ORGANIC CHEMISTRY "CRACK" MASTER NOTES

Biological Molecules

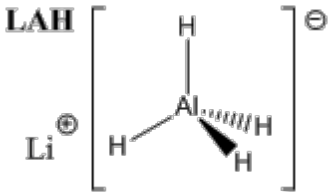
The Covalent Bond

sigma and pi bonds

- ... sigma and pi bonds is a repeat of general chemistry bonding
- hybrid orbitals (sp^3, sp^2, sp and respective geometries)
    - ... hybrid orbitals is a repeat of general chemistry bonding
- valence shell electron pair repulsion (VSEPR) theory, prediction of shapes of molecules (e.g., NH_3, H_2O, CO_2)
    - ... VSEPR is a repeat of general chemistry bonding
- structural formulas for molecules involving H, C, N, O, F, S, P, Si, Cl
    -

	# valence e^-	Usual # bonds	Typically found in
H	1	1	Hydrocarbon (alkane, alkene, alkyne), hydride. All organic compounds contain hydrogen.
C	4	4	Alkane, alkene, alkyne, aromatic rings. All organic compounds contain carbon.
N	5	3	Amine, amide, imine, hydrazone, oxime, nitro compound, diazo compound, nitrile/cyanide, azide
O	6	2	Alcohol, ether, aldehyde, ketone, carboxylic acid, acyl halide, anhydride, amide, ester, ozone
F	7	1	Fluoride
S	6	2 or 6	Thiol, sulfide, sulfate, sulfite
P	5	3 or 5	Phosphorous compound, phosphate, phosphite
Si	4	4	Silane, silicon dioxide
Cl	7	1	Chloride, hypochlorite, chlorite, chlorate, perchlorate

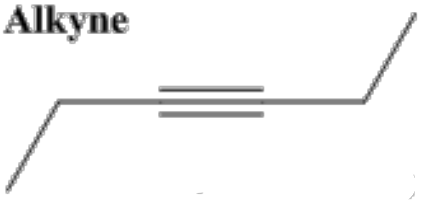
    - H and C



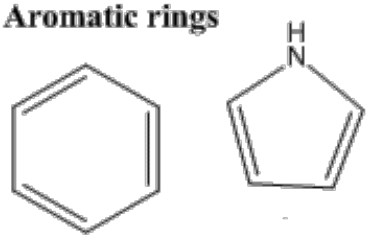
Alkane

Alkene

Alkyne

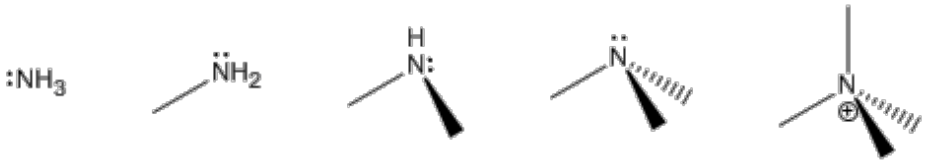


Aromatic rings



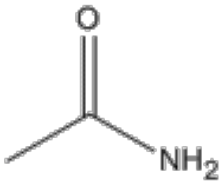
- N

Amines

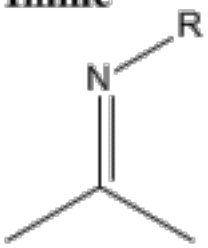


Ammonia Primary Secondary Tertiary Quaternary

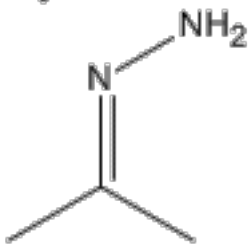
Amide



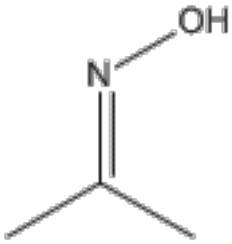
Imine



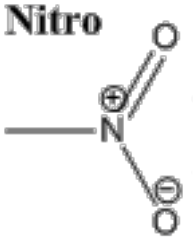
Hydrazone



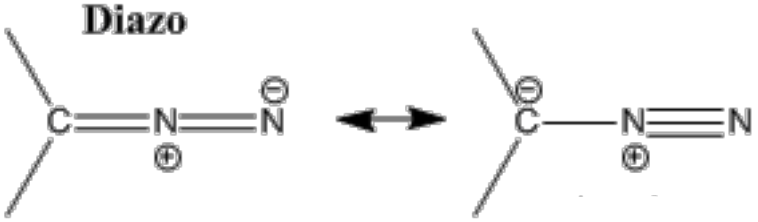
Oxime



Nitro

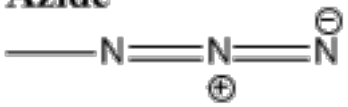


Diazo

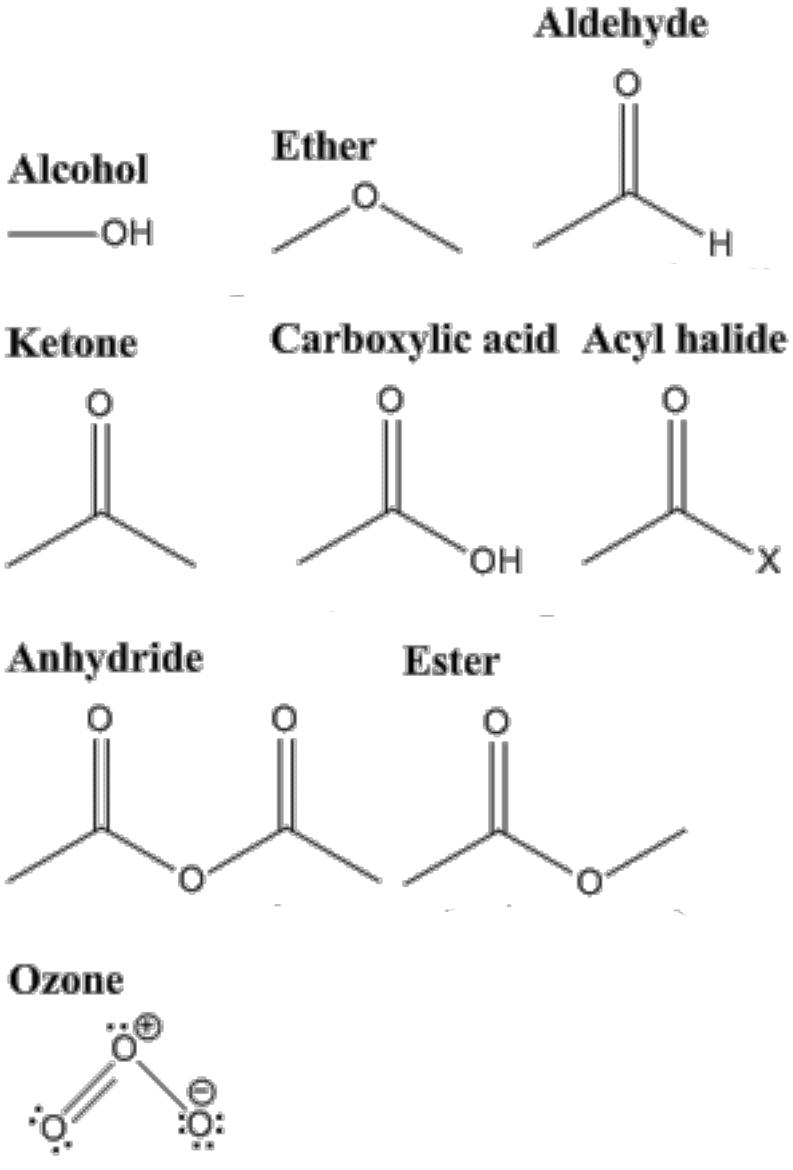


Nitrile / Cyanide

Azide



- O



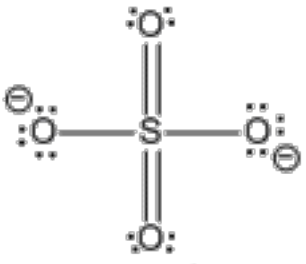
- F

Fluoride

——F

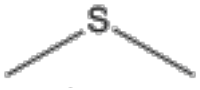
- S

Sulfate

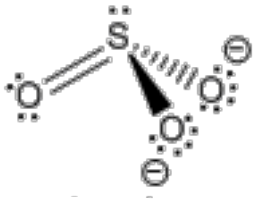


Thiol

Sulfide

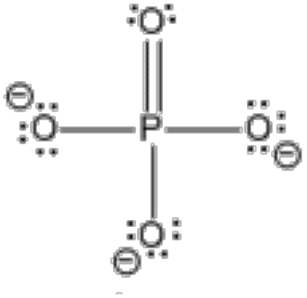


Sulfite



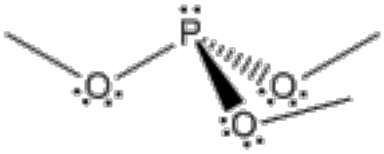
- P

Phosphate

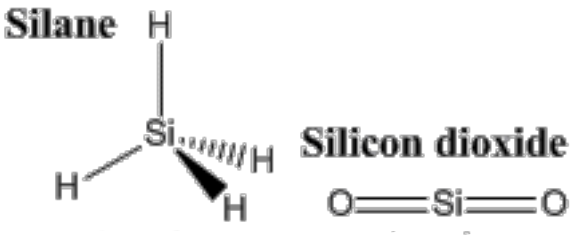


PBr_3

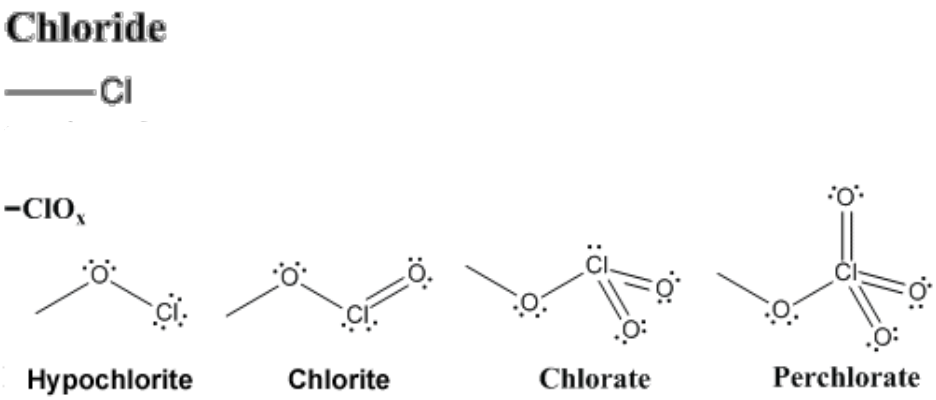
Phosphite



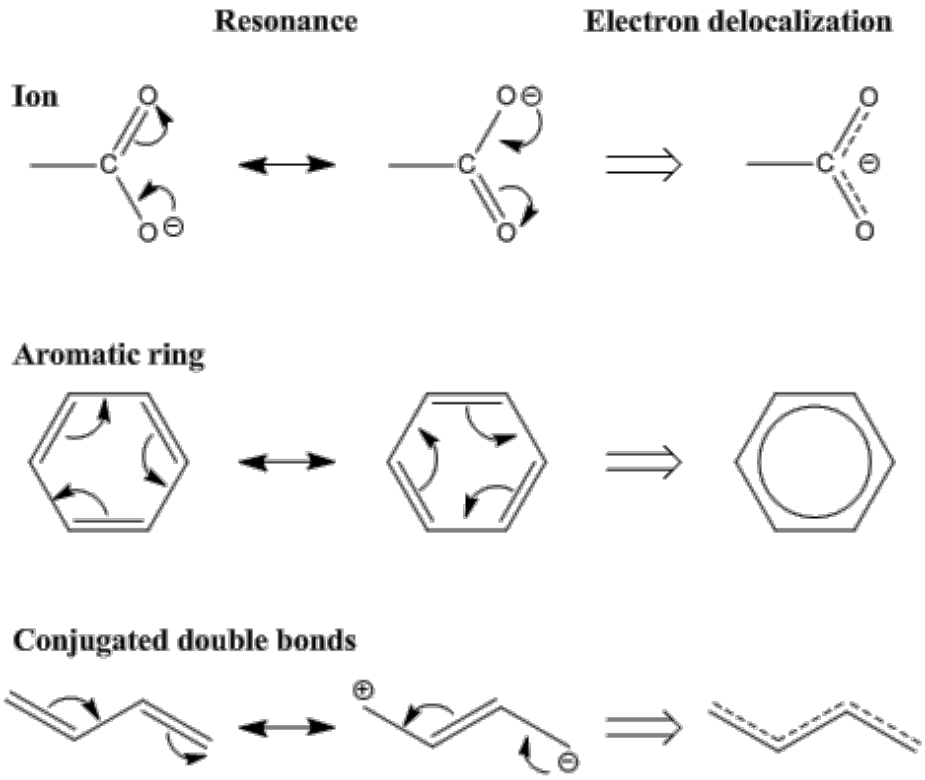
- Si



- Cl



- delocalized electrons and resonance in ions and molecules



-
    - Resonance structures result from electrons not being fixed in position (that's why you "push" electrons when drawing resonance structures).
    - When electrons are not fixed in position, they are delocalized electrons.
    - For all practical purposes, resonance and electron delocalization mean the same thing.
    - In ions, resonance and electron delocalization occurs to "distribute" the charge around.
    - In molecules, resonance and electron delocalization occurs in aromatic rings and conjugated double bonds.

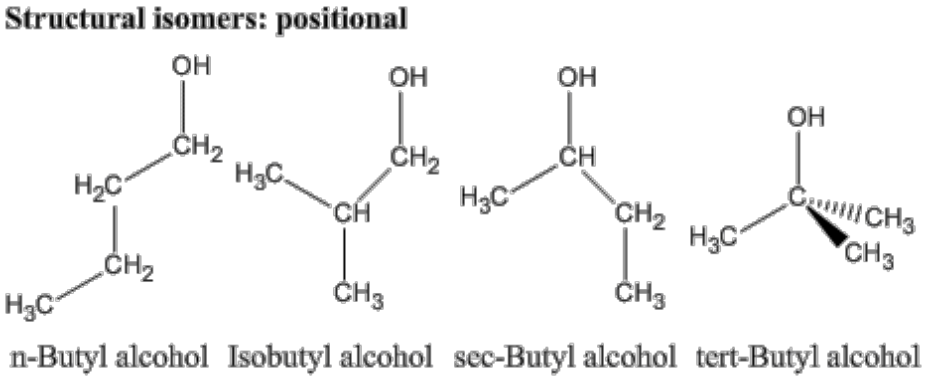
Multiple bonding

- its effect on bond length and bond energies
    - Multiple bonding decreases bond length.
    - Multiple bonding increases bond energy.
- rigidity in molecular structure

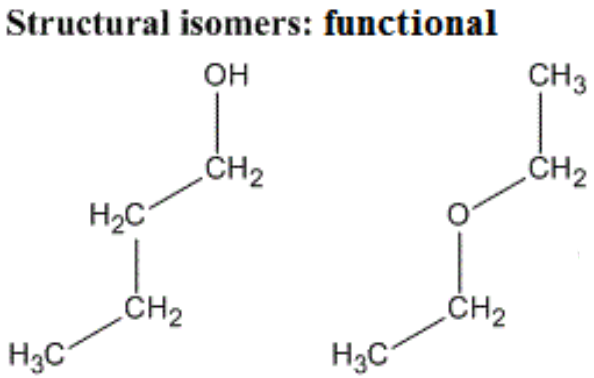
- Multiple bonding increases rigidity in molecular structure.
- Single bonds can rotate, but double and triple bonds can't.
- Even partial double bonds like those found in the peptide bond prevents free rotation.

Stereochemistry of covalently bonded molecules

- isomers
  - Same molecular formula, different structural formula.
  - "Same in writing, different in drawing..."
  - structural isomers



n-Butyl alcohol Isobutyl alcohol sec-Butyl alcohol tert-Butyl alcohol

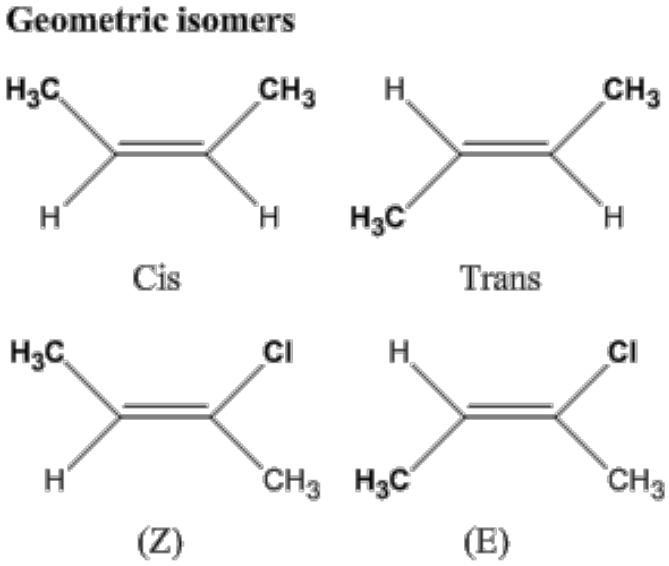


n-Butyl alcohol Diethyl ether

- Structural (constitutional) isomers have the same molecular formula, but different connectivity.

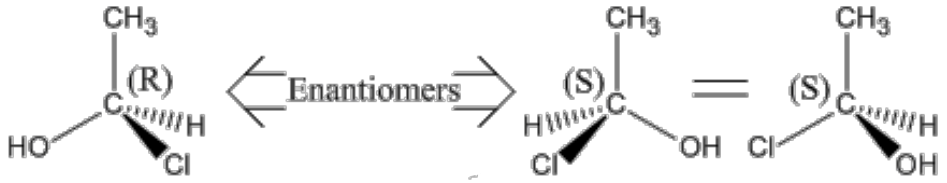
- Positional isomers: structural isomers that have the same functional groups positioned differently.
- Functional isomers: structural isomers that have different functional groups.

- geometric isomers

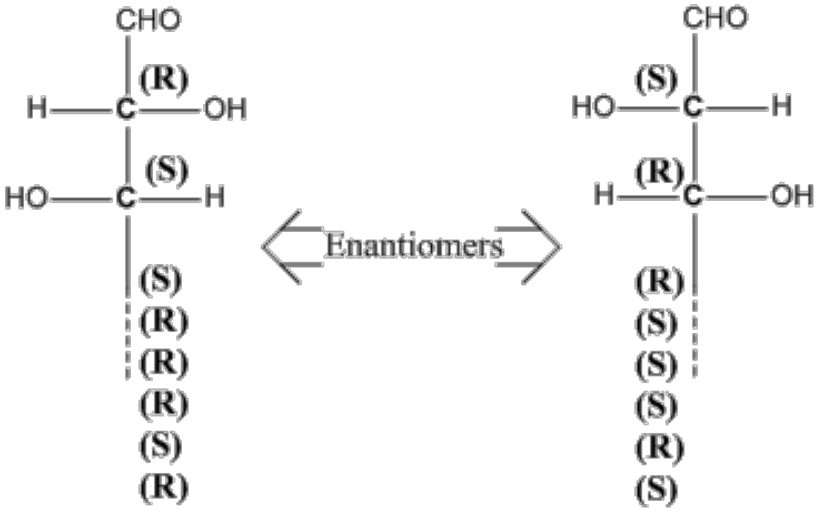


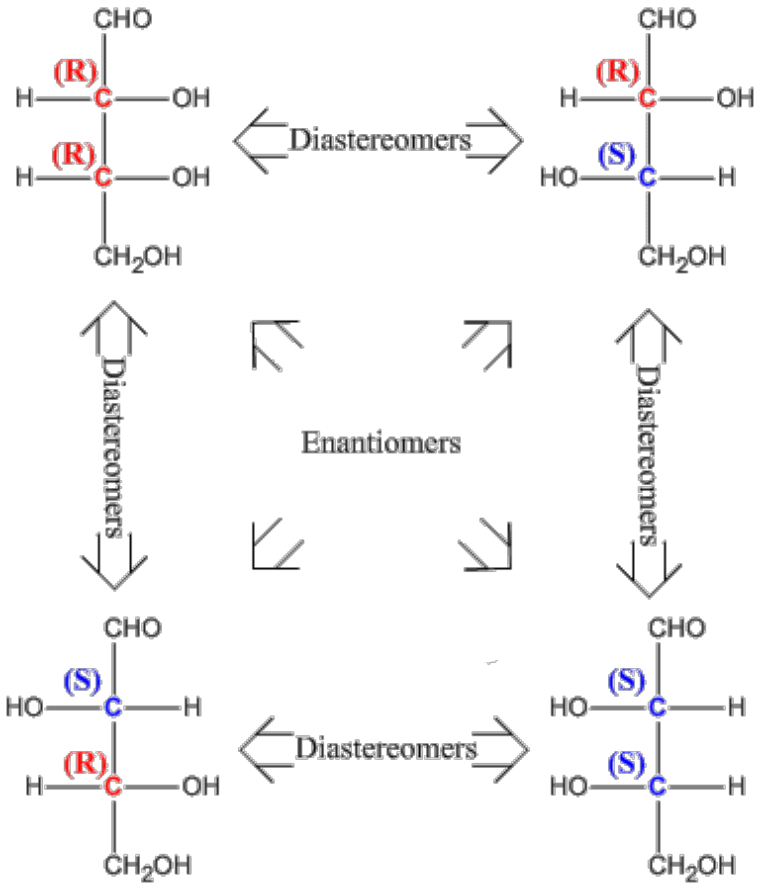
- Geometric isomers have the same molecular formula, same connectivity, but have different orientation across a double bond.
- When both sides of the double bond contains the same 2 groups, then cis and trans is used.
- Cis = same side, Trans = opposite sides.
- When different groups are attached to either side, Z and E is used.
- Z is when the higher priority groups (ranked according to the Cahn-Ingold-Prelog rules) are orientated on the same side across the double bond. Zusammen is the German word for together.
- E is when the higher priority groups are orientated on different sides across the double bond. Entgegen is the German word for opposed.

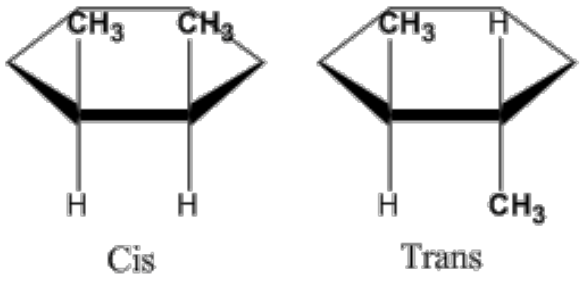
- stereoisomers (e.g. diastereomers, enantiomers, cis/trans isomers)

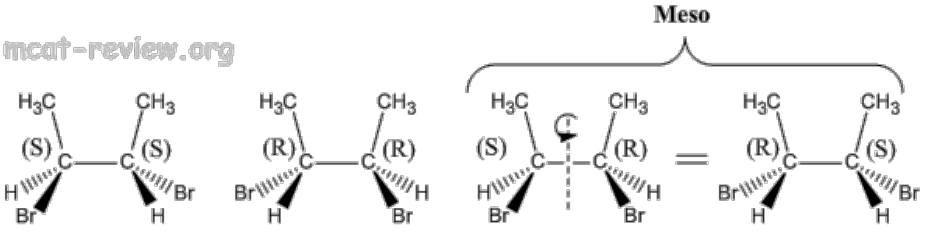
- 

(R)-1-chloro-ethanol (S)-1-chloro-ethanol

- 



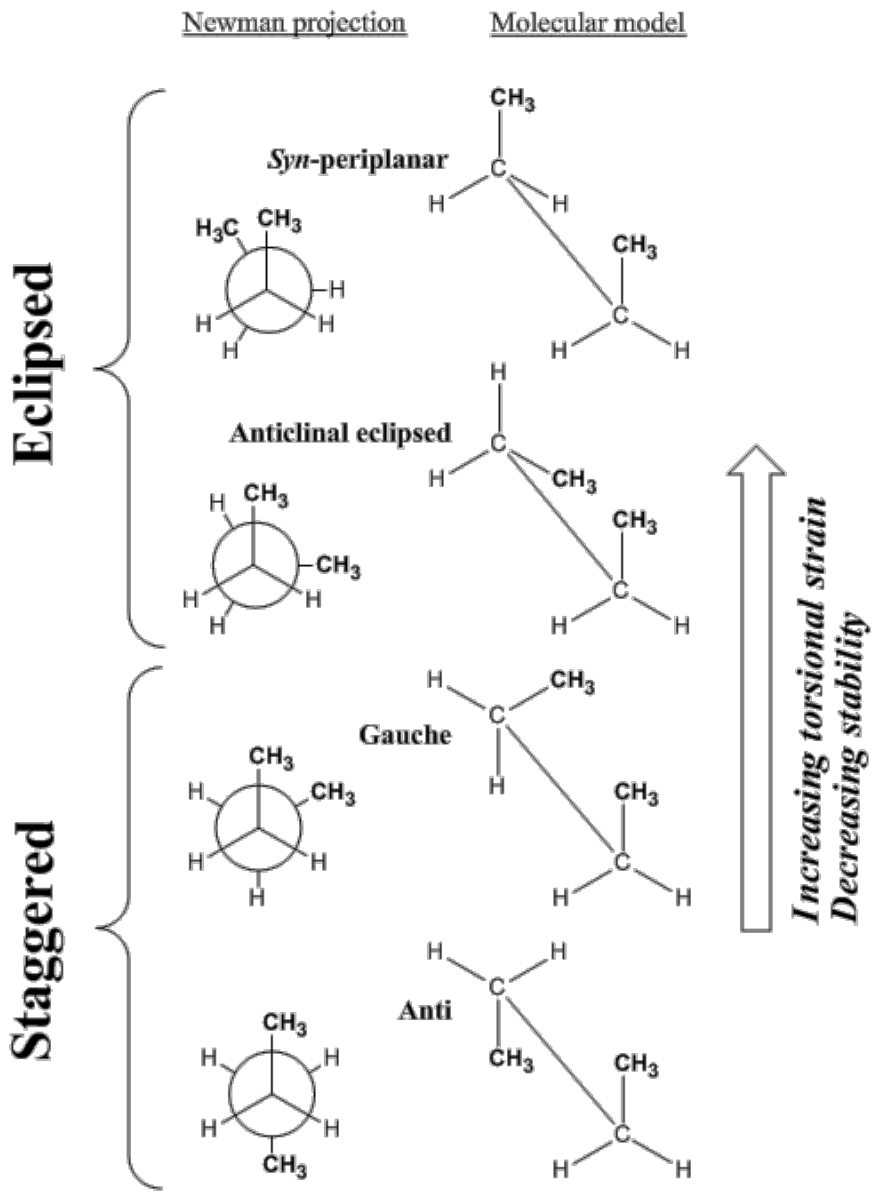
- 

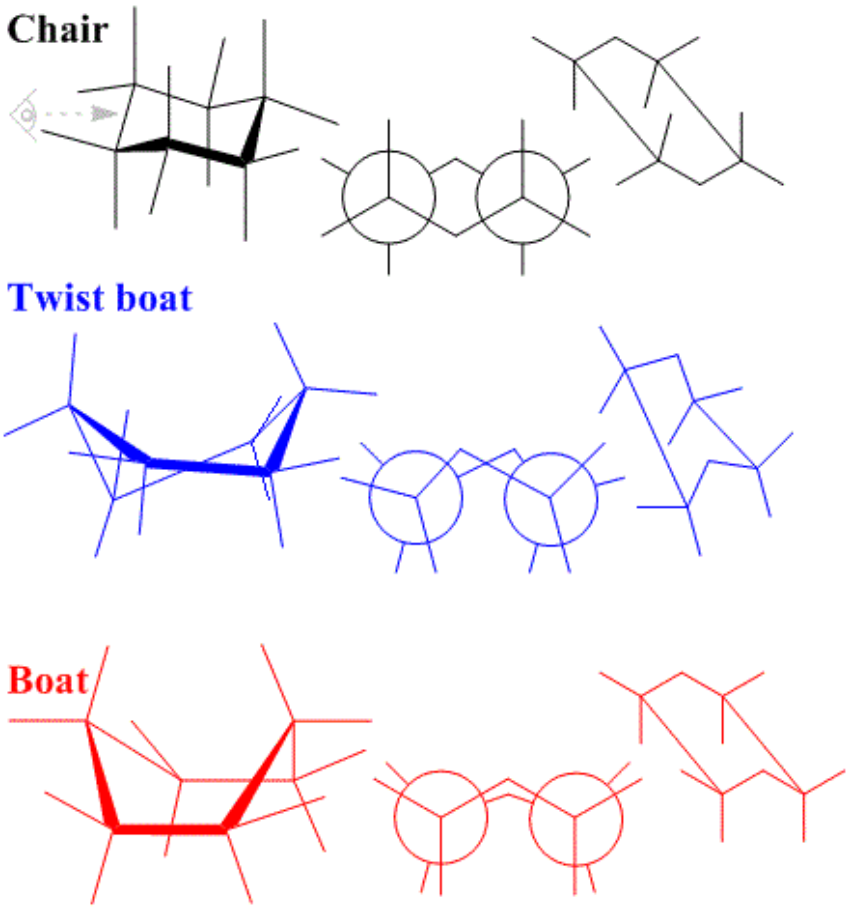
- 

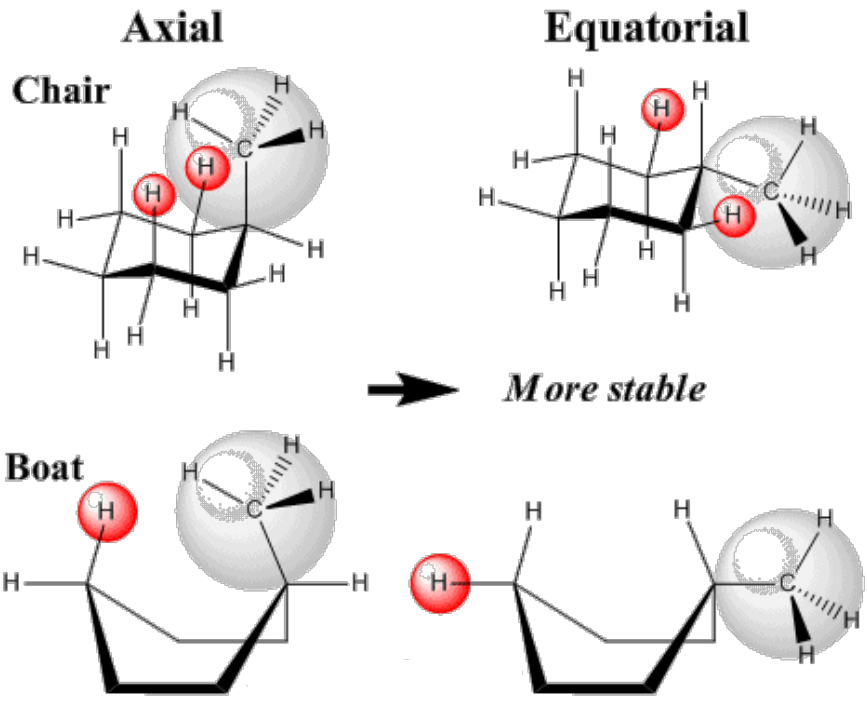
- $2^{\#chiral}$ - #meso = 2^2 - 1 = 3 different stereoisomers

- Stereoisomers have the same molecular formula, same connectivity, but have different 3-D arrangements across one or more asymmetric (chiral) centers.
- Chiral center is any atom with 4 different entities attached to it.
- Enantiomers are mirror images of each other. That means ALL chiral centers in one enantiomer is reversed in the other.
- You can't have stereoisomers if you don't have a chiral center.
- Diastereomers - more than one chiral center, inversion of stereochemistry on some but not all of its chiral centers. For examples, diastereomers would have stereochemistries of (R)-(R) vs (R)-(S). Another example of diastereomers would be (R)-(R)-(S)-(R) vs (R)-(R)-(R)-(R).
- In rings, it is easier to assign stereoisomers as cis/trans rather than R or S. Cis is having the same groups on the same side of the ring. Trans is having the same groups on different sides of the ring.
- A compound will have a total of $2^{\#\text{chiral centers}}$ stereoisomers if it is not meso.
- Meso compounds may have chiral centers, but as a molecule, they are achiral and optically inactive.
- Meso compounds reduce the total number of stereoisomers.
- Stereoisomers have the same chemical properties.
- Enantiomers have the same physical properties.
- Diastereomers have different physical properties.
- Note: in biological molecules, people use D and L for R and S, respectively.
- Caution: D and L (absolute configurations) are NOT the same as d and l (relative configuration). Read the section below on rotation of polarized of light for more details.

- conformational isomers


Newman projection
Molecular model
Eclipsed
Staggered
Syn-periplanar
Anticlinal eclipsed
Gauche
Anti
Increasing torsional strain
Decreasing stability


Chair
Twist boat
Boat

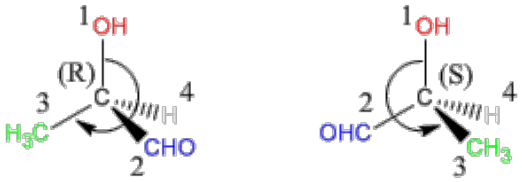

Axial
Equatorial
Chair
More stable
Boat

- Conformational isomers have the same molecular formula, same connectivity, same stereochemistry, but can rotate about a single bond to switch between different conformations.
- Technically, conformational isomers are not really isomers because you don't have to break any bonds to convert from one conformation to another. They are more accurately called conformers.
- Conformers about a single bond
    - Eclipsed
        - Syn-periplanar: highest torsional strain, most unstable, bulky groups eclipse each other.
        - Anticlinal eclipsed: high torsional strain, unstable, bulky groups eclipse hydrogens.
    - Staggered
        - Gauche: low torsional strain, stable, bulky groups 60° staggered.
        - Anti: lowest torsional strain, most stable, bulky groups 180° staggered.
    - Single bonds will rotate such that it achieves the most stable conformation.
- Conformers of cyclohexose
    - Chair: most stable, everything is staggered.
    - Twist boat: less stable, things are not completely eclipsed.
    - Boat: least stable, everything is eclipsed.
    - Hexose rings will twist and turn to achieve the most stable conformation.
- Torsional strain: the strain due to eclipsing of groups across a single bond.
- Steric interactions
    - Axial: most unstable because the axial groups are orientated with a high degree of clashing.

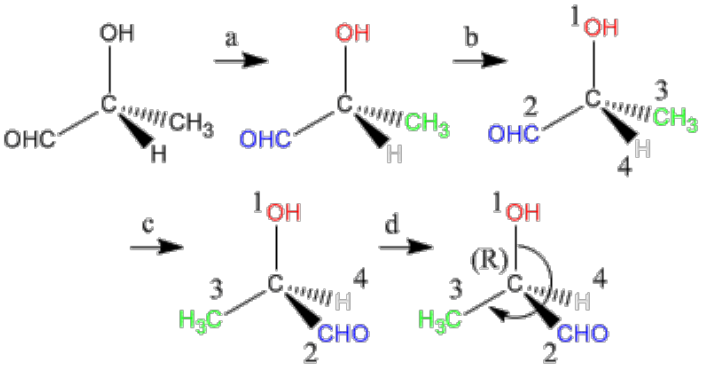
        - Equatorial: most stable because the equatorial groups are orientated away from one another.
        - Bulky groups like to be in the equatorial position.
    - Most stable conformation: completely staggered (chair), with bulky groups in the equatorial position.
    - Least stable conformation: completely eclipsed (boat), with bulky groups in the axial position.

- polarization of light, specific rotation
    - Light is an electromagnetic wave.
    - Electromagnetic waves are waves of electric and magnetic fields (in phase, but perpendicular to each other and also to the direction of propagation).
    - Normal light has the EM fields in all directions (in a 360° circle perpendicular to the direction of propagation).
    - Polarized light has EM fields all in one direction.
    - Specific rotation: chiral molecules containing a single enantiomer will rotate polarized light (to varying degrees) either to the left or to the right. This is why chiral molecules are said to be "optically active".
    - Left rotation: (-) or *l* or levorotatory.
    - Right rotation: (+) or *d* or dextrorotatory.
    - Caution: (+) or (-) does NOT correspond to R/S configurations.
    - Caution: d and l is NOT the same as D and L. The upper case letters denote absolute configurations in sugars.
- absolute and relative configuration

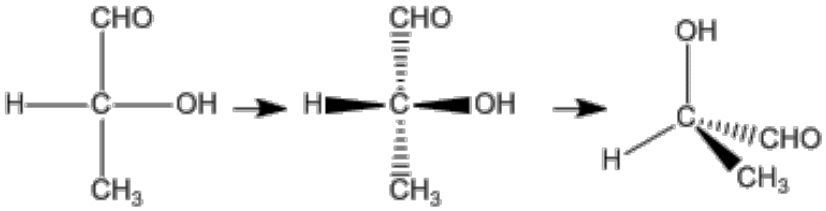
Assigning (R) and (S)

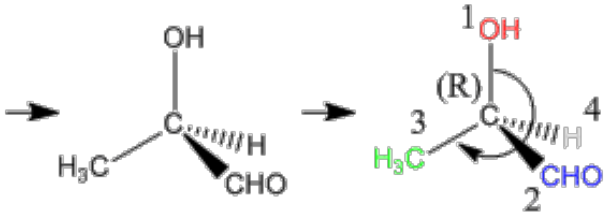


Steps involved



Fischer projection





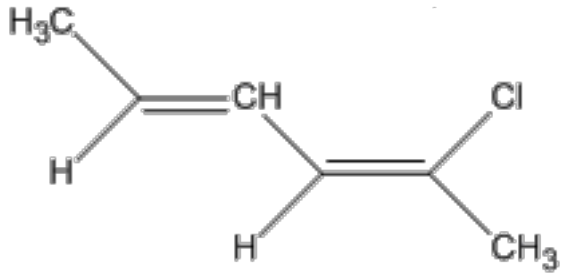
- Steps in assigning (R) and (S) - refer to figure above.
  - a. Is the carbon center chiral? For our molecule, the answer is yes because 4 different groups are attached to the carbon atom.
  - b. Assign priorities according to the Cahn-Ingold-Prelog rules (see below).
  - c. Turn the molecule such that the lowest priority group is at the back.
  - d. Rotate from the 1st to 2nd to 3rd priority group like a steering wheel. It's (R) if you end up turning right, and it's (S) if you end up turning left.

        - note: if you're good at visualizing stuff, you do this much faster by skipping step c.

- Absolute configuration is the (R) or (S) that's labeled on the chiral centers.
- Relative configuration is always defined in relationship to another chiral center. The direction that a molecule rotates plane-polarized light is the prime example of relative configuration.
- Before the mid-1800s, people did not have an understanding of the tetrahedral carbon atom, so they did not have absolute configurations. Instead, they used the relative configurations of which way a compound rotates plane-polarized light.
- The definition for relative configuration can be very broad. For example, you may arbitrarily assign one chiral center to be R* (even though it may or may not actually be R) as long as it is of opposite configuration to S* (which may or may not actually be S). Additionally, the cis or trans configuration that describes how one group is orientated relative to another group is also an example of relative configuration. Reactions can also proceed via retention or inversion, which describes the stereochemistry in relationship with the original reactant.
-

Configuration	Notation
Absolute (R)	R, D
Absolute (S)	S, L
Relative (rotate light right)	+, *d*
Relative (rotate light left)	-, *l*

- conventions for writing R and S forms
    - If only 1 chiral center
        - (R/S)-molecule, where R/S is the absolute configuration and molecule is the name of the compound.
        - For example, (R)-2-hydroxyl-propanal.
    - If more than 1 chiral center
        - (#R/S, #R/S)-molecule, where # is the carbon number (in ascending order), R/S is the absolute configuration, and molecule is the name of the compound.
        - For example, (2R,3S)-2,3,4-hydroxyl-butanal.

- conventions for writing E and Z forms
  - If only 1 double bond
    - (E/Z)-molecule, where E/Z is the geometric configuration across the double bond, and molecule is the name of the compound.
    - For example, (Z)-2-chloro-2-butene. (see geometric isomer figure)
  - If more than 1 double bond
    - (#E/Z, #E/Z)-molecule, where # is the carbon number (the smaller one in the double bond, in ascending order), and molecule is the name of the compound.
  - 

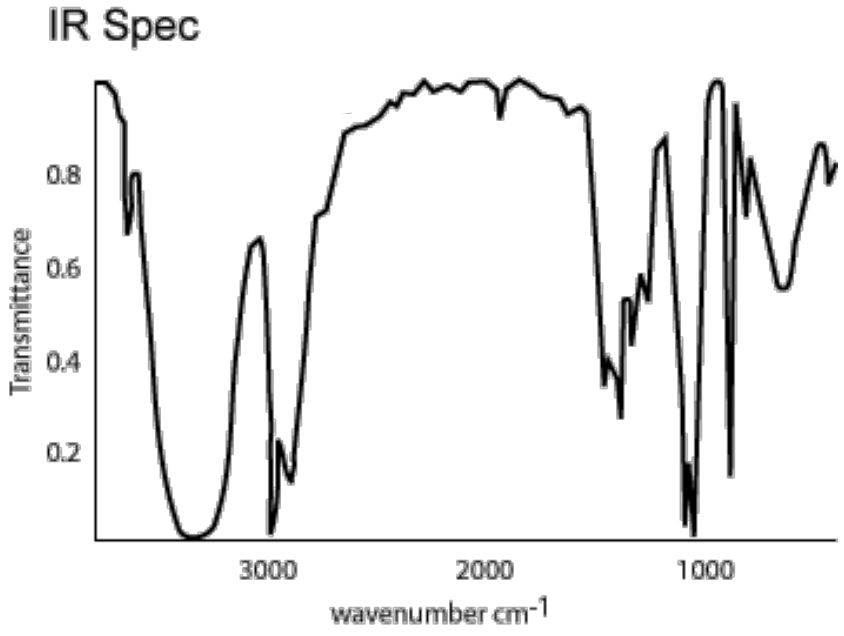
    (2Z,4E)-2-chloro-2,4-hexadiene
- Cahn-Ingold-Prelog rules for assigning priority
  - Start with shell 1, which is the atoms directly bonded to the chiral carbon.
    - The atom with the higher MW has greater priority.
    - If atoms are the same, look at next shell.
  - Shell 2, which are the atoms adjacent around shell 1 atoms.
    - The atom with the higher MW has greater priority.
    - If same atoms, the more # of the high MW species, or the more bonds to the high MW species wins.
    - For example, -CHO will have higher priority than -CH_2OH because the aldehyde has a double bond to oxygen.
    - For example, -$CH(OH)_2$ will have higher priority than -CH_2OH because the diol has 2 oxygens while the alcohol only has 1.

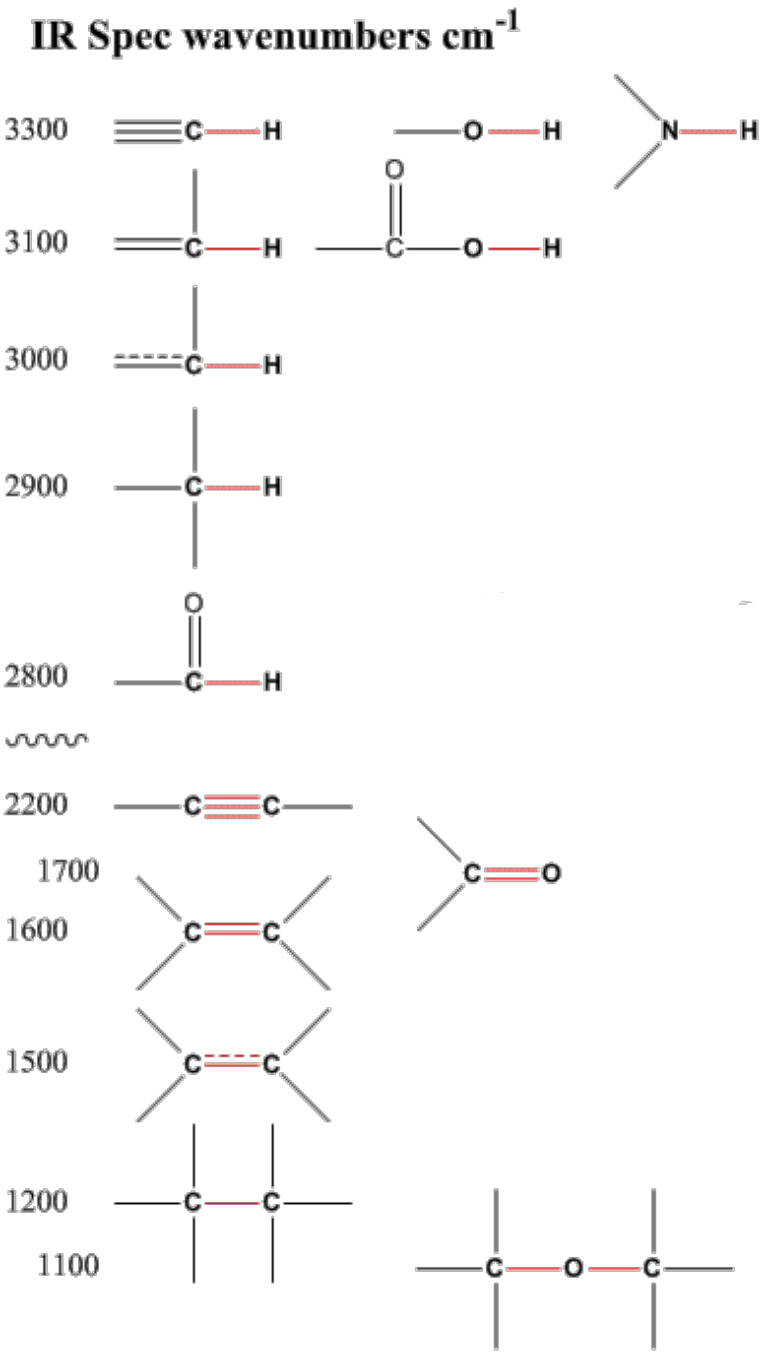
        - What about -$CH(OH)_2$ vs. CH_2F? Ans: It doesn't matter how many oxygens there are, because fluorine has greater molecular weight. So fluorine has higher priority.
        - If by now, everything is still the same, go to shell 3 and repeat the procedure.

- racemic mixtures, separation of enantiomers by biological means
    - Racemic mixtures contain equal amounts of both enantiomers. Another name for racemic mixtures is racemate.
    - Racemic mixtures do not rotate polarized light, so they are optically inactive.
    - Separation of enantiomers
        - Convert enantiomers to diastereomers.
        - Separation of diastereomers.
        - Convert diastereomers back to enantiomers.
    - Separation of enantiomers by biological means
        - Enzymes are highly specific and can differentiate between enantiomers. For example, if an enzyme digests or modifies all L-amino acids, then you'd be able to use that enzyme to separate a D/L racemic mixture.
        - In nature, all proteins are made up of L-amino acids.

Molecular Structure and Spectra

Absorption spectroscopy

- infrared region
  - 

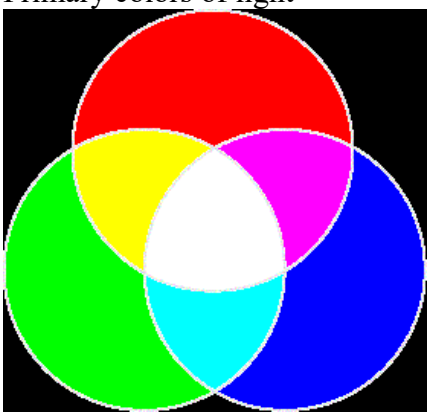


- intramolecular vibrations and rotations
  - Vibrations: bonds can stretch, compress and bend like a spring. It is this vibration that is measured in IR-spec.
  - Rotations: molecules can rotate. Rotations produce waves mainly in the microwave region. However, part of the rotation spectra does overlap with the vibration spectra.

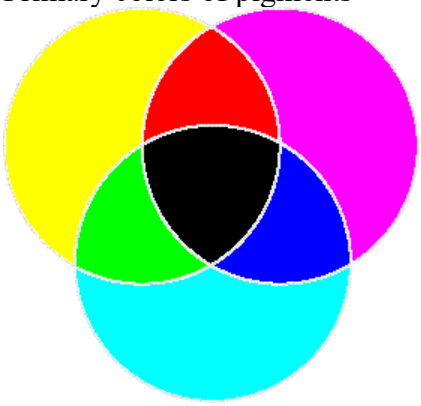
- Infrared spectra plots transmittance vs. wavenumbers, cm^{-1}
  - Transmittance increases as you go up the y-axis.
  - Where transmittance dips down, that's a region of absorbance.
  - Wavenumbers decrease from left to right.
  - Wavenumbers are correlated to frequency.
  - Peaks toward the left have higher frequency of vibration.
- recognizing common characteristic group absorptions, fingerprint region
  - Anything around 3000 cm^{-1} involves a hydrogen atom, be it O-H, N-H, or C-H.
  - Anything around 2000 cm^{-1} and below does not involve hydrogen, be it C=O, C=C, C-C, or C-O.
  - With the same atoms, the higher the bond order, the faster it vibrates, and so the higher the wavenumber.
  - 1700 cm^{-1} is for the carbonyl group. Remember this.
  - 3300 cm^{-1} can be O-H, N-H, or alkyne C-H. OH is the broadest, N-H slightly sharper, alkyne C-H is very sharp.
  - Broad peaks are due to hydrogen bonding (OH and NH).
  - Below 1300 cm^{-1} is called the fingerprint region.
  - Patterns in the fingerprint region are unique for each compound just like a fingerprint is unique for each person.

- visible region
  - absorption in visible region gives complementary color (e.g., carotene)
    - There are primary colors of light and primary colors of pigment.

- Primary colors of light



- Primary colors of pigments



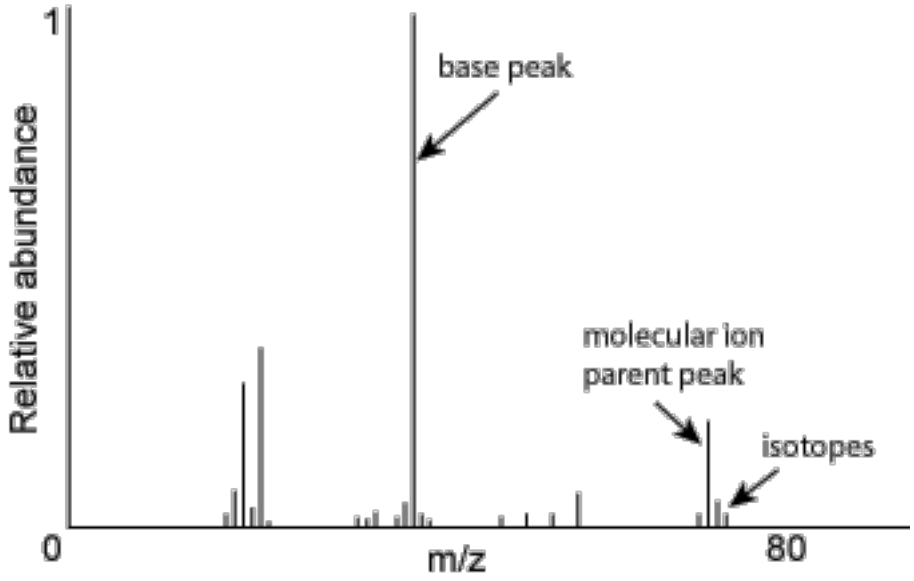
    - Complementary color is the color that's on the opposite side of the color wheel. For example, the complementary of red is cyan.
    - The absence of (when you absorb) a primary color of light, you end up with its complementary color.
    - The primary colors of pigments is exactly the complementary colors of the primary colors of light. This is because pigments absorb a certain color of light and reflect the rest back into your eyes.
    - Carotene absorbs blue light and reflect the others into your eyes. The absence of blue produces yellow, the complementary color of blue.

- effect of structural changes on absorption (e.g., indicators)
    - Changes to chemical structure can lead to changes in absorption.
    - H-indicator <--> H^+ + $Indicator^-$
    - H-indicator absorbs at a certain wavelength and is of one color.

        - Indicator$^-$ absorbs at a different wavelength so is of a different color.
        - At low pH, high [H+], H-indicator and its color will predominate.
        - At high pH, low [H+], indicator$^-$ and its color will predominate.
        - At neutral pH, both H-indicator and indicator$^-$ will co-exist in an equilibrium, so the color will be a mixture of the two.
        - You should know the colors of the universal indicator:
            - Red: very acidic
            - Orange: acidic
            - Yellow: weakly acidic
            - Green: neutral
            - Blue: basic
            - Purple: very basic
- ultraviolet region
    - pi-electron and non-bonding electron transition
        - Every time you have a bond, the atoms in a bond have their atomic orbitals merged together to form molecular orbitals.
        - Every time you have molecular orbitals, you get bonding molecular orbitals and non-bonding and/or anti-bonding orbitals.
        - Normally, electrons sit in their bonding orbitals because it is the most stable there. If bonding orbitals are full, then non-bonding orbitals are occupied.
        - Given enough energy (as in absorption), the electrons transition from the bonding or non-bonding orbitals to the anti-bonding orbitals.
        - If too much energy is absorbed, enough electrons escape the bonding orbitals / enter the anti-bonding orbitals to break the bond completely.
        - For UV absorption, we're not worried about breaking bonds. We're only interested in the pi-electrons of double bonds because their molecular orbital transitions result in UV absorption.

        - Double bonds absorb UV because the pi electrons transition from the bonding and non-bonding molecular orbitals to the anti-bonding orbitals.
    - conjugated systems
        - Conjugated systems decreases the energy of electromagnetic radiation that is absorbed.
        - The more conjugated double bonds there are, the longer the wavelengths of absorbed radiation.
        - If there are enough conjugated double bonds, the molecule will start to absorb in the visible region.

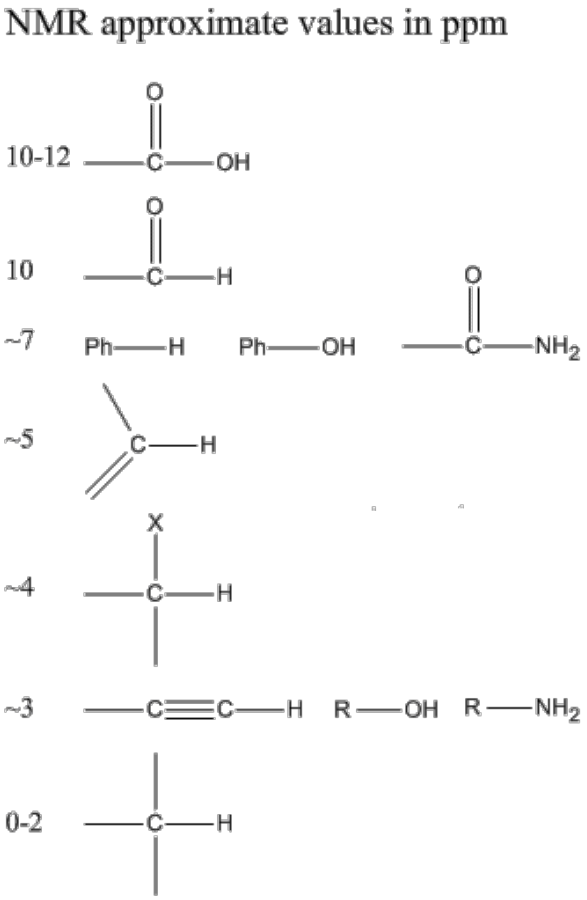
Mass spectrometry: m/e ratio, parent peak



- Mass spec is when you bombard a molecule with electrons.
- When electrons smash into your molecule, it is fragmented into ions.
    - What if the electrons "miss" your molecule? Ans: Your molecule is neither fragmented nor ionized. Uncharged molecules are not detected and are not included in the mass spectra.
    - What if the electrons do not break apart your molecule, but merely ionizes it? Ans: this "molecular ion" will be detected as the parent peak, also called the molecular ion peak.

    - What if the electrons not only ionize but also fragment your molecule? Ans: all the fragmented ions will be detected and plotted in the mass spectra.
    - The faster (higher energy) the bombarding electron, the more fragmentation.
    - The more fragmentation, the smaller the molecular ion peak.
- These ions have a characteristic mass to charge ratio (m/e or m/z).
- A magnetic field resolves (separates) the different m/z ions so they can be individually detected and plotted on a spectrum.
- The resulting spectrum plots Relative abundance vs. the m/z ratio.
- The parent peak, or the molecular ion peak, is the peak that depicts the ion of the molecule without fragmentation. It has the highest m/z ratio.
- Peaks clustered really close to one another depicts isotopes.
- The base peak is the tallest peak (most abundant species).
- Mass spec is useful for:
    - Measuring the molecular weight of a molecule.
    - Identify the molecule by fragmentation patterns.
    - Identity heteroatoms by their characteristic isotope ratios.

NMR spectroscopy



- protons in a magnetic field; equivalent protons
    - Protons have spins of up or down (+½ or -½, counterclockwise or clockwise. The detailed vectors are not important here, so simply up or down is fine).
    - With an even number of protons, the spins pair up and the up and down spins of all the protons cancel each other out.
    - With an odd number of protons, there is a net spin of up or down.
    - Normally, both up or down spins are equal in energy (they are degenerate). So, either way goes.
    - In the presence of a magnetic field, the spin that lines up with the magnetic field gets the lower energy. If the external magnetic field is up, then you better spin up. If the magnetic field is down, then you better spin down.
    - If we were to give the protons some energy (by radio wave absorption), then the protons can be promoted (flipped) to the higher energy spin, which is opposite to

the direction of the external magnetic field. This absorption is called resonance. The resonance frequency is the frequency of the radio wave that's needed to cause a flip in spin.

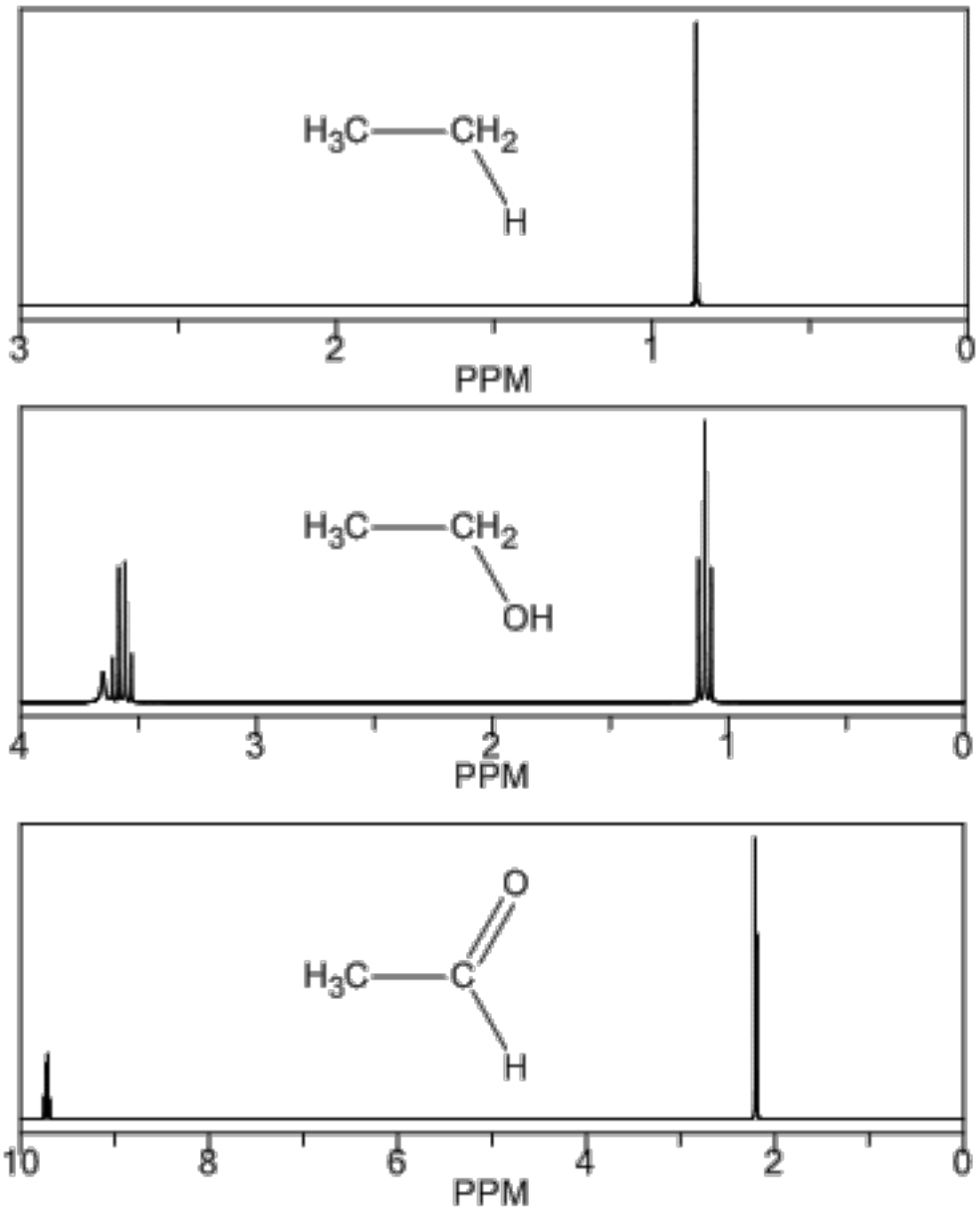
- The resonance frequency (or energy or field strength) of absorption is called the chemical shift.
- Different protons have different resonance frequencies.
- Equivalent protons have the same resonance frequencies.
- You can substitute X at any of the equivalent protons, and you should end up with the same new compound. If not, then they're not equivalent protons.
- What makes protons have different resonance frequencies depends on what atom they're close to.
- NMR measures the chemical shift relative to a standard called TMS (tetramethylsilane) in unit of ppm.
- The more "different" two protons are, the farther their chemical shifts
- What makes protons "different" is the degree of electron shielding or deshielding.
    - Next to stuff like carbon, hydrogen is shielded by electrons because carbon is not so electronegative.
    - Next to stuff like oxygen, hydrogen is deshielded because oxygen is very electronegative.
    - When things are shielded, the magnetic field is smaller and they have small chemical shifts and appear upfield (to the right).
    - When things are deshielded, the magnetic field is larger and they have large chemical shifts and appear downfield (to the left).

- NMR is nuclear magnetic resonance because the nuclear stands for protons; magnetic stands for the external magnetic field; the resonance stands for the absorption of radio waves.
- Signals by n equivalent protons add up to produce one signal the height n times the signal for a single proton.

- spin-spin splitting

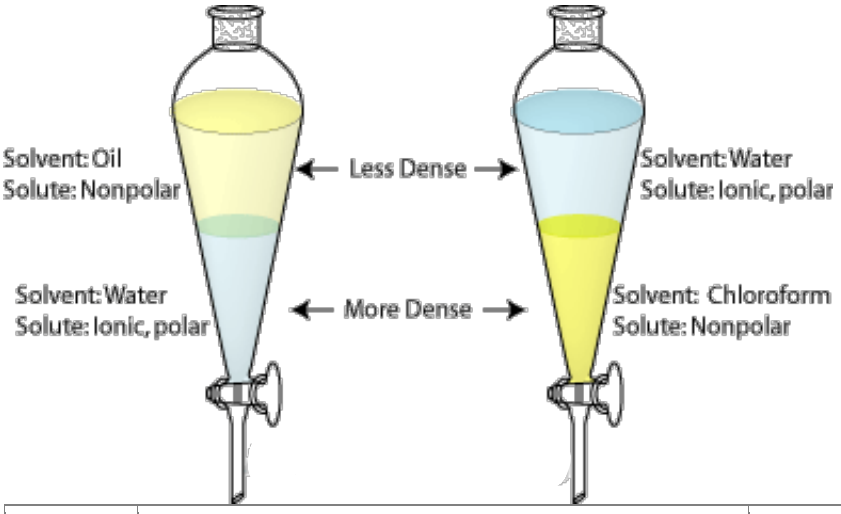
- Magnetic fields produced by neighboring protons cause spin-spin splitting.
- Neighboring is defined as 3 bonds away, which is the same thing as hydrogens attached to adjacent atoms.
- Things are split into n+1 peaks, where n is the number of neighboring protons.
- Aromatic protons can split over 3 bonds, which is why the NMR spectra for the aromatic region is a mess.
- The J value defines how far apart things get split.
- Protons across single and aromatic bonds get split approximately the same.
- Protons across double bonds get split farther apart.

NMR Spectra



Separations and Purifications

Extraction (Distribution of Solute Between Two Immiscible Solvents



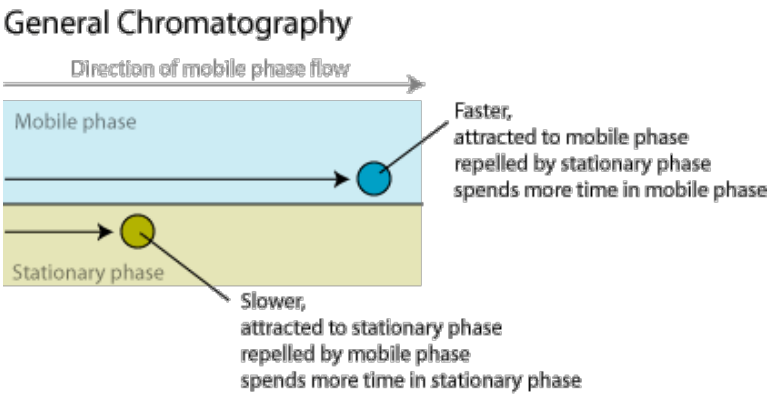
	Organic phase	Aqueous phase
Solvent	Nonpolar solvent	Water
Solute	Nonpolar solutes dissolve here	Ionic and polar solutes dissolve here
Density	The organic phase does not always float on top. Chloroform, for example, sinks below the aqueous phase.	Water is usually denser than other solvents, but some organic solvents are even denser.

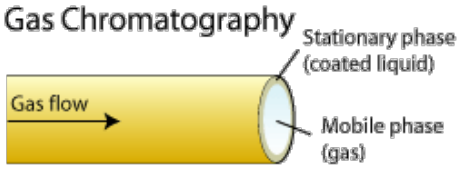
Distillation

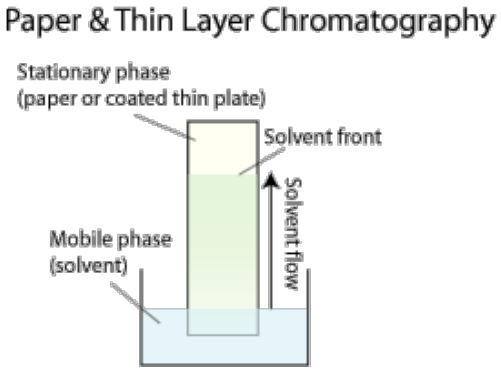
- Separates liquids based on boiling point. The stuff with the lower boiling point is boiled off and collected; the higher boiling point stuff remains behind.
- Simple distillation = done with a normal column = can separate two liquids if the difference in boiling point is large.
- Fractional distillation = done with a fractionating column = can separate two liquids with smaller differences in boiling point.

- Vacuum distillation = done under lower pressure (vacuum) = lowers the boiling point for all liquid components so you don't have to crank up the temperature so high (chemical might decompose).

Chromatography (Basic Principles Involved in Separation Process)







- Gas-liquid chromatography
    - Good if analyte can be promoted to gas phase.
    - Gas-liquid chromatography (GLC) is the same thing as gas chromatography (GC).
    - The gas part is the mobile phase, the liquid part is the stationary phase coated to the inside walls of the column.

    - Substrate equilibrates between mobile (gas) and stationary (liquid coat) phase.
    - Those with greater affinity for the stationary phase comes out of the column slower. Polar substrate has more affinity for polar stationary phase, and hydrophobic substrate has more affinity for hydrophobic stationary phase.
- Paper chromatography
    - Classically used to separate pigments in dyes.
    - Solvent = mobile phase. Paper = stationary phase.
    - Pigments in dyes stick to paper, solvent tries to wash them along, those with greater affinity to paper stays behind, those with greater affinity to solvent gets washed along.
    - R_f value = distance traveled by pigment / distance of solvent front.
    - R_f = 0 means that pigment has not moved.
    - R_f = 1 means that pigment moved as far as the solvent front.
- Thin-layer chromatography
    - Thin-layer chromatography = advanced paper chromatography.
    - Instead of paper, you have a plate coated with a specific stationary phase of your choosing.
    - R_f value used in the same way as paper chromatography.

Recrystalization (Solvent Choice from Solubility Data)

- Recrystalization = barely dissolving your compound, then let it recrystalize out of solution = compound ends up being more pure.
- Barely dissolving = use just enough to fully dissolve your compound under warm temperature = saturated solution.
- Recrystalize = solution cools, solubility decreases, compound comes out of solution.

- Solvent choice = choose a solvent in which your compound is soluble in at warm temperature, but not at cool temperature. Also, choose a solvent in which impurities are highly soluble.

- Impurities should remain dissolved in the solvent even when your compound recrystalizes out.

Hydrocarbons

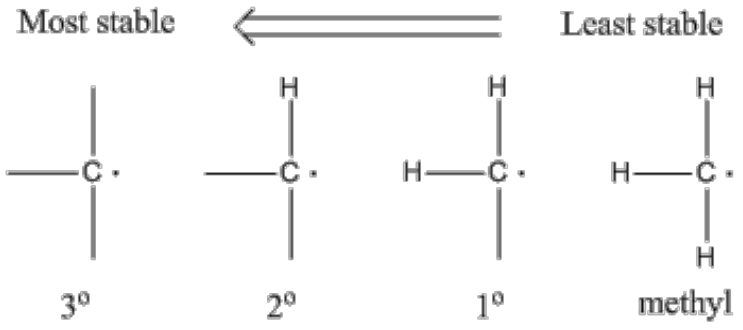
Aliphatic - alkanes

- Description
    - nomenclature
        -

# C atoms	Name for straight chain alkane	Name for cyclic alkane
1	Methane	N/A
2	Ethane	N/A
3	Propane	Cyclopropane
4	Butane	Cyclobutane
5	Pentane	Cyclopentane
6	Hexane	Cyclohexane
7	Heptane	Cycloheptane
8	Octane	Cyclooctane
9	Nonane	Cyclononane
10	Decane	Cyclodecane

        - After Decane, there is Undecane (11), Dodecane (12), Tridecane (13), Tetradecane (14), and so forth for eleven membered alkanes upwards.
    - physical properties
        - Hydrophobic.
        - London Dispersion Forces present only.
        - Lower boiling points than compounds the same size but with functional groups.
        - Very long alkanes can have very high boiling points due to the sum of all the dispersion forces. A useful reference is that heptane, the 7 membered alkane, has the same boiling point as water.

- Important reactions
    - combustion
        - Complete combustion of alkanes: alkane or cycloalkane + $O_2 \rightarrow CO_2 + H_2O$
        - Complete combustion of anything: fuel + oxygen → carbon dioxide + water
    - substitution reactions with halogens, etc.
        - Alkane + halogen + free radical initiator → alkyl halide
        - Free radical initiators = hv (UV light) or peroxides.
        - Substitution occurs via a free radical mechanism - see below.
- General principles
    - stability of free radicals; chain reaction mechanism; inhibition
        - The more substituted the radical, the more stable it is.
        - Stability: 3° > 2° > 1° > methyl.

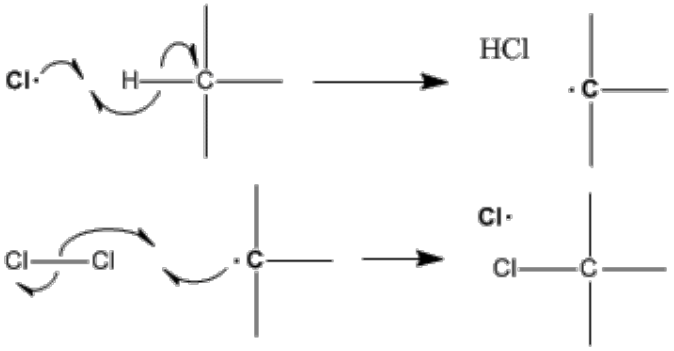


        -
        - Substitution will occur preferentially at the more substituted carbon atom.

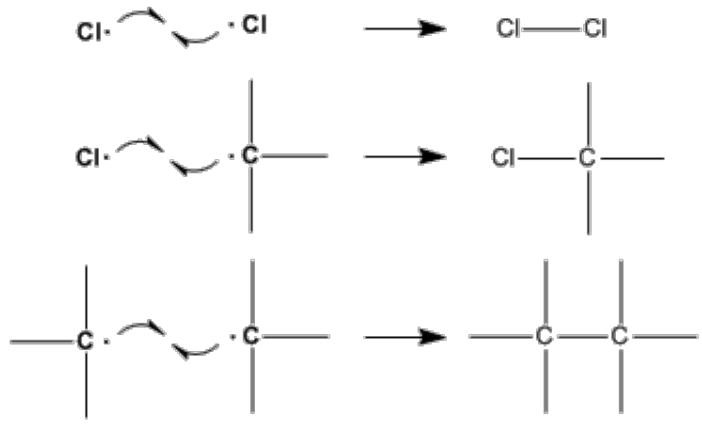
Radical Chain Reaction Mechanism

Initiation

Propagation



Termination

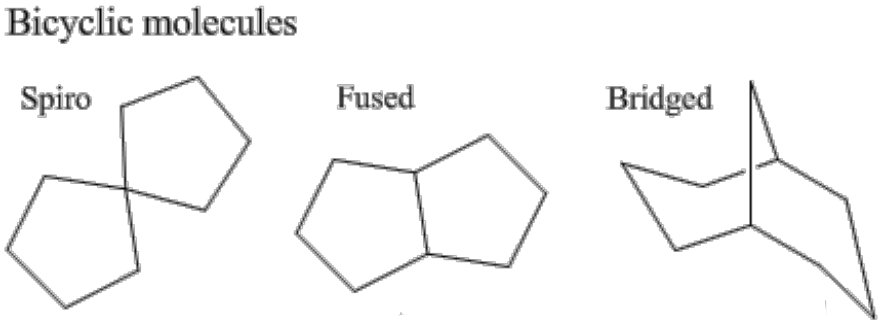


- The free radical chain reaction is dependent on the presence of free radicals. Therefore, anything that inhibits free radicals will inhibit this reaction. One example is antioxidants, which eats up free radicals and therefore inhibits the free radical chain reaction.

- ring strain in cyclic compounds
  - Cyclopropane has the highest ring strain.
  - Cyclobutane has the second highest ring strain.

- Cyclohexane has the lowest ring strain.
- Any ring with greater or equal to 14 carbon atoms has the next lowest ring strain.
- Stick with the above rule and you can answer any questions comparing ring strain. The exam will not require you to make weird ring strain comparisons, for example between cyclopropane and cycloheptane.
- Ring strain consists of Angle (Baeyer) strain and Torsional strain.
    - Angle (Baeyer) strain is caused by deviation from the ideal sp^3 tetrahedral bond angle of 109.5°
    - Torsional strain is caused by the molecule having eclipsed conformations instead of staggered ones.
    - Cyclopropane has both angle (Baeyer) strain and torsional strain.
    - Cyclohexane, in the chair conformation, has no angle (Baeyer) or torsional strain.
    - You'll frequently see people write Bayer strain instead of Baeyer strain. They mean the same thing.

- bicyclic molecules



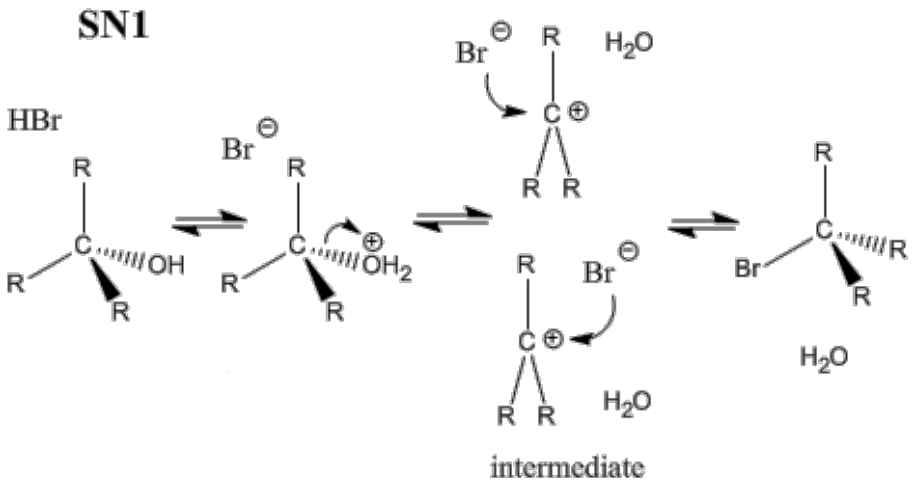
- Bicyclic molecules have more ring strain than monocyclic molecules. Except for spiro bicyclics, which have similar ring strain as their monocyclic counterparts.

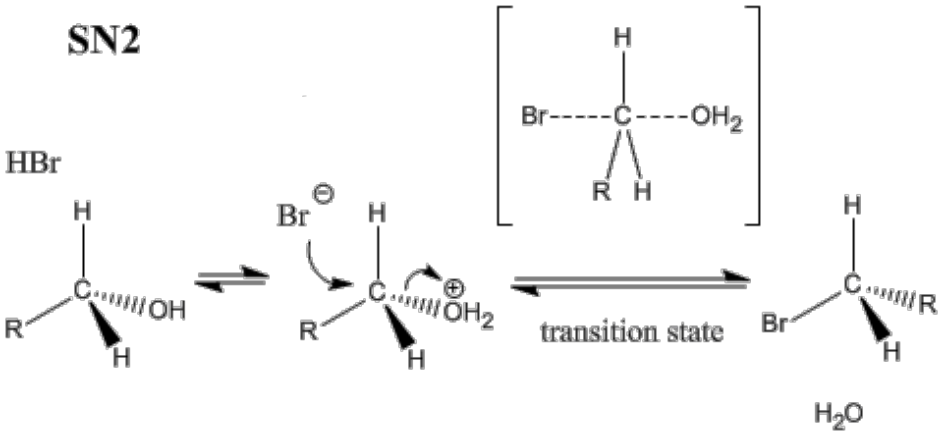
Oxygen Containing Compounds - Alcohols

Description

- nomenclature
    - Prefix: hydroxyl, hydroxy.
    - Suffix: -ol, alcohol.
- physical properties
    - Hydrogen bonding.
    - Higher boiling point than the same compound without the alcohol group.
    - Water soluble as long as molecule does not contain a long hydrophobic region.
- infrared absorption of OH group: 3300 cm^{-1} and broad due to hydrogen bonding.

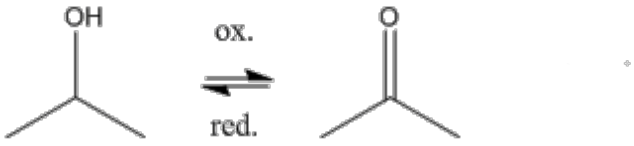
Important reactions

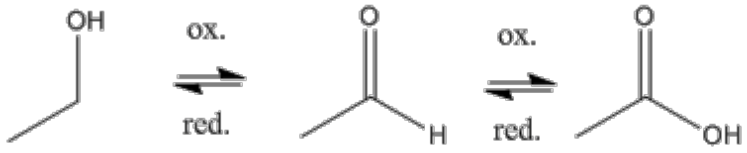
- substitution reactions: SN1 or SN2, depending on alcohol and derived alkyl halide
    - R-OH + HX <--> R-X + H_2O
    - 



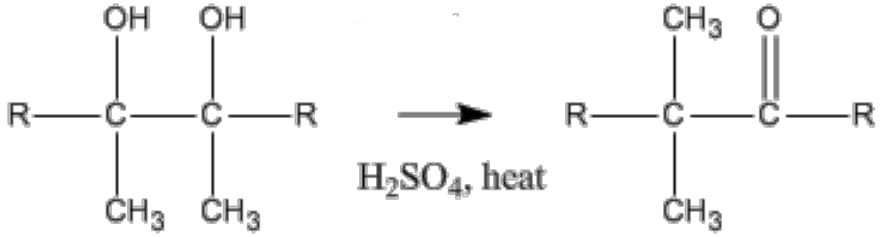
- Factors that favor sn1: stable carbocation, tertiary carbon center, protic solvent.
- Factors that favor sn2: unstable carbocation, primary carbon center, aprotic (but polar) solvent.
- All substitution reactions need a good leaving group.
- SN1 = unimolecular reaction, intermediate carbocation formed.
- SN2 = bimolecular reaction, passes through transition state.

- oxidation
  - KMnO4 and CrO3 will oxidize primary alcohols to carboxylic acids, but PCC (Pyridine Chlorochromate) and other weak oxidizing agents will only oxidize a primary alcohol to the aldehyde.
  - Secondary alcohols always oxidize to the ketone.
  - Tertiary alcohols do not oxidize.

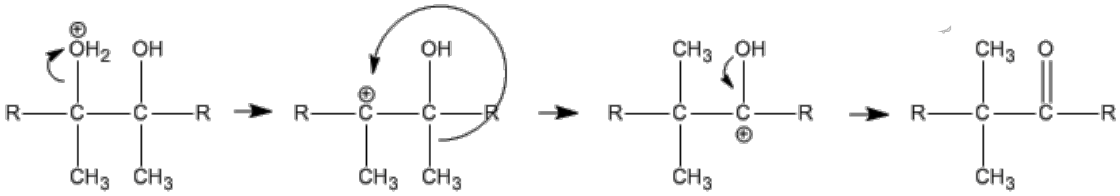


- 

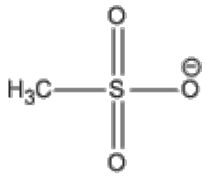
- pinacol rearrangement in polyhydroxyalcohols; synthetic uses

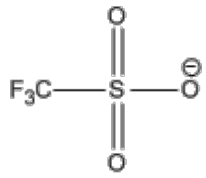


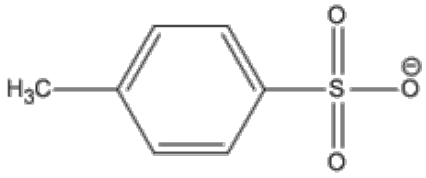
- Mechanism of pinacol rearrangement:

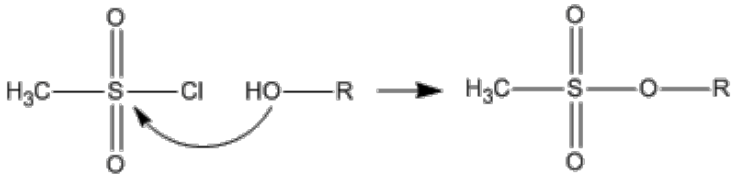


- protection of alcohols: the best protecting group for alcohol is the trimethylsilyl group.
    - To protect, add Cl-$SiMe_3$ to R-OH.
    - The alcohol gets "capped" into R-O-$SiMe_3$.
    - To deprotect, add F^-.
- reactions with SOCl2 and PBr3
    - R-OH + $SOCl_2$ --> R-Cl (by products: SO_2 + HCl)
    - R-OH + PBr_3 --> R-Br (by products: H_3PO_3, R_3PO_3, HBr)
- preparation of mesylates and tosylates



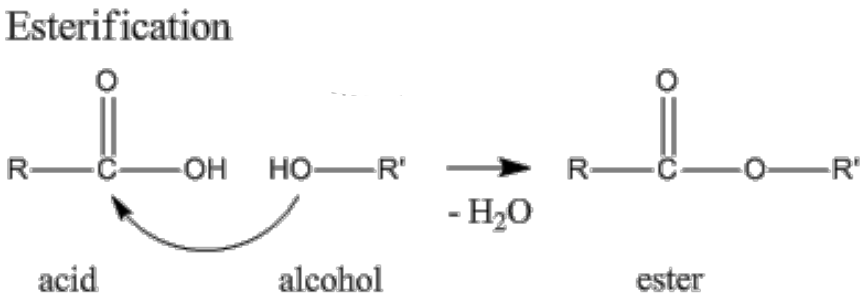


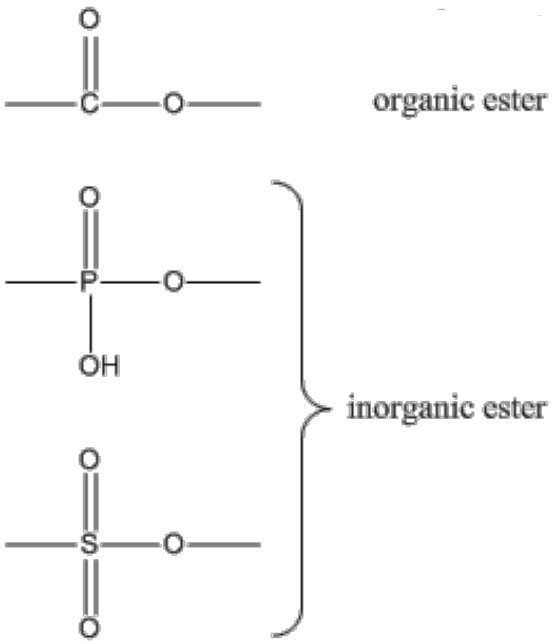




-
  - Sulfonates R-SO_3^- are good leaving groups.
  - The R can be:
    - Methane, which makes methanesulfonate.
    - Toluene, which makes tosylate.
    - Trifluoromethane, which makes triflate.
  - Mesylates can be prepared by reacting an alcohol (R-OH) with mesyl chloride (MsCl).
  - Tosylates can be prepared by reacting an alcohol (R-OH) with tosyl chloride (TsCl).

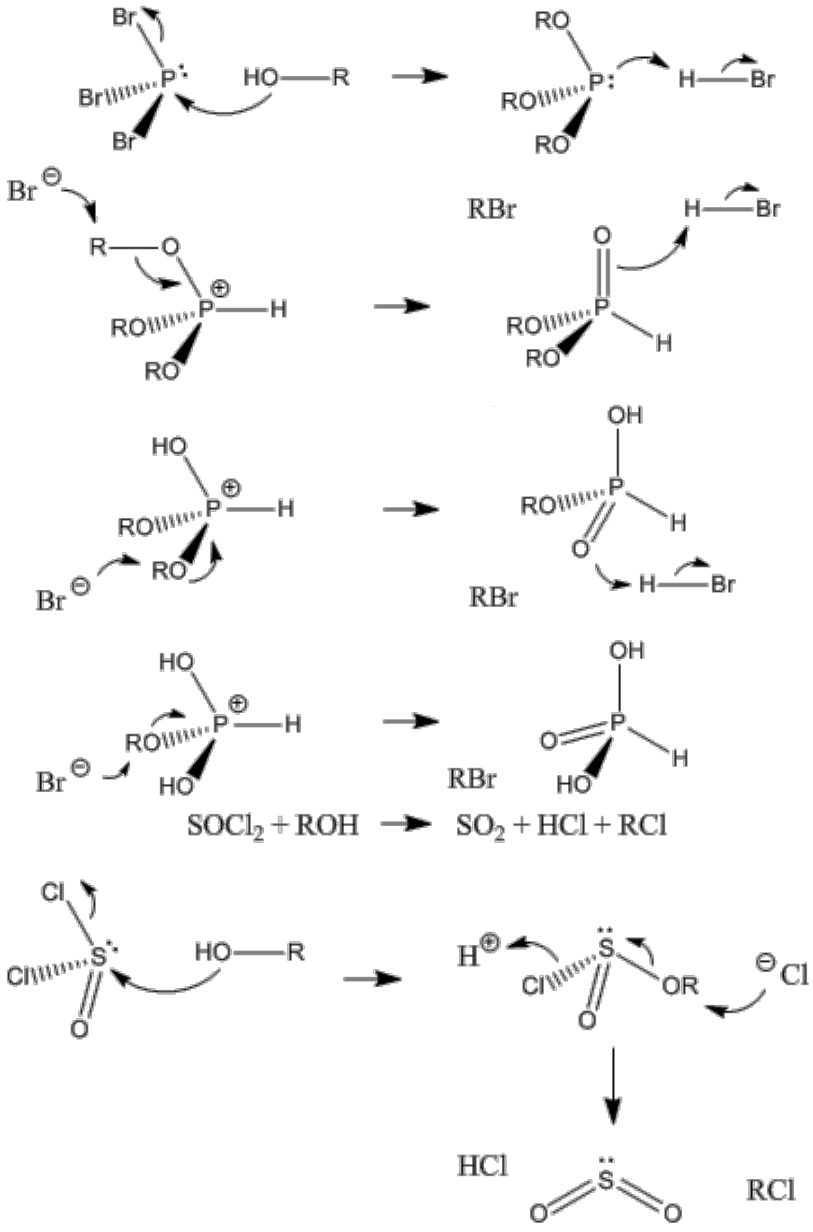
- esterification: acid + alcohol = ester

- 

- inorganic esters: replace the carbon of esters with a different atoms.
- 

- Reactions involving the formation of inorganic esters:

$$PBr_3 + 3ROH \rightarrow H_3PO_3 + 3RBr$$



- Formation of mesylates and tosylates are also reactions that involve inorganic esters.
- In biochemistry DNA/RNA polymerization, the 3'-OH alcohol group attacks the 5'-phosphate to form an inorganic ester linkage (phosphodiester linkage of DNA/RNA backbone).

General principles

- hydrogen bonding: hydrogen bonding in alcohols give them a higher boiling point than their corresponding alkanes.
- acidity of alcohols compared to other classes of oxygen-containing compounds: lower pKa = more acidic.
-

Compound	pKa
COOH (carboxylic acids)	5
ArOH (phenols)	10
H_2O (water)	16
ROH (alcohols)	16
-CH2(CO)-R (alpha hydrogen in aldehydes and ketones)	20
-CH2(CO)-OR (alpha hydrogen in esters)	25

- effect of chain branching on physical properties: going from straight chain to branched alkane (with same # carbons) = higher freezing/melting point, lower boiling point.

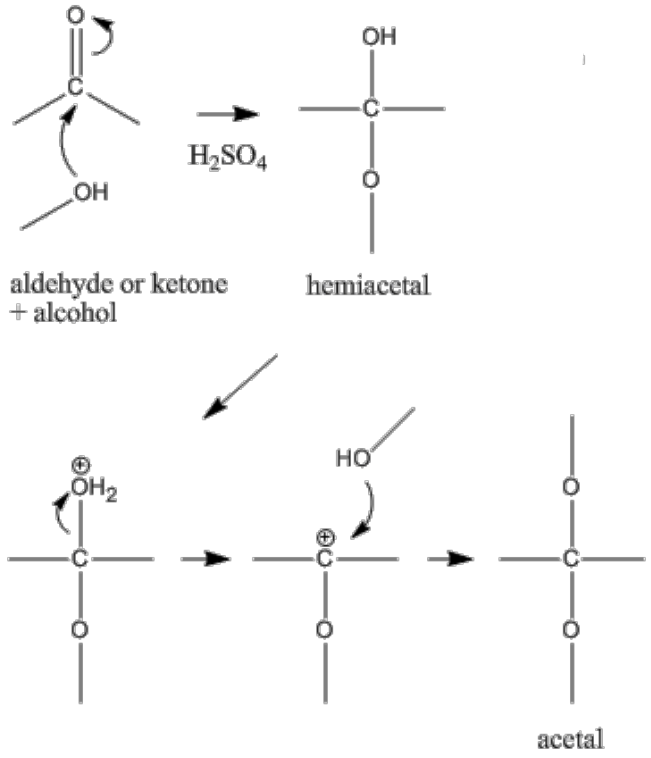
Oxygen Containing Compounds - Aldehydes and Ketones

Description

- nomenclature
    - Aldehyde suffix: -al, -aldehyde.
    - Ketone prefix: keto-, oxo-.
    - Ketone suffix: -one, ketone.
- physical properties
    - C=O bond is polar, with the carbon partially positive and oxygen partially negative.
    - Dipole-dipole interactions give these molecules higher boiling points than their corresponding alkanes, but not as high as the corresponding alcohols or carboxylic acids.
- infrared absorption of C=O bond: 1700 cm^{-1}

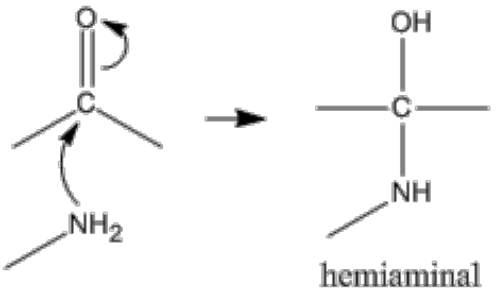
Important reactions

- nucleophilic addition reactions at C=O bond
    - acetal, hemiacetal

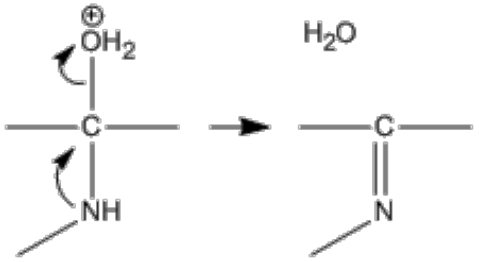


- Aldehydes and ketones react with 1 equivalent of alcohols to make hemiacetals.
- Aldehydes and ketones react with 2 equivalent of alcohols to make acetals.
- Hemiketal and ketal are the same as acetals except the starting compound must be a ketone and not an aldehyde. This is an old naming scheme that is no longer used.

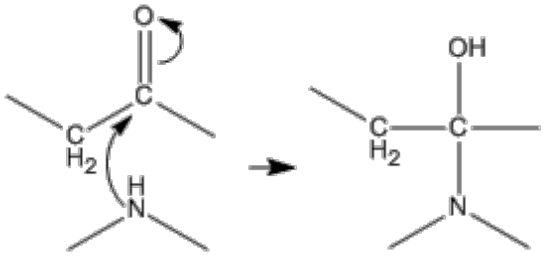
- imine, enamine



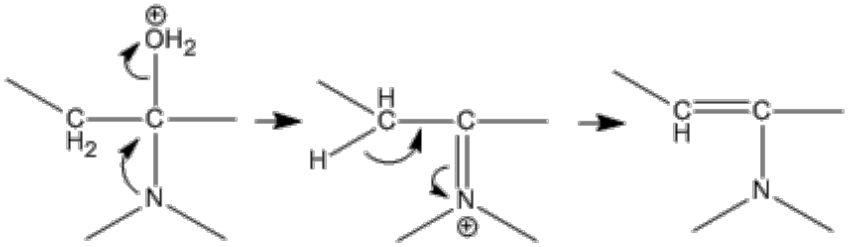
hemiaminal



imine

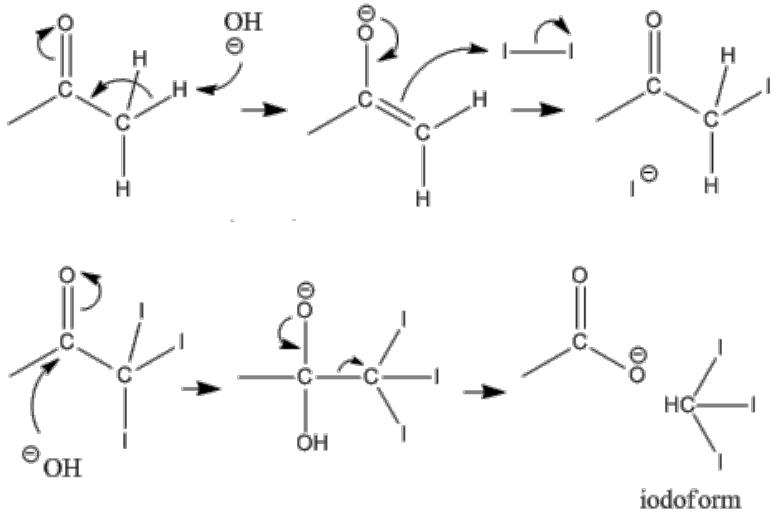


hemiaminal

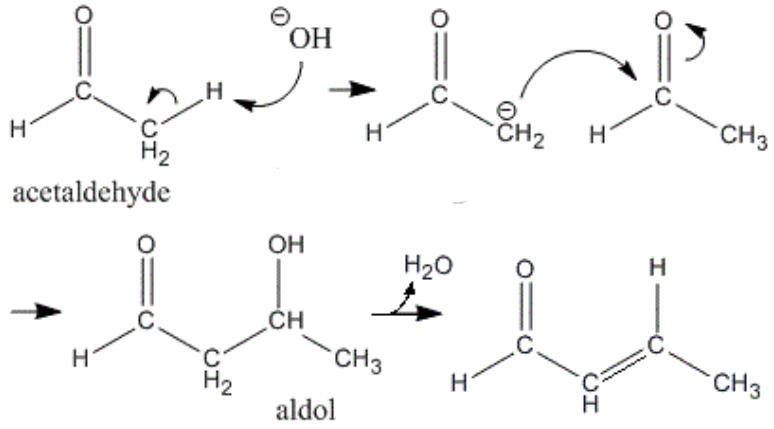


enamine

    - Primary amine + aldehyde or ketone = imine.
    - Secondary amine + aldehyde or ketone = enamine.
- reactions at adjacent positions
    - haloform reactions

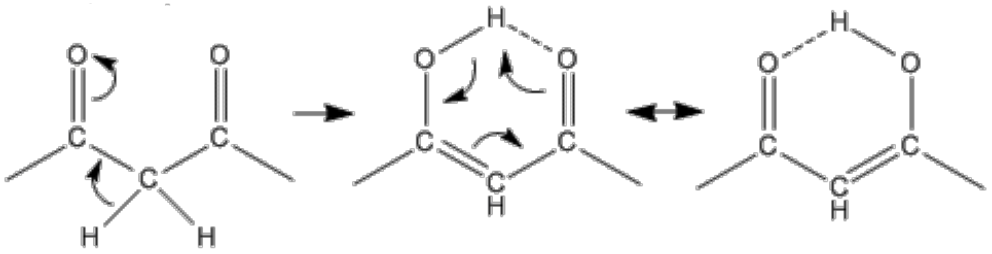


    - Ketones + halogen = halogenation of the alpha position (carbon adjacent to the C=O group).
    - Methyl ketone + halogen = haloform + carboxylate.
    - Trihalogenated methyl = good leaving group.
  - aldol condensation

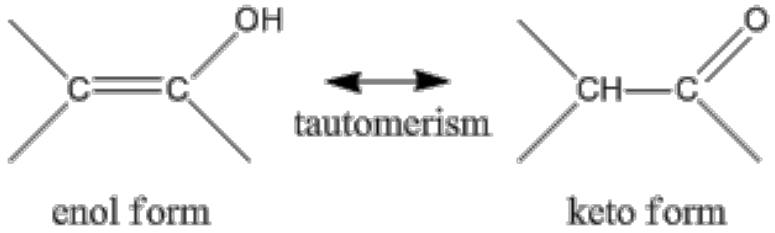


    - Occurs because of the acidic alpha proton.
    - 2 acetaldehyde -> aldo.
    - Works for carbonyl compounds with an acidic alpha proton.
  - oxidation: aldehydes oxidize to carboxylic acids. Ketones do not oxidize further.

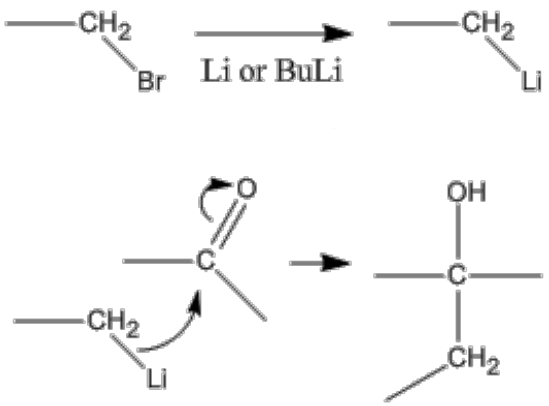
- 1,3-dicarbonyls: internal H-bonding



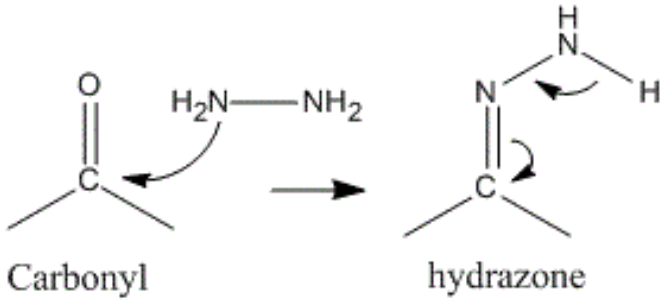
-
  - 1,3-dicarbonyls have 2 carbonyl groups flanking a carbon atom with an acidic proton.
  - Also referred to as active methylene compounds.
  - Tautomerism causes one of the carbonyls to switch to its enol form, which contains an -OH group that hydrogen bonds with the other carbonyl C=O group on the same molecule. This is called intramolecular (internal) hydrogen bonding.
- keto-enol tautomerism

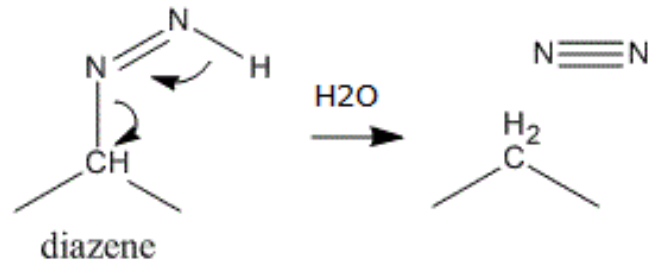


-
  - Enol form is the one with the alcohol.
  - Keto form is the one with the ketone.
  - Keto form is more stable, it is the predominant form.
- organometallic reagents



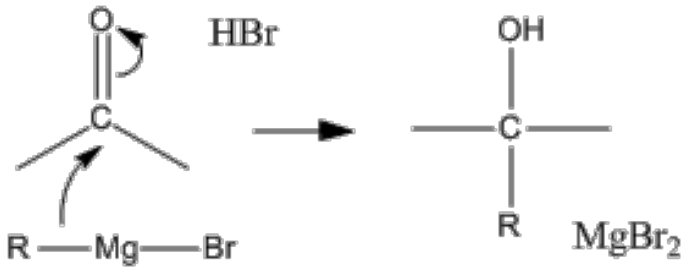
-
  - Organometallic compounds makes R^-, which attacks C=O to make R-C-OH.
  - The purpose of organometallic compounds is to make carbon-carbon bonds.
  - R-X + Li -> R-Li (byproduct: LiX)
  - R-X + BuLi -> R-Li (byproduct: Bu-X)
  - R-Li + C=O -> R-C-OH
- Wolff-Kishner reaction: reduces C=O to $-CH_2-$





-
  - C=O + NH_2NH_2 -> $-CH_2-$ + N_2

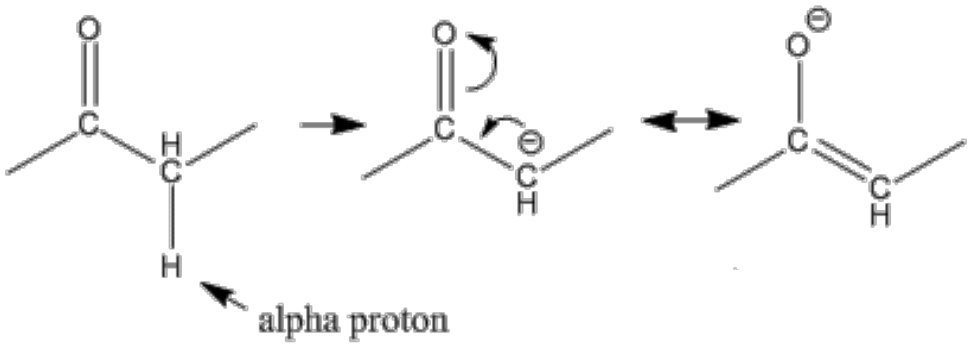
- Grignard reagents



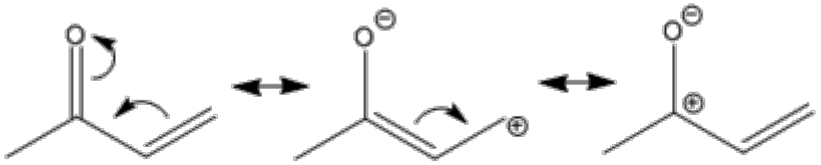
-
    - Grignard reagents are just like organometallic reagents, they produce R^-.
    - R-X + Mg -> R-Mg-X
    - R-Mg-X + C=O -> R-C-OH

General principles

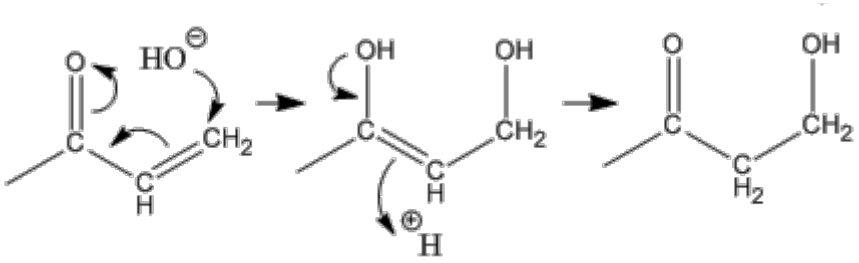
- effect of substituents on reactivity of C=O; steric hindrance: bulky groups on either side of C=O blocks access to the electrophilic carbon, so reactivity goes down.
- acidity of alpha H; carbanions



-
    - Alpha proton is acidic because the resulting carbanion is stabilized by resonance.
- alpha, beta-unsaturated carbonyls - resonance structures

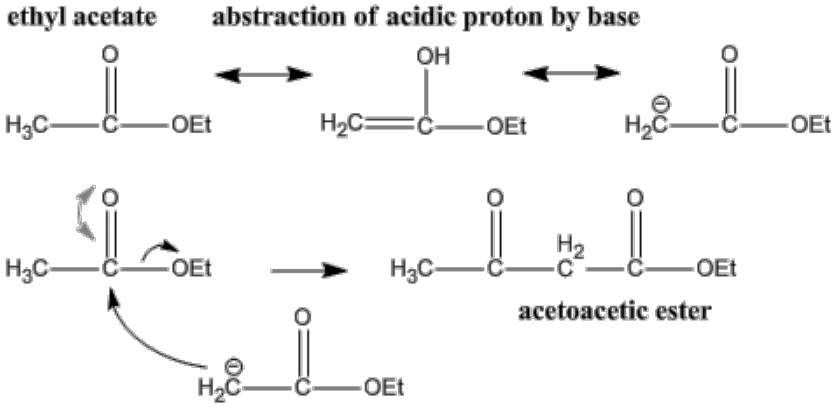


resonance structures of the beta unsaturated carbonyl

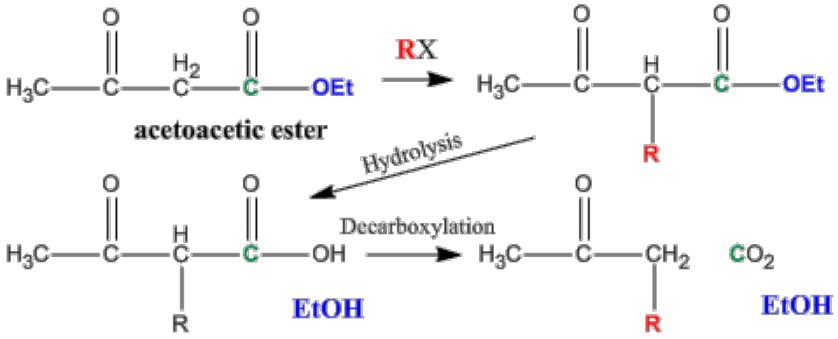


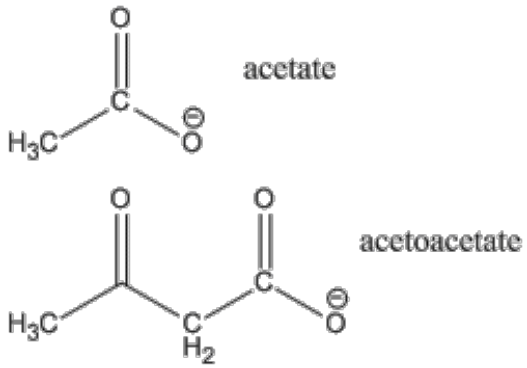
- nucleophilic attack on the beta unsaturated carbonyl
    - α,β-unsaturated carbonyl + nucleophile -> addition of the nucleophile at the β position.
    - Nucleophile attacks the beta carbon, pushing the α,β-unsaturated carbonyl into the enol form, which tautomerizes to the original carbonyl.

Synthesizing Acetoacetic Ester
(Acetoacetic Ester Condensation)



Acetoacetic Ester Synthesis
(Using Acetoacetic Ester to Synthesize)

- 

- 

    - Acetoacetic ester is synthesized by Claisen condensation of ethyl acetate in a process called acetoacetic ester condensation
        - 2 x ethylacetate → ethyl acetoacetate
        - acetoacetic ester = β-keto ester

        - Claisen condensation = 1. alpha proton of ester leaves, 2. the resulting carbanion attacks the carbonyl group of another ester molecule, 3. Carbonyl group reforms and kicks off the alcohol group.

    - "Acetoacetic ester synthesis" is a reaction where acetoacetic ester is used to synthesize a new ketone.

        1. Acidic alpha proton comes off, resulting carbanion attacks new R group.

        2. Hydrolysis of ester turns it into a β-keto carboxylic acid.

        3. β-keto acids undergo decarboxylation because the β-keto group stabilizes the resulting carbanion via enol formation. Enol converts back to keto form, and the net result of this reaction is that an R group is made to attach to the α carbon of acetone.

Oxygen Containing Compounds - Carboxylic Acids

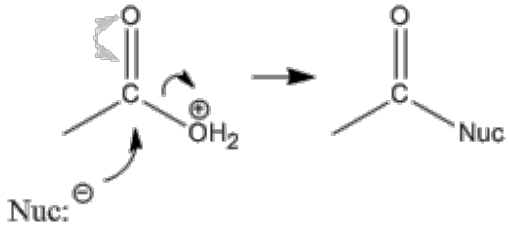
Description

- nomenclature
    - Suffix: -oic acid, carboxylic acid, -dioic acid.
- physical properties and solubility
    - High boiling point due to hydrogen bonding.
    - Soluble in water.
- infrared absorption
    - C=O at 1700 cm^{-1}
    - -OH at 3100 cm^{-1}

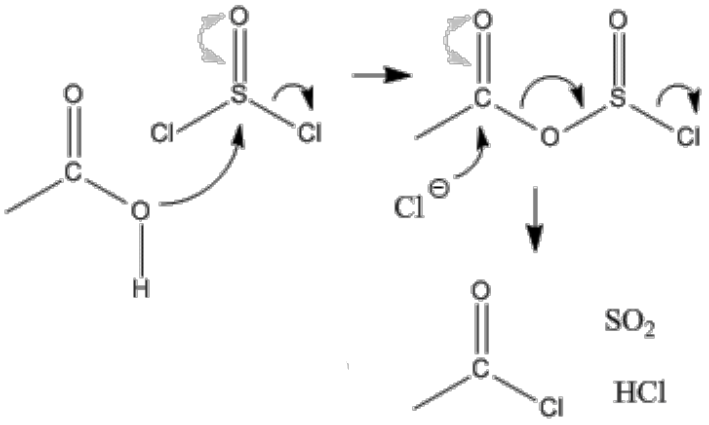
Important reactions

- carboxyl group reactions
    - nucleophilic attack

Nucleophilic attack on COOH

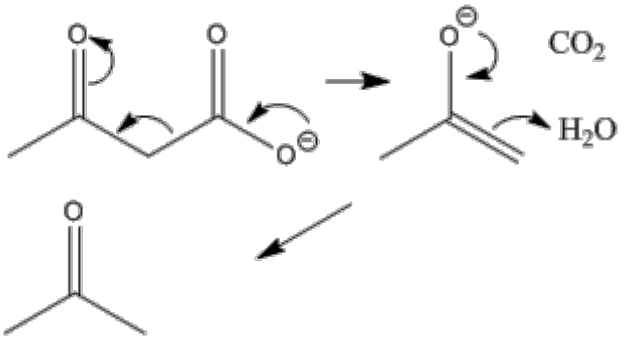


Nucleophilic attack by COOH

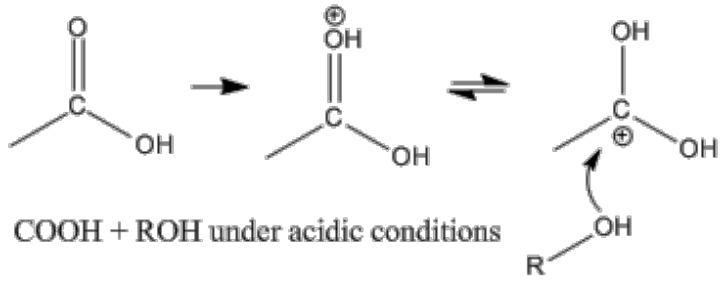


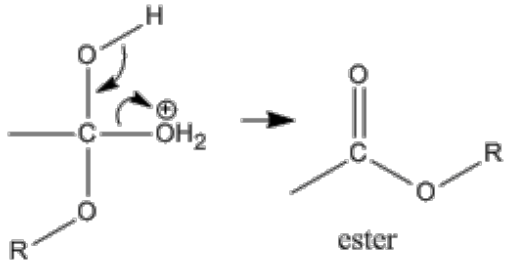
- Nucleophilic attack occurs on the electrophilic carbon of C=O.
- Nucleophilic attack occurs by the nucleophilic oxygen of COOH.

- reduction
  - $LiAlH_4$: COOH -> alcohol.
- decarboxylation: occurs for beta-keto acids

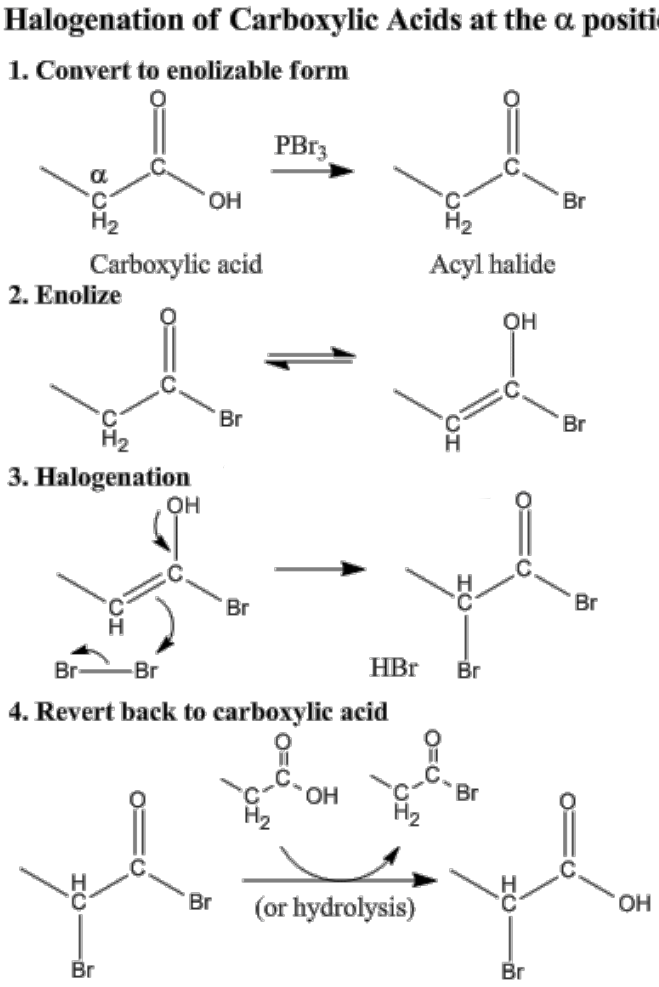


- esterification: COOH + ROH under acidic conditions = ester.





- reactions at 2 position
  - halogenation: RCOOH + X_2 -> halogenation at the alpha carbon (2 position).

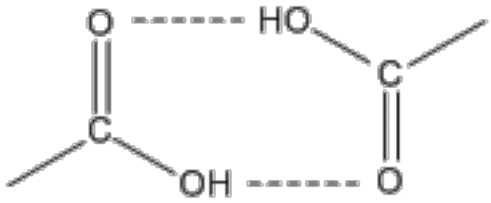
- 

- substitution reactions: RCOOH + E^+ -> substitution at the alpha carbon (2 position).
    1. Carboxylic acid converted to Acyl Halide, which can enolize.
    2. Acyl Halide tautomerizes to its enol form by abstraction of acidic alpha hydrogen.
    3. Halogen (or some other E^+) gets attacked by alpha position.
    4. Revert back to carboxylic acid. The net effect is that the alpha H get substituted by an electrophile.

General principles

- H bonding: COOH has high boiling point because of H bonding.

- dimerization: Hydrogen bonding causes dimerization of carboxylic acids.



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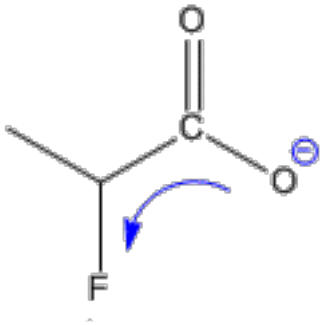
- acidity of the carboxyl group: pKa of COOH is about 5. pKa of H^+ is 0 while the pKa of water is 16. So, COOH can be classified as a weak acid. Vinegar is dilute acetic acid, which is CH_3COOH.

- inductive effect of substituents: electron withdrawing groups makes the acid stronger.



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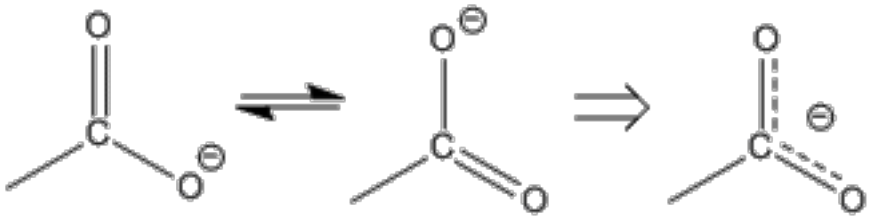
    - electron withdrawing groups attached to positions close to the COOH helps to distribute the charge of the COO^- and stabilize it.
    - A more stabilized carboxylate ion makes a stronger acid.

- resonance stability of carboxylate anion: the reason why COOH is a good acid is because the conjugate base (carboxylate ion) is stabilized by resonance.



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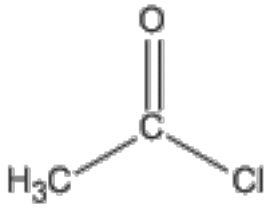
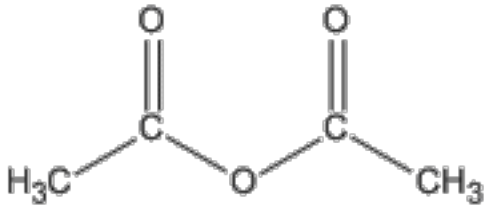
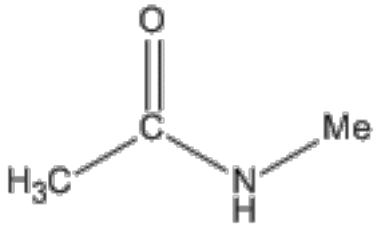
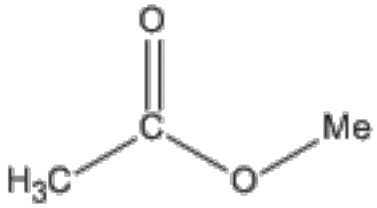
Acid Derivatives

Description

- nomenclature:

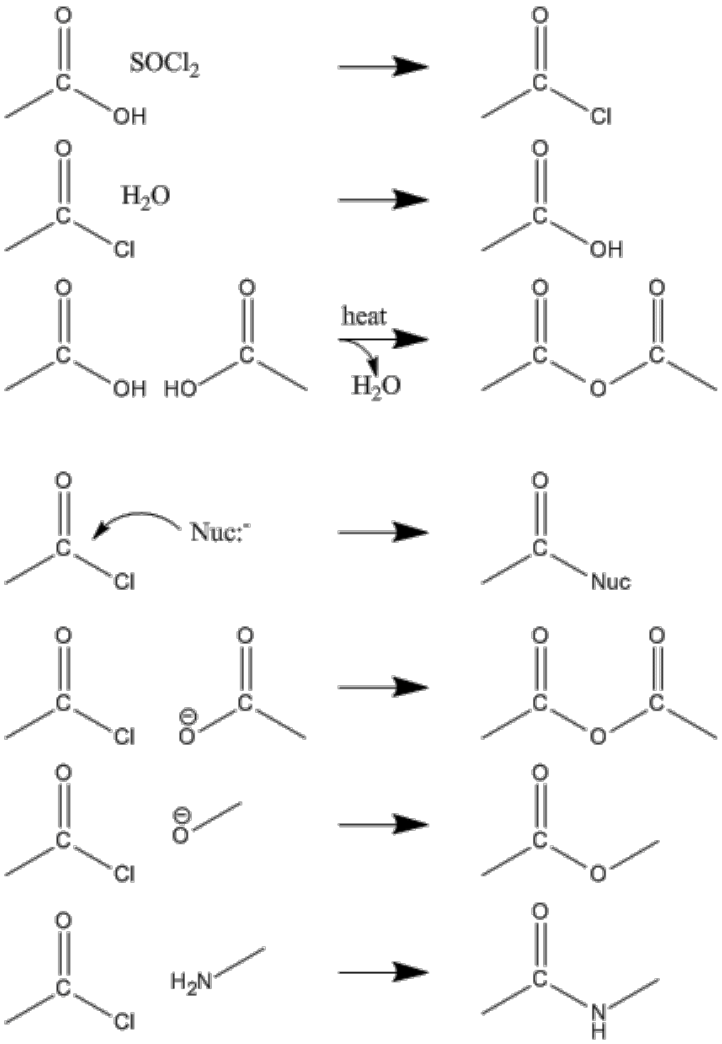
•	suffix	example
Acid chlorides	-oyl chloride	ethanoyl chloride 
Anhydrides	-oic anhydride	ethanoic anhydride 
Amides	-amide	N-methyl ethanamide 
Esters	-oate	methyl ethanoate 

-
- physical properties
    - C=O bond is polar, so there are dipole-dipole interactions.

    - No hydrogen bond exists in acid chlorides, anhydrides, or esters unless there is an -OH group somewhere.
    - Amides can hydrogen bond because of the N-H group. In fact, hydrogen bonding involving the amide backbone of polypeptides form the secondary structure of proteins.
    - Amides have higher boiling points than the other acid derivatives.
    - Acid derivatives have high boiling points than alkanes because of the C=O dipole interactions.
- infrared absorption
    - Acid chloride: the C=O will show up at greater than 1700 cm^{-1}, pretty close to 1800 cm^{-1}
    - Anhydride: the double C=O doesn't show up as a single band. Instead, 2 bands shows up between 1700 cm^{-1} and 1800 cm^{-1}.
    - Amide: the N-H shows up around 3300 cm^{-1}, the C=O shows up at 1700 cm^{-1}
    - Ester: C=O group shows up at 1700 cm^{-1}. The C-O ether stretch shows up around 1200 cm^{-1}

Important reactions

- preparation of acid derivatives
    - Carboxylic acid + $SOCl_2$ → Acid chloride.
    - Carboxylic acid + carboxylic acid + heat → Anhydride.
    - Acid chloride + carboxylic acid + base → Anhydride.
    - Acid chloride + alcohol + base → Ester.
    - Acid chloride + amine → Amide.
    - Acid chloride + water → Carboxylic acid.

- 

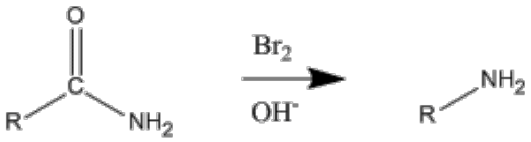
- nucleophilic substitution: Nucleophile attacks the carbon center of the C=O group.

- 

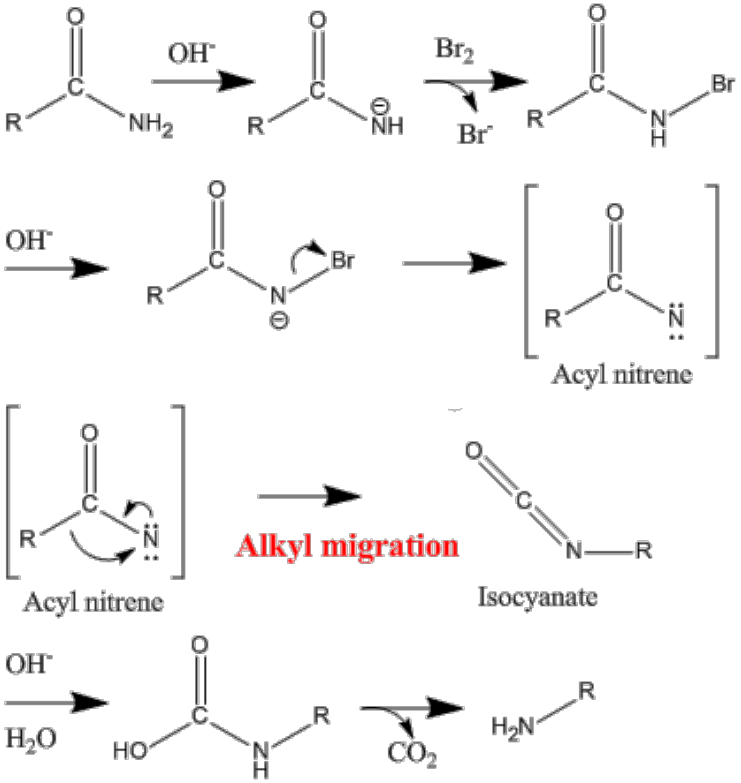
X = Cl > anhydride > ester > amide

- Hofmann rearrangement: Hofmann rearrangement takes away the C=O of an amide. The alkyl migration is basically how the -R group on the other side of the C=O migrates and attaches itself to the nitrogen atom. See figure below for detailed mechanism of the Hofmann degradation and how the aryl group migrates.

Hofmann Degradation of Amides

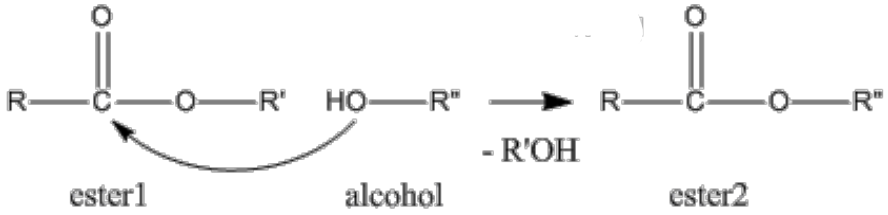


Migration of the Alkyl group (Hofmann mechanism)

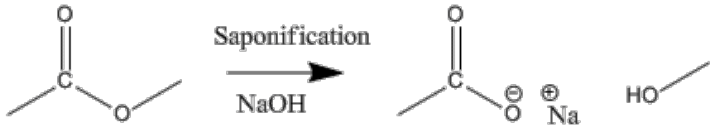


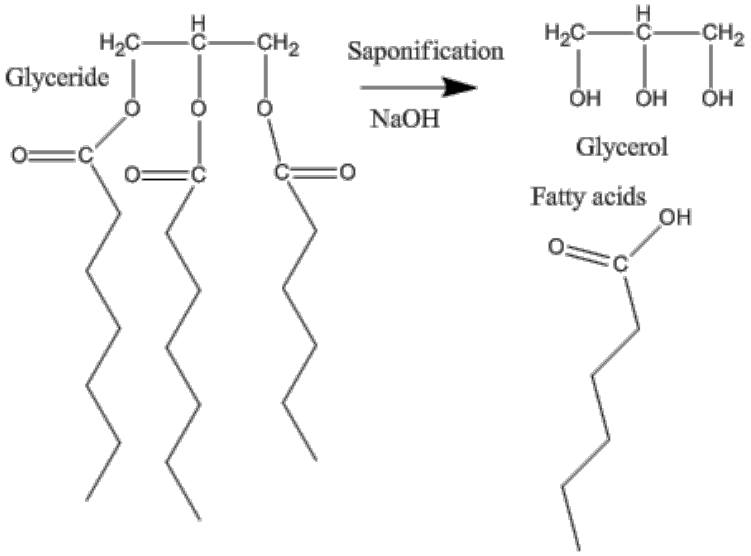
- transesterification: Ester + alcohol → new ester.

Transesterification

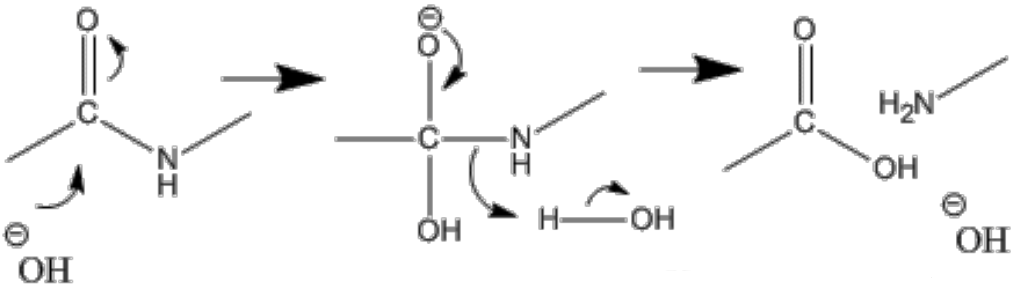


- hydrolysis of fats and glycerides (saponification): saponification is basically the hydrolysis of an ester in base.





- hydrolysis of amides: the leaving group is not NR_2^-, it is the neutral amine.



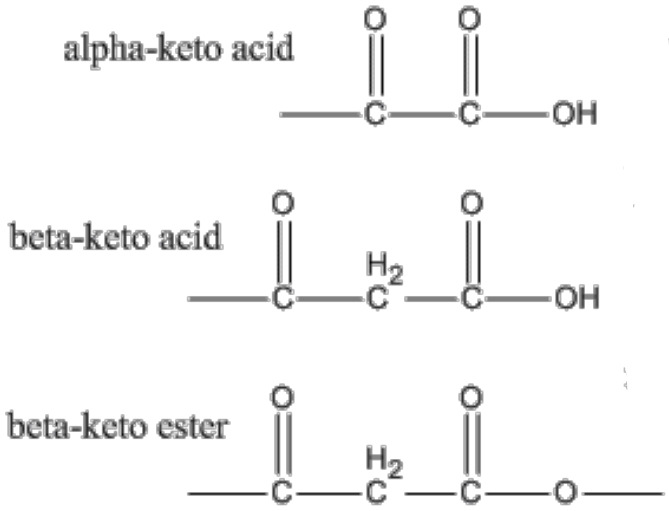
General principles

- relative reactivity of acid derivatives: Acid chloride > Anhydride > Esters > Amides
    - Acid halides are the most reactive derivatives because halides are very good leaving groups.
    - Amides are the most stable derivatives because NR_2^- is a terrible leaving group. Also, the C-N bond has a partial double bond characteristic. Proteins are made of peptide bonds, and they are very stable.

- steric effects: bulky groups around the C=O group helps protect the carbon center from nucleophilic attack.
- electronic effects: groups that can redistribute and stabilize negative charges are good leaving groups. For example, the anhydride has a good leaving group - the carboxylate ion - because the COO^- can redistribute the negative charge to both oxygens via resonance.
- strain (e.g., beta-lactams)
    - Amides have a double bond characteristic between the carbon and nitrogen. This means that the C-N bond can not rotate.
    - Normally, the sigma bonds in a ring rotate as to achieve the most stable conformation, but this can't occur for the C-N bond if the ring contains an amide.
    - Because C-N bond in an amide can not rotate, rings that contain amides have higher strain.
    - An example of this is the beta-lactam, which is basically a 4 membered ring with 1 amide in it.

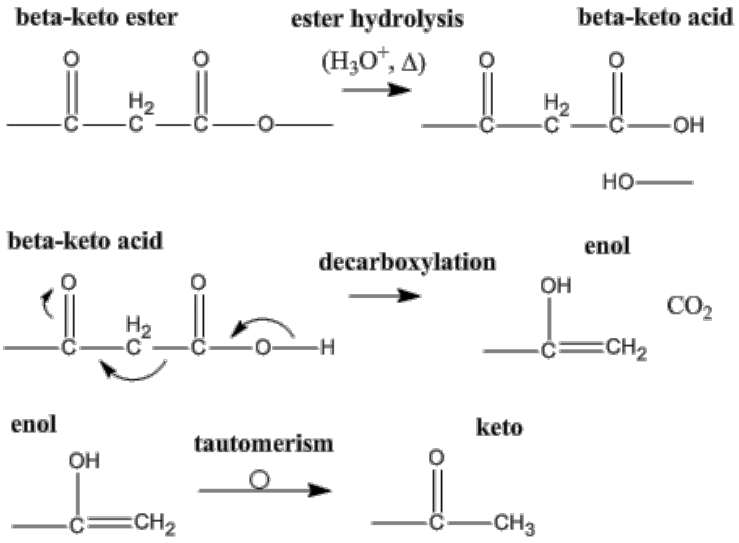
Oxygen Containing Compounds - Keto Acids and Esters

Description; nomenclature

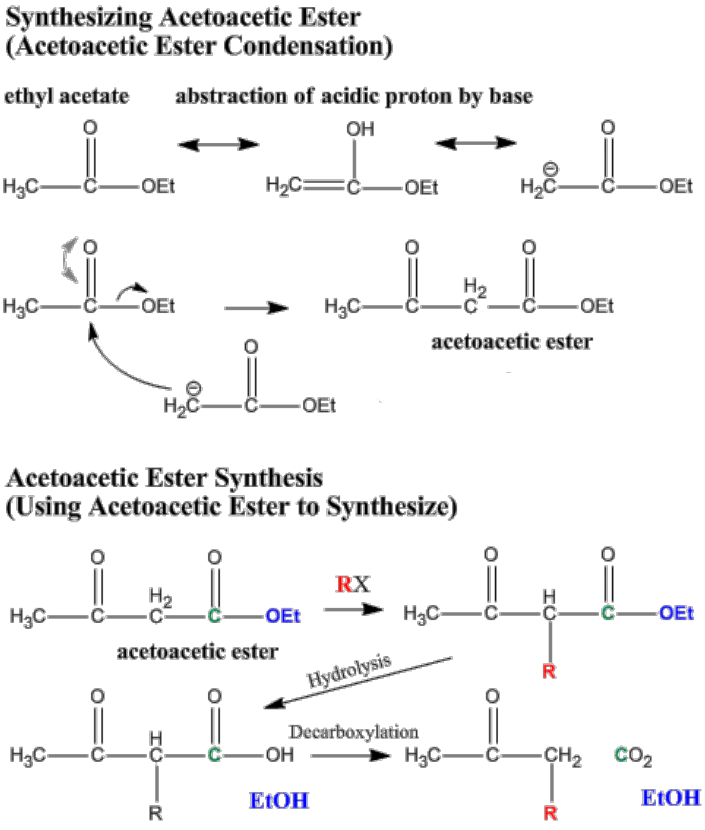


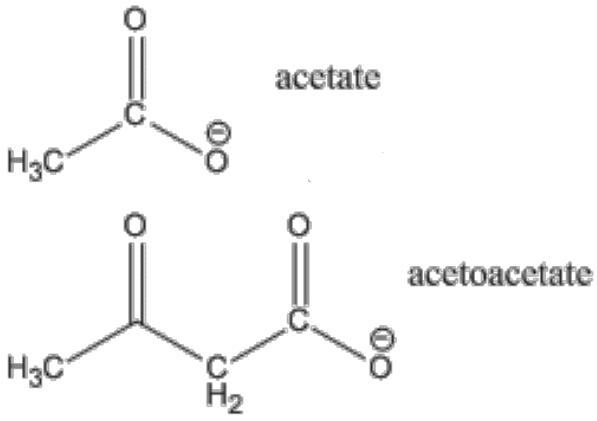
- α-keto acid = 2-oxo acid. For example: α-ketopropanoic acid = 2-oxopropanoic acid
- β-keto acid = 3-oxo acid.
- α-keto ester = 2-oxo ester.
- β-keto ester = 3-oxo ester. For example: methyl β-ketobutanoate = methyl 3-oxobutanoate

Important reactions

- decarboxylation
  - 

  - beta-keto esters → beta-keto acids → enols → ketos
  - decarboxylation of beta-keto acids is facile because the enol stabilizes the reaction intermediate.

- acetoacetic ester synthesis
  - 

  - 

  - Acetoacetic ester is synthesized by Claisen condensation of ethyl acetate in a process called acetoacetic ester condensation
    - 2 x ethylacetate → ethyl acetoacetate
    - acetoacetic ester = β-keto ester
  - "Acetoacetic ester synthesis" is a reaction where acetoacetic ester is used to synthesize a new ketone.

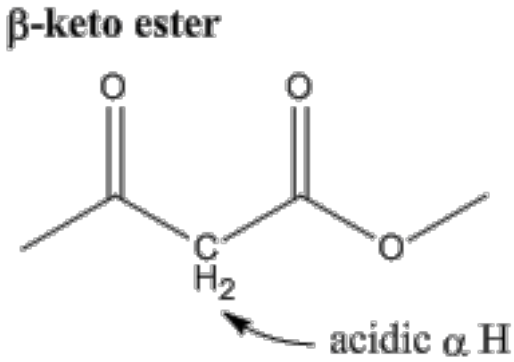
1. Acidic alpha proton comes off, resulting carbanion attacks new R group.

2. Hydrolysis of ester turns it into a β-keto carboxylic acid.

3. β-keto acids undergo decarboxylation because the β-keto group stabilizes the resulting carbanion via enol formation. Enol converts back to keto form, and the net result of this reaction is that an R group is made to attach to the α carbon of acetone.

General principles

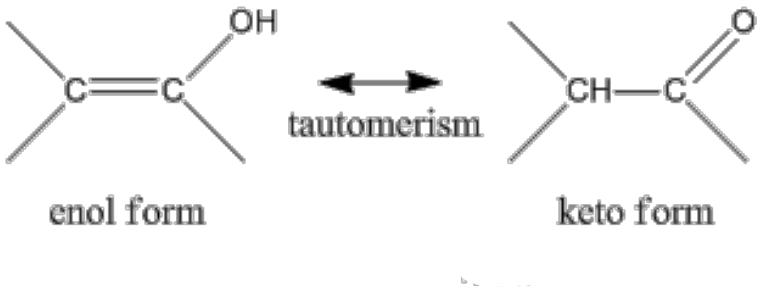
- acidity of alpha hydrogen and beta-keto ester



  - Any hydrogen alpha to (adjacent to) a carbonyl group is more acidic than a regular hydrogen. The alpha hydrogen of a beta-keto ester is even more acidic because it's adjacent to 2 carbonyl groups.

  - The reason for the acidity is the stabilization of the deprotonated species by the enolate ion resonance structures.

- keto-enol tautomerism

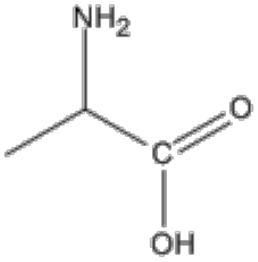


  - enol ends with an "ol" so it has an alcohol group.

- keto is a ketone group.
- enol → keto because the keto form is more stable.
- You can change a ketone to an enolate ion by abstracting the alpha hydrogen. However, that's not tautomerism.

Amine

- Description
  - nomenclature
    - Prefix: amino-
    - For example, 2-aminopropanoic acid.

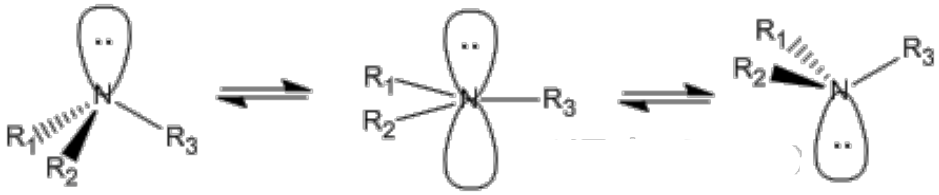


2-aminopropanoic acid

    - Suffix: -amine.
    - For example, propanamine.

propanamine

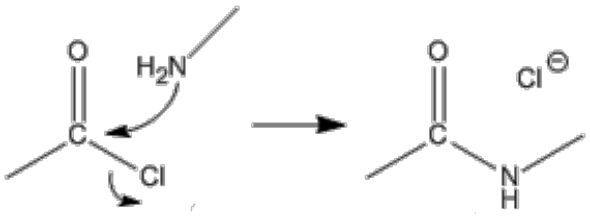
  - stereochemistry and physical properties
    -



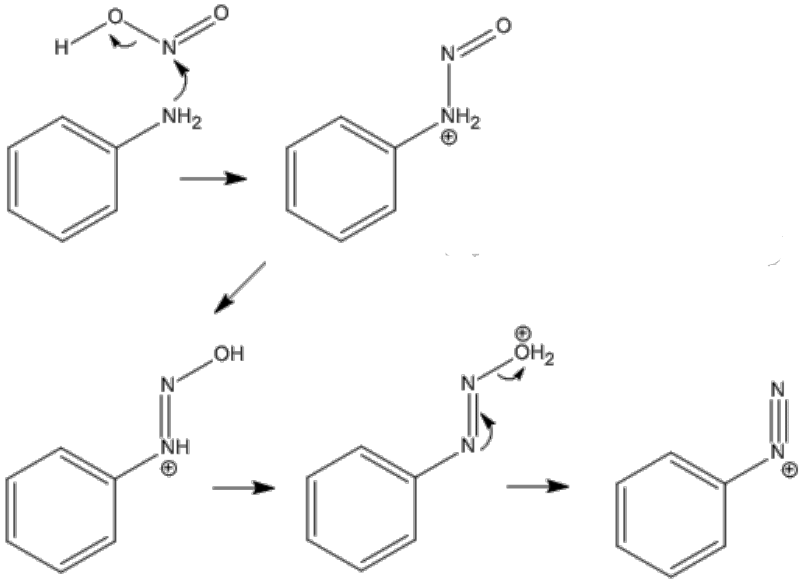
    - 3° amines can be chiral. But they are always racemic because of spontaneous inversions at room temperature.
    - Even protonated 3° amines undergo inversion because the proton comes on and off in an acid-base equilibrium.
    - 4° amines can be chiral and they stay chiral because they don't undergo inversion.
  - infrared absorption

        - primary amines = R-NH_2 = 2 N-H bonds = 2 peaks around 3300 cm^{-1}.
        - secondary amines = R_2-NH = 1 N-H bonds = 1 peak around 3300 cm^{-1}.
        - tertiary amines = R_3-N = no N-H bonds = 0 peak around 3300 cm^{-1}.

- Major reactions
    - amide formation



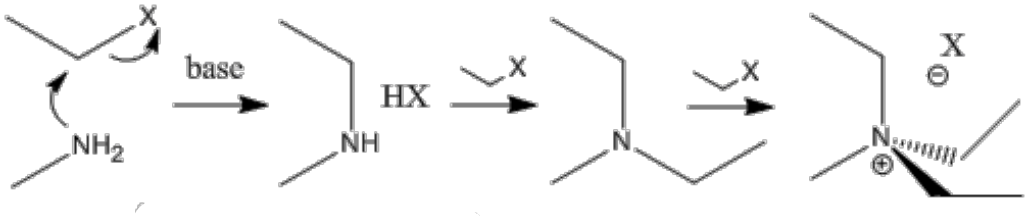
        - Amine + acid derivative with a good leaving group → amide
        - Usually the acide derivative is acyl chloride with chlorine as the leaving group. However, any other good leaving group will work.
        - An important biological amide formation is the peptide bond formation in protein synthesis. Here amine + carboxylic acid → amide. The leaving group is water (not OH^-).
    - reactions with nitrous acid
        - Ar-NH_2 + HONO → Ar-N_2^+ + H_2O + OH^-
        - nitrous acid = HNO_2 = HONO



- The reason why the nitrogen in nitrous acid can be attacked is the following:

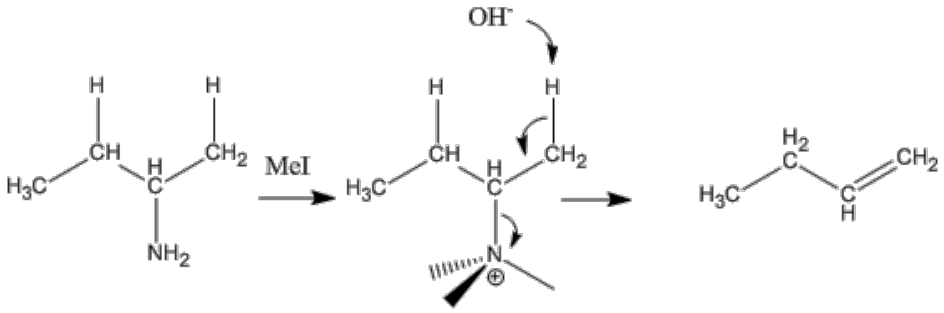
- $HONO \rightarrow NO^+ + OH^-$
- The NO^+ species is the strong electrophile.

- alkylation



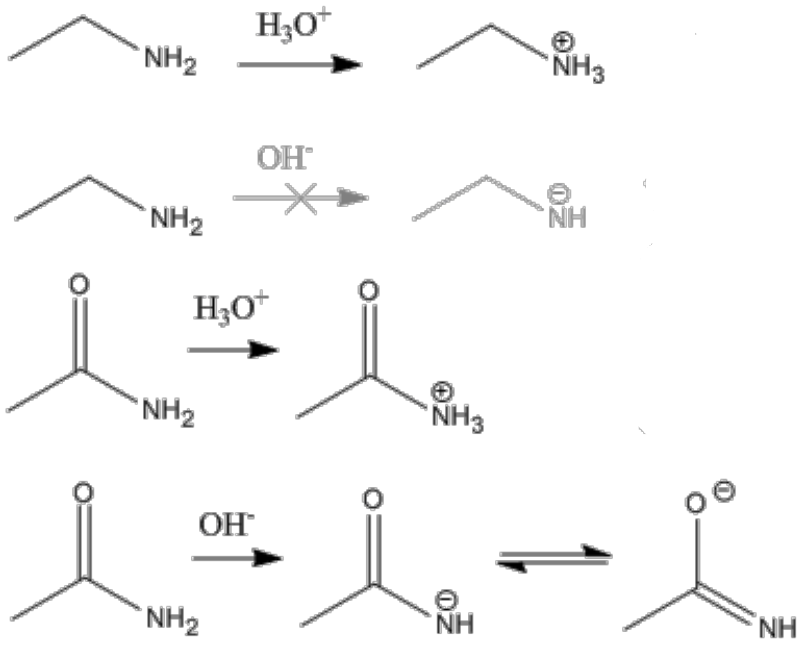
- multiple products formed from polyalkylation.

- Hoffman elimination (Hofmann elimination)



- amine + methyl iodide → exhaustive methylation of the amine → elimination with the methylated amine as leaving group.
- Unlike E1 reactions where the more substituted double bond is formed (Zaitsev), Hofmann elimination forms the less substituted double bond (Hofmann).
- A quick review of regiochemistry:
  - E1 = zaitsev
  - E2 with bulky base = Hofmann
  - Hofmann elimination = Hofmann
- Hoffman and Hofmann mean the same thing.

- General principles
  - basicity

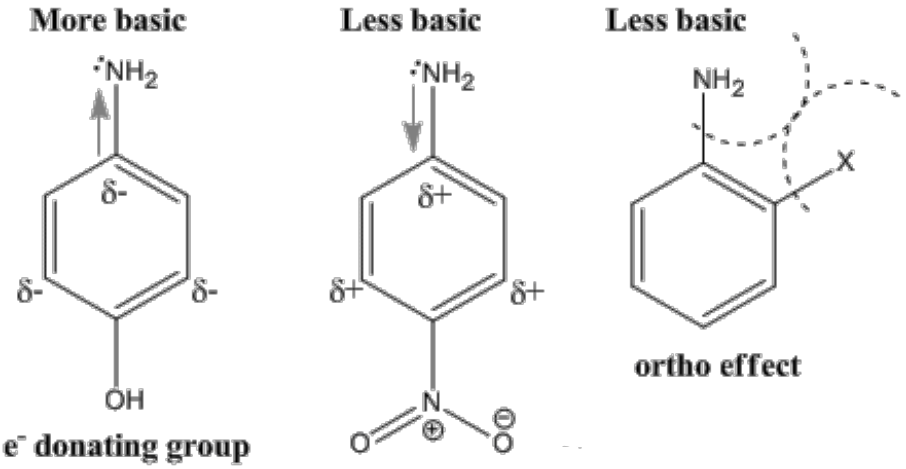


- Amines are basic. They like to gain a proton. R-NH_2 → R-NH_3^+
- It is very difficult for neutral amines to lose a proton.
- An amide, however, can lose a proton much more easily. This is because the carbonyl group next to the nitrogen contributes to a resonance structure that places the negative charge on the oxygen. Thus, the negative charge of the conjugate base is distributed over both nitrogen and oxygen.

- stabilization of adjacent carbonium ions (carbocations)

- The nitrogen of the amine donates its lone electron pair to the adjacent carbonium ion (carbocation).

- effect of substituents on basicity of aromatic amines

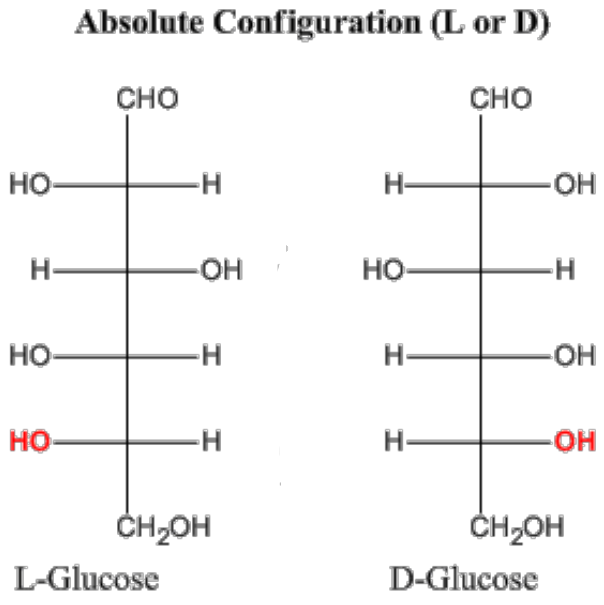


- Aromatic amines are weaker bases than aliphatic amines. This is because the amine donates its electron density to the aromatic ring. Also, the amine forms stable resonance structures with the aromatic ring, which is absent once the amine becomes protonated.
- Electron donating groups on the aromatic amine increase the basicity of aromatic amines. This is because the electron donating groups contribute to the electron density on the nitrogen.
- Electron withdrawing groups on the aromatic amine decrease the basicity of aromatic amines. This is because the electron withdrawing groups steal electron density from the nitrogen.
- Anything ortho to the amine, no matter whether it is electron donating or withdrawing, will decrease the basicity of the aromatic amine. This is because of the ortho effect, which is basically sterics. The protonated amine will have a greater steric interaction with the ortho group, so it will be less stable.

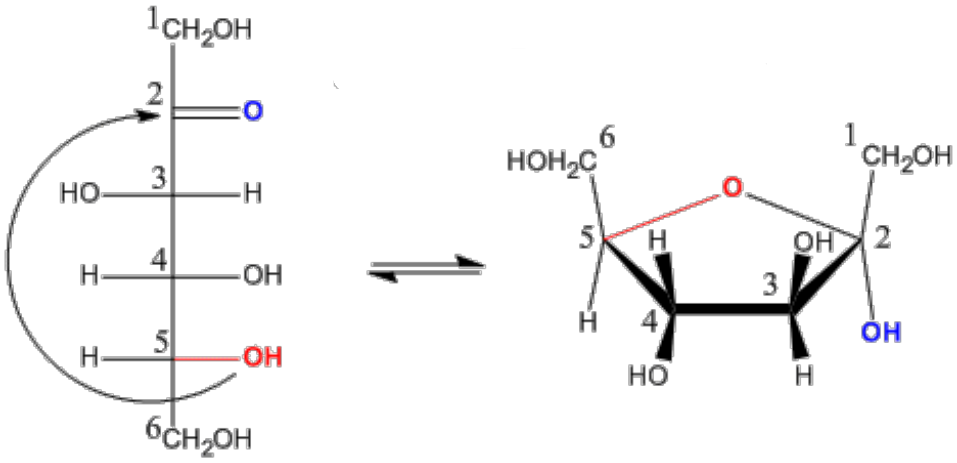
Biological Molecules - Carbohydrates

Description

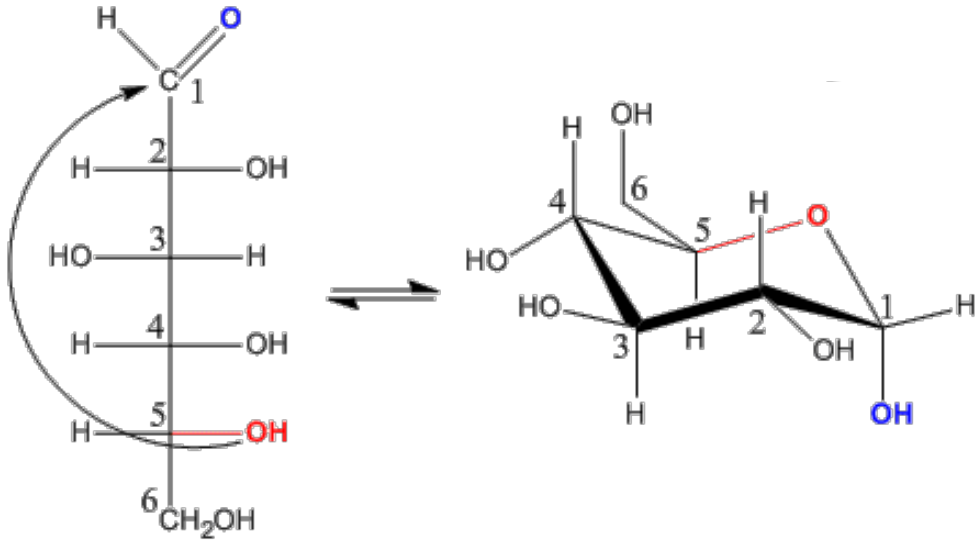
- nomenclature and classification, common names
    - nomenclature
        - Carbohydrate = Sugars, monosaccharides, disaccharides, polysaccharides
        - Prefix:
            - Deoxy = it has an -H in place of an -OH at a certain position.
            - D/L = absolute configuration = assigned based on the chirality of the carbon atom furthest from the carbonyl group.
            - α/β = anomeric configuration.
        - Suffix: all sugars end in -ose.
    - classification
        - aldose = sugars with an aldehyde group.
        - ketose = sugars with a ketone group.
        - pyranose = sugars in a 6 membered ring structure = hexagon shaped. For example, glucopyranose = glucose in a 6 membered ring.
        - furanose = sugars in a 5 membered ring structure = pentagon shaped. For example, fructofuranose = fructose in a 5 membered ring.
        - #ose = sugar with # carbon atoms. For example, hexose = sugar with 6 carbons. Another example: aldopentose = a five-carbon sugar with an aldehyde group.
        - In order to be classified as a carbohydrate, a molecule must have:

        - at least a 3 carbon backbone.
        - an aldehyde or ketone group.
        - at least 2 hydroxyl groups.
    - common names
        - Common names are used so you can say glucose instead of (2R,3S,4R,5R)-2,3,4,5,6-Pentahydroxyhexanal
        - See monosaccharides, disaccharides and polysaccharides
- absolute configuration
    - 

    - The chiral carbon furthest from the carbonyl group determines the absolute configuration L or D of the sugar.
    - If in the fischer projection, the OH group on the chiral carbon furthest from the carbonyl is pointing left, then it's L. If it's pointing right, then it's D.
    - Note: L and D are enantiomers, not epimers. So, every chiral carbon center inverts. It's just that you assign L and D based on the chiral carbon furthest from the carbonyl.
- cyclic structure and conformations of hexoses

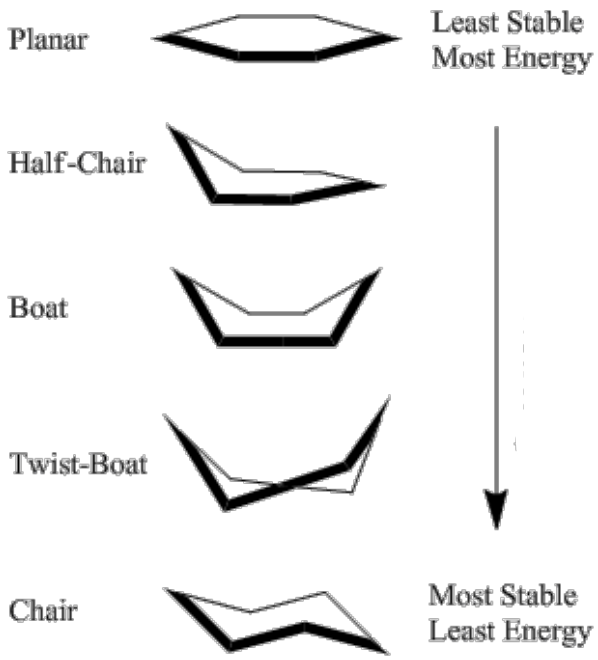


- Fructose forms a furanose when carbon 5 attacks the carbonyl carbon.



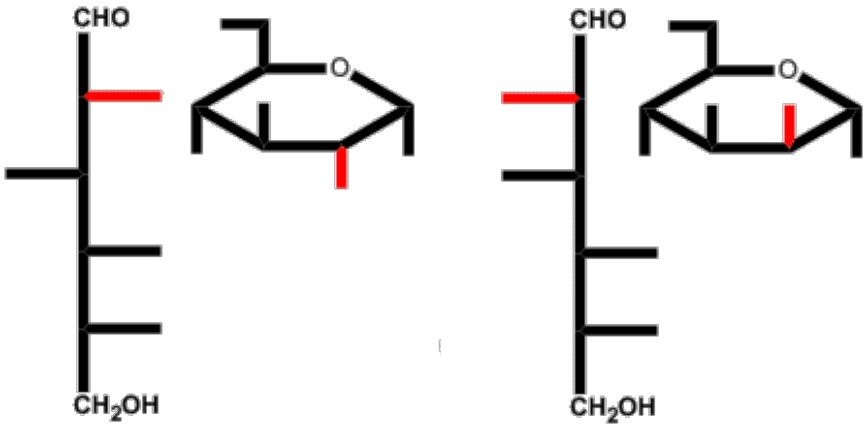
- Glucose forms a pyranose when carbon 5 attacks the carbonyl carbon.
- Convert a Fischer projection to Haworth (cyclic) form
  - -OH groups that are pointing Left on the Fischer becomes Up on the Haworth.
  - -OH groups that are pointing Right on the Fischer becomes Down on the Haworth.

        - The -OH group on the anomeric carbon (the Fischer carbonyl) can be either up (beta) or down (alpha).
        - The CH_2OH group on the absolute configuration carbon (carbon 5) points up for D, and down for L.



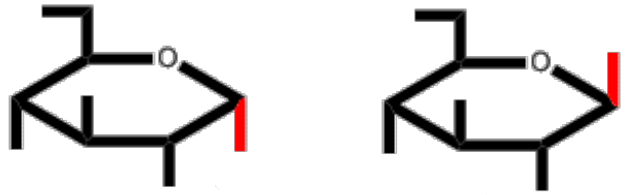
    - In the planar conformation, everything is eclipsed.
    - In the chair conformation, everything is staggered.
    - All the conformations in between are partially eclipsed.
    - The Boat conformation has Flagpole interactions because axial groups attached to the head and tail of the boat clash.
    - The Twist-boat conformation lessens these Flagpole interactions in addition to reducing the number of eclipsed interactions.
- epimers and anomers

- **Epimers**



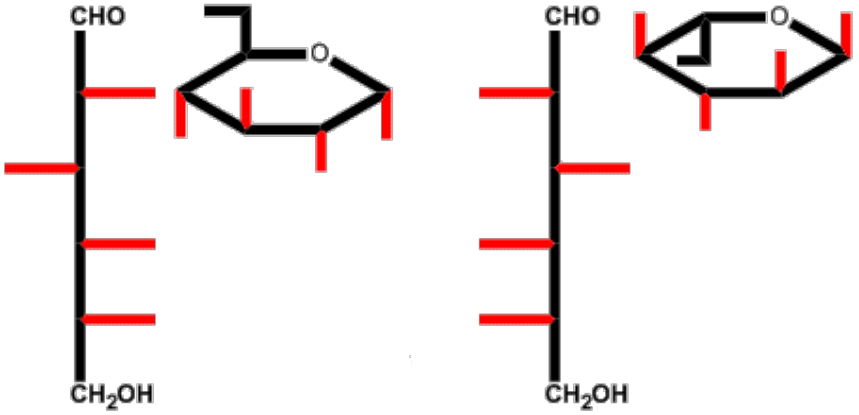
- Epimers = different configuration in just one chiral carbon.

- **Anomers**



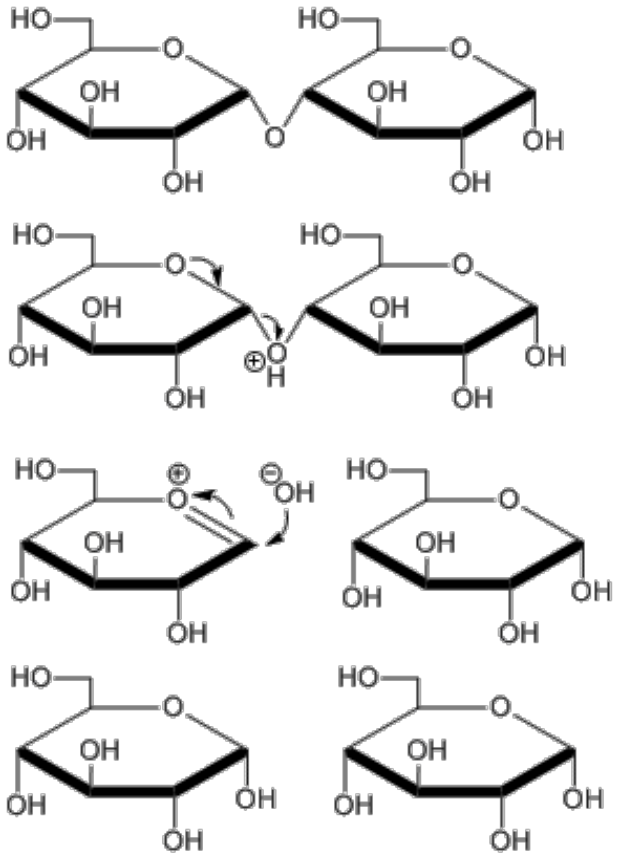
- Anomers = different configuration in the chiral, anomeric carbon when the molecule is in the cyclic form.
- Anomers are simply special types of epimers.
- Epimers are simply special types of diastereomers.
- Don't confuse with enantiomers (D/L configuration), in which everything changes configuration.

- **Enantiomers**



Hydrolysis of the glycoside linkage

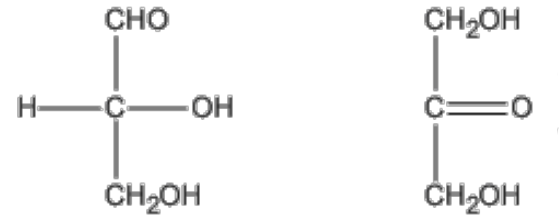
- Glycoside linkage = acetal linkage = linkage involving the hydroxyl group of the anomeric carbon.
- Glycoside linkage can also mean the linkage between the sugar and the base in nucleotides.
- Examples of glycosidic linkages = starch, glycogen, nucleotide.
- Hydrolysis of the glycosidic bond has the same mechanism as hydrolysis of the acetal bond.



- glycoside + H_2O + catalyst → hydrolysis.
- Catalysts include: Amylase for starch and glycosylase for nucleotide.

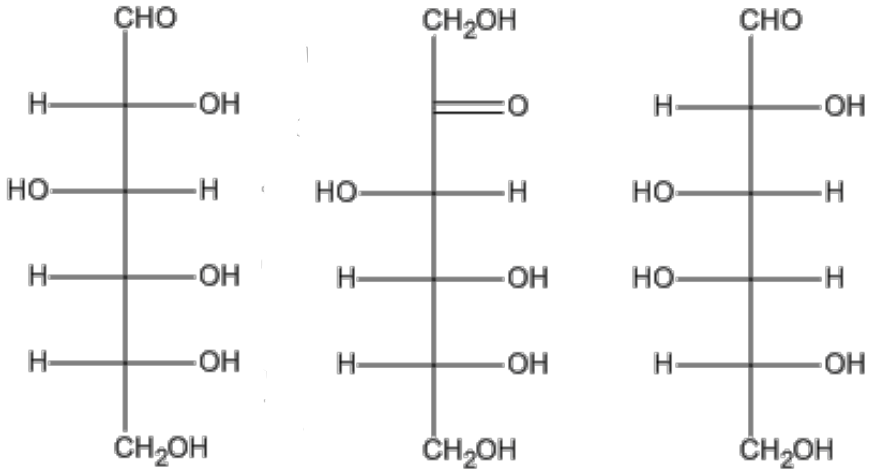
Monosaccharides

- **Smallest Carbohydrates**



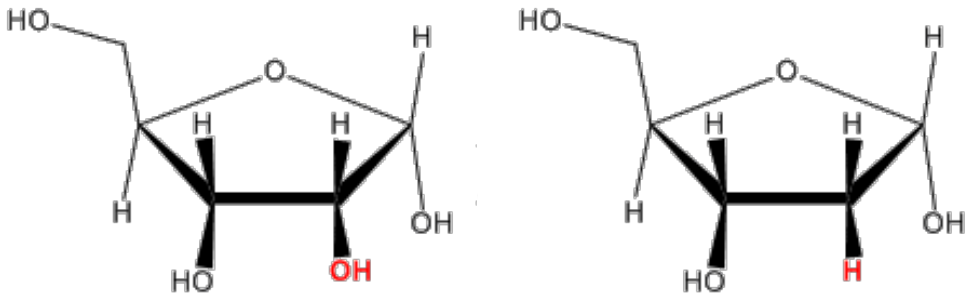
Glyceraldehyde Dihydroxyacetone

- The simplest, smallest carbohydrates are glyceraldehyde and dihydroxyacetone.



Glucose Fructose Galactose

- The 3 common monosaccharides are glucose, fructose, and galactose. Glucose is our blood sugar and the product of photosynthesis. Fructose is the sugar in fruits, and it is sweeter than glucose. Galactose is one of the monomers that make up lactose, which is the sugar in milk; it is less sweet than glucose.

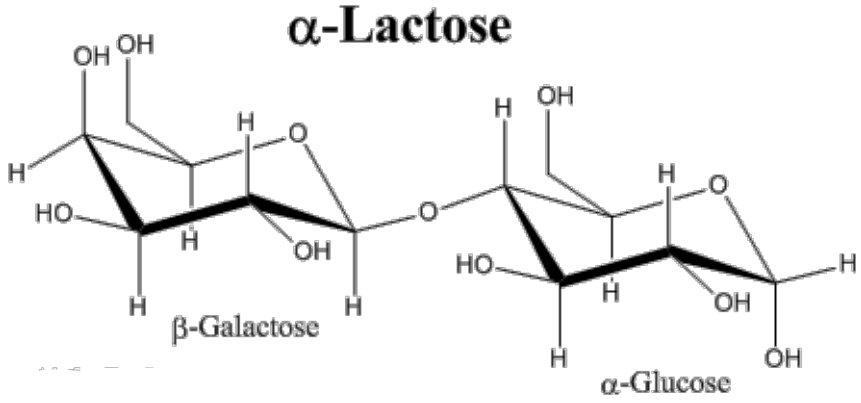


Ribose **Deoxyribose**

- The sugar that make up RNA is ribose, and for DNA it is deoxyribose (More precisely it's 2'-deoxyribose because the difference is at the 2 carbon).

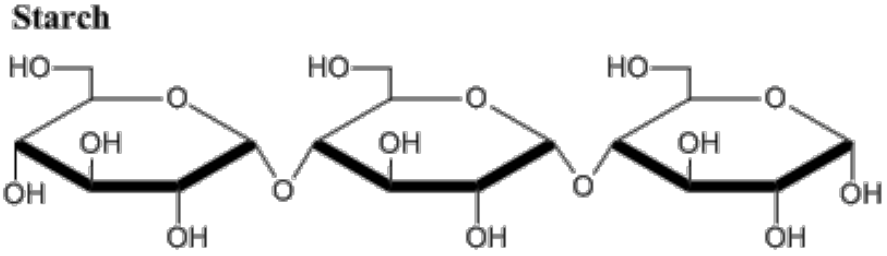
Disaccharides

- Sucrose is a disaccharide made from α-glucose and β-fructose joined at the hydroxyl groups on the anomeric carbons (making acetals). Sucrose is table sugar, the sugar we buy in stores.

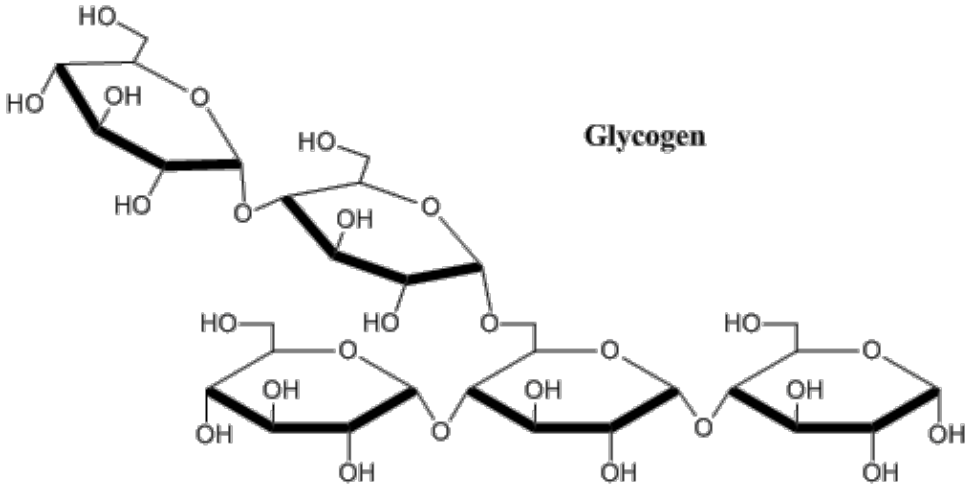


- Lactose is a disaccharide made from β-galactose and α/β-glucose joined by a 1-4 linkage.

Polysaccharides

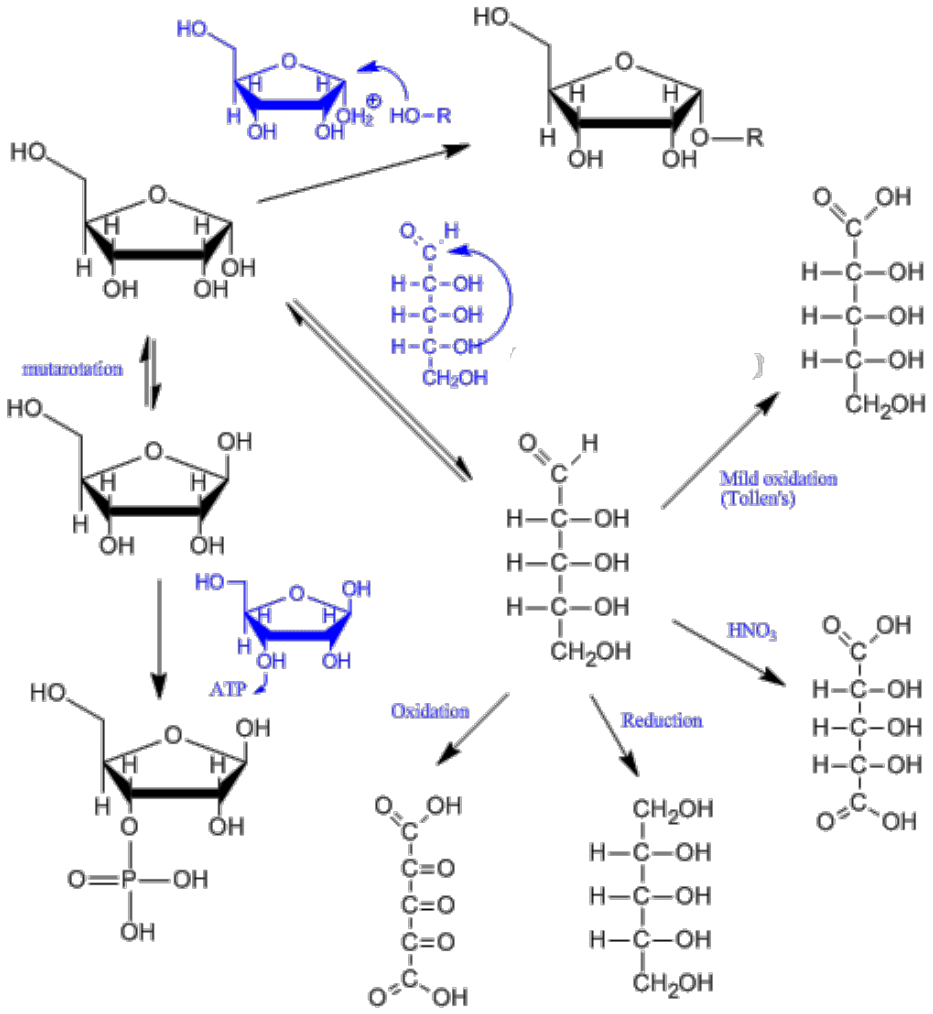


- Starch = glucose molecules joined by α1-4 linkage = energy storage in plants

- 

- Glycogen = same as starch, but with additional α1-6 linkages for branching = energy storage in animals (stored in the liver)

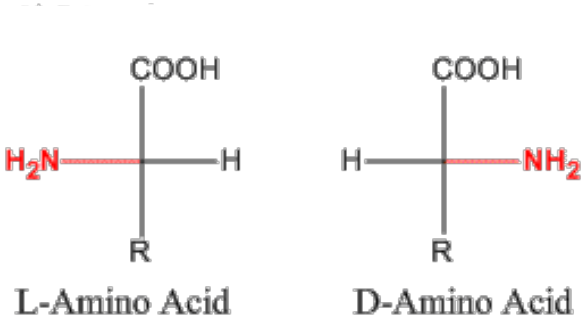
Reactions of Monosaccharides

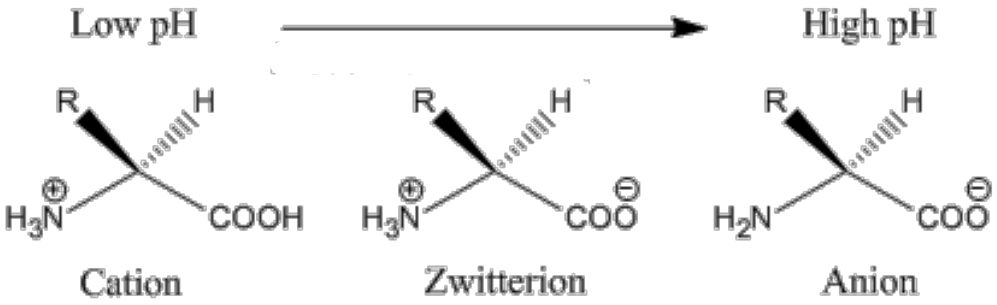


- Hemiacetal formation = -OH attacks carbonyl group = produces ring form.
- Acetal formation = another -OH attack on the same carbonyl group = produces polysaccharides if the -OH is from another monosaccharide.
- Mutarotation = equilibrium between the α and β anomers.
- Strong oxidation turns aldehyde and terminal hydroxyls to carboxylic acids, and other hydroxyls to ketones. The strongest kind of oxidation turns everything to CO_2, and this occurs in cellular respiration.
- Mild oxidation is more selective. Tollens agent (the test for aldoses, silver reagent) selectively oxidizes the aldehyde to carboxylic acid. Nitric acid oxidizes both the aldehyde and the terminal hydroxyl to carboxylic acids, but leaves the other hydroxyls alone.
- Reduction turns monosaccharides into polyalcohols.

Biological Molecules - Amino Acids and Proteins

Amino acid description

- Absolute configuration at the alpha position
  - 

  - L and D is different from R and S. L is not always S, and D is not always R.
  - If the priority of NH2 > COOH > R, then L=S and D=R. For example, L-Alanine = S-Alanine.
  - If the priority of NH2 > R > COOH, then L=R, and D=S. For example, L-Cysteine = R-Cysteine.
  - L-amino acids are the more common in nature, and are the type found in proteins. D-amino acids are less common in nature, and are never found in proteins.
- Amino acids as dipolar ions classification
  - 

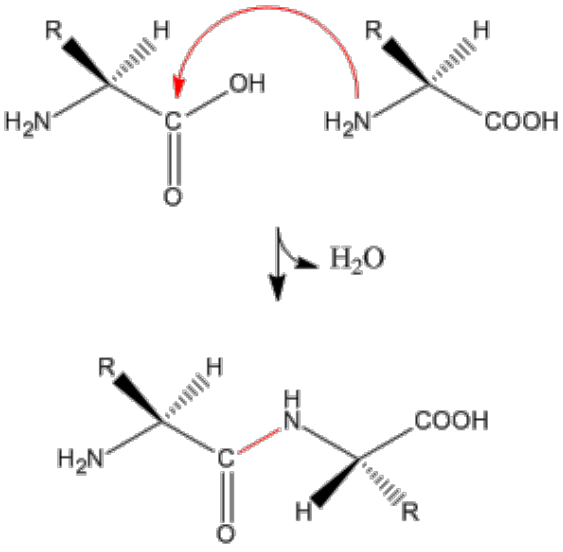
  - At low pH, amino acids exist in the cationic form.
  - At high pH, amino acids exist in the anionic form.

    - At pH = pI, amino acids exist in the zwitterion form, which is overall neutral.

- Classification
    - Acidic or basic
        - If the R group contains carboxylic acid, then it's an acidic amino acid. There are two acidic amino acids: aspartic acid and glutamic acid.
        - If the R group contains an amine group, then it's a basic amino acid. There are three basic amino acids: lysine, arginine, and histidine.
    - Hydrophobic or hydrophilic
        - Hydrophobic: If the R group doesn't contain any of the stuff below.
        - Hydrophilic: If the R group contains acids, bases, amines or alcohols.

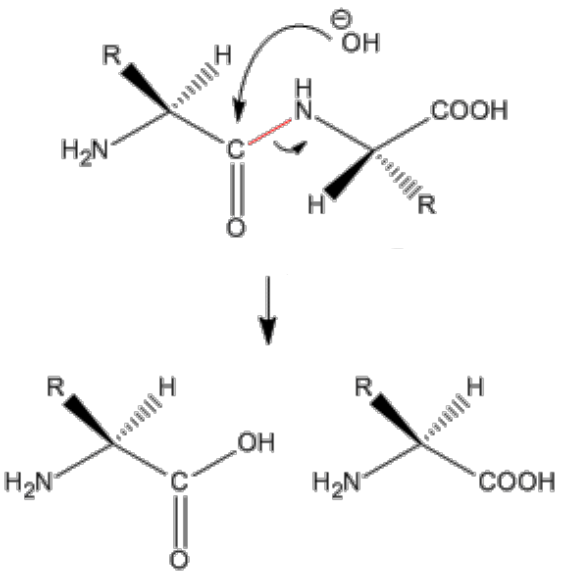
Amino acid reactions

- Sulfur linkage for cysteine and cystine
    - Cysteine = side chain with the thiol group
    - cystine = 2 cysteines forming a disulfide bond
- Peptide linkage



- Peptide bond = amide bond.
- The peptide bond is formed by the amine group attacking the carbonyl carbon.

- Hydrolysis



- The peptide bond is very difficult to hydrolyze. It requires a strong base, or a biological enzyme.

Protein structure

- Primary structure of proteins

    - Primary structure = sequence.
    - The primary structure of proteins is read from the N-terminus to the C-terminus.
- Secondary structure of proteins
    - Secondary structure = repetitive motifs formed by backbone interactions.
    - Backbone interactions = hydrogen bonding between the NH and C=O
    - The two most common secondary structures are α helices and β pleated sheets.
    - The α helix is right-handed, with the R groups sticking outward.
    - In β sheets, R groups stick out above and below the sheet.
- Tertiary structure
    - 3D structure of proteins
    - Caused electrostatic side chain - side chain interactions
- Quaternary structure
    - Separate chains/subunits joining together
    - Caused by covalent disulfide bonding of cysteine side chains

Protein conformational stability

- Folding = chain -> 3D structure
- Many proteins fold spontaneously, some require the assistance of chaperone proteins
- Denaturing = loss of the native 3D structure such that it no longer function
- Extreme heat, salt concentration, or pH denatures proteins

Separation techniques

- Isoelectric point
    - pH at which the molecule is neutral
    - Acidic amino acids and proteins with lots of acidic side chains have have a lower isoelectric point
    - Basic amino acids and proteins with lots of basic side chains have a higher isoelectric point
- Electrophoresis
    - Protein is charged
    - An electric field forces protein to travel through a gel
    - Larger charge = more electrical force = travels faster
    - Smaller protein = squeezes through easier = travels faster
    - Structure plays no role because SDS is usually added to denature the protein

Non-enzymatic protein function

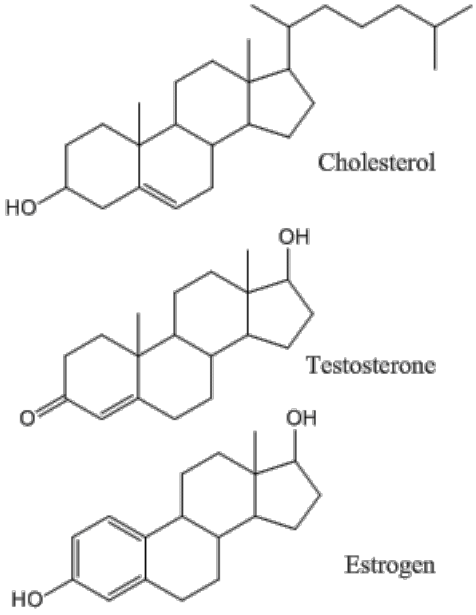
- Binding: the active site binds the substrate
- Stronger binding = lower Kd value
- Stronger binding doesn't necessarily mean a more efficient enzyme (if it binds the substrate and not let go, then it can't catalyze a new substrate)
- Stronger binding = better antibody
- Immune system
    - Antibody = proteins that bind antigen on pathogens, which promote their destruction by the immune system
    - Antigen = proteins expressed by pathogens. They can either directly bind to antibodies, or be presented by antigen presenting cells (such as macrophages and dendritic cells)

    - Complement = proteins that punch holes in cells to be destroyed by the immune system

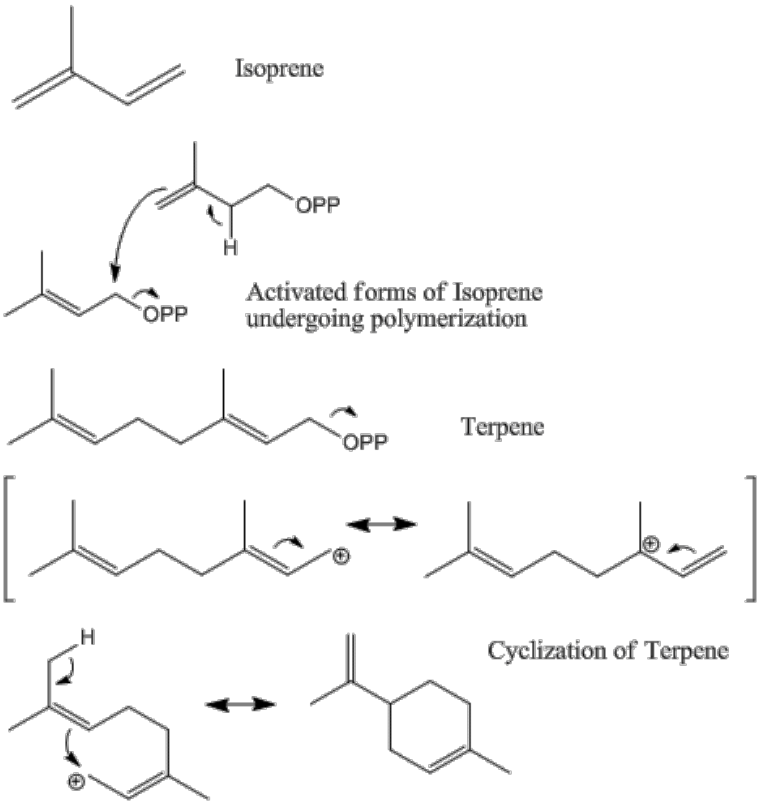
- Motors: uses ATP/GTP as energy to create motion
    - Flagella (bacteria, sperm)
    - ATP synthase (mitochondria, chloroplasts)
    - Motile cilia (trachea)
    - Myosin (muscle)
    - Kinesin/Dynein (intracellular transport)
    - Actin polymerization (Listeria)

Biological Molecules - Lipids

Description; structure

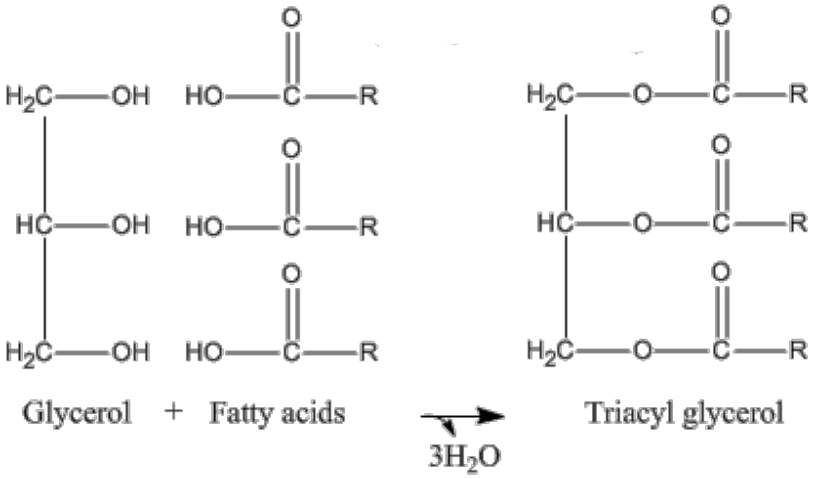
- steroids
  - 

    - Steroids are made from the cyclization of squalene, which is a terpene.
- terpenes



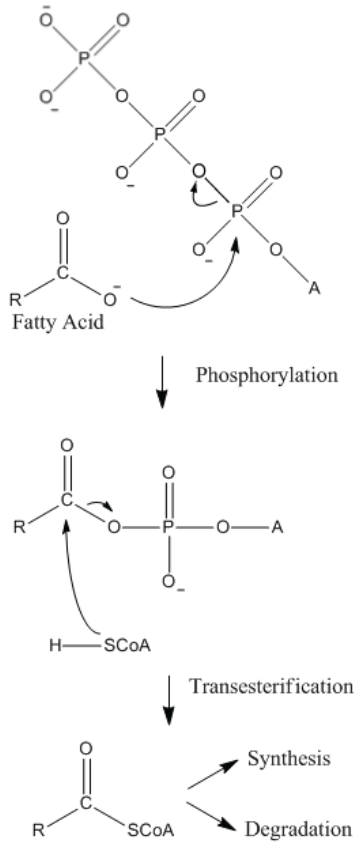
- Terpenes are made from the polymerization of isoprene.
- Terpenes contain double bonds, which gives the molecule the ability to undergo cyclization.
- Squalene, the precursor of steroids, is a terpene that consists of 6 isoprene subunits. A complex self-cyclization reaction converts squalene to make steroids.
- Squalene is classified as a triterpene. Triterpene = 6 isoprene subunits. Diterpene = 4 units. Monoterpene = 2 units.

- triacyl glycerols

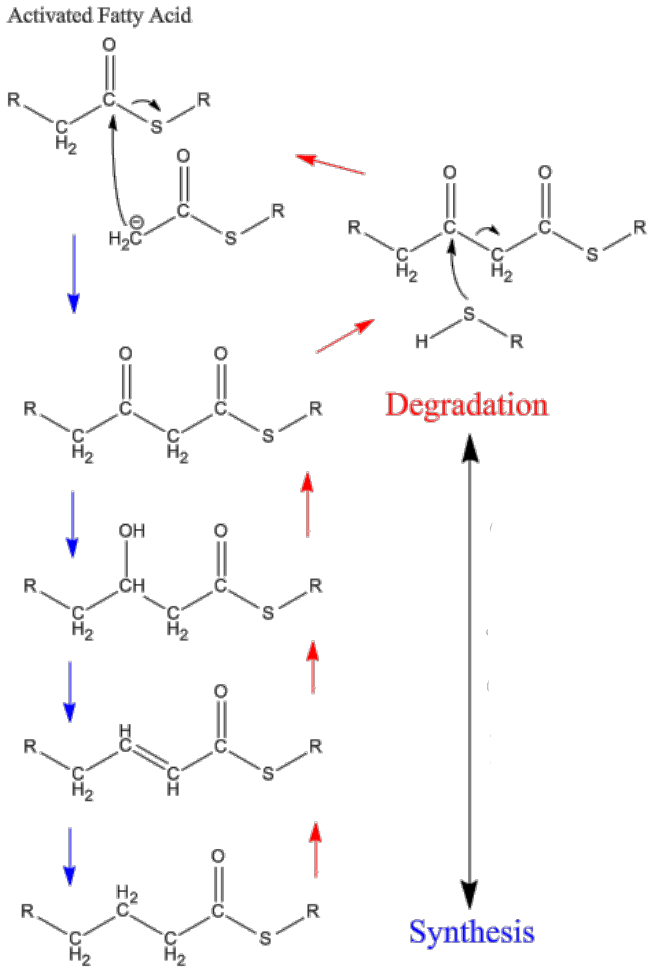


- Glycerol + 3 Fatty acids → Triacyl Glycerol.
- The reverse of triacyl glycerol synthesis is saponification.

- free fatty acids



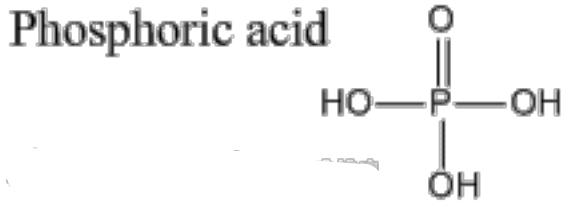
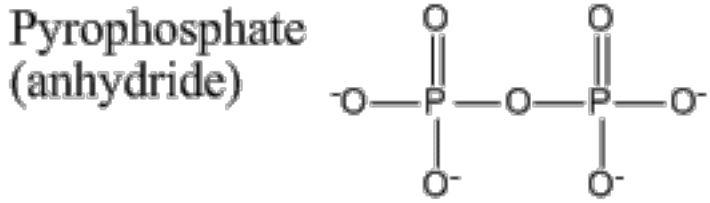
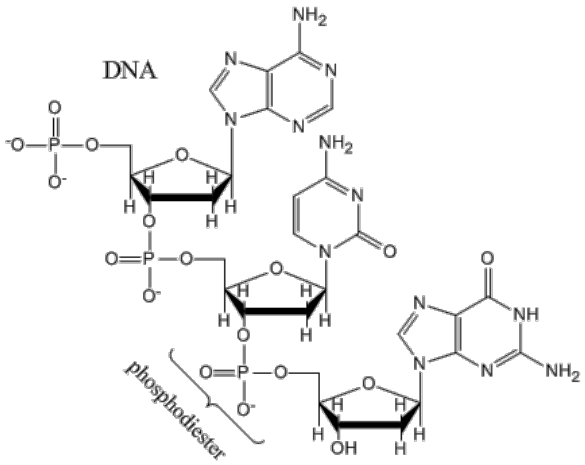
- Fatty acids can undergo phosphorylation and transesterification (commonly called activation by biochemists).

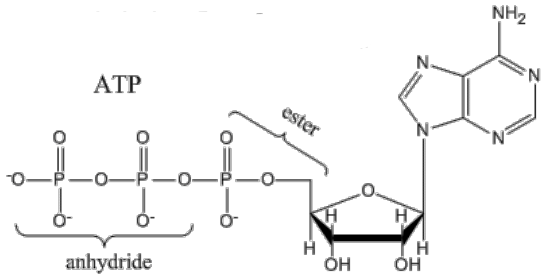
- 

- Fatty acid synthesis occurs via a mechanism similar to the claisen condensation.

Biological Molecules - Phosphorus Compounds

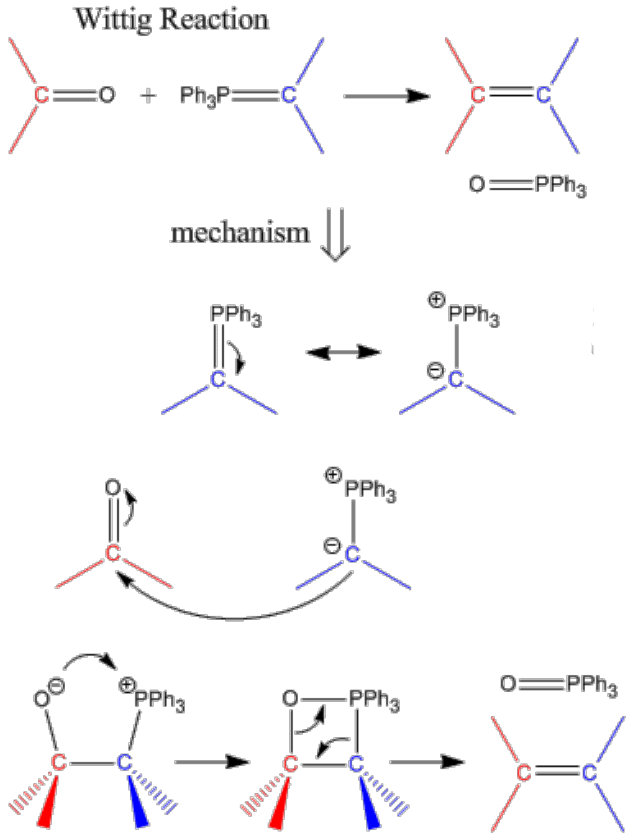
Description

- structure of phosphoric acids (anhydrides and esters)
  - Phosphoric acid 
  - Phosphoric acid = H_3PO_4
  - Pyrophosphate (anhydride) 
  - Pyrophosphate is the simplest phosphoric acid anhydride.
  - 

  - 

- Phosphodiester bonds link together the DNA and RNA backbone.
- Phosphoester bonds link the phosphates to the sugar in ATP.

Important reactions

- Wittig reaction
  - 

  - Carbonyl + Phosphorus Ylide → Alkene
  - The $C_1=O + Ph_3P=C_2 \rightarrow C_1=C_2$
  - Most Wittig reactions are not stereospecific.