

COLLEGE ORGANIC CHEMISTRY 2011 OUTLINES

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

Lewis Structures

Electrons and Bonding

wave functions (ψ) and probability functions (ψ^2)

sigma and pi bonds

atomic orbitals and molecular orbitals

hybridization

# of e ⁻ domains	Hybridization	Bond angle
2	sp	180°
3	sp ²	120°
4	sp ³	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

π 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.”

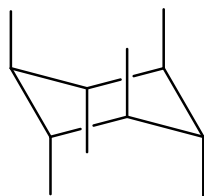
Newman Projections

Staggered and eclipsed conformations

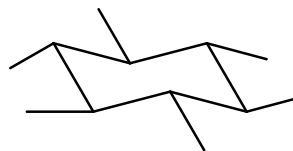
Gauche Interactions

Chair Conformations of Cyclohexane

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



Axial bonds



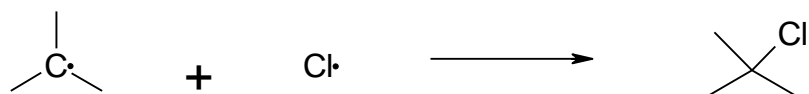
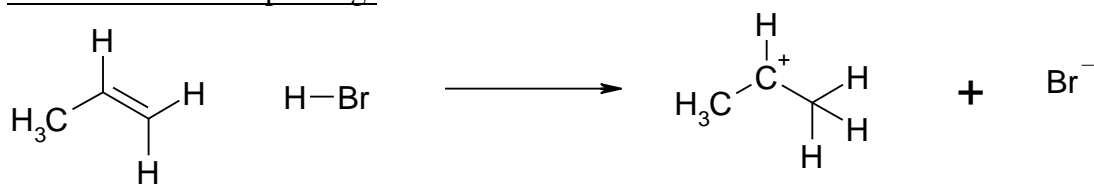
Equatorial bonds

1,3-diaxial interactions

Organic Chemistry Chapter 3 – Introduction to Reaction Mechanisms

Arrow Pushing

Show curved arrow pushing:



Reaction Coordinate Diagrams

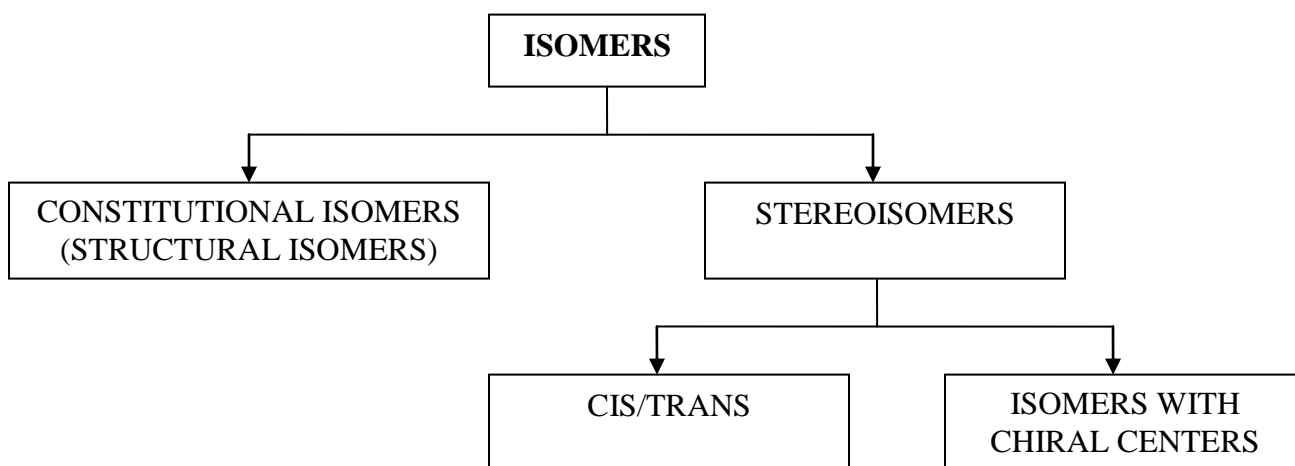
Endogonic vs Exergonic

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

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

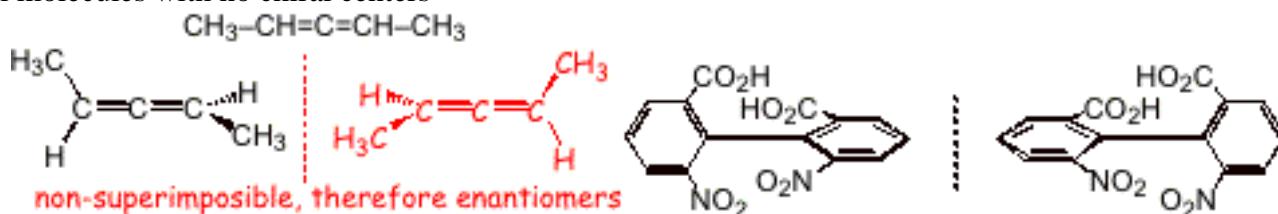
Multiple chiral centers

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 ⁺ and Br ⁻	Markovnikov	-	Possible
H ₃ O ⁺	H ⁺ and OH ⁻	Markovnikov	-	Possible
H ⁺ , ROH	H ⁺ and OR ⁻	Markovnikov	-	Possible
Br ₂ /CCl ₄ (or Cl ₂ /CCl ₄)	Br ⁺ and Br ⁻	-	Anti	Not possible
Br ₂ /H ₂ O Cl ₂ /H ₂ O	Br ⁺ and OH ⁻	Markovnikov	Anti	Not possible
Br ₂ /ROH Cl ₂ /ROH	Br ⁺ and OR ⁻	Markovnikov	Anti	Not possible
(1) Hg(OAc) ₂ , H ₂ O (2) NaBH ₄	H ⁺ and OH ⁻	Markovnikov	Anti	Not possible
(1) Hg(OAc) ₂ , ROH (2) NaBH ₄	H ⁺ and OR ⁻	Markovnikov	Anti	Not possible
(1) BH ₃ ·THF (2) H ₂ O ₂ , OH ⁻ , H ₂ O	H ⁺ and OH ⁻	Anti-Markovnikov	Syn	Not possible
H ₂ /catalyst (Catalyst = Pt/C, Pd/C, or Ni)	H and H	-	Syn	Not possible
HBr/ROOR (peroxide)	H ⁺ and Br ⁻	Anti-Markovnikov	-	Not possible
RCO ₃ H/K ₂ CO ₃ (MCPBA)	epoxide	-	Syn	Not possible
CH ₂ N ₂ /Δ (carbene)	cyclopropane	-	Syn	Not Possible

Stability (More substituted alkenes are more stable)

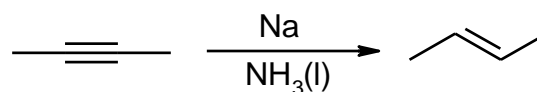
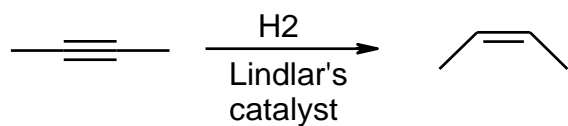
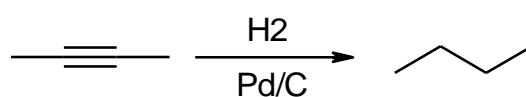
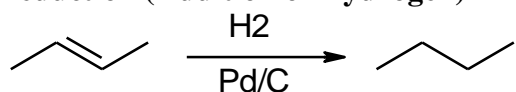
Heats of Hydrogenation

Organic Chemistry Chapter 6 – Alkynes

Nomenclature

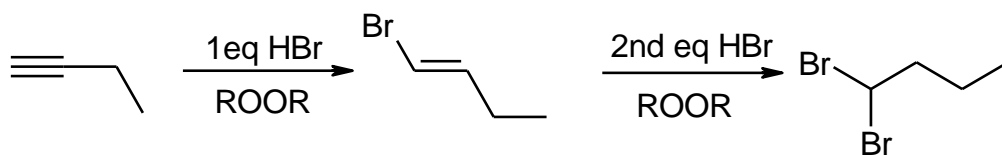
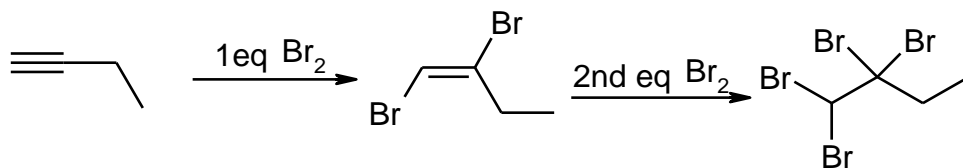
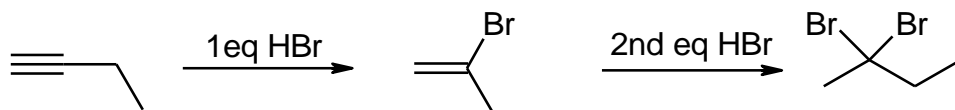
Acidity of alkynes

Reduction (Addition of Hydrogen)

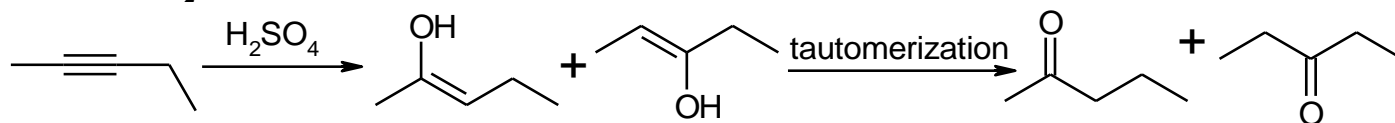


Addition of H-X or X₂

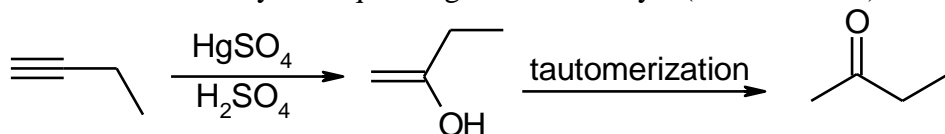
Alkynes are less reactive than alkenes in addition rxns



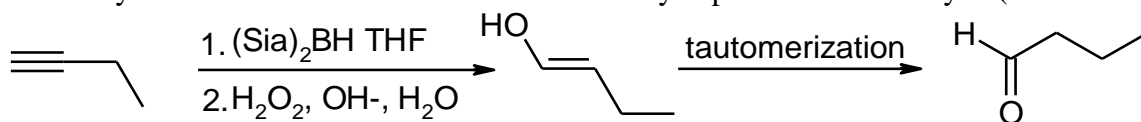
Addition of H₂O



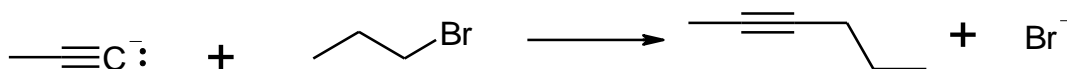
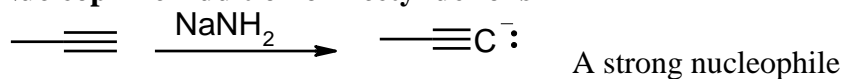
Terminal alkynes require HgSO₄ as a catalyst (Markovnikov)



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

π 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)

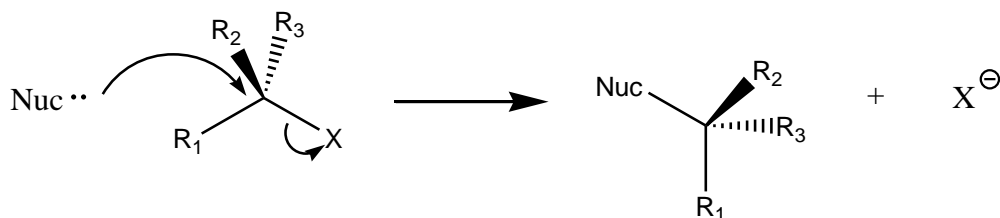
Frontier Molecular Orbital Theory (FMO Theory)

Conservation of orbital symmetry

Organic Chemistry Chapter 8 – Substitution Reactions

S_N2 reactions – Substitution Nucleophilic Bimolecular

Mechanism

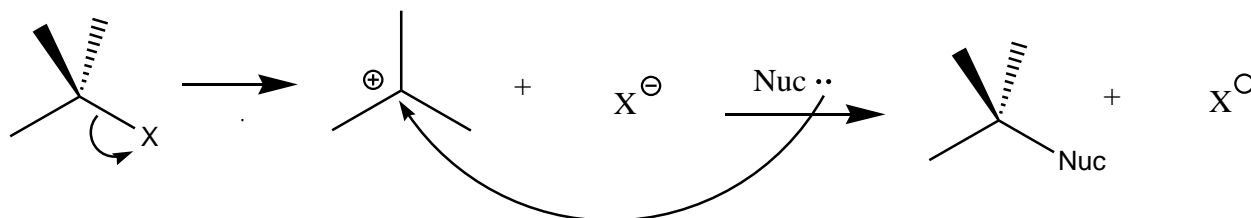


$$\text{rate} = k[\text{substrate}][\text{nucleophile}]$$

results in inversion of configuration

S_N1 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 AgNO₃ facilitates carbocation formation

S_N2 vs. S_N1

	S _N 2	S _N 1
Nucleophile	strong required	weak is ok
Electrophile (has LG)	CH ₃ > 1° > 2°	3° > 2°
Solvent	polar aprotic (preferred)	polar protic
Leaving Group	Good (I ⁻ > Br ⁻ > Cl ⁻ > F ⁻)	Good (I ⁻ > Br ⁻ > Cl ⁻ > F ⁻)
Rearrangements	Not Possible	Possible
Inversion	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

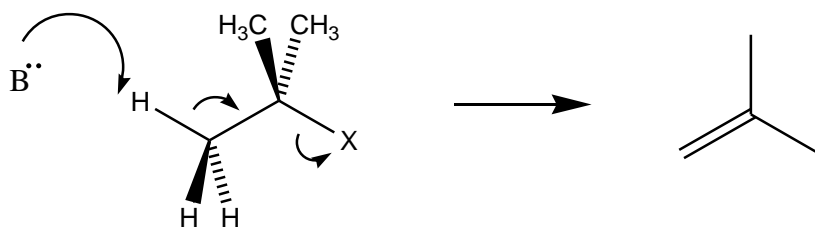
in aprotic solvent

Use of KF with crown ethers for S_N2 rxns

Organic Chemistry Chapter 9 – Elimination Reactions

E2 reactions – Elimination Bimolecular

Mechanism



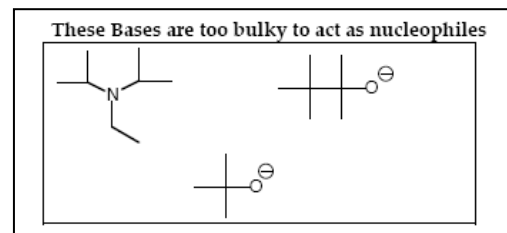
$$\text{rate} = k[\text{substrate}][\text{base}]$$

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

Forms most substituted double bond (Zaitsev's Rule)

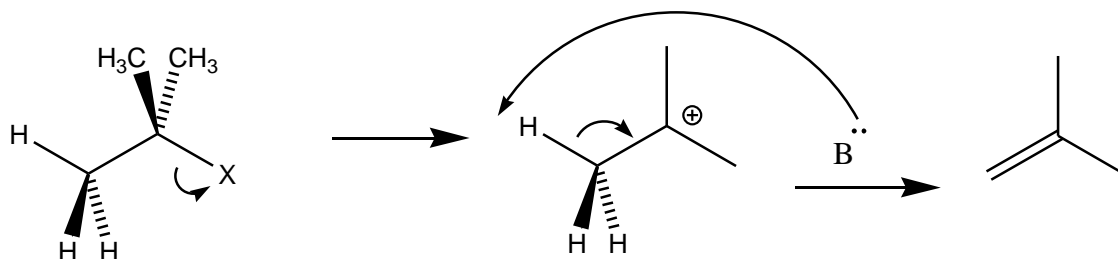
Forms least substituted (Hofmann) if F^- is the leaving group

Forms least substituted (Hofmann) if a bulky base is used with 3° halide



E1 reactions – Elimination Unimolecular

Mechanism



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

Carbocation rearrangements are possible

Forms most substituted double bond (Zaitsev's Rule)

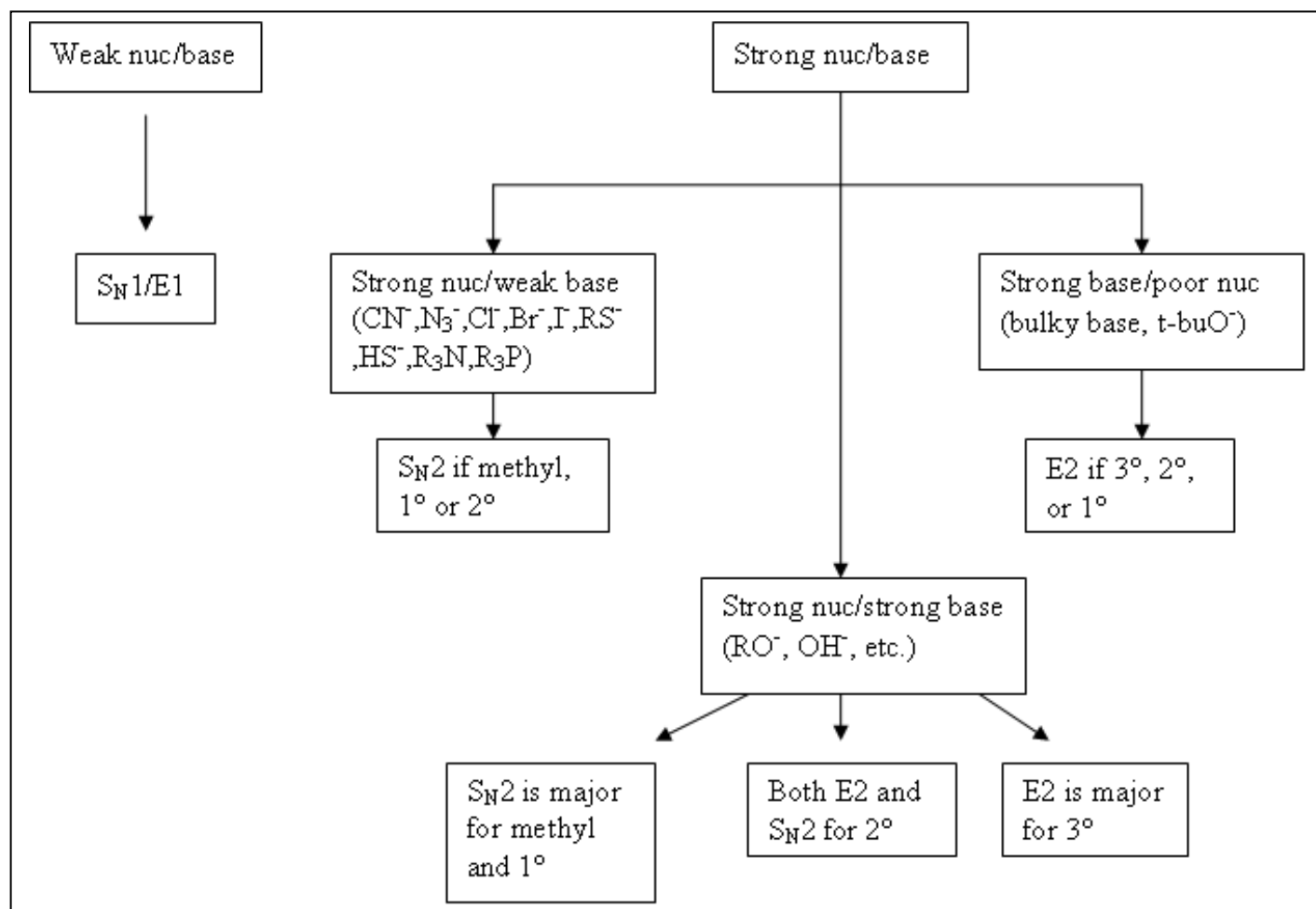
Favored by heat due to entropy

E2 vs. E1

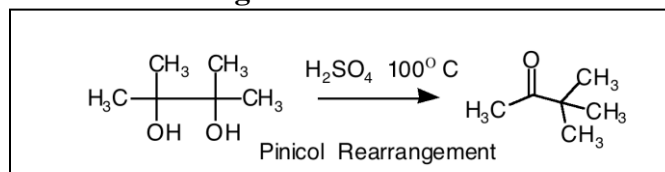
	E2	E1
Base	strong base	weak base
Electrophile (has LG)	$3^\circ > 2^\circ > 1^\circ$	$3^\circ > 2^\circ$
Solvent	polar aprotic (best)	polar protic
Leaving Group	Good ($\text{I}^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$)	Good ($\text{I}^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$)
Rearrangements	Not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

	S_N2	E2	S_N1	E1
Electrophile (has LG)	$\text{CH}_3 > 1^\circ > 2^\circ$	$3^\circ > 2^\circ > 1^\circ$	$3^\circ > 2^\circ$	$3^\circ > 2^\circ$
Nucleophile/Base	strong nuc	strong base	weak nuc	weak base
Solvent	polar aprotic (preferred)	polar aprotic (preferred)	polar protic	polar protic
Leaving Group	good	good	good	good

Substitution/Elimination Map



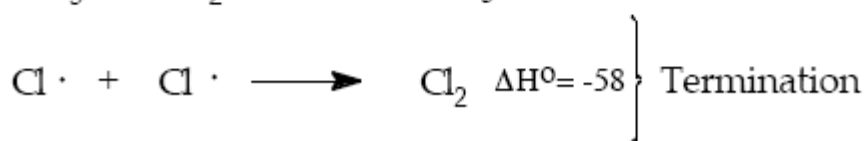
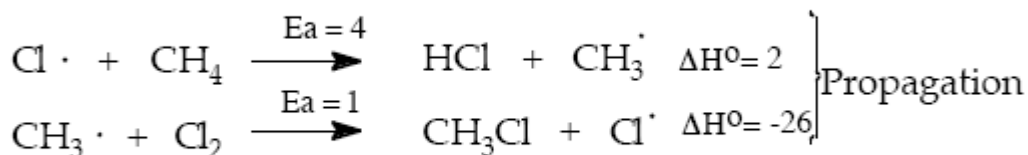
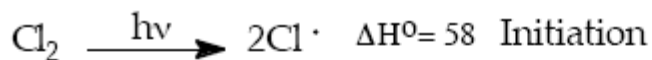
Pinacol Rearrangement



Organic Chemistry Chapter 10 – Radical Rxns

Chlorination vs Bromination

Mechanism

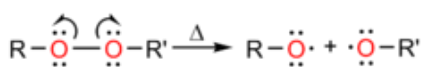


Selectivity

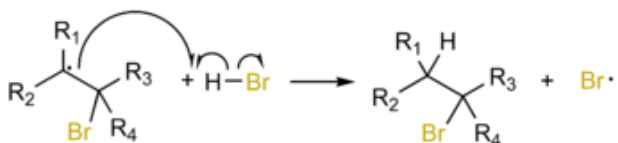
Addition of HBr/ROOR

Mechanism

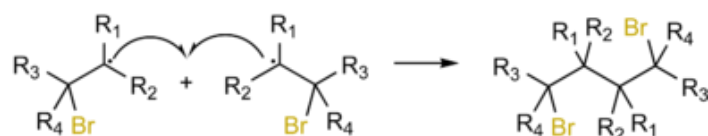
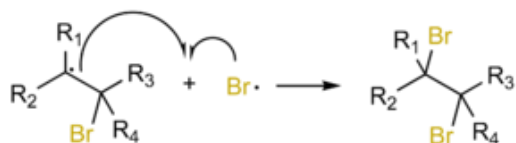
Initiation



Propagation



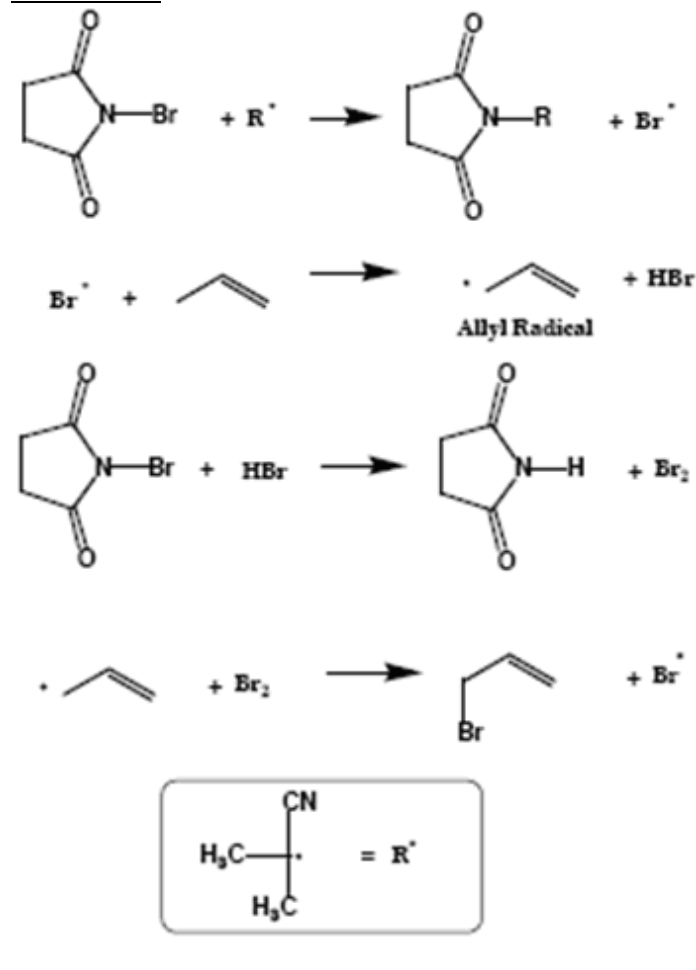
Termination



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)

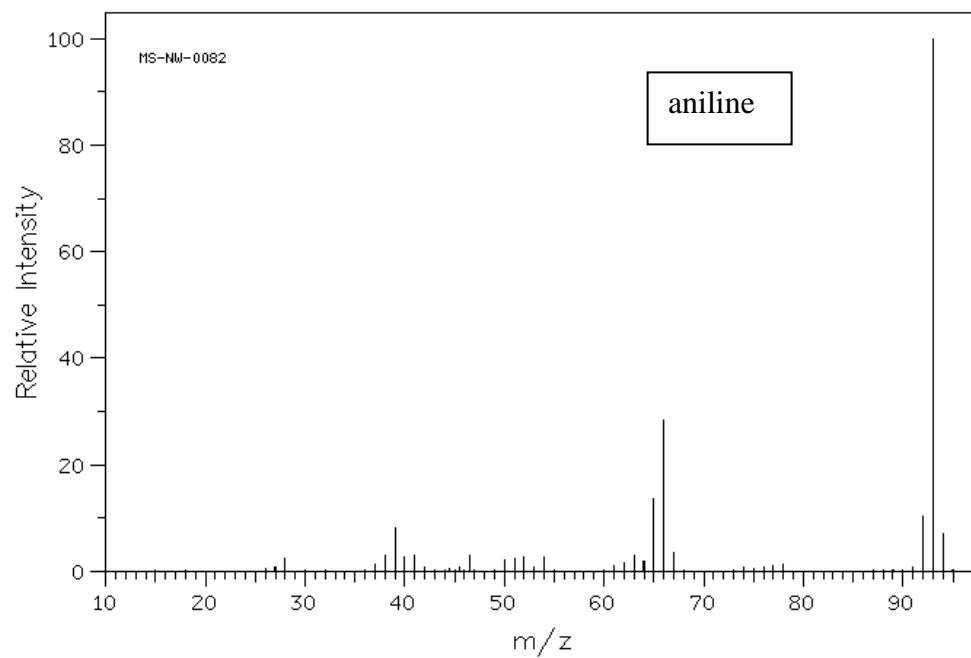
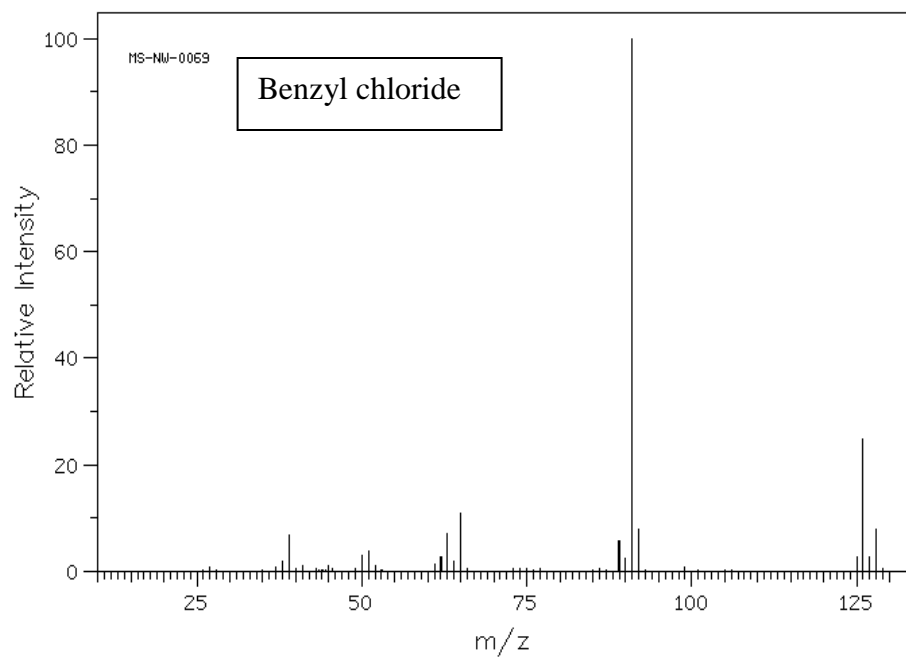
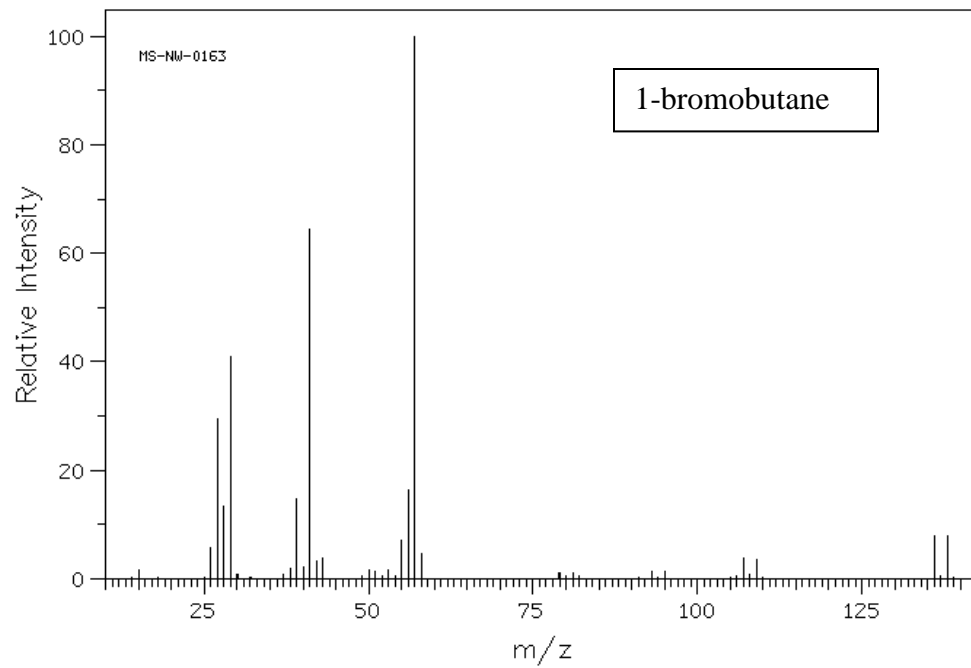
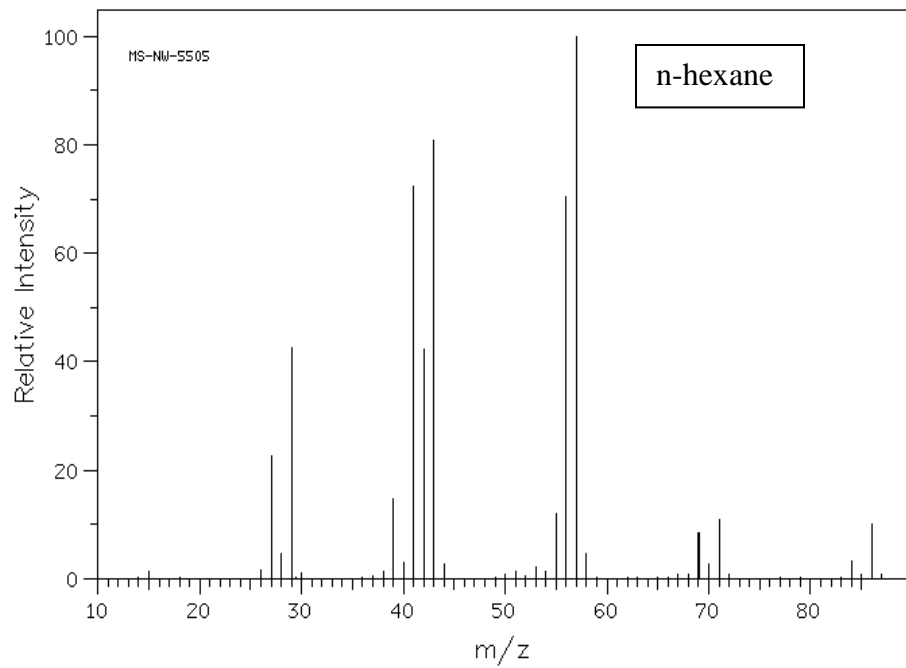
m/z 15 methyl group

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 (cm^{-1}) which are called wavenumbers.

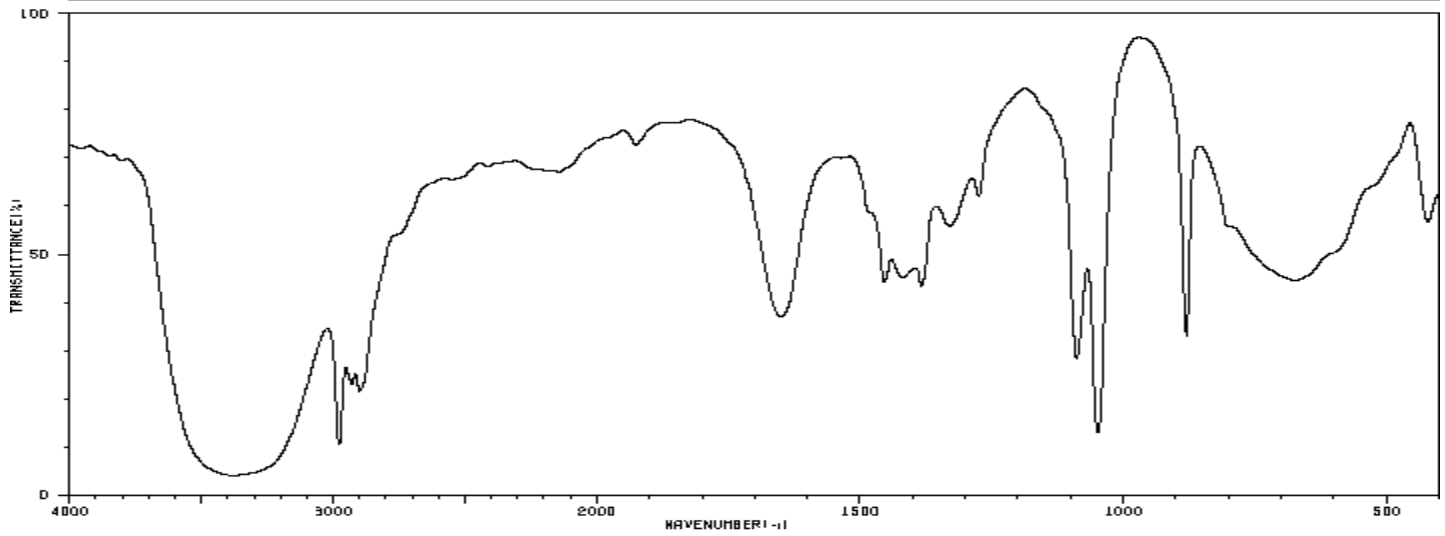
Stretching a bond must change the dipole of a molecule for the bond to be IR active.

You need to be able to identify the following absorptions:

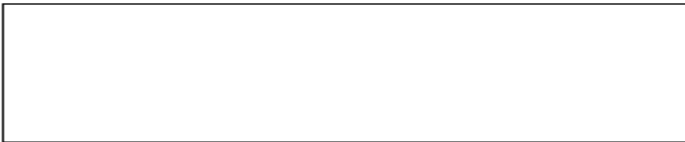
Aromatic C-C	two peaks usually in the range of 1500-1600 cm^{-1}
C=C	~1650 cm^{-1}
C=O	~1710 cm^{-1} (shifts to ~1735 cm^{-1} for esters)
C≡C	~2100-2300 cm^{-1}
C≡N	~2100-2300 cm^{-1}
C-H (aldehyde)	Two peaks at 2710 and 2810 cm^{-1}
sp^3 C-H	just to the right of 3000 cm^{-1}
sp^2 C-H	just to the left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

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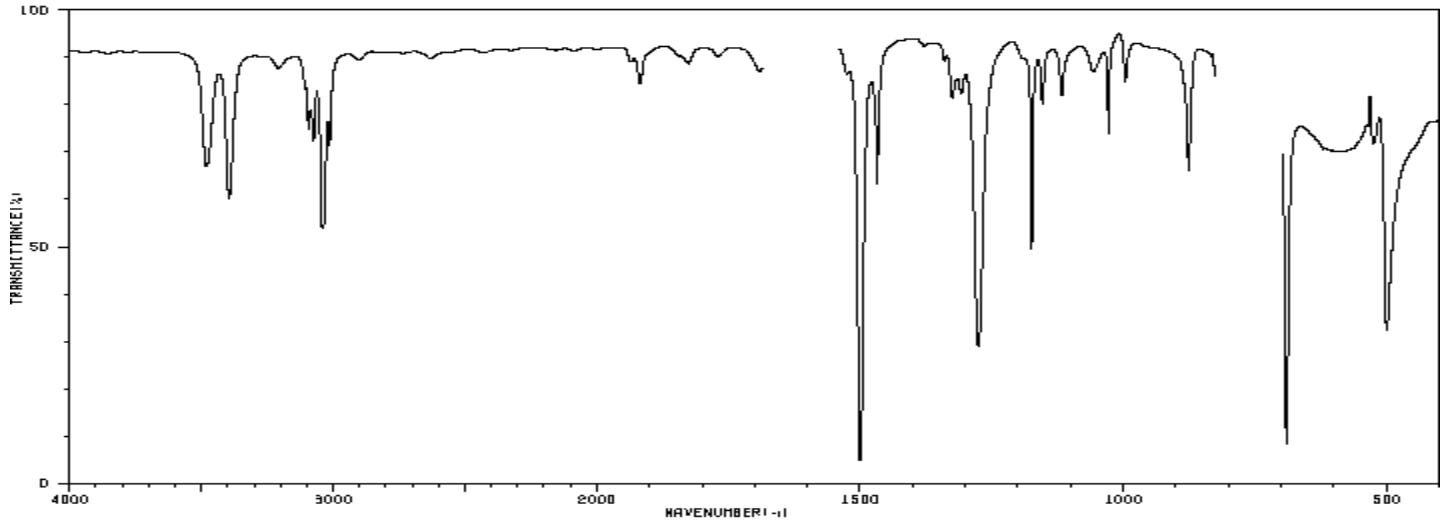
HIT-NO=1374 | SCORE= () | SDBS-NO=1300 | IR-NIDA-21941 : LIQUID FILM
 ETHYL ALCOHOL
 C_2H_6O



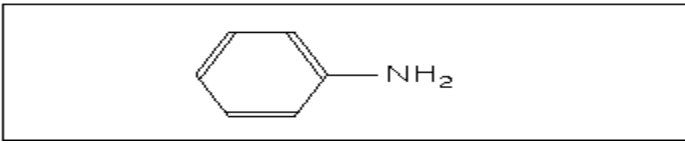
2977	4	1384	32
2930	13	1329	44
2899	12	1275	52
1926	62	1089	18
1650	26	1048	6
1454	33	880	22
1418	33		



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



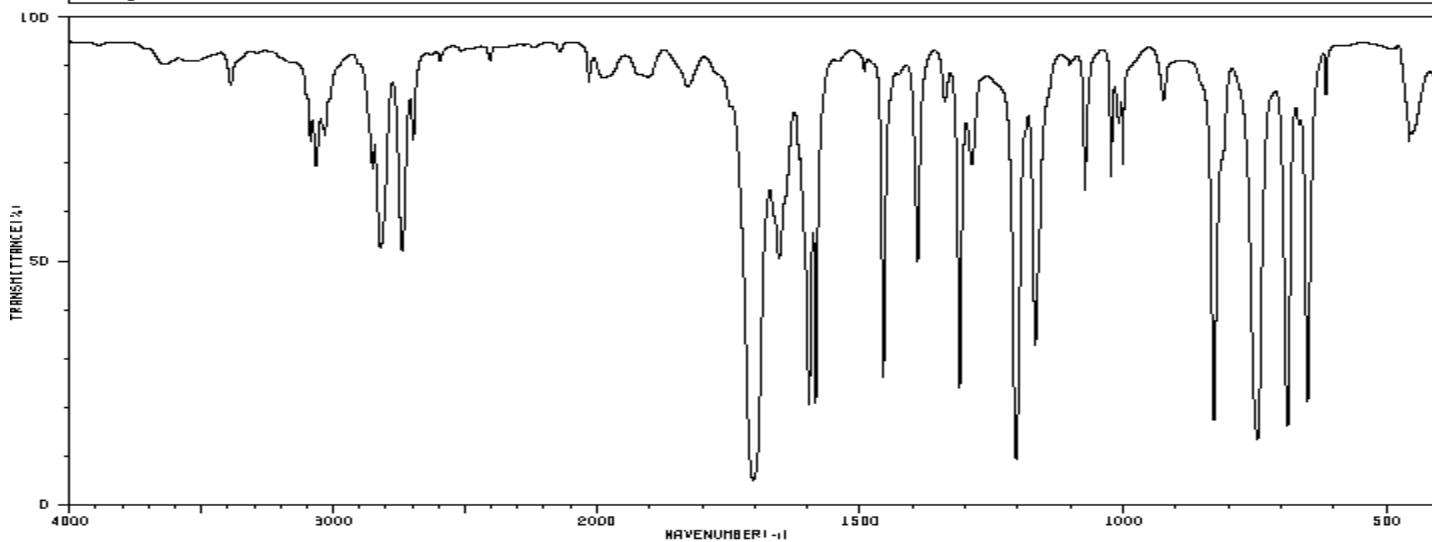
3480	64	2906	86	1340	86	1068	84
3395	58	2630	86	1325	79	1028	72
3209	84	1918	81	1306	79	996	81
3094	72	1833	86	1275	28	876	64
3074	70	1826	86	1174	47	690	8
3041	52	1500	4	1154	77	526	70
3013	68	1468	60	1117	79	500	31



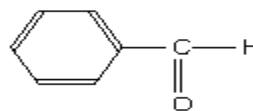
HIT-NO=1117 SCORE= () SOBS-NO=672 IR-NIDA-05223 : LIQUID FILM

BENZALDEHYDE

C₇H₆O



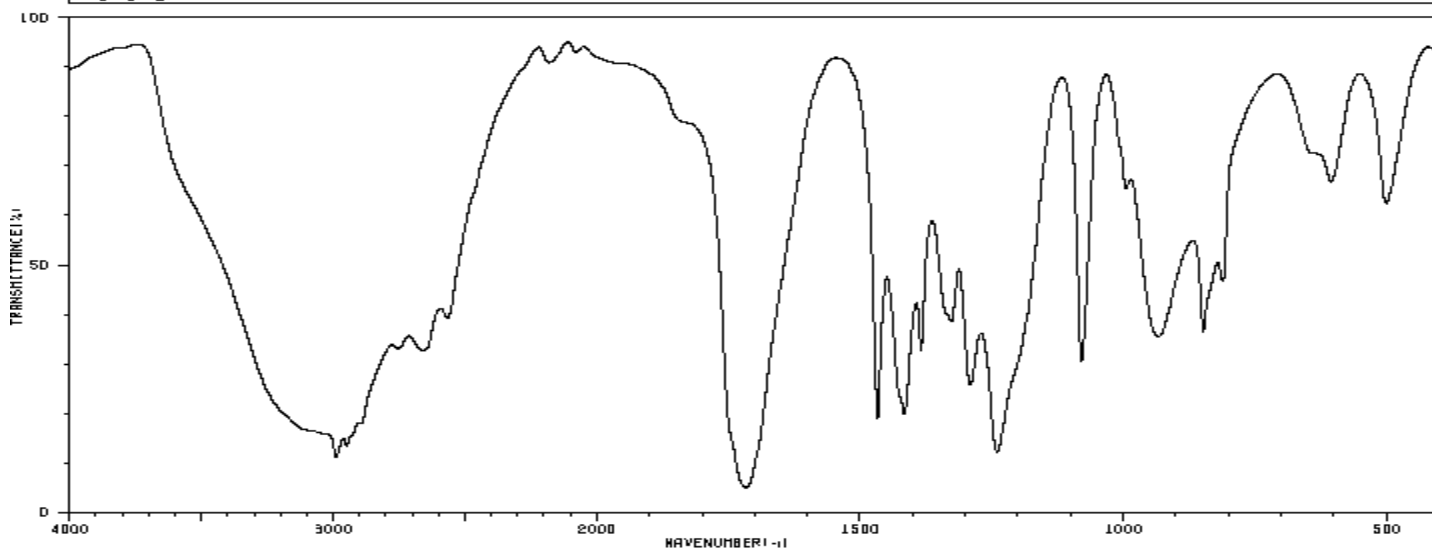
3086	72	1981	84	1597	20	1204	8	828	16
3065	86	1916	84	1584	20	1168	31	746	13
3031	72	1909	84	1456	25	1073	62	688	15
2860	66	1901	84	1391	47	1023	64	667	74
2820	50	1828	81	1339	79	1008	74	650	20
2736	50	1703	4	1311	23	1001	66	615	61
2696	72	1664	49	1288	68	924	79	467	72



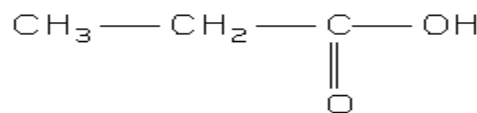
HIT-NO=1276 SCORE= () SOBS-NO=1033 IR-NIDA-05127 : LIQUID FILM

PROPIONIC ACID

C₃H₆O₂

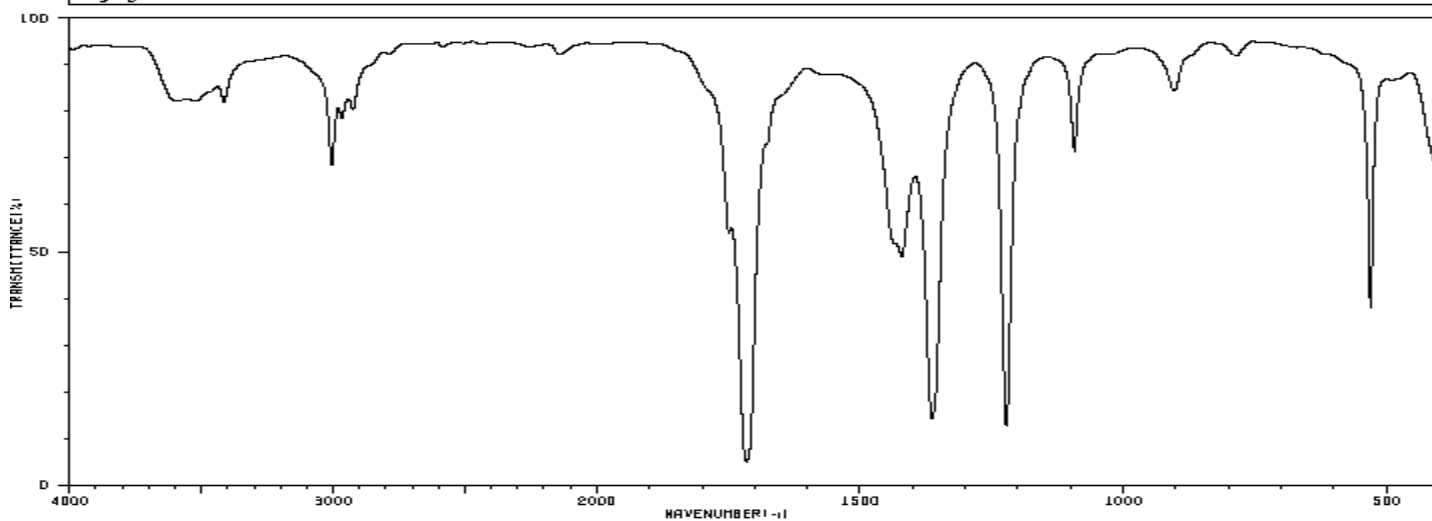


2986	10	1384	32	848	36
2948	12	1327	37	811	44
2860	31	1291	25	814	86
2666	38	1240	12	606	64
1716	4	1080	29	501	60
1467	18	995	62		
1416	19	933	34		

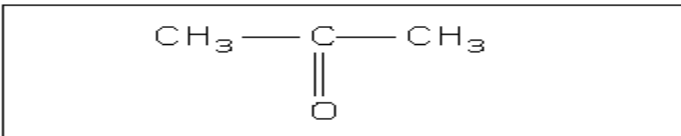


HIT-NO=960 SCORE= () SDBS-NO=319 IR-NIDA-63533 : LIQUID FILM
ACETONE

C₃H₆O



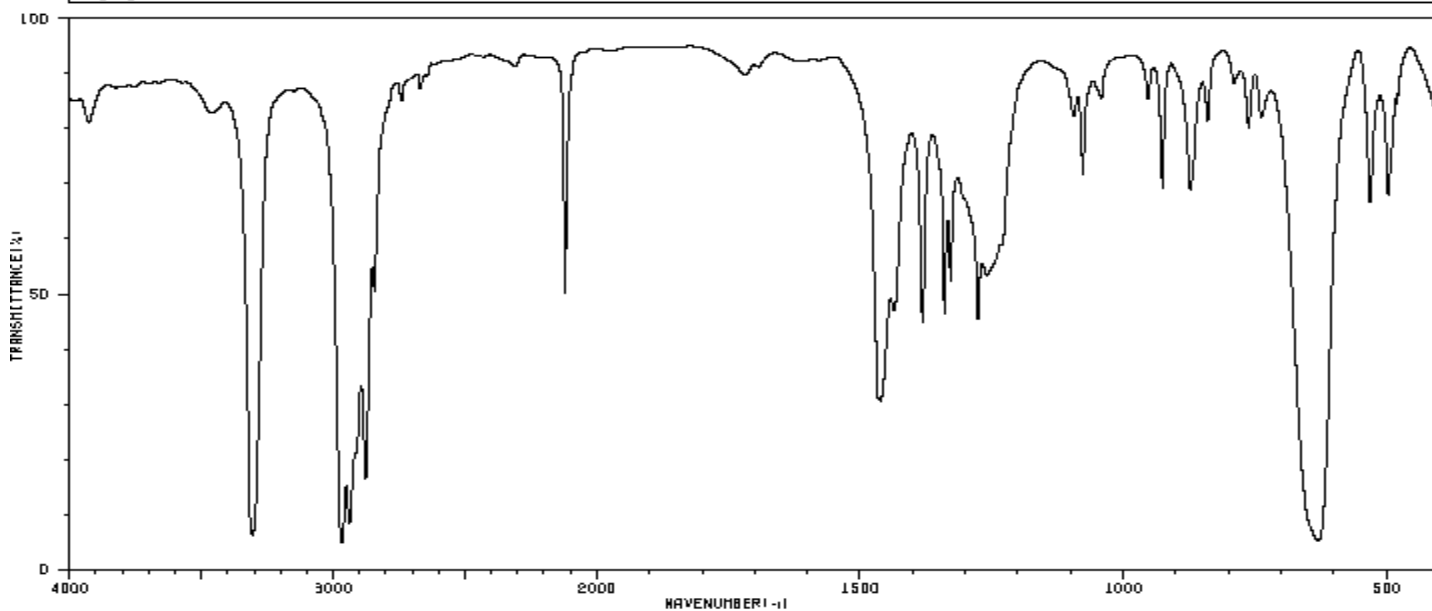
3414	79	1421	47
3005	66	1363	13
2966	74	1223	12
2926	77	1093	68
1749	52	903	81
1715	4	531	36
1434	49		



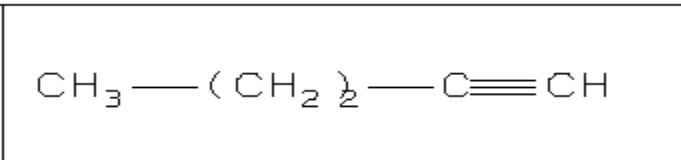
HIT-NO=2943 SCORE= () SDBS-NO=5386 IR-NIDA-13676 : LIQUID FILM

1-PENTYNE

C₅H₈



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		

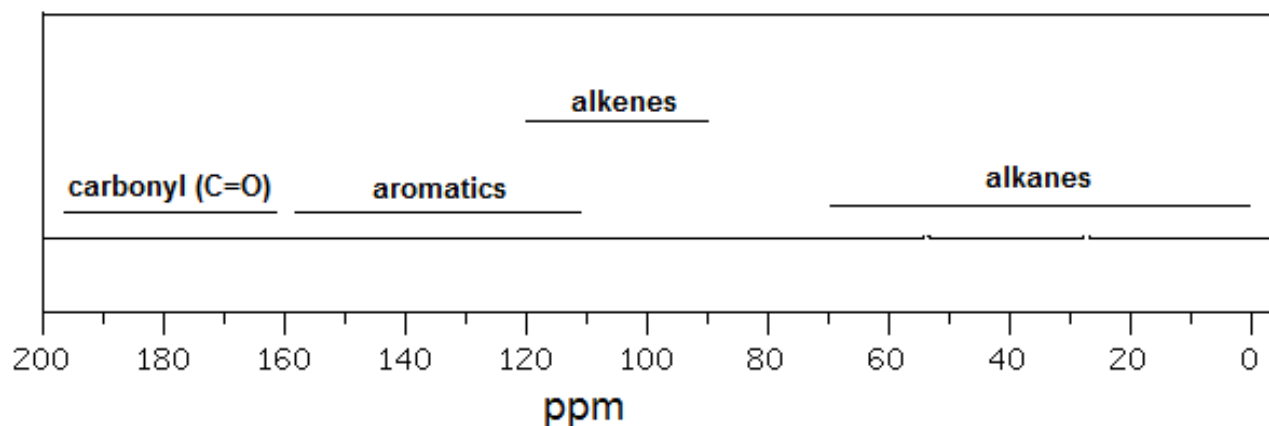


Organic Chemistry Chapter 13 – NMR Spectroscopy

^{13}C NMR

Gives the number of carbon environments in a molecule

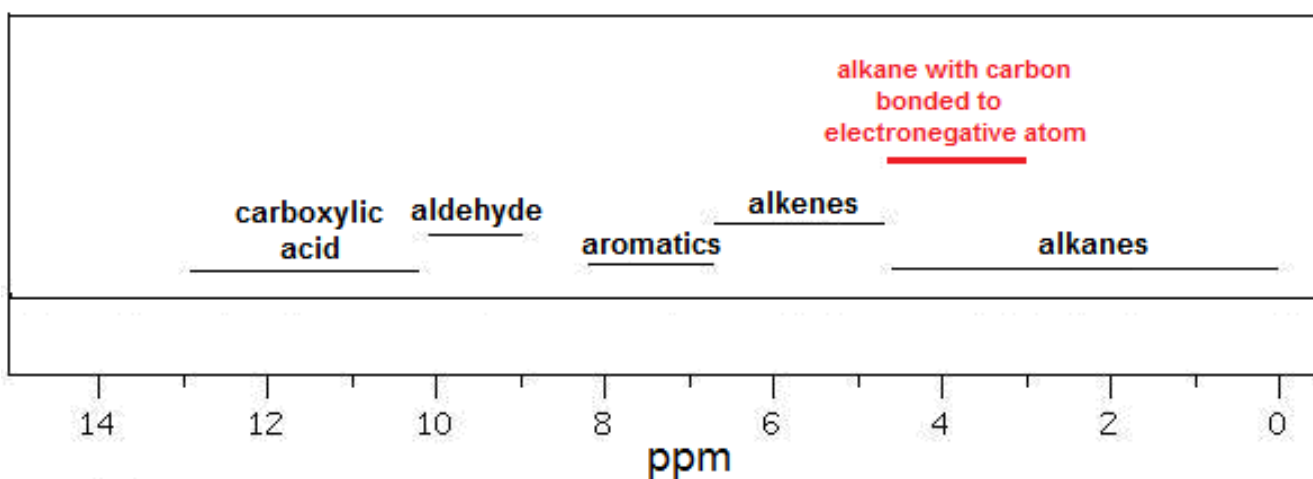
The chemical shift also tells whether the carbon is an alkane, alkene, aromatic, or carbonyl (C=O)

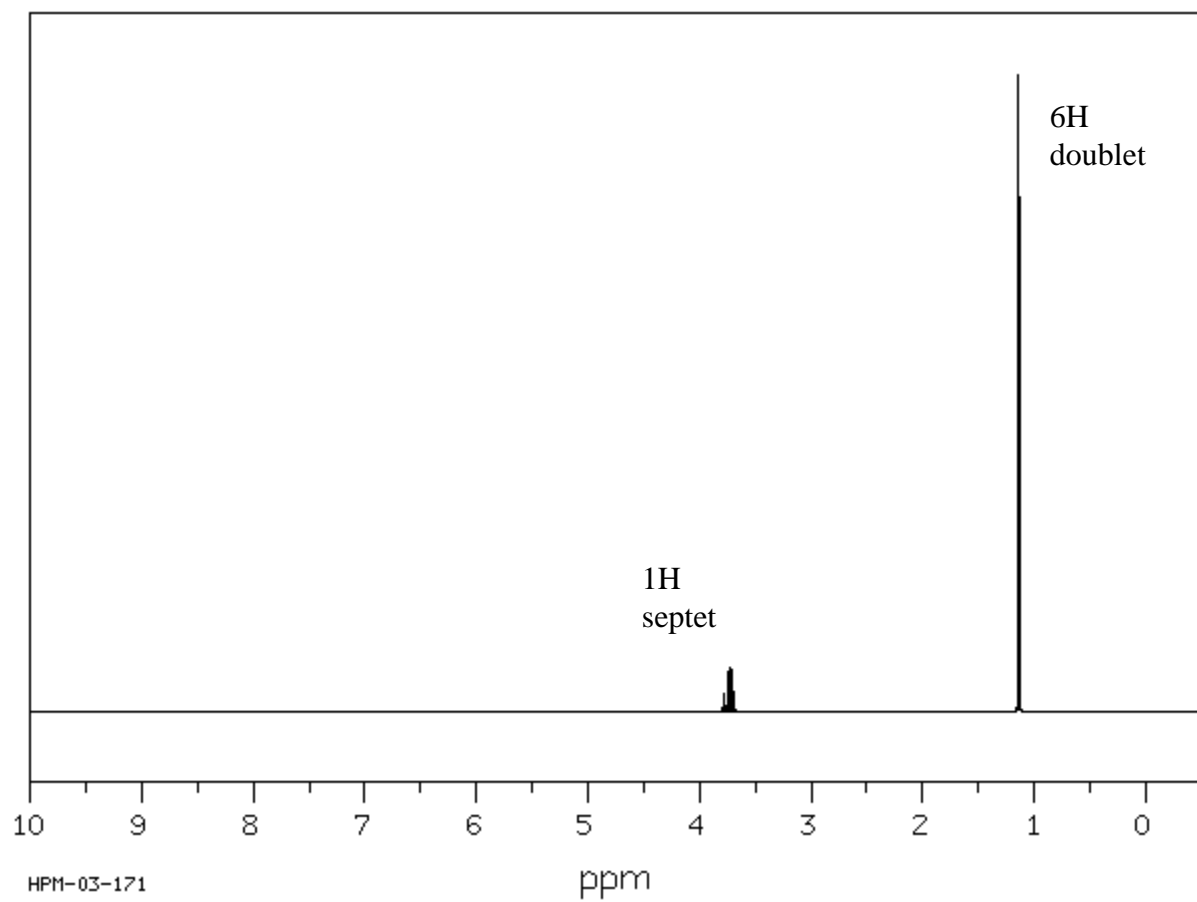
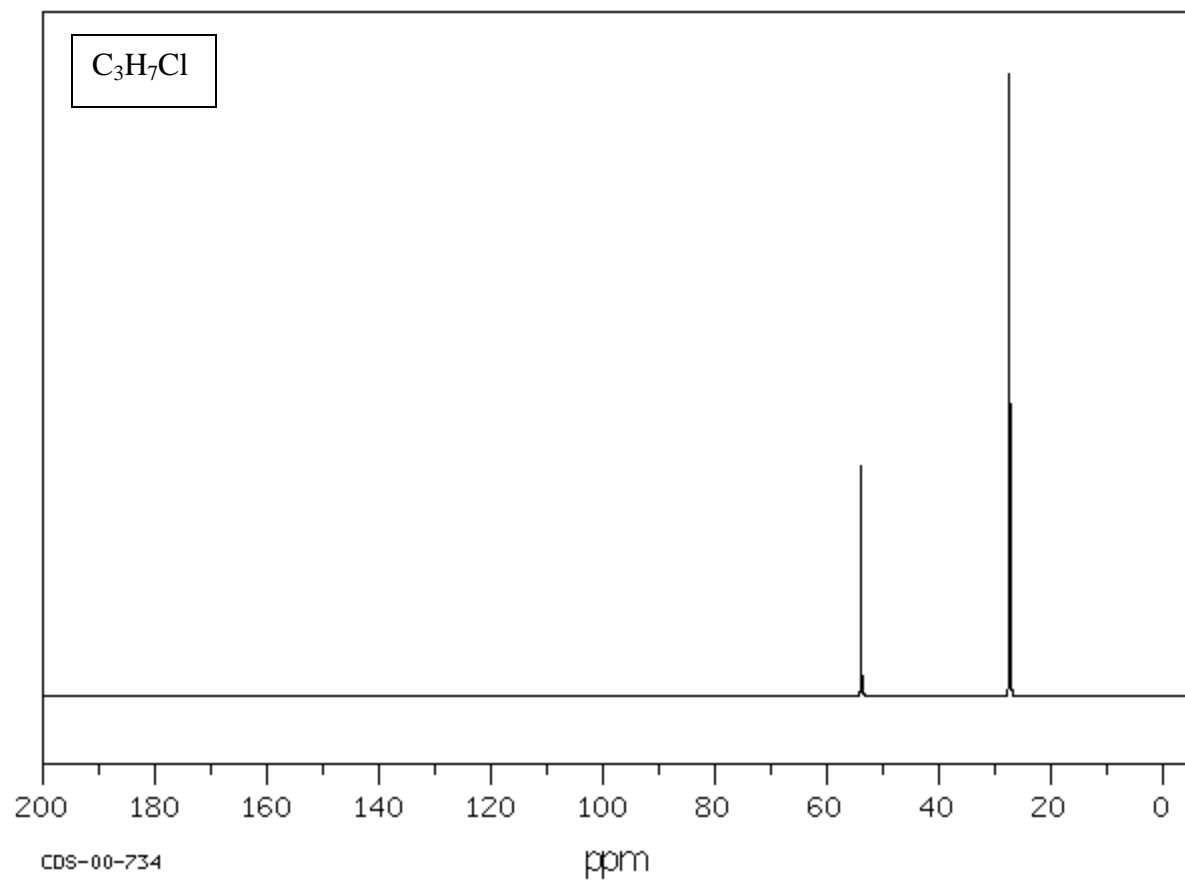


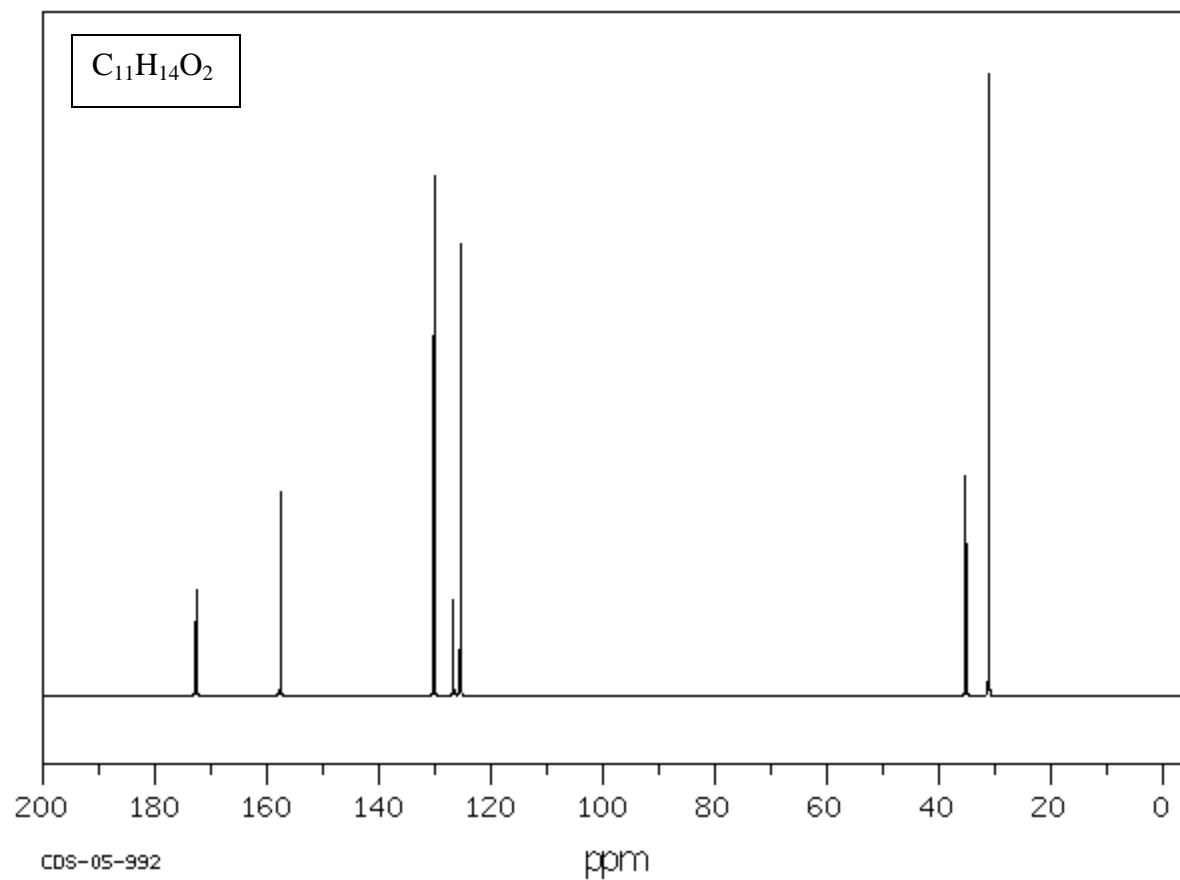
^1H NMR

Gives the number of hydrogen environments in a molecule

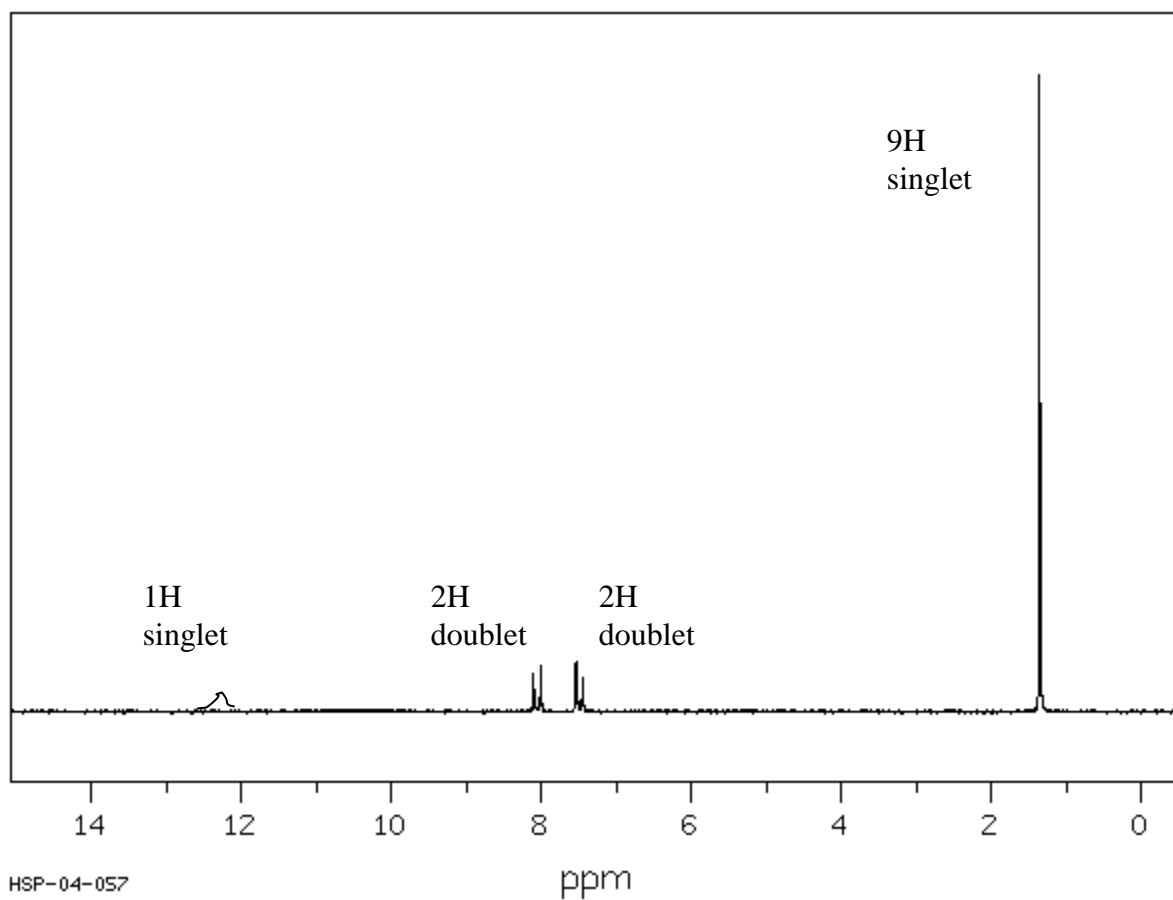
- 1) The chemical shift tells whether the hydrogen is an alkane, alkene, aromatic, aldehyde, or carboxylic acid
- 2) The area under the signal or integration tells how many hydrogens a signal represents (or at least the ratio)
- 3) The number of peaks tells the number of neighbors ($\# \text{ peaks}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

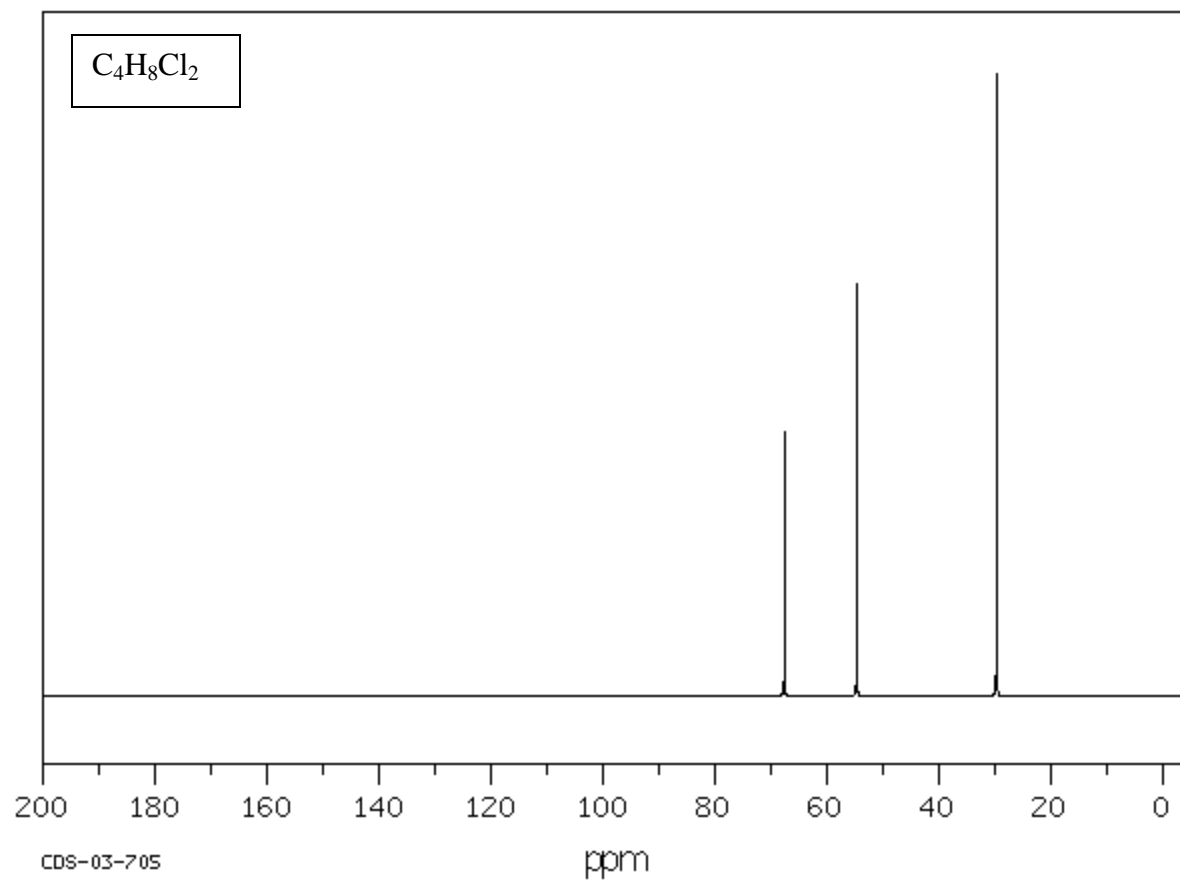




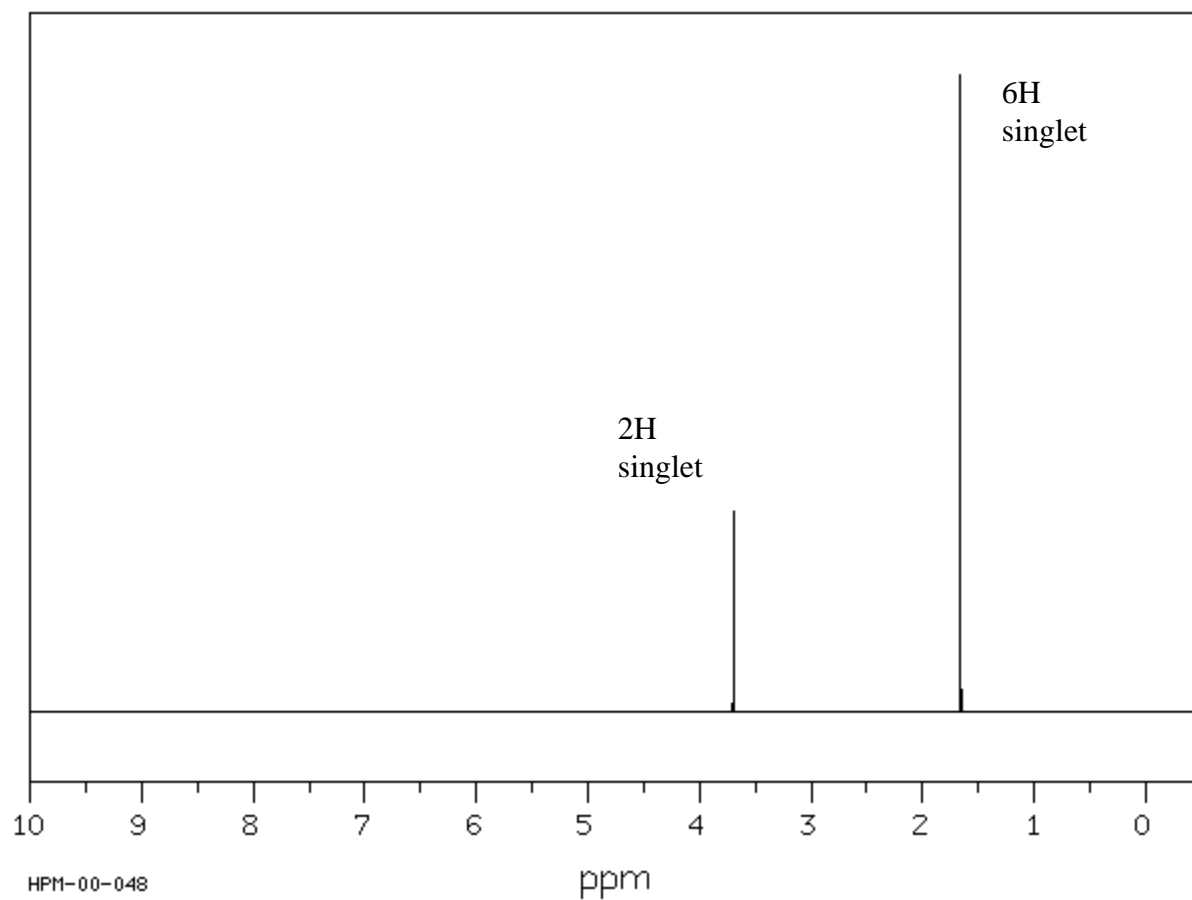


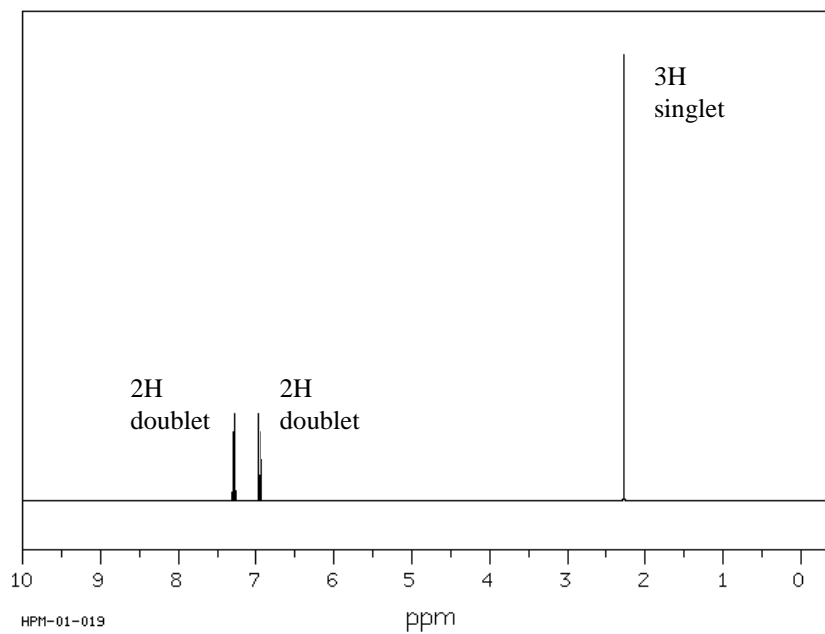
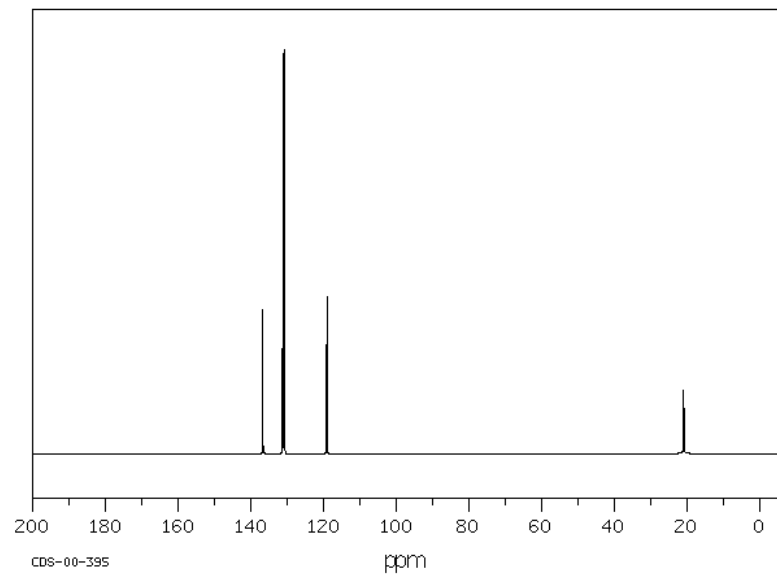
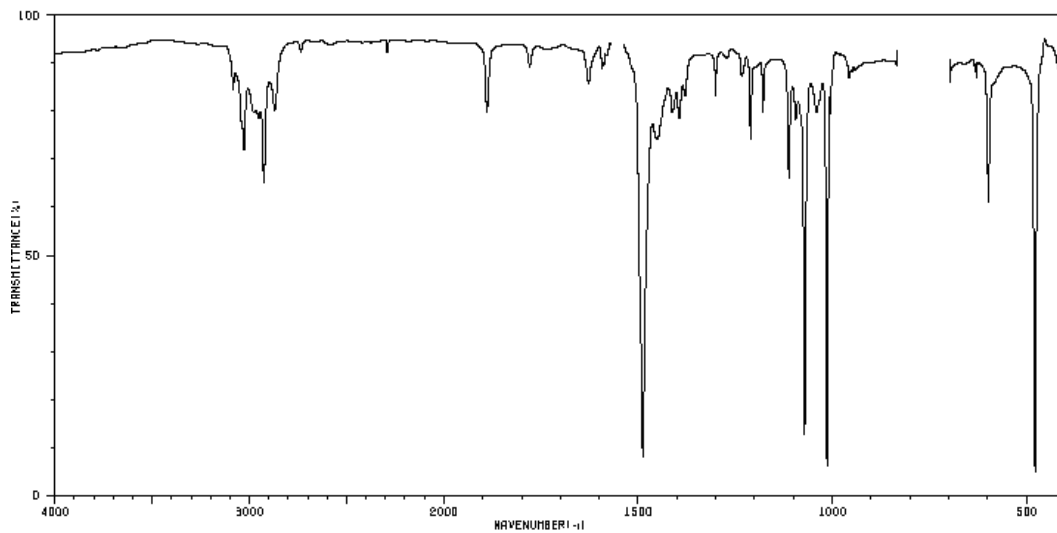
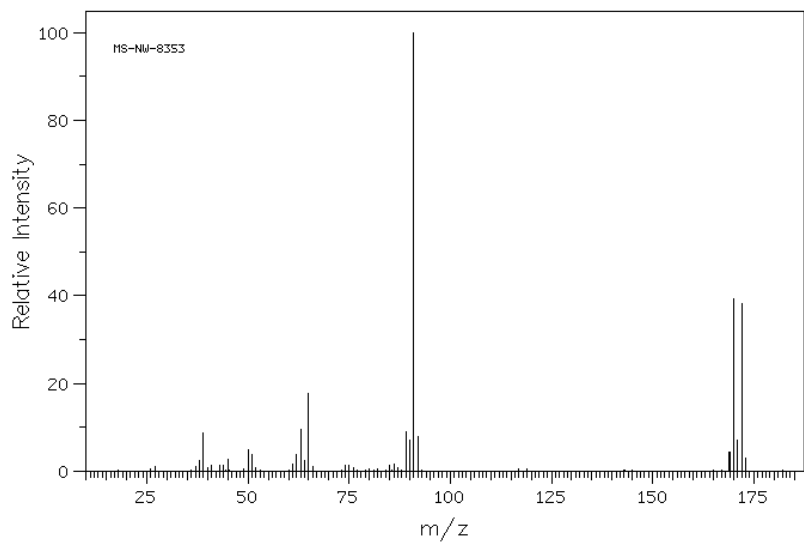
#2



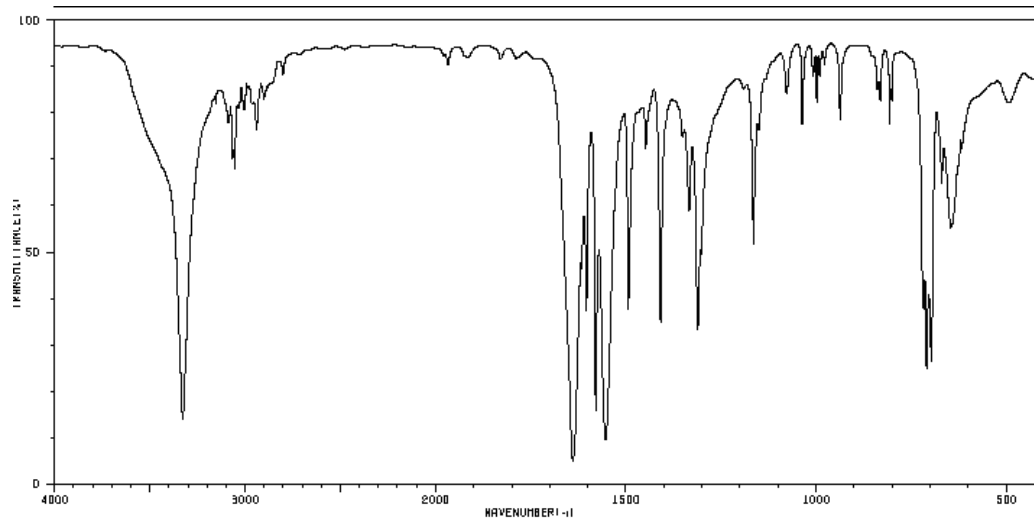
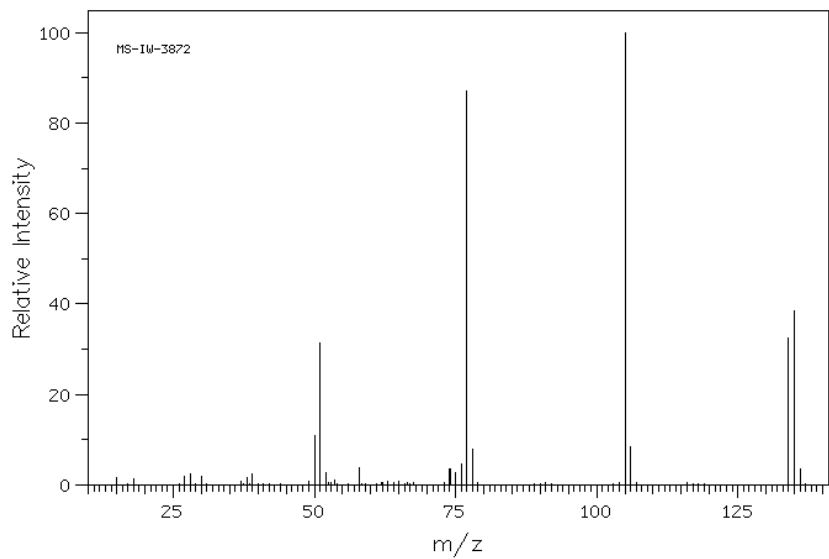


#3

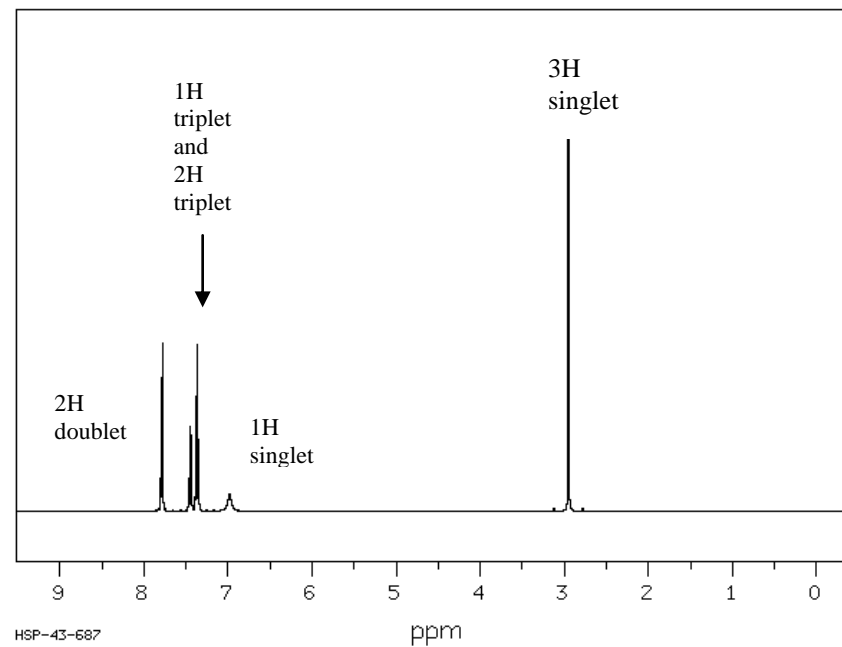
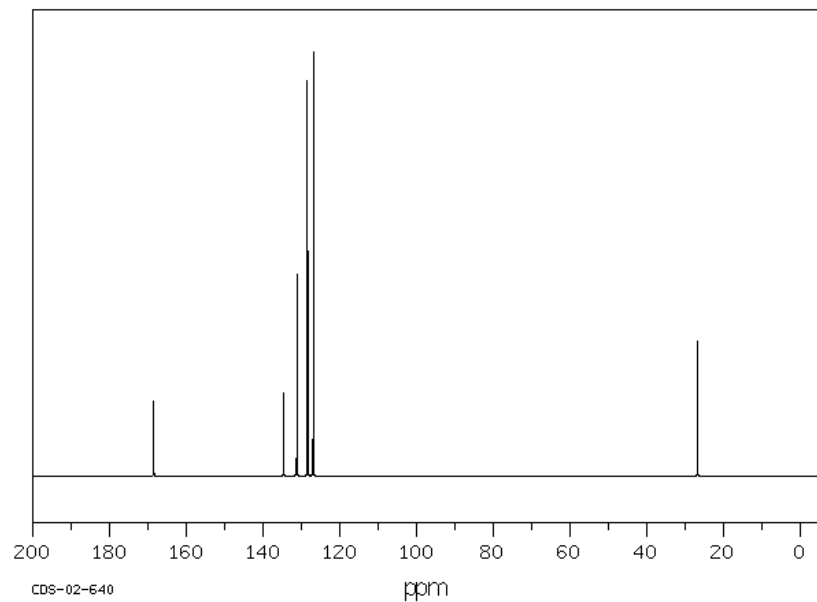




#4



#5

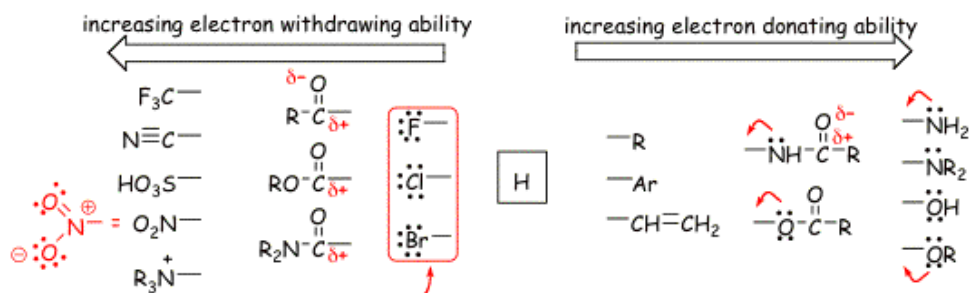
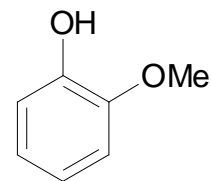
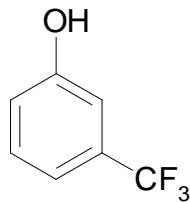
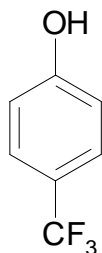
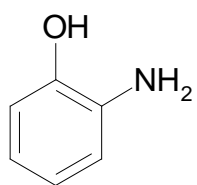


Organic Chemistry Chapter 14 – Alcohols, Ethers, and Epoxides

Alcohols

Nomenclature

Acidity



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

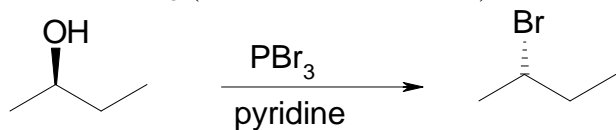
Reactions of Alcohols

Rxn with H-X (HBr or HCl/ZnCl₂)

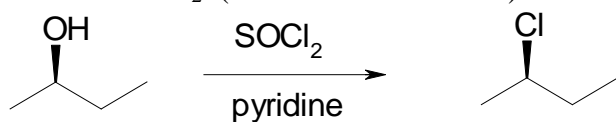
S_N1 for 2° and 3° alcohols

S_N2 for 1° alcohols

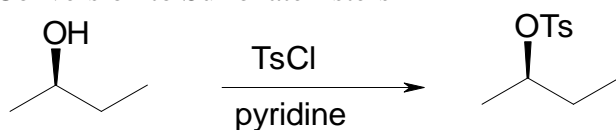
Rxn with PBr₃ (for 1° and 2° alcohols)



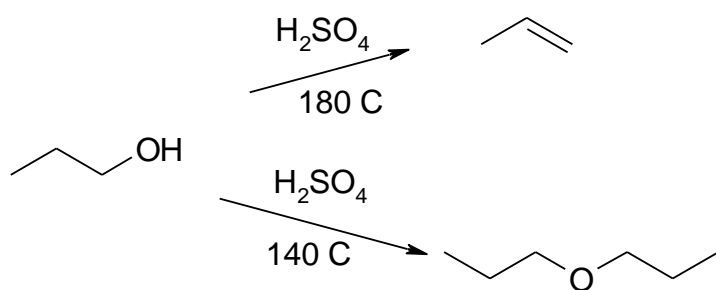
Rxn with SOCl₂ (for 1° and 2° alcohols)



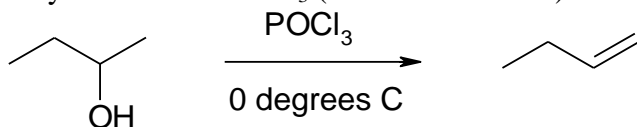
Conversion to Sulfonate Esters



Dehydration with H₂SO₄

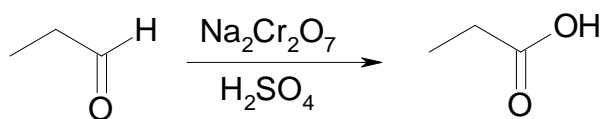
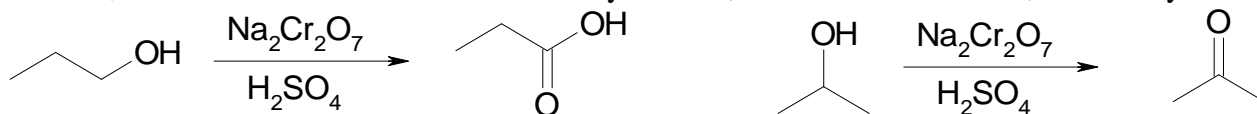


Dehydration with POCl₃ (Hofmann Product)



Oxidation

Na₂Cr₂O₇/H₂SO₄ 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

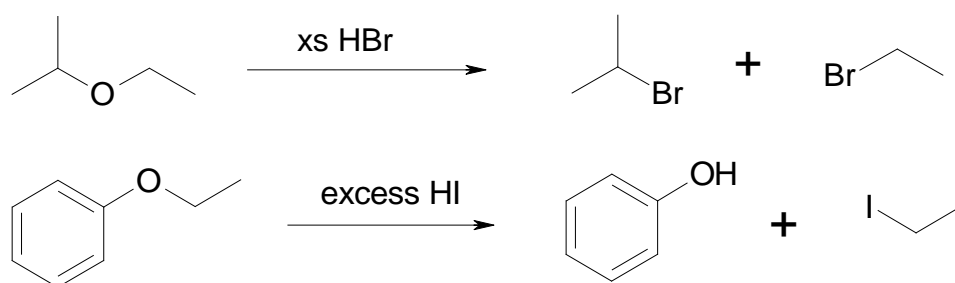
Nomenclature of Epoxides (Oxiranes)

Synthesis via Substitution (S_N2 or S_N1)

Williamson Ether Synthesis (S_N2)

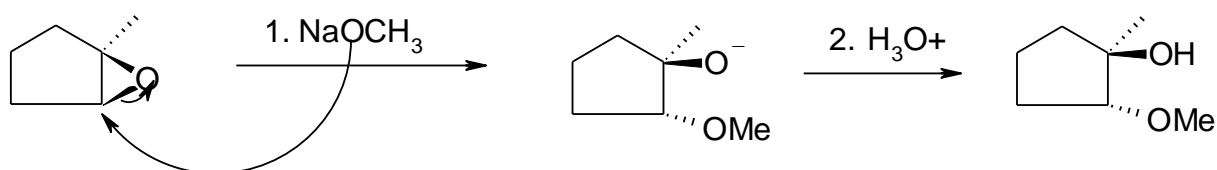


Rxn with H-X

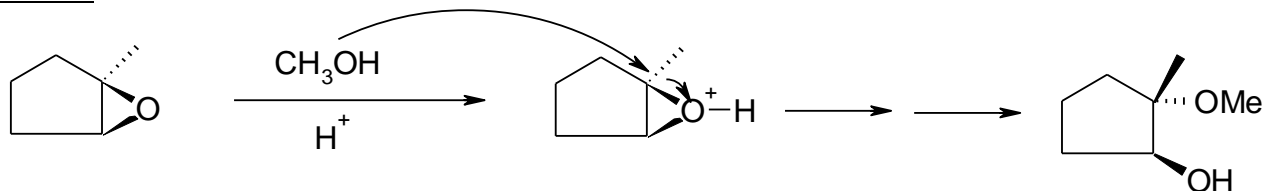


Ring Opening of Epoxides (In Acid or Base)

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)

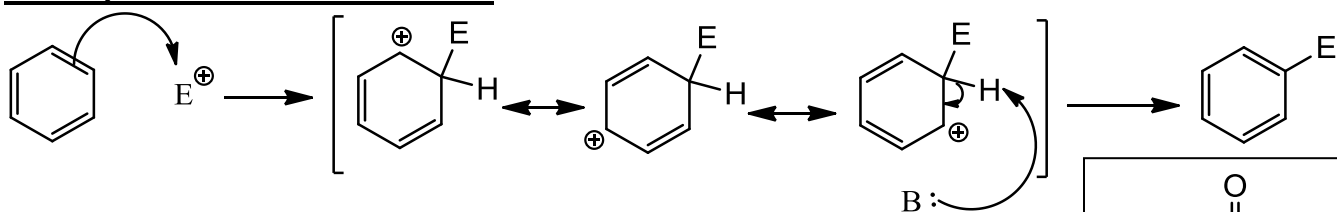
Antiaromatic compounds satisfy the first 3 rules above but delocalization of the pi electrons increases the electronic energy ($4N$ electrons)

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

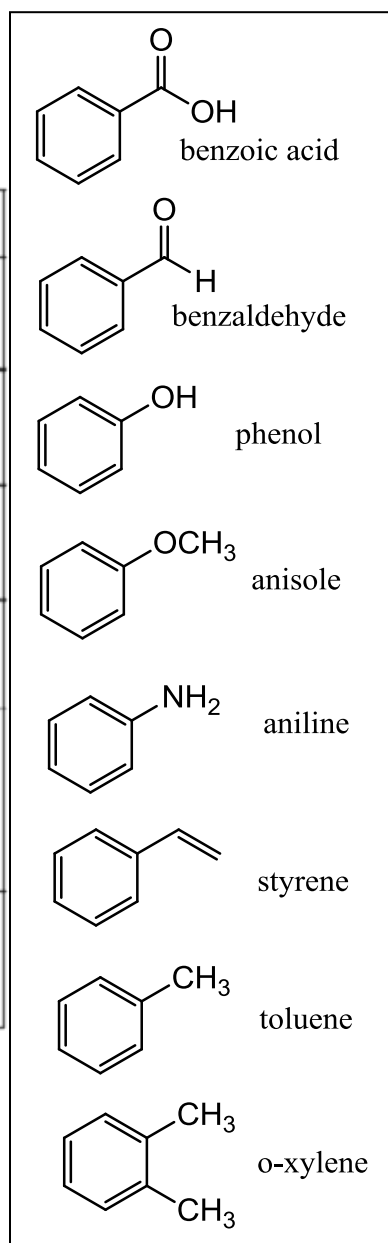
π Molecular Orbitals

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 $R-X/AlCl_3$

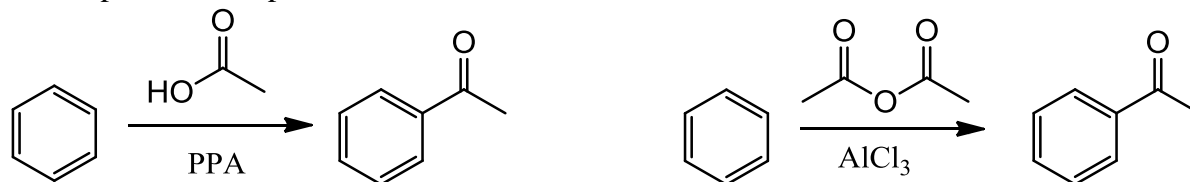
- 1) Fails with strongly deactivated benzenes (benzenes with strong electron withdrawing groups attached)
- 2) Carbocation rearrangement
- 3) Alkylation activates the ring: multiple alkylations are hard to avoid

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)

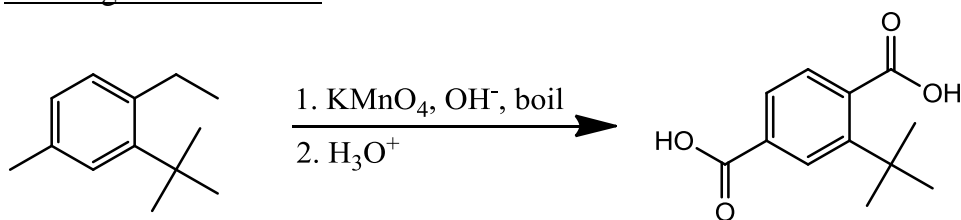
Meta Directors (Deactivating)

Strongest donating group usually directs when there are competing substituents

Activating		BENZENE	Deactivating		
π Donors	σ Donors		Halogens	Carbonyls	Other
$-\ddot{N}H_2$ $-\ddot{O}H$ $-\ddot{O}R$ $-\ddot{N}HCOCH_3$	$-\text{R}$ (alkyl)  (aryl)	$-\text{H}$	$-\text{F}$ $-\text{Cl}$ $-\text{Br}$ $-\text{I}$	$\begin{matrix} \text{O} \\ \\ -\text{C}-\text{R} \\ \text{O} \\ \\ -\text{C}-\text{OH} \\ \text{O} \\ \\ -\text{C}-\text{OR} \end{matrix}$	$-\text{SO}_3\text{H}$ $-\text{C}\equiv\text{N}$ $-\text{NO}_2$ $-\overset{+}{\text{N}}\text{R}_3$
Ortho/Para Directors			Meta Directors		

Side-Chain Reactions of Benzenes

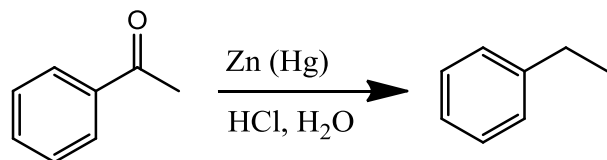
Permanganate Oxidation



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

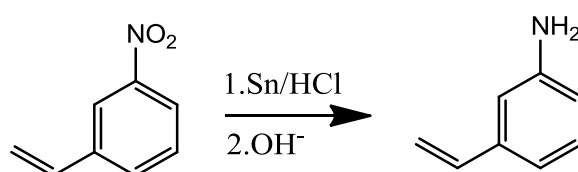
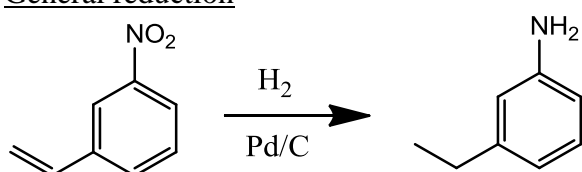
Side-chain Reduction

Clemmenson Reduction – reduces ketones and aldehydes to alkanes



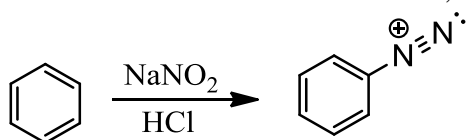
Wolff Kishner
Reduction does the
same thing with
 $\text{H}_2\text{NNH}_2, \text{OH}^-, \text{heat}$

General reduction

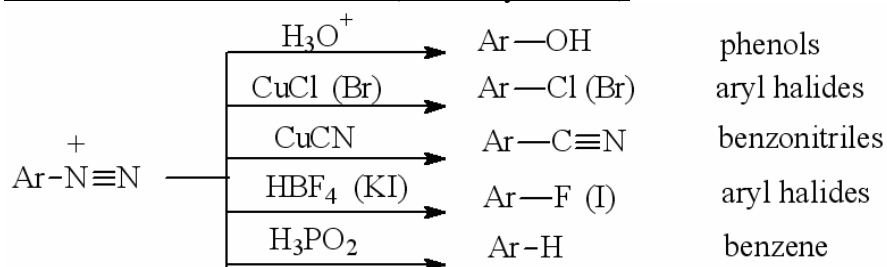


Rxn with Nitrous Acid - NaNO_2/HCl leads to formation of nitrosonium ion (NO^+)

1° become diazonium salts, 2° become nitrosamines



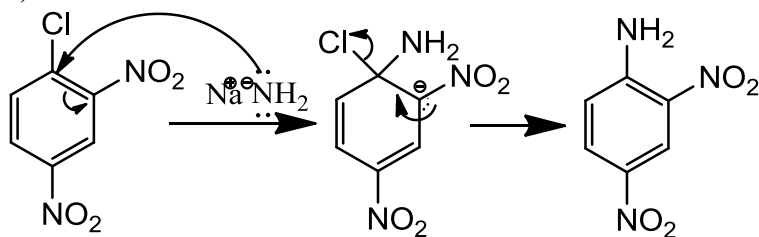
Rxns of arenediazonium salts (Sandmeyer Rxns)



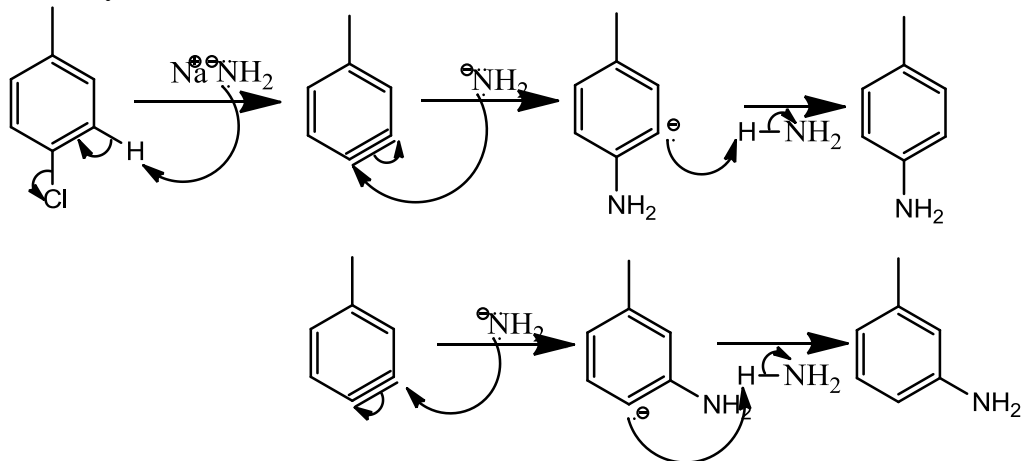
Nucleophilic Aromatic Substitution (NAS)

strong nucleophile (NH_2^- or OH^- for example) replaces halide
electron withdrawing groups ortho/para to halide facilitate reaction

1) Addition-Elimination mechanism

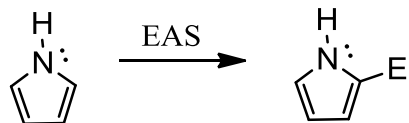


2) Benzyne mechanism (Elimination-Addition Mechanism)

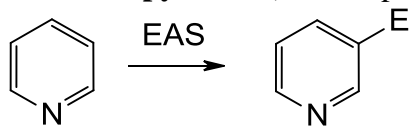


Non-benzenoid Aromatics

EAS with 5-membered Aromatic Heterocycles



EAS with pyridine (at the 3-position)



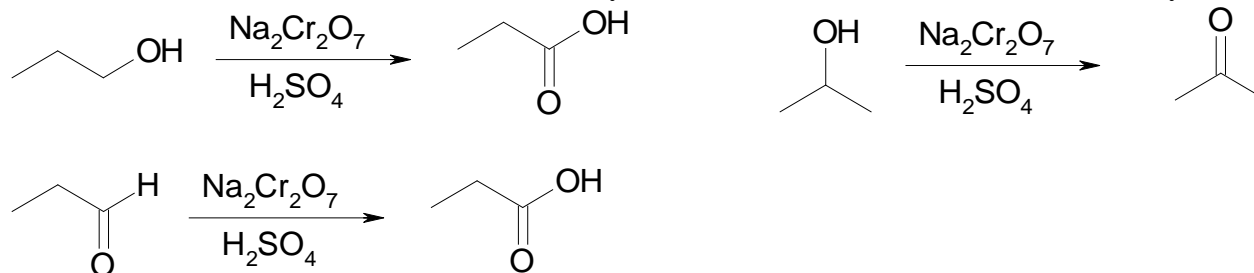
Organic Chemistry Chapter 16 – Ketones and Aldehydes

Nomenclature

Synthesis

Oxidation using chromic acid (H₂CrO₄) or PCC

Na₂Cr₂O₇/H₂SO₄ 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)O₃ (2) (CH₃)₂S

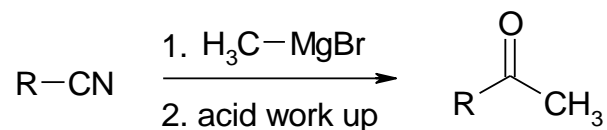
Friedel Crafts Acylation (a phenyl ketone) and Formylation (benzaldehyde)

Hydration of a Terminal Alkyne

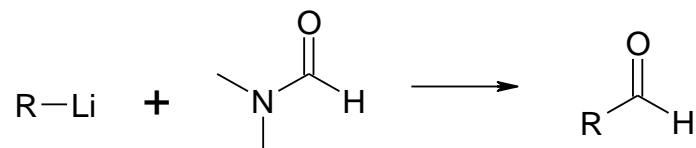
(1) (Sia)₂BH (2) H₂O₂, NaOH to yield an aldehyde (anti-Markovnikov addition)

HgSO₄, H₂SO₄, H₂O to yield a ketone (Markovnikov addition)

Grignard Addition to Nitriles



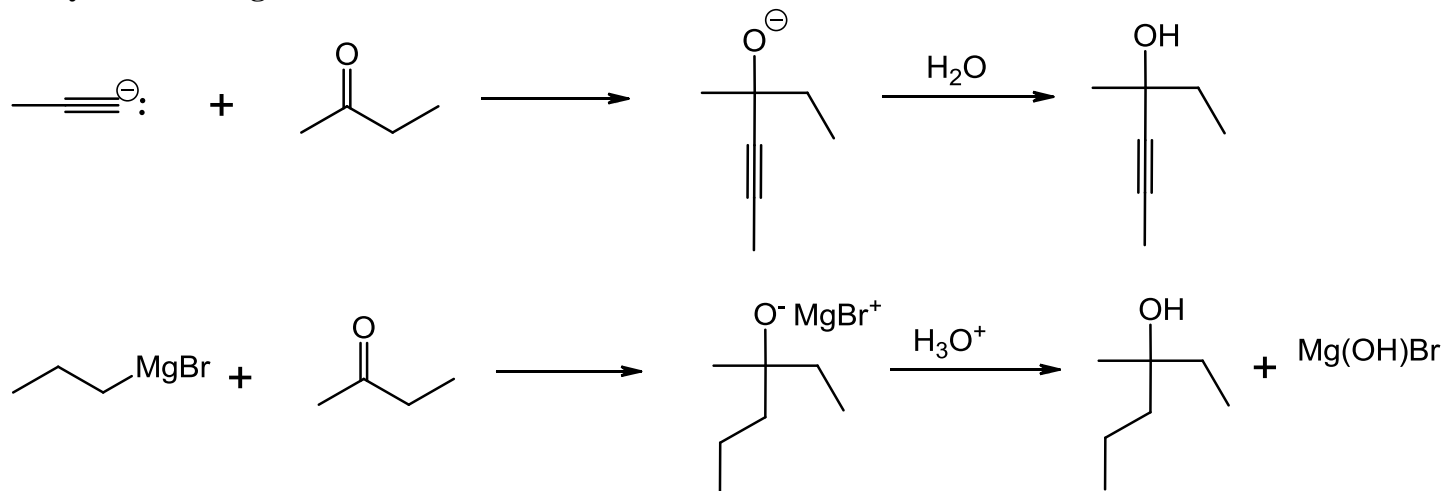
Organolithium Addition to DMF



Reactions of Ketones and Aldehydes

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

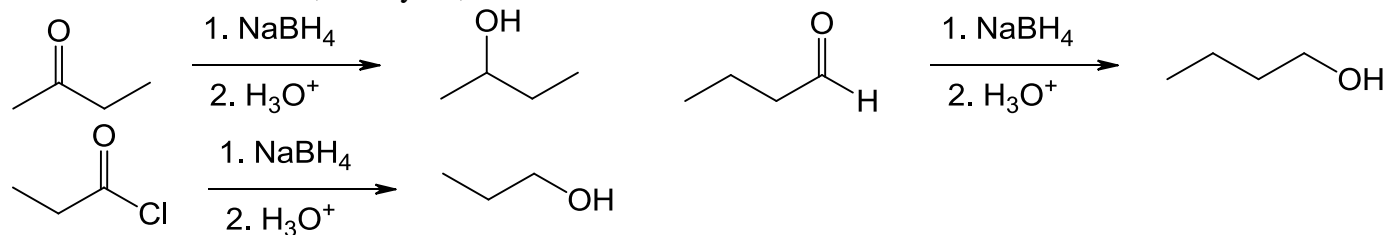
Acetylide and Grignard addition



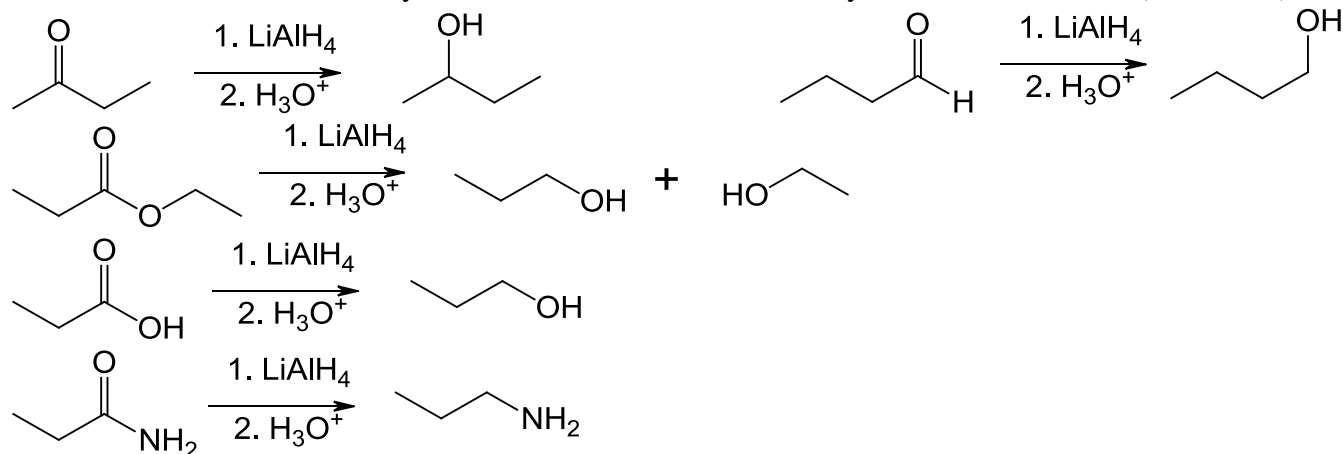
Grignard addition to acid halides, acid anhydrides, and esters

Hydride Reduction Rxns

NaBH₄ reduces ketones, aldehydes, and acid halides

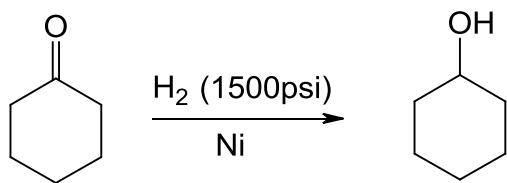
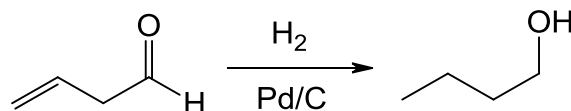
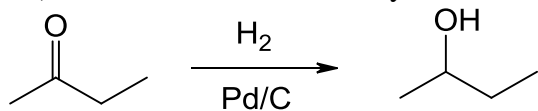


LiAlH₄ reduces ketones, aldehydes, acid chlorides, esters, carboxylic acids, and amides (and others)



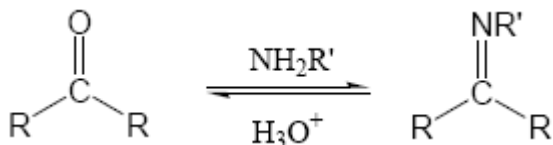
DIBALH reduces esters to aldehydes

H₂, Pd/C reduces alkenes, alkynes, and nitro groups



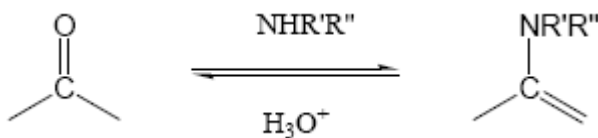
Formation of imines (Schiff bases) and imine derivatives

rxn with a 1° amine

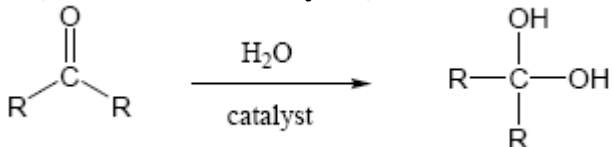


Formation of enamines

rxn with a 2° amine

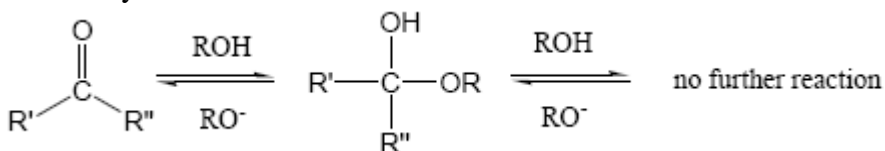


Hydration (Acid- or Base-catalyzed)



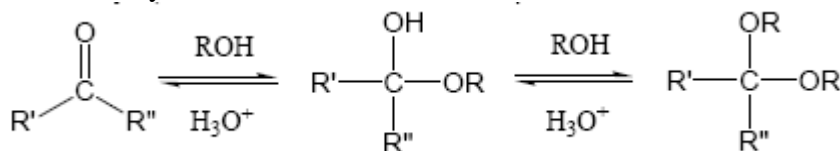
Addition of alcohols (formation of hemiacetals, acetals, hemiketals, and ketals) – acid- and base-catalyzed

Base-catalyzed



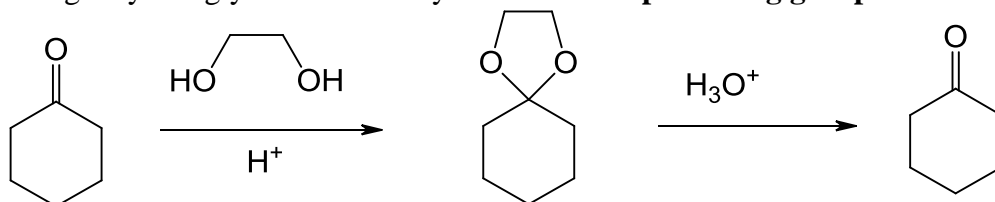
Forms hemiacetal

Acid-catalyzed



Forms acetal

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

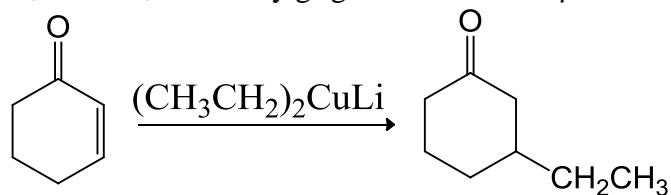


Addition to a Conjugated Carbonyl

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

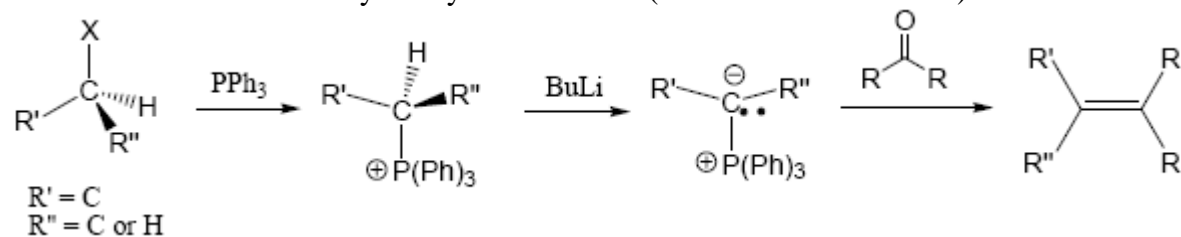
Grignards often result in both 1,2- and 1,4-addition

CN^- , OH^- , R_2CuLi , and bulky grignards add to the β 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 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° alcohols and aldehydes – $\text{Na}_2\text{Cr}_2\text{O}_7/\text{H}_2\text{SO}_4$

Cleavage of alkenes with KMnO_4 – conc. $\text{KMnO}_4/\text{heat}, \text{H}_3\text{O}^+$

Oxidation of alkylbenzenes to benzoic acids with KMnO_4 or chromic acid

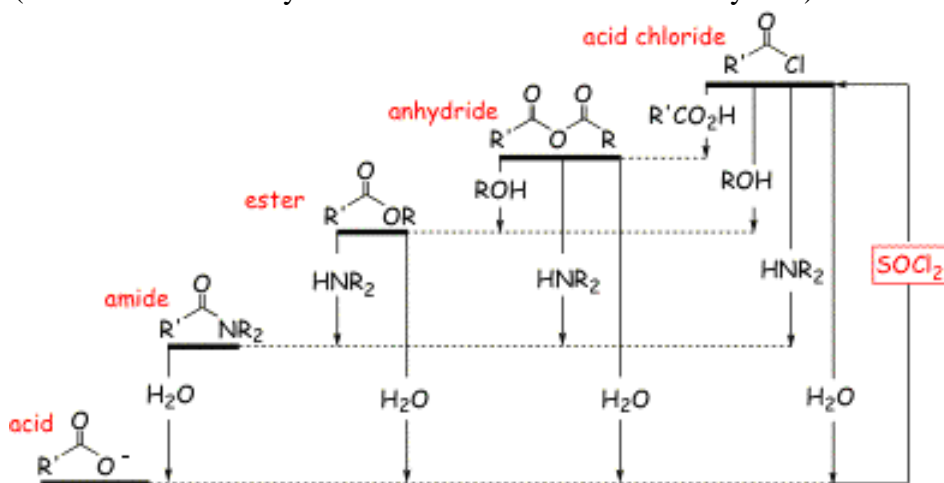
Carboxylic Acid Derivatives

Acid halides, anhydrides, esters, amides, and nitriles

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

Nucleophilic Acyl Substitution

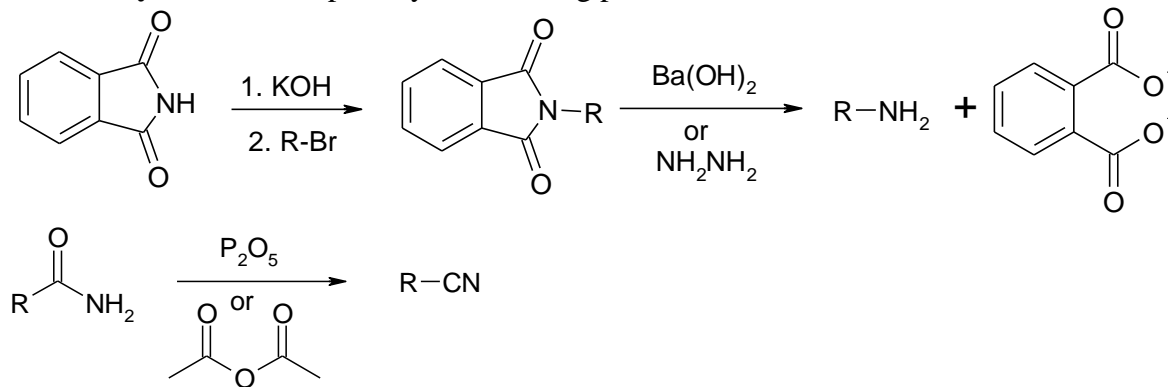
-Reactivity (acid chlorides > anhydrides > esters > amides > carboxylates)



• 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

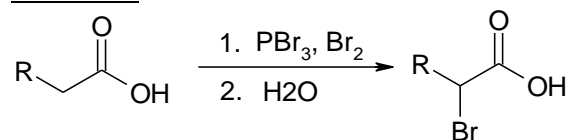
LDA (lithium diisopropyl amide) is a strong base used to form enolate ions

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° amine and α -alkylate followed by hydrolysis

Alkylation at Beta Carbon

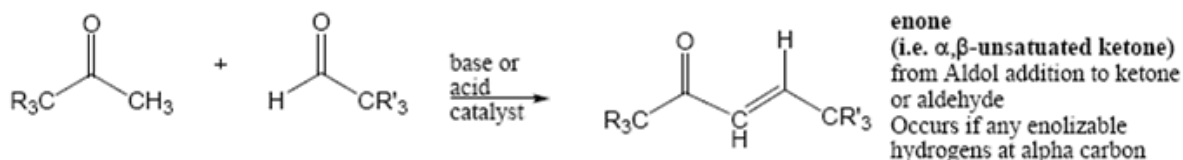
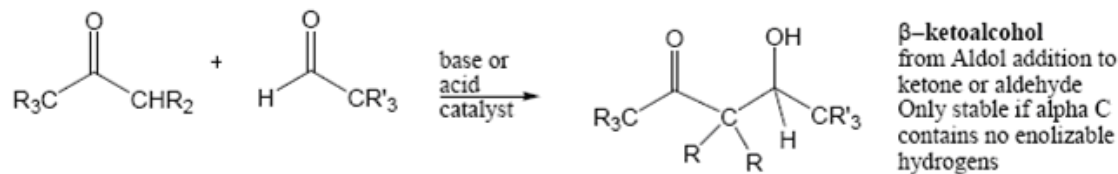
Michael addition – a 1,4-addition of a conjugated ketone

Michael donor is typically a stabilized enolate ion or R_2CuLi

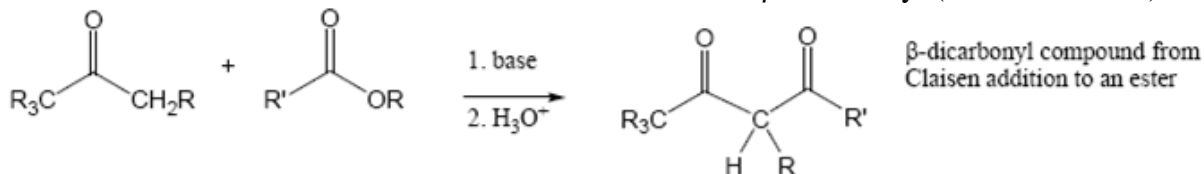
Acceptor is a conjugated carbonyl, cyano, or nitro group

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

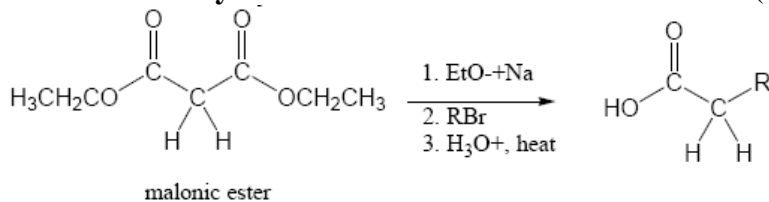
Base-catalyzed - **enolate** adds to a ketone or aldehyde



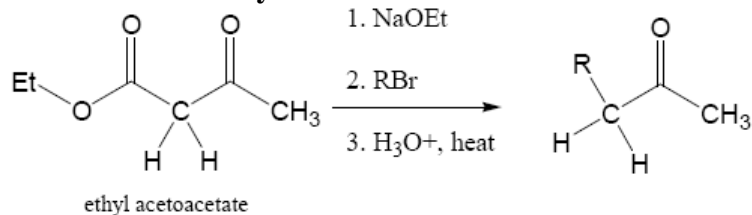
Claisen Condensation – enolate attacks an ester to form a β -dicarbonyl (self and crossed)



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)

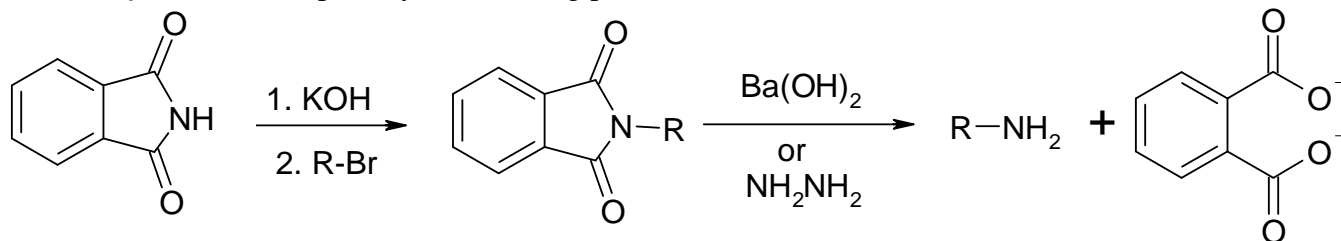
Organic Chemistry Chapter 19 – Amines

Nomenclature

Basicity

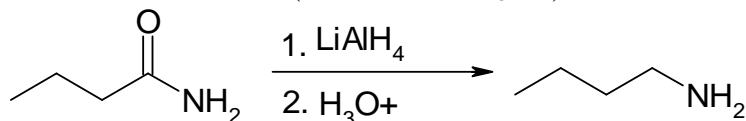
Synthesis

Gabriel Synthesis – template synthesis using phthalimide

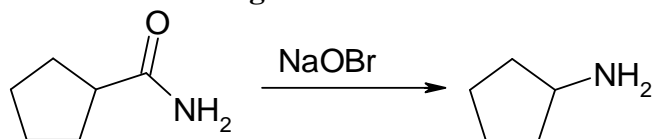


Reduction of nitro-compounds, azides, nitriles (H₂/Pd/C or LAH)

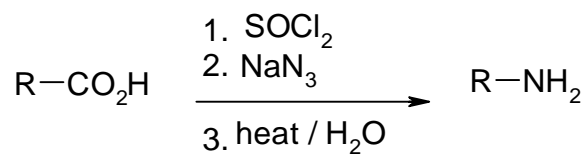
Reduction of Amides (1. LiAlH₄ 2. H₃O⁺)



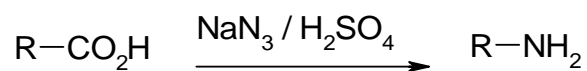
Hofmann Rearrangement



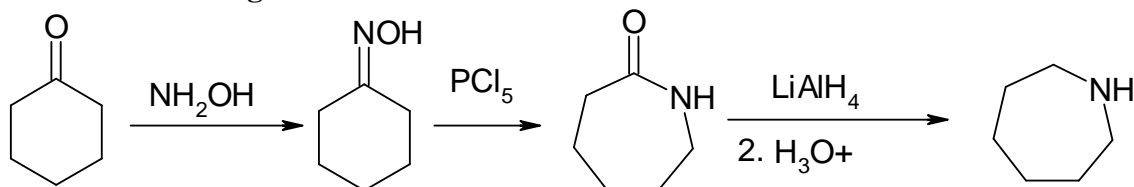
Curtius



Schmidt

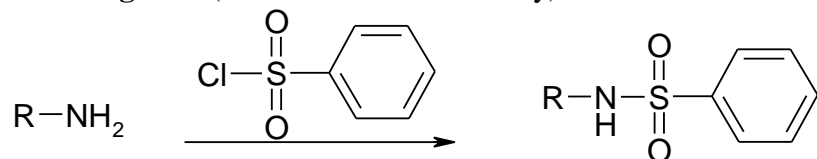


Beckman Rearrangement



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

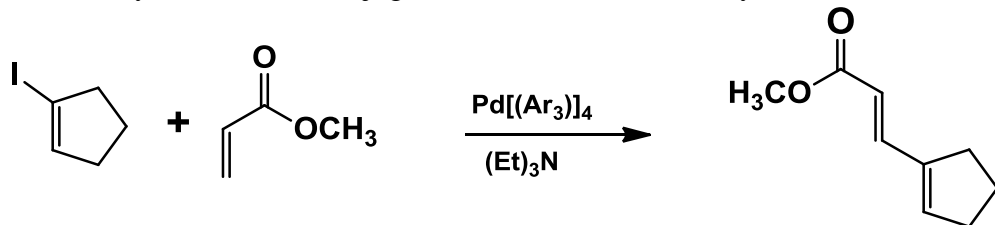
Phase Transfer Catalysis (with quaternary ammonium salts) TEBAC

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 Et_3N)



Suzuki

