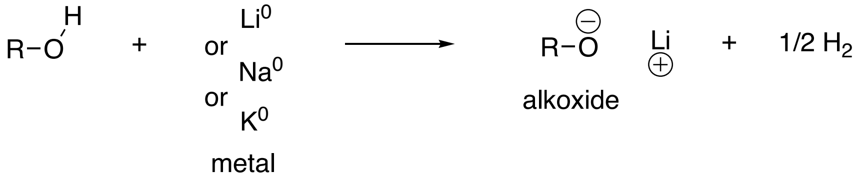
CHEM 263 **Oct 25, 2016**

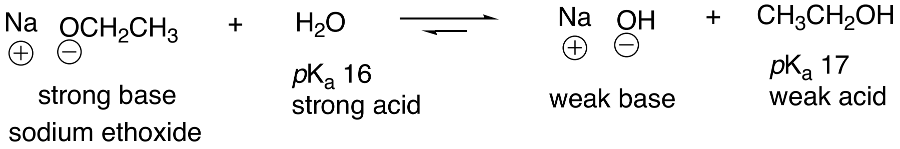
Reactions and Synthesis (Preparation) of R-OH

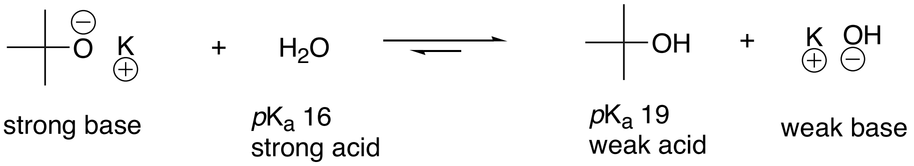
Breaking the O-H Bond of R-OH with Metals

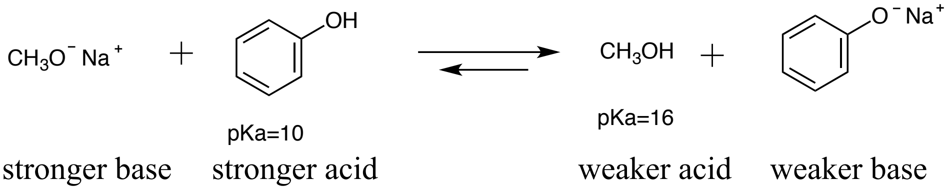


Breaking the O-H Bond of R-OH by Acid-Base Reaction

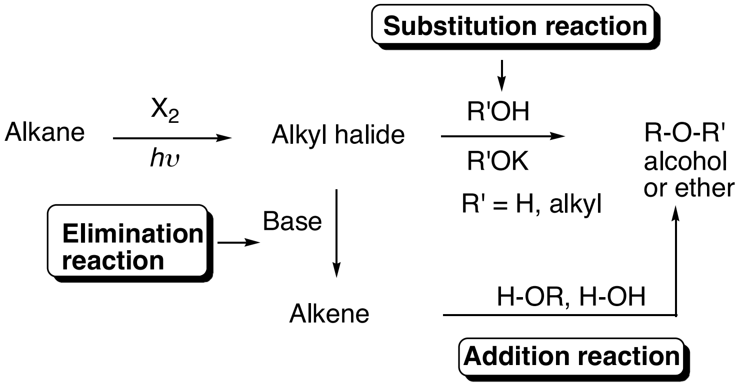
Examples:



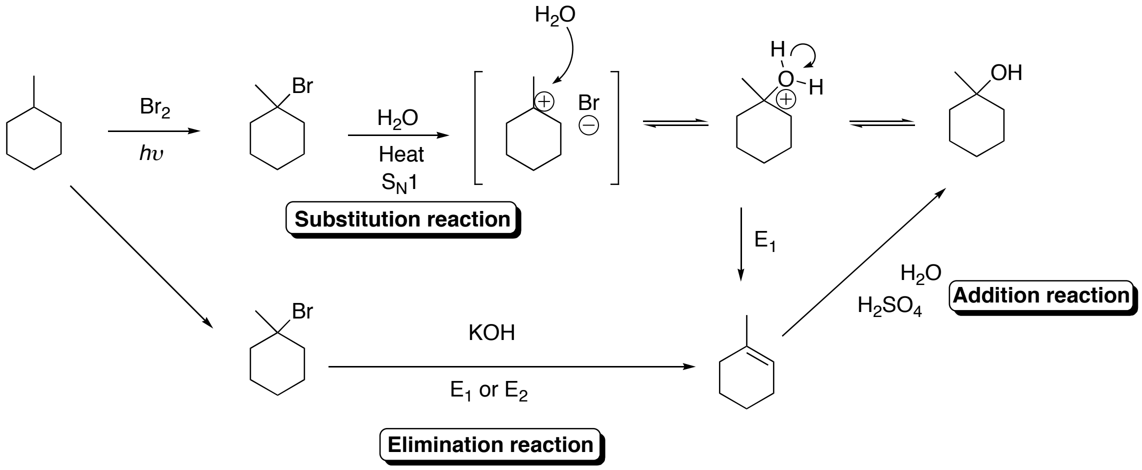




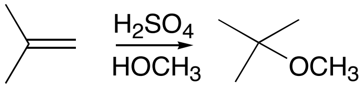
Preparation of Alcohols and Ethers from Alkanes



Example:

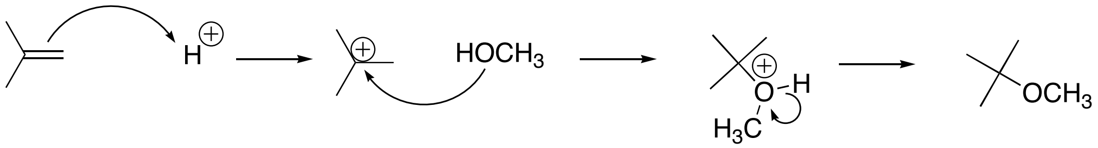


Preparation of Alcohols and Ethers from Alkenes

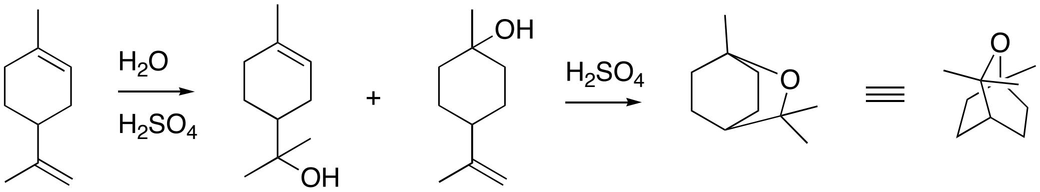


Markovnikov Addition

Mechanism:



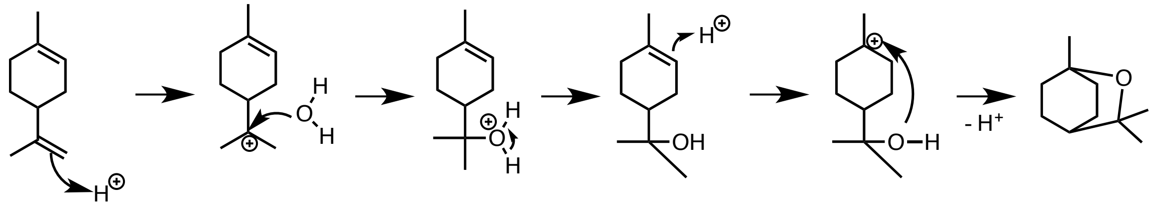
The alkene is first protonated to give a tertiary carbocation, which is then attacked by a lone pair on the oxygen of methanol. This is an **intermolecular** ether formation, where the reaction occurs between two molecules.



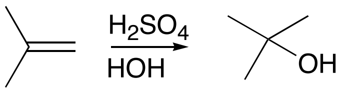
Cineol - seed germination inhibitor

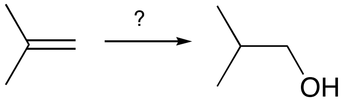
Above is and addition of water to limonene, followed by an **intramolecular** ether formation, where the reaction occurs within the molecule to give cineol. The high local concentration of the reacting groups and the formation of a six-membered ring drive the reaction forward.

Mechanism:



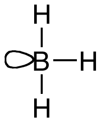
Markovnikov / Anti-Markovnikov Addition:





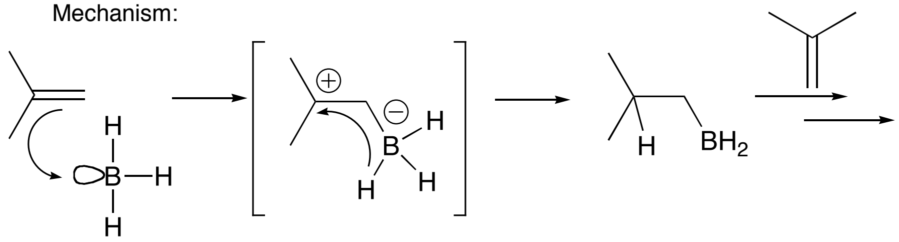
? = 1. B_2H_6
2. H_2O_2, NaOH

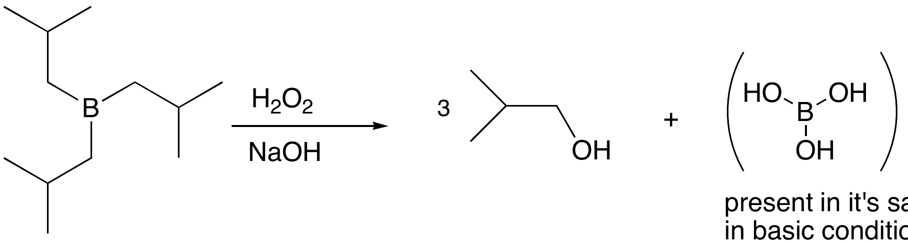
B_2H_6 behaves like BH_3, which is a Lewis acid:



The first step of this last example is called **hydroboration** (syn addition**)**, while the second is an oxidation. This is an example of **anti-Markovnikov** addition.

Mechanism:



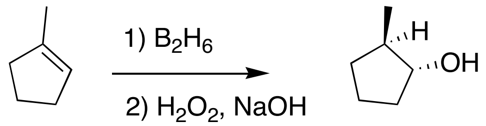


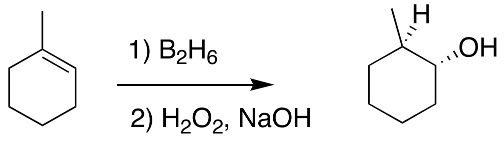
present in it's salt form
in basic condition

Anti-Markovnikov addition of water with retention of configuration

Borane adds to the least substituted carbon to give the more stable carbocation
Syn addition of borane and H
NaOH is used for deprotonation of hydrogen peroxide – replaces boron with retention of stereochemistry

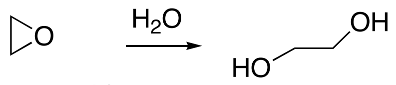
Examples:





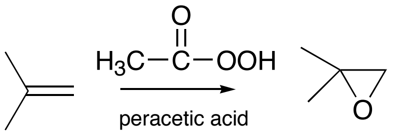
Note the **<u>cis-addition of H_2O.</u>**

Preparation of Ethers from Alkenes – Epoxidation – epoxides can be opened by water



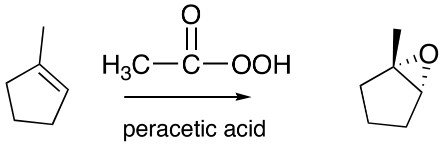
ethylene oxide

Epoxide formation:



an epoxide
aka oxirane
3 membered ether ring

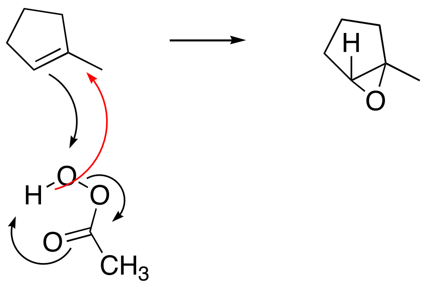
It is a **concerted** and **stereospecific** reaction



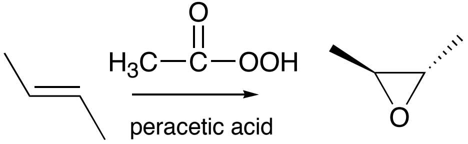
formed as racemate

(racemic mixture = 1:1 mix of enantiomers)

Concerted mechanism:



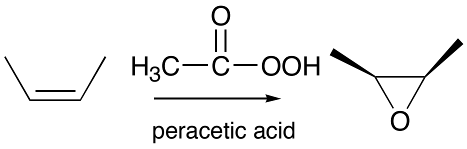
Examples:



formed as racemate

(**racemic mixture** =

1:1 mix of enantiomers)



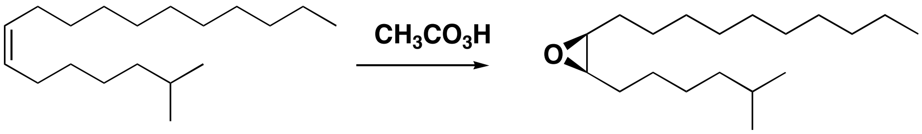
formed as single compound

(**meso compound** =

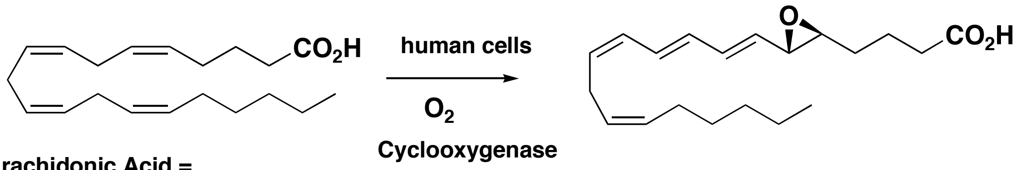
achiral but has stereocentres)

Note that achiral starting material and peracetic acid (achiral) gives a net achiral product(s). That is, the products are either racemic, or a meso compound.
Examples:

Is the product of the following reaction one enantiomer or racemic? (racemic – reagent equally likely to approach from the top or bottom)



Disparlure = sex pheromone of Gypsy Moth



Arachidonic Acid =

all Z 5,8,11,14-eicosatetraenoic acid

Leukotriene A_4

Leukotriene A_4 is an inflammatory signal for asthma and allergic reactions.

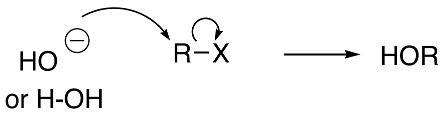
Alcohols and Ethers from Alkyl Halides

R-X → ROH
R-X → ROR'

X = Cl, Br, I, OSO_2R

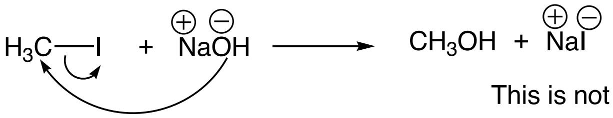
Substitution reactions (S_N2, S_N1)
S = Substitution N = Nucleophilic
2 or 1 = rate depends on 2 concentrations or 1 concentration

S_N2



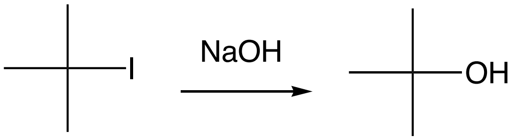
- Stereospecific (the stereochemistry of the reactants determines the stereochemistry of the products)
- Inversion of configuration (Walden Inversion)
- Concerted (bonds are broken and formed at the same time)
- Bimolecular
- 1° halides work the best
- 2° halides work ok
- 3° halides don't work
- In general C=C-X (vinyl halides) also fail for this type of reaction

Example:

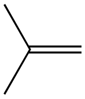


This is not reversible, because I- is more stable than OH-

Would the following reaction occur?



No, this involves a tertiary halide, which is too crowded. Elimination could occur though, to produce:



What reagents instead of NaOH could be used that would allow the above substitution reaction to occur?

Answer: H_2O, H_2SO_4 and heat would allow an S_N1 reaction to occur: