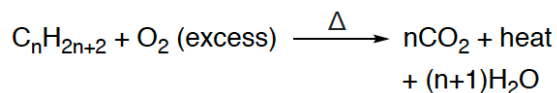


**Know the mechanism** for all reactions marked with an asterisk (\*)

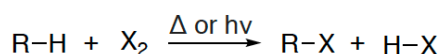
Reactions of Alkanes	General Characteristics
----------------------	-------------------------

#### Combustion



No heat, no reaction

#### \*Radical Halogenation



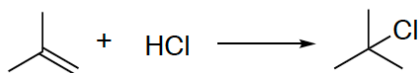
R = Alkyl

X = Cl, Br (only)

(Cl is more reactive & less chemoselective)

Reactions of Alkenes	General Characteristics
----------------------	-------------------------

#### \*Addition of HX

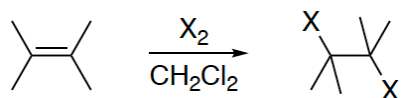


X = Cl, Br, I

Carbocation rearrangements possible

Markovnikov orientation

#### \*Addition of Halogens (X<sub>2</sub>)



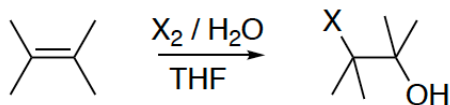
X=Br<sub>2</sub>, Cl<sub>2</sub>, also ICl or BrCl

Halonium ion intermediate

No rearrangements

Anti-addition

#### \*Halohydrin Formation



X=Br<sub>2</sub>, Cl<sub>2</sub>, I<sub>2</sub>

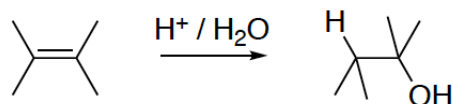
Anti-addition

*Modification:* NBS/H<sub>2</sub>O/Solvent (NCS or NIS)

Can use non H<sub>2</sub>O nucleophiles (ROH, RCO<sub>2</sub>H)

Halonium Ion (no rearrangements)

#### \*Addition of Water

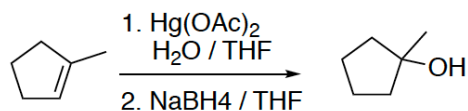


Brønsted acid catalyst

Nucleophiles besides H<sub>2</sub>O (ROH, RSH, etc.)

Carbocation rearrangements possible

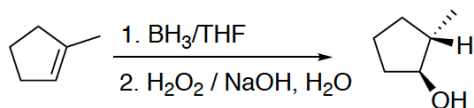
**\*Oxymercuration-Demercuration**



*\*Know mechanism for **step 1** only*

Mercurinium ion intermediate  
 No carbocation rearrangements  
 Can use ROH instead of  $\text{H}_2\text{O}$

**\*Hydroboration**

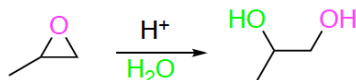


*\*Know mechanism for **step 1** only*

Also with **9-BBN** ( $\text{H}-\text{BR}_2$ ) and deuterated versions (**D-9-BBN**)  
 Anti-Markovnikov orientation  
 Syn addition of  $\text{H}_2\text{O}$   
 No carbocation rearrangement

**\*Ring-Opening of Epoxides**

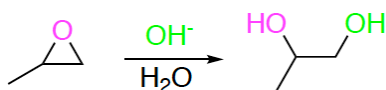
*Acid + Nucleophile*



*Mechanism summary:*

1) *protonate oxygen*  
 2) *nucleophilic attack*  
 Diol product – anti-addition  
 Can also use  $\text{H}_2\text{S}$ ,  $\text{ROH}$ ,  $\text{RSH}$

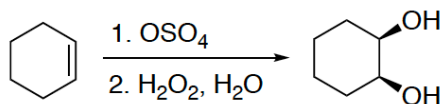
*Base/Nucleophile*



*Mechanism summary:*

1) *nucleophilic attack at less hindered carbon*  
 2) *protonate oxygen*  
 Diol product – anti-addition  
 Also  $\text{OR}^-$ ,  $\text{SR}^-$

**Hydroxylation**



Mild oxidation

Syn addition

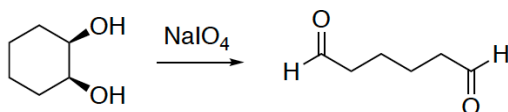
Variations:

Step 2.  $\text{NaHSO}_4, \text{H}_2\text{O}$

or

Step 2. N-methylmorpholine oxide (NMO)

**Oxydative Cleavage**

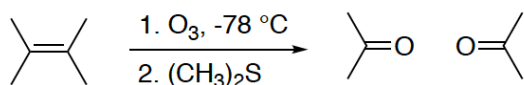


*Cis* diols only!

Aldehyde product

Mild oxidative cleavage

## Ozonolysis



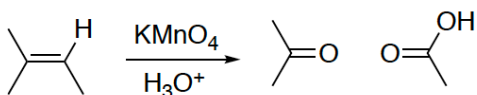
Mild Oxidation

Break double bond

End groups stay the same

May lead to mixtures with asymmetric alkenes

## Permanganate Oxidation



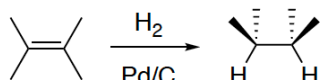
Vigorous Oxidation

Complete oxidation, does not stop at the aldehyde

## Comparisons:

	Ozonolysis	Vigorous Oxidation
$\text{H}_2\text{C}=\text{CH}_2$	$\text{H}_2\text{C}=\text{O}$ formaldehyde	$\text{O}=\text{C}=\text{O}$ carbon dioxide
$\text{RCH}=\text{CH}_2$	$\text{RCH}=\text{O}$ aldehyde	$\text{RCH}(\text{O})\text{OH}$ carboxylic acid
$\text{R}_2\text{C}=\text{CH}_2$	$\text{R}_2\text{C}=\text{O}$ ketone	$\text{R}_2\text{C}=\text{O}$ ketone

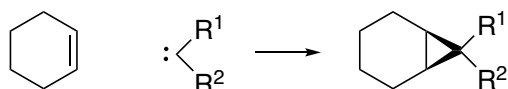
## Hydrogenation



Reduction to alkane

Syn addition of  $\text{H}_2$  (or  $\text{D}_2$ )

## Addition of Carbenes

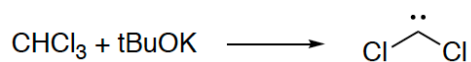


Highly reactive

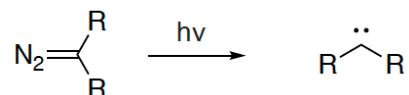
Unfilled octet

Formal charge on carbene carbon = 0

## Generation of Carbenes

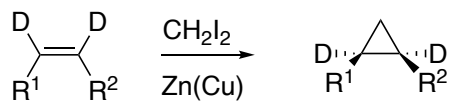


Dichlorocarbene only



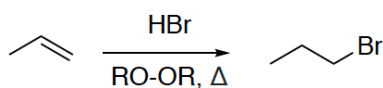
R = H, alkyl

### Simmons-Smith Cyclopropanation



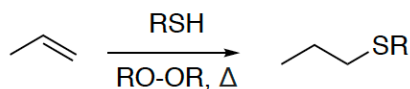
No carbene intermediate

### \*Radical Addition of HBr



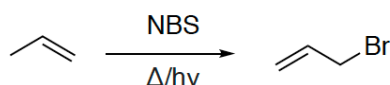
Anti-Markovnikov orientation  
Only HBr (or DBr), *no HI or HCl*  
Radical mechanism

### Thiol-ene Reaction



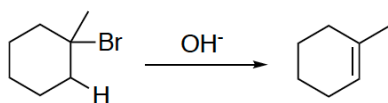
Anti-Markovnikov addition of SR  
Radical mechanism

### \*Allylic Bromination

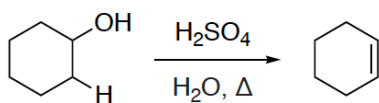


Radical mechanism *via* resonance stabilized allyl radical

### Synthesis of Alkenes (an introduction)



Elimination of HBr  
More substituted C=C (Saytzeff orientation)

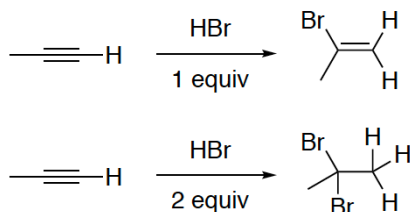


Elimination of H<sub>2</sub>O  
Need heat

## Reactions of Alkynes

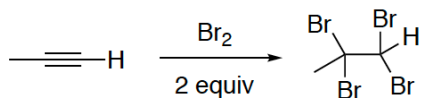
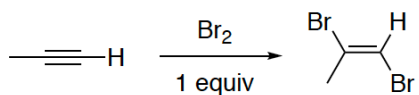
### General Characteristics

#### \*Addition of HX



Markovnikov orientation  
Similar to alkenes  
Via 2° vinylic carbocation first

**\*Addition of X<sub>2</sub>**

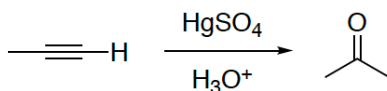


*Anti*-addition

Similar to alkenes

Via 2° vinylic carbocation first

**\*Oxymercuration**



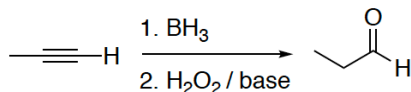
Ketone product

No analogous demercuration step

Via acid tautomerization

(know *tautomerism mechanism separately*)

**\*Hydroboration**



9-BBN (H-BR<sub>2</sub>) and **deuterated** variations

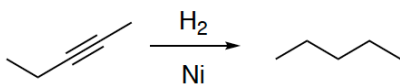
Aldehyde generation

Skip mechanism for step 2

Via base tautomerization

(know *tautomerism mechanism separately*)

**Full Reduction**



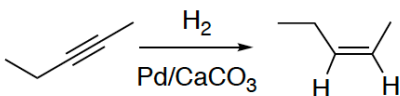
Also with D<sub>2</sub>

Other catalysts: Ni, Pt, Pd, PtO

Full reduction to alkane

No reaction without catalyst

**Partial Reduction**

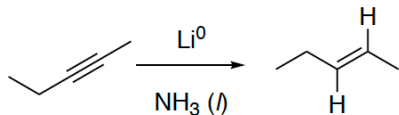


Lindlar's catalyst

Syn - addition (Z isomer)

D<sub>2</sub> also

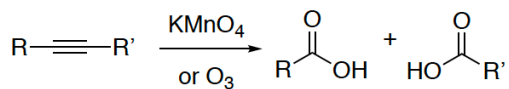
## Dissolving Metal Reduction



Anti – addition

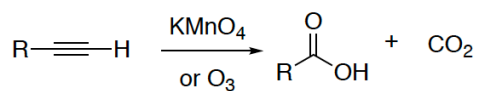
Also ND<sub>3</sub> instead of NH<sub>3</sub>

## Oxidative Cleavage



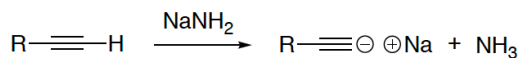
May lead to mixtures if asymmetric alkyne is used

Break alkyne to form carboxylic acids

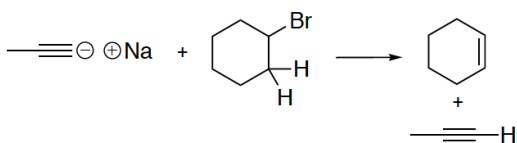
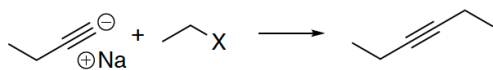


One product + CO<sub>2</sub> (g)

## \*Acetylides as Nucleophiles

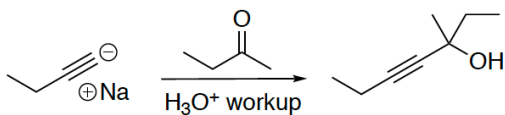


Acetylide can act as a nucleophile with 1° RX only



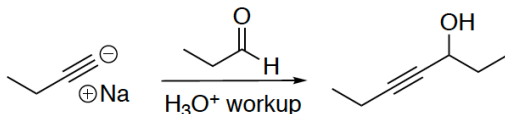
Acetylides can act as a base with 2° and 3° R-X

## \*Addition of Acetylides to Carbonyls

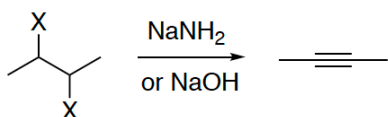


First, form acetylide

Need acidic workup

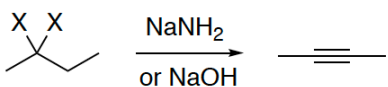


## \*Synthesis of Alkynes



X = Cl, Br, I

Dehydrohalogenation of vicinal dihalides



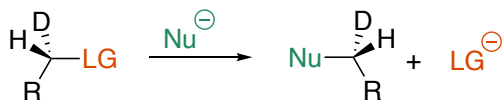
X = Cl, Br, I

Dehydrohalogenation of geminal dihalides

## Substitution / Elimination

## General Characteristics

### \*S<sub>N</sub>2



Second order kinetics

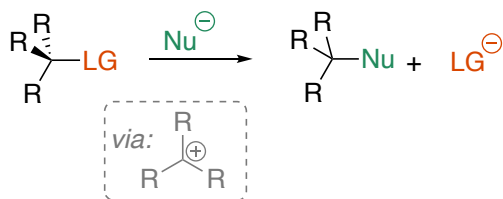
Backside attack on 1° and 2° R-LG

(LG = leaving group, R = alkyl)

Inversion of stereochemistry

Use polar aprotic solvents

### \*S<sub>N</sub>1



Second order kinetics

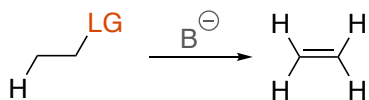
Best for R-LG where R leads to a stable carbocation

(LG = leaving group, R = alkyl)

Loss of stereochemistry

Use polar protic solvents

### \*E2



Second order kinetics

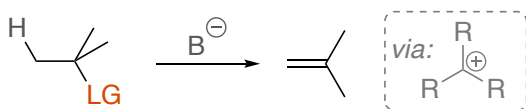
Kinetic isotope effect

Antiperiplanar orientation needed

B = Base

(LG = leaving group)

### \*E1



First order kinetics

B = Base

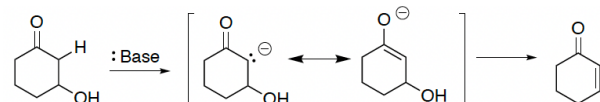
Best for R-LG where R leads to a stable carbocation

(LG = leaving group)

Saitsev's rule determines regiochemistry

E- alkene preferred stereochemistry

### \*E1cB



Via resonance-stabilized carbanion

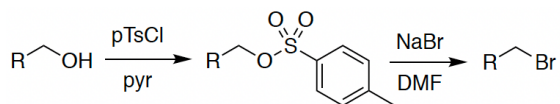
Strongly basic conditions

Poor leaving groups (e.g. -OH)

## Reactions of Alcohols

## General Characteristics

### \*ROH to Alkyl Halides from Tosylates

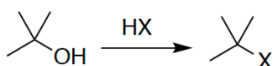


Turns -OH to better **LG**

Can use a good nucleophile for  $\text{S}_{\text{N}}2$

See additional  $\text{S}_{\text{N}}2$  requirements above

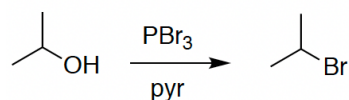
### \*Acid Catalyzed ROH to Alkyl Halides by $\text{S}_{\text{N}}1$



Protonates -OH to turn into better **LG**

See additional  $\text{S}_{\text{N}}1$  requirements above

### ROH to Alkyl Halides Using $\text{PX}_3$

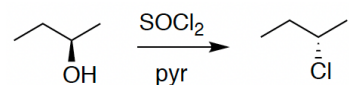


Works with  $\text{PCl}_3$ ,  $\text{PBr}_3$ ,  $\text{P} + \text{I}_2$

Net  $\text{S}_{\text{N}}2$

Best for  $1^\circ$  and  $2^\circ$  R-OH

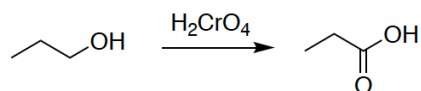
### ROH to R-Cl Using $\text{SOCl}_2$



Net  $\text{S}_{\text{N}}2$

Best for  $1^\circ$  and  $2^\circ$  R-OH

### Vigorous Oxidation of Alcohols



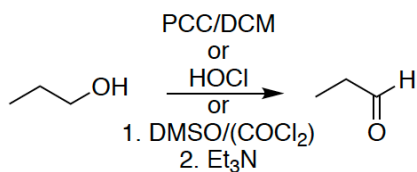
R-OH =

$1^\circ$  yields Carboxylic Acid

$2^\circ$  yields Ketone

$3^\circ$  no reaction

### Mild Oxidation of Alcohols



R-OH =

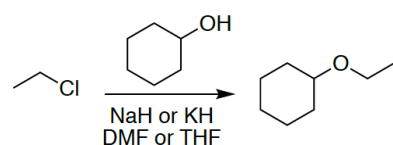
$1^\circ$  yields Aldehyde

$2^\circ$  yields Ketone

$3^\circ$  no reaction

See also, Swern oxidation

### \*Williamson-Ether Synthesis



$1^\circ$  R-X, ok for  $2^\circ$

Non-nucleophilic base

Aprotic polar solvent

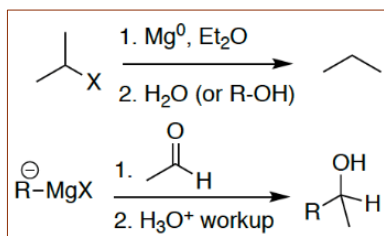
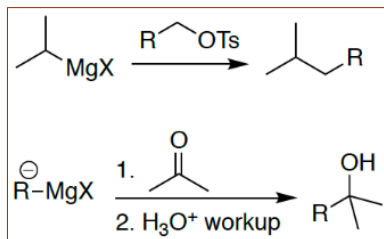
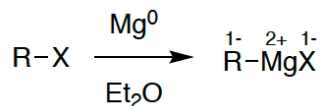
$\text{S}_{\text{N}}2$ -like mechanism



## Organometallic Reagents

## General Characteristics

### \*Grignard Reagents



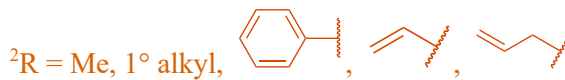
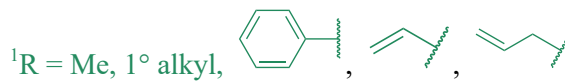
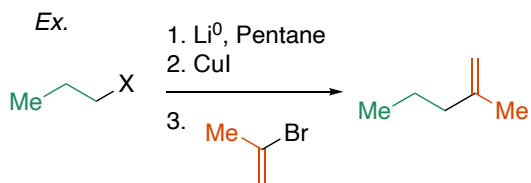
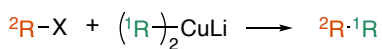
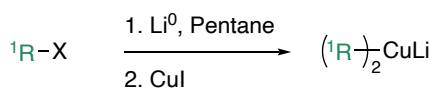
### Organomagnesium reagents

R = 1°, 2°, 3° RX, alkenyl, aryl, benzylic

X = Cl, Br, I

Makes alkanes

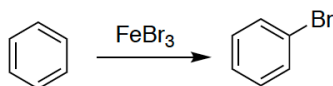
### \*Gillman Reagents



## Electrophilic Aromatic Substitution

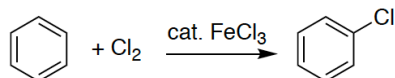
### General Characteristics

#### \*Bromination



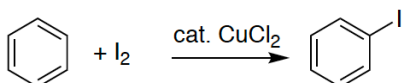
Br activated as electrophile  
RDS = breaking aromaticity  
Resonance stabilized carbocation

#### \*Chlorination



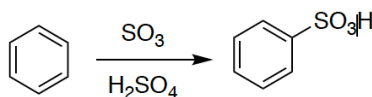
Same mechanism as bromination

#### \*Iodination



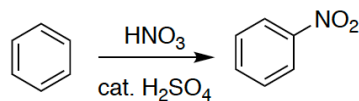
Same mechanism as bromination  
Also with  $\text{I}_2 + \text{H}_2\text{O}_2 + \text{H}_2\text{SO}_4$

#### \*Sulfonation



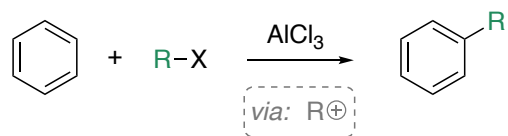
$\text{SO}_3$  activated as electrophile (fuming sulfuric acid)

#### \*Nitration



$\text{NO}_2$  activated as electrophile

#### \*Friedel-Crafts Alkylation



$\text{RX}$  used to generate carbocation, acts as good electrophile

Carbocation rearrangements allowed

$\text{R} = \text{Me}, 1^\circ, 2^\circ, 3^\circ$