

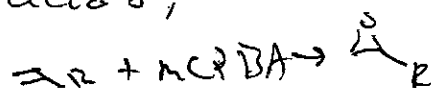
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Last lecture: - Synthesis of ethers

- Epoxide Introduction

- Synthesis via alkenes + peracids,

(concerted mechanism)

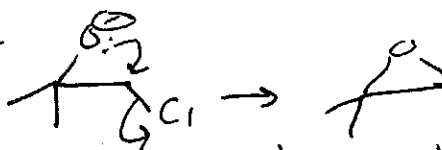


2) Cyclication of halohydrins



Consider

Mech:



intramolecular S<sub>N</sub>2!

⊖ OH can be a nucleophile!

⊖ OH intermolecular nucleophile

↳

In the ~~next~~ there is an advantage to the

intramolecular reaction, especially for the formation of a 3-6 membered ring!

Due to the entropy of ~~the~~ not having to bring 2 things together in an inter molecular fashion.

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

→ Entropy

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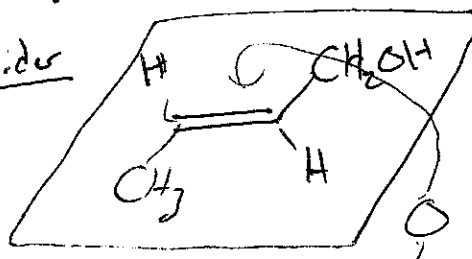
Synthesis of epoxides as single enantiomers

3) Asymmetrical synthesis of epoxides: Sharpless

(Nobel prize 2001)

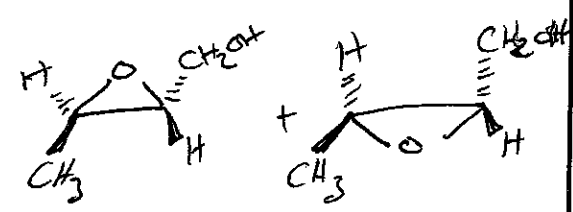
Epoxidation

Consider

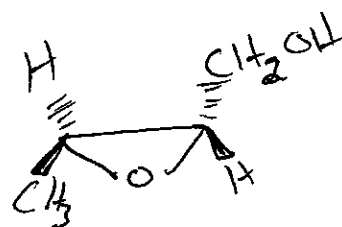
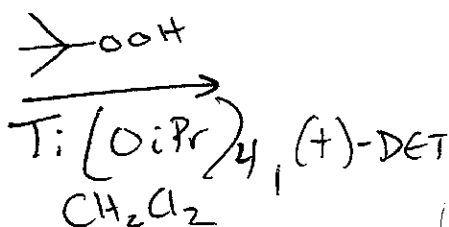
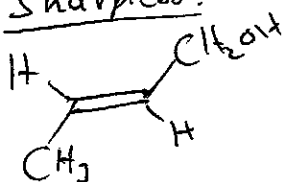


in plane of paper

O can add above or below



Sharpless:

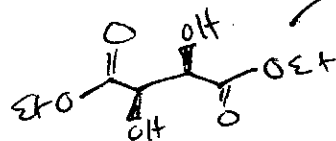


>95% this enantiomer

t-BuOOH  $\rightarrow$  oxidant (similar to mCPBA)

$\text{Ti}(\text{O}i\text{Pr})_4$   $\text{Ti}^{4+}$  w/  $4 \times \ominus \text{O}^-$   
 $\rightarrow$  Lewis acid  $\rightarrow$  not consumed  $\rightarrow$  catalyst  
 $\text{CH}_2\text{Cl}_2 \rightarrow$  solvent

(+)-DET  $\rightarrow$  diethyl tartrate



Chiral cofactor  $\rightarrow$  not consumed in rxn

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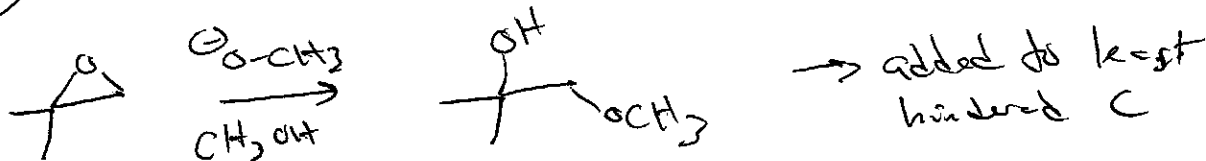
Other enantiomers of DET would give the  
 opposite epoxide enantiomer  $\rightarrow (-)$ -DET

$\rightarrow$  Lewis acid ( $Ti^{4+}$ ) w/ coordinate to the  
 oxygens giving this selectivity

### Reactions of Epoxides w/ Nucleophiles

Epoxides  $\rightarrow$  strained & electrophilic

1) Rxns w/ alkoxides (and similar nucleophiles)  $\rightarrow$   $S_N2$



Selective attack

$S_N2 \rightarrow$  least hindered substituent  
 due to steric bulk at more sub.

$\downarrow$  normally  $\ominus \text{OR}$  or  $\ominus \text{OH}$  is a bad L.G.!

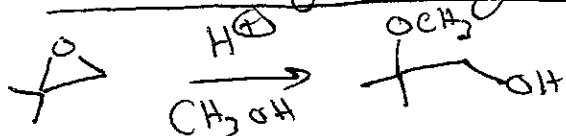
Here we have an exception  $\rightarrow$  if  $\ominus \text{OR}$  leaves we relieve

Ring strain

$\downarrow \ominus \text{OR}$  is our epoxide

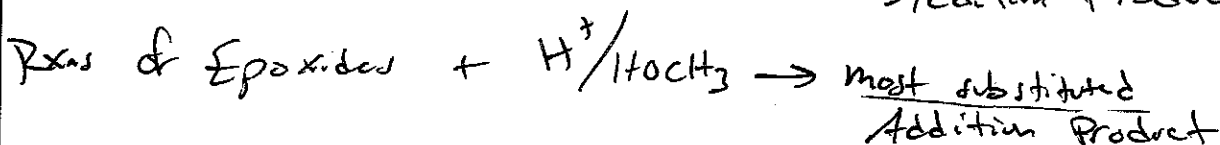
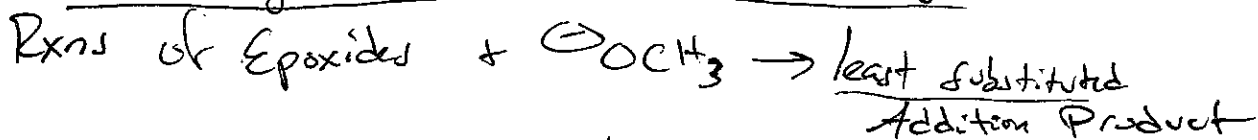
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2) Acid catalyzed ring opening

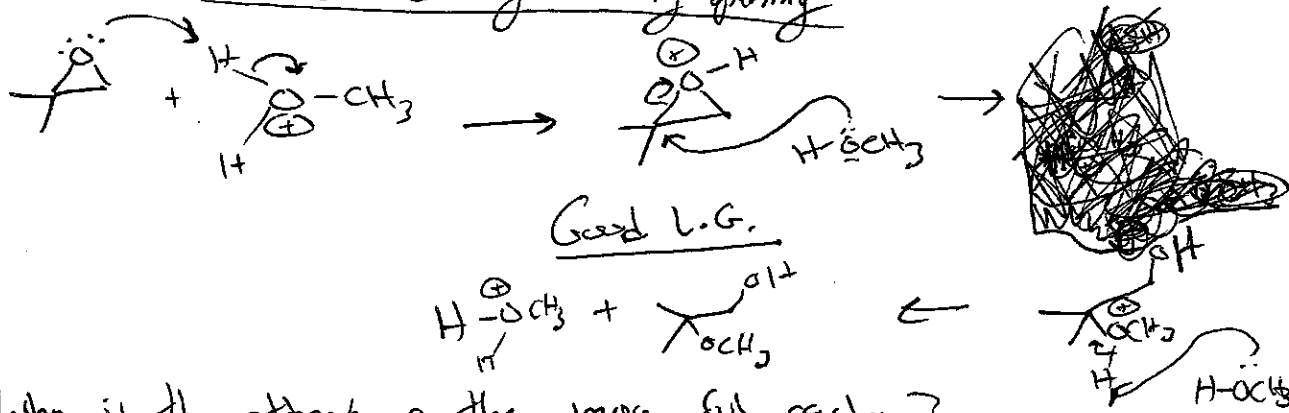


Attach on the most substituted Carbon

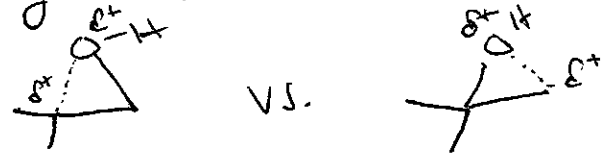
Contrasting rxn conditions change selectivity:



Mechanism of Acid catalyzed ring opening

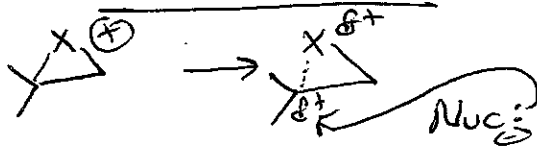


Why is the attack on the more sub carbon?



more stable  
 follows  $\text{C}^+$  stabilization

General Trend



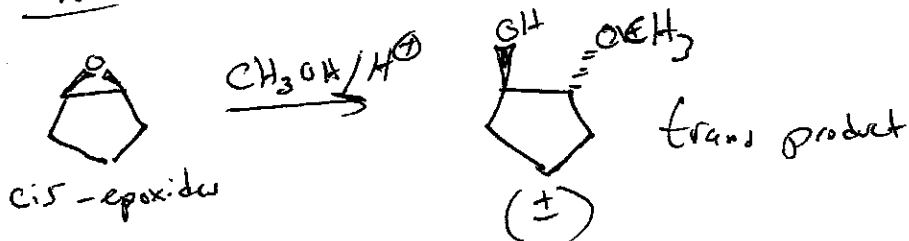
X = Br, Cl,  $\text{HgOAc}$   
 halonium oxymercuration

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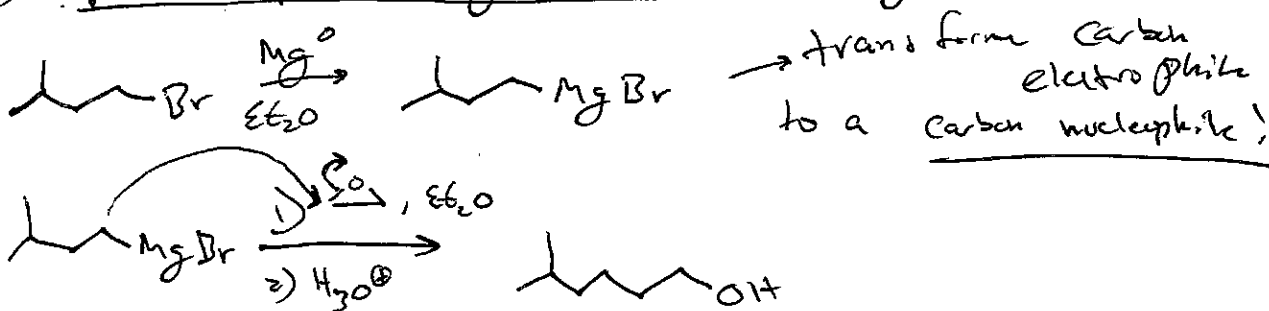
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### Stereochemical analysis

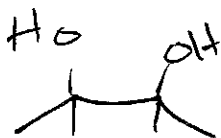
S<sub>N</sub>2 rxns → back s.i.c. attack



### 3) Epoxides plus Organometallic Reagents



Next time



1,2 Diols