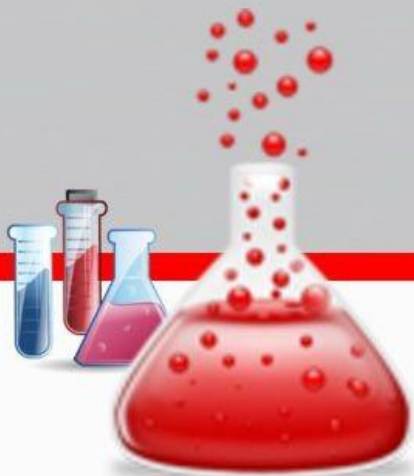


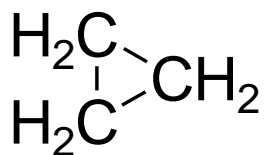
- **National University –SUDA**
- Faculty of Clinical and Industrial Pharmacy
- Second Year (**Batch-PA-14**)-Semester Four
  - Organic Chemistry in Pharmacy
- **Course Coordinator: Us.** Ghada Mustafa Eltayeb,
- Phone Number (**00249-912242444 / 00249-990997710**).
- **Assistant Coordinator: Us.** Maria Elamin Hamid,
  - Phone Number (**00249-913714903** )



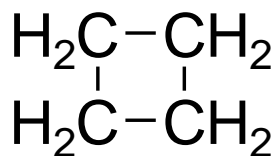
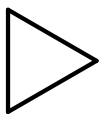
# Alicyclics

Aliphatic compounds containing rings, cycloalkanes, cycloalkyl halides, cycloalkyl alcohols, cyclic ethers, cycloalkenes, cycloalkadienes, etc.

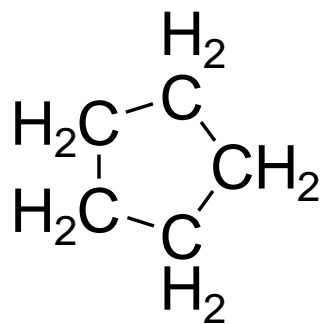
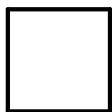
## Cycloalkanes



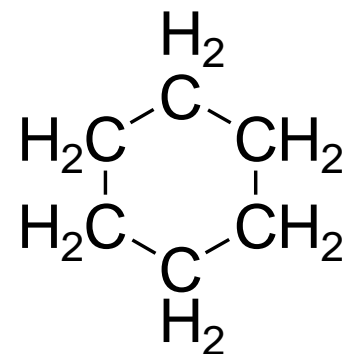
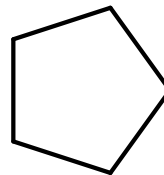
cyclopropane



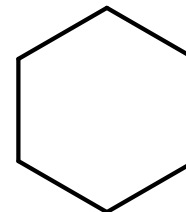
cyclobutane

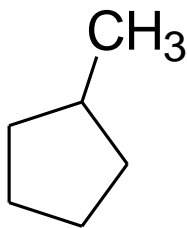


cyclopentane

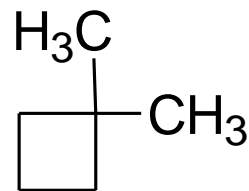


cyclohexane

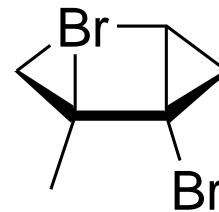
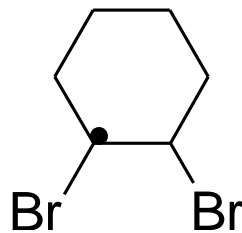
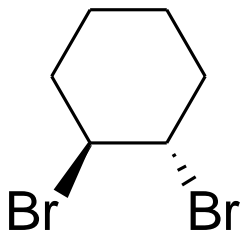




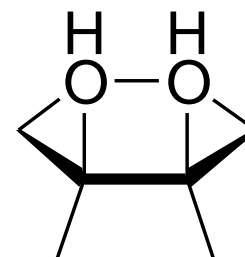
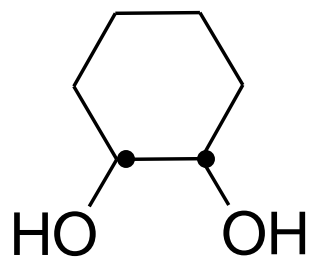
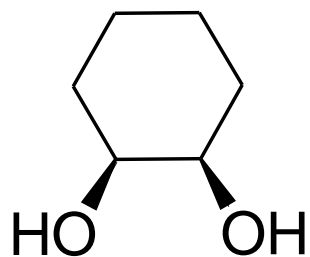
methylcyclopentane



1,1-dimethylcyclobutane

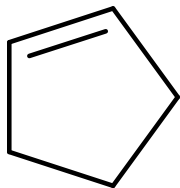


*trans*-1,2-dibromocyclohexane

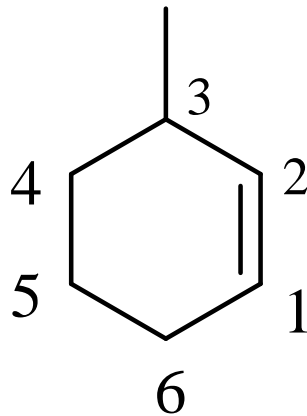


*cis*-1,2-cyclohexanediol

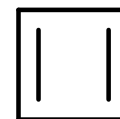
## cycloalkenes



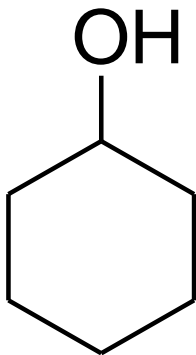
cyclopentene



3-methylcyclohexene

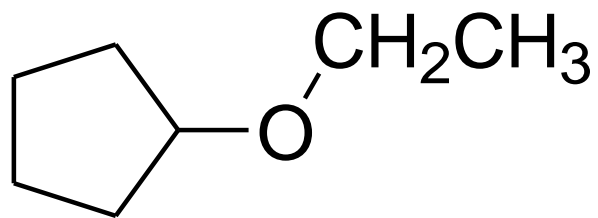


1,3-cyclobutadiene



cyclohexanol

cyclohexyl alcohol



ethyl cyclopentyl ether

## Cycloalkanes, syntheses:

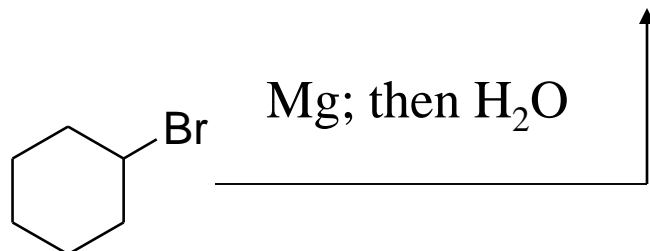
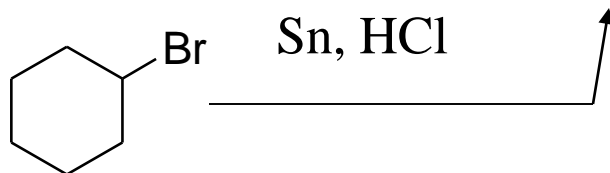
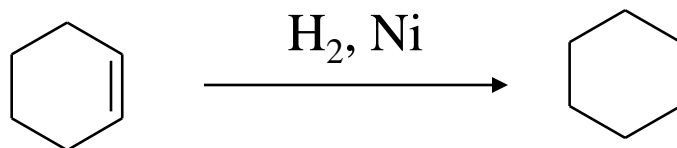
### A. Modification of a ring compound:

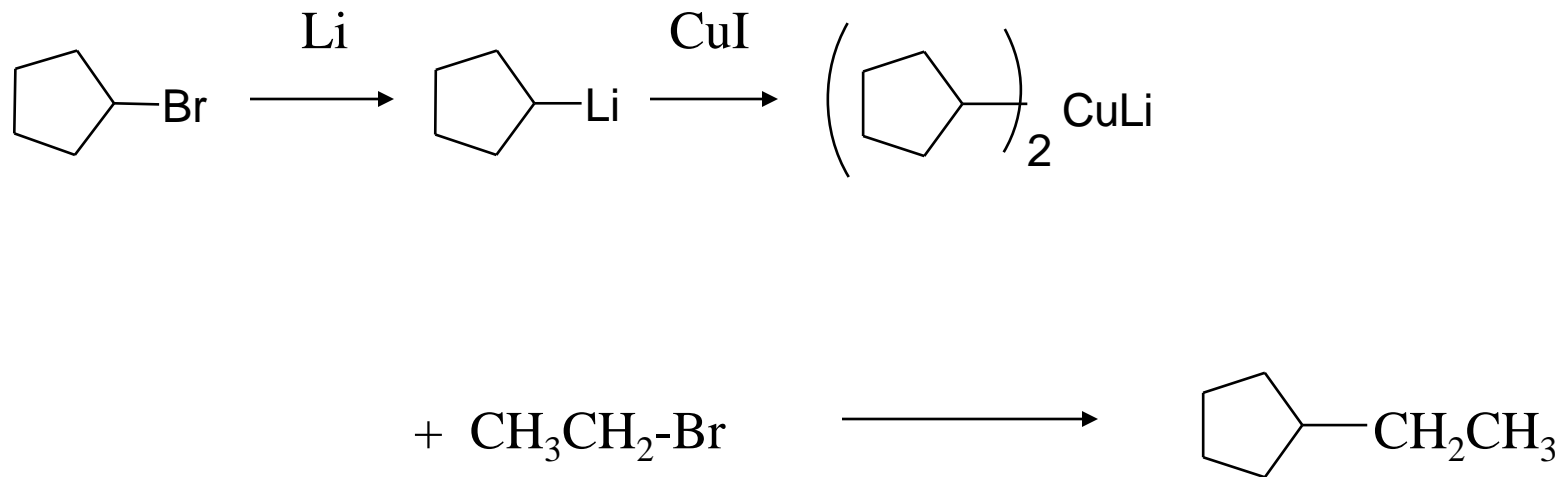
1. reduction of cycloalkene
2. reduction of cyclic halide
  - a) hydrolysis of Grignard reagent
  - b) active metal & acid
3. Corey House

### B. Ring closures



A. Modification of a cyclic compound:

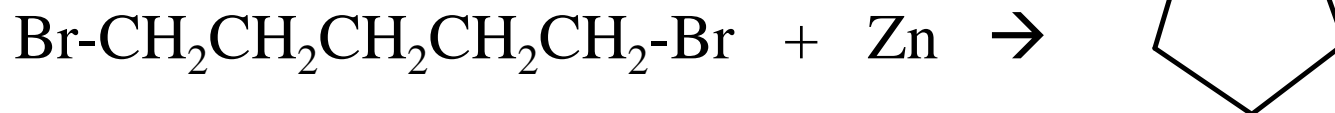
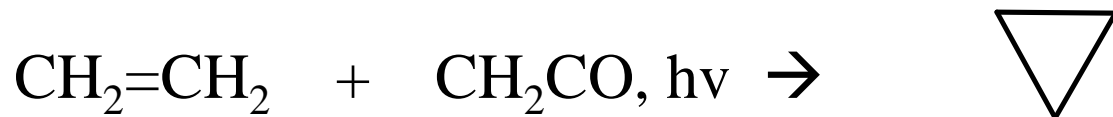




*must be 1°*

Corey-House

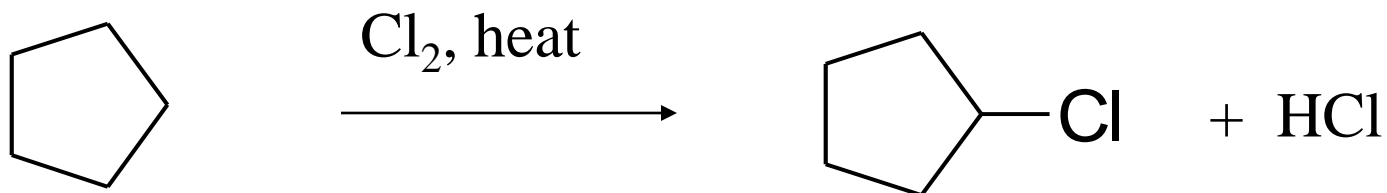
## B. ring closures



etc.

## cycloalkanes, reactions:

### 1. halogenation

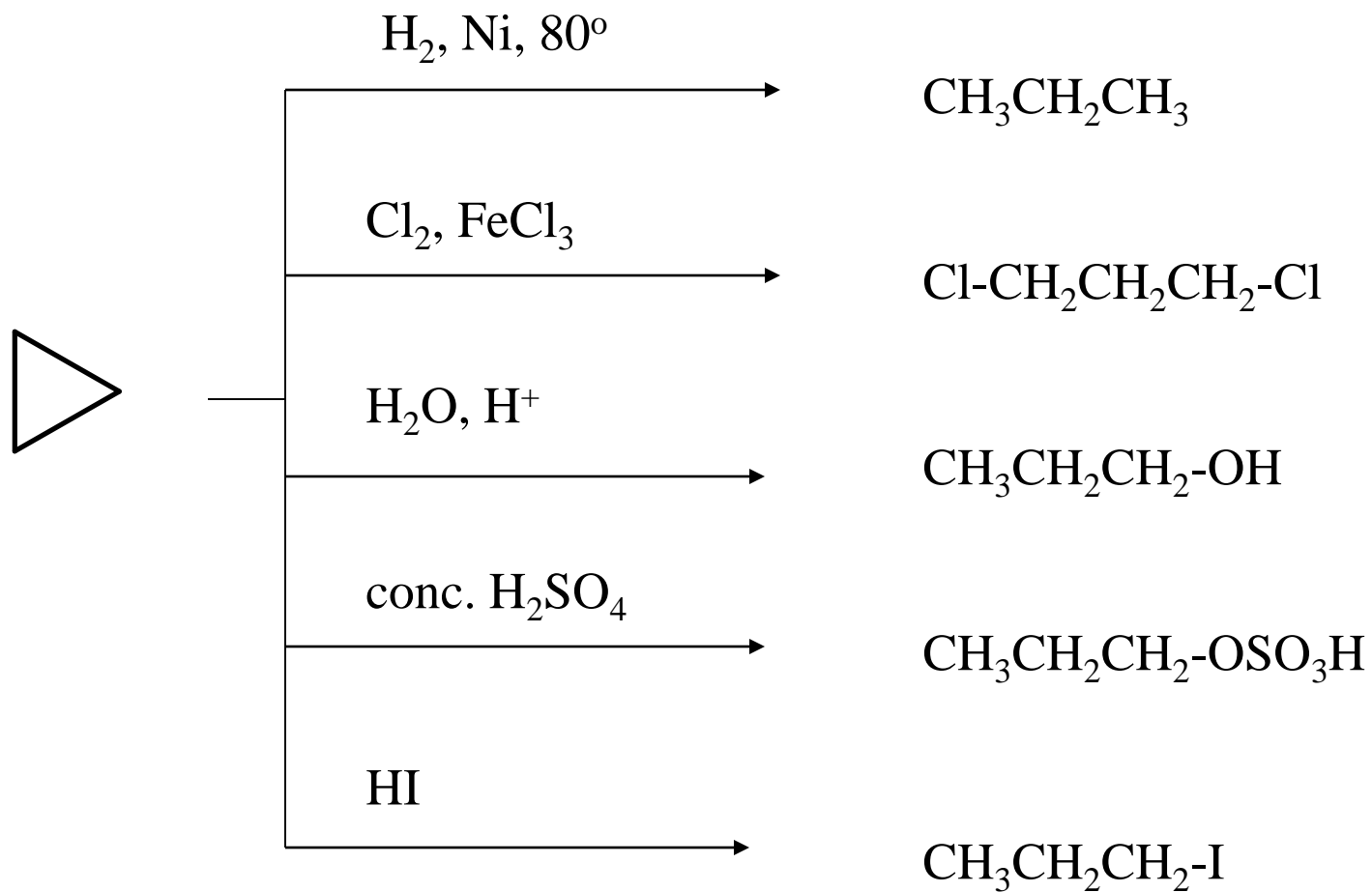


### 2. combustion

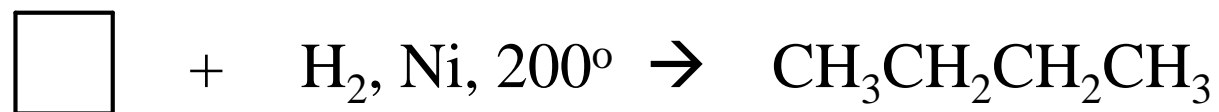
### 3. cracking

### 4. exceptions




exceptions:



exceptions (cont.)





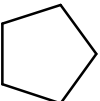
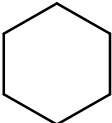
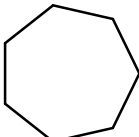
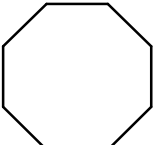
??????????

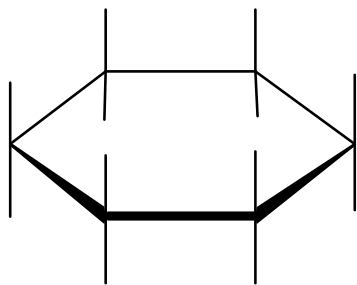
	internal bond angles	deviation from 109.5	heat of combustion
	60°	-49.5°	166.6
	90°	-19.5°	164.0
	108°	-1.5°	158.7

Cyclopropane undergoes addition reactions that other cycloalkanes and alkanes do not. This is because of **angle strain** in the small ring. Because the bond angles are less than the optimal  $109.5^\circ$  for maximum overlap, the bonds are weaker than normal carbon-carbon single bonds and can be added to.

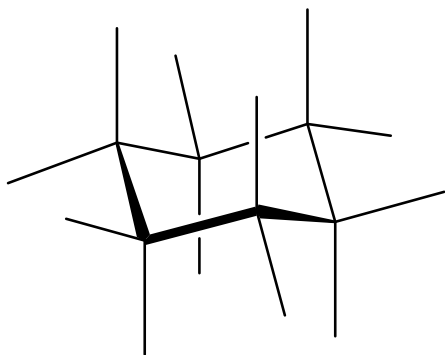
Cyclobutane has angle strain that is less than that for cyclopropane, reacts with  $\text{H}_2/\text{Ni}$  at a higher temperature, but does not react like cyclopropane in the other exceptional reactions.



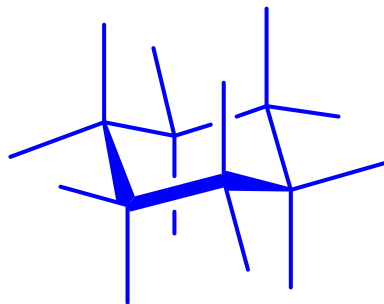
	internal bond angles	deviation from 109.5	heat of combustion
	60°	-49.5°	166.6
	90°	-19.5°	164.0
	108°	-1.5°	158.7
	120°	+11.5°	157.4
	128.5°	+19°	158.3
	135°	+25.5°	158.6



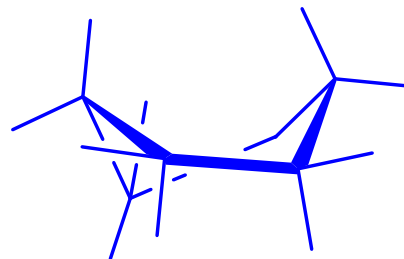
Cyclohexane does not have any angle strain! It isn't a flat molecule. By rotating about the carbon-carbon bonds, it can achieve  $109.5^\circ$  bond angles.



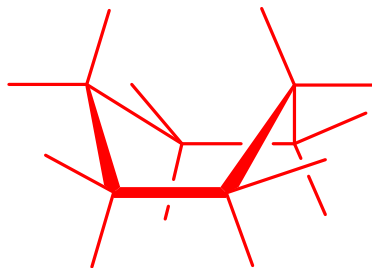
# conformations of cyclohexane



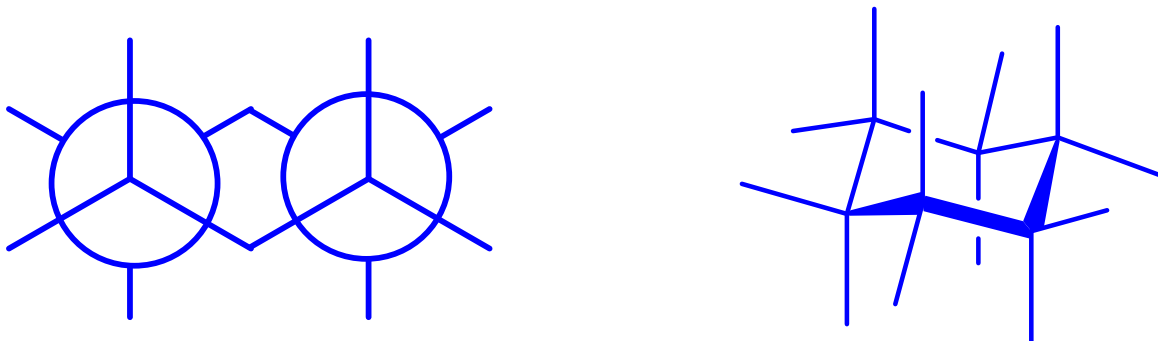
chair



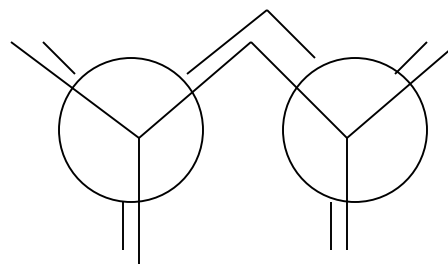
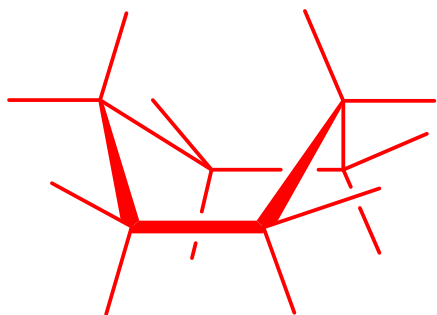
twist boat



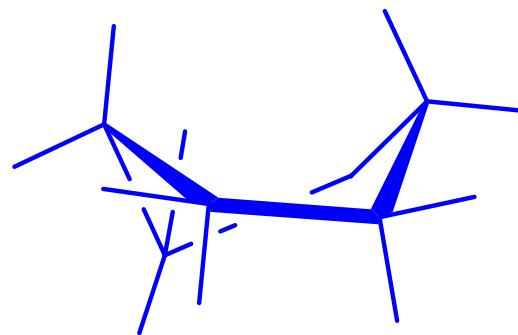
boat

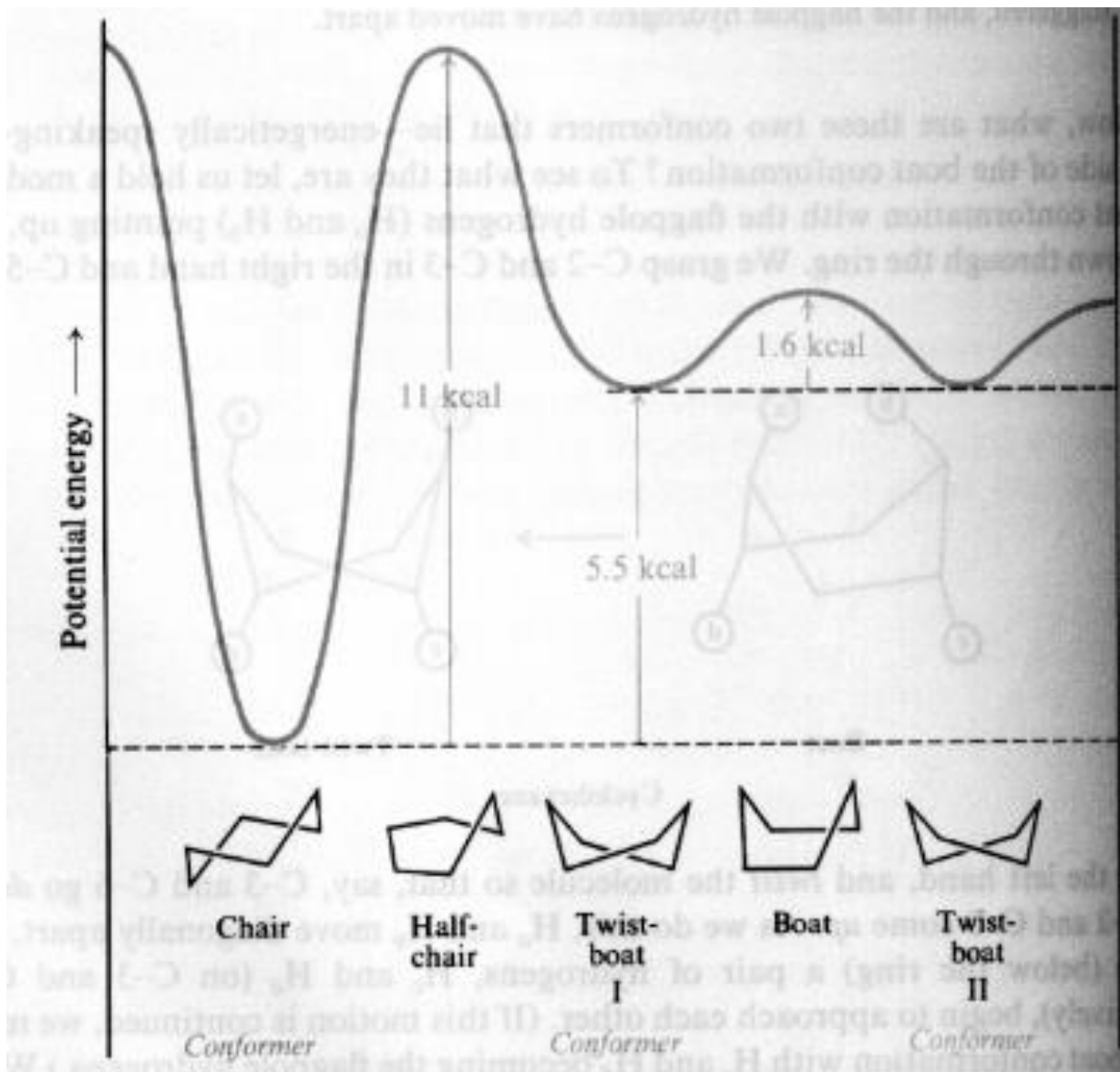


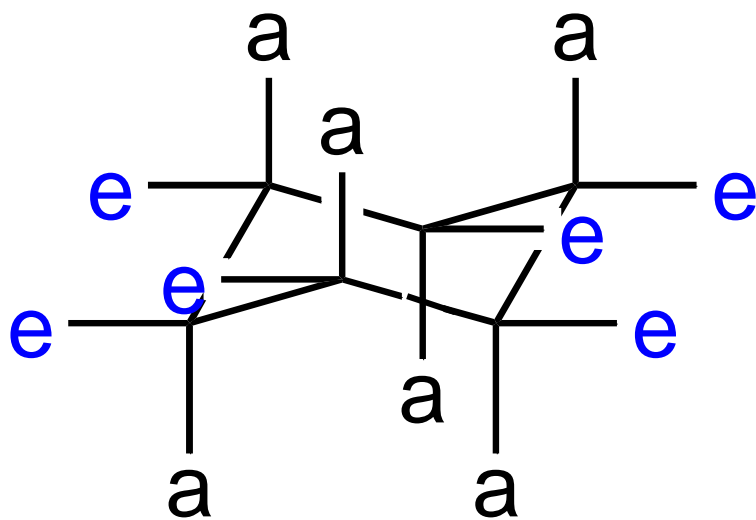
The **chair** conformation of cyclohexane is free of both angle strain and torsional strain (deviation from staggered). This is the **most stable** conformation.



The boat conformation is free of angle strain, but has a great deal of torsional strain (eclipsed). To relieve the strain, it twists slightly to form the twist boat:

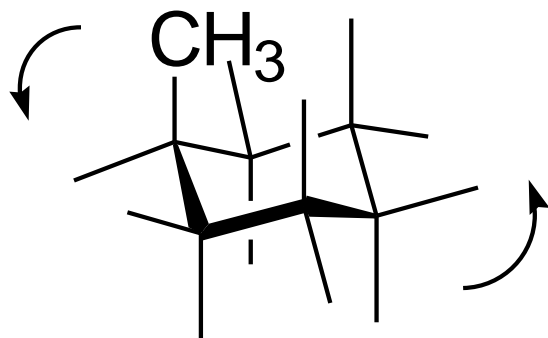




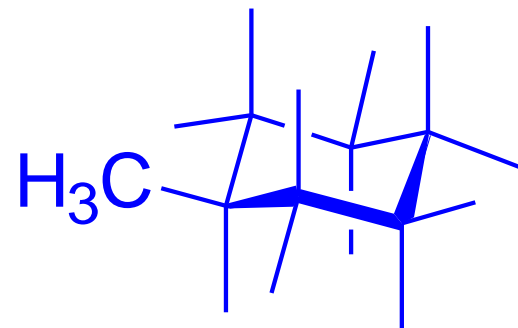


a = axial positions in the chair conformation

e = equatorial positions

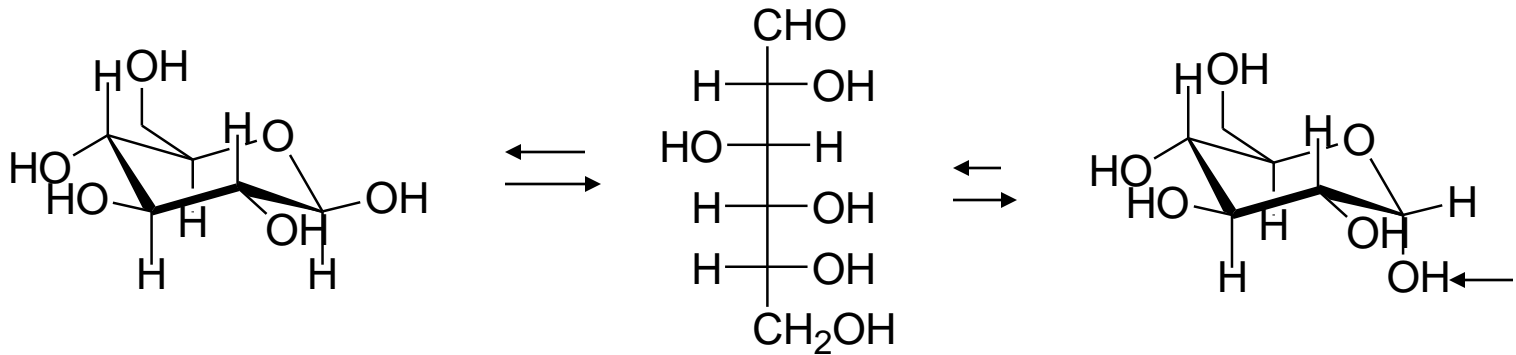


CH<sub>3</sub> in **axial** position



CH<sub>3</sub> in **equatorial** position  
is more stable





beta-D-glucose

all groups equatorial

more stable

alpha-D-glucose

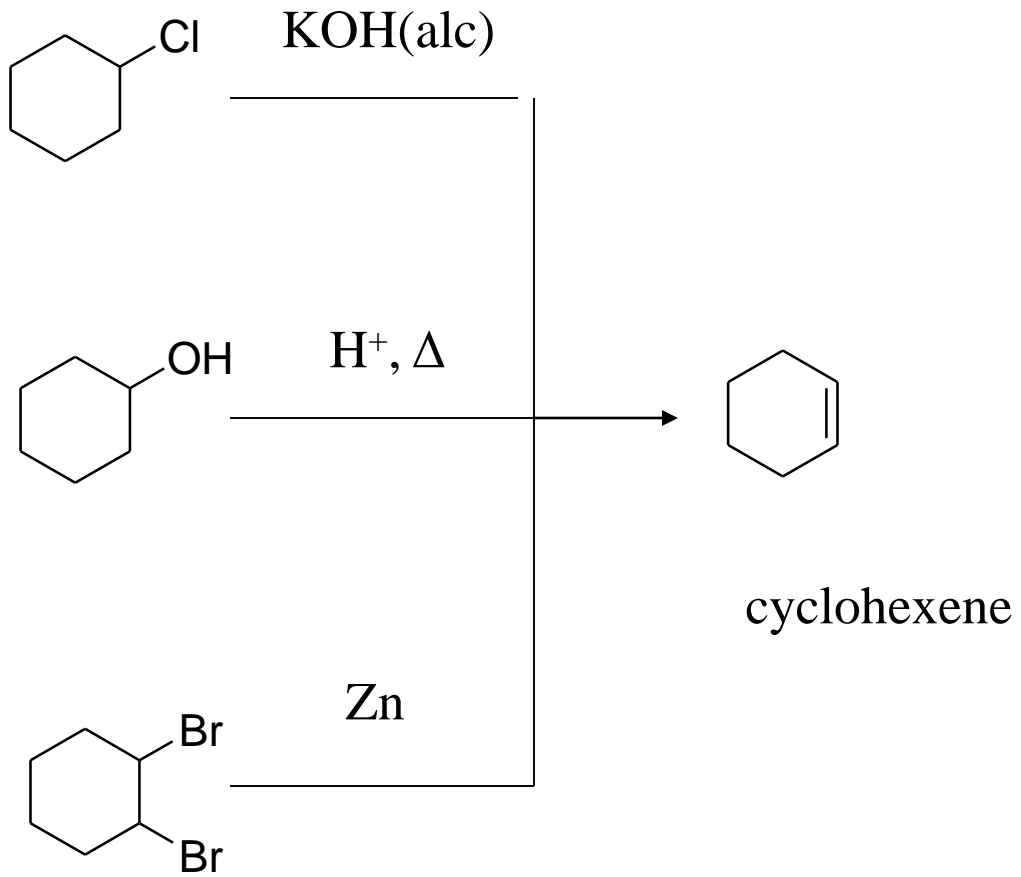
one group forced to be axial

## Cycloalkenes, syntheses:

### A. Modification of a ring compound:

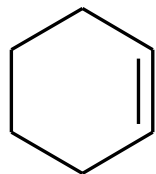
- 1) dehydrohalogenation of an alkyl halide
- 2) dehydration of an alcohol
- 3) dehalogenation of vicinal dihalides

### (B. Ring closures)

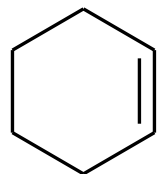
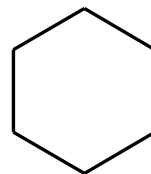
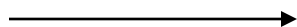


## Cycloalkenes, reactions:

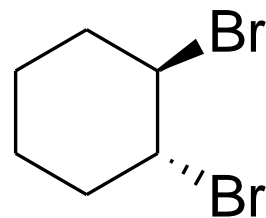
1. addition of  $H_2$
2. addition of  $X_2$
3. addition of  $HX$
4. addition of  $H_2SO_4$
5. addition of  $H_2O, H^+$
6. addition of  $X_2 + H_2O$
7. oxymerc-demerc.
8. hydroboration-oxid.
9. addition of free radicals
10. addition of carbenes
11. epoxidation
12. hydroxylation
13. allylic halogenation
14. ozonolysis
15. vigorous oxidation



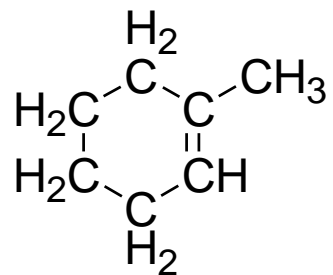
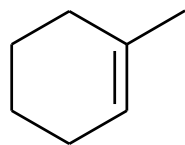
$\text{H}_2, \text{Pt}$



$\text{Br}_2, \text{CCl}_4$



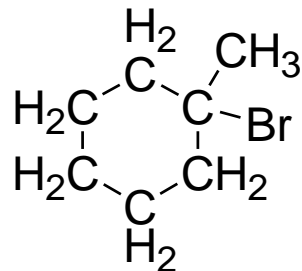
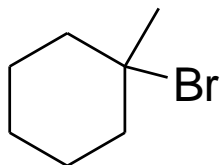
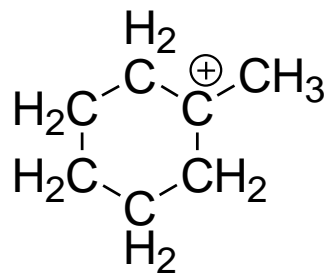
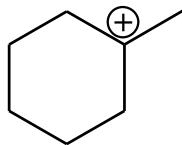
*trans*-1,2-dibromocyclohexane

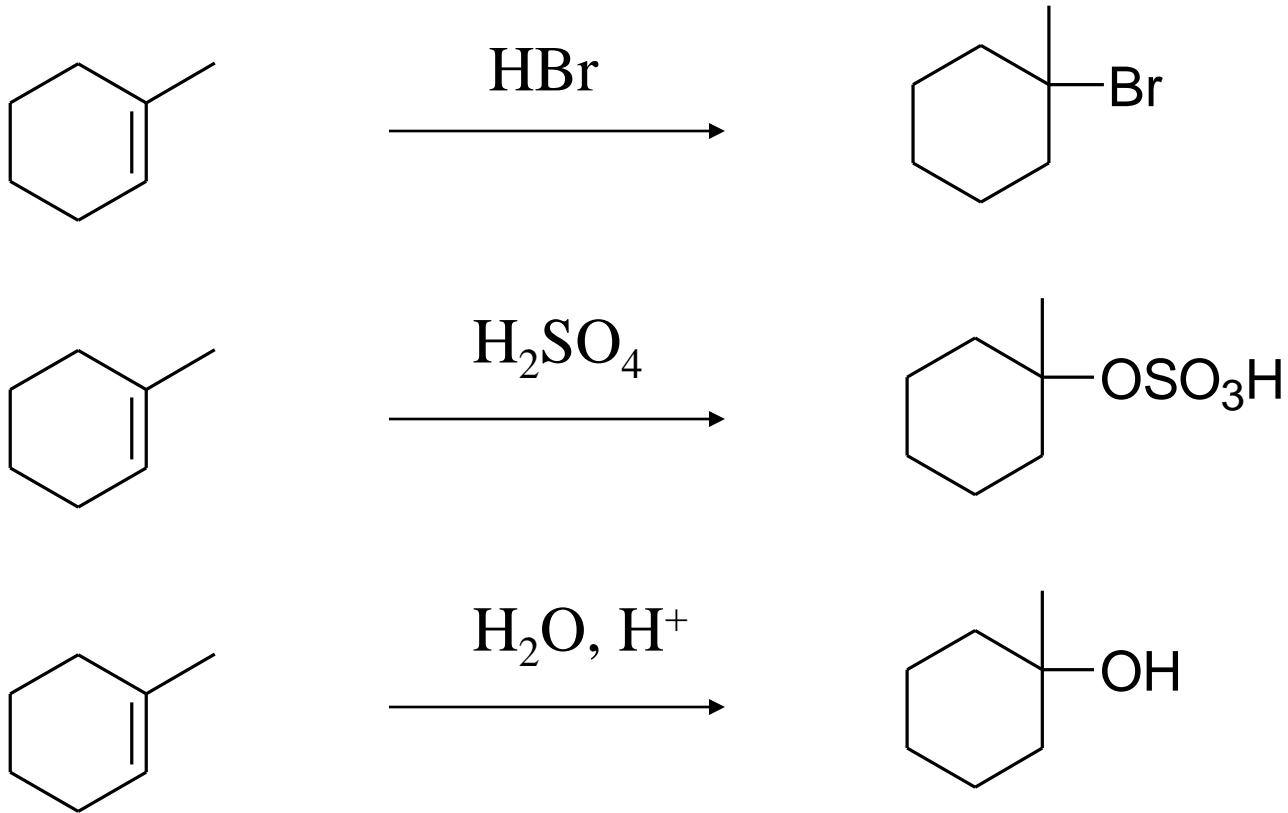


+ HBr

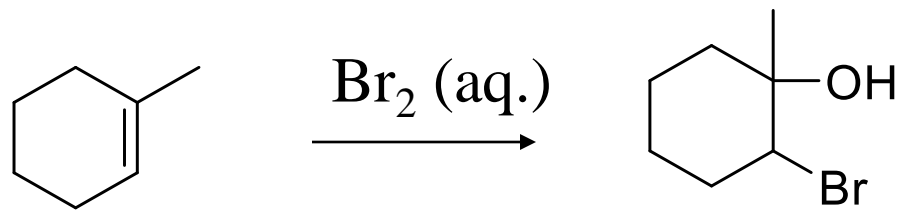


3° carbocation

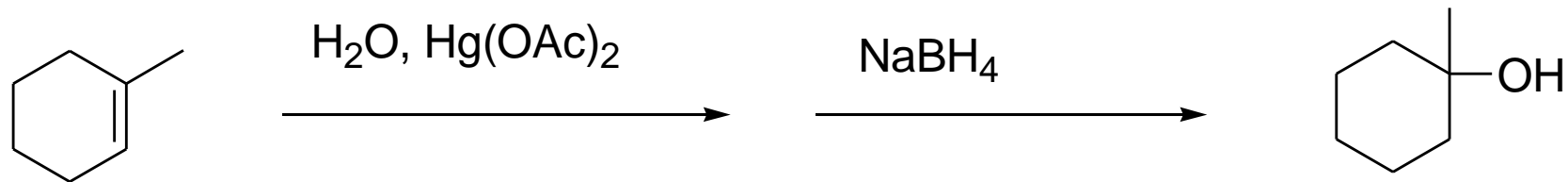




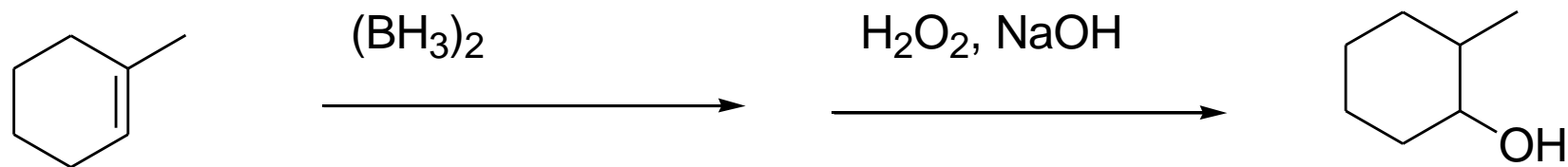
Markovnikov orientation



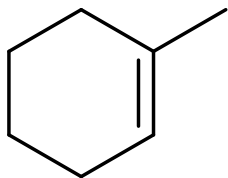




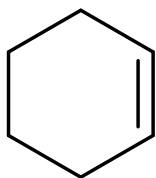
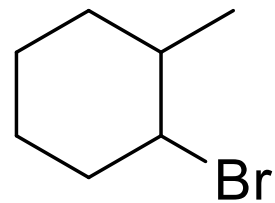
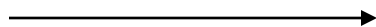
Markovnikov



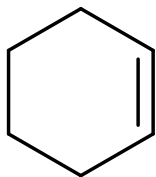
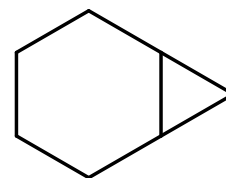
anti Markovnikov



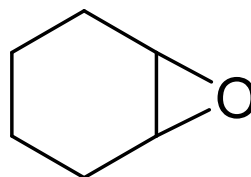
HBr, peroxides

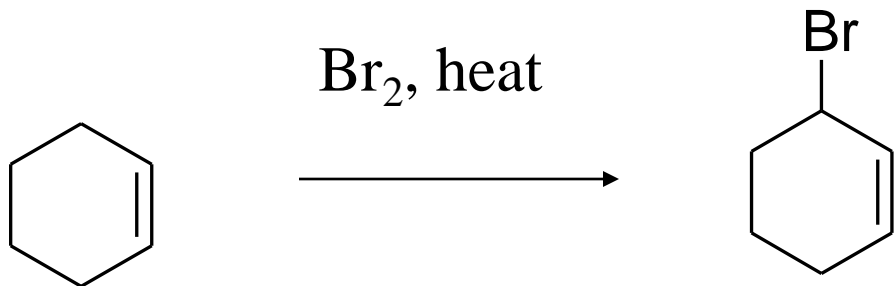
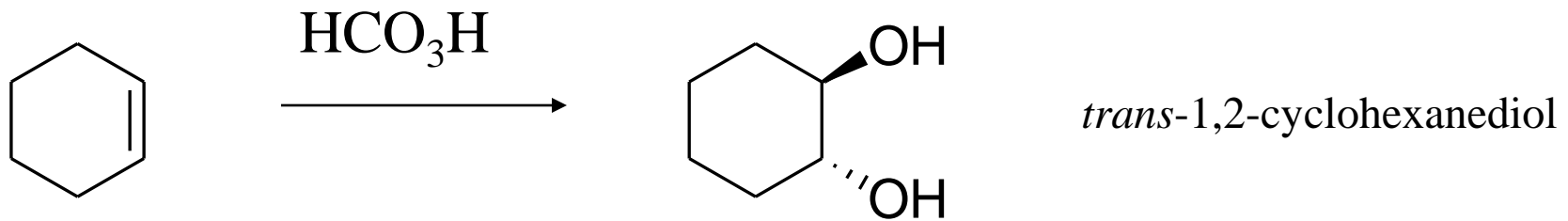
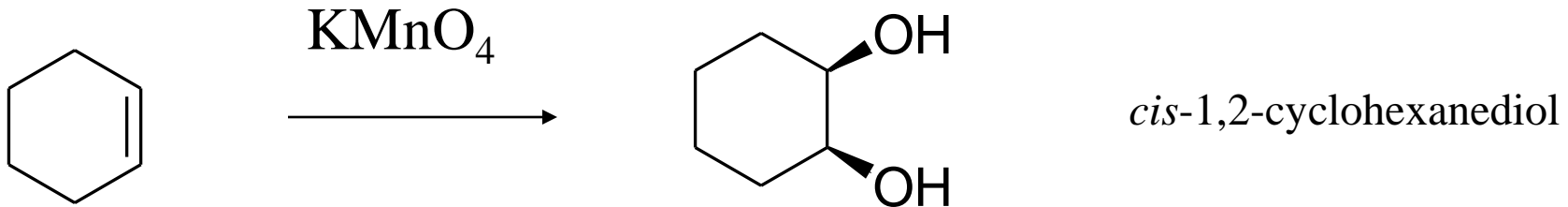


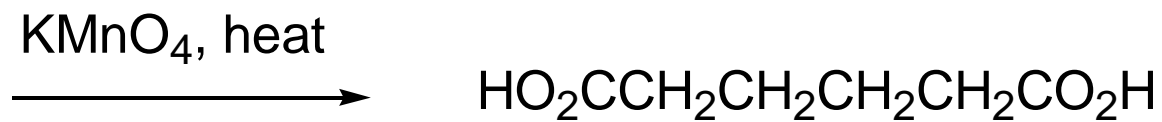
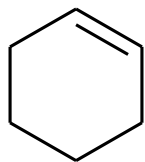
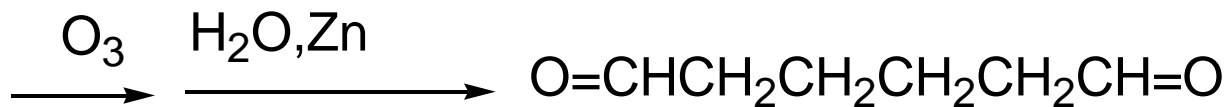
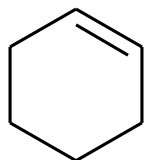
$\text{CH}_2\text{CO}$ ,  $h\nu$



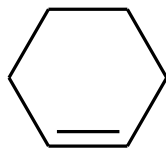
Peroxybenzoic acid



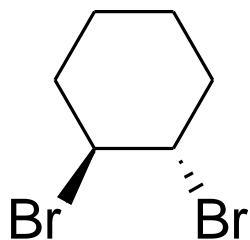




stereoselective

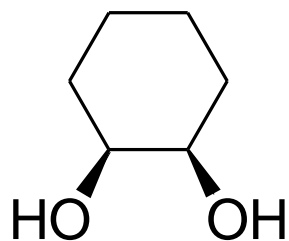


$\text{Br}_2$



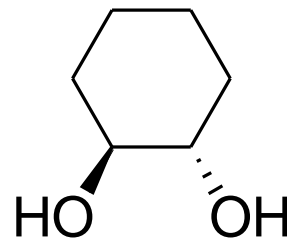
*anti*

$\text{KMnO}_4$



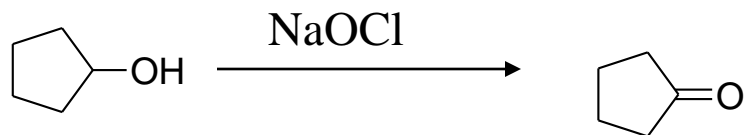
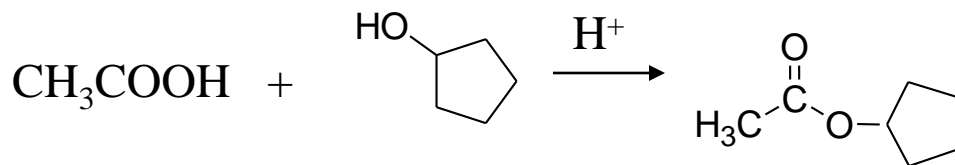
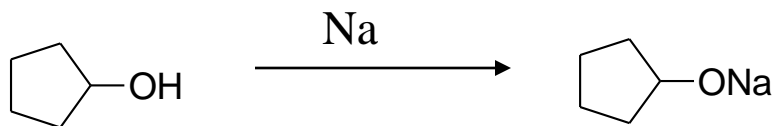
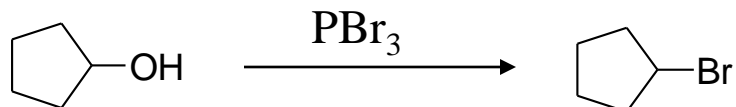
*syn*

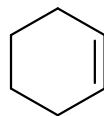
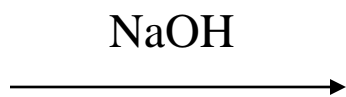
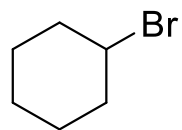
$\text{HCO}_3\text{H}$



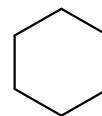
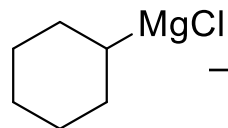
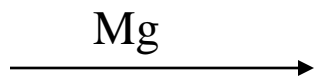
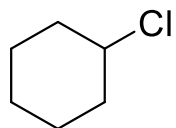
*anti*

cyclic alcohols, halides, ethers as expected:





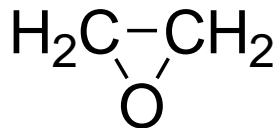
2° alkyl halide => E2



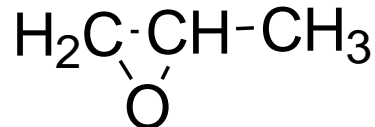
Alicyclic compounds are chemically like their open chain analogs. The exceptions are for small ring compounds where angle strain may give rise to reactions that are not typical of other molecules.



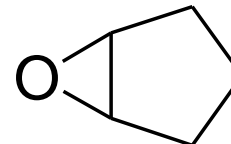
## Epoxides:



ethylene oxide  
(oxirane)

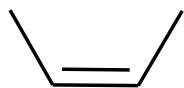


propylene oxide  
(methyloxirane)

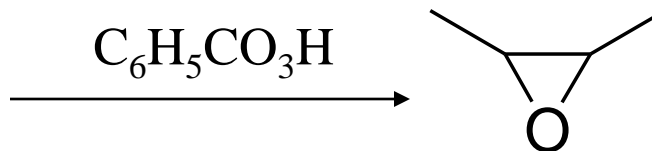


cyclopentene oxide

## Synthesis:



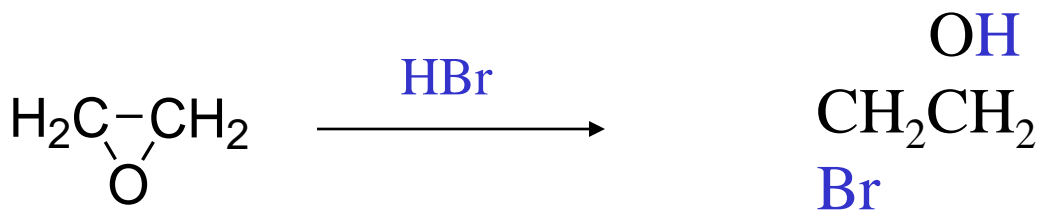
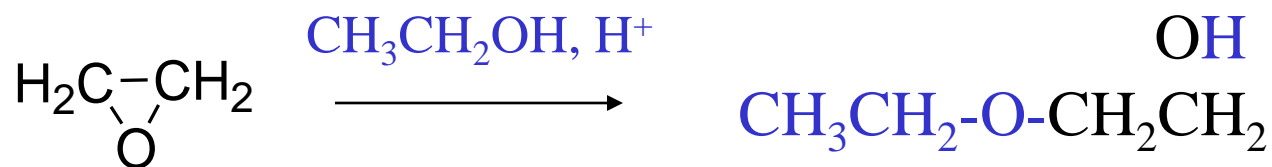
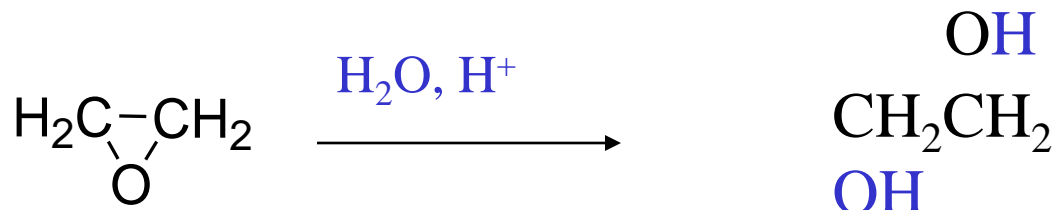
*cis*-2-butene



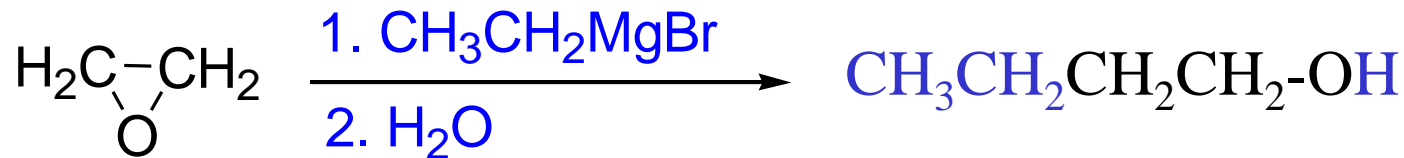
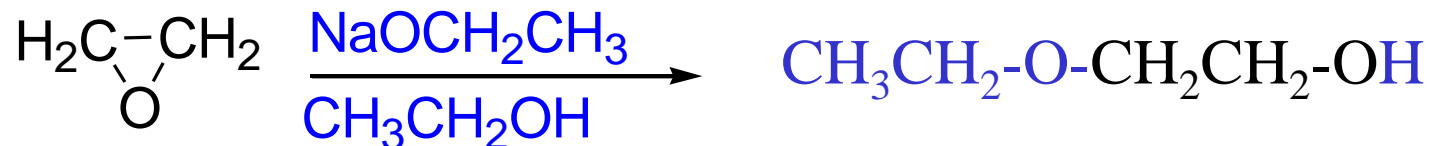
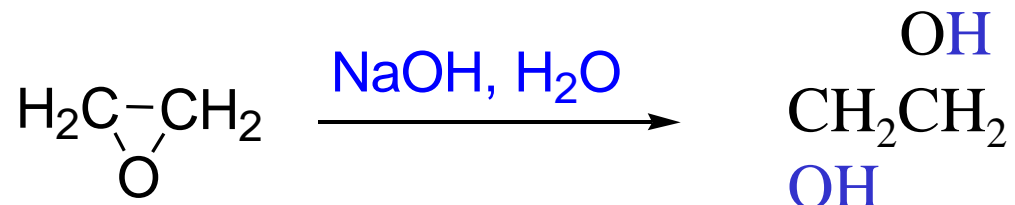
$\beta$ -butylene oxide

epoxides, reactions:

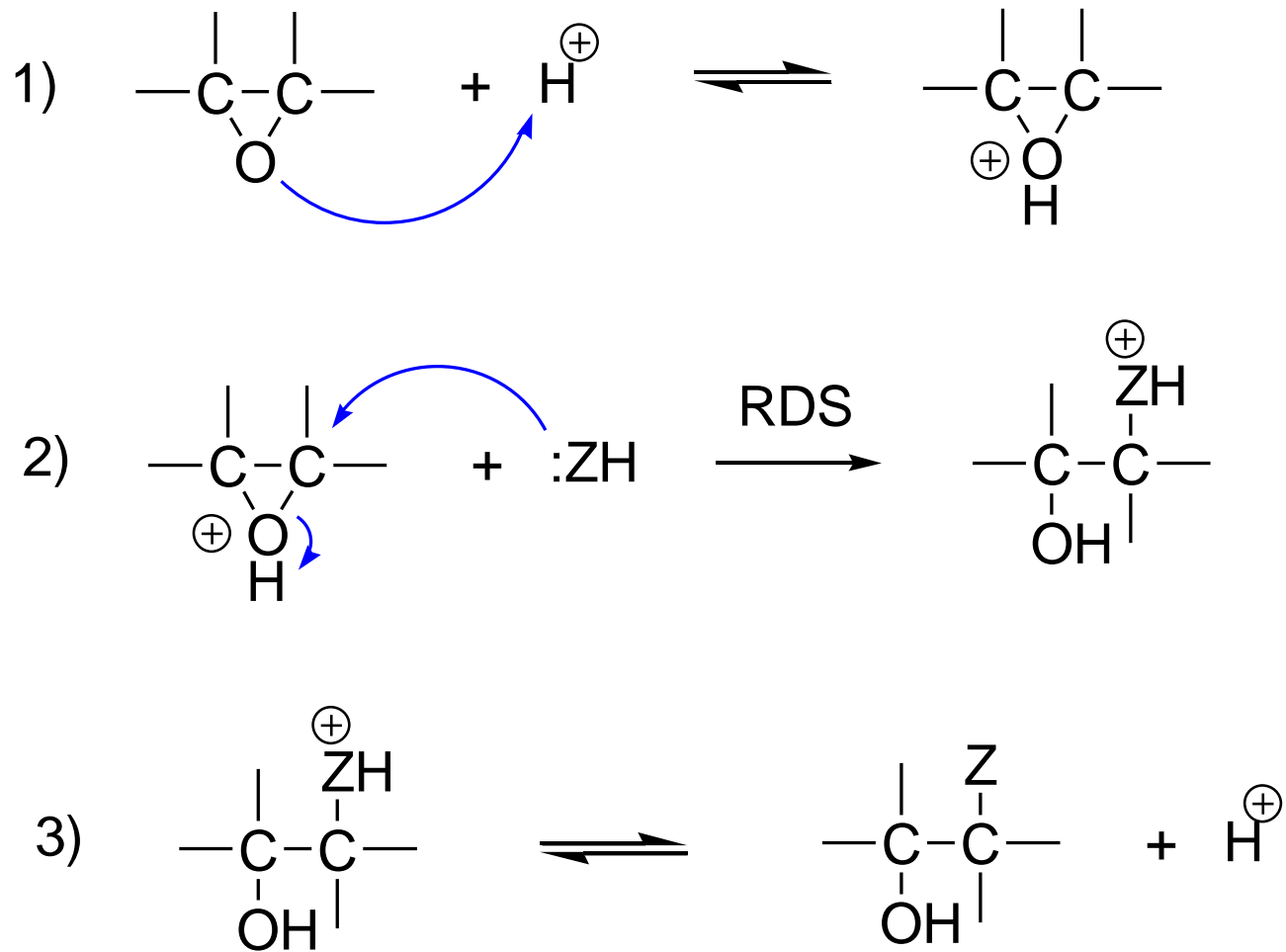
1) acid catalyzed addition



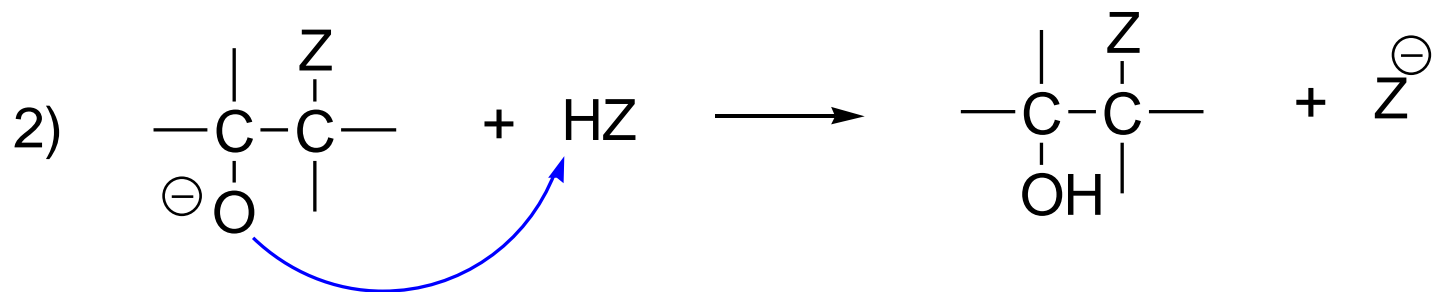
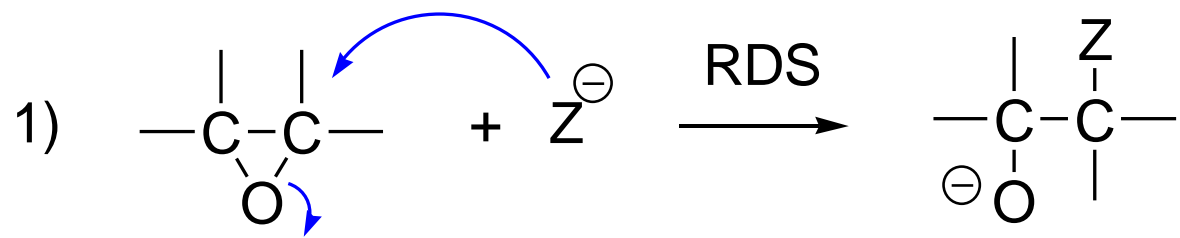
## 2. Base catalyzed addition



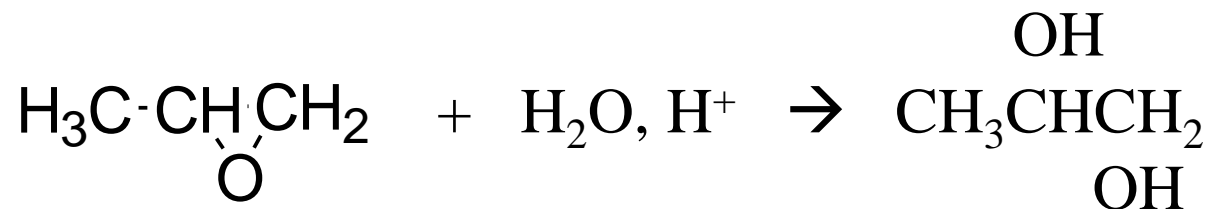
mechanism for acid catalyzed addition to an epoxide



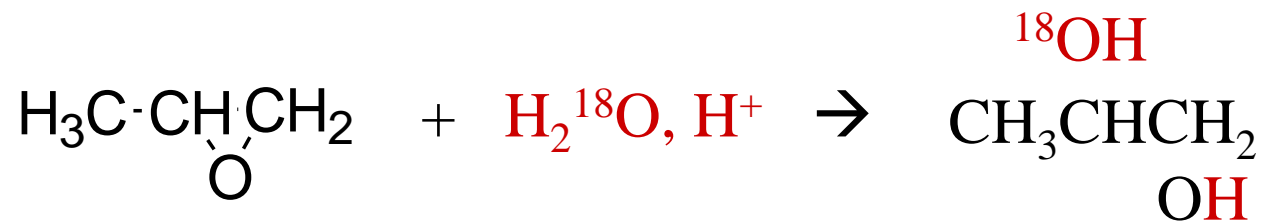
mechanism for base-catalyzed addition to an epoxide:

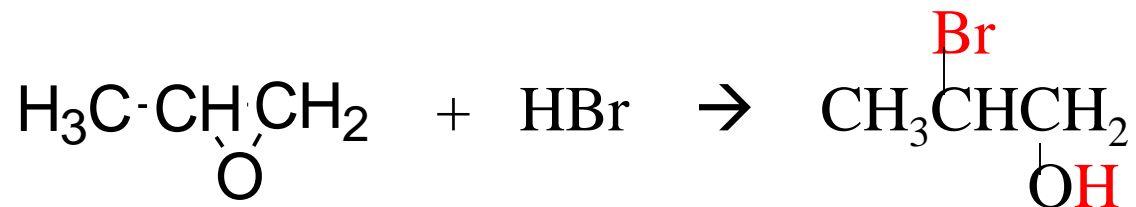
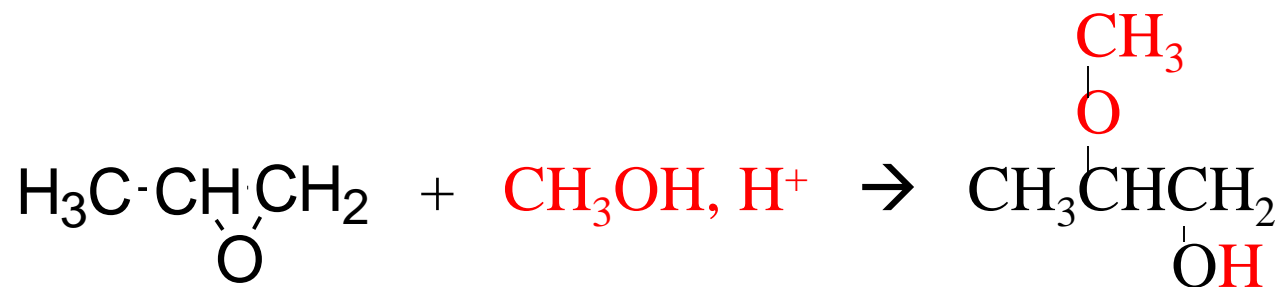


acid catalyzed addition to unsymmetric epoxides?

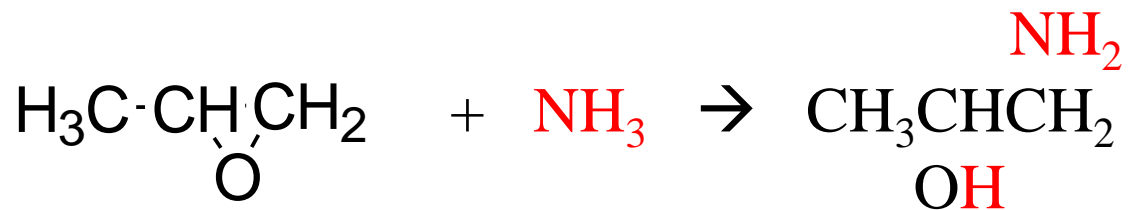
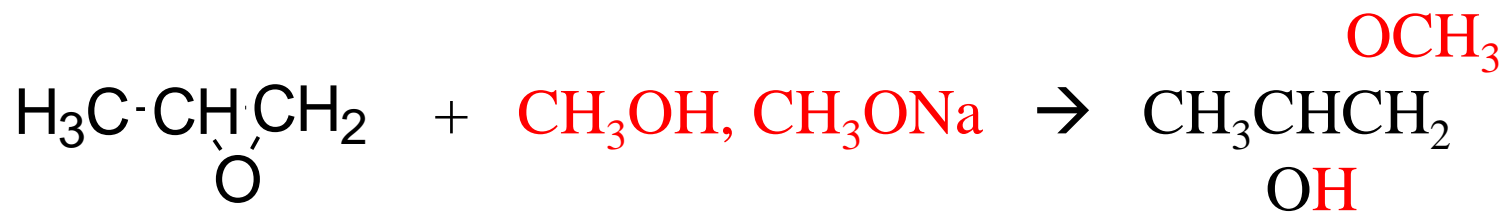
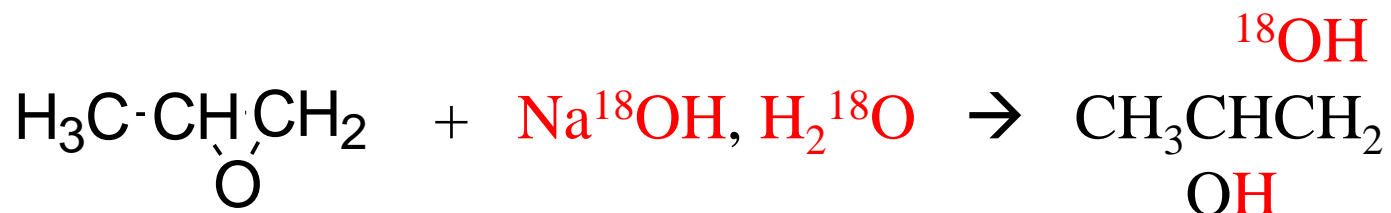


which oxygen in the product came from the water?



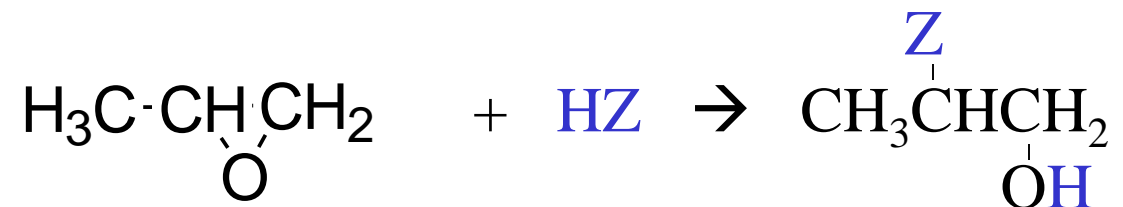


Base?





Acid:



Base:

