Chapter 11

Alcohols & Ethers

Created by
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About The Authors

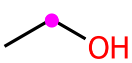
These Powerpoint Lecture Slides were created and prepared by Professor William Tam and his wife Dr. Phillis Chang.

Professor William Tam received his B.Sc. at the University of Hong Kong in 1990 and his Ph.D. at the University of Toronto (Canada) in 1995. He was an NSERC postdoctoral fellow at the Imperial College (UK) and at Harvard University (USA). He joined the Department of Chemistry at the University of Guelph (Ontario, Canada) in 1998 and is currently a Full Professor and Associate Chair in the department. Professor Tam has received several awards in research and teaching, and according to *Essential Science Indicators*, he is currently ranked as the Top 1% most cited Chemists worldwide. He has published four books and over 80 scientific papers in top international journals such as *J. Am. Chem. Soc., Angew. Chem., Org. Lett.,* and *J. Org. Chem.*

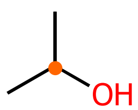
Dr. Phillis Chang received her B.Sc. at New York University (USA) in 1994, her M.Sc. and Ph.D. in 1997 and 2001 at the University of Guelph (Canada). She lives in Guelph with her husband, William, and their son, Matthew.

1. Structure & Nomenclature

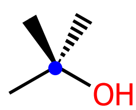
- Alcohols have a hydroxyl (–OH) group bonded to a *saturated* carbon atom (sp^3 hybridized)



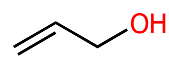
1°
Ethanol



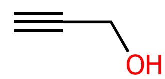
2°
2-Propanol (isopropyl alcohol)



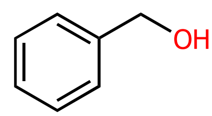
3°
2-Methyl-2-propanol (*tert*-butyl alcohol)



2-Propenol (allyl alcohol)

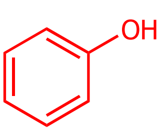


2-Propynol (propargyl alcohol)

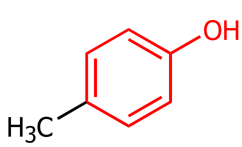


Benzyl alcohol

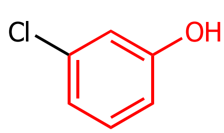
- Phenols
  - Compounds that have a hydroxyl group attached *directly* to a benzene ring



Phenol

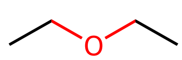


4-Methylphenol

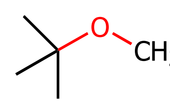


2-Chlorophenol

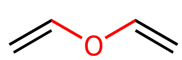
- Ethers
  - The oxygen atom of an ether is bonded to two carbon atoms



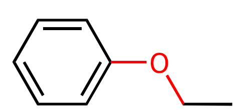
Diethyl ether



tert-Butyl methyl ether



Divinyl ether

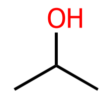


Ethyl phenyl ether

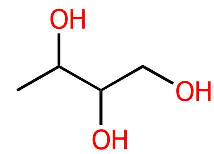
1A. Nomenclature of Alcohols

- Rules of naming alcohols
  - Identify the longest carbon chain that includes the carbon to which the –OH group is attached
  - Use the lowest number for the carbon to which the –OH group is attached
  - Alcohol as parent (suffix)
    - ending with "ol"

- Examples

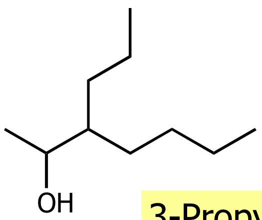


2-Propanol
(isopropyl alcohol)

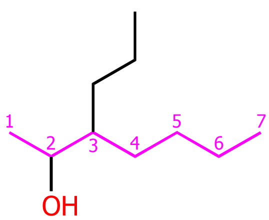


1,2,3-Butanetriol

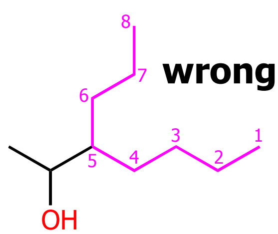
- Example



3-Propyl-2-heptanol



or

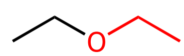


wrong

1B. Nomenclature of Ethers

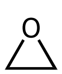
- Rules of naming ethers
  - Similar to those with alkyl halides
    - $CH_3O–$ Methoxy
    - $CH_3CH_2O–$ Ethoxy

- Example

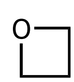


Ethoxyethane
(diethyl ether)

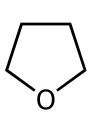
- Cyclic ethers



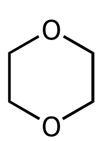
Oxacyclopropane
or oxirane
(ethylene oxide)



Oxacyclobutane
or oxetane



Oxacyclopentane
(tetrahydrofuran or THF)

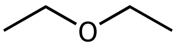


1,4-Dioxacyclohexane
(1,4-dioxane)

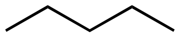
2. Physical Properties of Alcohols and Ethers

- Ethers have boiling points that are roughly comparable with those of hydrocarbons of the same molecular weight (MW)
- Alcohols have much higher boiling points than comparable ethers or hydrocarbons

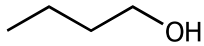
❖ For example



Diethyl ether
(MW = 74)
b.p. = 34.6°C



Pentane
(MW = 72)
b.p. = 36°C

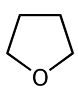


1-Butanol
(MW = 74)
b.p. = 117.7°C

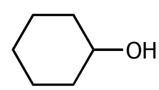
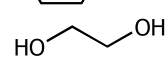
❖ Alcohol molecules can associate with each other through hydrogen bonding, whereas those of ethers and hydrocarbons cannot

❖ Water solubility of ethers and alcohols
- Both ethers and alcohols are able to form hydrogen bonds with water
- Ethers have solubilities in water that are similar to those of alcohols of the same molecular weight and that are very different from those of hydrocarbons
- The solubility of alcohols in water gradually decreases as the hydrocarbon portion of the molecule lengthens; long-chain alcohols are more "alkane-like" and are, therefore, less like water

❖ Physical Properties of Ethers

Name	Formula	mp (°C)	bp (°C) (1 atm)
Dimethyl ether	CH_3OCH_3	-138	-24.9
Diethyl ether	$CH_3CH_2OCH_2CH_3$	-116	34.6
Diisopropyl ether	$(CH_3)_2CHOCH(CH_3)_2$	-86	68
1,2-Dimethoxyethane (DME)	$CH_3OCH_2CH_2OCH_3$	-68	83
Oxirane		-112	12
Tetrahydrofuran (THF)		-108	65.4

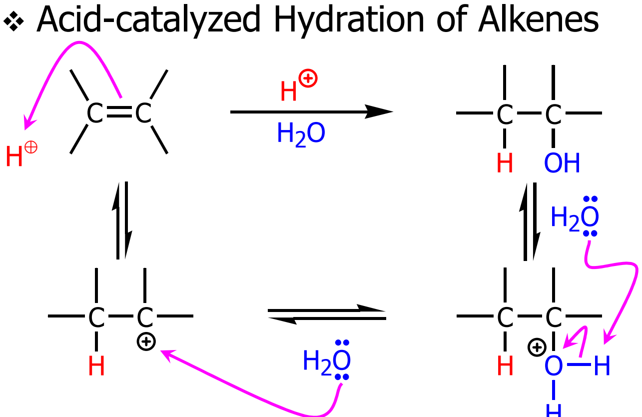
❖ Physical Properties of Alcohols

Name	Formula	mp (°C)	bp (°C) (1 atm)	*
Methanol	CH_3OH	-97	64.7	inf.
Ethanol	CH_3CH_2OH	-117	78.3	inf.
Isopropyl alcohol	$CH_3CH(OH)CH_3$	-88	82.3	inf.
tert-Butyl alcohol	$(CH_3)_3COH$	25	82.5	inf.
Hexyl alcohol	$CH_3(CH_2)_4CH_2OH$	-52	156.5	0.6
Cyclohexanol		24	161.5	3.6
Ethylene glycol		-12.6	197	inf.

* Water solubility (g/100 mL H_2O)

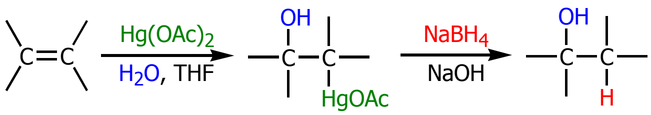
4. Synthesis of Alcohols from Alkenes

❖ Acid-catalyzed Hydration of Alkenes



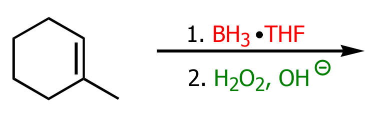
❖ Acid-Catalyzed Hydration of Alkenes
- Markovnikov regioselectivity
- Free carbocation intermediate
- Rearrangement of carbocation possible

❖ Oxymercuration–Demercuration



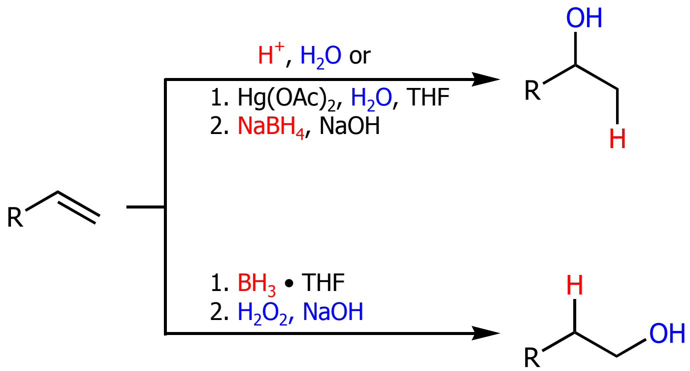
- Markovnikov regioselectivity
- Anti stereoselectivity
- Generally takes place without the complication of rearrangements
- Mechanism
  - ♦ Discussed in Section 8.6

❖ Hydroboration–Oxidation



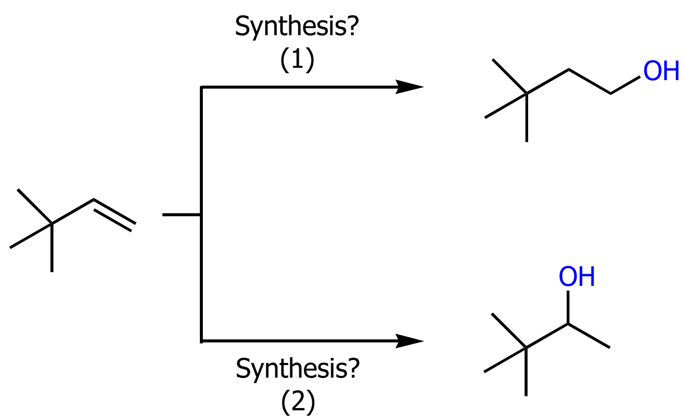
- Anti-Markovnikov regioselectivity
- Syn-stereoselectivity
- Mechanism
  - ♦ Discussed in Section 8.7

Markovnikov regioselectivity

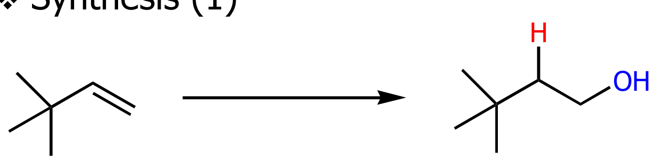


Anti-Markovnikov regioselectivity

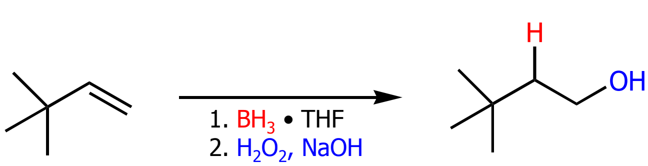
❖ Example



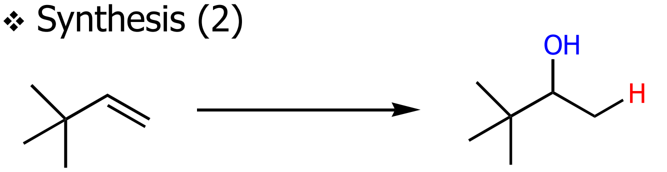
❖ Synthesis (1)



- Need anti-Markovnikov addition of H–OH
- Use hydroboration-oxidation

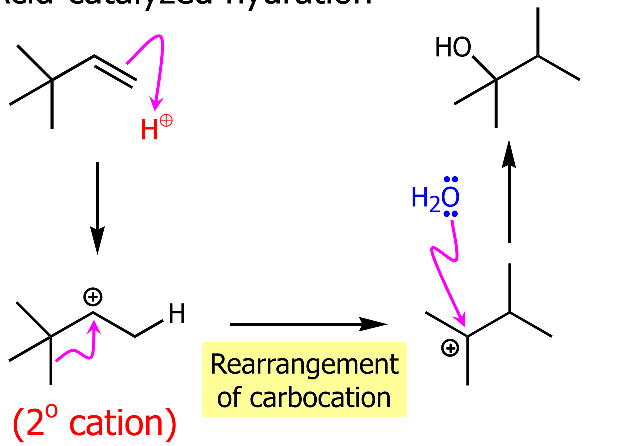


❖ Synthesis (2)

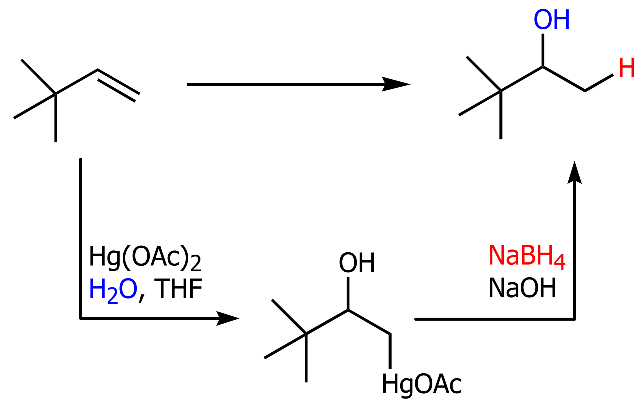


- Need Markovnikov addition of H–OH
- Use either
  - ♦ acid-catalyzed hydration or
  - ♦ oxymercuration-demercuration
- Acid-catalyzed hydration is **NOT** desired due to *rearrangement of carbocation*

❖ Acid-catalyzed hydration

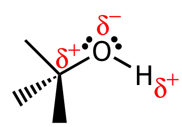


❖ Oxymercuration-demercuration



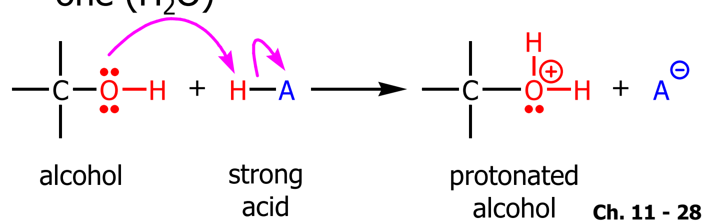
5. Reactions of Alcohols

❖ The reactions of alcohols have mainly to do with the following
- The oxygen atom of the –OH group is nucleophilic and weakly basic
- The hydrogen atom of the –OH group is weakly acidic
- The –OH group can be converted to a leaving group so as to allow substitution or elimination reactions

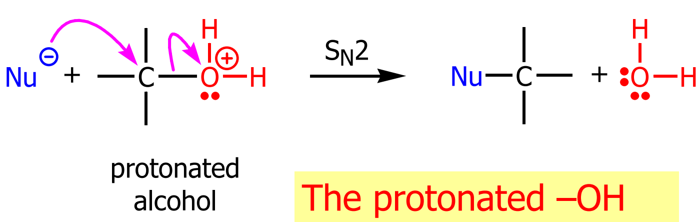


C–O & O–H bonds of an alcohol are polarized

❖ Protonation of the alcohol converts a poor leaving group ($OH^{\ominus}$) into a good one (H_2O)



❖ Once the alcohol is protonated substitution reactions become possible



The protonated –OH group is a good leaving group (H_2O)

6. Alcohols as Acids

❖ Alcohols have acidities similar to that of water

p*K*a Values for Some Weak Acids

Acid	pK_a
CH_3OH	15.5
H_2O	15.74
CH_3CH_2OH	15.9
$(CH_3)_3COH$	18.0

- Relative Acidity

H$_2$O & alcohols are the strongest acids in this series

$H_2O > ROH > RC{\equiv}CH > H_2 > NH_3 > RH$

← Increasing acidity

- Relative Basicity

$OH^{\ominus}$ is the weakest acid in this series

$R^{\ominus} > NH_2^{\ominus} > H^{\ominus} > RC{\equiv}C^{\ominus} > RO^{\ominus} > HO^{\ominus}$

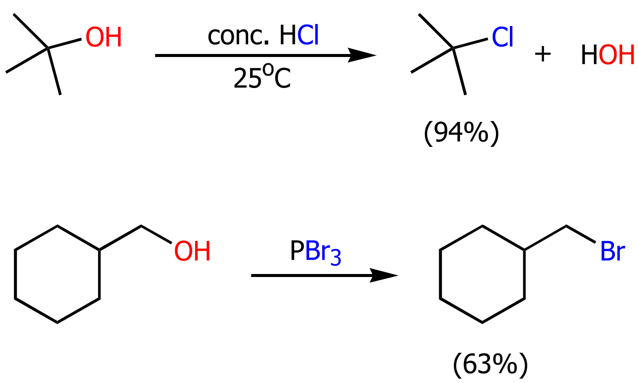
← Increasing basicity

7. Conversion of Alcohols into Alkyl Halides

$$R{-}OH \longrightarrow R{-}X$$

- HX (X = Cl, Br, I)
- PBr_3
- $SOCl_2$

- Examples



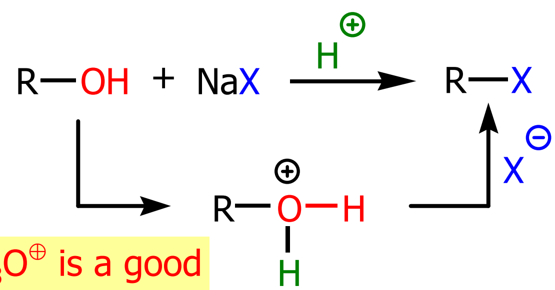
8. Alkyl Halides from the Reaction of Alcohols with Hydrogen Halides

$$R{-}OH + HX \longrightarrow R{-}X + H_2O$$

- The order of reactivity of alcohols
  - 3° > 2° > 1° < methyl
- The order of reactivity of the hydrogen halides
  - HI > HBr > HCl (HF is generally unreactive)

$$R{-}OH + NaX \longrightarrow \text{No Reaction!}$$

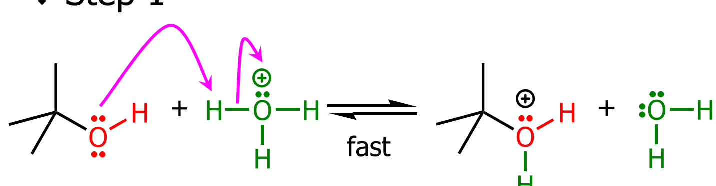
$OH^{\ominus}$ is a poor leaving group



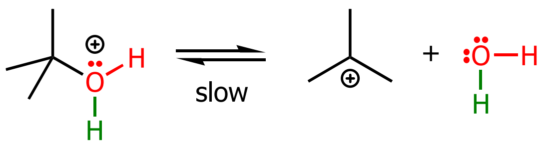
$H_3O^{\oplus}$ is a good leaving group

8A. Mechanisms of the Reactions of Alcohols with HX

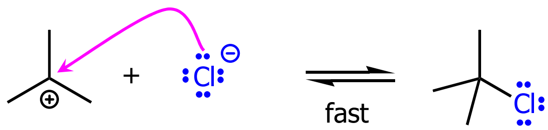
- Secondary, tertiary, allylic, and benzylic alcohols appear to react by a mechanism that involves the formation of a carbocation
- Step 1



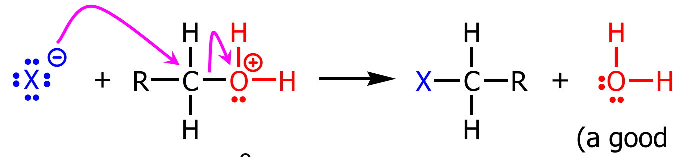
- Step 2



- Step 3



- Primary alcohols and methanol react to form alkyl halides under acidic conditions by an S_N2 mechanism



protonated 1° alcohol or methanol

(a good leaving group)

9. Alkyl Halides from the Reaction of Alcohols with PBr_3 or $SOCl_2$

- Reaction of alcohols with PBr_3

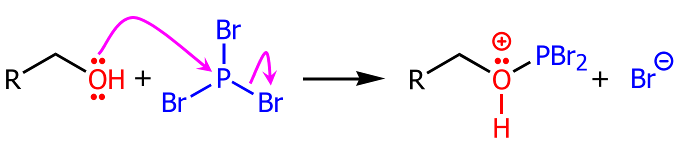
$$3\ R\text{—}OH + PBr_3 \longrightarrow R\text{—}Br + H_3PO_3$$

(1° or 2°)

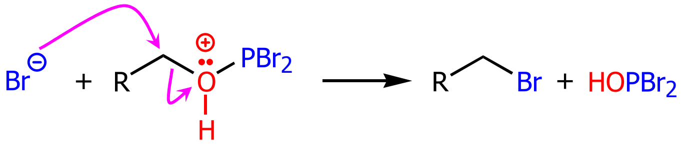
- The reaction does not involve the formation of a carbocation and *usually occurs without rearrangement* of the carbon skeleton (especially if the temperature is kept below 0°C)

- Reaction of alcohols with PBr_3
  - Phosphorus tribromide is often preferred as a reagent for the transformation of an alcohol to the corresponding alkyl bromide

- Mechanism



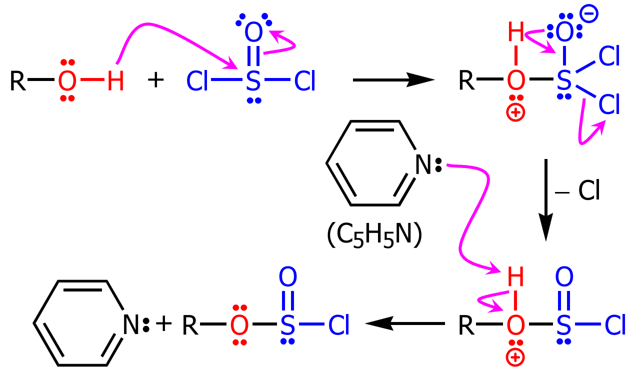
protonated alkyl dibromophosphite



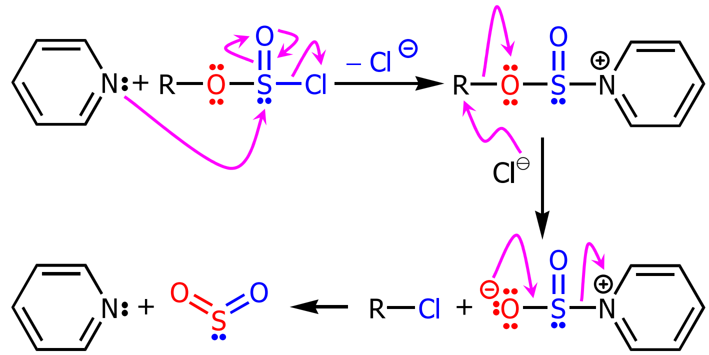
a good leaving group

- Reaction of alcohols with $SOCl_2$
  - $SOCl_2$ converts 1° and 2° alcohols to alkyl chlorides
  - As with PBr_3, the reaction does not involve the formation of a carbocation and *usually occurs without rearrangement* of the carbon skeleton (especially if the temperature is kept below 0°C)
  - Pyridine (C_5H_5N) is often included to promote the reaction

❖ Mechanism

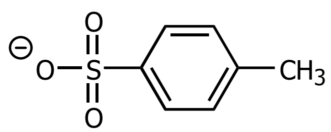


❖ Mechanism



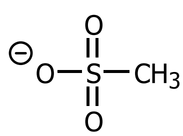
10. Tosylates, Mesylates, & Triflates: Leaving Group Derivatives of Alcohols

⊖OTs =



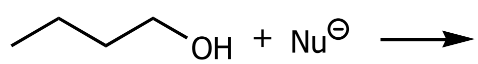
(Tosylate)

⊖OMs =



(Mesylate)

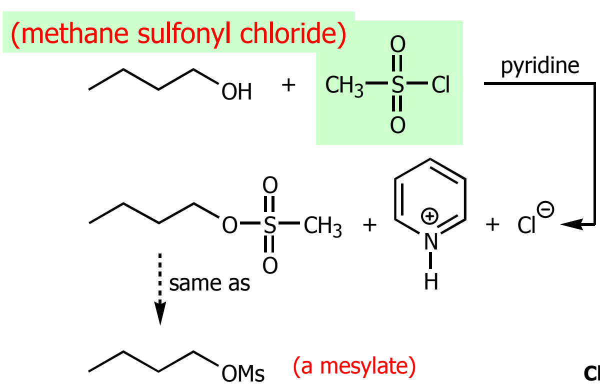
❖ Direct displacement of the –OH group with a nucleophile via an S_N2 reaction is not possible since $OH^{\ominus}$ is a very poor leaving group



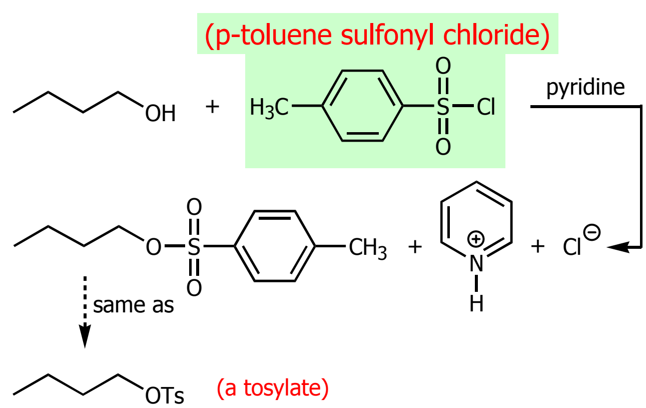
No Reaction!

❖ Thus we need to convert the $OH^{\ominus}$ to a better leaving group first

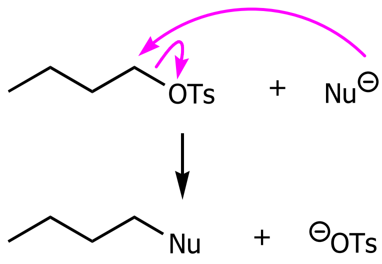
❖ Mesylates (OMs) and Tosylates (OTs) are good leaving groups and they can be prepared easily from an alcohol



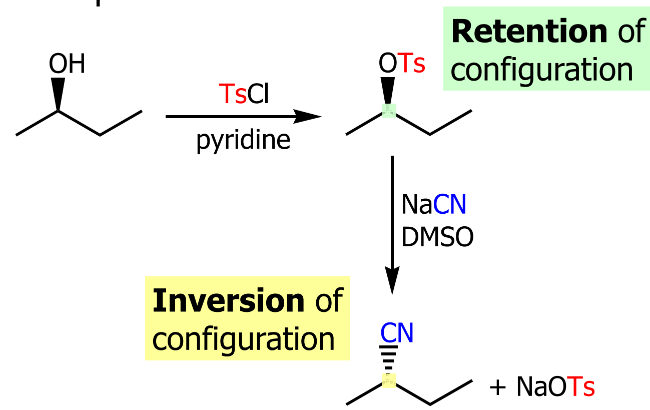
❖ Preparation of Tosylates (OTs) from an alcohol



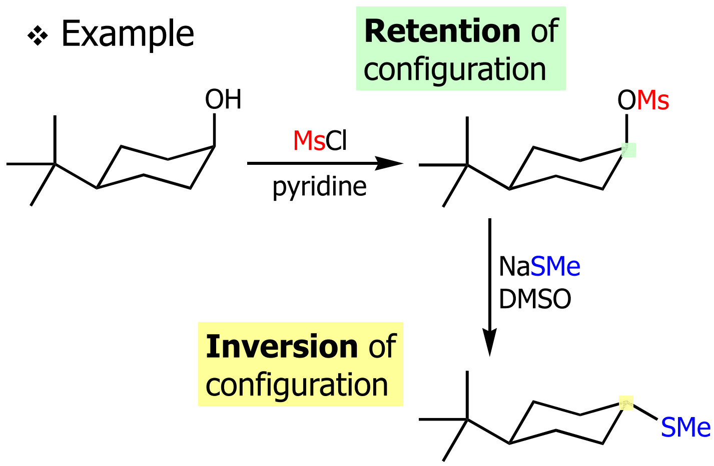
- S_N2 displacement of the mesylate or tosylate with a nucleophile is possible



- Example

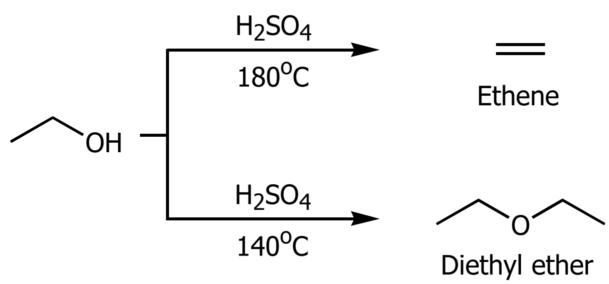


- Example

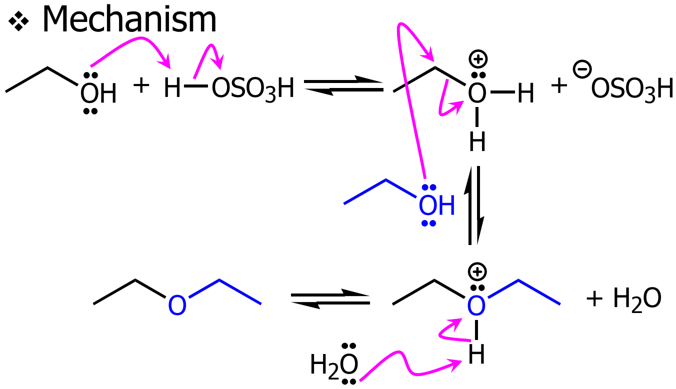


11. Synthesis of Ethers

11A. Ethers by Intermolecular Dehydration of Alcohols

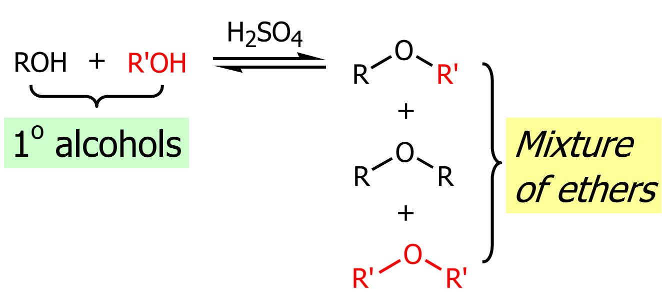


- Mechanism

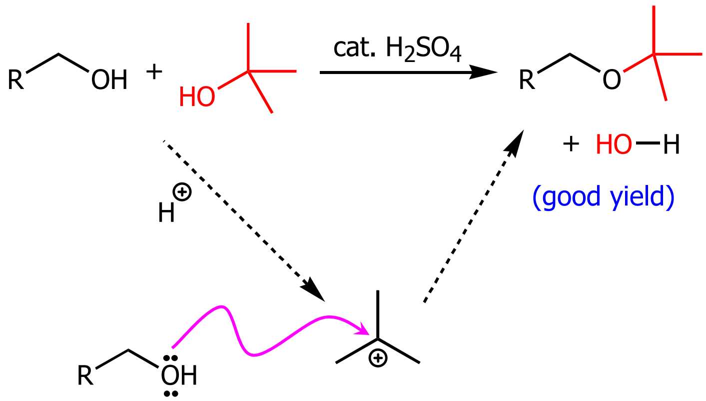


- This method is only good for synthesis of *symmetrical ethers*

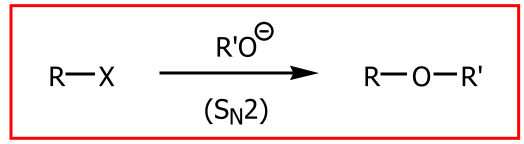
- For unsymmetrical ethers



❖ Exception

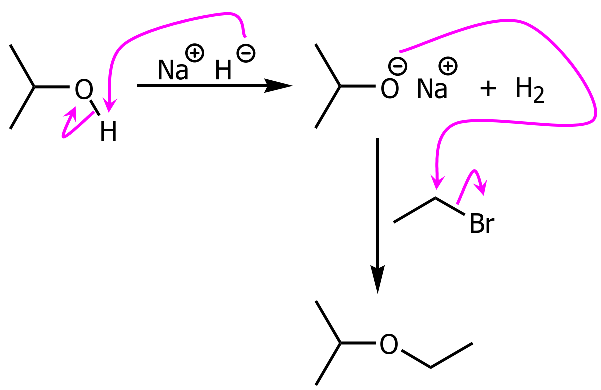


11B. The Williamson Synthesis of Ethers

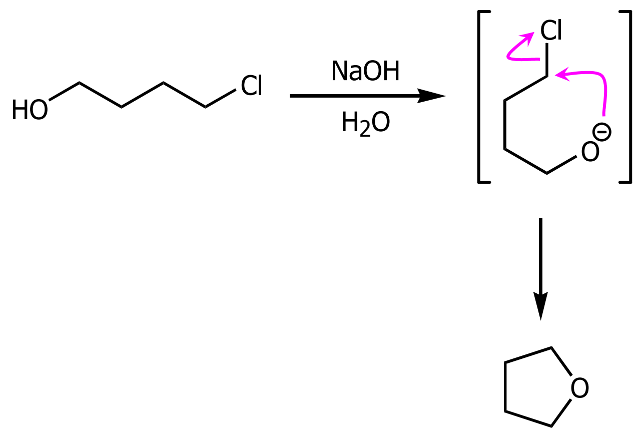


❖ Via S_N2 reaction, thus R is limited to 1° (but R' can be 1°, 2° or 3°)

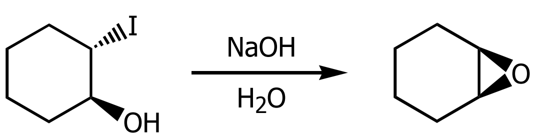
❖ Example 1



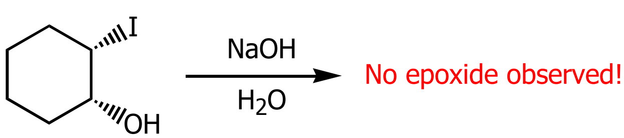
❖ Example 2



❖ Example 3

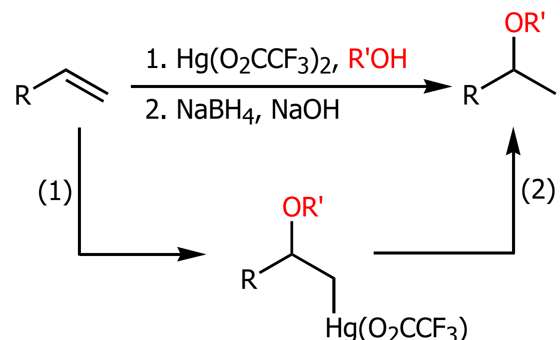


❖ However

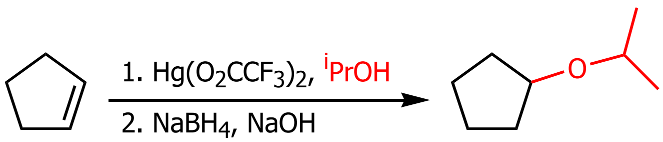


11C. Synthesis of Ethers by Alkoxy-mercuration–Demercuration

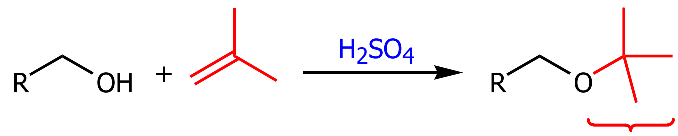
Markovnikov regioselectivity



- ❖ Example



11D. *tert*-Butyl Ethers by Alkylation of Alcohols: Protecting Groups

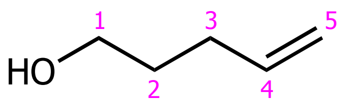


tert-butyl protecting group

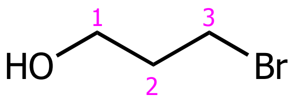
- ❖ A *tert*-butyl ether can be used to "protect" the hydroxyl group of a 1° alcohol while another reaction is carried out on some other part of the molecule
- ❖ A *tert*-butyl **protecting group** can be removed easily by treating the ether with dilute aqueous acid

- ❖ Example

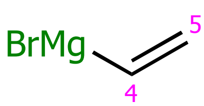
Synthesis of



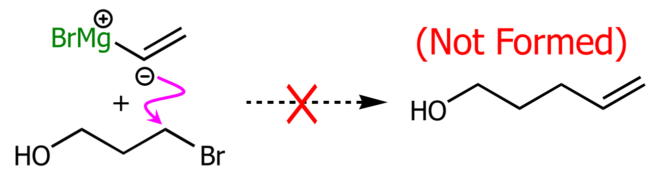
from



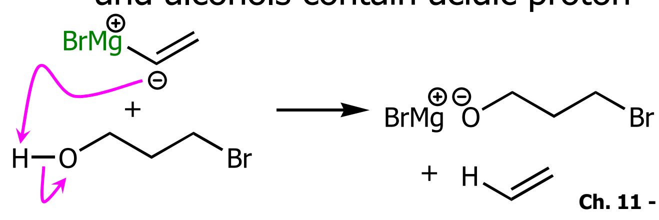
and



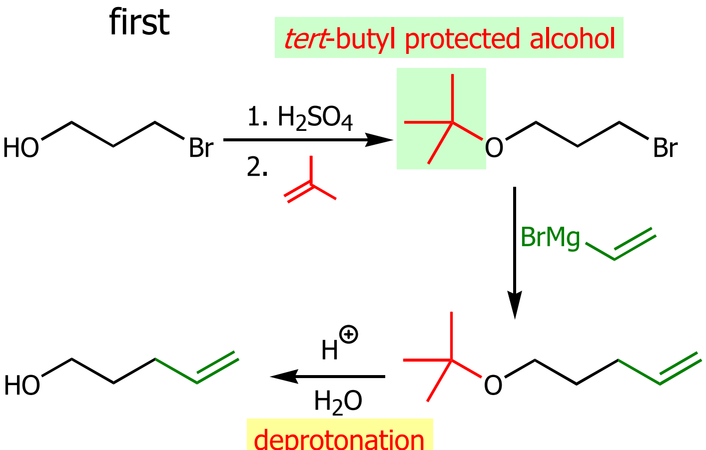
- Direct reaction will not work



- Since Grignard reagents are basic and alcohols contain acidic proton

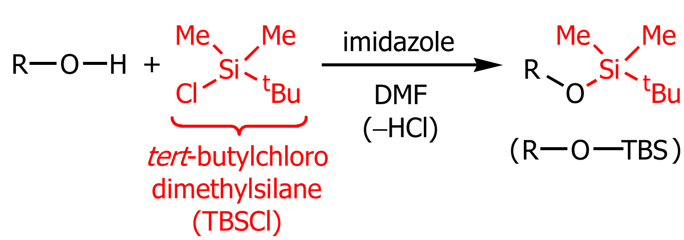


- Need to "protect" the –OH group first

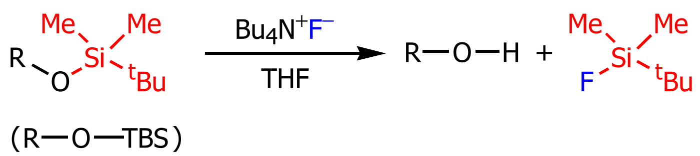


11E. Silyl Ether Protecting Groups

- ❖ A hydroxyl group can also be protected by converting it to a silyl ether group

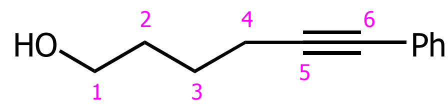


❖ The TBS group can be removed by treatment with fluoride ion (tetrabutylammonium fluoride or aqueous HF is frequently used)

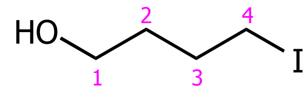


❖ Example

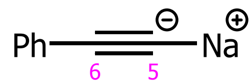
Synthesis of



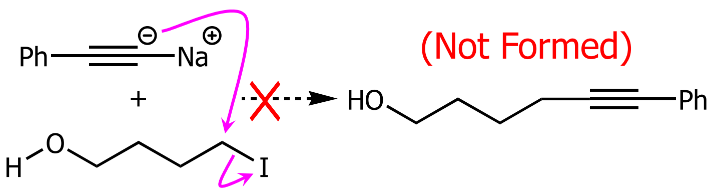
from



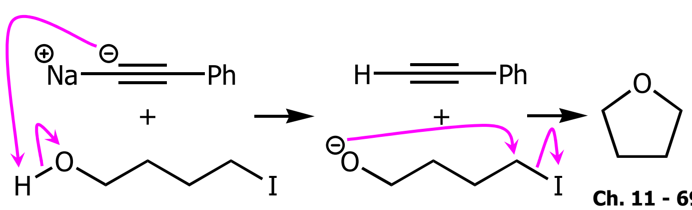
and



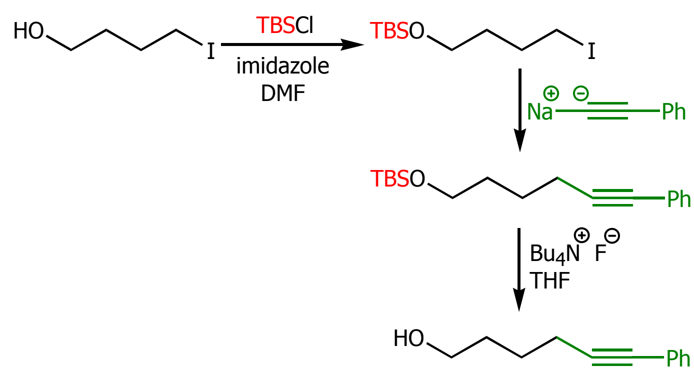
- Direct reaction will not work



- Instead

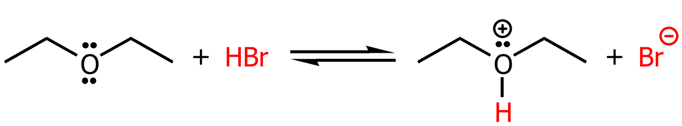


- Need to "protect" the –OH group first



12. Reactions of Ethers

❖ Dialkyl ethers react with very few reagents other than acids



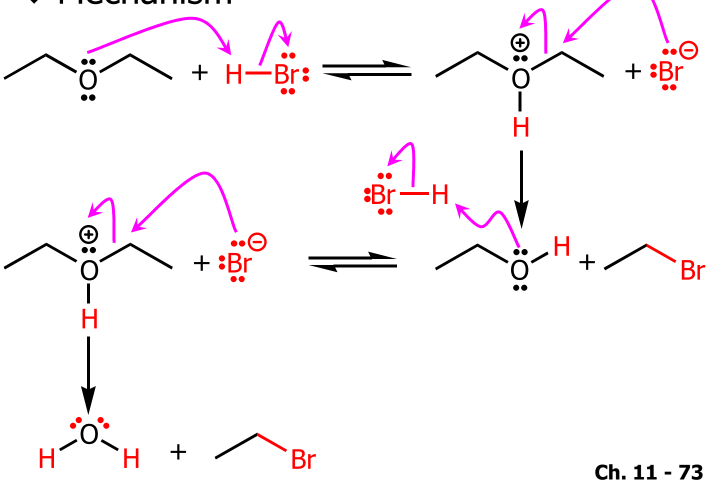
an oxonium salt

12A. Cleavage of Ethers

❖ Heating dialkyl ethers with very strong acids (HI, HBr, and H_2SO_4) causes them to undergo reactions in which the carbon–oxygen bond breaks

Cleavage of an ether

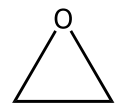
❖ Mechanism



13. Epoxides

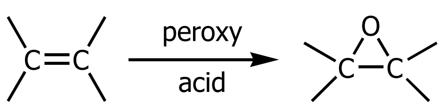
❖ Epoxide (oxirane)

- A 3-membered ring containing an oxygen

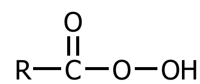


13A. Synthesis of Epoxides: Epoxidation

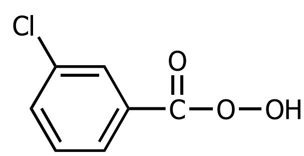
❖ Electrophilic epoxidation



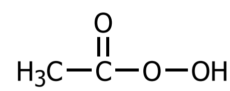
❖ Peroxy acids (peracids)



- Common peracids

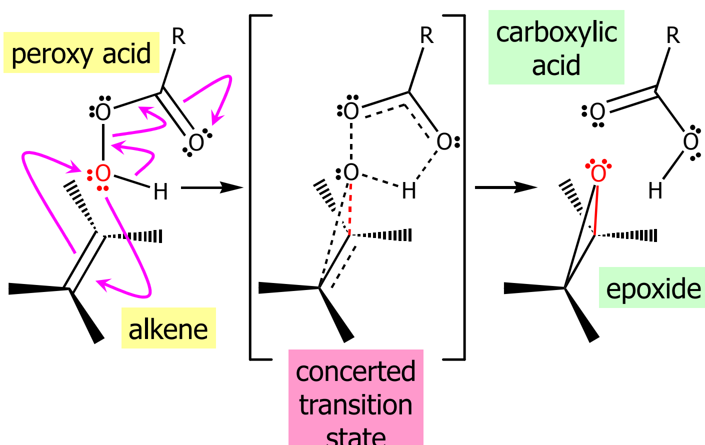


meta-chloroperbenzoid acid
(MCPBA)



peracetic acid

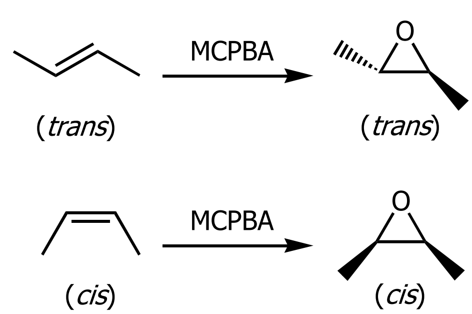
❖ Mechanism



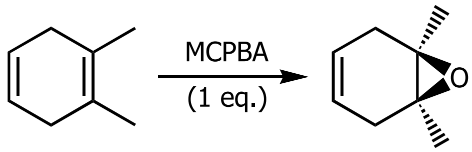
13B. Stereochemistry of Epoxidation

❖ Addition of peroxy acid across a C=C bond

❖ A stereospecific *syn* (*cis*) addition



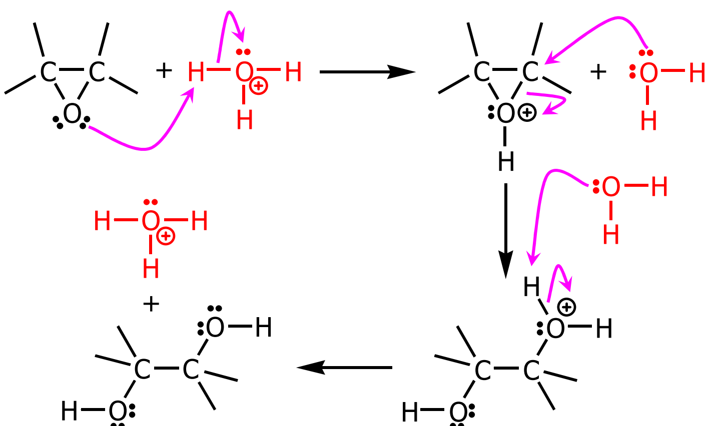
❖ Electron-rich double reacts faster



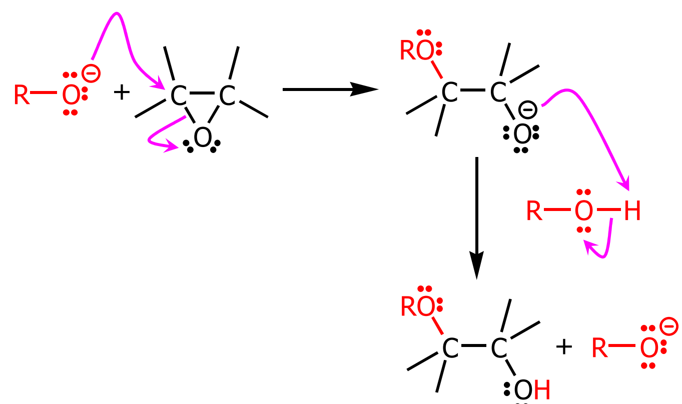
14. Reactions of Epoxides

❖ The highly strained three-membered ring of epoxides makes them much more reactive toward nucleophilic substitution than other ethers

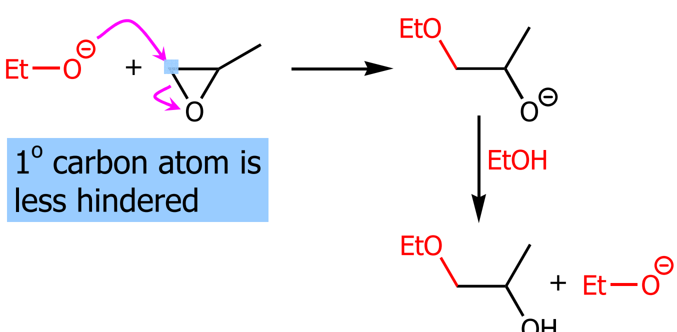
❖ Acid-catalyzed ring opening of epoxide



❖ Base-catalyzed ring opening of epoxide

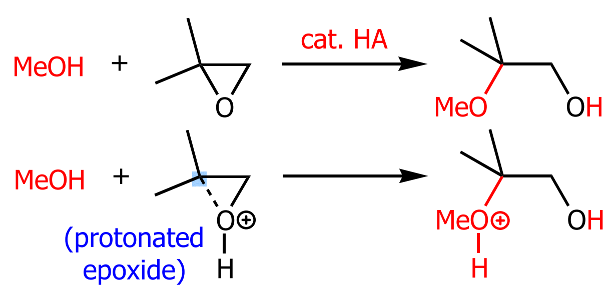


❖ If the epoxide is unsymmetrical, in the **base-catalyzed ring opening**, attack by the alkoxide ion occurs primarily ***at the less substituted carbon atom***



1° carbon atom is less hindered

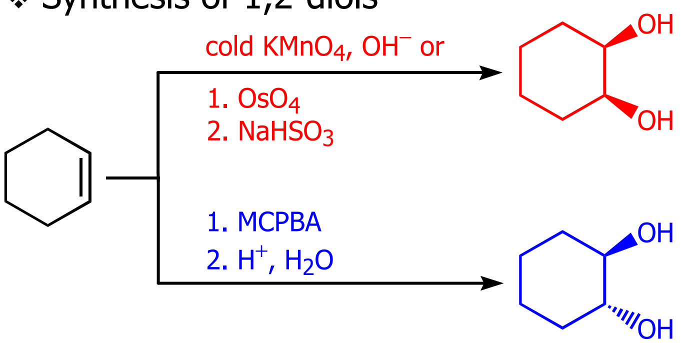
❖ In the **acid-catalyzed ring opening** of an unsymmetrical epoxide the nucleophile attacks primarily ***at the more substituted carbon atom***



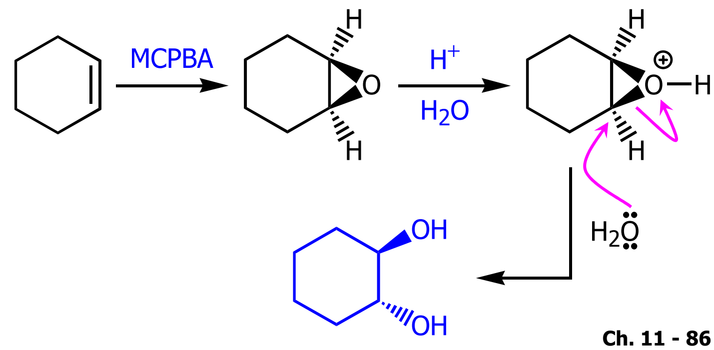
This carbon resembles a 3° carbocation

15. Anti 1,2-Dihydroxylation of Alkenes via Epoxides

❖ Synthesis of 1,2-diols



❖ *Anti*-Dihydroxylation
- A 2-step procedure via ring-opening of epoxides

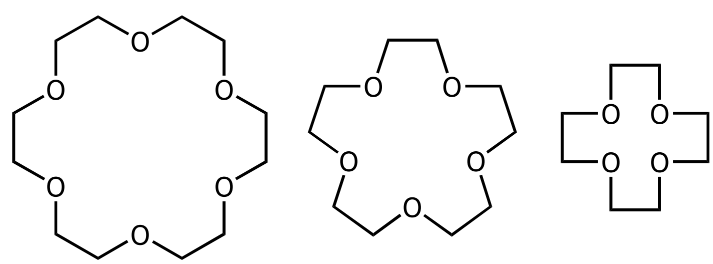


16. Crown Ethers

❖ Crown ethers are heterocycles containing many oxygens

❖ They are able to transport ionic compounds in organic solvents – ***phase transfer agent***

❖ Crown ether names: x-crown-y
- x = ring size
- y = number of oxygen

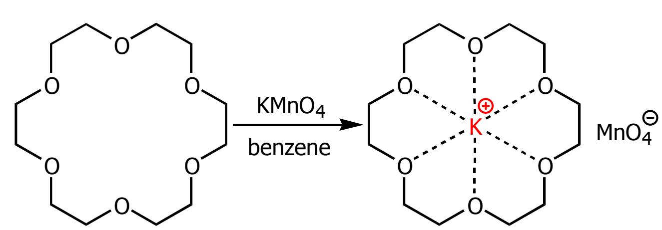


(18-crown-6) (15-crown-5) (12-crown-4)

❖ Different crown ethers accommodate different guests in this guest-host relationship
- 18-crown-6 for K^+
- 15-crown-5 for Na^+
- 12-crown-4 for Li^+

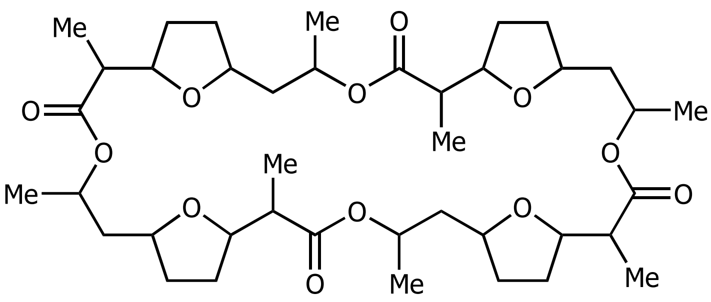
❖ 1987 Nobel Prize to Charles Pedersen (Dupont), D.J. Cram (UCLA) and J.M. Lehn (Strasbourg) for their research on ion transport, crown ethers

❖ Many important implications to biochemistry and ion transport



(18-crown-6) (purple benzene)

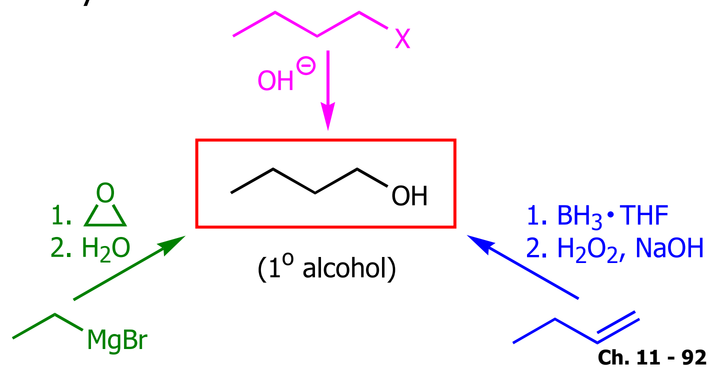
- Several antibiotics call **ionophores** are large ring polyethers and polylactones



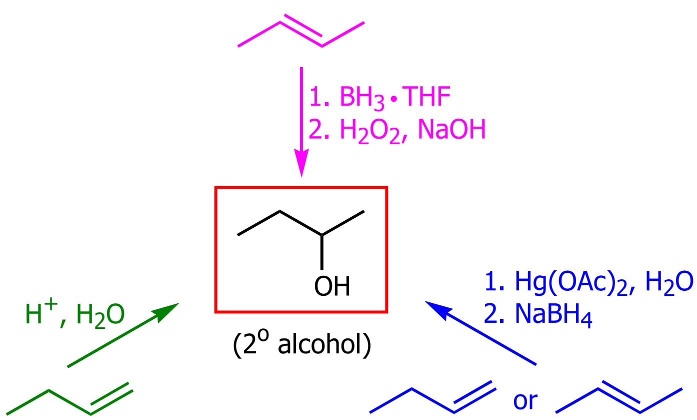
Nonactin

17. Summary of Reactions of Alkenes, Alcohols, and Ethers

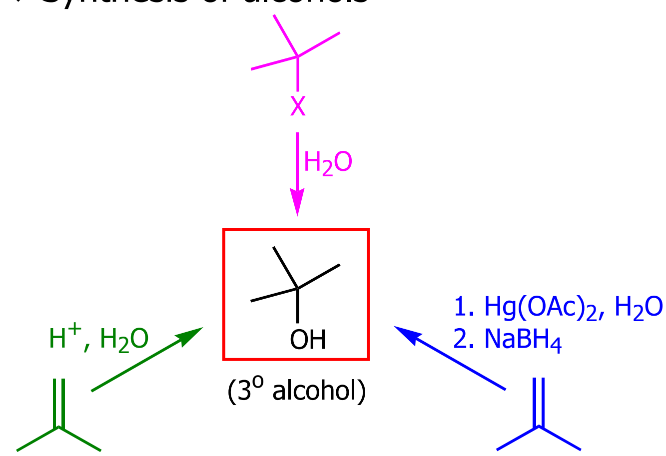
- Synthesis of alcohols



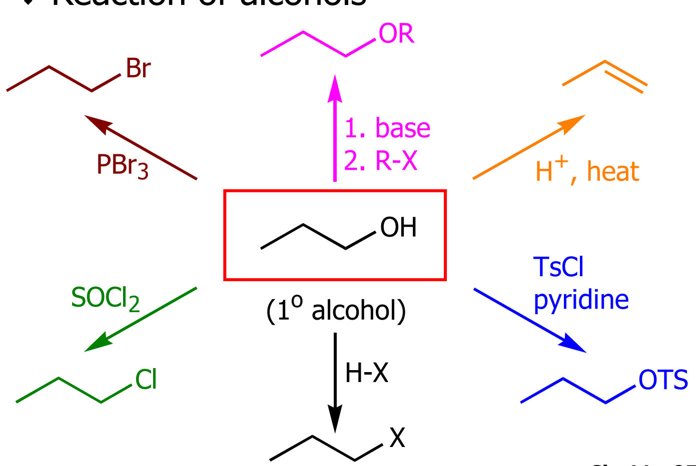
- Synthesis of alcohols



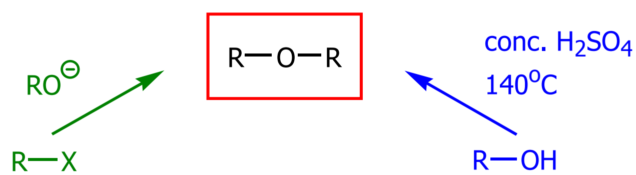
- Synthesis of alcohols



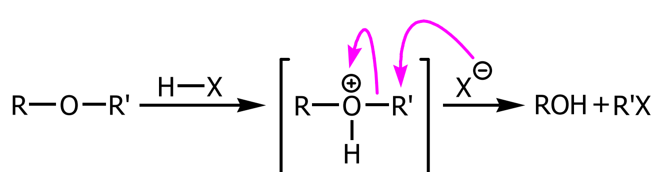
- Reaction of alcohols



- Synthesis of ethers



- Cleavage reaction of ethers



🔔 **END OF CHAPTER 11** 🔔