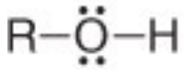
Alcohols, Ethers and Epoxides

Chapter 17-18

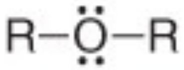
Organic Chemistry, *8th Edition*

John McMurry

Introduction—Structure and Bonding



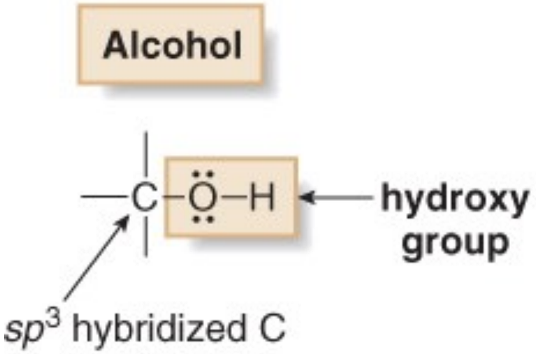
alcohol

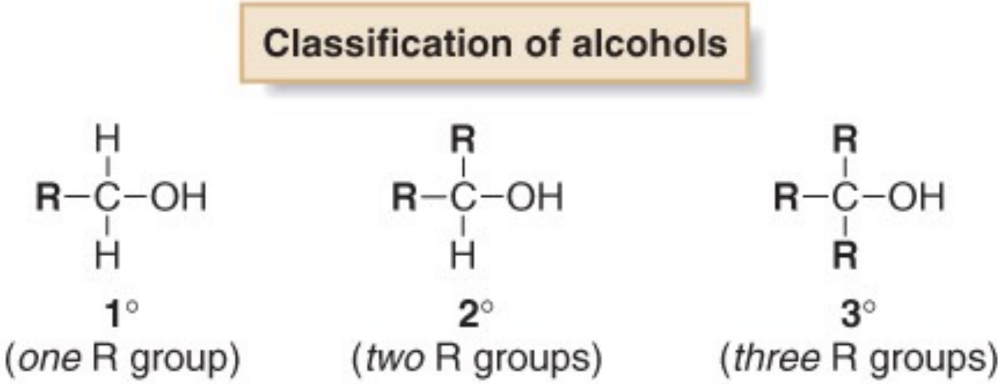


ether

epoxide

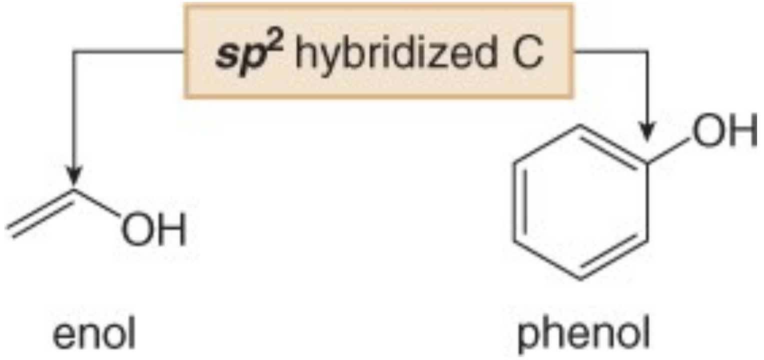
Alcohols contain a hydroxy group (OH) bonded to an sp3 hybridized carbon.



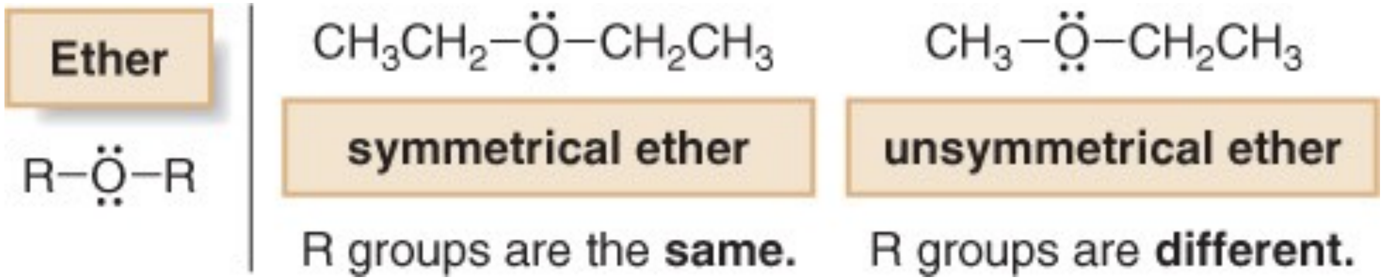


Introduction—Structure and Bonding

enols and phenols—undergo different reactions than alcohols.



Ethers have two hydrocarbon groups groups bonded to an oxygen atom.



Ether

$R-\ddot{\underset{..}{O}}-R$

$CH_3CH_2-\ddot{\underset{..}{O}}-CH_2CH_3$

symmetrical ether

R groups are the **same.**

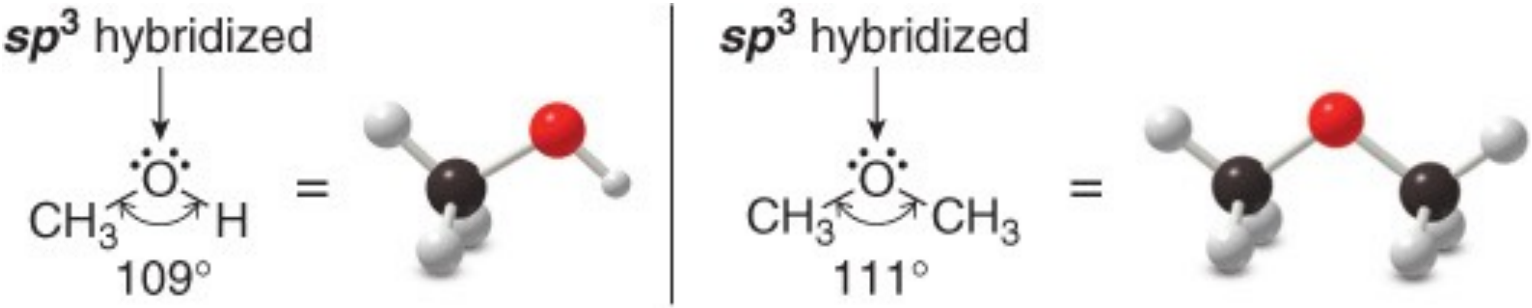
$CH_3-\ddot{\underset{..}{O}}-CH_2CH_3$

unsymmetrical ether

R groups are **different.**

Introduction—Structure and Bonding

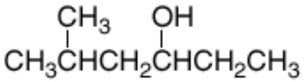
- The oxygen atom in alcohols, ethers and epoxides is *sp*³ hybridized. Alcohols and ethers have a bent shape like that in H_2O.
- The bond angle around the O atom in an alcohol or ether is similar to the tetrahedral bond angle of 109.5°.
- Because the O atom is much more electronegative than carbon or hydrogen, the C—O and O—H bonds are all polar.



Nomenclature of Alcohols

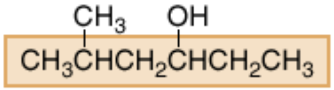
How To Name an Alcohol Using the IUPAC System

Example Give the IUPAC name of the following alcohol:



$CH_3\overset{CH_3}{\overset{|}{C}}HCH_2\overset{OH}{\overset{|}{C}}HCH_2CH_3$

Step [1] Find the longest carbon chain containing the carbon bonded to the OH group.



$\boxed{CH_3\overset{CH_3}{\overset{|}{C}}HCH_2\overset{OH}{\overset{|}{C}}HCH_2CH_3}$

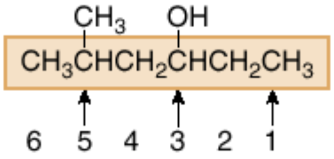
6 C's in the longest chain

6 C's ⇢ hexane ⇢ hexan*ol*

- Change the ***-e*** ending of the parent alkane to the suffix ***-ol.***

Step [2] Number the carbon chain to give the OH group the lower number, and apply all other rules of nomenclature.

a. **Number** the chain.

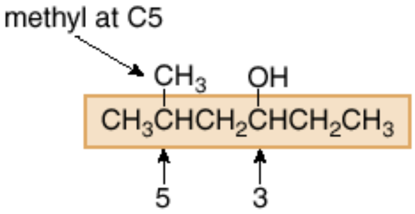


$\boxed{CH_3\overset{CH_3}{\overset{|}{C}}HCH_2\overset{OH}{\overset{|}{C}}HCH_2CH_3}$

- Number the chain to put the OH group at C3, not C4.

3-hexanol

b. **Name** and **number** the substituents.



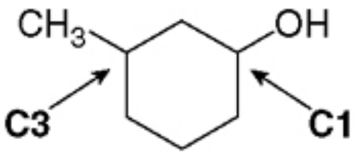
methyl at C5

$\boxed{CH_3\overset{CH_3}{\overset{|}{C}}HCH_2\overset{OH}{\overset{|}{C}}HCH_2CH_3}$

Answer: 5-methyl-3-hexanol

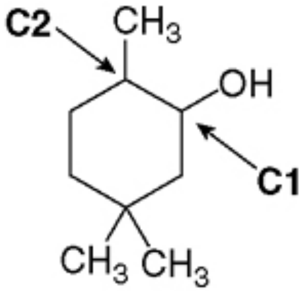
Nomenclature of Alcohols

- When an OH group is bonded to a ring, the ring is numbered beginning with the OH group. .



3-methylcyclohexanol

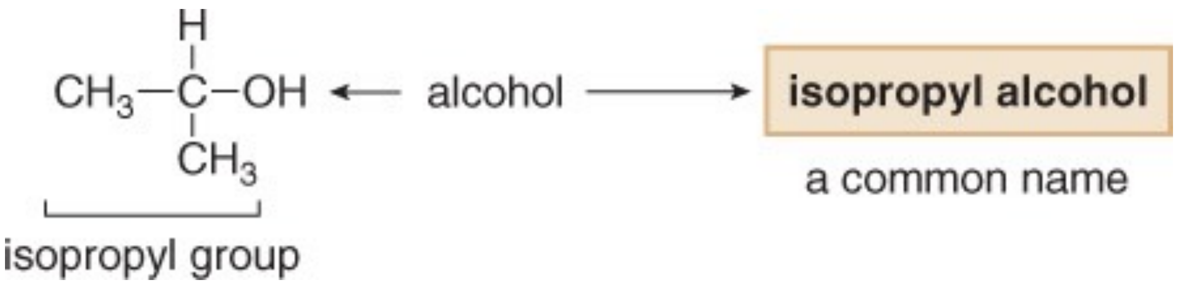
The OH group is at C1; the second substituent (CH_3) gets the lower number.



2,5,5-trimethylcyclohexanol

The OH group is at C1; the second substituent (CH_3) gets the lower number.

- Common names are often used for simple alcohols.



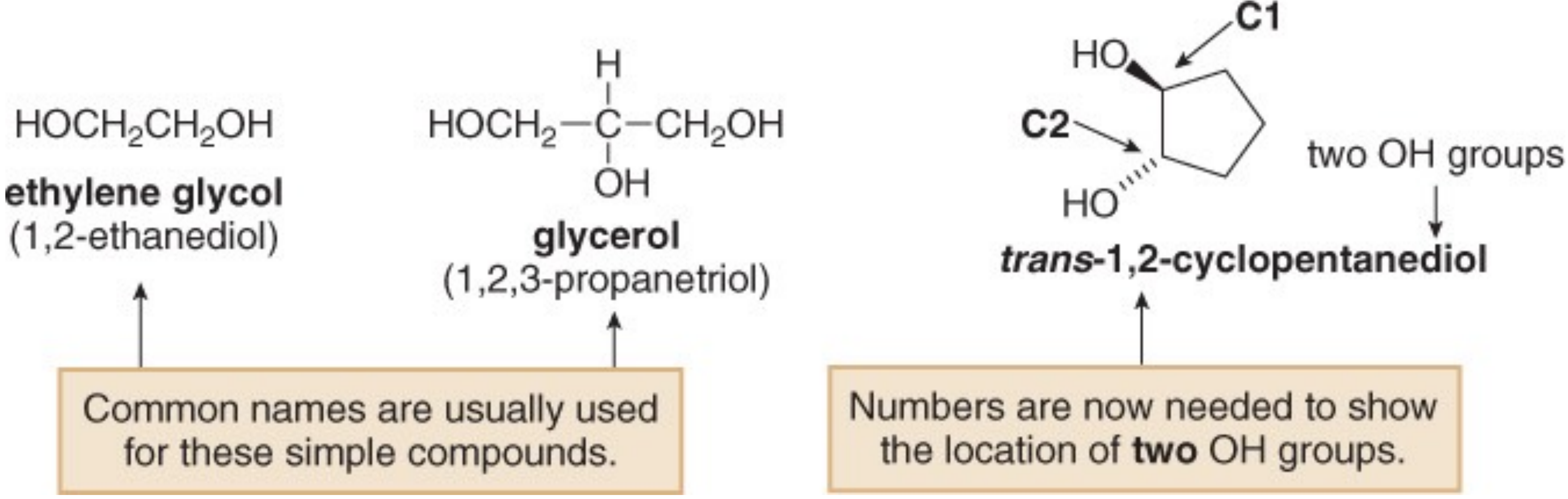
$$CH_3-\overset{\displaystyle H}{\underset{\displaystyle CH_3}{C}}-OH$$

isopropyl alcohol

a common name

Nomenclature of Alcohols

- Compounds with two hydroxy groups are called diols or glycols. Compounds with three hydroxy groups are called triols and so forth.



$HOCH_2CH_2OH$

ethylene glycol
(1,2-ethanediol)

$HOCH_2-CH(OH)-CH_2OH$

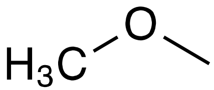
glycerol
(1,2,3-propanetriol)

trans-1,2-cyclopentanediol

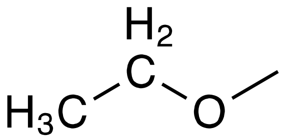
Common names are usually used for these simple compounds.

Numbers are now needed to show the location of **two** OH groups.

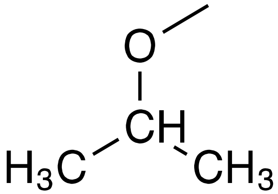
Nomenclature of Alcohols



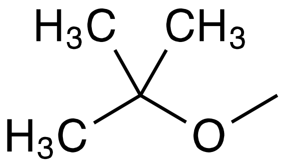
Methoxy



ethoxy



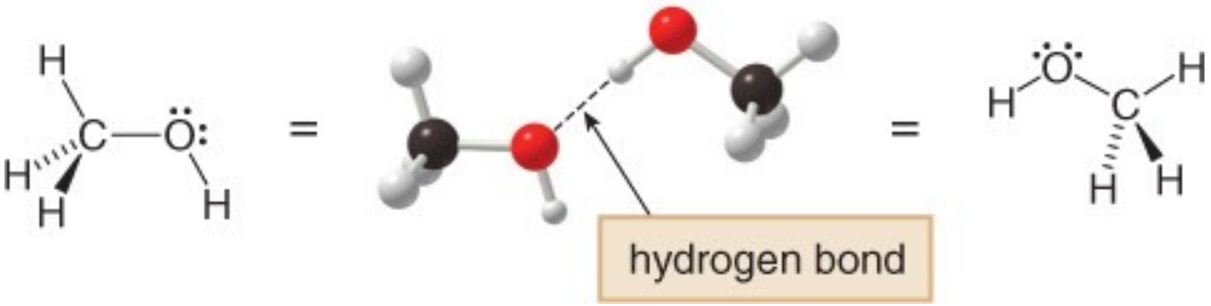
2-propoxy
isopropoxy



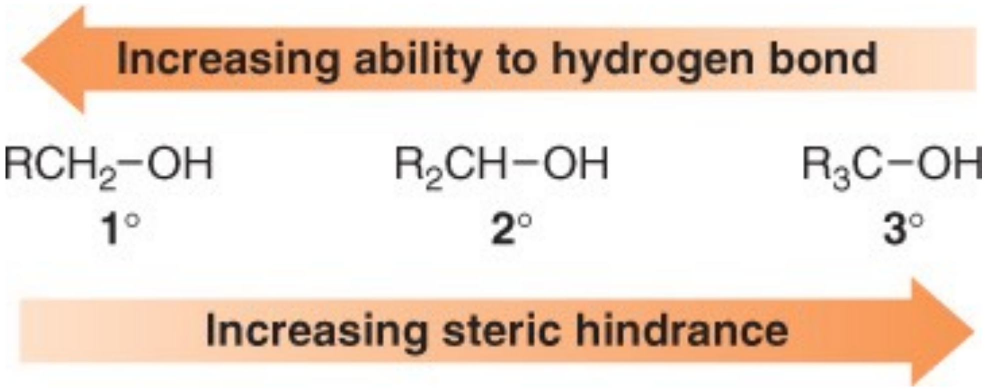
2-methyl-2-propoxy
terbutoxy

Physical Properties

- dipole-dipole interactions.
- intermolecular hydrogen bonding. Alcohols are more polar than ethers and epoxides.



- Steric factors affect hydrogen bonding.

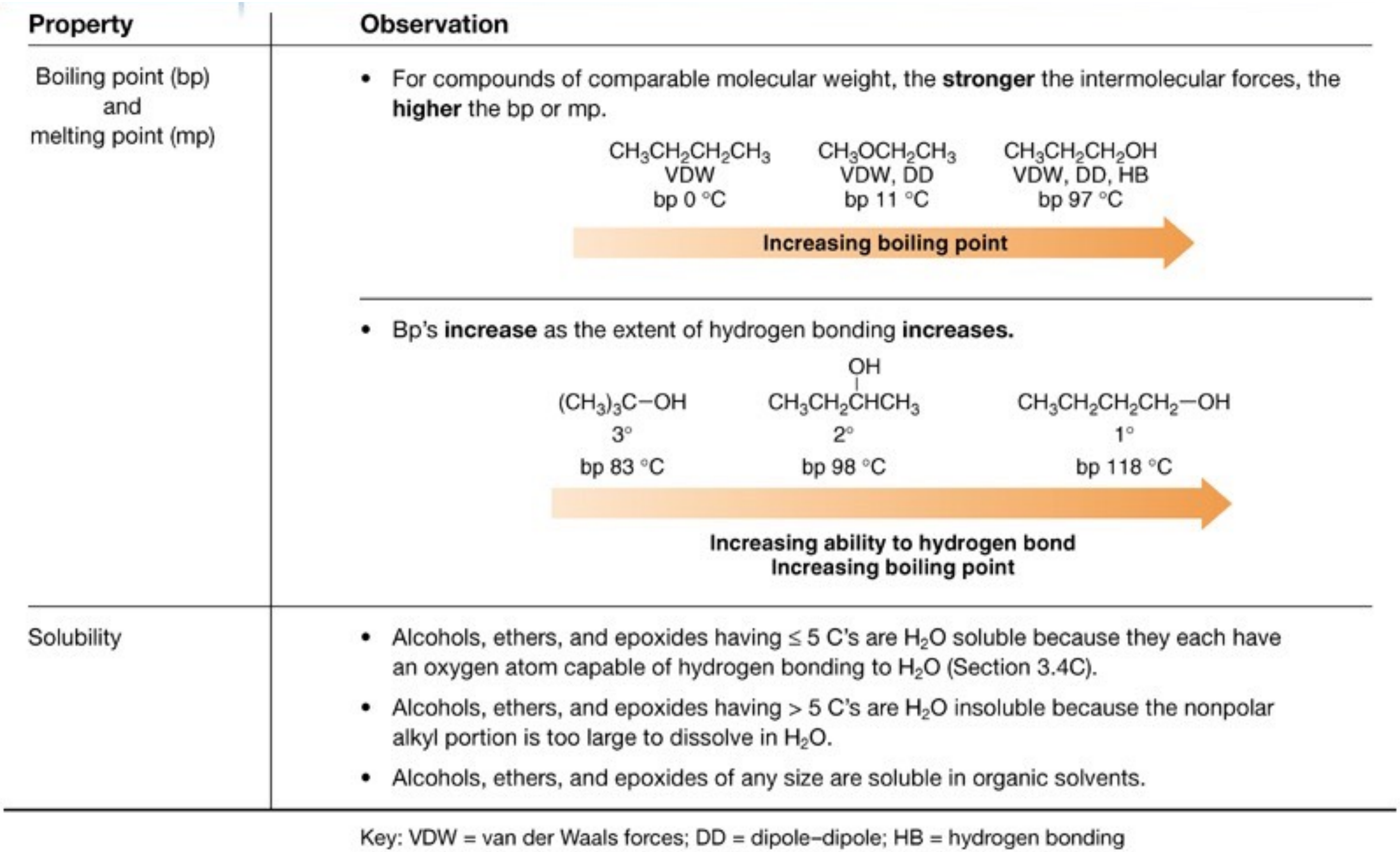


Increasing ability to hydrogen bond

RCH_2-OH	R_2CH-OH	R_3C-OH
1°	2°	3°

Increasing steric hindrance

Physical Properties

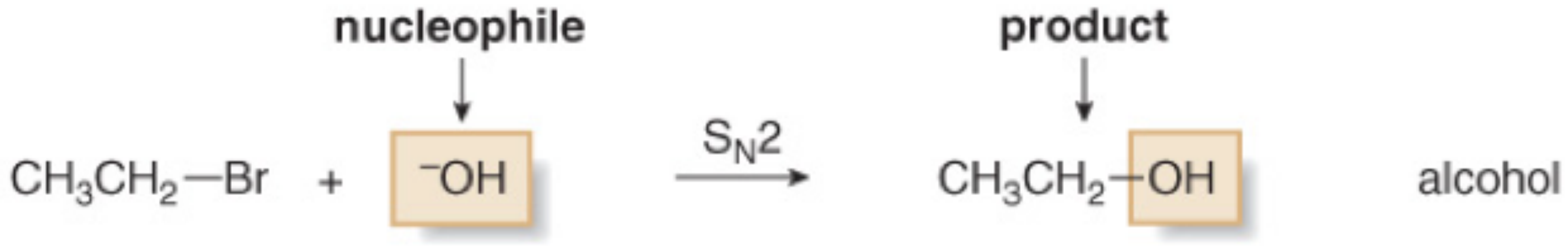


Property	Observation
Boiling point (bp) and melting point (mp)	• For compounds of comparable molecular weight, the **stronger** the intermolecular forces, the **higher** the bp or mp. $CH_3CH_2CH_2CH_3$ VDW bp 0 °C $CH_3OCH_2CH_3$ VDW, DD bp 11 °C $CH_3CH_2CH_2OH$ VDW, DD, HB bp 97 °C **Increasing boiling point**
	• Bp's **increase** as the extent of hydrogen bonding **increases.** $(CH_3)_3C{-}OH$ 3° bp 83 °C $CH_3CH_2\overset{OH}{C}HCH_3$ 2° bp 98 °C $CH_3CH_2CH_2CH_2{-}OH$ 1° bp 118 °C **Increasing ability to hydrogen bond** **Increasing boiling point**
Solubility	• Alcohols, ethers, and epoxides having ≤ 5 C's are H_2O soluble because they each have an oxygen atom capable of hydrogen bonding to H_2O (Section 3.4C). • Alcohols, ethers, and epoxides having > 5 C's are H_2O insoluble because the nonpolar alkyl portion is too large to dissolve in H_2O. • Alcohols, ethers, and epoxides of any size are soluble in organic solvents.

Key: VDW = van der Waals forces; DD = dipole–dipole; HB = hydrogen bonding

Preparation of Alcohols

- From alkyl halides

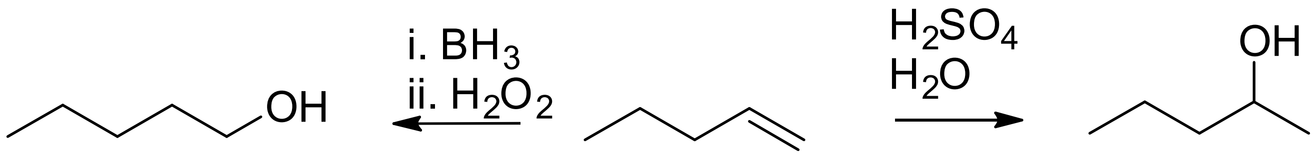


nucleophile **product**

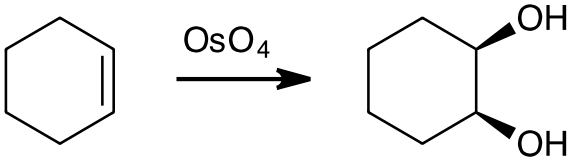
$$CH_3CH_2{-}Br + {}^{-}OH \xrightarrow{S_N2} CH_3CH_2{-}OH$$

alcohol

- Hydration/hydroboration of alkenes

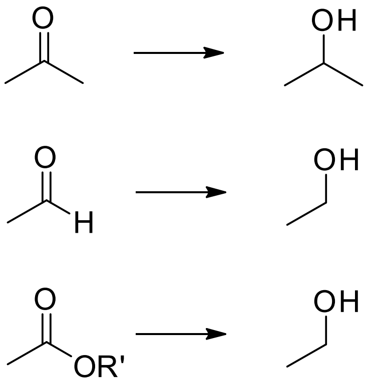


- Dihydroxylation of alkenes



Preparation of Alcohols

- Reduction of carbonyl compounds



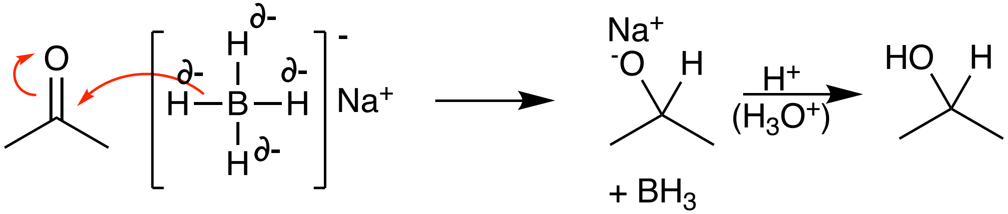
secondary alcohol

primary alcohol

H_2/Pd reduces also C=C

$NaBH_4$, $LiAlH_4$ selective for C=O

Mechanism: nucleophilic addition to the C=O bond



H is transferred as $[H^-]$

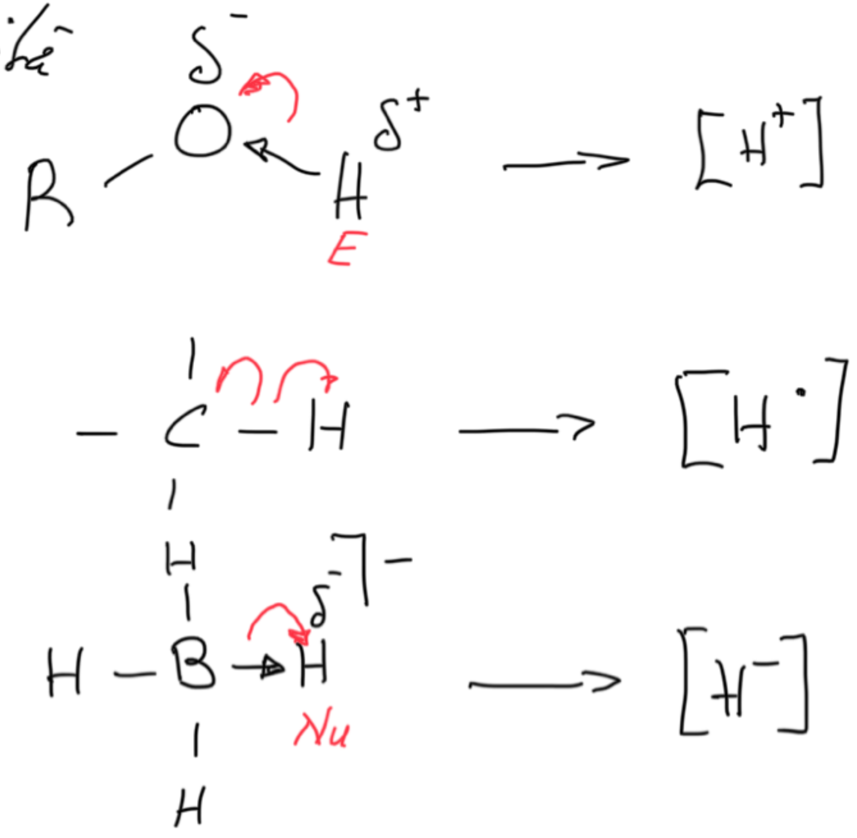
B and Al Hydrides

elettronegatività

$O > H$

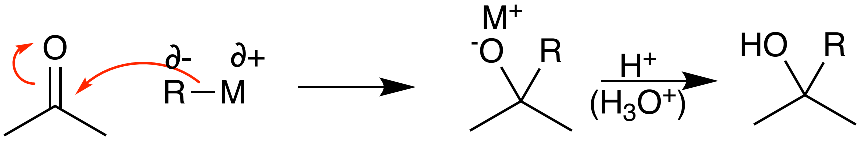
$C \simeq H$

$B < H$

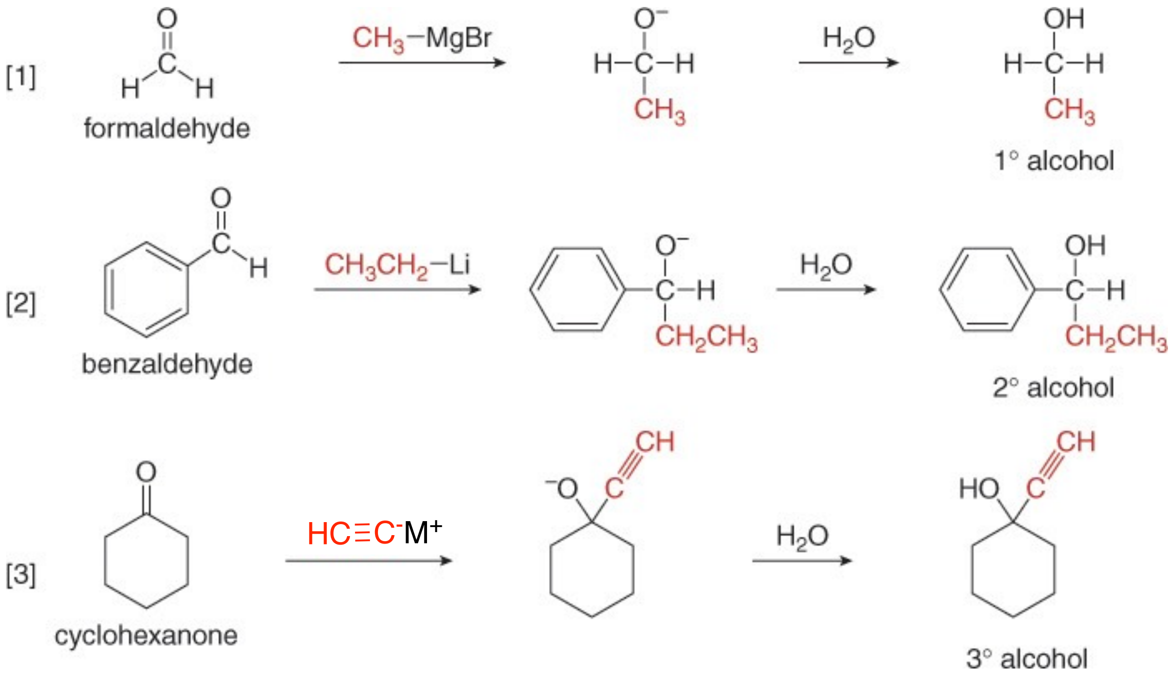


Reaction of carbonyl compounds with organometallic reagents

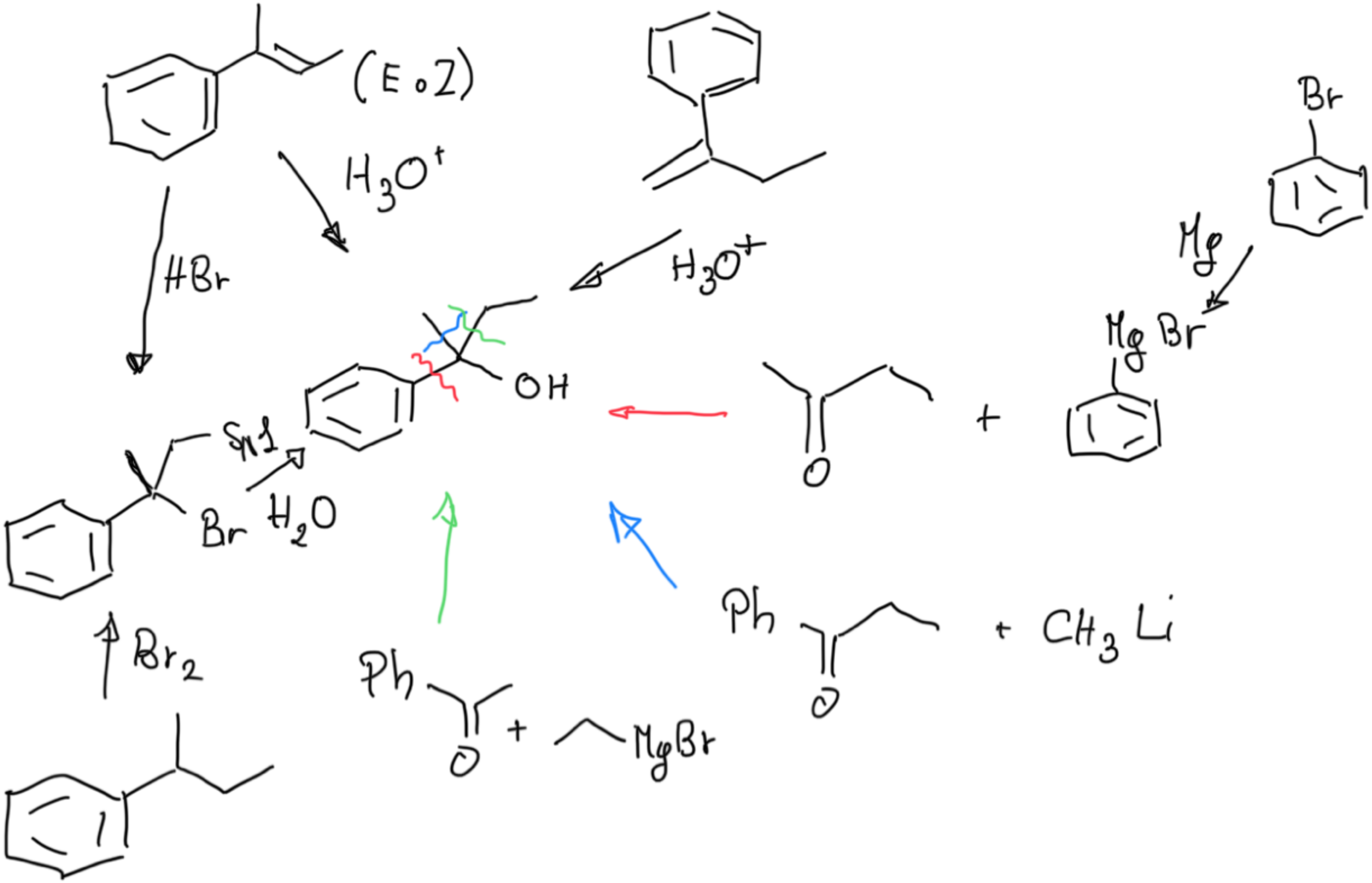
Mechanism: nucleophilic addition to the C=O bond



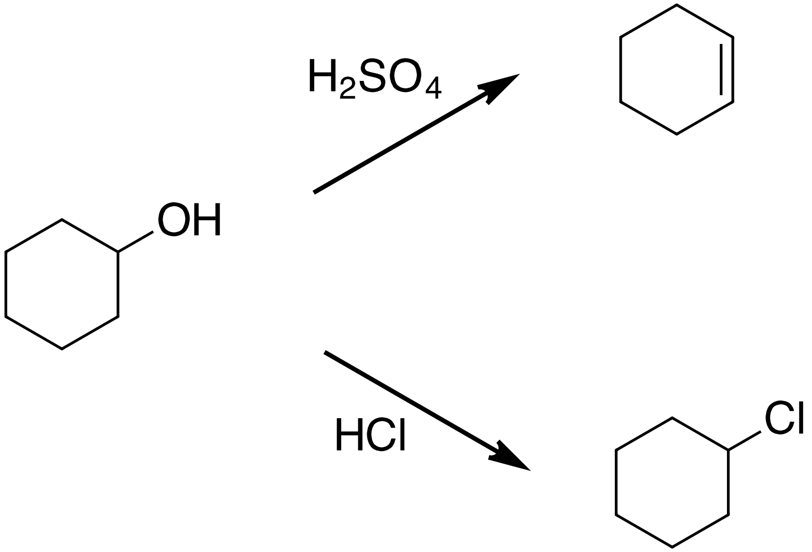
R is transferred as $[R^-]$



Synthesis of Alcohols



Reactions of Alcohols
OH as Leaving Group

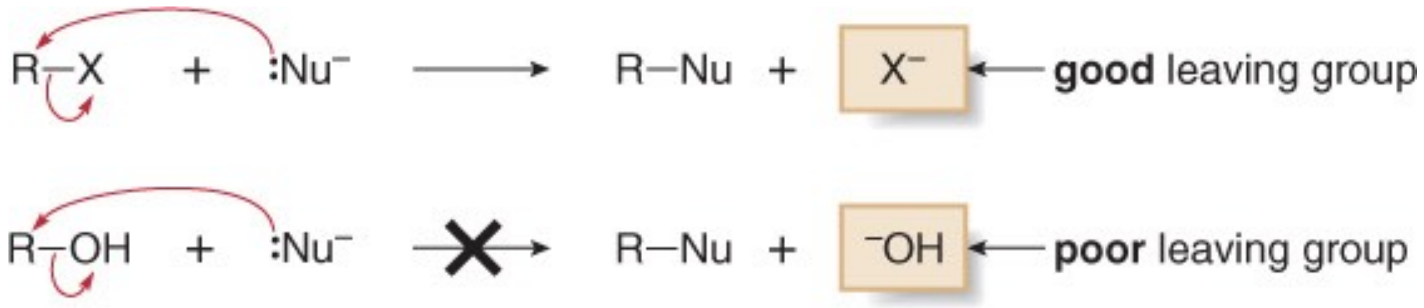


Elimination

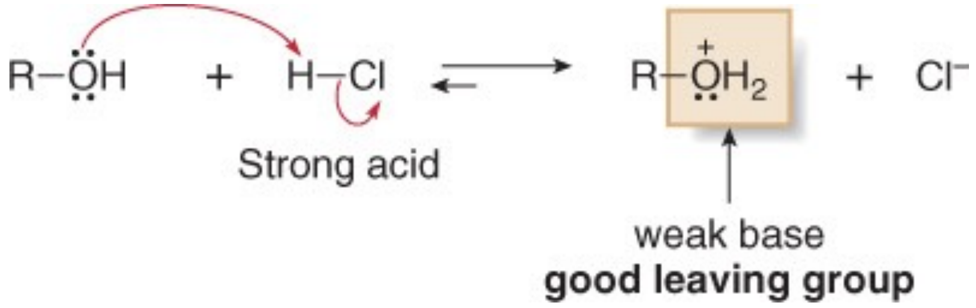
Substitution

Reactions of Alcohols
OH as Leaving Group

- The OH group in alcohols is a very poor leaving group.

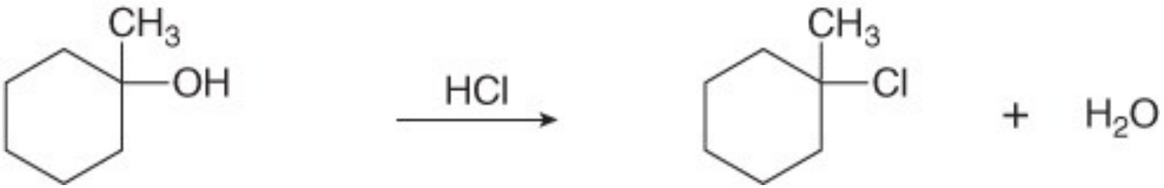


- By using acid, -OH can be converted into $–OH_2^+$, a good leaving group.

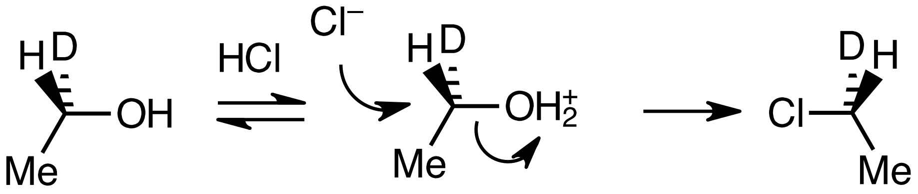


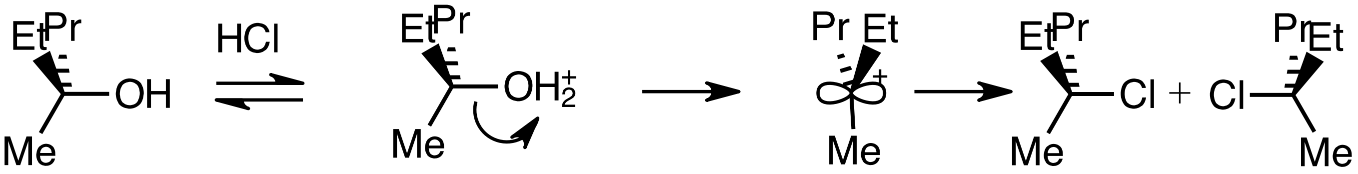
Conversion of Alcohols to Alkyl Halides

- The reaction of alcohols with HX (X = Cl, Br, I) is a general method to prepare alkyl halides.



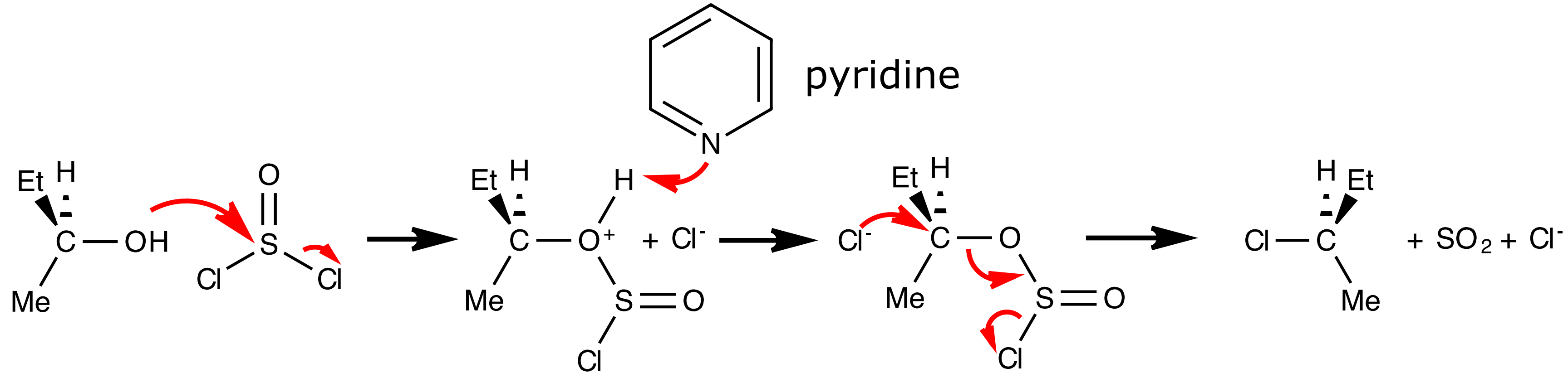
- Mechanism:
  - 1ry alcohols: S_N2
  - 2ry alcohols: S_N2 or S_N1
  - 3ry alcohols: S_N1

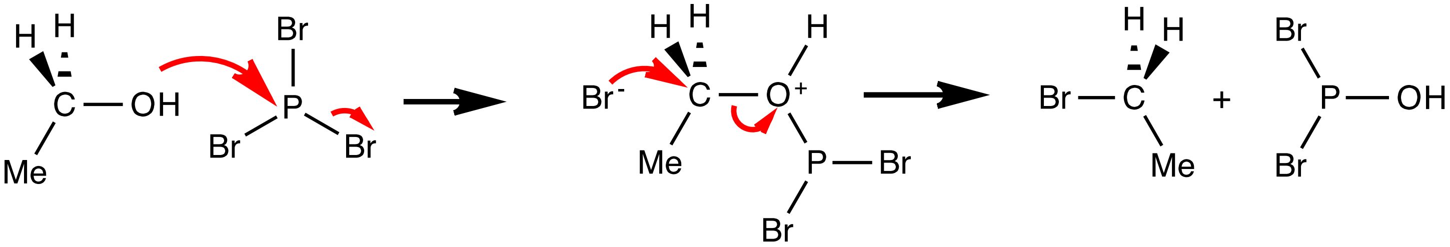




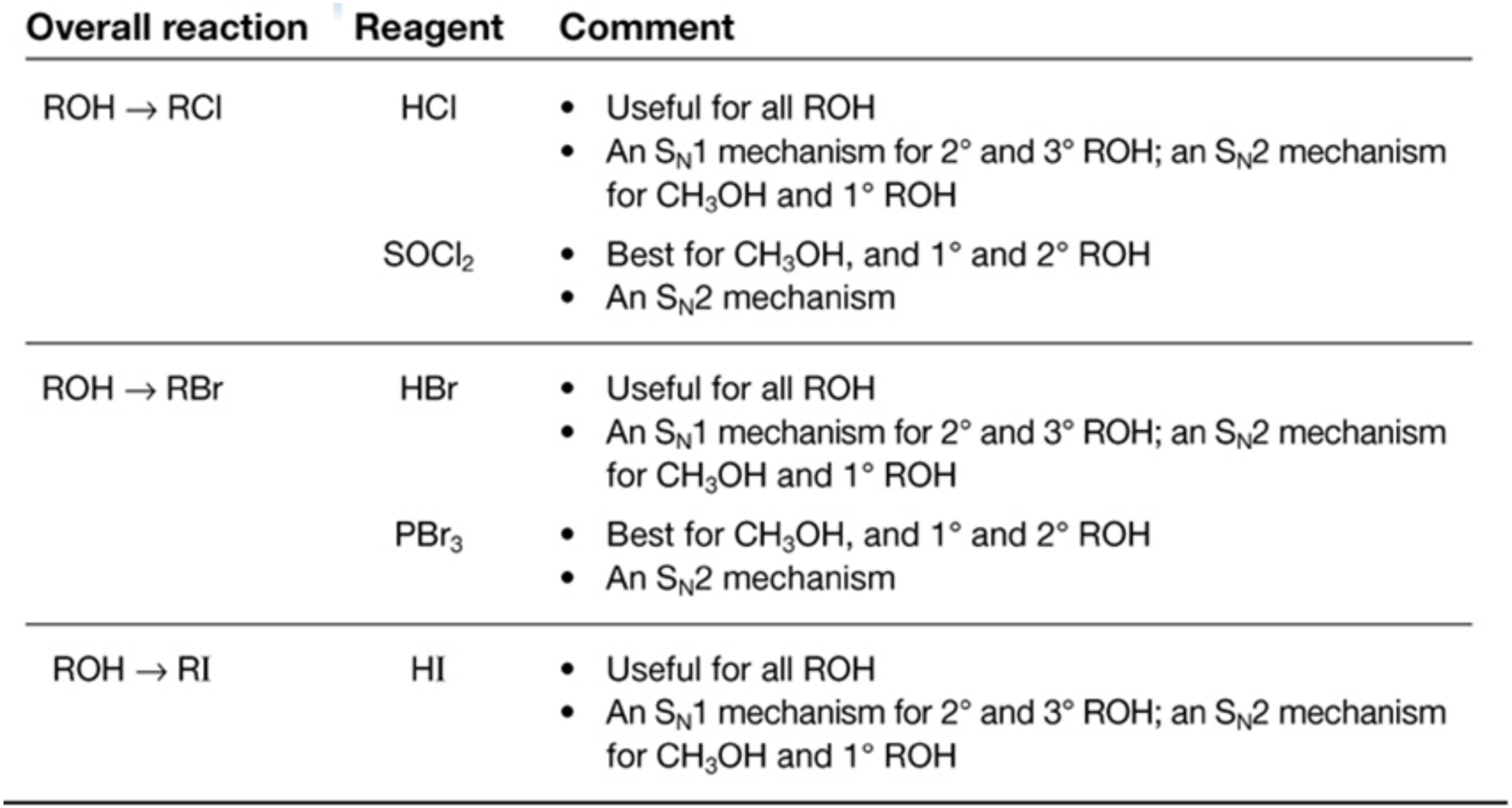
Conversion of Alcohols to Alkyl Halides with SOCl2 and PBr3

- Primary and secondary alcohols can be converted to alkyl halides using $SOCl_2$ (thionyl chloride) and PBr_3 (phosphorus tribromide)





Conversion of Alcohols to Alkyl Halides

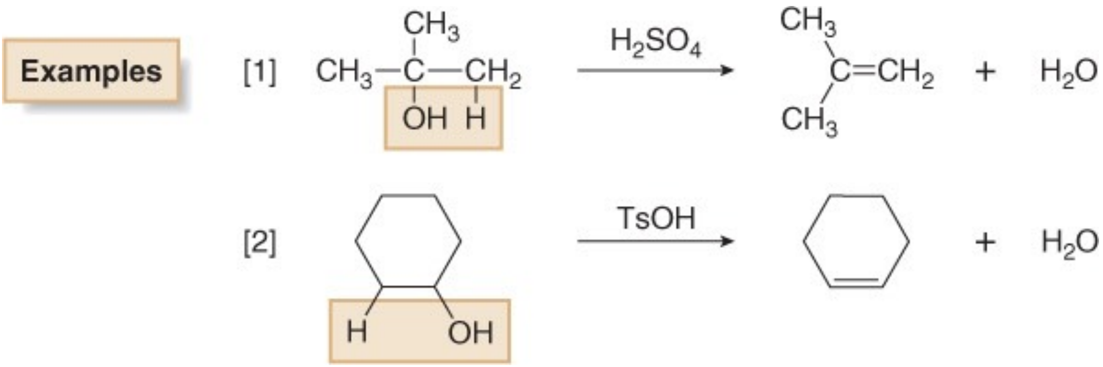


Overall reaction	Reagent	Comment
ROH → RCl	HCl	• Useful for all ROH • An S_N1 mechanism for 2° and 3° ROH; an S_N2 mechanism for CH_3OH and 1° ROH
	$SOCl_2$	• Best for CH_3OH, and 1° and 2° ROH • An S_N2 mechanism
ROH → RBr	HBr	• Useful for all ROH • An S_N1 mechanism for 2° and 3° ROH; an S_N2 mechanism for CH_3OH and 1° ROH
	PBr_3	• Best for CH_3OH, and 1° and 2° ROH • An S_N2 mechanism
ROH → RI	HI	• Useful for all ROH • An S_N1 mechanism for 2° and 3° ROH; an S_N2 mechanism for CH_3OH and 1° ROH

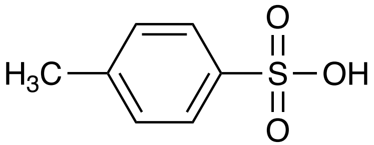
Reactions of Alcohols—Dehydration

- Dehydration, like dehydrohalogenation, is a β-elimination reaction in which the elements of OH and H are removed from the α and β carbon atoms respectively.

- Typical acids used for alcohol dehydration are H_2SO_4 or *p*-toluenesulfonic acid (TsOH).



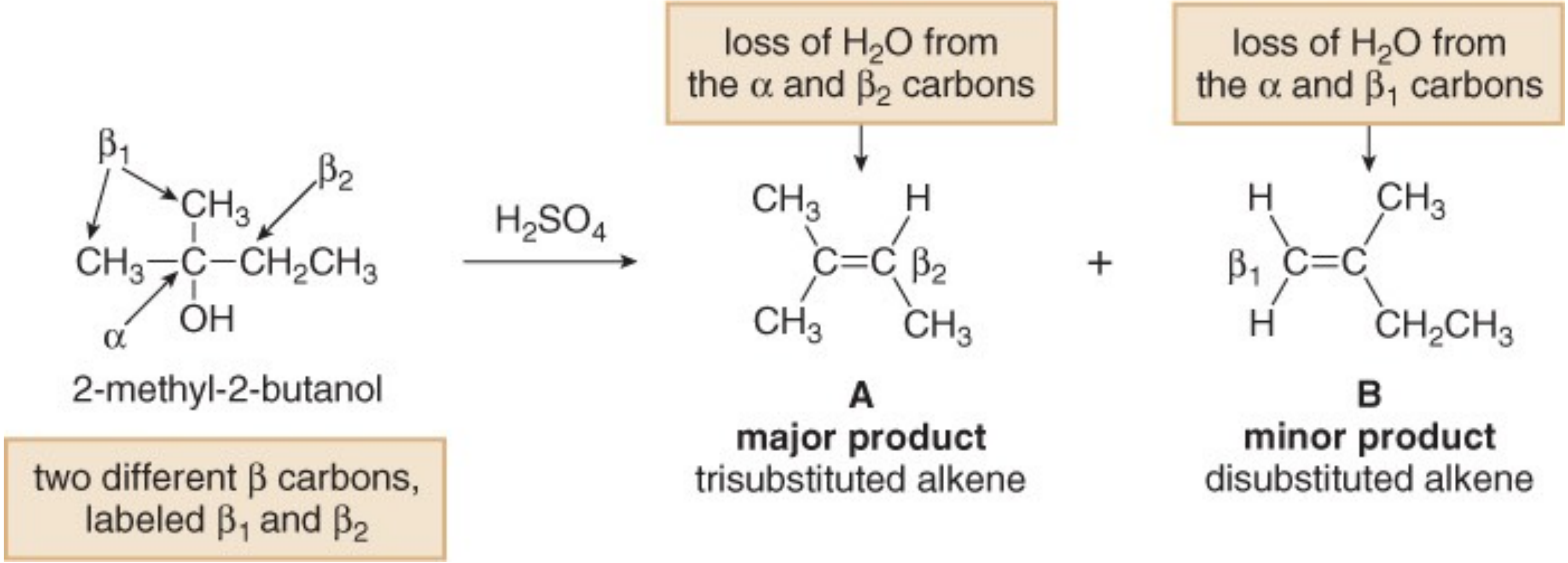
TsOH:



a strong organic acid with a non-nucleophilic anion

Reactions of Alcohols—Dehydration

- Dehydration is regioselective and follows the Zaitsev rule, giving the more substituted alcohol.



2-methyl-2-butanol

two different β carbons, labeled β_1 and β_2

loss of H_2O from the α and β_2 carbons

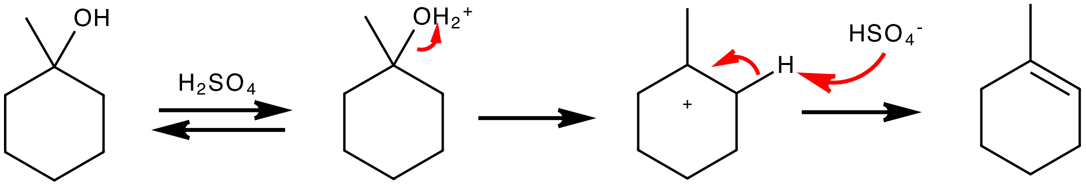
A
major product
trisubstituted alkene

loss of H_2O from the α and β_1 carbons

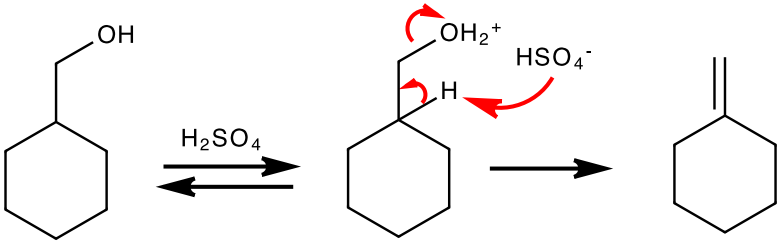
B
minor product
disubstituted alkene

Reactions of Alcohols—Dehydration

- Tertiary alcohols react by an E1 mechanism.

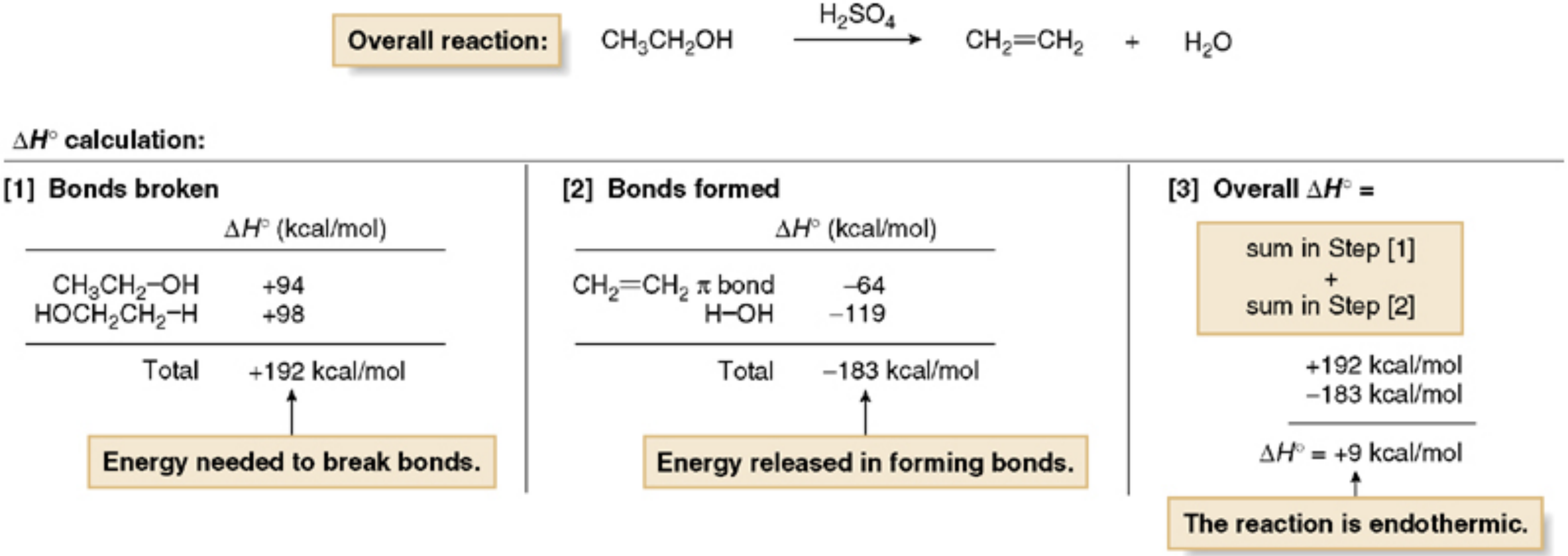


- 1^{ry} alcohols undergo dehydration following an E2 mechanism.



Reactions of Alcohols—Dehydration

- Although entropy favors product formation in dehydration (i.e., one molecule of reactant forms two molecules of product), enthalpy does not, since the σ bonds broken in the reactant are stronger than the σ and π bonds formed in the products.



Overall reaction: $CH_3CH_2OH \xrightarrow{H_2SO_4} CH_2{=}CH_2 + H_2O$

$\Delta H°$ calculation:

[1] Bonds broken

	$\Delta H°$ (kcal/mol)
$CH_3CH_2{-}OH$	+94
$HOCH_2CH_2{-}H$	+98
Total	+192 kcal/mol

Energy needed to break bonds.

[2] Bonds formed

	$\Delta H°$ (kcal/mol)
$CH_2{=}CH_2$ π bond	−64
H−OH	−119
Total	−183 kcal/mol

Energy released in forming bonds.

[3] Overall $\Delta H°$ =

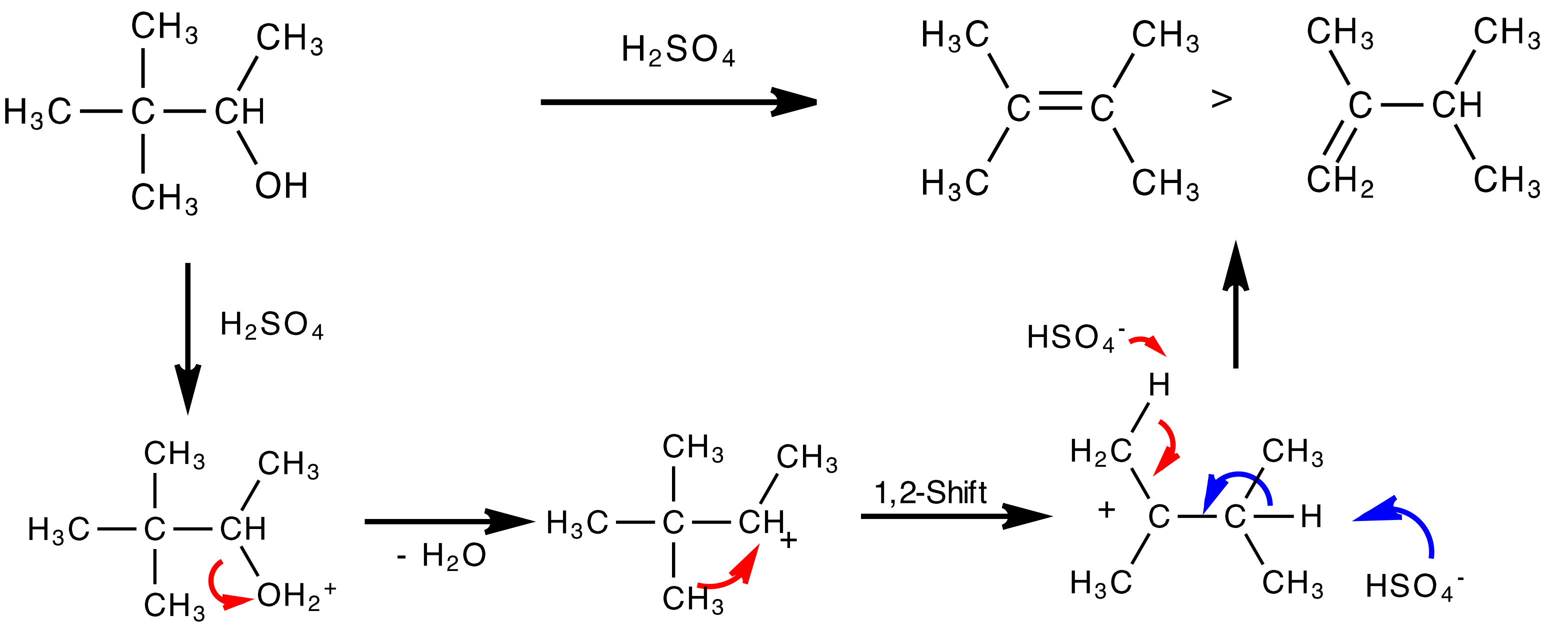
sum in Step [1]
+
sum in Step [2]

+192 kcal/mol
−183 kcal/mol

$\Delta H°$ = +9 kcal/mol

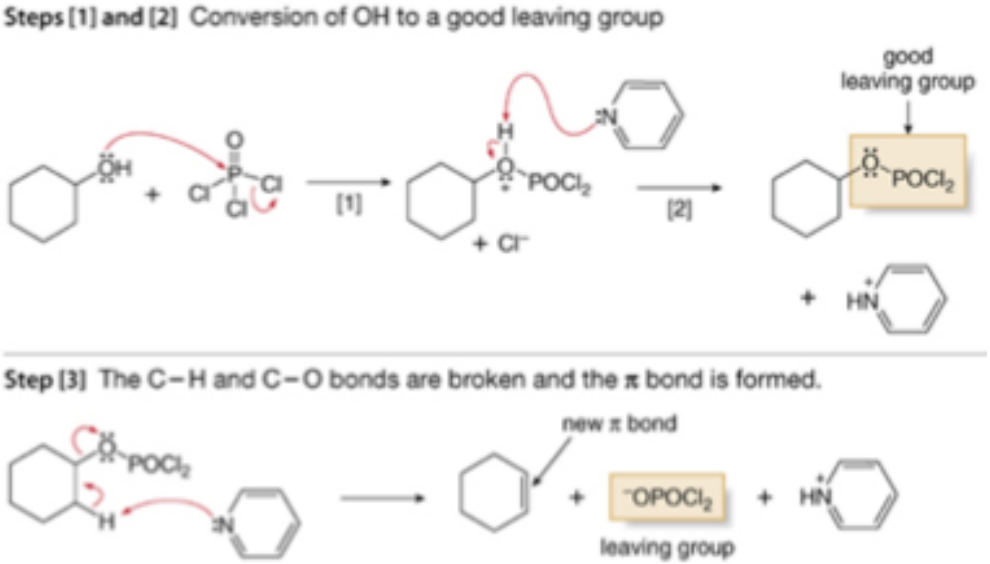
The reaction is endothermic.

Carbocation Rearrangements



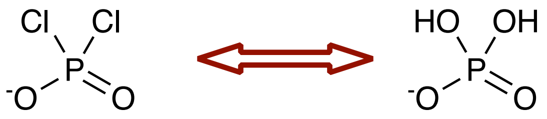
Dehydration of Alcohols with POCl3 and Pyridine

- Some organic compounds decompose in the presence of strong acid, so other methods have been developed to convert alcohols to alkenes.



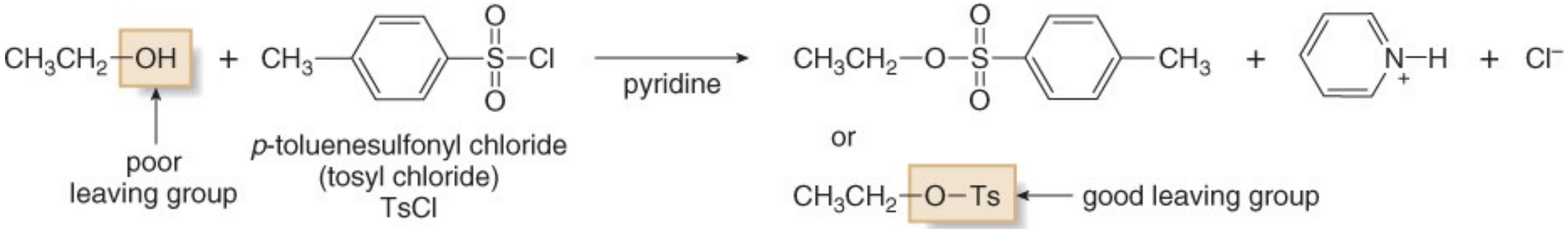
Steps [1] and [2] Conversion of OH to a good leaving group

Step [3] The C–H and C–O bonds are broken and the π bond is formed.



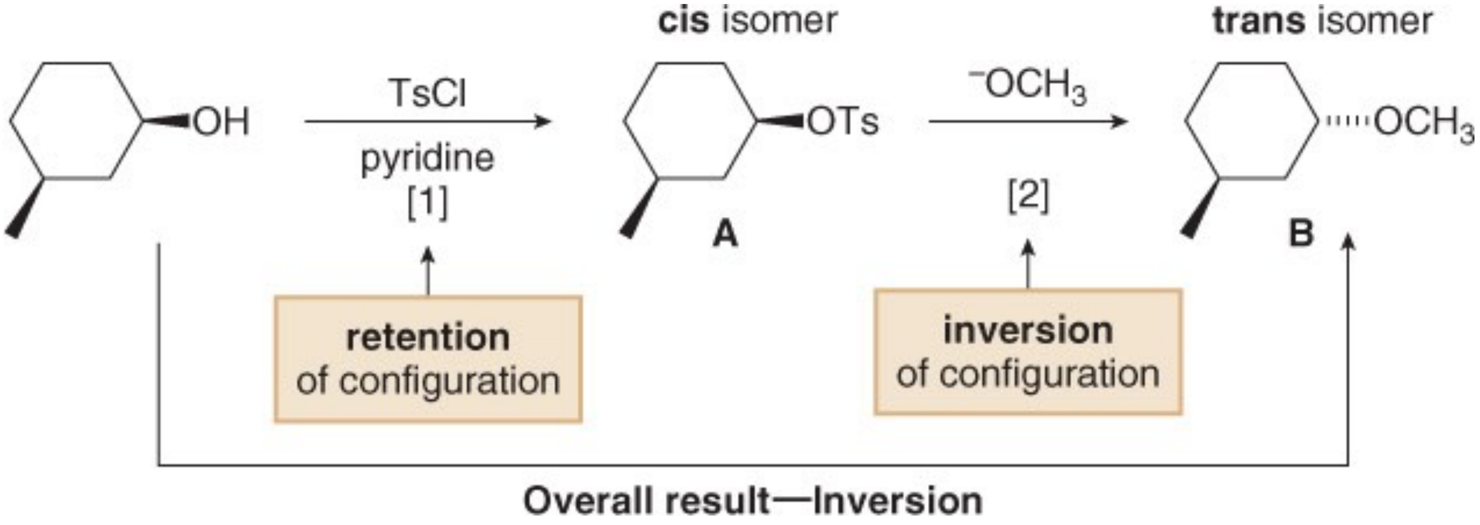
similar structure and stability

Tosylate—Another Good Leaving Group

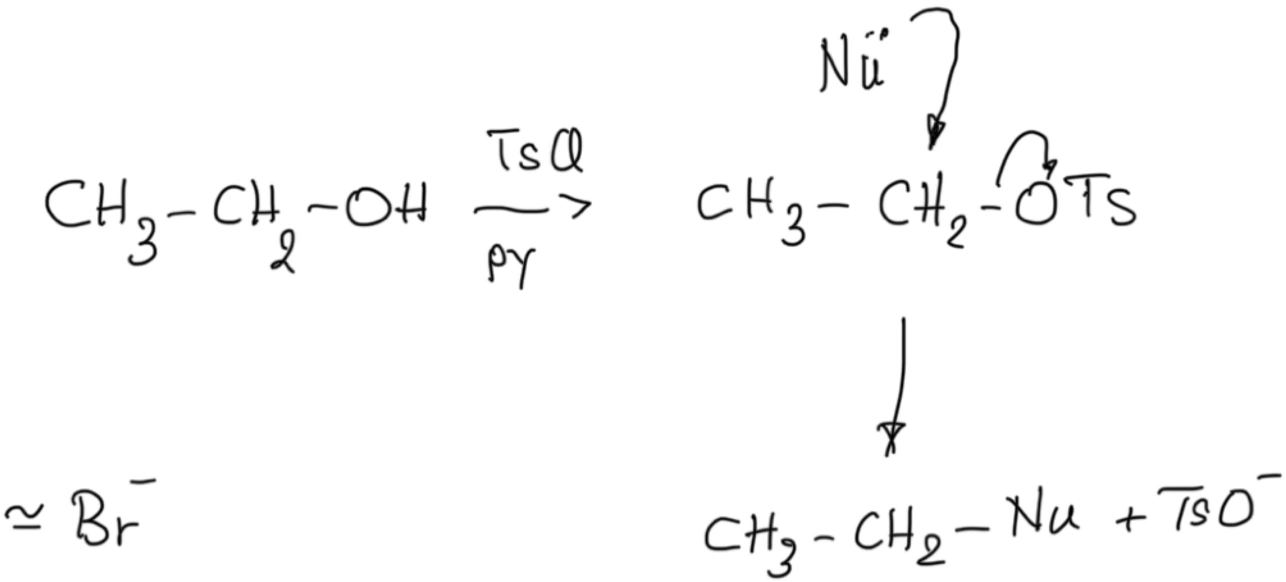


- Tosylate is a good leaving group because its conjugate acid, *p*-toluenesulfonic acid ($CH_3C_6H_4SO_3H$, TsOH) is a strong acid

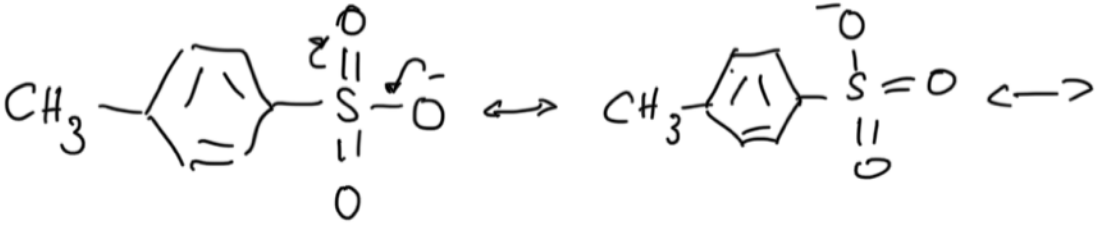
(pK_a = -7).



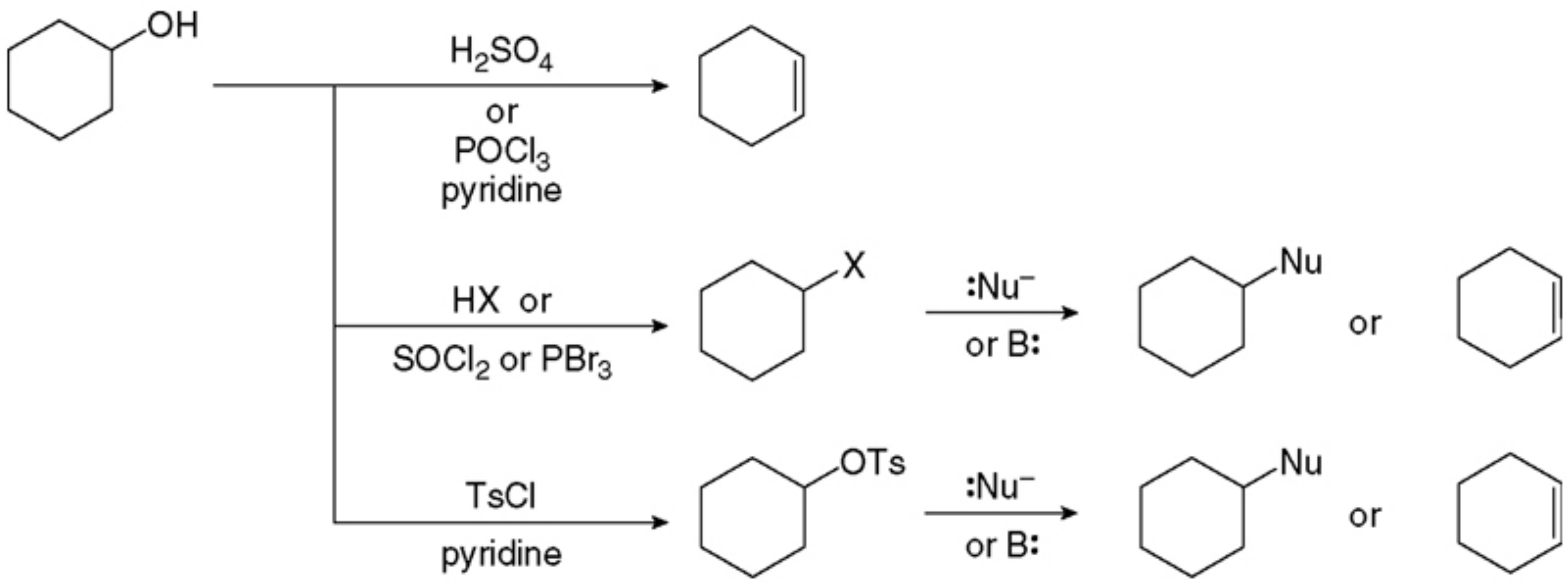
Tosylate—Another Good Leaving Group



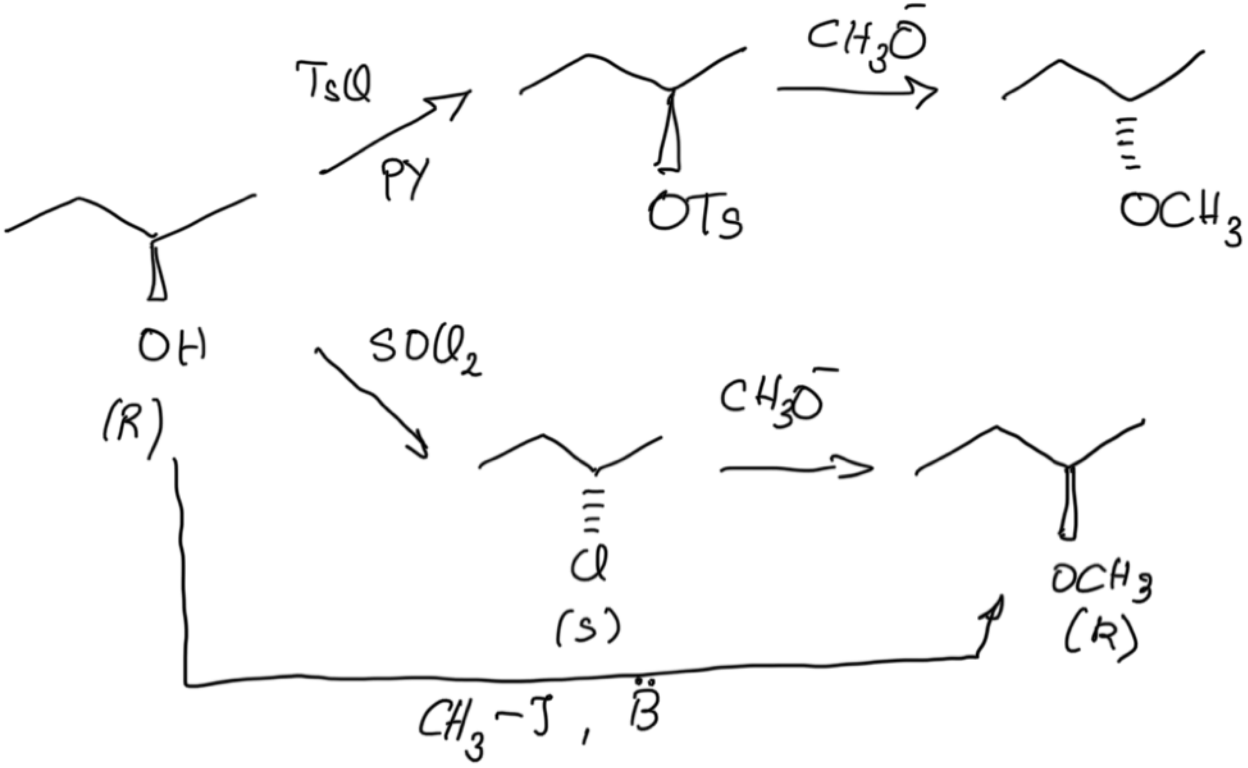
$TsO^- \simeq Br^-$



Nucleophilic substitution and β-elimination reactions of alcohols

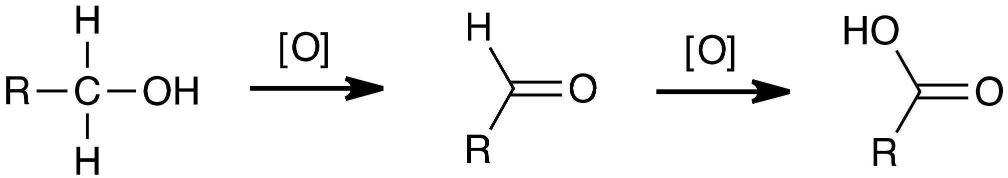


Nucleophilic substitutions of alcohols



Oxidation of Alcohols

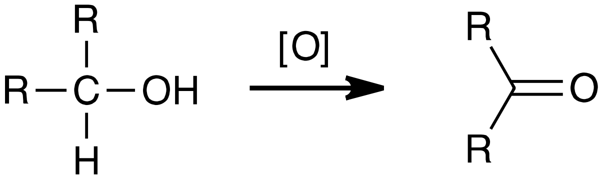
1° ALCOHOL



ALDEHYDE

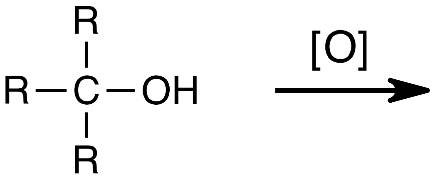
ACID

2° ALCOHOL



KETONE

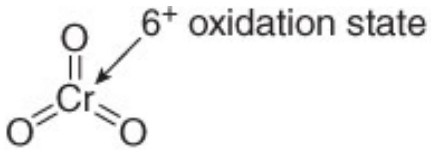
3° ALCOHOL



NO REACTION

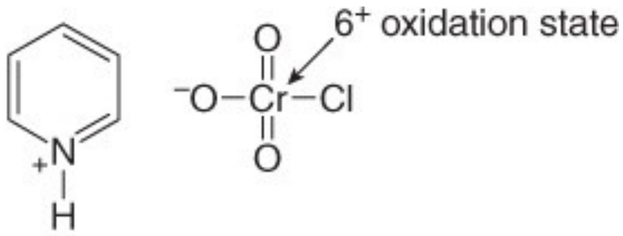
Oxidation of Alcohols

- The oxidation of alcohols to carbonyl compounds is typically carried out with Cr(VI) oxidants, which are reduced to Cr(III) products.
- CrO_3, $Na_2Cr_2O_7$, and $K_2Cr_2O_7$ are strong, nonselective oxidants used in aqueous acid ($H_2SO_4 + H_2O$).
- PCC is soluble in CH_2Cl_2 (dichloromethane) and can be used without strong acid present, making it a more selective, milder oxidant.



chromium(VI) oxide

CrO_3



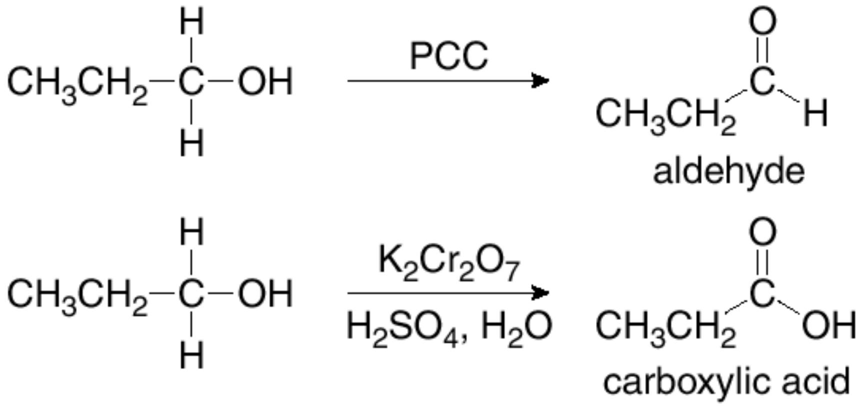
pyridinium chlorochromate

PCC

Oxidation of Alcohols

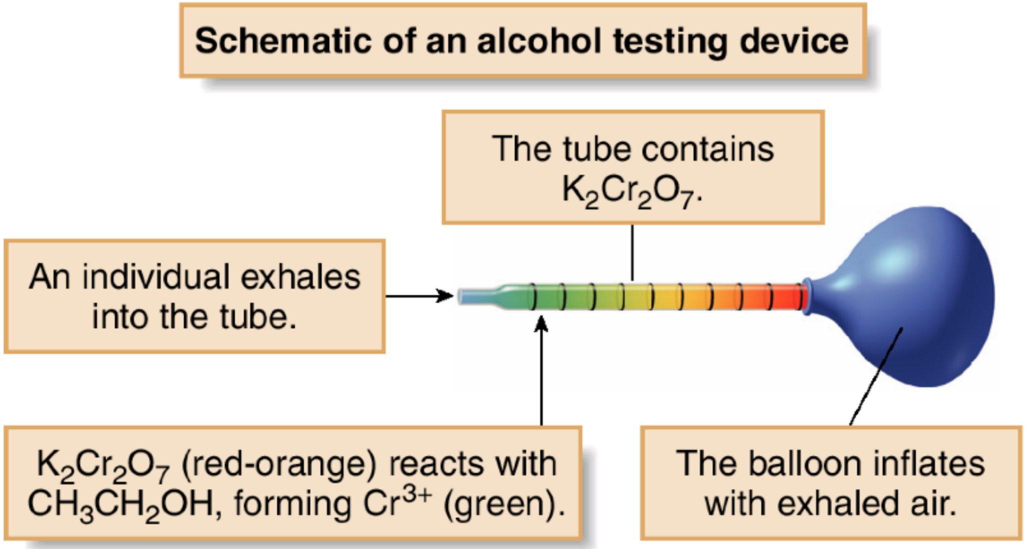
- 1° Alcohols are oxidized to aldehydes (RCHO) under mild reaction conditions—using PCC in CH_2Cl_2.
- 1° Alcohols are oxidized to carboxylic acids (RCOOH) under harsher reaction conditions: $Na_2Cr_2O_7$, $K_2Cr_2O_7$, or CrO_3 in the presence of H_2O and H_2SO_4.

1° Alcohols



The Alcohol Test

- The oxidation of CH_3CH_2OH with $K_2Cr_2O_7$ to form CH_3COOH and Cr^{3+} was the first available method for the routine testing of alcohol concentration in exhaled air. Some consumer products for alcohol screening are still based on this technology.



Schematic of an alcohol testing device

The tube contains $K_2Cr_2O_7$.

An individual exhales into the tube.

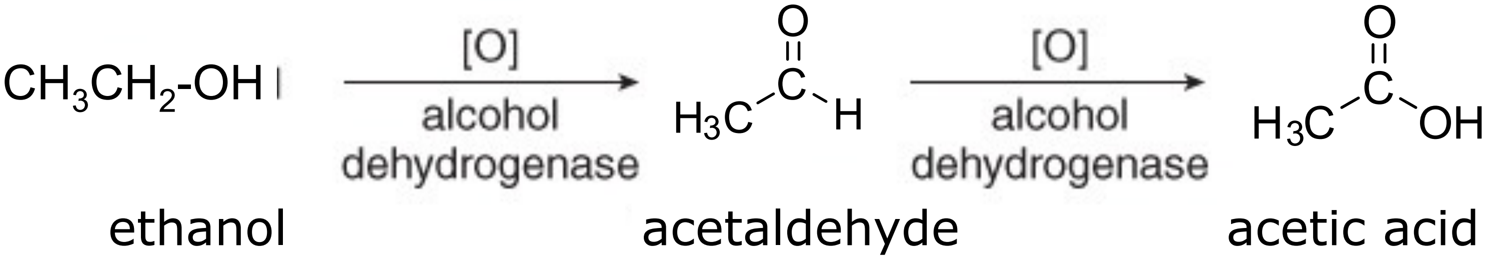
$K_2Cr_2O_7$ (red-orange) reacts with CH_3CH_2OH, forming Cr^{3+} (green).

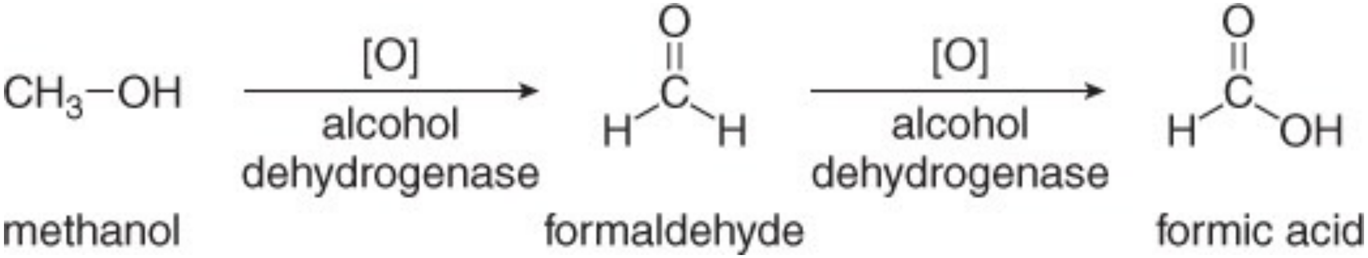
The balloon inflates with exhaled air.

Consumer product

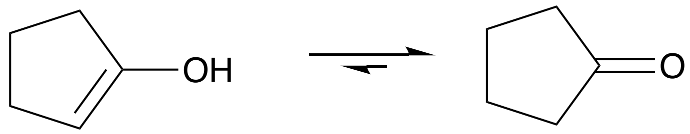
$K_2Cr_2O_7$

Ethanol Metabolism

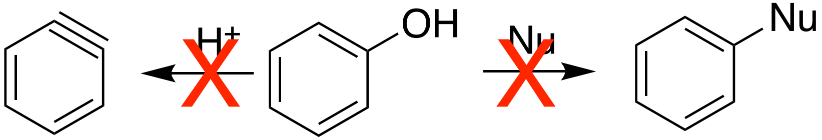




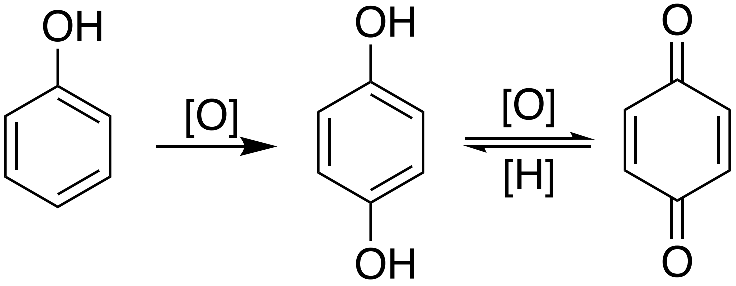
Phenols and Enols



Enols only exist in equilibrium with the more stable carbonyl compounds



Phenols do not give nucleophilic substitution nor elimination



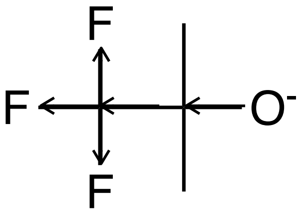
hydroquinone quinone

Phenol is oxidized by strong oxidizing agents. Hydroquinone is a common antioxidant

Acidity of Alcohols an Phenols

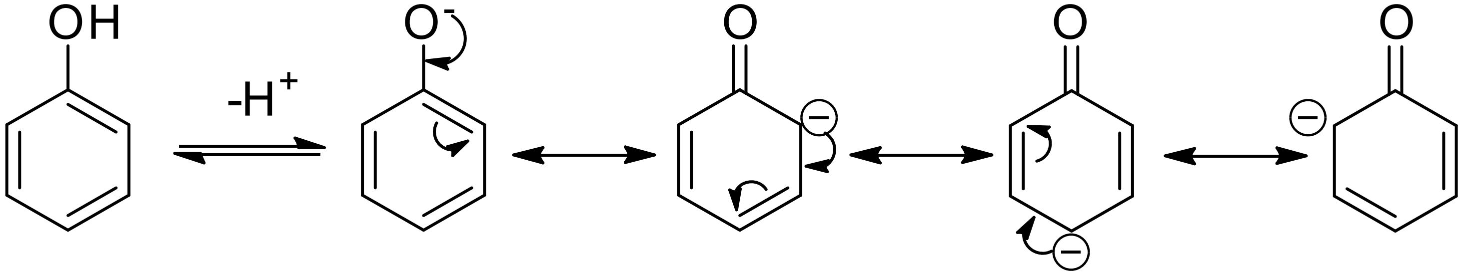
Compound	pK_a
CH_3CH_2OH	16.0
CF_3CH_2OH	12.4
C_6H_5OH	9.9
p-$NH_2C_6H_4OH$	10.5
p-$NO_2C_6H_4OH$	7.2

$CF_3CH_2O^-$: Inductively stabilized



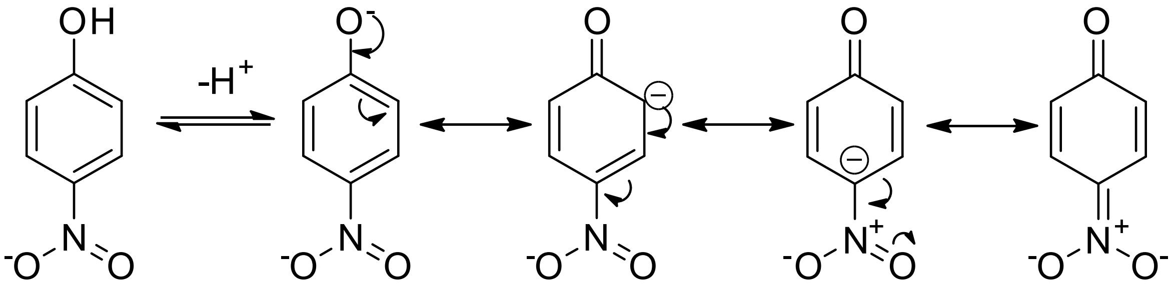
polarization of the C-F bond is transmitted along σ bonds and the negative charge is dispersed on several atoms

$C_6H_5O^-$: Resonance stabilized

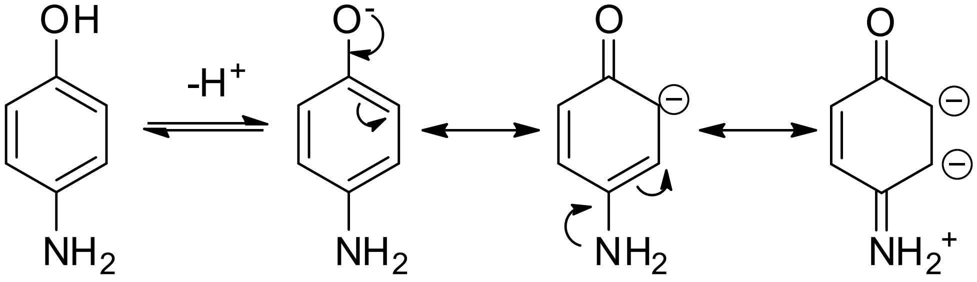


the negative charge is delocalized on the o- and p- positions of the aromatic ring

Substituent effects on acidity of phenols



Stabilized by delocalization



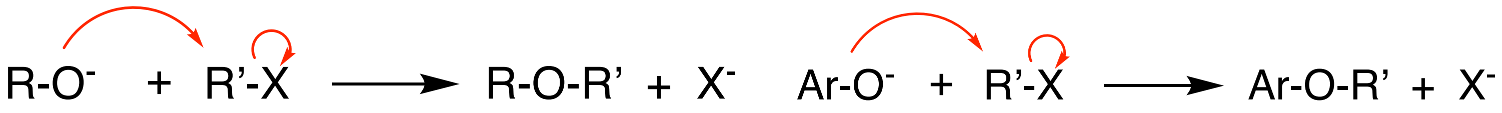
Destabilized by delocalization

Reactions of Alcohols
OH as Nucleophile

- Alcohols (R-OH) are weak nucleophiles; alcoxides ($R\text{-}O^-$) are strong nucleophiles.

- Phenols (Ar-OH) and phenoxides ($Ar\text{-}O^-$) are weaker nucleophiles than alcohols and alcoxides, respectively, because the Oxygen lone pair is delocalized on the ring.

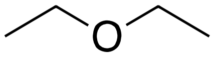
- Alcohols and phenols can be alkylated with alkyl halides in basic medium giving alkyl and aryl ethers.



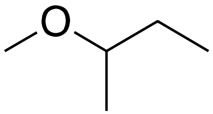
$$R\text{-}O^- + R'\text{-}X \longrightarrow R\text{-}O\text{-}R' + X^- \qquad Ar\text{-}O^- + R'\text{-}X \longrightarrow Ar\text{-}O\text{-}R' + X^-$$

Nomenclature of Ethers

- Common names:



diethyl ether

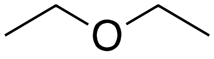


s-butyl methyl ether

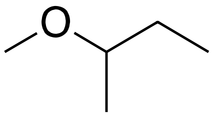
tetrahydrofuran

THF

- IUPAC names:



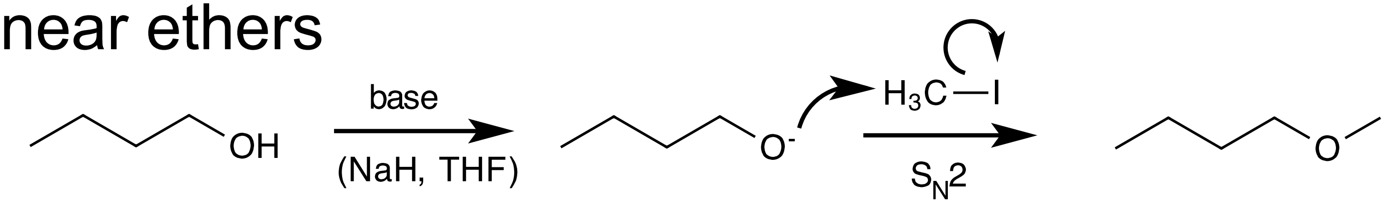
ethoxyethane



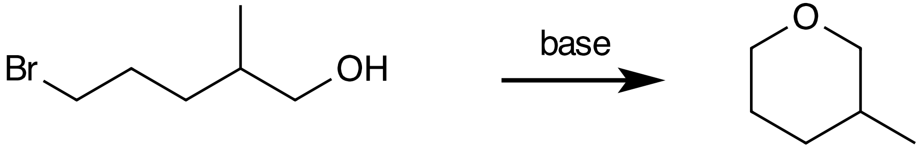
2-methoxybutane

Preparation of Ethers
Williamson synthesis

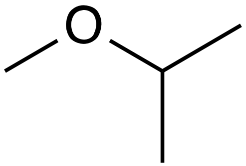
Linear ethers

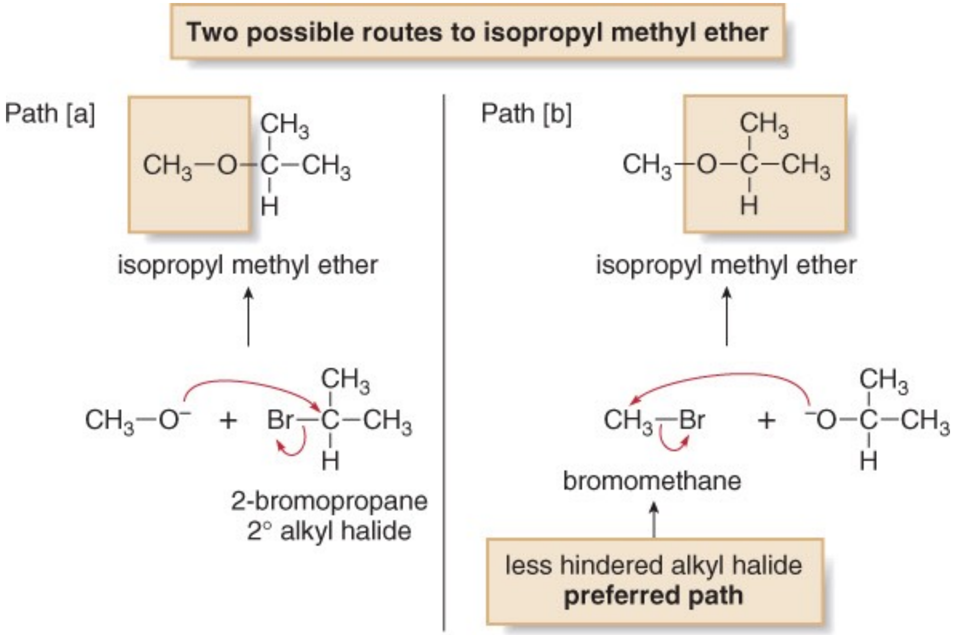


Cyclic ethers

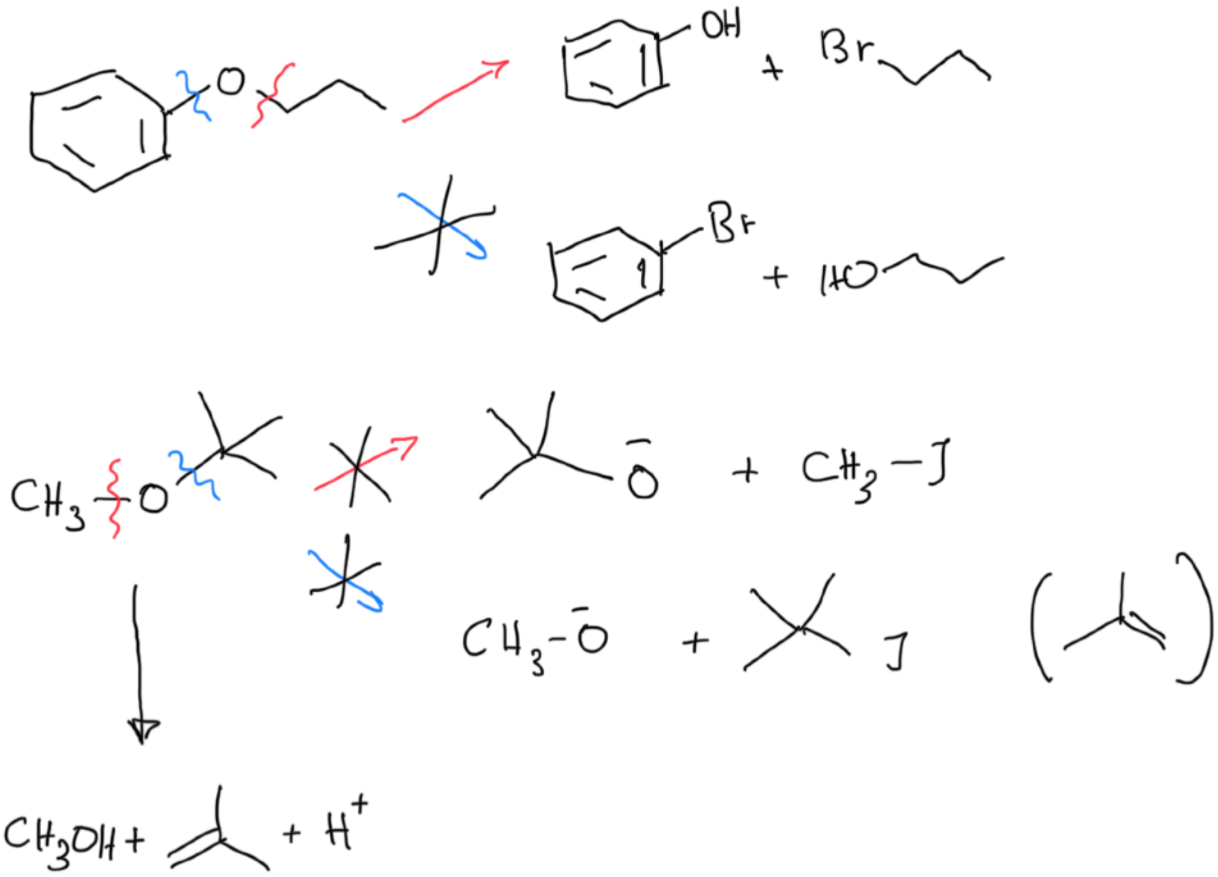


Preparation of Ethers
Williamson synthesis



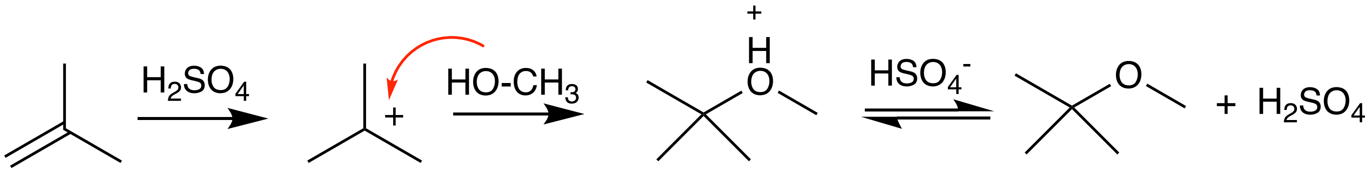


Preparation of Ethers
Williamson synthesis

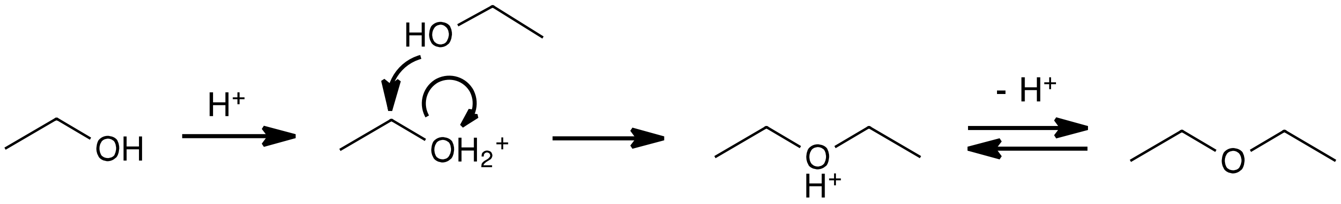


Preparation of Ethers

FROM ALKENES



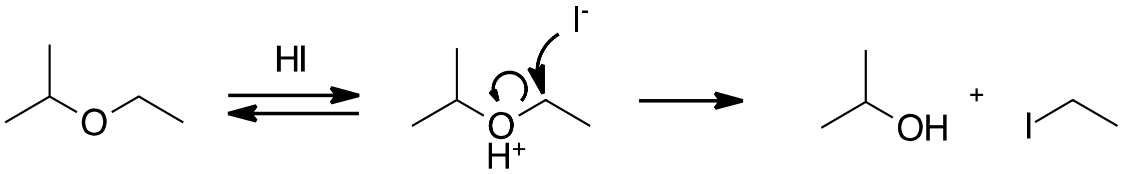
FROM ALCOHOLS (for symmetrical ethers)



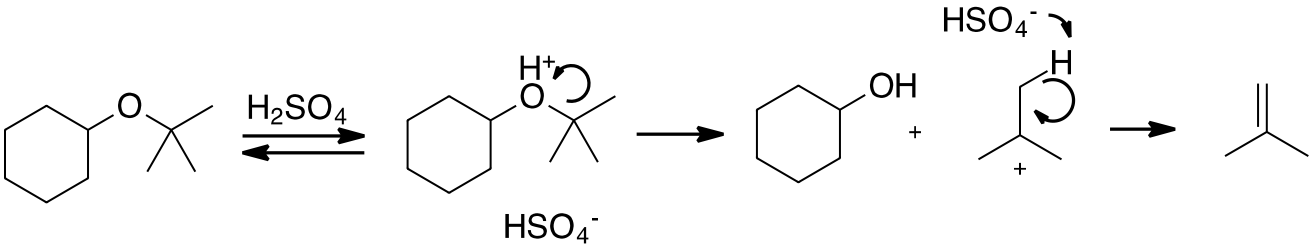
Reaction of Ethers with Strong Acid

- The ether bond is cleaved with strong acids to give an alcohol and a halide or an alkene

S_N2



$S_N1/E1$



Structure of Epoxides

- Epoxides are ethers having the oxygen atom in a three-membered ring. Epoxides are also called oxiranes.

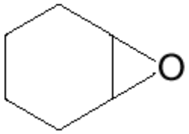
epoxide or **oxirane**

An epoxide is a special type of ether.

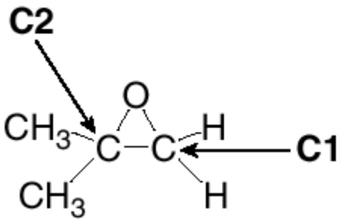
- The C—O—C bond angle for an epoxide must be 60°, a considerable deviation from the tetrahedral bond angle of 109.5°. Thus, epoxides have angle strain, making them more reactive than other ethers.

Nomenclature of Epoxides

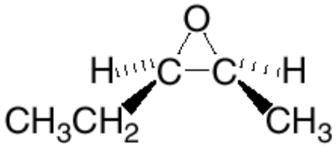
- Epoxyalkanes:



1,2-epoxycyclohexane



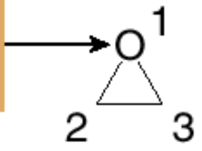
1,2-epoxy-2-methylpropane



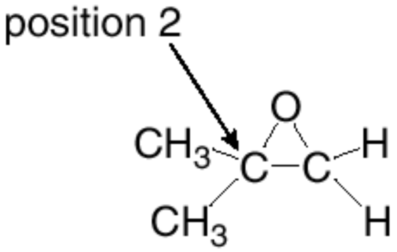
***cis*-2,3-epoxypentane**

- Oxiranes:

Number the ring beginning at the O atom.

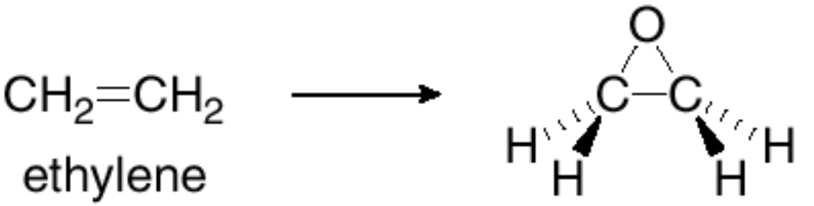


oxirane



2,2-dimethyloxirane

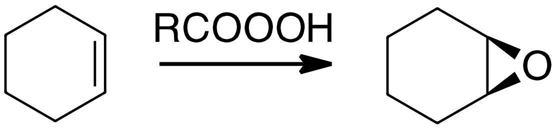
- Alkene oxides:



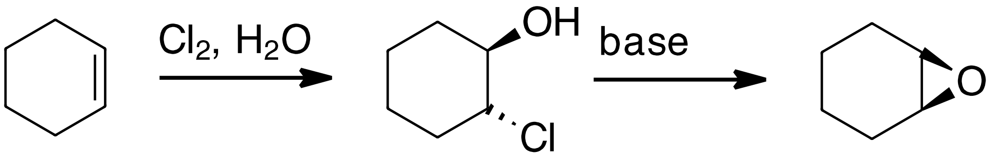
ethylene oxide
oxirane

Preparation of Epoxides

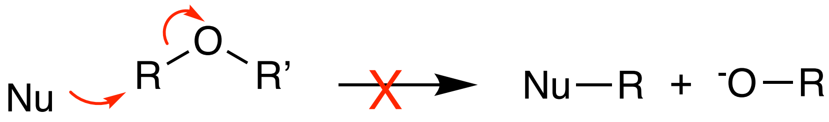
epoxidation of alkenes



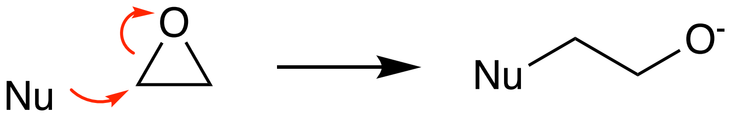
cyclization of halohydrins



Reactions of Epoxides



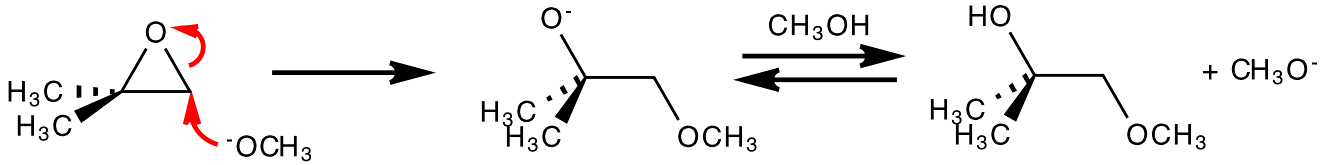
Ethers do not react with nucleophiles



strain is released

Epoxides are very reactive with nucleophiles

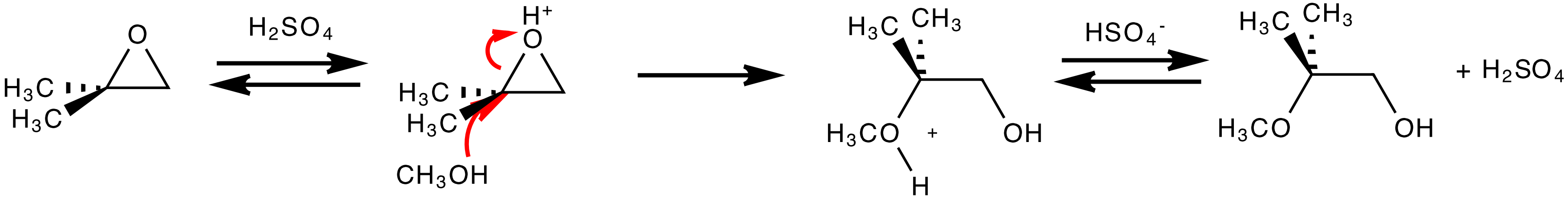
Nucleophilic attack opens the strained three-membered ring with an S_N2 mechanism, making it a favourable process even with a poor leaving group.



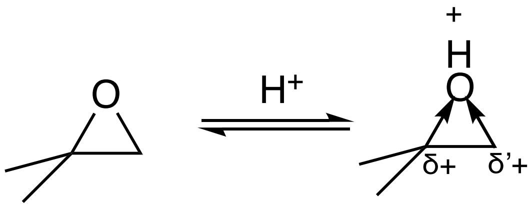
Backside attack on the less substituted carbon: steric control

Reactions of Epoxides

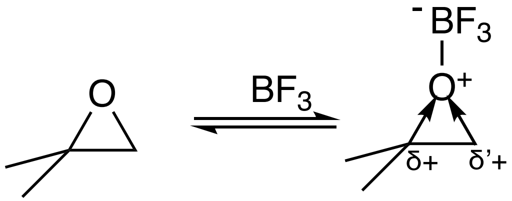
Acids catalyse epoxide ring opening by protonating the oxygen:



Backside attack on the more substituted carbon: electronic control



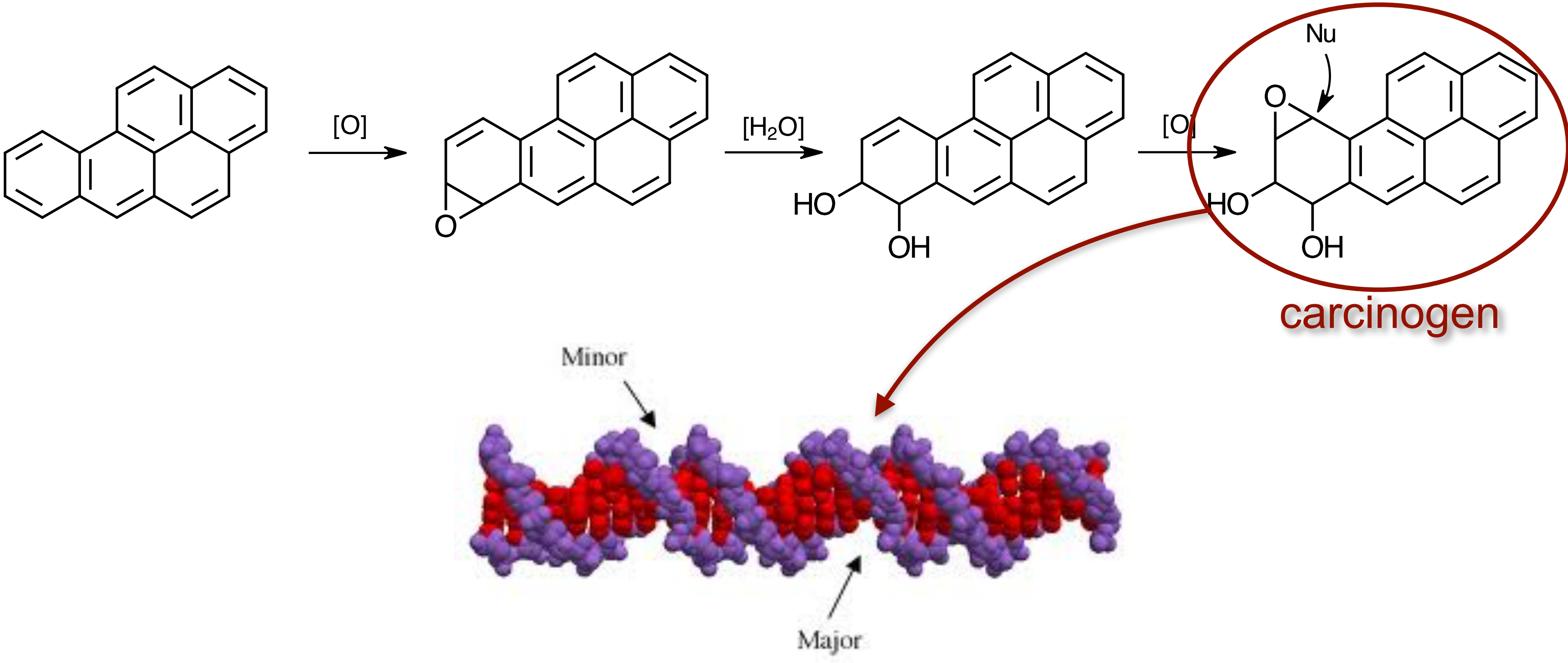
also with Lewis acids



δ+ > δ′+ : the partial charge is higher on the more substituted carbon

Reactions of Epoxides

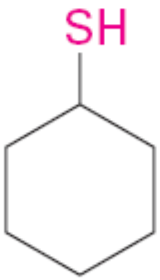
- When polyaromatic hydrocarbons are inhaled or ingested, they are oxidized in the liver to species that often contain a highly reactive epoxide ring.
- The strained three-membered ring reacts readily with biological nucleophiles such as DNA or enzymes, leading to ring-opened products that often disrupt cell function, causing cancer or cell death.



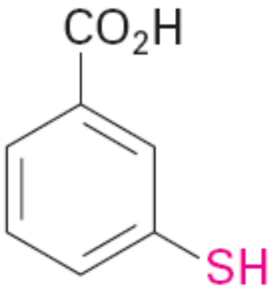
Thiols and Sulfides

CH_3CH_2SH

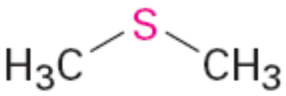
ethanethiol



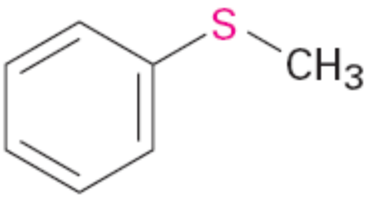
ciclohexanethiol



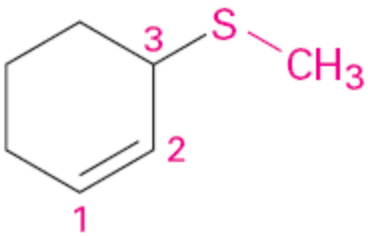
3-mercapto
benzoic acid



dimethylsulfide

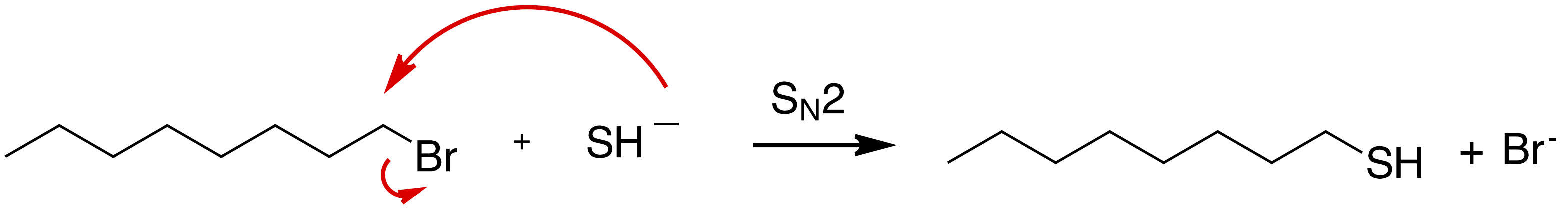


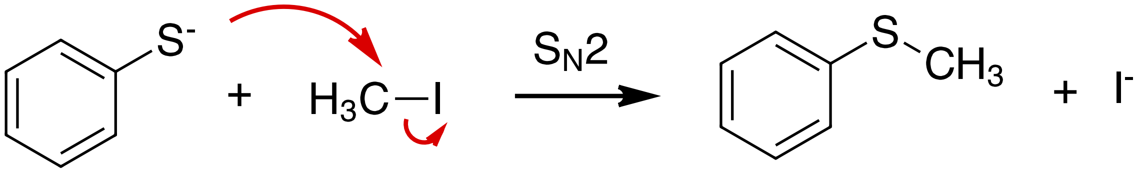
methyl phenyl
sulfide



3-(methylmercapto)
cyclohexene

Thiols and Sulfides: Synthesis

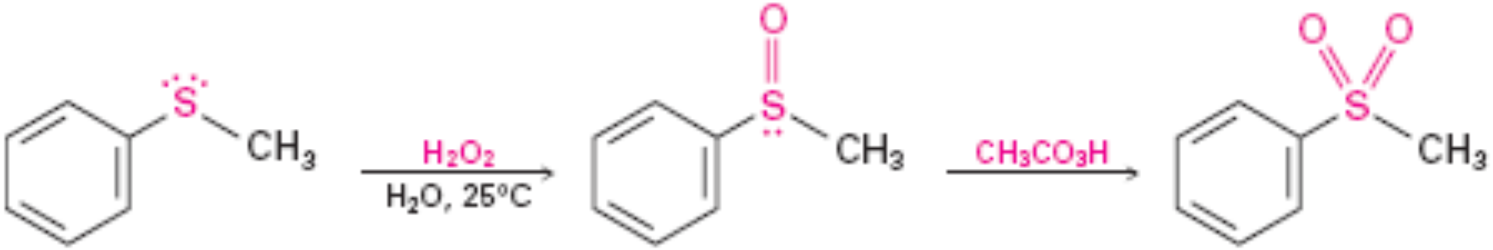




Thiols and Sulfides: Oxidation

$$2\ R{-}SH \underset{Zn,\ H^+}{\overset{I_2}{\rightleftharpoons}} R{-}S{-}S{-}R + 2\ HI$$

thiol disulfide



sulfide sulfoxide sulfone