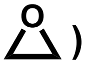
Klein-Starkey Chapter 13 Outline - Ethers (ROR') & Epoxides ()

I. Structure & Properties of ethers (13.1, 13.3)
II. Preparation of ethers (13.5)
  a) Williamson ether synthesis
  b) Epoxide formation (13.8)
III. Reactions of ethers with HBr and HI (13.6)
IV. Reactions of epoxides (13.9)
  a) Acid-catalyzed mechanism
  b) Base-catalyzed mechanism
  c) Stereochemistry of ring-opening
  d) Regiochemistry of ring-opening
V. Synthetic strategies (13.10)
VI. Thiols (RSH) and sulfides (RSR') (13.11)

Ether topic already covered *(with Ch. 12)*
- nomenclature (13.2 & SkillBuilder 13.1)

skip the following sections:
13.4 crown ethers
13.7 epoxide nomenclature
13.12 enantioselective epoxidation

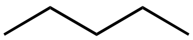
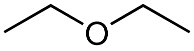
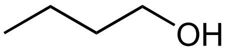
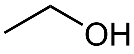
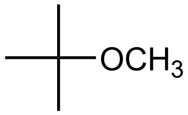
I. Properties of ethers (13.3) Ether R–O–R

- no "OH" group, so no hydrogen bonds between ether molecules

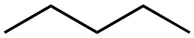
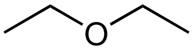
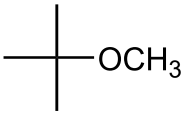
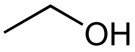
- polar, so ethers make good solvents

- can accept H-bonds from water, so ethers have some water solubility

Water Solubility (grams per 100 mL H_2O)

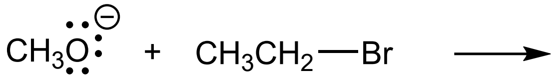
				
0 g	8.4 g	7.4 g	miscible	5.1 g

Boiling Points

	CH_3-O-CH_3				
	dimethyl ether	pentane	diethyl ether	MTBE	ethanol
bp (ºC)	-24	36	35	55	79

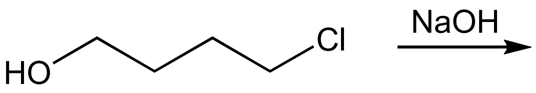
II. Preparation of ethers (13.5)

a) Williamson Ether Synthesis



$CH_3\ddot{\underset{\cdot\cdot}{O}}{:}^{\ominus} + CH_3CH_2{-}Br \longrightarrow$

Examples:



Intramolecular S_N2 (gives cyclic ethers)

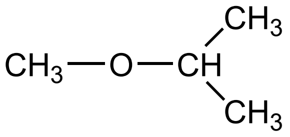
- good for 3-, 5- or 6-membered rings only
- favored over intermolecular S_N2 (due to entropy)

Planning an ether synthesis

synthesize this ether: R—O—R'

target molecule
(TM)

Example:



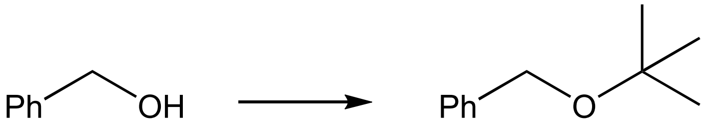
$CH_3{-}O{-}CH(CH_3)_2$

TM

this target molecule has two
possible disconnections

Example:
Starting with propanol as the only source of carbon atoms, synthesize dipropyl ether.

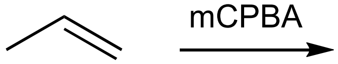
Transform:



II. b) Preparation of epoxides (13.8)

a) via Williamson Ether Synthesis

b) via oxidation



try SkillBuilder 13.2

III. Reactions of Ethers with HBr and HI (13.6)

- ethers are generally very stable, unreactive
- ethers have no leaving group, no acidic protons
- ethers make good solvents (polar, unreactive)

$R-O-R' \longrightarrow$

Any reaction possible? Yes! Reaction with HBr or HI...

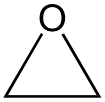
$$CH_3-O-CH_2CH_3 \xrightarrow[\text{(xs)}]{HBr} CH_3-Br + Br-CH_2CH_3$$

mechanism:

$H-Br$

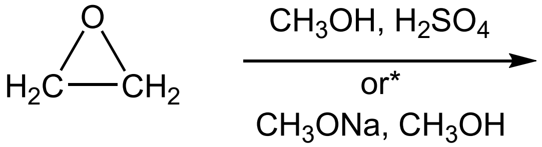
$CH_3-\underset{\cdot\cdot}{\overset{\cdot\cdot}{O}}-CH_2CH_3$

IV. Epoxide Ring-Opening Reactions (13.9)

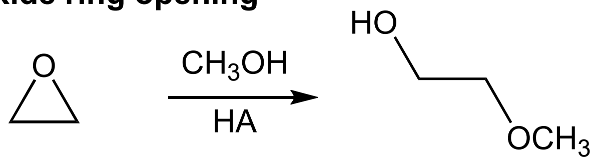


$RO^{\ominus}$ as a leaving group?! LG is bad, but ring strain is released

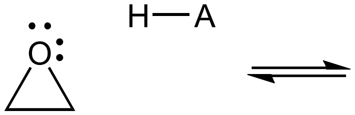
Example:



IV. a) Acid-catalyzed epoxide ring opening



Mechanism (P.A.D.):

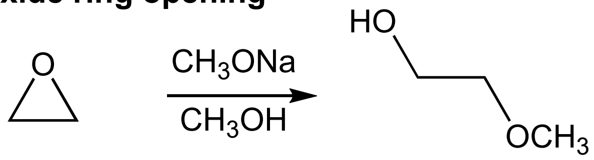


* Note: no O^- charges in acid (no HO^-, no RO^-)

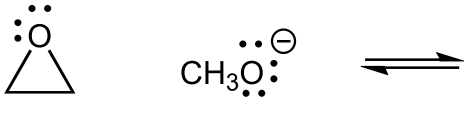
* Note: acid is a catalyst (used and regenerated - not consumed)

try SkillBuilder 13.5

IV. b) Base-catalyzed epoxide ring opening



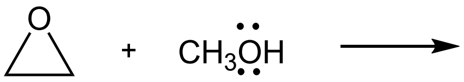
Mechanism:



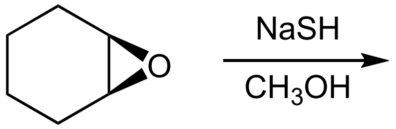
* Note: no O^+ charges in base (structures are neutral or negatively charged)

* Note: base is a catalyst (used and regenerated - not consumed)

** A catalyst is needed for epoxide ring opening (must be either strongly acidic or strongly basic) **

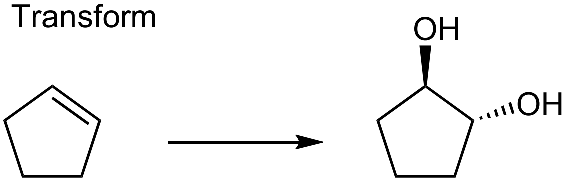


IV. c) Stereochemistry of epoxide ring opening (S_N2 mechanism)



acid or base mechanism?

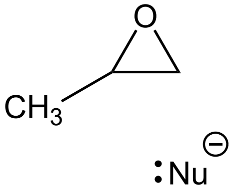
Example: Transform



(racemic)

IV. d) Regiochemistry of epoxide ring opening (depends on reaction conditions)

In base:

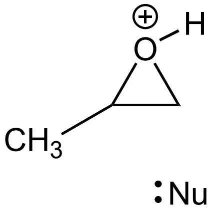


* Nucleophile attacks **neutral** epoxide

* S_N2 is controlled by *sterics*

* Nu: goes to

In acid:
(P.A.D.)



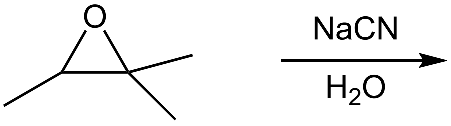
* Nucleophile attacks **protonated** epoxide

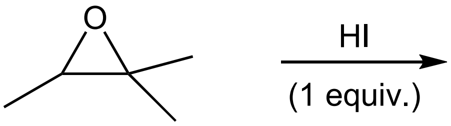
* S_N2 with some S_N1 character (due to + charge)

* reaction is controlled by *electronics*

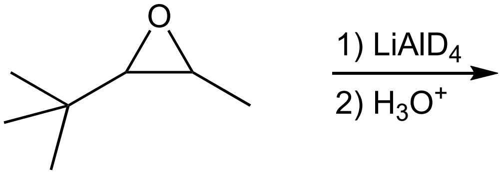
* Nu: goes to

Examples:



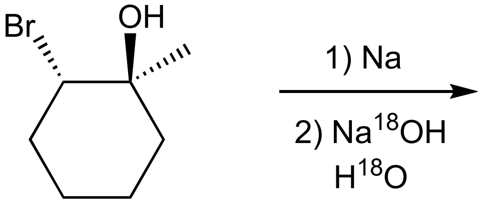


Grignard or Hydride as Nucleophile

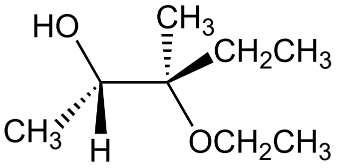


try SkillBuilder 13.4

Predict the Product



V. Synthetic strategies (13.12)



$\Longrightarrow$ epoxide + Nucleophile (Nu:)

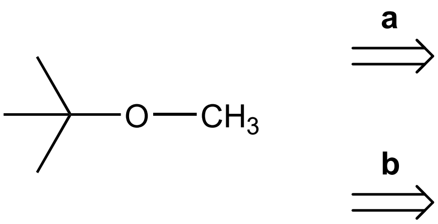
try SkillBuilders 13.6 & 13.7

Planning a Synthesis (additional examples)

$R{-}O{-}R' \Longrightarrow$

target molecule (TM)

Example: Synthesize TBME (*t*-butyl methyl ether) from alcohol starting materials:



target molecule
TBME