Chapter 1
Introduction to Organic Compounds

Concepts introduced in chapter 1:

1) Covalent versus Ionic bonding

Bonds in organic compounds are typically "covalent" bonds
-electrons are shared between two atoms

Vastly different than bonds between metals which are often ionic bonds
-atoms held together only by electrostatic interactions between opposite charges

H_3C ⬭ CH_3 $Na\oplus$ $\ominus$ $:Cl$

2)   Drawing Organic Compounds

There is a shorthand way to draw organic structures without
needing to explicitly indicate every atom
-the carbon framework is assumed to be saturated unless a double or triple bond is indicated
therefore must be enough hydrogens attached to each carbon to achieve this saturation
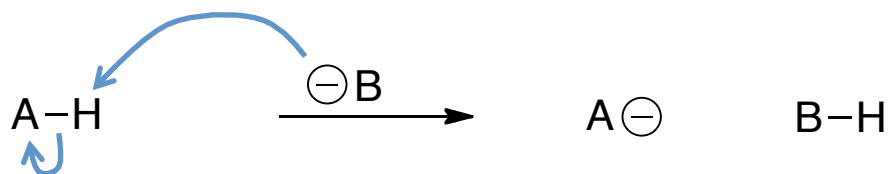

$CH_3CHBrCH_2CH_2CH_3$
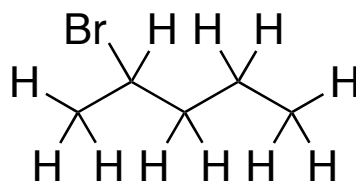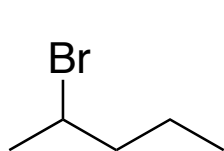
Can also draw structure in formula designation
-need to read from left to right
-becomes highly complicated as structure becomes larger

3)   Acid/Base Reactions

For organic compounds the key in acid/base reactions is predicting
the stability of the charged forms generated

$$A-H \qquad \overset{\ominus B}{\longrightarrow} \qquad A\ominus \qquad B-H$$

As the anion becomes more stable, the conjugate acid is more acidic

The stability is determined by how stable is the negatively charged structure
-anything that can stabilize the anion will make the conjugate more acidic

4)   Resonance

One way to stabilize negatively charged structures is through resonance

Resonance is whenever a charged can be delocalized over more than one atom

Need to have p orbitals in conjugation over continuous atoms to allow resonance to occur

Orbital picture   line angle drawing
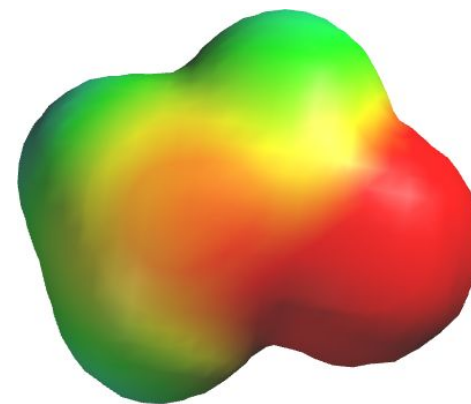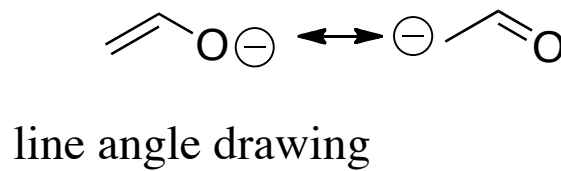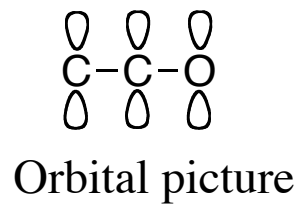
Excess electron density is on
terminal carbon and oxygen

Electrons must move in pairs

5)   Inductive Effect

Another way to stabilize charge is through an inductive effect
-inductive means "through bond"

While bonds are covalent in organic compounds, the electrons need not be shared equally
-a more electronegative atom will pull electrons closer to itself on time average

These bond dipoles can cause an inductive effect in a molecule by stabilizing charges
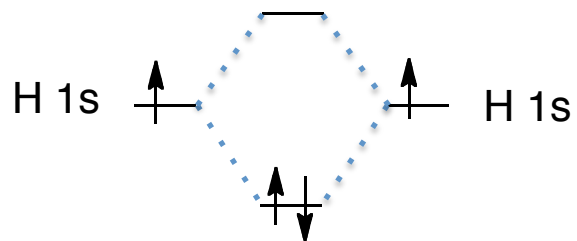elsewhere in the compound
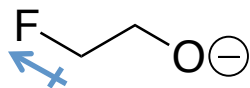
A strong dipole will also affect the neighboring bond

Inductive effects are highly dependent upon the strength of a bond dipole and also the
distance the bond is away from the charged site

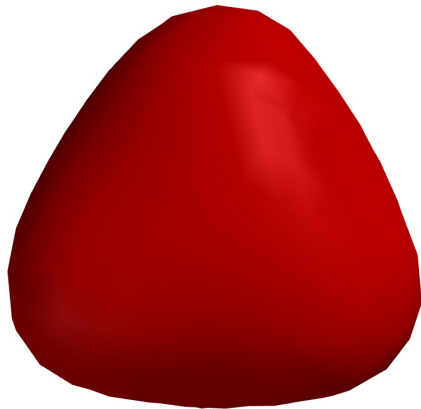Molecular Orbitals are formed by combining Atomic Orbitals
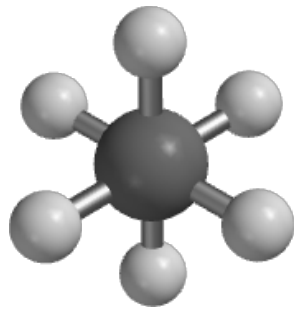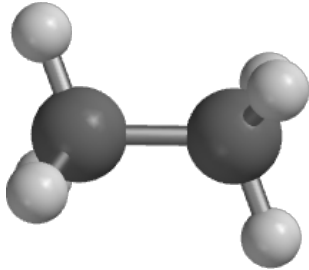
H 1s ⇡ ⟍⟋ ⇡ H 1s

Once atomic orbitals combine,
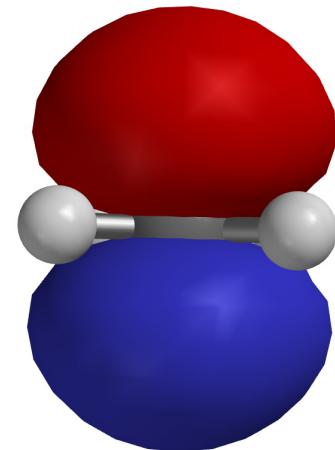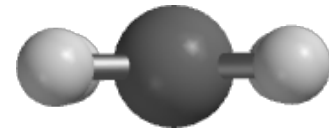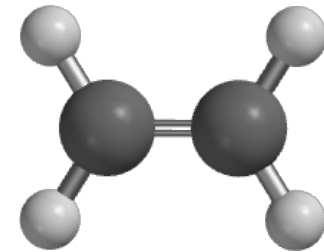they can form both bonding and antibonding molecular orbitals

Bonding

Two types of bonds can be formed
(sigma and pi bonds)

ethane

ethylene

Rotate molecules

Electron density symmetric
upon rotation
(sigma bond)
Electron density unsymmetric
upon rotation
(pi bond)

Hybrid Orbitals

In addition to atomic orbitals combining to form molecular orbitals,
atomic orbitals can first combine to form "hybrid" orbitals
which are then used to form molecular orbitals

The hybrid orbitals are a mathematical combination of the atomic orbitals
(the spatial orientation of an orbital is described by its "wave equation",
the hybrid orbitals are thus merely a result of combining these wave equations)

There are thus 3 types of hybrid orbitals that can form with 2nd row atoms:

$$1s + 1p = sp$$
$$1s + 2p = sp^2$$
$$1s + 3p = sp^3$$
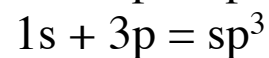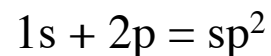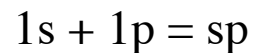
Molecular Geometry from Bonding

If we know what orbitals are being used to form a bond,
then we can predict the geometry of the resulting structure

Because the hybrid orbitals are a mathematical combination of the wave equations,
the geometry can be predicted

Atomic s orbital

combine

Atomic p orbital

With 2 atomic orbitals,
obtain 2 hybrid orbital
-each orbital 180° apart
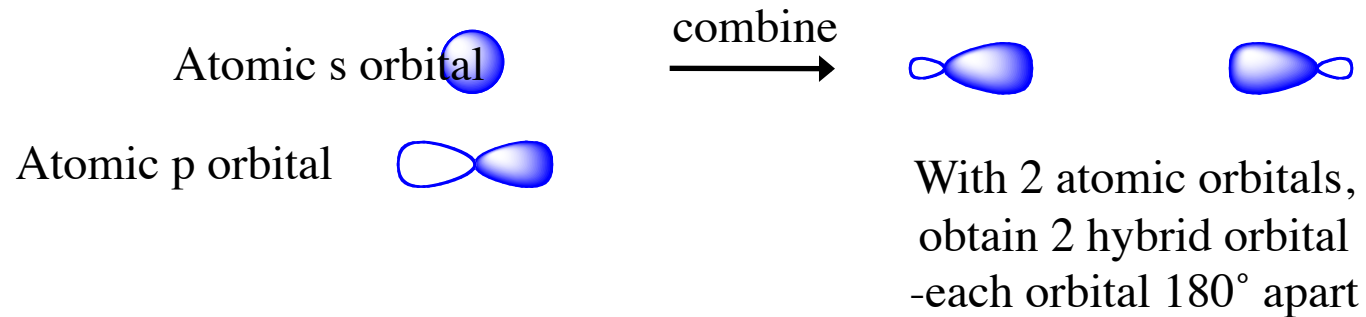
Can perform same operation to obtain 3 sp^2 hybrid orbitals (120° apart)
and 4 sp^3 hybrid orbitals (109.5° apart)

Chapter 3
Alkanes and Cycloalkanes

Knowing the geometry of a compound through the orbitals used to form bonds,
the structure of alkanes can be predicted

The naming of alkanes follow some straightforward rules:

Find the longest continuous carbon chain
-the length of the chain determines the root name

If all carbons are saturated then the compound is an alkane and use –ane suffix

Any atoms not part of the main chain are substituents and are named using the same rules

All substituents are placed in front of the root name in alphabetical order
(using a number to indicate which atom of the main chain the substituent is attached)

Conformers

A key aspect to organic compounds is that they are not static
-the compounds can rotate about bonds causing the formation of "conformers"

The distribution of conformers is controlled by Gibb's free energy
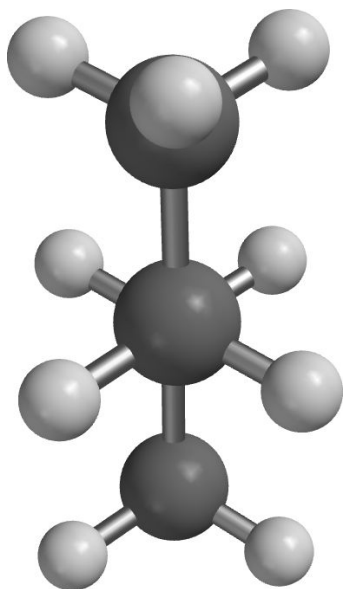depending upon the energy of each conformer

The most stable conformer is thus the low energy conformation
and it has the highest concentration
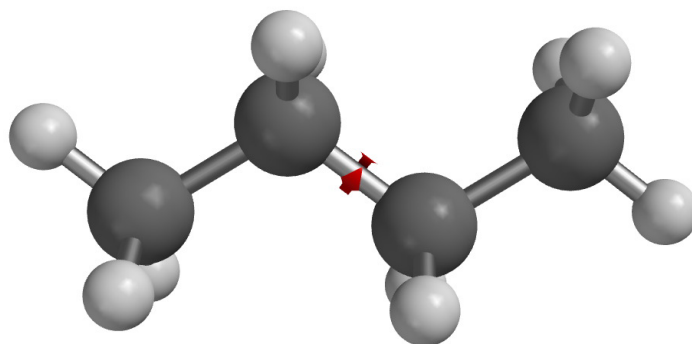
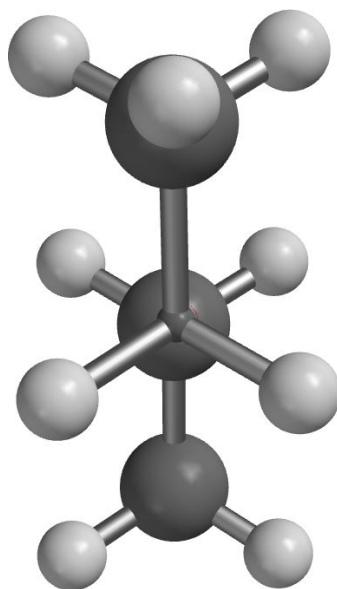# Newman Projections

In order to indicate which conformer is being discussed Melvin Newman
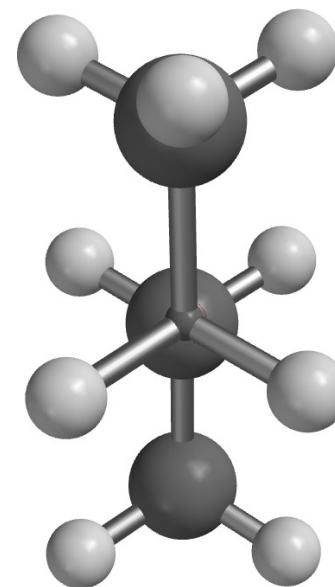invented the use of "Newman" projections

Convenient method to compare conformers
-draw conformer looking down one bond

Anti conformation of
n-butane

In Newman, front carbon
is point with substituents
to front carbon attached
to this point

Upon rotation, can detect
staggered and eclipsed
conformations

Cycloalkanes

With rings, cannot rotate freely about a carbon-carbon bond
due to the steric constraints of the ring

Cycloalkanes adopt certain low energy conformations

With a cyclohexane, the low energy conformation is called a "chair" conformation

In a chair conformation, substituents can be placed in either "equatorial" or "axial" positions

Axial
position

Equatorial
position

chair-chair
interconversion

Bromocyclohexane
-low energy conformation
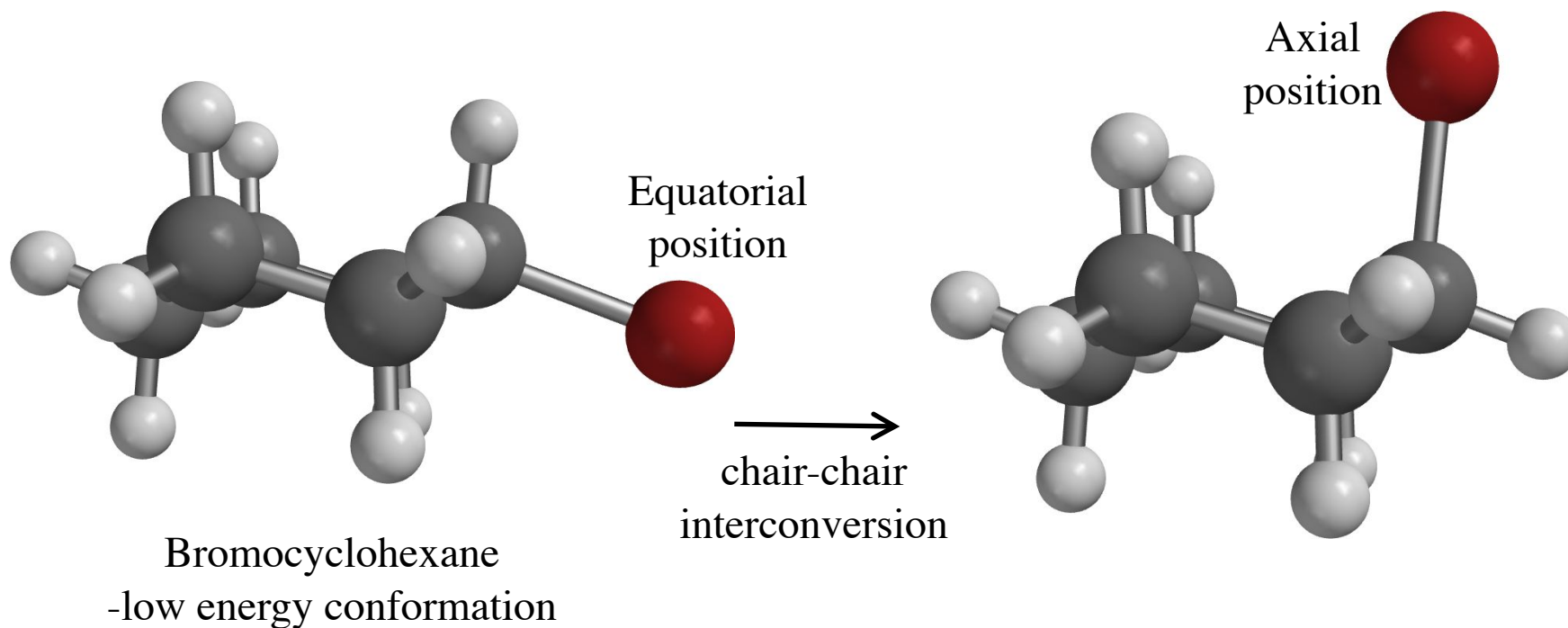
Chapter 5
Stereoisomers

In addition to compounds having conformers, some compounds are chiral
(chiral means "handedness")

An isomer means two compounds that possess the same molecular formula
-a constitutional isomer has the atoms bonded to different positions
-a stereroisomer has all the atoms bonded to same other atoms,
but there is a different three dimensionality between the isomers

Due to the sp^3 hybridization of carbon atoms,
some compounds are not superimposable with their mirror images causing stereoisomers

For a carbon atom, this means there must be 4 different substituents attached
(if two substituents are identical, then there would be an internal mirror plane)

Types of Stereoisomers

The three dimensional relationship between two stereoisomers
determines the type of relationship

If the two stereoisomers are nonsuperimposable mirror images,
then the stereoisomers are enantiomers

mirror

F

H₃C ⸺ Br

Cl

F

H₃C ⸺ Cl

Br
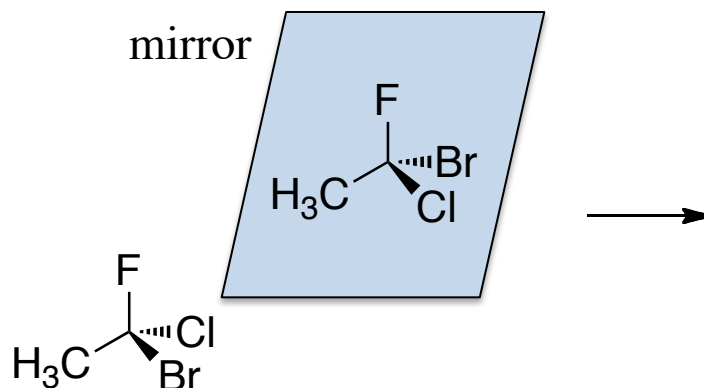
Two images are not
superimposable

If the two stereoisomers are not related by a mirror image, however,
then the stereoisomers are called diastereomers

Enantiomers have identical energy, but diastereomers are often quite different

Naming of Stereocenters

Cahn-Ingold-Prelog developed a naming system to label chiral atoms

The chiral atom is labeled either R or S
(*atom not the molecule)

To label chiral atom:
-prioritize substituents attached to chiral atom by molecular weight
-if there is a tie, continue with adjacent atoms until the tie is broken
-view atom with the lowest priority substituent towards the back
-determine if the remaining three substituents are placed clockwise or counterclockwise
when connecting first, second and then third priority substituent
-Clockwise is R (Rectus, to the right) and counterclockwise is S (Sinister, to the left)
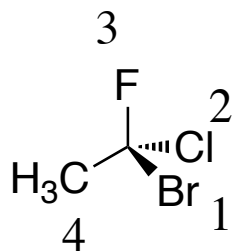

Prioritize substituents
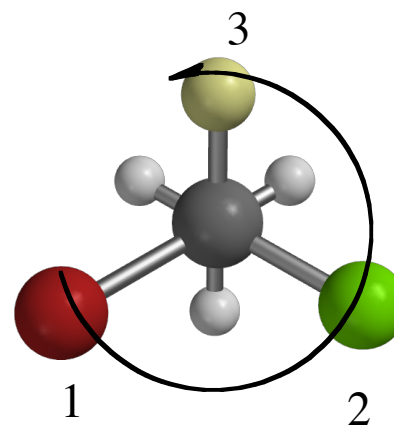
Look down bond
to lowest priority

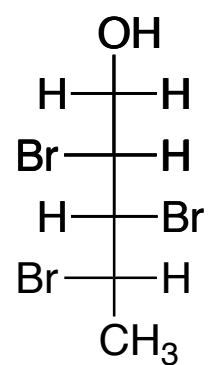Have counterclockwise
rotation, therefore S

Fischer Projections

Another tool to represent chiral compounds is to use a Fischer Projection
(very useful for extended carbon chains with multiple chiral centers)

Each horizontal cross point is coming out of the page toward viewer
Each vertical line represents extended carbon chain going away from viewer

View first
chiral center
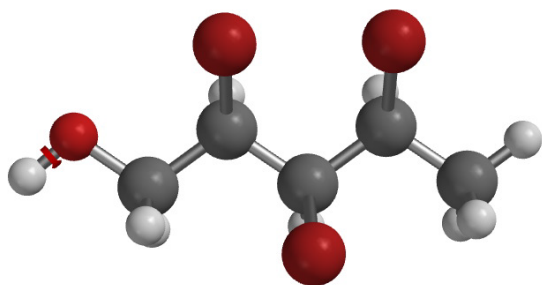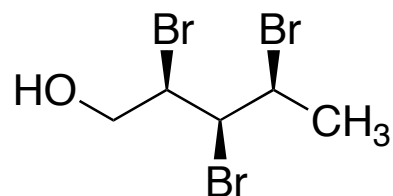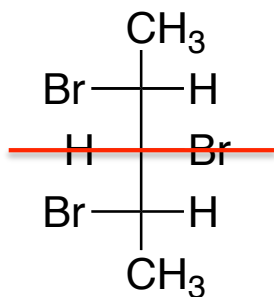
View second
chiral center
after rotation

View third
chiral center
after rotation

Need to rotate molecule so extended
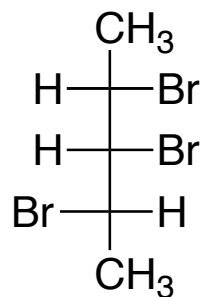carbon chain is along vertical axis

Meso Compounds

Another type of stereochemical relationship is called a MESO compound
-these compounds have chiral atoms, but the molecule is not chiral

There is an internal plane of symmetry

```
        CH3                         CH3
  Br ——— H                   H ——— Br
   H     Br                   H     Br
  Br ——— H                   Br ——— H
        CH3                         CH3

      Meso                      Diastereomer
```
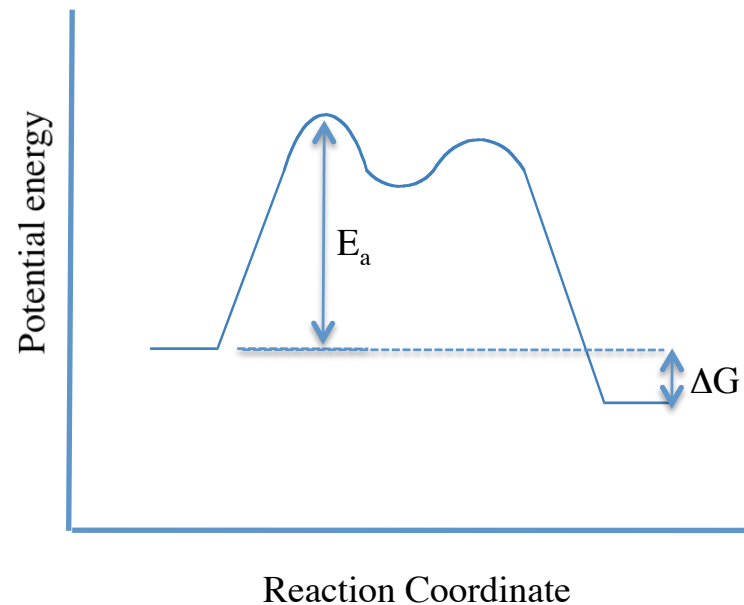
Information for reaction is included in a potential energy diagram

The kinetics is determined by the energy barrier for highest barrier

The thermodynamics are determined by the energy barrier between products and starting materials
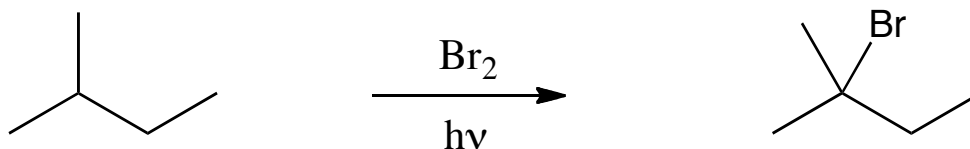

For any reaction therefore, the rate is dependent upon the structures along the highest energy barrier
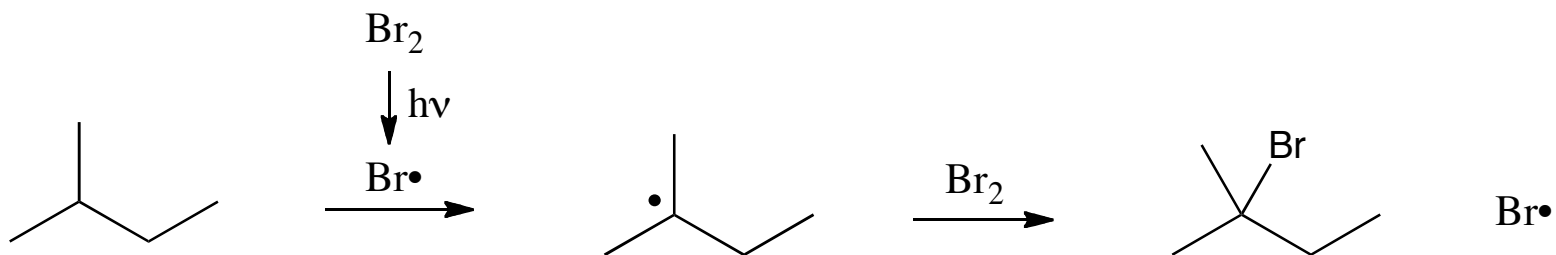If we know these structures we can predict how to increase the rate of a reaction

Halogenation Reaction

One type of reaction studied in chapter 4 is the halogenation of alkanes

Reaction proceeds through a radical intermediate

Reactivity versus Selectivity

In the halogenation reaction, we observe for the first time
the almost universal statement in organic chemistry –
"as reaction becomes faster, it is less selective"

Reactivity and selectivity are inversely related

In halogenation reactions, chlorine is faster than bromine,
therefore chlorination is less selective than bromination
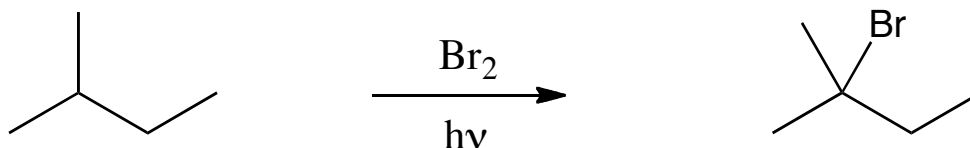
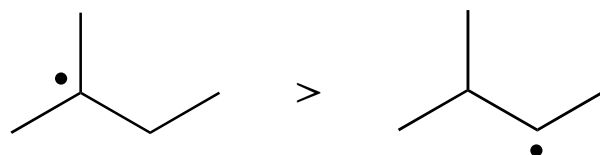Only most stable radical site is produced (selective)
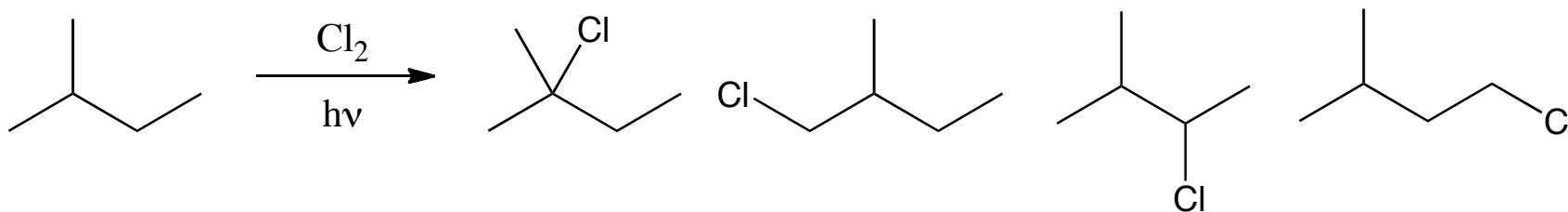
All radical sites are produced (unselective)

Reactive Intermediates

Radicals

Electron deficient

Any effect that can increase electron density (inductive or resonance) will stabilize radicals
(3° radical more stable than 2° radical)

Cations

Electron deficient
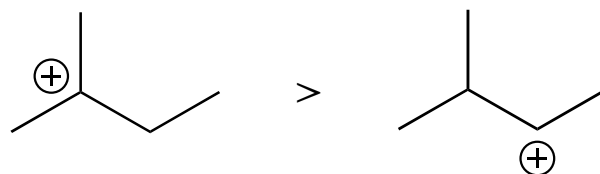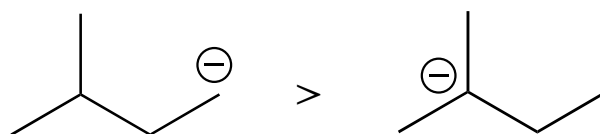
Any effect that can increase electron density (inductive or resonance) will stabilize cations
(3° cation more stable than 2° cation)

Anions

Excess electron density

Any effect that can decrease electron density will stabilize anion
(1° anion is more stable than 3° anion)

Chapter 6
Nucleophilic and Elimination Reactions

Very common mechanism for organic reactions

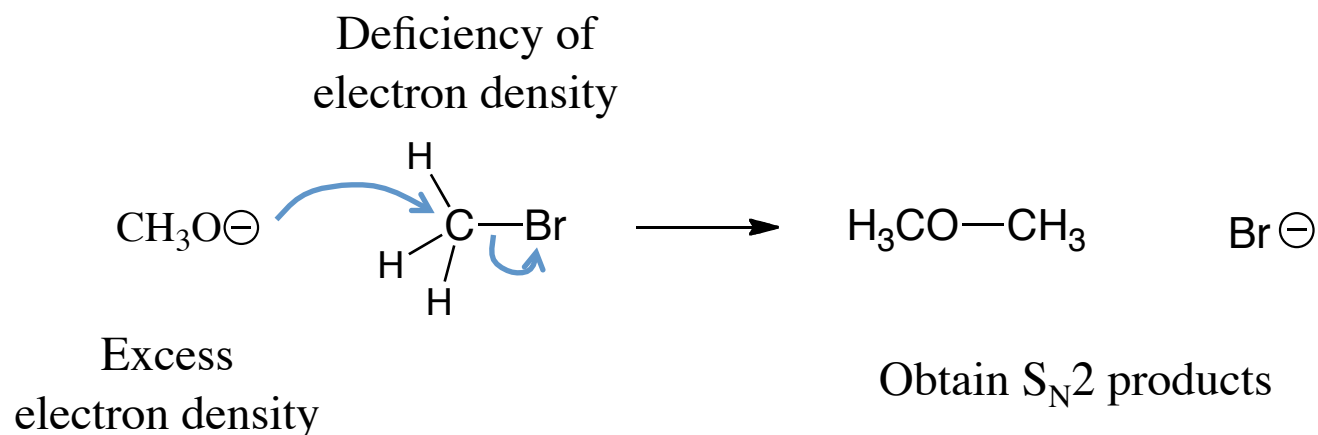Terminology comes from Lewis definition for species:

Nucleophile – something attracted to the nucleus
(therefore negatively charged or excess of electron density)

Electrophile – something attracted to electrons
(therefore positively charged or deficiency of electron density)

Understanding organic reactions, therefore, is directly related
to understanding where there is excess or deficiency of electronic charge

Reactivity Patterns

Deficiency of
electron density

$CH_3O^{\ominus}$ $\overset{H}{\underset{\underset{H}{H}}{C}}$—Br $\longrightarrow$ H_3CO—CH_3 $Br^{\ominus}$

Excess
electron density

Obtain S_N2 products

If trajectory is allowed (low sterics) then good nucleophiles will react
with good electrophiles in a S_N2 reaction

If sterics prevent attack at electrophilic carbon then good base will react in an E2 mechanism

Reactivity Trends

S_N2 reactions are favored with following trends:
-good nucleophiles
-weak bases
-low sterics at electrophilic carbon
(highly favored with methyl or 1° carbons)

E2 reactions are favored with following trends:
-strong bases
-bulky bases
-high sterics at electrophilic carbon

E1 and S_N1 reactions are thus only favored when E2 and S_N2 reactions are not:
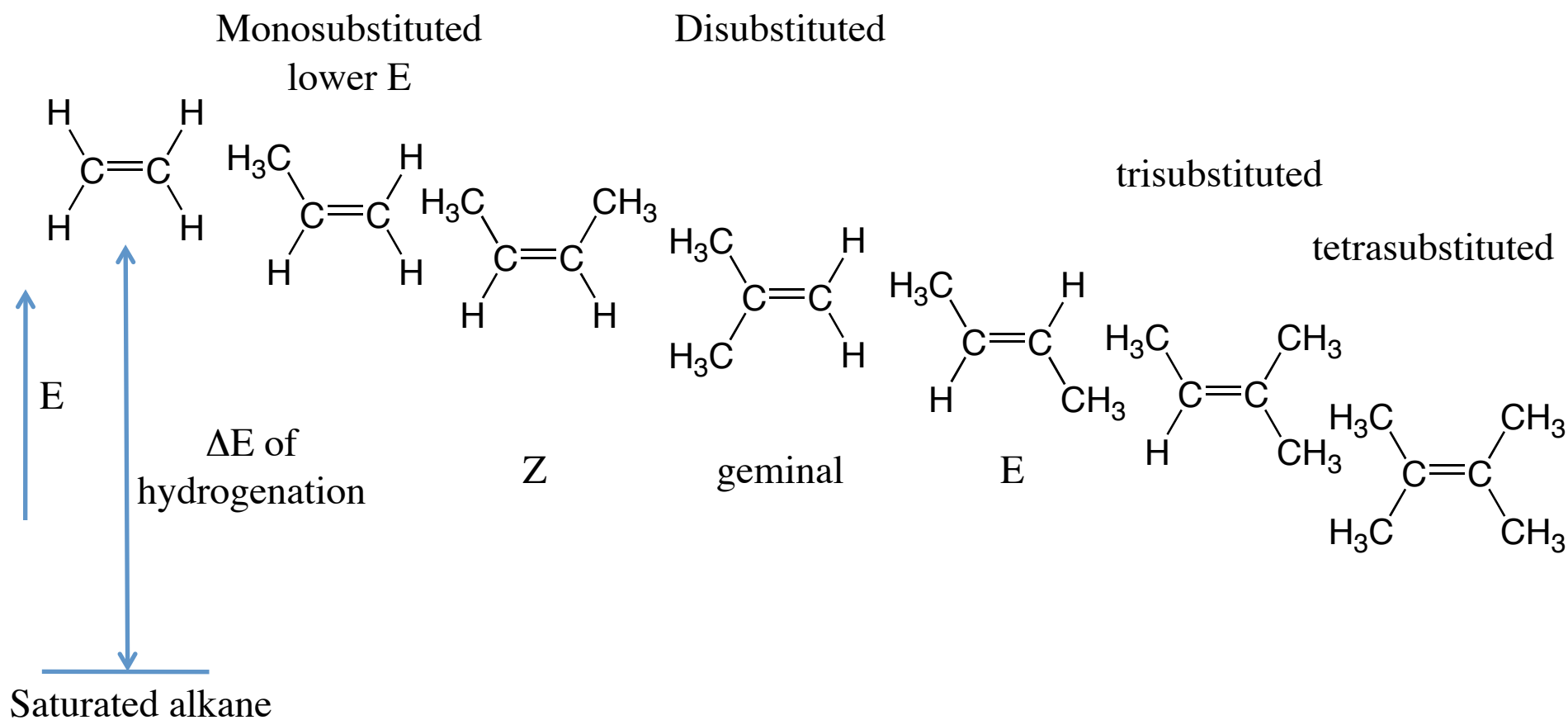-weak nuclephiles
-weak bases
-need high sterics at electrophilic carbon to allow carbocation formation

Another rule of thumb is that as base strength increases, elimination is favored

Chapters 7+8
Alkenes

The stability of alkenes is dependent upon the amount of electron density donated to electron deficient alkenes

Monosubstituted
lower E

Disubstituted

trisubstituted

tetrasubstituted

E

ΔE of hydrogenation
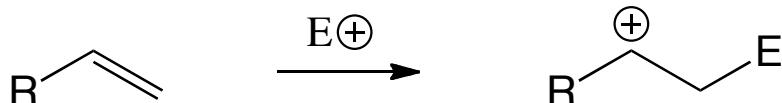
Z

geminal

E

Saturated alkane

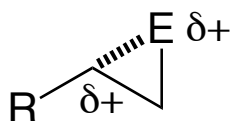Can predict relative stability due to alkyl substituents

Alkene Reactivity

Alkenes generally react with electrophiles in an initial step

The structure of the intermediate formed will dictate the properties of the product

Small electrophiles generate free carbocations
-more stable cation is formed
-can rearrange
(observed with H+)

Larger electrophiles form three
membered ring intermediates
-no rearrangements occur
-partial charge on more substituted site
(observed with Hg^{2+} and Br^+)

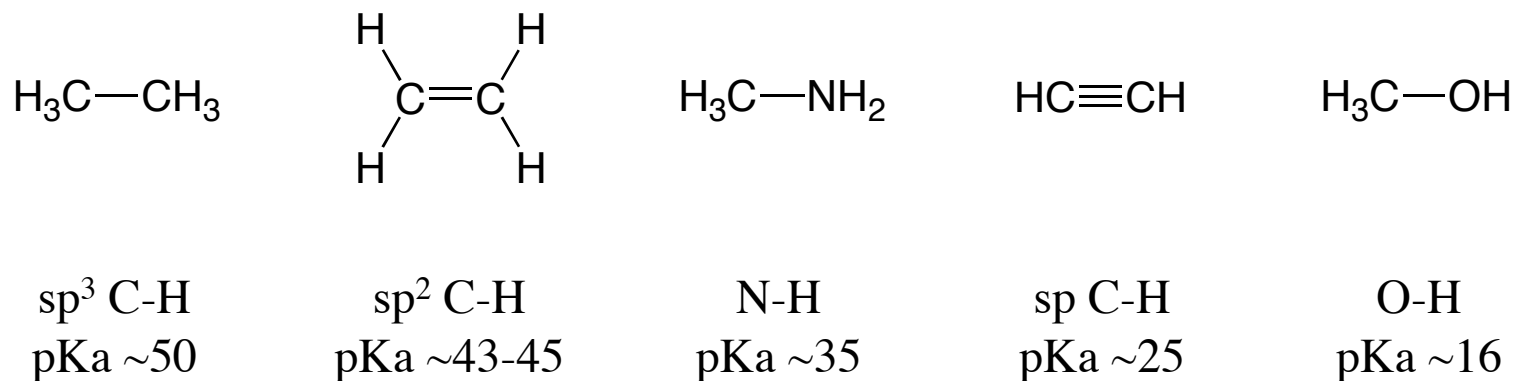Regio- and stereochemistry is thus controlled with type of intermediate
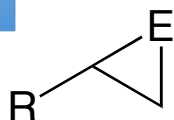
Some electrophiles can form stable three
membered rings
-can isolate compound
(observed with epoxides)

Chapter 9
Alkynes

Reactivity of alkynes is very similar to alkenes

Most notable difference is that there are 2 π bonds to react instead of 1

Another major difference is the generation of more acidic C-H bonds with terminal alkynes

H_3C-CH_3 $C=C$ (with H, H on top and H, H on bottom) H_3C-NH_2 $HC\equiv CH$ H_3C-OH

sp^3 C-H	sp^2 C-H	N-H	sp C-H	O-H
pKa ~50	pKa ~43-45	pKa ~35	pKa ~25	pKa ~16

Alkynes

Due to the 2 π bonds present in alkynes,
an intial reaction can add a reagent to the π bond

If an alcohol is added to a π bond the compound is called an enol
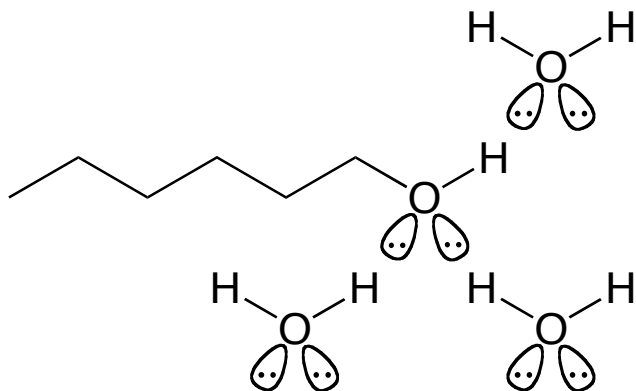Enols equilibrate to the carbonyl form
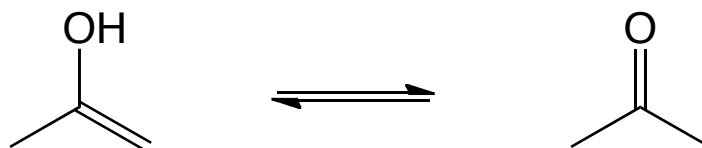
If two alcohols add to the same carbon, the geminal diol also equilibrates to a carbonyl
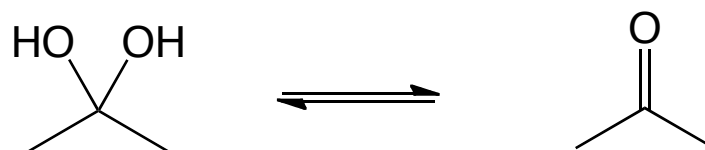
Chapter 10
Alcohols

A unique property of alcohols is the presence of a labile hydrogen

The hydrogen bonding affects many properties including boiling point and water solubility
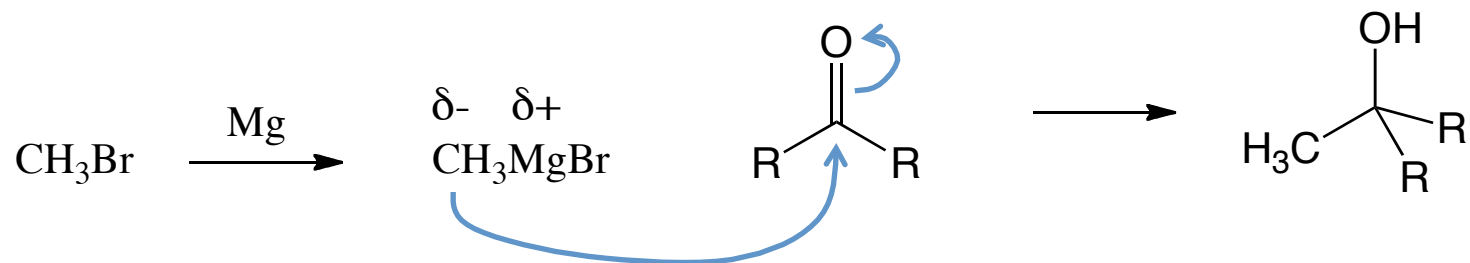
Alcohol Synthesis

Many reactions to form alcohols have been studied in previous chapters

Two unique approaches in chapter 10 include the use of Grignard reagents

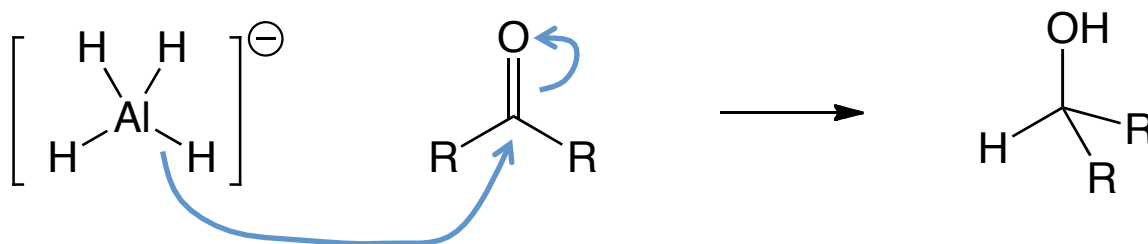Grignard reagents allow the use of carbon based anions in organic synthesis

Upon reaction with carbonyl compounds, alcohol products are observed

CH_3Br $\xrightarrow{Mg}$ $\overset{\delta-}{C}H_3\overset{\delta+}{Mg}Br$ + carbonyl $\longrightarrow$ alcohol product

Alcohol Synthesis

The second unique approach to synthesize alcohols is the use of hydride reducing agents

Both LAH and $NaBH_4$ reduce ketones and aldehydes to alcohols

Due to reactivity differences, LAH is more reactive, LAH is also less selective

LAH reduces a wide variety of carbonyl compounds
(including esters and acid chlorides) that $NaBH_4$ does not