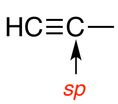
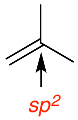
Organic Chemistry I Review

Introductory Material

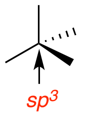
Molecular Shape and Hybridization



Linear
180° bond angle



Trigonal Planar
120° bond angle

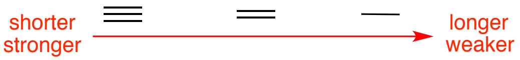


Tetrahedral
109.5° bond angle

Bond Dipoles

A bond dipole points from a less electronegative atom to a more electronegative atom.
Electronegativity increases diagonally up the periodic table from Fr to F.
An atom with more s-character is more electronegative.

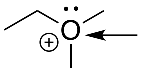
Bond Length & Bond Strength



For the atoms joined in a bond, increasing s-character corresponds to a stronger & shorter bond.

Formal Charge

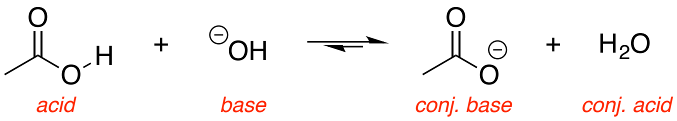
$$\boxed{FC = \text{Group \#} - \text{\# Bonds} - \text{\# non-bonding e-}}$$



FC = 6 - 3 - 2 = +1

Acids and Bases

More acidic molecules have more stable conjugate bases.
As acidity increases, pKa decreases.
Acid/Base Reactions lie to the side of the more stable conjugate base and weaker acid.

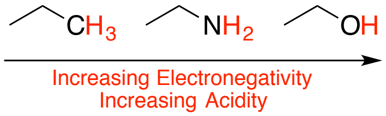


Rxn lies to the right. Water is the weaker acid. The conjugate base is more stable than the base.

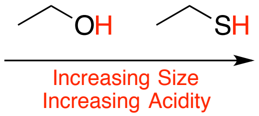
Factors that Stabilize the Conjugate Base

1) Atom Effect

Atoms in the same row: A negative charge is more stable if it is on a more e-neg atom

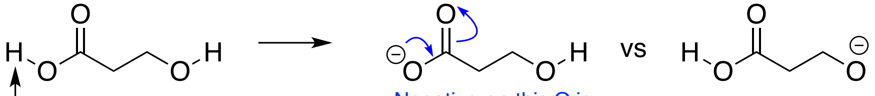


Atoms in the same column: A negative charge on a larger atom is more stable.



2) Resonance Effect

A conjugate base that is stabilized by resonance is more stable than one that is not.



Most acidic proton in the molecule

Negative on this O is resonance stabilized

3) Inductive Effect

Nearby electronegative atoms help to stabilize the conjugate base.

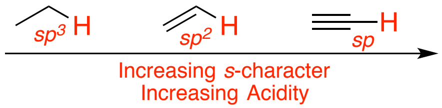
H_3C-H Cl_2HC-H Cl_3C-H F_3C-H $\longrightarrow$

Increasing Acidity

The size of the halogen does not matter since the acidic proton isn't directly attached.

4) Hybridization Effect

Electronegativity and acidity increases with increasing s-character.

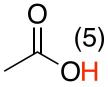


pKa Values:
Alkane C-H = 50
Alkene C-H = 45
Alkyne C-H = 25

Some Other Representative pKa Values

R–OH (16)

$R-NH_2$ (35)



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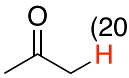

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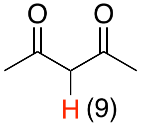

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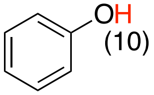


(10)

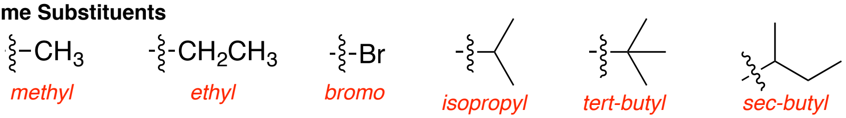
**Take note of the important unusual exception: Terminal Alkynes (pKa 25) are more acidic than amines (pKa 35)

Alkanes and Cycloalkanes

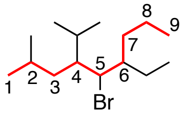
Alkane Nomenclature

1. Identify the Parent - the longest continuous carbon chain.
2. Name it based on the number of carbon atoms.
   1C = methane; 2C = ethane; 3C = propane; 4C = butane; 5C = pentane; 6C = hexane; 8C = octane; 9C = nonane; 10C = decane
3. Number the chain starting at the end that gives the 1st substitutent the lowest number.
4. Assemble the name by alphabetizing the substituent (with numbers) followed by the parent.

Some Substituents



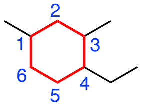
Example



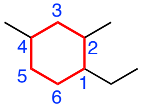
5-bromo-6-ethyl-4-isopropyl-2-methylnonane

Cycloalkane Nomenclature

1. Identify the Cycloalkane Parent
2. Number around the ring so as to get the lowest possible substituent numbering.
3. Assenble the name by alphabetizing the substituents followed by the parent name.



Substituents at 1,3,4
Adds up to 8
Incorrect Numbering



Substituents at 1,2,4
Adds up to 7 = Better
Correct Numbering

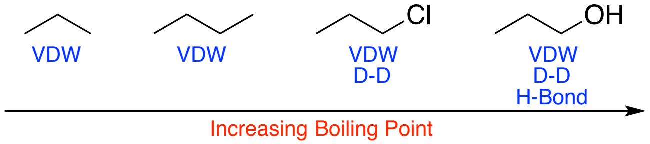
1-ethyl-2,4-dimethylcyclohexane

Intermolecular Forces & Boiling Point

As the strength of the intermolecular forces increases, the boiling point of a molecule increases.

Van der Waals Forces < Dipole-Dipole Interactions < Hydrogen Bonding $\longrightarrow$

Increasing IMF Strength

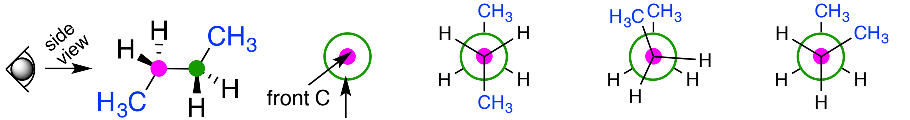


All covalent compounds have VDW Forces.
Butane has a larger surface area & thus stronger VDW forces than propane.

Organic Chemistry I Review

Newman Projections

A Newman projection is a way of visualizing the rotational conformations of an acyclic molecule.



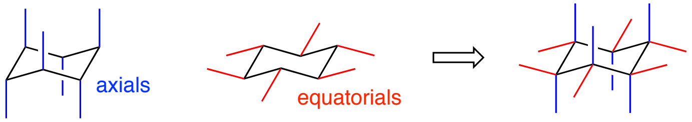
Staggered, Anti
Most Stable
Lowest Energy

Eclipsed
Least Stable
Highest Energy

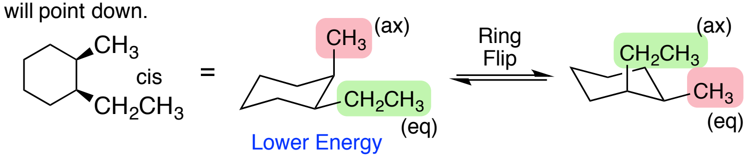
Staggered, Gauche

Chair Conformations

Every carbon in cyclohexane has two substituents. In chair cyclohexane each carbon has one axial (straight up or straight down) substituent and one equatorial (sideways) substituent.



Cis substituents should both point up or down. With trans substituents, one will point up and one will point down.



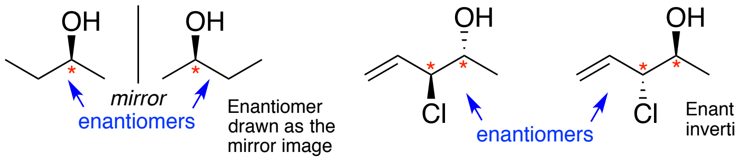
During a ring flip, axials become equatorials and equatorials become axials.

The lowest energy chair conformation is the one that puts the largest substituent(s) in the equatorial position.

Stereochemistry

Structural Relationships

Constitutional Isomers - Compounds with the same mol. formula, but different atom connectivity.
Stereoisomers - Compounds with different 3D arrangements of the atoms.
Enantiomers - Stereoisomers that are non-superimposable mirror images.
Diastereomers - Stereoisomers that are non-superimposable and are not mirror images.
Chiral Center - An atom that has four different groups attached to it.
Chiral Molecule - A compound that has one or more chiral centers, and no plane of symmetry.

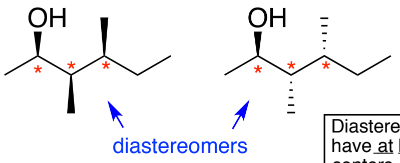


Enantiomer drawn as the mirror image

Enantiomer drawn by inverting *all* chiral centers.

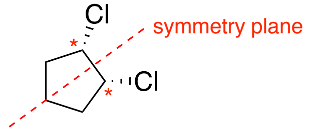
Enantiomers can have one or more chiral centers.

In a pair of diastereomers, at least one, but not all of the chiral centers are inverted.



Diastereomers must have at least 2 chiral centers. *Not including alkene diastereomers.*

A **meso compound** is a molecule that has two or more chiral centers, but is achiral due to the molecule having a plane of symmetry.



achiral (meso)

Assignment of *R/S* Configuration

R and *S* is used to assign the configuration at a chiral center.
A pair of enantiomers have opposite R/S assignments.

1. Look at four atoms directly attached to the chiral center.
2. Prioritize the atoms based on atomic number (Highest AN = Priority 1).
3. If there is a tie, move out to the next atom in the chain and compare.
4. Orient the molecule such that the priority 4 group is pointing back.
5. Draw a curved arrow from 1 to 2 to 3.

↻ R-Configuration ↺ S-Configuration

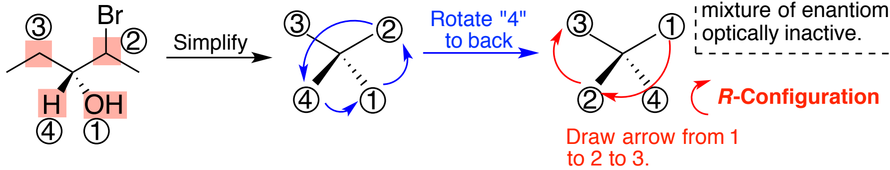
Optical Activity

A single enantiomer of a chiral molecule will be optically active - it will rotate plane polarized light in the (+) or (-) direction.

Achiral molecules are optically inactive

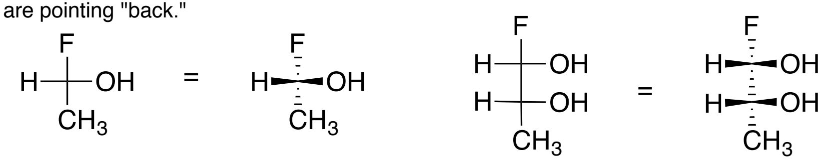
A racemic (±) mixture (1:1 mixture of enantiomers) is optically inactive.

Example



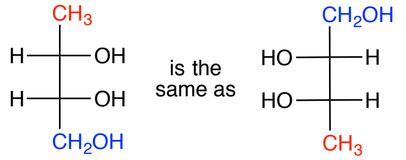
Fischer Projections

A Fischer projection is a way to view three dimensional structures.
By definition the horizontal bonds in a Fischer projection are pointing "out" and the vertical bonds are pointing "back."

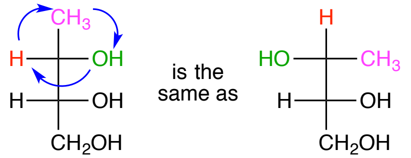


Manipulating Fischer Projections

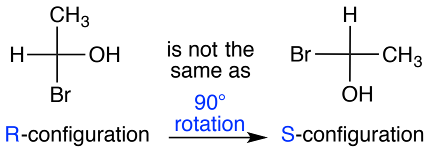
1. Fischer Projections can be rotated 180° without changing the molecule

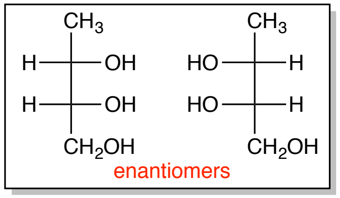


2. You can rotate the top three groups or the bottom three groups without chaning the molecule

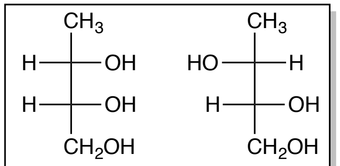


3. Rotating a Fischer Projection 90° changes the configuration at the chiral center



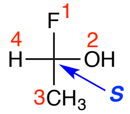


enantiomers



diastereomers

Assigning R/S Configuration

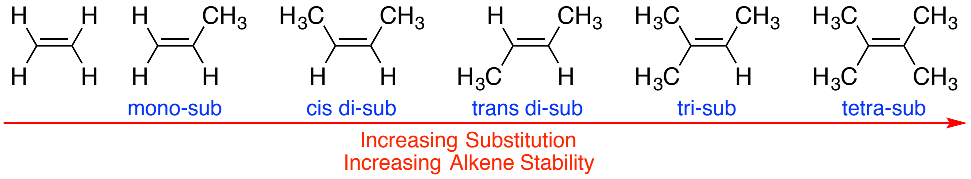


Trick: It looks like *R*-config, but since the H is pointing out (by definition) the configuration is actually *S*.

Organic Chemistry I Review

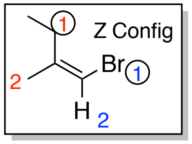
Alkenes

Alkene Stability



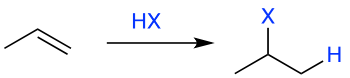
E/Z Assignment

Using the same priority rules as with assigning R/S configurations, the configuration of an alkene double bond can be assigned as *E* or *Z*.
E-Configuration - Priority 1 Groups on opposite sides of the double bond.
Z-Configuration - Priority 1 Groups on same side of double bond.

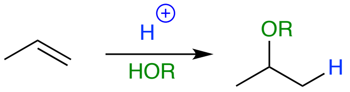


Reactions of Alkenes

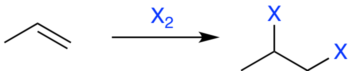
The most common reactions of alkenes are addition reactions where two atoms are added across the alkene π-bond.
Markovnikov Addition - H adds to the side with more H (less substituted side).
Anti-Markovnikov Addition - H adds to the side with less H (more substituted side).



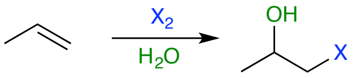
HX = HCl, HBr, HI
Markovnikov Addition



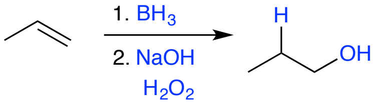
Markovnikov Addition



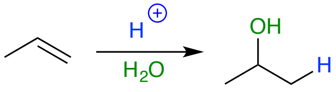
X_2 = Cl_2, Br_2, I_2
Halogenation



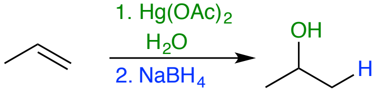
Halohydrin Formation



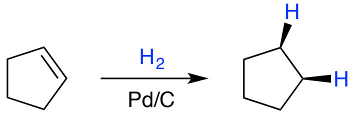
Hydroboration/Oxidation
Anti-Markovnikov Addition



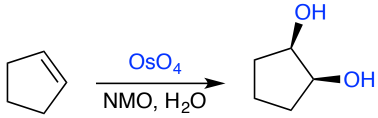
Hydration
Markovnikov Addition



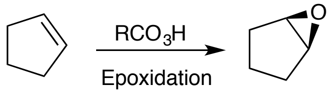
Oxymercuration/Demercuration
Markovnikov Addition



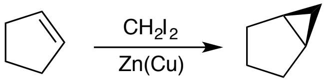
Hydrogenation



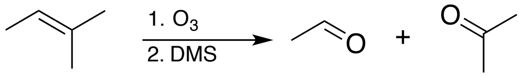
Syn-Dihydroxylation



Epoxidation



Simmons-Smith Cyclopropanation

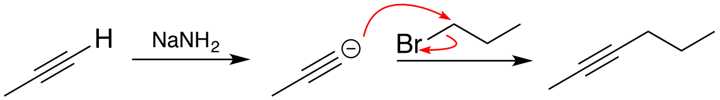


Ozonolysis - Reductive Workup

Alkynes

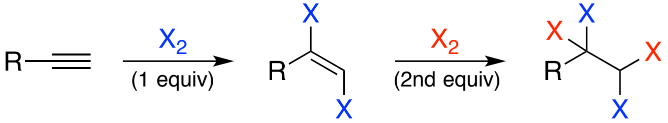
Alkyne Alkylation

Terminal alkynes can be alkylation by reacting the alkyne with a base followed by addition of R-X.

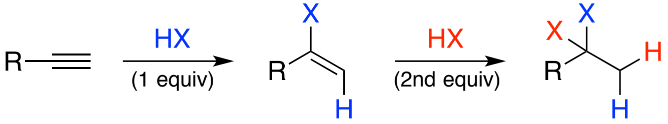


The carbon bonded to the halogen must be sp^3.

Addition Reactions

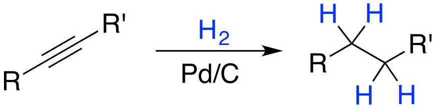


X = Cl, Br, I

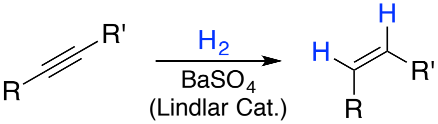


X = Cl, Br, I
HX adds to the terminal alkyne in Markovnikov fashion.

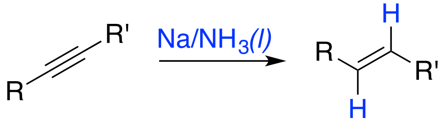
Hydrogenation (Also an Addition Reaction)



Complete reduction of the alkyne to an alkane



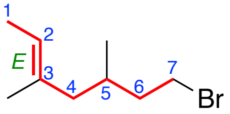
Lindlar's Catalyst gives partial reduction to the cis-alkene



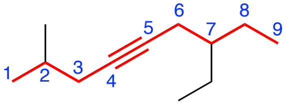
Sodium in liquid ammonia gives partial reduction to the trans-alkene

Alkene/Alkyne Nomenclature

1. Find the parent chain - the longest carbon chain that contains both carbons of the unsaturation.
2. Number the parent from the end that gives the unsaturation the lowest numbers.
3. Change parent ending -ane to -ene (alkene) or -ane to -yne (alkyne)
4. Assemble name: **Alkene:** *(E or Z)*-substitutents-alkene C #-parent
   Alkyne: substituents-alkyne C #-parent



(E)-7-bromo-3,5-dimethyl-2-heptene



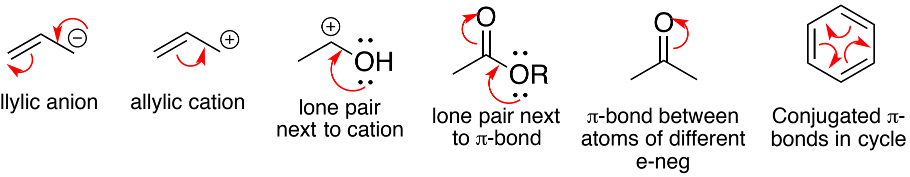
7-ethyl-2-methyl-4-nonyne

Organic Chemistry I Review

Delocalized Electrons and Resonance

Delocalization of electrons through resonance helps to stabilize a structure.

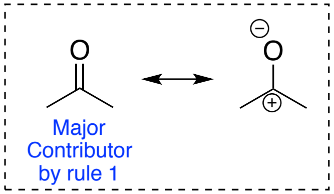
Common Resonance Patterns



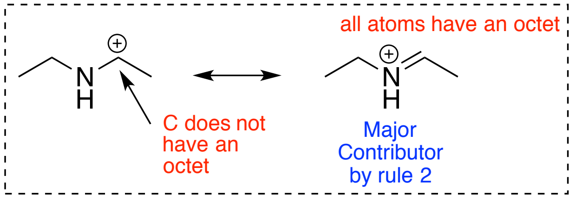
allylic anion | allylic cation | lone pair next to cation | lone pair next to π-bond | π-bond between atoms of different e-neg | Conjugated π-bonds in cycle

Assessing Relative Importance of Resonance Contributors

1. A resonance structure where charges are minimized is more important.
2. A resonance structure where all atoms have an octet is more important.
3. A resonance structure that puts the negative on the more e- neg atom is more important.



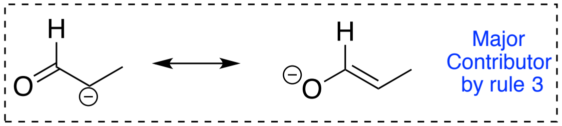
Major Contributor by rule 1



all atoms have an octet

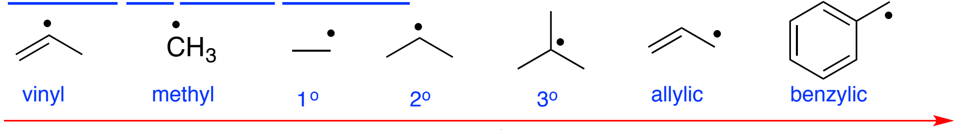
C does not have an octet

Major Contributor by rule 2



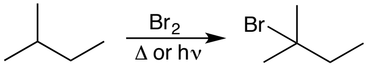
Major Contributor by rule 3

Radicals and Radical Reactions



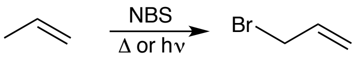
Increasing Stability

Radical Halogenation of Alkanes



Bromination Selectivity: 3°>2°>1°
Radical chlorination is much less selective

Allylic Bromination using NBS



Bromination at the allylic position. Proceeds via an allylic radical intermediate. NBS can also be used for benzylic bromination.

Radical Addition of HBr to Alkenes

Anti-Markovnikov addition - H goes to the more substituted carbon and Br goes to the less substituted carbon.

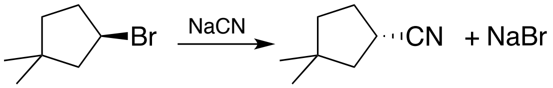
Substitution Reactions

S_N2 - Substitution Nucleophilic Bimolecular

$$H_3C{-}X \;+\; {:}\overset{\ominus}{Nu} \longrightarrow H_3C{-}Nu \;+\; X^{\ominus} \qquad \boxed{\text{Rate} = k\left[H_3C{-}X\right]\left[Nu^{-}\right]}$$

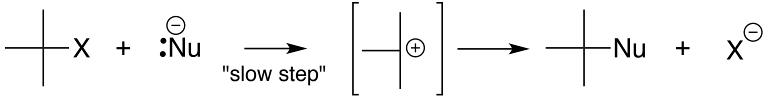
Only a single step in the reaction
This single step must then = slow step

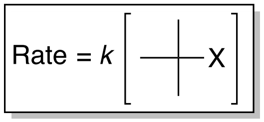
A Better Leaving Group = Faster Reaction
A Stronger Nu = Faster Reaction



In S_N2 the nucleophile adds from the backside of the leaving group providing the inversion product.

S_N1 - Substitution Nucleophilic Unimolecular

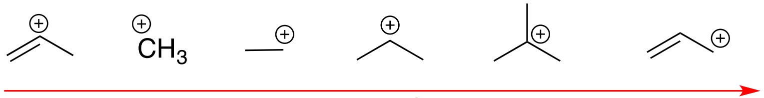




The S_N1 reaction involves a carbocation intermediate.
Formation of this carbocation is the rate determining step.
A Better Leaving Group = Faster Reaction
A More Stable Carbocation Intermediate = Faster Reaction

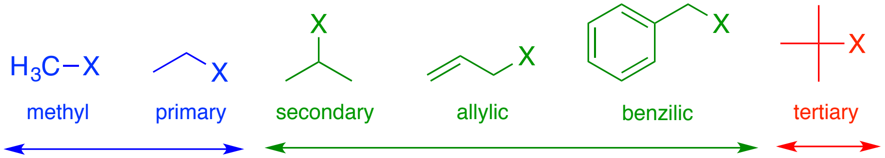
S_N1 reactions are sometimes referred to as solvolysis reactions.
A substrate is most likely to ionize in a polar protic solvent if it has a good leaving group and can form a relatively stable carbocation (allylic, benzylic, or tertiary).

Carbocation Stability



Increasing Stability

Alkyl Halide Reactivity

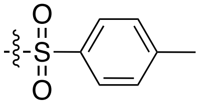


methyl | primary | secondary | allylic | benzilic | tertiary

S_N2 Only | S_N1 or S_N2 | S_N1 Only

Some Good Leaving Groups

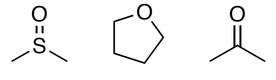
$R{-}I$ $R{-}Br$ $R{-}Cl$ $R{-}\overset{\oplus}{O}H_2$ $R{-}OTs$ Ts =



Reaction Solvent

S_N1 goes best in polar protic solvents: H_2O, ROH
S_N2 goes best in polar aprotic solvents.

Some Polar Aprotic Solvents

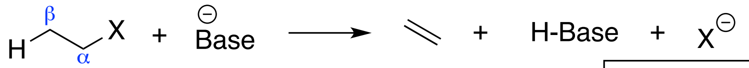


DMSO | THF | acetone

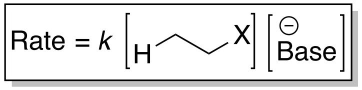
Organic Chemistry I Review

Elimination Reactions

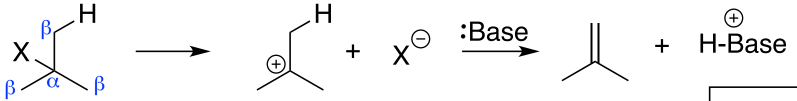
E2 - Elimination Bimolecular



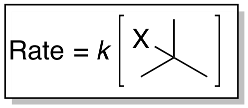
Rate depends on both the ability of the leaving group and the strength of the base.



E1 - Elimination Unimolecular



In E1, the base has no effect on the reaction rate.
The reaction involves a carbocation intermediate.
Tertiary, Benzylic, and Allylic Halides can undergo E1 Elimination

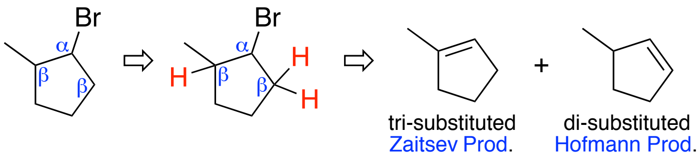


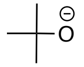
Solving an Elimination Problem

Identify α-C & β-C

Identify β-H

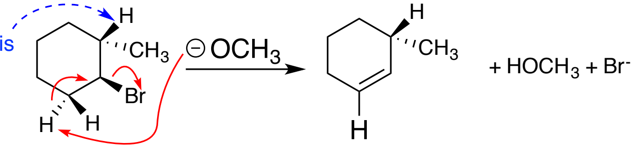
Eliminate HBr across all α,β bonds with α-H



Small Base	Bulky Base
HO^- RO^- H_2N^- Zaitsev Major	 Hofmann Major

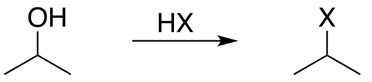
For E2 elimination, the H and Leaving Group must be antiperiplanar.
When dealing with a ring, the hydrogen eliminated and LG must be *anti.*

Not anti to Br so this β-H can't eliminate

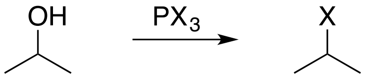


Reactions of Alcohols

Alcohol Substitution

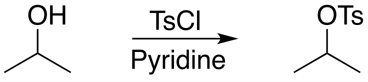


HX = HCl, HBr, HI



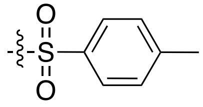
X = Cl, Br

Tosylate Formation

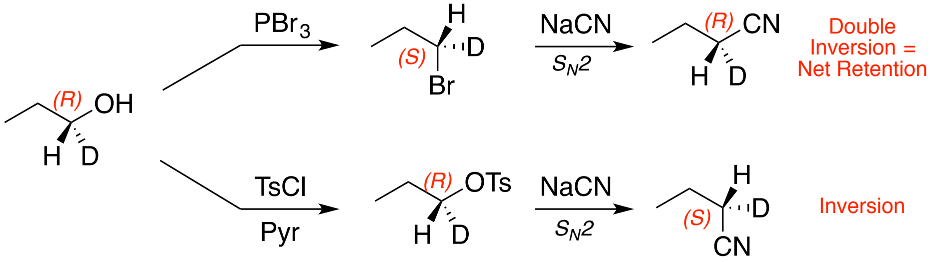


OTs is an **excellent** leaving group.

Ts =

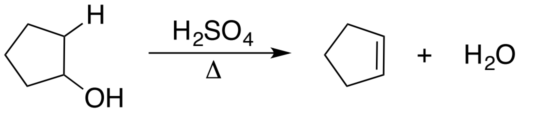


Inversion vs Retention of Configuration

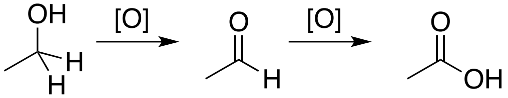


*Conversion of R-OH to R-OTs does not change configuration!

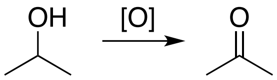
Dehydration of an Alcohol with Acid



Alcohol Oxidation

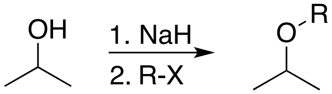


PCC will stop at aldehyde
$Na_2Cr_2O_7/H_2SO_4$ or CrO_3/H^+ will completely oxidize 1° OH to COOH.



PCC, $Na_2Cr_2O_7/H_2SO_4$, and CrO_3/H^+ will oxidize 2° OH to ketone

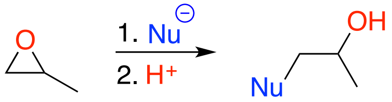
Williamson Ether Synthesis



NaH is one of several bases that can be used.

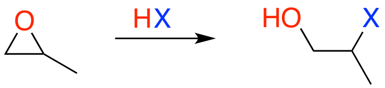
Reactions of Epoxides

Nucleophilic Opening



Under nucleophilic conditions, the nucleophile attacks the less substituted epoxide carbon.

Acidic Opening



Under acidic conditions, the acid protonates the epoxide oxygen. X^- then attacks the more substituted epoxide carbon.

Organic Chemistry I Review

Infrared Spectroscopy

-Useful for detecting functional groups in a molecule.
-Upon absorption of IR light, functional groups will exhibit characteristic stretching and bending vibrations.

Key IR Regions (Memorize These!)

Group	Region (cm^{-1})
OH & NH Stretch	3200-3600; fairly broad
Terminal Alkyne C-H	3300; sharp & narrow
Csp^2-H Stretch	Just above 3000
Csp^3-H Stretch	Just below 3000
C,â°C Stretch	~2100
C=O Stretch	~1700; strong
C=C Stretch	~1650
$-CH_3$ bending	Just below 1400

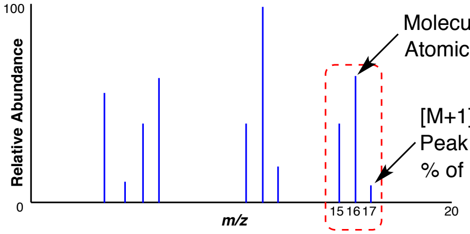
COOH derivatives tend to be higher. Conjugation lowers C=O stretch by ~20 wavenumbers.

Can be useful to distinguish constitutional isomers where one has a methyl group and the other doesn't.

Mass Spectrometry

Useful for obtaining the atomic mass and certain structural features for a molecule.

Typically focus in on the right most grouping of peaks. Often, the tallest peak in this group will correspond to the molecular ion (M^+). The *m/z* of this molecular ion = atomic mass of the molecule.

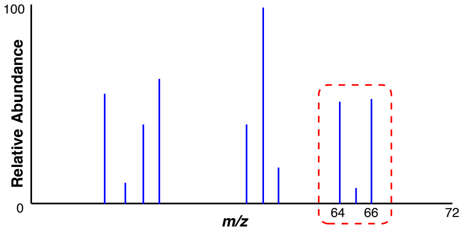


Molecular Ion $[M]^+$ at *m/z* 16
Atomic Mass of Molecule = 16

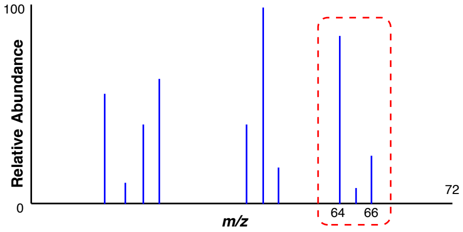
$[M+1]^+$ at *m/z* 17
Peak one mass unit higher than M^+, due to small % of ^{13}C in the sample.

Halogens in the Molecule

The presence of an $[M+2]^+$ peak indicates the presence of a halogen.



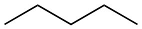
1:1 Ratio of $[M]^+$ and $[M+2]^+$
Indicative of Br



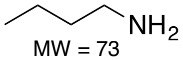
3:1 Ratio of $[M]^+$ and $[M+2]^+$
Indicative of Cl

Nitrogen Rule

-An odd molecular weight indicates the presence of an odd # of N in the molecule.
-An even molecular weight indicates the presence of no nitrogen or an even number of N in the molecule.



MW = 72



MW = 73

MW = 74

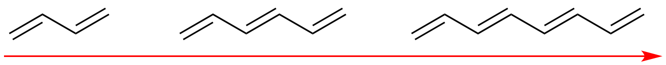
UV-Vis Spectroscopy

Upon irradiation of UV light, conjugated compounds absorb light energy promote a π-electron from the HOMO to the LUMO.

Increasing conjugation decreases the energy gap between the HOMO and LUMO levels. A smaller HOMO-LUMO gap means less energy is required excitation.

$$\boxed{E = \frac{hc}{\lambda}}$$

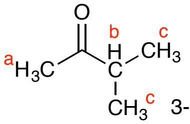
As conjugation increases, the energy required for excitation decreases. Since E and λ are inversely proportional, lower E = Higher λ_{max}.



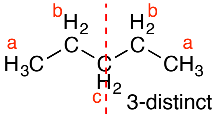
Increasing Conjugation — Decreasing E gap — Increasing λ_{max}

NMR Spectroscopy

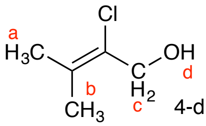
^1H NMR - Every distinct type of proton in a molecule gives rise to a signal.
^{13}C NMR - Every distinct type of carbon in a molecule gives rise to a signal.



3-distinct H

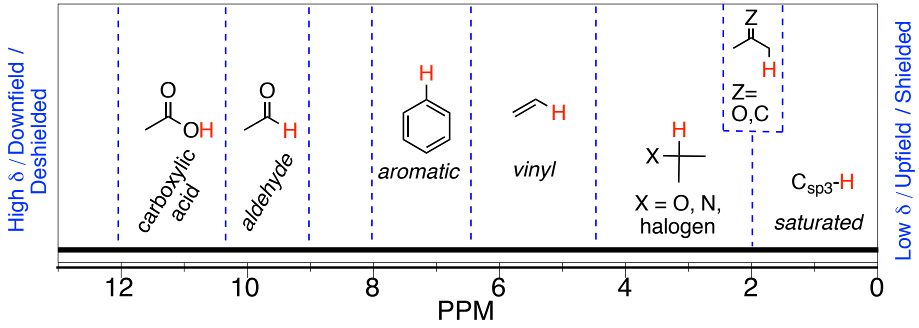


3-distinct H



4-distinct H

Chemical Shift Regions (Memorize these Regions!)

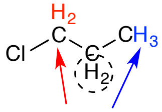


Integration

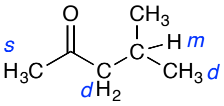
The area under each signal is proportional to the number of hydrogen that the signal represents.

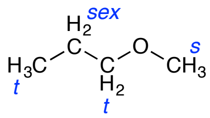
Splitting (Coupling)

For simple systems, the signal corresponding to a particular proton is split into (n+1) peaks where n = the number of hydrogen on the adjacent atom(s).



n = 2 + 3 = 5
n + 1 = 5 + 1 = 6 **(sextet)**





<u>multiplicities:</u> s (singlet); d (doublet), t (triplet), q (quartet), quin (quintet), sex (sextet), sep (septet), m (multiplet)