16.9

Preparation of Epoxides: A Review and a Preview

Preparation of Epoxides

Epoxides are prepared by two major methods.
Both begin with alkenes.

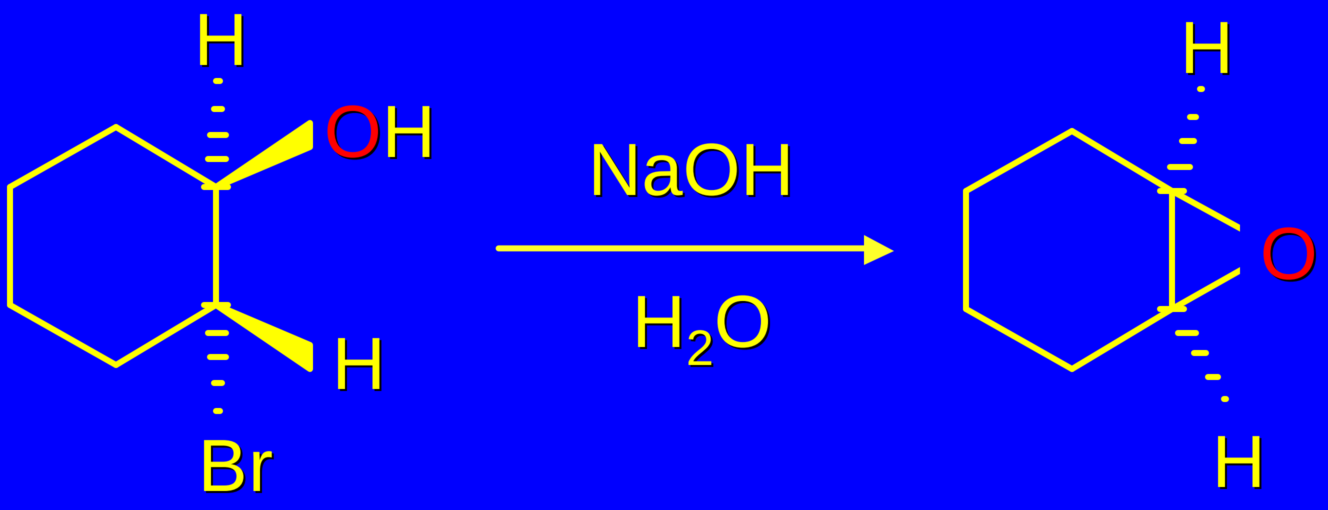
reaction of alkenes with peroxy acids (Section 6.18)

conversion of alkenes to vicinal halohydrins, followed by treatment with base (Section 16.10)

16.10

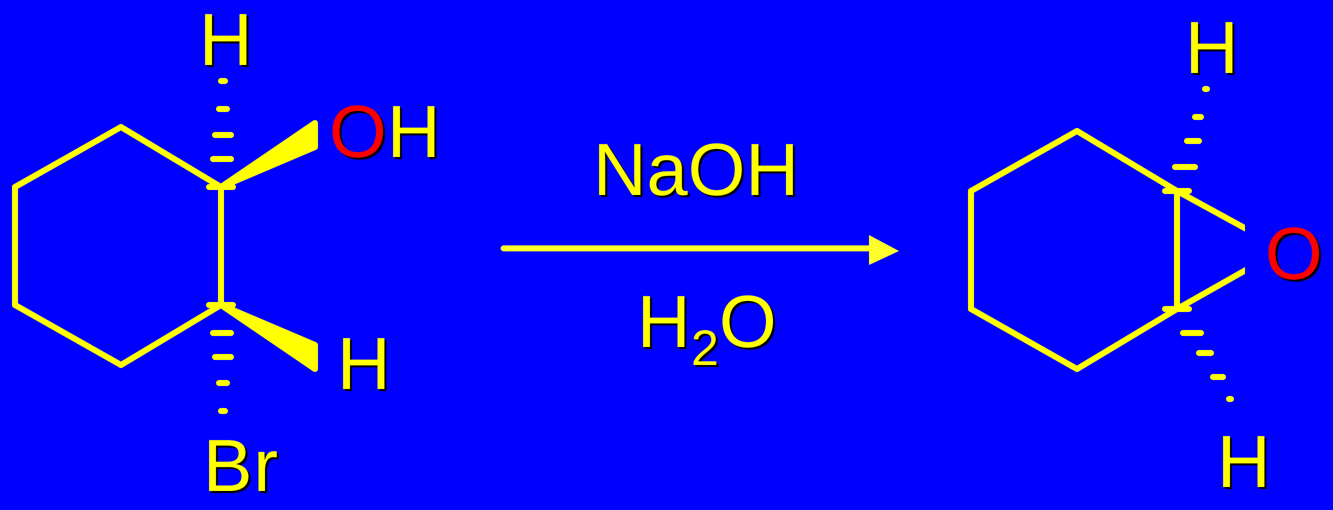
Conversion of Vicinal Halohydrins to Epoxides

Example



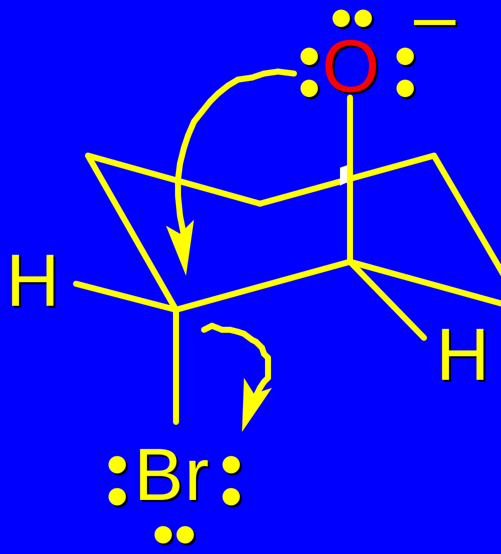
(81%)

Example

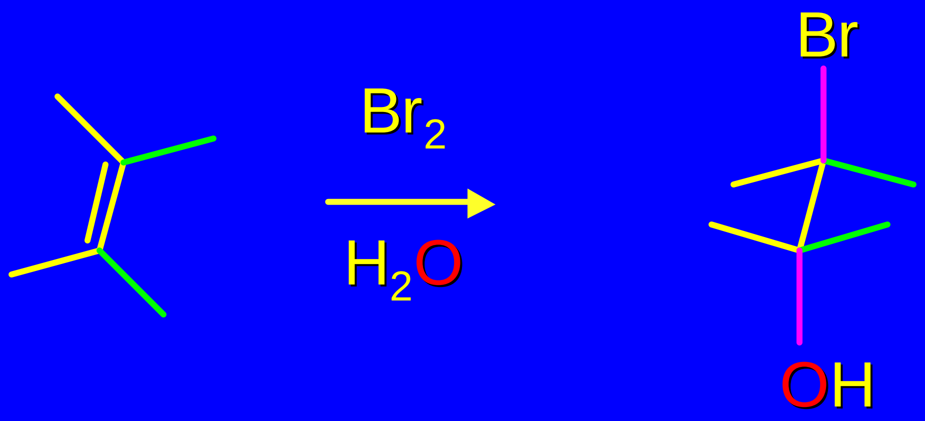


(81%)

via:

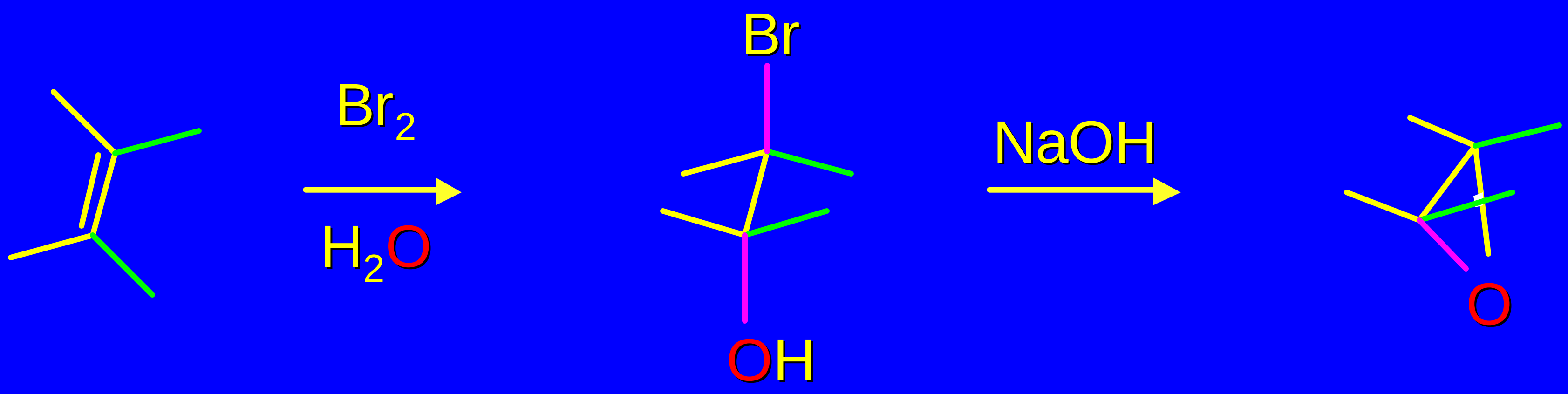


Epoxidation via Vicinal Halohydrins



anti addition

Epoxidation via Vicinal Halohydrins

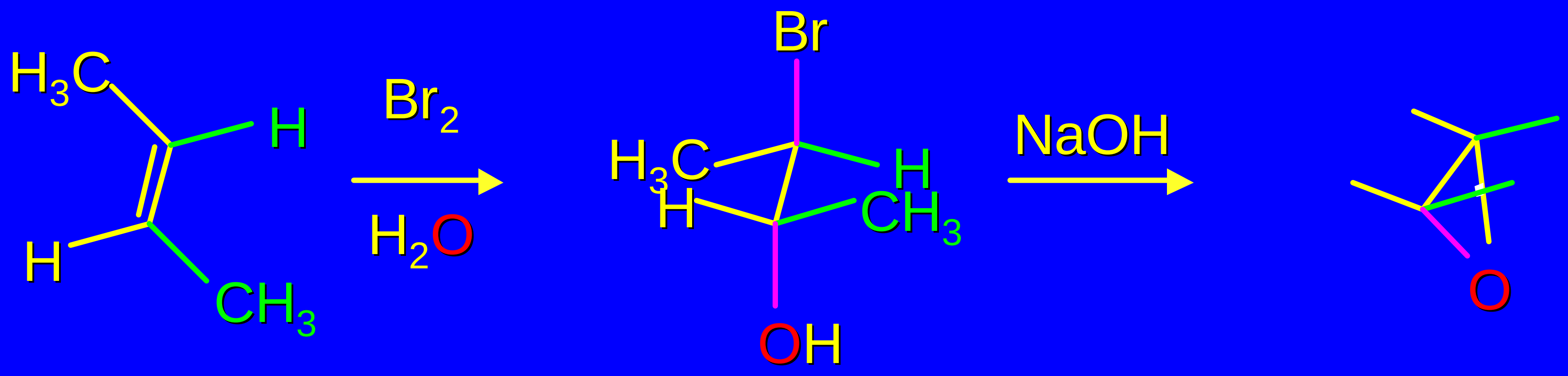


anti addition

inversion

corresponds to overall syn addition of oxygen to the double bond

Epoxidation via Vicinal Halohydrins

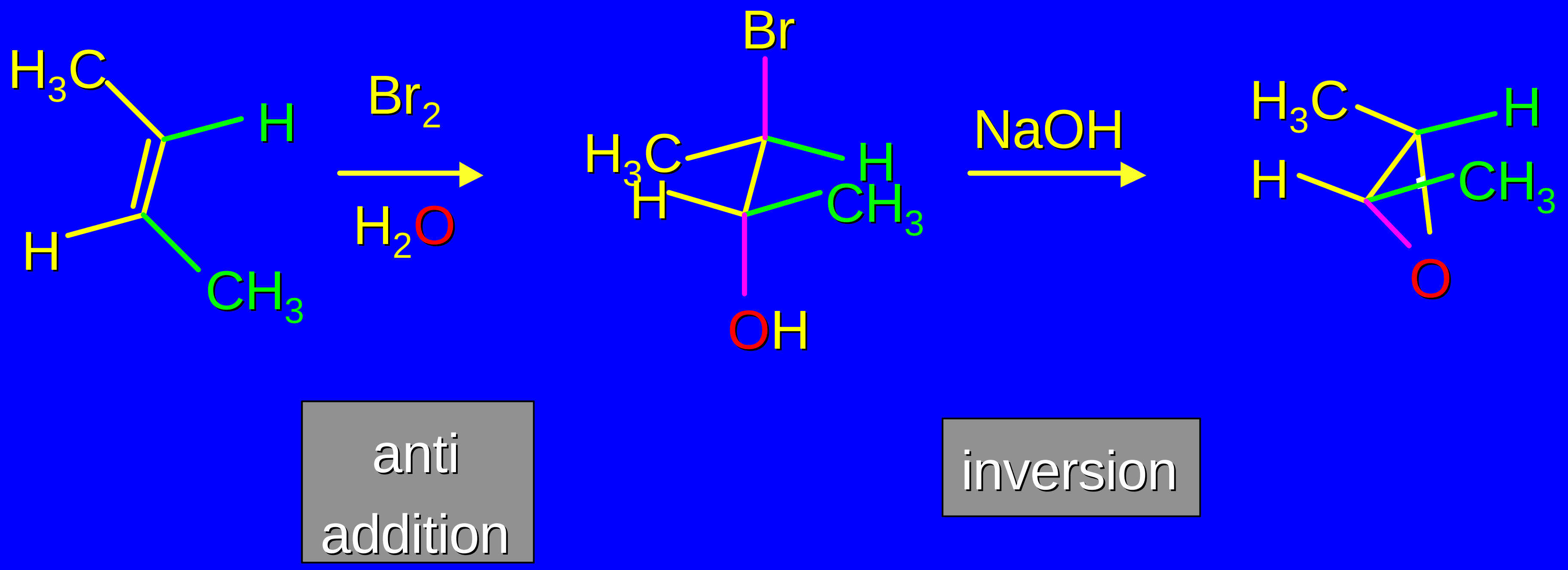


anti addition

inversion

corresponds to overall syn addition of oxygen to the double bond

Epoxidation via Vicinal Halohydrins



anti addition

inversion

corresponds to overall syn addition of oxygen to the double bond

16.11

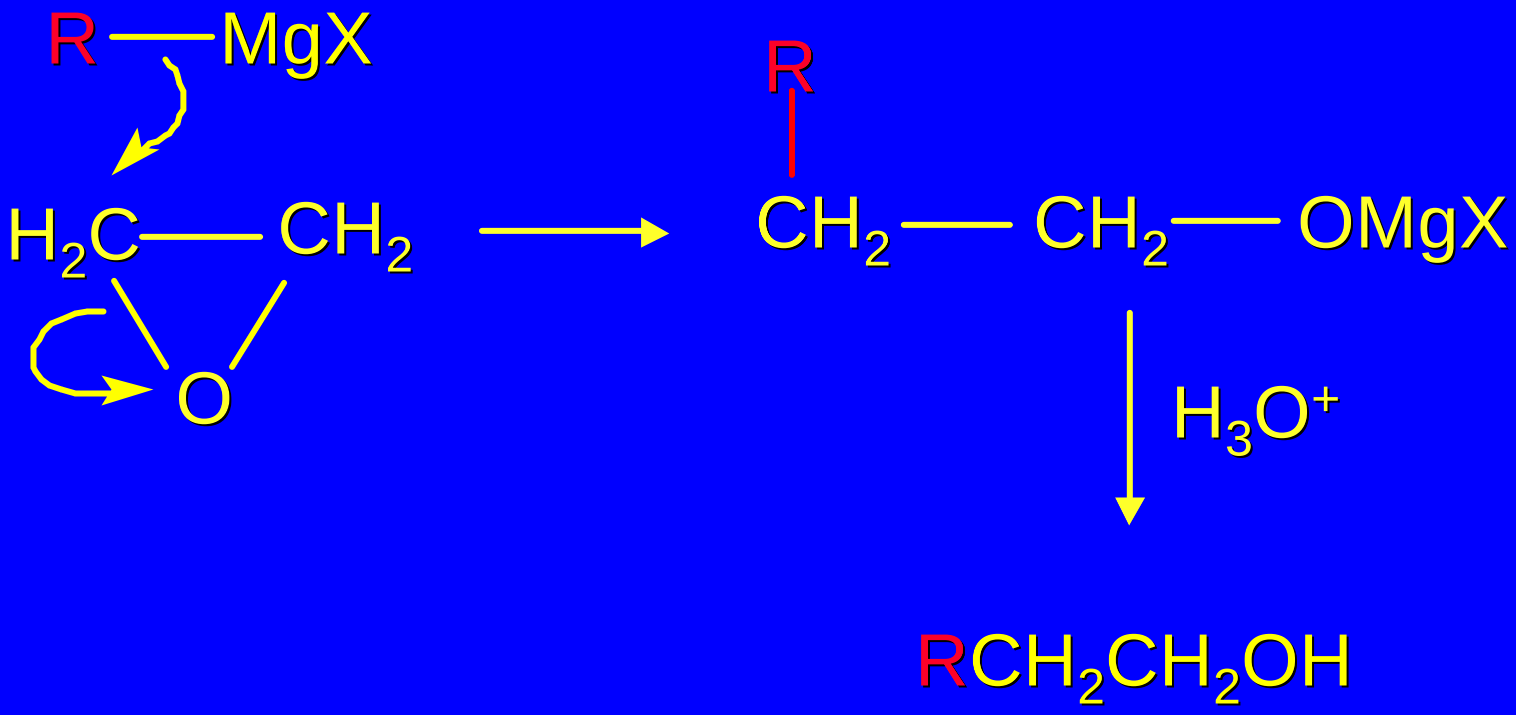
Reactions of Epoxides: A Review and a Preview

Reactions of Epoxides

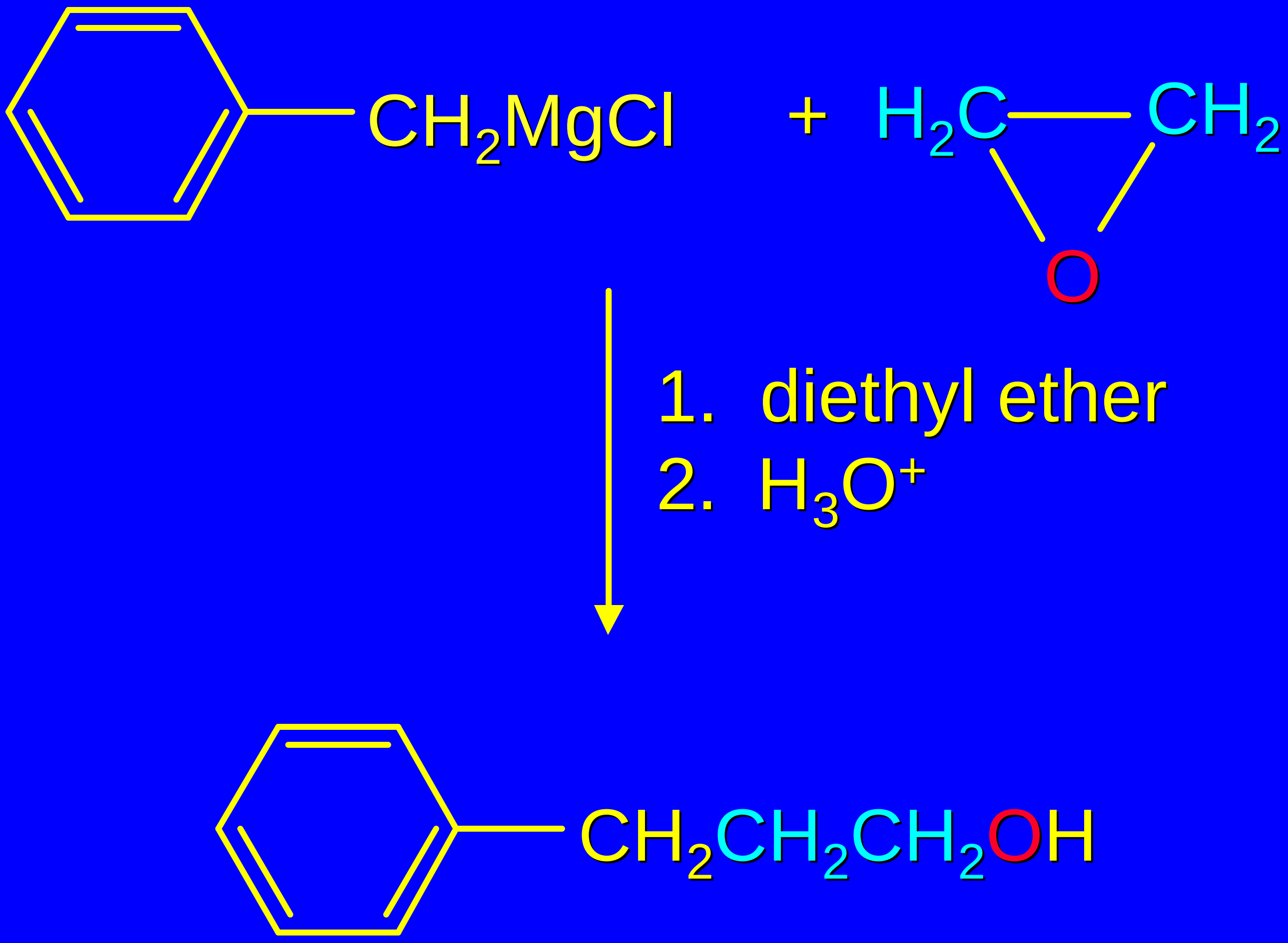
All reactions involve nucleophilic attack at carbon and lead to opening of the ring.

An example is the reaction of ethylene oxide with a Grignard reagent (discussed in Section 15.4 as a method for the synthesis of alcohols).

Reaction of Grignard Reagents with Epoxides



Example

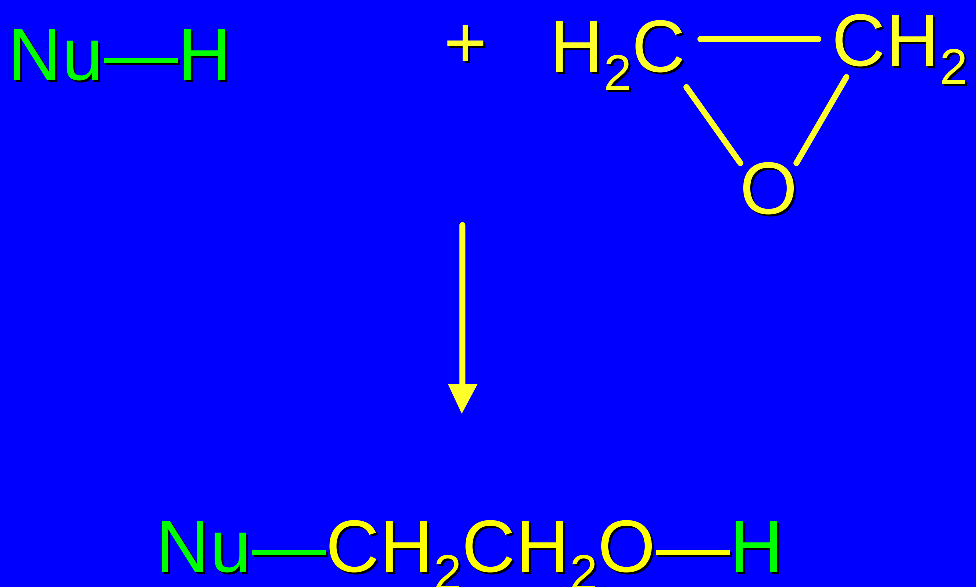

$C_6H_5CH_2MgCl$ + H_2C—CH_2 O
1. diethyl ether
2. H_3O^+
$C_6H_5CH_2CH_2CH_2OH$

(71%)

In general...

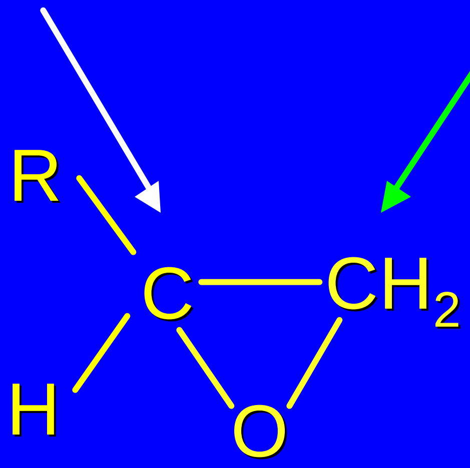
Reactions of epoxides involve attack by a nucleophile and proceed with ring-opening.

For ethylene oxide:



In general...

For epoxides where the two carbons of the ring are differently substituted:



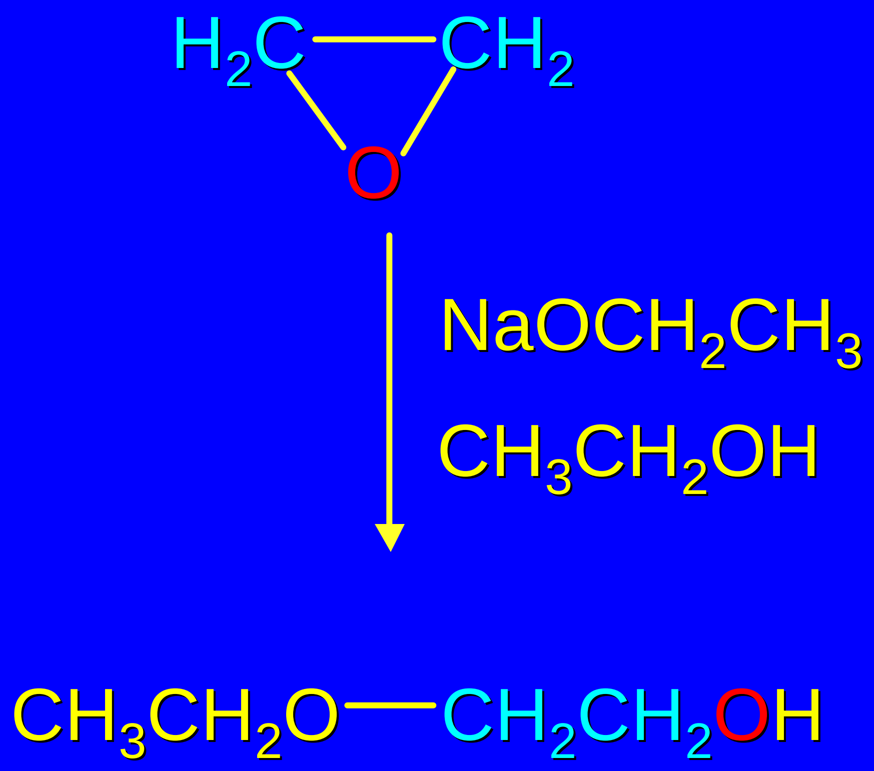
Nucleophiles attack here when the reaction is catalyzed by acids:

Anionic nucleophiles attack here:

16.12

Nucleophilic Ring-Opening Reactions of Epoxides

Example



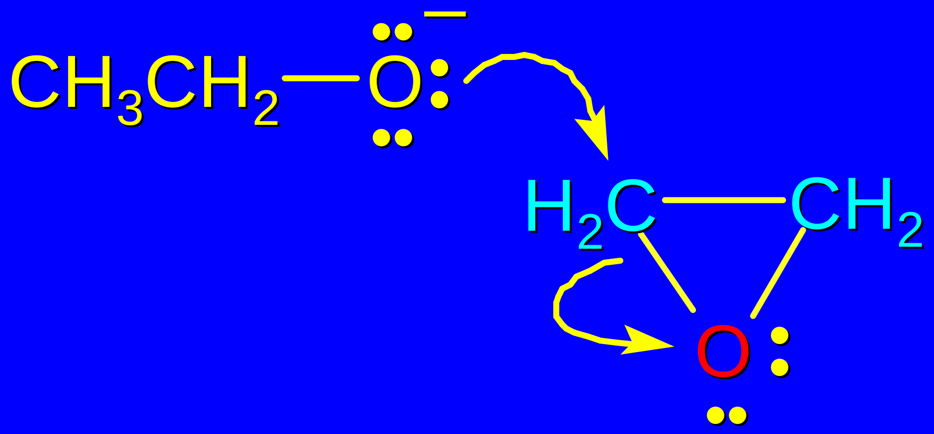
$NaOCH_2CH_3$

CH_3CH_2OH

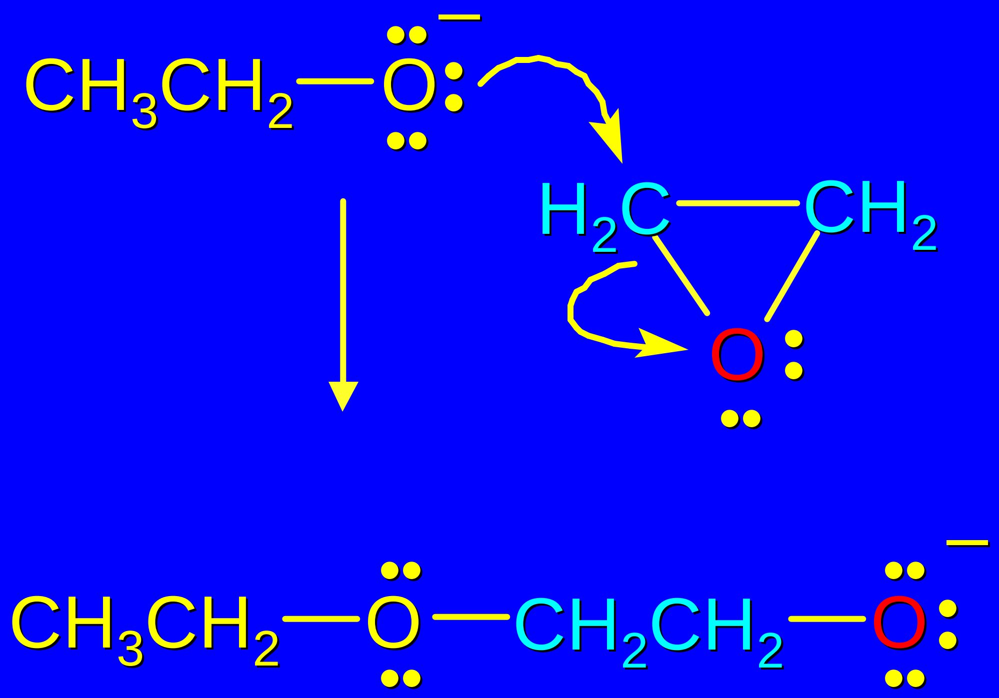
$CH_3CH_2O—CH_2CH_2OH$

(50%)

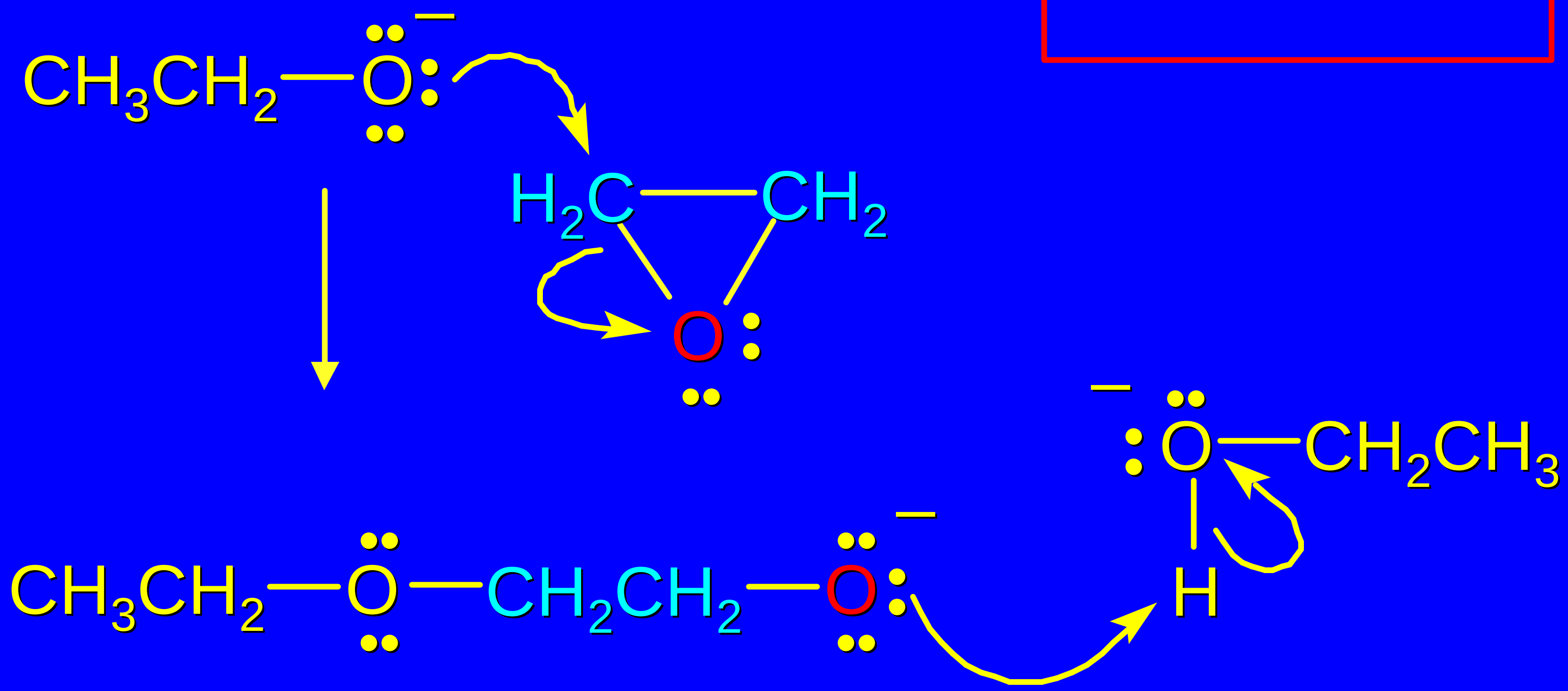
Mechanism



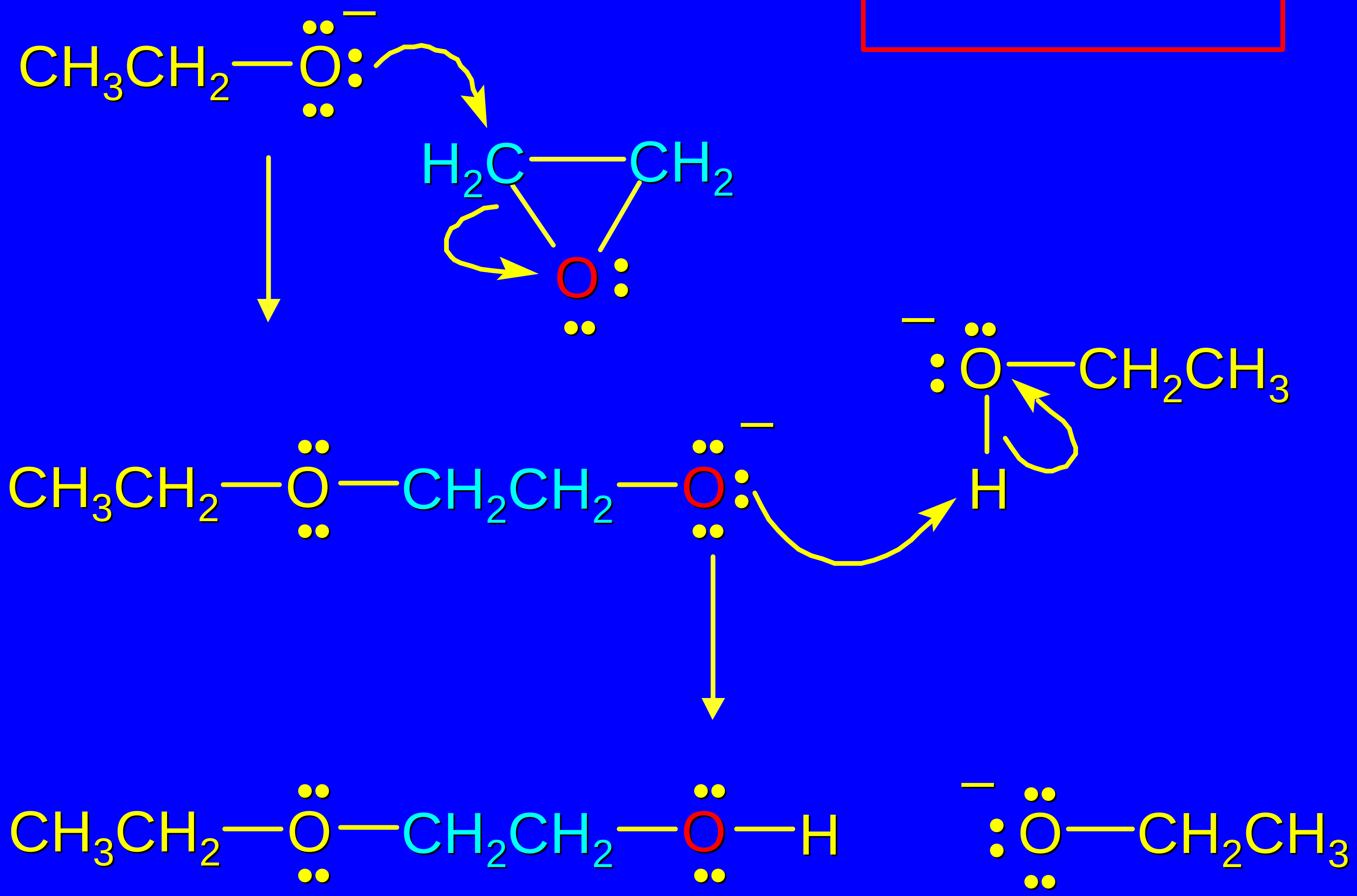
Mechanism



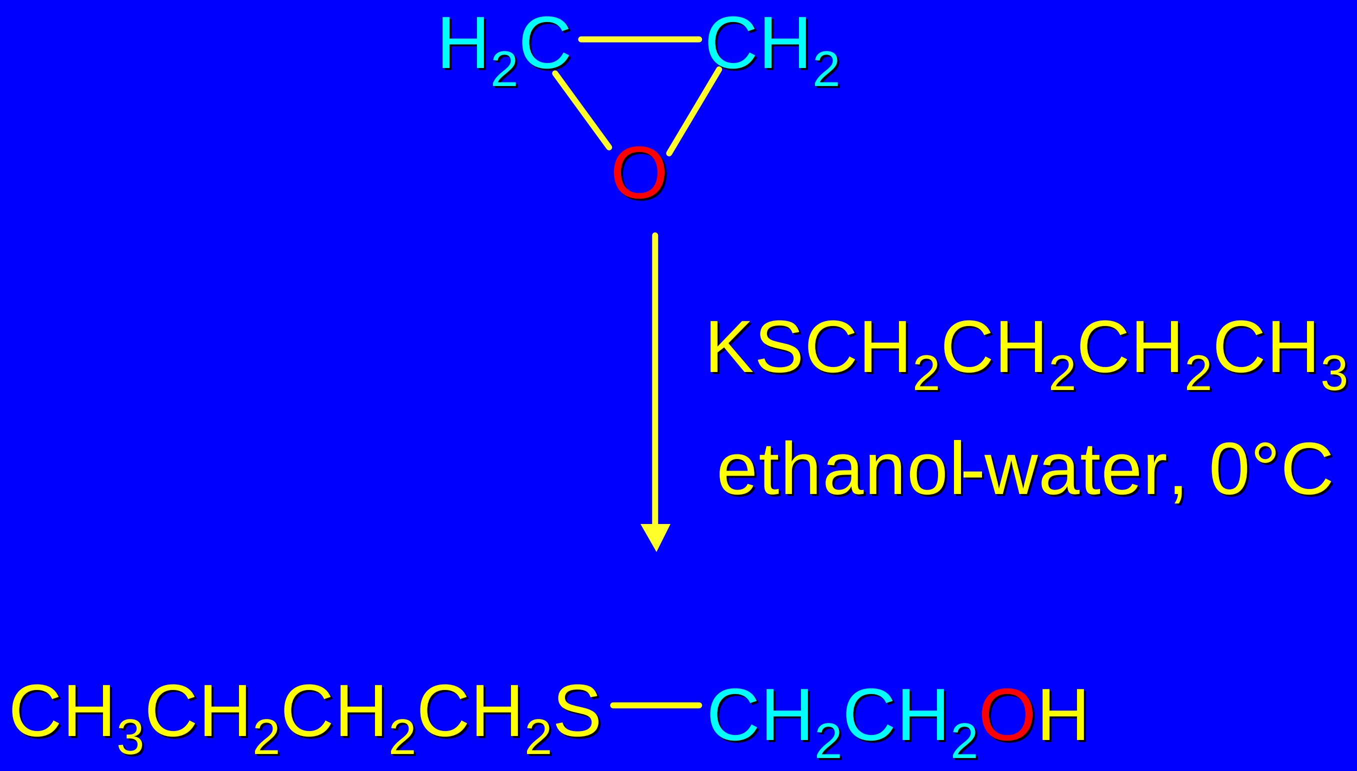
Mechanism



Mechanism


$CH_3CH_2-\ddot{O}:^-$
H_2C-CH_2
O
$CH_3CH_2-O-CH_2CH_2-O:^-$
$^-:O-CH_2CH_3$
H
$CH_3CH_2-O-CH_2CH_2-O-H$
$^-:O-CH_2CH_3$

Example



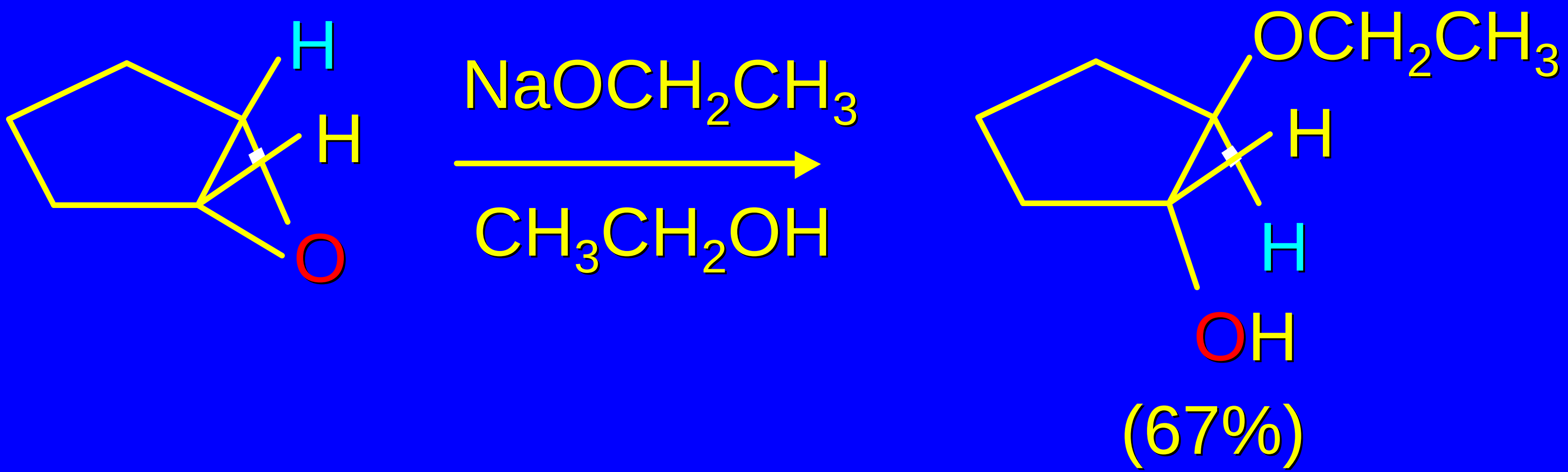
$KSCH_2CH_2CH_2CH_3$

ethanol-water, 0°C

$CH_3CH_2CH_2CH_2S-CH_2CH_2OH$

(99%)

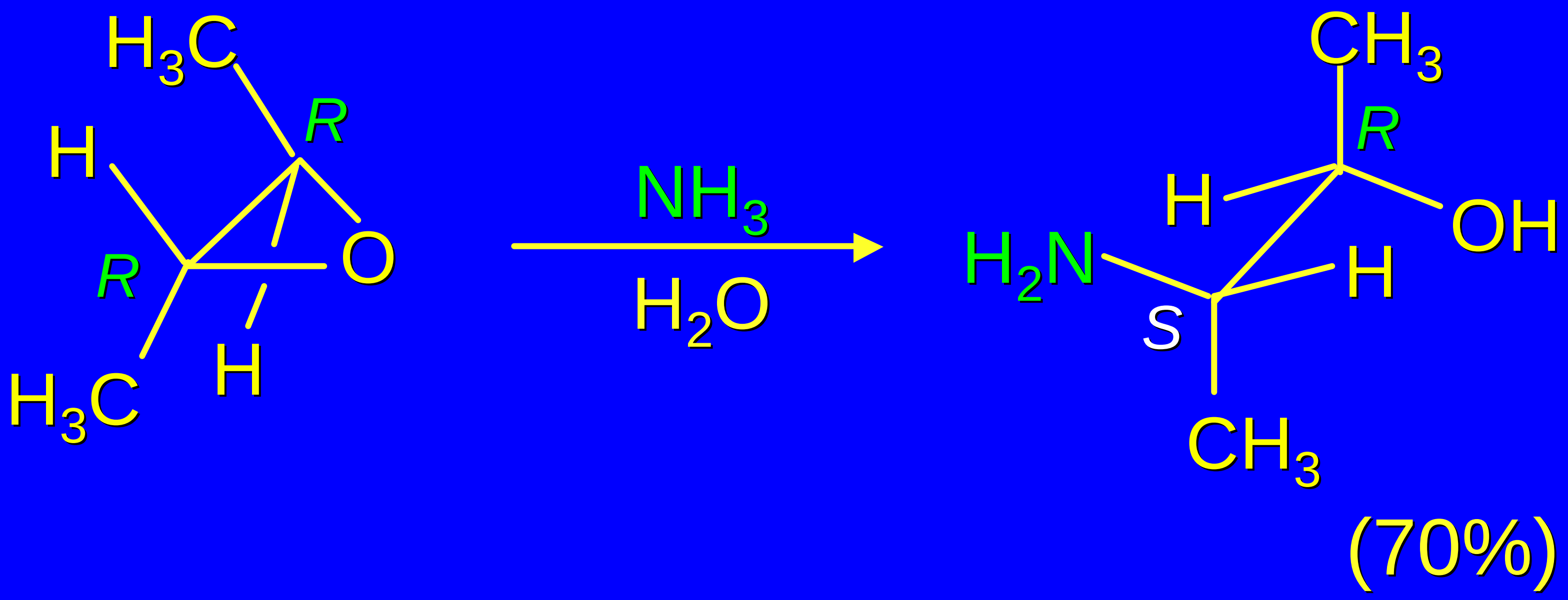
Stereochemistry



Inversion of configuration at carbon being attacked by nucleophile

Suggests S_N2-like transition state

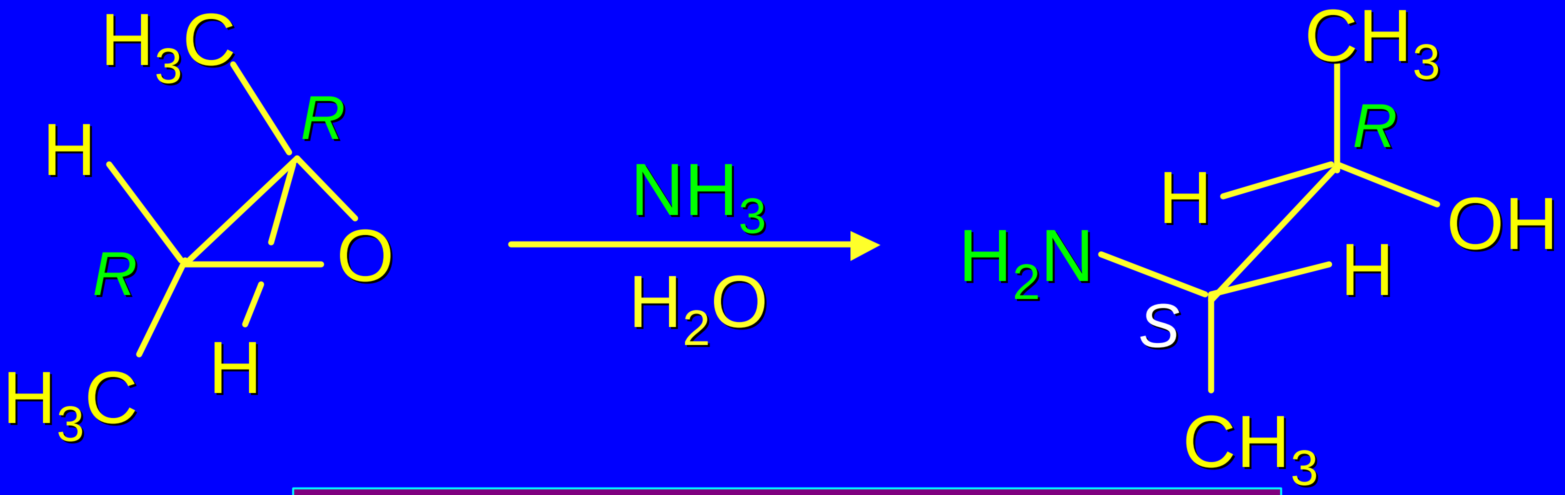
Stereochemistry



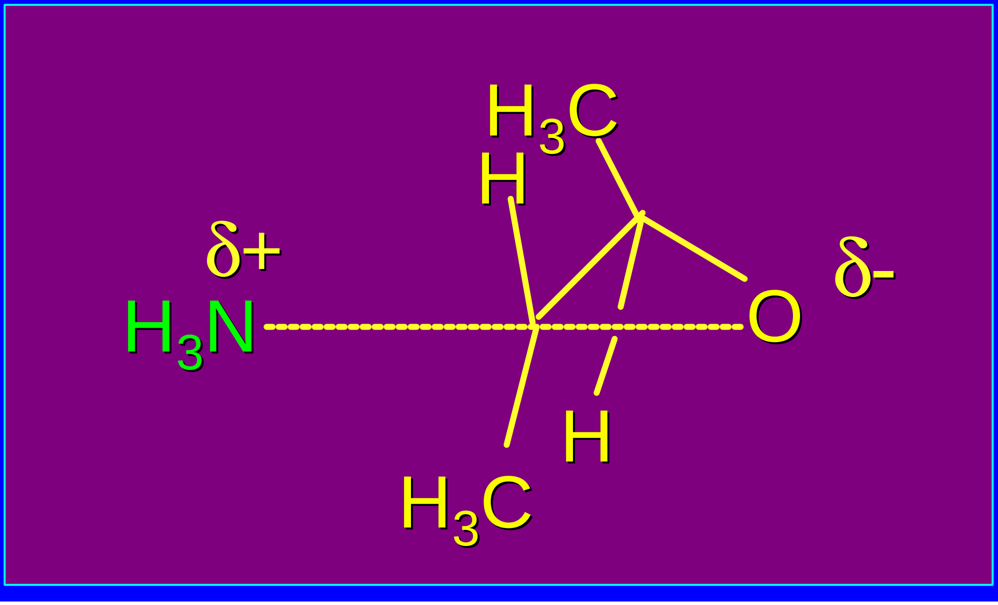
Inversion of configuration at carbon being attacked by nucleophile

Suggests S_N2-like transition state

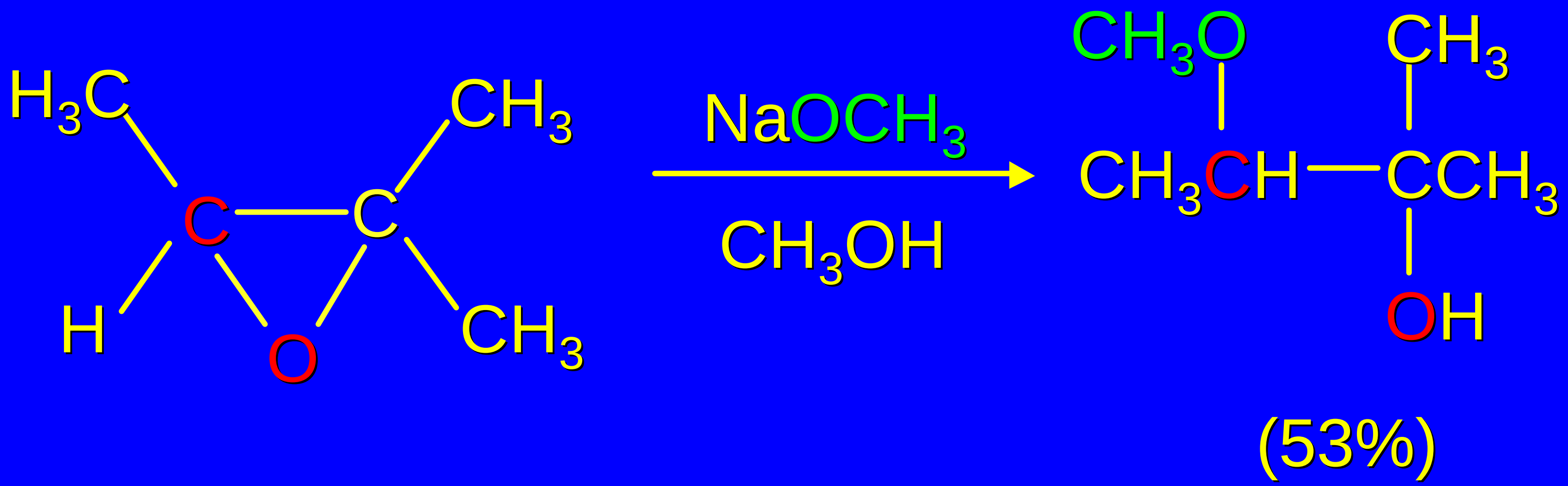
Stereochemistry



(70%)

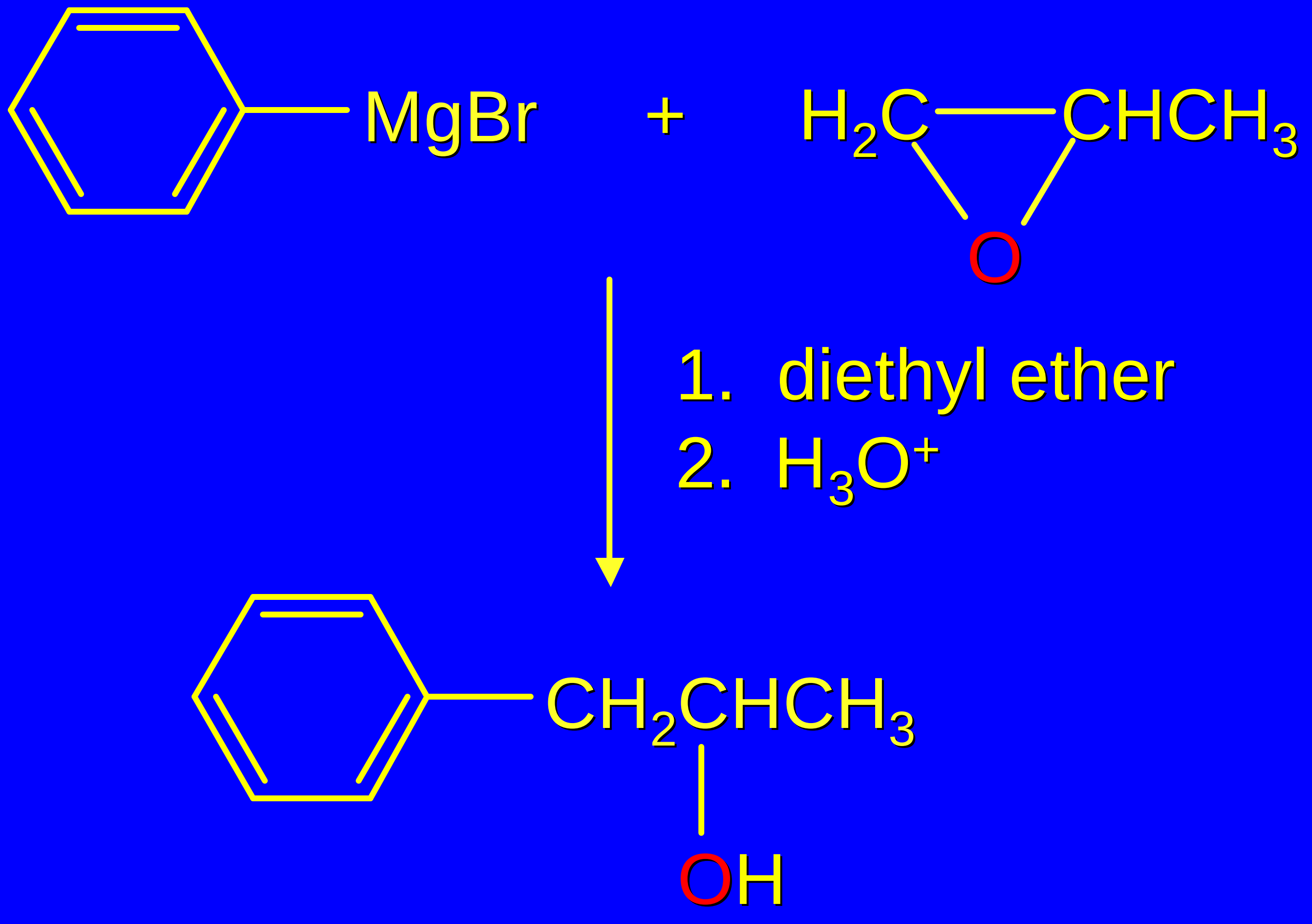


Anionic nucleophile attacks less-crowded carbon



consistent with S_N2-like transition state

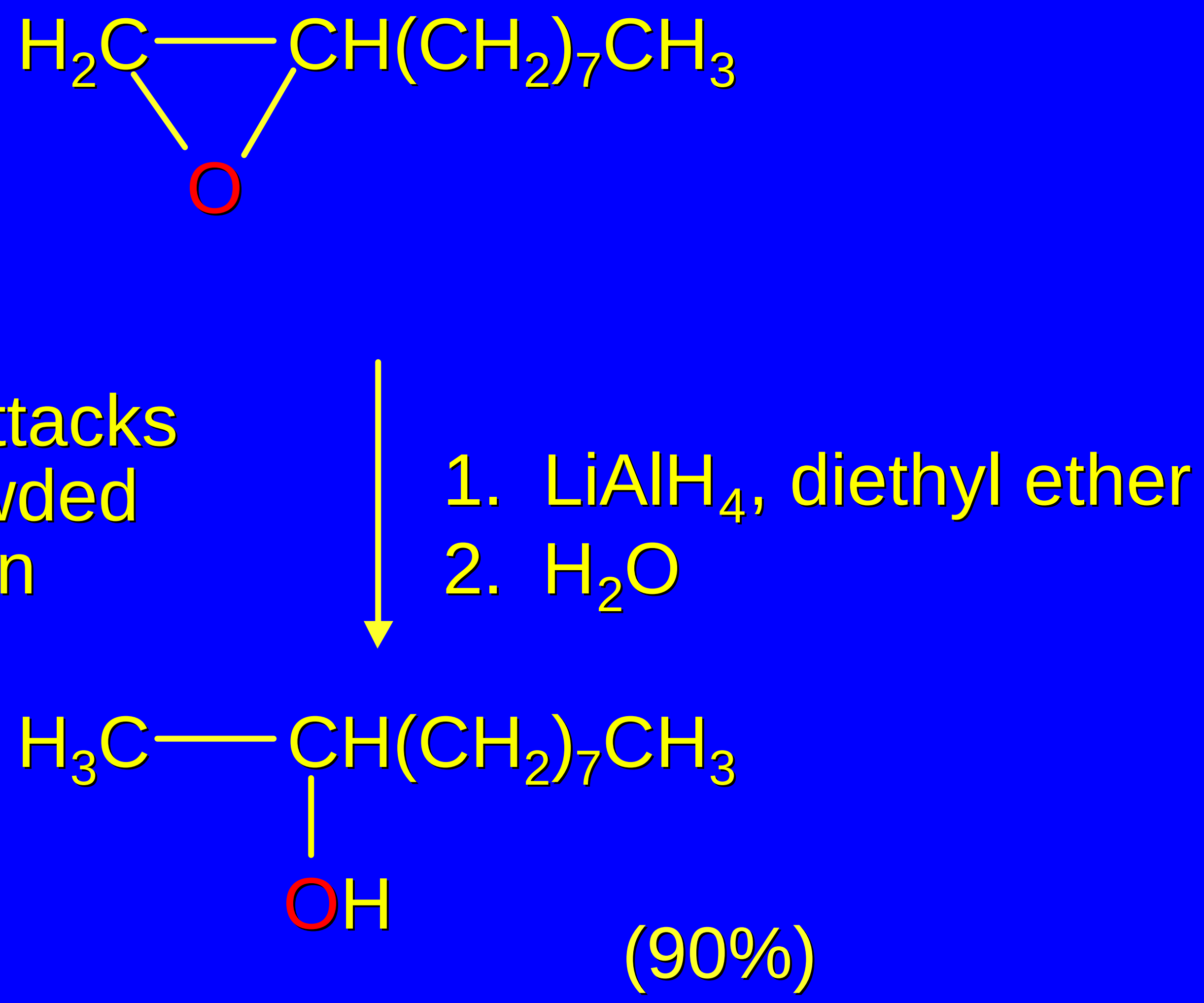
Anionic nucleophile attacks less-crowded carbon



1. diethyl ether
2. H_3O^+

(60%)

Lithium aluminum hydride reduces epoxides



Hydride attacks
less-crowded
carbon

1. $LiAlH_4$, diethyl ether
2. H_2O

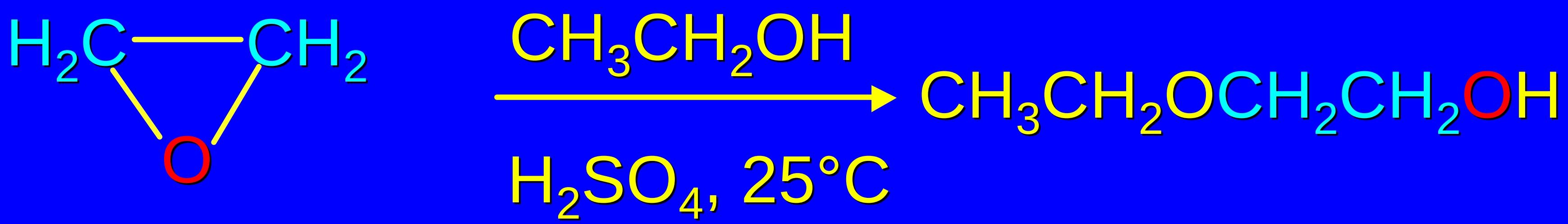
$H_3C{-}CH(OH)(CH_2)_7CH_3$

(90%)

16.13

Acid-Catalyzed Ring-Opening Reactions of Epoxides

Example

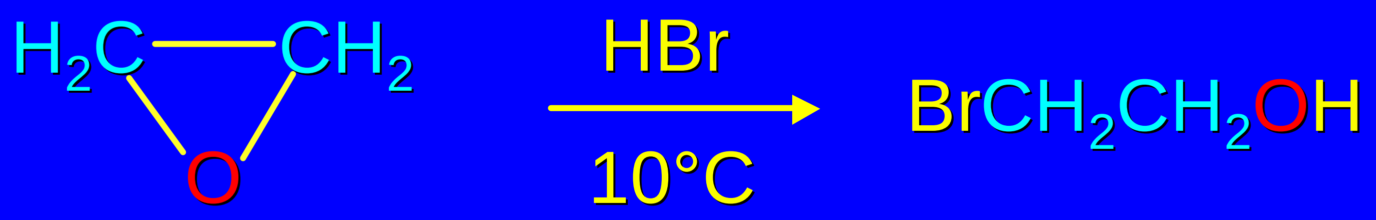


$$H_2C\text{—}CH_2\ (O) \xrightarrow[H_2SO_4,\ 25°C]{CH_3CH_2OH} CH_3CH_2OCH_2CH_2OH$$

(87-92%)

$CH_3CH_2OCH_2CH_2OCH_2CH_3$ formed only on heating and/or longer reaction times

Example

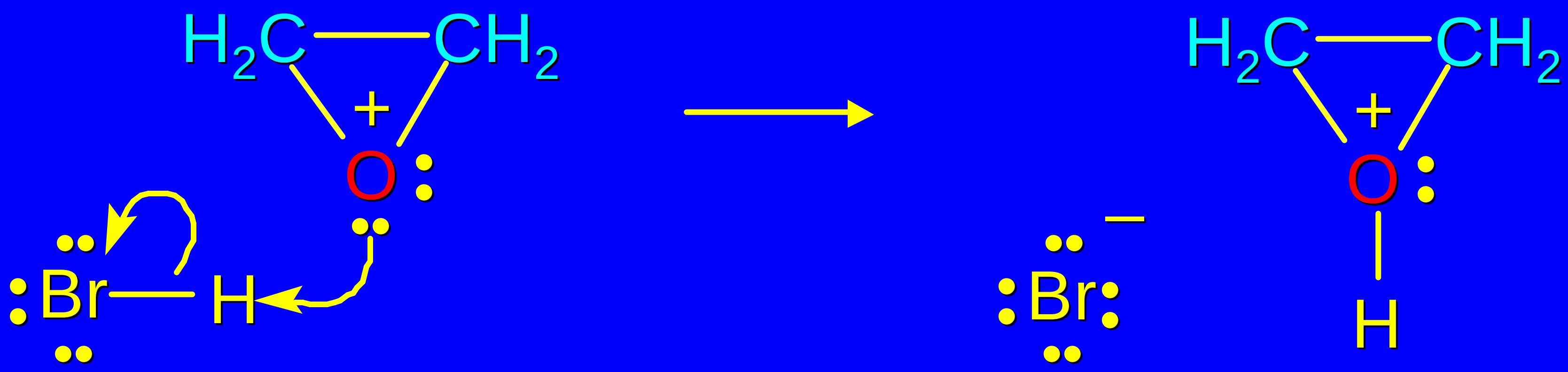


H_2C-CH_2 (O) $\xrightarrow[10°C]{HBr}$ $BrCH_2CH_2OH$

(87-92%)

$BrCH_2CH_2Br$ formed only on heating and/or longer reaction times

Mechanism



Mechanism

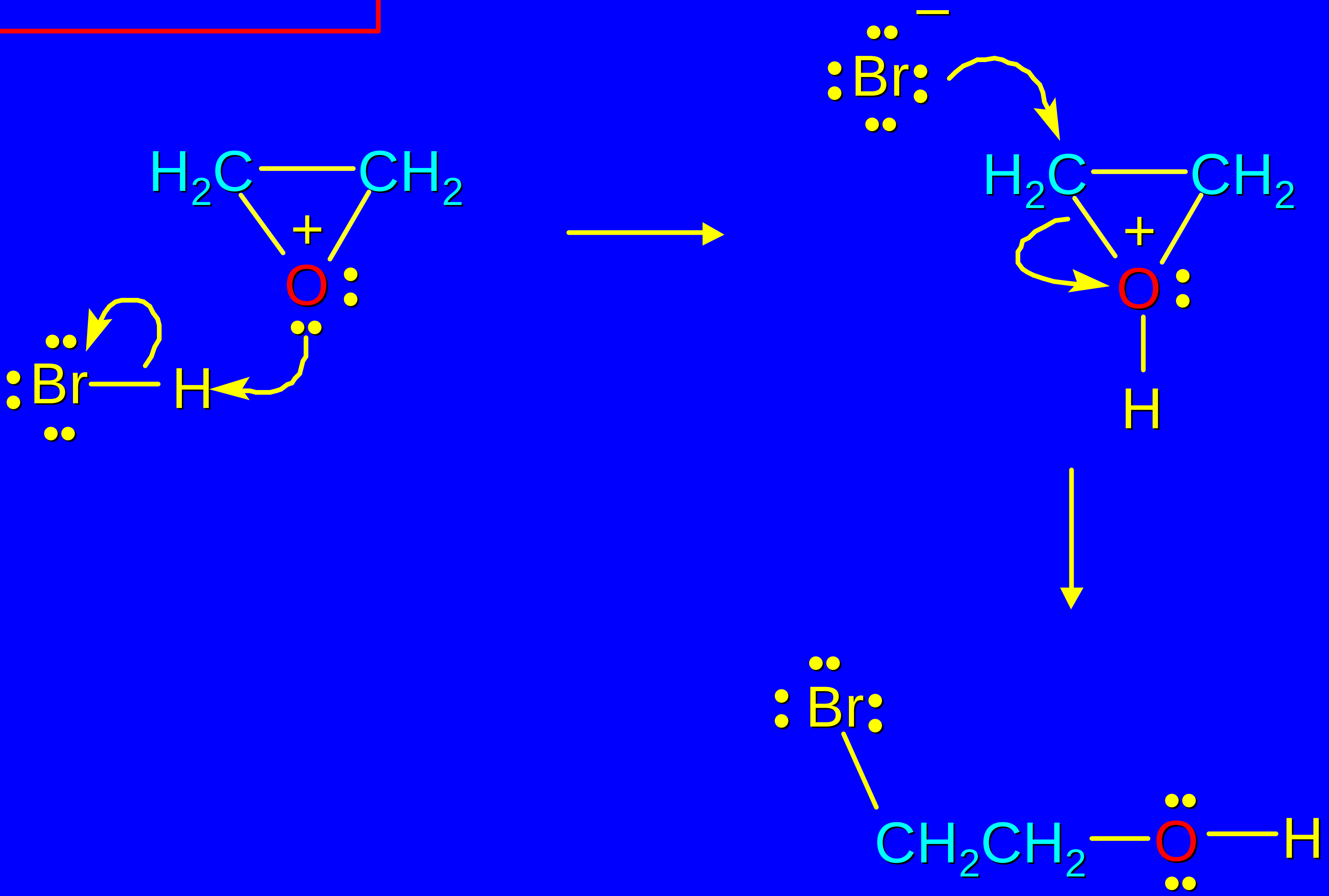


Figure 16.6
Acid-Catalyzed Hydrolysis of Ethylene Oxide

Step 1

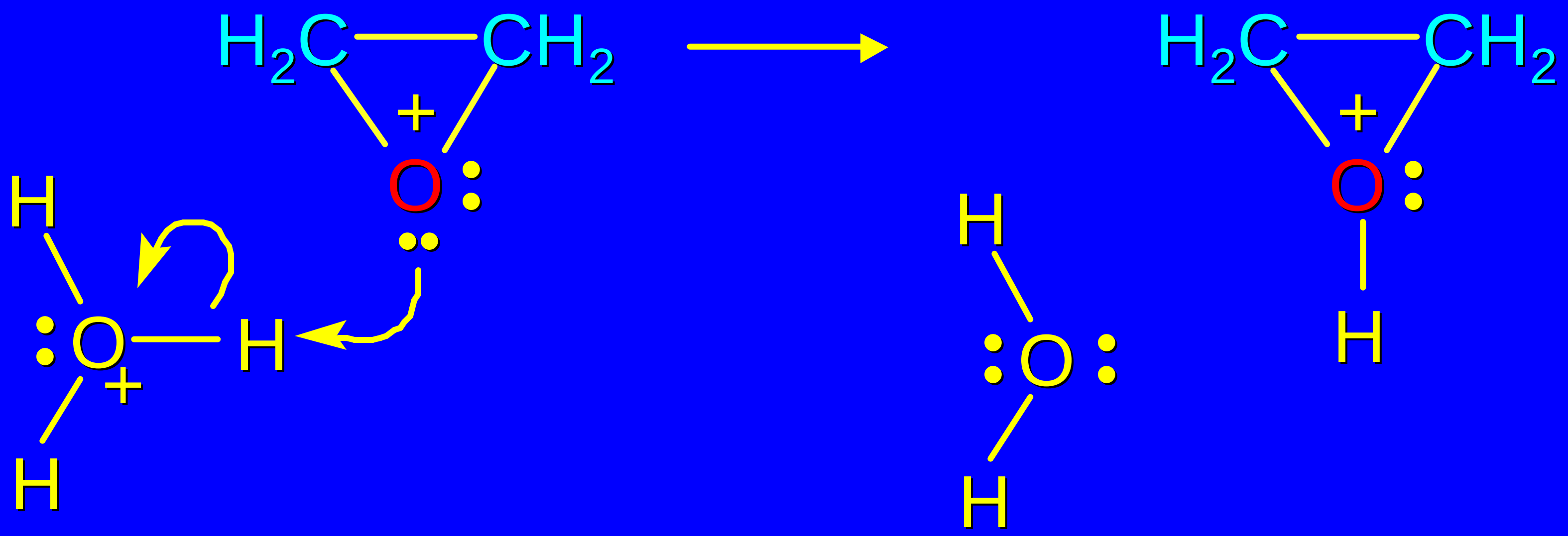


Figure 16.6
Acid-Catalyzed Hydrolysis of Ethylene Oxide

Step 2

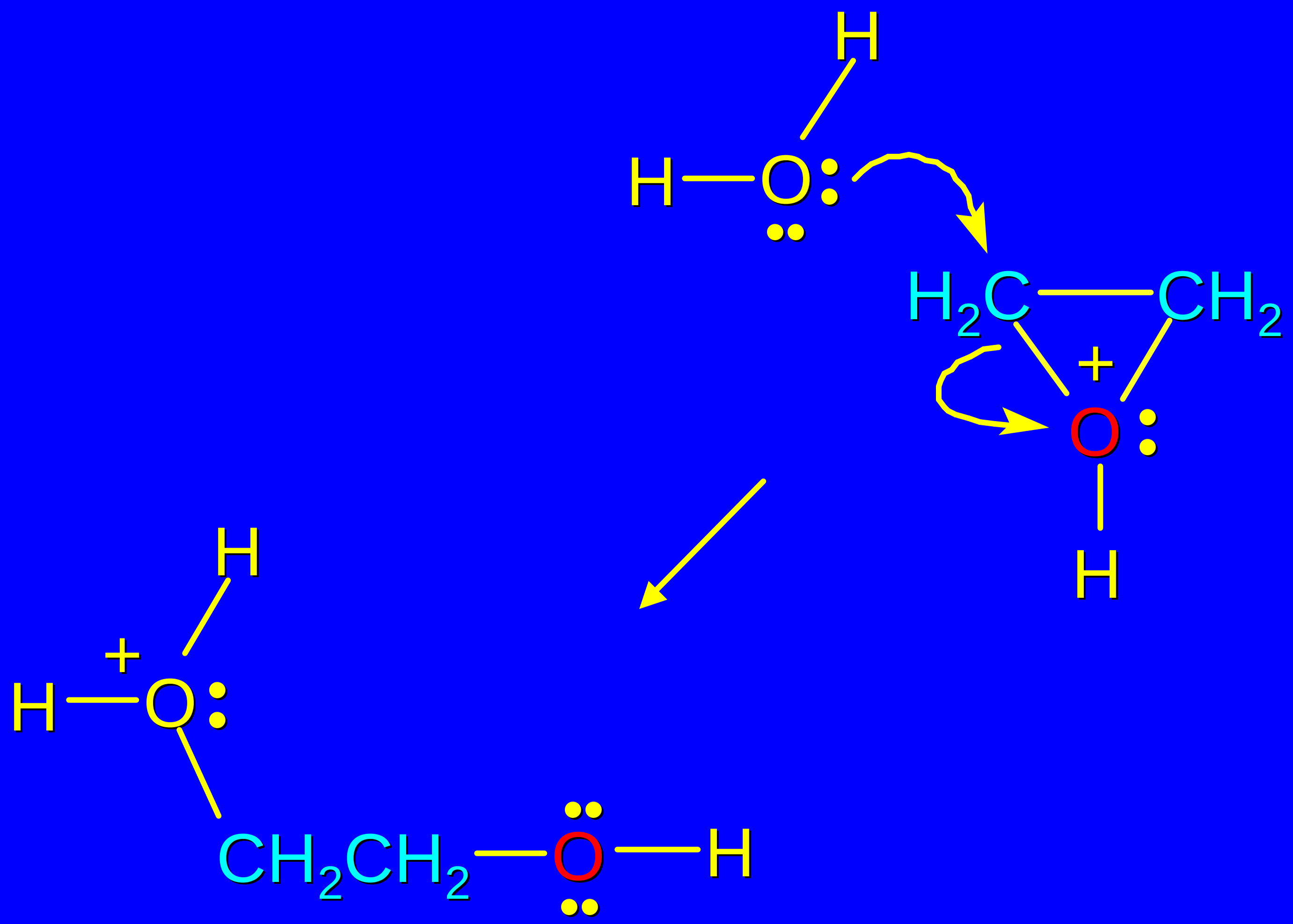
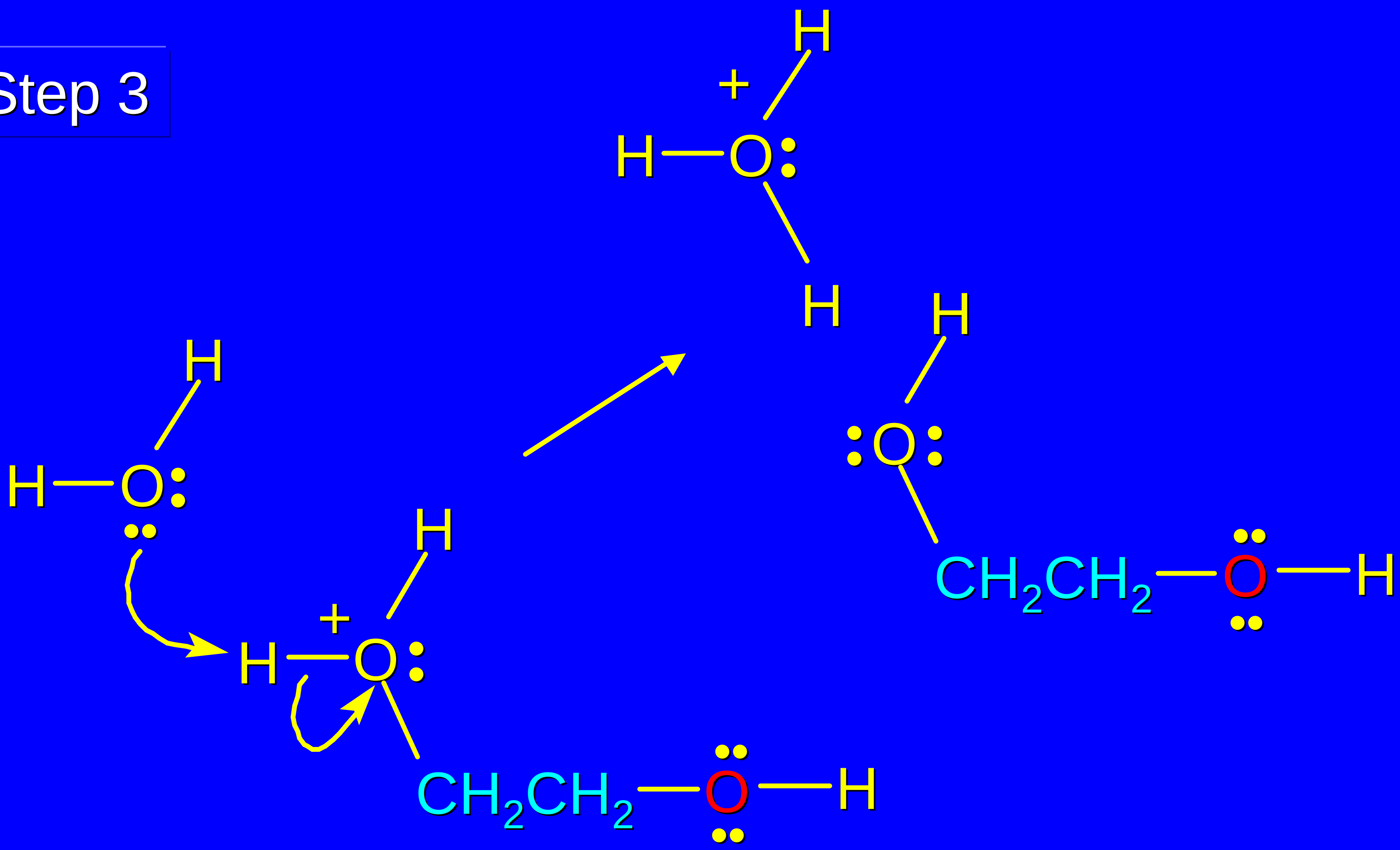


Figure 16.6

Acid-Catalyzed Hydrolysis of Ethylene Oxide

Step 3



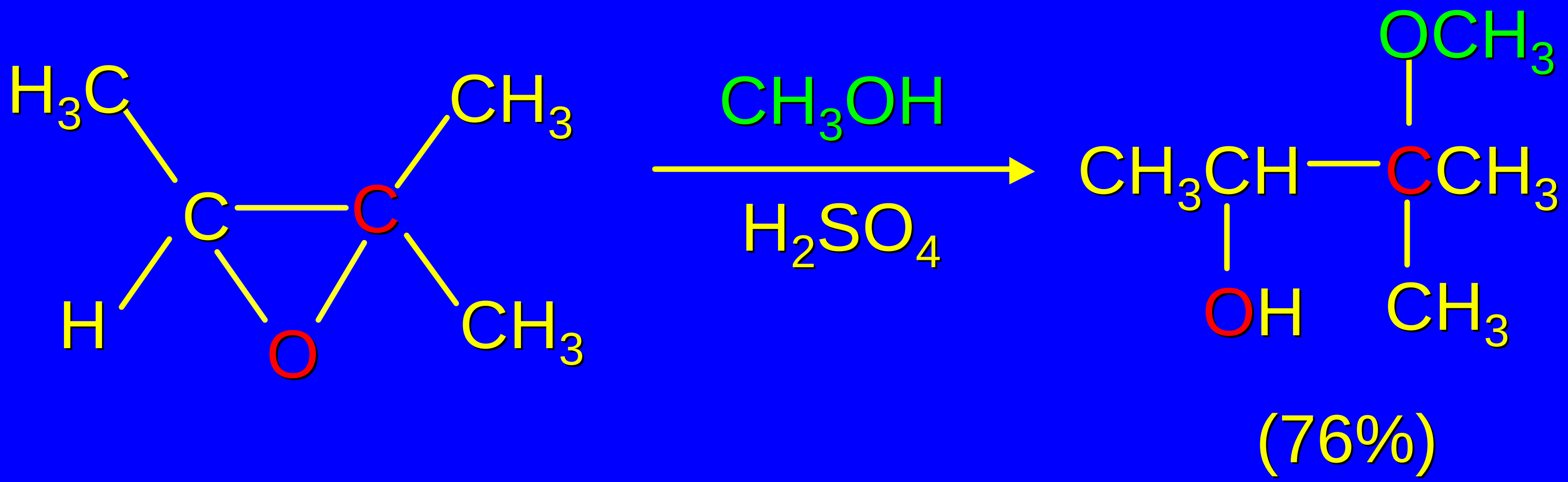
Acid-Catalyzed Ring Opening of Epoxides

Characteristics:

nucleophile attacks more substituted carbon of protonated epoxide

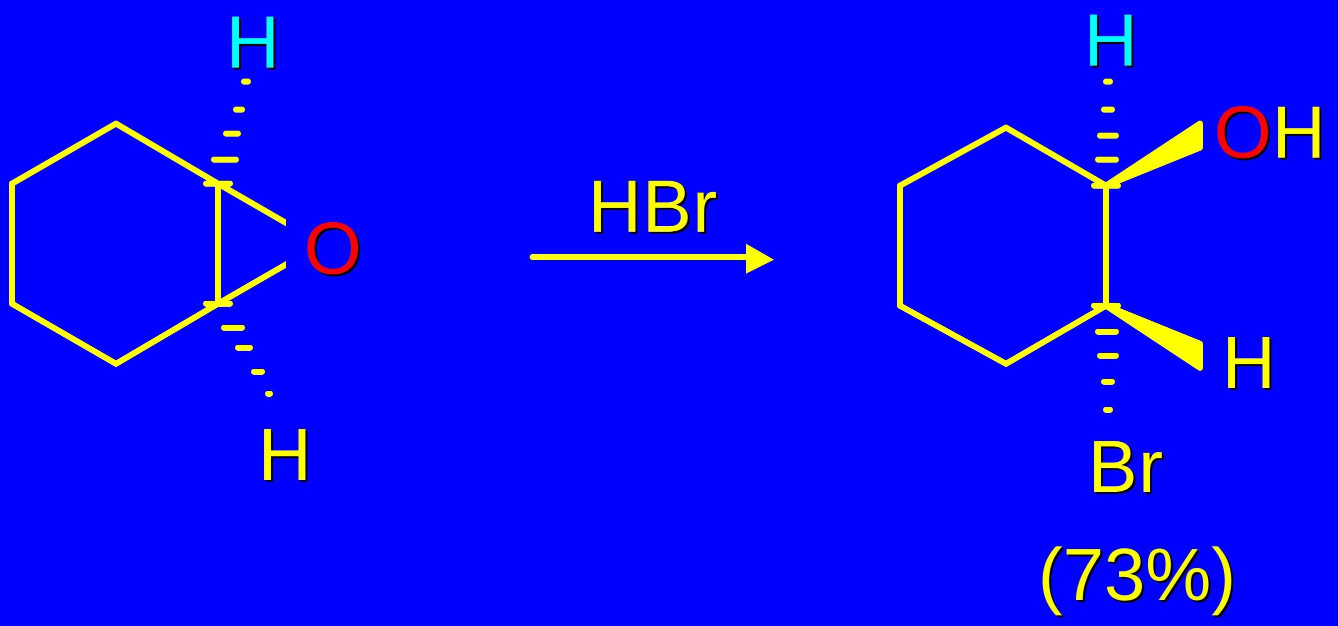
inversion of configuration at site of nucleophilic attack

Nucleophile attacks more-substituted carbon



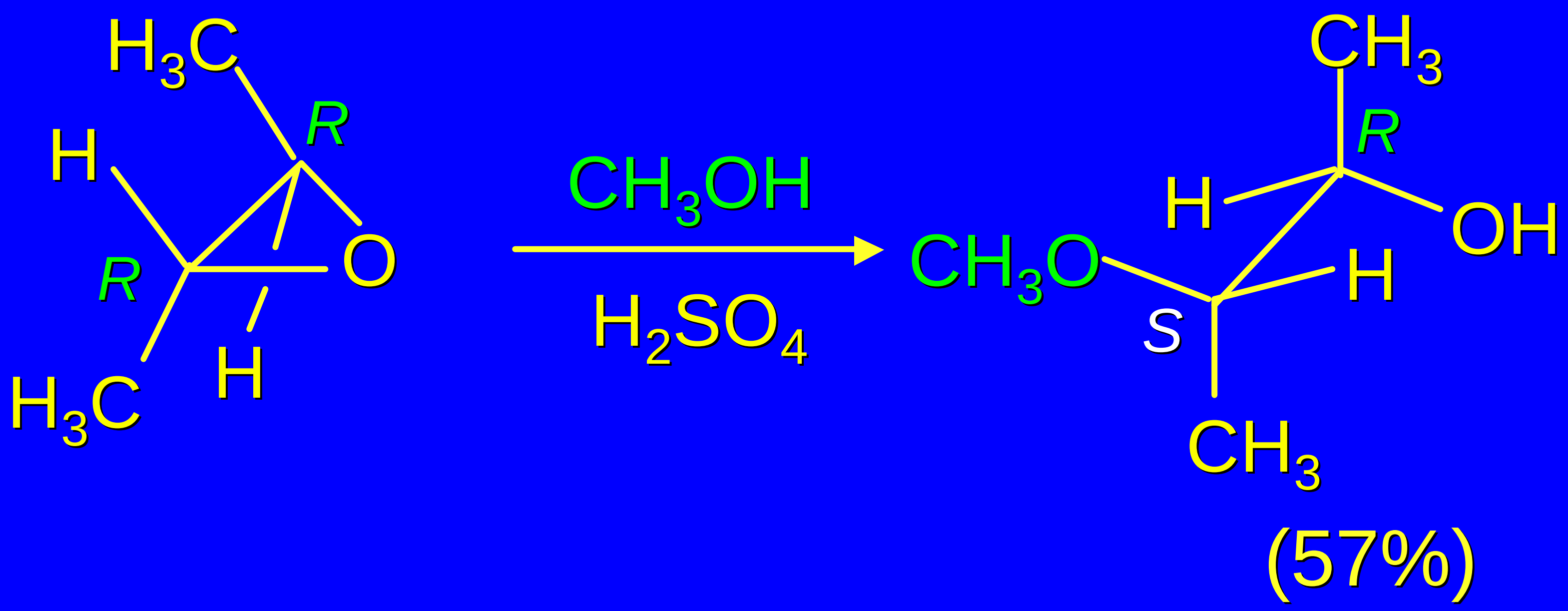
consistent with carbocation character at transition state

Stereochemistry



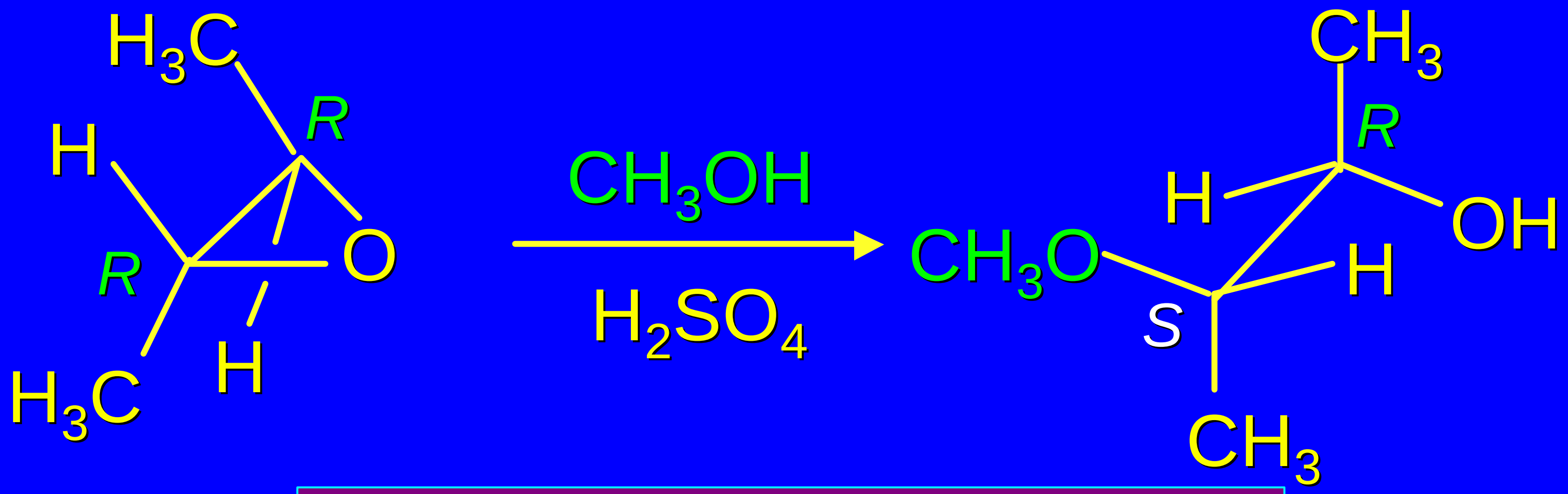
Inversion of configuration at carbon being attacked by nucleophile

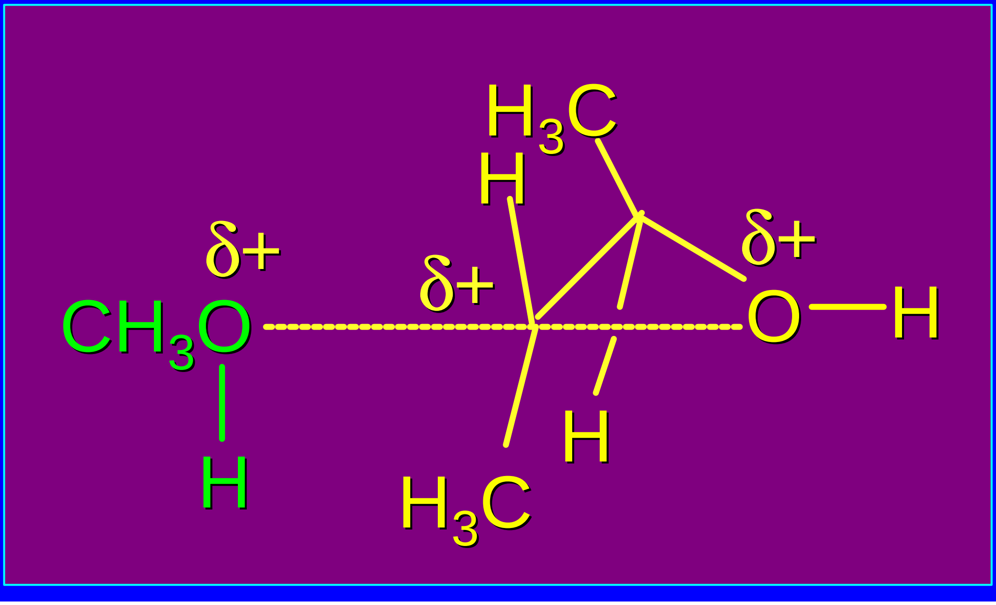
Stereochemistry



Inversion of configuration at carbon being attacked by nucleophile

Stereochemistry





anti-Hydroxylation of Alkenes