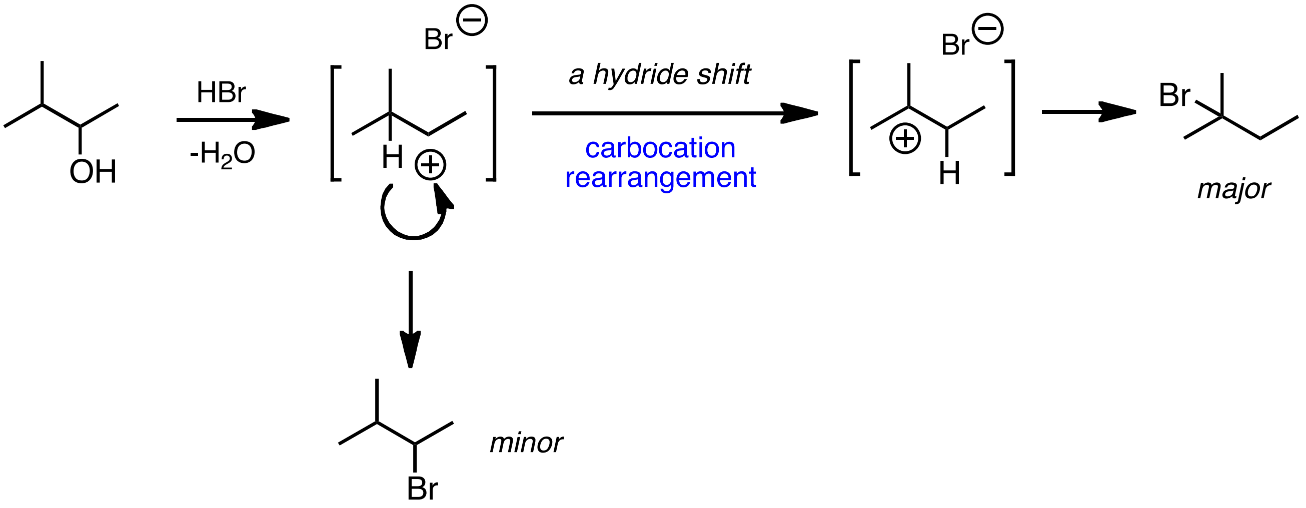
Chemistry 0310 - Organic Chemistry 1

Chapter 9. Alcohols & Ethers

Alcohols and ethers are among the most common functional groups in organic molecules. THF and dioxane as well as diethyl ether are popular solvents for organic reactions.

Deprotonation of alcohols greatly increases their nucleophilicity and can be accomplished with bases of pK_a>18 (LDA, BuLi, KH, NaH, etc.) or by treatment with alkali metals. Protonation of alcohols with strong acids (pK_a<-2) greatly increases their leaving group abilities. Elimination of H_2O from the intermediate oxonium ion generates **carbocations** that can undergo S_N1 reactions or eliminations. In the latter case, overall a dehydration has occurred. Depending on the lifetime of the carbocation, it can also undergo rearrangement reactions:

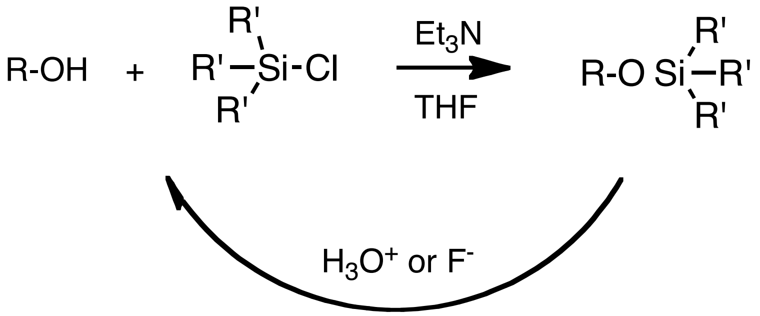


In addition to hydride shifts, alkyl shifts are also possible if the resulting carbocation is more stabilized than its precursor (e.g. pinacol→pinacolone rearrangement).

The **formation of ethers** often involves organosulfonates and halides as starting materials. Organosulfonates are formed from alcohols and alkyl- or arylsulfonylchlorides in the presence of pyridine under retention of configuration of the C-O bond. In the presence of base, treatment of alcohols with halogenating agents such as PX_3, PX_5 or $SOCl_2$ (thionyl chloride), leads to halide formation with inversion of configuration at carbon. When thionyl chloride is used in ether without base, a different mechanism leads to retention of configuration at carbon

The dehydration of alcohols by heat and strong anhydrous acids as well as, especially, the Williamson ether synthesis are the most popular methods of ether formation. Ethers with tertiary substituents are prepared by acid-catalyzed S_N1 addition of alcohols to alkenes.

Silyl ethers are important protective groups of alcohols in organic synthesis. Protective groups reversibly modify a functional group during subsequent synthetic transformations that are incompatible with the original functionality. The protective group should be removable when desired under mild conditions and in high yield to regenerate the original functional group. Specifically, with silyl ethers the acidic OH is removed and the nucleophilicity of the oxygen is considerably reduced.



Oxiranes (epoxides) are three-membered cyclic ethers. They are prepared from alkenes and peracids such as MCPBA. In contrast to the relatively chemically inert ethers, oxiranes are relatively reactive electrophiles and easily undergo *anti*-opening with nucleophiles. With aqueous acid, *anti*-diols are isolated. This constitutes a method for the *anti*-dihydroxylation of alkenes.