O-Chem Day 1-Basics

Nomenclature

Nomenclature

1) Find the longest continuous carbon chain to determine base name.
2) Number the carbons, starting on the end closest to the first sutstituent.
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 no 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

Bonding and Geometry

Electron Domains	Hybridization	Bond Angle	Geometry
2	sp	180°	Linear
3	sp^2	120°	Trigonal planar
4	sp^3	109.5°	Tetrahedral

Sigma and Pi Bonds

Physical Properties of Hydrocarbons

Intermolecular Forces

1) Hydrogen Bonding – a super strong dipole-dipole force
   -must have hydrogen bonded to F, O, or N to H-bond as a pure liquid
   - only need F, O, N to hydrogen bond with protic compounds
2) Dipole-Dipole Forces – interaction between molecules having permanent dipole moments
   -the larger the dipole moment, the larger the force
3) London Dispersion Forces – weak interactions due to a transient (temporary) dipole
   -all molecules have these; the larger the molecule, the larger the force

Effects on melting pt and boiling pt

Branching (usually) decreases the boiling pt, but increases the melting pt

Solubility – Like dissolves like.

Ranking Boiling Points

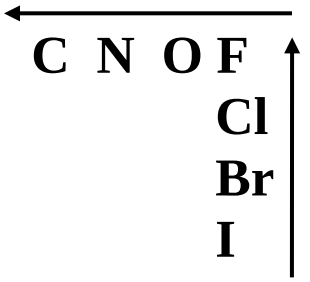
1) Network Covalent ($C_{diamond}$, SiO_2)
2) Ionic
3) Hydrogen Bonding
4) Dipole-Dipole
5) London Forces

Miscellaneous

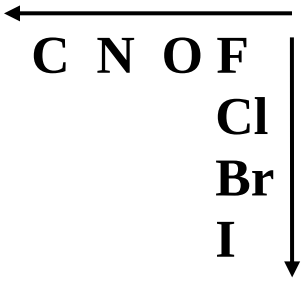
Nucleophiles and Electrophiles

Most strong nucleophiles have a negative charge (must have lone pairs of electrons)

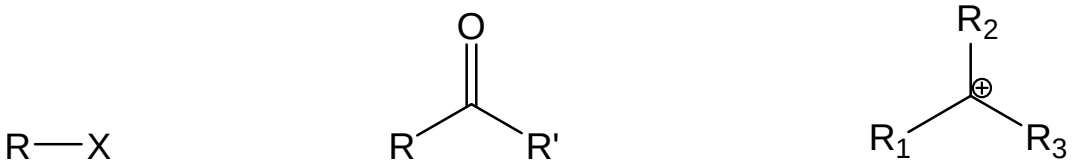
Nucleophile Strength in Aprotic Solvents



Nucleophile Strength in Protic Solvents



Common Electrophiles



Reaction intermediates (carbocations, radicals, carbanions)

Carbocation Stability	Radical Stability	Carbanion Stability
3° > 2° > 1° > Me	3° > 2° > 1° > Me	Me > 1° > 2° > 3°

Resonance Stabilization (electron delocalization)

Inductive Effects

Oxidation/Reduction Rxns (Identifying)

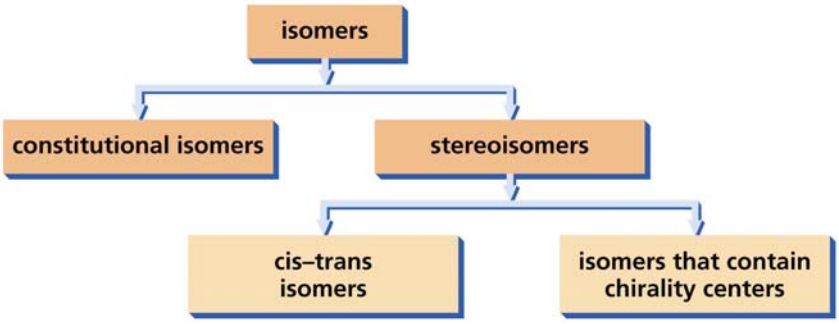
Degrees of Unsaturation (C_NH_{2N+2})

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: $sp > sp^2 > sp^3$

O-Chem Day 2 – Isomers, Newman Projections, Cycloalkanes, Substitution, Elimination

Isomerism



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.

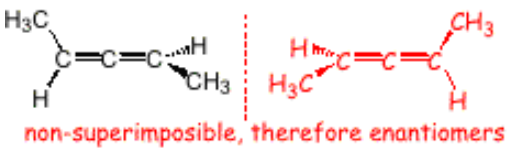
Chirality centers are tetrahedral centers with four different substituents (i.e. asymmetric centers).
R vs. S

Fischer projections

Multiple chiral centers
Diastereomers
Meso compounds (achiral but having chiral centers)

Amine inversion

Chiral molecules with no chiral centers

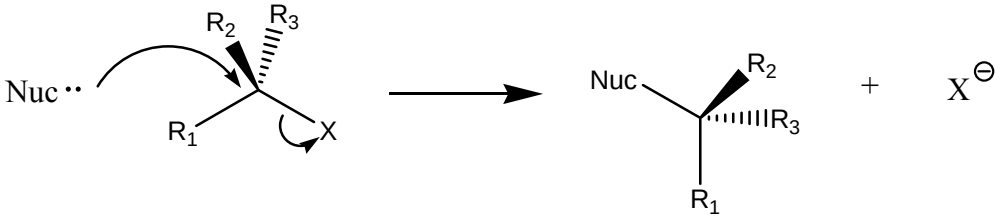


Newman Projections
Staggered, eclipsed, anti, gauche

Cycloalkanes
Ring strain
Chair Conformations of Cyclohexane
Equatorial positions are lower in energy (i.e. more stable) than axial positions due to 1,3-diaxial interactions

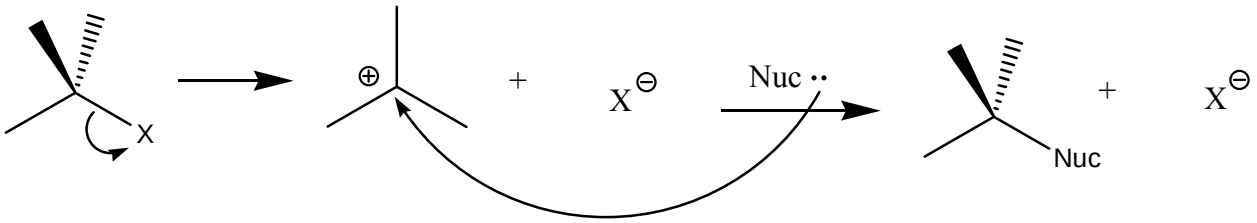
Substitution Reactions

S_N2 reactions – Substitution Nucleophilic Bimolecular Mechanism



rate = k[substrate][nucleophile]

S_N1 reactions – Substitution Nucleophilic Unimolecular Mechanism



Rate = k[substrate]

S_N2 vs. S_N1

	S_N2	**S_N1**
Electrophile	CH_3 > 1° > 2°	3° > 2°
Nucleophile	strong required	weak is ok
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, ethers

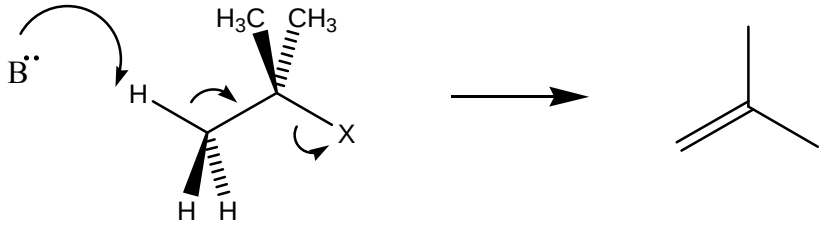
aryl and vinyl halides are unreactive (leaving group can't be on an sp^2 carbon)

nucleophile strength in aprotic and protic solvents

Elimination Reactions

E2 reactions – Elimination Bimolecular

Mechanism



rate = k[substrate][base]

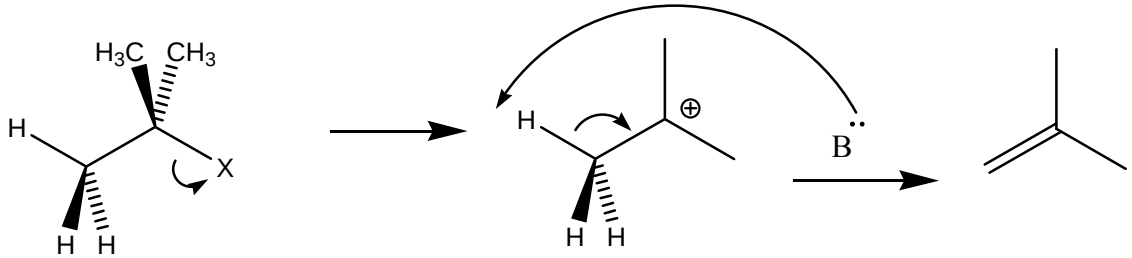
H and X (leaving group) should be anti-coplanar (anti-coplanar)

Forms most substituted double bond (Zaitsev's Rule)

Forms least substituted if substrate is 3° and if a bulky base is used like t-butoxide $(CH_3)_3CO^-$

E1 reactions – Elimination Unimolecular

Mechanism



Rate = k[substrate

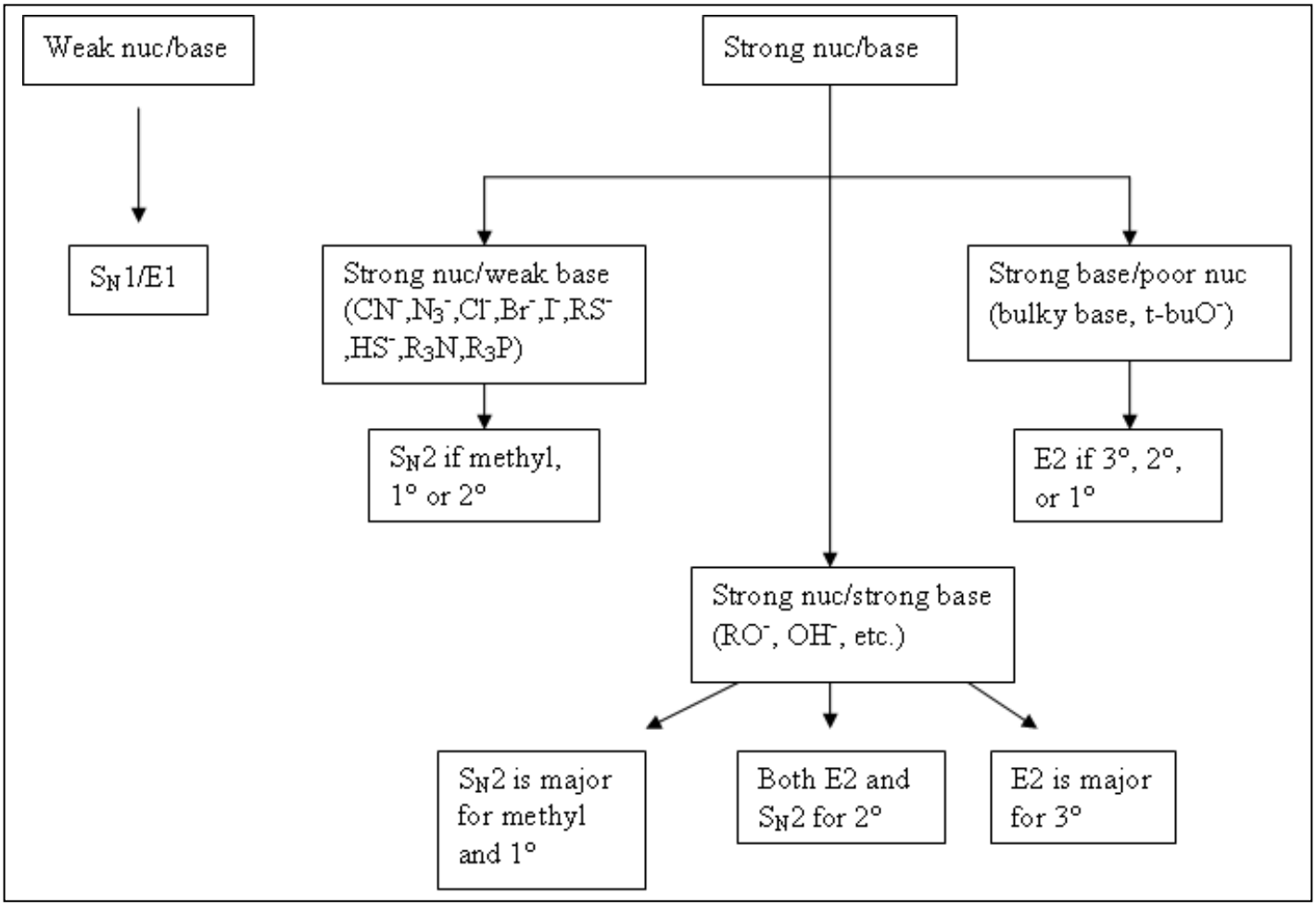
Forms most substituted double bond (Zaitsev's Rule)

E2 vs. E1

	E2	**E1**
Electrophile	3° > 2°>1°	3° > 2°
Base	strong base	weak base
Solvent	polar aprotic (preferred)	polar protic
Leaving Group	Good (I^->Br^->Cl^->F^-)	Good (I^->Br^->Cl^->F^-)
Rearrangements	Not possible	Possible
Stereochemistry	Anti-coplanar	None

	S_N2	**E2**	**S_N1**	**E1**
Electrophile	CH_3 > 1° > 2°	3° > 2°>1°	3° > 2°	3° > 2°
Nucleophile/Base	strong nuc	strong base	weak nuc	weak base
Solvent	polar aprotic	polar aprotic	polar protic	polar protic
Leaving Group	good	good	good	good

Substitution/Elimination Map



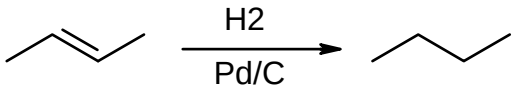
O-Chem Day 3: Alkene/Alkyne Rxns, Halogenation and EAS

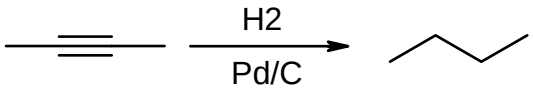
Electrophilic Addition Reactions

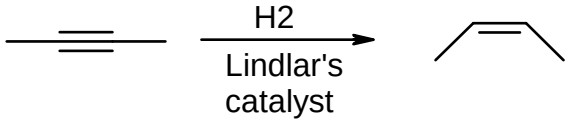
Reagents	What's added	Regioselectivity	Stereoselectivity	Intermediate	Rearrangements
HBr (or HCl, HI)	H^+ and Br^-	Markovnikov	-	carbocation	Possible
H_3O^+	H^+ and OH^-	Markovnikov	-	carbocation	Possible
H^+, ROH	H^+ and OR^-	Markovnikov	-	carbocation	Possible
Br_2/CCl_4 (or Cl_2)	Br^+ and Br^-	-	Anti	bromonium ion	Not possible
Br_2/H_2O Cl_2/H_2O	Br^+ and OH^- Cl^+ and OH^-	Markovnikov	Anti	bromonium ion	Not possible
Br_2/ROH Cl_2/ROH	Br^+ and OR^- Cl^+ and OR^-	Markovnikov	Anti	bromonium ion	Not possible
(1) $Hg(OAc)_2$, H_2O (2) $NaBH_4$	H^+ and OH^-	Markovnikov	Anti	mercurinium ion	Not possible
(1) $Hg(OAc)_2$, ROH (2) $NaBH_4$	H^+ and OR^-	Markovnikov	Anti	mercurinium ion	Not possible
(1) BH_3·THF (2) H_2O_2, OH^-, H_2O	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)	$H^\cdot$ and $Br^\cdot$	Anti-Markovnikov	-	radical	Not possible
(1) RCO_3H (2) H_3O^+	OH and OH	-	Anti		Not possible
(1) OsO_4 (2) H_2O_2	OH and OH	-	Syn		Not possible
$KMnO_4$ (cold, dilute)/ OH^-	OH and OH	-	Syn		Not possible

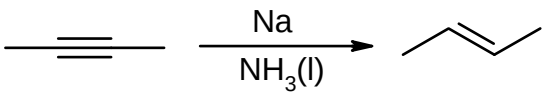
Alkynes

Reduction (Addition of Hydrogen)

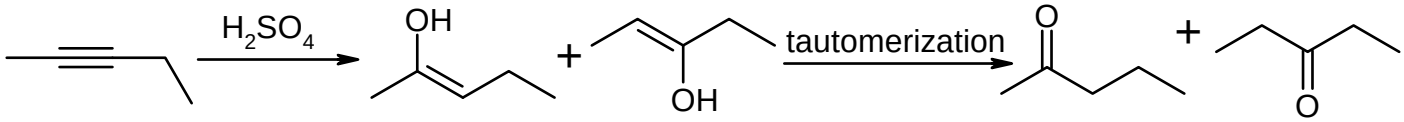




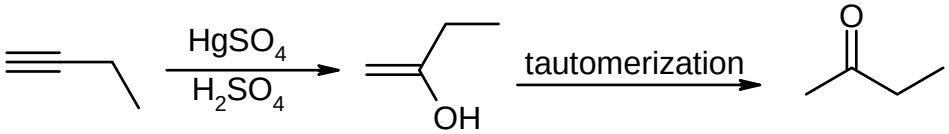




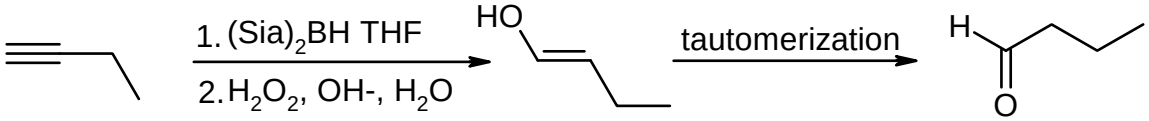
Addition of H_2O



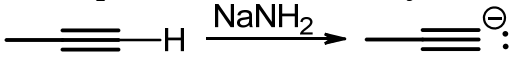
Terminal alkynes require $HgSO_4$ as a catalyst (Markovnikov)



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



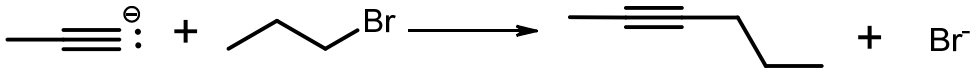
Nucleophilic Addition of Acetylide Ions



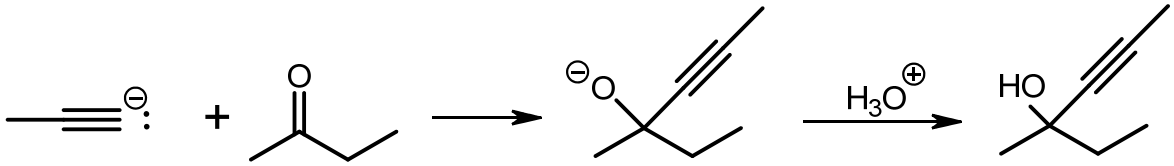
(A strong nucleophile)

An acetylide ion attacks 3 typical electrophiles:

1) an alkyl halide



2) a carbonyl (C=O)

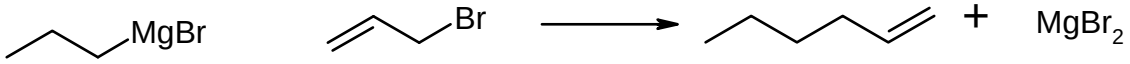


3) an epoxide (adds to least substituted side)

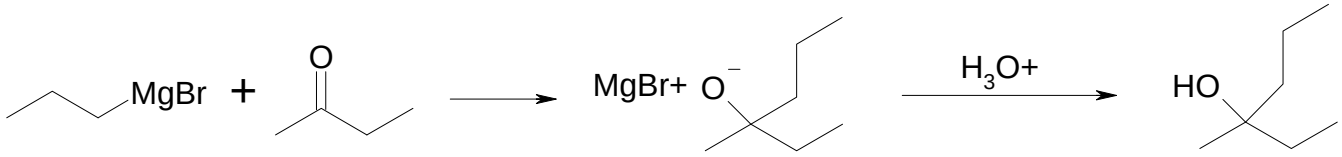
<u>Organometallic Reactions</u>

Formed by combining an alkyl halide with Li or Mg

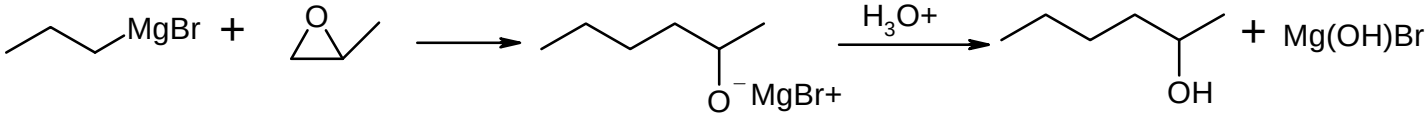
1) an allylic or benzylic halide



2) a carbonyl (C=O)



3) an epoxide (adds to the least substituted side)



<u>Oxidative Cleavage of Alkenes</u>

<u>Reducing conditions</u>

B. (1) O_3, -78°C (2) Zn/H_2O or $(CH_3)_2S$

<u>Oxidizing conditions</u>

A. $KMnO_4$ (hot, concentrated)/OH^- (or with H_3O^+)

B. (1) O_3 (2) H_2O_2

Free Radical Halogenation

1) Initiation
2) Propagation
3) Termination

Selectivity and stability of radicals (chlorination vs. bromination)

Criteria for Aromatic Compounds

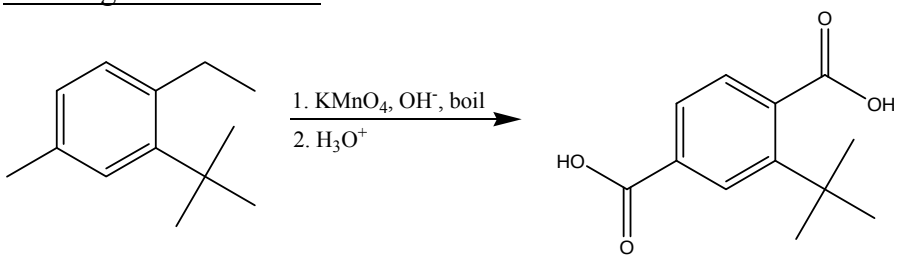
1) cyclic and containing conjugated pi bonds
2) each atom in the ring must have an unhybridized p orbital
3) planar structure
4) delocalization of the pi electrons must lower the electronic energy (4N+2 π electrons)

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

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

Side-Chain Reactions of Benzenes

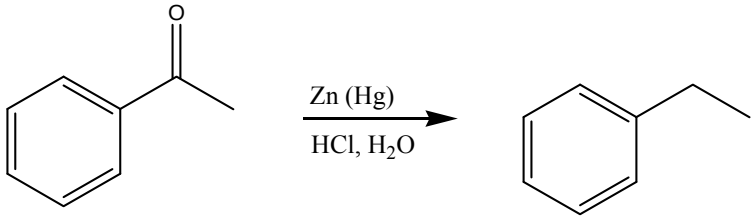
Permanganate Oxidation



Chromic acid ($Na_2Cr_2O_7$ / H_2SO_4) achieves the same reaction

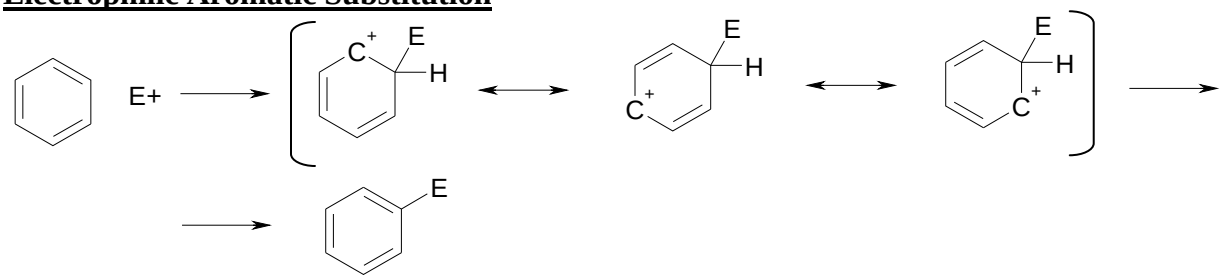
Side-chain Reduction

Clemmenson Reduction – reduces ketones and aldehydes to alkanes

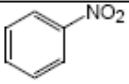
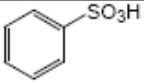
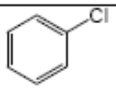
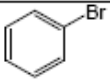
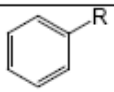
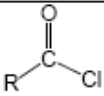
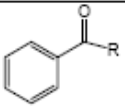


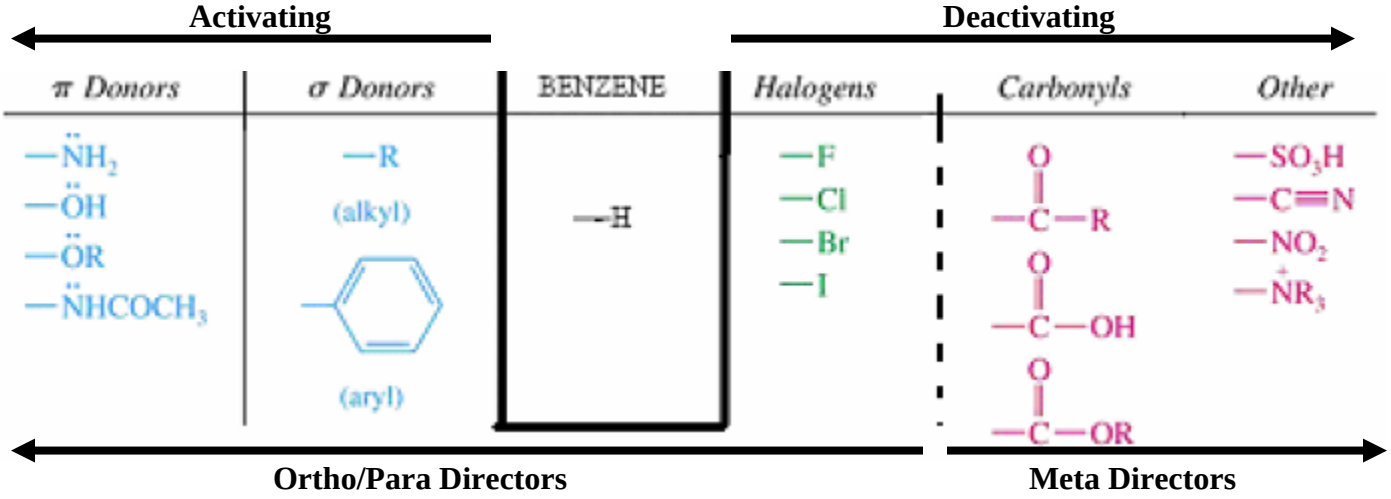
Wolff Kishner Reduction does the same thing with H_2NNH_2, OH^-, heat

Electrophilic Aromatic Substitution



Summary of suitable EAS electrophiles, reagents, and reactions

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^+	Cl_2	$AlCl_3$		Chlorination
	Br^+	Br_2	$FeCl_3$		Bromination
	I^+	I_2	HNO_3		Iodination
	R^+	RX or R-OH or RX	$AlCl_3$ or $FeBr_3$ BF_3 $AgNO_3$		Friedel –Craft Alkylation Or alkylation
	$O{=}C^+R$		$AlCl_3$		Friedel-Craft Acylation



O-Chem Day 4: Alcohols, Nucleophilic Addition, Nucleophilic Acyl Substitution and Alpha Addition

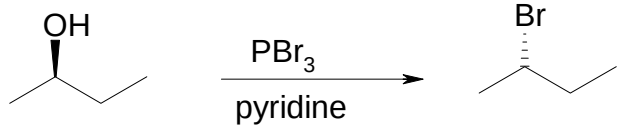
Alcohols

Acidity of Phenols

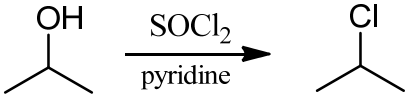
Rxn with H-X (HBr or $HCl/ZnCl_2$)

S_N1 for 2° and 3° alcohols; S_N2 for methanol 1° alcohols

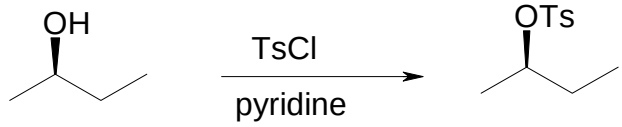
Rxn with PBr_3 (for 1° and 2° alcohols)



Rxn with $SOCl_2$ (for 1° and 2° alcohols)

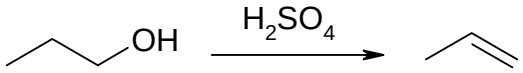


Conversion to Sulfonate Esters



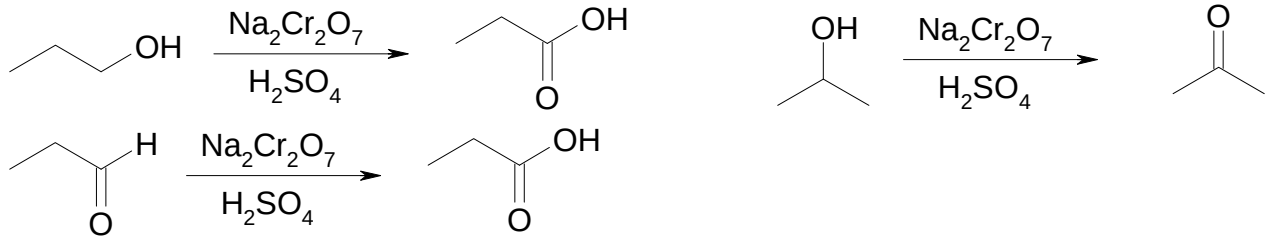
Good leaving group!

Dehydration with H_2SO_4 (or H_3PO_4)



Oxidation

$Na_2Cr_2O_7/H_2SO_4$ oxidizes 1° alcohols to carboxylic acids, 2° alcohols to ketones, and aldehydes to acids



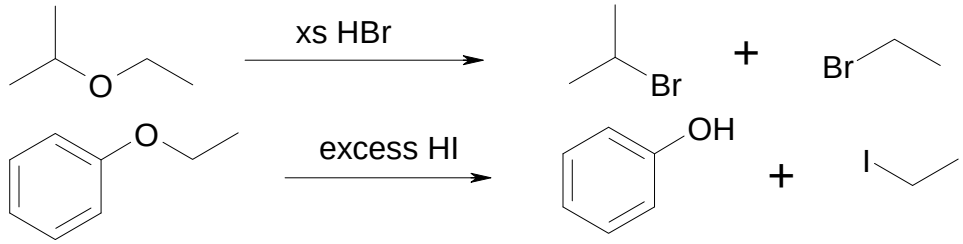
PCC oxidizes 1° alcohols to aldehydes and 2° alcohols to ketones

Ethers

Synthesis via Substitution (S_N2 or S_N1)

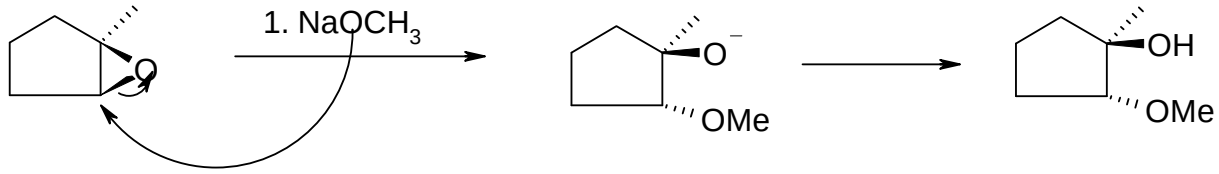
Williamson Ether Synthesis (S_N2)

Rxn with H-X

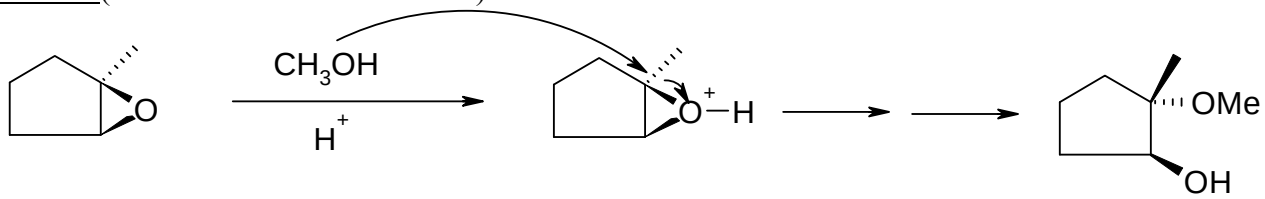


Ring Opening of Epoxides (In Acid or Base)

In Base (Attack less substituted side)



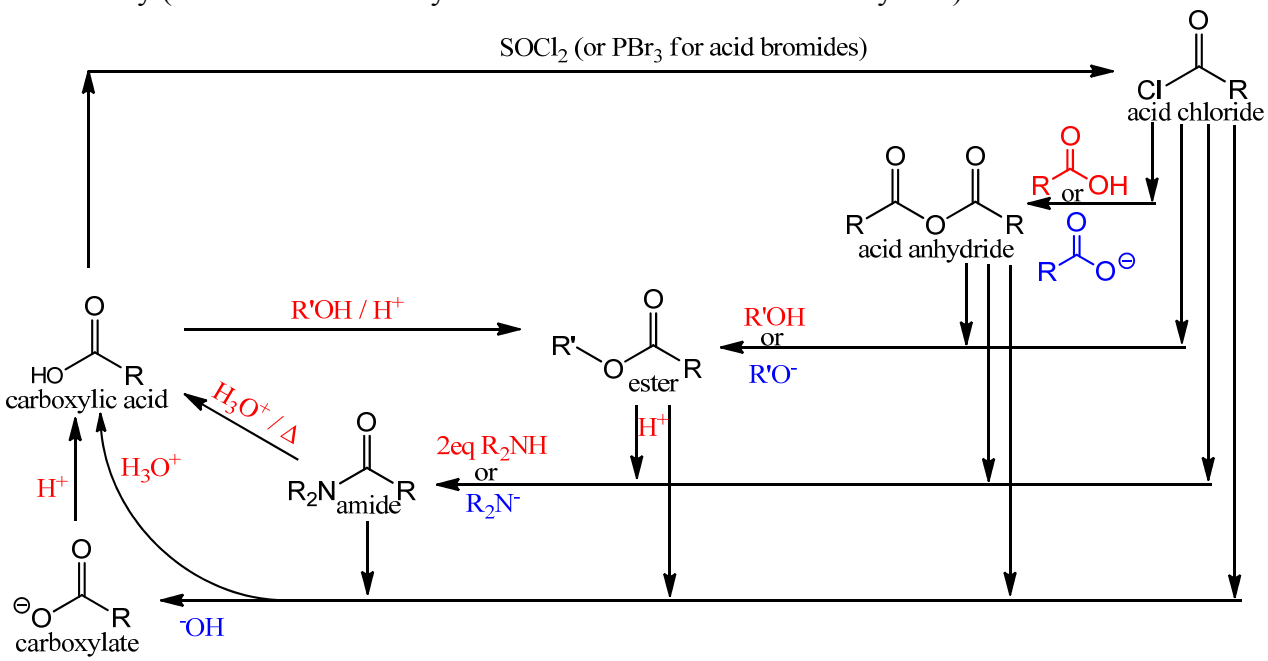
In Acid (Attack more substituted side)



Carboxylic Acids and Derivatives

Nucleophilic Acyl Substitution

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



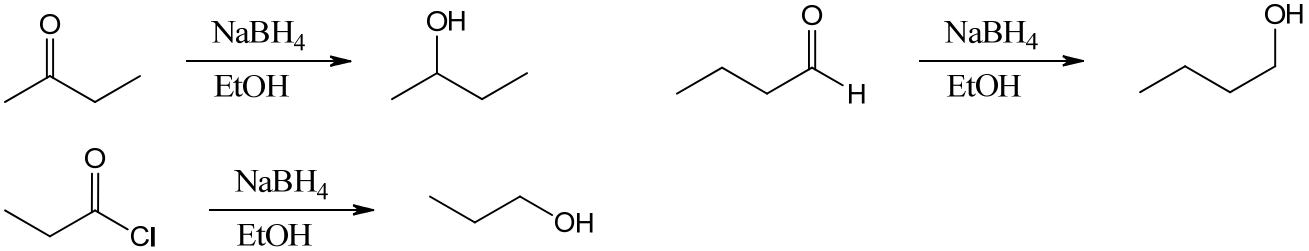
Fischer Esterification

Saponification

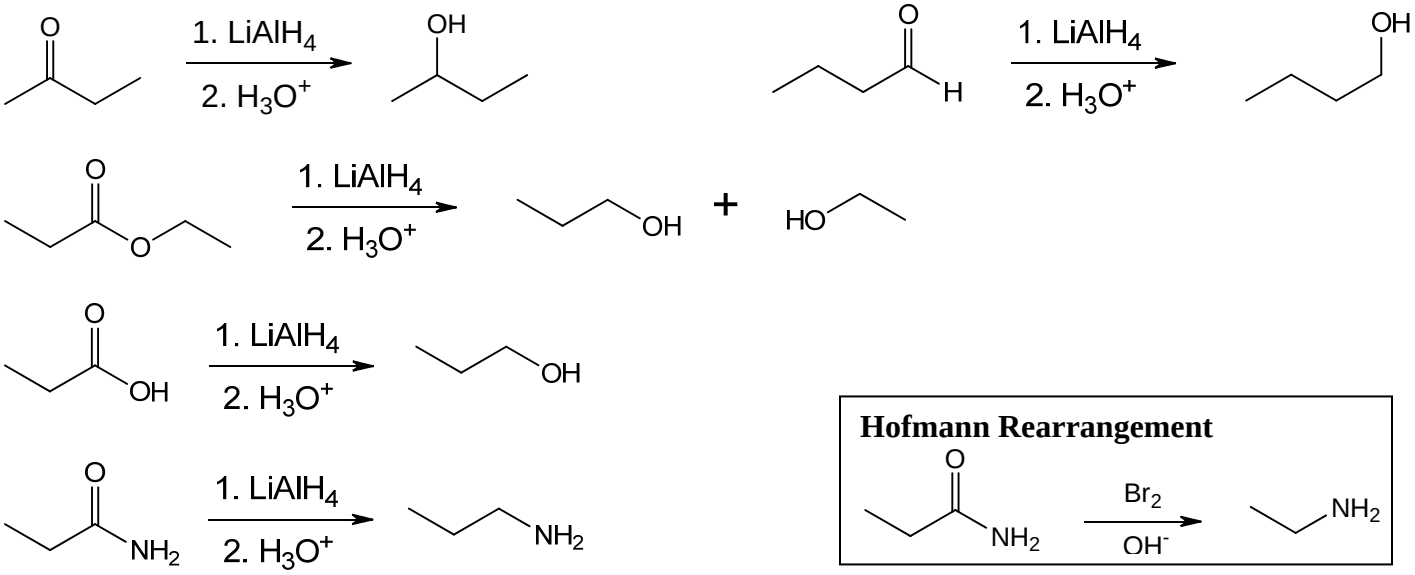
Cycloadditions (Diels-Alder Rxns)

Reduction Rxns

$NaBH_4$ reduces ketones, aldehydes, and acid halides



$LiAlH_4$ reduces ketones, aldehydes, acid chlorides, esters, carboxylic acids, and amides (and others)



Hofmann Rearrangement

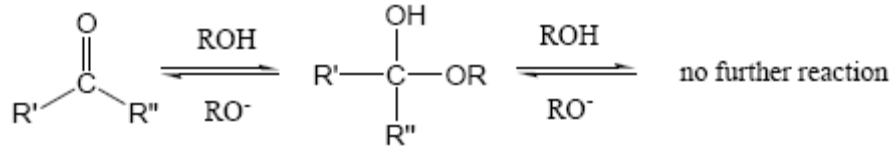
Aldehydes and Ketones

Nucleophilic Addition (Carbonyls as electrophiles)
Alpha Addition (Carbonyls as nucleophiles (enolates and enols))
    Acidity of α-hydrogens
Keto/enol tautomerism

Reactions of Ketones and Aldehydes

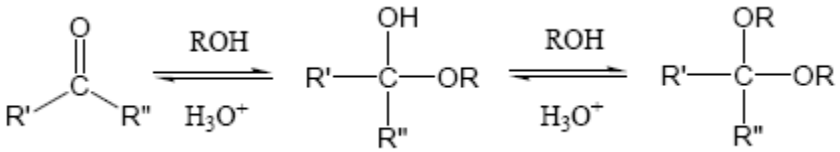
Addition of alcohols (formation of hemiacetals, acetals, hemiketals, and ketals) – acid- and base-catalyzed

Base-catalyzed



Forms hemiacetal/hemiketal

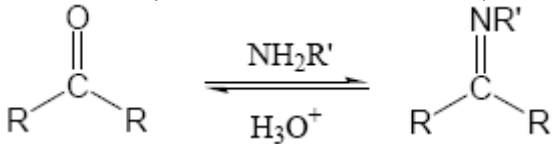
Acid –catalyzed



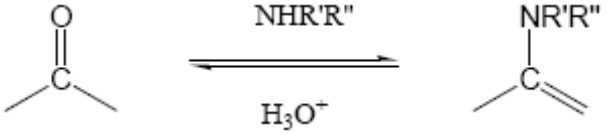
Forms acetal/ketal

Protecting Groups with ethylene glycol

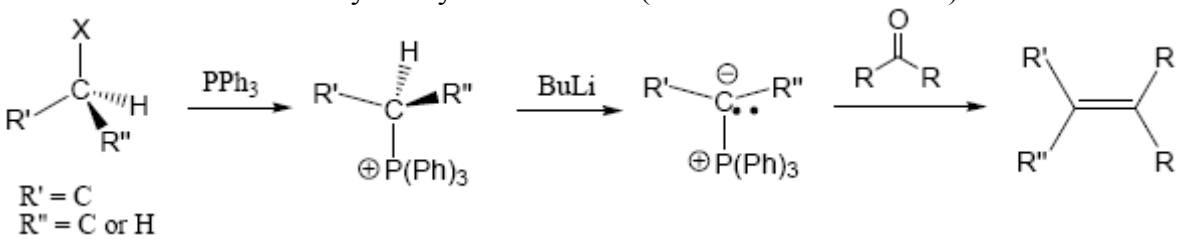
Formation of imines (Schiff bases) and imine derivatives (rxn with a 1° amine)



Formation of enamines (rxn with a 2° amine)



Wittig Rxn – $P(Ph)_3$ + R-X + BuLi gives a phosphorous ylide
-ylide reacts with a ketone or aldehyde to yield an alkene (C=O converted to C=C)



R' = C
R" = C or H

Michael Rxn (Alkylation at Beta Carbon)

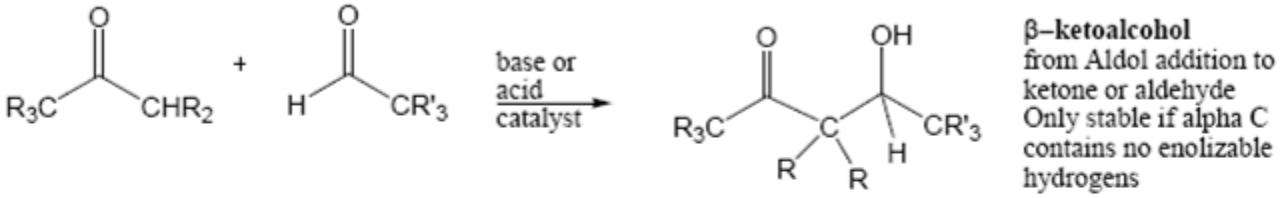
Michael addition – a 1,4-addition of a conjugated ketone

Michael donor is typically a stabilized enolate ion or R_2CuLi

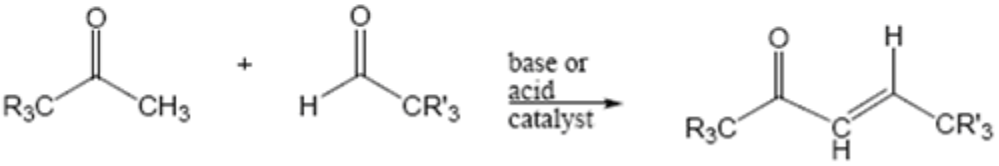
Acceptor is typically a conjugated carbonyl

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

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

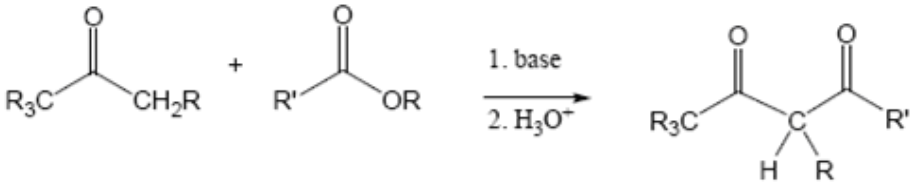


β–ketoalcohol
from Aldol addition to ketone or aldehyde
Only stable if alpha C contains no enolizable hydrogens



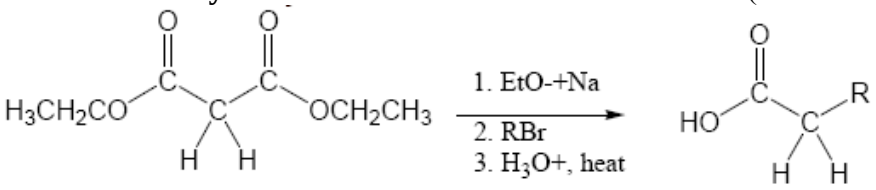
enone
(i.e. α,β-unsatuated ketone)
from Aldol addition to ketone or aldehyde
Occurs if any enolizable hydrogens at alpha carbon

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



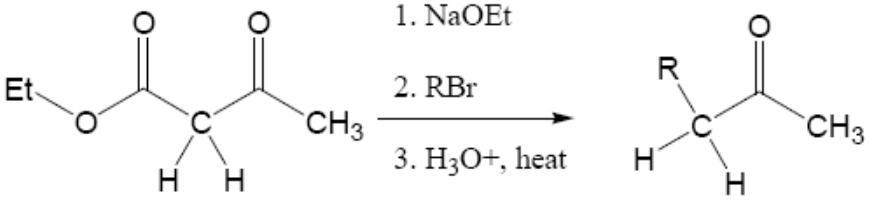
β-dicarbonyl compound from Claisen addition to an ester

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



malonic ester

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



ethyl acetoacetate

O-Chem Day 5: Lab Techniques and Spectroscopy

Lab Techniques
Melting Pt Determination

Extractions

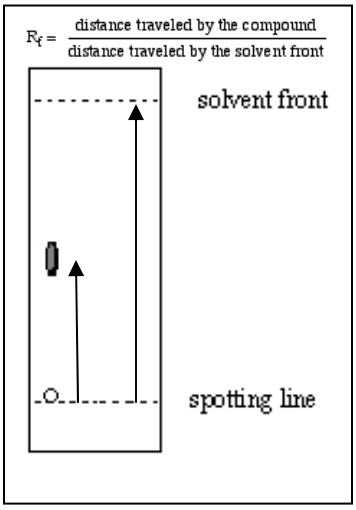
1. Aqueous Extractions

2. Acid/Base Extractions
   a) Amines removed by HCl
   b) Carboxylic acids removed by $NaHCO_3$ or NaOH
   c) Phenols removed by NaOH

Crystallization
Purification (separation) due to a difference in solubility
Solute has a higher solubility at high temps but lower solubility at low temps

Chromatography

1. TLC (thin layer chromatography)
   Separation due to difference in polarity
   More polar solutes have a lower R_f value
   Less polar solutes have a higher R_f value



2. GC (gas chromatography)
   Separation due to difference in boiling point
   The compound with a lower boiling pt is eluted first
   Areas under peaks gives relative abundances

Distillation

1. Simple distillation
   Liquids with lower boiling pts are distilled before liquids with higher boiling pts

2. Fractional distillation
   Equivalent to many simple distillations

Spectroscopy/Spectrometry

Mass Spectometry

Base Peak and Parent Peak

IR (infra-red)

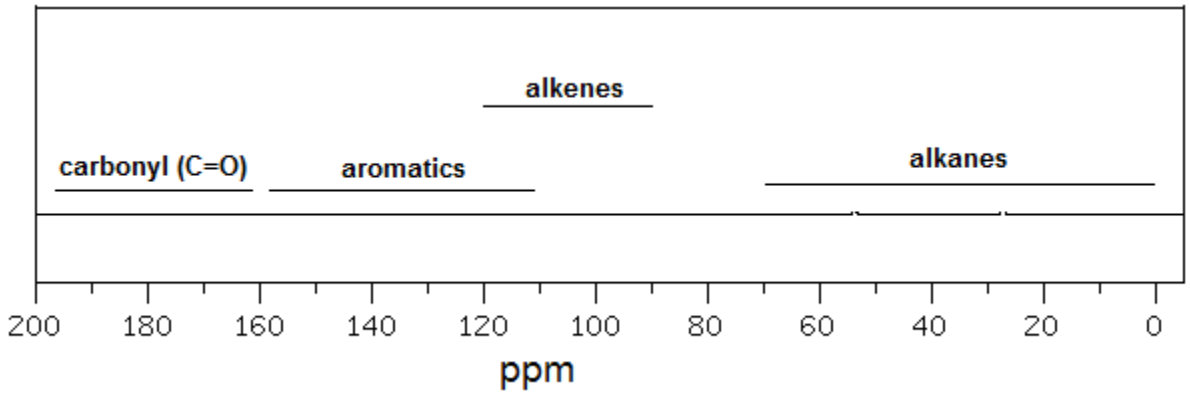
Infra-red light results in the stretching and/or bending of bonds

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)

^{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)



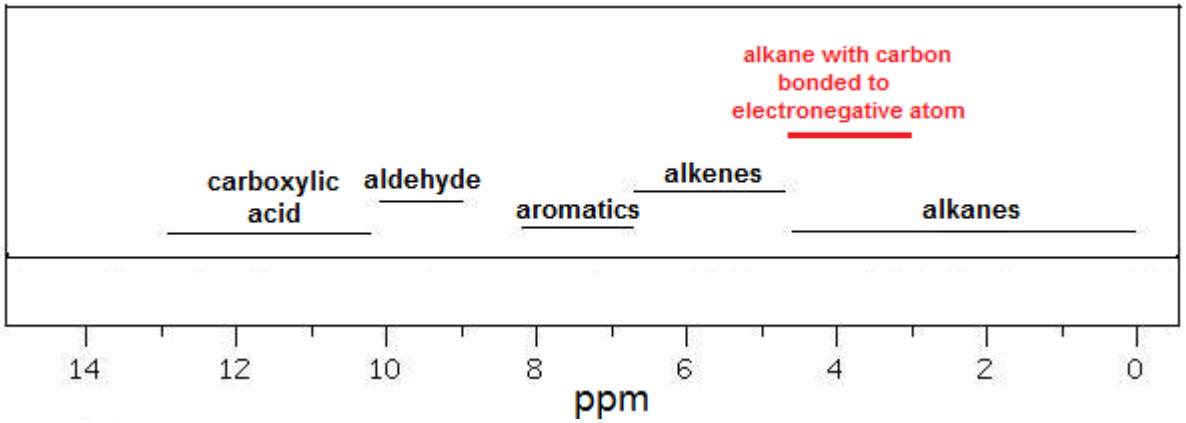
^{1}H NMR

Gives the number of hydrogen environments in a molecule

1) Chemical shift tells whether the hydrogen is an alkane, alkene, aromatic, aldehyde, or carboxylic acid

2) Integration or area under the signal tells how many hydrogens a signal represents (or at least the ratio)

3) Splitting **# of peaks = n + 1** where n = # of neighbors



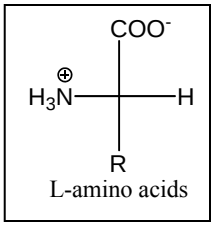
Fast Proton Transfer (Proton Exchange) – H bonded to O or N can be exchanged with protic solvents (like D_2O)

O-Chem Day 6: Proteins, Carbohydrates, Lipids, Nucleic Acids

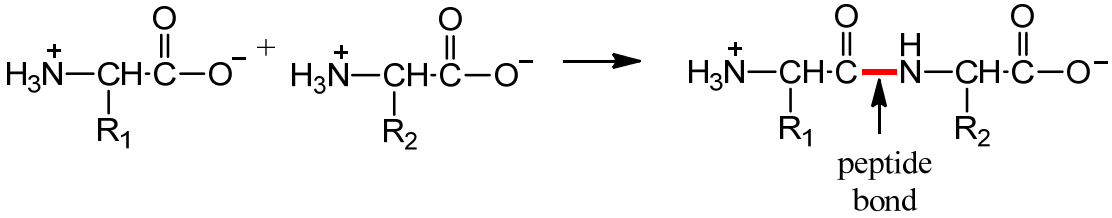
Proteins

Amino Acids

D vs. L-amino acids



Essential amino acids can't be synthesized by an organism and so must be part of the dietary intake.

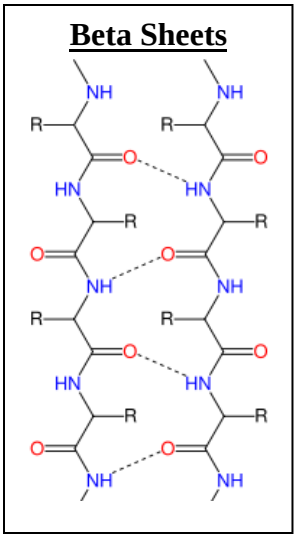


Polar (hydrophilic) vs Non-polar (hydrophobic) side chains
Acidic vs. Basic
Proline puts kinks into the peptide structure
pKas and pI

Primary Structure

Amino Acid Sequence

Secondary Structure (Held together by H-bonding in the backbone)
Alpha-helix
Beta-sheet



Tertiary Structure

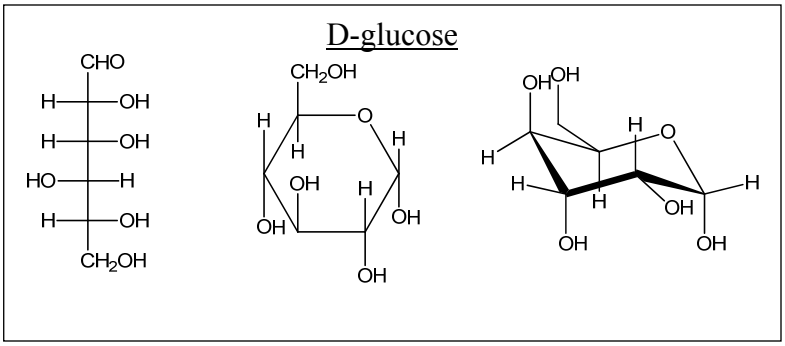
Organization of secondary structures
In globular proteins, hydrophobic residues are sequestered in the interior of the protein while hydrophobic residues are on the outer surface.
Disulfide bridges between cysteine residues

Quaternary Structure

Interaction of multiple subunits (separate peptide chains) as in hemoglobin

Carbohydrates

Monosaccharides – glucose, fructose, galactose,
Oligosaccharides – sucrose (glucose and fructose) and lactose (glucose and galactose) are disaccharides
Polysaccharides – starch, glycogen, cellulose, chitin, etc.

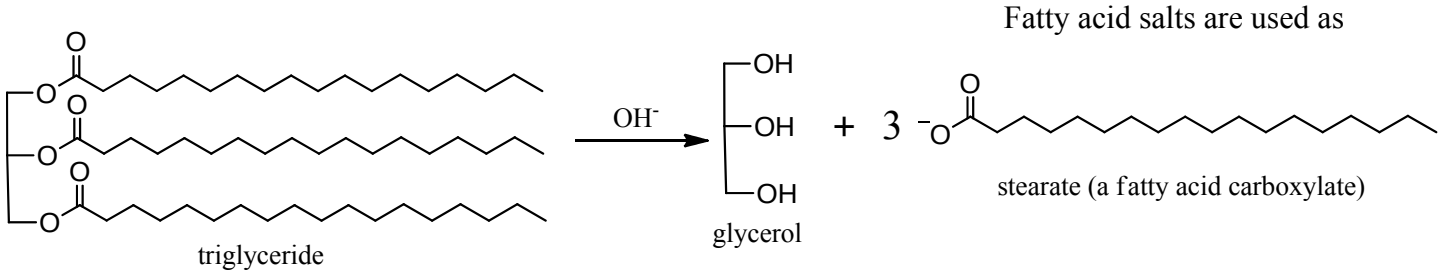


D vs. L-sugars
Aldose vs. Ketose
Pentose vs. Hexose
Furanose vs Pyranose
Acetals (ketals) and Hemi-acetals (hemi-ketals)
Anomeric carbon and alpha (down) vs. beta (up)

Reducing sugars (Benedict's Test)
All open chain aldoses and most ketoses and hemi-acetals/hemi-ketals are reducing
All acetals/ketals are non-reducing sugars

Lipids

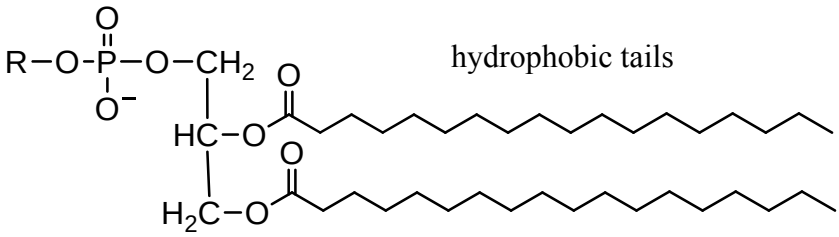
Triacylglycerols (triglycerides)



Phospholipids

Lipid Bilayer

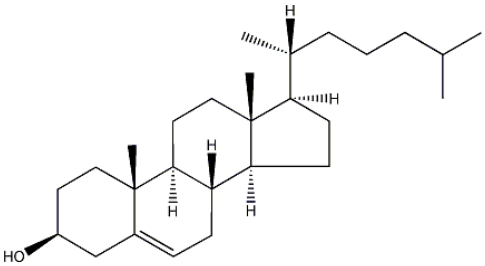
hydrophilic head



Cholesterol

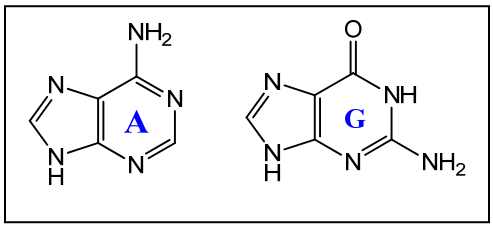
Membrane fluidity

Steroid precursor

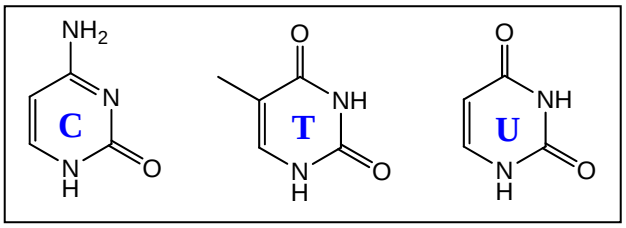


Nucleic Acids

Purines (**A**denine and **G**uanosine)



Pyrimidines (**C**ytidine, **T**hymidine, **U**racil)



ATP hydrolysis and pyrophosphate hydrolysis