

Summary Sheet - Hybridization And Bonding

"Master Organic Chemistry"
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Note - this sheet is not meant to be comprehensive. Your course may provide additional material, or may not cover some of the reactions shown here. Your course instructor is the final authority.

What is bonding and why does it occur?

In a chemical bond, electrons are shared between atoms.

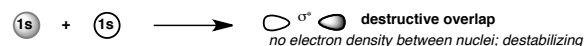
This is energetically favorable (more stable) because of Coulomb's law (opposite charges attract; negatively charged electrons held between two positively charged nuclei)

Constructive end-on-end overlap between **atomic orbitals** results in a σ ("sigma") **molecular orbital**



What is antibonding?

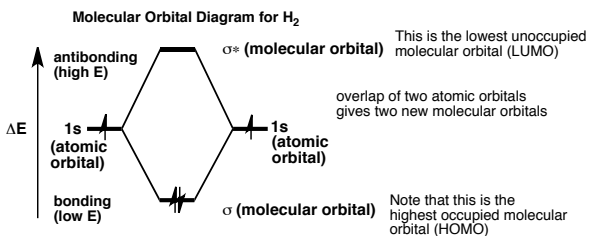
Destructive overlap between atomic orbitals gives an **antibonding** molecular orbital. This means that two positively charged nuclei are held closely together without any electrons between them to "glue" them together; repulsion between nuclei makes this a very unstable situation



Can't we just have bonding without antibonding?

No. When atomic orbitals come together, the number of molecular orbitals has to equal the number of atomic orbitals. Bringing together two atomic orbitals will always result in two new molecular orbitals, one bonding ("constructive overlap") and one antibonding ("destructive overlap")

Sigma bonds are formed through **end-on** overlap of two atomic orbitals, as distinguished from **pi bonds** (see later section).



Why care about antibonding if it's usually empty?

- In the diagram above for H_2 , if we added a third electron, it would have to go to the antibonding orbital because there's nowhere else to put it.
- Antibonding orbitals can be filled when electrons absorb energy of a certain frequency (promoting a bonding electron to antibonding) or if an extra electron is added to a molecule where all orbitals are already full.

What is Pi (π) bonding?

Pi bonding occurs when orbitals overlap in a "side-on" fashion. This is possible when neighboring atoms have electrons in unhybridized p orbitals (like alkenes and alkynes)

Pi bonding occurs when orbitals overlap in a "side-on" fashion.

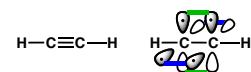
Electron density is shared between neighboring p orbitals, resulting in a π bond.

Atoms involved in pi bonding cannot be rotated, since this would destroy overlap.

Pi bonding not possible here because these p orbitals are at 90° to each other

There are also π^* orbitals (not shown)

It is possible for two pi bonds to be present; this involves the side-on overlap of two p orbitals, each at 90° to each other

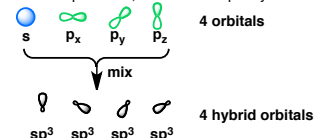


Hybridization

Type	s	hybridized p	leftover (unhybridized) p	orbital geometry
sp^3	1	3	0	tetrahedral
sp^2	1	2	1	trigonal planar
sp	1	1	2	linear

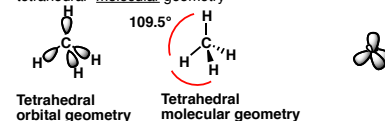
sp^3 Hybridization

The bond angles in CH_4 are 109.5° . The orbitals containing each pair of electrons are neither "pure p" or "pure s". They are a hybrid between p and s. Since we are hybridizing one s orbital and three p orbitals, we call this " sp^3 " hybridization

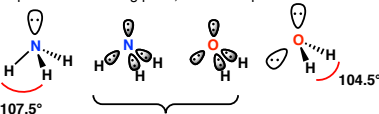


(Each 109.5° apart - "tetrahedral" orbital geometry)

In CH_4 the hydrogens are arranged in a tetrahedral fashion around the central carbon atom. We say CH_4 has "tetrahedral" molecular geometry



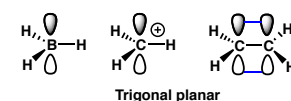
Molecules such as NH_3 and H_2O also have four electron pair domains that are arranged tetrahedrally around the central atom; some of these are "lone pairs" that are not bonded to an atom. The lone pairs take up slightly more space than bonding pairs, which compresses the bond angles



"Trigonal pyramidal" molecular geometry
"Bent" molecular geometry

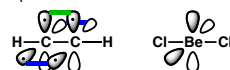
sp^2 Hybridization

If one s orbital is hybridized with two p orbitals we obtain three hybrid orbitals that will be 120° apart. We will have one "leftover" unhybridized p orbital. This is the geometry of the central atom in trivalent boron compounds, carbocations, and atoms with a single pi bond



sp Hybridization

If one s orbital is hybridized with one p orbital we obtain two hybrid orbitals 180° apart. We have two "leftover" unhybridized p orbitals. This is the geometry of the central atom in beryllium compounds (e.g. $BeCl_2$) as well as that of atoms with triple bonds

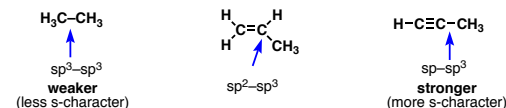


Some examples

Example	Hybridization	Orbital Geometry	Molecular geometry
CH_4	sp^3	tetrahedral	tetrahedral
NH_3	sp^3	tetrahedral	trigonal pyramidal
H_2O	sp^3	tetrahedral	bent
$\ominus NH_2$	sp^3	tetrahedral	bent
$\ominus CH_3$	sp^3	tetrahedral	trigonal pyramidal
BH_3	sp^2	trigonal planar	trigonal planar
$\oplus CH_3$	sp^2	trigonal planar	trigonal planar
$BeCl_2$	sp	linear	linear
$H_2C=CH_2$	sp^2	trigonal planar	trigonal planar
$H_2C=O$	sp^2	trigonal planar	trigonal planar
$H_2C=N^+$	sp^2	trigonal planar	trigonal planar
$H_2C=C^+$	sp^2	trigonal planar	trigonal planar

How does hybridization affect bond strength?

s orbitals are closer to the nucleus and more tightly held. The more "s-character" a bond has, the stronger (and shorter) it will be



The Shortcut For Finding The Hybridization Of Any Atom

Count the number of surrounding atoms (A) + lone pairs (LP)

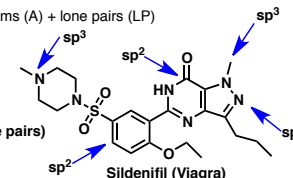
If $A+LP = 4$ hybridization is sp^3

If $A+LP = 3$ hybridization is sp^2

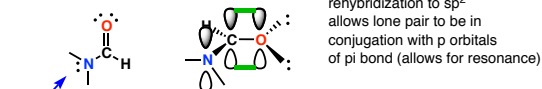
If $A+LP = 2$ hybridization is sp

Try it with Viagra!

(don't forget the "hidden" lone pairs)



Exception - not always covered - if atom with lone pair next to pi bond, rehybridization occurs to put that lone pair in a p orbital. So it's actually sp^2 not sp^3



atom with lone pair adjacent to sp^2 hybridized atom; lone pair will be in p orbital, not sp^2 orbital. Nitrogen is **sp^2 not sp^3**

Omissions, Mistakes, Suggestions?

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Formal Charge, Dipoles, Boiling Points, and Curved Arrows

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How To Calculate Formal Charge Of An Atom

1. Start with the number of valence electrons, "V"

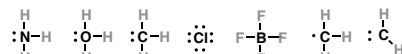
e.g.

B	C	N	O	F
---	---	---	---	---

"V"

3	4	5	6	7
---	---	---	---	---

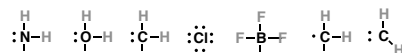
2. Count the number of non-bonded electrons, "N"



"N"

2	2	2	8	0	1	2
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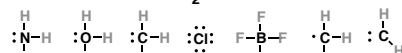
3. Count the number of bonding electrons, "BE" [2 electrons per bond]



"BE"

6	6	6	0	8	6	4
---	---	---	---	---	---	---

$$\text{Formal charge} = V - \left[N + \frac{1}{2} \text{BE} \right]$$



Charge

0	+1	-1	-1	-1	0	0
---	----	----	----	----	---	---

Alternative: instead of multiplying the # of bonding electrons "BE" by 1/2, count the number of bonds, "B" around the atom instead

$$\text{Formal charge} = V - [N + B]$$

Dipoles

Atomic nuclei differ in their ability to pull electrons toward themselves. This property is called "electronegativity", and is measured on a scale from roughly 1.0 (low) to 4.0 (high). The higher the electronegativity, the "greedier" that atom is for electrons.

B	H	P	S	C	I	Br	N	Cl	O	F
2.0	2.2	2.2	2.6	2.6	2.7	3.0	3.0	3.2	3.4	4.0

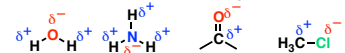
A consequence of electronegativity is that electrons in bonds between atoms with different electronegativities are not equally shared. The more electronegative atom will have a greater "share" of the bonding electrons, giving it a partial negative charge, and the less electronegative atom will have a lesser "share" of the bonding electrons, giving it a partial positive charge.

This is what is known as a **dipole**

example: $\delta^+ \text{H}-\text{F} \delta^-$ the δ^- means that fluorine bears a partial negative charge

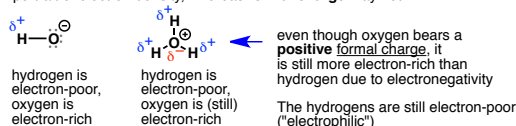
hydrogen bears a partial positive charge
electronegativities: 2.2 (H), 4.0 (F)

Representative examples (with largest dipoles shown)



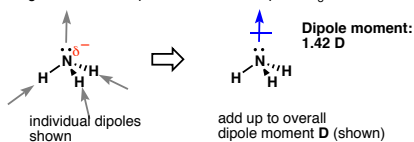
Understanding dipoles is KEY for comprehending boiling points (this sheet) but also many aspects of reactivity!

One important thing to keep in mind: dipoles always give an accurate portrait of electron density, whereas formal charge may not

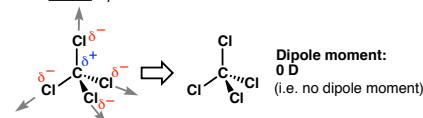


Dipole Moments

The dipoles of bonds in a molecule add up (as vectors) to give an overall **dipole moment**. Example: NH_3



Some molecules with dipoles along individual bonds will have no overall dipole moment since the vectors cancel



A good rule of thumb: the larger the dipole moment, the more polar the molecule

Polar molecules: tend to have larger dipole moments, higher water solubility, lower solubility in non-polar solvents, and relatively higher boiling and melting points than non-polar molecules.

Factors That Affect Boiling Points

Boiling occurs when enough energy is added to a liquid to overcome the attractive forces between molecules.

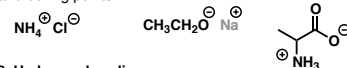
The greater the attractive forces, the higher the boiling point.

As bonds become more polarized, the charges on the atoms become greater, which leads to stronger intermolecular attractions, which leads to higher boiling points

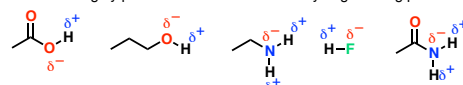
There are four types of attractive forces between molecules. Here they are in order from largest to smallest:

Ionic > Hydrogen Bonding > VDW Dipole-Dipole > VDW Dispersion (VDW = Van der Waals)

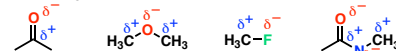
1. **Ionic forces**
Attraction between point charges. Ionic compounds have the highest melting and boiling points.



2. **Hydrogen bonding**
The next-strongest intermolecular force. Look for O-H, N-H, or F-H bonds. These are highly polarized and lead to relatively large boiling points.



3. **Van der Waals Dipole interactions**
Look for bonds between C and highly electronegative elements like O, N, or halogens. Smaller differences in electronegativity than with hydrogen bonding, but still significant

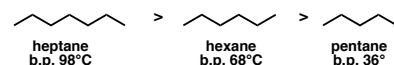


4. **Van der Waals Dispersion interactions**

Temporary (instantaneous) dipoles; weakest attractive interactions Present in all molecules (even hydrocarbons and noble gases)

Generally will increase with surface area

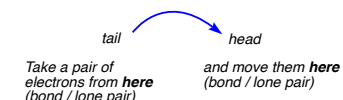
This is why boiling points increase with increasing chain lengths



Curved Arrows

Curved Arrows: A way to show the "movement" of electrons.

Electrons move from the tail to the head



- The curved arrow shows "movement" of a pair of electrons... it's an extremely useful accounting system that lets us keep track of changes in **bonding and charge**
- The tail **must** be at a source of electrons, **either a lone pair or a bond**.
- The head **must** be able to accept a pair of electrons without breaking the octet rule

There are only three "moves" possible for a curved arrow



Simple example:



Oxygen goes from "owning" a lone pair to "sharing", so its formal charge becomes less negative by 1

Negative charges can stand in for lone pairs. It's OK to draw the tail from a negative charge, so long as the atom has a lone pair of electrons

The pair of electrons in the bond will become a new lone pair on Cl

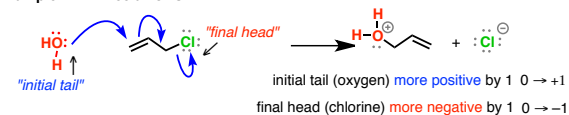
Note change in formal charge at oxygen: -1 → 0

Note change in formal charge at chlorine: 0 → -1

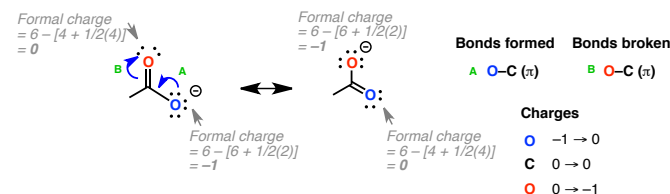
Cl goes from "sharing" this pair to "owning" it so the charge becomes more negative by 1

Only two charges are changed: the initial tail becomes more positive and the final head becomes more negative

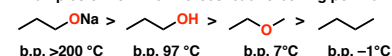
Example with three arrows:



Resonance example:

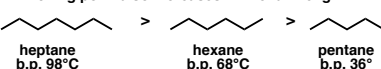


Examples of how the 4 forces lead to boiling point differences:



[Ionic] [H-bonding] [Dipole-dipole] [Dispersion]

Boiling point also increases with chain length



Omissions, Mistakes, Suggestions?

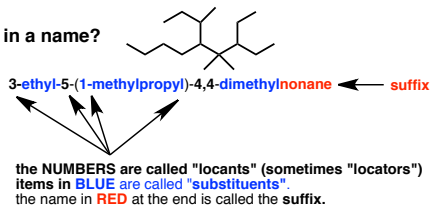
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Introduction to Alkane Nomenclature

<http://masterorganicchemistry.com>

What's in a name?



The purpose of this sheet is to demonstrate the rules by which alkanes are named.

ORDER OF BUSINESS

A. Determine the priority of functional groups (not covered here since we're dealing with alkanes only)

B. Find the longest linear chain of your molecule, or the largest ring (whichever is greatest). This is the **Chain length rule** which defines both the "main chain" and also the suffix.

tiebreaker: where more than one "path" along the molecule leads to the longest chain, the **main chain is the one that contains the most substituents.**

C. Identify the substituents along your main chain. Substituents are classified according to length of carbon chain and the suffix "yl" is attached.

D. Number your chain from one of the ends. The LOWEST LOCATOR RULE determines which end is chosen as carbon #1: "Number the chain such as to provide the lowest possible locators for the chain."

tiebreaker for lowest-locator rule: alphabetization

E. Multiple instances of substituents are given the prefixes di, tri, tetra, etc.

note: must have locator for all substituents. Example: 2,2-dimethyl is correct. 2-dimethyl is incorrect.

F. Branched substituents are numbered and named separately from the main chain, and put in brackets.

G. The FINAL name is assembled such as to arrange the substituents in alphabetical order.

-di-, tri-, tetra- are ignored for alphabetization purposes.

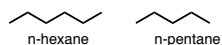
-prefixes like "n-", "tert-", "i-" and "sec-" are ignored for alphabetization purposes.

THE EXCEPTION is "isopropyl" and "isobutyl". For some reason these count as "i" - not covered here, but this is also where one puts in descriptors like "cis", "trans", (R), (S) (E), (Z) and so on.

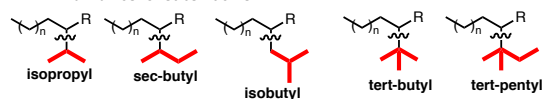
Names for Hydrocarbon Chains and Rings

1 methane		3 cyclopropane
2 ethane		4 cyclobutane
3 propane		5 cyclopentane
4 butane		6 cyclohexane
5 pentane		7 and higher follow the same pattern.
6 hexane		
7 heptane		
8 octane		
9 nonane		
10 decane		
11 undecane		
12 dodecane		
20 eicosane		

Sometimes you will see "n" in front to indicate that it is a straight-chain alkane



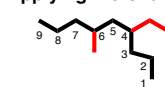
Trivial names for substituents



A. Determining the Priority of Functional Groups.

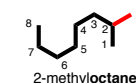
Too big a subject to cover on one sheet! This paper will focus on alkanes. Determining functional group priority will be the subject of a subsequent sheet.

B. Applying the Chain Length Rule



4-ethyl-6-methylnonane
Longest chain is 9 carbons - suffix will be **nonane**

Watch out! Longest chain might not be drawn as a "straight chain"



2-methyloctane
Longest chain is 8 carbons - suffix will be **octane**

Chains vs. rings

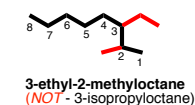
Rings take priority over chains, assuming there are only alkyl groups in the chain. ***see note below



propylcyclobutane butylcyclopropane

Tiebreaker: Alphabetization

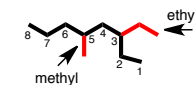
Where more than one "longest chain" exists, the more substituted chain is chosen as the "longest chain"



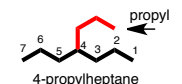
3-ethyl-2-methyloctane
(NOT 3-isopropyloctane)

C. Identifying Substituents

Substituents are carbon fragments branching off the main chain. They are named according to the number of carbons like the main chain would be, except the "ane" is dropped and replaced with "yl"



3-ethyl-5-methyloctane

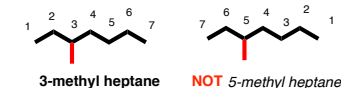


4-propylheptane

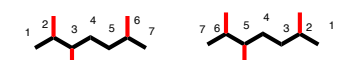
*** IUPAC 61.2 says, "Choice between these methods [either choosing rings or chains as the root] is made according to the more appropriate of the following principles: (a) the maximum number of substituents into a single unit of structure; (b) treatment of a smaller of structure as a substituent into a larger."

D. Applying the Lowest Locator Rule

Number the chain from one end so as to provide the lowest locator possible for the first substituent.



This also applies for subsequent substituents, if either direction would give the same number.



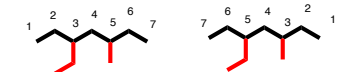
2,3,6-trimethylheptane NOT 2,5,6-trimethylheptane
For rings with one substituent, the locator "1" can be dropped. Why? Imagine a street that had only one house on it. Would the house really need a number?



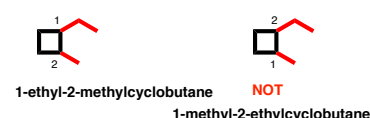
methylcyclohexane the same as 1-methylcyclohexane

Tiebreaker: Alphabetization

If the same locators are obtained from either direction of the chain, the chain is numbered according to alphabetical order of the substituents.

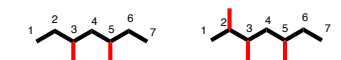


3-ethyl-5-methylheptane NOT 3-methyl-5-ethylheptane



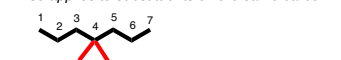
E. Multiples of the Same Substituent

Multiples of the same substituent are given the prefixes "di", "tri", "tetra", etc. The lowest locator rule still applies.



3,5-dimethylheptane 2,3,5-trimethylheptane

Also applies to substituents on the same carbon:



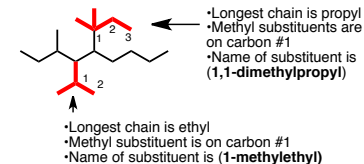
4,4-dimethylheptane

NOT 4-dimethylheptane
NOT 4,4-methylheptane

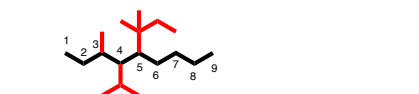
Extremely common mistakes!

F. Dealing With Branched Substituents (the IUPAC Way)

Treat each branched substituent as its own naming problem. Carbon #1 of the branched substituent will be where it meets the main chain.



We put the name in brackets to avoid confusing the numbers of the branched substituent with the numbers of the main chain.



3-methyl-4-(1-(1-methylethyl)-5-(1,1-dimethylpropyl)nonane
In certain instances, you may see the trivial names isopropyl, isobutyl, tert-butyl, tert-pentyl used.

e.g. 4-isopropyl-3-methyl-5-tert-pentylnonane.

The official IUPAC nomenclature system will never let you down. It would probably be best to just go with that.

G. Putting the Name Together.

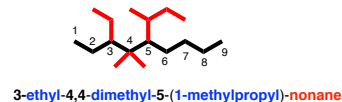
1. Put your substituents together in alphabetical order. For alphabetization purposes: IGNORE "di", "tri", "tet", etc. "sec-", "tert-", "n-", "cyclo-"

DO NOT IGNORE "iso". For some reason "isopropyl" is alphabetized under "i" and not "p".

2. Affix the locators.

3. Make sure any branched substituents are in brackets.

4. Attach the suffix at the end.



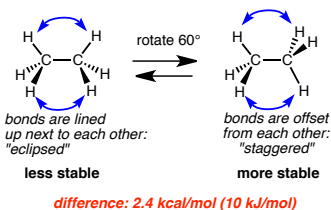
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Errors/omissions/suggestions? james@masterorganicchemistry.com

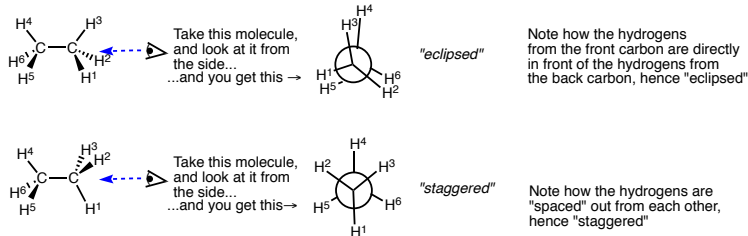
For more complete resources on nomenclature consult:
1) "Organic Chemistry Online" by William Reusch: <http://www2.chemistry.msu.edu/80/faculty/reusch/VirtTxJml/intro1.htm>
2) IUPAC "Blue Book" <http://www.acdlabs.com/iupac/nomenclature/>

What are conformations?

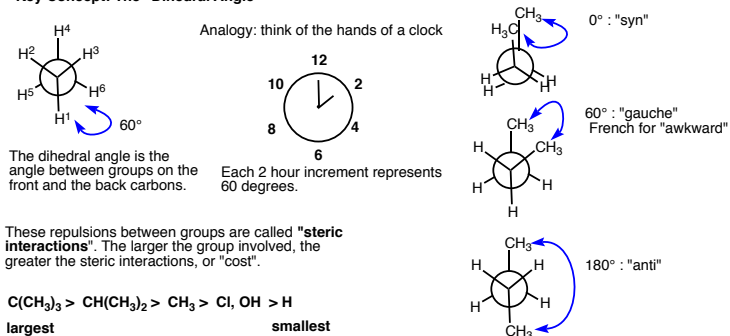
•Sigma bonds (single bonds) are free to rotate.
 •Through the rotation of bonds, molecules can adopt different 3-dimensional shapes. These are called **conformations**. Two identical molecules with different 3-D shapes are called **conformational isomers**.
 •Not all conformations are equal in energy. Because electron clouds repel, conformations which maximize the distance between atoms are generally favored (i.e. lower in energy).



Key Tool: The Newman projection



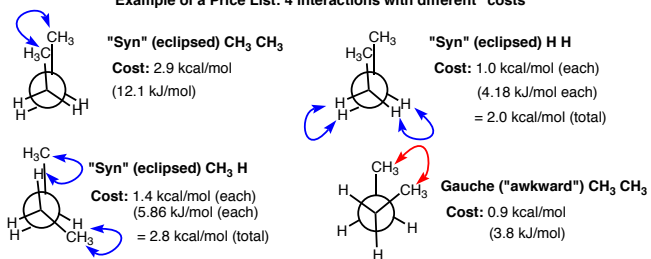
Key Concept: The "Dihedral Angle"



Interestingly, CH_3 is larger than Cl or OH , since it "sweeps out" a larger area

Repulsions between groups cause **strain**, which can be relieved through bond rotation; this is often called **"torsional strain"**.

Example of a Price List: 4 interactions with different "costs"



Example: how to figure out the rotational energies for butane ($CH_3CH_2CH_2CH_3$) ?

Step 1: like a clock, pick one group as the "hour hand" and one as the "minute hand". Then rotate that "hand" through 360°, in 60° (2h) increments.

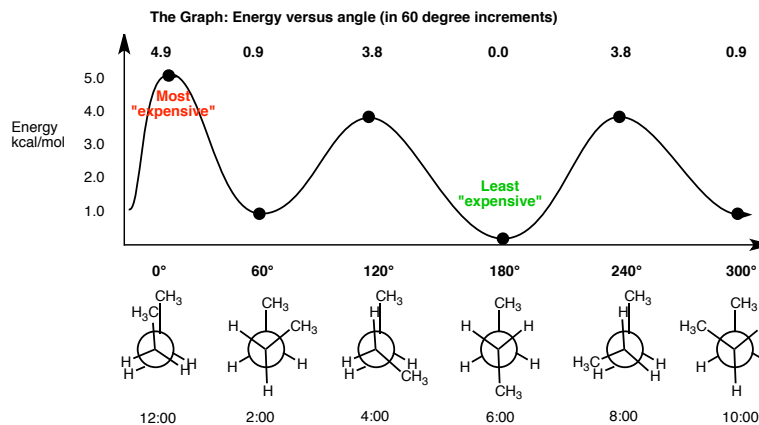
In this example, it's best to pick the two methyl groups as your "hands" since there is only one on each carbon.

Step 2: Calculate the "costs" for each of the six conformations

Example: Adding up the "costs" of each conformation for butane

"Time"	12:00	2:00	4:00	6:00	8:00	10:00
Dihedral angle	0°	60°	120°	180°	240°	300°
Eclipsed CH_3-CH_3	2.9	-	-	-	-	-
Eclipsed CH_3-H	-	-	2 x 1.4	-	2 x 1.4	-
Eclipsed H-H	2 x 1.0	-	1.0	-	1.0	-
Gauche CH_3-CH_3	-	0.9	-	-	-	0.9
Total Cost (kcal/mol)	4.9	0.9	3.8	0.0	3.8	0.9
	Most "expensive"			Least "expensive"		

Step 3: Make a graph



Omissions, Mistakes, Suggestions?

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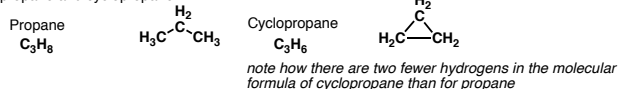
Introduction to Cycloalkanes

"Master Organic Chemistry"
 masterorganicchemistry.com
 Mar 2015. Version 1.2

Note - this sheet is not meant to be comprehensive. Your course may provide additional material, or may not cover some of the reactions shown here. Your course instructor is the final authority.

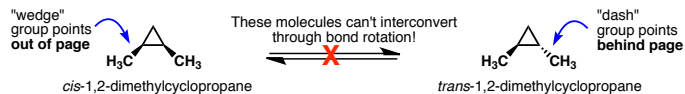
Cyclic molecules

Molecules in organic chemistry don't just exist as chains - they can also exist as **rings**. Compare propane and cyclopropane.



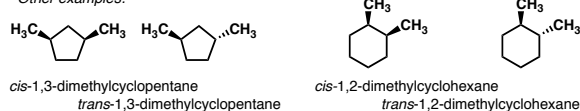
Stereochemistry

When groups are on a ring, they are constrained - they can't rotate in the same way that linear molecules can. This can give rise to "cis" and "trans" isomers - stereoisomers.



stereoisomers: same molecular formula, different boiling points/melting points

Other examples:



Ring Strain

In contrast to chains, where sp^3 hybridized carbons can adopt their ideal geometry of 109.5° , the geometry of carbons in some cycloalkanes can be far from ideal, leading to **ring strain**



Name: Cyclopropane Cyclobutane Cyclopentane Cyclohexane
 Interior angle: 60° 90° 108° * see below

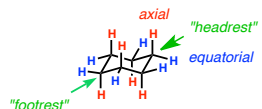
Ring strain (kcal/mol) 27.6 kcal/mol 26.4 kcal/mol 6.5 kcal/mol 0
 (kJ/mol) 115.5 kJ/mol 110.4 kJ/mol 27.2 kJ/mol 0

Ring strain is a combination of **angle strain** (where geometry of the carbon deviates from the ideal) and **torsional strain** (arising from eclipsing interactions)

The Chair Conformation of Cyclohexane

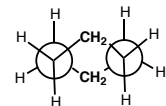
The cyclohexane ring is not a flat hexagon. Why not? Two reasons: 1) the bond angles would be 120° (creating angle strain) and 2) the neighboring hydrogen atoms would be eclipsed with each other. Instead cyclohexane adopts a **chair** conformation where all bond angles are close to 109 degrees and all neighboring groups are staggered.

Groups that point "straight" up and down are said to be "axial" - in red



Groups that point "somewhat" up or down are said to be "equatorial" - in blue

Newman projection of chair

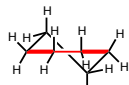


In the chair form, all substituents are staggered along every C-C bond

Other conformations of cyclohexane (higher in energy than the chair)

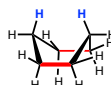


Planar
 angle strain (120°)
 eclipsing strain
 (two hydrogens omitted for clarity)



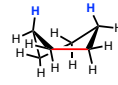
"Half-Chair"
 eclipsing strain
 steric crowding

10.7 kcal/mol less stable than chair



"Boat"
 eclipsing strain
 steric crowding

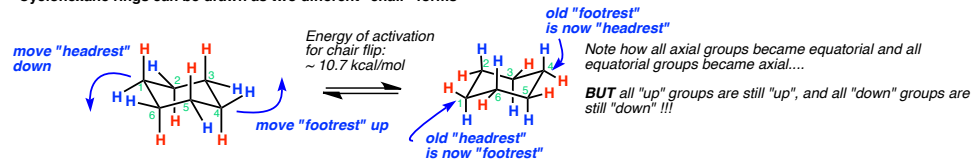
6.9 kcal/mol less stable than chair



"Twist boat"
 eclipsing strain
 steric crowding

5.3 kcal/mol less stable than chair

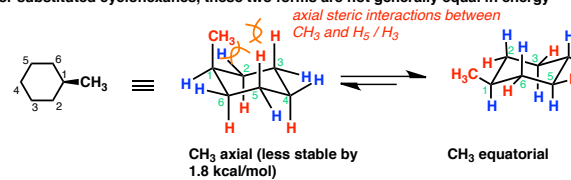
Cyclohexane rings can be drawn as two different "chair" forms



Note how all axial groups became equatorial and all equatorial groups became axial...

BUT all "up" groups are still "up", and all "down" groups are still "down" !!!

For substituted cyclohexanes, these two forms are not generally equal in energy



The axial position is less favored for substituents since it can undergo unfavorable steric interactions with other axial substituents. These are avoided in the equatorial position.

(Technically these are "gauche" interactions)

Each interaction between axial CH_3 and axial H "costs" ~ 0.9 kcal/mol, for a total of about 1.75 kcal/mol.

Using this value we can calculate the % of 1-methylcyclohexane that is present in the axial form at equilibrium:

$$\Delta G = -RT \ln K \quad K = e^{-\Delta G/RT}$$

At 1.75 kcal/mol this gives us $K = 0.052$, or approximately 95:5 ratio in favor of the equatorial CH_3

This value: 1.75 kcal/mol is sometimes referred to as the "A" value of CH_3

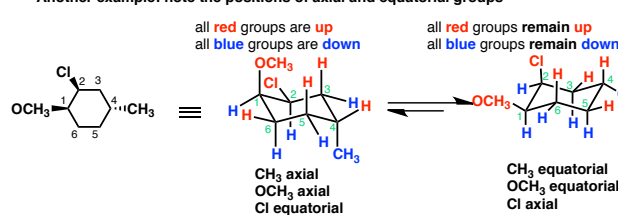
The size of the A value is related to the magnitude of the steric interactions between axial substituents

Group	A Value	Group	A Value
CH ₃	1.74	Cl	0.43
CH ₂ CH ₃	1.75	OH	0.87
i-Pr	2.15	OCH ₃	0.6
t-Bu	4.7	NH ₂	1.6

This table gives an idea of the preference of the substituent for the equatorial position. For example t-Bu is the bulkiest of these groups, whereas Cl is the least bulky.

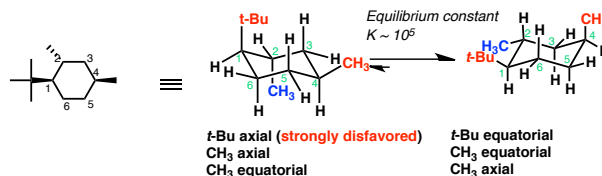
Using the Gibbs equation it's possible to calculate the position of the equilibrium for each substituent.

Another example: note the positions of axial and equatorial groups



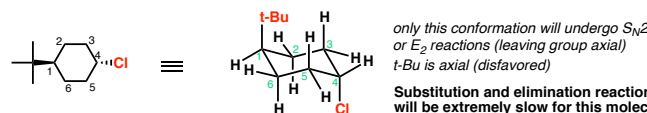
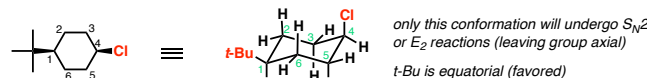
Important: the t-butyl group is conformationally "locked" in the equatorial position

The t-butyl group is so bulky that the axial position is extremely disfavored. Equilibrium favors the equatorial position to such an extent that one can consider the chair to be "locked" in the conformation with t-Bu equatorial



Application in substitution and elimination reactions (S_N2 and $E2$)

Understanding the proportions of different chair forms is important because S_N2 and $E2$ reactions will only occur when the leaving group is in the axial position.



Omissions, Mistakes, Suggestions?

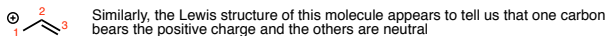
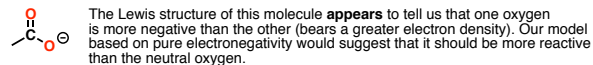
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1. What is Resonance?

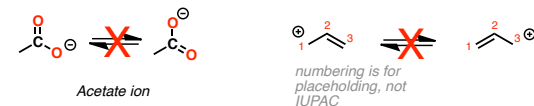
The true distribution of electrons in a molecule cannot always be accurately depicted through a single Lewis structure. Resonance is a tool to show this.

So what about applying this concept to these molecules?

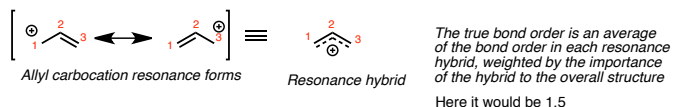
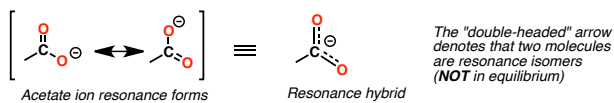


In reality, the charge in both of these molecules is distributed equally between the different ends

Important: this is **not** an equilibrium!

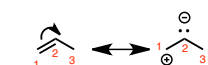


Instead, the "true" structure of the molecule is a **hybrid** of these two forms.

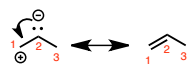


2. How to Use Curved Arrows

There are only **three** legal "moves" we can do with curved arrows to show resonance.

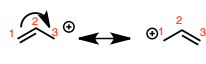
 π Bond \rightarrow Lone pair

Tail is at π bond between C1 and C2
Head is at C2
Arrow shows movement of electrons from the C1-C2 π bond to become a lone pair on carbon 2.

Lone pair \rightarrow π Bond

Tail is on lone pair of C2
Head is between C1 and C2.
Arrow shows movement of electrons from the lone pair on C2 to become a π bond between C1 and C2

*only possible if an sp^2 or sp hybridized carbon is next door (i.e. don't break the octet rule)

 π Bond \rightarrow π Bond

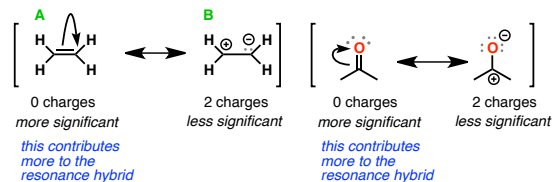
Tail is at π bond between C1 and C2
Head is at π bond between C2 and C3
Arrow shows movement of electrons from the C1-C2 π bond (which breaks) to the C2-C3 π bond (which forms).

*only possible if an sp^2 or sp hybridized carbon is next door (i.e. don't break the octet rule)

3. When Resonance Forms are Not Equal: How to tell which are most significant?

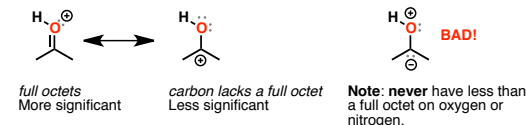
Rule #1 - The Fewer Charges, the Better

Resonance forms decrease in importance as their charges increase



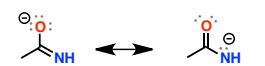
Rule #2 - Full Octets Are Preferred

A resonance form in which all atoms have a full octet is more significant than one where at least one atom lacks a full octet.



Rule #3 - Place a negative charge on the least basic atom

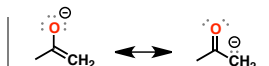
"Amide anions"



negative charge is on least basic atom (O)

negative charge is on most basic atom (N)

"Enolates"



negative charge is on least basic atom (O)

negative charge is on most basic atom (C)

If given a choice, the best place to put a negative charge on a resonance form is on the **least basic atom**

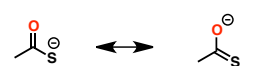
Use acidity trends to determine the "best" resonance form in these cases

• Electronegativity

• Polarizability

• Induction

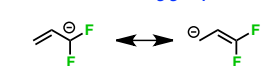
Polarizability



negative charge is on least basic atom (S)

negative charge is on most basic atom (O)

Electron withdrawing groups



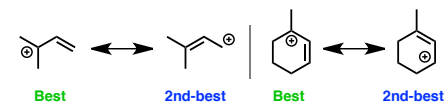
negative charge is on least basic atom

negative charge is on most basic atom

Rule #4 Stabilizing positive charge

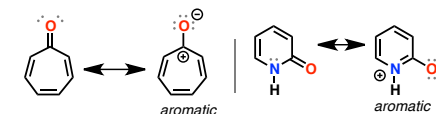
If the resonance form has a positive charge, try and find a resonance form in which all octets are full (Rule #2)

If all octets are **not** full, place positive charge on the atom best able to support a carbocation (i.e. the most substituted carbon)



Rule #5 - Aromaticity (Org 2 Topic)

A resonance form that is aromatic will have a disproportionate contribution to the resonance hybrid

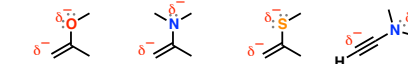


4. Applications of Resonance

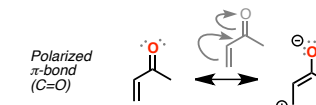
1) π -donation

Alkenes attached to an atom with a lone pair such as O, N, S, etc. (often called "heteroatoms") have an important resonance form with a negative charge adjacent to the carbon-atom bond.

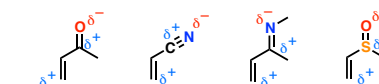
Example:

2) π -accepting

When double bonds are connected to a polarized π bond, the molecule will have a significant resonance form where there is positive charge on the adjacent carbon.



This effect makes these alkenes more electrophilic (electron-poor)



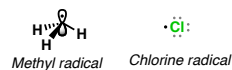
Omissions, Mistakes, Suggestions?

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Summary Sheet - Free Radicals

Free radicals contain an unpaired electron in their valence shell



As free radicals contain less than a full octet of electrons, they are electron-deficient and therefore are highly reactive

Properties: Neutral (formal charge of zero)

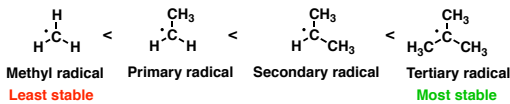
geometry of methyl radical is a "shallow" trigonal pyramid

What Factors Stabilize Free Radicals?

The same factors which stabilize carbocations. Keep these two general principles in mind: 1) electron-poor species (like radicals) are stabilized by electron-rich neighbors, or 2) by being able to spread electron density out over a greater volume.

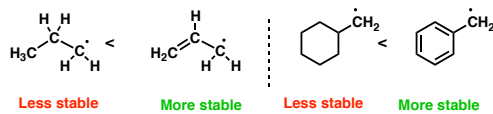
1. Substitution

Stability increases with the number of attached carbons. Neighboring alkyl groups can donate electron density to the electron-poor radical



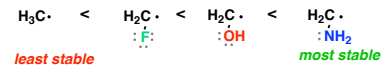
2. Free Radicals Are Stabilized By Resonance

Radicals are stabilized if they can be delocalized over several atoms (as in resonance)



3. (Advanced) Atoms With Adjacent Lone Pairs

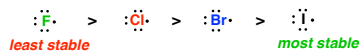
Adjacent lone pairs stabilize free radicals through "hyperconjugation"



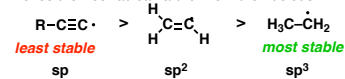
Stability increases with increasing donor ability of adjacent atom with lone pairs

Other Factors Affecting Free Radical Stability

Polarizability: Stability increases with increasing distance of the half-filled orbital from the nucleus; in other words, with increasing size of the atom (stability increases going down the periodic table)



Hybridization: Stability increases with decreasing s-character, which moves the free radical farther from the nucleus

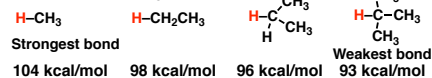


Electron-Withdrawing Groups: Groups which withdraw electron density from the free radical (without being able to donate a lone pair) destabilize radicals



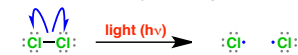
Bond strengths are a useful guide to free radical stability

Since bond dissociation energies measure homolytic cleavage. It's possible to discern trends in free radical stability by examining bond dissociation energies.



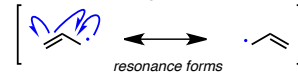
Electron movement is shown with "single-barbed" arrows

Example #1 - homolytic cleavage

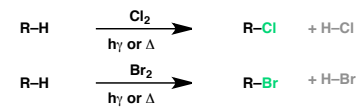


Each barbed arrow shows the movement of one electron

Example #2 - showing interconversion of resonance forms



Key Reaction: Halogenation of Alkanes With Cl₂ or Br₂

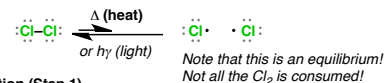


Iodination doesn't work well (thermodynamically unfavorable) and fluorination is difficult to control

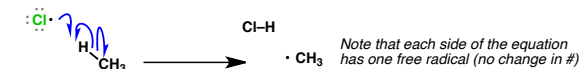
The Three Key Mechanistic Steps In Free-Radical Halogenation Are Initiation, Propagation, and Termination

- Initiation steps have a net **increase** in the number of free radicals
- Propagation steps have **no net change** in the number of free radicals
- Termination steps have a net **decrease** in the number of free radicals

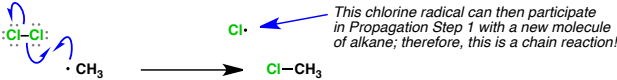
Initiation



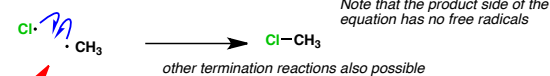
Propagation (Step 1)



Propagation (Step 2)



Termination

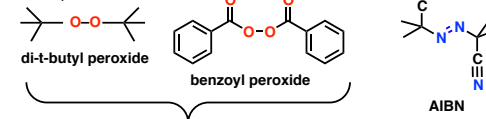


Avoid the common mistake of writing this step as Propagation Step 2! Note how the number of free radicals decreases from 2 to zero; therefore it is a termination step

Free Radical Initiators

Free radical "initiators" generate free radicals when heated. They generally have a weak bond (such as O-O) that readily undergoes homolytic cleavage.

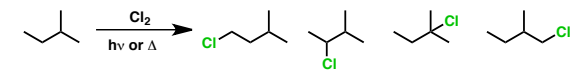
Examples:



Often just abbreviated as "RO-OR" or "peroxides"

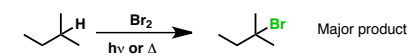
Chlorination Reactions Are Less Selective Than Bromination Reactions

Example: Chlorination can lead to substitution at primary, secondary, and tertiary positions



4 possible products formed here; chlorination occurs at primary, secondary and tertiary positions

Bromination tends to be very selective for substitution at tertiary C-H

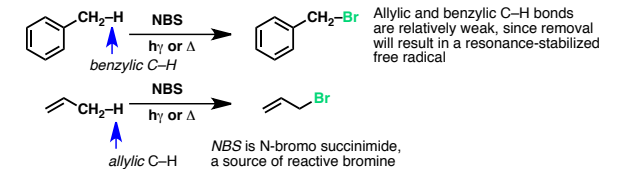


How much more selective is Br· than Cl· ?

Selectivity of Radicals Towards Alkyl Hydrogens

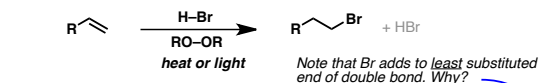
Radical	CH ₃ -H (methyl)	CH ₃ CH ₂ -H (primary)	(CH ₃) ₂ CH-H (secondary)	(CH ₃) ₃ C-H (tertiary)
Br·	0.007	1	220	19,400
Cl·	0.004	1	4.3	6.0

Allylic And Benzylic Bromination

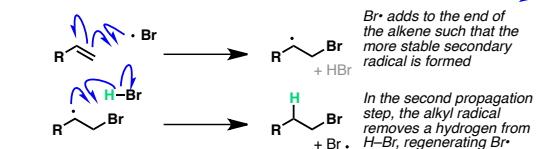


Allylic and benzylic C-H bonds are relatively weak, since removal will result in a resonance-stabilized free radical

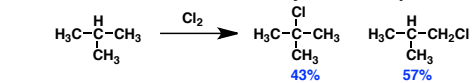
Free-Radical Addition of H-Br To Alkenes



After initiation forms peroxide radical, and peroxide radical removes H from H-Br to give Br·, this key step occurs:



How To Calculate Selectivity? An Example



Here there are two types of C-H bonds; a tertiary C-H and a primary C-H. How selective is the reaction for tertiary C-H? We can't compare by the yields directly [43% and 57%] because there is one tertiary C-H and 9 primary C-H. To adjust for this statistical factor we divide 57 by 9.

This gives us 6.3. Now we divide 43 by 6.3, which gives us 6.8.

Therefore the reaction is 6.8 times more selective for tertiary C-H than primary C-H

Omissions, Mistakes, Suggestions?

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Introduction to Acids and Bases

"Master Organic Chemistry"
masterorganicchemistry.com

Note - this sheet is not meant to be comprehensive. Your course may provide additional material, or may not cover some of the reactions shown here. Your course instructor is the final authority.

1. Introduction

Two definitions of acids:

Bronsted definition: An acid donates a proton (H⁺)

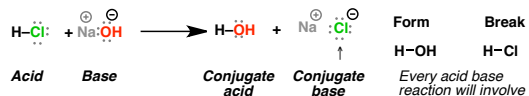
Lewis definition: An acid accepts a lone pair of electrons

Two definitions of bases:

Bronsted definition: A base accepts a proton (H⁺)

Lewis definition: A base donates a lone pair of electrons

Simple example of an acid-base reaction



The four actors:

Acid: donates a proton (or - accepts a lone pair)

Base: accepts a proton (or - donates a lone pair)

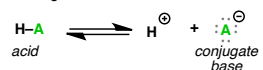
"**Conjugate base**": is what remains of the acid after it donates H⁺

"**Conjugate acid**" is the species formed when the base accepts H⁺

2. How Do We Define and Measure Acidity?

Acidity is defined as the position of the equilibrium between an acid and its conjugate base. We obtain this number through **experimental measurement**.

For a generic acid-base reaction:



The acidity constant, K_a is:

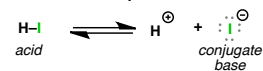
$$K_a = \frac{[\text{A}^-][\text{H}^+]}{[\text{H}-\text{A}]}$$

solvent is technically a part of the acid-base equation, but we can ignore this because all K_a's are expressed in the same solvent

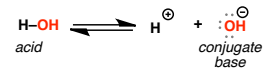
These values can differ by an extremely large amount (10⁶⁰) so it is convenient to work with the logarithm of this number, defined as the pK_a:

$$\text{pK}_a = -\log K_a$$

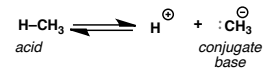
3 concrete examples:



$$K_a = 1 \times 10^{10} \quad \text{pK}_a = -10 \quad \text{Strong acid!}$$



$$K_a \sim 1 \times 10^{-15} \quad \text{pK}_a = 15.7 \quad \text{Weak acid}$$



$$K_a = 1 \times 10^{-50} \quad \text{pK}_a = 50 \quad \text{Extremely weak acid!}$$

3. What factors make an acid strong or weak?

Generally, the strength of an acid is related to the **stability** of the conjugate base.

The greater the stability of the conjugate base, the stronger the acid.

The lower the stability of the conjugate base, the weaker the acid.

A different way to put it: **stability is inversely related to basicity**.

Stable conjugate base = a "weak" base

Unstable conjugate base = a "strong" base

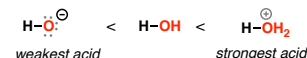
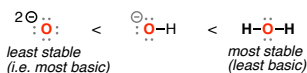
The stronger the acid, the weaker the conjugate base

The weaker the acid, the stronger the conjugate base.

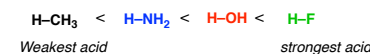
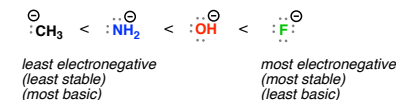
The best way to understand acidity/basicity is to understand the factors that stabilize negative charge (i.e. high electron density)

There are seven important factors (placed here in roughly decreasing order of importance).

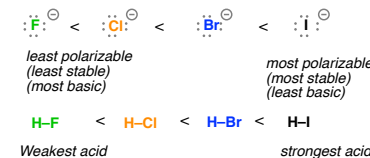
Factor #1: The less charge, the better



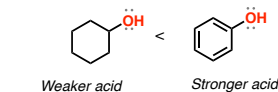
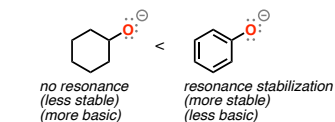
Factor #2: Going **across** the periodic table, greater electronegativity stabilizes negative charge.



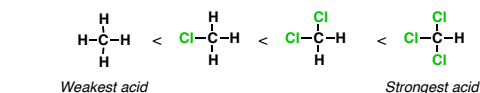
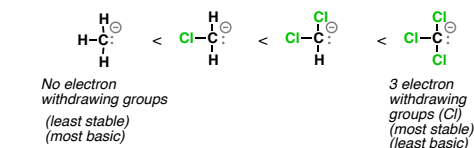
Factor #3: Going **down** the periodic table, greater polarizability stabilizes negative charge.



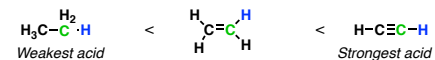
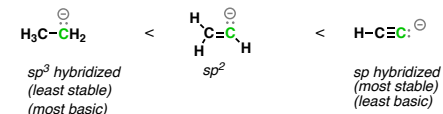
Factor #4: Negative charge is stabilized by resonance, which delocalizes electron density



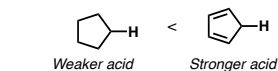
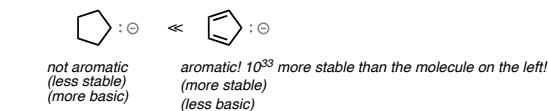
Factor #5: Negative charge is stabilized by adjacent electron withdrawing groups (inductive effects)



Factor #6: Negative charge is stabilized as the hybridization includes greater s character



Factor #7: A Special case - negative charge is especially stable if the electrons are part of an aromatic π-system



4. What makes an acid-base reaction favorable (or not)?

Key principle: In **favorable** acid-base reactions, a stronger acid adds to a stronger base to give a weaker acid and a weaker base

Key questions to ask: Is the "acid" stronger than the "conjugate acid"? Is the "base" stronger than the "conjugate base"? **If so, the acid-base reaction will be favorable.**

How do you tell which acid is stronger or weaker?

A **pK_a table** collates **experimental measurements** of acidity, and thus incorporates all the factors mentioned above.

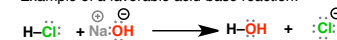
Strong acids have **low** pK_a values. Weak acids have **high** pK_a values.

A very abridged pK_a table:

Acid	pK _a	Conjugate Base
H-Cl	-8	Cl ⁻
H-OH₂⁺	-1.7	H ₂ O
H-O-C(=O)CH₃	4.5	O=C(=O)CH ₃
H-NH₃⁺	10	:NH ₃
H-OH	15.7	OH ⁻
H-OCH₂CH₃	16	OCH ₂ CH ₃ ⁻
H-C≡C-H	25	C≡C ⁻
H-NH₂	38	NH ₂ ⁻
H-CH₃	~50	CH ₃ ⁻

↑ strongest acid / weakest acid ↓
 ↓ weakest base / strongest base ↑

Example of a favorable acid-base reaction:



pK_a -8

pK_a ~15

Here, we're going from a stronger acid (HCl, pK_a -8) to a weaker acid (H₂O, pK_a 15) so this acid-base reaction is favorable.

Omissions, Mistakes, Suggestions?

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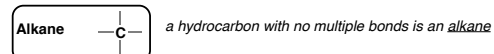
Summary of Functional Groups (1)

"Master Organic Chemistry"
masterorganicchemistry.com
 2015 Version

Note - this sheet is not meant to be comprehensive. Your course may provide additional material, or may not cover some of the reactions shown here. Your course instructor is the final authority.

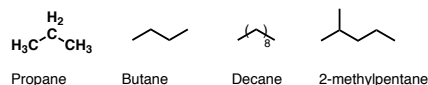
What Are Functional Groups?

Functional groups are collections of atoms that have a common pattern of chemical reactivity



Suffix: "-ane". As a substituent: "alkyl"

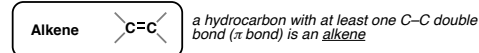
Examples:



Characteristics: nonpolar

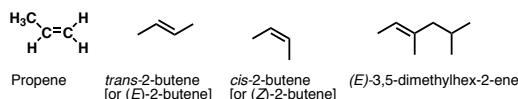
Geometry: tetrahedral (sp^3 hybridized)

Reactivity: **free radical reactions** (e.g. free radical chlorination or bromination)



Suffix: "-ene". As a substituent: "alkenyl"

Examples:

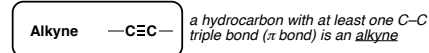


Characteristics: nonpolar. Molecule cannot rotate along double bond.

Geometry: trigonal planar (sp^2 hybridized)

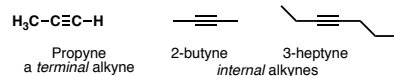
Reactivity: undergo **addition reactions**, as well as **oxidative cleavage**

Stability increases with increasing # of carbons attached



Suffix: "-yne". As a substituent: "alkynyl"

Examples:

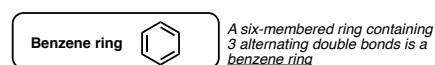


Alkynes with a C-H bond are called "terminal" alkynes

Geometry: linear (sp hybridized)

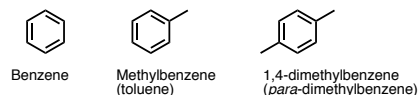
Characteristics: non polar

Reactivity: **addition reactions**
oxidative cleavage reactions
acid-base reactions (terminal alkynes are unusually acidic)



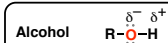
Suffix: "benzene". As a substituent: "phenyl"

Examples:



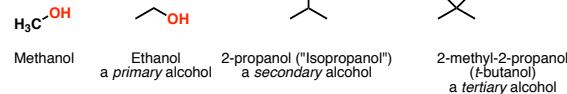
Reactivity: **substitution reactions** (e.g. electrophilic aromatic substitution or nucleophilic aromatic substitution)

Less reactive than normal alkenes due to aromatic stability



Suffix: "-ol". As a substituent: "hydroxy"

Examples:

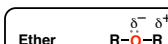


Characteristics: polar (O-H group participates in hydrogen bonding)

Reactivity: **acid-base reactions** (can act as acids or bases)

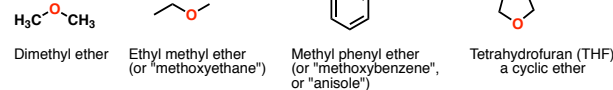
substitution reactions (can act as nucleophiles)

oxidation reactions (primary and secondary alcohols (and methanol) can be oxidized to aldehydes, ketones, or carboxylic acids, depending on structure and reagent used)



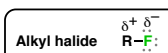
As a substituent: "alkoxy"

Examples:



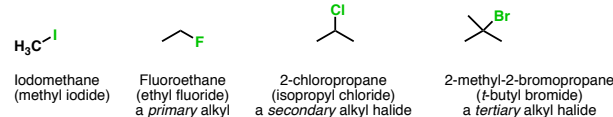
Characteristics: borderline between nonpolar and polar (due to dipole-dipole)

Reactivity: **acid-base reactions** (oxygen can act as a very weak base)



Suffix: "-ane". As a substituent: "haloalkyl"

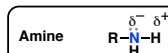
Examples:



Characteristics: generally considered non polar (but more polar than alkanes)

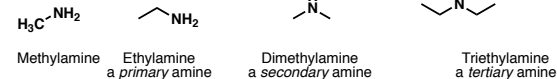
Reactivity: **substitution reactions** (Cl, Br, I can be good leaving groups)

elimination reactions (Cl, Br, I can be good leaving groups)



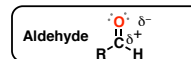
Suffix: "-ine". As a substituent: "amino"

Examples:



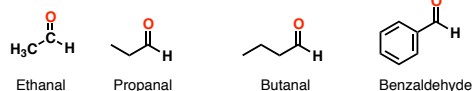
Characteristics: polar (N-H group participates in hydrogen bonding, although not as much as a hydroxy group)

Reactivity: **acid-base reactions** (tend to act as bases)
substitution reactions (can act as nucleophiles)



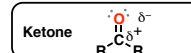
Suffix: "-al" (if attached to ring: carbaldehyde) As a substituent: "oxo"

Examples:



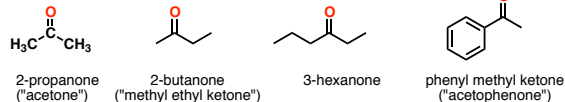
Characteristics: the C=O bond is somewhat polar

Reactivity: **addition reactions** (the carbonyl carbon reacts easily with nucleophiles)



Suffix: "-one". As a substituent: "oxo"

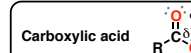
Examples:



Characteristics: the C=O bond is somewhat polar (less so than O-H however)

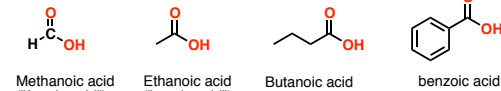
Reactivity: **addition reactions** (the carbonyl carbon reacts easily with nucleophiles)

acid-base reactions (carbons adjacent to the ketone can be deprotonated to give enolates)



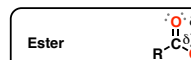
Suffix: "-oic acid"

Examples:



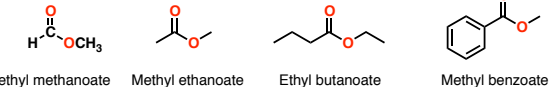
Reactivity: **acid-base reactions** (the O-H is acidic)

acyl substitution reactions (can replace OH with other groups under acidic conditions)



Suffix: "-oate"

Examples:



Reactivity: **acyl substitution reactions** (can replace OR with other functional groups under acidic conditions)
addition reactions (the carbonyl carbon reacts easily with nucleophiles)

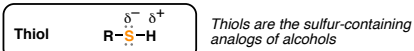
Omissions, Mistakes, Suggestions?

jesames@masterorganicchemistry.com

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<http://masterorganicchemistry.com>

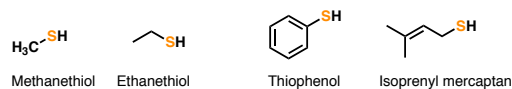
What Are Functional Groups?

Functional groups are collections of atoms that have a common pattern of chemical reactivity

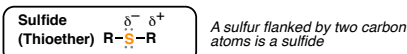


Suffix: "-thiol". As a substituent: "mercapto"

Examples:

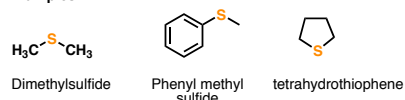


Reactivity: **acid-base reactions** (thiols can act as weak acids)
substitution reactions (thiols are good nucleophiles)

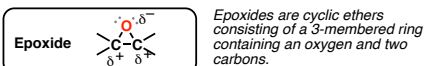


Suffix: "-sulfide".

Examples:

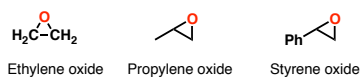


Reactivity: **reduction reactions** (will reduce the intermediate of ozonolysis reactions); sulfide is oxidized to "sulfoxide"

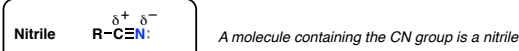


Suffix: "-oxide"

Examples:

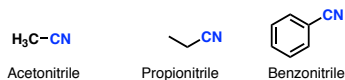


Reactivity: epoxides have considerable ring strain, and will undergo **ring opening** when treated with various types of nucleophiles (e.g. Grignard reagents, organolithium reagents)



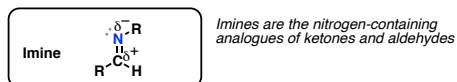
Suffix: "-nitrile"

Examples:



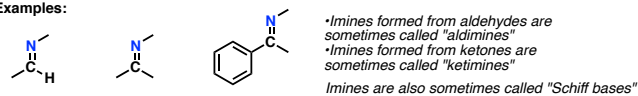
Reactivity: **reduction reactions** (nitriles can be reduced to amines with strong reductants such as LiAlH_4)
hydrolysis reactions (nitriles can be converted to carboxylic acids with aqueous acid)

Summary of Functional Groups (2)

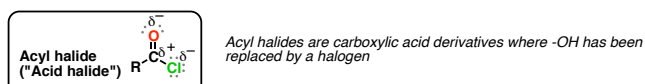


Suffix: "-imine".

Examples:

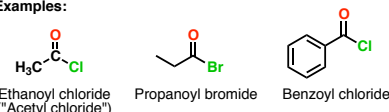


Reactivity: **reduction reactions** (imines can be reduced to amines)
hydrolysis reactions (imines can be hydrolyzed to give back aldehydes or ketones)

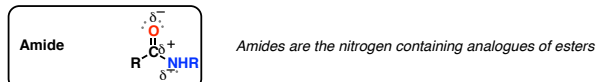


Suffix: "-oyl halide"

Examples:

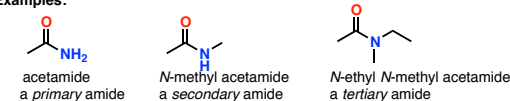


Reactivity: **acyl substitution reactions** (halides are good leaving groups and can be replaced by good nucleophiles)

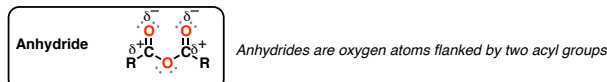


Suffix: "-amide"

Examples:

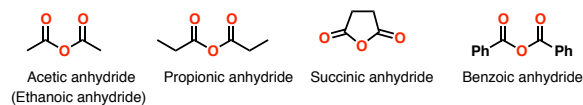


Reactivity: **reduction reactions** (amides can be reduced to amines with strong reductants such as LiAlH_4)
hydrolysis reactions (amides can be hydrolyzed to carboxylic acids with aqueous acid)

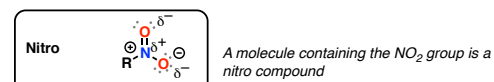


Suffix: "-anhydride"

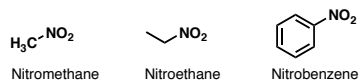
Examples:



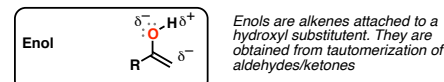
Reactivity: **acyl substitution reactions** (anhydrides can be cleaved with good nucleophiles)
reduction reactions (anhydrides can be reduced to aldehydes with various reducing agents)



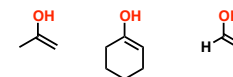
Examples:



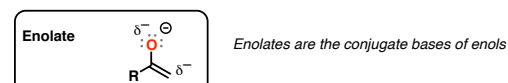
Reactivity: **reduction reactions** (nitro groups can be reduced to amines)
acid-base reactions (C-H bonds adjacent to the NO_2 group are acidic)



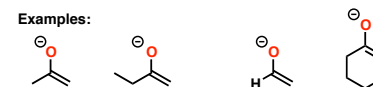
Examples:



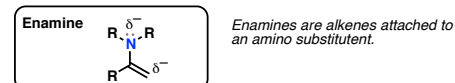
Reactivity: enols are good nucleophiles. They will perform **addition reactions** to aldehydes and ketones, among other reactions.
 Enols will **tautomerize** to aldehydes/ketones



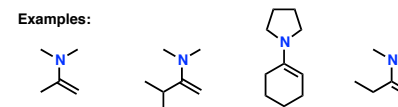
Examples:



Reactivity: enolates are excellent nucleophiles (better than enols) They will perform **addition reactions** to aldehydes and ketones, as well as **substitution reactions** with alkyl halides (among others)



Examples:



Reactivity: enamines are excellent nucleophiles. They will perform **addition reactions** to aldehydes and ketones, as well as **substitution reactions** with alkyl halides (among others)

Omissions, Mistakes, Suggestions?







james@masterorganicchemistry.com

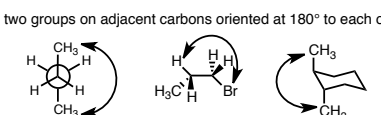
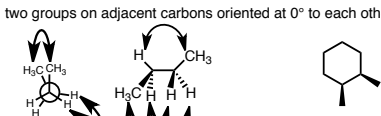
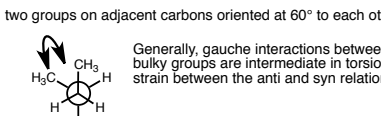
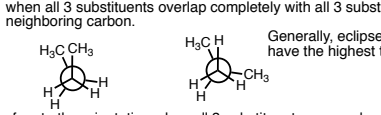
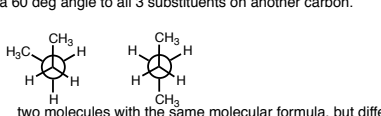
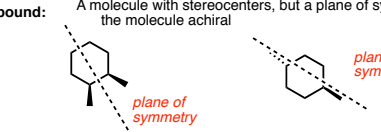
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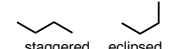
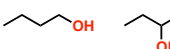
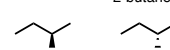

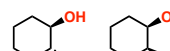
Introduction to Stereochemistry

"Master Organic Chemistry"
masterorganicchemistry.com
 2015 Version

Note - this sheet is not meant to be comprehensive. Your course may provide additional material, or may not cover some of the reactions shown here. Your course instructor is the final authority.

Symbols	Example
 "wedge" denotes a group pointing "out of the page"	
 "dash" denotes a group pointing "into the page"	
 "squiggle" undefined (mixture of stereoisomers) Rarely used.	

Terms
<p>anti two groups on adjacent carbons oriented at 180° to each other</p> 
<p>syn two groups on adjacent carbons oriented at 0° to each other</p> 
<p>gauche two groups on adjacent carbons oriented at 60° to each other</p>  <p>Generally, gauche interactions between bulky groups are intermediate in torsional strain between the anti and syn relations</p>
<p>eclipsed when all 3 substituents overlap completely with all 3 substituents on a neighboring carbon.</p>  <p>Generally, eclipsed conformations have the highest torsional strain</p>
<p>staggered refers to the orientation when all 3 substituents on a carbon are arranged at a 60 deg angle to all 3 substituents on another carbon.</p> 
<p>isomers two molecules with the same molecular formula, but different in their structures</p>
<p>configuration the 3-D arrangement of bonds around a carbon.</p>
<p>racemic mixture a 50:50 mixture of two enantiomers</p>
<p>Meso compound: A molecule with stereocenters, but a plane of symmetry that makes the molecule achiral</p> 
<p>Cis on the same side of a double bond or ring</p>
<p>Trans on opposite sides of a double bond or ring.</p>
<p>Chiral molecule a molecule with an enantiomer; cannot possess a plane of symmetry</p>
<p>Stereocenter Has 4 different constituents</p>
<p>Torsional Strain Strain that arises from the proximity of bonds (and the electrons in them) - generally eclipsing</p>

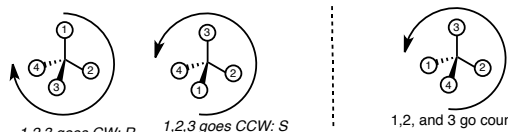
Types of isomers	Isomers: same empirical formula, different structural formula.			Example	
Type	Connectivity?	Configuration?	3-D Shape?	Physical properties	
Conformational isomers	Same	Same	Different	Identical, as long as they can interconvert through bond rotation	 staggered eclipsed
Constitutional isomers	Different			Different boiling points, melting points, and other physical properties	 1-butanol 2-butanol
Stereoisomers	Same	Different			
Enantiomers	Stereoisomers that are non-superimposable mirror images			Identical. Differ in optical rotation	 (R)-2-butanol (S)-2-butanol
Diastereomers	Stereoisomers that are NOT non-superimposable mirror images			Different boiling points, melting points, etc.	 trans-2-butene cis-2-butene
					 (trans)-cyclohexane 1,2-diol (cis)-1,2-cyclohexanediol

Note: another name for stereoisomers is "configurational isomers": they have the same connectivity, but differ in the configurations of the carbons.

The R,S convention

Rank according to atomic number
Put #4 ranked substituent in back.

What if #4 is in the front? One approach is to trace 1,2 and 3 as you normally would. Then flip!

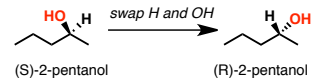


1,2,3 goes CW: R 1,2,3 goes CCW: S

1,2, and 3 go counterclockwise.
4 ranked substituent is in front
Therefore, flip: this is R!

The single swap rule:

Single swap rule: switching any two groups on a stereocenter will flip (R) to (S) and vice versa.



(S)-2-pentanol → (R)-2-pentanol

works for any other two groups as well
(e.g. OH and CH₃, H and CH₃, OH and CH₂CH₂CH₃, etc.)

Recognizing Enantiomers/Diastereomers Using Only Their Names

Diastereomers: same name, but R/S designations are not exactly opposite

Example: (2S, 3R)-2-bromo-3-chlorobutane and (2S, 3S)-2-bromo-3-chlorobutane
 (2S, 3S, 4S, 5R)-2-bromo-3-chloro-4-methyl-5-propyldecane
 and (2S, 3R, 4R, 5S)-2-bromo-3-chloro-4-methyl-5-propyldecane
also, diastereomers will have the same name, but differ in E/Z (or cis/trans).

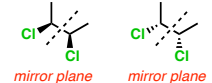
e.g. (Z)-2-butene and (E)-2-butene.
 cis-1,2-dimethylcyclohexane and trans-1,2-dimethylcyclohexane

Enantiomers: same name, but have all stereocenters have opposite R/S designations

Example: (R)-2-butanol, (S)-2-butanol
 (2S, 3R)-2-bromo-3-chlorobutane and (2R, 3S)-2-bromo-3-chlorobutane
 (2S, 3S, 4S, 5R)-2-bromo-3-chloro-4-methyl-5-propyldecane
 and (2R, 3R, 4R, 5S)-2-bromo-3-chloro-4-methyl-5-propyldecane

Important exception: If the molecule has a mirror plane, then it is **meso**, and the two "enantiomers" are in fact the same molecule

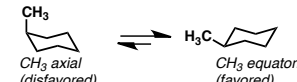
Example: (2R,3S)-2,3-dichlorobutane and (2S,3R)-2,3-dichlorobutane are the same



mirror plane mirror plane

Cyclohexane chair conformations

in the cyclohexane chair conformation: all C-C bonds staggered



CH₃ axial (disfavored) ↔ CH₃ equatorial (favored)

Chair flips: all axial groups become equatorial, and all equatorial groups become axial.
BUT all groups that are "up" stay "up" and all groups that are "down" stay "down".
 Bulky groups prefer the equatorial position.
 The bulkier the group, the greater the energy difference will be.
Bulkiness:
 tertiary C (3°) > secondary C (2°) > primary C (1°), methyl (CH₃) >> H
 The energy difference between two different chair forms (in ΔG) is related to the equilibrium constant by
 $K = e^{-\Delta G/RT}$

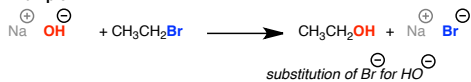
Omissions, Mistakes, Suggestions?
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Substitution and Elimination - Page 1 of 2

Nucleophilic Substitution Bimolecular (S_N2)

Key points:
 • Nucleophilic substitution is swapping of one functional group for another
 • Structure of alkyl halide is key: primary > secondary >> tertiary
 • Mechanism proceeds through backside attack
 • Stereochemistry proceeds with **inversion**
 • Rate depends on concentration of **both** nucleophile and alkyl halide
 • Reaction occurs faster in **polar aprotic solvents**

Example:



The S_N2 Reaction is Sensitive to Steric Effects.

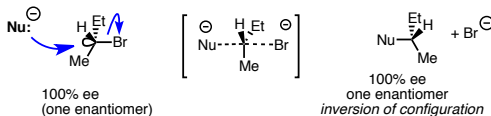
In the S_N2 the electrophile is the antibonding orbital. as you populate the antibonding orbital with electrons **R groups shield backside from nucleophilic attack** you weaken the bond to the leaving group



Fast **Intermediate** **So slow it doesn't happen.**

The S_N2 Mechanism: The Backside Attack Leads to Inversion

The nucleophile (electron pair) attacks the empty antibonding orbital which is on the **backside** of the carbon-leaving group bond



The Rate Limiting Step of the S_N2 Is Bimolecular

$$\text{Rate} = k [\text{Substrate}] [\text{Nucleophile}]$$

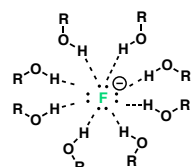
Rate	[R-X]	[Nu]	
x	1	1	Doubling the concentration of either component will double the rate.
2x	2	1	
2x	1	2	
4x	2	2	

Polar aprotic solvents are the best for the S_N2

Because of the charges involved in the S_N2 mechanism polar solvents are better than nonpolar solvents.

Two types of polar solvents: polar protic (have O-H or N-H bonds)
 Polar aprotic (has dipoles but cannot hydrogen bond).

Why? **Polar protic solvents make a "jacket" around nucleophiles through hydrogen bonding, decreasing the reactivity of the nucleophile.**

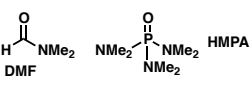


Examples of polar protic solvents:

H₂O, CH₃OH, CH₃CH₂OH, CH₃COOH, i-PrOH, CH₃CH₂CH₂NH₂

Polar aprotic solvents:

DMSO Acetone Me-C≡N



Note that in polar aprotic solvent reactivity of halides **reverses** because there is no hydrogen bonding to solvent

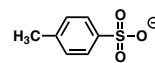
$\text{F}^- > \text{Cl}^- > \text{Br}^- > \text{I}^-$

What Makes A Good Leaving Group?

One main thing: **Good Leaving Groups are Weak Bases**

Good Leaving Groups

pKa of conjugate acid	I ⁻	Br ⁻	Cl ⁻	TsO ⁻	H ₂ O	AcO ⁻
	-9	-8	-7	-3	-1.7	4



TsO = p-methyltoluenesulfonate

Conjugate base of the strong acid tosic acid, similar in strength to H₂SO₄ (sulfuric acid)

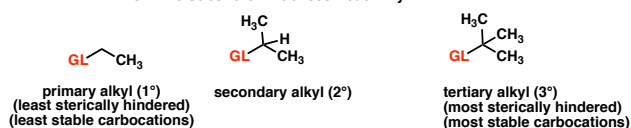
Bad Leaving Groups

pKa of conjugate acid	F ⁻	OH ⁻	RO ⁻	H ₂ N ⁻	H ⁻	alkyl, alkenyl
	1	16	16-18	~38	42	>45

With the exception of F⁻, these are all **strong bases** Fluorine forms very strong bonds and is thus a very bad leaving group

Note how HO⁻ is not a good leaving group but H₂O is: therefore, HO⁻ can be made into a good leaving group by adding a strong acid

How The Substrate Influences Reactivity



S_N2 (unhindered)
 E₂ (provided a proton is on the β carbon)

S_N1/E1: not observed

S_N2 (slower than primary)
 E₂ (provided a proton is on the β carbon)
 S_N1/E1: can occur when LG is OH and a strong acid is added watch out for rearrangements! Generally poor when LG is a halide.

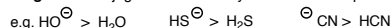
S_N2: Not observed
 E₂ (provided a proton is on the β carbon)
 S_N1/E1: strongly favored if LG = halide, good reaction if LG = OH, requires acid

Note that hybridization in all cases here is sp³

These reactions do not occur for alkenyl and alkynyl halides under normal conditions.

What Factors Influence Nucleophilicity?

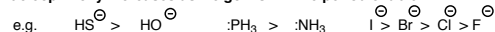
1. **Charge:** The conjugate base is always a better nucleophile than the conjugate acid



2. **Electronegativity:** The less tightly held a pair of electrons are, the more readily they can be donated.

Nucleophilicity increases as we go to the **LEFT** along the periodic table: C > N > O > F:

Nucleophilicity increases as we go **DOWN** the periodic table:



Another term for how "tightly held" electrons are is **polarizability**.

Nucleophilicity increases with polarizability.


3. **Solvent:** Polar protic solvents will hydrogen bond with nucleophiles (see column on left) which decreases their nucleophilicity.

• More polarizable nucleophiles will be less affected by polar protic solvents, since hydrogen bonding ability is greatest for most electronegative nucleophiles.

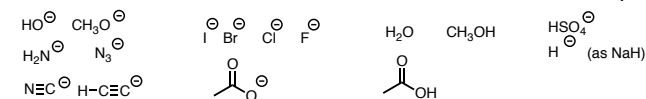
• Polar aprotic solvents **will not** hydrogen bond: therefore they are good solvents for the S_N2

Note that in polar aprotic solvent reactivity of halides **reverses** because there is no hydrogen bonding to solvent

4. **Steric bulk:** If a sterically bulky group surrounds the nucleophilic atom, this will decrease its nucleophilicity.

Example: CH₃O⁻ is more nucleophilic than  for this reason

"Good Nucleophiles" "OK Nucleophiles" "Weak Nucleophiles" "Non-Nucleophiles"



These are examples only, not comprehensive

Elimination, Bimolecular (E2)

Key points:

• Elimination is the loss of a leaving group from the α-carbon and a hydrogen from the β-carbon resulting in the **formation of a double bond**

• The major product is the more substituted alkene (Zaitsev product) and the bulkiest groups will be **trans**

• Use of a bulky base will result in formation of more of the less substituted alkene

• Requires strong base

• The leaving group and the hydrogen must be oriented **anti-periplanar**

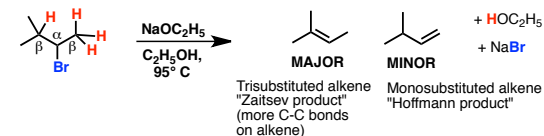
• Can occur with primary, secondary, tertiary substrates **provided there is a hydrogen on the β-carbon that can orient itself anti to the leaving group**

• Rate determining step is **bimolecular**

• Solvent is generally polar protic

• Reaction is favored with heat

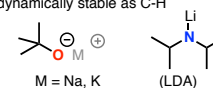
Example: Elimination of HBr



The Major Product is the Most Substituted Alkene

Why? Because alkenes become more thermodynamically stable as C-H bonds are replaced with C-C bonds

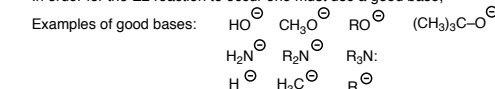
Exception: Bulky bases will give less of the Zaitsev product because deprotonation on the less substituted carbon becomes favored.



Exception #2 is when the leaving group is bulky (e.g. NR₃⁺)

A Strong Base Is Required

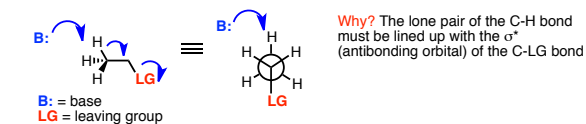
In order for the E2 reaction to occur one must use a good base,



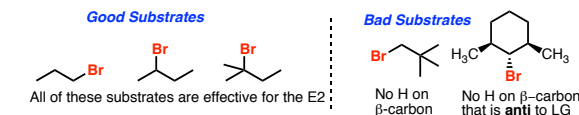
Basicity increases going to the left along the periodic table: C > N > O > F:

Basicity increases going up the periodic table: F⁻ > Cl⁻ > Br⁻ > I⁻

The H and Leaving Group MUST be Anti-Periplanar



The E2 Can Occur With Primary, Secondary, and Tertiary Substrates



The Rate Limiting Step of the E2 Is Bimolecular

$$\text{Rate} = k [\text{Substrate}] [\text{Base}]$$

Rate	[R-LG]	[B]	
x	1	1	Doubling the concentration of either component will double the rate.
2x	2	1	
2x	1	2	
4x	2	2	

Solvent is Generally Polar Protic - not in all instances, but polar protic will favor E2 in cases where it competes with the S_N2. (see left)

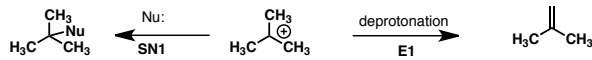
The E2 Is Favored By Heat

• Keep this in mind when considering substrates that could go E2 or S_N2
 • Heat favors elimination due to higher entropy

Substitution and Elimination - Page 2 of 2

Substitution Nucleophilic Unimolecular (S_N1) and Elimination, Unimolecular (E1)

- These reactions have a **lot** in common and often occur together.
- They represent different fates of the same carbocation



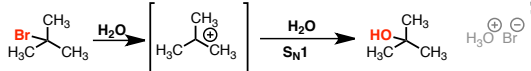
The S_N1 is nucleophilic attack at the carbocation

The E1 is deprotonation of the carbon adjacent to the carbocation

What the S_N1 and E1 Have In Common

- The rate-limiting step is **formation of a carbocation**
- The rate-limiting step is **unimolecular** and **only** depends on the concentration of the **substrate** (e.g. alkyl halide)
- The rate is also proportional to the **stability of the carbocation** (see column on right)
- Tertiary carbocations > secondary carbocations >> primary carbocations > methyl carbocations
- Carbocations are **ions** (polar) so according to "like dissolves like", polar solvents are favored. In particular, **polar protic solvents** help

S_N1 Example:

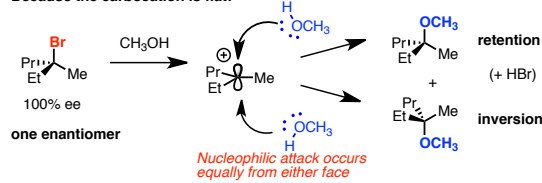


The S_N1 involves two steps that occur in sequence:

- 1) departure of the leaving group
 - 2) attack of the nucleophile at the carbocation
- The reaction proceeds with **weak/moderate nucleophiles** (e.g. H₂O, ROH)
 - If the carbon is chiral, the chiral carbon becomes **racemized**
 - **The S_N1 is always accompanied by some E1** (~95:5)

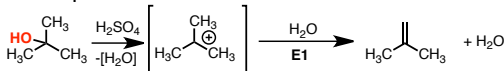
Why does the S_N1 lead to a mixture of stereoisomers?

Because the carbocation is flat!



A racemic mixture is obtained

E1 Example:



The E1 also involves two steps that occur in sequence:

- 1) departure of the leaving group
- 2) deprotonation of the carbon adjacent to the carbocation

- The proton is removed by a **weak base**
- The **more substituted double bond** is favored (Zaitsev product)
- The major product will have the bulkiest groups *trans* to each other across the double bond
- The reaction is favored by **heat**
- (The base can be the solvent, the leaving group, or the counter-ion of the acid (whichever is strongest))

The Rate Limiting Step of the S_N1 and E1 Is Unimolecular

$$\text{Rate} = k [\text{Substrate}] [\text{Nucleophile/Base}]$$

Rate	[R-X]	[Nu]	Effect
x	1	1	Doubling the concentration of the substrate doubles the rate.
2x	2	1	Doubling the concentration of the nucleophile/base has no effect
x	1	2	
2x	2	2	

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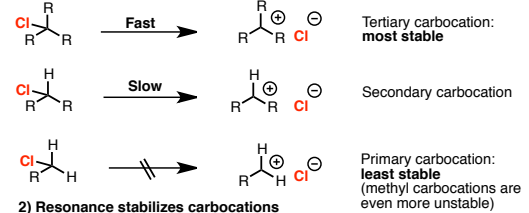
All About Carbocations

- Carbocations are flat (trigonal planar) - the central carbon is sp² hybridized
- They are stabilized by 1) increasing substitution at carbon and 2) resonance
- Tertiary carbocations > secondary carbocations >> primary carbocations
- They can be formed in several ways: 1) dissolving a tertiary alkyl halide in a polar protic solvent 2) adding acid to a secondary or tertiary alcohol
- They are more stable in polar solvents
- Secondary carbocations can rearrange to tertiary carbocations through hydride or alkyl shifts

What influences carbocation stability?

1) Carbon substituents stabilize carbocations

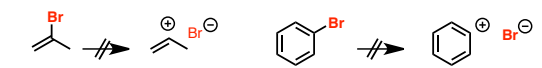
Tertiary > secondary >> primary > methyl



2) Resonance stabilizes carbocations



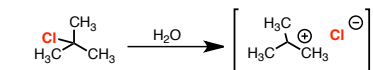
3) Vinyl and aryl carbocations are very unstable



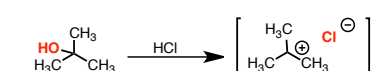
How are Carbocations formed?

Three ways.

1) dissolve a tertiary alkyl halide in a polar protic solvent.

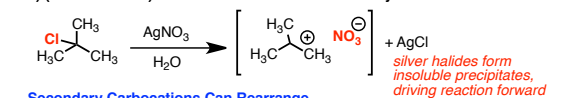


2) Add an acid to a secondary or tertiary alcohol:



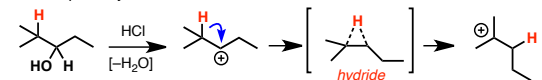
Can also be done for secondary alcohols - watch out for rearrangements!

3) (Less common) - addition of silver salts to an alkyl halide

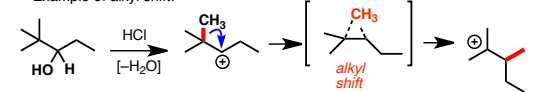


Secondary Carbocations Can Rearrange

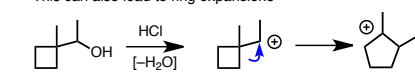
Driving force is formation of more stabilized carbocation



Example of alkyl shift:

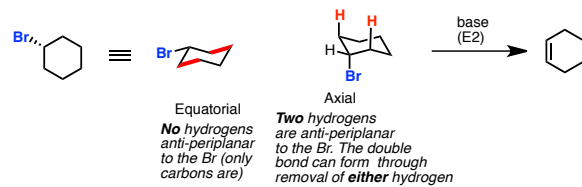


This can also lead to ring expansions

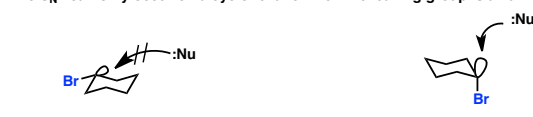


Further Notes on the S_N2 / E₂ (more advanced topics)

The E2 can only occur when the leaving group is axial:



The S_N2 can only occur on a cyclohexane when the leaving group is axial

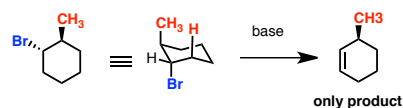


Why?

When the leaving group is equatorial, the antibonding orbital points *into* the center of the ring, making it sterically inaccessible

When the leaving group is **axial**, the antibonding orbital points **above** the ring, where it can be attacked by a nucleophile

If there is no hydrogen *anti* to the leaving group, then the double bond cannot form



One hydrogen are anti-periplanar to the Br. Therefore only **one** double bond can form

Relative Rate of S_N2 Reactions where X is a leaving group

CH ₃ X	30
H ₂ CH ₂ CH ₂ C-X	1
H ₂ CH ₂ C-X	0.4
(CH ₃) ₂ CH-X	0.025
(CH ₃) ₃ C-X	1 x 10 ⁻⁵

rate decreases with increasing steric bulk

note that even though X is on a primary carbon, it is adjacent to a quaternary carbon, which results in a very slow reaction

Additions to Alkenes

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Note - this sheet is not meant to be comprehensive. Your course may provide additional material, or may not cover some of the reactions shown here. Your course instructor is the final authority.

Note: the alkene is drawn in perspective. Imagine it lying flat on a table - the H is coming toward you, that's why it's drawn as a "wedge"

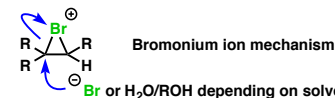
Reaction	Regiochemistry"	Stereochemistry"
Hydroboration	Anti-Markovnikoff	syn addition
Oxymercuration	Markovnikoff	syn + anti
Acid-catalyzed addition of H ₂ O (hydration)	Markovnikoff	syn + anti
Addition of HX	Markovnikoff	syn + anti
Addition of HX	Markovnikoff	syn + anti
Bromination	N/A	anti addition
Halohydrin Formation	Markovnikoff	anti addition
Chlorination	N/A	anti addition
Dihydroxylation	N/A	syn addition
Dihydroxylation	N/A	syn addition
Epoxidation	N/A	syn addition
Hydrogenation	N/A	syn addition
Radical addition of HBr	Anti-Markovnikoff	syn + anti
Ozonolysis (Reductive workup)		
Ozonolysis (Oxidative Workup)		
Cyclopropanation	N/A	syn addition

Sometimes you might see BH₃·THF or B₂H₆ used here: it's the same reagent in a slightly different form. The base (can be NaOH, KOH, identity unimportant) helps make H₂O₂ more reactive. The reaction is *anti*-Markovnikoff because the H-B bond is polarized toward H (electronegativity of H = 2.2, B = 2.0) - the H adds to the carbon best able to stabilize positive charge (i.e. the most substituted one).

This reaction goes through 3-membered "mercurinium" ion. The NaBH₄ step removes the mercury. While the addition is anti, the overall reaction is stereorandom because this step involves a carbon based free radical (usually not discussed). Alternatively, an alcohol used in place of water will produce an ether.

Strong acid protonates the alkene, generating free carbocation. Watch out for possibility of rearrangements when a tertiary carbocation could be generated through a 1,2 shift. HSO₄⁻ anion is not strongly nucleophilic, hence it does not add. Gives a mixture of syn and anti products due to the free carbocation.

HCl and HBr (as well as HI, not pictured) protonate the alkene to give a free carbocation which can then be trapped by the halide anion. Gives a mixture of syn and anti



Br⁻ or H₂O/ROH depending on solvent

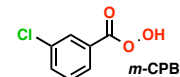
The key detail in these reactions is solvent: water and alcohol solvents will form the halohydrin products (the ones containing the OH and Br). All other solvents (you might see CCl₄, CHCl₃, hexane, etc.) provide the dibromide.

As with bromination, above. Although not depicted, use of water or alcohol as solvent will also lead to formation of the halohydrin product (also anti).

Osmium is a transition metal. The tools won't be given in this course to fully understand how this reaction works. Occasionally a second reagent like NaHSO₃, H₂S, or Na₂S₂O₃ is also given as a reactant in this reaction - minor detail, it's used to remove the osmium from the hydroxyl groups.

Keywords are "cold, dilute". **NOTE:** If "heat" or "acid" is mentioned in the conditions, the diol will be cleaved to provide carbonyl compounds (same reaction as ozonolysis with **oxidative workup**, below).

RCO₃H is a peroxyacid. A common peroxy acid for this reaction is *m*-CPBA (*m*-chloroperoxybenzoic acid). If H₃O⁺, heat is written afterwards, this is opening of the epoxide to give the diol (anti-selective)



The catalyst can vary - you might see Pt or Ni as well. All provide the same product with the same stereochemistry.

Peroxides generate the Br[·] radical, which adds to the double bond in the way that will generate the most stable radical (i.e. the radical will go on to the most substituted carbon). This explains the selectivity for the anti-Markovnikoff product. It gives a mixture of syn and anti because it goes through a free radical process.

Reductive workup: Zinc (Zn), or dimethyl sulfide (DMS, Me₂S) is a reducing agent. It reduces excess ozone, allowing for isolation of the aldehyde.

Oxidative workup: Hydrogen peroxide is used to obtain the carboxylic acid instead of the aldehyde.
Can also use KMnO₄ and acid

This reaction goes through addition of a *carbene* (actually, "carbenoid") to the double bond. The reaction is stereospecific. Another set of conditions to provide a cyclopropane is **CHCl₃ with strong base (NaOH)**, which makes the dichlorocyclopropane.

Omissions, Mistakes, Suggestions?

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Summary of Alkene Reaction Patterns

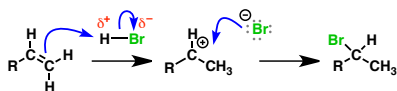
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Note - this sheet is not meant to be comprehensive. Your course may provide additional material, or may not cover some of the reactions shown here. Your course instructor is the final authority.

Pattern 1: The Carbocation Pathway

These reactions proceed through attack of an alkene upon an acid, which results in formation of a carbocation. The carbocation is then attacked by a nucleophile, which can occur from either face of the carbocation.

Example: addition of H-Br to alkenes



Regiochemistry: Markovnikov-Selective. In other words, **hydrogen** ends up bonded to the **less** substituted carbon of the alkene, and (in this case) Br ends up attached to the **most** substituted end of the alkene.

Stereochemistry: Mixture of syn + anti. In other words the H and the other group (e.g. Br) do not add exclusively "syn" or "anti", but provide a mixture of the two

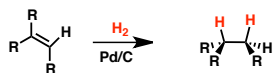
Reactions in this category: Addition of H-Cl
 Addition of H-Br
 Addition of H-I
 Addition of H₃O⁺
 (sometimes written as H₂O / H₂SO₄)

Note: since this reaction goes through a carbocation, **rearrangements are possible.**

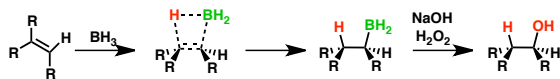
Pattern 3: The "Concerted" Pathway

Although these reactions do not share a common mechanism, they each form two new bonds on the same side of the alkene, a consequence of a "concerted" reaction mechanism.

Example 1 - hydrogenation



Example 2 - hydroboration



Regiochemistry: anti-Markovnikov-Selective (for BH₃). Note how hydrogen adds to the **most** substituted end of the alkene, and OH ends up on the **least** substituted end.

Stereochemistry: Syn. The two bonds are formed on the same side of the alkene

Reactions in this category: Hydroboration: BH₃, then H₂O₂/NaOH
 Hydrogenation: Pd/C, H₂
 Epoxidation: RCO₃H (e.g. mCPBA)
 Dihydroxylation: OsO₄
 Cyclopropanation: CH₂I₂, Zn-Cu
 Dichlorocyclopropanation CHCl₃, NaOH

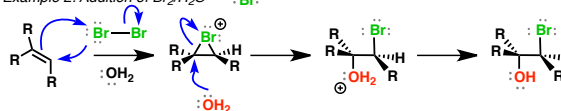
Pattern 2: The 3-Membered Ring Pathway

These reactions proceed through formation of a 3-membered ring cation, which is then attacked from the backside by a nucleophile, on the most substituted carbon.

Example 1: addition of Br₂ to alkenes



Example 2: Addition of Br₂/H₂O



Regiochemistry: Markovnikov-Selective (where appropriate). For example, with Br₂/H₂O, water adds to the **most** substituted carbon of the alkene.

Stereochemistry: Anti. The two groups add to opposite faces of the alkene.

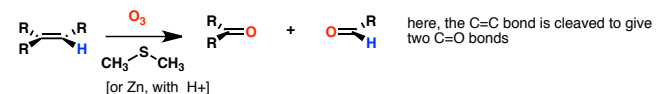
Reactions in this category: Addition of halogens: Cl-Cl, Br-Br, I-I
 Addition of halogens in the presence of nucleophilic solvents: Br₂/H₂O, Br₂/R-OH
 Oxymercuration: Hg(OAc)₂, H₂O, then NaBH₄
 Oxymercuration (with an alcohol as solvent) Hg(OAc)₂, ROH, then NaBH₄
 Opening of epoxides under acidic conditions

Pattern 4: Two miscellaneous reactions

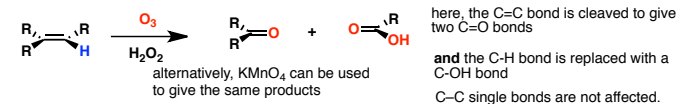
Two reaction patterns of note

Oxidative cleavage: Addition of an oxidant (such as ozone, O₃) leads to cleavage of the carbon-carbon double bond and formation of two new carbon-oxygen double bonds.

Ozonolysis (Reductive workup)

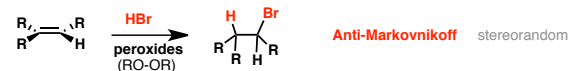


Ozonolysis (Oxidative Workup)



Radical addition of HBr

Here, addition of HBr to alkenes in the presence of a radical initiator (peroxides) leads to **anti-Markovnikov** addition of H-Br to the alkene; the Br adds to the least substituted carbon of the alkene, and the H adds to the most substituted.



Regiochemistry: anti-Markovnikov-Selective. Note that the Br adds to the less substituted end of the alkene.

Stereochemistry: Mixture of syn + anti.

H and Br do not add exclusively "syn" or "anti" across the alkene.

Omissions, Mistakes, Suggestions?

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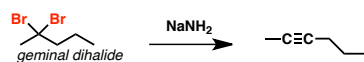
Introduction to Reactions of Alkynes

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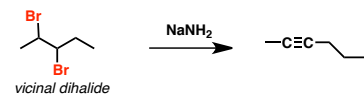
Note - this sheet is not meant to be comprehensive. Your course may provide additional material, or may not cover some of the reactions shown here. Your course instructor is the final authority.

Synthesis of Alkynes

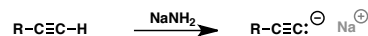
Elimination of Hydrogen halides



NaNH₂ is a strong base and will lead to elimination of HBr. According to Zaitsev's rule, the most substituted alkyne should form.

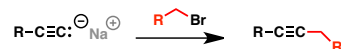


Deprotonation



Alkynes are relatively acidic [pK_a = 25]. A strong base like NaNH₂ will remove the C-H to provide the acetylide anion. The resulting anion is an excellent nucleophile. Can also use strong bases like *n*-BuLi, or Grignard reagents (RMgBr, etc.)

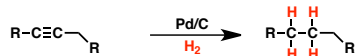
Reaction with Electrophiles



Deprotonated alkynes are excellent, useful nucleophiles and will react with alkyl halides in S_N2 reactions

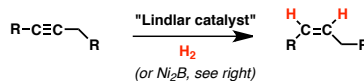
Addition Reactions to Alkynes

Hydrogenation



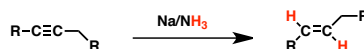
Can also use Pt, Ni, etc. as hydrogenation catalysts. These will also reduce alkynes to alkanes.

Partial Hydrogenation



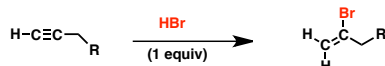
Lindlar catalyst is a "poisoned" palladium catalyst for the partial hydrogenation of alkynes. It contains palladium (Pd), lead (Pb), and quinoline, and is selective for the *cis*-alkene. Sometimes also see "Pd, CaCO₃".

Reduction (Dissolving metal reduction)



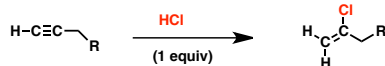
Sodium (Na) is a very strong reducing agent, and will reduce alkynes (but not alkenes). Selective for the *trans*-alkene. The NH₃ provides the hydrogens in the final product.

Addition of Hydrogen bromide to form gem-dibromides



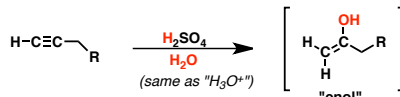
Markovnikov

Addition of Hydrogen chloride to form gem-dichlorides



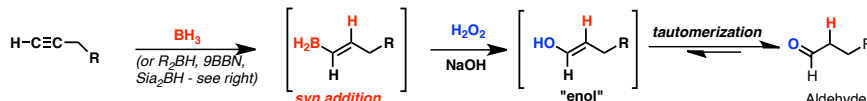
Markovnikov

Acid-catalyzed Hydration to provide ketones



Markovnikov

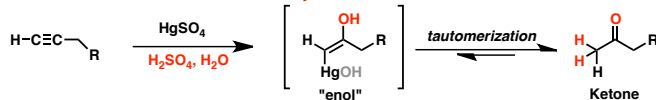
Hydroboration to form aldehydes



syn addition

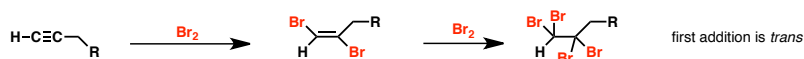
Anti-Markovnikov

Oxymercuration to provide ketones



Markovnikov

Bromination



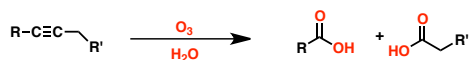
first addition is *trans*

Chlorination



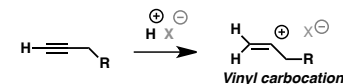
first addition is *trans*

Ozonolysis



If R = H, then one product will be CO₂ [O=C=O]

The key intermediate in all three of these reactions is an intermediate *vinyl carbocation* which is formed upon protonation of the alkyne by strong acid. The carbocation forms on the more substituted side of the carbon, according to Markovnikov's rule.

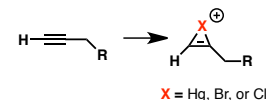


This carbocation will then be attacked by the nucleophile in question, leading to the formation of substituted products.

tautomerization (keto-enol tautomerization in this case) is the interconversion of enols and aldehydes/ketones through the movement of a proton and the shifting of bonding electrons. It is an equilibrium which generally favors the *keto* form.

Note: Hydroboration on internal alkynes will give mixture of ketones.

The first intermediate in each of these three reactions is a cyclic ion, which undergoes attack by a nucleophile at the more substituted carbon (Markovnikov)



Omissions, Mistakes, Suggestions?

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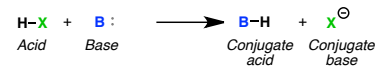
Common Reaction Patterns (Org 1)

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Note - this sheet is not meant to be comprehensive. Your course may provide additional material, or may not cover some of the reactions shown here. Your course instructor is the final authority.

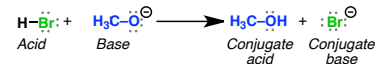
Pattern #1 - Acid Base Reactions

Generic example:



Bonds Formed	Bonds Broken
B-H	H-X

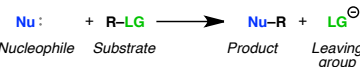
Specific example:



Notes: Favorable acid base reactions will involve a stronger acid and a stronger base reacting to give a weaker acid and weaker base. Relative strengths of acids and bases can be obtained through consulting a pKa table

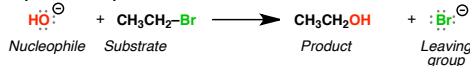
Pattern #2 - Nucleophilic Substitution Reactions

Generic example:



Bonds Formed	Bonds Broken
C-Nu	C-LG

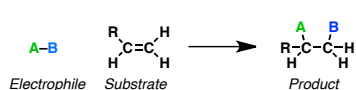
Specific example:



Notes: Substitution reactions can proceed through two pathways. The S_N2 pathway is concerted, and C-Nu bond formation occurs at the same time as C-LG bond breakage. Steric hindrance is paramount. In the S_N1 pathway, the leaving group leaves first to give a carbocation, which is then attacked by a nucleophile. In the S_N1 pathway rearrangements can occur depending on carbocation stability. Good nucleophiles tend to have a loosely held lone pair of electrons. Good leaving groups are weak bases.

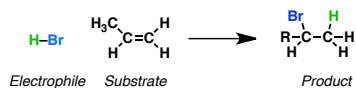
Pattern #3 - Electrophilic Addition

Generic example:



Bonds Formed	Bonds Broken
C-A	C-C (π)
C-B	A-B

Specific example:



Notes: Note that every addition reaction involves breakage of a C-C π bond and formation of two new single bonds to C. For stepwise addition reactions, the tendency will be to place positive charge on the carbon best able to accept it (i.e. the carbon attached to the most carbon atoms). This gives rise to "Markovnikov's rule", where H always adds to the least substituted carbon. [Notable exception is hydroboration-oxidation, which is "anti-Markovnikov."] Stereochemistry of the two new bonds can be syn, anti, or a mixture of both, depending on mechanistic pathway.

Pattern #7 - Oxidative Cleavage

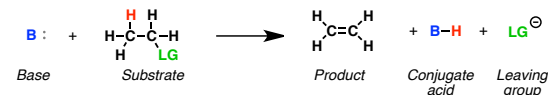
Specific example:



Bonds Formed	Bonds Broken
C-O (2)	C-C (2)
C-O (π) (2)	C-C (π) (2)

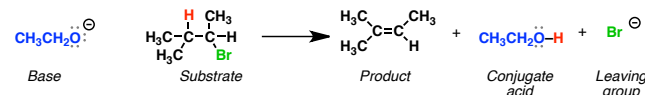
Pattern #4 - Elimination Reactions

Generic example:



Bonds Formed	Bonds Broken
C-C (π)	C-H
B-H	C-LG

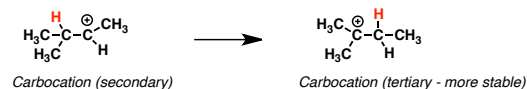
Specific example:



Notes: Note that every elimination reaction involves the formation of a new C-C π bond. Since alkene stability increases as the number of attached carbons increases, eliminations tend to favor formation of the more substituted alkene ("Zaitsev's rule"). An important exception is when more hindered bases (such as *t*-BuO⁻) are used, which gives the less substituted alkene. Two dominant mechanisms for elimination are the concerted pathway (E2) which occurs in one step, requiring *anti*-periplanar arrangement of H and leaving group. The second pathway is the stepwise E1 pathway, which occurs with loss of leaving group followed by deprotonation. A third (rare) pathway involves deprotonation, followed by loss of leaving group, called the E1-conjugate base (E1cb) pathway. All elimination reactions tend to be favored by heat.

Pattern #5 - Carbocation Rearrangements

Hydride shift example:



Bonds Formed	Bonds Broken
C-H	C-H

Alkyl shift example:

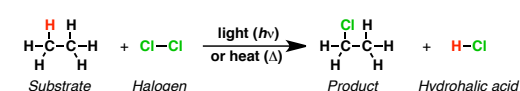


Bonds Formed	Bonds Broken
C-C	C-C

Notes: Rearrangements are favorable when the migration of hydride or alkyl leads to a more stable carbocation. Recall that carbocation stability proceeds in the order tertiary > secondary >> primary. Resonance can also stabilize carbocations. Hydrogen tends to migrate preferentially over carbon. Relief of ring strain can also be a major contributing factor with rearrangement reactions.

Pattern #6 - Free Radical Substitution

Generic example:



Bonds Formed	Bonds Broken
C-Cl	C-H
H-Cl	Cl-Cl

Notes: Free radical reactions proceed in three steps: initiation, propagation, and termination. Light (hν) or heat (Δ) is used to initiate the reaction. Chlorine is quite unselective relative to bromine, which will only react with tertiary and allylic/benzylic C-H bonds (which are weakest). Iodine does not perform this reaction.

If multiple equivalents of chlorine are present, chlorination can occur multiple times until all C-H bonds are replaced with C-Cl.

Notes: Oxidation of C-C multiple bonds (π bonds) can be achieved with ozone (O₃) or potassium permanganate (KMnO₄). With ozone, reductive workup (using Zn or dimethyl sulfide) leaves all C-H bonds intact. With KMnO₄ or O₃ using oxidative workup, sp² hybridized C-H bonds are oxidized to C-OH.

A different type of oxidative cleavage can occur with vicinal diols using NaIO₄, HIO₄, or Pb(OAc)₄. These oxidants will cleave C-C single bonds and form C=O (π) bonds

Omissions, Mistakes, Suggestions?

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Introduction to Chemical Reactivity, Nomenclature, Boiling Points, and Water Solubility

<http://masterorganicchemistry.com>

Reactant #1	Reactant #2	Product	Example	Notes
Alkene	Pd/C + H ₂	Alkane		cis addition (hydrogens go on same side of alkene)
Amine	Acid	Ammonium salt		amines but NOT amides (amides are not basic on nitrogen)
Carboxylic acid	Base	Salt (Carboxylate salt)		
Carboxylic acid	Alcohol, acid, heat	Ester		Alcohols used as solvent
Ester	Water, acid, heat	Carboxylic acid		This is the reverse of the above reaction. Here we use water as solvent.
Ester	Water, base	Carboxylic acid		This is called ester hydrolysis or saponification

The Four Types of Intermolecular Bonding in Organic Chemistry

Name	Type of Interaction	Found in	Example	Strength	Notes
Ionic	Attraction between point charges	Salts		Strongest	gives rise to greatest water solubility (most polar) also highest boiling points
Hydrogen Bonding	Attraction between positively charged H and negatively charged O, N or F.	Water, alcohols, carboxylic acids, amides, amines		2nd strongest	2nd greatest for effect on water solubility and boiling points
Dipole-Dipole	Attraction between dipole moments caused by differences in electronegativity	ketones, aldehydes, esters, alkyl halides, etc. - any molecule with a strongly electronegative element (O, N, F, Cl, Br)		2nd weakest	Increases as electronegativity difference increases 3rd greatest for effect on water solubility and boiling points
Van Der Waals (London forces)	Attraction between temporary dipoles	Hydrocarbons	Name	Weakest	Increases with surface area (increasing length of carbon chains) worst for water solubility (least polar) best for solubility in non-polar solvents (e.g. pentane)

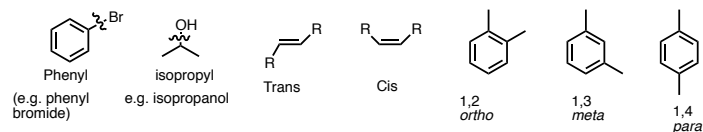
Alkene	Water, acid	Alcohol		alcohol forms on most substituted carbon (Markovnikov rule) proceeds through carbocation
Alkene	Strong acid	Alkyl halide		halide adds to most substituted carbon (Markovnikov rule) proceeds through carbocation
Alkene	Br ₂	Dibromide		Results in trans product
Alcohol	K ₂ CrO ₇	Carboxylic acid (primary alcohol) OR ketone (secondary alcohol)		
				Note that secondary alcohols stop at the ketone stage
Alcohol	KMnO ₄	Carboxylic acid (primary alcohol)		
Alkane	Cl ₂ , hv (or peroxides)	Alkyl chloride		Free-radical reaction (number of new C-Cl bonds depends on # of equivalents)
Benzene derivative	Br ₂ , FeCl ₃	Aryl bromide		Also gives 1,4 (para) product but never 1,3 (meta) product
Thiol	"Oxidant"	Disulfide		

# Carbons	Root
1	Meth-
2	Eth-
3	Prop-
4	But-
5	Pent-
6	Hex-
7	Hept-
8	Oct-
9	Non-
10-	Dec-

Primary carbon: attached to ONE carbon atom
Secondary: attached to TWO carbon atoms
Tertiary: attached to THREE carbon atoms
Quaternary: attached to FOUR carbon atoms

Functional Group	Name	Example	Name
R-	Alkyl		Pentane
-OH	Hydroxyl		Pentanol or pentyl alcohol
-Cl, -Br, -F, -I	Halide		Pentyl chloride
-NH ₂	Amine		Pentylamine
R-O-R	Ether		Pentyl methyl ether
-SH	Thiol		Pentane thiol
C=C	Alkene		Pentene
R-C(=O)-H	Aldehyde		Pentanal
R-C(=O)-R	Ketone		Butyl methyl ketone OR 2-pentanone
R-C(=O)-OH	Carboxylic acid		Pentanoic acid
R-C(=O)-OR	Ester		Methyl pentanoate
R-C(=O)-NH ₂	Amide		N-methyl pentamide

Other important nomenclature terms to remember



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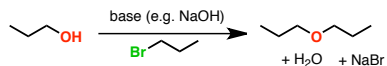
Introduction to Alcohols and Ethers

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Note - this sheet is not meant to be comprehensive. Your course may provide additional material, or may not cover some of the reactions shown here. Your course instructor is the final authority.

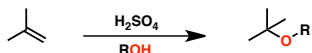
Ethers from alcohols and alkyl halides

The Williamson Ether synthesis: alcohol, base, alkyl halide (or tosylate)



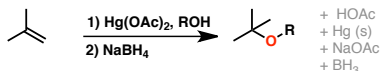
This is an S_N2 reaction; it works best for primary alkyl halides (and alkyl tosylates)

Ethers from alkenes



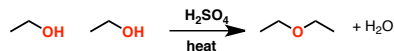
The reaction is similar to the hydration of alkenes with aqueous acid. Acid leads to the formation of a carbocation, which is then trapped by the alcohol as solvent. Carbocation rearrangements (hydride and alkyl shifts) can occur in certain cases.

Ethers from alkenes through oxymercuration



The reaction is similar to the hydration of alkenes with aqueous acid. The **key difference** is that it does **not** proceed through a carbocation, so **no rearrangements** can occur.

Ethers from alcohols through dehydration



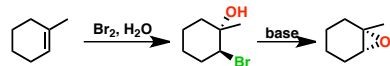
Strong acid (and heat) leads to protonation of the alcohol, followed by nucleophilic attack of a second molecule of alcohol to give the ether. Only practical for the synthesis of *symmetrical* ethers.

Epoxides from alkenes



m-CPBA (meta-chloroperoxybenzoic acid, a peroxyacid) converts alkenes to epoxides, a cyclic ether. Other peroxyacids can be used (e.g. $\text{CH}_3\text{CO}_3\text{H}$)

Epoxides from halohydrins



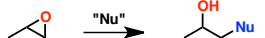
Formation of the halohydrin from the alkene is stereospecific for the **trans** product. Deprotonation of the alcohol by base results in S_N2 (with inversion at carbon bearing the leaving group) to give the epoxide.

Opening of epoxides

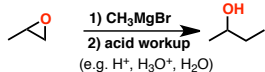
Due to ring strain, epoxides are highly reactive towards nucleophiles. They will react with nucleophiles under both acidic and basic conditions. However the *patterns* are different.

Under basic conditions

Under basic conditions, nucleophiles will attack epoxides at the **least sterically hindered position** (primary [fastest] > secondary > tertiary [slowest])
 The reaction is essentially an S_N2 reaction!



Example: reaction of epoxides with Grignard reagents

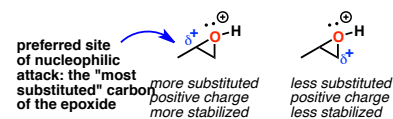


Under acidic conditions

Under acidic conditions, the epoxide oxygen is protonated:

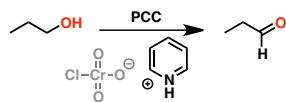


The nucleophile will attack the carbon best able to stabilize positive charge - which is the more substituted carbon. Just like Markovnikov's rule!

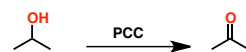


Oxidation of alcohols

Oxidation of primary alcohols to aldehydes

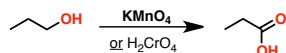


Oxidation of secondary alcohols to ketones



Can also use KMnO_4 or H_2CrO_4 (or DMP or Swern, see right)

Oxidation of primary alcohols to carboxylic acids



Common source of confusion:
 Another way of writing H_2CrO_4 is $\text{K}_2\text{Cr}_2\text{O}_7 / \text{H}_2\text{SO}_4$ or $\text{Na}_2\text{Cr}_2\text{O}_7 / \text{H}_2\text{SO}_4$

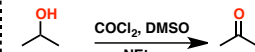
Alternative reagents for oxidation of primary alcohols to aldehydes and secondary alcohols to ketones (not seen in all courses):

Dess-Martin Periodinane (DMP)

Dess-Martin Periodinane (DMP)
 •oxidizes primary alcohols to aldehydes
 •oxidizes secondary alcohols to ketones

Swern oxidation

•oxidizes primary alcohols to aldehydes
 •oxidizes secondary alcohols to ketones



(often just written, "Swern")

(COCl_2)₂ is oxalyl chloride
 DMSO is dimethyl sulfoxide
 and NEt_3 is triethylamine (base)

Conversion of alcohols to good leaving groups

The hydroxide group (HO^-) of alcohols is a strong base and a poor leaving group. Converting to a halogen or "sulfonate" (e.g. tosylate or mesylate) greatly facilitates substitution reactions.

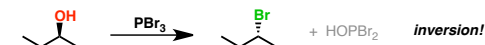
Alcohols to alkyl chlorides



Alcohols to alkyl bromides



One thing to note - these reactions occur with inversion of configuration. For example:



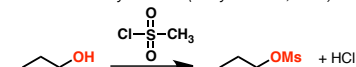
Alcohols to alkyl halides by using acids



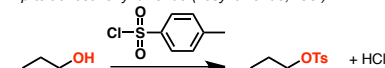
These reactions can proceed through an S_N1 or S_N2 pathway depending on the structure of the alcohol

Alcohols to tosylates and mesylates ("sulfonate esters")

Methanesulfonyl chloride (mesyl chloride, MsCl)



p-toluenesulfonyl chloride (Tosyl chloride, TsCl)

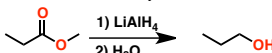


One thing to note - these reactions do not change the stereochemistry of the alcohol.

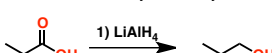


Alcohols through reduction

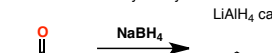
Reduction of esters by lithium aluminum hydride (LiAlH_4)



Reduction of carboxylic acids by lithium aluminum hydride (LiAlH_4)

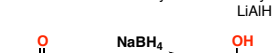


Reduction of aldehydes by sodium borohydride (NaBH_4)



LiAlH_4 can also do this reaction.

Reduction of ketones by sodium borohydride (NaBH_4)



LiAlH_4 can also do this reaction.

Omissions, Mistakes, Suggestions?

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