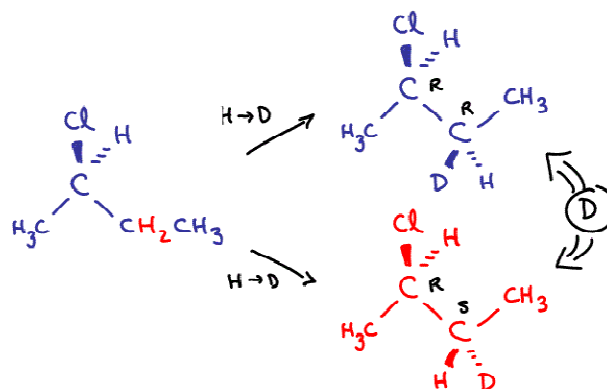
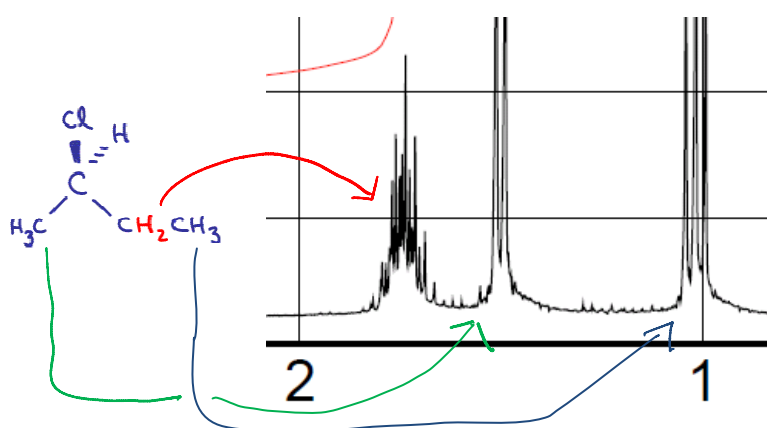


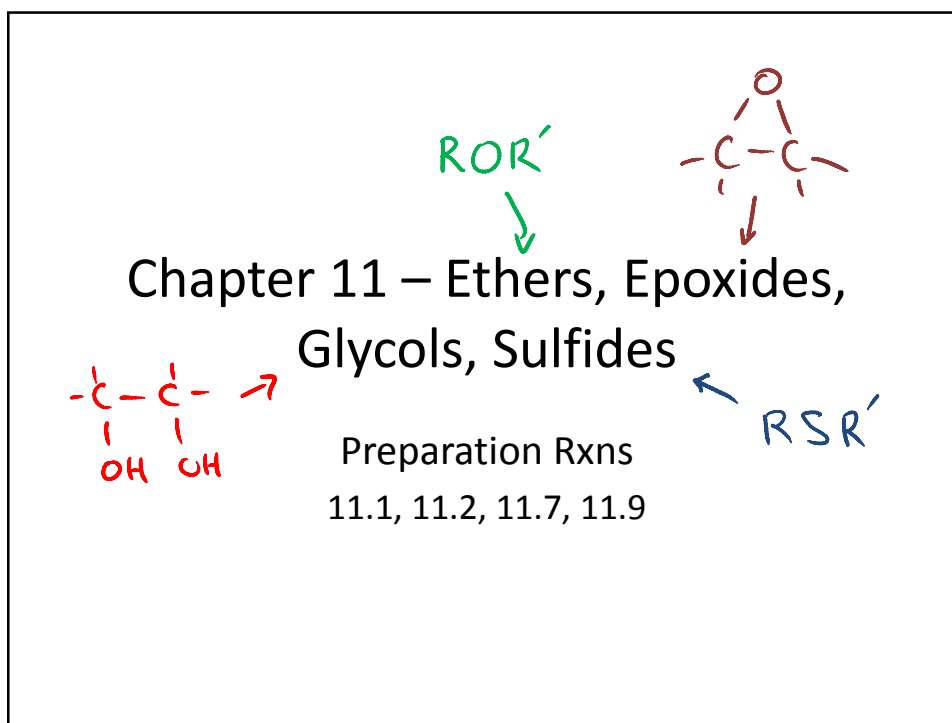
Equivalent H?

- Constitutional
- Homotopic, Enantiotopic, Diastereotopic
- NMR



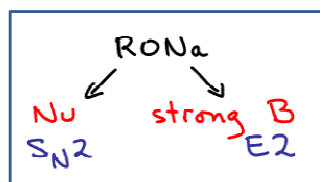
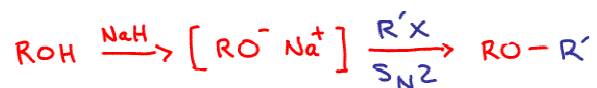
NMR Spectrum



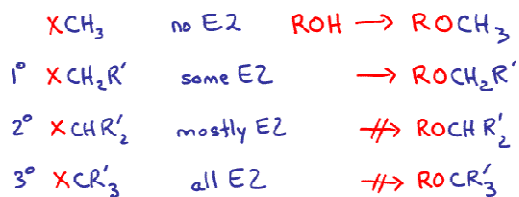


Preparation of Ethers

- Williamson Ether Synthesis (familiar)

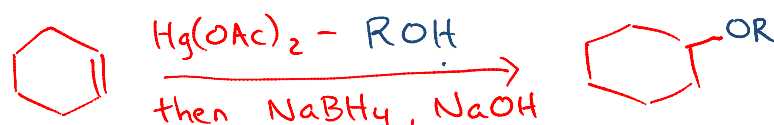
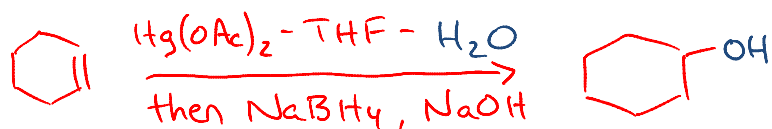


not all R'X successful



Preparation of Ethers

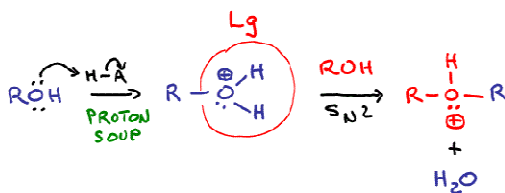
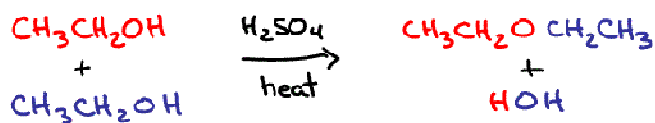
- Alkoxymercuration-Reduction (semi-familiar)



THF may not be needed
if C1=CCCCC1 dissolves in ROH

Preparation of Ethers

- Alcohol Dehydration (semi-familiar)

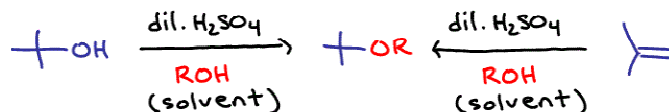


"NOT USEFUL IN LAB"

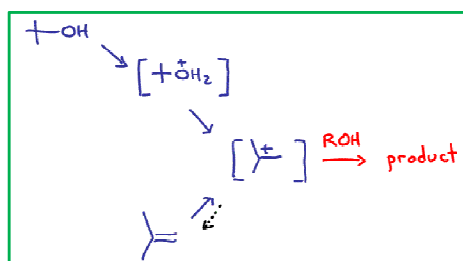
- not generally applicable
- expensive apparatus
- difficult to control
- hazardous reagents
- ...

Preparation of Ethers

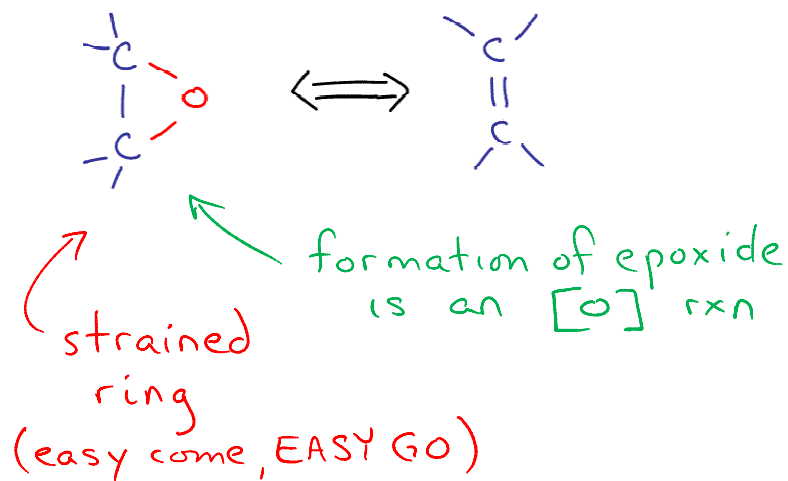
- Alcohol Dehydration – Alkene Addition (semi-familiar)



many limitations
 ① must have 3° ROH
 ② must have CHEAP ROH to waste

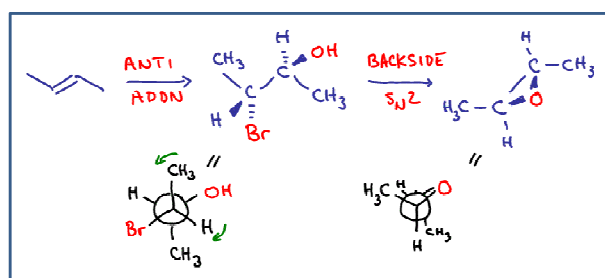
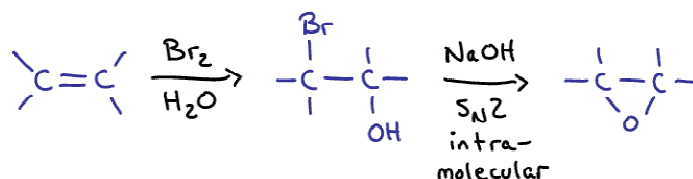


Preparation of Epoxides (Oxiranes)



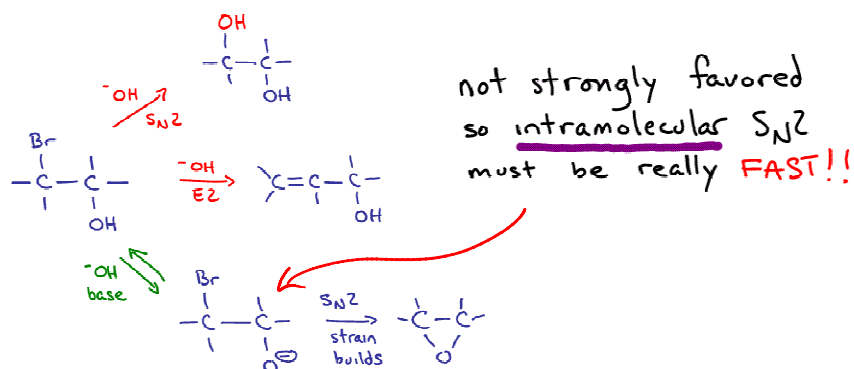
Preparation of Epoxides (Oxiranes)

- Halohydrin route

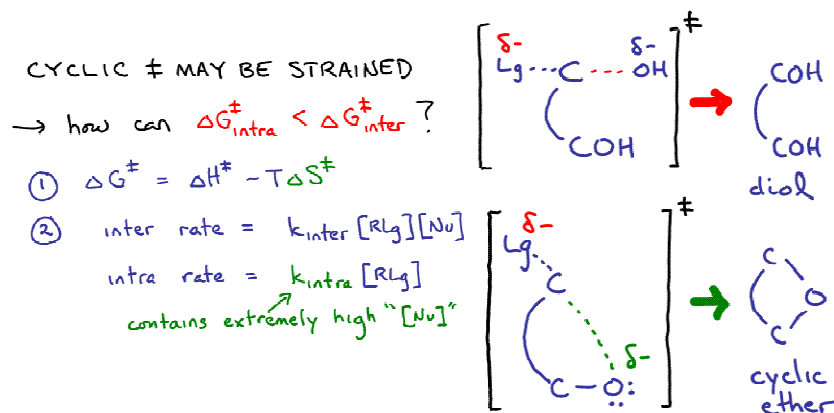


A Puzzle Concerning Ring Closure

- Why Does a Strained Ring Form?
 - Especially when so much else can happen!



Why Are Intramolecular Rxns So Fast ?



The Proximity (Entropy) Effect

reflects probability of atoms
adopting geometry needed in \ddagger

$$\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger$$

reflects difficulty of bond changes
e.g. STRAIN, steric hindrance, etc.

The Proximity (Entropy) Effect

$$\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger$$

① strain in \ddagger raises ΔH^\ddagger
 $\Delta H_6^\ddagger < \Delta H_5^\ddagger < \Delta H_4^\ddagger \approx \Delta H_3^\ddagger$

② \ddagger more ordered than reactants
 $\rightarrow \Delta S^\ddagger < 0$
 but intramolecular rxns much more probable

$$\Delta S_{\text{inter}}^\ddagger \ll \Delta S_6^\ddagger < \Delta S_5^\ddagger < \Delta S_4^\ddagger < \Delta S_3^\ddagger$$

$$-T\Delta S_{\text{inter}}^\ddagger \gg -T\Delta S_6^\ddagger > \dots > -T\Delta S_3^\ddagger$$

$-T\Delta S_{\text{intra}}^\ddagger$
 lowers $\Delta G_{\text{intra}}^\ddagger$
 by 30-45 kJ/mol

High Probability = High "Effective" Molarity

$$\frac{\text{rate intra}}{\text{rate inter}} = \frac{k_{\text{intra}} [\text{R/Lg}]}{k_{\text{inter}} [\text{R/Lg}] [\text{Nu}]} = \frac{k_{\text{intra}}}{k_{\text{inter}} [\text{Nu}]}$$

① if $-T\Delta S^\ddagger$ (45 kJ/mol) is only factor at work

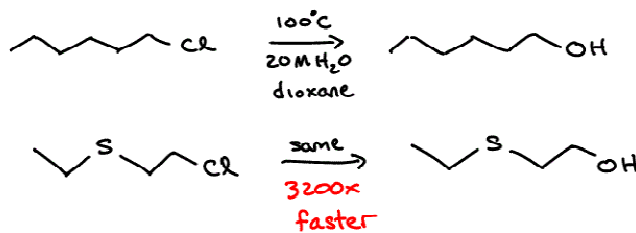
$$\frac{k_{\text{intra}}}{k_{\text{inter}}} = 10^{\Delta(\Delta G^\ddagger)/2.3RT} = 10^{45/5.7} \approx 10^8$$

② to put it another way, $[\text{Nu}] \approx 10^8 \text{ M}$ would make
 $\text{rate intra} = \text{rate inter}$

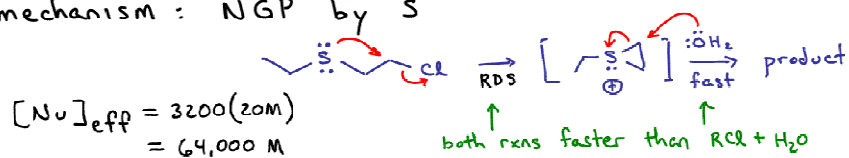
③ **EFFECTIVE MOLARITY** defined as $[\text{Nu}]$
 that makes $\text{rate intra} = \text{rate inter}$

Neighboring Group Participation

- Unexpected **rate enhancement** or **stereochemical outcome** due to an intramolecular reaction



mechanism: NGP by S



$$\begin{aligned}
 [\text{Nu}]_{\text{eff}} &= 3200(20\text{M}) \\
 &= 64,000 \text{ M}
 \end{aligned}$$