

# COLLEGE ORGANIC CHEMISTRY 2011 OUTLINES

## Organic Chemistry Chapter 1 – Structure, Bonding, Acids and Bases, Nomenclature

### Lewis Structures

#### Electrons and Bonding

wave functions ( $\psi$ ) and probability functions ( $\psi^2$ )

sigma and pi bonds

atomic orbitals and molecular orbitals

hybridization

# of e <sup>-</sup> domains	Hybridization	Bond angle
2	sp	180°
3	sp <sup>2</sup>	120°
4	sp <sup>3</sup>	109.5°

the bond angle decreases if the central element has non-bonding electrons and is in period two

#### **Resonance**

Non-bonding electrons can move to an adjacent bond

$\pi$  electrons can move to an adjacent atom or adjacent bond

Electrons tend to move toward a '+' formal charge and/or away from a '-' formal charge

#### **Acids and Bases**

$\downarrow$ pKa = stronger acid,  $\downarrow$ pKb = stronger base

The stronger the acid, the weaker its conjugate base and vice-versa.

The more stable the base, the weaker the base.

#### **Ranking Acids and Bases**

- 1) Charge - More negatively charged species are typically more basic, and more positively charged species are typically more acidic.
- 2) Atom - The larger and/or more electronegative the atom with a negative charge, the more stable it is.
- 3) Resonance stabilization.
- 4) Dipole Induction - Electron withdrawing groups (i.e., electronegative atoms) near the atom that has the negative charge stabilize the ion/molecule.
- 5) Orbitals – a pair of electrons is more stable as follows:  $sp > sp^2 > sp^3$

#### **Nomenclature**

Alkanes

- 1) Find the longest continuous carbon chain to determine base name.
- 2) Number the carbons, starting on the end closest to the first substituent.
- 3) Name the substituents attached to the chain. Use the chain number as the locator. Multiple substituents use di-, tri-, tetra- etc.
- 4) List substituents in alphabetical order. Ignore numerical prefixes and hyphenated prefixes (*tert-* and *sec-*), but not iso and cyclo.
- 5) If there is more than one way of numbering the chain to give the substituents the lowest possible numbers, rank the substituents by alphabetical order giving the lower number to the substituent beginning with the the letter closer to 'A.'
- 6) If there is more than way of to come up with the longest parent chain, then choose the one with the most substituents.

1	meth
2	eth
3	prop
4	but
5	pent
6	hex
7	hept
8	oct
9	non
10	dec
11	undec
12	dodec

Naming Complex substituents

Naming alkyl halides, ethers, alcohols, amines, alkenes

## Organic Chemistry Chapter 2 – Molecular Interactions and Conformations

### Intermolecular Forces

London Dispersion Forces (van der Waals Forces) – weak interactions due to a transient (temporary) dipole  
-all molecules have these; the larger you are, the larger the force

Dipole-Dipole Forces – interaction between molecules having permanent dipole moments  
-the larger the dipole moment, the larger the force

Hydrogen Bonding – a super strong dipole-dipole force  
-must have hydrogen bound to F, O, N to H-bond as a pure liquid  
-must only have F, O, N to hydrogen bond with water

### Effects on melting pt and boiling pt

Branching decreases the boiling pt, but increases the melting pt

Solubility - “Like dissolves like.”

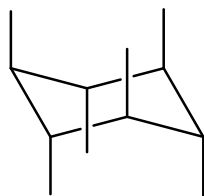
### Newman Projections

Staggered and eclipsed conformations

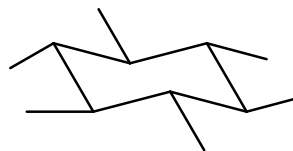
Gauche Interactions

### Chair Conformations of Cyclohexane

Substituents in equatorial positions are lower in energy (i.e. more stable) than when in axial positions



Axial bonds



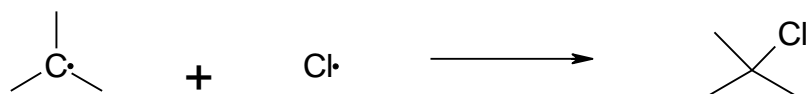
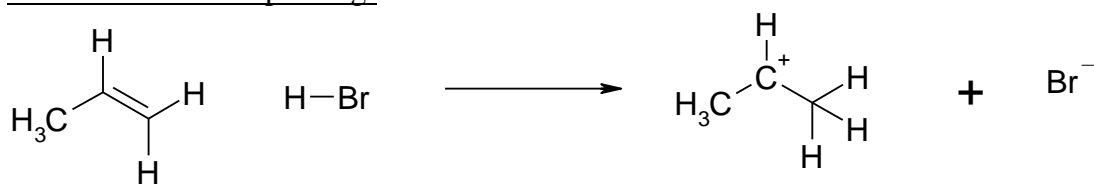
Equatorial bonds

1,3-diaxial interactions

## Organic Chemistry Chapter 3 – Introduction to Reaction Mechanisms

### Arrow Pushing

Show curved arrow pushing:



### Reaction Coordinate Diagrams

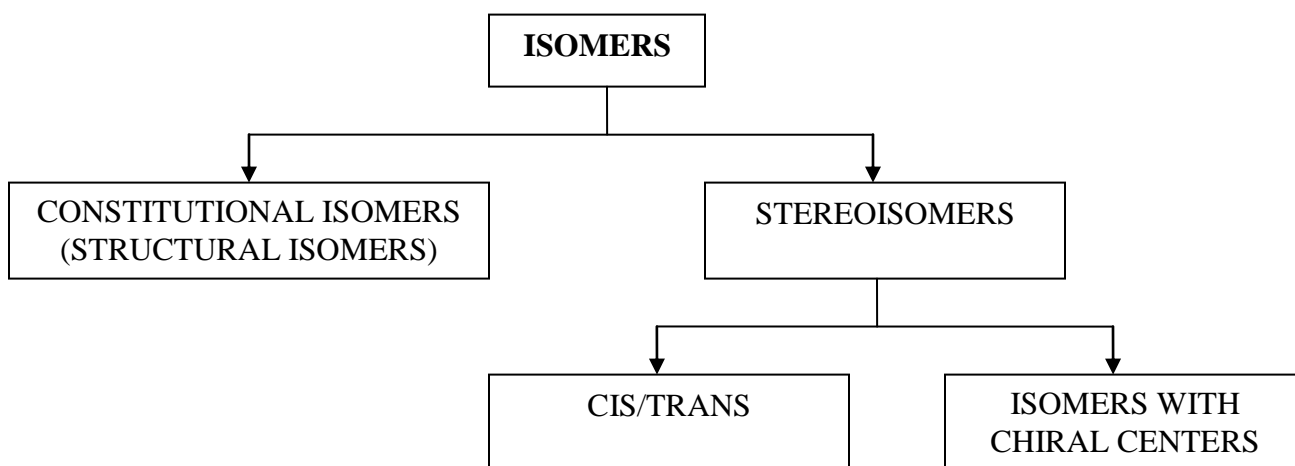
Endogonic vs Exergonic

$$\Delta G = -RT \ln K_{eq}$$

Transition state, activation energy, rate constant

Hammond Postulate

## Organic Chemistry Chapter 4 – Isomers and Stereochemistry



**Chiral** compounds have non-superimposable (non-identical) mirror images called *enantiomers*.

**Achiral** compounds have mirror images that are superimposable (identical).

Chiral compounds are said to be *optically active*.

A 50/50 mixture of enantiomers is called a *racemic mixture* and is optically inactive.

Chirality centers are tetrahedral centers with four different substituents (i.e. asymmetric centers).

R vs. S

Fischer projections

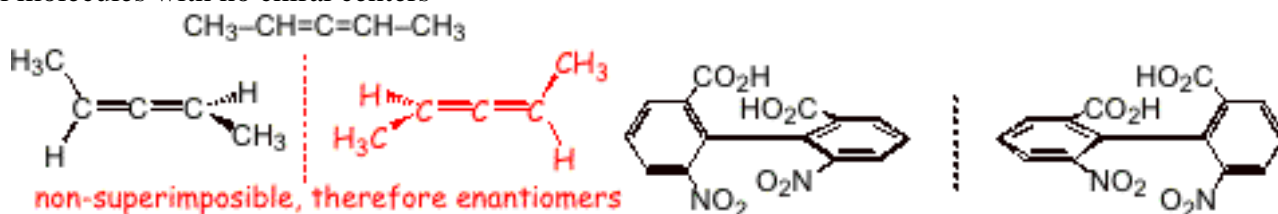
Multiple chiral centers

**Diastereomers**

**Meso** compounds (achiral but having chiral centers)

Amine inversion

Chiral molecules with no chiral centers



Optical Activity

Specific rotation  $[\alpha] = \frac{\alpha \text{ (observed)}}{c \cdot l}$

$c$  = concentration (in g/ml)     $l$  = path length (in dm)

Optical purity =  $\frac{\text{observed specific rotation}}{\text{specific rotation of pure enantiomer}}$

Enantiomeric excess =  $\frac{\text{excess of single enantiomer}}{\text{entire mixture}}$

## Organic Chemistry Chapter 5 – Alkenes

### Nomenclature

-E/Z

### Addition Reactions to Alkenes

Reagents	What's added	Regioselectivity	Stereoselectivity	Rearrangements
HBr (or HCl, HI)	H <sup>+</sup> and Br <sup>-</sup>	Markovnikov	-	Possible
H <sub>3</sub> O <sup>+</sup>	H <sup>+</sup> and OH <sup>-</sup>	Markovnikov	-	Possible
H <sup>+</sup> , ROH	H <sup>+</sup> and OR <sup>-</sup>	Markovnikov	-	Possible
Br <sub>2</sub> /CCl <sub>4</sub> (or Cl <sub>2</sub> /CCl <sub>4</sub> )	Br <sup>+</sup> and Br <sup>-</sup>	-	Anti	Not possible
Br <sub>2</sub> /H <sub>2</sub> O Cl <sub>2</sub> /H <sub>2</sub> O	Br <sup>+</sup> and OH <sup>-</sup>	Markovnikov	Anti	Not possible
Br <sub>2</sub> /ROH Cl <sub>2</sub> /ROH	Br <sup>+</sup> and OR <sup>-</sup>	Markovnikov	Anti	Not possible
(1) Hg(OAc) <sub>2</sub> , H <sub>2</sub> O (2) NaBH <sub>4</sub>	H <sup>+</sup> and OH <sup>-</sup>	Markovnikov	Anti	Not possible
(1) Hg(OAc) <sub>2</sub> , ROH (2) NaBH <sub>4</sub>	H <sup>+</sup> and OR <sup>-</sup>	Markovnikov	Anti	Not possible
(1) BH <sub>3</sub> ·THF (2) H <sub>2</sub> O <sub>2</sub> , OH <sup>-</sup> , H <sub>2</sub> O	H <sup>+</sup> and OH <sup>-</sup>	Anti-Markovnikov	Syn	Not possible
H <sub>2</sub> /catalyst (Catalyst = Pt/C, Pd/C, or Ni)	H and H	-	Syn	Not possible
HBr/ROOR (peroxide)	H <sup>+</sup> and Br <sup>-</sup>	Anti-Markovnikov	-	Not possible
RCO <sub>3</sub> H/K <sub>2</sub> CO <sub>3</sub> (MCPBA)	epoxide	-	Syn	Not possible
CH <sub>2</sub> N <sub>2</sub> /Δ (carbene)	cyclopropane	-	Syn	Not Possible

Stability (More substituted alkenes are more stable)

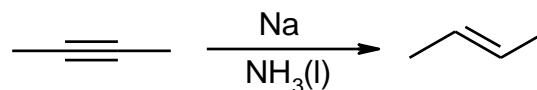
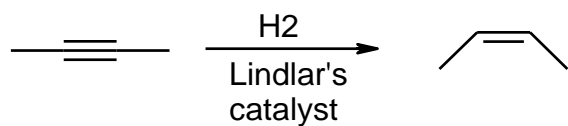
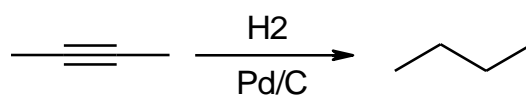
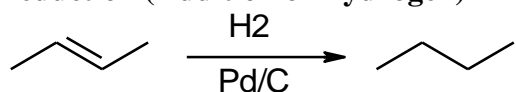
Heats of Hydrogenation

## Organic Chemistry Chapter 6 – Alkynes

### Nomenclature

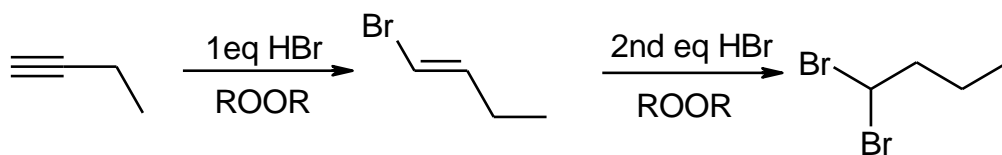
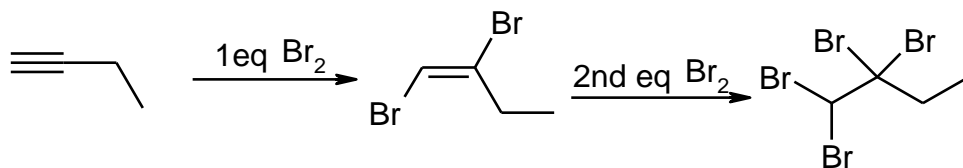
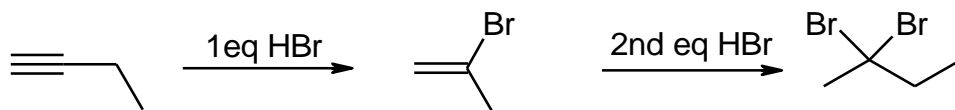
### Acidity of alkynes

### Reduction (Addition of Hydrogen)

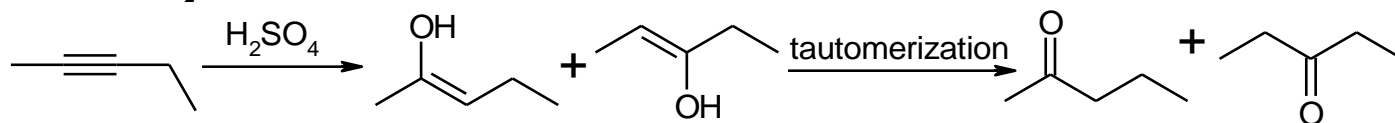


### Addition of H-X or X<sub>2</sub>

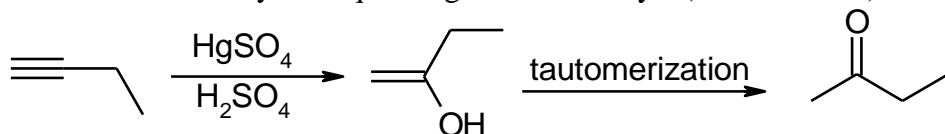
Alkynes are less reactive than alkenes in addition rxns



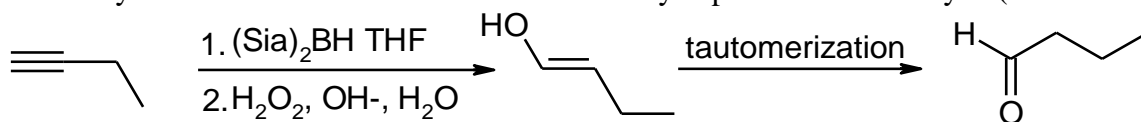
### Addition of H<sub>2</sub>O



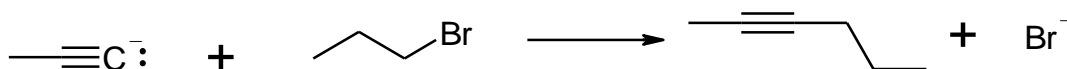
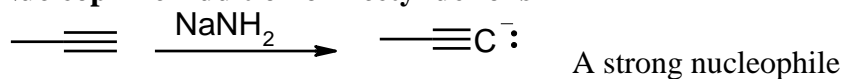
Terminal alkynes require HgSO<sub>4</sub> as a catalyst (Markovnikov)



Hydroboration oxidation with a terminal alkyne produces an aldehyde (anti-Markovnikov)



### Nucleophilic Addition of Acetylide Ions



## Organic Chemistry Chapter 7 – Conjugated Systems

### Addition Rxns to Conjugated Dienes

Kinetic Product – has lowest activation energy (has most stable transition state)

Major product at lower temperatures

Thermodynamic Product – most stable product (i.e. most substituted alkene)

Major product at higher temperatures

### $\pi$ Molecular Orbitals

1,3-butadiene

allyl system

benzene

### Diels-Alder Rxns ([4 + 2] cycloaddition)

concerted syn addition between dienophile and electron-deficient diene

diene must be in the s-cis conformation

only 1,2 and 1,4 products observed with unsymmetrical reagents (relationship of D to W)

Frontier Molecular Orbital Theory (FMO Theory)

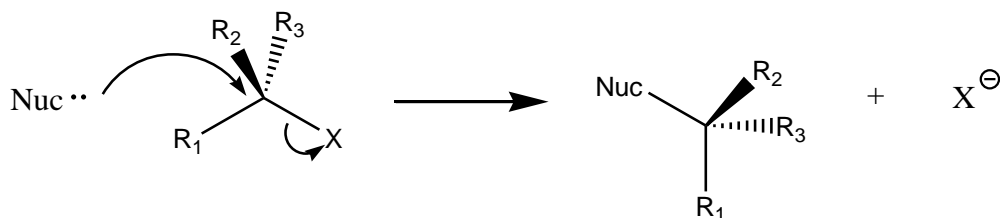
Conservation of orbital symmetry



## Organic Chemistry Chapter 8 – Substitution Reactions

### S<sub>N</sub>2 reactions – Substitution Nucleophilic Bimolecular

Mechanism

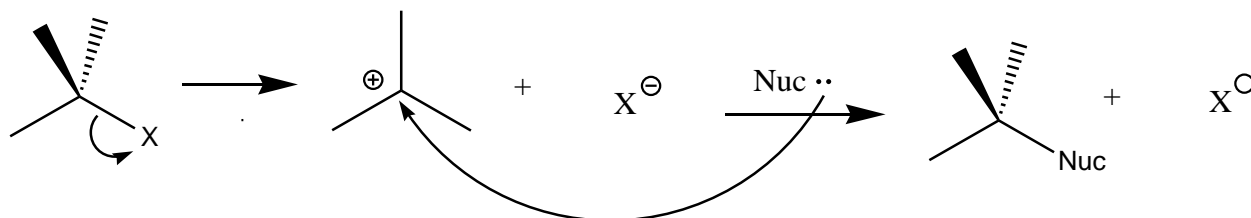


$$\text{rate} = k[\text{substrate}][\text{nucleophile}]$$

results in inversion of configuration

### S<sub>N</sub>1 reactions – Substitution Nucleophilic Unimolecular

Mechanism



$$\text{Rate} = k[\text{substrate}]$$

Carbocation rearrangements are possible

Results in both inversion and retention of configuration (racemization)

Weak nucleophiles (or low concentrations of strong nucleophiles) are ok as it isn't in the RDS

Addition of AgNO<sub>3</sub> facilitates carbocation formation

### S<sub>N</sub>2 vs. S<sub>N</sub>1

	S <sub>N</sub> 2	S <sub>N</sub> 1
<b>Nucleophile</b>	strong required	weak is ok
<b>Electrophile</b> (has LG)	CH <sub>3</sub> > 1° > 2°	3° > 2°
<b>Solvent</b>	polar aprotic (preferred)	polar protic
<b>Leaving Group</b>	Good (I <sup>-</sup> > Br <sup>-</sup> > Cl <sup>-</sup> > F <sup>-</sup> )	Good (I <sup>-</sup> > Br <sup>-</sup> > Cl <sup>-</sup> > F <sup>-</sup> )
<b>Rearrangements</b>	Not Possible	Possible
<b>Inversion</b>	Yes	No (Racemization)

polar aprotic solvents include DMSO, acetone, DMF, and acetonitrile (know structures)

benzylic and allylic substrates

aryl and vinyl halides are unreactive

nucleophile strength

in protic solvent

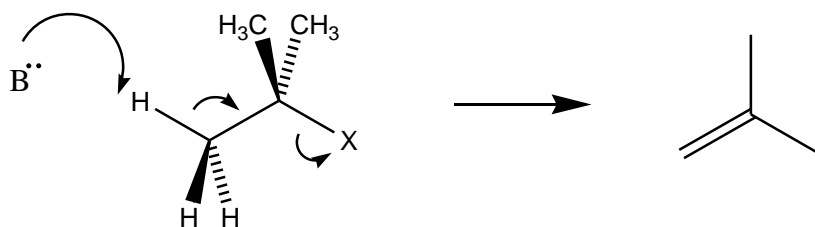
in aprotic solvent

Use of KF with crown ethers for S<sub>N</sub>2 rxns

## Organic Chemistry Chapter 9 – Elimination Reactions

### E2 reactions – Elimination Bimolecular

Mechanism



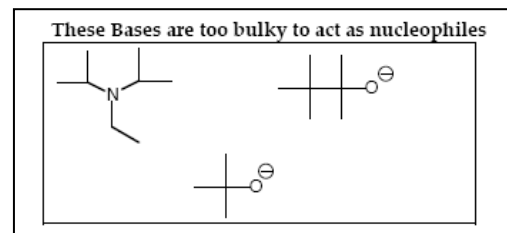
$$\text{rate} = k[\text{substrate}][\text{base}]$$

H and X (leaving group) should be anti-periplanar (anti-coplanar)

Forms most substituted double bond (Zaitsev's Rule)

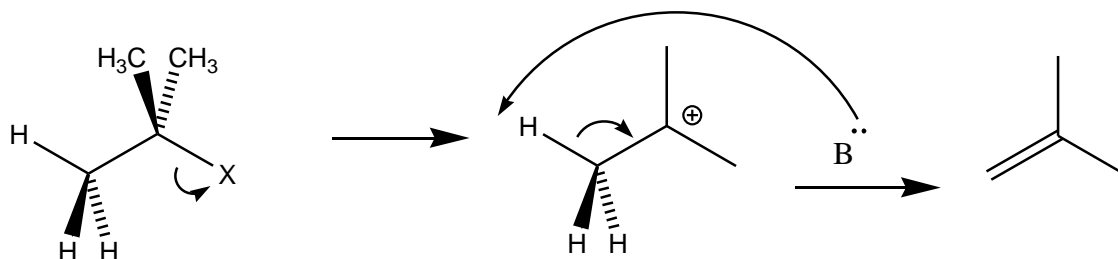
Forms least substituted (Hofmann) if  $\text{F}^-$  is the leaving group

Forms least substituted (Hofmann) if a bulky base is used with  $3^\circ$  halide



### E1 reactions – Elimination Unimolecular

Mechanism



$$\text{Rate} = k[\text{substrate}]$$

Carbocation rearrangements are possible

Forms most substituted double bond (Zaitsev's Rule)

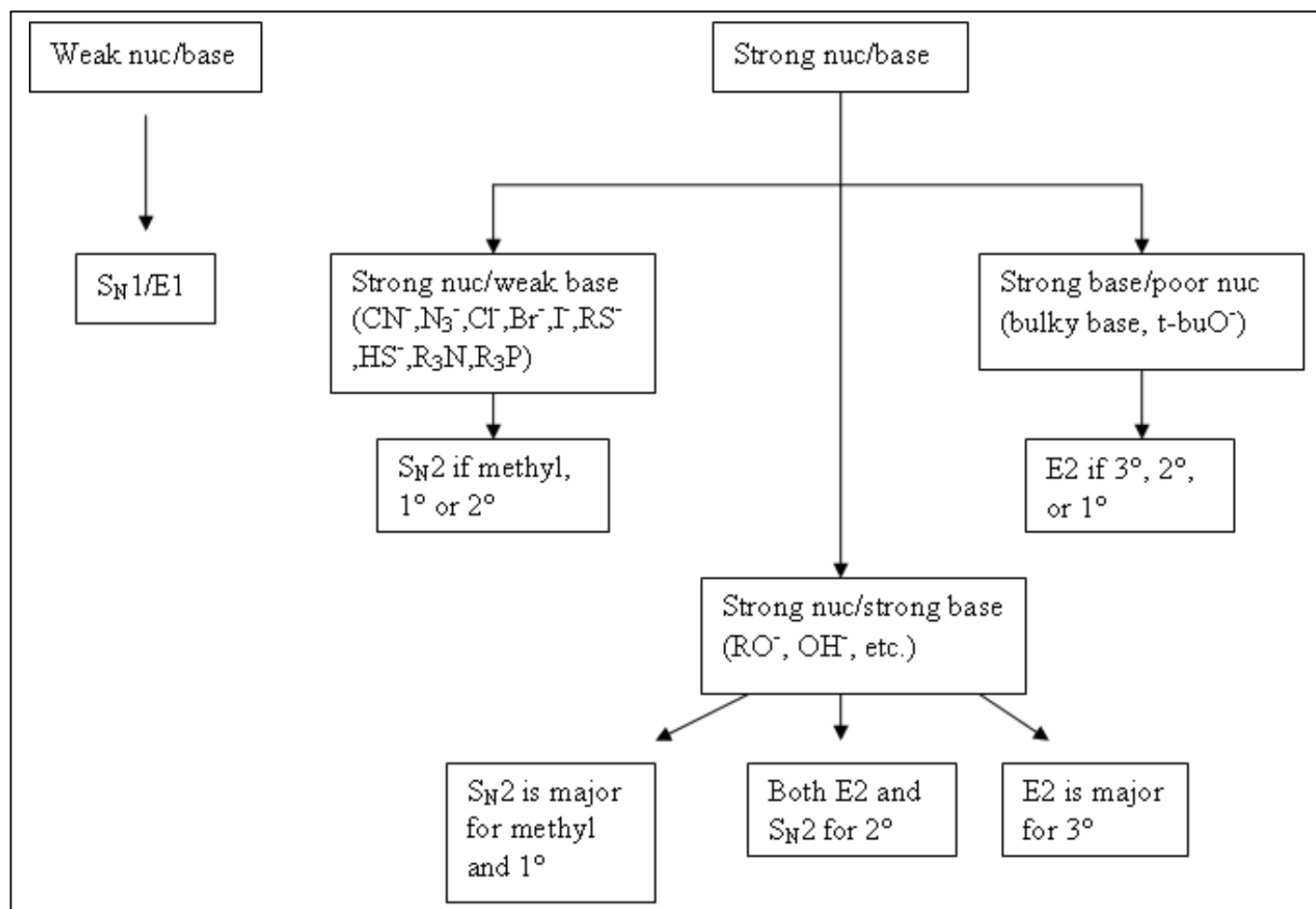
Favored by heat due to entropy

### E2 vs. E1

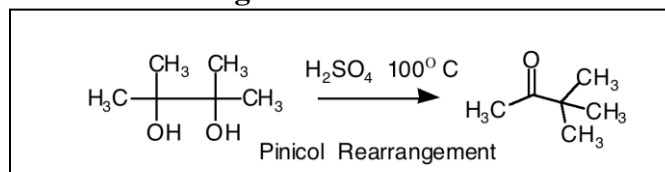
	<b>E2</b>	<b>E1</b>
<b>Base</b>	strong base	weak base
<b>Electrophile</b> (has LG)	$3^\circ > 2^\circ > 1^\circ$	$3^\circ > 2^\circ$
<b>Solvent</b>	polar aprotic (best)	polar protic
<b>Leaving Group</b>	Good ( $\text{I}^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$ )	Good ( $\text{I}^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$ )
<b>Rearrangements</b>	Not possible	Possible
<b>Stereochemistry</b>	Anti-coplanar	None

	<b>S<sub>N</sub>2</b>	<b>E2</b>	<b>S<sub>N</sub>1</b>	<b>E1</b>
<b>Electrophile</b> (has LG)	$\text{CH}_3 > 1^\circ > 2^\circ$	$3^\circ > 2^\circ > 1^\circ$	$3^\circ > 2^\circ$	$3^\circ > 2^\circ$
<b>Nucleophile/Base</b>	strong nuc	strong base	weak nuc	weak base
<b>Solvent</b>	polar aprotic (preferred)	polar aprotic (preferred)	polar protic	polar protic
<b>Leaving Group</b>	good	good	good	good

## Substitution/Elimination Map



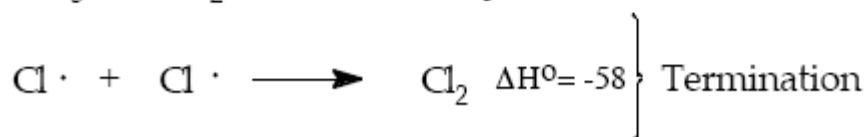
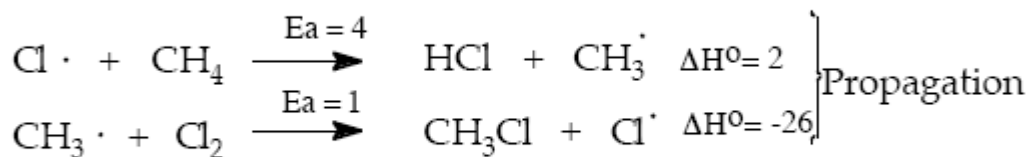
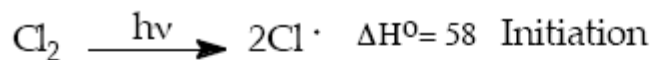
## Pinacol Rearrangement



## Organic Chemistry Chapter 10 – Radical Rxns

### Chlorination vs Bromination

#### Mechanism

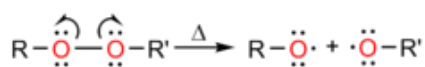


Selectivity

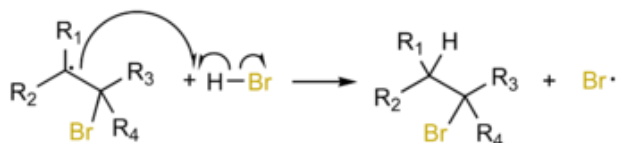
### Addition of HBr/ROOR

#### Mechanism

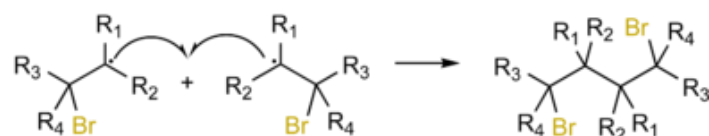
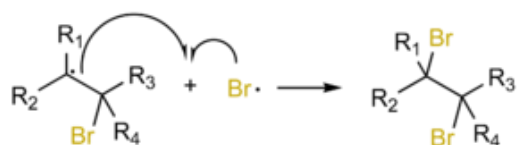
##### Initiation



##### Propagation



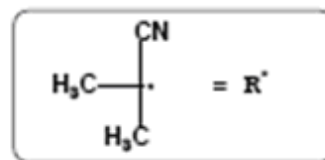
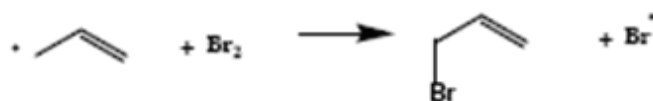
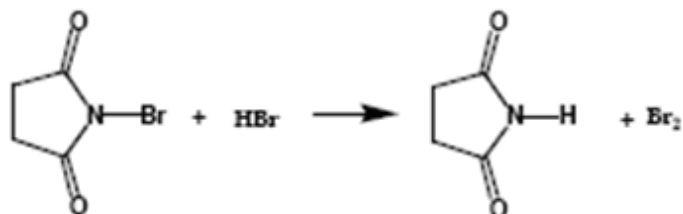
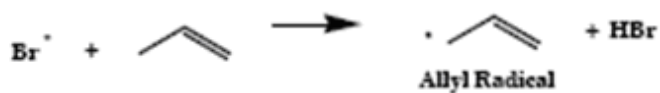
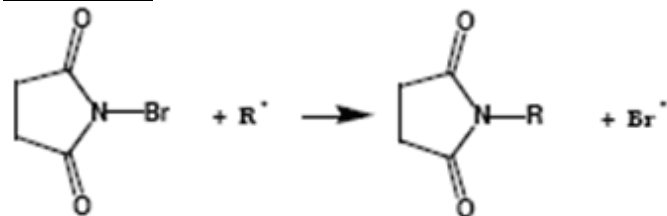
##### Termination



### Bromination with NBS

Useful for brominating allylically

#### Mechanism



## Organic Chemistry Chapter 11 – Mass Spectrometry

A beam of electrons is used to remove an electron (or electrons) from a molecule.

If the molecule doesn't fragment, this results in a radical cation which is called the molecular ion.

The molecule may also fragment forming a radical and a cation.

**Only the cation is detected!**

The tallest peak on the spectrum is called the base peak.

The rest of the peaks are given values expressed as a percentage of the height of the base peak.

Predicting fragmentation patterns

The most stable fragments will yield the tallest peaks.

Resonance-stabilized and more substituted carbocations are more stable.

Patterns to identify

**Bromine's  $M+2$  peak is nearly as tall as its  $M^+$  peak**

**Chlorine's  $M+2$  peak is about 1/3 the size of its  $M^+$  peak**

**Nitrogen-containing compounds have an odd  $m/z$  for the  $M^+$  peak**

Iodine-containing compounds have a large 'gap' in the spectrum corresponding to the MW of 127 for iodine; often there is a peak at 127 as well.

Alcohols don't typically have a true parent peak, but usually have an  $M-18$  peak as the peak furthest to the right corresponding to the loss of  $H_2O$

***Substituted benzenes typically fragment to form the tropylium ion ( $m/z$  91)***

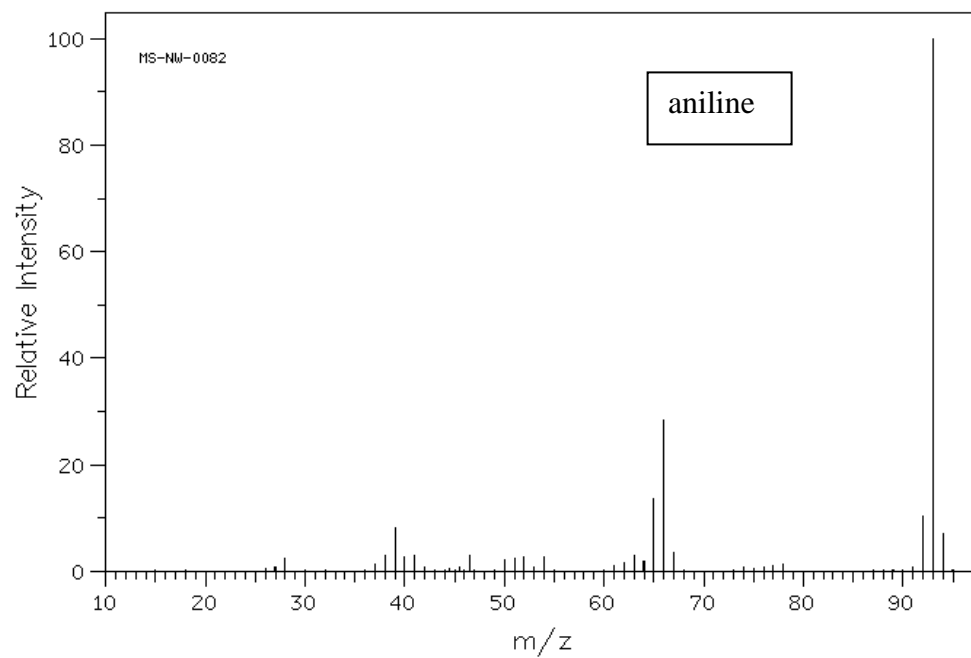
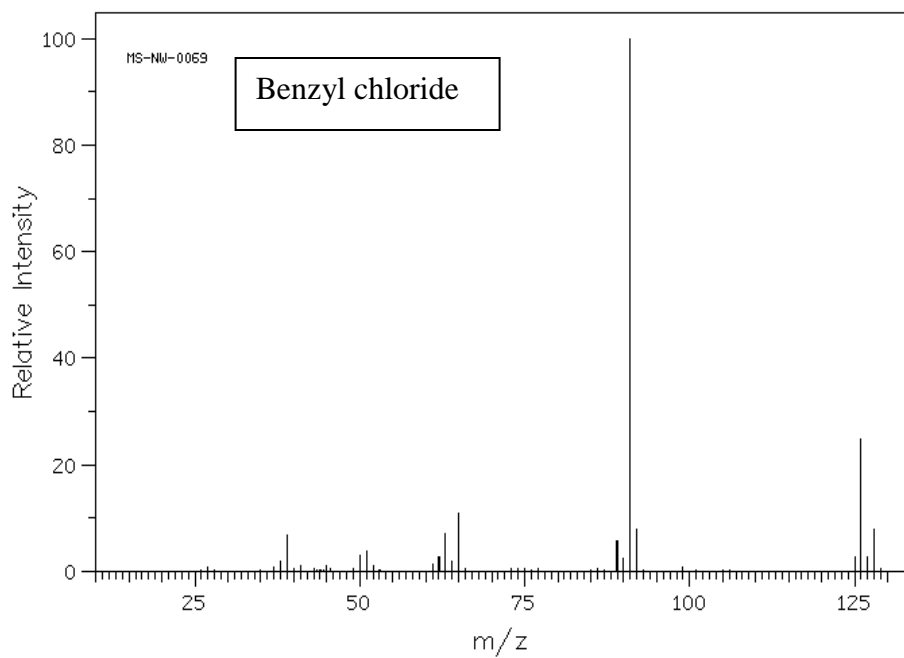
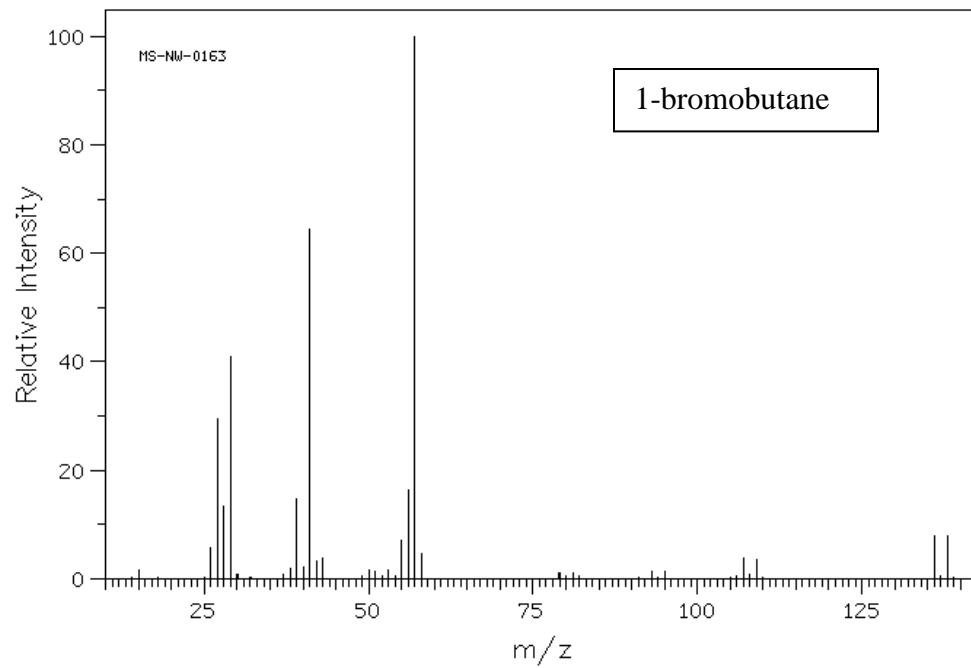
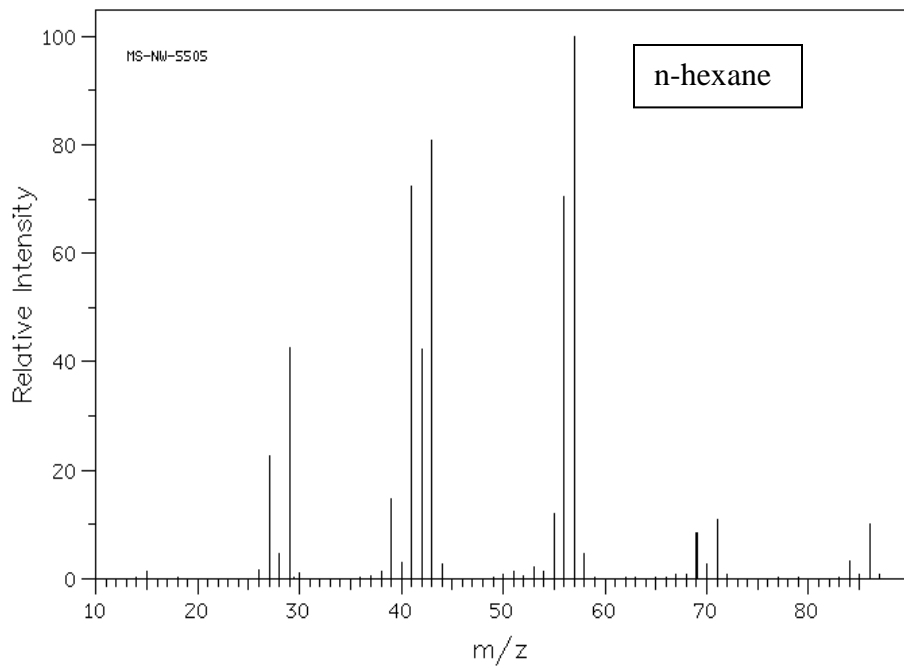
$m/z$  15          methyl group

$m/z$  29          ethyl group

$m/z$  43          propyl group

$m/z$  57          butyl group

$m/z$  41          allyl group



## Organic Chemistry Chapter 12 – IR Spectroscopy

Infra-red light results in the stretching and/or bending of bonds.

Bonds will stretch or bend at characteristic frequencies that allow us to determine the type of bond.

This allows us to identify many of the functional groups.

Frequencies are measured in inverse cm ( $\text{cm}^{-1}$ ) which are called wavenumbers.

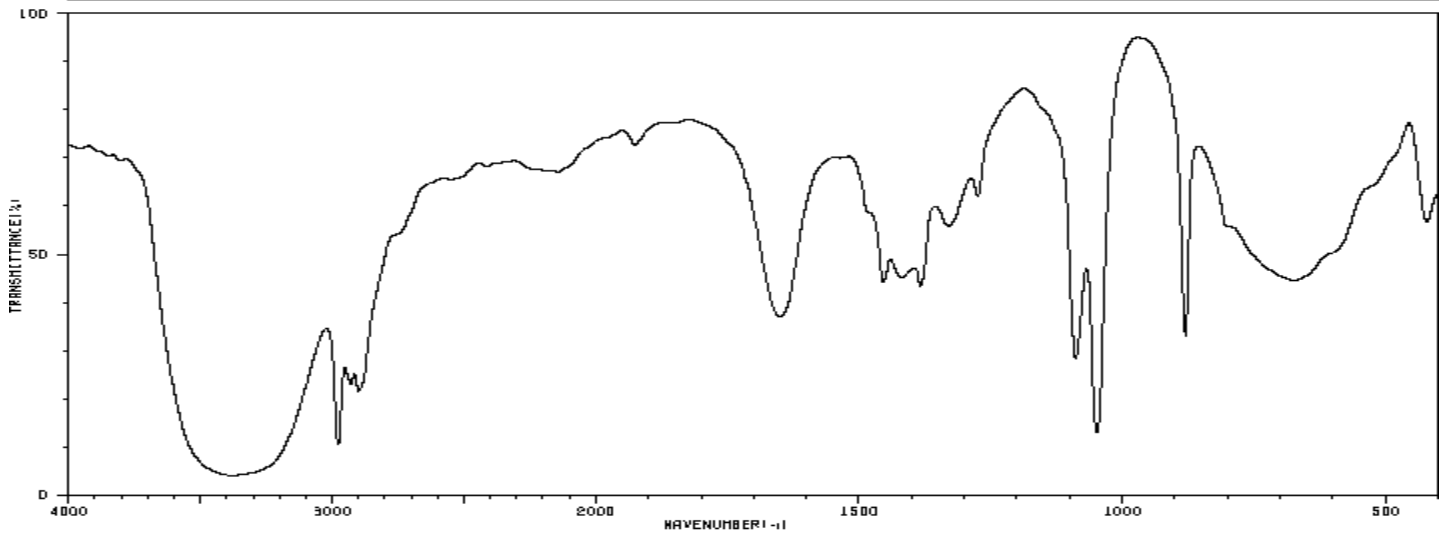
Stretching a bond must change the dipole of a molecule for the bond to be IR active.

You need to be able to identify the following absorptions:

Aromatic C-C	two peaks usually in the range of 1500-1600 $\text{cm}^{-1}$
C=C	$\sim 1650 \text{ cm}^{-1}$
C=O	$\sim 1710 \text{ cm}^{-1}$ (shifts to $\sim 1735 \text{ cm}^{-1}$ for esters)
C $\equiv$ C	$\sim 2100\text{-}2300 \text{ cm}^{-1}$
C $\equiv$ N	$\sim 2100\text{-}2300 \text{ cm}^{-1}$
C-H (aldehyde)	Two peaks at 2710 and 2810 $\text{cm}^{-1}$
sp <sup>3</sup> C-H	just to the right of 3000 $\text{cm}^{-1}$
sp <sup>2</sup> C-H	just to the left of 3000 $\text{cm}^{-1}$
sp C-H	$\sim 3300 \text{ cm}^{-1}$
N-H	$\sim 3300 \text{ cm}^{-1}$ (one peak for -NH-, two peaks for -NH <sub>2</sub> )
O-H (alcohol)	$\sim 3400 \text{ cm}^{-1}$ (a broad, smooth peak)
O-H (acid)	$\sim 2500\text{-}3500 \text{ cm}^{-1}$ (a very broad, ugly peak—not smooth)

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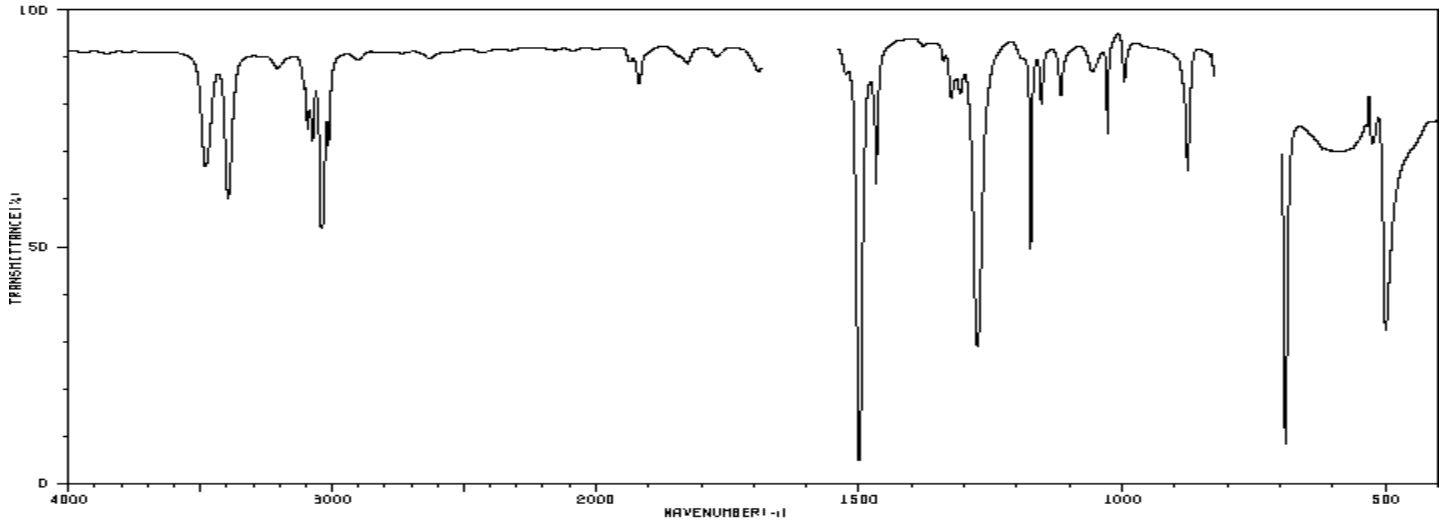
HIT-NO=1374 | SCORE= ( ) | SDBS-NO=1300 | IR-NIDA-21941 : LIQUID FILM  
 ETHYL ALCOHOL  
 $C_2H_6O$



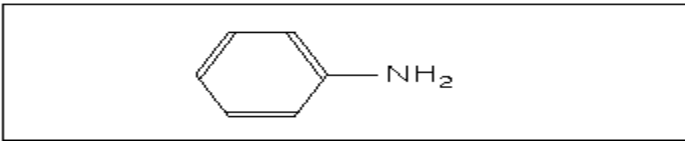
2977	4	1384	32
2930	13	1329	44
2899	12	1275	52
1925	62	1089	18
1650	26	1048	6
1454	33	880	22
1418	33		



HIT-NO=1070 | SCORE= ( ) | SDBS-NO=905 | IR-NIDA-08669 : CCL4 SOLUTION  
 ANILINE  
 $C_6H_7N$



3480	64	2906	86	1340	86	1068	84
3395	58	2630	86	1325	79	1028	72
3209	84	1918	61	1306	79	996	61
3094	72	1833	66	1275	28	876	64
3074	70	1826	66	1174	47	690	8
3041	52	1500	4	1154	77	525	70
3013	68	1468	60	1117	79	500	31

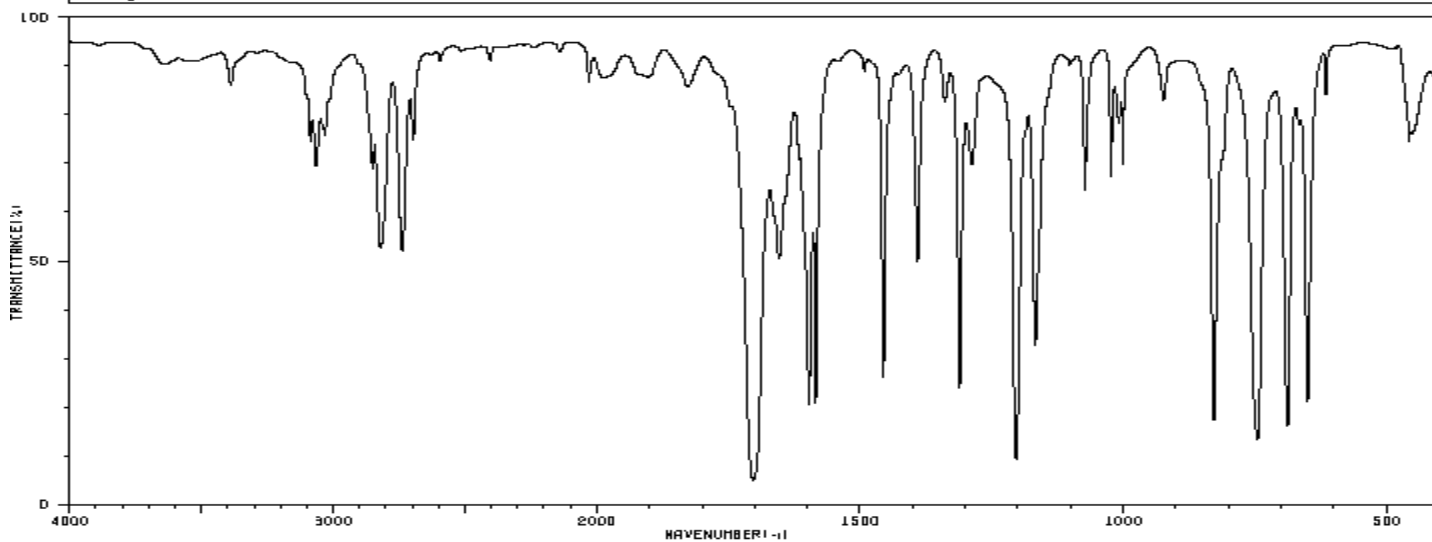




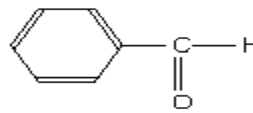
HIT-NO=1117 SCORE= ( ) SOBS-NO=672 IR-NIDA-05223 : LIQUID FILM

BENZALDEHYDE

C<sub>7</sub>H<sub>6</sub>O



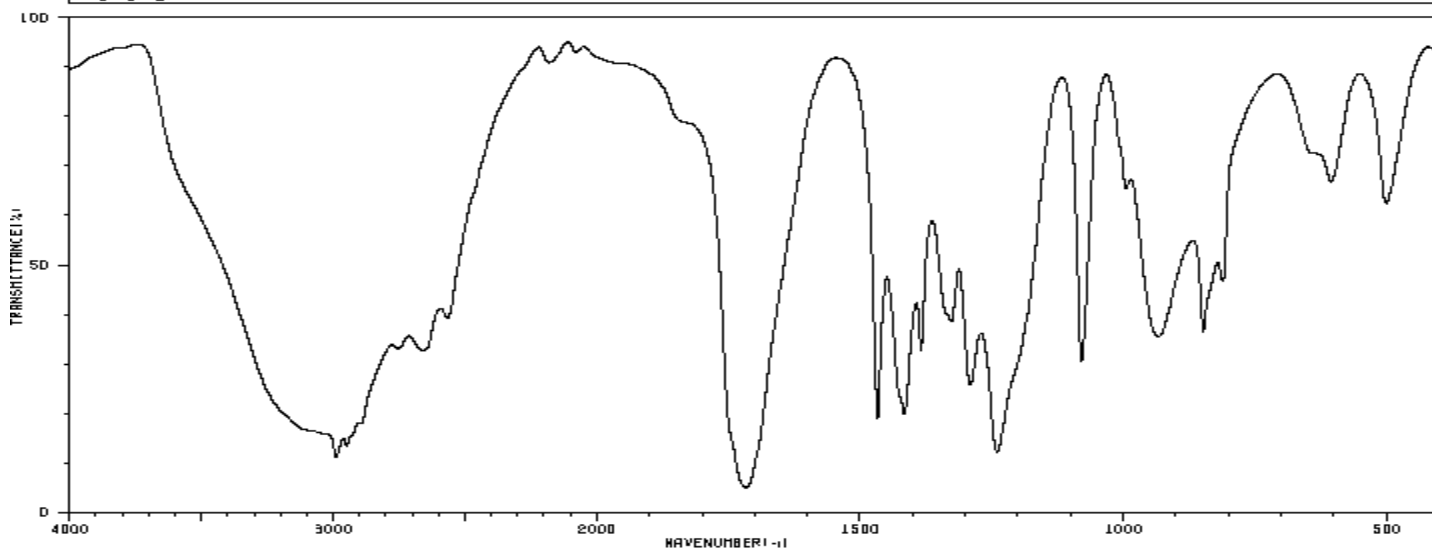
3086	72	1981	84	1597	20	1204	8	828	16
3065	86	1916	84	1584	20	1168	31	746	13
3031	72	1909	84	1456	25	1073	62	688	15
2860	66	1901	84	1391	47	1023	64	667	74
2820	50	1828	81	1339	79	1008	74	650	20
2736	50	1703	4	1311	23	1001	66	615	61
2696	72	1664	49	1288	68	924	79	467	72



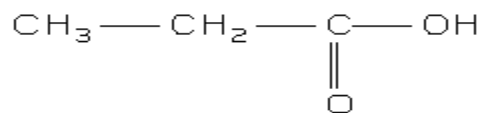
HIT-NO=1276 SCORE= ( ) SOBS-NO=1033 IR-NIDA-05127 : LIQUID FILM

PROPIONIC ACID

C<sub>3</sub>H<sub>6</sub>O<sub>2</sub>

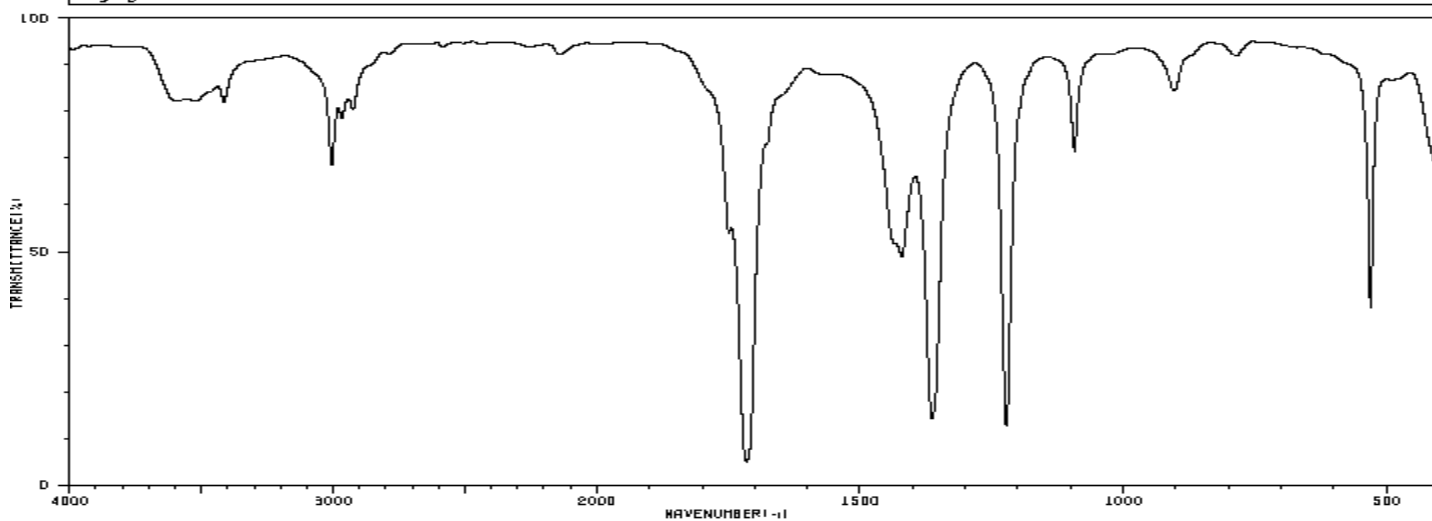


2986	10	1384	32	848	36
2948	12	1327	37	811	44
2860	31	1291	25	814	86
2666	38	1240	12	606	64
1716	4	1080	29	501	60
1467	18	995	62		
1416	19	933	34		

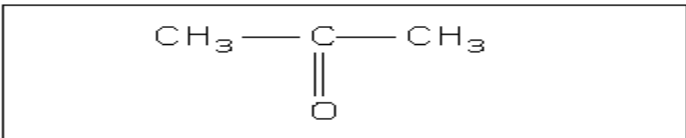


HIT-NO=960 SCORE= ( ) SDBS-NO=319 IR-NIDA-63533 : LIQUID FILM  
 ACETONE

C<sub>3</sub>H<sub>6</sub>O

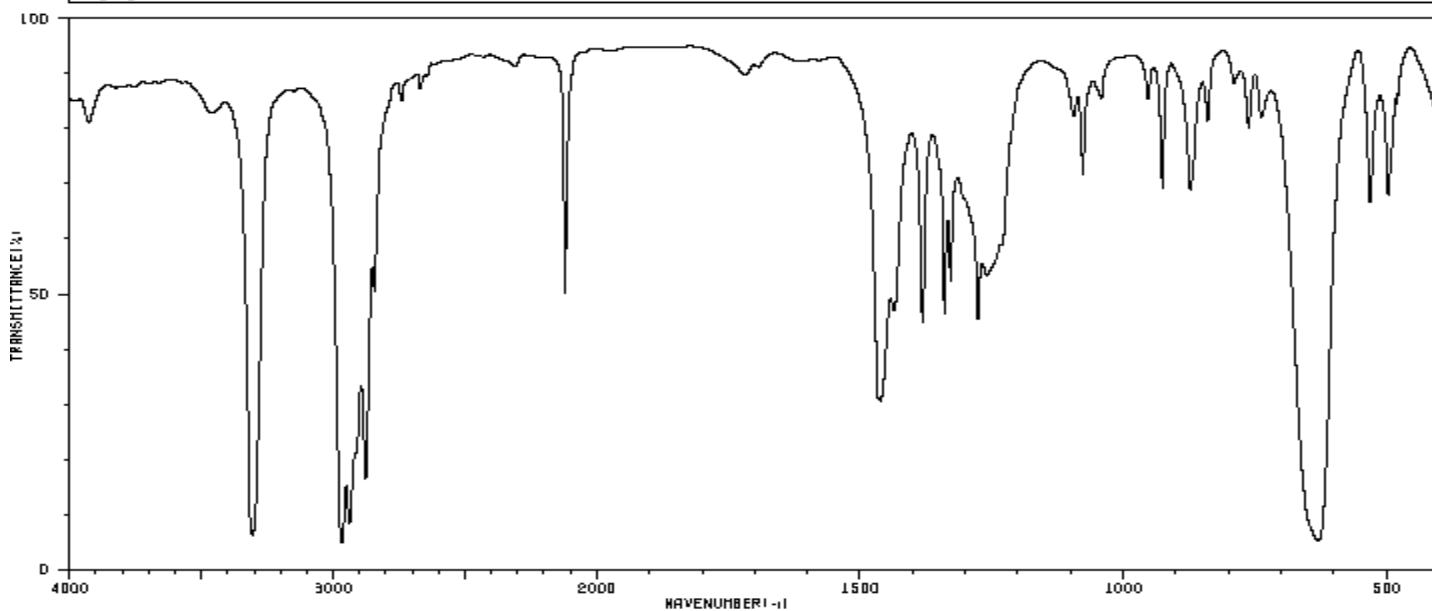


3414	79	1421	47
3005	66	1363	13
2966	74	1223	12
2926	77	1093	68
1749	52	903	81
1715	4	531	36
1434	49		

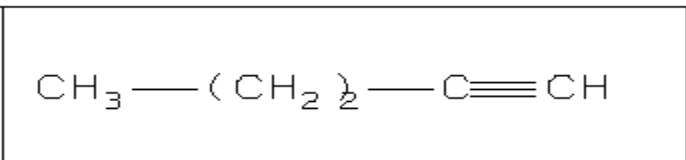


HIT-NO=2943 SCORE= ( ) SDBS-NO=5386 IR-NIDA-13676 : LIQUID FILM  
 1-PENTYNE

C<sub>5</sub>H<sub>8</sub>



3928	79	2741	81	1381	43	1041	81	739	79
3457	79	2670	84	1340	44	954	81	630	5
3307	6	2120	47	1328	50	926	66	532	64
2968	4	1718	86	1276	43	872	66	497	66
2938	7	1466	29	1259	52	840	79	481	81
2876	16	1460	29	1095	79	791	84		
2843	49	1436	44	1077	68	762	77		

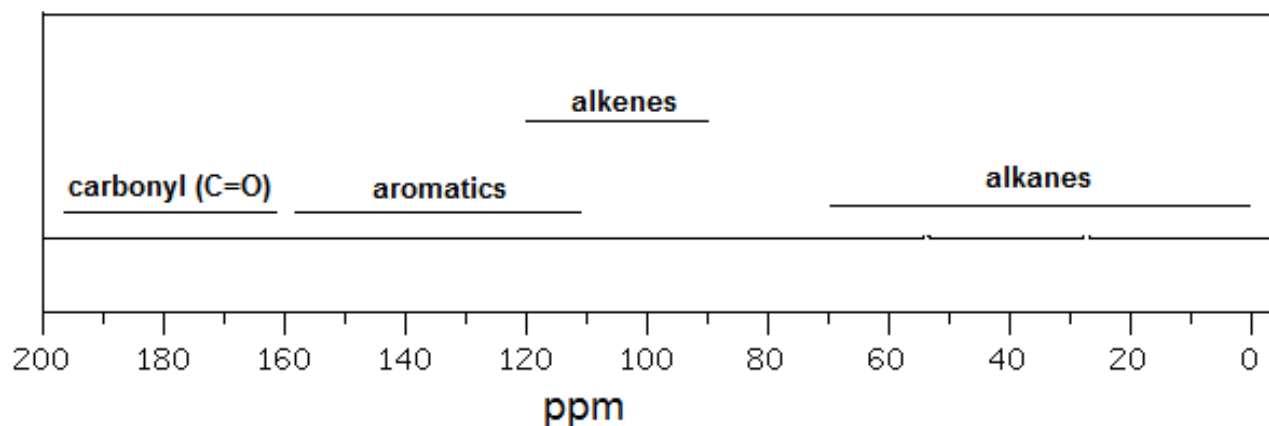


## Organic Chemistry Chapter 13 – NMR Spectroscopy

### $^{13}\text{C}$ NMR

Gives the number of carbon environments in a molecule

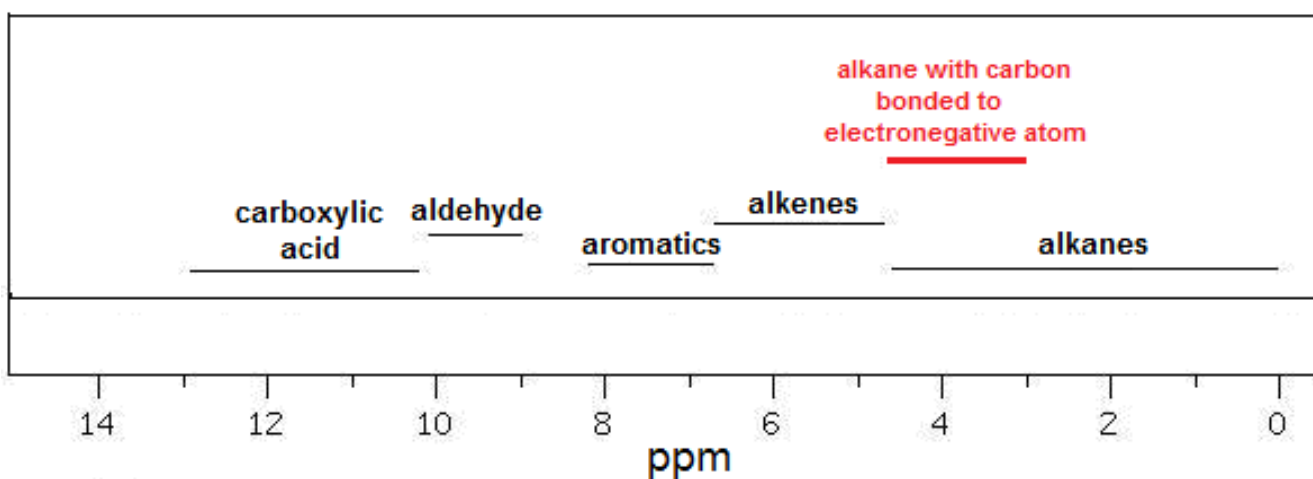
The chemical shift also tells whether the carbon is an alkane, alkene, aromatic, or carbonyl (C=O)

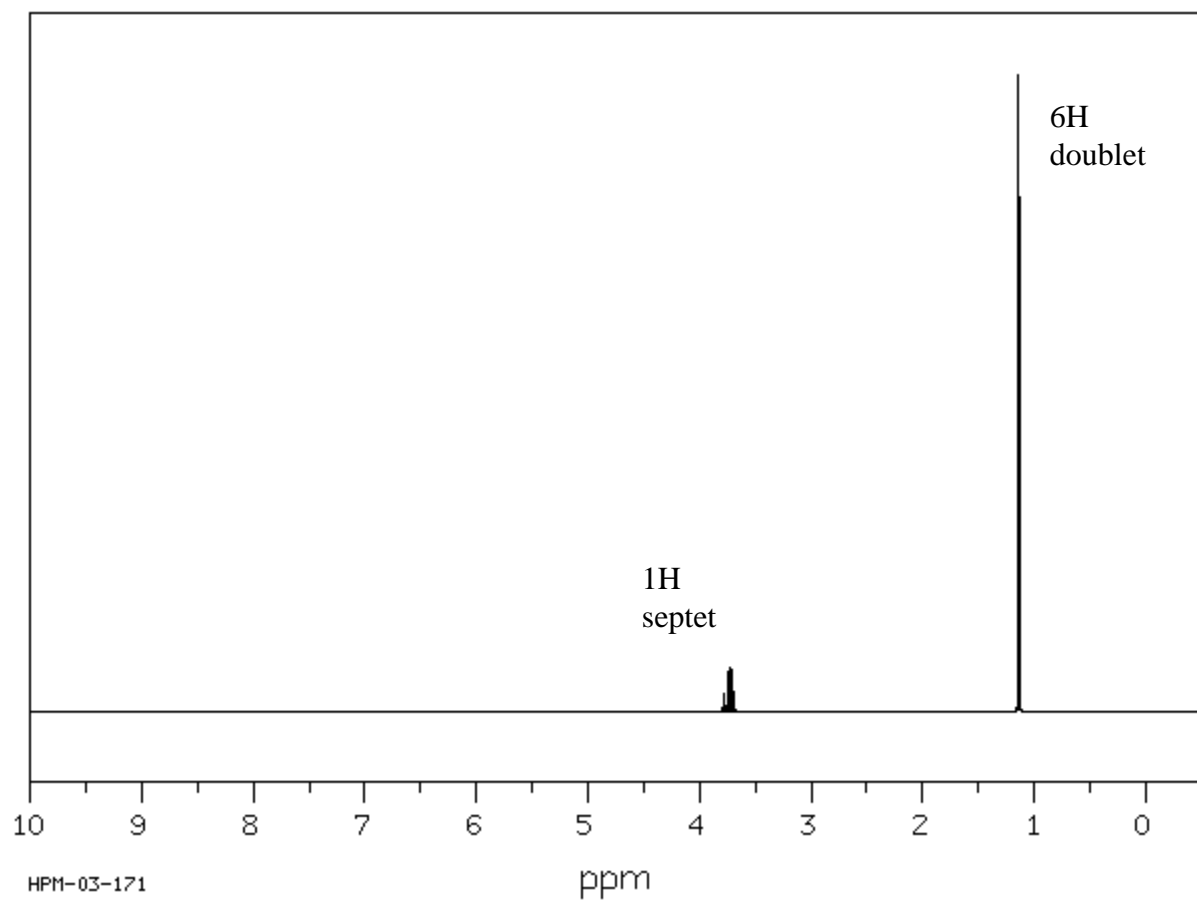
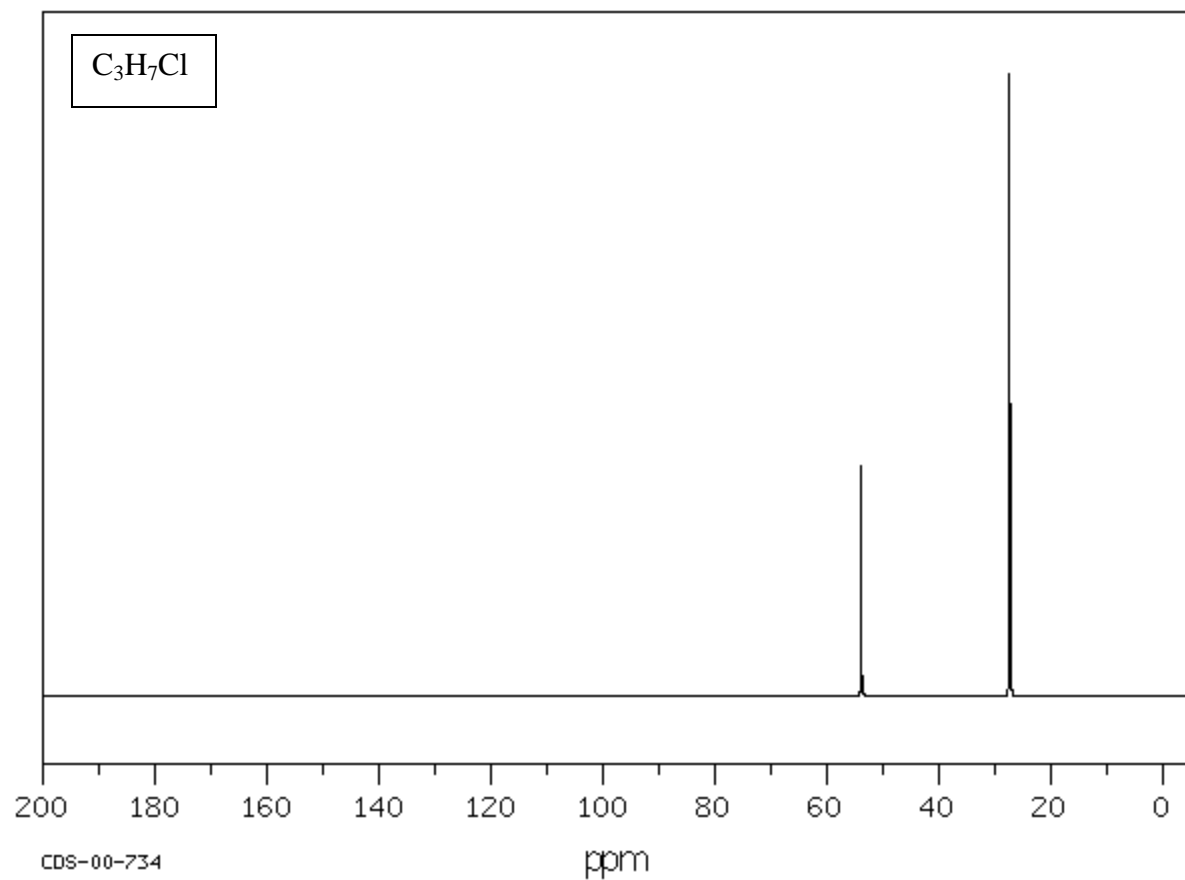


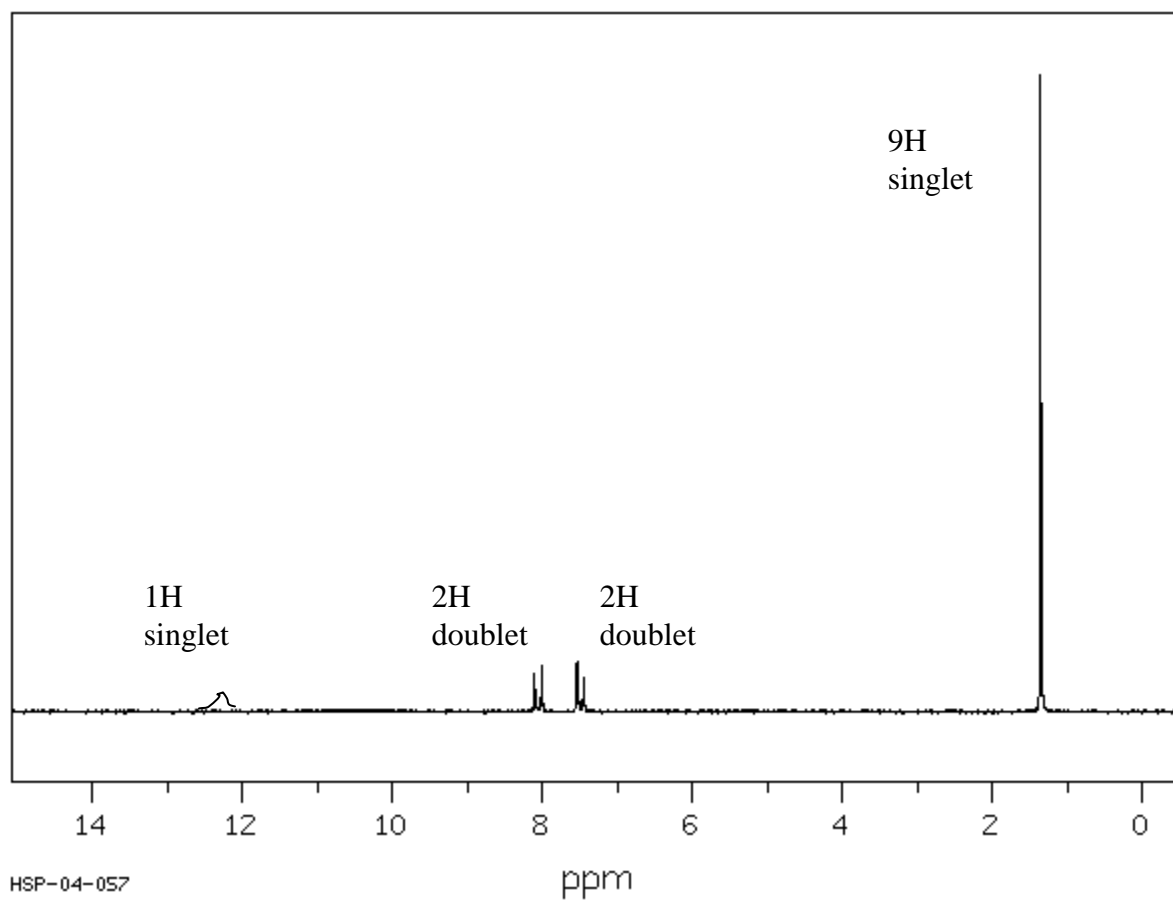
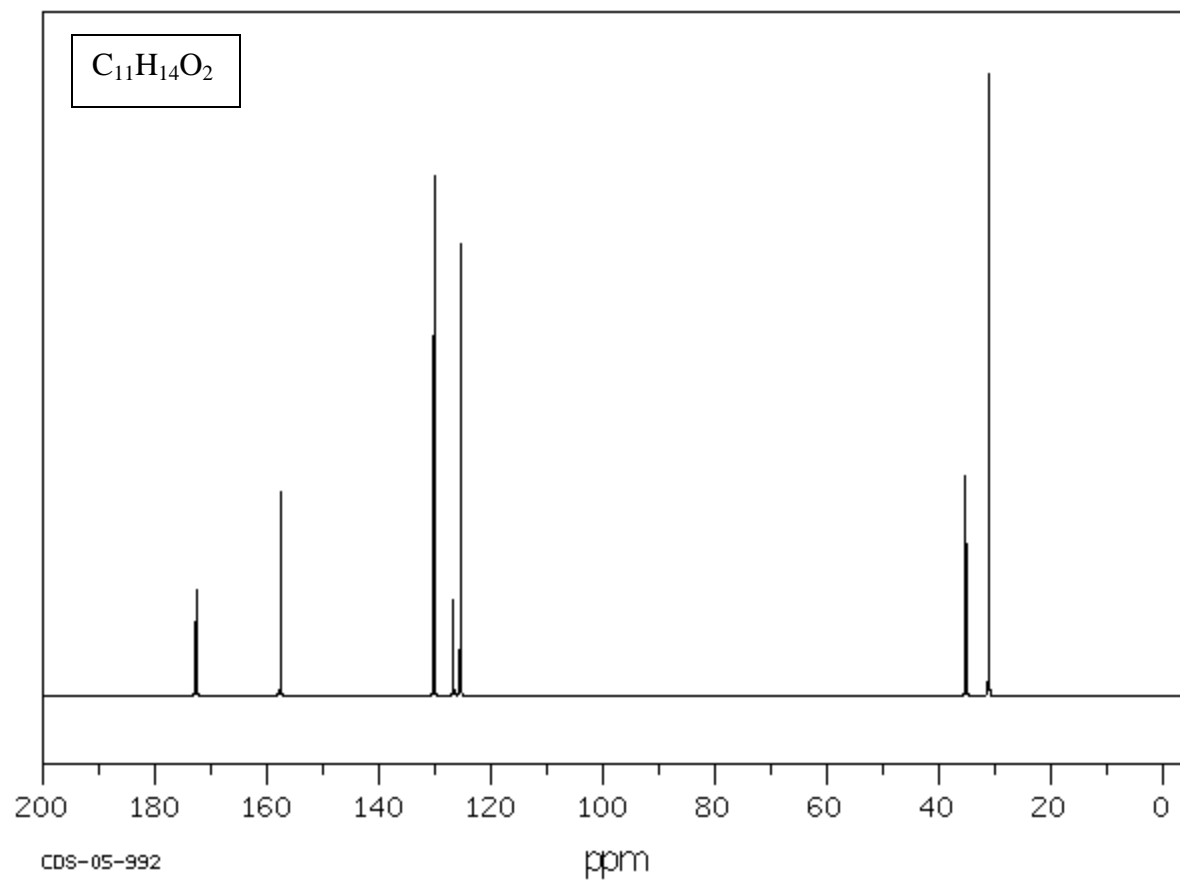
### $^1\text{H}$ NMR

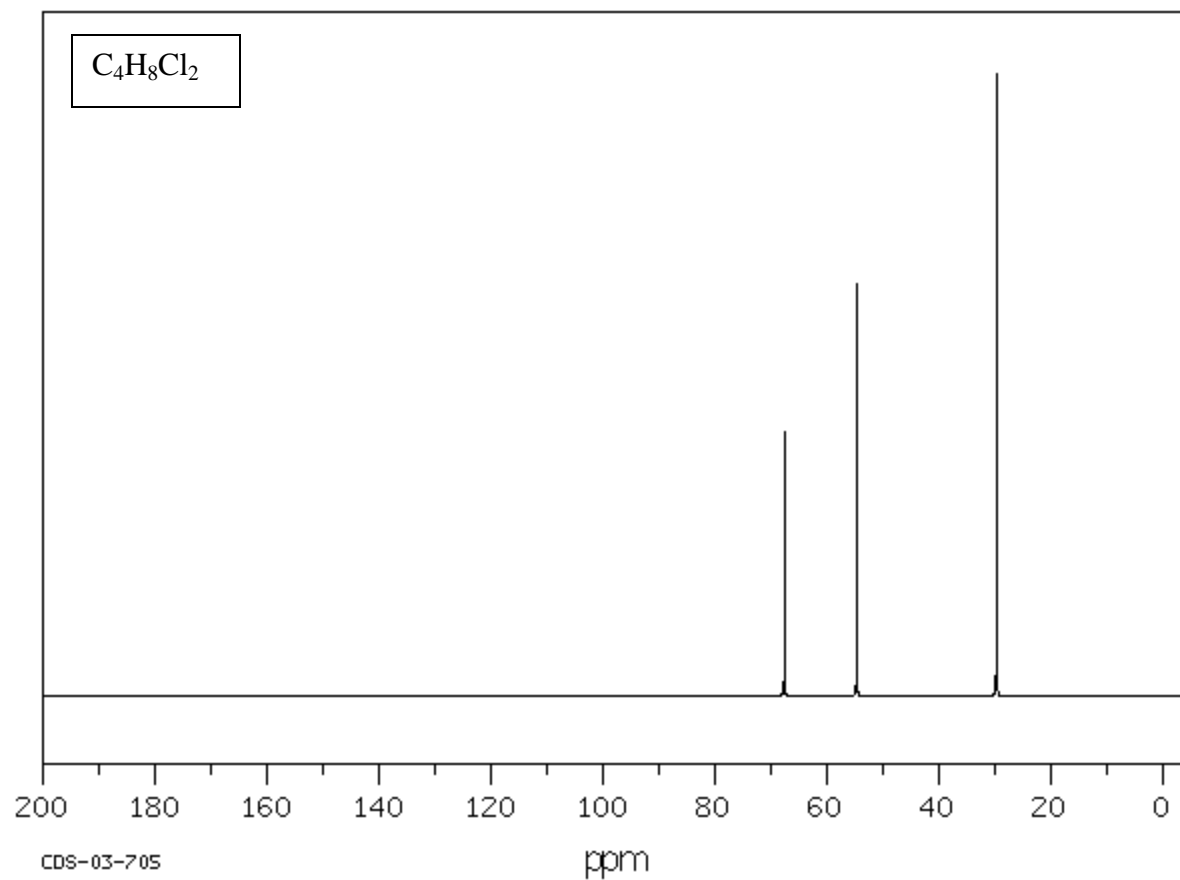
Gives the number of hydrogen environments in a molecule

- 1) The chemical shift tells whether the hydrogen is an alkane, alkene, aromatic, aldehyde, or carboxylic acid
- 2) The area under the signal or integration tells how many hydrogens a signal represents (or at least the ratio)
- 3) The number of peaks tells the number of neighbors ( $\# \text{ peaks} = n + 1$ )

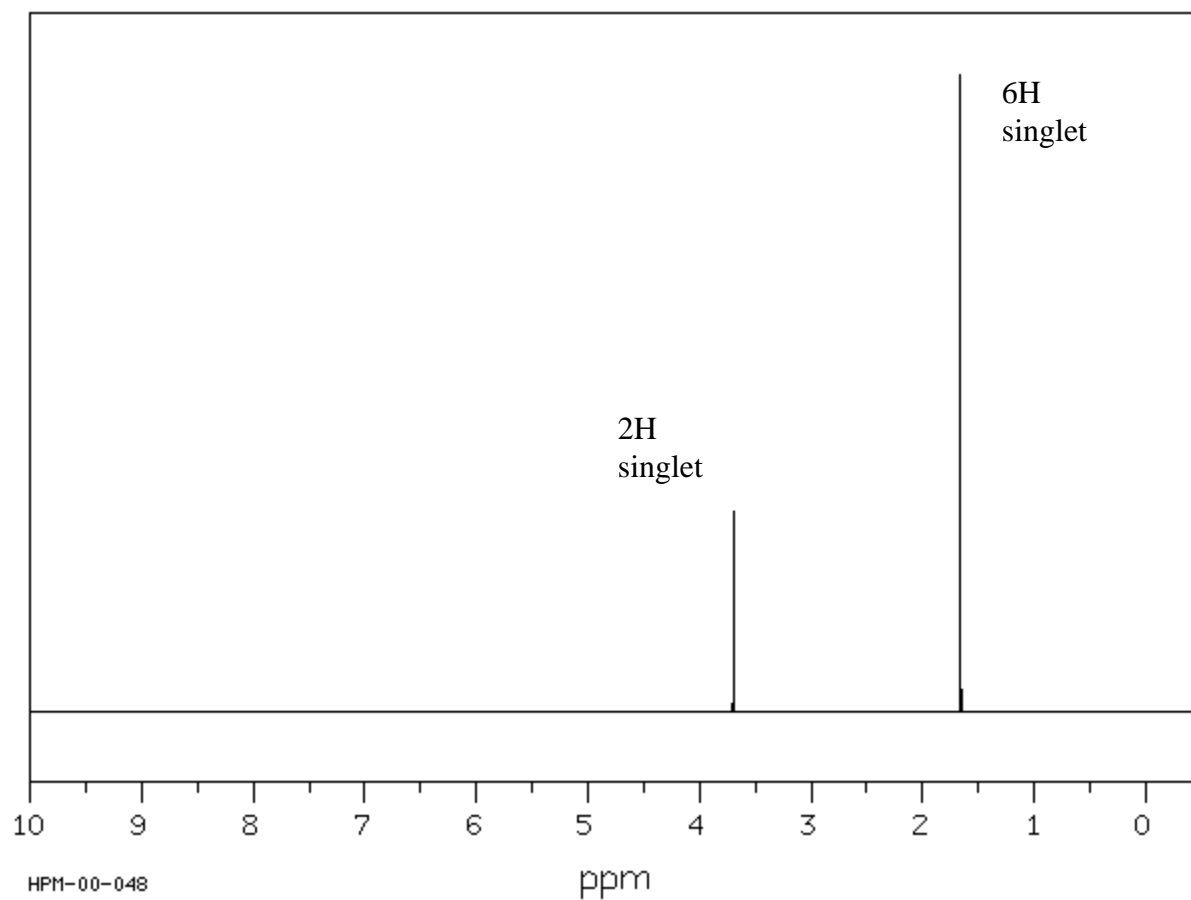


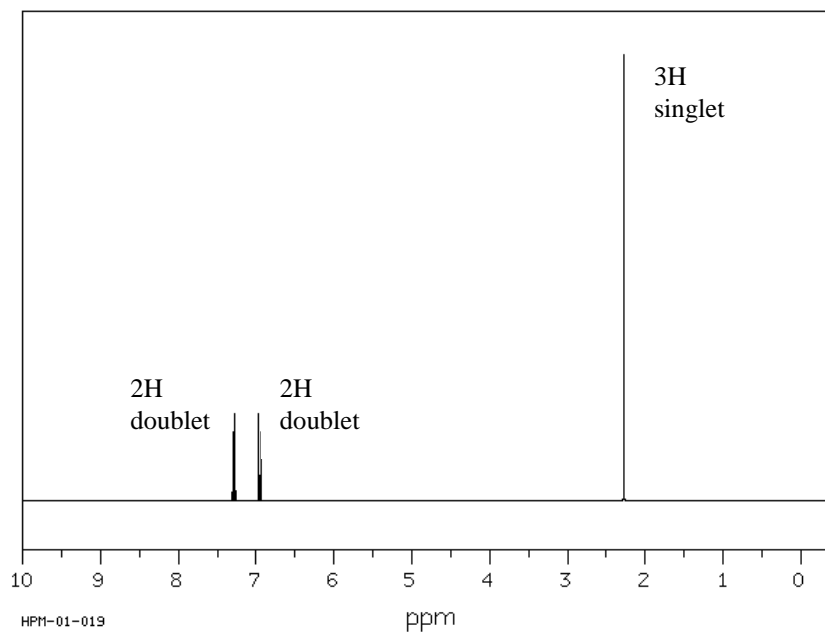
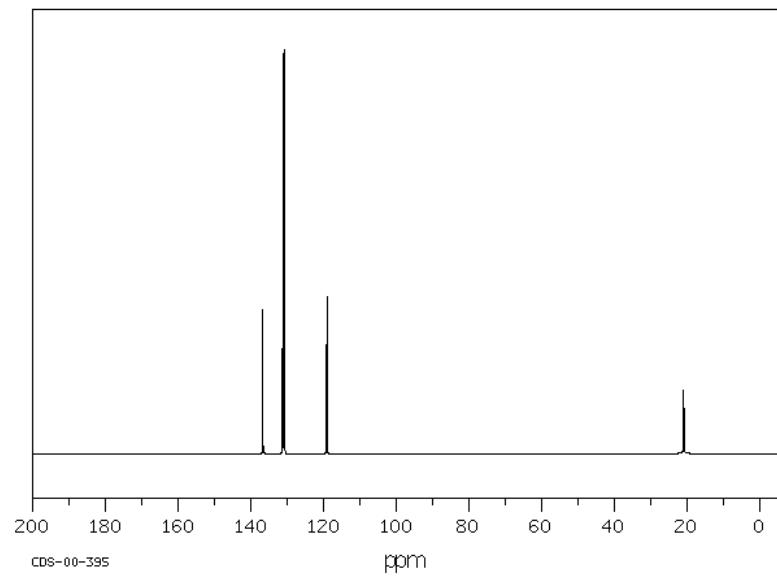
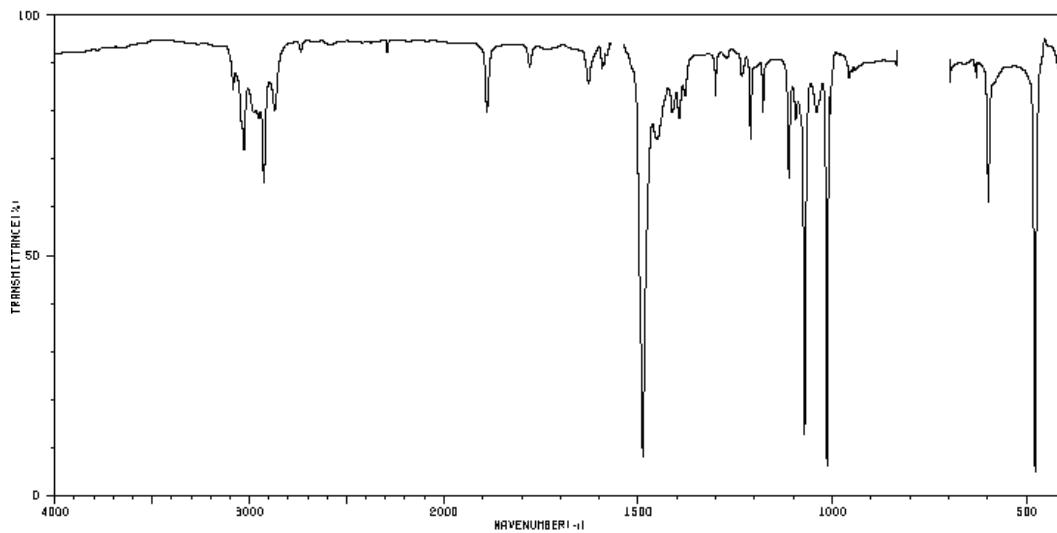
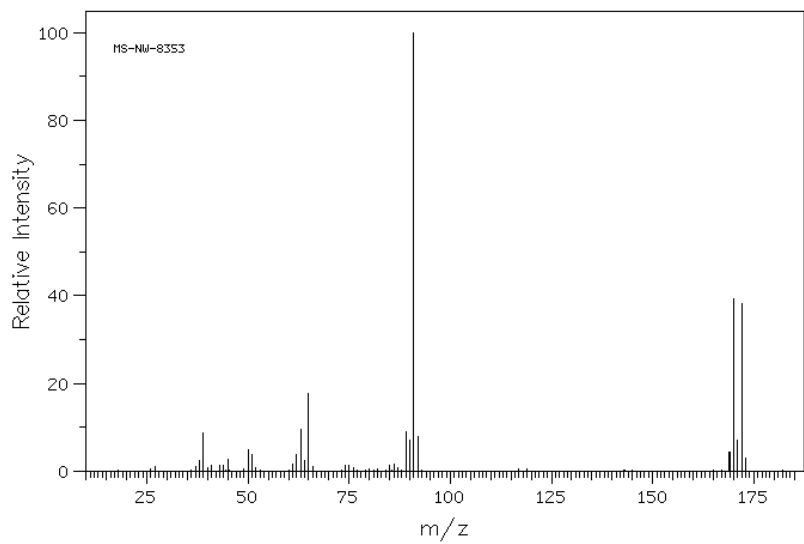




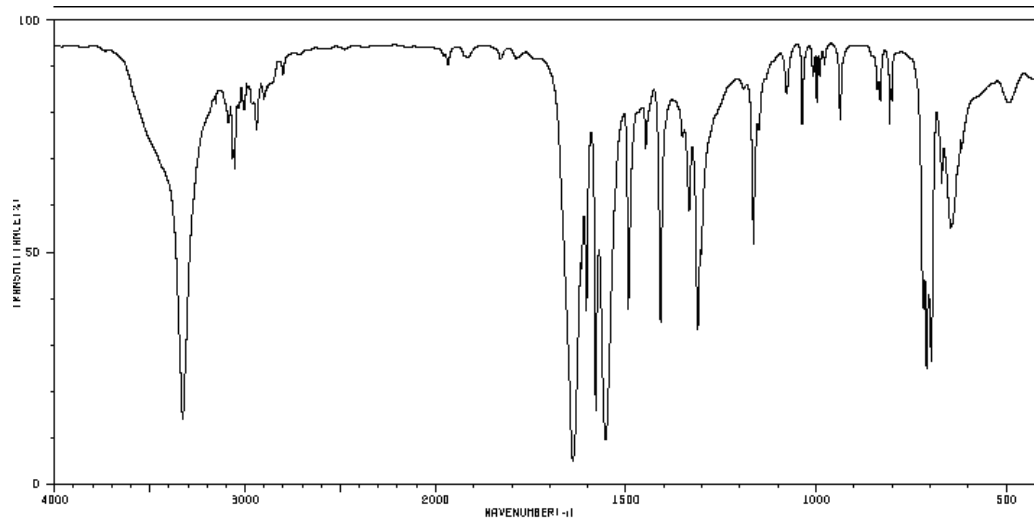
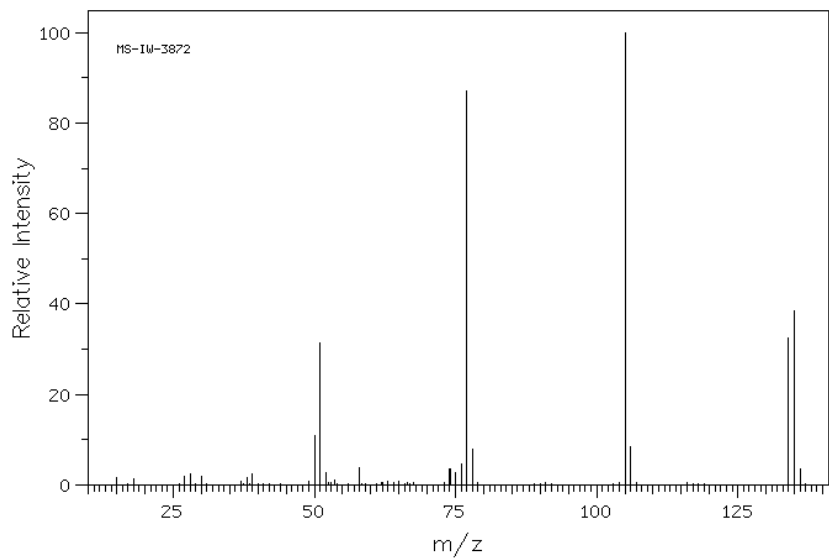


#3

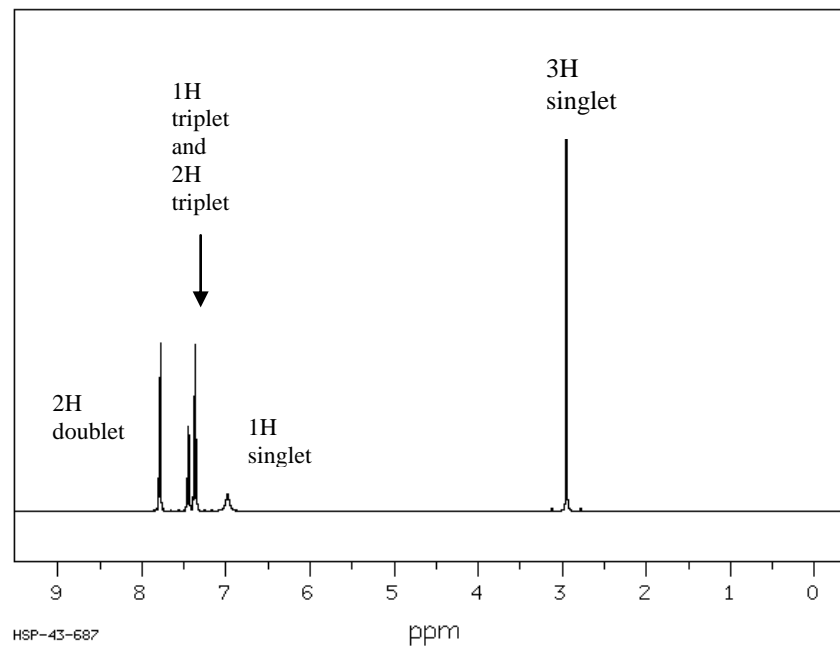
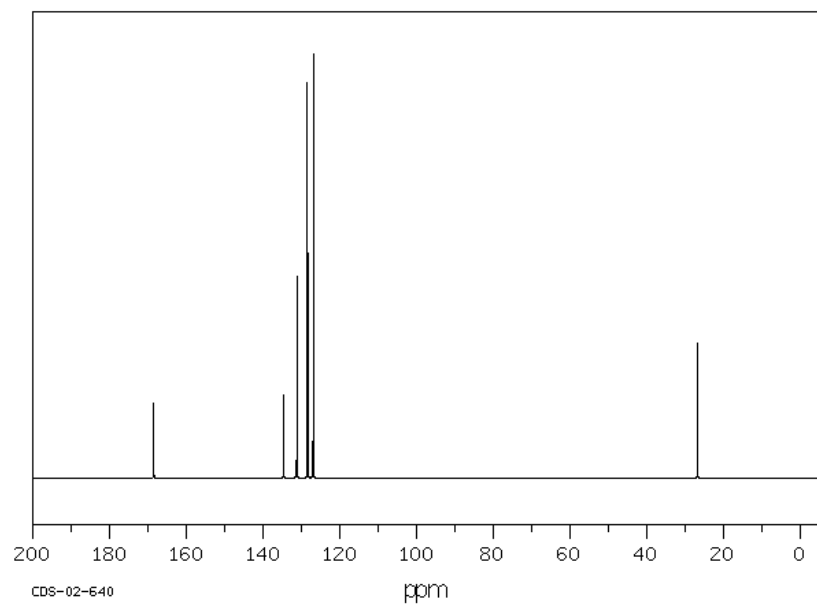




#4



#5



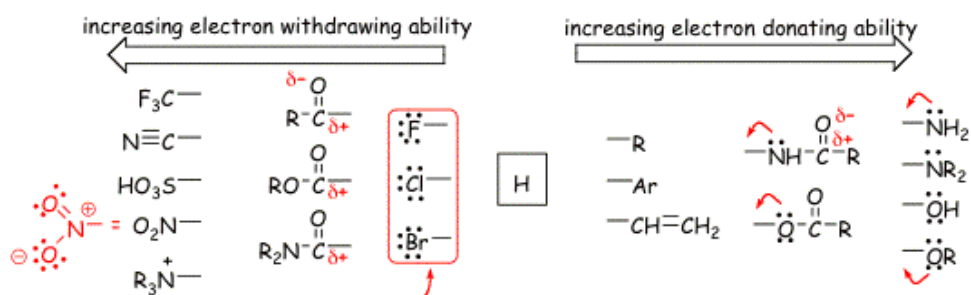
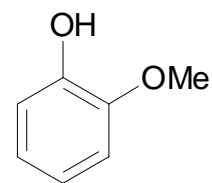
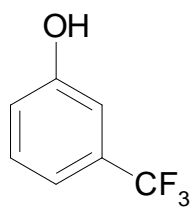
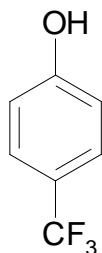
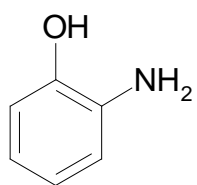


# Organic Chemistry Chapter 14 – Alcohols, Ethers, and Epoxides

## Alcohols

### Nomenclature

### Acidity



the halogens are electron withdrawing when attached to a  $\pi$ -system even though they have non-bonding electrons due to electronegativity

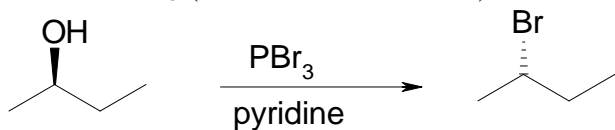
## Reactions of Alcohols

Rxn with H-X (HBr or HCl/ZnCl<sub>2</sub>)

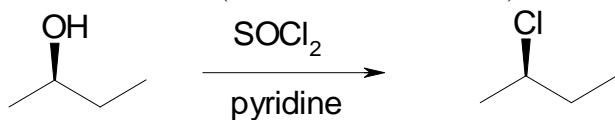
S<sub>N</sub>1 for 2° and 3° alcohols

S<sub>N</sub>2 for 1° alcohols

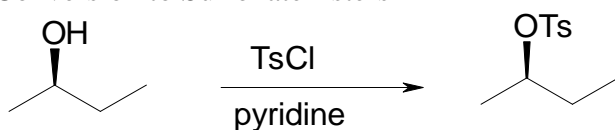
Rxn with PBr<sub>3</sub> (for 1° and 2° alcohols)



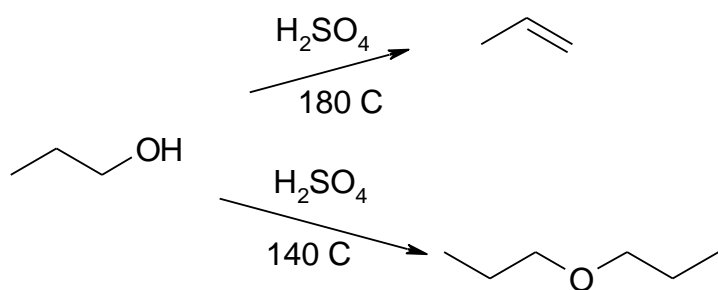
Rxn with SOCl<sub>2</sub> (for 1° and 2° alcohols)



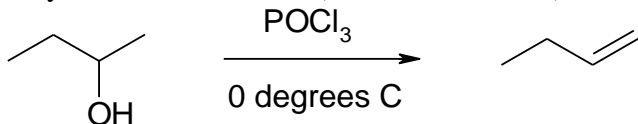
Conversion to Sulfonate Esters



Dehydration with H<sub>2</sub>SO<sub>4</sub>

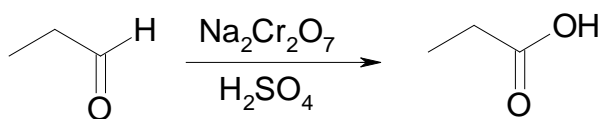
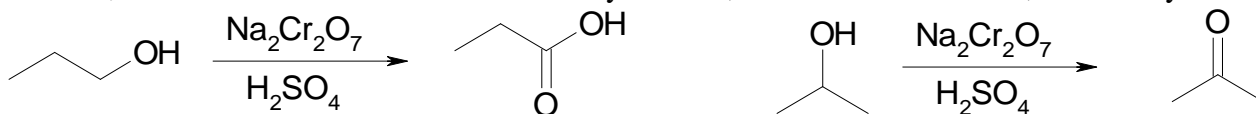


Dehydration with POCl<sub>3</sub> (Hofmann Product)



## Oxidation

Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>/H<sub>2</sub>SO<sub>4</sub> oxidizes 1° alcohols to carboxylic acids, 2° alcohols to ketones, and aldehydes to acids



PCC oxidizes 1° alcohols to aldehydes and 2° alcohols to ketones



## Ethers

### Nomenclature

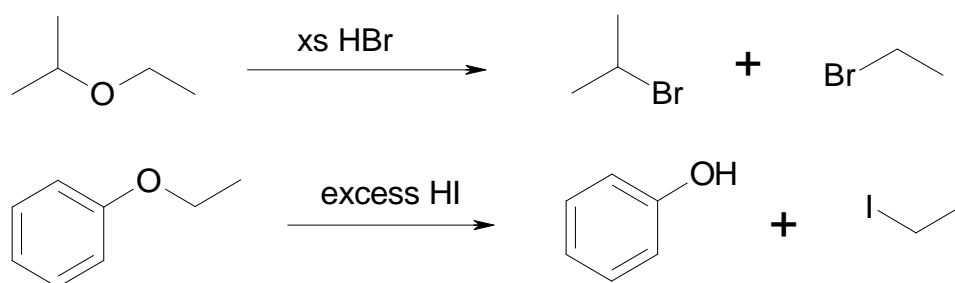
#### Nomenclature of Epoxides (Oxiranes)

#### Synthesis via Substitution ( $S_N2$ or $S_N1$ )

##### Williamson Ether Synthesis ( $S_N2$ )

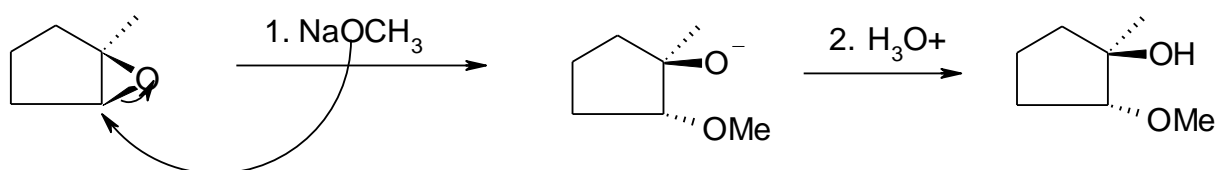


#### Rxn with H-X

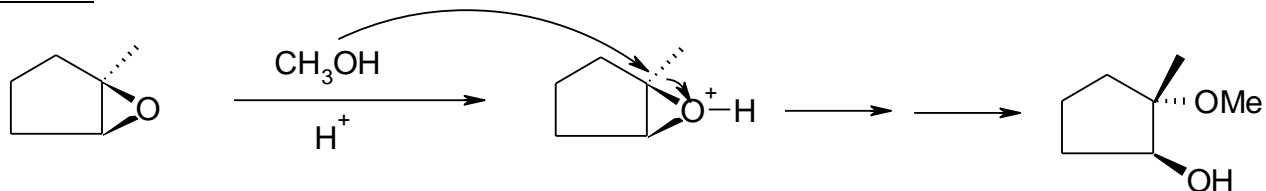


#### Ring Opening of Epoxides (In Acid or Base)

##### In Base



##### In Acid



## Organic Chemistry Chapter 15 – Aromatic Compounds

### Criteria for Aromatic Compounds

- 1) cyclic and containing conjugated pi bonds
- 2) each atom in the ring must have an unhybridized p orbital (no  $sp^3$  atoms in ring)
- 3) planar structure
- 4) delocalization of the pi electrons must lower the electronic energy ( $4N+2$  electrons)

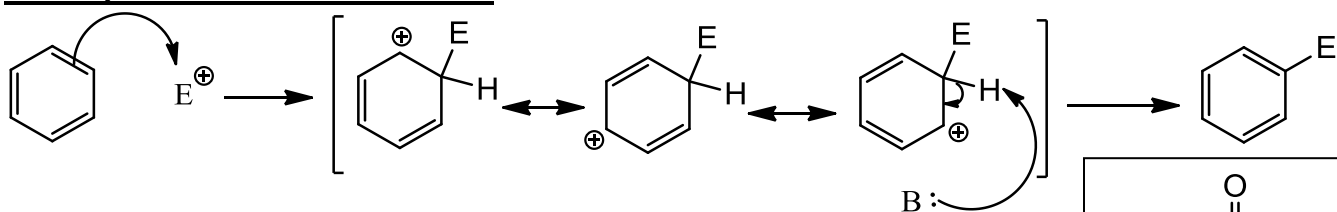
*Antiaromatic* compounds satisfy the first 3 rules above but delocalization of the pi electrons increases the electronic energy ( $4N$  electrons)

*Nonaromatic* compounds are those that don't satisfy one or more of the first 3 rules above

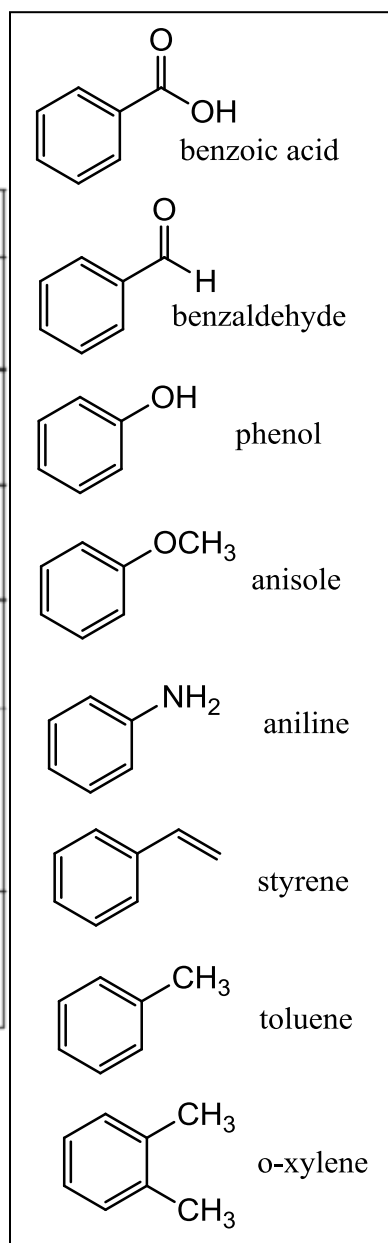
### $\pi$ Molecular Orbitals

benzene

### Electrophilic Aromatic Substitution



Reactant	$E^+$	Reagents	Catalyst	Product(s)	Type of EAS	
	$NO_2^+$	$HNO_3, H_2SO_4$	---		Nitration	
	$SO_3H^+$	$SO_3, H_2SO_4$	---		Sulfonation	
		$Cl_2$	$AlCl_3$		Chlorination	
		$Br_2$	$FeCl_3$		Bromination	
		$R^+$	$RX$ or $R-OH$ or alkene	$AlCl_3$ or $FeBr_3$  $H_2SO_4$  $HF$		Friedel-Craft Alkylation  Or alkylation
		$O=C^+R$		$AlCl_3$		Friedel-Craft Acylation



## Friedel-Crafts Alkylation $R-X/AlCl_3$

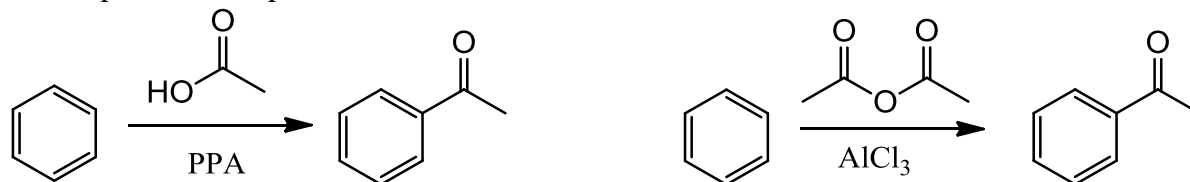
- 1) Fails with strongly deactivated benzenes (benzenes with strong electron withdrawing groups attached)
- 2) Carbocation rearrangement
- 3) Alkylation activates the ring: multiple alkylations are hard to avoid

## Friedel-Crafts Acylation

Fails with strongly deactivated rings

Mechanism involves acylium ion

Favors para if ortho/para director is on benzene due to bulkiness



Formylation (adds one carbon to form an aldehyde)  $CO, HCl, AlCl_3/CuCl$


Called the Gatterman-Koch synthesis

Ortho/Para Directors (Activating except for halogens)

**halogens are deactivating ortho/para directors (pi donating but withdrawing inductively)**

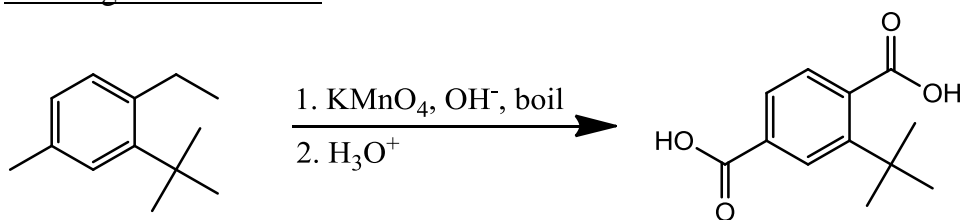
Meta Directors (Deactivating)

Strongest donating group usually directs when there are competing substituents

Activating		BENZENE	Deactivating		
$\pi$ Donors	$\sigma$ Donors		Halogens	Carbonyls	Other
$-NH_2$ $-OH$ $-OR$ $-NHC(=O)CH_3$	$-R$ (alkyl)  (aryl)	$-H$	$-F$ $-Cl$ $-Br$ $-I$	$O$ $  $ $-C-R$ $O$ $  $ $-C-OH$ $O$ $  $ $-C-OR$	$-SO_3H$ $-C\equiv N$ $-NO_2$ $-NR_3^+$
Ortho/Para Directors			Meta Directors		

## Side-Chain Reactions of Benzenes

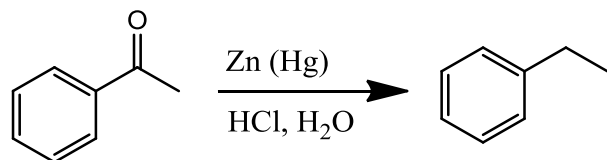
### Permanganate Oxidation



Chromic acid  
( $\text{Na}_2\text{Cr}_2\text{O}_7 / \text{H}_2\text{SO}_4$ )  
achieves the same  
reaction

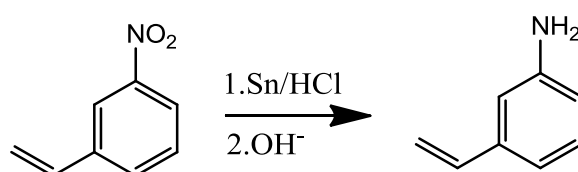
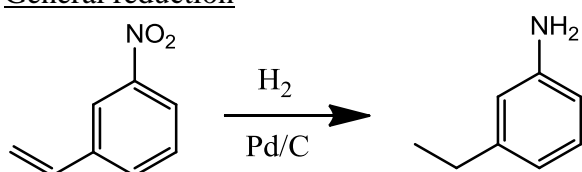
### Side-chain Reduction

Clemmenson Reduction – reduces ketones and aldehydes to alkanes



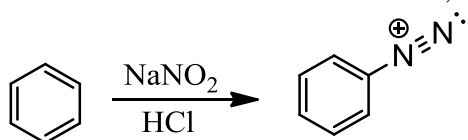
Wolff Kishner  
Reduction does the  
same thing with  
 $\text{H}_2\text{NNH}_2, \text{OH}^-$ , heat

### General reduction

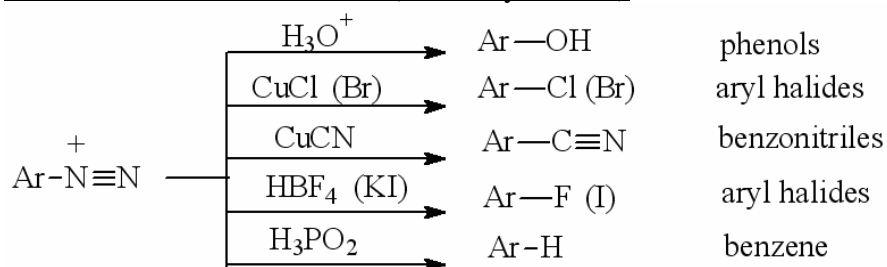


Rxn with Nitrous Acid -  $\text{NaNO}_2/\text{HCl}$  leads to formation of nitrosonium ion ( $\text{NO}^+$ )

1° become diazonium salts, 2° become nitrosamines



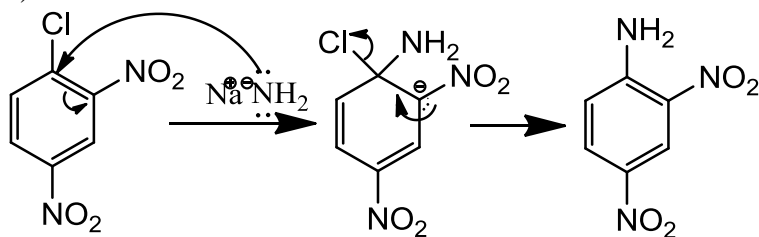
### Rxns of arenediazonium salts (Sandmeyer Rxns)



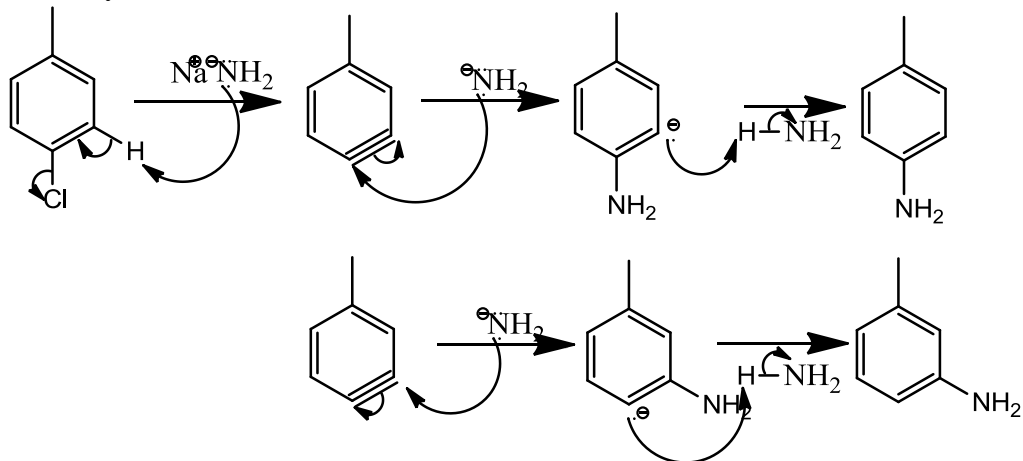
## Nucleophilic Aromatic Substitution (NAS)

strong nucleophile ( $\text{NH}_2^-$  or  $\text{OH}^-$  for example) replaces halide  
electron withdrawing groups ortho/para to halide facilitate reaction

1) Addition-Elimination mechanism

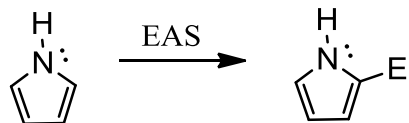


2) Benzyne mechanism (Elimination-Addition Mechanism)

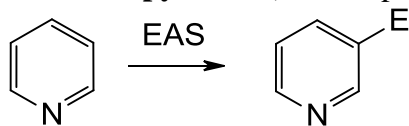


## Non-benzenoid Aromatics

EAS with 5-membered Aromatic Heterocycles



EAS with pyridine (at the 3-position)



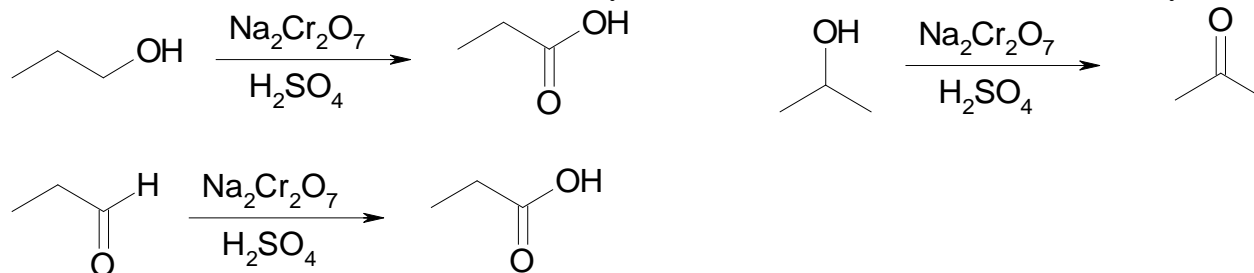
## Organic Chemistry Chapter 16 – Ketones and Aldehydes

### Nomenclature

#### Synthesis

##### **Oxidation using chromic acid (H<sub>2</sub>CrO<sub>4</sub>) or PCC**

Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>/H<sub>2</sub>SO<sub>4</sub> oxidizes 1° alcohols to carboxylic acids, 2° alcohols to ketones, and aldehydes to acids



PCC oxidizes 1° alcohols to aldehydes and 2° alcohols to ketones



##### **Ozonolysis of alkenes - (1)O<sub>3</sub> (2) (CH<sub>3</sub>)<sub>2</sub>S**

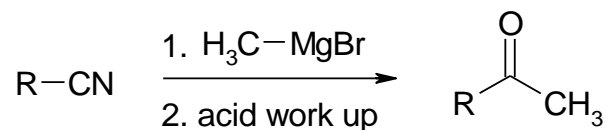
##### **Friedel Crafts Acylation (a phenyl ketone) and Formylation (benzaldehyde)**

##### **Hydration of a Terminal Alkyne**

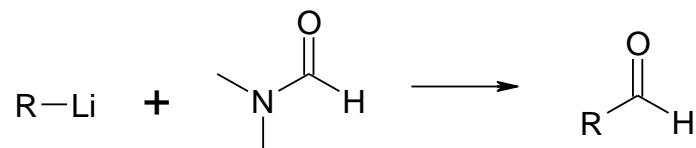
(1) (Si<sub>a</sub>)<sub>2</sub>BH (2) H<sub>2</sub>O<sub>2</sub>, NaOH to yield an aldehyde (anti-Markovnikov addition)

HgSO<sub>4</sub>, H<sub>2</sub>SO<sub>4</sub>, H<sub>2</sub>O to yield a ketone (Markovnikov addition)

##### **Grignard Addition to Nitriles**



##### **Organolithium Addition to DMF**

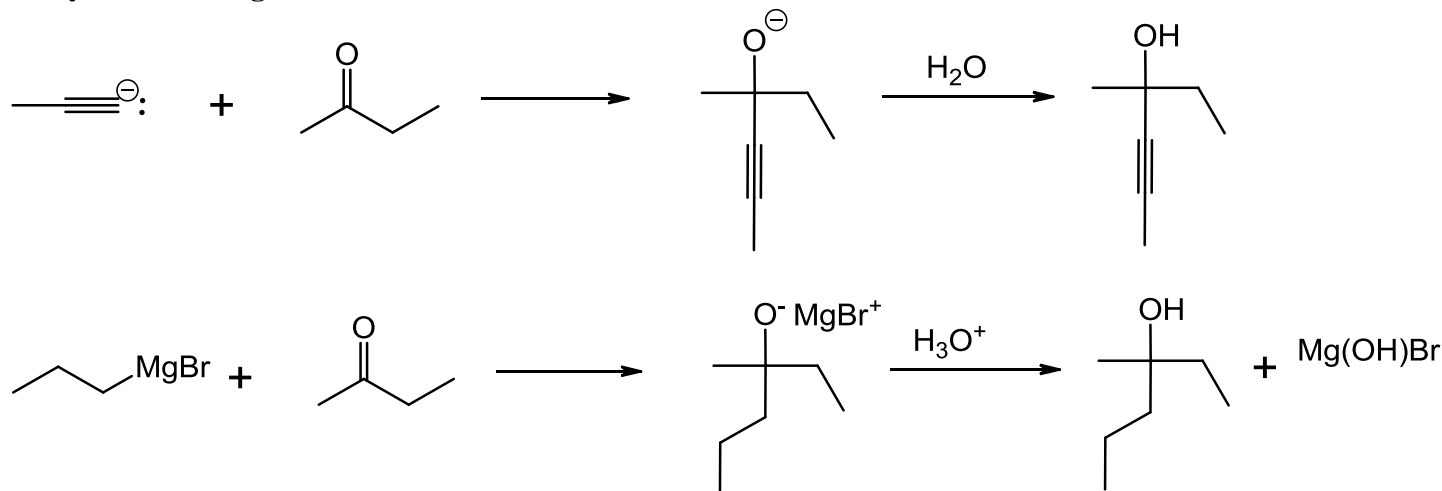




## Reactions of Ketones and Aldehydes

Nucleophilic addition to a carbonyl (with and without acid catalysis)  
aldehydes are more reactive than ketones

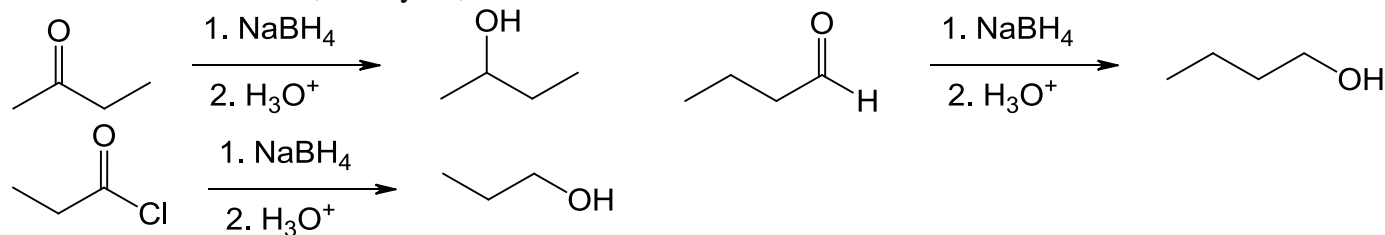
### Acetylide and Grignard addition



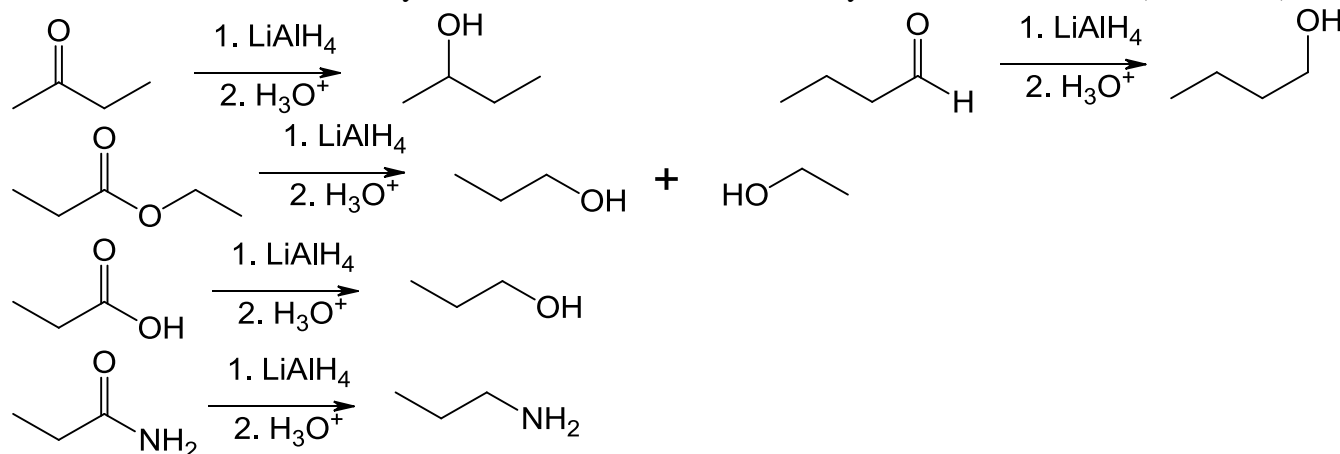
Grignard addition to acid halides, acid anhydrides, and esters

### Hydride Reduction Rxns

**NaBH<sub>4</sub>** reduces ketones, aldehydes, and acid halides

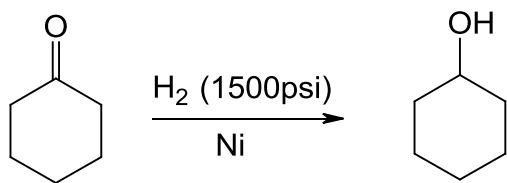
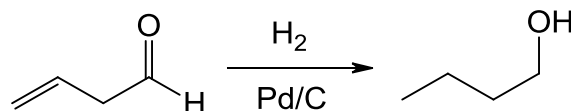
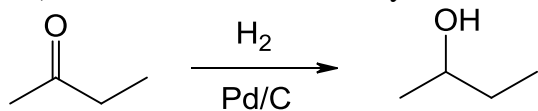


**LiAlH<sub>4</sub>** reduces ketones, aldehydes, acid chlorides, esters, carboxylic acids, and amides (and others)



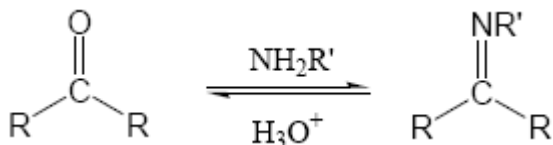
**DIBALH** reduces esters to aldehydes

$\text{H}_2$ , Pd/C reduces alkenes, alkynes, and nitro groups



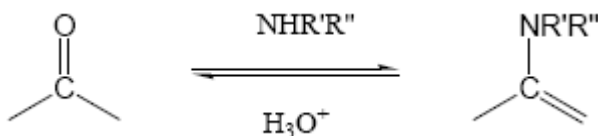
**Formation of imines (Schiff bases) and imine derivatives**

rxn with a  $1^\circ$  amine

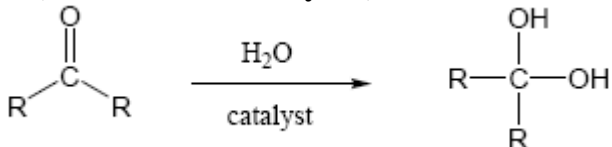


**Formation of enamines**

rxn with a  $2^\circ$  amine

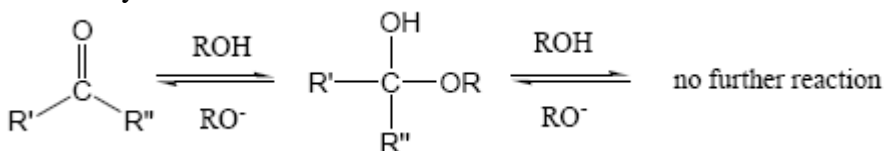


**Hydration (Acid- or Base-catalyzed)**



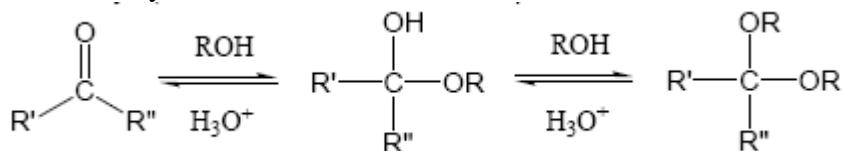
**Addition of alcohols** (formation of hemiacetals, acetals, hemiketals, and ketals) – acid- and base-catalyzed

Base-catalyzed



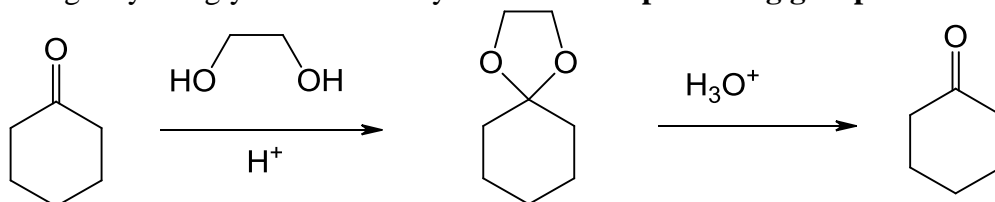
Forms hemiacetal

Acid-catalyzed



Forms acetal

Using ethylene glycol to form a cyclic acetal as a **protecting group**

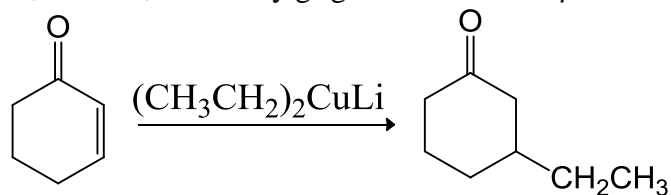


### Addition to a Conjugated Carbonyl

$\text{NaBH}_4/\text{CeCl}_3$  and organolithium add to the carbonyl (1,2-addition)

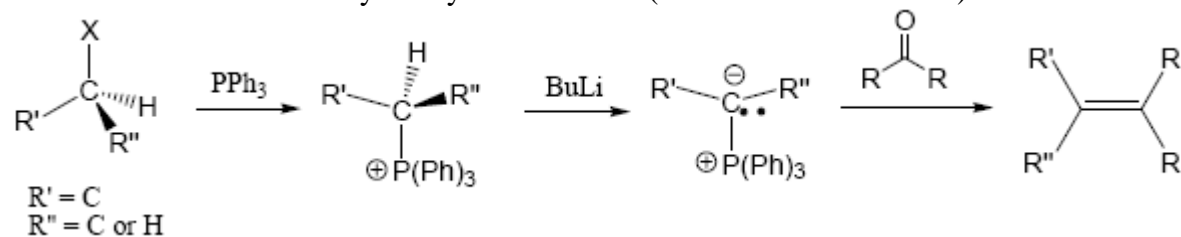
Grignards often result in both 1,2- and 1,4-addition

$\text{CN}^-$ ,  $\text{OH}^-$ ,  $\text{R}_2\text{CuLi}$ , and bulky grignards add to the  $\beta$  carbon (1,4-addition)



**Wittig Rxn** –  $\text{P}(\text{Ph})_3 + \text{R-X} + \text{BuLi}$  gives a phosphorous ylide

-ylide reacts with a ketone or aldehyde to yield an alkene ( $\text{C}=\text{O}$  converted to  $\text{C}=\text{C}$ )



## Organic Chemistry Chapter 17 – Carboxylic Acids and Carboxylic Acid Derivatives

### Carboxylic Acids

Nomenclature

#### Synthesis

Grignard addition to  $\text{CO}_2$  (Adds 1 carbon)

Hydrolysis of Nitriles –  $\text{R-CN} + \text{H}_3\text{O}^+ \leftrightarrow \text{RCOOH}$  (Adds 1 carbon)

Oxidation of  $1^\circ$  alcohols and aldehydes –  $\text{Na}_2\text{Cr}_2\text{O}_7/\text{H}_2\text{SO}_4$

Cleavage of alkenes with  $\text{KMnO}_4$  – conc.  $\text{KMnO}_4/\text{heat}, \text{H}_3\text{O}^+$

Oxidation of alkylbenzenes to benzoic acids with  $\text{KMnO}_4$  or chromic acid

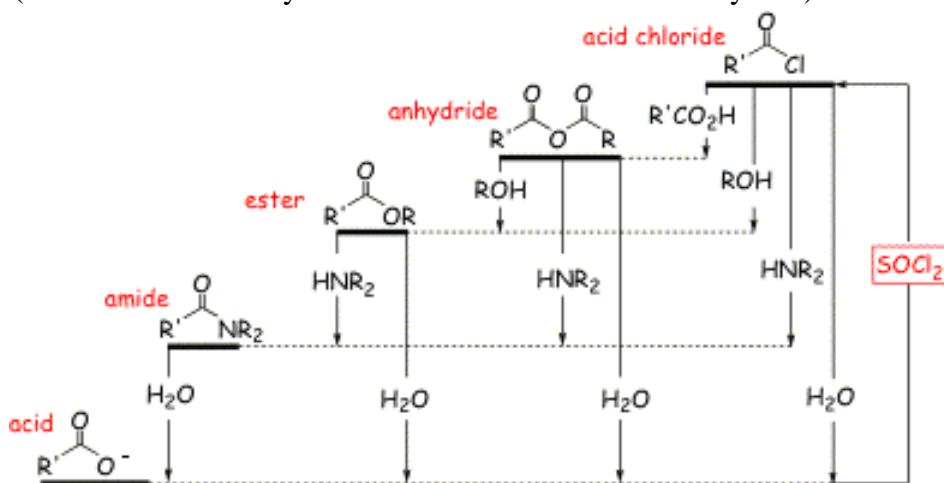
### Carboxylic Acid Derivatives

Acid halides, anhydrides, esters, amides, and nitriles

Nomenclature (acid halides, anhydrides, esters, cyclic esters, amides, cyclic amides, and nitriles)

#### Nucleophilic Acyl Substitution

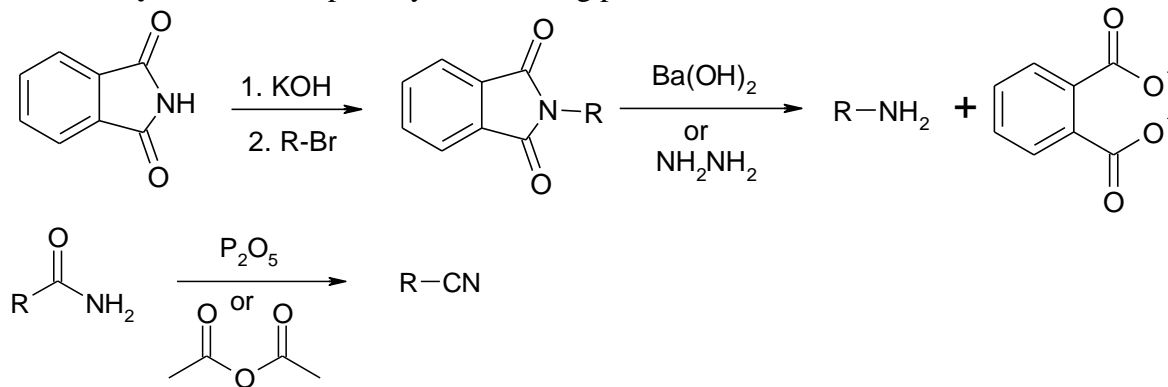
-Reactivity (acid chlorides > anhydrides > esters > amides > carboxylates)



• can convert *more* reactive derivatives into *less* reactive derivatives, not the other way around!!

Saponification of Esters

Gabriel Synthesis – template synthesis using phthalimide



## Organic Chemistry Chapter 18 – Alpha Additions

Acidity of alpha hydrogens

Keto-enol tautomerism

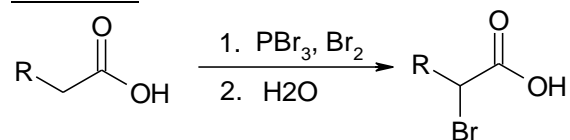
LDA (lithium diisopropyl amide) is a strong base used to form enolate ions

### Alpha halogenation

Base-promoted ( $X_2/OH^-, H_2O$ )

Acid-catalyzed halogenation of ketones

HVZ Rxn



### Alpha alkylation

Alkylation of enolate ions ( $S_N2$  rxn with an enolate attacking an alkyl halide); only for ketones

Stork rxn – convert ketone to enamine with  $2^\circ$  amine and  $\alpha$ -alkylate followed by hydrolysis

### Alkylation at Beta Carbon

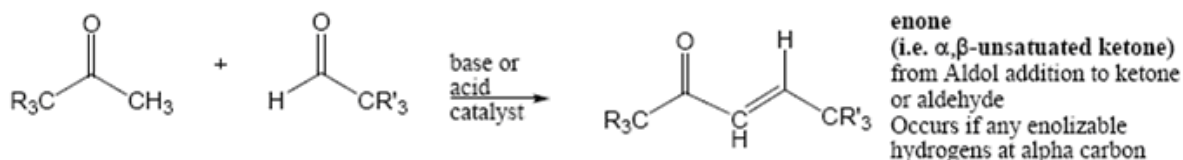
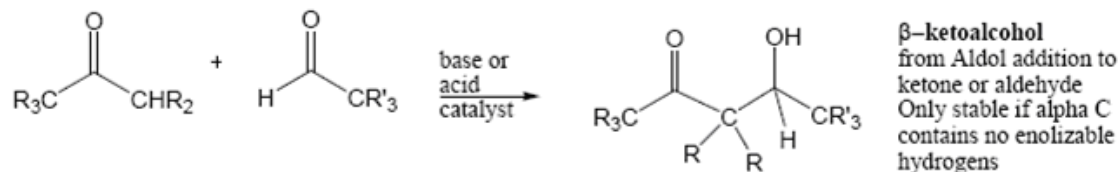
Michael addition – a 1,4-addition of a conjugated ketone

Michael donor is typically a stabilized enolate ion or  $R_2CuLi$

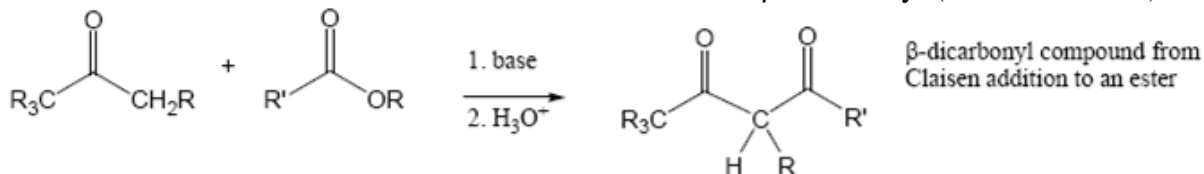
Acceptor is a conjugated carbonyl, cyano, or nitro group

**Aldol Condensation** – Acid catalyzed – **enol** adds to a ketone or aldehyde

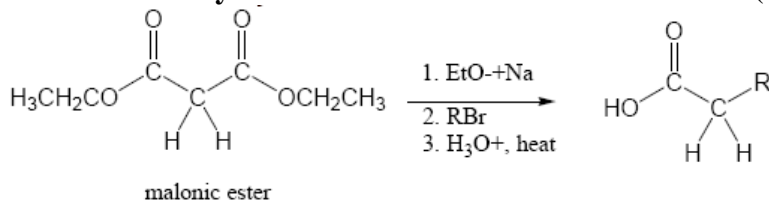
Base-catalyzed - **enolate** adds to a ketone or aldehyde



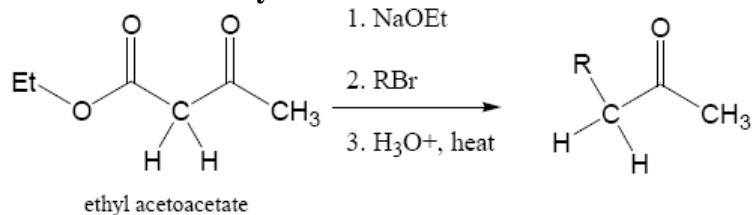
**Claisen Condensation** – enolate attacks an ester to form a  $\beta$ -dicarbonyl (self and crossed)



**Malonic Ester Synthesis** – forms a substituted acetic acid (adds 2 carbons)



**Acetoacetic Ester Synthesis** – forms a substituted acetone (methyl ketones)



### Robinson Annulation

- 1) Michael Rxn
- 2) Aldol (Intramolecular)

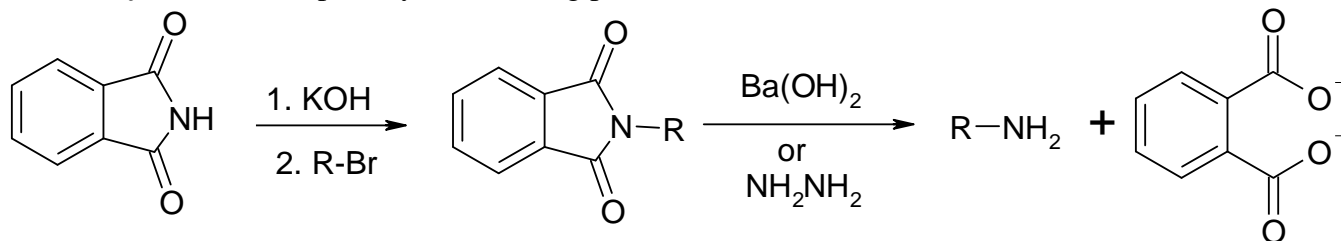
## Organic Chemistry Chapter 19 – Amines

### Nomenclature

### Basicity

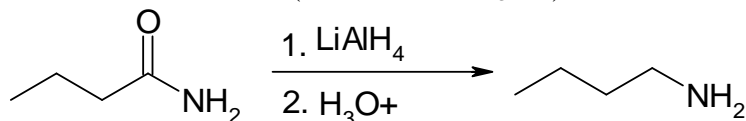
### Synthesis

**Gabriel Synthesis** – template synthesis using phthalimide

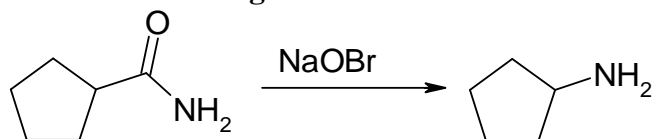


**Reduction of nitro-compounds, azides, nitriles** (H<sub>2</sub>/Pd/C or LAH)

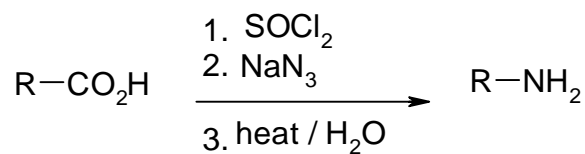
**Reduction of Amides** (1. LiAlH<sub>4</sub> 2. H<sub>3</sub>O<sup>+</sup>)



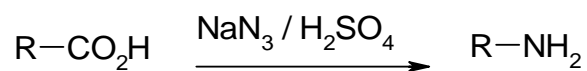
**Hofmann Rearrangement**



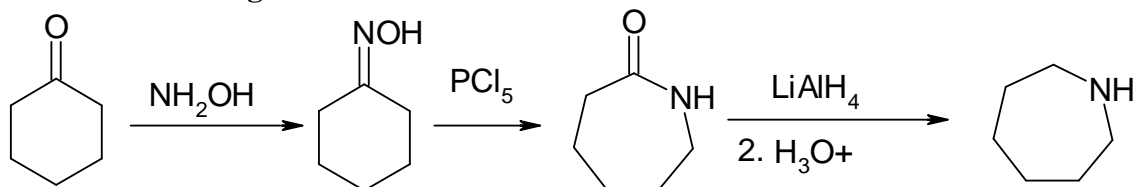
**Curtius**



**Schmidt**

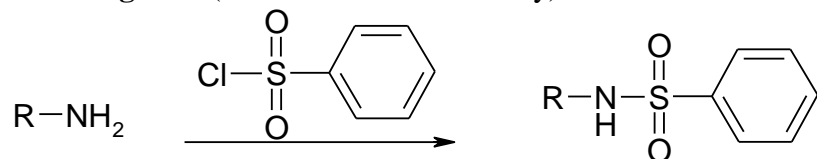


**Beckman Rearrangement**



## Rxns of Amines

**Hinsberg Test** (for 1° and 2° amines only)



Product with 1° amine is soluble in base while product with 2° amine is not

## **Hofmann Elimination**

(1) Excess  $CH_3I$  (2)  $Ag_2O/H_2O$  (3) Heat

## **Cope Elimination** (elimination of an amine-oxide)

(1)  $H_2O_2$  (2) Heat

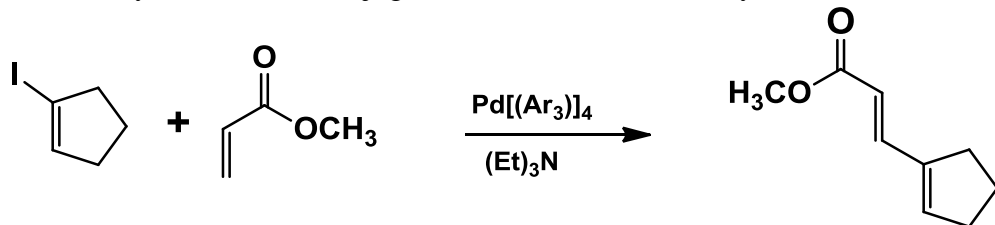
## **Phase Transfer Catalysis** (with quaternary ammonium salts) TEBAC

## **Reductive Amination**

## Organic Chemistry Chapter 20 – Carbon-Carbon Coupling Reactions

**Gilman Reagent** (lithium dialkyl cuprate with conjugated carbonyl)

**Heck** (vinyl halide with conjugated ester, nitrile, or aldehyde with  $\text{Pd}(\text{PAr}_3)_4$  and  $\text{Et}_3\text{N}$ )



**Suzuki**

