Chapter 9

Reactions of Alcohols, Ethers, Epoxides, Amines, and Thiols

Paula Yurkanis Bruice
University of California, Santa Barbara

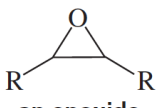
More About the Families in Group III

Group III

R—X (X = F, Cl, Br, I)
an alkyl halide

R—OH
an alcohol

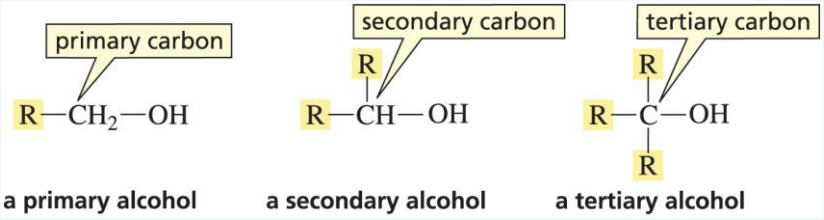
R—OR
an ether



an epoxide

The families in Group III all have an electronegative atom or group that is attached to an sp^3 carbon.

Classification of Alcohols



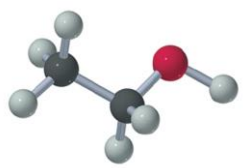
Primary alcohol = OH is on a primary carbon.
Secondary alcohol = OH is on a secondary carbon.
Tertiary alcohol = OH in on a tertiary carbon.

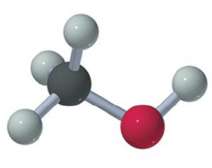
Common Names of Alcohols

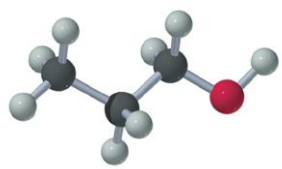
CH_3CH_2OH
ethyl alcohol

$CH_3CH_2CH_2OH$
propyl alcohol

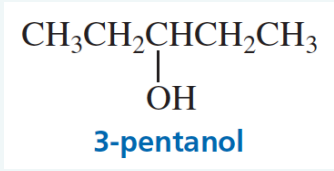
$CH_3CHOHCH_3$
isopropyl alcohol


ethyl alcohol


methyl alcohol

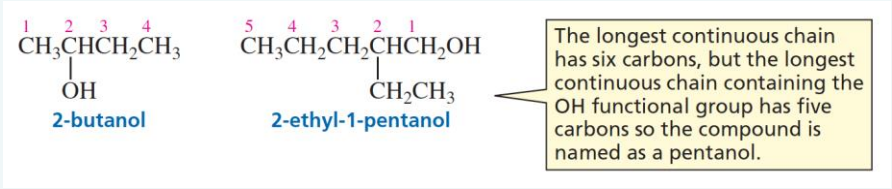

propyl alcohol

Systematic Names of Alcohols



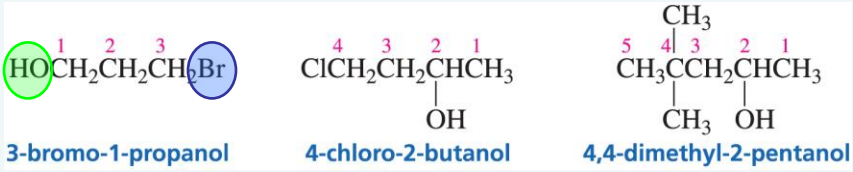
- The OH is the "functional group."
- Systematic nomenclature uses a suffix to denote a functional group.
- Alcohols are named by replacing the "e" at the end of the parent hydrocarbon with the suffix "ol."

Systematic Names of Alcohols



The parent hydrocarbon is the longest chain containing the functional group.

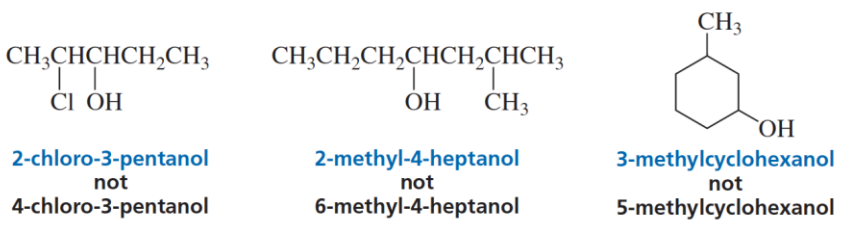
Systematic Names of Alcohols



3-bromo-1-propanol | 4-chloro-2-butanol | 4,4-dimethyl-2-pentanol

When there is both a functional group and a substituent, the functional group gets the lowest number.

Systematic Names of Alcohols

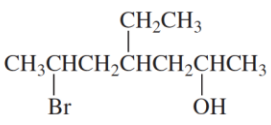


2-chloro-3-pentanol
not
4-chloro-3-pentanol

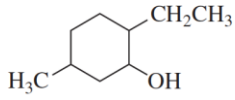
2-methyl-4-heptanol
not
6-methyl-4-heptanol

3-methylcyclohexanol
not
5-methylcyclohexanol

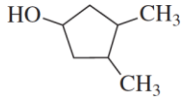
Systematic Names of Alcohols



6-bromo-4-ethyl-2-heptanol

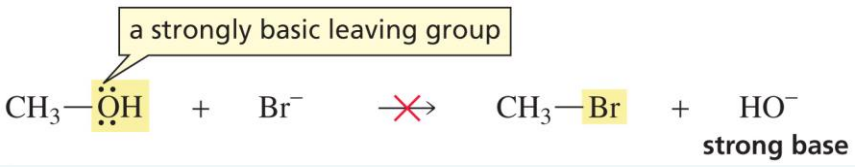


2-ethyl-5-methylcyclohexanol

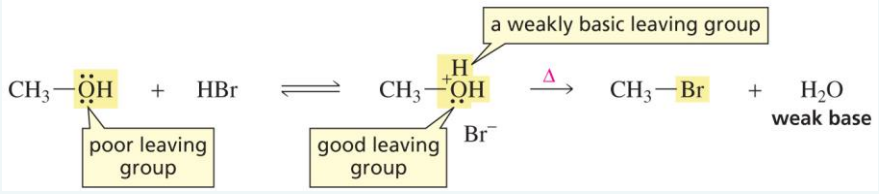


3,4-dimethylcyclopentanol

Strongly Basic Leaving Groups cannot be displaced



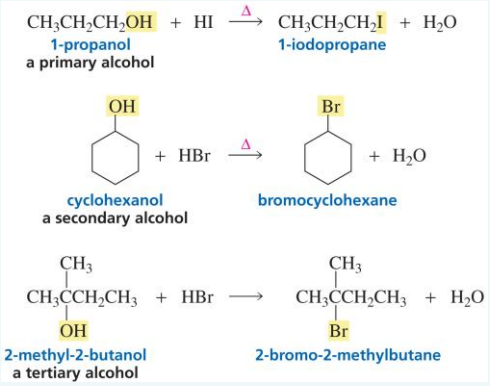
Acid converts the Poor Leaving Group into a Good Leaving Group



Alcohols have to be "activated" before they can react.

Only weakly basic nucleophiles can be used.
Strongly basic nucleophiles would react with the proton.

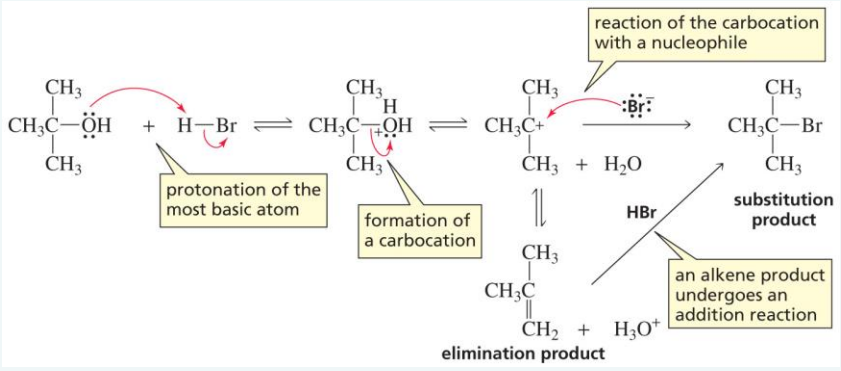
Converting Alcohols to Alkyl Halides



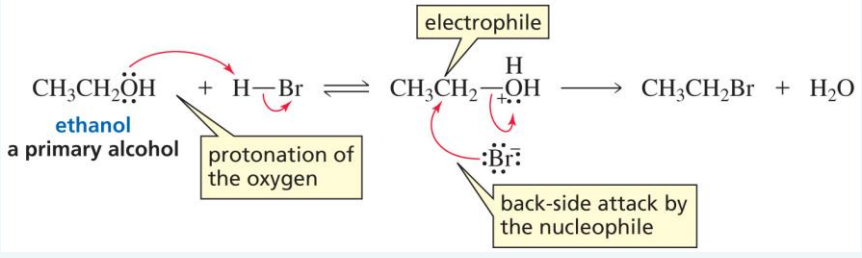
Primary and secondary alcohols require heat for this reaction.

Tertiary alcohols do not.

The Reactions of Secondary and Tertiary Alcohols with Hydrogen Halides are S_N1 Reactions

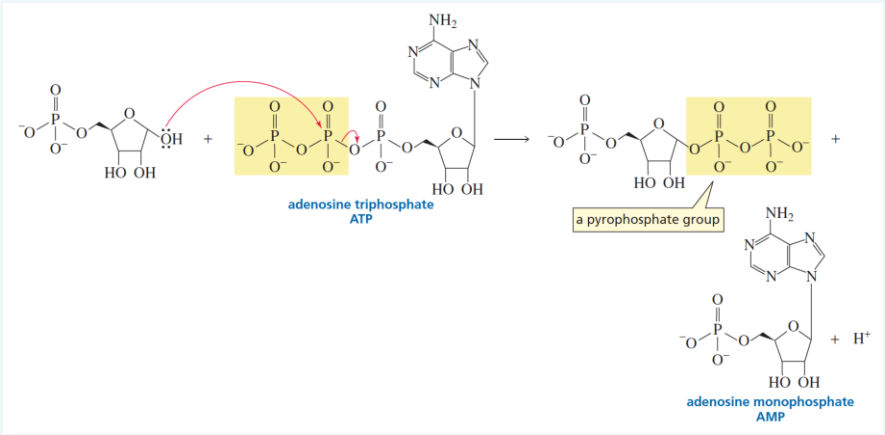


The Reactions of Primary Alcohols with Hydrogen Halides are S_N2 Reactions

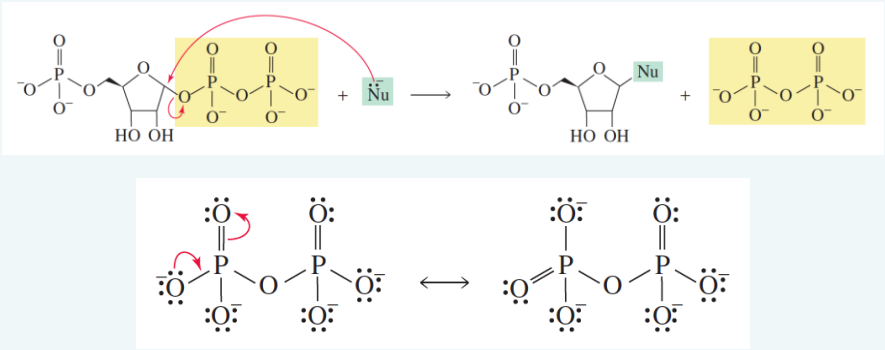


Alcohols undergo S_N1 reactions unless they would have to form a primary carbocation.

Activating an OH Group for Nucleophilic Substitution in a Cell

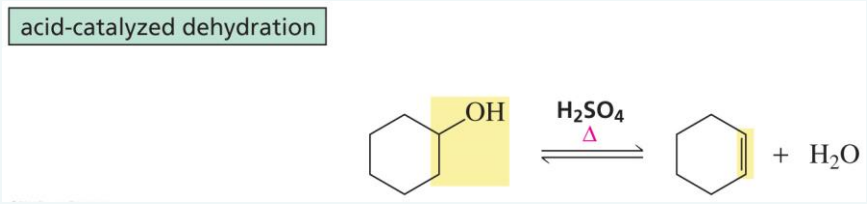


Activating an OH Group for Nucleophilic Substitution in a Cell



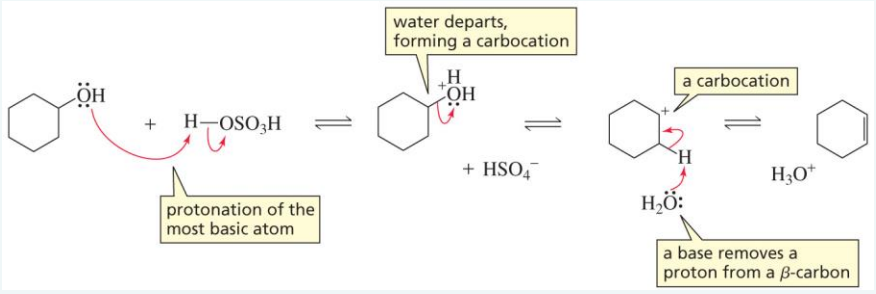
Pyrophosphate is a good leaving group (weak base).

Dehydration of an Alcohol

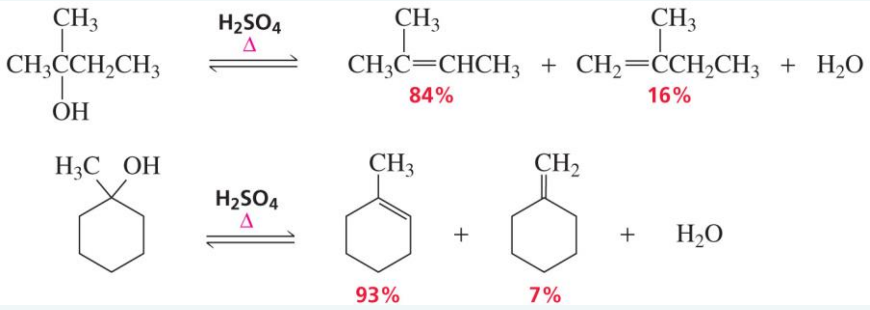


Dehydration of an alcohol is an elimination reaction.

Dehydration of Secondary and Tertiary Alcohols are E1 Reactions

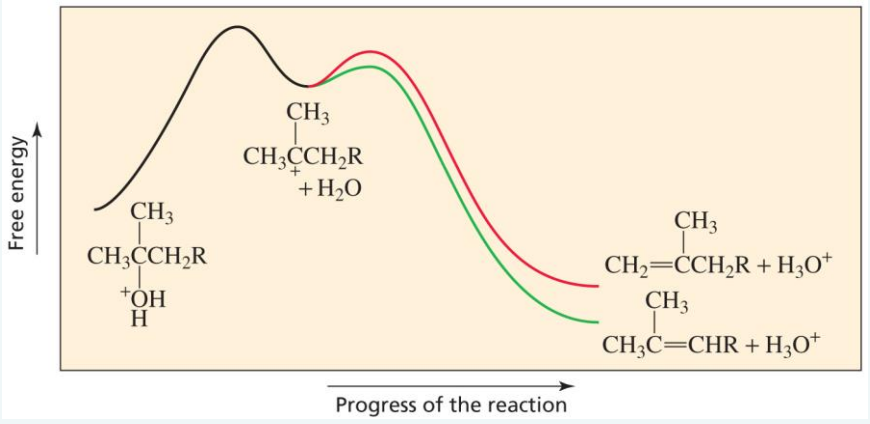


Dehydration is a Regioselective Reaction

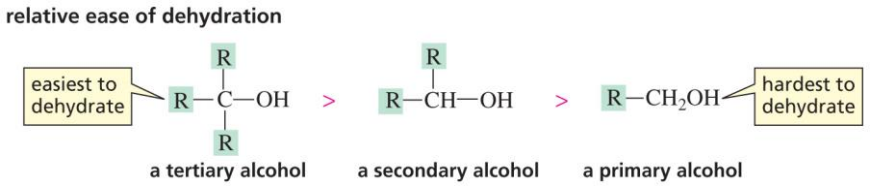


The major product is the more stable alkene.

The more stable Alkene has the more stable Transition State leading to its formation

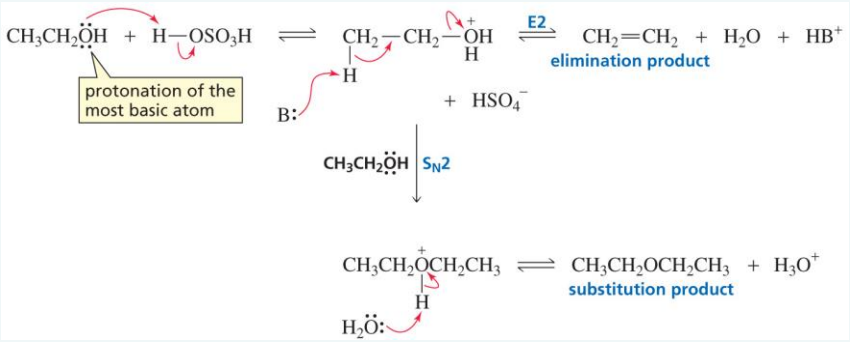


Tertiary Alcohols are the Easiest to Dehydrate



The rate of dehydration reflects the ease of carbocation formation.

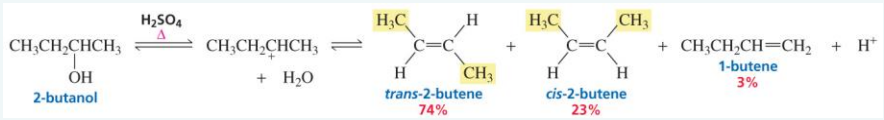
Dehydration of a Primary Alcohol is an E2 Reaction



Both E2 and S_N2 products are obtained.

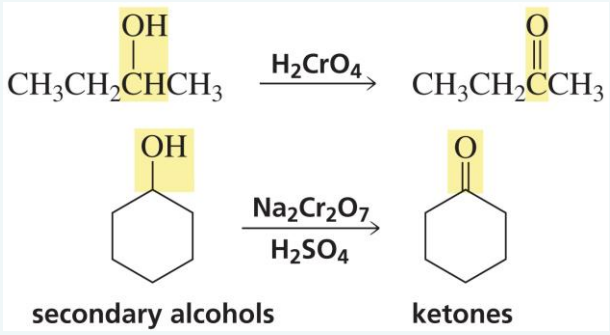
Alcohols undergo E1 reactions unless they would have to form a primary carbocation.

The major product is the Stereoisomer with the largest groups on opposite sides of the Double Bond

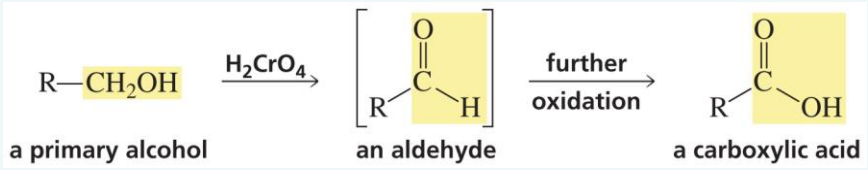


The major product has the CH_3 groups on opposites sides of the double bond.

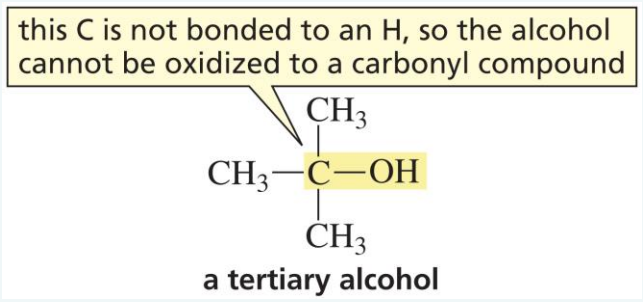
Oxidation of Secondary Alcohols



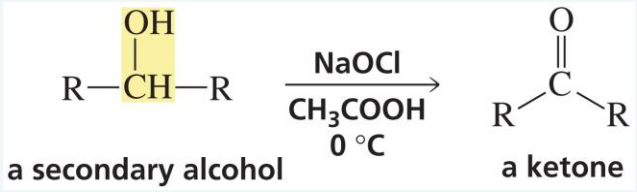
Oxidation of Primary Alcohols

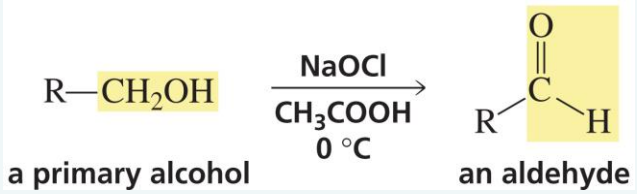


Tertiary Alcohols cannot be Oxidized to a Carbonyl Compound

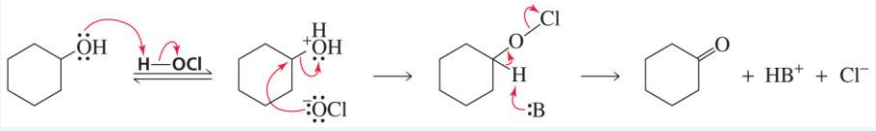


Oxidation by Hypochlorous Acid (HOCl)

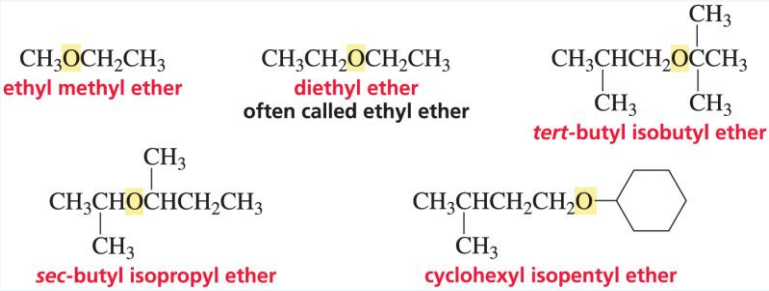




The Mechanism

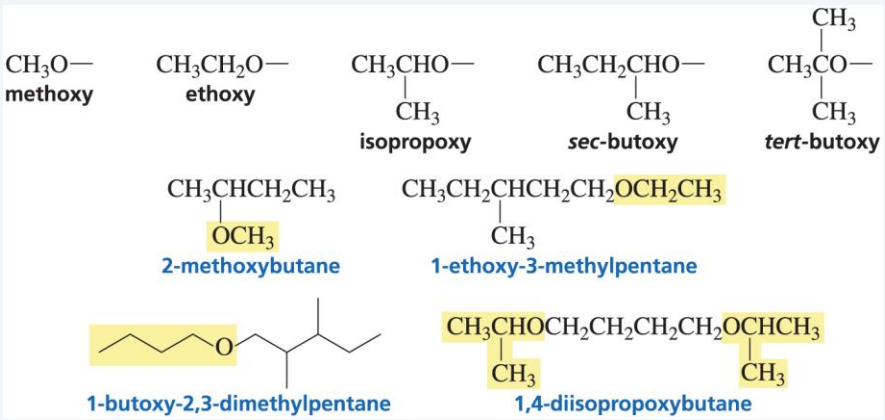


Nomenclature of Ethers



The substituents are listed in alphabetical order.

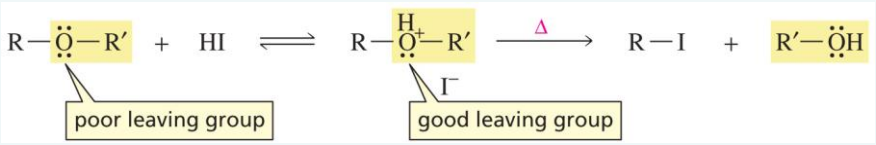
Systematic Names of Ethers



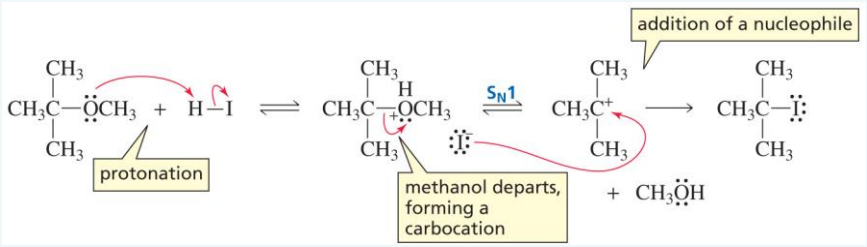
Alcohols and Ethers have similar Leaving Groups

Alcohols and ethers have to be "activated" before the compounds can react.

The Leaving Group of an Ether can be activated by Protonation

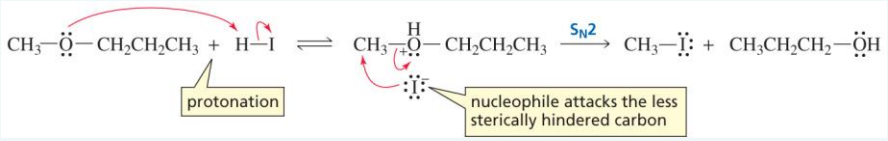


The Mechanism



If a relatively stable carbocation will be formed when ROH leaves, it will be an S_N1 reaction.

The Mechanism

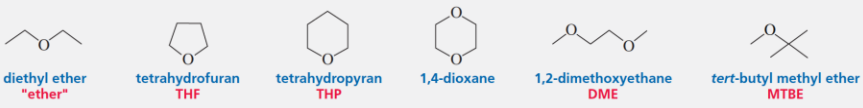


If a relatively stable carbocation would not be formed when ROH leaves, it will be an S_N2 reaction.

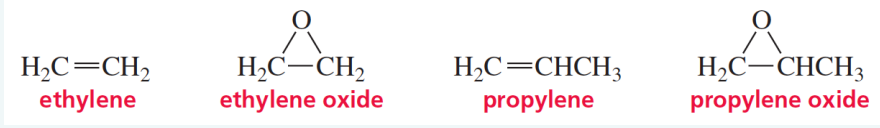
Ethers undergo S_N1 reactions unless they would have to form a primary carbocation.

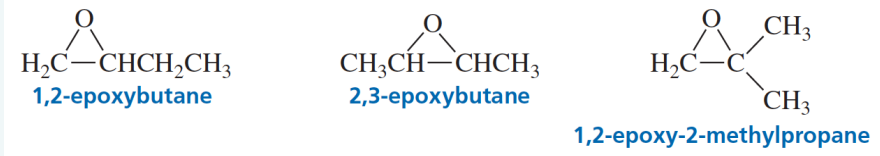
Ethers are common Solvents because they react only with Hydrogen Halides

Table 9.1 Some Ethers Are Used as Solvents

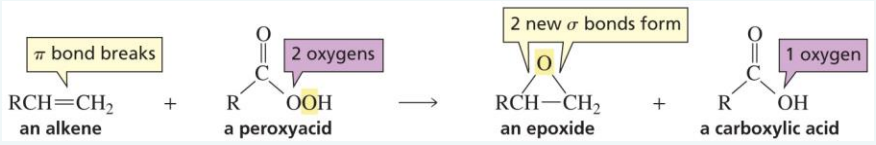


Nomenclature of Epoxides

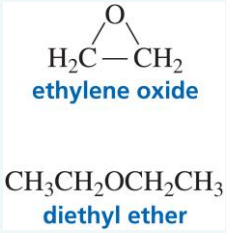


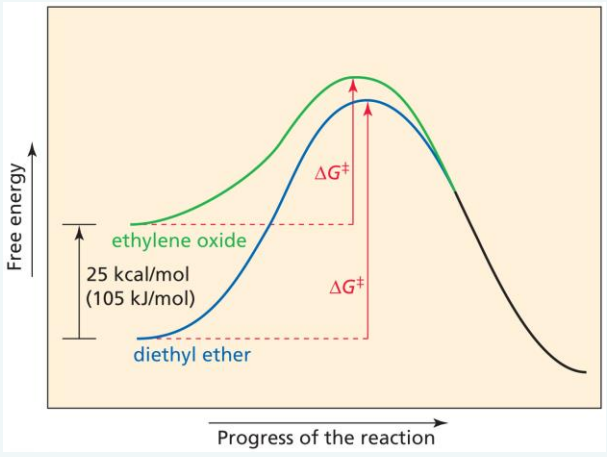


Synthesis of an Epoxide

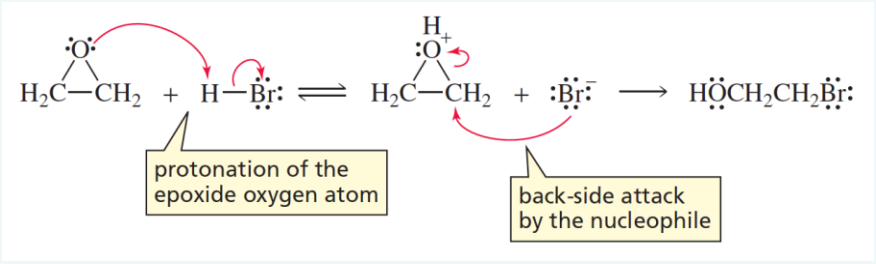


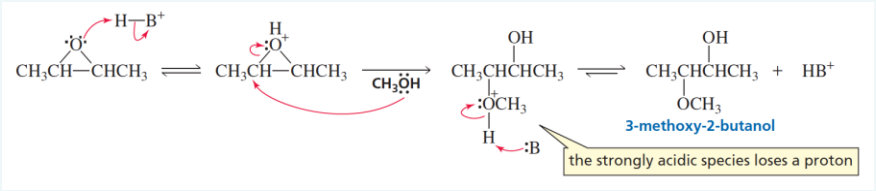
Epoxides are more reactive than Ethers because of Ring Strain



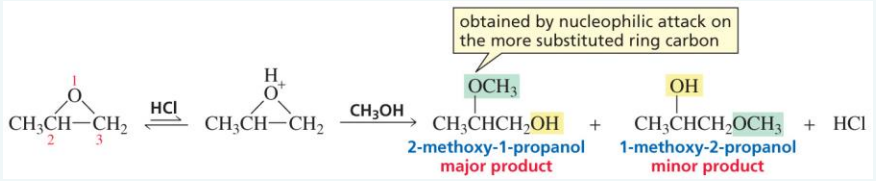


Nucleophilic Substitution of Epoxides: The Acid-Catalyzed Mechanism

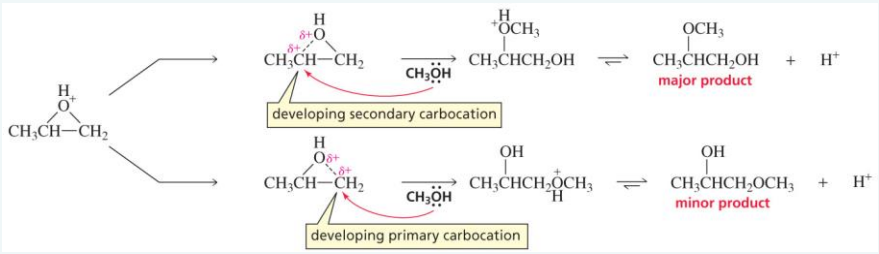




Under acidic conditions, the Nucleophile attacks the more substituted Ring Carbon

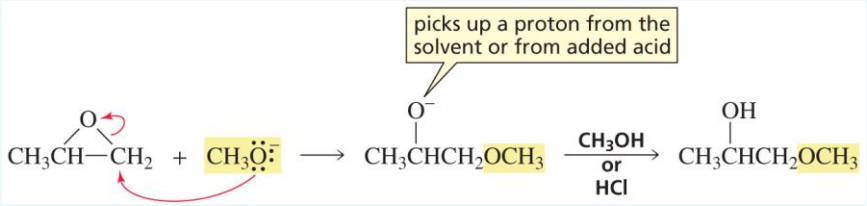


Why the more Substituted Ring Carbon is attacked under acidic conditions



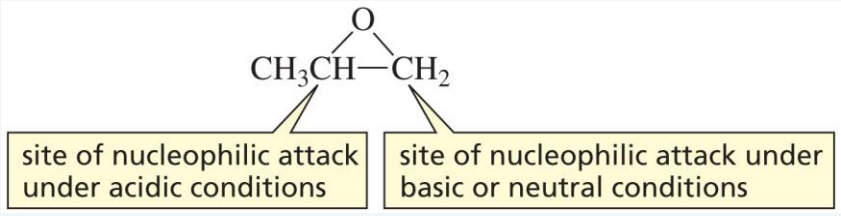
The nucleophile attacks the more substituted ring carbon.

Under neutral or basic conditions, the Nucleophile attacks the less substituted Carbon

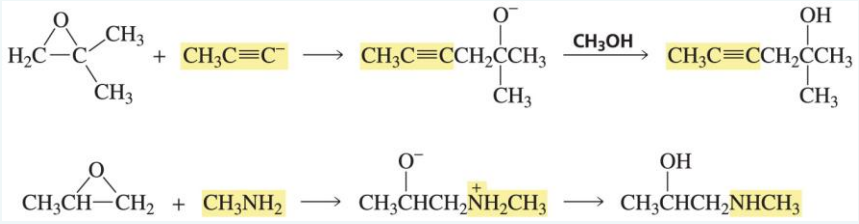


The nucleophile attacks the less substituted ring carbon.

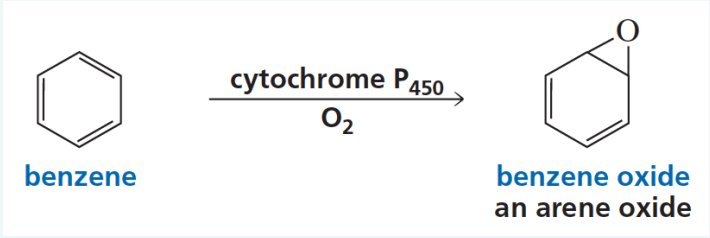
The conditions determine the Site of Nucleophilic Attack

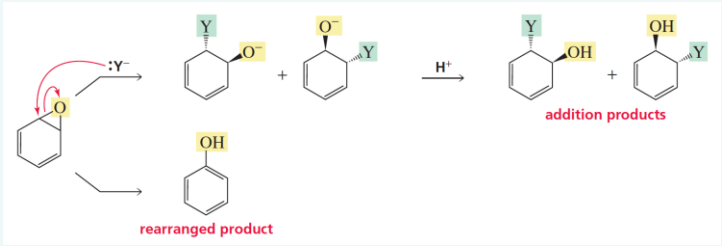


Using Epoxides in Synthesis

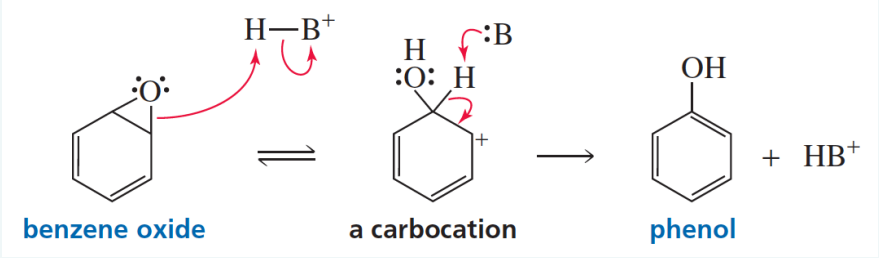


Carbocation Stability determines the Carcinogenicity of an Arene Oxide

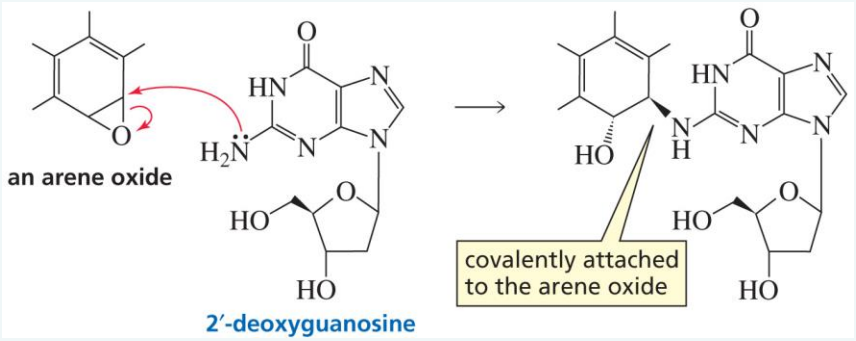




The more stable the Carbocation, the more likely the Phenolic Product will be formed

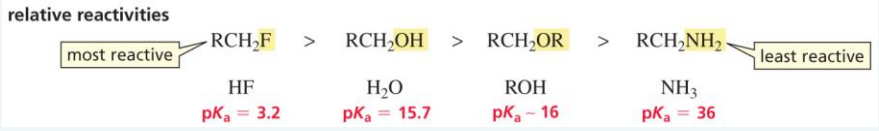


Addition Products can be Carcinogenic



If formation of the addition products is faster than formation of the phenol, the arene oxide can be carcinogenic.

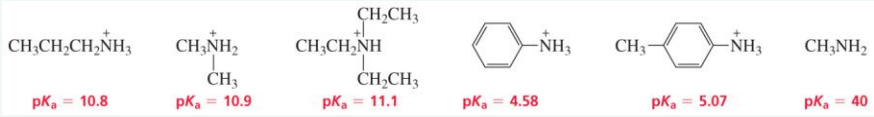
Relative Reactivity of Amines



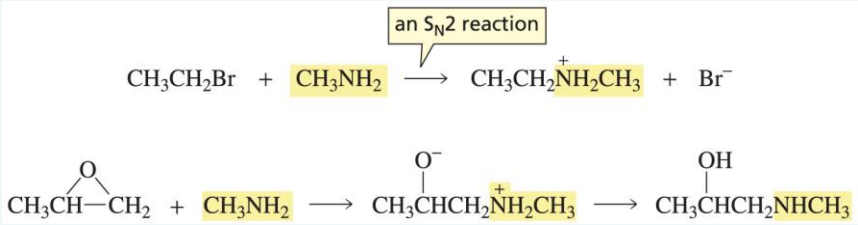
Protonating an Amine does not form a Compound with a Good Leaving Group

Amines cannot undergo substitution and elimination reactions.

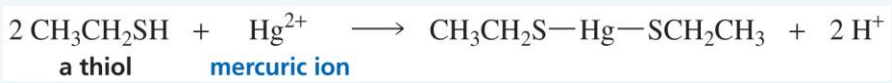
Amines are common Organic Bases



Amines are common Nucleophiles

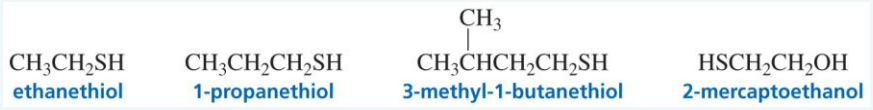


Thiols

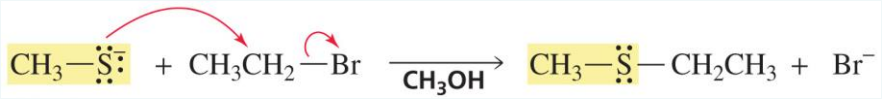


Thiols used to be called mercaptans because they capture mercury.

Nomenclature of Thiols



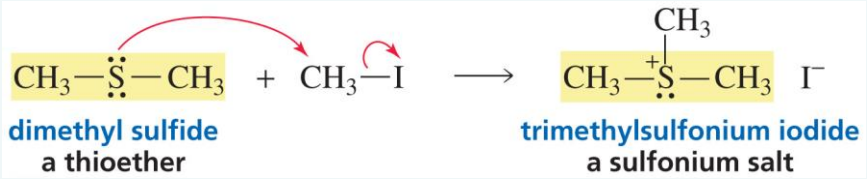
Thiols are good Nucleophiles in a Protic Solvent



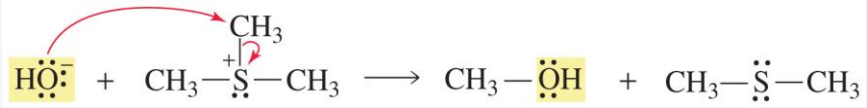
Thiolate ions are better nucleophiles because they are less solvated than are alkoxide ions.

The product is a sulfur analogue of an ether (thioether or a disulfide).

Thioethers are also Nucleophiles

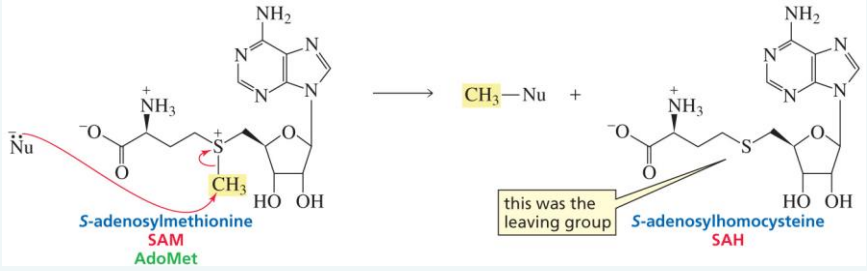


A Sulfonium Ion is an Alkylating Agent

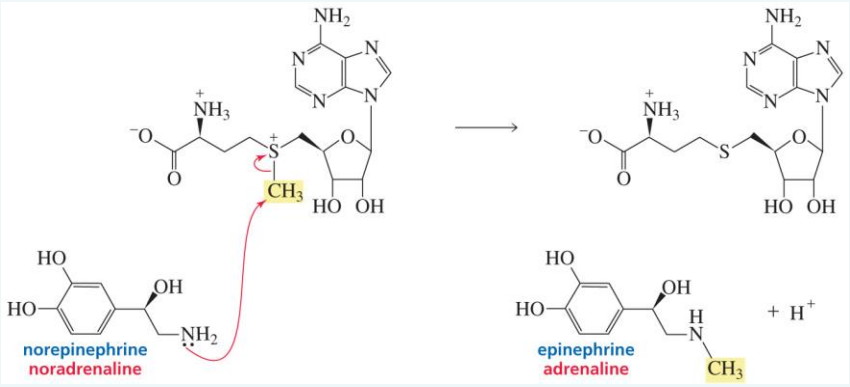


Methylation by a Chemist

Methylation by a Cell



Noradrenaline to Adrenaline



The Families in Group III