

# Organic Chemistry I

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# 1 The Basics Bonding and Molecular Structure

## 1.1 We Are Stardust

- Organic chemistry is simply the study of carbon-based compounds, hydrocarbons, and their derivatives

## 1.2 Atomic Structure

- In atoms, the electrons are what create most of the volume
  - Most of the atom is actually empty space
- The letter  $Z$  is used to denote the atomic number of an element

## 1.3 The Structural Theory of Organic Chemistry

- **Constitutional Isomers:** Different compounds that have the same molecular formula but differ in the sequence in which their atoms are bonded, that is, their connectivity but not number of bonds (older term: structural isomers)<sup>1</sup>

## 1.4 Chemical Bonds: The Octet Rule; How to Write Lewis Structures; Exceptions to the Octet Rule

- **Electronegativity:** The ability of an atom to attract electrons
- Elements of the third period and beyond have  $d$  orbitals that can be used for bonding and thus can exceed the octet rule (eg: S or P)
- Elements such as boron and beryllium can have fewer than eight electrons (eg:  $\text{BF}_3$ )
- Oxygens are very rarely bonded to other oxygens in stable molecules because these peroxy groups are very unstable and reactive

## 1.5 Formal Charges

- $F = Z - (1/2)S - U$ , where  $F$  is the formal charge,  $Z$  is the group number,  $S$  is the number of shared electrons, and  $U$  is the number of unshared electrons
  - An alternate formula is  $F = Z - (B + U)$ , where  $B$  is one electron for each covalent bond
- An easier way to think about formal charges is to just take the group number and subtract the number of free electrons as well as the number of bonds connected to that atom

## 1.6 Resonance Theory

- In resonance structures, one structure can be converted to another on paper via the movement of electrons (and therefore changing bonds) with the atoms still in the same arrangement in 3-space and *obeying conservation of charge*<sup>2</sup>
- To show the movement of electrons, a curved arrow,  $\curvearrowright$ , is drawn with the tail of the arrow beginning at the current position of the electron pair and the head of the arrow pointed to where the electron pair will be in the next structure

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<sup>1</sup>Constitutional isomers can't be the same if rotated (eg: not tetrahedral geometries)

<sup>2</sup>Do not move atoms when drawing resonance structure. It is a common mistake to move hydrogen atoms.

- Resonance structures are not real representations of the actual molecule (not an equilibrium state)
  - The actual molecule is a hybrid of all resonance contributors
- A double-headed arrow,  $\leftrightarrow$ , is used to equate resonance structures
- To depict what a hybrid structure may be both solid lines and dashed lines are used for bonds where the dashed lines indicate the superimposed bonds of the **resonance contributors**. Partial charges,  $\delta$ , are also used
- The energy of the resonance hybrid is lower than the energy of any contributing structure
- Resonance structures stabilize a molecule or ion, especially when the resonance structures are equivalent and is known as **resonance stabilization**
- The more stable an individual resonance contributor is on its own, the greater its contribution to the overall hybrid structure

### 1.6.1 Determination of Stability for Resonance Structures

The following is in order of decreasing significance:

1. The more covalent bonds a structure has, the more stable it is
2. Charge separation (formal charges) decreases stability
3. Negative charges on the more electronegative elements and positive charge on the more electropositive elements are more favorable<sup>3</sup>

## 1.7 Quantum Mechanics and Atomic Structure

- Each **wave function**,  $\psi$ , corresponds to a different energy state for an electron
- Each energy state is a sublevel where one or two electrons can reside
- The relative probability of finding an electron in a given region of space can be found with  $\psi^2$  and is known as the **electron probability density**
- **Constructive interference** occurs when wave functions with the same phase sign interact and reinforce the amplitude of the resultant wave (bonding MO)
- **Destructive interference** occurs when wave functions with opposite phase signs interact and subtract the amplitude of the resultant wave (antibonding MO)

## 1.8 Atomic Orbitals and Electron Configuration

### 1.8.1 Orbitals

- An **orbital** is a region of space where the probability of finding an electron is high
- **Atomic orbitals** are plots of  $\psi^2$  in three dimensions
- All **s orbitals** are spheres with higher levels having an inner nodal surface where  $\psi^2 = 0$  (eg:  $2s$  is a large sphere with a smaller sphere inside separated by a node)
- All **p orbitals** are shaped like dumbbells with a nodal plane separating the two lobes of a p-orbital, and the three  $p$  orbitals of a given energy level are arranged along the  $x$ ,  $y$ , and  $z$  axes

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<sup>3</sup>For the purposes of drawing all resonance structures, it is not considered a violation of the octet rule if a second-row element, like carbon, has fewer than an octet. It is simply less likely but still imperative to draw.

### 1.8.2 Configurations

- Electrons of lower quantum numbers have lower energy since they are closest to the nucleus
- For orbitals of the same quantum number, the higher  $l$  quantum number (shape of the atomic orbital) has more energy (eg: a  $2p$  orbital has more energy than a  $2s$  orbital)
- Orbitals of equal energy (such as the three  $2p$  orbitals) are called **degenerate orbitals**

### 1.8.3 Rules of Configuration

- The **Aufbau Principle** states that orbitals are filled so that those of lowest energy are filled first
- The **Pauli Exclusion Principles** states that a maximum of two electrons may be placed in each orbital but only when the spins of the electrons are paired ( $\uparrow$  and  $\downarrow$  can be paired but never  $\uparrow\uparrow$  or  $\downarrow\downarrow$ )
- **Hund's Rule** states that, when degenerate orbitals are considered, we add one electron to each with their spins unpaired until each degenerate orbital contains one electron. Afterward, the second set of electrons are added to pair the spins

## 1.9 Molecular Orbitals

- The ideal internuclear distance between two atoms is known as the **bond length**
- The **Heisenberg Uncertainty Principle** states that we cannot simultaneously know the position and momentum of an electron
- A **Molecular Orbital (MO)** represents the region of space where one or two electrons of a molecule are likely to be found (remember that **atomic orbitals** represent an analogous probability but for isolated atoms)
- When atomic orbitals combine to form molecular orbitals, the number of molecular orbitals that result always equal the number of atomic orbitals that combine
- A **bonding molecular orbital** ( $\psi_{molecular}$ ) results when two orbitals of the same phase overlap
- An **antibonding molecular orbital** ( $\psi_{molecular}^*$ ) results when two orbitals of opposite phase overlap
- In the **Linear Combination of Atomic Orbitals (LCAO) Method**, wave functions for atomic orbitals are combined in a linear fashion in order to obtain new wave function for MOs
- The energy of a bonding molecular orbital is less than the energy for the corresponding atomic orbital while the energy of an antibonding molecular orbital is higher than the energy for the corresponding atomic orbital

### 1.10 The Structure of Methane and Ethane: $sp^3$ Hybridization

- **Orbital Hybridization** combines individual wave functions for  $s$  and  $p$  orbitals to form new orbitals known as **hybrid atomic orbitals**
- The type of hybridization directly correlates to the molecular geometry for the structure:  $sp$  is linear,  $sp^2$  is trigonal planar,  $sp^3$  is tetrahedral, etc.
- A bond formed from the overlap of an  $sp^3$  orbital and a  $1s$  orbital is an example of **sigma ( $\sigma$ ) bond**
- A sigma bond has a circularly symmetrical orbital cross section, and all single bonds are sigma bonds
- Rotation of groups joined by a single bond do not require a lot of energy input

- More  $s$  (less  $p$ ) character means bonds are shorter
  - Bonds involving  $sp$  hybrids are shorter than  $sp^2$  hybrids, which are shorter than  $sp^3$  hybrids, etc.
- The contributing structure with the largest bond angle will determine the overall geometry as well as level of hybridization for molecules with a lone pair that participates in resonance since the geometry of an atom must be representative of all possible resonance forms<sup>4</sup>
- Each  $\pi$  bond is a degree of saturation, and a ring is an example of a degree of unsaturation that can be used to eliminate hydrogen atoms from a molecular formula

### 1.11 The Structure of Ethene: $sp^2$ Hybridization

- The common name for ethene is ethylene and propylene for propene
- Hydrocarbons whose molecules contain a carbon-carbon double bond are known as **alkenes**
- Sideways overlap of  $p$  orbitals and sharing of the two electrons between atoms leads to a **pi ( $\pi$ ) bond**
  - $\pi$ -bonds, and thus  $p$  orbitals, overlap above and below the plane of the  $\sigma$ -bond framework
- When two  $p$  atomic orbitals combine to form a  $\pi$ -bond, two molecular orbitals form: one is a bonding MO, and one is an antibonding MO
- Bonding  $\pi$  MOs form when  $p$  orbitals of like signs overlap and vice versa for antibonding  $\pi$  MOs
- The energy diagram for a standard MO set of bonds is, in order of increasing energy,  $\sigma$ ,  $\pi$ ,  $\pi^*$ ,  $\sigma^*$
- There is a large energy barrier to rotation associated with a group that has a  $\pi$ -bond because rotating one carbon of a double bond breaks the  $\pi$  bond
- Since *-cis* and *-trans* isomers have identical connectivity (just on different sides), they are not constitutional isomers but are rather **stereoisomers** or **conformational isomers**<sup>5</sup>

### 1.12 The Structure of Ethyne (Acetylene): $sp$ Hybridization

- The common name of ethyne is acetylene
- Hydrocarbons composed of triple bonds are known as **alkynes**

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<sup>4</sup>Important: Most carboxylic amides have the functional group's nitrogen as  $sp^2$  regardless of geometry!

<sup>5</sup>Not to be confused with conformers

### 1.13 Techniques for Drawing Resonance Structures Systematically

First Step: Always draw out the electron pairs!

Factor 1: A lone pair next to a  $\pi$  bond<sup>6</sup>

- Move the two electrons that compose the lone pair and turn them into a bond to make a new  $\pi$  bond
- Turn the  $\pi$  bond that was originally next to the lone pair into a  $\sigma$  bond and add an electron pair to the atom attached to the new  $\sigma$  bond atom as compensation for the loss of 2 electrons. Check to see if this option can be performed again

Factor 2: A lone pair next to a positive charge

- Simply “slide” the lone electron pair to the nearby bond of the positively charged atom to make all formal charges zero and a new  $\pi$  bond

Factor 3: A  $\pi$  bond next to a positive charge

- Simply shift the  $\pi$  bond to the  $\sigma$  bond of the positively charged atom. If there is conjugation of double bonds, shift them all for another structure. This will make the positive formal charge move to the opposite end of the molecule

Factor 4: A  $\pi$  bond between two atoms where one is electronegative

- Turn the  $\pi$  bond into a  $\sigma$  bond, and give the pair of electrons lost from this to the electronegative atom

Factor 5:  $\pi$  bonds going all the way around a ring

- Simply change the  $\pi$  bonds to  $\sigma$  bonds and vice versa

Important Note: Resonance structure where two carbon atoms bear opposite charges are typically considered insignificant contributing structures

### 1.14 How to Interpret and Write Structural Formulas; Applications of Basic Principles

- The **dot structure** includes all the valence electrons
- Atoms joined by single bonds can rotate relatively freely with respect to one another
- **Dash structural formulas** are used to indicate the way in which atoms are attached, also known as the **connectivity**, to distinguish constitutional isomers
- **Condensed structural formulas** have the hydrogen atoms written immediately after the carbon
  - In fully condensed formulas all of the atoms that are attached to the carbon are written immediately after the carbon, listing hydrogens first
- A **bond-line formula** has no carbons or hydrogens written (on occasion, hydrogens may be added to indicate the geometry if ambiguous)
  - Lines represent bonds, and carbon atoms are inferred at each bend or end
  - The number of hydrogen atoms is inferred based on the octet rule



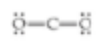

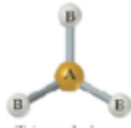
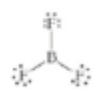
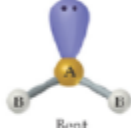
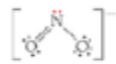
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<sup>6</sup>“Next to” means that the lone pair is separated from the double bond by exactly one single bond




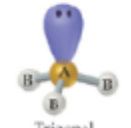

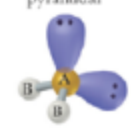

## 1.15 Molecular Geometry: The Valence Shell Electron Repulsion (VSEPR) Model

Graphic from *Chemistry: The Central Science*, 12th ed., Pearson, Prentice Hall

**TABLE 9.2** Electron-Domain Geometries and Molecular Shapes for Molecules with Two, Three, and Four Electron Domains Around the Central Atom

| Number of Electron Domains | Electron-Domain Geometry   | Bonding Domains | Nonbonding Domains | Molecular Geometry   | Example  |        |
|----------------------------|--|-----------------|--------------------|--|--|--------|
| 2                          | <br>Linear          | 2               | 0                  | <br>Linear          |  | 180°   |
| 3                          | <br>Trigonal planar | 3               | 0                  | <br>Trigonal planar |  | 120°   |
|                            |  | 2               | 1                  | <br>Bent            |  | < 120° |

**TABLE 9.2** Electron-Domain Geometries and Molecular Shapes for Molecules with Two, Three, and Four Electron Domains Around the Central Atom

| Number of Electron Domains | Electron-Domain Geometry   | Bonding Domains | Nonbonding Domains | Molecular Geometry  | Example  |                   |
|----------------------------|--|-----------------|--------------------|---|--|-------------------|
| 4                          | <br>Tetrahedral | 4               | 0                  | <br>Tetrahedral        |  | 109.5°            |
|                            |  | 3               | 1                  | <br>Trigonal pyramidal |  | 107°              |
|                            |  | 2               | 2                  | <br>Bent               |  | < 109.5° (104.5°) |

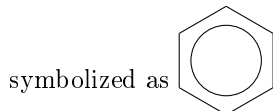
## 2 Families of Carbon Compounds

### 2.1 Hydrocarbons: Representative Alkanes, Alkenes, Alkynes, and Aromatic Compounds

- **Hydrocarbons** are compounds that contain only hydrogen and carbon
- **Alkanes** are hydrocarbons that are entirely composed of single bonds, C–C, between carbon atoms (members of this family have suffixes of -ane)
- **Alkenes** contain at least one C=C bond (members of this family have suffixes of -ene)
- **Alkynes** contain at least one C≡C bond (members of this family have suffixes of -yne)
- **Aromatic compounds** contain a special type of ring, the most common being a benzene ring
- Compounds with only single bonds are known as **saturated compounds** because they contain a maximum number of hydrogen
- Compounds with multiple bonds are known as **unsaturated compounds** because they contain fewer than the maximum possible number of hydrogen atoms

- A benzene ring using the so-called **Kekulé structure** is indicated as 

- The Kekulé structure is not accurate because of the resonance nature of benzene. A correct hybrid is



- As a result, all of the carbon-carbon bonds are 1.5 bonds, have a bond length in between that of a single and double bond, and have a bond angle of 120°
- The six electrons associated with the *p* orbitals that have overlapping lobes above and below the ring are said to be **delocalized** about the six carbon atoms in benzene

### 2.2 Polar Covalent Bonds

- A complete transfer of electrons, unlike the shared nature of a covalent bond, produces an **ionic bond**
- **Electronegativity** is simply the ability of an atom to attract electrons that it is sharing in a covalent bond
  - If an electronegativity difference exists between two bonded atoms, and they are not large enough to produce an ionic bond, the electrons are not shared equally and produce a **polar covalent bond**
- If there is a partial charge ( $\delta+$  or  $\delta-$ ) on an atom, the molecule ends up having a **dipole moment** and is said to be a **dipole**
  - The direction of polarity of a polar bond can be symbolized by  $\text{+} \rightarrow$  with the cross being the positive end and the arrow head being the partially negative end
    - \* A **debye** is the unit for dipole moment
- **Functional groups** are defined groups of atoms in a molecule that give rise to the function of the molecule, and, many times, polar covalent bonds composed these groups
- Atoms that form covalent bonds and have unshared electron pairs, such as oxygen, nitrogen, and sulfur, are known as **heteroatoms**

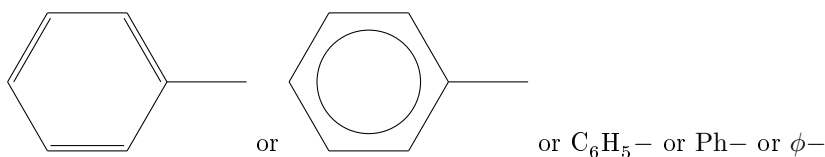


## 2.3 Polar and Nonpolar Molecules

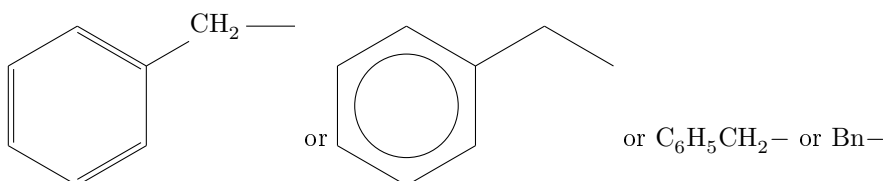
- A molecule with a dipole moment is known as a **polar molecule**
  - A molecule can have polar covalent bonds and still be nonpolar due to symmetry in its molecular geometry

## 2.4 Functional Groups

- **Alkyl groups** are the functional groups that we identify for purposes of naming compounds if a hydrogen atom is removed from the alkane (eg: For ethane,  $\text{CH}_3\text{CH}_3$ , the alkyl group is ethyl,  $\text{CH}_3\text{CH}_2-$ , with an abbreviation of Et-)
  - For propane,  $\text{CH}_3\text{CH}_2\text{CH}_3$ , there is a propyl group of  $\text{CH}_3\text{CH}_2\text{CH}_2-$  if a hydrogen is taken off of the end of the chain, but a hydrogen atom can be taken off from the middle to make an isopropyl group
- When a benzene ring is attached to some other group of atoms it is called a **phenyl group** and can be represented by some of the following ways:



- The combination of a phenyl group and a **methylene group** ( $-\text{CH}_2-$ ) is called a **benzyl group**, which can be written in the following ways:



## 2.5 Alkyl Halides or Haloalkanes

- Alkyl halides, or **haloalkanes**, are compounds in which a halogen atom replaces a hydrogen atom of an alkane (ie:  $\text{RX}$ )
- If the carbon that bears the halogen is attached to only one other carbon, the carbon atom is said to be a **primary carbon atom** with the alkyl halide being classified as a **primary alkyl halide** ( $1^\circ$ )
- If the carbon that bears the halogen is attached to two other carbon atoms, it is the **secondary carbon** of a **secondary alkyl halide** ( $2^\circ$ )
- If the carbon that bears the halogen is attached to three other carbon atoms, then it is the **tertiary carbon** of a **tertiary alkyl halide** ( $3^\circ$ )

## 2.6 Alcohols and Ethers

- An **alcohol** has the functional group known as a hydroxyl group,  $-\text{OH}$ , that attaches to an  $sp^3$ -hybridized carbon atom
- In an analogous method described previously with the alkyl halides, alcohols can be classified into a primary alcohol, secondary alcohol, or tertiary alcohol
- **Ethers** have the general formula of  $\text{R}-\text{O}-\text{R}'$  where the two groups are composed of different alkyl (or phenyl) groups

## 2.7 Amines

- **Amines** have the functional group of  $-\text{NH}_2$ ,  $-\text{NH}$ , or  $-\text{N}$  depending on the type of amine
- The classification of primary, secondary, or tertiary amine is different from alcohols and alkyl halides and, instead, refers to the number of organic groups that are attached to the nitrogen atom
  - If there is only one organic group, the amine is primary and has a general functional group of  $-\text{NH}_2$
  - If there are two organic groups attached to the nitrogen atom, the amine is secondary and has a general functional group of  $-\text{NH}$
  - If there are three organic groups attached to the nitrogen atom, the amine is tertiary and has a general functional group of simply  $-\text{N}$

## 2.8 Aldehydes and Ketones

- An **aldehyde** can be classified as  $\text{R}-\overset{\cdot\cdot}{\text{O}}=\text{C}-\text{H}$  while a **ketone** can be classified as  $\text{R}-\overset{\cdot\cdot}{\text{O}}=\text{C}-\text{R}'$
- Both aldehydes and ketones have the **carbonyl group**, which is the carbon atom double-bonded to the oxygen ( $\text{C}=\text{O}$ )
  - The carbonyl group of an aldehyde is bonded to one hydrogen atom and one carbon atom except for formaldehyde, which is the only aldehyde bearing two hydrogen atoms (R group is H)
  - The carbonyl group of a ketone is bonded to two carbon atoms

## 2.9 Carboxylic Acids, Esters, Amides, and Nitriles

- **Carboxylic acids** have a carboxyl group, which is represented as  $-\text{COOH}$ , since it comes from the carbonyl group and a hydroxyl group
  - Carboxylic acids thus are classified as  $\text{RCOOH}$
- **Esters** have the general formula of  $\text{RCOOR}'$  with a carbonyl group bonded to an alkoxy group ( $-\text{OR}$ )
- Esters can be produced from the reaction of a carboxylic acid and an alcohol through the acid-catalyzed loss of a molecule of water with the OH taken from the carboxylic acid and the other H taken from the alcohol
  - Example:  $\text{CH}_3\text{COOH} + \text{HOCH}_2\text{CH}_3 \longrightarrow \text{CH}_3\text{COOCH}_2\text{CH}_3 + \text{H}_2\text{O}$
- **Amides** have a carbonyl (look for that  $\text{C}=\text{O}$ ) group bonded to a nitrogen atom bearing hydrogen and/or alkyl groups and therefore have the possible general formulas of  $\text{RCONH}_2$ ,  $\text{RCONHR}'$ , and  $\text{RCONR}'\text{R}''$
- A **nitrile** has a cyanide group attached to the carbon to make a general formula of  $\text{R}-\text{CN}$  with linear *sp*-hybridization

## 2.10 Summary of Important Families of Organic Compounds

| Alkane                     | Alkene   | Alkyne                     | Aromatic         | Haloalkane                   | Alcohol                             | Ether                                 |
|----------------------------|--|----------------------------|------------------|------------------------------|-------------------------------------|---------------------------------------|
| C—H<br>and<br>C—C<br>bonds |  | $\text{—C}\equiv\text{C—}$ | Aromatic<br>ring | $\text{—C—}\ddot{\text{X}}:$ | $\text{—C—}\ddot{\text{O}}\text{H}$ | $\text{—C—}\ddot{\text{O}}\text{—C—}$ |
| RH                         | RCH=CH <sub>2</sub><br>RCH=CHR<br>R <sub>2</sub> C=CHR<br>R <sub>2</sub> C=CR <sub>2</sub> | RC≡CH<br>RC≡CR             | ArH              | RX                           | ROH                                 | ROR                                   |

| Amine   | Aldehyde      | Ketone         | Carboxylic Acid | Ester          | Amide  | Nitrile                    |
|---|---------------|----------------|-----------------|----------------|--|----------------------------|
| $\text{—C—N:}$  |               |                |                 |                |  | $\text{—C}\equiv\text{N:}$ |
| RNH <sub>2</sub><br>R <sub>2</sub> NH<br>R <sub>3</sub> N | $\text{RCHO}$ | $\text{RCOR}'$ | $\text{RCOOH}$  | $\text{RCOR}'$ | $\text{RC(=O)NH}_2$<br>$\text{RC(=O)NHR}'$<br>$\text{RC(=O)NHR}''$ | RCN                        |

## 2.11 Physical Properties of Molecular Structure

### 2.11.1 State Changes

- The **melting point** of a substance is the temperature at which an equilibrium exists between the well-ordered crystalline state and the more random liquid state
- The **boiling point** of a liquid is the temperature at which the vapor pressure of the liquid equals the pressure of the atmosphere above it
  - If pressure is reduced then boiling point is subsequently reduced
  - Molecules that are symmetrical have abnormally high melting points
  - Heavier molecules boil at higher boiling points because it takes more kinetic energy to get them to the speed at which they separate from one another to form a gas
- The **ion-ion forces** of an ionic compound are the strong electrostatic lattice forces that act between the positive and negative ions in the solid state
  - Therefore, boiling points of ionic compounds are higher than covalent compounds and oftentimes decompose before they are able to boil<sup>7</sup>

### 2.11.2 Intermolecular Forces

- Intermolecular forces (IMFs) that are dispersion forces are also referred to as **van der Waals forces**
- **Dipole-Dipole Forces** are due to a permanent dipole moment resulting from a nonuniform distribution of bonding electrons in polar molecules

<sup>7</sup>Be careful when distinguishing boiling point and solubility. For instance, consider ethanol and decanol. The solubility (in water) of ethanol will be higher due to a more polar structure. However, decanol will have a higher boiling point due to a larger overall structure causing much more London Dispersion forces.

- **Hydrogen bonding** is a very strong dipole-dipole force between hydrogen atoms bonded to oxygen, nitrogen, or fluorine and nonbonding electron pairs on other such electronegative atoms
  - Since H-bonding is a strong IMF, it raises the boiling point of water, which is why it's a liquid at STP
- **(London) Dispersion forces** can be thought of as an instantaneous dipole moment that can induce other dipole moments in neighboring molecules
  - The more **polarizable** a molecule is, the larger dispersion forces it has since it can have a larger instantaneous dipole moment
  - Large atoms are easily polarizable and small atoms are not. Also, atoms with unshared electron pairs are more polarizable than atoms with only bonding pairs
  - Molecules that are longer and flatter (long chains) have more surface area and thus have larger dispersion forces
  - A higher molecular weight increases boiling point because there is a higher energy needed to reach necessary velocities and because there is more surface area
- The **solubility** of a solid substance is how well it dissolves in a liquid
- Water dissolves solute particles by **hydrating** or **solvating** the ions due to its high polarity (large **ion-dipole forces**<sup>8</sup>)

### 2.11.3 Solubility

- **Hydrophobic** means incompatible with water while **hydrophilic** means compatible with water (“like-dissolves-like”)
- The **hydrophobic effect** is when a hydrocarbon chain, for instance, with a large hydrophobic portion does not dissolve in a polar solvent even though it has a hydrophilic functional group like –OH
  - The reason for the hydrophobic effect is that there is an **unfavorable entropy change** because water must become more ordered around the hydrocarbon chain in order to solvate it, and this goes against the favorable entropy flow of the universe
- With soaps and detergents there is a long hydrophobic chain with a strong hydrophilic group at the end of the chain
  - The long chain embeds itself in the oily layer of what we wash while the hydrophilic ion portion attract the polar water molecules
- Compounds with one to three carbon atoms are water soluble if the compound has only one hydrophilic group
  - Compounds with four to five carbons are borderline, and compounds with six or more carbons are insoluble

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<sup>8</sup>An ionic compound forms with an electronegativity difference between atoms of  $> 1.7$ . Polar bonds are for differences of  $0.5 - 1.7$ , and a nonpolar bond is for differences  $< 0.5$

## 2.12 Summary of Attractive Forces

### 2.12.1 Strength of Attractive Forces

Here are the forces in order of increasing strength:

1. London Dispersion
2. Dipole-Dipole
3. Hydrogen Bonding
4. Ion-Dipole
5. Ion-Ion

### 2.12.2 Degrees of Unsaturation

- A degree of unsaturation is either a  $\pi$  bond or a ring structure
- **Formula:**  $\frac{2C + 2 + N - H - X}{2}$  where the variables are carbons, nitrogens, hydrogens, and halogens

## 3 An Introduction to Organic Reactions and Their Mechanisms

### 3.1 Reactions and Their Mechanisms

- **Substitutions** are the characteristic reactions of saturated compounds such as alkanes and alkyl halides and of aromatic compounds where one group replaces another
- **Additions** are characteristic of compounds with multiple bonds where all parts of the adding reagent appear in the product
- **Eliminations** are the opposite of additions where one molecule loses the elements of another small molecule
  - Eliminations are useful in creating compounds with multiple bonds
- **Rearrangements** are when a molecule undergoes a reorganization of its constituent parts
- In cases where we want to indicate one electron moving (not a pair), we use a one-barbed arrow like the following:  $\rightarrow$
- **Heterolysis** is when a bond breaks such that one fragment takes away *both* electrons of the bond
  - Heterolysis produces **ions** and is termed an **ionic reaction** with a broken bond that has been cleaved heterolytically
  - Heterolysis requires separation of oppositely charged ions, so it needs some input of energy typically from the addition of a molecule with an unshared pair that can form a bond to one of the atoms
- **Homolysis** is when a bond breaks so that each fragment takes away *one* electron from the bond
  - Homolysis produces fragments with unpaired electrons known as **radicals**

### 3.2 Acid-Base Reactions

- Brønsted-Lowry acid-base reactions involve the transfer of protons
- A **Brønsted-Lowry acid** is a substance that can donate a proton
- A **Brønsted-Lowry base** is a substance that can accept a proton
- The molecule or ion that forms when an acid loses its proton is the **conjugate base**
- The molecule or ion that forms when a base accepts a proton is the **conjugate acid**
- The hydronium ion,  $\text{H}_3\text{O}^+$ , is the strongest acid that can exist in water with all stronger acids forming hydronium ions due to the leveling effect
- The hydroxide ion,  $\text{OH}^-$ , is the strongest base that can exist in water with all stronger bases forming hydroxide ions due to the leveling effect
- **Spectator ions** do not play a part in an acid-base reaction

### 3.3 Lewis Acids and Bases

- According to **Lewis acid-base theory**, acids are electron pair acceptors while bases are electron pair donors
- By definition, Lewis theory includes Brønsted-lowry reactions as well as more like electron-deficient atoms and metals such as elements of group IIIA, atoms with vacant orbitals, zinc, and iron(III) halides

### 3.4 Heterolysis of Bonds to Carbon: Carbocations and Carboanions

- A **carbocation** is an ion with a positive charge on the carbon atom while a **carbanion** is an ion with a negatively charge carbon atom
- Carbocations act as lewis acids while carbanions act as lewis bases
- Carbocations, and all lewis acids, are **electrophiles**, which means that they are electron-seeking reagents to achieve a full octet
  - Even without a formal charge, a carbon atom can be an electrophile if it is electron poor ( $\delta+$ ) due to bond polarity.
- Carbanions, and all lewis bases, are **nucleophiles**, which means they seek a positive center other than a proton, especially that of a positively charged carbon atom

### 3.5 How to Use Curved Arrows in Illustrating Reactions

- A curved arrow points from electrons to the atom receiving the electrons
- As an example, if a curved arrow has its tail at a lone pair of electrons on an oxygen atom of one molecule and the head of the arrow at the hydrogen atom of another second molecule, this means that the hydrogen from the second molecule is going to move to the first molecule and form a bond where the lone pair once was

### 3.6 The Strength of Brønsted-Lowry Acids and Bases: $K_a$ and $pK_a$

- **Acid strength** is characterized in terms of **acidity constant**,  $K_a$ , or  $pK_a$  values
- The generic expression for weak acid in water is  $\text{HA} + \text{H}_2\text{O} \rightleftharpoons \text{H}_3\text{O}^+ + \text{A}^-$  with an expression for the acidity constant as  $K_a = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{HA}]}$
- A large  $K_a$  value means the acid is a strong acid while a small value means the acid is weak
  - The stronger the acid, the weaker its conjugate base
- The larger the value of  $pK_a$ ,  $-\log(K_a)$ , the weaker the acid
  - The larger the  $pK_a$  value of the conjugate acid, the stronger the base

### 3.7 How to Predict the Outcome of Acid-Base Reactions

- Acid-base reactions, which are under equilibrium control, always favor the formation of the weaker acid and the weaker base
- Some water-insoluble compounds, like amines and carboxylic acids of many carbon atoms, can be dissolved readily in hydrochloric acid or sodium hydroxide, respectively, due to an acid-base reaction

### 3.8 Relationships Between Structures and Acidity

- Bond strength to the proton decreases as we move down a group. Therefore, acidity increases as we move down a group.
- Acidity increases as we go across a period because electronegativity increases in the same fashion
- Having more  $s$  character means that the electrons of the anion will, on average, be lower in energy, and the anion will be more stable. Consequently, more  $s$  character causes a molecule to be more acidic.
- The **inductive effect**, which weakens with distance from the group, is an electronic effect transmitted through bonds that can be **electron donating** or **electron withdrawing**
  - Eg: If we have  $\text{CH}_3\text{CH}_2\text{F}$ , the fluorine will have  $\delta^-$ . The  $\text{CH}_3$  and  $\text{CH}_2$  will have  $\delta^+$

### 3.9 Energy Changes

- Chemical energy is a form of potential energy, and the more potential energy an object has, the less stable it is
- **Enthalpies**,  $H$ , represent the relative potential energies of molecules
- The sign for the **enthalpy change**,  $\Delta H^\circ$ , for **exothermic** reactions is negative while it is positive for **endothermic** reactions

### 3.10 The Relationship Between the Equilibrium Constant and the Standard Free-Energy Change, $\Delta G^\circ$

- Equation for **standard free-energy change**:  $\Delta G^\circ = -RT \ln(K_{eq})$
- A negative value of  $\Delta G^\circ$  is spontaneous while a positive value is nonspontaneous
- The relationship between enthalpy, entropy ( $\Delta S^\circ$ ), and free-energy changes is:  $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$
- Exothermic reactions and increases in molecular disorder, entropy, lead to spontaneous reactions

### 3.11 The Acidity of Carboxylic Acids

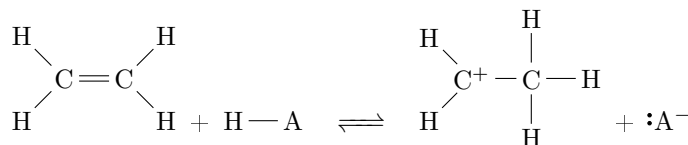
- Carboxylic acids are weak acids while alcohols have negligible acidity
- Carboxylic acids are weakly basic because the carboxylate anion produced is relatively stable due to delocalization of charge from resonance structures as well as an inductive electron-withdrawing effect
- Charge delocalization due to resonance structures always increases stability
- The inductive electron-withdrawing effect for carboxylate anions is due to its two oxygen atoms versus the one oxygen atom of an alkoxide<sup>9</sup> anion. The negative charge is distributed through both the electronegative oxygen atoms in the carboxylate anion, but it is only distributed through one oxygen atom in an alcohol thus making the carboxylate anion more stable
  - Also, there is an inductive effect in the neutral molecule of the carboxylate because the two oxygen atoms create a larger polarized O-H bond, which makes it easier for the H to dissociate in solution
- The **substituent effect** is the acid-strengthening effect of other electron-attracting groups
- Any factor that stabilizes the conjugate base of an acid increases the strength of the acid

### 3.12 The Effect of the Solvent on Acidity

- A **protic solvent** is one that has hydrogen bonding
- Solvation of any species decreases the entropy of the solvent because the solvent molecules become much more ordered as they surround the solute ( $\Delta S = -$ )

### 3.13 Organic Compounds as Bases

- The conjugate acid of an alcohol is called a **protonated alcohol**, **alkyloxonium ion**, or **oxonium ion**
- Since an atom with an unshared electron pair makes for a basic molecule, many organic molecules go through proton transfer reactions as a first step in a mechanism because of unshared electron pairs on an oxygen or nitrogen atom
- A  $\pi$  bond, such as on an alkene, can also create basicity in a molecule in the presence of a strong acid by breaking the  $\pi$  bond and taking the proton away from the strong acid
- As seen in the reaction below, the  $\pi$  bond is broken, the bond between the proton and the atom, A, is broken, and a bond between a carbon of the alkene and the proton is formed, leaving that carbon with a formal positive charge (unstable carbocation)

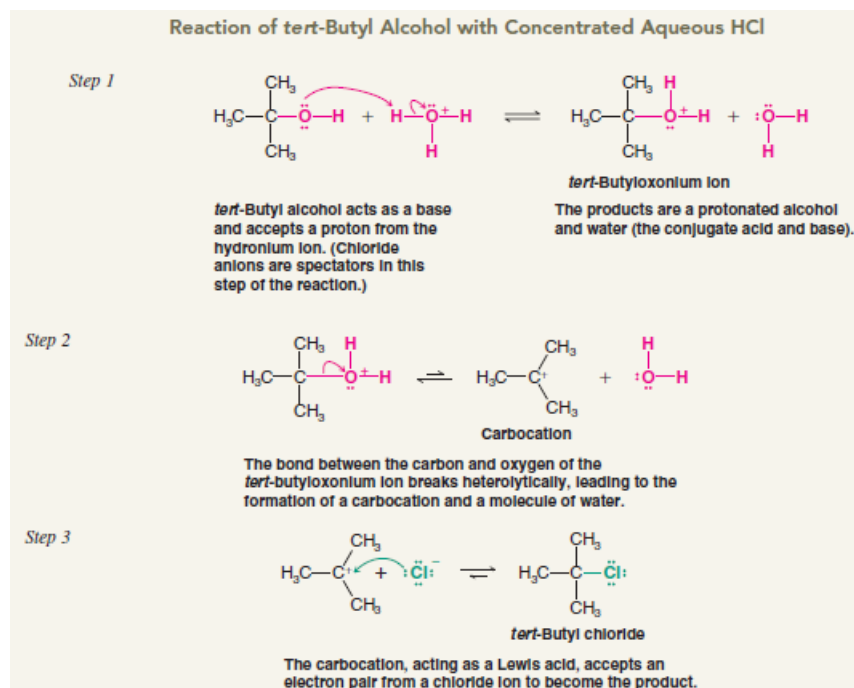


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<sup>9</sup>The anion of an alcohol



### 3.14 A Mechanism for an Organic Reaction



### 3.15 Acids and Bases in Nonaqueous Solutions

- The **leveling effect** only applies to aqueous (water as solvent) solutions, so bases and acids stronger than the hydroxide anion and hydronium cation, respectively, can be created if a different solvent is used
- **Terminal alkynes** are alkynes with a proton attached to a triple bonded carbon

### 3.16 Acid-Base Reactions and the Synthesis of Deuterium and Tritium-Labeled Compounds

- Using deuterium ( $^2\text{H}$ ) or tritium ( $^3\text{H}$ ) in an organic molecule is useful to label particular hydrogen atoms
- If a very strong base is reacted with  $\text{D}_2\text{O}$  or  $\text{T}_2\text{O}$ , a good example being  $\text{NH}_2^-$ , an acid-base reaction can occur to add the hydrogen isotope to the organic molecule (as well as  $\text{OD}^-$  or  $\text{OT}^-$ )
- The deuterium or tritium will replace the hydrogen atoms that, when removed and turned into an electron pair, can form a resonance structure

### 3.17 Systematic Approach to Acids and Bases

- The more stable the conjugate is, the stronger the parent acid/base. This will influence how acidic a parent molecule is

Factors Affecting Acidity (in decreasing significance)<sup>10</sup>: ARIO

1. Atom
2. Resonance Stabilization
3. Induction Effect
4. Orbital (*s* character)

Factors Explained:

1. Look at what atom the charge is on for the conjugate base. Use periodic trends mentioned earlier
2. Look at resonance structures. The more atoms the charge of the conjugate anion is spread over the better because it will stabilize it
3. Look for inductive effect. Many electronegative atoms that pull electron density towards themselves create more stable anions and thus more acidic molecules. However, if there are many alkyl groups, this is a process called hyperconjugation, and the molecule is less stable
4. Look at the orbital where the negative charge for the conjugate base is. More *s* character of a bond with hydrogen makes it more acidic

## 4 Nomenclature and Conformations of Alkanes and Cycloalkanes

### 4.1 Introduction to Alkanes and Cycloalkanes; Shapes of Alkanes

- **Alkanes** are hydrocarbons with all carbon-carbon single bonds
- **Alkenes** are hydrocarbons with a carbon-carbon double bond
- **Alkynes** are hydrocarbons with a carbon-carbon triple bond
- **Cycloalkanes** are alkanes in which all or some of the carbon atoms are arranged in a ring
- Alkanes have the general formula of  $C_nH_{2n+2}$
- Cycloalkanes with a single ring have the formula  $C_nH_{2n}$
- An **unbranched** chain means that each carbon atom is bonded to no more than two other carbon atoms and that there are only primary and secondary carbon atoms

### 4.2 IUPAC Nomenclature of Alkanes, Alkyl Halides, and Alcohols

#### 4.2.1 Suffixes

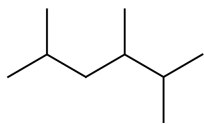
- Endings of alkane names end in *-ane*, and the standard prefixes apply to how many carbon atoms there are (*meth-*, *eth-*, *prop-*, *but-*, *pent-*, etc.)
- An **alkyl group** has one hydrogen removed from an alkane, and the names have a suffix of *-yl*
- An alcohol group has the name ending of *-ol*

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<sup>10</sup>This general trend is not always perfectly applicable. However, it is usually a very good indicator for acidities

### 4.2.2 Branched-Chain Alkanes

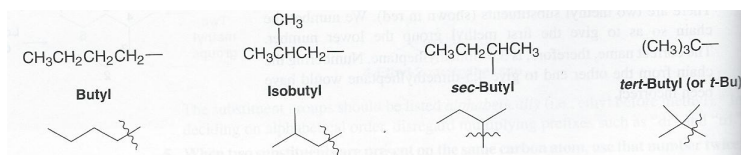
1. Locate the longest continuous chain of carbon atoms. This chain determines the parent (prefix) name for the alkane.
  - (a) Always start numbering from the end of a chain
2. Number the longest chain beginning with the end of the chain nearer the substituent
3. Use the numbers obtained by application of Rule 2 to designate the location of the substituent group
4. When two or more substituents are present, give each substituent a number corresponding to its location on the longest chain
  - (a) Name them in alphabetical order
5. When two substituents are present on the same carbon atom, use that number twice
6. When two or more substituents are identical, indicate this by the use of alternate prefixes (*di-*, *tri-*, *tetra-*, etc.)
7. When two chains of equal length compete for selection as the parent chain, choose the chain with the greatest number of substituents
8. When branching first occurs at an equal distance from either end of the longest chain, choose the name that gives the lower number at the first point of difference



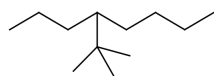
This is 2,3,5-Trimethylhexane

### 4.2.3 Branched Alkyl Groups

- A 1-methylethyl alkyl group is also known as an **isopropyl group** and is derived from the removal of the terminal hydrogen of propane
- The common names of **isobutyl**, **sec-butyl**, and **tert-butyl** are also IUPAC approved and are as follows:



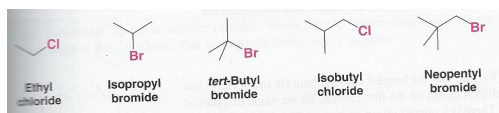
- The 2,2-dimethylpropyl group, also known as the neopentyl group, is also important to know with 2,2-dimethylpropane being neopentane



This is 4-(1,1-Dimethylethyl)octane or 4-tert-butyloctane

#### 4.2.4 Alkyl Halides

- When a parent chain has both a halogen substituent and alkyl substituent, start the numbering from the end nearest the first substituent, regardless of its type. If two substituents are at equal distances from one another, number the chain nearer the substituent that has alphabetical precedence
- The **functional class nomenclature** is the common naming system for haloalkanes and are as follows:

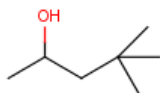


#### 4.2.5 Alcohols

- A **substitutive nomenclature** name may have four features: **locants**, **prefixes**, **parent compound**, and **suffixes**
- Numbering of the chain always begins at the end nearer the group named as a suffix

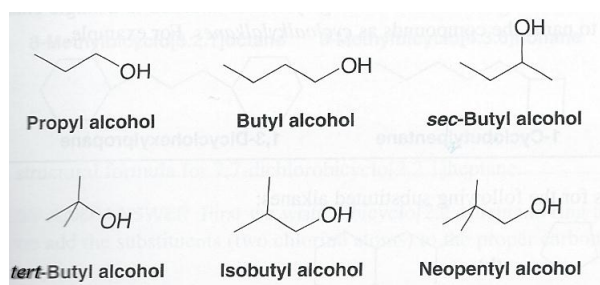
Steps:

1. Select the longest continuous carbon chain to which the hydroxyl is directly attached. Change the name of the alkane corresponding to this chain by dropping the final *-e* and adding the suffix *-ol*
2. Number the longest continuous carbon chain so as to give the carbon atom bearing the hydroxyl group the lower number. Indicate the position of the hydroxyl group by using this number as a locant. Indicate the positions of other substituents by using the numbers corresponding to their positions along the carbon chain as locants



This is 4,4-Dimethyl-2-pentanol or 4,4-dimethylpentan-2-ol

Common names also apply to alcohols. Aside from methyl alcohol, ethyl alcohol, and isopropyl alcohol, here are some more:



Alcohols containing two hydroxyl groups are known as **glycols** and are named as **diols**



### 4.3 Nomenclature for Cycloalkanes

- Cycloalkanes with only one ring are named by attaching the prefix *cyclo* to the names of the alkanes
- When two substituents are present, we number the ring beginning with the substituent first in the alphabet and number in the direction that gives the next substituent the lowest number possible
- When three or more substituents are present, we begin at the substituent that leads to the lowest set of locants
- When a single ring system is attached to a single chain with a greater number of carbon atoms, or when more than one ring system is attached to a single chain, then it is appropriate to name the compounds as cycloalkylalkanes

### 4.4 Nomenclature for Bicyclic Compounds

- **Bicycloalkanes** are compounds containing two fused or bridged rings with the name of the alkane corresponding to the total number of carbon atoms
- The carbon atoms common to both rings are known as bridgeheads with each bond or chain of atoms connecting the bridgehead atoms being called a bridge
- With the name, we also interpose an expression in brackets that denotes the number of carbon atoms in each bridge in order of decreasing length. Fused rings have zero carbon atoms in the bridge (eg: Bicyclo[2.2.1]heptane)
- Number the largest cyclic section first from the bridgehead

### 4.5 Nomenclature of Alkenes and Cycloalkenes

- Some common alkene names are ethylene, propylene, and isobutylene for ethene, propene, and 2-methylpropene, respectively

Steps:

1. Determine the parent name by selecting the longest chain that contains the double bond and change the ending of the name of the alkane of identical length from *-ane* to *-ene*
2. Number the chain so as to include both carbon atoms of the double bond, and begin numbering at the end of the chain nearest the double bond. Designate the location of the double bond by using the number of the first atom of the double bond as a prefix. The locant for the alkene suffix may precede the parent name or come after the suffix
3. Indicate the locations of the substituent groups by the numbers of the carbon atoms to which they are attached
4. Number substituted cycloalkenes in the way that gives the carbon atoms of the double bond the 1 and 2 positions and that also gives the substituent groups the lower numbers at the first point of difference.
5. Name compounds containing a double bond and an alcohol group as alkenols or cycloalkenols and give the alcohol carbon the lower number (ignore Step 4)
6. If two identical or substantial groups are on the same side of the double bond, the compound can be designated with *cis* if they are on the same side or *trans* if they're on opposite sides. If applicable, always indicate *cis* and *trans* with a double bond on a hydrocarbon chain

## 4.6 Nomenclature of Alkynes

- Unbranched alkynes are named by replacing -ane with -yne
- The chain is numbered to give the carbon atoms of the triple bond the lower possible numbers
- The lower number of the two carbon atoms of the triple bond is used to designate the location of the triple bond
- The locations of substituent groups of branched alkynes and substituted alkynes are also indicated with numbers
- Monosubstituted acetylenes or 1-alkynes are called **terminal alkynes**, and the hydrogen attached to the carbon of the triple bond is called the **acetylenic hydrogen atom**

## 4.7 Hierarchy of Naming

- What if we have more than one functional group? Which do we make the suffix? It goes as follows in decreasing order: carboxylic acid (-oic acid), ester (-oate), aldehyde (-al), ketone (-one), alcohol (-ol), and then amine (-amine)
- We start numbering carbons in an order that produces the longest chain, but what are some other factors? Well, there is a hierarchy for the following groups in decreasing order: functional group, double bond, and triple bond. You number in a way that creates the longest chain and includes whichever factor from this list is highest in the hierarchy as the lowest possible number


## 4.8 Sigma Bonds and Bond Rotation


### 4.8.1 Definitions

- Two groups bonded by only a single bond can undergo rotation about that bond with respect to each other
- The temporary molecular shapes that result from such a rotation are called **conformations** of the molecule
- Each possible structure is called a **conformer**
- An analysis of the energy changes that occur as a molecule undergoes rotations about single bonds is called a **conformational analysis**

### 4.8.2 Newman Projection Formula

- We imagine ourselves taking a view from one atom (usually a carbon) directly along a selected bond axis to the next atom (also usually a carbon atom)

- The front carbon and its other bonds are represented by 

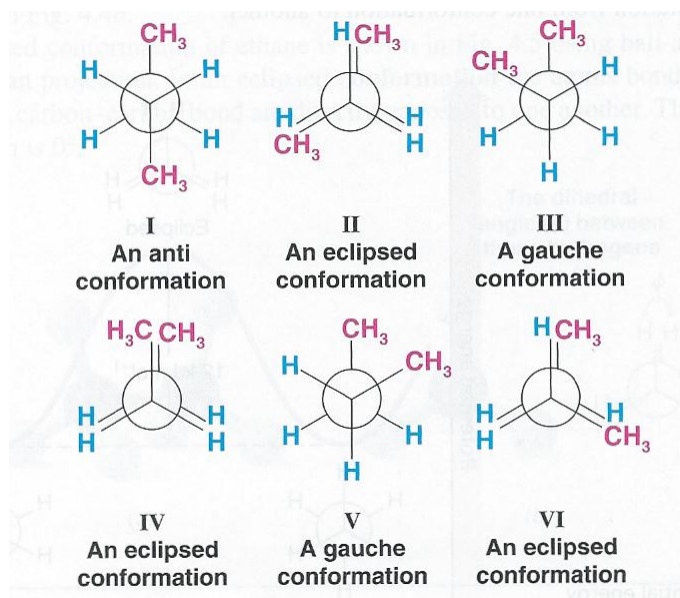
- The back carbon and its bonds are represented by 

- The **staggered conformation** of a molecule is that conformation where the **dihedral angle**,  $\phi$ , between the bonds at each of the carbon-carbon bonds is  $180^\circ$  and where atoms or groups bonded to carbons at each end of a carbon-carbon bond are as far apart as possible
- In an **eclipsed conformation**, the atoms bonded to carbons at each end of a carbon-carbon bond are directly opposed to one another with a dihedral angle of  $0^\circ$  between them

- The phenomenon of electron delocalization via orbital overlap from a filled bonding orbital to an adjacent unfilled orbital is called **hyperconjugation**
- The **torsional barrier** is the potential energy barrier between the staggered and eclipsed conformations
- The factors involved in the rotational barrier are called the **torsional strain**
- **Steric hindrance** between electron clouds of bonded groups are repulsive interactions

## 4.9 Conformational Analysis of Butane

Below shows the conformers for butane:



- In the **anti conformation**, there is no torsional strain from steric hindrance because the groups are staggered. Therefore, it is the most stable
- In the **gauche conformation**, the methyl groups are much closer and repel one another thus giving it more potential energy and less stability
- The eclipsed conformations here have the most potential energy with the staggered having the least
- **Stereoisomers** have the same molecular formula and connectivity but different arrangements of atoms in 3-space
- **Conformational stereoisomers** are related to one another by bond rotations

## 4.10 The Relative Stabilities of Cycloalkanes: Ring Strain

- Ring strain is composed of angle strain and torsional strain
- **Angle strain** is the result of deviation from ideal bond angles caused by inherent structural constraints
- **Torsional strain** is from dispersion forces that can't be relieved due to restricted conformational mobility

## 4.11 Conformations of Cyclohexane: The Chair and the Boat

- The most stable conformation of cyclohexane is the **chair conformation** (no angle or torsional strain) because the bond angles are  $109.5^\circ$



## 4.12 Substituted Cyclohexanes: Axial and Equatorial Hydrogen Groups

### 4.12.1 Definitions

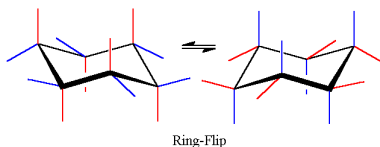
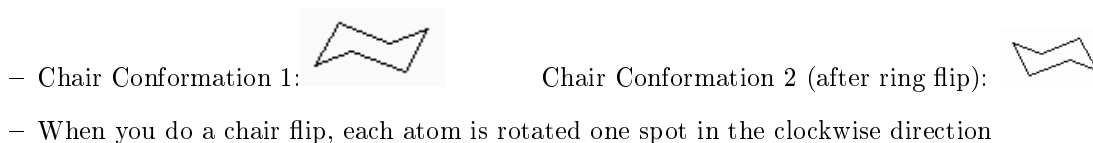
- The **axial** bonds of cyclohexane are those that are perpendicular to the average plane of the ring
- The **equatorial** bonds of cyclohexane are those that extend from the perimeter of the ring
- The most stable conformation for a monosubstituted cyclohexane ring is the conformation where the substituent is equatorial

### 4.12.2 Drawing Chair Structures

- Start numbering carbons from the North-East corner of the chair. At this spot, it is simple to make it have axial up/equatorial down. There can never be both up or both down for axial/equatorial at the same carbon. Also, the positions for up and down for axial and equatorial switch with each carbon atom. For example, the second carbon (typically easy to move clockwise around the chair) has axial down/equatorial up.
- A solid wedge in a structural formula is up in a chair structure while a dashed wedge is down

### 4.12.3 Ring Flipping

- The axial groups become equatorial and vice versa
- When doing a ring flip, whether a group is up or down does not change
- During a ring flip, the skeleton of the chair is flipped over an arbitrary vertical axis



## 4.13 Disubstituted Cycloalkanes: Cis-Trans Isomerism; Bicyclic and Polycyclic Alkanes

- When one ring substituent group is larger than the other and they cannot both be equatorial, the conformation with the larger group equatorial will be more stable



## 4.14 Synthesis of Alkanes and Cycloalkanes

- A **hydrogenation** reaction converts a carbon-carbon double bond to a single bond
  - This will convert an alkene to an alkane. It can also convert an alkyne to an alkene or alkane depending on the reaction conditions
- One molar equivalent of hydrogen is needed to reduce an alkene, and two molar equivalents are needed to convert an alkyne to an alkane

## 5 Stereochemistry

### 5.1 Chirality, Stereochemistry, and Isomerism

- **Chiral** objects are those that can exist in right and left handed forms
  - If the mirror image of an object can be superposed onto itself then it is considered achiral
- **Isomers** are different compounds that have the same molecular formula
- **Constitutional isomers** have the same molecular formula but different connectivity
- **Stereoisomers** have their atoms connected in the same sequence, but they differ in the arrangement of their atoms in space (eg: *cis* and *trans* isomers)
- **Enantiomers** are stereoisomers whose molecules are nonsuperposable mirror images of each other (optical isomers)
- **Diastereomers** are stereoisomers whose molecules are not mirror images of each other
  - To create a diastereomer given the structure of one molecule simply change a dashed wedge to a solid wedge<sup>11</sup>, or vice versa without it creating a mirror image or do a *cis-trans* swap
- A **chiral molecule** is one that is not superposable on its mirror image (therefore, all enantiomers are pairs of chiral molecules)
  - A molecule will not be chiral if it possess a **plane of symmetry**

### 5.2 A Single Chirality Center

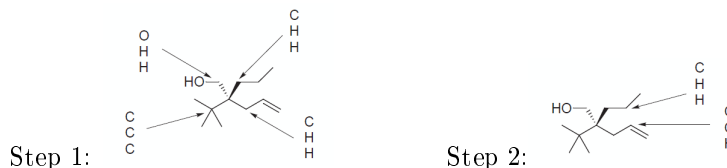
- Even though tetrahedral molecules cannot have geometric isomers, they can, however, be chiral if all four atoms attached to the tetrahedron are different. Such molecules are said to have **chirality centers**
- The presence of a single chirality center makes a molecule chiral, but having more than one (or zero) chirality centers does not guarantee this
- Interchanging any two groups of the chirality center of an enantiomer converts it into the other
- Any atom at which an interchange of groups produces a stereoisomer is called a **stereogenic center**
- Enantiomers do not interconvert spontaneously (need large amounts of energy)
- A chirality center is a type of stereogenic center, but not all stereogenic centers are chirality centers
  - MIT 5.512: “A stereogenic center is an element where the interchange of two substituents will lead to a stereoisomer. A chiral center is a specific type of stereogenic center where reflection of the molecule results in a non-superposable mirror image”

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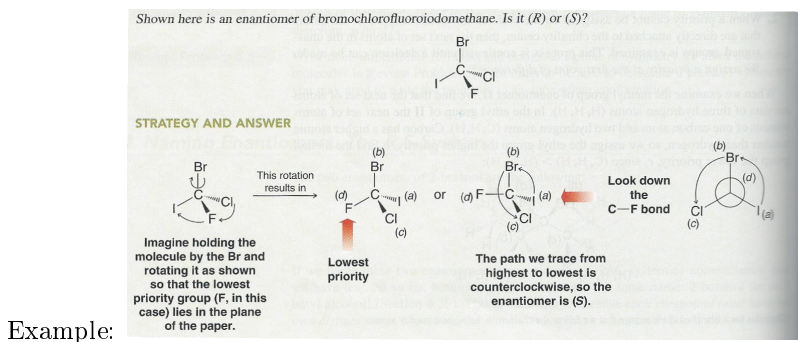
<sup>11</sup>Remember solid and dashed wedges are drawn on the same side of the carbon atom

### 5.3 Naming Enantiomers: The R-, S-System

- Each of the four groups attached to the chirality center is assigned a **priority** or **preference** of a, b, c, or d. Priority is assigned first on the basis of the **atomic number** of the atom that is directly attached to the chirality center. The group with the highest atomic number gets the highest priority and vice versa
- When a priority cannot be assigned on the basis of atomic number of the atoms, then the next set of atoms in the unassigned groups is examined. This process is continued until a decision can be made at the first point of difference

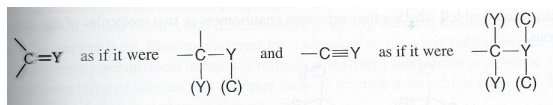


- We now rotate the structure so that the group with the lowest priority is directed away from the viewer. That is, priority number 4 should be made into a dashed wedge if it's not already
- Next, trace a path from a to b to c. If, as we do this, the direction of the path is clockwise, the enantiomer is designated with an R. If the direction is counterclockwise, the enantiomer is designated with an S



Example:

- For compounds containing at least one  $\pi$  bond, another rule is needed. Groups containing double or triple bonds are assigned priorities as if both atoms were duplicated or triplicated, which affects the priority:



- Note: There is a trick. The trick is this:
  - If the 4th atom is a dashed wedge (downward): Analyze if the numbers (1  $\rightarrow$  2  $\rightarrow$  3  $\rightarrow$  4) go clockwise or counterclockwise. If the 4th atom is *not* a dash, then interchange the dashed atom with the 4th atom. Clockwise indicates that the molecule is “R,” while counterclockwise indicates the molecule is “S.”
  - If the 4th atom is a solid wedge (upward): Analyze this “intermediate” molecule to see if the numbers go clockwise or counterclockwise. Clockwise indicates that the original molecule is “S,” while counterclockwise indicates the molecule is “R.”

## 5.4 Properties of Enantiomers: Optical Activity

- Enantiomers have identical properties for many physical traits such as boiling point, solubility, infrared spectra, etc. when comparing the S enantiomer with the R enantiomer
  - Mixtures of enantiomers have different physical properties when compared to a solution of just an isolated sample
- When a beam of plane-polarized light passes through an enantiomer, the plane of polarization **rotates**
- Separate enantiomers rotate the plane of polarized light in equal amounts but in opposite directions and are **optically active compounds**
  - Chiral molecules are optically active (not the same as having a chirality center)
- A polarizer makes light waves oscillate in only one plane, which is known as **plane-polarized light**
- A substance that rotates plane-polarized light in the clockwise (+) direction is said to be **dextrorotatory**
- A substance that rotates plane-polarized light in the counterclockwise (-) directions is said to be **levorotatory**
- **Specific rotation** is the number of degrees that the plane of polarization is rotated as the light passes through a solution of an enantiomer
  - Specific rotation is dependent on temperature and wavelength
- There is no correlation between R and S enantiomers and + or specific rotation
- A **racemic mixture** is one that has an equimolar mixture of two enantiomers
- An **enantiomerically pure** sample is one that consists of a single enantiomer (also said to have an **enantiomeric excess** of 100%)
- Reactions carried out with achiral reactants can create a chiral molecule, but the resultant mixture is racemic. This is not the case if there is/are chiral molecule(s) and/or chiral influences like chiral enzymes/catalysts or chiral solvent

## 5.5 Molecules with More than One Chirality Center

- In compounds whose stereoisomerism is due to chirality centers, the total number of stereoisomers will not exceed  $2^n$ , where  $n$  is the number of chirality centers
- Diastereoisomers have different physical properties, unlike enantiomers
- A **meso compound** is an achiral molecule that contains chirality centers and are not optically active since they are not chiral
  - To quickly determine if a molecule is a meso compound, check to see if it has a plane of symmetry and/or if its mirror image is identical to the original. A meso compound can also exist if it has a center of inversion<sup>12</sup>
- If a molecule has two chirality centers, make all wedges planar. Then, if there is internal symmetry it is achiral and meso
- To name a molecule with more than one chirality centers, locants must be used to describe whether each chirality center is R or S (eg: (2R,3R)-2,3-dibromobutane)

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<sup>12</sup>A center of inversion can be seen if everything can be inverted around the center to regenerate the same thing

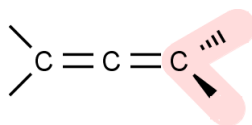
## 5.6 Configurations and Cyclic Compounds

- If a reaction takes place in a way so that no bonds to the chirality center are broken, the product will have the same general configuration of groups (same relative position) around the chirality center as the reactant. This is a reaction that **proceeds with retention of configuration**
- Chirality centers in different molecules have the same relative configuration if they share three groups in common and if these groups with the central carbon can be superposed
- The **absolute configuration** of a chirality center is its R or S designation
- A cyclic molecule can have an enantiomer that is apparent after a ring flip, but they might not be able to be separated because of rapid interconversion. Therefore, they represent different conformations of the same compound known as **conformational stereoisomers** (conformers)

## 5.7 Compounds with Chirality Centers other than Carbon; Chiral Molecules that do not Possess a Chirality Center

- Elements in the same group as carbon can form tetrahedral compounds and thus can have chirality centers if all four groups connected to the central atom are different
- Conformational isomers that are stable, isolable compounds are known as **atropisomers** (from such large rotational barriers between conformers)
- Allenes are compounds that exhibit stereoisomerism due to the geometry of the  $\pi$  bond (not cis-trans but still chiral with different substituents on the end of the carbon atom)

General Allene:

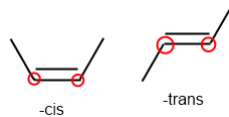


## 5.8 Confused about Stereochemistry?

### 5.8.1 Quick Tips

- The main thing is to recognize that *there is a difference between rotation around an axis and reflection over an axis*. Reflection over an  $x$  or  $y$  axis isn't going to change the solid or dashed wedge nature of that atoms in 3-space, but a rotation around that axis will!
- Sometimes it might be necessary to check to see if a pair of potential enantiomers are the same by rotating one of them over the  $y$  axis and then the  $x$  axis (double rotation)
- When given a chair structure, draw out the planar hexagon form, but make sure the orientation is correct
- The configuration ( $R$  or  $S$ ) is unique to each individual molecule, hence the  $2^n$  formula for permutations
- Diastereomers have swapped R and S configurations

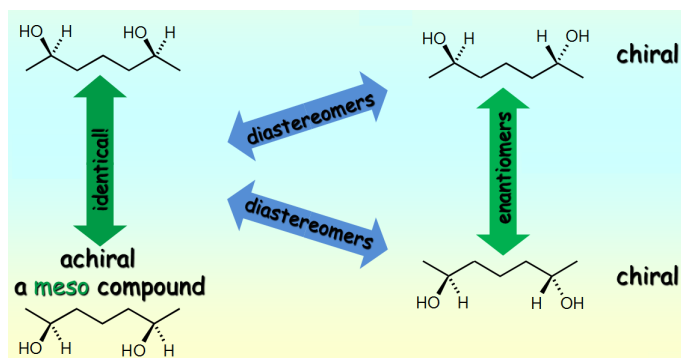
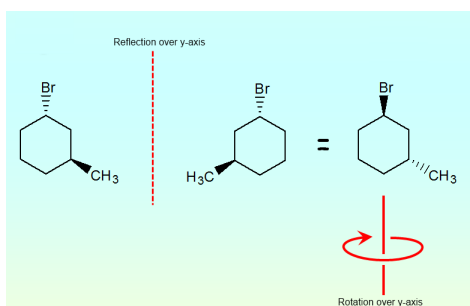
- With rings, *cis* and *trans* describe the solid/dashed wedges of atoms, but this is different with regular double bonded hydrocarbons! Double bonded hydrocarbons do not have tetrahedral geometries for the carbon atoms attached to the double bond; it is (trigonal) planar.



- As a result,

- All meso compounds have an internal plane of symmetry, so they have an *R, S* configuration or *S, R*, but not all *S, R/R, S* compounds are meso
- Number of Stereoisomers is  $2^n$ , where  $n$  is the number of chirality centers. However, if *cis* and *trans* can be made due to double bond, then you need to make sure you are careful, as the formula is not as straight forward.

### 5.8.2 Examples<sup>13</sup>



## 6 Ionic Reactions

### 6.1 Organic Halides

- **Vinyl** or **phenyl halides** are compounds in which a halogen atom is bonded to an  $sp^2$ -hybridized carbon
- $\text{CH}_2=\text{CHCl}$  is **vinyl chloride** with  $\text{CH}_2=\text{CH}-$  being the **vinyl group**
- Vinyl halides have a halogen attached to a carbon atom that is double-bonded to another carbon

<sup>13</sup>Credit to Stony Brook University CHE 327 PowerPoint slides

- Phenyl halides have a halogen attached to a benzene ring and are part of a larger group known as **aryl halides**
- Together, vinylic and phenyl halides are part of a bigger group known as **organic halides** or **organohalogen compounds**

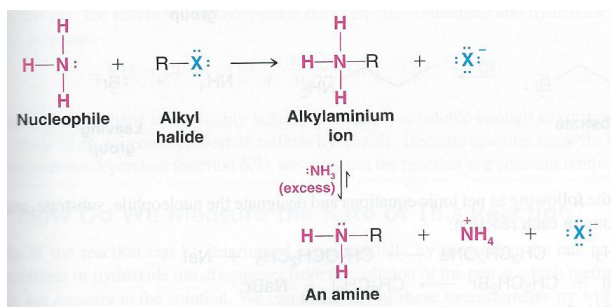
## 6.2 Nucleophilic Substitution Reactions

- General nucleophilic substitution<sup>14</sup> is  $\text{Nu} :^- + \text{R-LG} \longrightarrow \text{R-Nu} + : \text{LG}^-$
- The molecule that undergoes substitution is called the **substrate**
- The nucleophile is always a lewis base

## 6.3 Nucleophiles and Leaving Groups

- A nucleophile is a reagent that seeks a positive center and gains a positive charge, relatively speaking
- Any negative ion or uncharged molecule with an unshared electron pair is a potential nucleophile
- A deprotonation step is always required to complete the reaction when the nucleophile was a neutral atom that bore a proton

Example showing deprotonation<sup>15</sup>:



- A good leaving group is a substituent that can leave as a relatively stable, weakly basic molecule/ion
- The leaving group gains a negative charge, so it must have originally bore a positive formal charge if it ends up being neutral

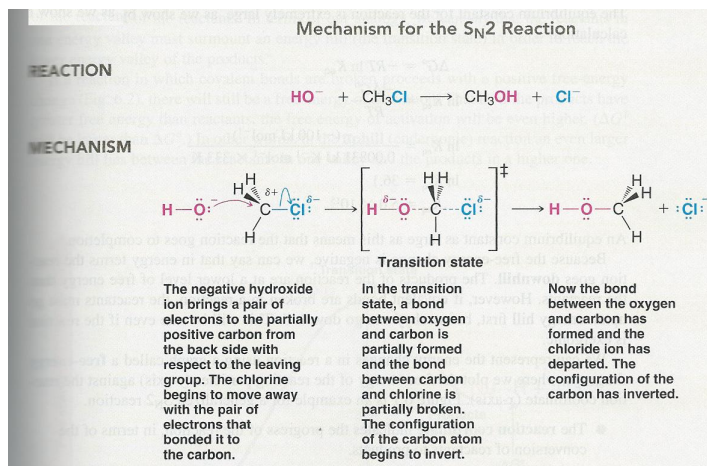
## 6.4 Mechanism for an S<sub>N</sub>2 Reaction

- For a rate,  $\text{Rate} = k [\text{A}]^a [\text{B}]^b$ , the overall order is  $a + b$
- A bimolecular reaction has two species involved in the rate-determining step
- S<sub>N</sub>2 stands for substitution, nucleophilic, bimolecular
- The nucleophile approaches the carbon bearing the leaving group from the back side (from the side directly opposite the leaving group)
- As the nucleophile forms a bond and the leaving group departs, the substrate carbon atom undergoes inversion where its tetrahedral bonding configuration is turned inside out

<sup>14</sup>Nu stands for nucleophile while LG stands for leaving group

<sup>15</sup>Deprotonation is normally seen as H<sub>3</sub>O<sup>+</sup> in water, but when there is a different solvent in excess it will be different

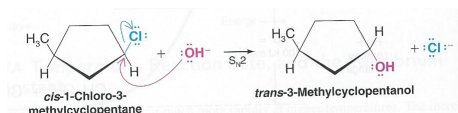
- The  $S_N2$  reaction proceeds in a single step through an unstable arrangement of atoms known as the **transition state**



- The  $S_N2$  reaction is a **concerted reaction** where bond forming and breaking occur simultaneously through a single transition state

## 6.5 The Stereochemistry of an $S_N2$ Reaction

- In a molecule containing chirality centers, the nucleophile ends up being bonded on the opposite side of the atom it replaces:



- When an  $S_N2$  reaction breaks a bond to a chirality center, the configurations swap

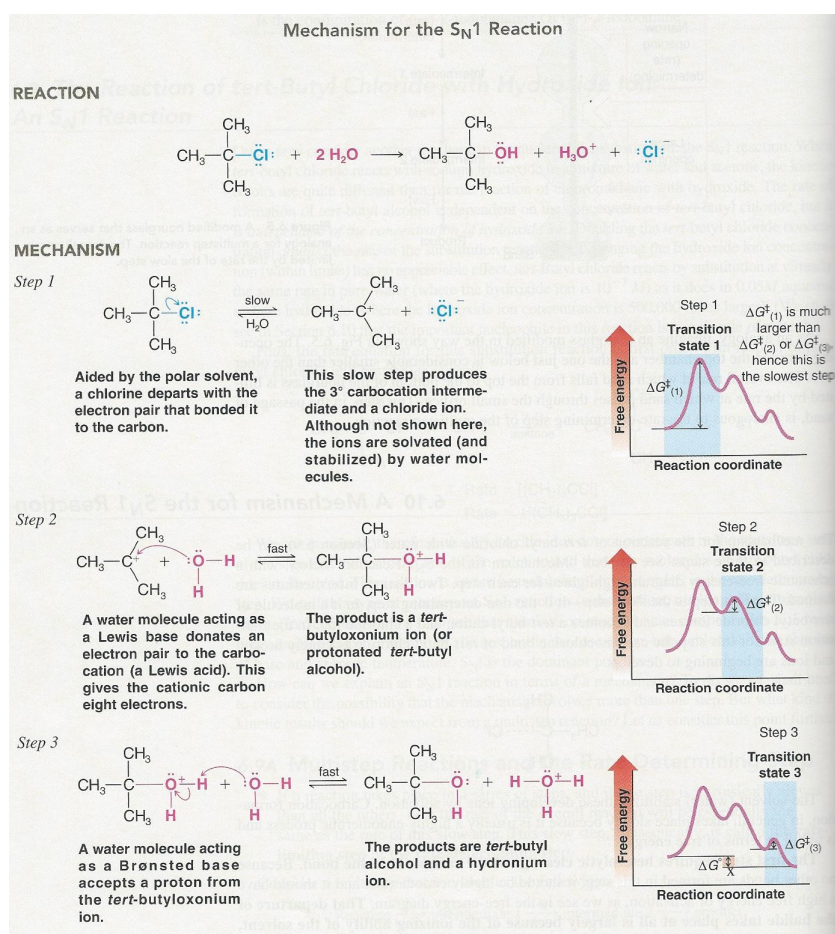
## 6.6 Transition State Theory: Free-Energy Diagrams

- A reaction that proceeds with  $-\Delta G$  is **exergonic** and is **endergonic** if it's  $+\Delta G$
- The top of the energy curve has the transition state
- The **free energy of activation** ( $\Delta G^\ddagger$ ) for the reaction is the difference in energy between the reactants and the transition state
- The free energy change ( $\Delta G^\circ$ ) is the difference in energy between the reactants and products
- The reaction with lower  $\Delta G^\ddagger$  will occur *exponentially* faster than a reaction with a higher  $\Delta G^\ddagger$

## 6.7 Mechanism for an $S_N1$ Reaction

- An  $S_N1$  reaction is an abbreviation for substitution, nucleophilic, *unimolecular*
  - An example: The reaction of tert-butyl chloride with the hydroxide ion is an  $S_N1$  reaction, and it is unimolecular because the hydroxide ion concentration does *not* alter the rate

- The slowest step of a multi-step mechanism is the **rate-limiting** or **rate-determining** step
- Two distinct intermediates (note: different from transition states) are formed in an  $S_N1$  reaction
- The first step is rate-determining and requires heterolytic cleavage of the carbon-leaving group bond. This is an endothermic reaction with a high  $\Delta G^\ddagger$
- The leaving group atom departs because of the ionizing ability of the polar solvent, typically water
  - Solvent molecules surround and stabilize the cation and anion that are produced
- The second step has the intermediate carbocation, a Lewis acid, reacting rapidly with the polar solvent, a Lewis base, to produce a second combined intermediate cation
- The third step has a rapid transfer of a proton to a molecule of the solvent, leaving the main product with a neutral charge



## 6.8 Stereochemistry for an $S_N1$ Reaction

- Since tetrahedral structures are achiral if all four groups are not all different, the product of an  $S_N1$  reaction will be identical whether there is a back-side attack or front-side attack
- A reaction that transforms an optically active compound into a racemic form proceeds with **racemization**



- An  $S_N1$  reaction reacts with water at equal rates from either side to form enantiomers if the leaving group was attached to a chiral carbon
- A **solvolysis** reaction is a nucleophilic substitution in which the nucleophile is a molecule of the solvent (called hydrolysis with water as solvent or methanolysis if the solvent is methanol)

## 6.9 Carbocations

- Carbocations are trigonal planar with  $sp^2$ -hybridization
- The central carbon atom in a carbocation is electron deficient with only six valence electrons (due to + formal charge)
- Tertiary carbocations are the most stable, and the methyl carbocation is the least stable
  - Order of Stability:  $3^\circ > 2^\circ > 1^\circ > \text{Methyl}$
- **Hyperconjugation** involves electron delocalization from a filled bonding orbital to an adjacent unfilled orbital
  - Any time a charge can be delocalized by hyperconjugation, inductive effect, or resonance, the system is stabilized

## 6.10 Overview of Factors Affecting the Rates of $S_N1$ and $S_N2$ Reactions

- Important factors that affect the relative rates of  $S_N1$  and  $S_N2$  reactions are: the structure of the substrate, the concentration and reactivity of the nucleophile, the effect of the solvent, and the nature of the leaving group
- A **steric effect** is an effect on the relative rates caused by the space-filling properties of those parts of a molecule attached at or near the reacting site (explanation for why neopentyl halide is very unreactive)
- **Steric hindrance** is when the spatial arrangement of atoms or groups at or near a reacting site of a molecule hinders or retards a reaction
  - Bulky substituents at or near the carbon atom have a dramatic inhibiting effect by increasing  $\Delta G^\ddagger$  of the transition state and  $\Delta G^\circ$
- The only organic compounds that undergo reactions by an  $S_N1$  path at a reasonable rate are those that are capable of forming relatively stable carbocations (exception for reactions in strong acids)
- Although not absolute, it is general to say that tertiary halides react mainly by an  $S_N1$  mechanism
- Tertiary carbocations are stabilized because the three sigma bonds contribute electron density to the  $p$  orbital by hyperconjugation
  - Therefore, hyperconjugation increases rate of  $S_N1$  due to increased stabilization of the carbocation intermediate

## 6.11 List of Effects for $S_N1$ and $S_N2$ Reactions

- Simple *alkyl halides* show the following trend for order of reactivity in  $S_N2$  reactions:
  - Methyl > primary > secondary  $\gg$  (tertiary-unreactive)

### 6.11.1 Nucleophiles

- The nucleophile does not participate in the rate-determining step of an  $S_N1$  reaction; therefore, the rate is not dependent on its concentration or identity
- The rates of  $S_N2$  reactions depend on both the concentration and identity of the attacking nucleophile
- The relative strength of a nucleophile, known as its **nucleophilicity**, is measured in terms of the relative rate of its  $S_N2$  reaction with a given substrate
  - A negatively charged nucleophile is always a more reactive nucleophile than its conjugate acid
- In a selection of nucleophiles in which the nucleophilic atom is the same, nucleophilicities parallel basicities:
  - $\text{RO}^- > \text{HO}^- \gg \text{RCO}_2^- > \text{ROH} > \text{H}_2\text{O}$
- Nucleophiles parallel basicity when comparing atoms in the same period
  - When the nucleophilic atoms are different, nucleophilicities may not parallel basicities
  - Nucleophiles do not parallel basicity and, instead, parallel size when comparing atoms of the same group
- ROH is a weak nucleophile, and, thus, does not favor  $S_N2$ , making  $S_N1$  have a competitive edge

### 6.11.2 Leaving Group

- Leaving groups depart with the electron pair that was used to bond them to the substrate
- The best leaving groups are weak bases after they depart
- The order of best leaving group is opposite basicity among halogens: iodine ion is the best while fluorine is the worst
- Strongly basic ions rarely act as leaving groups
- Very powerful bases, such as  $\text{H}^-$  and  $\text{R}^-$ , never act as leaving groups

### 6.11.3 Polar Protic Solvent

- A **protic solvent** is a molecule of a solvent that has hydrogen bonding
- Hydrogen bonding encumbers a nucleophile and hinders its reactivity in a substitution reaction
- A strongly solvated nucleophile must shed some of its solvent molecules to react (**solvent effect**)
- Hydrogen bonds to a small nucleophilic atom are stronger than those to larger nucleophilic atoms among elements in the same group
  - A larger anion will be more weakly solvated and thus be the stronger nucleophile (when comparing in the same group)
- Larger atoms have greater polarizability. Therefore, a larger nucleophilic atom can also donate a greater degree of electron density to the substrate

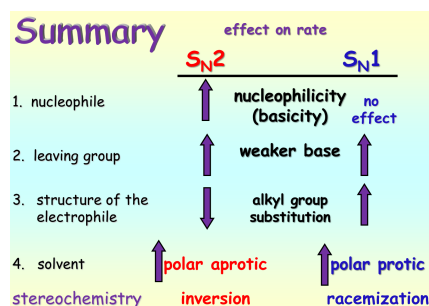
#### 6.11.4 Polar Aprotic Solvent

- Many polar aprotic solvents are useful in  $S_N2$  reactions
- Aprotic solvents do not solvate anions due to their lack of hydrogen bonding thus making nucleophiles highly reactive
- The rates of  $S_N2$  reactions generally are vastly increased when they are carried out in polar aprotic solvents

#### 6.11.5 Solvent Effects on an $S_N1$ Reaction

- A polar protic solvent will increase the rate of carbocation formation of an alkyl halide in any  $S_N1$  reaction because of its ability to solvate cation and anions effectively
- The **dielectric constant** is a rough indication of a solvent's polarity (higher polarity = higher  $S_N1$  rate)

#### 6.11.6 Summary



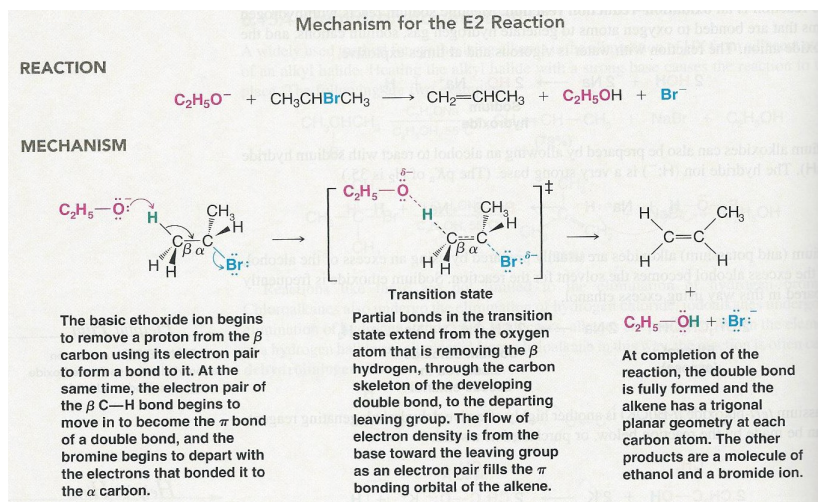
### 6.12 Organic Synthesis: Functional Group Transformations Using an $S_N2$ Reaction

- Vinylic and allylic compounds cannot go through  $S_N1$  or  $S_N2$
- **Functional group transformation (interconversion)** is the process of converting one functional group to another
- $S_N2$  reactions always occur with **inversion of configuration** at the atom that bears the leaving group
- Vinylic and phenyl halides are unreactive in  $S_N1$  and  $S_N2$  reactions due to instability for  $S_N1$  reactions and unreactiveness for  $S_N2$  reactions

### 6.13 Elimination Reactions of Alkyl Halides

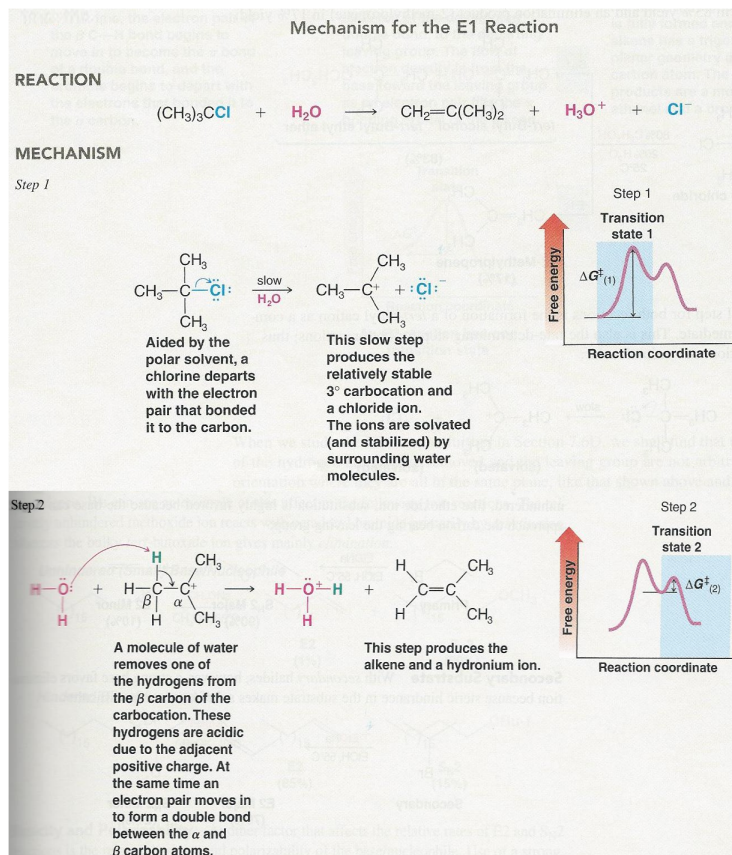
- In an **elimination reaction**, the fragments of some molecule are removed from adjacent atoms of the reactant to create a  $\pi$  bond
- When the elements of a hydrogen halide are eliminated from a haloalkane, the reaction is called **dehydrohalogenation**
- The carbon atom that bears the leaving group is the **alpha ( $\alpha$ ) carbon** atom, and any carbon atom adjacent to it is a **beta ( $\beta$ ) carbon** atom
- A hydrogen atom attached to a  $\beta$  carbon is called a  $\beta$  hydrogen atom. Therefore, these are  $\beta$  eliminations or 1,2 eliminations
- The E2 reaction is bimolecular in the rate-determining step while the E1 reaction is unimolecular

## 6.14 The E2 Reaction



- Notice that the geometry required here is similar to  $S_N2$  where the nucleophile must push out the leaving group from the opposite side
- There must be an anticoplanar nature

## 6.15 The E1 Reaction



- E1 reactions almost always accompany  $S_N1$  reactions to some extent

## 6.16 How to Determine Whether Substitution or Elimination is Favored

- Reagents are written over the reaction arrow, solvents and temperatures are written under the arrow, and only the substrate and major organic products are written to the left and right of the reaction arrows

### 6.16.1 Comparing $S_N2$ Reactions and $E2$ Reactions

- When the nucleophile attacks a  $\beta$  hydrogen atom, elimination occurs. When the nucleophile attacks the carbon atom bearing the leaving group, substitution results
- When the substrate is a primary halide and the base is strong and unhindered, substitution is highly favored because the base can easily approach the carbon bearing the leaving group
- When the substrate is a secondary halide, a strong base favors elimination because steric hindrance in the substrate makes substitution more difficult
- When the substrate is a tertiary halide, steric hindrance in the substrate is severe and an  $S_N2$  reaction can't even take place. Elimination is highly favored, especially at higher temperatures, and any substitution that occurs is through  $S_N1$
- Increasing the reaction temperature favors both types of elimination over substitution
- If *tert*-butoxide is used, sterics must be considered to find out which hydrogen it takes through the  $E2$  reaction
- A strong base can be  $RO^-$ ,  $RN^-$ , and the more substituted double bond is more stable

### 6.16.2 Tertiary Halides: $S_N1$ and $E1$

- $E1$  is likely in the same ways that  $S_N1$  is (eg: tertiary halides, weak base nucleophiles, polar protic solvents)
- In most unimolecular reactions, the  $S_N1$  reaction is favored over  $E1$ , especially at lower temperatures

### 6.16.3 Summary

**TABLE 6.7 Overall Summary of  $S_N1$ ,  $S_N2$ ,  $E1$ , and  $E2$  Reactions**

|                        | $CH_3X$<br>Methyl                        | $\begin{array}{c} H \\   \\ R-C-X \\   \\ H \end{array}$<br>$1^\circ$                                       | $\begin{array}{c} R \\   \\ R-C-X \\   \\ H \end{array}$<br>$2^\circ$  | $\begin{array}{c} R \\   \\ R-C-X \\   \\ R \end{array}$<br>$3^\circ$   |
|------------------------|--|---|--|---|
|                        | Bimolecular ( $S_N2/E2$ ) Reactions Only |   |  | $S_N1/E1$ or $E2$   |
| Gives $S_N2$ reactions |  | Gives mainly $S_N2$ except with a hindered strong base [e.g., $(CH_3)_3CO^-$ ] and then gives mainly $E2$ . | Gives mainly $S_N2$ with weak bases (e.g., $I^-$ , $CN^-$ , $RCO_2^-$ ) and mainly $E2$ with strong bases (e.g., $RO^-$ ). | No $S_N2$ reaction. In solvolysis gives $S_N1/E1$ , and at lower temperatures $S_N1$ is favored. When a strong base (e.g., $RO^-$ ) is used, $E2$ predominates. |

- Note: Secondary molecules can have  $S_N1$  or  $E1$  in polar protic solvents despite what it says in the textbook graphic
- Note:  $N_3^-$  and  $RS^-$  are other reactive nucleophiles/weak bases

## 7 Alkenes and Alkynes I

### 7.1 The *E* – *Z* System

- To determine *E* or *Z*, look at the two groups attached to one carbon atom of the double bond and decide which has higher priority. Then, repeat this at the other carbon atom. This system is not used for cycloalkenes
  - If the two groups of higher priority are on the same side of the double bond, the alkene is designated *Z*. If the two groups of higher priority are on opposite sides of the double bond, the alkene is designated *E*
- Hydrogenation is a syn/cis addition

### 7.2 Relative Stabilities of Alkenes

- The trans isomer is generally more stable than the cis isomer due to electron repulsions
- The addition of hydrogen to an alkene, hydrogenation, is exothermic (heat of hydrogenation)
- The greater number of attached alkyl groups, the greater the stability of an alkene

### 7.3 Synthesis of Alkenes via Elimination Reactions and Dehydrohalogenation of Alkyl Halides

#### 7.3.1 How to Favor E2

- Reaction conditions that favor elimination by E1 should be avoided due to the highly competitive  $S_N1$  mechanism
- To favor E2, a secondary or tertiary alkyl halide should be used
- If there is only a possibility for a primary alkyl halide, use a bulky base
- Use a higher concentration of a strong and nonpolarizable base, like an alkoxide
- EtONa/EtOH favors the more substituted double bond while *t*-EtONa/*t*-BuOH favors in making the less substituted double bond via elimination
  - Remember, an E2 reaction must be anticoplanar, typically seen with an RO<sup>−</sup> base like EtONa
- Use elevated temperature

#### 7.3.2 Stability of Product

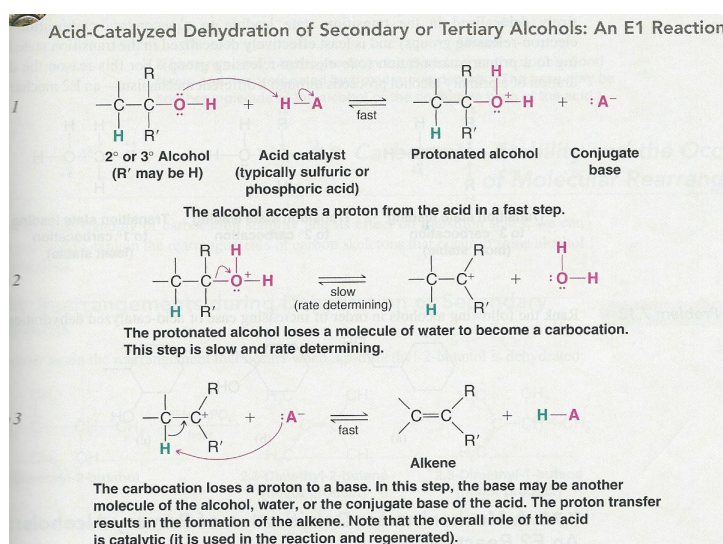
- If a small base such as ethoxide or hydroxide is used, the major product of the reaction will be the more substituted alkene<sup>16</sup>
- Whenever an elimination occurs to give the more stable, more highly substituted alkene, the elimination follows the **Zaitsev Rule**
- Carrying out dehydrohalogenations with a bulky base, such as *tert*-butoxide, favors the formation of the **less substituted alkene** due to sterics
- When an elimination yields the less substituted alkene, it follows the **Hofmann Rule**
- If there is an E2 elimination where there are two anticoplanar  $\beta$  hydrogens, the *major* product will be one that follows Zaitsev's rule

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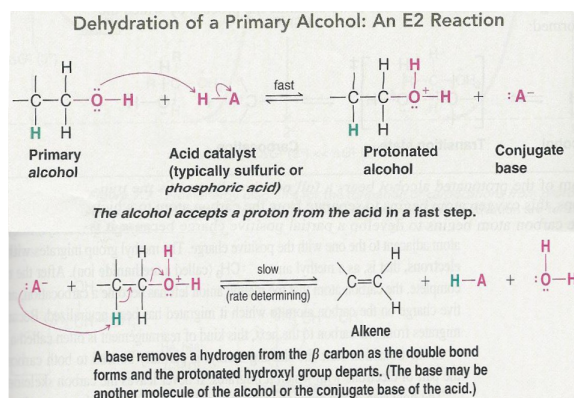
<sup>16</sup>To determine the degree of substitution, look at *both* carbon atoms of the double bond. Count how many alkyl groups are attached to *both* carbon atoms total.

## 7.4 Acid-Catalyzed Dehydration of Alcohols

- Most alcohols undergo dehydration to form an alkene when heated with a strong acid
- The temperature and concentration of acid required to dehydrate an alcohol depend on the structure of the alcohol substrate
- The relative ease with which alcohols undergo dehydration is as follows: 3° alcohol > 2° alcohol > 1° alcohol
- Some primary and secondary alcohols also undergo rearrangements of their carbon skeletons during dehydration
- The mechanism for dehydration of secondary and tertiary alcohols is an E1 reaction with a protonated alcohol substrate



- The mechanism for dehydration of a primary alcohol is an E2 reaction



- Due to the leveling effect, a strong acid in aqueous solution is effectively as a hydronium cation and will act as a catalyst that is both a reactant *and* a product

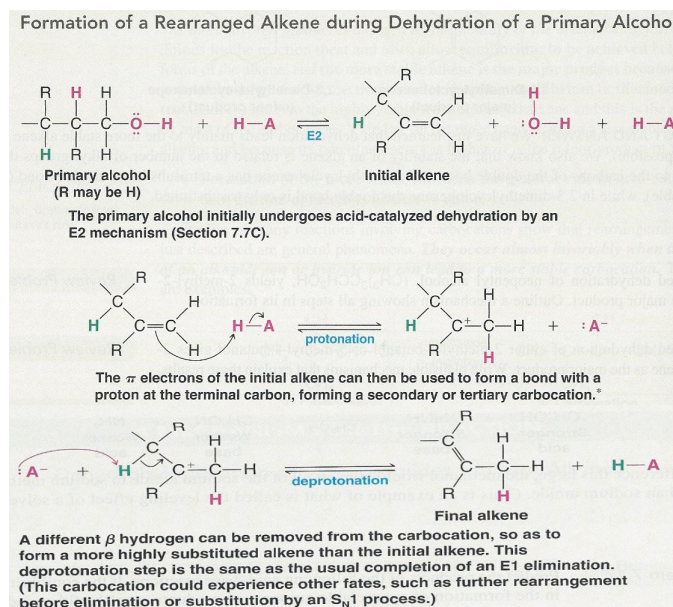


## 7.5 Carbocation Stability and the Occurrence of Molecular Rearrangements

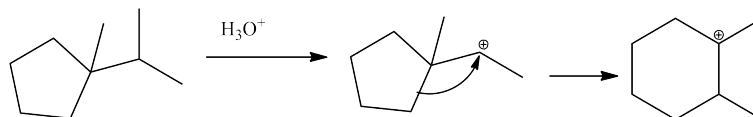
### 7.5.1 Rearrangements During Dehydration of Secondary Alcohols

- The positive formal charge shifts away from the first carbocation to the carbon that donated an alkyl anion. This is a **1,2 shift**
- The more favored product in this final step is dictated by the stability of the alkene being formed (eg: more substituted double-bonded carbons)
- Rearrangements occur naturally when the migration of an alkyl anion (alkyl anion) ion or hydride ion can lead to a more stable carbocation. *Never* do two migrations!
  - Note: When doing a hydride shift, make sure the arrow comes from the *bond* connected to the hydrogen atom and goes to the positive formal charge

### 7.5.2 Rearrangements after Dehydration of Primary Alcohols



- A ring can change in size due to a methyl shift, especially if it reduces ring strain
- Here is an alkyl rearrangement from lecture. There are two more stable products. This is the trickier one:



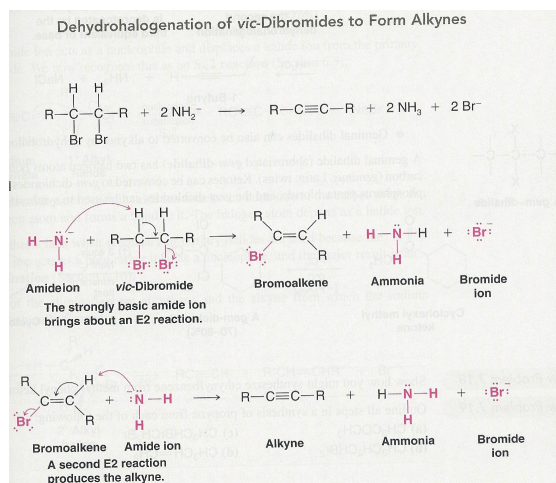
## 7.6 The Acidity of Terminal Alkynes

- The hydrogen atom bonded to the carbon of a terminal alkyne is called an **acetylenic hydrogen** and is more acidic than those bonded to carbons of an alkene or alkane (more *s* character)
- Relative Acidity: H<sub>2</sub>O > HOR > H-C≡CR > NH<sub>3</sub> > CH<sub>2</sub>=CH<sub>2</sub> > CH<sub>3</sub>CH<sub>3</sub>
- Relative Basicities: Reverse of above molecules but just deprotonated



## 7.7 Synthesis of Alkynes

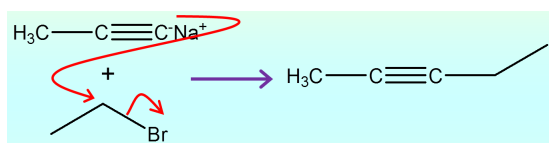
- Alkynes can be synthesized from alkanes via compounds called **vicinal dihalides**, which are compounds bearing the halogens on adjacent carbons
- This synthesis tool is quite useful after a  $\text{Br}_2$  attack to an alkene. Note that it requires the use of  $\text{NH}_2^-$ , which can frequently be found as  $\text{NaNH}_2$  with  $\text{NH}_4\text{Cl}$



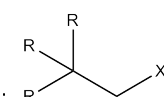
- Geminal dihalides**, which are compounds that have two halogen atoms bonded to the same carbon atom, can be converted to alkynes by dehydrohalogenation

## 7.8 Substitution of the Acetylenic Hydrogen Atom of a Terminal Alkyne

- Sodium alkynides are useful intermediates for the synthesis of other alkynes
- These syntheses can be accomplished by treating the sodium alkynide with a primary alkyl halide
- The alkynide ion acts as a nucleophile next and displaces a halide ion from the primary alkyl halide (an  $S_N2$  reaction)
- The unshared electron pair of the alkynide ion does a back-attack and  $S_N2$  proceeds. We already know this reaction mechanism from Chapter 6!



- The synthesis fails when a secondary or tertiary halide is used because the alkynide ion acts as a base rather than a nucleophile with a major result being an E2 elimination, as seen below,

- Another exception is that you *cannot* use this primary halide: 
- Note that a strong base is needed in conjunction with the primary halide

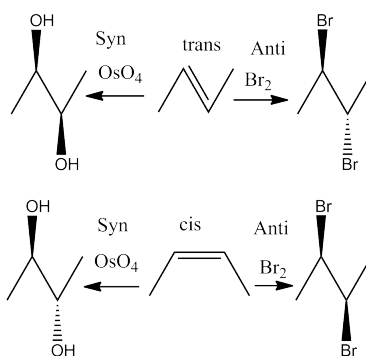
## 7.9 Hydrogenation

### 7.9.1 Overview

- Hydrogenation reactions involve finely divided insoluble platinum, palladium, or nickel catalysts
- If the catalyst is insoluble in the reaction mixture, it is **heterogeneous catalysis** while a soluble catalyst is **homogeneous catalysis**
- An **addition reaction** has a product, an alkane, that results from the addition of hydrogen to an alkene
- Alkanes are said to be **saturated compounds**
- Alkenes and alkynes, due to their  $\pi$  bonds, are said to be **unsaturated**

### 7.9.2 Specific Reactions

- Catalytic hydrogenation is, for this case, synonymous with addition reaction
- Normal metal catalyzed  $H_2$  addition to an alkyne (eg:  $H_2/Pd-C$ ) produces an alkane
- Controlled metal catalyzed  $H_2$  addition to an alkyne (eg:  $H_2$  and Lindlar's Catalyst<sup>17</sup>) produces an alkene with syn-addition (cis). This is also for  $H_2/Ni_2B(P-2)$
- Chemical reduction of an alkyne produces an alkene with anti-addition (trans). Sodium metal and liquid  $NH_3$  is one example. Another is  $Li, C_2H_5$  with  $NH_4Cl$
- Note:  $NaNH_2$  and liquid  $NH_3$  is different in that it deprotonates a terminal alkyne
- When using a hydrogenation reaction, keep the backbone the same. It will help with orientations in 3-space,



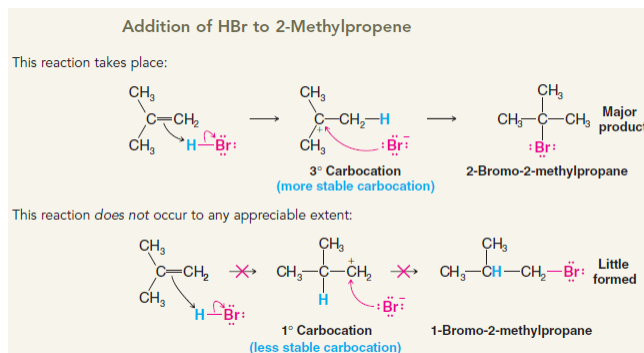
## 8 Alkenes and Alkynes II

### 8.1 Addition Reactions of Alkenes: Mechanism and Markovnikov's Rule

- Electrons in the  $\pi$  bond of alkenes react with electrophiles
- Hydrogen halides can add to the double bond of alkenes
- The order of reactivity of the hydrogen halides in alkene addition is  $HI > HBr > HCl > HF$

<sup>17</sup>Lindlar's Catalyst is  $Pd/CaCO_3/Pb$

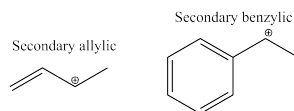
- **Markovnikov's rule** states that in the addition of HX to an alkene, the halide atom adds to the carbon atom of the original double bond with the fewer amount of hydrogen atoms. The hydrogen of HX will bond to the carbon atom of the greater amount of hydrogen atoms. This is precisely the same thing as stabilizing a carbocation intermediate by having the nucleophile go to the more substituted carbon
- More accurately, the negative portion of an unsymmetrical ionic addition reagent will bond to the carbon of the double bond with the fewer amount of hydrogen atoms while the more positive reagent will restore the stability of the carbocation
- Note that this is *not* in water. Typically, this will happen when the solvent is not listed



- A reaction is **regioselective** if it can potentially yield two or more constitutional isomers but produces a predominance of one

## 8.2 Stereochemistry of the Ionic Addition to an Alkene, Addition of Sulfuric Acid, and Allylic/Benzylic Carbocations

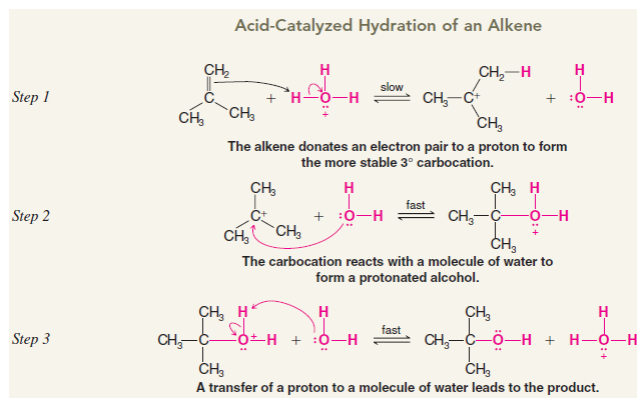
- The enantiomers are produced in equal amounts because the carbocation is trigonal planar with ionic addition to an alkene
- Addition of sulfuric acid to alkenes adds a hydroxide group onto the alkene via Markovnikov's Rule
- Resonance can stabilize a product



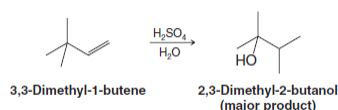
- Revised Carbocation Stability Trend:
- Methyl < Primary < Secondary  $\approx$  Primary allylic  $\approx$  Primary benzylic < Tertiary  $\approx$  Secondary allylic  $\approx$  Secondary benzylic < Tertiary allylic  $\approx$  Tertiary benzylic

## 8.3 Addition of Water to Alkenes: Acid-Catalyzed Hydration

- This, too, follows Markovnikov's Rule
- HX in H<sub>2</sub>O is the same as H<sub>3</sub>O<sup>+</sup> because HX will be a strong acid (except for HF), and the solvent is in larger quantities. An analogous reaction will occur with CH<sub>3</sub>OH that will add OCH<sub>3</sub> to the more substituted carbon because of HX dissociation

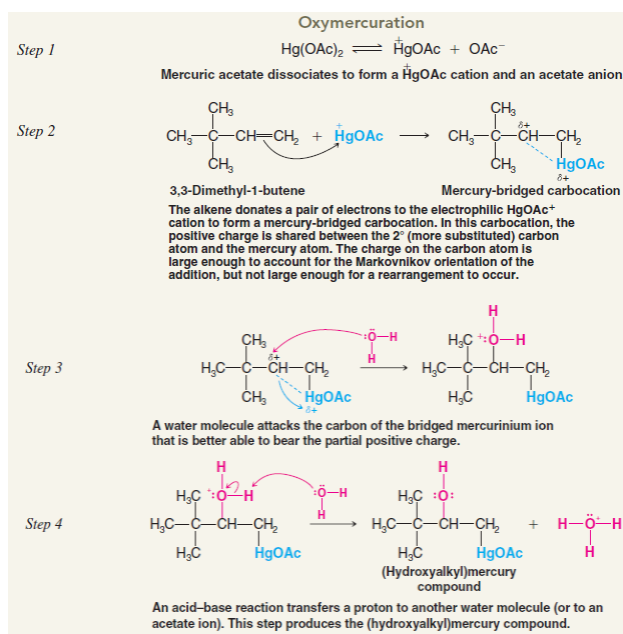


- Rearrangements occur in alkene hydration because the first step is the formation of a carbocation, so this will be rearranged to a more stable position. Example shown below:



## 8.4 Alcohols from Alkenes through Oxymercuration-Demercuration: Markovnikov Addition

- The first step, known as oxymercuration, has the water and mercuric acetate adding to the double bond
- The second step, known as demercuration, has sodium borohydride reduce the acetoxymercury group and replace it with hydrogen (note: OAc is acetate)
- Oxymercuration-demercuration follows Markovnikov's Rule
- Rearrangements rarely occur in oxymercuration-demercuration reactions
- The net result of oxymercuration-demercuration is anti addition of H and OH



## 8.5 Alcohols from Alkenes through Hydroboration-Oxidation: Anti-Markovnikov Syn Hydration

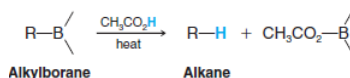
- The use of  $B_2H_6$  or a solution of  $BH_3 \cdot THF$  can cause Anti-Markovnikov hydration of a double bond
- The addition of a boron atom and a hydrogen atom to a double bond is called hydroboration
- Hydroboration-oxidation takes place with syn stereochemistry
- After hydroboration, the alkylborane intermediate is oxidized and hydrolyzed to an alcohol and boric acid
- In each addition step, the boron atom becomes attached to the least substituted carbon due to electronic and steric factors

## 8.6 Oxidation and Hydrolysis of Alkylboranes

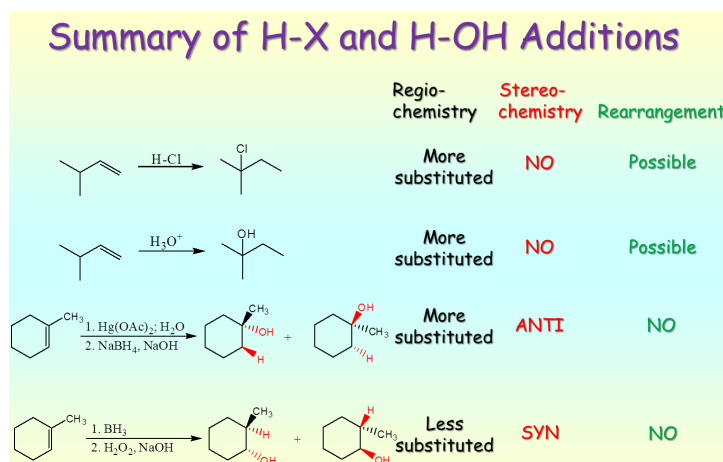
- The net result of hydroboration-oxidation is anti-Markovnikov addition of water to an alkene in the form of a hydroxyl group and hydrogen (makes an alcohol)
- Hydroboration-oxidation reactions are syn additions for the H and OH
- The hydroxyl group replaces the boron atom where it stands in the alkylboron compound

## 8.7 Protonolysis of Alkylboranes

- Hydrogen replaces the boron where it stands in the alkylborane during protonolysis of an alkylborane
- The overall stereochemistry is syn
- Requires heating an alkylborane with acetic acid



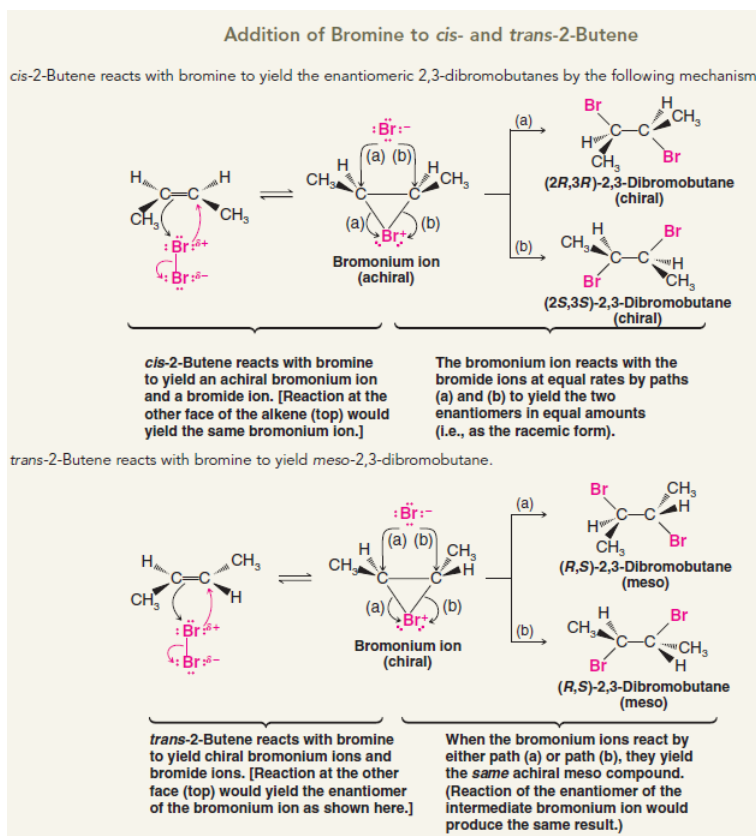
## 8.8 Summary of Alkene Hydration Methods



## 8.9 Electrophilic Addition of Bromine and Chlorine to Alkenes

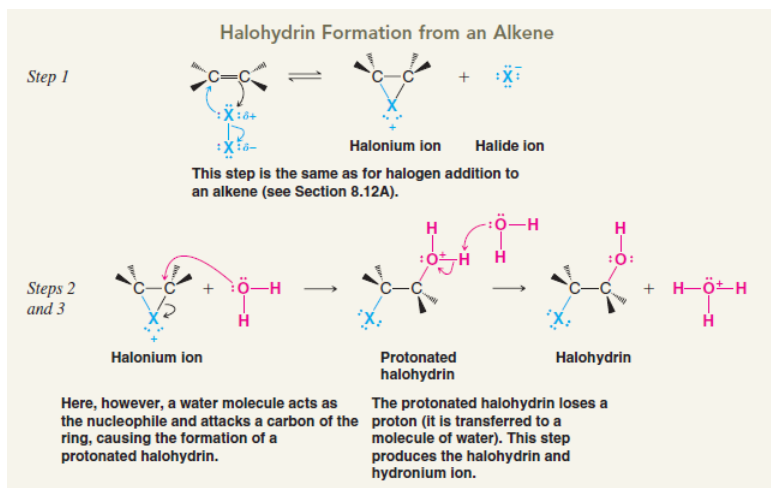
- Alkenes react rapidly with bromine or chlorine in nonnucleophilic solvents to form vicinal dihalides (anti addition)
- I personally like to think of this reaction as some bad-ass bromines attacking the life out of the carbon-carbon  $\pi$  bond. To get the most out of this attack, the bromine atoms attack from opposite sides

## 8.10 Stereospecific Reactions



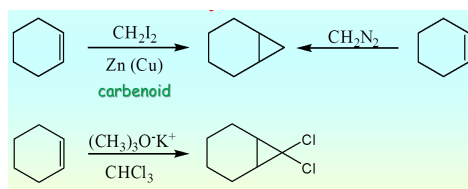
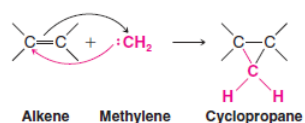
## 8.11 Halohydrin Formation

- A halohydrin (halo alcohol) is produced when the halogenation of an alkene is carried out in an aqueous solution as opposed to a nonnucleophilic solvent
- If the alkene is unsymmetrical, the halogen is added to the carbon atom with the greater number of hydrogen atoms (Anti-Markovnikov)



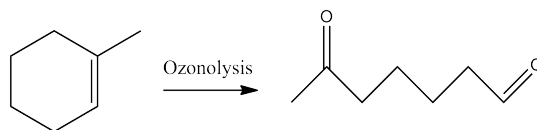
## 8.12 Divalent Carbon Compounds: Carbenes

Carbenes have carbon atoms that only form two bonds

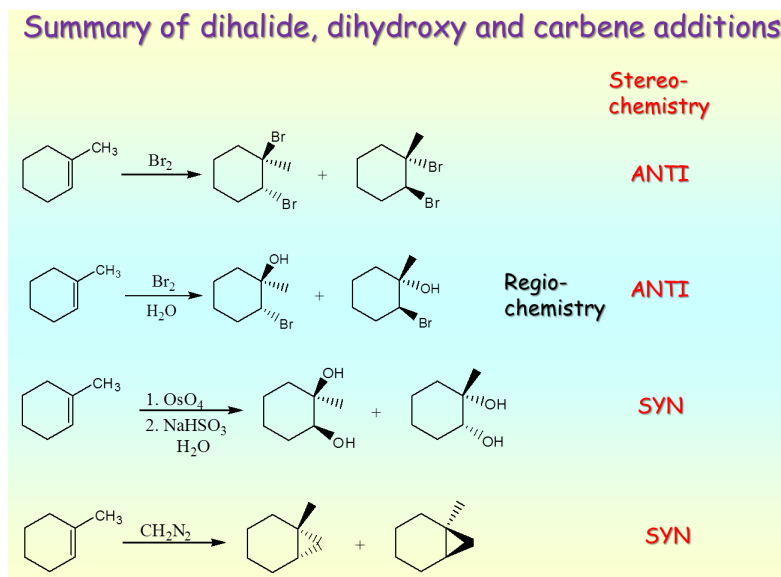


## 8.13 Oxidation of Alkenes; Oxidative Cleavage of Alkenes

- $\text{O}_3$  or  $\text{KMnO}_4$  can perform oxidative cleavage of alkenes with syn additions (useful for adding on multiple hydroxyl groups)
- Hot, basic  $\text{KMnO}_4$  cleaves the double bond of an alkene. Disubstituted alkene *carbons* are oxidatively cleaved to ketones, monosubstituted alkene carbons are cleaved to carboxylic acids, and unsubstituted alkene carbons are oxidized to carbon dioxide
- Ozone is the best method to cleave alkenes (ozonolysis)
- Ozonolysis can also open up cycloalkenes, as in this example, if inside a ring



## 8.14 Summary for Dihalide, Dihydroxy, and Carbene Additions

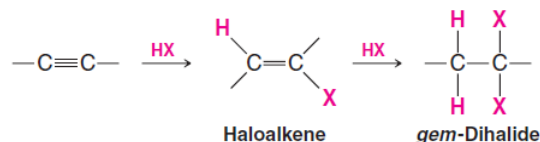


## 8.15 Electrophilic Addition of Bromine and Chlorine to Alkynes

- Alkynes show the same kind of haloaddition as alkenes (anti addition)
- Addition may occur once or twice depending upon the molar equivalents of the halogen

## 8.16 Addition of Hydrogen Halides to Alkynes

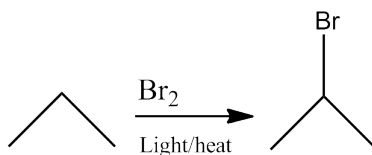
- Alkynes react with one molar equivalent of HX to form haloalkenes and with two molar equivalents to form geminal dihalides via Markovnikov's Rule



- Anti-Markovnikov addition occurs when peroxides are present

## 8.17 Oxidative Cleavage of Alkynes and Other Reactions

- Oxidative cleavage of alkynes with ozone will yield two carboxylic acids
- Br<sub>2</sub> and heat/light can perform the following halogen addition (only for synthesis) to the more substituted carbon of an alkane,



- HBr with a peroxide (ROOR) will have the bromine added to the least substituted carbon of an alkene



## 8.18 Alkene Addition Reaction Summary

| Summary and Review Tools                               |  |   |                        |                                       |                      |                             |          |
|--|--|---|------------------------|---------------------------------------|----------------------|-----------------------------|----------|
| Mechanism Review: Summary of Alkene Addition Reactions |  |   |                        |                                       |                      |                             |          |
|  | Reaction Conditions  | Electrophile  | Nucleophile            | Key Intermediates or Transition State | Regiochemistry       | Stereochemistry of Addition | Product* |
| <b>Hydrohalogenation</b>                               | H—X  | $\delta^+ \text{H} - \delta^- \text{X}^-$             | $:\ddot{\text{X}}^-$   |                                       | Markovnikov          | Not controlled              |          |
| <b>Hydration (acid cat.)</b>                           | Cat. HA, H <sub>2</sub> O  | $\text{H} - \overset{\delta+}{\text{O}}^+ - \text{H}$ | $\text{H}_2\text{O}$   |                                       | Markovnikov          | Not controlled              |          |
| <b>Halogenation</b>                                    | X <sub>2</sub><br>(non nucleophilic solvent)   | $\delta^+ \text{X} - \delta^- \text{X}^-$             | $:\ddot{\text{X}}^-$   |                                       | Not applicable       | Anti                        |          |
| <b>Halohydrin Formation</b>                            | X <sub>2</sub> , ROH; R = H or C<br>(nucleophilic solvent)                                     | $\delta^+ \text{X} - \delta^- \text{X}^-$             | $\text{ROH}$           |                                       | Markovnikov          | Anti                        |          |
| <b>Oxymercuration-Demercuration</b>                    | (1) Hg(OAc) <sub>2</sub> , HOR;<br>THF (R = H or C)<br>(2) NaBH <sub>4</sub> , OH <sup>-</sup> | HgOAc   | $\text{ROH}$           |                                       | Markovnikov          | Not controlled              |          |
| <b>Hydroboration-Oxidation</b>                         | (1) BH <sub>3</sub> :THF<br>(2) H <sub>2</sub> O <sub>2</sub> , HO <sup>-</sup>                | $\text{H} - \text{B} - \text{H}$                      | $\text{H}_2\text{O}_2$ |                                       | Net anti-Markovnikov | Syn                         |          |
| <b>1,2-Dihydroxylation</b>                             | (1) OsO <sub>4</sub><br>(2) aq NaHSO <sub>3</sub>  |   |                        |                                       |                      | Syn                         |          |

\*The generic alkene chosen has a substitution pattern that allows both regiochemistry and stereochemistry of the products to be discerned.

\*The products are formed as a mixture of enantiomers in each case.

## 9 Alcohols and Ethers

### 9.1 Structure and Nomenclature

- The common naming names alcohols as alkyl alcohols (eg: methyl alcohol)
- The common names of ethers have the groups attached to the oxygen atom listed in alphabetical order followed by the word “ether” (eg: Ethly methyl ether)
- The RO group is called an alkoxy group (eg: OCH<sub>3</sub> is methoxy)

### 9.2 Physical Properties of Alcohols and Ethers

- Ethers have boiling points that are roughly comparable with those of hydrocarbons of the same molecular weight (unlike alcohols, which have higher)
- Ethers can form hydrogen bonds with other molecules (eg: water) but not with other ethers and are, therefore, similarly soluble to those of alcohols of the same molecular weight

### 9.3 Synthesis of Alcohols from Alkenes

- Well, here's where you cry yourself a river if you don't remember (or want to remember) acid-catalyzed hydration of alkenes, oxymercuration-demercuration, and hydroboration-oxidation reactions
- What's different about this chapter is that the starting reactants are alcohols, not alkenes/alkynes

### 9.4 Reactions of Alcohols

- The reactions of alcohols has to do with improving the poor nature of the hydroxyl leaving group
- Protonation of the alcohol converts a poor leaving group (eg: OH) into a good one (eg: H<sub>2</sub>O)
- In H<sup>+</sup>, the hydroxyl group is protonated, becomes a good LG, and a nucleophile substitutes on
- If the nucleophile is ROH, OR substitutes on to make an ether

### 9.5 Alcohols as Acids

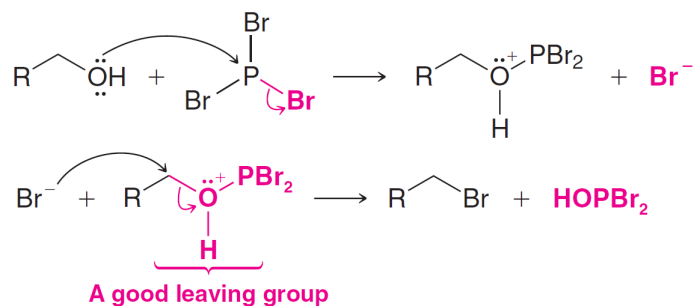
- Alcohols are about as acidic as water
- Sterically hindered alcohols are less acidic/more basic
- All alcohols are stronger acids than terminal alkynes, hydrogen, ammonia, and alkanes
- Conjugate bases of compounds with higher  $pK_a$  values than an alcohol will deprotonate it

### 9.6 Alkyl Halides from the Reaction of Alcohols with Hydrogen Halides

- 2°, 3°, allylic, and benzylic alcohols go through an S<sub>N</sub>1 reaction with the protonated alcohol acting as the substrate when reacted with concentrated HX
- 1° alcohols and methanol react to form alkyl halides in concentrated HX by an S<sub>N</sub>2 mechanism where the halide anion substitutes for the water molecule LG
- Rearrangements still typically occurs here, as we've done time and time again in Chapter 8
- Racemic mixtures are produced due to the creation of the carbocation
- Elimination does not occur due to the high concentration of X<sup>-</sup> anions in the concentrated HX solution

### 9.7 Alkyl Halides from the Reaction of Alcohols with PBr<sub>3</sub> or SOCl<sub>2</sub>

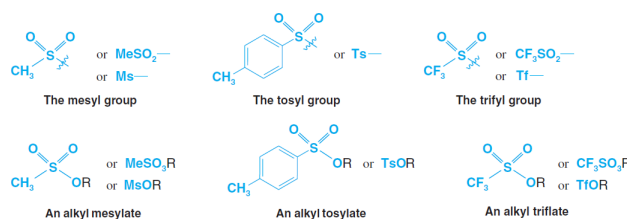
- PBr<sub>3</sub> or SOCl<sub>2</sub> can be used to convert a 1° or 2° alcohol to a leaving group without worrying about rearrangement
- The reaction of an alcohol with PBr<sub>3</sub> does not involve the formation of a carbocation, and, therefore, does *not* go through rearrangement
- $3\text{ROH} + \text{PBr}_3 \longrightarrow 3\text{RBr} + \text{H}_3\text{PO}_3$ , only where ROH is 1° or 2°



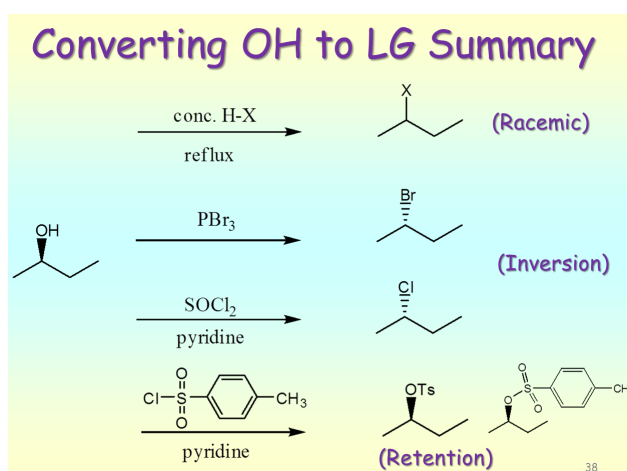
- $\text{SOCl}_2$  converts  $1^\circ$  and  $2^\circ$  alcohols to alkyl chlorides with  $\text{C}_2\text{H}_5\text{N}$  (pyridine) included to promote the reaction
- **Inversion of configuration occurs** with  $\text{PBr}_3$  and  $\text{SOCl}_2$  since it's  $\text{S}_\text{N}2$

## 9.8 Tosylates, Mesylates, and Triflates: Leaving Group Derivatives of Alcohols

- The hydroxyl group of an alcohol can be converted to a good LG by conversion to a sulfonate ester derivative like the ones shown below,



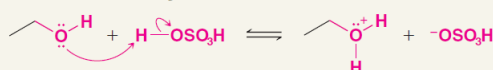
- We can prepare sulfonate esters with DMAP or pyridine and the chlorinated sulfonate derivative
- There is **retention of configuration** in the formation of a sulfonate ester because the C-O bond is not involved, as with pyridine



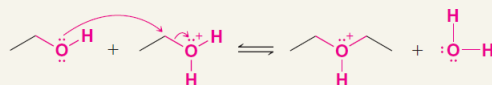
## 9.9 Synthesis of Ethers

- Alcohols can dehydrate to form alkenes, as done in Chapter 7. Also,  $1^\circ$  alcohols can dehydrate to form ethers

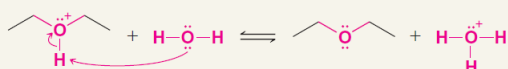
### Intermolecular Dehydration of Alcohols to Form an Ether



This is an acid-base reaction in which the alcohol accepts a proton from the sulfuric acid.



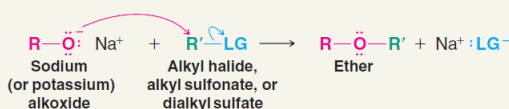
Another molecule of the alcohol acts as a nucleophile and attacks the protonated alcohol in an  $S_N2$  reaction.



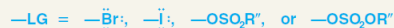
Another acid-base reaction converts the protonated ether to an ether by transferring a proton to a molecule of water (or to another molecule of the alcohol).

- Alkenes form too easily for  $2^\circ$  and  $3^\circ$  alcohols to form ethers
- Acid-catalyzed dehydration is not useful for preparing unsymmetrical ethers from different  $1^\circ$  alcohols because the reaction leads to a mixture of products ( $ROR$ ,  $ROR'$ , and  $R'OR'$ )
- A **Williamson Synthesis** converts the hydroxyl group to an alkoxide ion

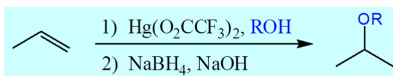
### The Williamson Ether Synthesis



The alkoxide ion reacts with the substrate in an  $S_N2$  reaction, with the resulting formation of an ether. The substrate must be unhindered and bear a good leaving group. Typical substrates are  $1^\circ$  or  $2^\circ$  alkyl halides, alkyl sulfonates, and dialkyl sulfates, that is,

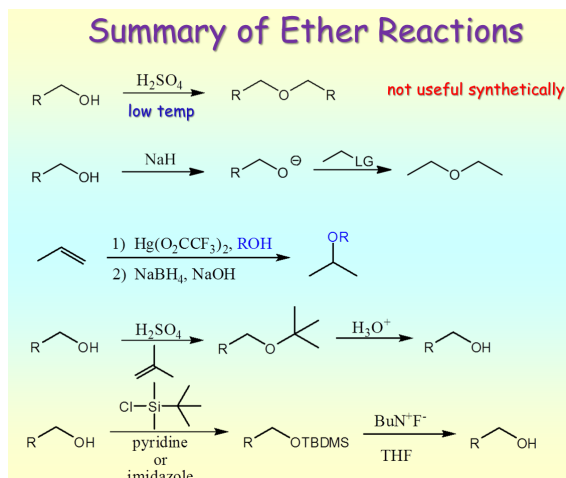


- When NaH is a reactant, the hydride anion acts as a base to form hydrogen gas thus turning the alcohol into a good nucleophile with  $\text{O}^-$
- Alkoxymercuration-demercuration is a method for synthesizing ethers directly from alkenes, like in the example below, and parallels oxymercuration-demercuration

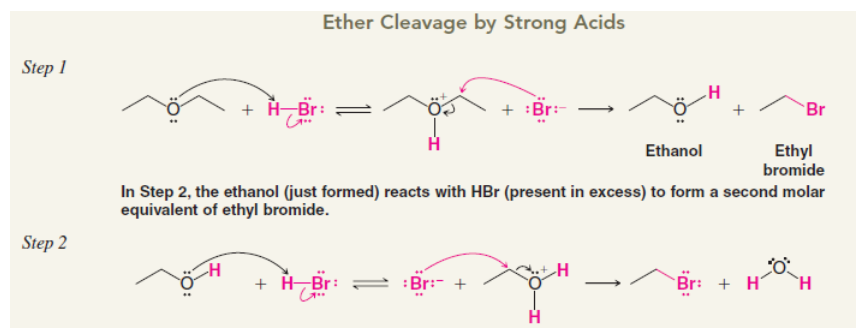


- An OH group can be protected by converting the alcohol to a temporary ether
- The reaction of 2-methylpropene and  $\text{H}_2\text{SO}_4$  with a primary alcohol can create a *tert*-butyl ether where the bulky substituent is a protecting group of the hydroxyl group
- Note: MTBE stands for methyl *tert*-butyl ether
- The protecting group can be removed if treated with  $\text{H}_3\text{O}^+$
- A hydroxyl group can also be protected by converting it to a silyl ether group with TBDMS-Cl (chicken-footed silicon structure) as a reactant
- A fluorine anion in THF will knock out the protecting group

## 9.10 Ether Summary

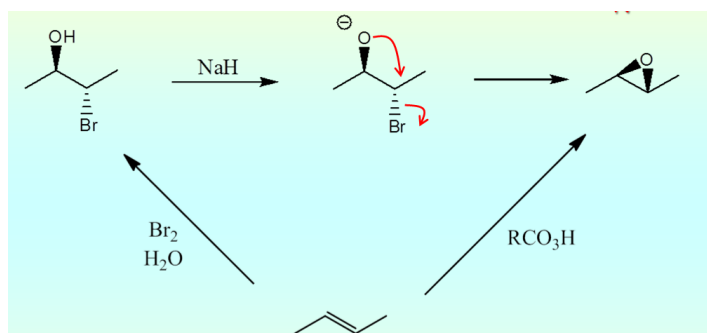


## 9.11 Ether Cleavage



## 9.12 Epoxides; Anti 1,2, Dihydroxylation of Alkenes Via Epoxides

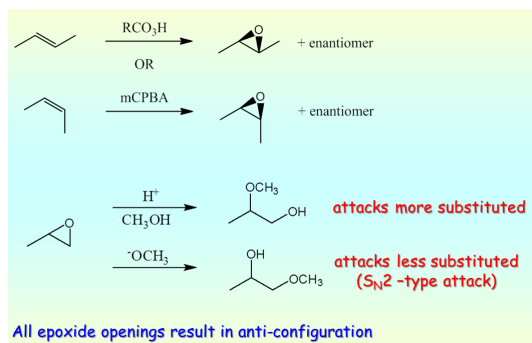
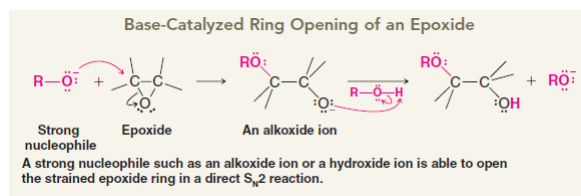
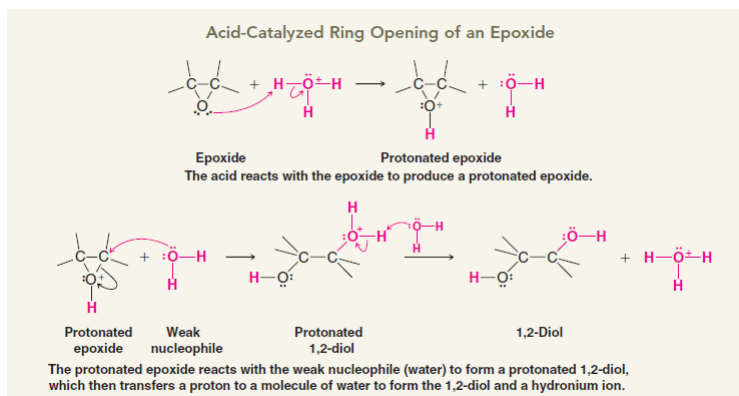
- Epoxides are cyclic ethers with three-membered rings and can be prepared with an intramolecular  $S_N2$  attack



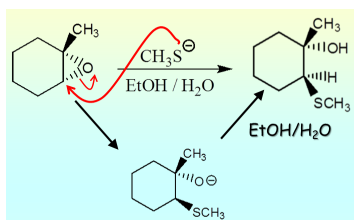
- For this reaction to occur, make sure the stereochemistry of the reactant is in a way that can allow for a center of inversion of, what was originally, the halide atom
- Epoxidation is a syn addition that is stereospecific
- $RCO_3H$  can be used to make an epoxide from an alkene (syn)

## 9.13 Reactions of Epoxides

- Two Types: Acid-Catalyzed and Base-Catalyzed (both ring-opening and anti-configuration)
- BLAM: Basic = Less Substituted      Acidic = More Substituted
- The acid-catalyzed ring opening is analogous to a halohydrin reaction ( $\text{Br}_2$  in ROH)



- The following is an example of an epoxide reaction with stereochemistry shown,



## 10 Alcohols from Carbonyl Compounds

### 10.1 Structure of the Carbonyl Group

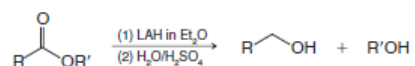
- Carbonyl compounds can go through nucleophilic addition where a pair of electrons from the C=O double bond moves up to the oxygen atom to make a negative formal charge and the nucleophile bonds to the carbon atom
- Hydride ions and carbanions are important nucleophiles in these reactions
- RedOx reactions also occur with carbonyl compounds

### 10.2 Oxidation-Reduction Reactions in Organic Chemistry

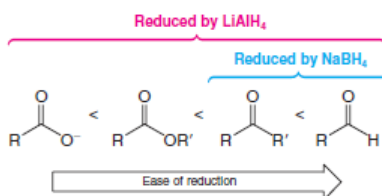
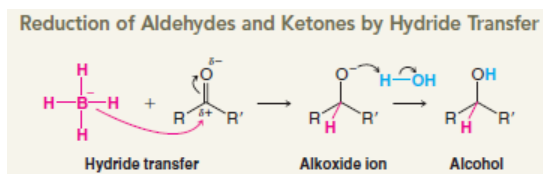
- Reduction to an organic molecule typically involves increasing hydrogen content or decreasing oxygen content
- Oxidation typically occurs with increasing oxygen content or decreasing hydrogen content
- The symbol [H] refers to reduction while [O] refers to oxidation

### 10.3 Alcohols by Reduction of Carbonyl Compounds

- Reduction converts a carboxylic acid to a primary alcohol by taking off an oxygen from C=O
- Reduction converts an ester into two 1° alcohols, one derived from the carbonyl part of the ester group, and the other from the alkoxy part of the ester
- Reduction converts a ketone to a 2° alcohol and an aldehyde to a 1° alcohol



- Aldehydes and ketones are easily reduced by NaBH<sub>4</sub>

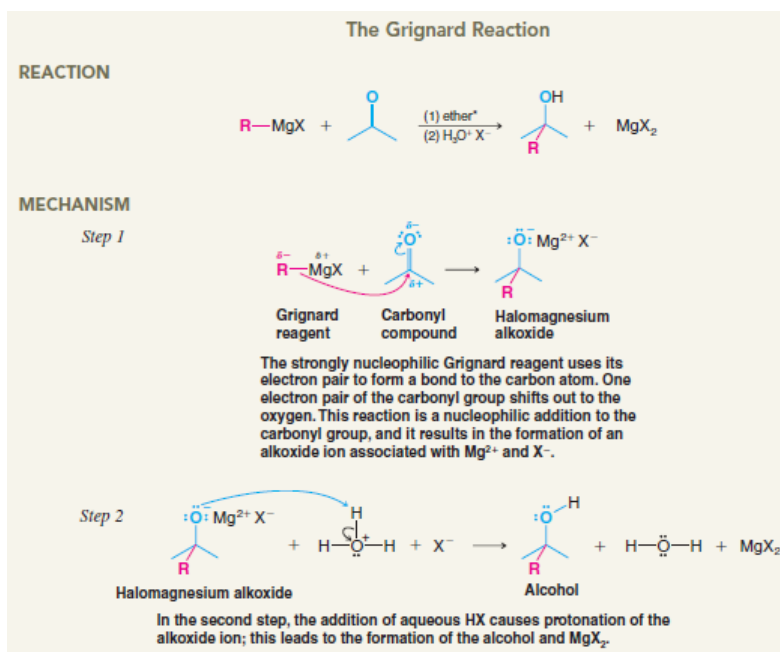


## 10.4 Oxidation of Alcohols

- 1° alcohols can be oxidized to aldehydes and carboxylic acids
- PCC will convert a 1° alcohol to an aldehyde and oxidize a 2° alcohol to a ketone. NOT 3°.
- $\text{KMnO}_4$  or  $\text{H}_2\text{CrO}_4$  (Jones Reagent) can oxidize a 1° alcohol to a carboxylic acid
- Oxidizing agents based on Cr(VI) can oxidize a 2° alcohol to a ketone. One example is  $\text{H}_2\text{CrO}_4$

## 10.5 Organometallic Compounds; Grignard Reagents

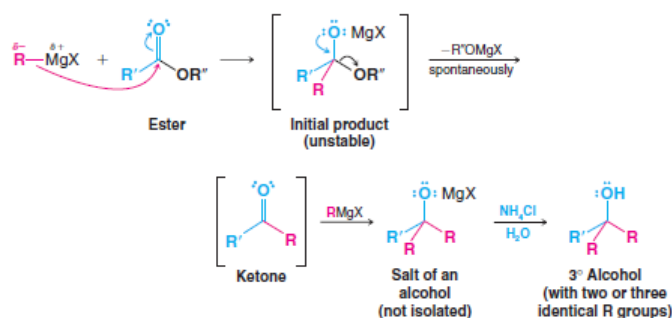
- Organometallic compounds contain carbon-metal bonds
- The general reaction to create organolithium compounds is,  $\text{RX} + 2\text{Li} \longrightarrow \text{RLi} + \text{LiX}$
- Grignard reagents are organomagnesium halides and are prepared by,  $\text{RX} + \text{Mg} \longrightarrow \text{RMgX}$
- Grignard Reagents react with any compound that has a hydrogen attached to an atom of high electronegativity (eg: oxygen, nitrogen, sulfur, etc.)
- Grignard Reagents react well with compounds that have carbonyl groups



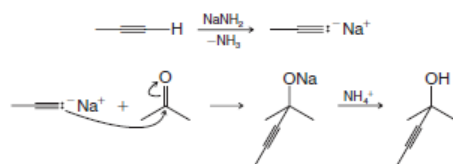


## 10.6 Alcohols from Grignard Reagents

- When a Grignard reagent adds to the carbonyl group of an ester, the initial product breaks down to a ketone. Then, the ketone reacts with the excess Grignard reagent and then goes through hydrolysis to form a tertiary alcohol with two identical alkyl groups



- It is not possible to prepare a Grignard reagent from a compound that contains any hydrogen more acidic than the hydrogen atoms of an alkane or alkene
- We're essentially limited to alkyl halides or analogous organic halides containing carbon-carbon double bonds, intermolecular triple bonds, ether linkages, and NR<sub>2</sub> groups
- Acetylenic Grignard reagents can be made by allowing terminal alkynes to react with alkyl Grignard reagents (similar to what we did with NaNH<sub>2</sub>)
- Organolithium reagents react with carbonyl compounds in the same way as Grignard reagents
- Sodium alkynides react with aldehydes and ketones to yield alcohols



## 10.7 Protecting Groups

- Protecting groups can be used to perform a Grignard synthesis with a compound that has a relatively acidic hydrogen by protecting that group and then taking off the protecting group with a fluoride anion