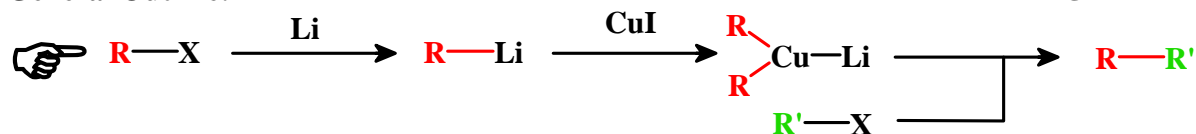


Lithium Dialkyl Cuprates: The Corey-House Synthesis

General Outline:

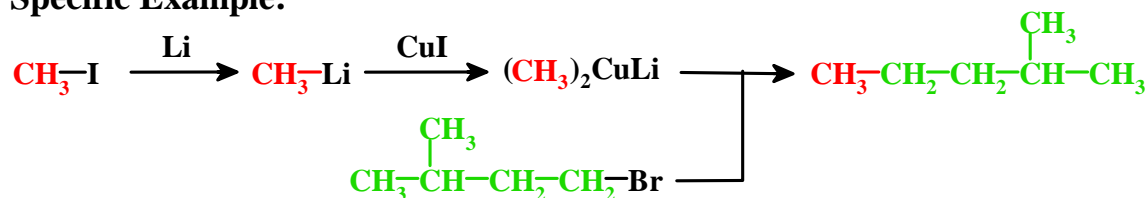
Wade, 6th Ed., Pages 443



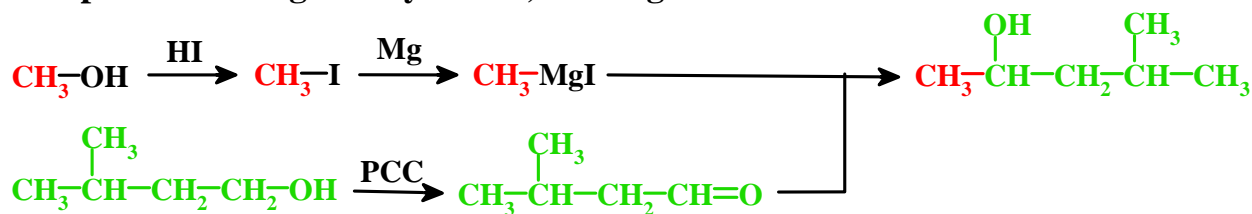
R may be methyl, primary alkyl, vinylic, allylic, or aryl.

R' may be methyl, primary alkyl, vinylic, allylic, aryl, or benzylic.

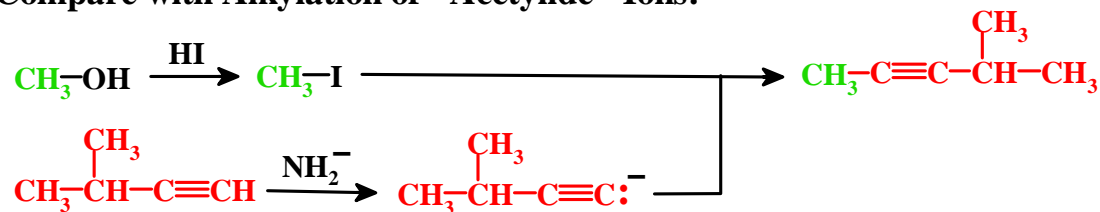
Specific Example:



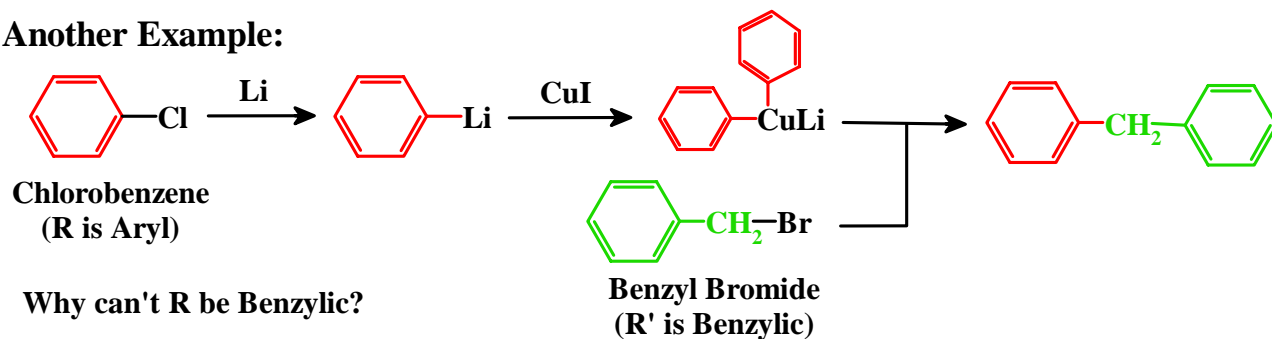
Compare with Grignard synthesis, starting with alcohols:



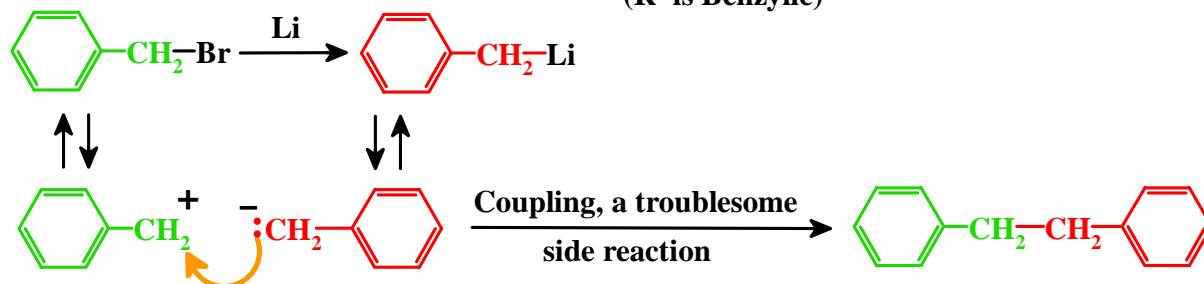
Compare with Alkylation of "Acetylide" Ions:



Another Example:

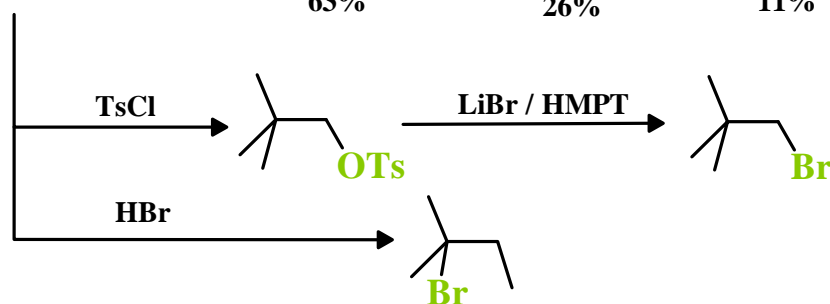
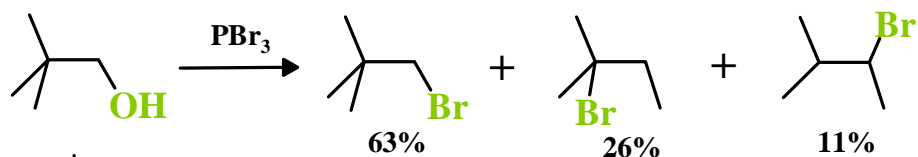
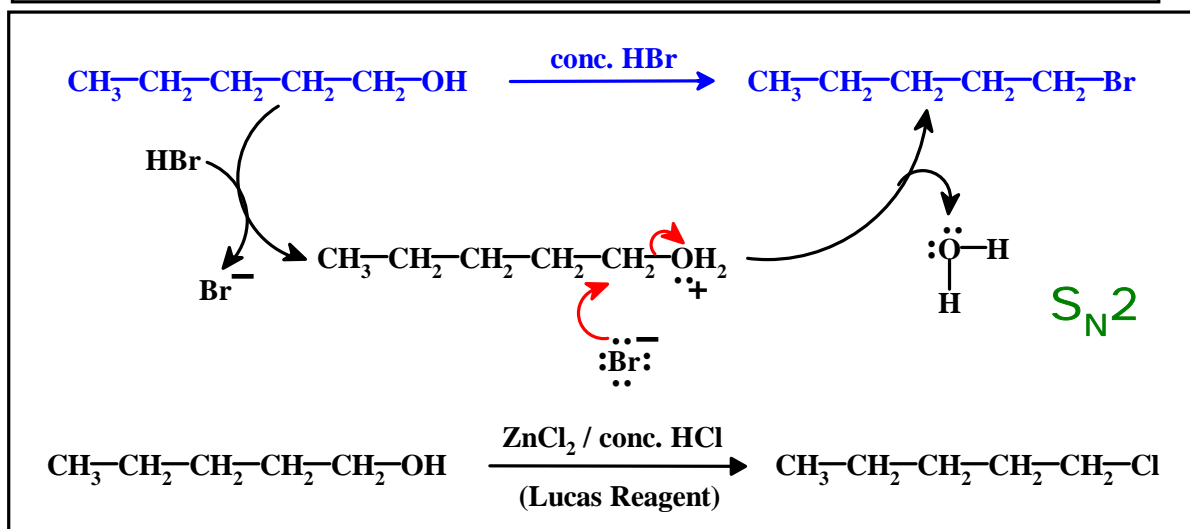
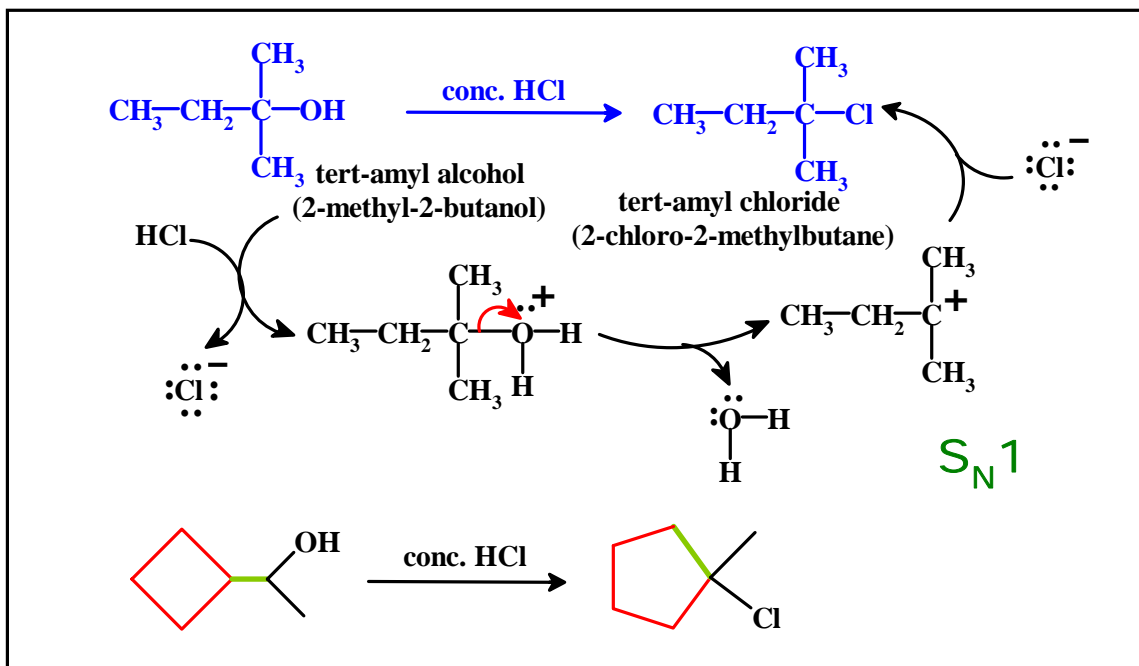


Why can't R be Benzylic?



Very stable carbocation and carbanion.

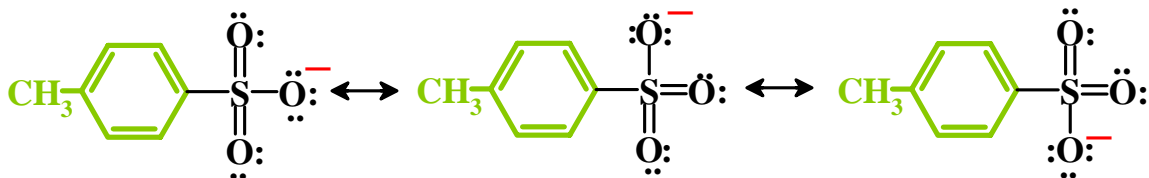
ALCOHOLS TO ALKYL HALIDES



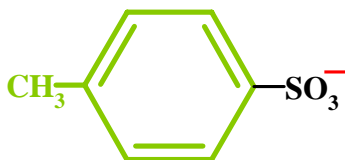
Sulfonate Anions As Leaving Groups

p-Toluenesulfonate (Tosylate, TsO⁻)

(a) a weak base: the negative charge is delocalized over three oxygen atoms:

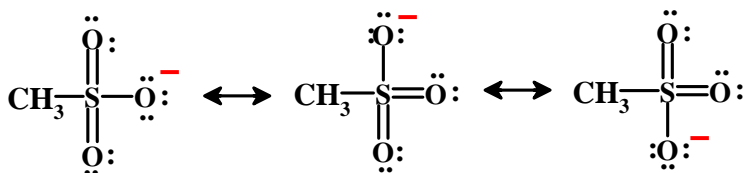


(b) a bulky group: lots of steric strain is relieved when TsO⁻ departs because of the size of the aromatic ring:



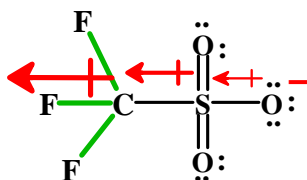
Methanesulfonate (Mesylate, MsO⁻)

Good leaving group, but not as good as tosylate; not as much steric strain relieved.

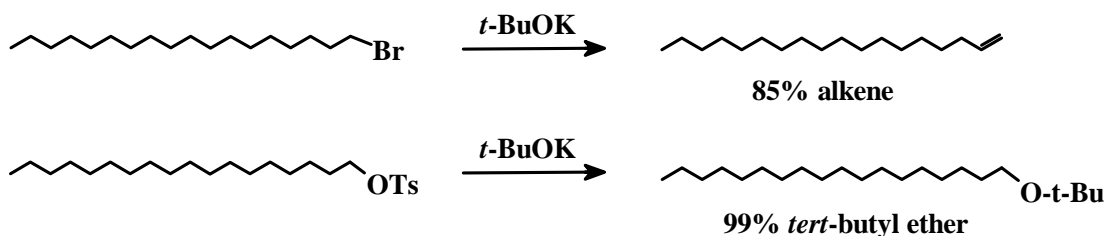


Trifluoromethanesulfonate (Triflate, TfO⁻)

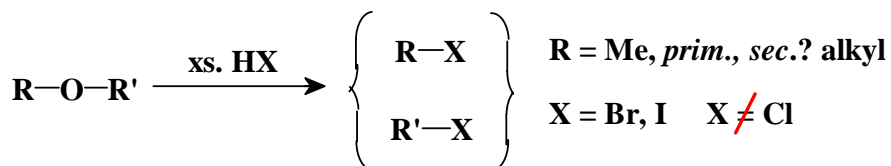
MUCH better leaving group than tosylate



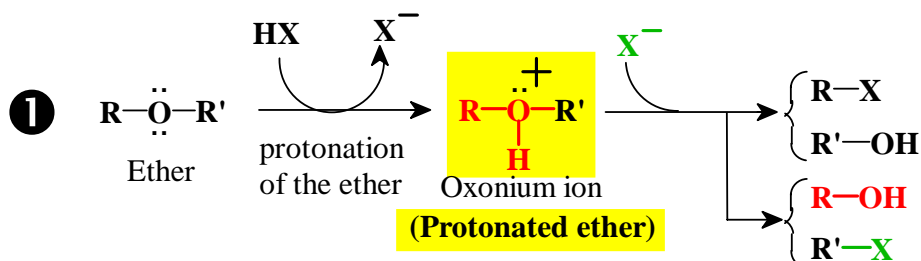
Very large **dipole moments** in **C—F bonds** produce an inductive effect that delocalizes the negative charge very effectively



CLEAVAGE OF ETHERS

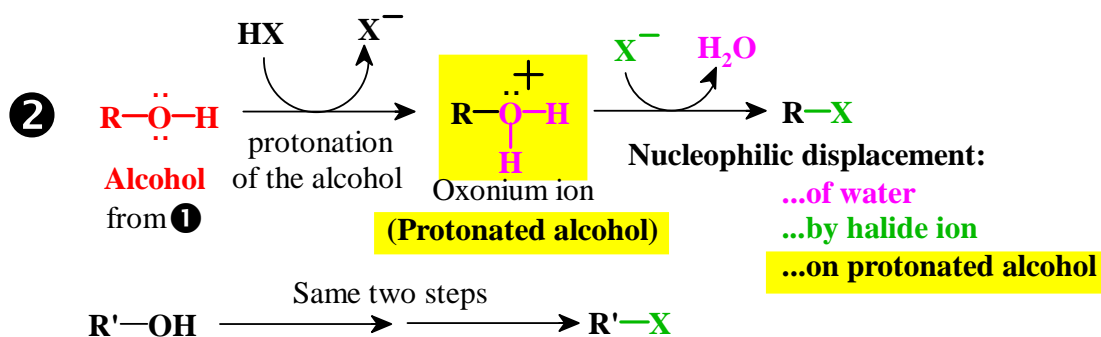


Two consecutive mechanisms:

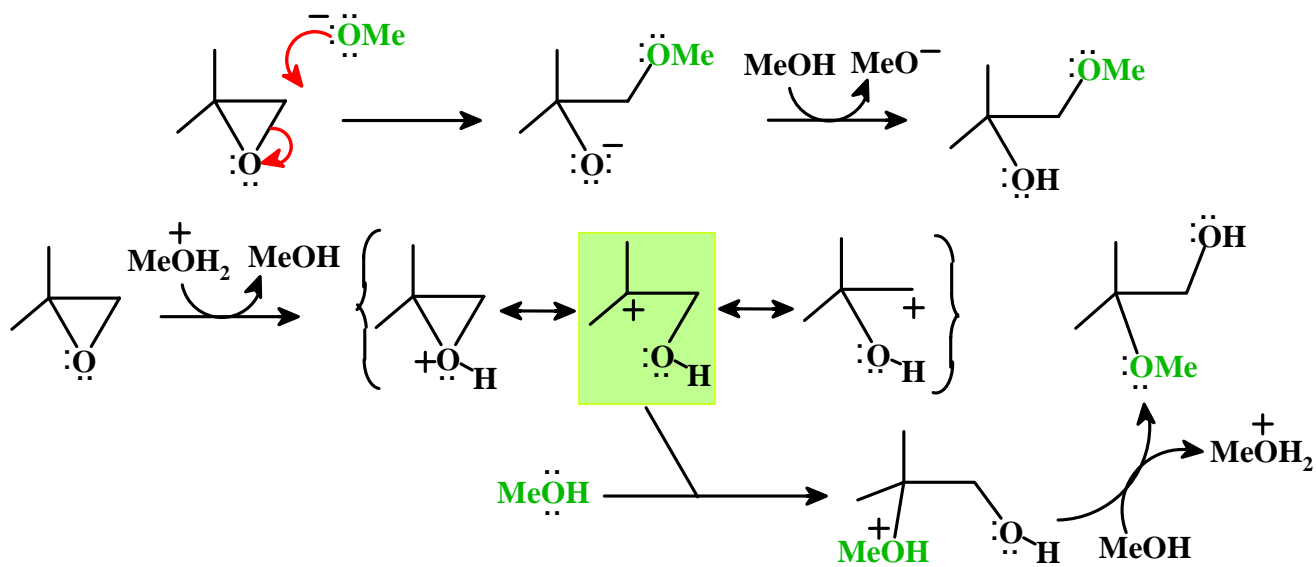


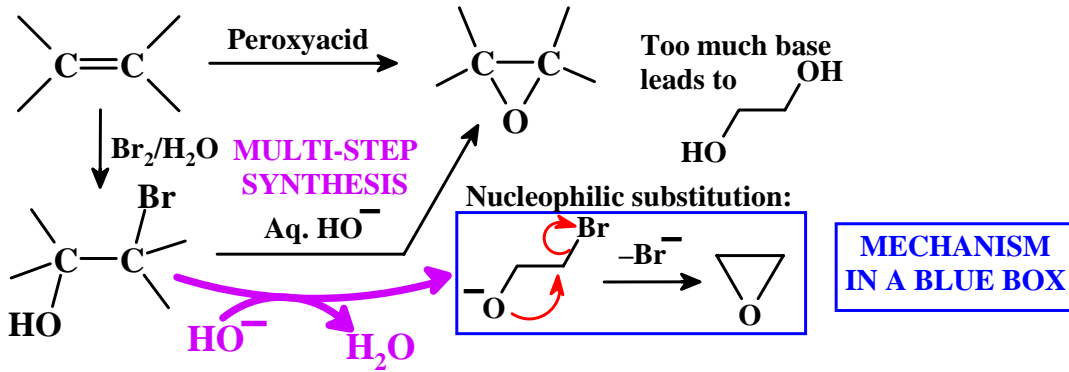
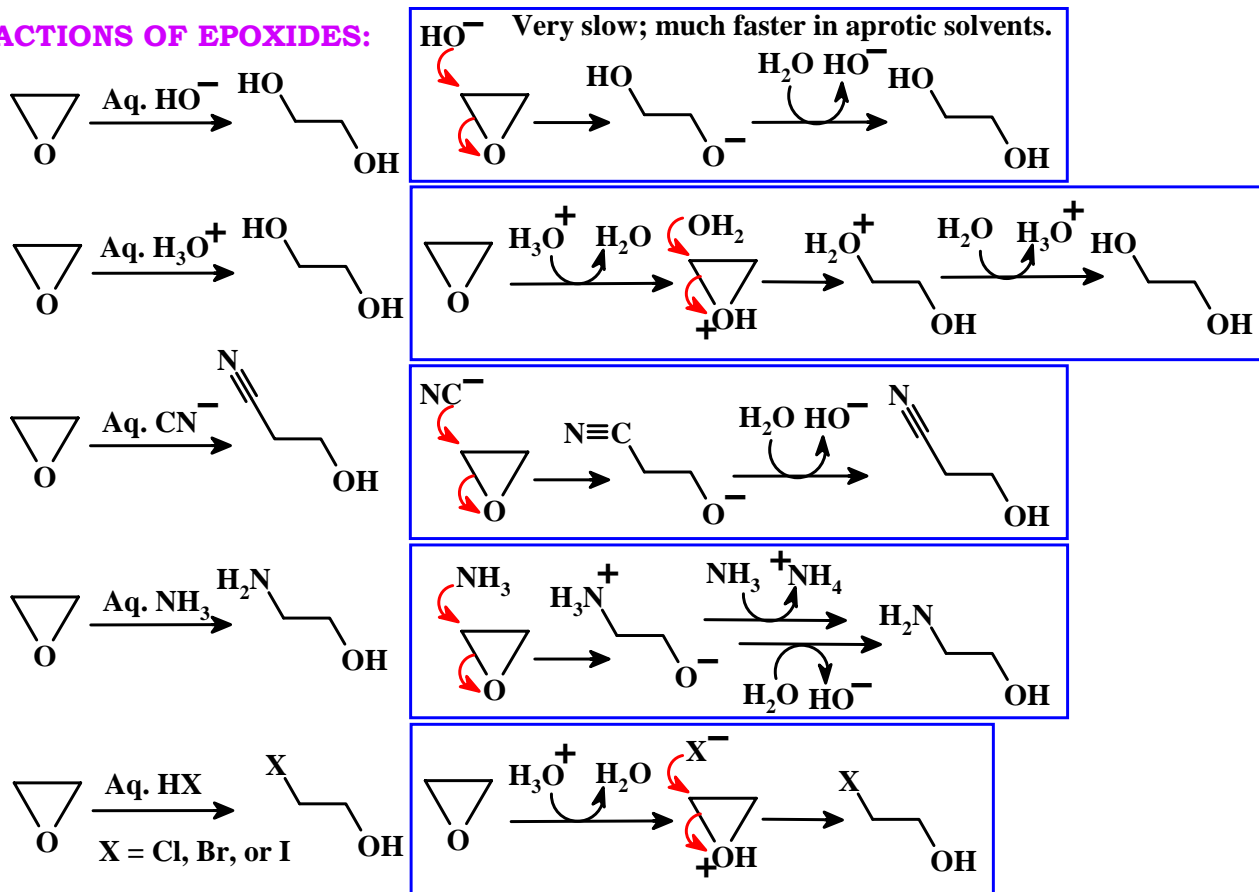
Nucleophilic displacement:

...of alcohol
...by halide ion
...on protonated ether

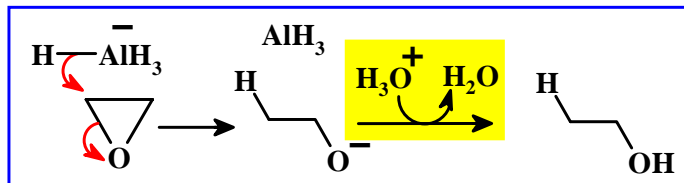
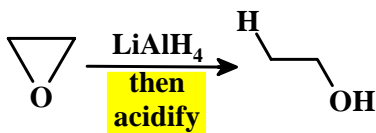
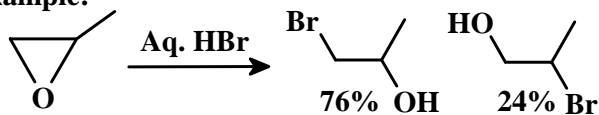


METHANOLYSIS OF EPOXIDES IN BASIC AND ACIDIC MEDIA

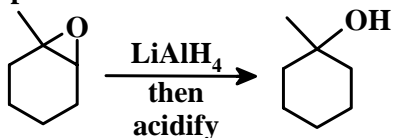


FORMATION OF EPOXIDES:**REACTIONS OF EPOXIDES:**

Example:



Example:



Wade 6, pages 484-487

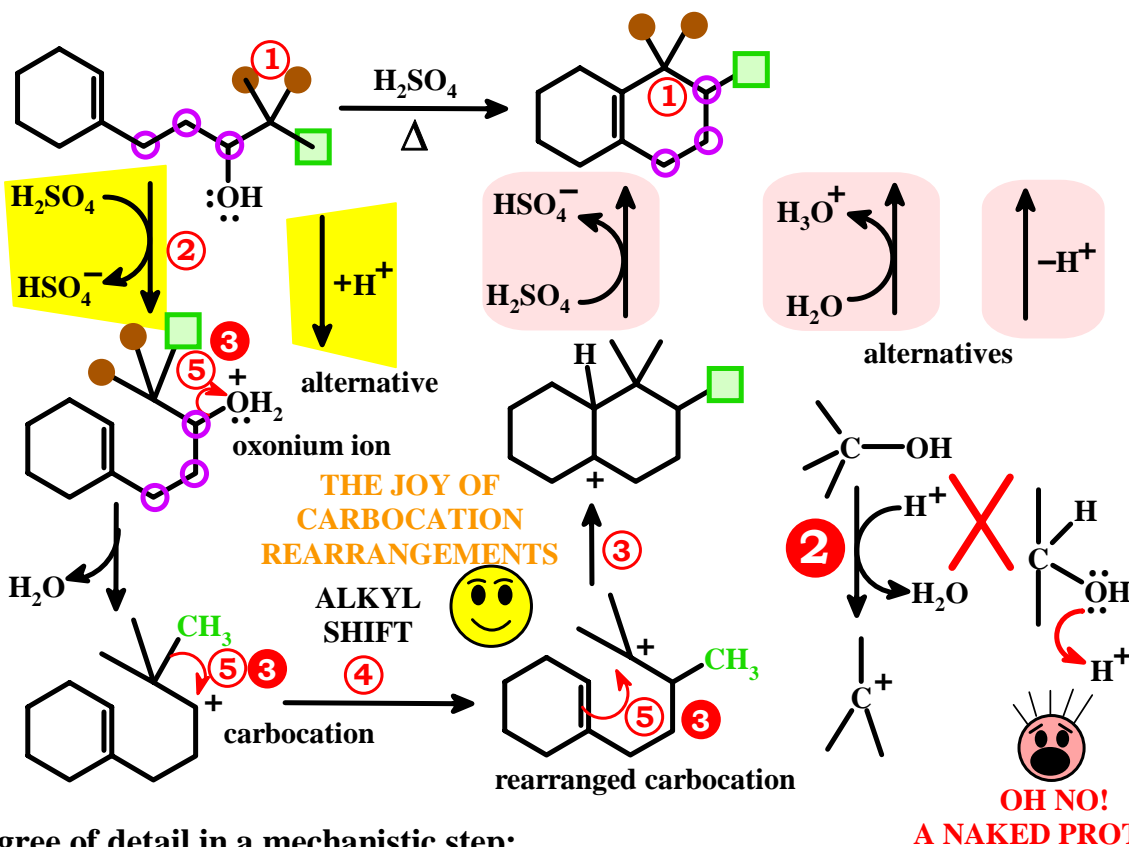
STRATEGY FOR WRITING MECHANISMS

Reactions involving strong electrophiles (carbocations)

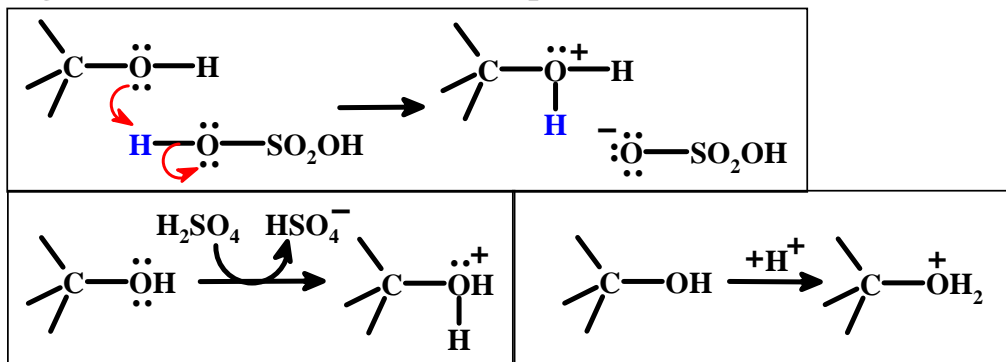
- ① Where did the carbons go?
- ② Acidic solution? Protonate something.
- ③ Consider possible nucleophile-electrophile interactions. (donor-acceptor). ↑↓ Confusion?
- ④ Consider possible carbocation rearrangements.
- ⑤ Use the fishhooks (curved arrows) to indicate electronic reorganization. ONE STEP AT A TIME.

AVOIDING COMMON MISTAKES

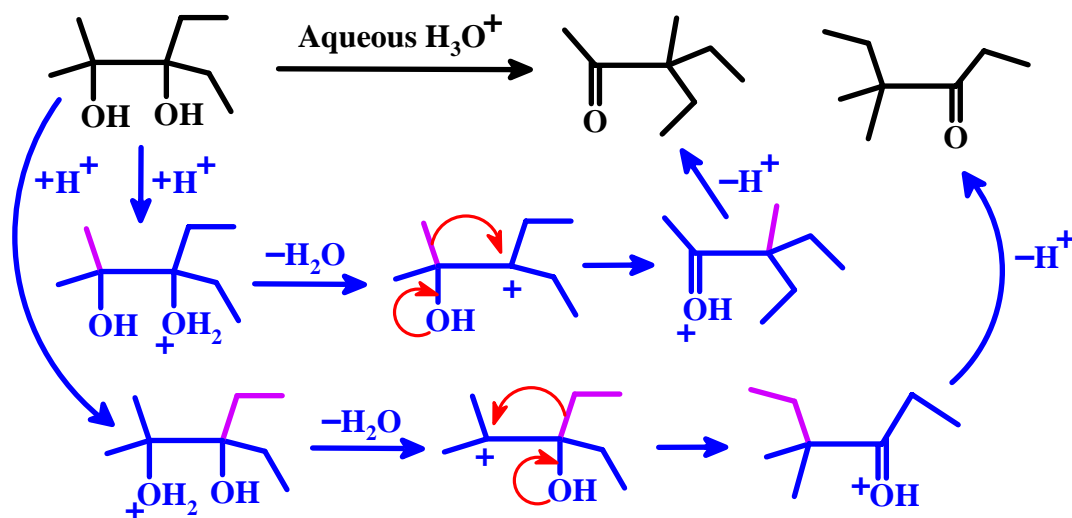
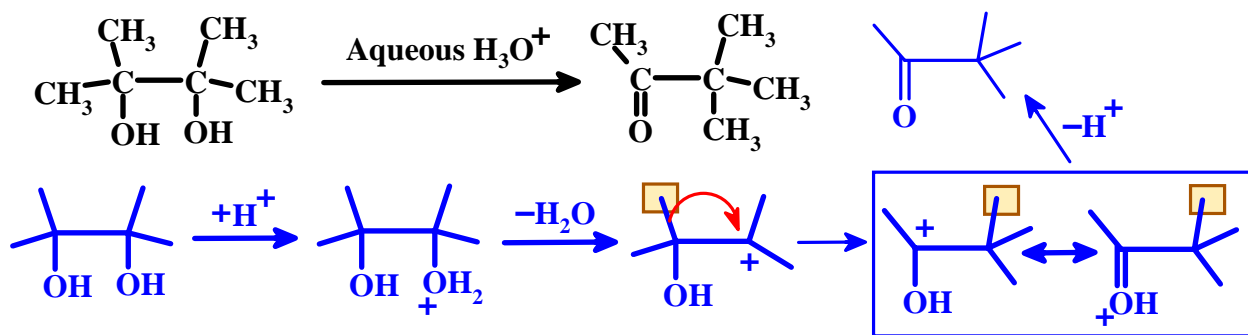
- ① Draw all bonds at reaction sites
- ② ONE STEP AT A TIME
- ③ Use fishhooks judiciously. Make sure they point the right way!



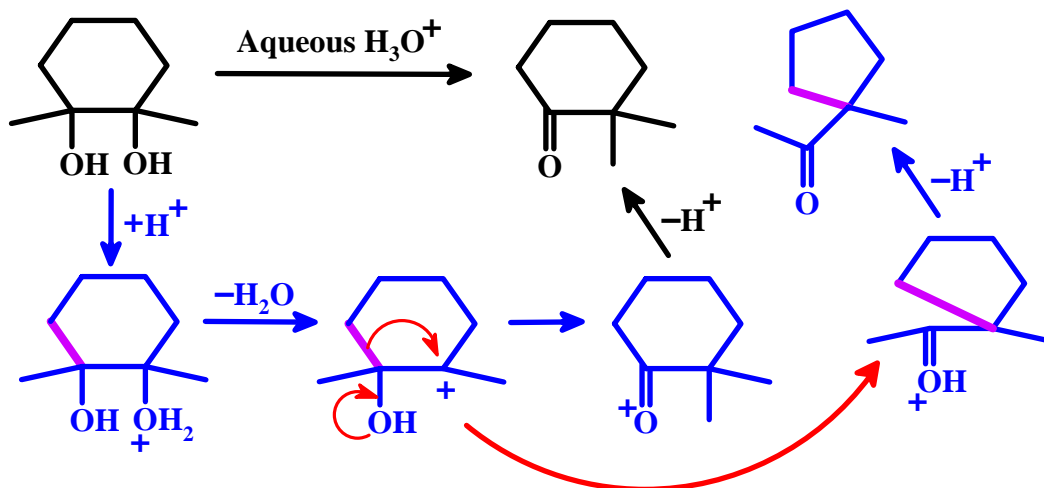
Degree of detail in a mechanistic step:



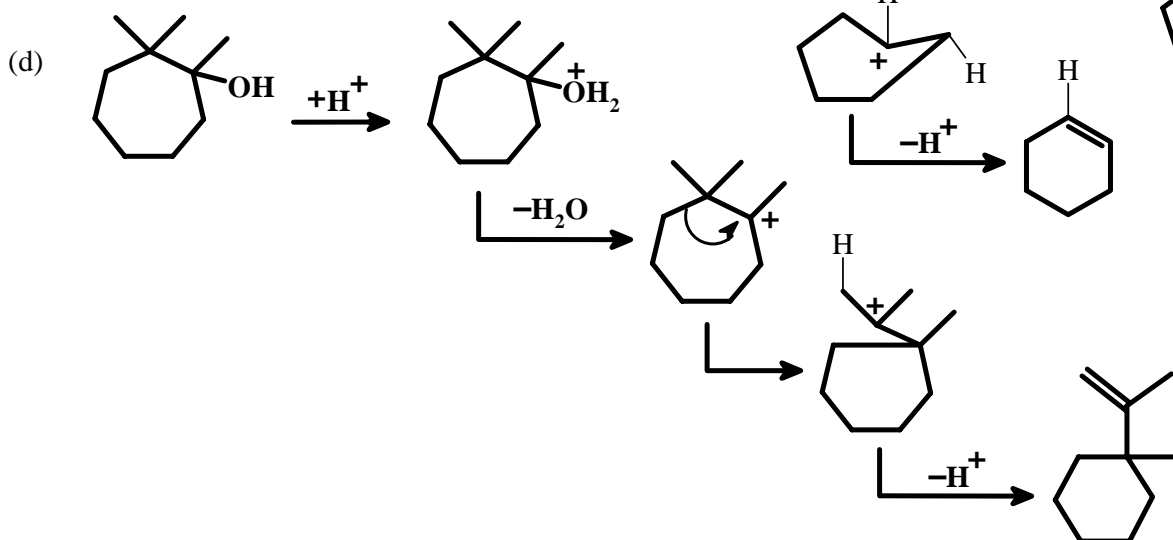
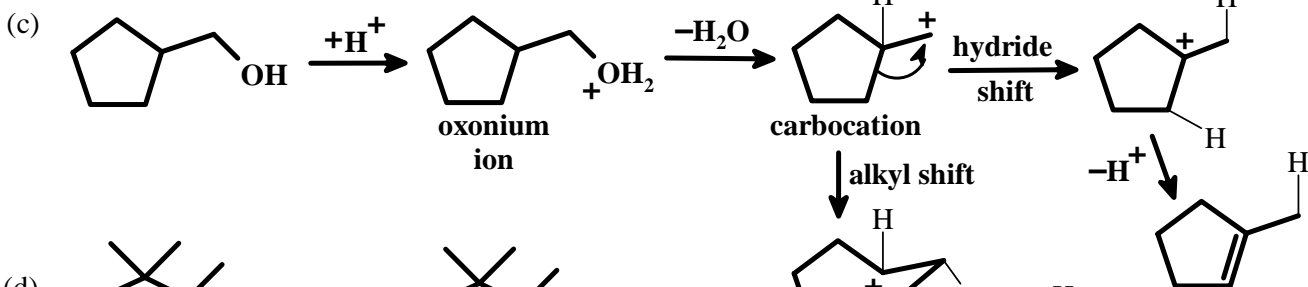
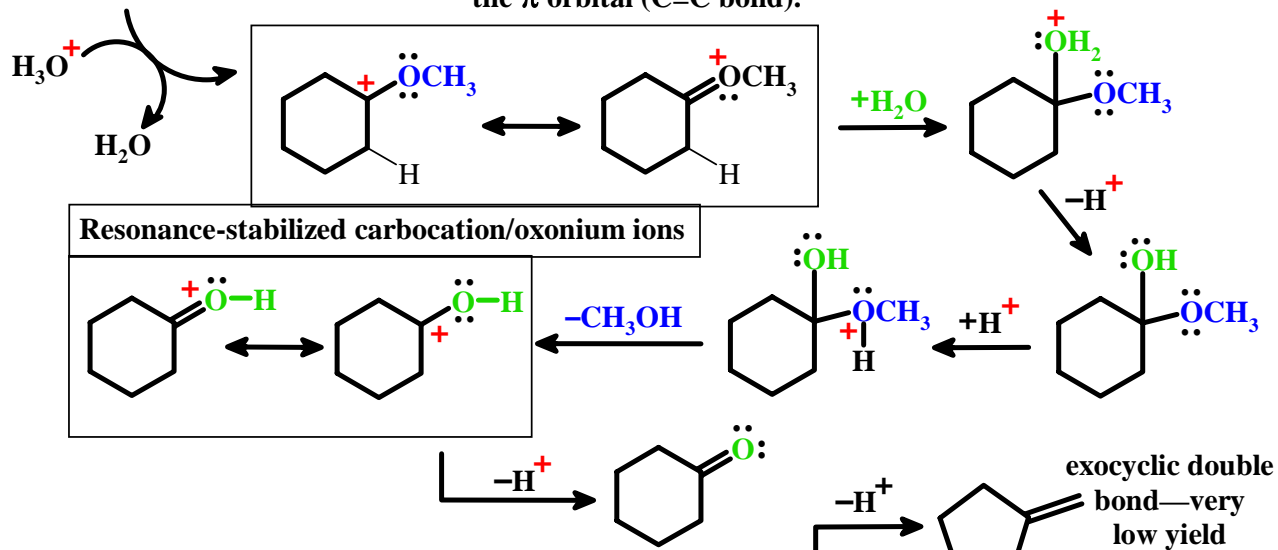
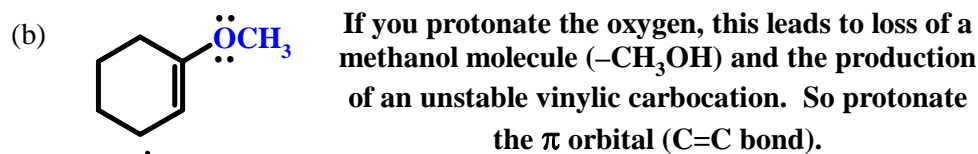
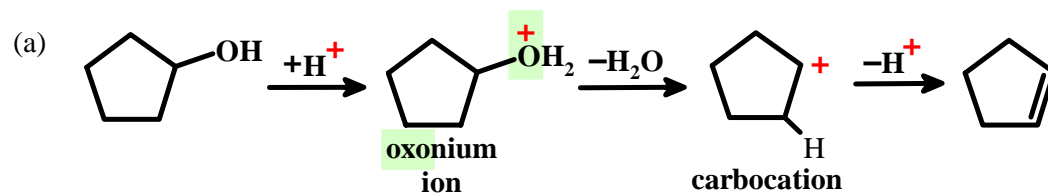
PINACOL REARRANGEMENT



Problem 11-28 (a)



PROBLEM 11-27



Practice Problems: Synthesis**Wade, Chapters 10, 11, and 14**

1. Outline a Grignard synthesis of 1-propanol, starting with alcohols of two carbon atoms or less. $\text{CH}_3\text{-CH}_2\text{-CH}_2\text{-OH}$

2. Outline a Corey-House synthesis of propane, starting with alkyl halides of two carbon atoms or less. (See Wade, 5th Ed., PROBLEM 10-21, pages 429-430). $\text{CH}_3\text{-CH}_2\text{-CH}_3$

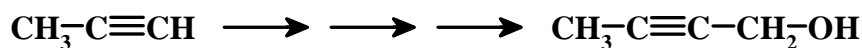
3. Outline a multi-step synthesis of propyne, starting with alkyl halides and/or dihalides of two carbon atoms or less. $\text{CH}_3\text{-C}\equiv\text{CH}$

4. Outline a multi-step synthesis of ethyl methyl ether, starting with alcohols of two carbon atoms or less. $\text{CH}_3\text{-O-CH}_2\text{-CH}_3$

5. Outline a Grignard synthesis of 2-methyl-2-propen-1-ol, starting with propyne.



6. Outline a Grignard synthesis of 2-buten-1-ol, starting with propyne:



7. Outline a multi-step synthesis of 1-ethoxy-2-methyl-2-propanol, starting with isobutylene:

