Chapter 1 - Structure and Bonding

Electron Structures

- Atom has dense positive nucleus
- Electron Density highest @ nucleus, drops off exponentially moving away

2p Orbitals 2 lobes per p orbital (labeled according its axis (x, y, z)) Different than s orbital bc of xyz orientation

3 2p orbitals oriented at ⊥ to each other

Isotopes - $^{12}_{6}C$ (Mass Number)

↳ Have same # of protons but diff. # of neutrons

Electron Configuration

Valence e⁻ are outermost electrons on the shell of the atom ← furthest from nucleus

Aufbau principle - fill lowest orbitals first

Hund's rule - when 2+ orbitals of same energy, e⁻ go into diff. orbitals rather than pairing up in same orbital

electrons in s orbital are less reactive than those in p orbital

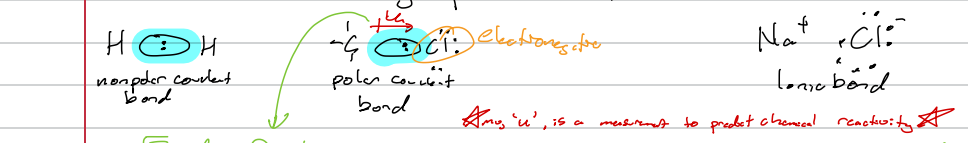
Octet Rule - want to have noble gas configuration

Ionic - Cation and anion

Covalent Bonding

Shared Evenly = nonpolar covalent, aka pure covalent

Not Shared Evenly = polar covalent



Any 'u', is a measurement to predict chemical reactivity

End of the arrow points to negative part of covalent bond

Bonding Patterns

	–C–	–N–	–O–	–H	–Cl:
Valence:	4	3	2	1	1
Lone pairs:	0	1	2	0	3

Nonbonding Electrons or lone pairs

- are valence shell electrons that are not shared btwn. atoms

> More accessible

Multiple Bonding

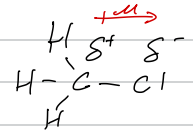
2 pairs shared = Double, 3 pairs = Triple

Dipole Moment

- A mount of charge separation (δ) multiplied by the bond length (μ)

Electronegative values → predict bond type > F is most electronegative

C and H are so close in EN, nonpolar

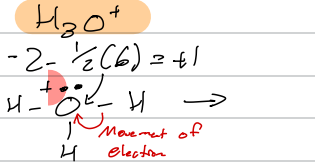


Formal Charges = (group #) − (nonbonding e⁻) − ½(shared e⁻)

Keeps track of electrons

H_3O^+

6 − 2 − ½(6) = +1



NO^+

6 − 2 − ½(6) = +1

:N≡O:

5 − 2 − ½(6) = 0

Know how to determine Formal Charge!

SUMMARY TABLE 1-1 Common Bonding Patterns in Organic Compounds and Ions

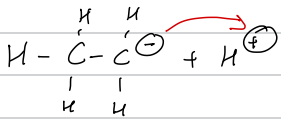
Atom	Valence Electrons	Positively Charged (Cation)	Neutral	Negatively Charged (Anion)
B	3		—B— (no octet)	—B—
C	4	—C⁺— (no octet)	—C— (stable)	—C⁻—
N	5	—N⁺—	—N—	—N⁻—
O	6	—O⁺—	—O—	—O⁻
halogens	7	—Cl⁺—	—Cl:	:Cl⁻

Negative Carbon is worse bc Carbon tends to be positive

Know the negative here

PROBLEM-SOLVING HINT

This is a very important table. Work enough problems to become familiar with these bonding patterns so that you can recognize other patterns as being either unusual or wrong.



Resonance Forms

Follow the 4 criteria, try to meet all criteria

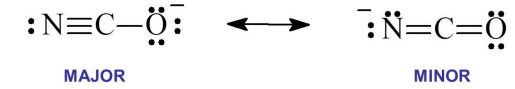
- Structures of some compounds not adequately represented by a single Lewis
- True structure is a hybrid of the contributing resonance forms

1. Have as many octets as possible
2. Has as many bonds as possible
3. Negative charge on most electronegative atom
4. Has little negative charge as possible

Major and Minor Contributors not specifically on exam but helpful to know

Which Resonance Structure is more logical than the other

If both Res. forms obey octet rule, major contributor is the one w/ neg. charge on most EN atom



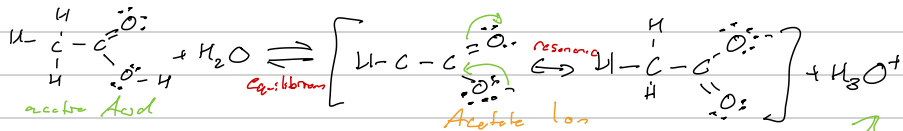
MAJOR MINOR

Non Equivalent Resonance

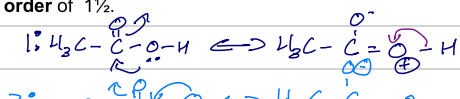
- Opposite charges should be on adjacent atoms

Resonance on the Acetate Ion

- When acetic acid loses a proton, the resulting acetate ion has a negative charge delocalized over both oxygen atoms.
- Each oxygen atom bears half of the negative charge, and this delocalization stabilizes the ion.
- Each of the carbon–oxygen bonds is halfway between a single bond and a double bond and is said to have a **bond order** of 1½.

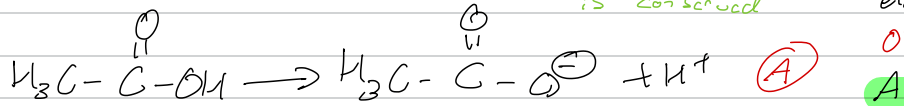


Note How total charge is conserved



Structure 2 is more favorable. O is electronegative, and likes a negative charge.

O^+ is so incredibly stinky why would nature make that



A

B

As product can have resonance, B cannot as e^- is localized

Know how to draw condensed structures quickly

[Lewis ⟺ Condensed]

Wave Properties of electrons

- Sigma (σ) bond is stronger than a p: (π) bond
- Wave function can describe electron probability
  - ↳ +/− separated by a node (amp. = 0) ← 0 probability of finding e^- here
- +/− overlap leads to anti bonding ← called out of phase overlap

Out of phase: Waves cancel out

In Phase: Wave amplitudes added together → inc.

Need to know δ^+ and δ^- in covalent bonds

Combination of Atomic Orbitals (Linear)

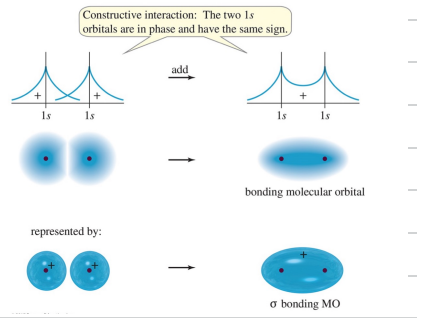
- Two different atoms combining orbitals → bond formation
- Combining orbitals on the same atom → hybridization

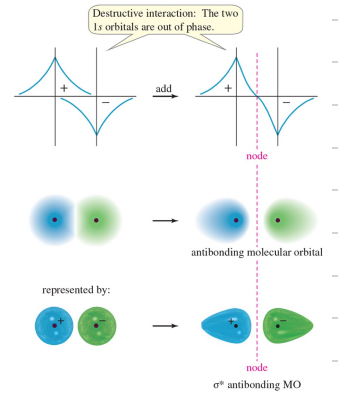
Alkane: sp
Alkene: sp^2
Alkyne: sp^3

Remember this connection

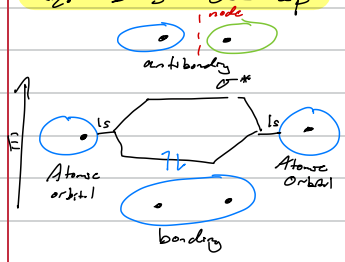
σ- bonding molecular orbital (MO)

- When 2 1s orbitals overlap out of phase, they destructively to form antibonding MO
- Constructively overlapped 1s orbitals are in phase and they form a bonding MO
- Antibonding is higher energy

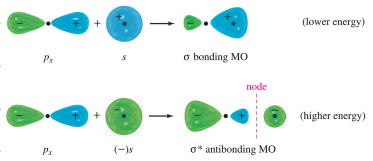




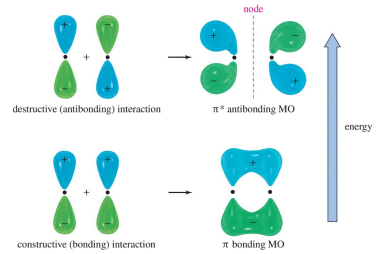
H_2: S–S overlap



S and p orbital overlap



Pi bonding and Antibonding

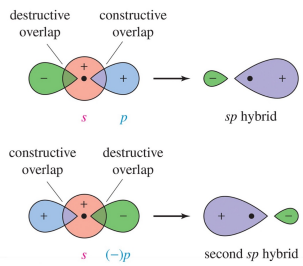


σ* * means antibonding

π* π is weaker than σ

In a reaction the π bond will go first because it is weaker than the σ bond

Sp Hybrid Orbitals



- Advantagous for Carbon to hybridize
- Linear e⁻ pair geometry (180° bond angle)
- Results when two orbitals combine to form two sp orbitals

Carbon

$2p_x$ — $2p_y$ — $2p_z$ —

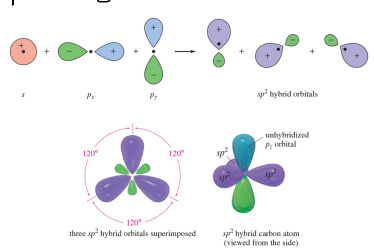
$2s$ —

Make sp

Can now be used to form π bonds

Makes this type of hybrid orbital the most reactive

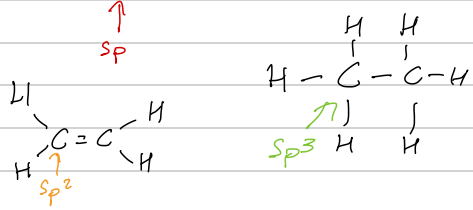
sp^2 Hybrid Orbitals



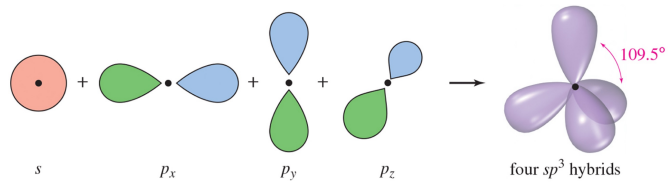
- Three orbitals (one and two p) combine to form 3 sp^2 orbitals
- Trigonal Planar geometry (120°)

H–C≡C–H

sp



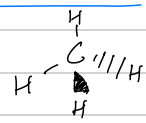
sp^3 Hybrid Orbitals



- Four orbitals (one s and three p) combine to form 4 sp^3 orb.
- Tetrahedral e⁻-pair geometry (109.5°)

Molecular Model

Methane:



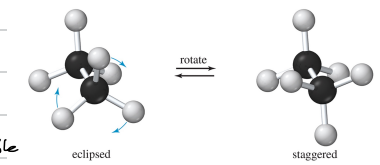
- Dashed is pointing away
- Solid is pointing towards

SUMMARY Hybridization and Geometry

Hybrid Orbitals	Hybridization	Geometry	Approximate Bond Angles
2	$s + p = sp$	linear	180°
3	$s + p + p = sp^2$	trigonal	120°
4	$s + p + p + p = sp^3$	tetrahedral	109.5°

Rotation in Single Bonds

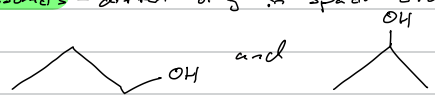
- Single bonds are allowed to rotate giving a variety of combinations
- Eclipsed has higher energy = less stable
- Staggered → bonding e⁻ farthest away from others, less energy = more stable



Isomerism

- Molecules with same molecular formula but diff. atom arrangement
- Constitutional (structural) – differ in their bonding sequence
- Stereoisomers – differ only in spatial arrangement

Example:

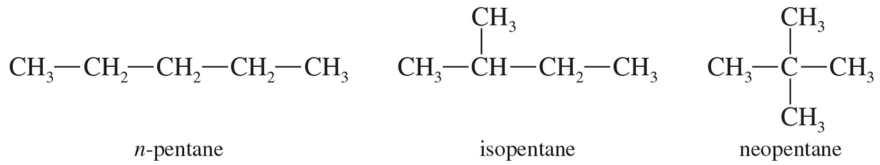


These are isomers

The different location of the hydroxyl changes the molecules properties

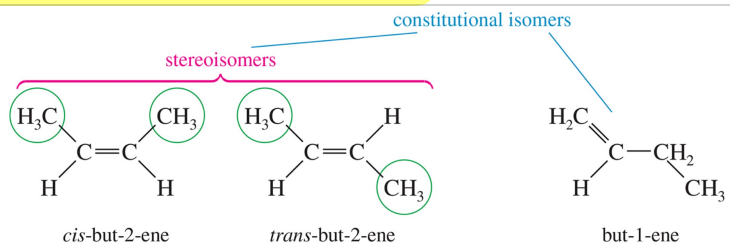
Example:

Isomers bc these cannot be superimposed in space



- Know about uncommon names like iso- and neo-

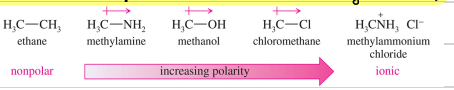
Geometric Isomers: Cis and Trans



- These occur when there is a double bond in the compound

Chapter 2 - Acids and Bases

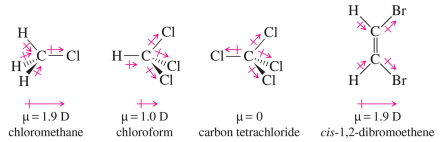
Bond Dipole Moments (debyes or D)



- Dipole Moments resulted from EN differences
- Depend on amt of charge and distance

Know the Difference!
A molecule can have bond dipole moments, but have nonpolar molecular dipole moments!

Molecular Dipole moment



- Vector sum of the bond dipole moment
- Depends on bond polarity and bond angles
- Lone pairs of e⁻ contribute to dipole moments

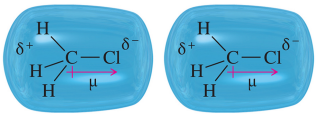
Intermolecular Forces ← Influences b.p., m.p., and solubility

Classifications:
- Dipole-Dipole
- London Dispersion (Van der Waals)
- Hydrogen Bonding

You can rank bond strength when you know the melting points or boiling points for given compounds

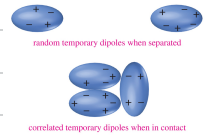
Dipole-Dipole Interactions

- Result from approach of two polar molecules
- Positive end wants negative of other molecule
  - ↳ same thing reversed
- Positive - positive or neg-neg ends will not attraction (common)



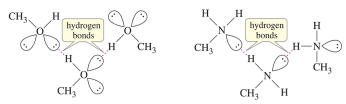
London Dispersion Forces

- Temp. Dipole moments can induce nearby temp. dipoles
  - ↳ called polarization
- Main force in nonpolar molecules
- Larger atoms = more polarizable

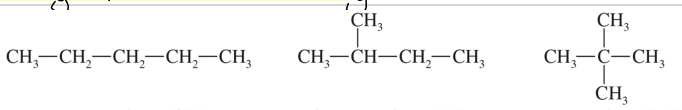


Hydrogen Bonding

- Strong Dipole-Dipole attraction
- Organic must have O-H or N-H to be H-bonded
- O-H is stronger than N-H
  - ↳ alcohols stronger H-bonding
- H on one molecule is very attracted to a lone pair on the nitrogen/oxygen



Boiling Points and Branching



- n-pentane has highest surface area → highest b.p.
- inc. branching → more spherical → lower surface area → lower b.p.

Shows that London dispersion forces dependent on surface area

Example: Boiling Points and Intermolecular Forces

Compare ethanol with dimethyl ether and ethyl amine

Ethanol: H_3C-CH_2-OH, C_2H_6O (b.p.) = 78°C

Dimethyl Ether: CH_3-O-CH_3 b.p. = -25°C

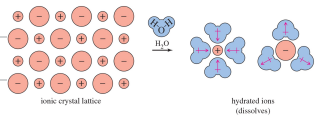
Ethyl amine: $H_3C-CH_2-NH_2$ (b.p. = 17°C)

The more polar a molecule is, the stronger the interactions is. Stronger interactions = higher b.p.s

Polarity Effects on Solubility

"like dissolves like" (same for nonpolar)

- Polar solutes dissolve polar solvents
- Molecules with similar intermolecular forces will mix freely



→ Hydration releases energy, entropy increases

More examples on slides 18-20 of ch. 2 lecture

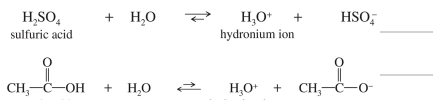
Functional Groups

classes: hydrocarbons, oxygen containing, or nitrogen containing

Arrhenius Acids:

substances that dissociate in water to give H_3O^+ ions

↳ Stronger acids dissociate to a greater degree!



Arrhenius Bases:

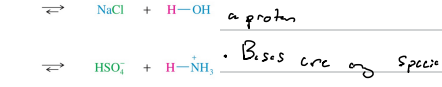
substances that dissociate in water to give OH^- ions

↳ stronger bases dissociate to a greater degree

$NaOH \rightleftharpoons Na^+ + {}^-OH$

$Mg(OH)_2 \rightleftharpoons Mg^{2+} + 2\ {}^-OH$

Bronsted-Lowry Acids and Bases:



- Acids are any species that donate a proton
- Bases are any species that accept a proton

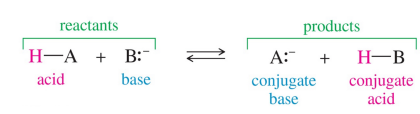
Acid Strength:

expressed in its extent of ionization in water.

Recall: $K_a = \frac{[H_3O^+][A^-]}{[HA]}$, stronger acids have higher K_a

Know and Understand: $pK_a = -\log(K_a)$, inverse relation when comparing K_a, low pK_a = strong acid

- Acid Base equilibrium favors formation of weaker acid and weaker base
- Weaker acids have larger pK_a. Weaker base has larger pK_b
- Weak acid and weak base are always on the same side of the reaction



Solvent Effects on Acids and Bases

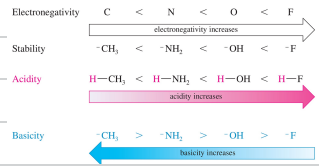
$$HCl + H_2O \longrightarrow Cl^- + H_3O^+$$

HCl: stronger acid, $pK_a = -7$ — H_2O: base — Cl^-: conjugate base — H_3O^+: conjugate acid, $pK_a = -1.7$, weaker acid

- Water is amphoteric, it can act as an acid or a base
  - ↳ its conj. acid is the hydronium ion, its conj. base is the hydroxide ion

Effect of EN on pKa

- More EN element bears neg. charge more easily, giving a more stable conjugate base and a stronger acid



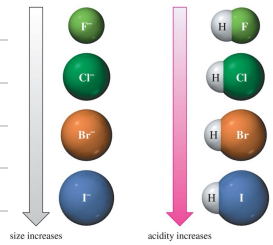
Summary on Limitations

SUMMARY Acidity and Basicity Limitations in Common Solvents

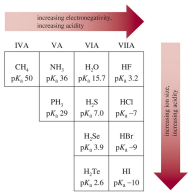
Solvent	Structure	Typical pK_a Limit	Limiting Species	Typical pK_a Limit	Limiting Species
water	H—O—H	−1.7	H_2O^+	−1.7	HO^-
alcohols	R—O—H	−2.4	ROH_2^+	−1.9	RO^-
ethers	R—O—R	−3.6	R—O(H)—R	none	none
ammonia	NH_3	9.2	NH_4^+	−22	NH_2^-
alkanes	R—H	none	none	none	none

Effect of Size on pKa

- Negative charge of an anion is more stable if it is spread over a larger region of space.
- Acidity increases down a column of the periodic table.

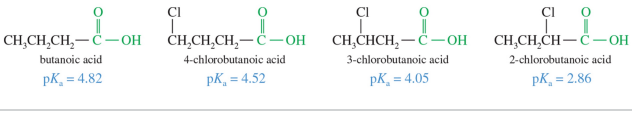


Summary of EN and size effects

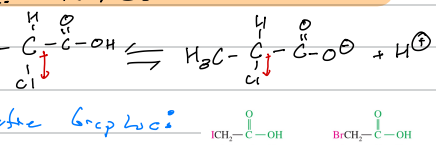


Inductive Effects on Acidity

- Electron withdrawing atoms and groups can stabilize a conjugate base through the sigma bonds of the molecule. Magnitude of this inductive effect depends on the number of bonds between the EN element and the side of the negative charge



Example: Chlorine's Inductive Effects

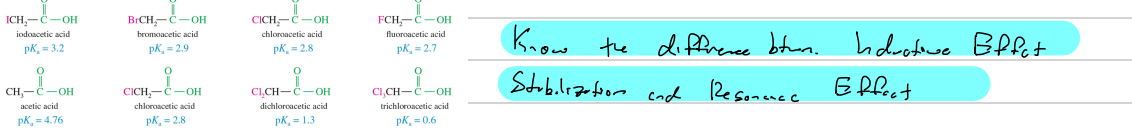


how does the Chlorine help break the OH bond?

The resonance structure of the product is more favorable. Inductive Effect delocalizes through the sigma bond, while resonance is through π bond

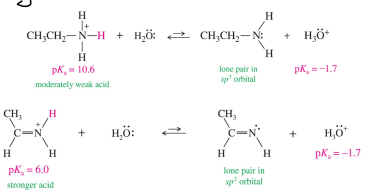
Illustrative Group Lists:

- sp^3 - σ bonds only
- sp^2 - 3σ, 1π
- sp - 2σ, 2π



Know the difference btwn. Inductive Effect Stabilization and Resonance Effect

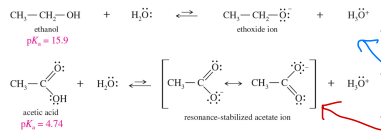
Hybridization Effects on Acidity



- All σ bonds (sp^3) hybridized → higher pKa
- sp^2 orbital
- More s characteristic means lower pKa

Compound	Conjugate Base	Hybridization	s Character	pK_a
H—C(H)(H)—C(H)(H)—H	H—C(H)(H)—C(H)(H)⁻	sp^3	25%	50
H—C(H)=C(H)—H	H—C(H)=C(H)⁻	sp^2	33%	44
H—C≡C—H	H—C≡C⁻	sp	50%	25

Resonance Effect on pKa



- If negative charge on an atom can be delocalized over two or more atoms, it will have a greater acidity

Localized e⁻, more acidic

Negative charge in the conj. base is delocalized

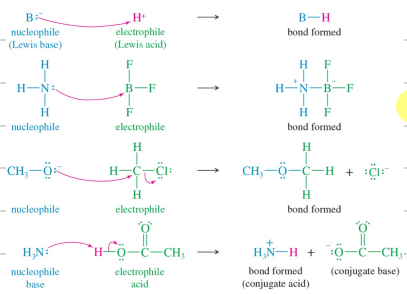
Lewis Acids and Bases

- Lewis bases (nucleophiles): Species with available electrons that can be donated to form a new bond ← Donates
- Lewis acid (electrophiles): Accepts a pair of e⁻ ← Accepts

When breaking a bond, the more EN atom receives the electrons

Resonance stabilizes More than Inductive Effects

Curly arrow describes movement of e⁻. Read about it in the appendix



- Indicate Mechanisms that break or form bonds

The Most EN group will be the leaving group

Hydrocarbons

- **Alkanes** – sp^3, single bonds only
- **Cycloalkanes** – sp^3 in a ring
- **Aromatic**: Contain Benzene
- **Alkenes**: sp^2, double bonds present
- **Cycloalkenes**: Double bonds in a ring
- **Alkynes**: sp, triple bonds

Naming Review

TABLE 2-3 CORRESPONDENCE OF PREFIXES AND NUMBERS OF CARBON ATOMS

Alkane Name	Number of Carbons	Alkane Name	Number of Carbons
*meth*ane	1	*hex*ane	6
*eth*ane	2	*hept*ane	7
*prop*ane	3	*oct*ane	8
*but*ane	4	*non*ane	9
*pent*ane	5	*dec*ane	10

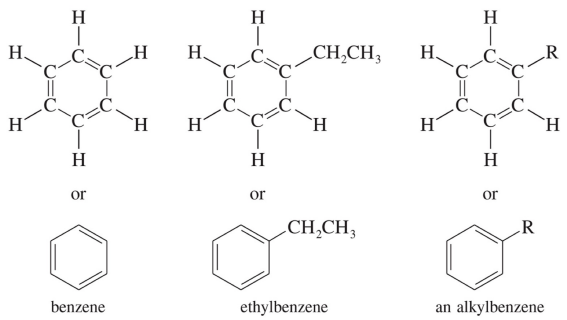
CH_4 methane; $CH_3—CH_3$ ethane; $CH_3—CH_2—CH_3$ propane; $CH_3—CH_2—CH_2—CH_3$ butane; $CH_3—CH(CH_3)—CH_3$ isobutane

- Know how to identify functional Group locations.
- Be able to draw structures based off of IUPAC Name

$CH_2=CH_2$ ethene (ethylene); $CH_2=CH—CH_3$ propene (propylene)

$\overset{1}{CH_2}=\overset{2}{CH}—\overset{3}{CH_2}—\overset{4}{CH_3}$ but-1-ene; $\overset{1}{CH_3}—\overset{2}{CH}=\overset{3}{CH}—\overset{4}{CH_3}$ but-2-ene

The π bond is a functional group! Not 'C-C' or 'C-H'



Don't touch the Benzene ring!

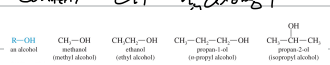
- **Alcohols**: Contain the hydroxyl group as the main functional group
- **Ethers**: Contain two alkyl groups bonded to an oxygen
- **Aldehydes** and **ketones**: Contain the carbonyl group, C=O
- **Carboxylic acids**: Contain the carboxyl group, —COOH

Four classes of Oxygen containing compounds. Differ by how Oxygen is connected to compound

Oxygen Containing Compounds

Alcohols

Organic Compounds that contain —OH hydroxyl

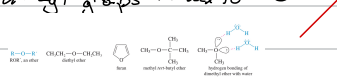


Ethers

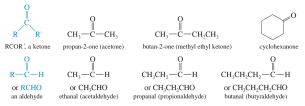
dissolves in water

Composed of two alkyl groups bonded to O

Does not H bond w/ itself because it lacks an OH group [lower BP]

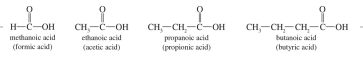


Aldehydes and Ketones



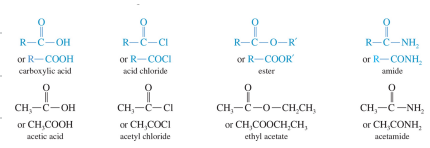
Carboxylic Acids

–COOH as the functional group



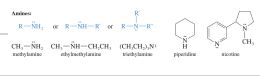
Carboxylic Acid Derivatives

- Includes acid chlorides, Amides, and Esters
- Go very in depth in higher level courses

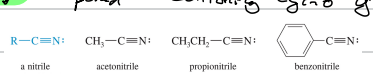


Compounds Containing Nitrogen

Amine: Alkylated derivatives of Ammonia

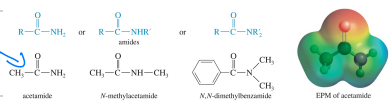


Nitrile: Compound Containing Cyano group



Amides: Derivatives that result from a combination of an acid with ammonia or amide

Acidic because



EPM of acetamide

Chapter 3 - Structure and Stereochemistry of Alkanes

Alkanes General Formula: C_nH_{2n+2}

↳ Small alkanes ⇒ lower bp so they're usually gasses

- $-CH_2-$ Group is called a methylene group

Constitutional Isomers

- Same molecular formulas but their carbons are connected differently

Example:

$CH_3CH_2CH_2CH_3$ n-butane

$CH_3CH(CH_3)CH_3$ isobutane

bp questions have nothing to do with the breaking of σ bonds!

n-butane > isobutane b.p. bc of forced ID in n-butane bc of higher surface area

IUPAC and Formal Nomenclature ← need to know how to draw them

① Longest cts HC chain is base name

If there are 2 longest chains of equal length go w/ the one that has most substituents

② Start chain numbering nearest the first substituent

③ Change ending of alkyl groups

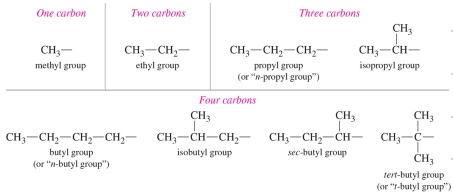
Important: Memorize common names

Alkanes	
CH_4	methane
CH_3-CH_3	ethane
$CH_3-CH_2-CH_3$	propane
$CH_3-(CH_2)_2-CH_3$	butane
$CH_3-(CH_2)_3-CH_3$	pentane

Alkyl Groups	
CH_3-	methyl group
CH_3-CH_2-	ethyl group
$CH_3-CH_2-CH_2-$	propyl group
$CH_3-(CH_2)_2-CH_2-$	butyl group
$CH_3-(CH_2)_3-CH_2-$	pentyl group (n-amyl group)

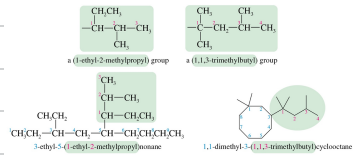
④ Multiple groups labeled numerically and alphabetically in order. Some groups get di-, tri-, tetra-, etc.

Common Names



On exam, Nomenclature is given in question and you need to draw it based on that

- Substituents can be complex, but IUPAC Naming still applies:



General Property: Increased # of Carbons → more van der waals → bp ↑

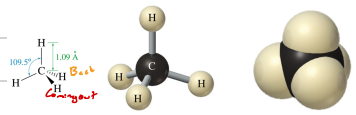
↳ recall that straight chain alkanes have higher bp than branched

Melting point is similar but odd # Hydrocarbons have higher than even numbered

Methane Representations

- Tetrahedral Carbon is sp^3

↳ likes to be 109.8°



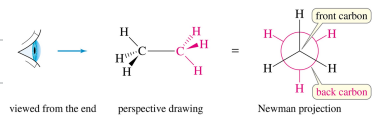
Ethane Representation

- Two sp^3 Carbons
- Conformations are different arrangements of atoms caused by free rotation about a single bond

Different than isomers because its only rotation

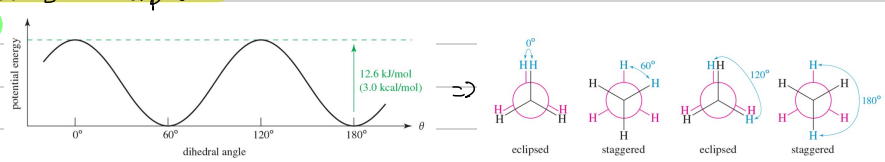
Newman Projections be able to convert easily

- The best way to judge stability of different conformations of a molecule



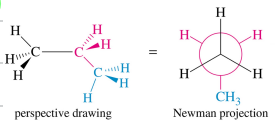
Conformations Explored

Ethane:

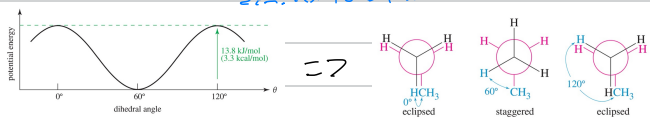


Eclipsed has higher energy, so staggered is more stable bc of lower Potential Energy observed.

Propane:

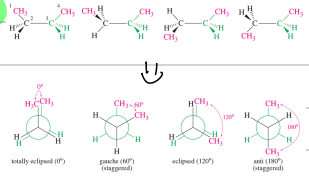


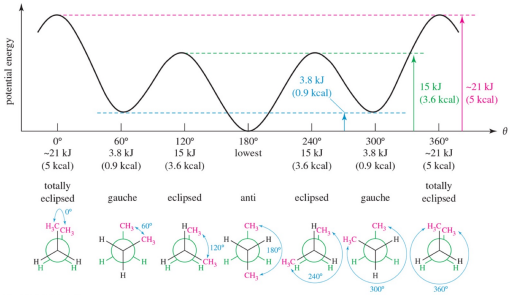
Similar to Ethane



Torsional - Bond
Steric - Size

Butane:





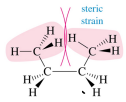
With rotation, there are different angles and these angles are reflected by their stability

total eclipsed has overlapped CH_3

↳ have some torsional strength

Practice Drawing Newman Projections based off of a requested angle

Steric Strain



Two bulky groups interacting like this is called steric strain. Has higher energy

Cycloalkanes do not have free rotation

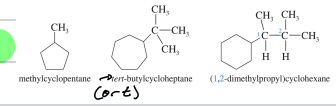
Cycloalkanes

← relatively nonpolar, inert, and bp dependent on weight

- No Number present if only one substituent

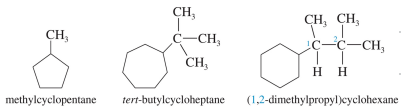
-yl ending is always a substituent, goes for these as well

Nomenclature:



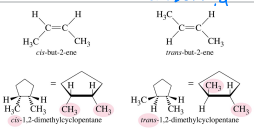
(ort)

Preferred numbering



Geometric Isomers:

Not conformers!!



Because there is no rotation in cycloalkanes, there can be cis-trans isomers

Important be cis-trans isomers reactivity?

Stability of Cycloalkanes

- Five- and Six-C rings are most common in nature
- require bond angle of 109.5° bc of sp^3 in cycloalkanes
- Angle strain, or Baeyer strain, is caused when a carbon is not 109.5°

① Cyclobutane is not stable, as the bonds are compressed to 90° bond angle
↳ Adopts a non planar geometry to avoid eclipsed situations

② Cyclopropane is even less stable because of the compressed 60° angle

③ Cyclopentane is more stable. Adopts envelope form to avoid eclipse

④ Cyclohexane is not flat! benzene's the hole

Chair has no eclipsed. It is most stable

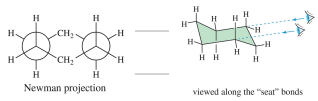
Boat conformation has twist and symmetrical form. less stable

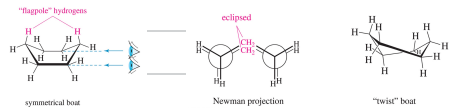
- Torsional strain occurs when all bonds are eclipsed

Be able to explain types of strain

Eclipsed = less stable
not as favorable

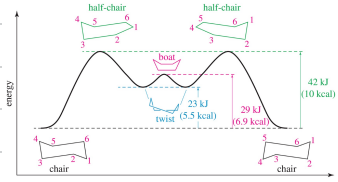
Must be comfortable drawing chair conformations





Eclipsed causes torsional strain

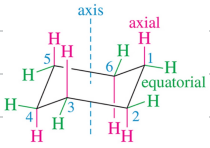
Conformational Energy Diagram:

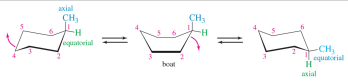


Axial / Equatorial

- Axial are directed vertically ∥ to the axis of ring ← parallel
- Equatorial are directed outward toward equator

Need to know!

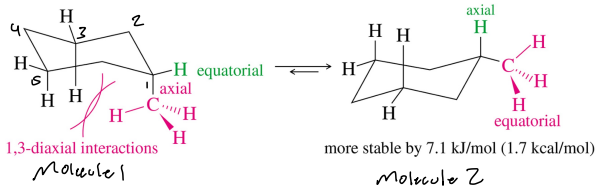




Must notch textbook

She will take off a lot of points if you draw the axial/equitorial wrong

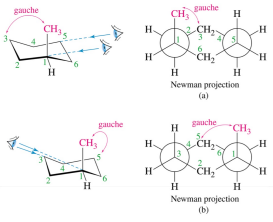
if equitorial/axial not drawn exactly not partial credit



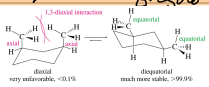
Molecule 1 Molecule 2

The axial substituent on molecule 1 interferes with the axial hydrogens on Carbons 3 and 5. This is called 1-3, diaxial interaction

Gauche interactions:

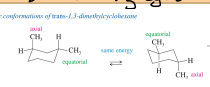


Cis-1,3-dimethylcyclohexane



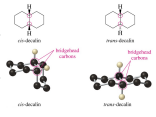
- Both methyl groups in axial positions or both equitorial
↳ both equitorial is more stable

Trans-1,3-dimethylcyclohexane



- Both conformations have one axial and one equitorial
↳ have the same energy

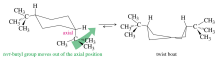
Cis = Substituents in same phase
Trans = opposite phase



Write neatly on exams!

Cis-1,4-di-tert-butylcyclohexane

Size of substituents plays role in stability



- twist boat is more stable here.

Bicyclic Systems

This is not tested on this course exams

- Fused rings: share two adjacent carbon atoms with the bond btwn them
- Bridged rings: share two non-adjacent carbon atoms and one or more C atoms bridge btwn them
- Spiro cyclo compounds: rare; the two rings only share one carbon

Chapter 4 - The Study of Chemical Reactions

Recall: A mechanism is a step-by-step description of how the reaction happens

Thermodynamics and Kinetics need to be used to properly describe products and perform chemical reactions

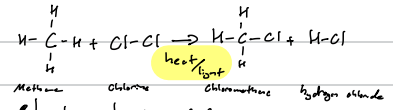
↳ **Thermo:** Study of energy changes
Kinetics: Study of reaction rates

These are not the same things!

Forming bonds
- generate energy

Breaking bonds
- require energy

Chlorination of Methane



- heat or light needed
- many molecules of the product are formed from absorption of only one photon of light

Mechanisms used to describe how a reaction like this occurs

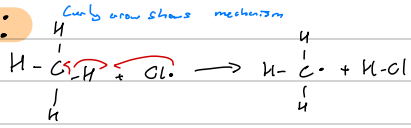
The Free-Radical Chain Reaction

- **Initiation:** generates a radical intermediate
- **Propagation:** Intermediate reacts with a stable molecule to produce another reactive intermediate (and a product molecule)
- **Terminations:** Side reactions that destroy reaction intermediates

Initiation Step: :Cl:Cl: + photon → :Cl· + ·Cl:
radical

Propagation step 1: Curly arrow shows mechanism

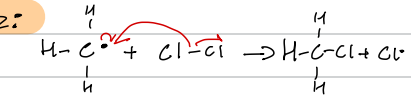
One fish hook



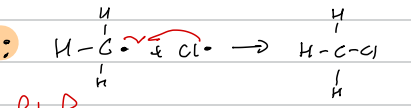
One e⁻ moving

use correct # of fish hooks on arrows

Propagation Step 2:



Termination Step:



Lewis Structures of free radicals

- Species w/ odd # of e⁻
- Halogens have 7 valence e⁻, so one of them will be unpaired (radical)

Equilibrium Constant

$aA + bB \rightleftharpoons cC + dD$

$$K_{eq} = \frac{[products]}{[reactants]} = \frac{[C]^c[D]^d}{[A]^a[B]^b}$$

These are helpful for chem B to generate favorable reactions

Larger K_{eq} favors products

Thermo

Gibbs Free Energy Change

- ΔG = energy of products − energy of reactants
  ↳ amount of energy available to do work

$\Delta G^\circ = -RT(\ln K_{eq}) = -2.303RT(\log_{10} K_{eq})$*

Recall: ΔH is enthalpy ← important!
ΔS is entropy ← not covered here

$\Delta G = \Delta H - T\Delta S$* *T is in Kelvin

Enthalpy

- ΔH is heat released or absorbed
- Exothermic: heat is released ($-\Delta H$)
- Endothermic: heat is absorbed ($+\Delta H$)
- Reactions favor products with the lowest enthalpy

For O-chem, entropy is negligable!

Negative $-\Delta G$ favors products, Exothermic does too @ negligable entropy

Bond Dissociation Enthalpies (BDE)

- If bond dissociation requires energy (+BDE)
- If bond dissociation releases energy (−BDE)
- Can be used to estimate ΔH for reactions

Homolytic Cleavage: Bond breaks → each atom gets one e⁻
↳ must be single fish hook arrow

Heterolytic Cleavage: Bond breaks → most EN atom gets both e⁻
↳ must be double fish hook arrow

Examples of BDE Cleavage

Homolytic (free radicals)

A:B → A· + ·B

Heterolytic (ions result)

A:B → A⁺ + ⁻:B

Enthalpy Changes in Chlorination

Add Energy on each side of rxn.
- Positive E on breaking
- Negative E on forming

Kinetics (Study of reaction rates)

- Rate of reaction is a measure of how the concentrations of products increase as starting materials decrease
- Rate laws show the relationship between conc. of reactants and observed rxn. rate
  ↳ determined experimentally

Rate Constant: $A + B \rightarrow C + D$

$rate = k_r[A]^a[B]^b$

k_r is rate constant

a is order w/ respect to A
b is order w/ respect to B
a+b is overall rxn. order

Order is the number of molecules of that reactant which is present at rate determining step of mechanism → The slowest step

k_r is big = fast
k_r is small = slow

Do not confuse k_r with Equilibrium K_{eq}

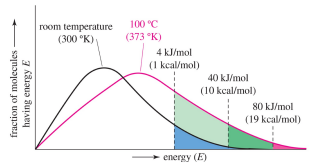
Activation Energy

- K_r depends on conditions of the rxn.

$$K_r = Ae^{-E_a/RT}$$

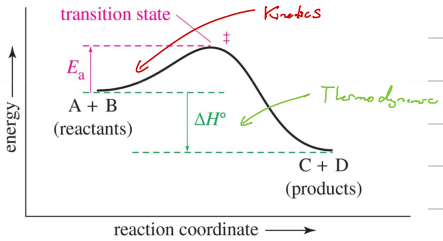
- A is constant (frequency factor)
- E_a = activation energy
- R = gas constant = $8.314\ J/K\cdot mol$
- T = absolute temperature (Kelvin)

At higher temperatures, more molecules have the required energy to react.



Energy Diagram of an Exothermic Reaction

- y-axis is always energy
- Transition state (‡) is the highest point on the graph
- Activation energy is difference between reactants and transition state

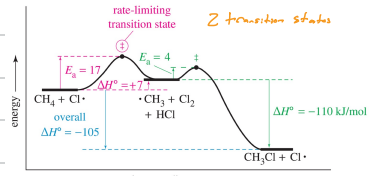


Know how to draw and interpret

The reaction here is exothermic because reactants energy > products energy

Rates of Multistep

- Highest points are transition states
- Lowest points in diagram are intermediates
- The rxn step with the highest E_a is the slowest → rate-limiting



Rate, E_a, and Temperature

$X\cdot + CH_4 \rightarrow HX + \cdot CH_3$

Reaction	E_a (per mole)	Relative Rate ($e^{-E_a/RT} \times 10^9$) 27 °C (300 °K)	227 °C (500 °K)
$F\cdot + CH_4 \longrightarrow HF + \cdot CH_3$	5 kJ (1.2 kcal)	140,000	300,000
$Cl\cdot + CH_4 \longrightarrow HCl + \cdot CH_3$	17 kJ (4 kcal)	1300	18,000
$Br\cdot + CH_4 \longrightarrow HBr + \cdot CH_3$	75 kJ (18 kcal)	9×10^{-8}	0.015
$I\cdot + CH_4 \longrightarrow HI + \cdot CH_3$	140 kJ (34 kcal)	2×10^{-19}	2×10^{-9}

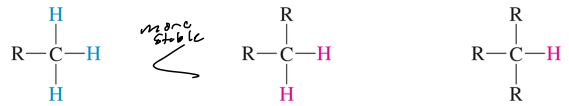
not as stereo, works with not many steric problems

- reacts explosively
- reacts moderately
- must be heated to react
- does not react

- Higher temperature → more Kinetic Energy
  - ↳ Means more molecules have their E_a
- Rate decreases as E_a increases
- Rate increases as temp increases

Primary, Secondary, and Tertiary Hydrogens

Must need to know how to identify these



At this point, if you can explain something, its probably stability

Bond Dissociation Energies for the Formation of Free Radicals

Formation of a methyl radical — *Bond-dissociation enthalpy*

$CH_4 \longrightarrow H\cdot + \cdot CH_3$ — $\Delta H° = 439$ kJ (105 kcal)

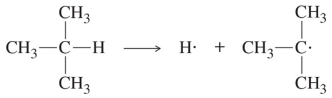
Formation of a primary (1°) radical

$CH_3{-}CH_2{-}CH_3 \longrightarrow H\cdot + CH_3{-}CH_2{-}\dot{C}H_2$ — $\Delta H° = 423$ kJ (101 kcal)

Formation of a secondary (2°) radical

$CH_3{-}CH_2{-}CH_3 \longrightarrow H\cdot + CH_3{-}\dot{C}H{-}CH_3$ — $\Delta H° = 413$ kJ (99 kcal)

Formation of a tertiary (3°) radical

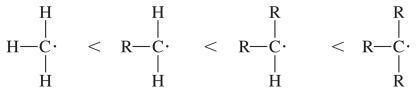


$\Delta H° = 403$ kJ (96 kcal)

Stability of Free Radicals

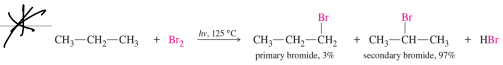
Must be known on exams

- Highly substituted radicals = more stable



Me· < 1° < 2° < 3°

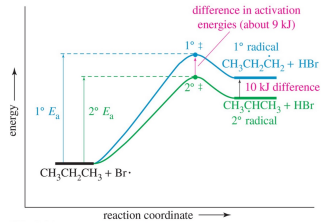
methyl < primary < secondary < tertiary



Look into this more

Bromination of Propane

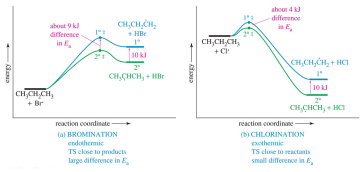
- Endothermic, so the energy of products > reactants. This is not as reactive
- Need a lot of heat to start



Hammond Postulate

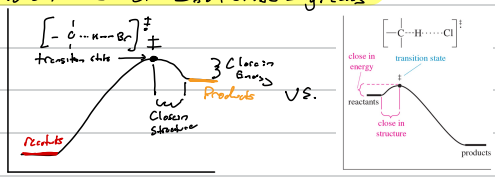
- Related species that are similar in energy are also similar in structure.
- The structure of the transition state resembles the structure of the closest stable species.
- **Endothermic reaction**: Transition state resembles the product.
- **Exothermic reaction**: Transition state resembles the reactant.

Compare Chlorination vs. Bromination



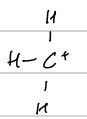
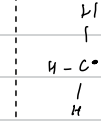
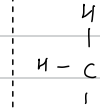
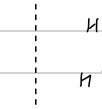
Here, the y-axis is enthalpy

Endothermic and Exothermic Diagrams



Reactive Intermediates

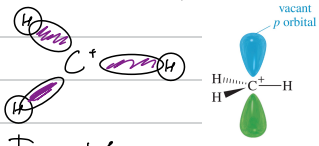
- Short lived species
- Never present in high conc. bc they react as quickly as formed

Carbocation	Radical	Carbanion	Carbene
			

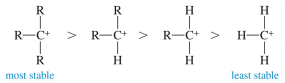
Know how Primary, Secondary, Tertiary effects stability and reactivity

Carbocation Structure

- Positively charged carbon
- Carbon is sp^2 hybridized with a vacant p orbital



Top View



3° > 2° > 1° > methyl

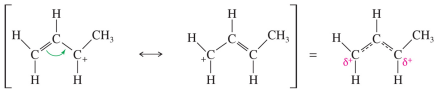
Know this and how it works

Stabilized intro vgs

- Inductive Effect: e⁻ density along bonds
- Hyperconjugation: Overlap of σ bonding orbitals with empty p orbitals

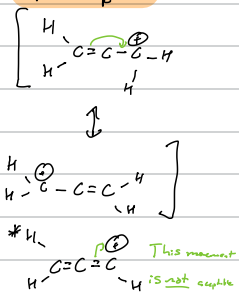
Unsaturated Carbocations

- Also stabilized by resonance



- If a π bond is adjacent to a carbocation, the filled p orbitals of the bond will overlap with the empty p orbital of the carbocation

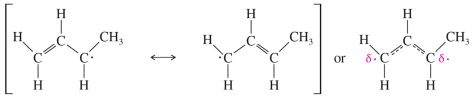
Examples



*Do not do this on exams!

Carbon Radicals

- Can also be stabilized by resonance
  - ↳ only one e⁻ moving



- Also follows 3° > 2° > 1° > methyl.

Carbanions

- sp^3 hybridized
- Negative charges are nucleophilic and basic
- Exact opposite of Carbocations
  - ↳ methyl > 1° > 2° > 3°

Basicity of Carbanions

- Stronger nucleophile than an amine. Neg charge = more powerful base

Basic enough to remove a proton from ammonia

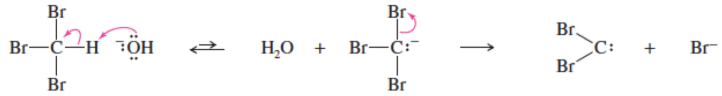
$R_3C:^- + :NH_3 \longrightarrow R_3CH + {}^-:\ddot{N}H_2$

Carbenes

- Neutral

- Can act as an electrophile or nucleophile

This carbanion expels bromide ion to give dibromocarbene.



Summary of Reactive Species

	Structure	Stability	Properties
carbocations	$-C^+$	3° > 2° > 1° > $^+CH_3$	electrophilic strong acids
radicals	$-C\cdot$	3° > 2° > 1° > $\cdot CH_3$	electron-deficient
carbanions	$-C:^-$	$^-:CH_3$ > 1° > 2° > 3°	nucleophilic strong bases
carbenes	$>C:$		both nucleophilic and electrophilic

Know this well enough to not even need it on the cheat sheet

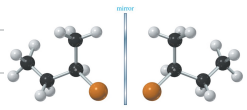
Chapter 5 - Stereochemistry

Chirality "Handedness": Right hand glove does not fit the left hand

An object is **chiral** if its mirror image is different from the original object

Achiral: Mirror images that can be superimposed

Enantiomers: compounds that are nonsuperimposable mirror images



↳ practice doing this with your model

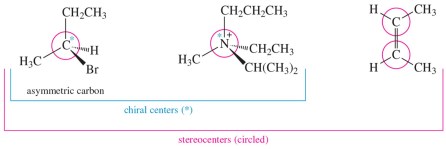
Chiral Carbon can also be called asymmetric

Achiral Carbon is Attached to Four different groups!

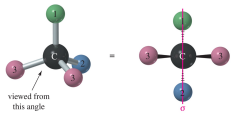
Stereocenters

- An asymmetric carbon is the most common example of a chirality center
- Chirality centers belong to the broad group: stereocenters ← any atom where the interchange of two groups gives a stereoisomer

↳ cis-trans isomers and double bonded carbons are most common example



A molecule that has a plane of symmetry is achiral



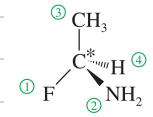
Even non planar molecules like cis cyclo structures can be superimposed along a line of symmetry

Trans Cyclo Compounds doesn't have a plane of symmetry → molecule will have 2 enantiomers

Priority Scale: I > Br > Cl > S > F > O > N > 13C > 12C > Li > 2H > 1H

(R) and (S) Configurations Gives a way to distinguish btwn enantiomers

Know how to number



① Assign Priority: Atoms with higher atomic numbers receive higher priorities

If you have isotopes, the one with the higher mass gets priority

Break Ties: Use next atoms along chain to break ties

Multiple Bonds: Treat as if there's bonds to separate atoms

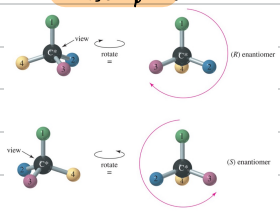
② Assign configuration: Put Lowest priority in back

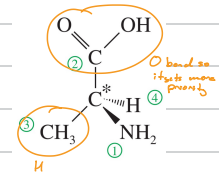
Draw arrow from highest to lowest

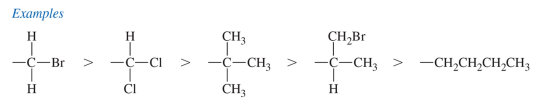
Arrows: Clockwise = (R)

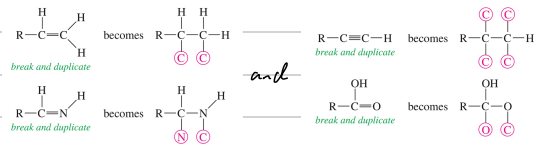
Counter Clockwise = (S)

Examples





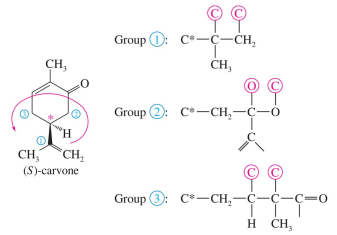




When modeling, always put lowest priority to the back!!!

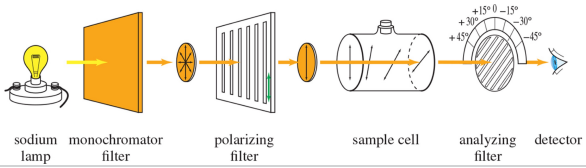
Be able to make R and S configurations based on different compound presentations

Example: Absolute Configuration in Cyclo Compounds



Properties of Enantiomers

- Same melting point, boiling point, density, and refractive index
- Rotate polarized light in opposite directions
- Different interactions with other chiral molecules



R and S is just a name, this process isn't related to R and S

↳ enantiomers rotate the light in equal magnitudes, but opposite directions/signs

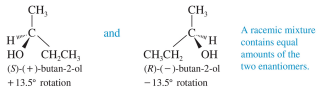
Called a Polarimeter, the light is clockwise (+) and counterclockwise (−)

Do not get this confused with R and S, they are not the same!

Important!

- (R) and (S) are absolute configurations
- (+) and (−) are reflecting polarized light

Racemic Mixtures



- 50/50 or equal quantities of enantiomers
- The mixture must have different bp and mp from the enantiomers
- Notation: (d, l) or (±)

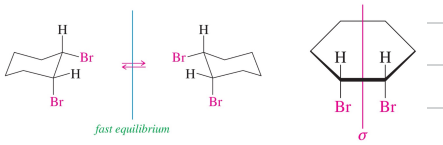
Optical Purity is sometimes called enantiomer excess

Racemic Products

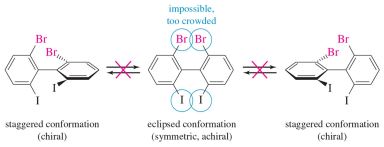
- If optically inactive reagents combine to form a chiral molecule, a racemic mixture is formed.

Chirality of Conformers

- If equilibrium exists btwn two chiral conformers, the molecule is not chiral
- Judge chirality by looking at the most symmetrical conformer
- Cyclohexane can be considered to be planar, on average



Non mobile Conformers

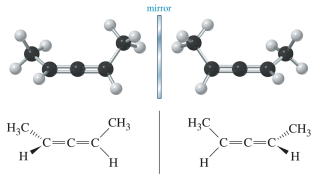


- Planar conformation of the biphenyl derivative is too sterically crowded
- The compound has restricted rotation around central C–C bond → conformationally locked
- Staggered conformers are chiral

Allenes

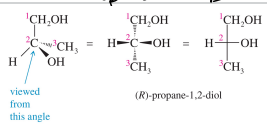
- Some allenes are chiral despite lacking a chiral carbon
- Central carbon is sp hybridized
- To be chiral, the groups at the end carbons must have different groups

Penta-2,3-diene Is Chiral



Required to assign stereochemistry from Fischer Projections

- Flat rep of 3D



Lowest and Highest Priority into front

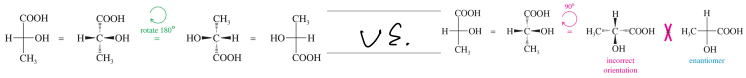
Fischer Projections always looked at through lowest and highest priority pointing out

- Carbon chain on vertical
- Highest oxidized carbon on

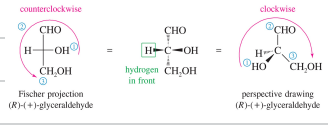
{ 180° is allowed, no impact
{ 90° is not allowed

Vertical = behind plane Horizontal = into plane

Explained Rotation rules:

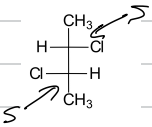


Example Glyceraldehyde



Recall: CHO gets priority of double bond rule

Fischer (R) and (S) Example



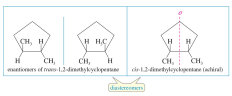
Two or more Chiral Carbons

- Have enantiomers, diastereomers, or meso isomers

Enantiomers: Opposite config @ chiral

Diastereomers: Some matching same equiv

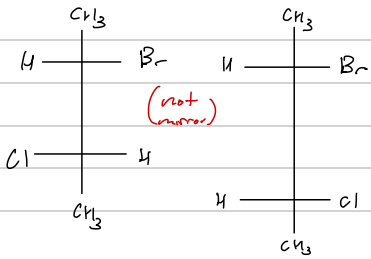
Meso: Have internal mirror planes



Diastereomers: Cis–Trans Isomers:

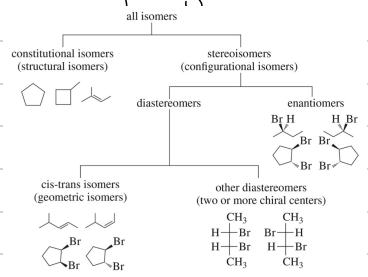
Def: Stereoisomers that are not mirror images of each other

Cis Trans Isomers are not mirror images of each other, so they are diastereomers



- Two or more chiral carbons
- Not superimposable

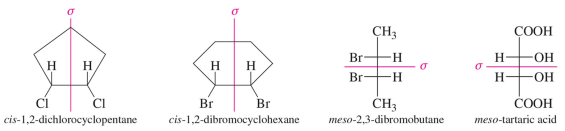
Comparing Structures



Meso Compounds

achiral

- Have a plane of symmetry
- 180° Rotation → superimposible



2^n rule in slides but not tested

Absolute vs. Relative Config

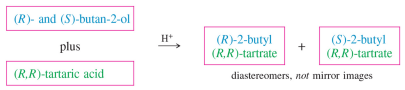
- Absolute: Detailed protein, Arrangement in space
- Relative: Experimental

Diastereomers Properties

- Different physical properties, easy to work with as opposed to enantiomers

It is useful to convert enantiomers into diastereomers and then separate the racemic mixture

Example of this process:



Chapter 6 - Alkyl Halides; Nucleophilic Substitution

Alkyl Halides: Halogen directly to sp^3 carbon

Vinyl Halides: Halogen bonded to an sp^2 carbon of an alkene

Aryl Halides: Halogen bonded to an sp^2 carbon of benzene ring

C–H bond = nonpolar

X is Halogen: C–X bond = polar

Always break Carbon Halogen bond 1st

IUPAC Nomenclature important to know be you can identify carbons by number

She only cares about IUPAC for numbering, so be able to do it quickly and comfortably

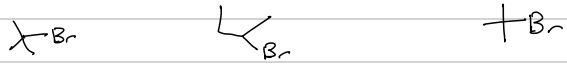
2-chloro butane

4-(2-fluoroethyl) heptane

Be able to name these quickly

She loves curly arrows, and mechanism steps/products

Recall: iso butyl, sec-butyl, t-butyl

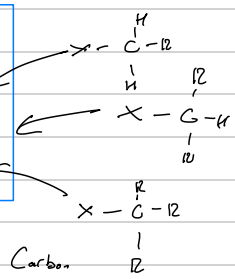


Methyl Halide: X to methyl, CH_3X

(1°) Primary Halide: X to only one carbon

(2°) Secondary Halide: X to two carbons

(3°) tertiary Halide: X to three carbons



Common Names

- CH_2X_2 methylene Halide
- CHX_3 is haloform
- CX_4 is carbon tetra halide

Halide replaced with atom 'X'

D. Halide: Geminal: Halogens are on identical Carbon

Vicinal: Halogens on Adjacent Carbons

This is linked to Ch 4 radical reactions

Dipole Moments

Size Matters

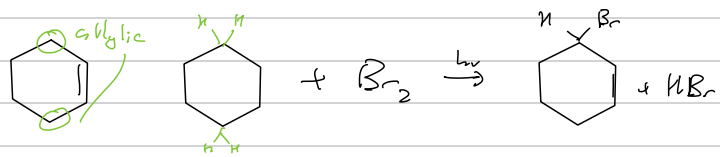
- EN Rank: F > Cl > Br > I
- Bond Dipoles: C–Cl > C–F > C–Br > C–I

This is due to polarizability

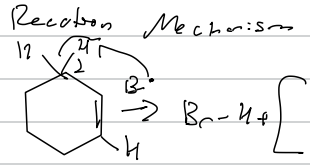
Recall: Molecule Dipoles depend on geometry

Same bp and dipole rules from earlier chapters

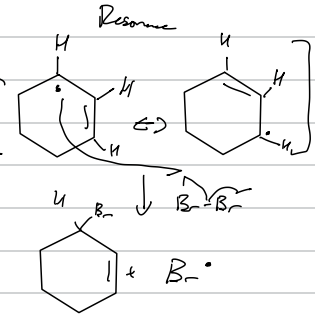
Allylic Bromination



Reaction Mechanism



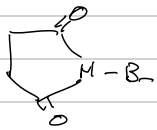
Resonance



Delocalization is good as it lowers E_a

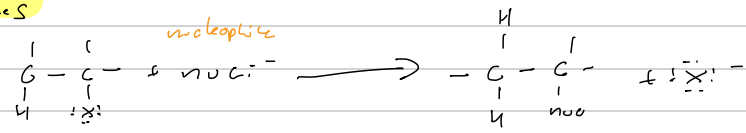
NBS

- N-Bromosuccinimide is an allylic bromination agent
- Keeps concentration of Br_2 low



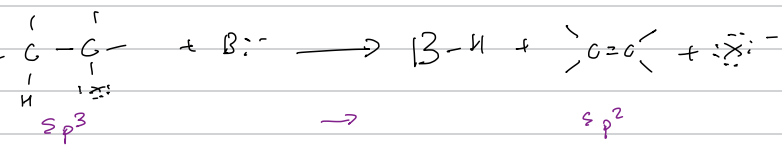
Reactions of Alkyl Halides

Nucleophilic Substitution: Very similar to acid-base



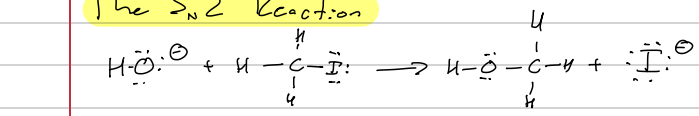
Nucleophiles, by def, are e^- rich entities

Elimination: Abstracts Proton

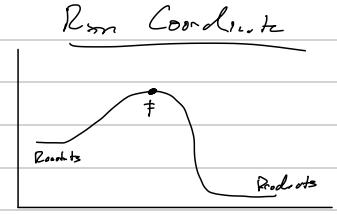


Be very comfortable with stability of 1°, 2°, 3° and carbocation stability

The S_N2 Reaction



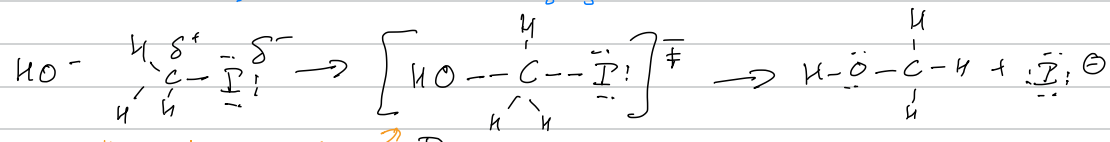
Know when to use single vs. double fishhook in mechanism



- Halogen on the Alkyl Halide replaced with the nucleophile, OH^- here

Since the Halogen is more EN than carbon, the C–I bond breaks heterolytically → I leaves

Mechanism:



Can have "S bonds" in ‡ as the dashed lines are happening at the same time!

Transition State

- One step Reaction! No intermediates
- Transition State is highest Energy

Nucleophile Strength: (in S_N2)

Stronger nucleophiles react faster

↳ Strong bases are strong nucleophiles, but not all strong nucleophiles are basic

Basicity vs. Nucleophilicity

- Basicity – defined by the eq. constant for abstracting a proton
- Nucleophilicity – defined by rate of attack on electrophilic Carbon

Examples of Trends

① Negatively charged > neutral
② Decreases from Left → right
③ Increases down periodic table ← size and polarizability increase

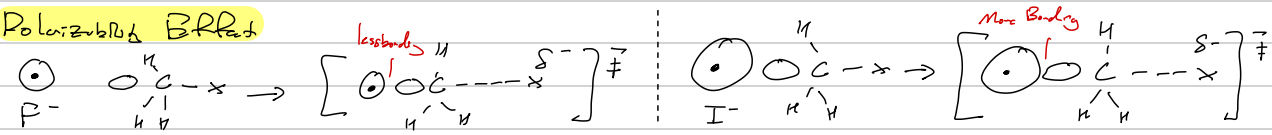
Trends

$-:\ddot{O}H > H_2\ddot{O}$ or $-:\ddot{S}H > H_2\ddot{S}$ or $-:\ddot{N}H_2 > :NH_3$

$-:\ddot{N}H_2 > -:\ddot{O}H > :\ddot{F}:^-$ or $:NH_3 > H_2\ddot{O}$ or $(CH_3CH_2)_3P: > (CH_3CH_2)_2\ddot{S}:$

$:\ddot{I}:^\ominus > :\ddot{Br}:^\ominus > :\ddot{Cl}:^\ominus > :\ddot{F}:^\ominus$

Polarizability Effect

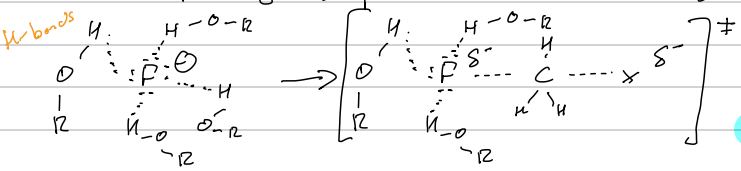


Bigger atoms have a soft shell that can overlap with carbon from further away

Exam will test individual parameters in questions

Solvent Effects: Protic Solvents

- Polar Protic Solvents have acidic hydrogens → solvate nucleophile → reduce nucleophilicity
- Nucleophilicity in protic solvents ↑ as size of atom ↑



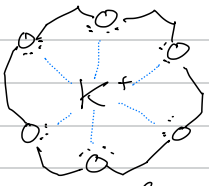
- Polar aprotic solvents do not have acidic protons → no H-bonds
- S_N2 reactions proceed faster in aprotic solvents!!!

S_N2 prefers Aprotic Solvents

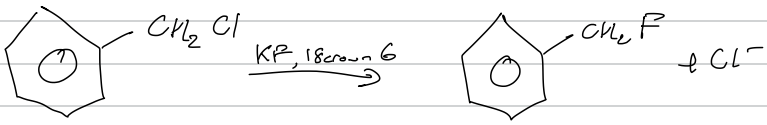
Crown Ethers

- Solvate the cations → nucleophilic strength of anion increases

↳ Fluoride becomes a good nucleophile



18-crown-6



Degree is based off # of alkyl groups connected to carbon with halide!

Leaving groups

Best Leaving groups are:

- e^- withdrawing to polarize the carbon atom
- Stable once they leave (not a strong base after leaving)
- Polarizable, to stabilize ‡

Structure of Substrate on S_N2

- Relative Rate:

$CH_3X > 1^\circ > 2^\circ >> 3^\circ$

Tertiary halides do not react via S_N2 mechanism bc of steric hindrance

Tertiary Tertiary

Know the Effects of Substituents on the S_N2 Rxn Rates

Stereochemistry of S_N2

S_N2 is Backside Attack

- Result in an inverted configuration also called Walden inversion
  - ↳ This is why steric effect plays such a large role, too big groups → no backside attack from halide

S_N1 Reaction ← Racemization occurs

- Unimolecular nucleophilic substitution — Mixture of stereoisomers in S_N1!
- Has a carbocation intermediate
- Rate = K_r [alkyl halide] ← rate dependent only on alkyl halide unlike S_N2

Mechanism:

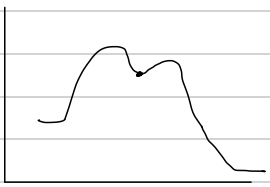
1. Forming Carbocation ← rate limiting step

   $R-\ddot{X}: \rightleftharpoons R^+ + :\ddot{X}:^{\ominus}$

   ↳ $G^{\ddot{}}$

2. Attack of Nucleophile
3. Product + protonated nucleophile

S_N1 has 3 steps!



Order of reactivity

- Opposite of S_N2

  $3^\circ > 2^\circ > 1^\circ >> CH_3X$ ← 3° carbocation > 1° carbocation in terms of stability ↳ lower E_a so this favorable here

- Better leaving group → rate↑

Recall Carbocation Stability

$3^\circ > 2^\circ > 1^\circ > CH_3$

Solvent Effect on S_N1

- Polar protic solvents best bc it can solvate both ions strongly through H-bonding

Structure of Carbocation ← Effects S_N1

- Carbocations are sp^2, empty p orbital on both sides

Nucleophile attack can occur from either side, producing mixtures of retention and inversion if chiral

Stereochemistry of S_N1: Produces mixtures of enantiomers. Usually more inversion than retention

Rearrangements: Carbocations can rearrange to form a more stable carbocation

- Move smallest group on the adjacent carbon

Know Hydride and Methyl Shifts

Hydride Shift: H^- on adjacent carbon moves

Methyl Shift: CH_3 on adjacent carbon moves

S_N1 of S_N2 Mechanism

S_N2	S_N1
$CH_3 > 1^\circ > 2^\circ$	$3^\circ > 2^\circ$
Strong Nucleophile	weak Nucleophile
Polar aprotic solvent	polar protic solvent
Rate = K_r [alkyl Halide][Nu:]	Rate = K_r [alkyl Halide]
Inversion at chiral C	Racemization
No rearrangements	rearranged products

Take your time on this so you know exactly what criteria correspond to S_N1 vs. S_N2

Memorize these for the exam!

More in-depth on Sides

Chapter 7 - Structure and Synthesis of Alkenes

Alkenes (Olefins) - Characterized by its C=C. They are sp^2 hybridized (120°)

↳ Their hybridization results in unhybridized p orbitals

- More % s character compared to alkanes

↳ Bond Length ≈ 1.33 Å compared to 1.54 Å in alkanes

IUPAC

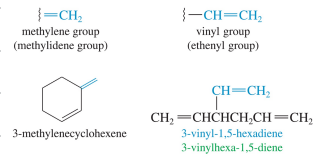
- -ene ending
- Double Bond gets Priority
- In ring, Double bond is btwn 1 and 2
  - ↳ Lowest number on Alkene and Substituents

di, tri, etc. apply for multiple

Exhibit Cis-Trans Isomerism ← no rotation around double bond; no interconversion

Know the common names to the left on exams

She likes to use vinyl on exams



Cis-Trans Isomerism (continued)

Similar groups on same side of bond = cis

Similar groups on opposite side = trans

- Not all alkenes exhibit cis-trans isomerism

Cyclic Compounds

- Trans cycloalkenes not stable unless ring has at least 8 carbons
- All cycloalkenes are assumed to be cis unless specifically named trans

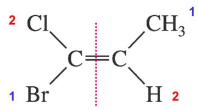
E-Z Nomenclature

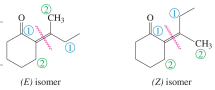
- Use Cahn-Ingold-Prelog Principle to assign priorities
- High priority groups on same side of bond = Z
- High priority groups on opposite side = E

E and Z reserved for Alkenes

R and S reserved for Alkanes

E-1-bromo-1-chloropropene

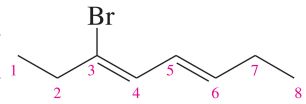




Be able to distinguish E-Z well

Take your time on cyclics!

Stereochemistry in Dienes



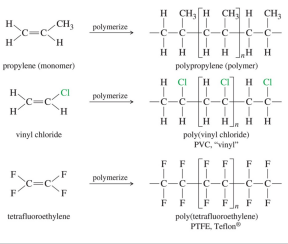
(3Z,5E)-3-bromoocta-3,5-diene

- If there are multiple double bonds, the configuration of all the double bonds should be specified!

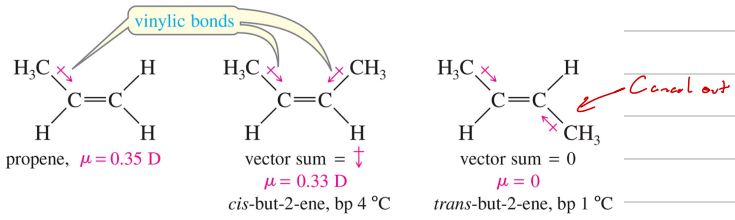
Polymers!

- Not testable
- Cool application
  - ↳ Ethylene used

Evaluate bc p: bond is nice for addition



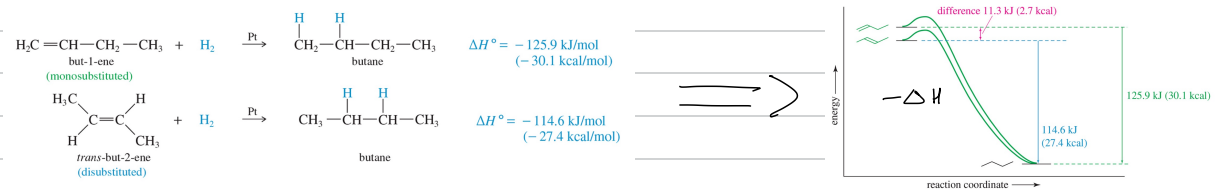
Different Polarity than Alkanes



Cis alkenes very slightly polar. Cis alkenes have higher bp. than trans alkenes

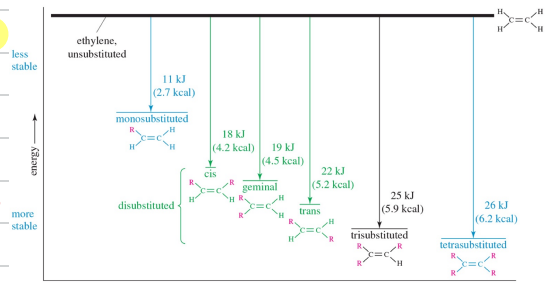
Heat of Hydrogenation

- Combustion of an alkene and hydrogenation of an alkene can provide stability information
- More substituted Double bond → Lower heat of hydrogenation



Relative Stability

Stable molecules not good reactants, but they are good products



Cycloalkenes

- A ring makes a difference only if there is ring strain, either be of a small ring or a trans double bond
- Rings that are 5-membered or larger easily accomodate double bonds, and these cycloalkenes react more and more like straight-chained alkenes

Cis more stable than Trans in small cycloalkenes
↳ For cyclodecene and above, trans ≈ cis in stability

} At least 8 carbons needed to have a stable double bond

Bridged bicyclo compounds cannot have a double bond unless one ring > 8 carbons

Physical Properties of Alkenes (Class discussion notes)

- Low b.p., increasing with mass
- Branched alkenes have lower b.p.

} Same reasons as Alkanes

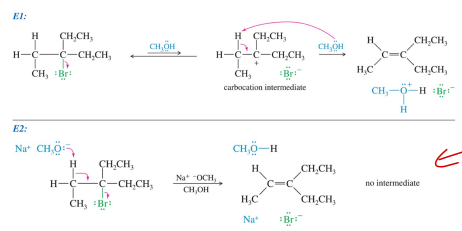
- Slightly Polar ← π bonds polarizable

Alkene Synthesis Overview

- E2 dehydrohalogenation (–HX)
- E1 dehydrohalogenation (–HX)
- Dehalogenation of vicinal dibromides (–X2)
- Dehydration of alcohols (–H2O)

Elimination Rxns

- Produce Double bonds
- Also called dehydrohalogenation (–HX)
- E1 and S_N1 compete with each other frequently
- E_2 is similar to S_N2



Look over Hydride and Methyl Shift

← Very Specific like S_N2

The E1 Rxn

- Unimolecular elimination
- A hydrogen and the halide are lost
- Nucleophile acts as a base
- E1 and S_N1 have same conditions

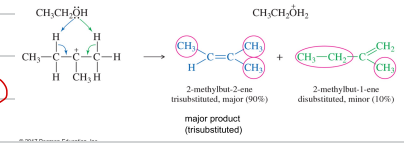
Zaitsev Rule

If more than one elimination products is possible, the most substituted alkene is the major product (most stable)

Don't just name drop, explain whats happening on exams!

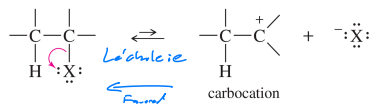
Stability

If you see a negative charge immediately think E2 or S_N2

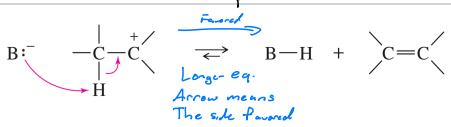


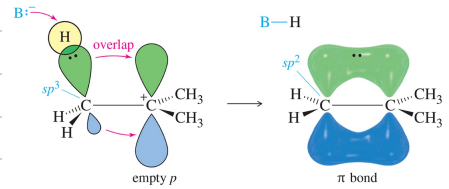
Mechanism

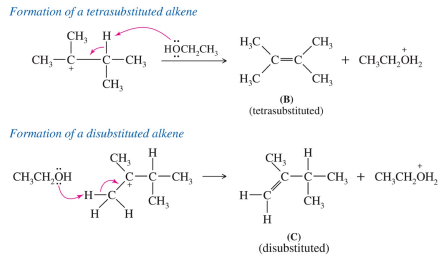
① Ionization to form carbocation



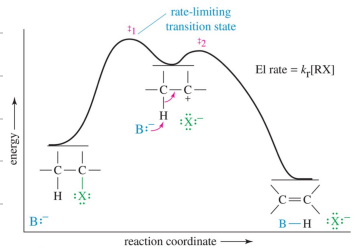
② Solvent abstracts proton to form alkene







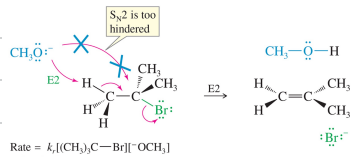
E1 Energy Diagram



- Similar to S_N1 Diagram
- Product is lower than Reactants

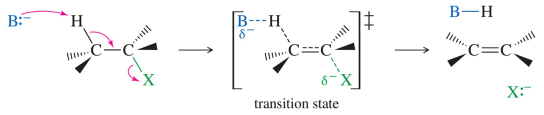
E2 Rxn

- Elimination, bimolecular
- Requires a strong base
- Everything happens in one step



A mixture may form, but Zaitsev product will dominate

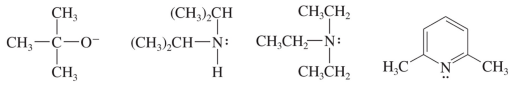
Mechanism



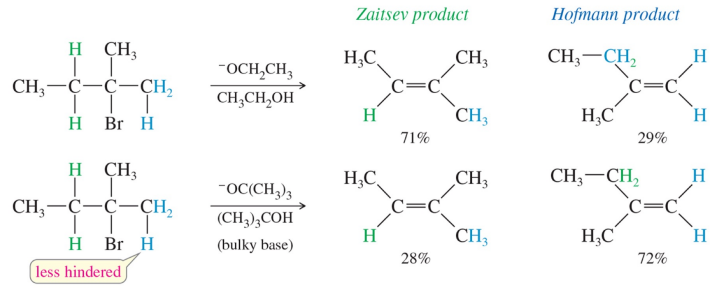
Order of Reactivity of Alkyl Halides: 3° > 2° > 1°

Zaitsev vs. Hofmann Products

Hoffman Product



- If the substrate in an E2 elimination is prone to substitution, we can minimize the amount of substitution by using a bulky base.
- Bulky bases can accomplish dehydrohalogenations that do not follow the Zaitsev rule. They form the **Hofmann product**.



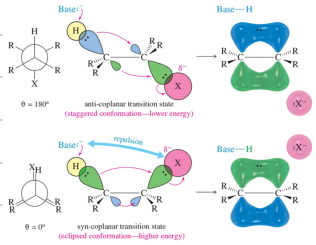
Be able to identify 1,2 hydride shift or 1,2 methyl shift

E2 Stereochemistry

- Halide and proton to be abstracted must be anti-coplanar to each other ($\theta = 180°$)
- Orbitals of Hydrogen atom and halide must be aligned

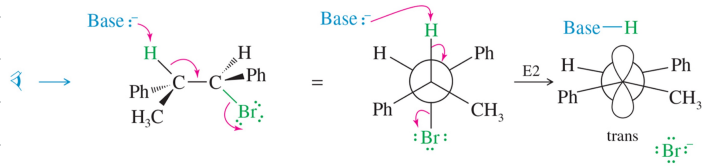
Anti-coplanar minimizes steric strain btwn base and leaving group

- When eclipsed e⁻ density are closer. This leads to a transition state with higher energy, which is less favorable



Most E2 reactions go through an anti-coplanar ↑

- Geometry is most apparent when looking at a Newman Projection

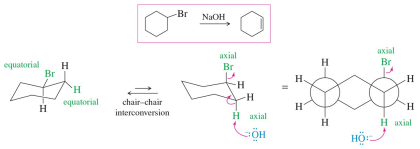


When doing E2 mechanism, make sure all of the arrows, or e⁻ movement, occurs in the same step

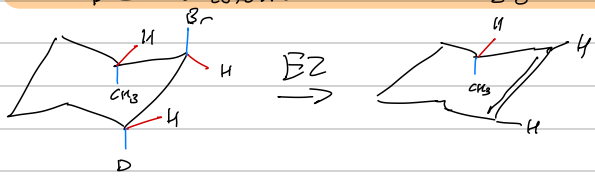
E2 Rxns on Cyclohexanes

Understand how axial/equitorial impact elimination rxns.

- An anti-coplanar conformation can only be achieved when both the Hydrogen and the halogen occupy axial positions
- The chair must flip to the conformation with the axial halide for elimination to take place



Example: deuterated 1-bromo-2-methylcyclohexane



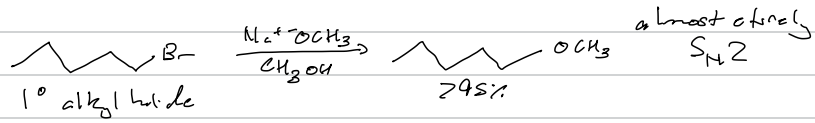
Substitution or Elimination

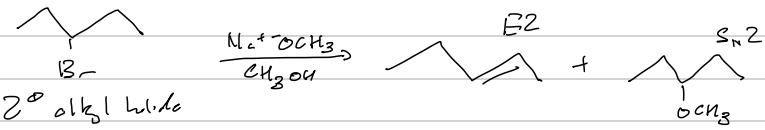
Rules to follow or summary

- Strength of nucleophile determines the order: Strong nucleophiles or bases promote bimolecular rxns.
- Primary Halides usually undergo S_N2
- Tertiary halides are a mixture of S_N1, E1, or E2. They cannot undergo S_N2
- High temperature (120°C) favors elimination
- Bulky bases favor elimination ← Hofmann dominates here

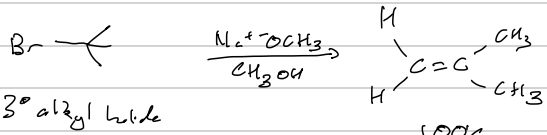
Know when Zaitsev or Hofmann will dominate

Examples of Common Rxn types





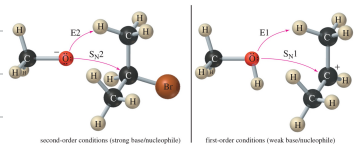
Proportions of each depend on conditions



Entirely E2

Secondary Alkyl Halides ← more challenging

Example

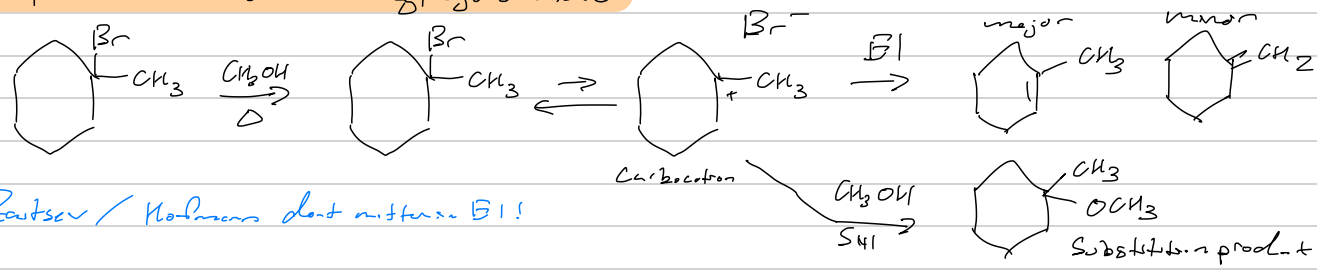


- Strong Nucleophiles promote S_N2 / E2
- Weak Nucleophiles promote S_N1 / E1

} Consider nucleophile strength first to narrow down problem!

- Strong nucleophiles with limited basicity favor S_N2.
  - ↳ Bromide and iodide are good examples

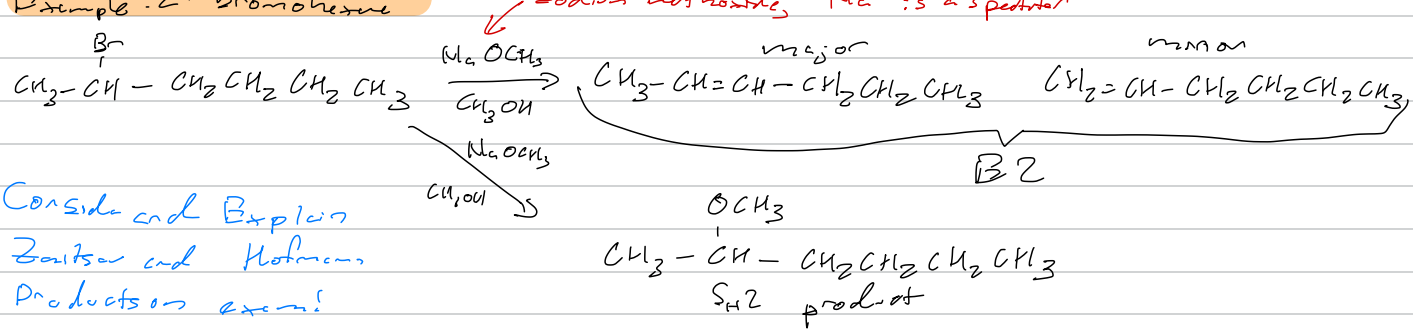
Example: 1-bromo-1-methyl cyclohexane



Zaitsev / Hofmann don't matter in E1!

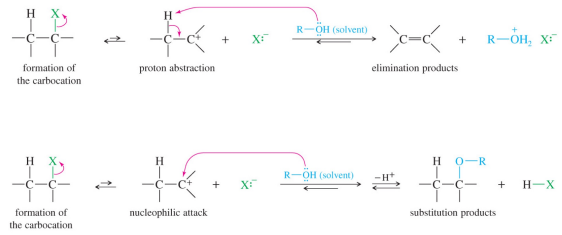
Example: 2-bromohexane

Sodium methoxide, Na is a spectator



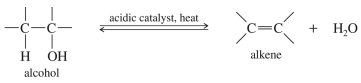
Consider and Explain Zaitsev and Hofmann Products on exam!

E1 vs. S_N1 Mechanisms



Dehydration of Alcohols

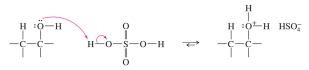
- Concentrated H_2SO_4 or H_3PO_4 → remove low-boiling alkene as it forms to shift eq.
- E1 mechanism
- Rearrangements are common
- Obeys Zaitsev's rule



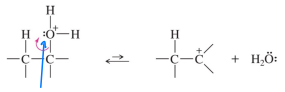
Lookout for Hydride or Methyl shift. Only do it when you can create a more stable carbocation

Mechanism of Dehydration: E1

Step 1: Protonation of the hydroxyl group (fast equilibrium)



Step 2: Ionization to a carbocation (slow; rate limiting)



Positive charge on oxygen is not favorable

Step 3: Deprotonation to give the alkene (fast)

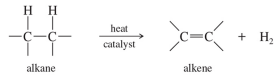
Catalytic Cracking of Alkanes ← not testable, just fun fact

- Long chain alkane heated with a catalyst to produce an alkene and shorter alkane
- Complex mixtures are produced

Dehydrogenation of Alkanes

- Removal of H_2 from a molecule, forming an alkene
- Unfavorable enthalpy change but favorable entropy change

Ex. →



ΔH° = +80 to +120 kJ/mol (+20 to +30 kcal/mol) ΔS° = +125 J/kelvin-mol

Summary of Rxn Mechanisms

1. First, Look at nucleophile strength and structure of alkyl halide ← narrow down possible rxn mechanisms
   ↳ Both of these should be looked at

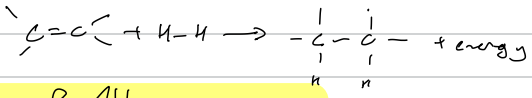
Strong Nucleophile = weak Nucleophile =

Look for patterns in Questions asked!

2. Next look at Rxn conditions like heat and size of base

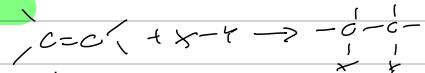
Chapter 8 - Reactions of Alkenes

Carbon Double bond - Unsaturated. Most common rxn bonds $\pi \rightarrow \sigma$

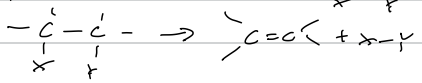


Types of Alkene rxns

Addition:



Elimination:



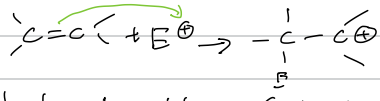
Substitution:

Bonding in Alkenes

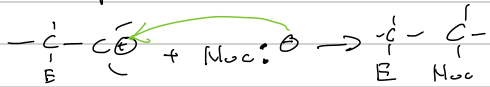
- Electrons in pi bonds are loosely held.
- The double bond acts as a nucleophile attacking electrophilic species.
- Carbocations are intermediates in some of these reactions.
- These reactions are called **electrophilic additions**.

Electrophile Addition Mechanism

① π e^- attack the electrophile



② Nucleophile attacks Carbocation



Types of Additions Table

TABLE 8-1
Types of Additions to Alkenes

Type of Addition [Elements Added][a]	Product	Type of Addition [Elements Added][a]	Product
hydration [H_2O]	H OH	halogenation [X_2], an oxidation	X X
hydrogenation [H_2], a reduction	H H	halohydrin formation [HOX], an oxidation	X OH
dihydroxylation [HOOH], an oxidation	OH OH	HX addition [HX] (hydrohalogenation)	H X
oxidative cleavage [O_3], an oxidation	C=O O=C	cyclopropanation [CH_2]	H H
epoxidation [O], an oxidation	O		

[a]These are not the reagents used, but simply the groups that appear in the product.

Addition of Hydrogen-Halide (HX) to Alkenes

① Protonation of the double bond

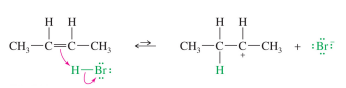
↳ Form most stable carbocation possible

② Nuc attacks carbocation → alkyl halide

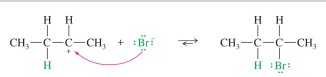
↳ HBr, HCl, and HI can be added through this rxn

Mechanism

①



②

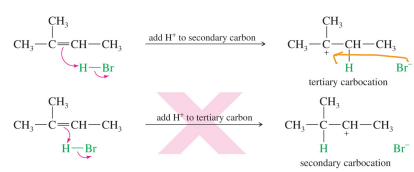


Regio Selectivity

Markovnikov's rule: The addition of a proton to the double bond of an alkene results in a product with the acidic proton bonded to the carbon atom that already holds the greater number of hydrogens.

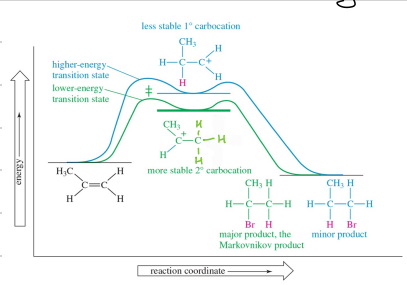
Markovnikov's rule (extended): In an electrophilic addition to the alkene, the electrophile adds in such a way that it generates the most stable intermediate.

Markovnikov Rule



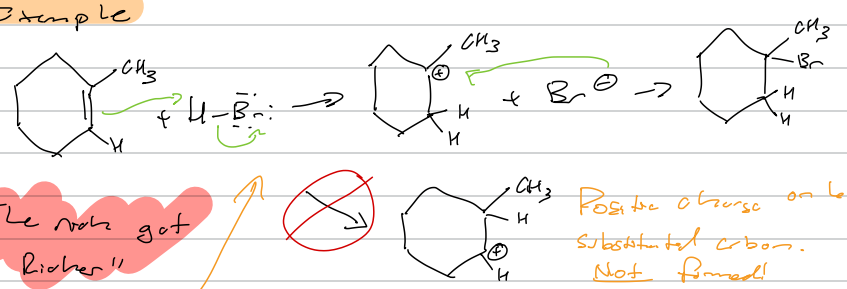
Acid Proton will bond to Carbon 3 in order to produce the most stable carbo cation

Rxn Coordinate Diagram



Markovnikov Product is more Stable

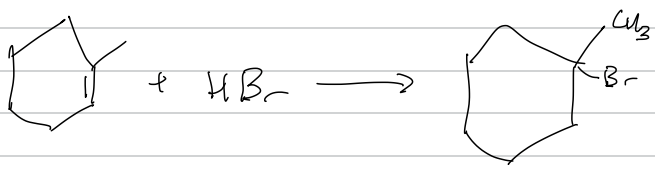
Example



"The rich got richer"

Positive charge on less substituted carbon. Not formed!

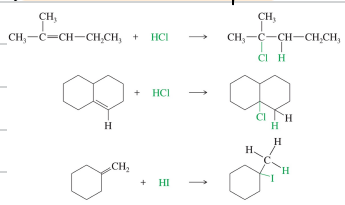
Example: How would you convert 1-methylcyclohexene to 1-bromo-1-methyl cyclohexane



Addition adding a halide

logical choice: HBr

More Examples



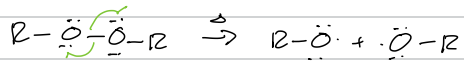
Place ⊕ on the more substituted carbon

Free-Radical Addition of HBr

- In presence of peroxides, HBr adds to an alkene to form the "anti-markovnikov" product
- Peroxides produce free radicals
- Only HBr has just the right reactivity for each step to take place

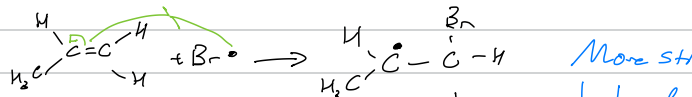
Free Radical Mechanism

Initiation — Peroxide bond breaks homolytically



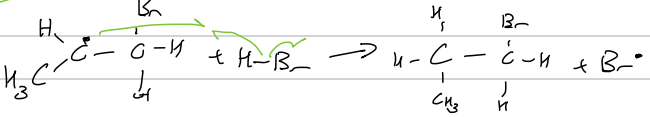
Hydrogen is abstracted from HBr

Prop 1 — Bromine adds to double bond, forming most stable radical

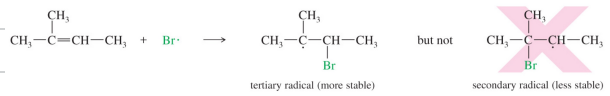


More stable intermediate is formed

Prop 2 — Hydrogen abstracted from HBr



Anti-markovnikov Stereochemistry



- Intermediate tertiary (3°) radical forms faster because it is more stable

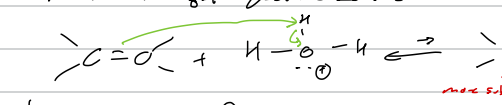
Hydration of Alkenes

- Addition of water to double bond forms an alcohol
- Follows markovnikov's rule
- Reverse of dehydration of alcohol
- Uses dilute solutions of H_2SO_4 or H_3PO_4

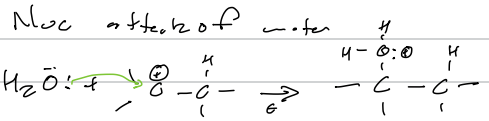
Mechanism of Hydration

Do not put OH in acidic conditions or Exam

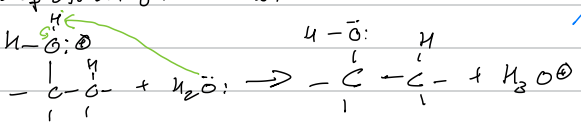
(1) Protonation of double bond → carbocation



(2) Nuc attack of water

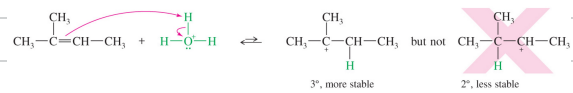


(3) Deprotonation of alcohol



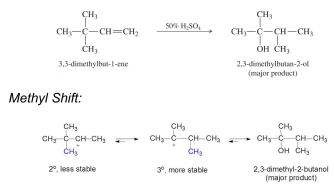
Tons of mechanisms on exam

Orientation of Hydration



Follow markovnikov rule here!

Rearrangements are possible



A methyl shift after protonation will produce the more stable tertiary carbocation

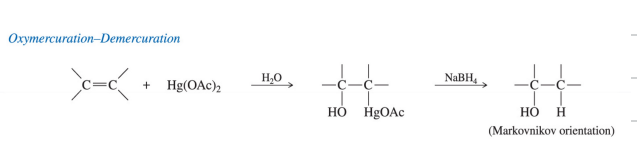
Look out for 1,2 methyl or 1,2 hydride shift on exams

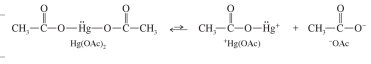
Oxymercuration–Demercuration Rxn

- Markovnikov addition of water to the double bond
- Milder conditions than direct hydration
- No rearrangements or polymerization

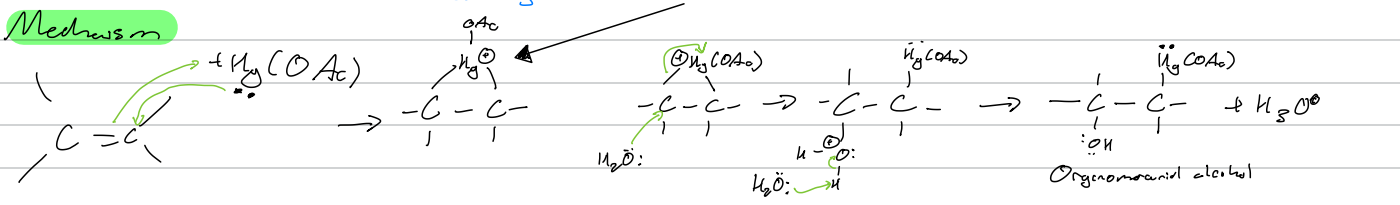
$NaBH_4$, H is negative here!

- The reagent is Hg(II) acetate, which dissociates slightly to form $^+Hg(OAc)$
  ↳ Intermediate is a 3-membered ring called the mercurinium ion





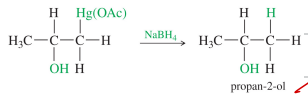
Mechanism



Stereochemistry of Mercurinium Ion opening

- Water adds to the more substituted carbon to form the Markovnikov product.
- Water approaches the mercurinium ion from the side opposite the ring (anti addition).

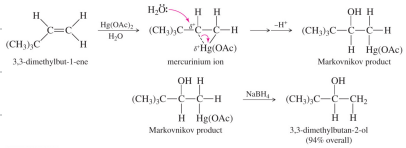
Must remove Mercury now



Demercuration

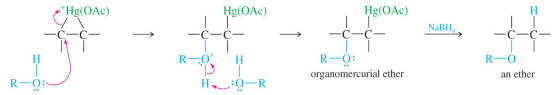
Oxymercuration – Demercuration of 3,3-Dimethyl but-1-ene

Does not suffer from rearrangements because there is no carbocation intermediate



Alkoxymercuration – Demercuration

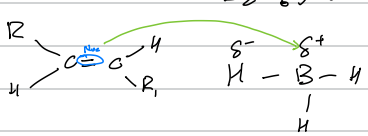
If the nuc is a alcohol instead of water an ethers produced with the same mechanism



Hydroboration of Alkenes

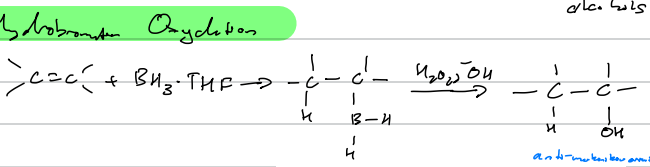
- Diborane (B_2H_6) adds to alkenes with anti-markovnikov orientation to form alkyl borines → oxidation → anti-m. alcohols

anti-markovnikov alcohol



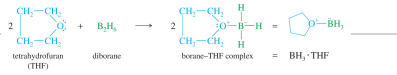
This is the base reaction below how borane works!

Hydroboration Oxydation



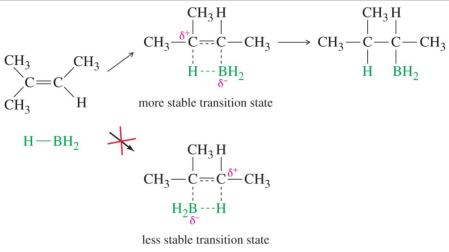
Diborane

- A dimer of borane in equilibrium with a small amount of BH_3
- Complex of borane with tetrahydrofuran is the most commonly used form



Mechanism of Hydroboration

- Borane adds to double bond in a single step, with boron adding to less substituted carbon and Hydrogen to the more substituted carbon
  - ↳ places δ+ on the more highly substituted carbon atom in the transition state

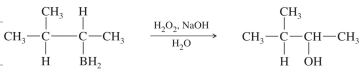


Concerted Mechanism!

↑ no carbocation formed!

Oxidation to Alcohol

- Oxidation of alkyl borane with basic H_2O_2 produces the alcohol

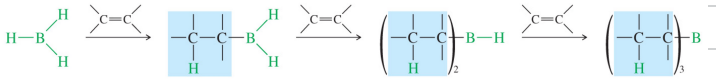


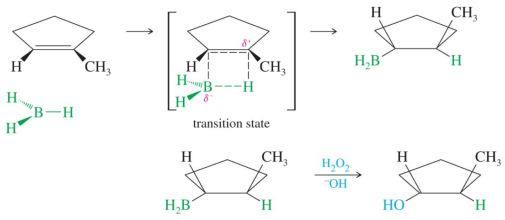
← Orientation is anti-markovnikov

Stereochemistry of Hydroboration

- 3 moles of alkene react with Each mole of borane
- Hydroboration step adds H and B to same side of double bond (Syn addition)
- When the boron is oxidized, OH keeps its orientation

Look @ Syn vs. anti



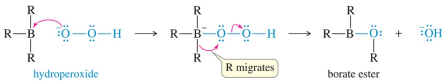


trans-2-methylcyclopentanol
(85% overall)
(racemic mixture of enantiomers)

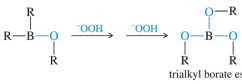
Role of the Hydroperoxide Ion

Formation of hydroperoxide ion

Addition of hydroperoxide and migration of the alkyl group

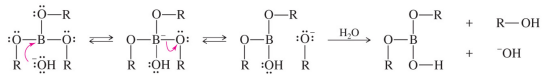


Twice more to oxidize the other two alkyl groups



Oxidation of Trialkylborane

Hydrolysis of the borate ester



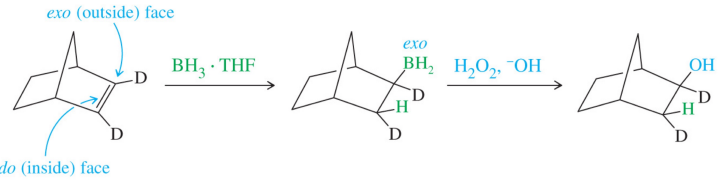
(The other two OR groups hydrolyze similarly.)

Work Backwards for Optional Points

↳ Draw product, determine intermediate, and get reaction from there. If you are any be sure to consider stereochemistry

There is a ton of contention to 3rd essay use space wisely!

Example: Solved Problem 4 ← slide 45 for question + explanation

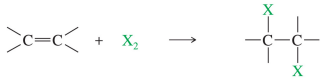


deuterium-labeled norbornene → alkylborane → alcohol (racemic mixture)

Addition of Halogens

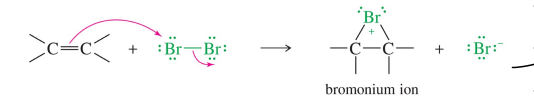
(adds addition of halides)

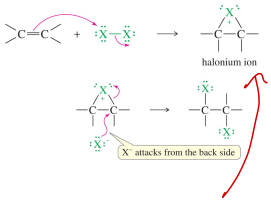
- Cl_2, Br_2, or I_2 add to double bond to form vicinal dihalide



(X_2 = Cl_2, Br_2, sometimes I_2) — usually anti addition

Mechanism of Halogen Addition



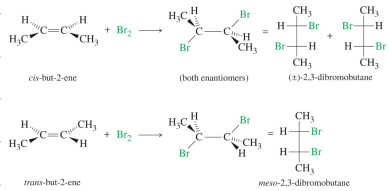


Intermediate here is called halonium ion

Stereochemistry of Halogen Addition

- Anti stereochemistry results from the backside attack of the Nuc on the bromonium ion
- Back-side attack ensures anti

Examples of Stereospecificity

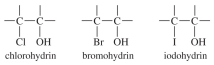


Bromine test for unsaturation

- If Br loses color, double bond found and reacted

Formation of Halohydrins

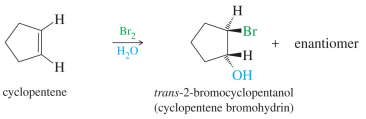
- Formed if halogen added in the presence of water as a solvent (the nucleophile)
- Markovnikov addition: Bromide (electrophile) → less substituted



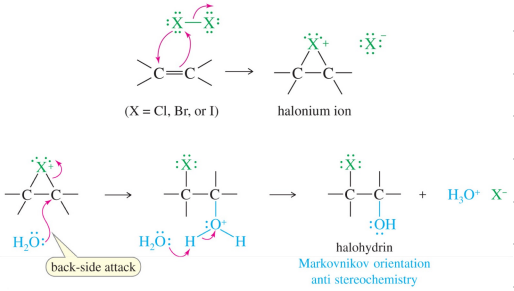
Make sure you know what meso and racemic is

Stereochemistry of Halohydrins

- Involvement of halonium → anti

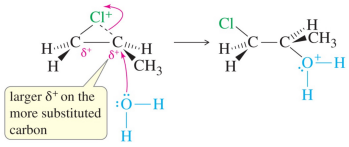


Mechanism of Halohydrin Formation

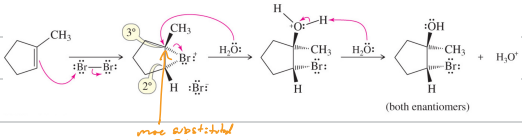


Orientation of Halohydrin Formation

- More substituted carbon of the chloronium ion bears more positive charge than less substituted one
- Attack by water on more substituted → markovnikov product



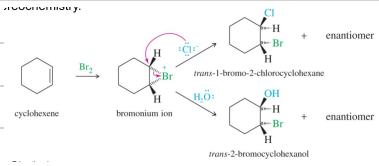
Example 5: Propose mechanism for rxn of 1-methylcyclopentene with bromine water



more substituted → δ+ greater → OH

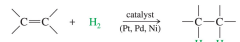
Problem 6 Solution

↳ Slide 57 for Q and Exp.



Cyclo Hydrogenation of Alkenes

- Hydrogen can be added across the double bond in this process
- Reaction only takes place if a catalyst is used!



Example

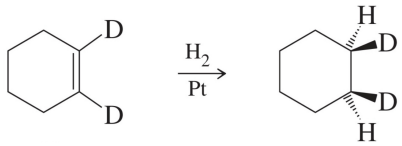
$CH_3—CH=CH—CH_3 + H_2 \xrightarrow{Pt} CH_3—CH_2—CH_2—CH_3$

Consider poisonous catalysts in your response

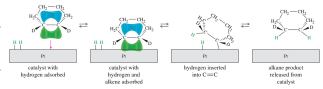
Mechanism of Catalytic Hydrogenation

Syn addition stereochemistry

↳ both hydrogens added to same side of bond



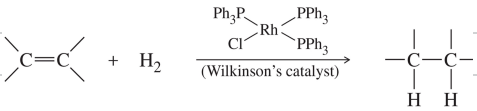
Syn Stereochemistry in Catalytic Hydrogenation

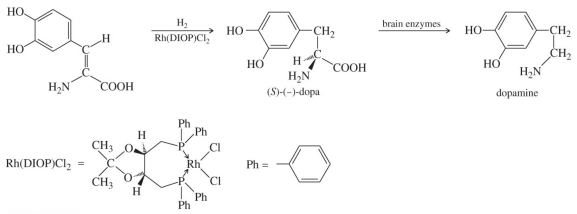


Need for Chiral Catalysts ← medical applications

Wilkinson's Catalyst

Soluble homogeneous catalyst that catalyzes hydrogenation of C double bond



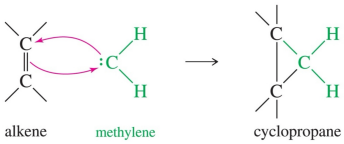


Just know that Wilkinson's is asymmetric!

Addition of Carbenes

- Insertion of the $—CH_2$ group into a double bond produces cyclopropane ring
- Three methods
  1. Diazomethane
  2. Simmons Smith
  3. Alpha elimination of haloform

Unstable but better than carbene



Preparation of Simmons Smith Reagent

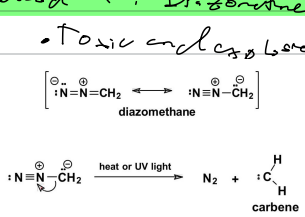
$CH_2I_2 + Zn(Cu) \rightarrow ICH_2ZnI$

Simmons–Smith reagent

If asked to make cyclopropane think about using carbene

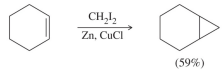
Method 1: Diazomethane

- Toxic and explosive



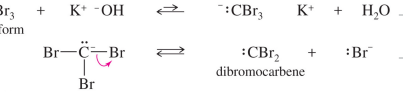
Simmons Smith Rxn

- Best method for this

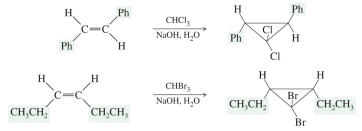


Alpha Elimination Rxn

- Presence of chloroform or bromoform can be dehydrohalogenated to form carbene

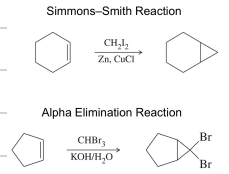


Cyclopropane Stereospecificity



Cis-trans

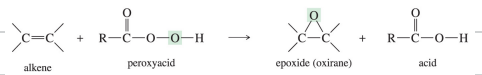
Carbene Examples



Epoxidation

Don't confuse with H_2O_2

- Alkene reacts with a peroxyacid to form an epoxide (or an oxirane)

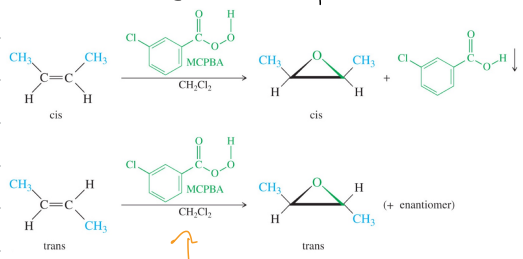


Mechanism of Epoxidation

- One step rxn of peroxyacid and the alkene to produce the epoxide and a molecule of acid

Dashed lines means simultaneous bond formation and breaking

Stereochemistry of Epoxidation

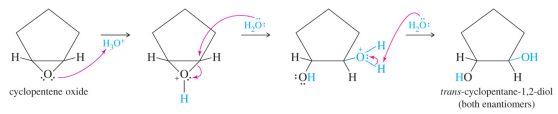


Draw MCPBA on exam to get credit!

- cis-trans determined by R-S config
- MCPBA is most common. Draw structure of this reagent on exams

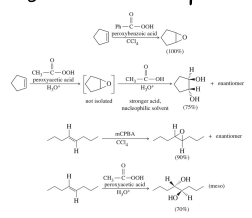
Opening the epoxide ring

- Process is acid-catalyzed
- Water attacks protonated epoxide on opposite side of ring (backside attack)
- Anti-diol is formed



OH is only a good leaving group with a positive charge.

Reagents for Epoxidation

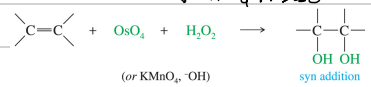


Acid catalyzing ring opening can be a problem so having base-catalyzed can be better. This is later!

Syn Hydroxylation of Alkenes

- Alkene converted to a syn-1,2-diol
- Two Reagents
  - OsO4 mixture tetroxide, OsO4, followed by H2O2
  - Cold, dilute solution of KMnO4 in base

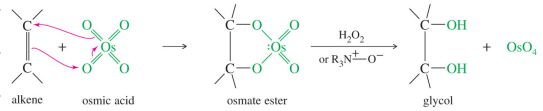
Regiochemistry to the conditions!



Mechanism with OsO4

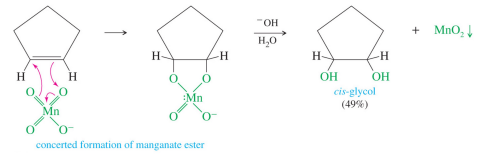
concerted mechanism

- OsO4 → double bond of alkene to form osmate ester
  - ↳ Osmate ester can be hydrolyzed to produce a cis-diol and reoxidate the OsO4



Permanganate Dihydroxylation

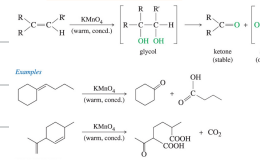
- Syn stereochemistry



Oxidative Cleavage of Alkenes

- Aldehydes are oxidized to carboxylic acids under conditions where KMnO4 solution is too warm, acidic or concentrated

Examples!



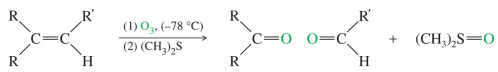
Oxidative Cleavage with KMnO4

- Too warm, acidic or concentrated, be careful
  - ↳ Disubstituted carbons become ketones.
  - Monosubstituted carbons become carboxylic acids.

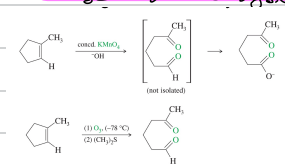
Ozonolysis

← Milder than KMnO4 and will not oxidize aldehydes further!

- Ozone oxidatively cleaves (breaks) double bond → aldehydes and ketones made
- Second step of this is the reduction of intermediate by Zinc or dimethyl sulfide



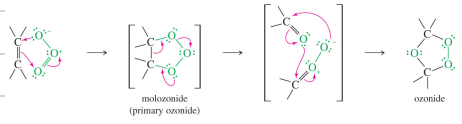
Comparison of KMnO4 Cleavage and Ozonolysis



Slide 83 for more info

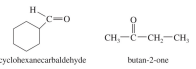
Mechanism of Ozonolysis

- Ozone adds to double bond, forming a five-membered ring intermediate called molozonide ← rearranges to ozonide

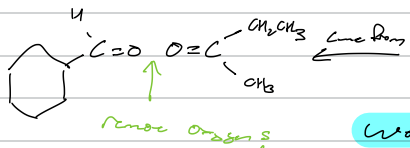


Example

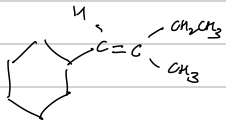
Ozonolysis–reduction of an unknown alkene gives an equimolar mixture of cyclohexanecarbaldehyde and butan-2-one. Determine the structure of the original alkene.



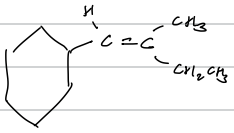
Product ← most likely?



remove oxygens and reconstruct double bond



or



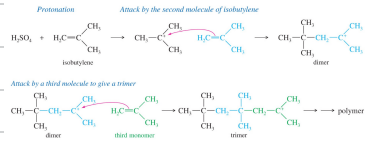
Work backwards on organic synthesis

Polymerization

- Alkene monomer add to another 'like' molecule to form polymer chain

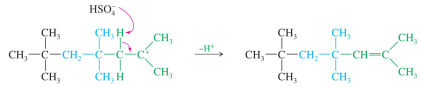
3 methods:
- Cationic ← carbocation
- Free radical
- Anionic ← carbanion (rare)

Cationic Polymerization

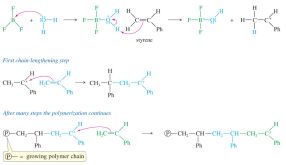


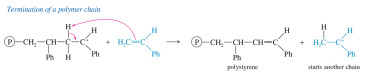
Termination Step

- Chain growth ends when protonation is abstracted by the conjugate base of the acid to initiate the rxn
- Loss of H forms an alkene which ends chain growth & terminates step



Cationic Polymerization Using BF_3 as catalyst



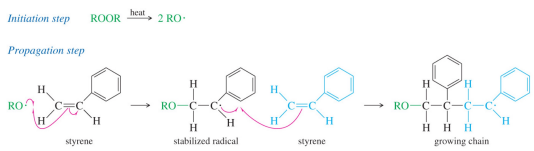


Termination

Radical Polymerization

- Presence of an initiator such as peroxide, free-radical polymerization occurs

single arrow rxns

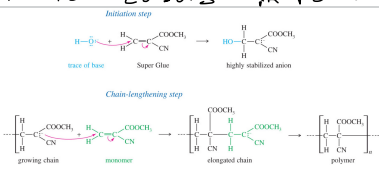


Anionic Polymerization

Don't destroy benzene's 223

For an alkene to gain electrons, strong e⁻ withdrawing groups such as nitrogen or carbonyl must be attached to the carbons in the double bond

rare but possible

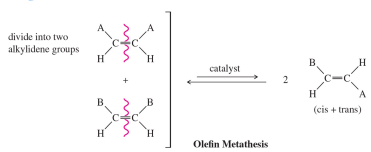


You need e⁻ withdrawing group directly attached to polymerization carbon for this to happen

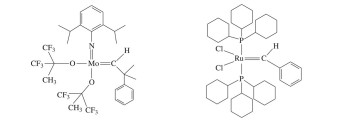
Olefin Metathesis

← different single step rxn

- Can think of a double bond as two alkylidene groups (=CHR)
- Olefin metathesis is any reaction that trades and interchanges alkylidene groups

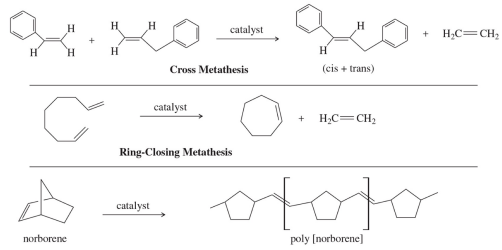


Catalysts for Olefin Metathesis



It's not necessary to draw catalyst structure for olefin. Identify reactant based on product

Examples for Olefin Metathesis



Lure made it! Addition Table

TABLE 8-1
Types of Additions to Alkenes

Type of Addition [Elements Added][a]	Product	Type of Addition [Elements Added][a]	Product
hydration [H_2O]	H, OH	halogenation [X_2], an oxidation	X, X
hydrogenation [H_2], a reduction	H, H	halohydrin formation [HOX], an oxidation	X, OH
dihydroxylation [HOOH], an oxidation	OH, OH	HX addition [HX] (hydrohalogenation)	H, X
oxidative cleavage [O_3], an oxidation	C=O, O=C	cyclopropanation [CH_2]	H, H
epoxidation [O], an oxidation	O		

[a]These are not the reagents used, but simply the groups that appear in the product.

Chapter 9 - Alkynes

- Alkynes are triple bonds
- C_nH_{2n-2} general formula
- Two elements of unsaturation for triple bond
- Most reactive one
- Some reactions resemble reactions of alkenes, like addition and oxidation
  - ↳ Some rxns specific to alkynes

All other functional groups except ethers and halides, have a higher priority than alkynes.

Least Chapter in textbook for Priority

Common Name

methylacetylene

$CH_3-\boxed{C\equiv CH}$ Ethyne / Acetylene

$CH_3-\overset{CH_3}{\overset{|}{CH}}-CH_2-C\equiv C-\overset{CH_3}{\overset{|}{CH}}-CH_3$

isobutylisopropylacetylene

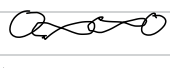
Physical Properties

- Nonpolar — insoluble in water
  - ↳ soluble in most organic solvents
- BP similar to an alkane of same size
- Less dense than water
- Up to 4 carbons, gas at room temp

Internal Alkyne behave differently than Terminal bc of proton presence.

Molecular Structure of Acetylene

- Triple bond have sp orbitals
- Each C has two unhybridized p orbitals with one unbonded e^-



Acidity

$R-C\equiv C:$ Strong Nuc

Alkane < Alkene < Alkyne < Alcohols

weaker acid — Must be Terminal — Stronger acid

sp is 50% s character, more stable conj base

S characteristic increases relative electronegativity of specific carbon

Terminal Alkynes can be deprotonated with strong bases

Creates Acetylide Ions

Deprotonation done with $Na^+ \ ^-NH_2$, not $-OH$! ← This is bc of base strength

Acetylide Ions in S_N2 Reactions

$CH_3CH_2-C\equiv C:^{\ominus}\ Na^{\oplus} + H_3C-I \longrightarrow CH_3CH_2-C\equiv C-CH_3 + NaI$

- 1° alkyl Halides lengthen Alkyne chain

Unhindered better, as per S_N2 criteria of backside attack

Be able to do a multi-step synthesis on the final exam

Acetylide Ions as Strong Bases

$CH_3CH_2-C\equiv C:^{\ominus} + H_3C-\overset{Br}{\overset{|}{CH}}-CH_3 \xrightarrow{E2} CH_3CH_2-C\equiv C-H + H_2C=CH-CH_3 + Br^{\ominus}$

- Acetylide Ions are also strong bases. If S_N2 is not possible, E2 will occur

Solved Problem 1

Starting: acetylene and reagents

Product: 3-decyne

Indicate reaction steps with numbers next to reagents

$H-C\equiv C-H \xrightarrow[(2)\ CH_3(CH_2)_5Br]{(1)\ NaNH_2} CH_3(CH_2)_5-C\equiv C-H$

oct-1-yne

$CH_3(CH_2)_5-C\equiv C-H \xrightarrow[(2)\ CH_3CH_2Br]{(1)\ NaNH_2} CH_3(CH_2)_5-C\equiv C-CH_2CH_3$

Work Backwards "reverse synthesis"

Addition to Carbonyl Compounds

- Nuc can attack Carbonyl carbon, forming an alkoxide ion that forms an alcohol upon protonation

$Nuc:^- \longrightarrow \overset{|}{C}=O \longrightarrow Nuc-\overset{|}{C}-\ddot{O}:^{\ominus}$ alkoxide ion

$Nuc-\overset{|}{C}-\ddot{O}:^{\ominus}$ (alkoxide) + $H-\ddot{O}-H$ (H2O) $\longrightarrow Nuc-\overset{|}{C}-OH + {}^{\ominus}OH$ (alcohol)

If Nuc is Acetylene you can do mechanism of Acetylinic Alcohol formation

Addition to Aldehyde

$R'-C\equiv C:^{\ominus} + H-C(=O)-R \longrightarrow R'-C\equiv C-\overset{R}{\overset{|}{\underset{H}{\underset{|}{C}}}}-\ddot{O}:^{\ominus}$ ...

Addition to Ketone

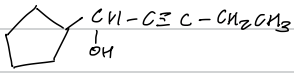
- Tertiary Alcohol Product

$R-C\equiv C:^{\ominus} + R_2C=O \longrightarrow R-C\equiv C-\overset{R}{\overset{|}{\underset{R}{\underset{|}{C}}}}-\ddot{O}:^{\ominus}$ ...

Solved Problem 2

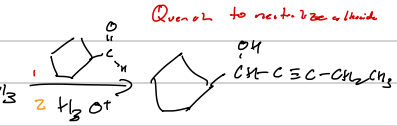
Try to work backwards

Missing step of H-C≡C-H to H-C≡C-CH2CH3



Synthesize this!

H-C≡C-CH2CH3 $\xrightarrow{NaNH_2}$ Na+ −:C≡C-CH2CH3



Quench to neutralize alkoxide

Synthesis Questions on Exams limited to around 5 steps max

Synthesis of Alkynes by Elimination Rxns

- Removal of two molecules of HX from a vicinal or geminal dihalide produces an alkyne
- Dehydrohalogenation of a geminal or vicinal dihalide gives a vinyl halide
- Under strongly basic conditions, a second dehydrohalogenation may occur to form an alkyne

Reagents for Elimination

- Molten KOH or alcoholic KOH @ 200°C forms an internal alkyne
- Sodium Amide, $NaNH_2$, at 150°C, followed by water forms a terminal alkyne

Addition Reactions

- Similar to addition to alkenes
- π bond becomes two σ bonds
- Usually E stereo
- One or two molecules may add

Catalytic Hydrogenation of Alkynes

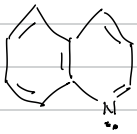
- Pd, Pt, or Ni must be used

Risky because it will make Alkyne → Alkene → Alkane

Hydrogenation with Lindlar's Catalyst

- A 'poisoned' catalyst
- Produces Alkenes with cis stereochemistry

Cis



$BaSO_4$

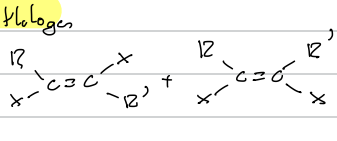
Asked for as Alkene? Use this!

Reduction of Alkynes with Metal Ammonia

Trans

- Forms a trans alkene
- Na/NH_3 ← not Na+, it is sodium not Na

Addition of 1 mole of Halogen

R-C≡C-R' + X_2 → 

X_2 = Cl_2 or Br_2

- May add syn or anti so product is a mixture of cis/trans isomers
- It is difficult to stop the reaction at the dihalide ← remaining π bond wants to keep reacting

Mechanism of Hydrogen Halide Addition

- Triple bonds abstract protons from HX, forming vinyl cation
- Proton adds to the least substituted carbon → vinyl cation

Markovnikov
H added → X
Anti-Markovnikov
X added → H

Anti-Markovnikov Addition of HBr to Alkynes

- Using peroxides, HBr can be added to a terminal alkyne anti markovnikov

Requires peroxide

Bromine attaches to least substituted carbon → anti-Markovnikov

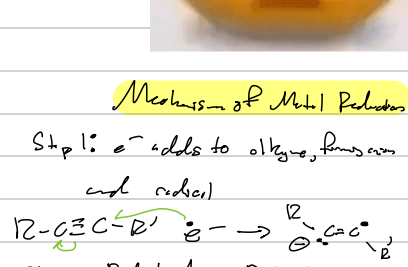
Enol mechanism on exam, know it well

Hydration of Alkynes

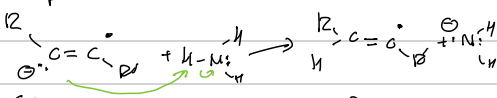
- Mercuric sulfate in sulfuric acid adds H-OH to one π bond with Markovnikov orientation forming vinyl alcohol (enol)
- Hydroboration-Oxidization adds H-OH with an anti-Markovnikov orientation

Mechanism of Metal Reduction

Step 1: e⁻ adds to alkyne, forming anion and radical

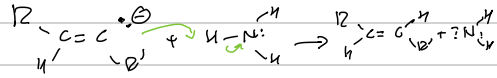
R-C≡C-R' + e⁻ → 

Step 2: Radical Anion Protonated



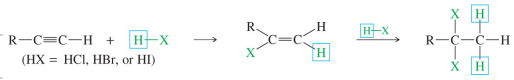
Step 3: e⁻ adds to alkyne to form Anion

Step 4: Protonation of anion gives alkene



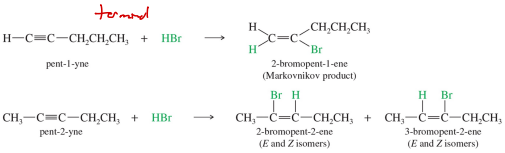
Addition of HX

- Hard to control 2 mols of HX added leads to geminal dihalide
- Markovnikov addition

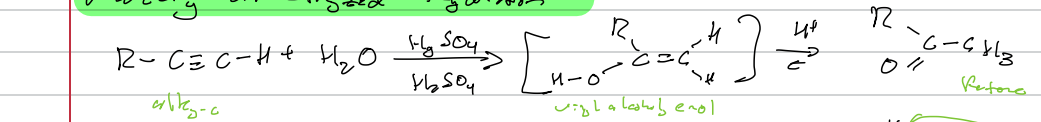


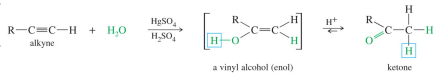
One mole addition forms vinyl halides

Examples of HX Addition

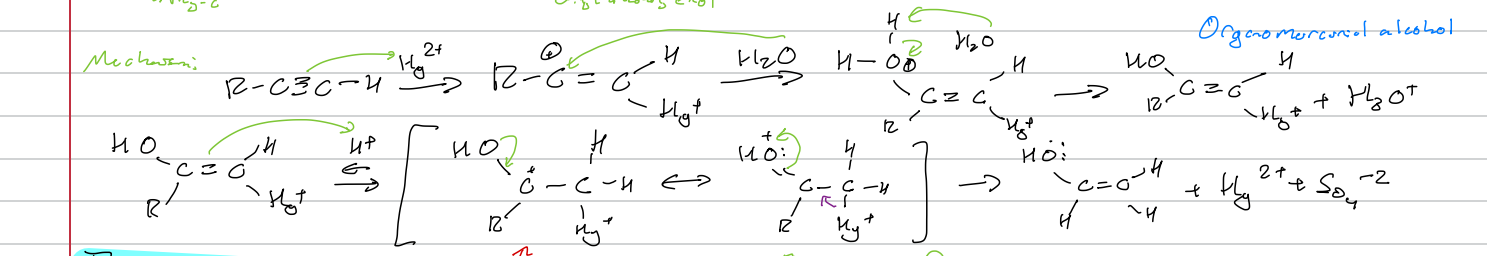


Mercury Ion-Catalyzed Hydration





Mechanism:



There will be One Exam Question on this

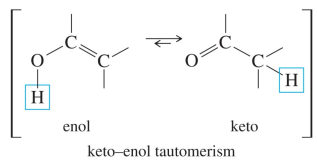
Not forming two positive charges close to each other

This resonance form explains how Mercury is removed

Mercury bond breaks easily to stabilize $O^{\oplus}$

Keto-Enol Tautomerism

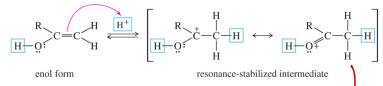
- Enols not stable and they isomerize to the corresponding aldehyde or ketone using the process



Know how acid-catalyzed works vs. base catalyzed.

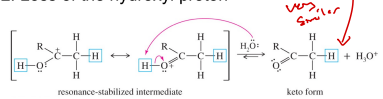
Acid-Catalyzed Tautomerism

Step 1: Addition of a proton at the methylene group



Do not have stable OH Photo around in Acids

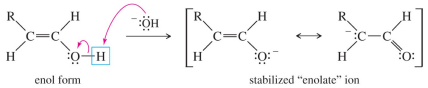
Step 2: Loss of the hydroxyl proton



very similar

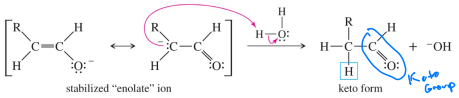
Base-Catalyzed Tautomerism

Step 1: Loss of the hydroxyl proton



Do not have stable HO Photo around in base!

Step 2: Reprotonation on the adjacent carbon atom

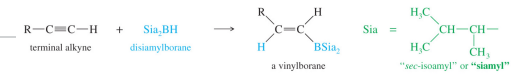


Ozonolysis

Produces Carboxylic Acids

Hydroboration-Oxidation Rxn

- Anti-Markovnikov addition of water across triple bond
- Hindered alkyl borane must be used to prevent two molecules of borane from adding to the triple bond.



Disiamylborane has two bulky alkyl groups

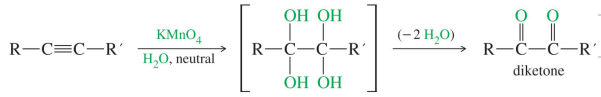
Oxidation of Boranes

- In 2nd Step, a basic solution of peroxides added to vinyl borane → oxidize boron and replace with hydroxyl group
- Once enol is formed, it rapidly tautomerizes in base to the more stable aldehyde

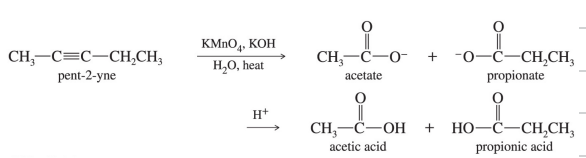
Oxidation of Alkynes

- Similar to oxidation of alkenes
- Dilute neutral solution of $KMnO_4$ oxidizes alkyne → diketone
- Warm, basic $KMnO_4$ cleaves triple bond
- Ozonolysis followed by hydrolysis cleaves triple bond

Permanganate Oxidation of Alkynes to Diketones



Permanganate Oxidation of Alkynes to Carboxylic Acids



Chapter 10 - Structure and Synthesis of Alcohols

$CH_3—CH_2—OH$	$CH_3—OH$	$CH_3—CH(OH)—CH_3$
ethyl alcohol	methyl alcohol	isopropyl alcohol
ethanol	methanol	propan-2-ol

Alcohols Overview

Organic Molecules with a hydroxyl group

Some of the most useful molecules in labs, nature, and everyday use

-OH, hydroxyl group

- sp^3 hybridized and tetrahedral
- H-O-H is 104.8°
- C-O-H is 108.9°
- Carbonil Carbon atoms the one bonded to -OH

Classifications of Alcohols

Primary: Carbonil Carbon to one other carbon $R-CH_2-OH$

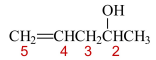
Secondary: Carbonil Carbon to two other carbons $R-CH(OH)-R$

Tertiary: Carbonil Carbon to three other carbons $R-C(OH)(R)-R$

Called Phenols → Aromatic: -OH on benzene ring ← distributes ring in 2,3,5

Alkenols (Enol)

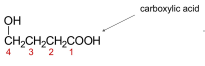
- OH gets priority, assign carbonil with lowest number
- Both -ene and -ol in name



Old: 4-penten-2-ol
New: pent-4-ene-2-ol

Hydroxy Substituent

If -OH is higher priority group, it is called hydroxy



4-hydroxybutanoic acid
also known as γ-hydroxybutyric acid (GHB)

Know all 11 chapters for 8th Exam

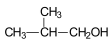
Priority of Nomenclature

TABLE 10-1
Priority of Functional Groups in Naming Organic Compounds

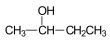
acids (highest)
esters
aldehydes
ketones
alcohols
amines
alkenes, alkynes
alkanes
ethers
halides (lowest)

Common Names

- Can be named as alkyl alcohols
- Only necessary for small molecules



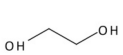
isobutyl alcohol
IUPAC: 2-methylpropan-1-ol



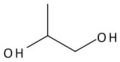
sec-butyl alcohol
IUPAC: butan-2-ol

Glycols

- 1,2-diols are called glycols
- Common names for these use the name of the alkene from which they are made



IUPAC: ethane-1,2-diol
ethylene glycol



IUPAC: propane-1,2-diol
propylene glycol

Phenol Nomenclature

- OH is assumed to be on Carbon 1

Ortho: 1,2
Meta: 1,3
Para: 1,4

Disubstituted Phenol rules

3-chlorophenol
(*meta-chlorophenol*)

4-methylphenol
(*para-cresol*)

- Methyl Phenols are cresols

Table of Physical Properties

TABLE 10-2
Physical Properties of Selected Alcohols

IUPAC Name	Common Name	Formula	mp (°C)	bp (°C)	Density (g/mL)
methanol	methyl alcohol	CH_3OH	−97	65	0.79
ethanol	ethyl alcohol	CH_3CH_2OH	−114	78	0.79
propan-1-ol	n-propyl alcohol	$CH_3CH_2CH_2OH$	−126	97	0.80
propan-2-ol	isopropyl alcohol	$(CH_3)_2CHOH$	−89	82	0.79
butan-1-ol	n-butyl alcohol	$CH_3(CH_2)_3OH$	−90	118	0.81
butan-2-ol	sec-butyl alcohol	$CH_3CH(OH)CH_2CH_3$	−114	100	0.81
2-methylpropan-1-ol	isobutyl alcohol	$(CH_3)_2CHCH_2OH$	−108	108	0.80
2-methylpropan-2-ol	tert-butyl alcohol	$(CH_3)_3COH$	25	83	0.79
pentan-1-ol	n-pentyl alcohol	$CH_3(CH_2)_4OH$	−79	138	0.82
3-methylbutan-1-ol	isopentyl alcohol	$(CH_3)_2CHCH_2CH_2OH$	−117	132	0.81
2,2-dimethylpropan-1-ol	neopentyl alcohol	$(CH_3)_3CCH_2OH$	52	113	0.81
cyclopentanol	cyclopentyl alcohol	cyclo-C_5H_9OH	−19	141	0.95
hexan-1-ol	n-hexyl alcohol	$CH_3(CH_2)_5OH$	−52	156	0.82
cyclohexanol	cyclohexyl alcohol	cyclo-$C_6H_{11}OH$	25	162	0.96
heptan-1-ol	n-heptyl alcohol	$CH_3(CH_2)_6OH$	−34	176	0.82
octan-1-ol	n-octyl alcohol	$CH_3(CH_2)_7OH$	−16	194	0.83
nonan-1-ol	n-nonyl alcohol	$CH_3(CH_2)_8OH$	−6	214	0.83
decan-1-ol	n-decyl alcohol	$CH_3(CH_2)_9OH$	6	233	0.83
prop-2-en-1-ol	allyl alcohol	$H_2C=CH—CH_2OH$	−129	97	0.86
phenylmethanol	benzyl alcohol	$Ph—CH_2OH$	−15	205	1.05
diphenylmethanol	diphenylcarbinol	Ph_2CHOH	69	298	
triphenylmethanol	triphenylcarbinol	Ph_3COH	162	380	1.20
ethane-1,2-diol	ethylene glycol	$HOCH_2CH_2OH$	−13	198	1.12
propane-1,2-diol	propylene glycol	$CH_3CH(OH)CH_2OH$	−59	188	1.04
propane-1,2,3-triol	glycerol	$HOCH_2CH(OH)CH_2OH$	18	290	1.26

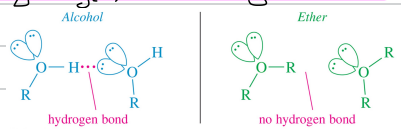
Physical Properties

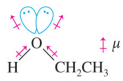
- Higher BP be of H-bonding
- Solubility in water decreases as alkyl group gets longer

Boiling Points of Alcohols

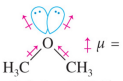
- Higher than alkanes and ethers as stronger interactions between molecules require more energy to break

Hydrogen Bonding Review





‡ μ = 1.69 D
ethanol, MW 46
bp 78 °C



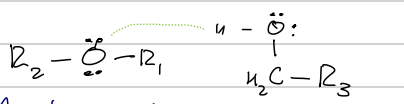
‡ μ = 1.30 D
dimethyl ether, MW 46
bp −25 °C

μ = 0.08 D
propane, MW 44
bp −42 °C

Draw Hydrogen bonds as dotted lines

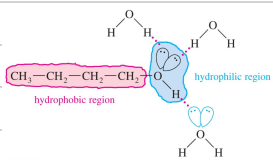
Know H-bond donor vs. acceptor

Ether and Alcohols are soluble



As long as there is a H-bond donor and an H-bond Acceptor Hydrogen bonding will occur!!

Solubility in Water



Small alcohols are miscible in water, but solubility ↓ as alkyl group size ↑

Alcohol	Solubility in Water
methyl	miscible
ethyl	miscible
n-propyl	miscible
tert-butyl	miscible
isobutyl	10.0%
n-butyl	9.1%
n-pentyl	2.7%
cyclohexyl	3.6%
n-hexyl	0.6%
phenol	9.3%
hexane-1,6-diol	miscible

Methanol "Wood Alcohol"

- 100mL toxic Dose
- You go blind and psycho

Ethanol "Good Stuff"

- 200mL Toxic Dose
- Fermentation of sugar substrates in grains
- Denatured Alcohol used as solvent in labs

Propan-2-ol "Isopropyl Rubbing Alcohol"

- Catalytic Hydration of propylene
- Isopropyl alcohol used as rubbing alcohol

Acidity of Alcohols

- pKa range: 15.5–18.0 (water is 15.7)
- Acidity ↓ as substitution on alkyl ↑
- Halogens and other e⁻ withdrawing groups increase acidity
- Phenols are 100 million times more acidic than cyclohexanol groups

Ka and pKa Table

Alcohol	Structure	K_a	pK_a
methanol	$CH_3—OH$	3.2×10^{-16}	15.5
ethanol	$CH_3CH_2—OH$	1.3×10^{-16}	15.9
2-chloroethanol	$Cl—CH_2CH_2—OH$	5.0×10^{-15}	14.3
2,2,2-trichloroethanol	$Cl_3C—CH_2—OH$	6.3×10^{-13}	12.2
isopropyl alcohol	$(CH_3)_2CH—OH$	3.2×10^{-17}	16.5
tert-butyl alcohol	$(CH_3)_3C—OH$	1.0×10^{-18}	18.0
cyclohexanol	$C_6H_{11}—OH$	1.0×10^{-18}	18.0
phenol	$C_6H_5—OH$	1.0×10^{-10}	10.0
	Comparison with Other Acids		
water	H_2O	1.8×10^{-16}	15.7
acetic acid	CH_3COOH	1.6×10^{-5}	4.74
hydrochloric acid	HCl	$1 \times 10^{+7}$	−7

Formation of Alkoxide Ions

- Ethanol reacts with Na (metal) to form $NaOCH_2CH_3$, sodium ethoxide. This is a strong base typically used for elimination rxns
- More hindered alcohols like 2-propanol or t-butanol react faster with K than Na

$$R—O—H + Na \longrightarrow R—O^-Na^+ + \tfrac{1}{2}H_2\uparrow$$

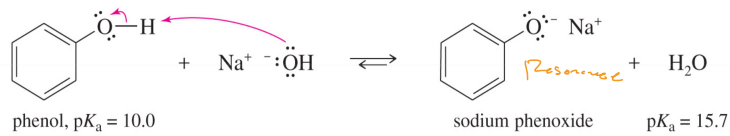
Example

$$CH_3CH_2OH + Na \longrightarrow CH_3CH_2O^-Na^+ + \tfrac{1}{2}H_2\uparrow$$

ethanol; sodium metal; sodium ethoxide; hydrogen gas

Formation of Phenoxide Ion

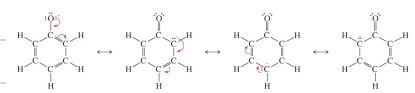
Aromatic alcohol phenol is more acidic than aliphatic alcohols due to the ability of aromatic rings to delocalize negative charge of the oxygen with carbons in the ring



phenol, $pK_a = 10.0$ — sodium phenoxide — $pK_a = 15.7$

Phenol Stronger Acid bc its conjugate base is more stable

Charge Delocalization on the Phenoxide Ion



Overview of Alcohol Synthesis

- Alcohols can be created through S_N2 usually
- Addition of H_2O to Double bonds also works
  - → Oxymercuration–demercuration
  - → Hydroboration–oxidation

Organometallic Reagents

Polarize EN

- Carbon is negatively charged, so this bonded to a metal (usually Mg or Li)
- will attack a partial positive carbon
  - ↳ C–X or C=O
- Good for forming Carbon–Carbon bonds

Sodium Acetylides

"Usually Nucleophiles

$$R—C\equiv C—H + NaNH_2 \longrightarrow R—C\equiv C:^-Na^+ + NH_3$$

terminal alkyne; sodium amide; a sodium acetylide; ammonia

$$R—C\equiv C:^- + R'—CH_2—X \longrightarrow R—C\equiv C—CH_2—R' + X^-$$

acetylide; alkyl halide; substituted alkyne

$$R—C\equiv C:^- + R'_2C=O \longrightarrow R—C\equiv C—C(R')_2—O^- \xrightarrow{H_3O^+} R—C\equiv C—C(R')_2—OH$$

acetylide; ketone or aldehyde; alkoxide; acetylenic alcohol

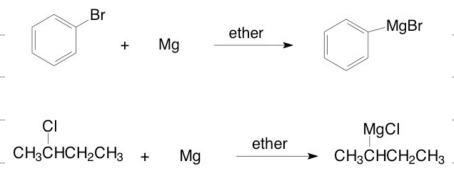
Grignard Reagents

$$R—X + Mg \xrightarrow{CH_3CH_2OCH_2CH_3} R—Mg—X$$

(X = Cl, Br, or I); organomagnesium halide (Grignard reagent); reacts like $R^-\ ^+MgX$

- Formula: R–Mg–X
- Ethers used to stabilize complex
- Iodides are most reactive ← Fluorides doesn't generally react
- Mg is formed from 1°, 2°, or 3° alkyl halides

Formation and Reactivity of Grignards



Cannot use Acidic Reagents

↑ Quenches too early!!

reactivity: R—I > R—Br > R—Cl ≫ R—F

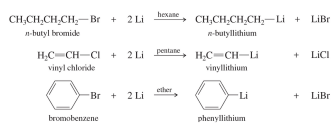
Organolithium Reagents

$$R—X + 2\,Li \longrightarrow Li^+X + R—Li$$

(X = Cl, Br, or I); organolithium; reacts like $R:^-Li^+$

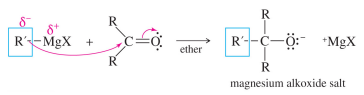
- Reacts same way as Grignard
- Cabc produced from alkyl, vinyl, or aryl halides, just like grignards
- Ether is not necessary, a wide variety of solvents can be used as long as the solvent is not acidic

Examples of Organolithium Reagents



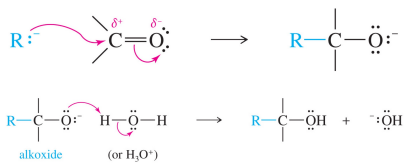
Addition to Carbonyl Compounds

- Carbonyl is partial positive (electrophilic)
- Nu will attack carbonyl → alkoxide



magnesium alkoxide salt

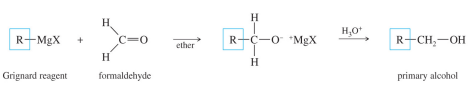
Mechanism of Addition of Organometallic to Carbonyl



alkoxide; (or H_3O^+)

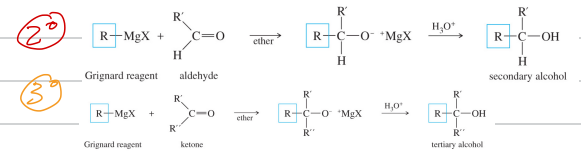
This is an appropriate answer on an exam. Short Synthesis always desirable

Formation of Primary Alcohols using Organometallics



Grignard Reagent allows this to happen

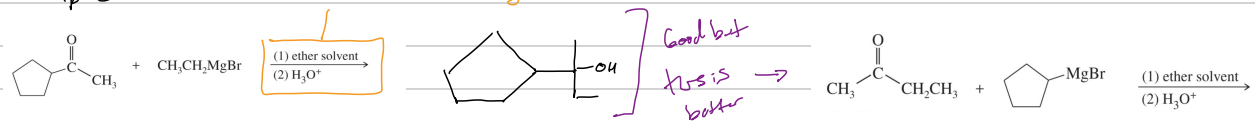
Synthesis of 2° and 3° Alcohols



Exam Review
Synthesis Exercise
On Canvas Prior to Exam 3

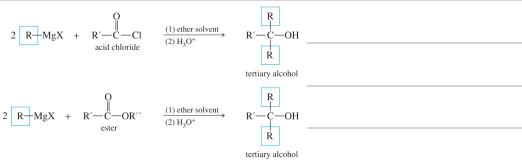
Example

Need Ether as Solvent for Grignard!

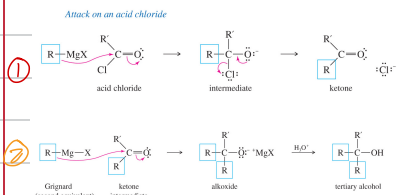


Grignard Rxns w/ Acid Chlorides and Esters

- 2 mols Grignard
- Product is 3° Alcohol w/ two identical Alkyl Groups
- Ketone Intermediate Produced

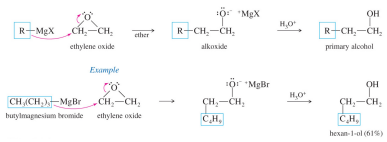


Mechanism with Acid Chloride



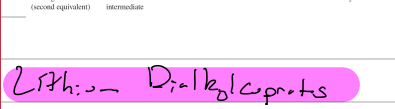
Addition to Ethylene Oxide

- Grignard and Lithium Reagents attack epoxides and open them → alcohols
- Epoxide ring strain relieved so rxn is preferred



Commonly Used to extend Carbon chain by 2 atoms

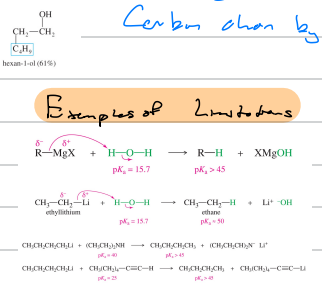
Lithium Dialkylcuprates



Limitations of Organometallics

- Grignards and organolithiums are good nucleophiles, but in the presence of acidic protons they will act as strong bases.
  - O—H, N—H, S—H, C≡C—H
- In the presence of multiple bonds with a strong electronegative element, the organometallics will act as a nucleophile.
  - C≡O, CN, C≡N, S≡O, N≡O

Examples of Limitations



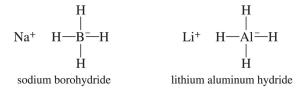
Do not use acidic Solvents!

Reduction of Carbonyl

- Hydride reagents add a hydride ion ($H^\ominus$) to reduce carbonyl group
- Protonation gives the alcohol.
- Reduction of aldehyde yields 1° alcohol.
- Reduction of ketone yields 2° alcohol.

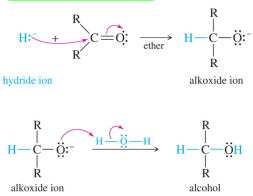
Hydride Reagents

- Called Complex hydrides as they do not have a simple hydride structure
- Bonding to metal = more Nuc less basic



- Lithium is stronger as a reducing agent
  - Dangerous to work with and can cause undesirable rxns.

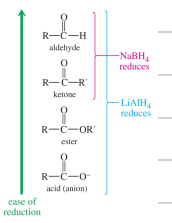
Mechanism



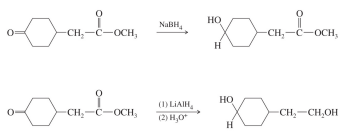
For Rxn Coord Diagrams do not put time on x-axis

Reducing Agents

- $NaBH_4$ can reduce aldehydes and ketones but not esters or carboxylics
- $LiAlH_4$ is stronger and reduces all carbonyls!



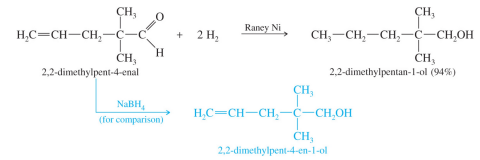
Comparison



Catalytic Hydrogenation

- Raney Ni is Heterogeneous
  - Same reactive as Pd or Pt catalysts
- Not commonly used bc it can react to or when its not needed

Selective Reductions



Thiols

- Sulfur analogues of alcohols
- Mercapto is the –SH group
- Named w/ suffix –thiol

CH3—SH OH	CH3CH2CH2CH2—SH	HS—CH2CH2—	Usedin
methanethiol methyl mercaptan	butane-1-thiol *n*-butyl mercaptan	2-mercaptoethanol	Common Names!

- More Acidic than Alcohols

$CH_3—CH_2—SH$ (ethanethiol, $pK_a = 10.5$) + ^-OH ⇌ $CH_3—CH_2—S^-$ (ethanethiolate) + H_2O ($pK_a = 15.7$)

—SH (benzenethiol (thiophenol), $pK_a = 7.8$) + ^-OH ⇌
—S^- (benzenethiolate) + H_2O ($pK_a = 15.7$)

For comparison

$CH_3—CH_2—OH$ (ethanol, $pK_a = 15.9$) + ^-OH ⇌ $CH_3—CH_2—O^-$ (ethoxide) + H_2O ($pK_a = 15.7$)

Mechanism of Thiols

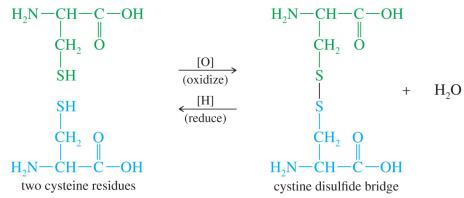
- Commonly made through S_N2 rxn → primary alkyl halides better
- Excess of sodium hydrosulfide to prevent a second alkyl addition

Na^+ $H—\ddot{\underset{..}{S}}:^-$ (sodium hydrosulfide) + $R—X$ (alkyl halide) ⟶ $R—SH$ (thiol) + Na^+ ^-X

Thiol Oxidation

- Can be oxidized to disulfides

Example



Chapter 11 - Reactions of Alcohols

Oxidation States

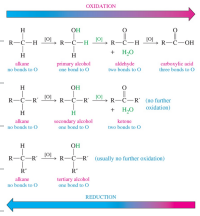
Inorganic

1. Oxidation = loss of e⁻
2. Reduction = gain of e⁻

Organic

1. Oxidation = Gain of O, O_2, or X_2; loss of H_2
2. Reduction = Gain of H_2 (or $H^\oplus$); loss of O or O_2 and loss of X_2
3. Neither = Gain or Loss of $H^\oplus$, H_2O, -OH, HX

Like S_N2

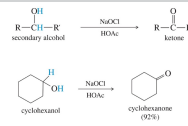


Oxidation of 2° alcohols

- 2° alcohol → Ketone
- $Na_2Cr_2O_7$ in H_2SO_4 is a traditional oxidizing agent
- H_2CrO_4 or $HCrO_4^\ominus$ is active reagent
  - ↳ dangerous and toxic so not good for class B

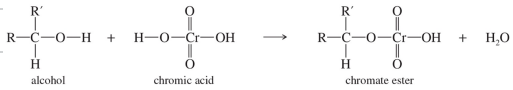
Formation of the Acid Chromate Ion

- CrO_3 will also produce chromic acid in H_2SO_4 and H_2O

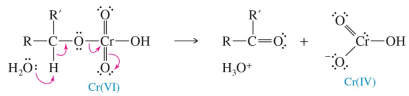


Oxidation Mechanism

Formation of the chromate ester

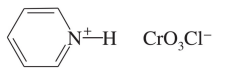


Elimination of the chromate ester and oxidation of the carbinol carbon



Pyridinium Chlorochromate

Pyridinium chlorochromate (PCC):



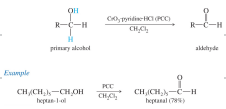
$CrO_3 \cdot pyridine \cdot HCl$
or $pyH^+ CrO_3Cl^-$

Do not name (PCC) drop on exam, draw this out

↓ same

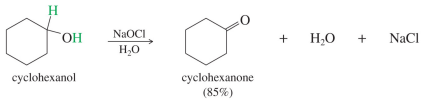
3° Alcohols cannot oxidize

- Carbon has no H so it cannot be oxidized



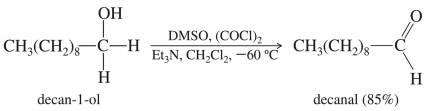
NaOCl Sodium Hypochlorite (bleach)

- Can oxidize alcohols w/o heavy metals and without bad waste
- Much better option for acid-sensitive chemicals



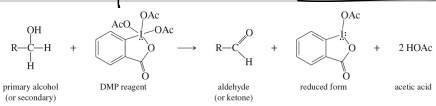
Swern Oxidation

- Dimethylsulfoxide (DMSO) with
- oxalyl chloride and hindered base
- Need Specific Conditions



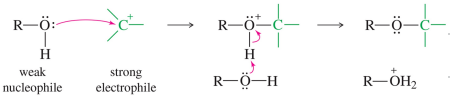
Dess-Martin Periodinane (DMP)

- Can oxidize primary alcohols to aldehydes and 2° to ketones
- Take place under mild conditions → excellent yields



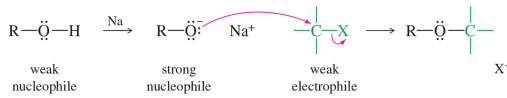
Alcohols as a Nuc

- Alcohols weak Nucs
- Alkoxides RO⊖ are strong
- New C-O bond, O-H broken

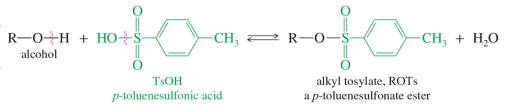


Alcohols as an electrophile

- Alcohols make Elec. as OH not good leaving group
- Protonation of hydroxyl group converts it into a good leaving group (H_2O)



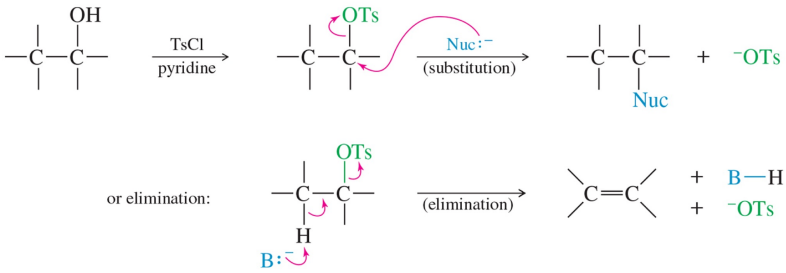
Tosylate Esters



- Can be converted to tosylate esters (ROTs) through condensation
- This is an excellent leaving group

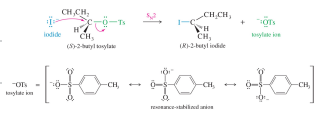
Substitution and Elimination Rxns using Tosylates

Summary



S_N2 Rxns w/ Tosylates

- Rxn shows S_N2 displacement of -OTs from alkyl to have inverted config
- Tosylate ion is quite clearly stable as an anion

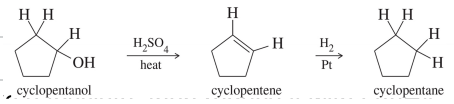


Summary of Tosylate Reactions

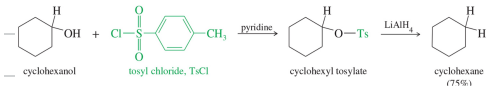
R—OTs	+	$^-$OH hydroxide	⟶	R—OH alcohol	+	$^-$OTs
R—OTs	+	$^-$C≡N cyanide	⟶	R—C≡N nitrile	+	$^-$OTs
R—OTs	+	Br^- halide	⟶	R—Br alkyl halide	+	$^-$OTs
R—OTs	+	R′—O$^-$ alkoxide	⟶	R—O—R′ ether	+	$^-$OTs
R—OTs	+	:NH_3 ammonia	⟶	R—NH_3^+ $^-$OTs amine salt		
R—OTs	+	$LiAlH_4$ LAH	⟶	R—H alkane	+	$^-$OTs

Reduction of Alcohols

- Dehydrate w/ concentrated H_2SO_4 → H_2

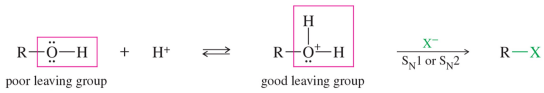


- Make a tosylate → reduce w/ $LiAlH_4$



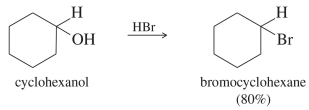
Reaction of Alcohols with Acids

- Hydroxyl group protonated by an acid to convert it into a good leaving group
- Once alcohol is protonated, a substitution or elimination rxn can take place

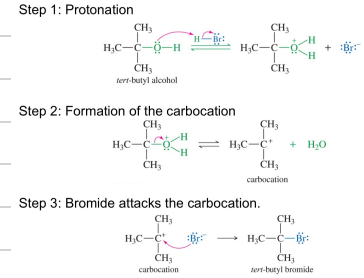


Reactions of Alcohols w/ HBr

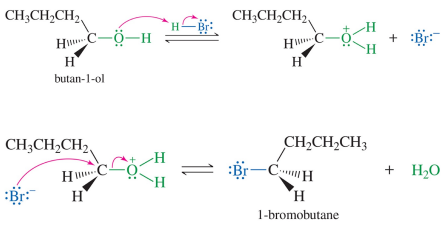
- -OH of alcohol is protonated → $-\overset{+}{O}H_2$ good LG
- 3° and 2° alcohols react with Br^- via S_N1
- 1° alcohols react via S_N2



S_N1 Mechanism for Alcohols



S_N2 Mechanism for Alcohols



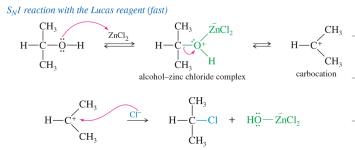
Reaction of Alcohols w/ HCl

- Cl is weaker Nuc than Br
  - ↳ smaller and less polarizable
- Addition of $ZnCl_2$
- Lucas test: $ZnCl_2$ in HCl
  - ③ 1° bad
  - ② 2° react well (1–5 min)
  - ① 3° react very well (1 min)

Lucas Reagent: HCl and $ZnCl_2$

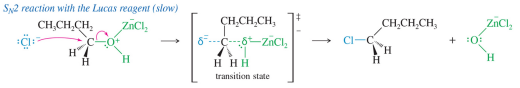
S_N1 Rxn w/ Lucas Reagent

- 2° and 3° alcohols react with Lucas by S_N1



S_N2 rxn with Lucas Reagent

- 1° alcohols react with Lucas via S_N2
- Rxn is very slow



Limitations of HX Rxns

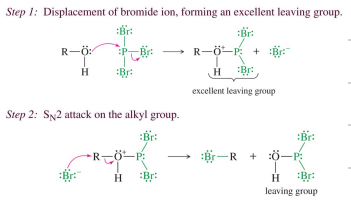
- Poor yields of alkyl chlorides from 1° and 2°
- Elimination vs. Substitution
- $C^\oplus$ may rearrange
- Limited ability to make alkyl halides

Rxns w/ Phosphorus Halides

- Good yields w/ 1° and 2°
- PCl_3 for alkyl chlorides ($SOCl_2$ better)
- PBr_3 for alkyl bromides
- P and I_2 for alkyl iodides (PI_3 unstable)

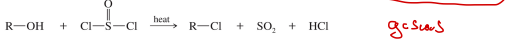
Mechanism w/ PBr_3

- O may attack phosphorus
- Br^- attacks S_N2 (back-side)

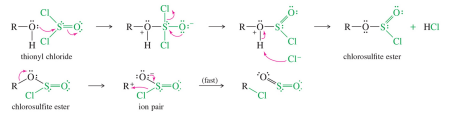


Reaction of Alcohols w/ Thionyl Cl

- Thionyl chloride ($SOCl_2$) can convert alcohols to corresponding alkyl chloride in a simple rxn producing HCl and SO_2

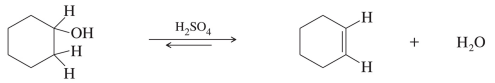


Mechanism of Thionyl Cl Rxn



Dehydration Rxns

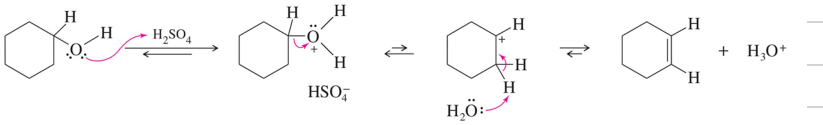
- Concentrated H_2SO_4 produces alkene
- $C^{\oplus}$ intermediate for 2° and 3° alcohols
- Zaitsev Product
- Bimolecular dehydration produces ether
- Low temp (140°C and below) favors ethers
- High temp (180°C and above) favors alkenes



cyclohexanol, bp 161 °C — cyclohexene, bp 83 °C (80%) (distilled from the mixture)

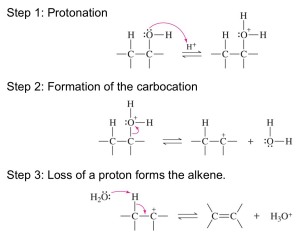
Dehydration of Alcohols

- Alcohol dehydration generally takes place through E1 mechanism
- Rearrangements are possible
- The rate of reaction follows same rate of $C^{\oplus}$: 3° > 2° > 1°
- Primary Alcohols rearrange, so this is isn't good for 1° alcohols → alkenes

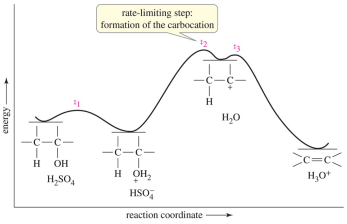


OH is not a good LG, so protonate it so it wants to leave

Mechanism of Dehydration: E1



Energy Diagram, E1



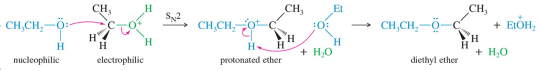
- Do not place time on the x-axis!

Unique Reactions of Diols

- Vicinal diols can undergo the following rxns:
  - Pinacol rearrangement
  - Periodic acid cleavage

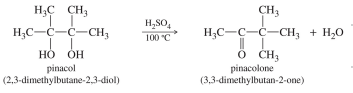
Industrial Bimolecular Condensation to form ethers

- Protonated alcohol may be attacked by another molecule of the alcohol and undergo an S_N2 displacement
- Net rxn is bimolecular dehydration → ether
  - ↳ this is a type of condensation
- Low temp rxn (140°C)



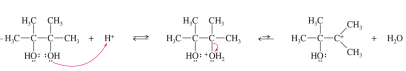
Pinacol Rearrangement

- Vicinal diol converts to a ketone called pinacolone in acidic conditions with heat present
- Rxn is described as dehydration

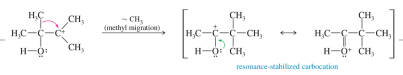


Mechanism of Pinacol Rearrangement

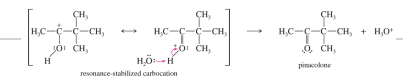
- Protonation and loss of water → $C^{\oplus}$



- Methyl shift forms resonance stabilized $C^{\oplus}$

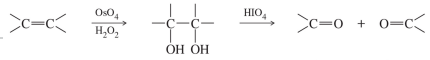


- Deprotonation by water yields product



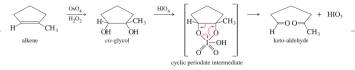
Periodic Acid Cleavage

- Glycols can be oxidatively cleaved by periodic acid (HIO_4) to form corresponding ketones and aldehydes
- Useful for determining the structures of sugars



Mechanism of HIO_4 Cleavage

- Cyclic Periodate Intermediate is usually involved

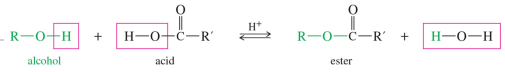


Esterification

- Fischer: Alcohol + carboxylic acid
- Tosylate esters
- Sulfate esters
- Nitrate esters
- Phosphate esters

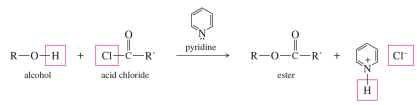
Rxns!

Fischer Ester Reaction

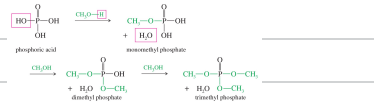


- Rxn of an alcohol and carboxylic acid produces an ester
- Sulfuric acid is a catalyst
- Rxn is an eq. between reactants and products, which results in less or use of this to produce esters!

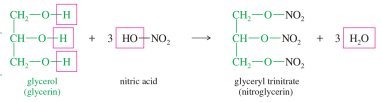
Reaction with Acyl Chlorides



Phosphate Esters



Nitrate Esters

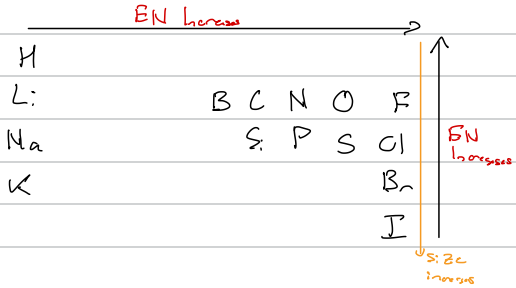


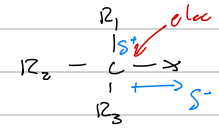
Alkoxide Ions: Williamson Ether Synthesis

- S_N2 displacement
- Alkoxide acts as basic if 2° or 3° hindered

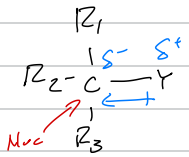
Retrosynthetic Analysis

Recent HW 1pt, not 0 pt, 6pt BC on exam





Nuc: e⁻ rich
Elec: e⁻ deficient

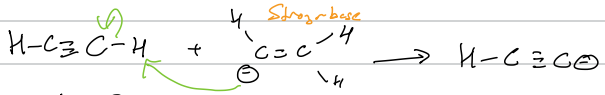


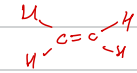
Grignard Leads Lithiates

Acidity of a H-bond to sp hybridized carbon

$sp > sp^2 > sp^3$ Relate EN of carbon atoms

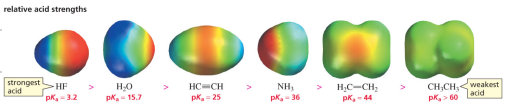
acetylene →		
$HC\equiv CH$	$H_2C=CH_2$	CH_3CH_3
ethyne	ethene	ethane
$pK_a = 25$	$pK_a = 44$	$pK_a > 60$



Conjugate acid: 

Negative charge not efficient

EN against Acid Strength



Strong base = weak conj. Stry Acid = weak base

relative base strength

$CH_3CH_2^- > H_2C{=}CH^- > H_2N^- > HC{\equiv}C^- > HO^- > F^-$

Strength of Acid/Base and Conjugates

$RC{\equiv}CH + {}^-NH_2 \rightleftharpoons RC{\equiv}C^- + NH_3$

stronger acid	stronger base	acetylide ion weaker base	weaker acid
	amide ion		

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$RC{\equiv}CH + HO^- \rightleftharpoons RC{\equiv}C^- + H_2O$

weaker acid	weaker base	stronger base	stronger acid
	hydroxide anion	acetylide anion	

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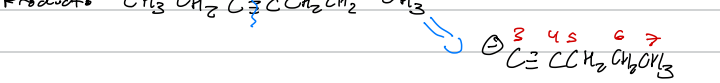
Synthesis One

$CH_3CH_2C{\equiv}C^- + CH_3CH_2CH_2Br \longrightarrow CH_3CH_2C{\equiv}CCH_2CH_2CH_3 + Br^-$

Product: $CH_3\,CH_2\,C\equiv C\,CH_2CH_2-CH_3$



These work as reactants too

Stable starting product

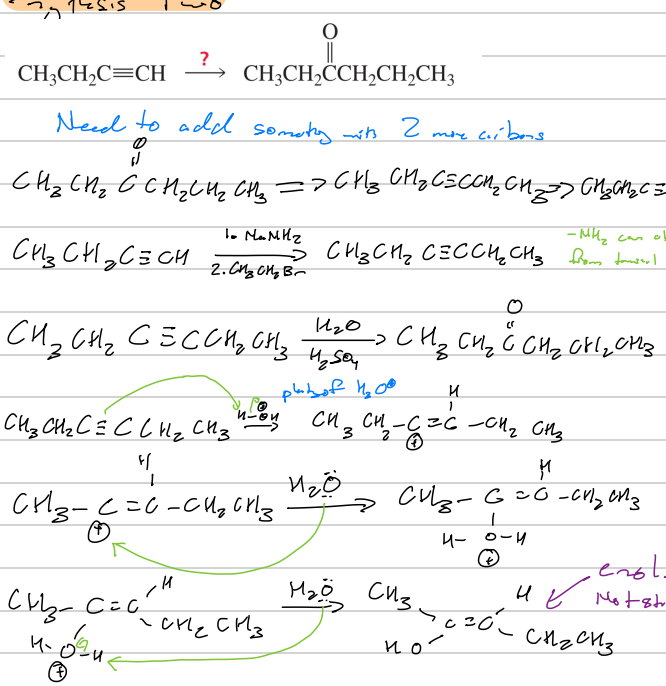
$CH_3CH_2Br + H-C\equiv CCH_2CH_2CH_3 \xrightarrow{-NH_2}$

$CH_3CH_2CH_2C\equiv C-H \xrightarrow[2.\ CH_3CH_2Br]{1.\ -NH_2} CH_3CH_2CH_2C\equiv C-CH_2CH_3$

Synthesis Two

$HC{\equiv}CH \xrightarrow{?} CH_3CH_2C{\equiv}CH$ ($CH_3CH_2\overset{O}{\overset{\|}{C}}CH_2CH_2CH_3$)

Need to add something with 2 more carbons



Keto-enol Tautomerism! Acid or base mediated

Synthesis Three

$HC{\equiv}CH \xrightarrow{?} CH_3CH_2CH_2CHCH_3$ (Br)

ethyne → 2-bromopentane

Adding 3 carbons!

$CH_3CH_2CH_2\,CH\,CH_3 \Rightarrow CH_3CH_2CH_2CH=CH_2$ (Br)

Add HBr Mark!

$CH_3CH_2CH_2C\equiv CH \Rightarrow HC\equiv CH$

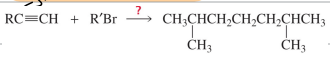
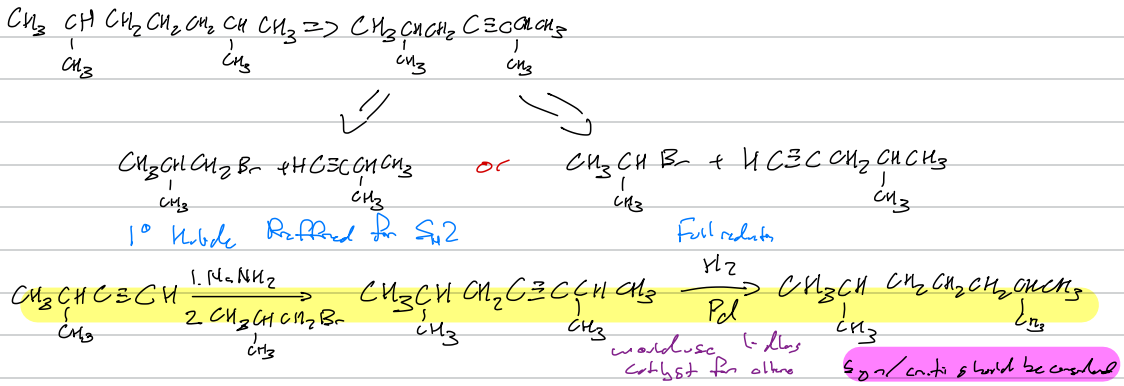
$HC\equiv CH \xrightarrow[2.\ CH_3CH_2CH_2Br]{1.\ NaNH_2} CH_3CH_2CH_2C\equiv CH$

$CH_3CH_2CH_2C\equiv CH \xrightarrow[\text{Lindlar}]{H_2,\ Pd/BaSO_4} CH_3CH_2CH_2CH=CH_2$

$CH_3CH_2CH_2CH=CH_2 \xrightarrow{HBr} CH_3CH_2CH_2CH-CH_3$ (Br)

Use Peroxide for anti-mark

Synthesis Four



2,6-dimethylheptane