

# CHEM 222 section 01

## LECTURE #05

Tues., Sept.18, 2007

### Lecture topics & readings

#### Today's class

- Ch.10: amines, ethers, epoxides, thiols, sulfides

#### Before next class

- **practice** Ch.10 reactions & problems
- read rest of Ch.10

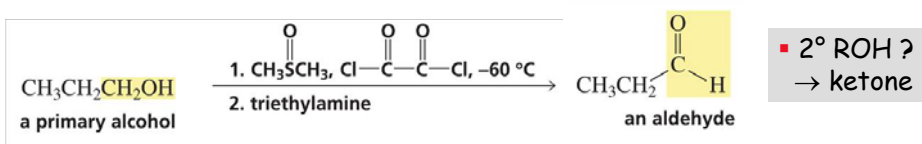
#### Next class

- organometallic reagents: 10.12, 10.13 (Gilman rgts only)
- start characterization techniques:
  - first topic: mass spectrometry (Ch.12)

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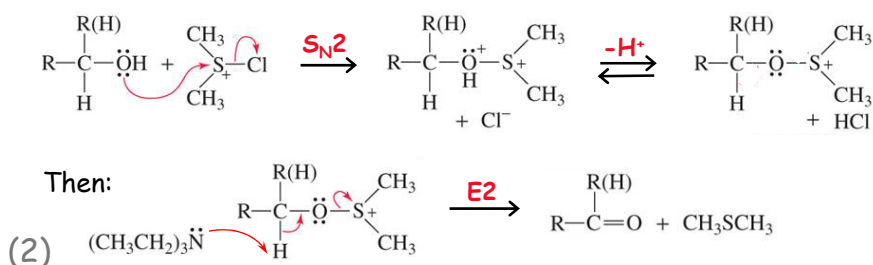
### 19.2: Other ways to oxidize alcohols to carbonyl comp'ds

Swern oxidation: oxalyl chloride + DMSO, followed by Et<sub>3</sub>N



**Mechanism:** almost same as chromic acid oxidation...

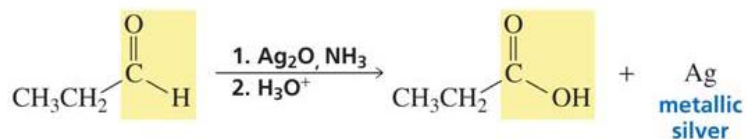
- *Not shown:* Activation of oxidant: (was H<sup>+</sup> for H<sub>2</sub>CrO<sub>4</sub>)
  - DMSO's lone pair on S attacks highly polarized δ<sup>+</sup>C=O
  - forms dimethylchlorosulfonium ion = the oxidant
- ROH attacks oxidant via S<sub>N</sub>2 rxn ⇒ adds on new good LG (then -H<sup>+</sup>)
- E2 elimination, B = Et<sub>3</sub>N ⇒ lose new good LG & create C=O bond



### 19.3: Other ways to oxidize carbonyls to carboxylic acids

"The Tollens test" for aldehydes:

- Weak oxidant  $\Rightarrow$  can only oxidize aldehydes  
 $\Rightarrow$  cannot oxidize ROH or other functional groups

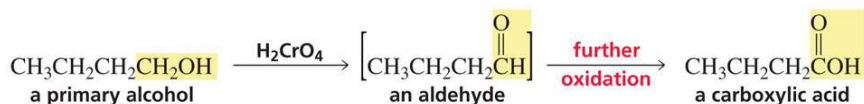


Party trick:  
Makes a  
silver mirror...

(For your information)

(3)

### 19.3: 1° ROH over-oxidize to yield acids unless use PCC...



Why does this happen?

- In aqueous acidic media: aldehydes form *hydrates*  $\Rightarrow$  2 OH groups!
- ...react again with  $\text{CrO}_3$  via same mechanism  $\Rightarrow$  2<sup>nd</sup> round of oxidation

Mechanism on board

Note: doesn't happen with PCC

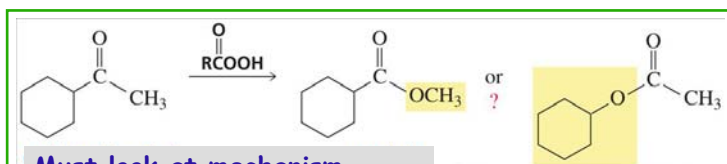
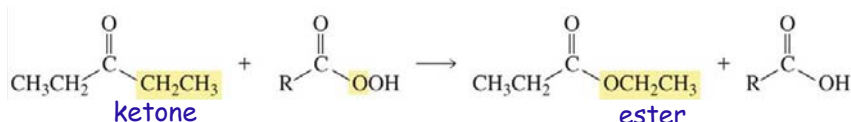
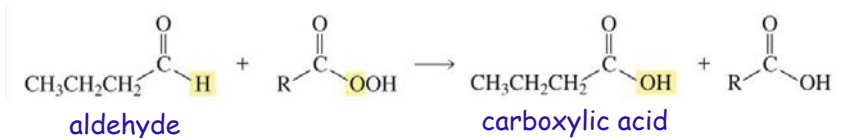
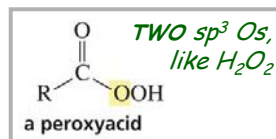
- Anhydrous organic solvent used  
 $\Rightarrow$  no hydrate forms!

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## 19.3: Other ways to oxidize carbonyls to carboxylic acids

### Baeyer-Villiger oxidation: using peroxyacids

- Inserts peroxyacid's "extra" O atom
- Bond  $\alpha$  to aldehyde/ketone's C=O is cleaved



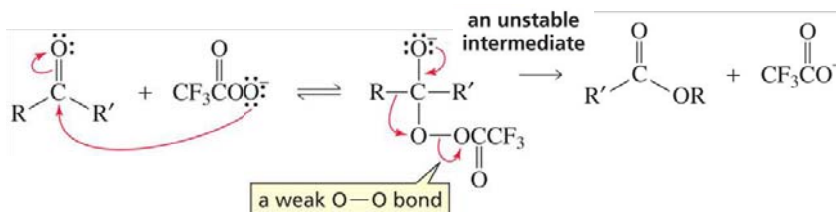
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Must look at mechanism...

## Baeyer-Villiger oxidation of carbonyl compds: mechanism

Note: mechanism shown has been simplified to focus on key points:

- 1<sup>st</sup>: peroxyacid protonates the C=O oxygen
- 2<sup>nd</sup>: acid's anion attacks the  $\delta^+\text{C}=\text{O}^+\text{H} \rightleftharpoons$  form Td ( $sp^3\text{-C}$ ) intermediate
- 3<sup>rd</sup>: a base (water...) de-H's the intermediate
- 4<sup>th</sup>: intermediate collapses via R migration to yield product



**Collapse of the Td intermediate:** an  $\alpha$  R group migrates onto O as LG leaves

most likely to migrate  $\rightarrow$  H > *tert*-alkyl > *sec*-alkyl = phenyl > primary alkyl > methyl  $\leftarrow$  least likely to migrate

Thus: aldehydes  
(R=H) always yield  
carboxylic acids...

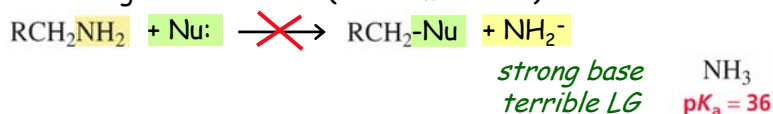
But otherwise:  
Bulkier R groups  $\Rightarrow$  migrate better

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## 10.6 Amines (only briefly)

$\text{CH}_3\text{NH}_2$   $\text{p}K_a = 40$

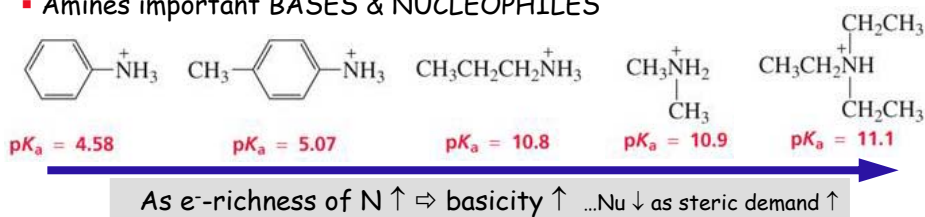
- Do not undergo substitutions (nor eliminations)



- Protonation helps - but not as much as with alcohols



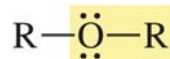
- Amines important BASES & NUCLEOPHILES



*aryl groups on N*  
(7) *stabilize lone pair ( $\pi$ -overlap)*

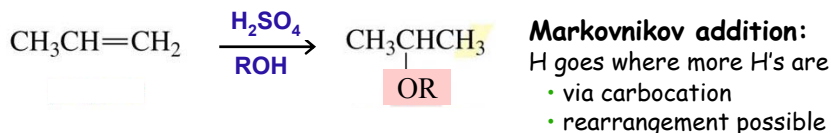
*alkyl groups*  
*= EDGs*

## 10.7 Ethers: preparation & reactivity

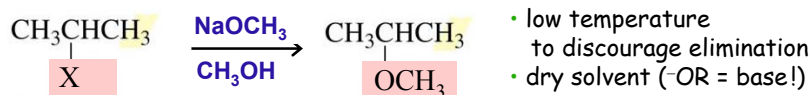


### Preparation:

- Rxn of alkenes with alcohols (review 4.5)



- Williamson ether synthesis:  $\text{S}_\text{N}2$  using Nu =  $-\text{OR}$  (review 9.9)



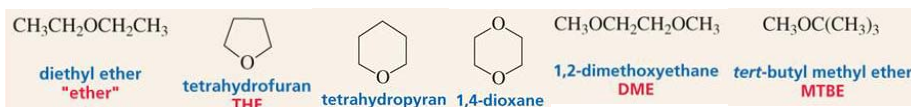
on board • To 1<sup>st</sup> make alkoxide salt: deprotonate an alcohol:

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## Uses of ethers: as solvents & chelators

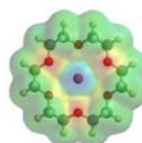
Ethers are relatively unreactive (except towards acids & very strong Bs...)

- OR is a poor LG, strong B... recall HOR  $pK_a \sim 15$
- "Exotic" reagents that activate ROHs do not activate ethers.
- THUS: Ethers often used as solvents



### Crown ethers: macrocyclic polyethers

- large rings with several oxygens  
= cyclic array of donor atoms
- coordinate  $M^{n+}$ s that fit inside



Section 10.10  
[18]-crown-6 +  $K^+$   
# atoms in ring    #Os    guest

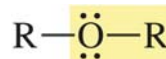
### Utility:

- Help inorganic salts dissolve in organic solvents
- Make anionic Nu's more reactive by sequestering their counter-ions

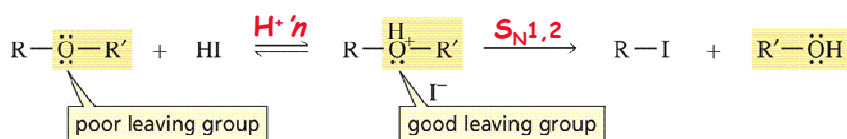
Ex. (2)  
on board

(9)

## Reactions of Ethers: cleavage by Nu



Undergo substitutions (or eliminations) if protonated: use strong acid



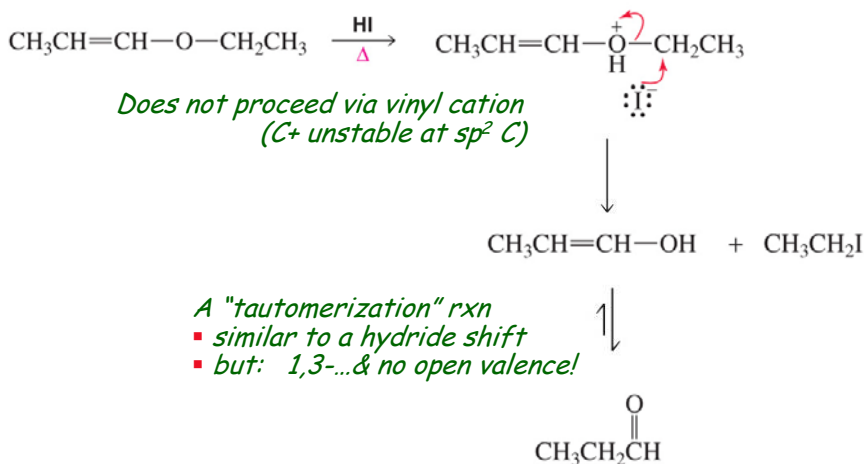
- $2^\circ, 3^\circ \Rightarrow S_N1$  pathway: quite fast - good LG, relatively stable  $C^+$ ...  
*find your own example...*
- $1^\circ$  ROR  $\Rightarrow S_N2$  pathway: quite slow - Nu's here not that strong  
Nu will attack less hindered R  $\Rightarrow$  R-Nu prod.

Ex. on board

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## Bruice solved problem #22

An enol product: converts to aldehyde naturally



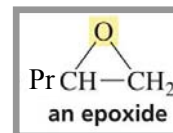
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## Epoxides: 3-membered cyclic ethers (4.9)

2 ways to systematically name epoxides:

- 1) 3-memb. ring as "oxirane": *OR* 2) As epoxyalkane
  - O as position 1
  - Rest of ring 2&3, + substituents
  - Alkane with "substituent"
  - 2 atom #s define pos'n

*2-propyloxirane*                      *2,3-epoxypentane*



Preparation: Rxn of alkenes with peroxyacids (Bruice 4.9)



Mechanism: concerted, with cyclic ‡

on board

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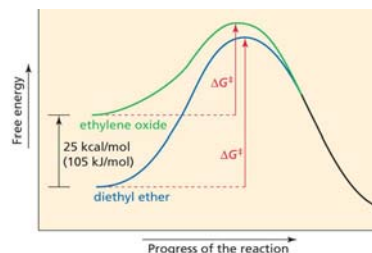
## 10.8 Reactions of epoxides

Less stable, more reactive than ethers

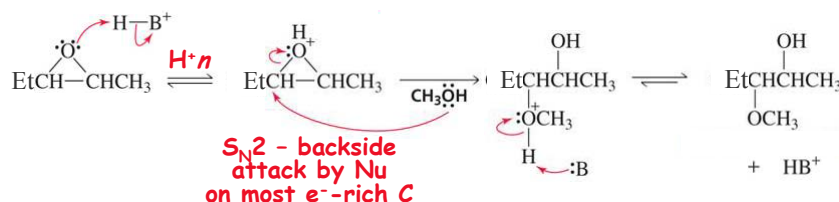
- Because of ring strain
- Rxns open the epoxide ring

Protonated epoxides = highly reactive

- Can be opened even by weak Nu's
- Route to: Halohydrins *using H-X*
- Diols *H<sup>+</sup> + H<sub>2</sub>O*
- Alkoxy-alcohols *H<sup>+</sup> + ROH*

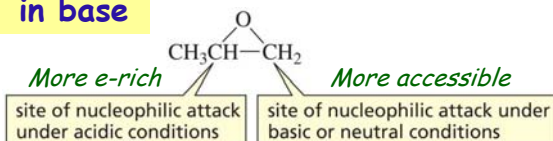


Mechanism: ① H<sup>+</sup>n... ② S<sub>N</sub>2, but † resembles C<sup>+</sup> ⇒ directs regiochem...



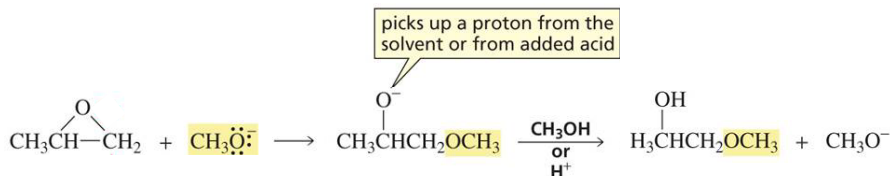
(13) **Major product: From Nu attack at more substituted C**

### Reactions of epoxides: in base

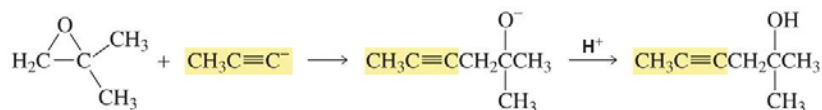


Mechanism: pure S<sub>N</sub>2

- Not activated 1<sup>st</sup>: C-O bond doesn't start breaking until Nu attacks
- less substituted C more accessible to Nu ⇒ preferred site of rxn

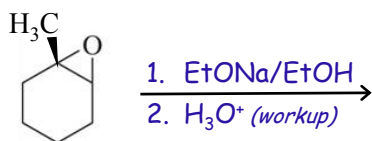


Utility: substitutions with strong base Nu's

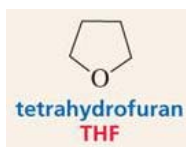


(14)

cf Bruice p.455: Give the major product for... (include stereochem.)



Bruice Problem 24: What do you think?



Would you expect a 5-membered cyclic ether to react more like...?

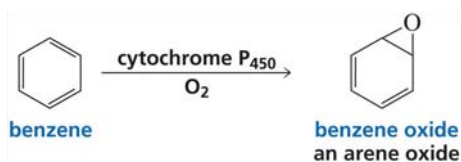
- (a) An acyclic ether
- (b) An epoxide

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## 10.10 Arene oxides

Read it on your own - for interest's sake & context

- relevant to metabolism of benzene & polycyclic aromatic hydrocarbons
  - explains about carcinogenic properties
  - very interesting...



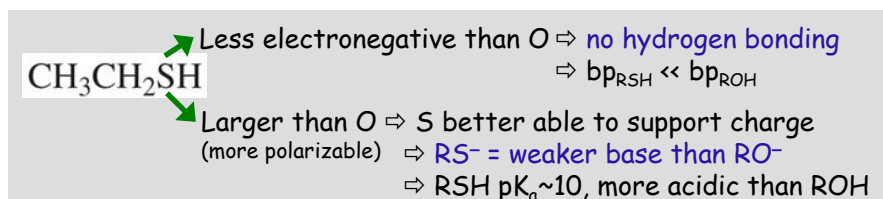
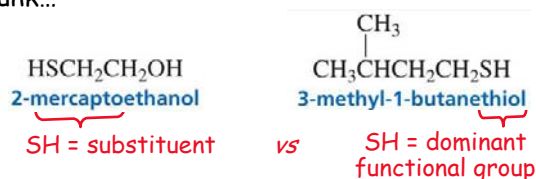
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## 10.11 S-containing cmpds: thiols, sulfides & sulfonium salts

**Thiols, RSH (aka mercaptans): S-analogs of ROH**

- strong odour: garlic, skunk...



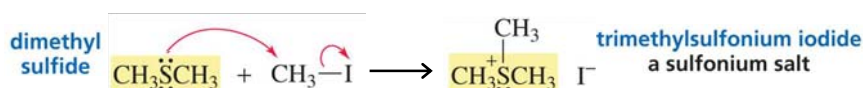
**Thiolates,  $\text{RS}^-$  = useful Nu's**

- soft S atom  $\Rightarrow$  less shielded in protic solvents *cf* alkoxides

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## 10.11 S-containing cmpds: thiols, sulfides & sulfonium salts

**Sulfides,  $\text{RSR}$  (aka thioethers) = also useful Nu's, unlike ethers...**



**Sulfonium salts = good "alkylating agents" *i.e.*, for R-group transfers**

- built-in sulfide = good LG
- biological methylating agent: **SAM** (section 8.12, for your interest)
  - Important role in stress response: noradrenaline  $\rightarrow$  adrenaline

