

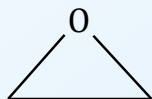
**Epoxides**  
**Nomenclature**  
**Synthesis and Reactions**

*Dr. Sapna Gupta*

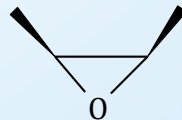
# Epoxides

Epoxide is a cyclic ether in which oxygen is one atom of a three-membered ring. Simple epoxides are named as derivatives of oxirane. When the epoxide is part of another ring system, it is shown by the prefix epoxy-.

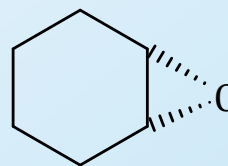
Common names are derived from the name of the alkene from which the epoxide is formally derived.



Oxirane  
ethylene oxide



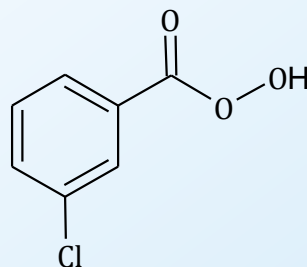
2,3-dimethyloxirane  
2-butene oxide



1,2-epoxycyclohexane  
cyclohexene oxide

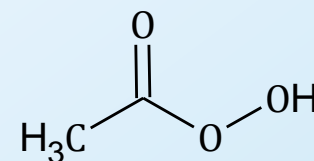
# Synthesis of Epoxides

1) **From Peracids:** The most common method is oxidation of an alkene using a peroxycarboxylic acid (a peracid).



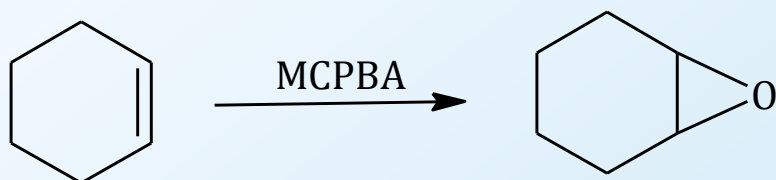
meta-chloroperbenzoic acid  
MCPBA

## Reagents

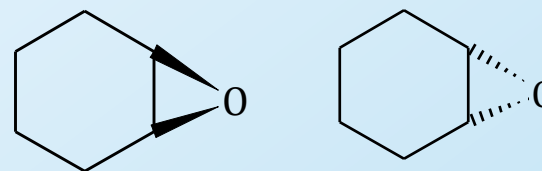


Peracetic acid

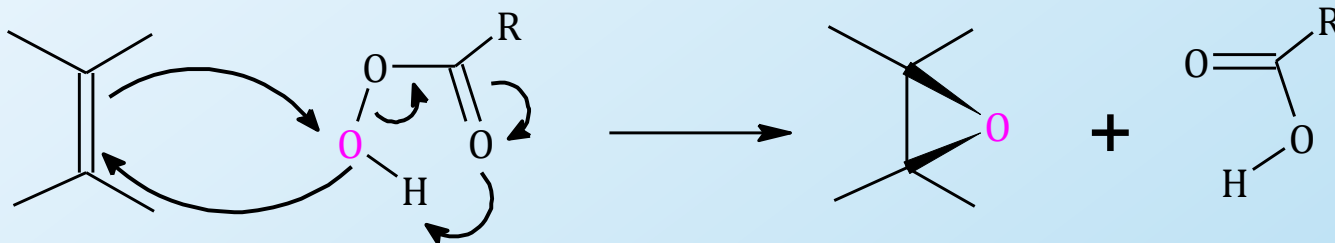
## Example



**Stereospecificity:** The addition is always syn. An enantiomer will also form.



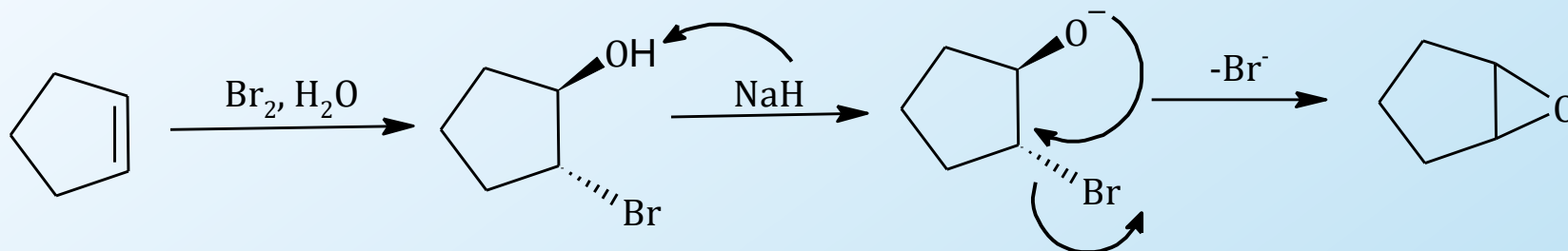
**Mechanism:** This is called concerted mechanism, meaning there is no specific nucleophile or electrophile and everything happens in one step.



# Synthesis of Epoxides, contd...

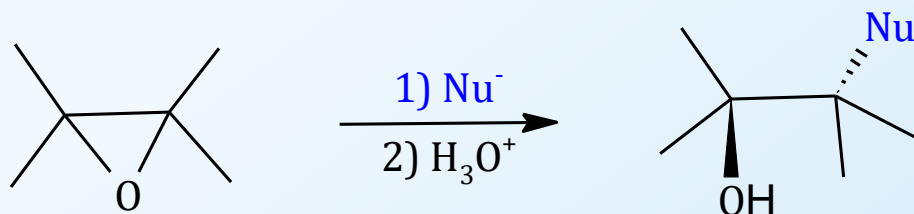
2) **Cyclization of Halohydrin**: Intramolecular Williamson synthesis can be carried out when the alcohol and halide are vicinal to each other. The best way to make this halohydrin is from an alkene using halogen and water. The halogen should be either chlorine or bromine.

The first step is generating an oxide of the alcohol using a strong base. The oxide then undergoes intramolecular  $S_N^2$  to form the epoxide as shown below.

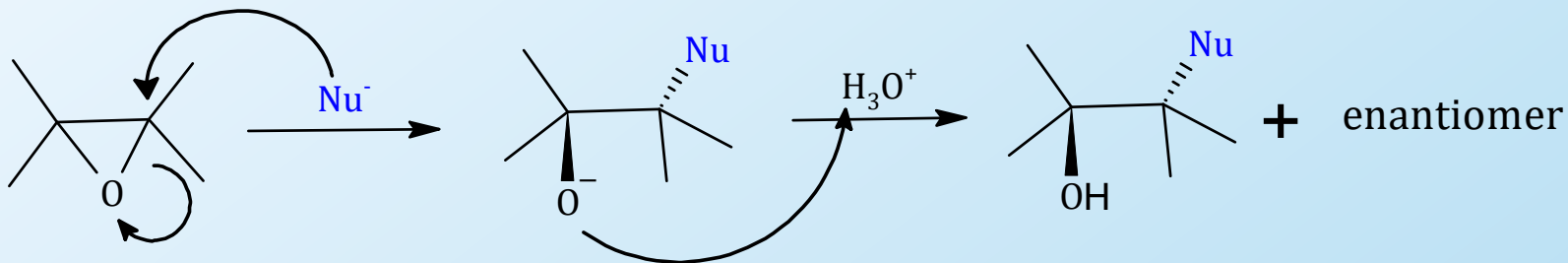


# Reactions of Epoxides – Nucleophilic Mechanism

Ethers can undergo both nucleophilic and electrophilic reactions.

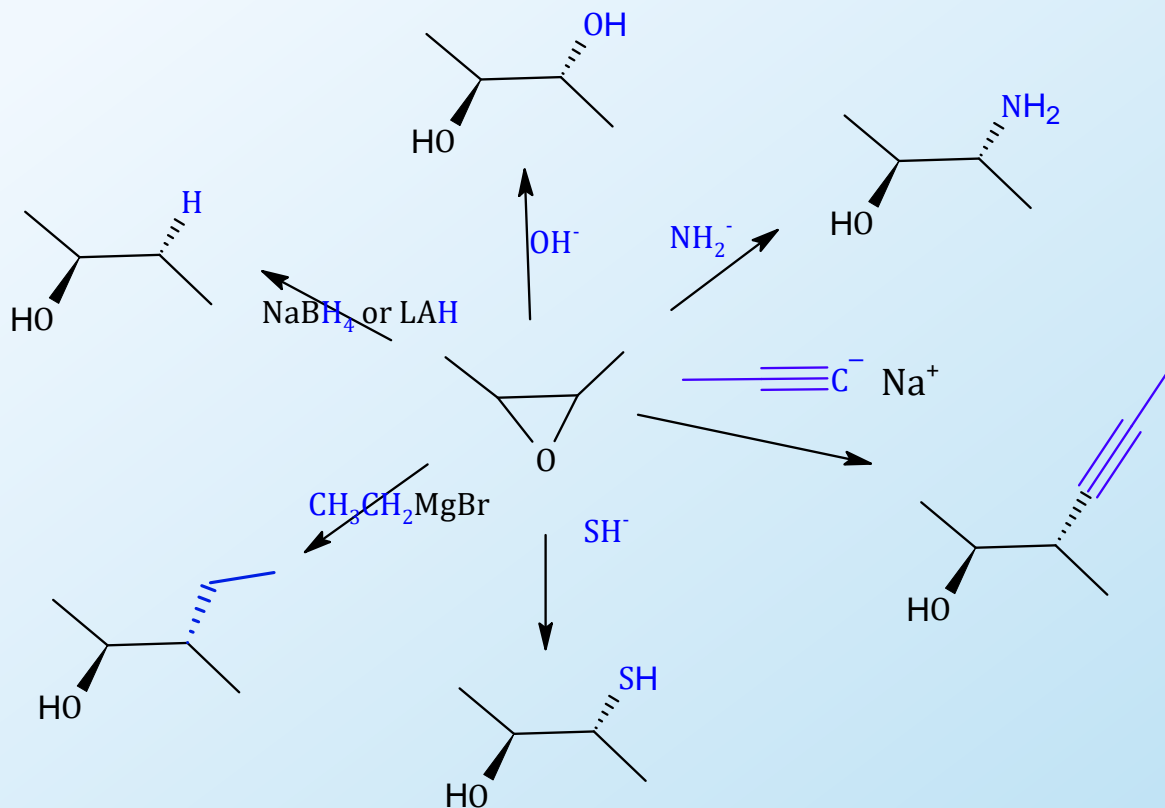


Nucleophilic mechanism: In this mechanism the nucleophile attacks from behind the epoxy ring. The carbons attached to the oxygen are partially positive hence, electrophilic. The backside attack will cause the epoxide ring to open to give an alkoxide which is then protonated during workup with acid to give an alcohol. The  $\text{Nu}^-$  and  $\text{OH}$  will be **anti** to each other in the product. The enantiomer will also be formed.



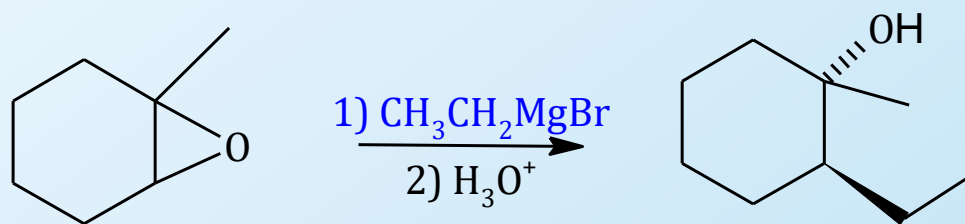
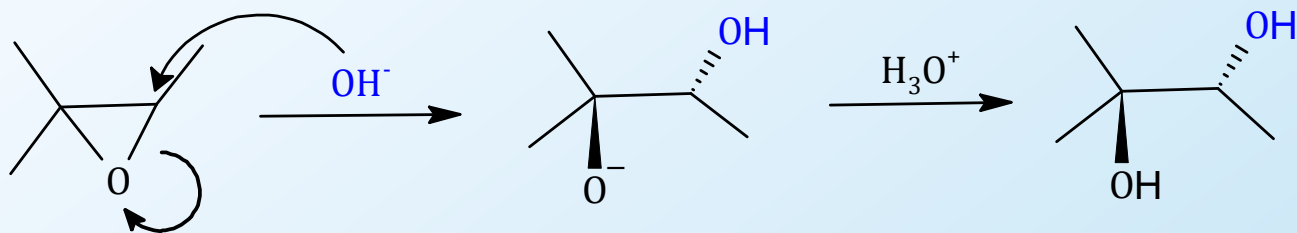
# Reactions of Epoxides – Nucleophilic - 2

A number of nucleophiles can react with the epoxide ring that are good for creating a variety of functional groups. An alcohol will always result from ring opening. Below are some examples. Note that I am starting with a symmetrical epoxide in all these examples. Also, I am not writing the second step of protonating the oxide, but that is understood.



# Reactions of Epoxides – Nucleophilic - 3

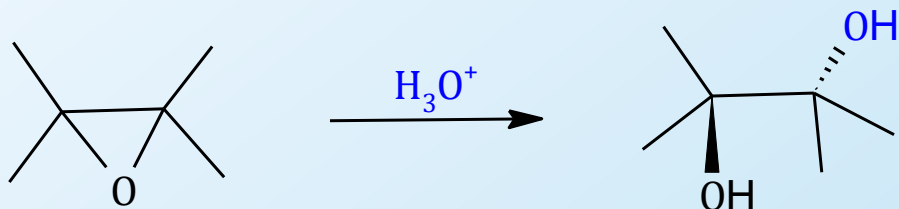
When the epoxide is symmetrical the nucleophile can attack either of the two electrophilic carbons of the epoxide. But when the epoxide is asymmetric, then the nucleophile will attack the less sterically hindered carbon, because the mechanism resembles the  $S_N^2$  mechanism.



# Reactions of Epoxides - Electrophilic

Ring opening in electrophilic mechanism gives similar anti stereochemistry as nucleophilic, but mechanism is different, and thus the products can be different depending on the ether. Electrophilic ring opening is used when the nucleophile is weak e.g., water and/or alcohol.

The acid generally used will be dilute sulfuric acid or phosphoric acid. An enantiomer will also form.

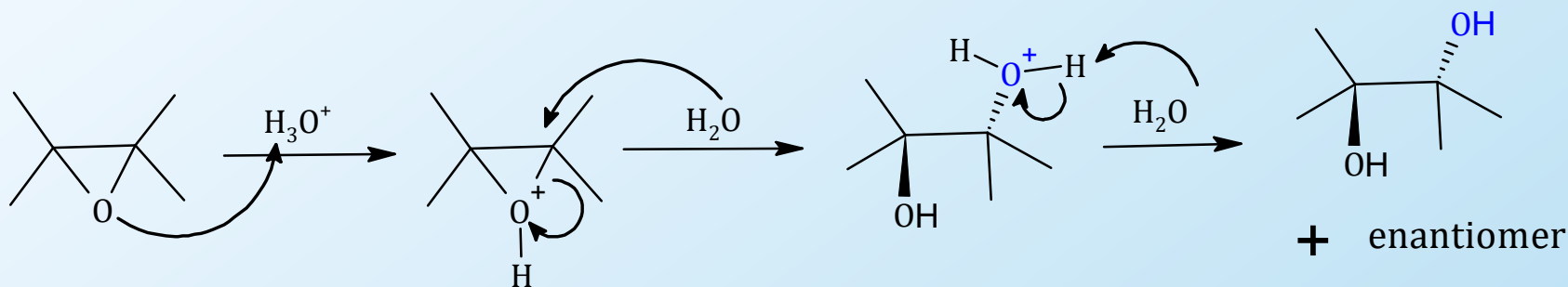




# Reactions of Epoxides – Electrophilic Mechanism

In electrophilic mechanism, the medium is always acidic.

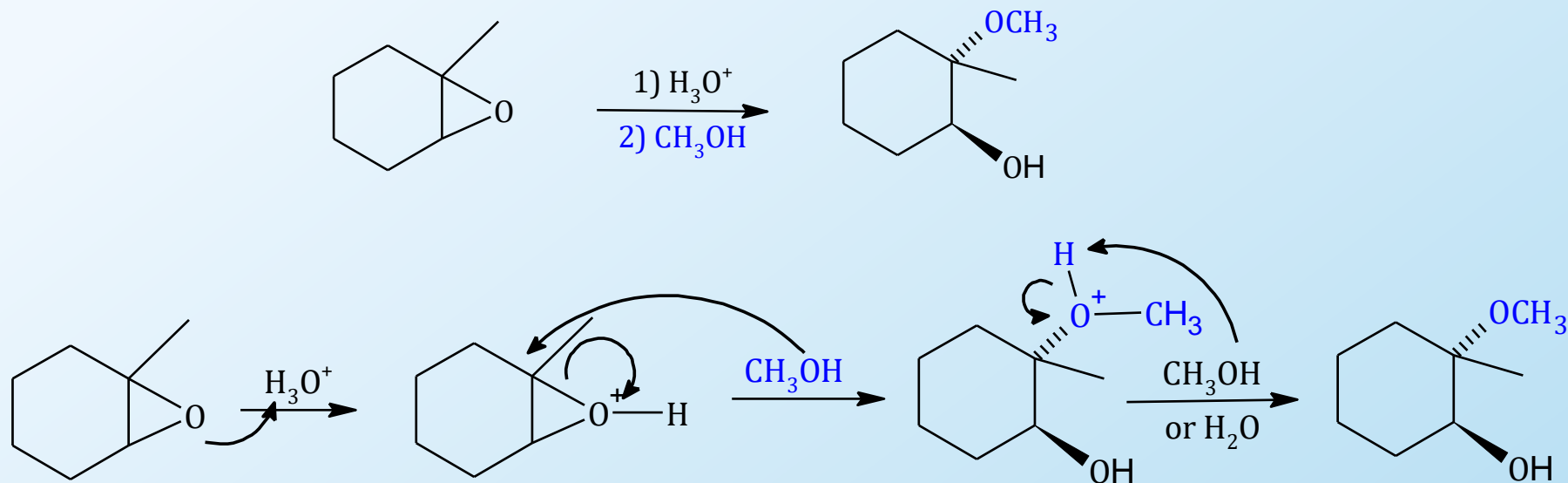
Reaction starts when oxygen of epoxide is protonated from the acid, forming an oxonium ion. The weak nucleophile, water or alcohol attacks from the backside of the epoxy ring causing the epoxide ring to open forming an alcohol. The protonated nucleophile eventually gets deprotonated from another water or alcohol molecule. The Nu<sup>-</sup> and OH are anti to each other. An enantiomer will also be formed.



# Reactions of Epoxides – Electrophilic contd..

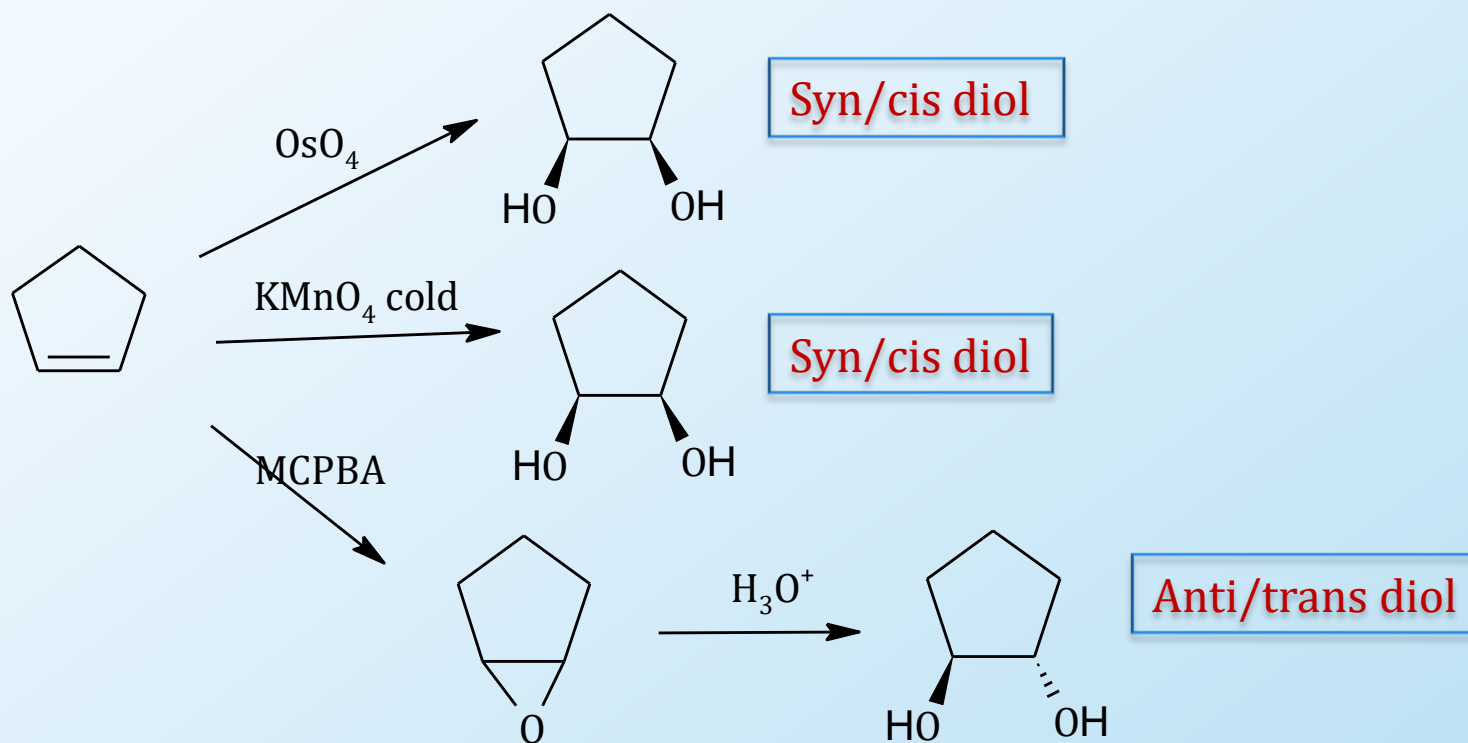
Here is an example with alcohol as the nucleophile. Here we will use an asymmetric epoxide as in example in acidic medium.

In asymmetric epoxide, the weak Nu will attack the more substituted carbon, as this mechanism resembles the  $S_N^1$  mechanism. More substituted carbons are like the more substituted carbocations, hence more stable.



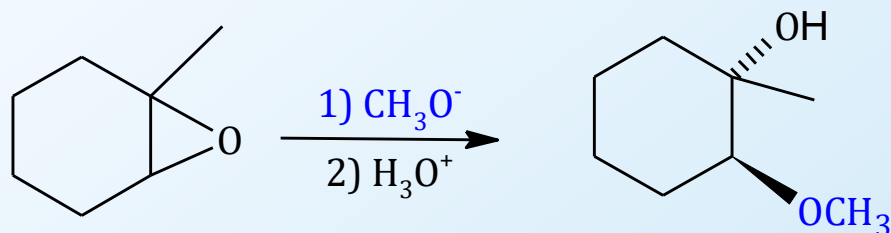
# Epoxides to Form Diols

Diols can be *cis* or *trans* depending on the reagents used. Alkenes will give *cis* diols on using osmium tetroxide or potassium permanganate (cold). The mechanism is a *syn* addition. To make *trans* diols, epoxides are used and then ring opened in electrophilic or nucleophilic manner to give the *anti* addition.

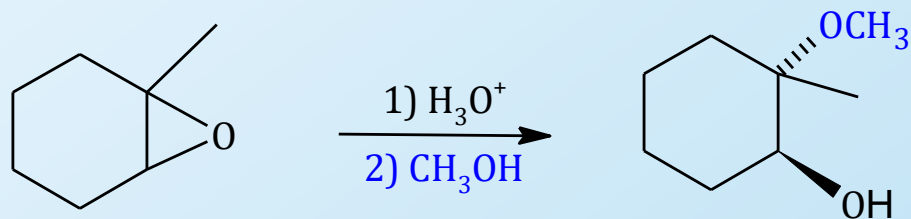


# Reactions - Epoxide Ring Opening: Nucleophilic Vs Electrophilic

**Nucleophilic Substitution:** In case of asymmetric epoxide, strong nucleophiles will attack the less sterically hindered carbon. Mechanism is  $S_N^2$ .

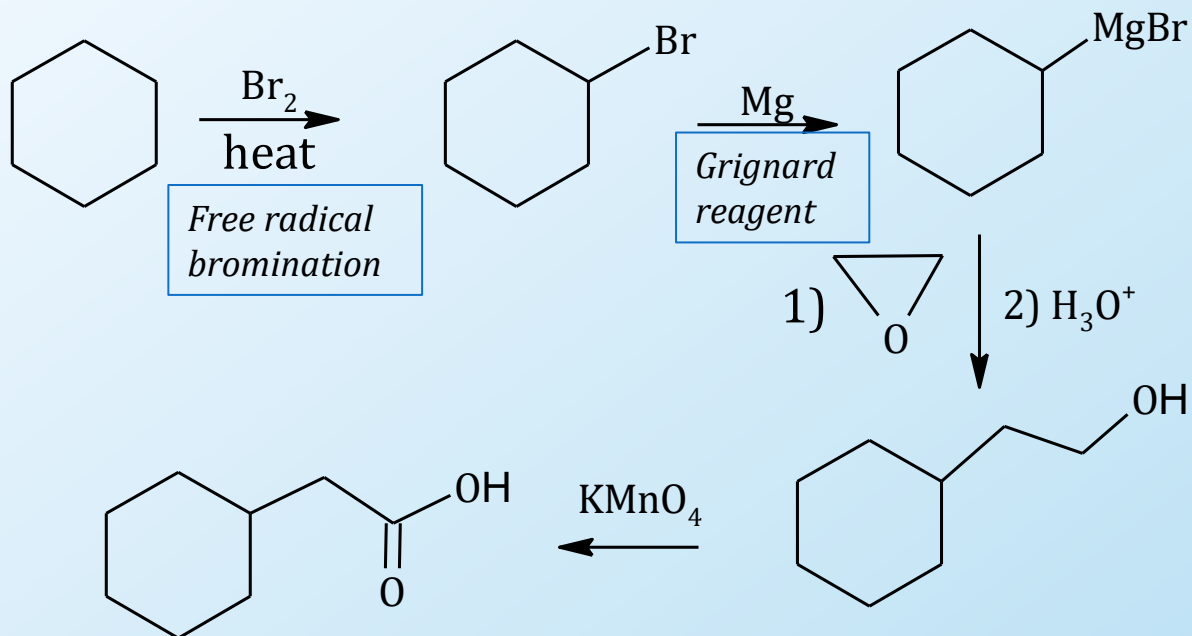
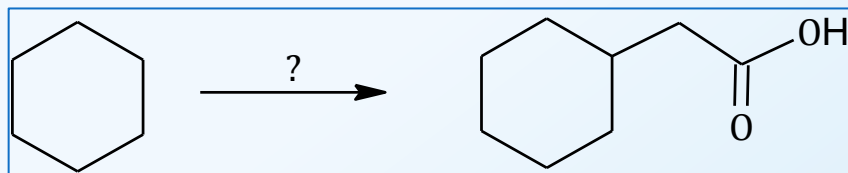


**Electrophilic Substitution:** In case of asymmetric epoxide, electrophile first protonates the oxygen and then the weak nucleophiles will attack the more substituted carbon. Mechanism is similar to  $S_N^1$  thus carbocation stability is considered during the  $Nu^-$  attack.



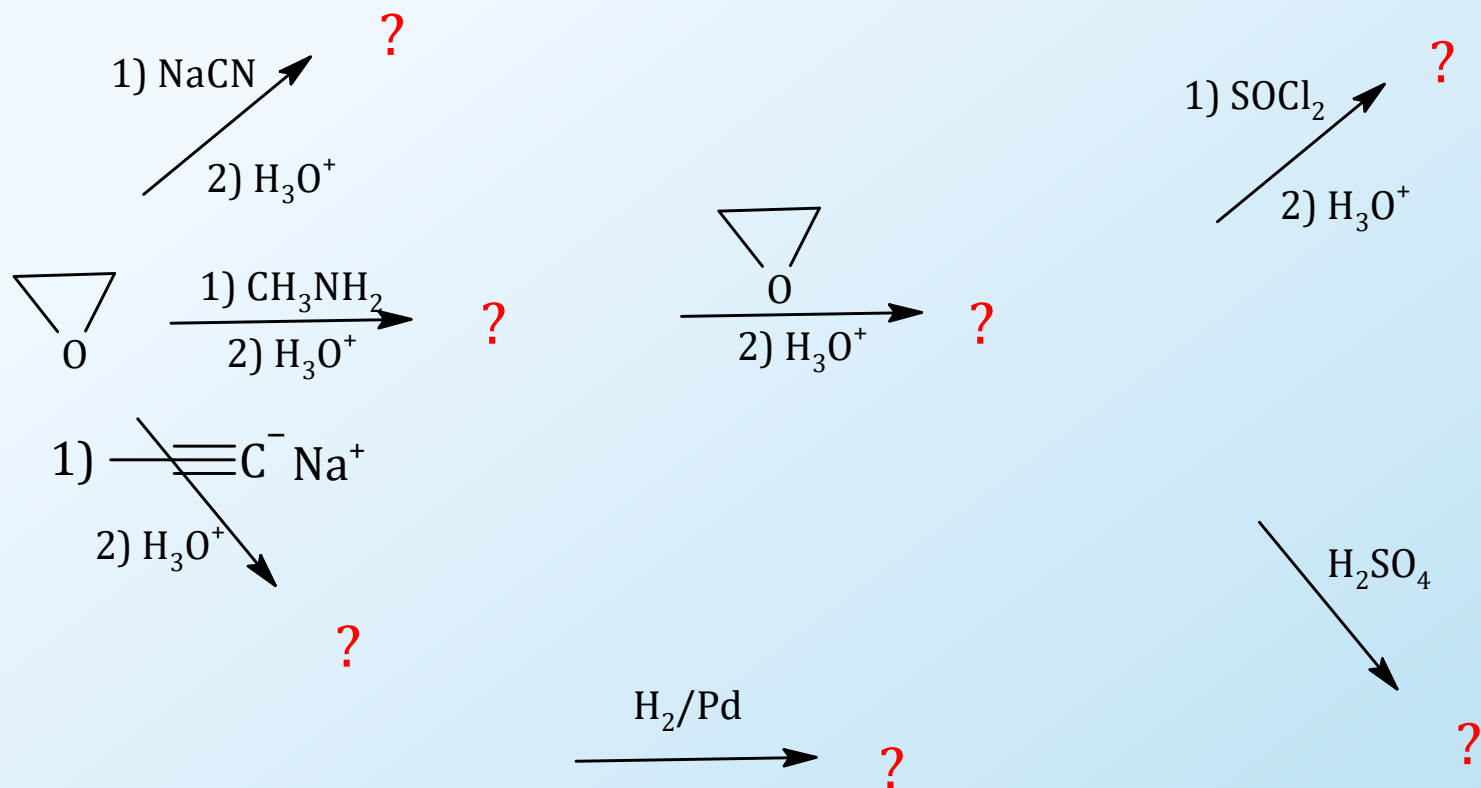
# Example of Epoxides and Synthesis

Epoxides are used as building blocks in organic synthesis. They are a great way to add carbons to any compound and form alcohol in the process. Here is a synthesis on how to add two carbons and make a primary alcohol during the synthetic steps.



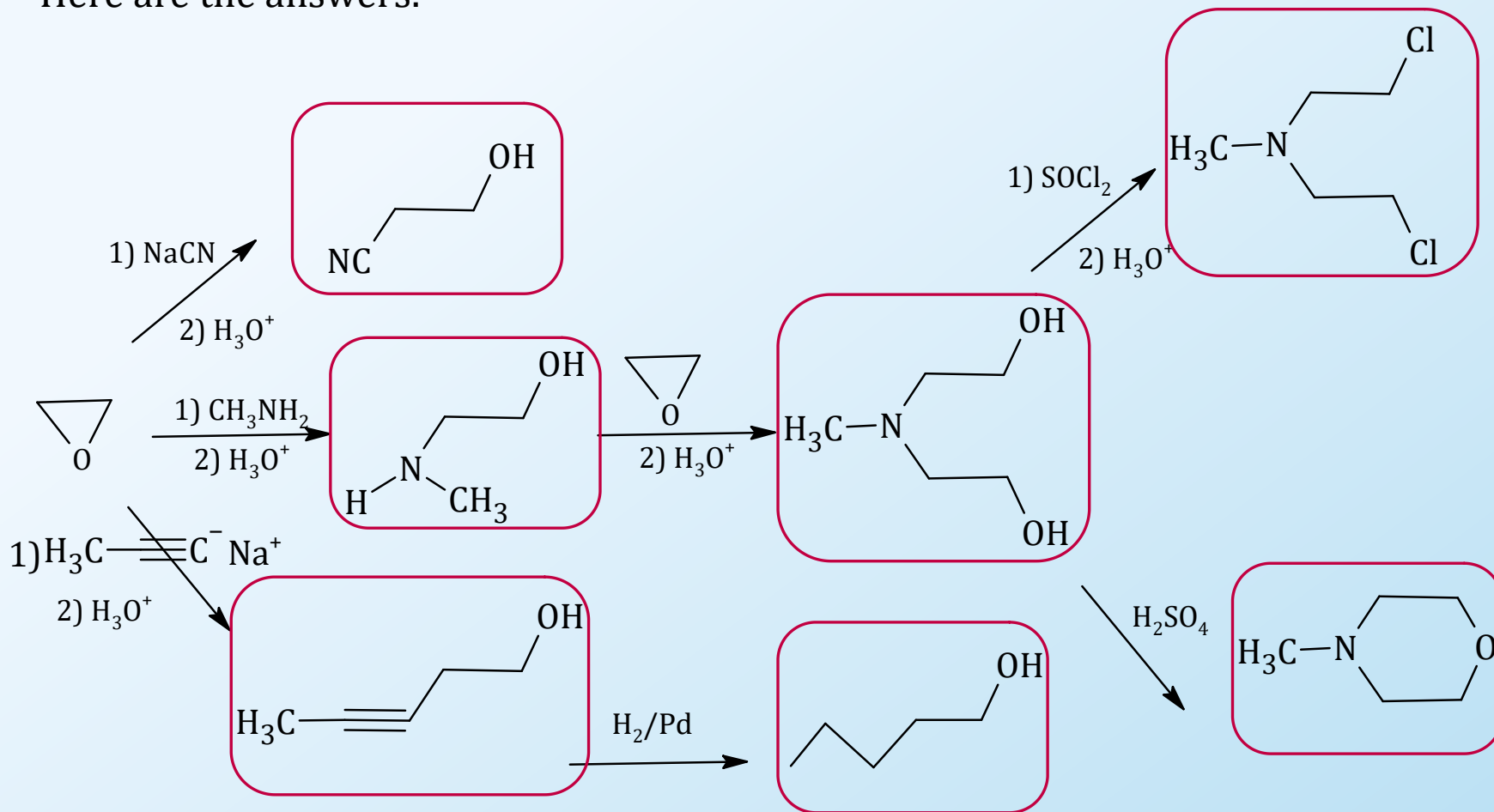
# Example - Ethylene Oxide Reaction Scheme

Ethylene oxide is a valuable building block for organic synthesis because each of its carbons may be converted to a functional group. Try the example of reaction scheme below. The answers are on the next slide.



# Example - Ethylene Oxide Reaction Scheme - Answer

Here are the answers.



# Key Concepts

- Epoxides
- Peracids
- Ring openings
  - Stereospecific